7457127

THE UNITED STATES OF AMERICA

TO ALL TO WHOM THESE PRESENTS SHALL COME:

UNITED STATES DEPARTMENT OF COMMERCE

United States Patent and Trademark Office

January 14, 2014

THIS IS TO CERTIFY THAT ANNEXED IS A TRUE COPY FROM THE RECORDS OF THIS OFFICE OF THE FILE WRAPPER AND CONTENTS OF:

APPLICATION NUMBER: *10/322,348*
FILING DATE: *December 17, 2002*
PATENT NUMBER: *7668730*
ISSUE DATE: *February 23, 2010*

Certified by

David J. Kappos

Under Secretary of Commerce
for Intellectual Property
and Director of the United States
Patent and Trademark Office

PATENT APPLICATION FEE DETERMINATION RECORD
Effective January 1, 2003

Application or Docket Number

CLAIMS AS FILED - PART I

	(Column 1)	(Column 2)
TOTAL CLAIMS	25	
FOR	NUMBER FILED	NUMBER EXTRA
TOTAL CHARGEABLE CLAIMS	25 minus 20=	* 5
INDEPENDENT CLAIMS	4 minus 3 =	* 1
MULTIPLE DEPENDENT CLAIM PRESENT		☐

* If the difference in column 1 is less than zero, enter "0" in column 2

SMALL ENTITY TYPE ☐		OR	OTHER THAN SMALL ENTITY	
RATE	FEE		RATE	FEE
BASIC FEE	$375	OR	BASIC FEE	$750
X$ 9=	45	OR	X$18=	
X42=	42	OR	X84=	
+140=		OR	+280=	
TOTAL	462	OR	TOTAL	

CLAIMS AS AMENDED - PART II

AMENDMENT A

	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA
Total	*	Minus	**	=
Independent	*	Minus	***	=
FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM				☐

SMALL ENTITY		OR	OTHER THAN SMALL ENTITY	
RATE	ADDITIONAL FEE		RATE	ADDITIONAL FEE
X$ 9=		OR	X$18=	
X42=		OR	X84=	
+140=		OR	+280=	
TOTAL ADDIT. FEE		OR	TOTAL ADDIT. FEE	

AMENDMENT B

	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA
Total	*	Minus	**	=
Independent	*	Minus	***	=
FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM				☐

RATE	ADDITIONAL FEE		RATE	ADDITIONAL FEE
X$ 9=		OR	X$18=	
X42=		OR	X84=	
+140=		OR	+280=	
TOTAL ADDIT. FEE		OR	TOTAL ADDIT. FEE	

AMENDMENT C

	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA
Total	*	Minus	**	=
Independent	*	Minus	***	=
FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM				☐

RATE	ADDITIONAL FEE		RATE	ADDITIONAL FEE
X$ 9=		OR	X$18=	
X42=		OR	X84=	
+140=		OR	+280=	
TOTAL ADDIT. FEE		OR	TOTAL ADDIT. FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20."
***If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3."
The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.

12-19-02

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of: Dayton T. Reardan et al.
Title: SENSITIVE DRUG DISTRIBUTION SYSTEM AND METHOD
Attorney Docket No.: 101.031US1

PATENT APPLICATION TRANSMITTAL

BOX PATENT APPLICATION
Commissioner for Patents
Washington, D.C. 20231

We are transmitting herewith the following attached items and information (as indicated with an "X"):

X Return postcard.
X Utility Patent Application under 37 CFR § 1.53(b) comprising:
  X Specification (18 pgs, including claims numbered 1 through 25 and a 1 page Abstract).
  X Formal Drawing(s) (16 sheets).
  X Unsigned Combined Declaration and Power of Attorney (4 pgs).
X Applicant claims small entity status under 37 C.F.R 1.27.

The filing fee (NOT ENCLOSED) will be calculated as follows:

	No. Filed	No. Extra	Rate	Fee
TOTAL CLAIMS	25 - 20 =	5	x 9 =	$45.00
INDEPENDENT CLAIMS	4 - 3 =	1	x 42 =	$42.00
[ ] MULTIPLE DEPENDENT CLAIMS PRESENTED				$0.00
BASIC FEE				$370.00
TOTAL				$457.00

THE FILING FEE WILL BE PAID UPON RECEIPT OF THE NOTICE TO FILE MISSING PARTS.

SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.
P.O. Box 2938, Minneapolis, MN 55402 (612-373-6900)

By: Bradley A. Forrest
Atty: Bradley A. Forrest
Reg. No. 30,837

Customer Number 21186

"Express Mail" mailing label number: EV 149 506 149 US
Date of Deposit: December 17, 2002
This paper or fee is being deposited on the date indicated above with the United States Postal Service pursuant to 37 CFR 1.10, and is addressed to The Commissioner for Patents, Box Patent Application, Washington, D.C. 20231.

[redacted]

Sensitive Drug Distribution System and Method

Field of the Invention

The present invention relates to distribution of drugs, and in particular to the distribution of sensitive drugs.

Background of the Invention

Sensitive drugs are controlled to minimize risk and ensure that they are not abused, or cause adverse reactions. Such sensitive drugs are approved for specific uses by the Food and Drug Administration, and must be prescribed by a licensed physician in order to be purchased by consumers. Some drugs, such as cocaine and other common street drugs are the object of abuse and illegal schemes to distribute for profit. Some schemes include Dr. shopping, diversion, and pharmacy thefts. A locked cabinet or safe is a requirement for distribution of some drugs.

Certain agents, such as gamma hydroxy buterate (GHB) are also abused, yet also are effective for therapeutic purposes such as treatment of daytime cataplexy in patients with narcolepsy. Some patients however, will obtain prescriptions from multiple doctors, and have them filled at different pharmacies. Still further, an unscrupulous physician may actually write multiple prescriptions for a patient, or multiple patients, who use cash to pay for the drugs. These patients will then sell the drug to dealers or others for profit.

There is a need for a distribution system and method that directly addresses these abuses. There is a further need for such a system and method that provides education and limits the potential for such abuse.

Summary of the Invention

A drug distribution system and method utilizes a central pharmacy and database to track all prescriptions for a sensitive drug. Information is kept in a central database regarding all physicians allowed to prescribe the sensitive drug, and all patients receiving the drug. Abuses are identified by monitoring data in the database for prescription patterns by physicians and prescriptions obtained by patients. Further verification is

made that the physician is eligible to prescribe the drug by consulting a separate database for a valid DEA license, and optionally state medical boards to determine whether any corrective or approved disciplinary actions relating to controlled substances have been brought against the physician. Multiple controls beyond those for traditional drugs are imposed on the distribution depending on the sensitivity of the drug.

Education is provided to both physician and patient. Prior to shipping the drug for the first time, the patient is contacted to ensure that product and abuse related educational materials have been received and/or read. The patient may provide the name of a designee to the central pharmacy who is authorized to accept shipment of the drug. Receipt of the initial drug shipment is confirmed by contacting the patient. Either a phone call or other communication to the patient within a set time after delivery may be made to ensure receipt. Further, a courier service's tracking system is used to confirm delivery in further embodiments. If a shipment is lost, an investigation is launched to find it.

In one embodiment, the drug may be shipped by the central pharmacy to another pharmacy for patient pick-up. The second pharmacy's ability to protect against diversion before shipping the drug must be confirmed. This ability may be checked through NTIS and State Boards of Pharmacy.

Prescription refills are permitted in the number specified in the original prescription. In addition, if a prescription refill is requested by the patient prior to the anticipated due date, such refills will be questioned. A lost, stolen, destroyed or spilled prescription/supply is documented and replaced to the extent necessary to honor the prescription, and will also cause a review or full investigation.

The exclusive central database contains all relevant data related to distribution of the drug and process of distributing it, including patient, physician and prescription information. Several queries and reports are run against the database to provide information which might reveal potential abuse of the sensitive drug, such as early refills.

Brief Description of the Drawings

FIG. 1 is a block diagram of a computer system for use in implementing the system and method of the present invention.

FIG.s 2A, 2B and 2C are a flowchart describing a method for sensitive drug distribution at least partially utilizing a computer system such as that shown in FIG. 1.

FIG. 3 is a flowchart of a physician success program at least partially implemented on a computer system such as that shown in FIG. 1.

FIG.s 4A and 4B are a flowchart describing a method for handling refill requests at least partially utilizing a computer system such as that shown in FIG. 1.

FIG. 5 is a flowchart of a process for requesting special reimbursement when a patient is uninsured or underinsured at least partially utilizing a computer system as that shown in FIG. 1.

FIG. 6 is a flowchart of a process for inventory control at least partially utilizing a computer system such as that shown in FIG. 1.

FIG. 7 is a block diagram of database fields.

FIG. 8 is a block diagram showing a list of queries against the database fields.

FIG. 9 is a copy of one example prescription and enrollment form.

FIG. 10 is a copy of one example of a NORD application request form for patient financial assistance.

FIG. 11 is a copy of one example voucher request for medication for use with the NORD application request form of FIG. 10.

FIG. 12 is a copy of certificate of medical need.

FIG.s 13A, 13B and 13C are descriptions of sample reports obtained by querying a central database having fields represented in FIG. 7.

Detailed Description of the Invention

In the following description, reference is made to the accompanying drawings that form a part hereof, and in which is shown by way of illustration specific embodiments in which the invention may be practiced. These embodiments are described in sufficient detail to enable those skilled in the art to practice the invention, and it is to be understood that other embodiments may be utilized and that structural, logical and electrical changes may be made without departing from the scope of the present invention. The following description is, therefore, not to be taken in a limited sense, and the scope of the present invention is defined by the appended claims.

[redacted]

The functions or algorithms described herein are implemented in software or a combination of software and human implemented procedures in one embodiment. The software comprises computer executable instructions stored on computer readable media such as memory or other type of storage devices. The term "computer readable media" is also used to represent carrier waves on which the software is transmitted. Further, such functions correspond to modules, which are software, hardware, firmware of any combination thereof. Multiple functions are performed in one or more modules as desired, and the embodiments described are merely examples. The software is executed on a digital signal processor, ASIC, microprocessor, or other type of processor operating on a computer system, such as a personal computer, server or other computer system.

A sensitive drug is one which can be abused, or has addiction properties or other properties that render the drug sensitive. One example of such a drug is sodium oxybate, also known as gamma hydroxy butyrate (GHB $C_4H_7NaO_3$) which is useful for treatment of cataplexy in patients with narcolepsy. GHB is marketed under the trademark of Xyrem® (sodium oxybate oral solution), which trademark can be used interchangeably with GHB herein. Sensitive drugs also include narcotics or other drugs which require controls on their distribution and use to monitor behaviors to prevent abuse and adverse side effects.

In one embodiment, Xyrem® is subject to a restricted distribution program. One aspect of the program is to educate physicians and patients about the risks and benefits of Xyrem, including support via ongoing contact with patients and a toll free helpline. Initial prescriptions are filled only after a prescriber and patient have received and read the educational materials. Further, patient and prescribing physician registries are maintained and monitored to ensure proper distribution.

In a further embodiment, bulk sodium oxybate is manufactured at a single site, as is the finished drug product. Following manufacture of the drug product, it is stored at a facility compliant with FDA Schedule III regulations, where a consignment inventory is maintained. The inventory is owned by a company, and is managed by a central pharmacy, which maintains the consignment inventory. Xyrem® is distributed and dispensed through a primary and exclusive central pharmacy, and is not stocked in retail

[redacted]

pharmacy outlets. It is distributed by overnight carriers, or by US mail in one embodiment to potentially invoke mail fraud laws if attempts of abuse occur.

FIG. 1 is a simplified block diagram of a computer system 100, such as a personal computer for implementing at least a portion of the methods described herein. A central processing unit (CPU) 110 executes computer programs stored on a memory 120. Memory 120 in one embodiment comprises one or more levels of cache as desired to speed execution of the program and access to data on which the programs operate. The CPU is directly coupled to memory 120 in one embodiment. Both CPU 110 and memory 120 are coupled to a bus 130. A storage 140, I/O 150 and communications 160 are also coupled to the bus 130. Storage 140 is usually a long term storage device, such as a disk drive, tape drive, DVD, CD or other type of storage device. In one embodiment, storage 140 is used to house a database for use with the present invention. I/O 150 comprises keyboards, sound devices, displays and other mechanisms by which a user interacts with the computer system 100. Communications 160 comprises a network, phone connection, local area network, wide area network or other mechanism for communicating with external devices. Such external devices comprise servers, other peer computers and other devices. In one embodiment, such external device comprises a database server that is used in place of the database on storage 140. Other computer system architectures capable of executing software and interacting with a database and users may also be used. Appropriate security measures such as encryption are used to ensure confidentiality. Further, data integrity and backup measures are also used to prevent data loss.

FIG.s 2A, 2B and 2C represent an initial prescription order entry process for a sensitive drug, such as Xyrem. At 202, a medical doctor (MD) sends a Rx/enrollment form via mail, fax, email or other means to an intake/reimbursement specialist at 204, who makes a copy of the RX/enrollment form that is stamped "copy". The original fax is forwarded to a pharmacy team. The enrollment form contains prescriber information, prescription information, checkboxes for the prescriber indicating they have read materials, educated the patient, understand the use in treatment, and understand certain safety information, and also contains patient information.

The prescriber information contains standard contact information as well as license number, DEA number and physician specialty. Patient and prescription

[redacted]

information includes name, social security number, date of birth, gender, contact information, drug identification, patient's appropriate dosage, and number of refills allowed, along with a line for the prescriber's signature. Patient insurance information is also provided.

There are two workflows involved at the pharmacy team, intake reimbursement 206 and pharmacy workflow 208, which may proceed in parallel or serially. The intake work flow 206 starts with an intake reimbursement specialist entering the patient and physician information into an application/database referred to as CHIPS, which is used to maintain a record of a client home infusion program (CHIP) for Xyrem®. A check is made to ensure the information is complete at 212. If not, at 214, an intake representative attempts to reach the MD or prescriber to obtain the missing information. If the missing information has not been obtained within a predetermined period of time, such as 24 hours at 216, the Rx/Enrollment form is sent back to the MD with a rejection explanation. A note is entered in CHIPS that the application was rejected.

If the information is complete at 212, the MD is contacted at 220 to verify receipt and accuracy of the patient's Rx. This contact is recorded in CHIPS. The intake and reimbursement specialist then sends a consent form and a cover letter to the patient at 224. The insurance provider is contacted at 226 to verify coverage and benefits. At 228, a determination is made regarding coverage for the drug. If it is not available, it is determined at 230 whether the patient is willing and able to pay. If not, a process is performed for handling patients who are uninsured or underinsured. In one embodiment, the process is referred to as a NORD process.

If the patient is willing and able to pay at 230, the patient is informed of the cost of the product and is given payment options at 234. At 236, once payment is received, the intake reimbursement specialist submits a coverage approval form with the enrollment form to the pharmacy team as notification to process the patient's prescription. If coverage is approved at 228, the intake reimbursement specialist also submits the coverage approval form with the enrollment form to the pharmacy team as notification to process the patient's prescription. Processing of the prescription is described below.

[redacted]

Upon receipt and initial processing of the prescription enrollment form and sending an original to the pharmacy work flow block 208, the patient is shipped a Xyrem® success packet via mail. In one embodiment, the Xyrem® success packet contains educational material for a patient that advises of the proper use, care and handling of the drug and consequences of diversion at 268. The medical doctor's credentials are checked to determine if the physician has a current DEA license to prescribe controlled substances and if he or she has had any actions related to misuse/misprescribing of controlled drugs against him or her, within a predetermined time, such as three months at 270. If they have, a pharmacist holds the prescription until receiving a coverage approval form from the intake reimbursement specialist at 272.

If the credentials have not been recently checked, the pharmacist verifies the credentials and enters all findings in the database at 274. If the credentials are approved at 276, the physician is indicated as approved in a physician screen populated by information from the database at 280. The prescription is then held pending coverage approval at 282.

If any disciplinary actions are identified, as referenced at block 278, management of the pharmacy is notified and either approves processing of the prescription with continued monitoring of the physician, or processing of the prescription is not performed, and the physician is noted in the database as unapproved at 284. The enrollment form is then mailed back to the physician with a cover letter reiterating that the prescription cannot be processed at 288. The patient is also sent a letter at 290 indicating that the prescription cannot be processed and the patient is instructed to contact their physician.

Actual filling of the approved prescription begins with receipt of the coverage approval form as indicated at 240. The patient is contacted by the pharmacy, such as by a technician to complete a technician section of a patient counseling checklist. If a pharmacist verifies that the program materials were not read at 242, the receipt of the material is confirmed at 244 and another call is scheduled to counsel the patient before the drug is shipped.

If the program materials were read at 242, the checklist is completed at 246 and the technician transfers the patient to the pharmacist who reviews the entire checklist and completes remaining pharmacist specified sections. At 248, the pharmacist indicates in

[redacted]

the database that the patient counseling and checklist was successfully completed, indicating the date completed.

At 250, the pharmacist schedules the patient's shipment for the next business day or the next business day that the patient or designee is able to sign for the package. Further, as indicated at 252, the shipment must be sent to the patient's home address unless the patient is traveling or has moved. In that event, the pharmacist may determine that an exception may be made. The patient or the patient's designee who is at least 18 years old, must sign for the package upon delivery.

At 254, the pharmacist enters the prescription order in the database, creating an order number. The pharmacist then verifies at 256 the prescription and attaches a verification label to the hard copy prescription. At 258, a pick ticket is generated for the order and the order is forwarded to the pharmacy for fulfillment. The shipment is confirmed in the database at 260, and the order is shipped by USPS Express Mail. Use of the US mail invokes certain criminal penalties for unauthorized diversion. Optionally, other mail services may be used. Potential changes in the law may also bring criminal penalties into play. Following shipment, the patient is called by the central pharmacy to confirm that the prescription was received.

As noted at 266, for the sensitive drug, Xyrem, all inventory is cycle counted and reconciled with the database system quantities before shipments for the day are sent. This provides a very precise control of the inventor.

A physician success program materials request process begins at 310 in FIG. 3. At 320, the MD calls to the central pharmacy to request program materials. A special phone number is provided. MD demographics, DEA number, and data or request are entered into the database at 330. At 340, a request is made to ship the materials to the MD via a fulfillment website, or other mechanism. The request process ends at 350.

A refill request process begins at 302 in FIG.s 4A and 4B. There are two different paths for refills. A first path beginning at 404 involves generating a report from the central database of patients with a predetermined number of days or product remaining. A second path beginning at 406 is followed when a patient calls to request an early refill.

In the first path, a copy of the report is provided to an intake reimbursement specialist at 408. No sooner than 8 days before the medication depletion, a pharmacy

[redacted]

technician contacts the patient at 410 to complete the pre-delivery checklist. At 412, if the patient is not reached, a message is left mentioning the depletion, and a return number at 414. A note is also entered into the database indicating the date the message was left at 416.

If the patient is reached at 412, the next shipment is scheduled at 418, the prescription is entered into the database creating an order at 420, the pharmacist verifies the prescription and attaches a verification label at 422 and the shipment is confirmed in the database at 424. Note at 426 that the inventory is cycle counted and reconciled with the database quantities before the shipments for a day or other time period are sent. A pick ticket is generated for the order and the order is forwarded for fulfillment at 428, with the first path ending at 430.

The second path, beginning at 406 results in a note code being entered into the database on a patient screen indicating an early refill request at 432. The pharmacist evaluates the patient's compliance with therapy or possible product diversion, misuse or over-use at 436. In one embodiment, cash payers are also identified. The pharmacist then contacts the prescribing physician to alert them of the situation and confirm if the physician approves of the early refill at 438. If the physician does not approve as indicated at 440, the patient must wait until the next scheduled refill date to receive additional product as indicated at 442, and the process ends at 444.

If the physician approves at 440, the pharmacist enters a note in the database on a patient screen that the physician approves the request at 446. The pharmacist notifies an intake reimbursement specialist to contact the patient's insurance provider to verify coverage for the early refill at 448. If the insurance provider will pay as determined at 450, the specialist submits the coverage approval form as notification that the refill may be processed at 452. At 454, the pharmacy technician contacts the patient to schedule shipment of the product for the next business day, and the process of filling the order is continued at 456 by following the process beginning at 240.

If the insurance provider will not pay at 450, it is determined whether the patient is willing and/or able to pay at 458. If not, the patient must wait until the next scheduled refill date to receive additional product at 460. If it was determined at 458 that the patient was willing and able to pay, the patient is informed of the cost of the product and is given

[redacted]

payment options at 462. Once payment is received as indicated at 464, the specialist submits a coverage approval form to the pharmacy team as notification that the refill request can be processed at 466. At 468, the pharmacy technician contacts the patient to schedule shipment. The process of filling the order is continued at 470 by following the process beginning at 240.

A process, referred to as a NORD process in one embodiment is used to determine whether donated, third party funds are available for paying for prescriptions where neither insurance will, nor the patient can pay. The process begins at 510 upon determining that a patient is uninsured or underinsured. A reimbursement specialist explains the NORD program to the patient and faxes an application request form to NORD for the patient. At 515, the intake reimbursement specialist documents in the database that an application has been received through NORD. At 520, NORD mails an application to the patient within one business day.

A determination is made at 525 by NORD whether the patient is approved. If not, at 530, NORD sends a denial letter to the patient, and it is documented in the database at 540 that the patient was denied by NORD. If the patient is approved, NORD sends an acceptance letter to the patient and faxes a voucher to the central pharmacy (SDS in one embodiment) to indicate the approval at 545. At 550, an intake reimbursement specialist submits a coverage approval form to the pharmacy team as notification that the patient has been approved for coverage. The process of filling the order is continued at 555 by following the process beginning at 240.

An inventory control process is illustrated in FIG. 6 beginning at 610. Each week, a responsible person at the central pharmacy, such as the director of the pharmacy transfers inventory for the week's shipments to a segregated warehouse location for production inventory. At 620, a purchase order is generated for the inventory transferred to the production location and is sent, such as by fax, to a controller, such as the controller of the company that obtained approval for distribution and use of the sensitive drug. At 630, the controller invoices the central pharmacy for the product moved to production. The process ends at 640.

The central database described above is a relational database running on the system of FIG. 1, or a server based system having a similar architecture coupled to

[redacted]

workstations via a network, as represented by communications 160. The database is likely stored in storage 140, and contains multiple fields of information as indicated at 700 in FIG. 7. The organization and groupings of the fields are shown in one format for convenience. It is recognized that many different organizations or schemas may be utilized. In one embodiment, the groups of fields comprise prescriber fields 710, patient fields 720, prescription fields 730 and insurance fields 740. For purposes of illustration, all the entries described with respect to the above processes are included in the fields. In further embodiments, no such groupings are made, and the data is organized in a different manner.

Several queries are illustrated at 800 in FIG. 8. There may be many other queries as required by individual state reporting requirements. A first query at 810 is used to identify prescriptions written by physician. The queries may be written in structured query language, natural query languages or in any other manner compatible with the database. A second query 820 is used to pull information from the database related to prescriptions by patient name. A third query 830 is used to determine prescriptions by frequency, and a n^{th} query finds prescriptions by dose at 840. Using query languages combined with the depth of data in the central database allows many other methods of investigating for potential abuse of the drugs. The central database ensures that all prescriptions, prescribers and patients are tracked and subject to such investigations. In further embodiments, the central database may be distributed among multiple computers provided a query operates over all data relating to such prescriptions, prescribers and patients for the drug.

An example of one prescription and enrollment form is shown at 900 in FIG. 9. As previously indicated, several fields are included for prescriber information, prescription information and patient information.

FIG. 10 is a copy of one example NORD application request form 1000 used to request that an application be sent to a patient for financial assistance.

FIG. 11 is a copy of one example application 1100 for financial assistance as requested by form 1000. The form requires both patient and physician information. Social security number information is also requested. The form provides information for approving the financial assistance and for tracking assistance provided.

[redacted]

FIG. 12 is a copy of one example voucher request for medication for use with the NORD application request form of FIG. 10. In addition to patient and physician information, prescription information and diagnosis information is also provided.

FIG.s 13A, 13B and 13C are descriptions of sample reports obtained by querying a central database having fields represented in FIG. 7. The activities grouped by sales, regulatory, quality assurance, call center, pharmacy, inventory, reimbursement, patient care and drug information. Each report has an associated frequency or frequencies. The reports are obtained by running queries against the database, with the queries written in one of many query languages.

While the invention has been described with respect to a Schedule III drug, it is useful for other sensitive drugs that are DEA or Federally scheduled drugs in Schedule II-V, as well as still other sensitive drugs where multiple controls are desired for distribution and use.

[redacted]

Claims

1. A method of distributing a sensitive drug, the method comprising:

receiving prescription requests from a medical doctor containing information identifying the patient, the sensitive drug, and various credentials of the doctor;

entering the information into a central database for analysis of potential abuse situations;

checking the credentials of the doctor;

confirming with the patient that educational material has been read prior to shipping the sensitive drug;

confirming receipt of the sensitive drug; and

generating periodic reports via the central database to evaluate potential abuse patterns.

2. The method of claim 1 wherein receipt of the sensitive drug is confirmed by telephone call from the central pharmacy to the patient.

3. The method of claim 1 and further comprising launching an investigation of lost shipments.

4. The method of claim 1 and further comprising recording the confirmation with the patient that the educational material has been read in the central database.

5. The method of claim 1 and further comprising verifying the patient's home address.

6. The method of claim 1 and further comprising recording a designee identified by the patient to receive the sensitive drug.

7. The method of claim 1 and further comprising establishing a delivery date.

[redacted]

8. The method of claim 1 wherein prescription refills requested prior to an anticipated date are questioned by the pharmacist.

9. The method of claim 1 and further comprising shipping comprehensive printed materials to the physician if the physician is a first time prescriber of the sensitive drug.

10. The method of claim 1 wherein the credentials of the doctor comprise DEA (Drug Enforcement Agency) and state license numbers.

11. A method of monitoring potential abuse of a sensitive drug by use of an exclusive central database, the method comprising:

generating queries of prescription information from a database containing selected information for all prescriptions of the sensitive drug, wherein the queries comprise prescriptions by physician specialty, prescriptions by patient name, prescriptions by frequency and prescriptions by dose.

12. The method of claim 11 and further comprising running multiple predetermined reports based on data in the exclusive central database.

13. The method of claim 12 wherein such reports are selected from groups of reports consisting of sales, regulatory, quality assurance, pharmacy, inventory, reimbursement, patient care, and drug information.

14. The method of claim 13 wherein sales reports are selected from the group consisting of prescriptions by zip code, prescriptions by physician by zip code and total dollars by zip code.

15. The method of claim 13 wherein regulatory reports are selected from the group consisting of number of physician registries, number of denied physician registries and reasons, number of completed patient registries, number of problem identification, number of cycle counts performed.

[redacted]

16. The method of claim 13 wherein inventory reports are selected from the group consisting of number of returned products and reasons, number of outdated bottles of product, inventory counts of consignment and production inventory, number of units received, and lots received.

17. The method of claim 13 wherein patient care reports are selected from the group consisting of number of adverse events, number of dosing problems and type, number of noncompliance episodes and reason, number of patients counseled and reason, number of discontinued and reason, number of patients referred to physician and reason, number of active patients, number of new patents, number of restart patients, and number of discontinued patients and reason.

18. The method of claim 13 wherein selected reports are run weekly, monthly or quarterly.

19. A method of obtaining FDA (Food and Drug Administration) approval for a sensitive drug, the method comprising:

determining current and anticipated patterns of potential abuse of the sensitive drug;

selecting multiple controls for distribution by an exclusive central pharmacy maintaining a central database, the controls selected from the group consisting of communicating prescriptions from a physician to the central pharmacy, identifying the physicians name, license and DEA (Drug Enforcement Agency) registration information, verifying the prescription; obtaining patient information, verifying the physician is eligible to prescribe the sensitive drug by consulting the National Technical Information Services to determine whether the physician has an active DEA number and check on whether any actions are pending against the physician, provide comprehensive printed materials to the physician, contacting the patient's insurance company if any, verifying patient registry information, providing comprehensive education information to the patient, verifying the patient has reviewed the educational materials, verifying the home

[redacted]

address of the patient, shipping via US postal service or similar shipping service, receiving the name of an at least 18 year old designee to receive the drug, confirming receipt of an initial shipment of the drug to the patient, returning the drug to the pharmacy after two attempts to deliver, launching an investigation when a shipment is lost, shipping to another pharmacy for delivery, requiring manufacture at a single location, releasing inventory in a controlled manner to the central pharmacy, questioning early refills, flagging repeat instances of lost, stolen, destroyed or spilled prescriptions, limiting the prescription to a one month supply, requiring rewriting of the prescription periodically, making the database available to the DEA for checking for abuse patterns in the data, cash payments, inappropriate questions; and

negotiating with the FDA by adding further controls from the group until approval is obtained.

20. The method of claim 19 wherein initially selected controls comprise communicating prescriptions from a physician to the central pharmacy, identifying the physicians name, license and DEA registration information, verifying the prescription; obtaining patient information, verifying the physician is eligible to prescribe the sensitive drug by consulting the National Technical Information Services to determine whether the physician has an active DEA number and check on whether any actions are pending against the physician, verifying patient registry information, providing comprehensive education information to the patient, verifying the patient has reviewed the educational materials, verifying the home address of the patient, shipping via US postal service, confirming receipt of an initial shipment of the drug to the patient releasing inventory in a controlled manner to the central pharmacy, flagging repeat instances of lost, stolen, destroyed or spilled prescriptions, and making the database available to the DEA for checking for abuse patterns in the data

21. The method of claim 19 wherein the sensitive drug is a scheduled drug in Schedule II-V.

22. A method of distributing a sensitive drug, the method comprising:

[redacted]

determining current and anticipated patterns of potential abuse of the sensitive drug;

selecting multiple controls for distribution of the sensitive drug; and

adding additional controls to provide sufficient reassurance to a governmental regulatory body that the sensitive drug distribution can be adequately controlled in order to obtain marketing approval by the governmental regulatory body.

23. The method of claim 22 wherein the system allows marketing of a drug product pursuant to FDA subpart 4 regulation embodied in Title 21, CFR Part 314.

24. The method of claim 22 wherein distribution of the sensitive drug is controlled by a central distribution center sufficient to allow the DEA (Drug Enforcement Agency) to approve the central distribution center.

25. The method of claim 22 wherein the governmental regulatory body comprises a state regulatory agency that approves distribution of the sensitive drug in a state.

[redacted]

Abstract of the Disclosure

A drug distribution system and method utilizes a central pharmacy and database to track all prescriptions for a sensitive drug. Information is kept in the database regarding all physicians allowed to prescribe the sensitive drug, and all patients receiving the drug. Abuses are identified by monitoring data in the database for prescription patterns by physicians and prescriptions obtained by patients. Further verification is made that the physician is eligible to prescribe the drug by consulting a separate database, and optionally whether any actions are taken against the physician. Multiple controls beyond those for normal drugs are imposed on the distribution depending on the sensitivity of the drug.

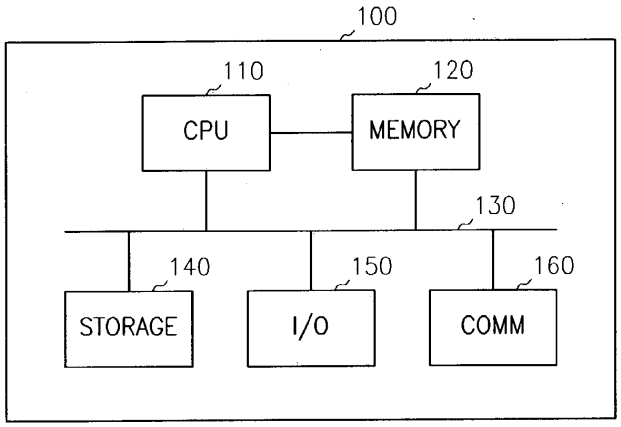


FIG. 1

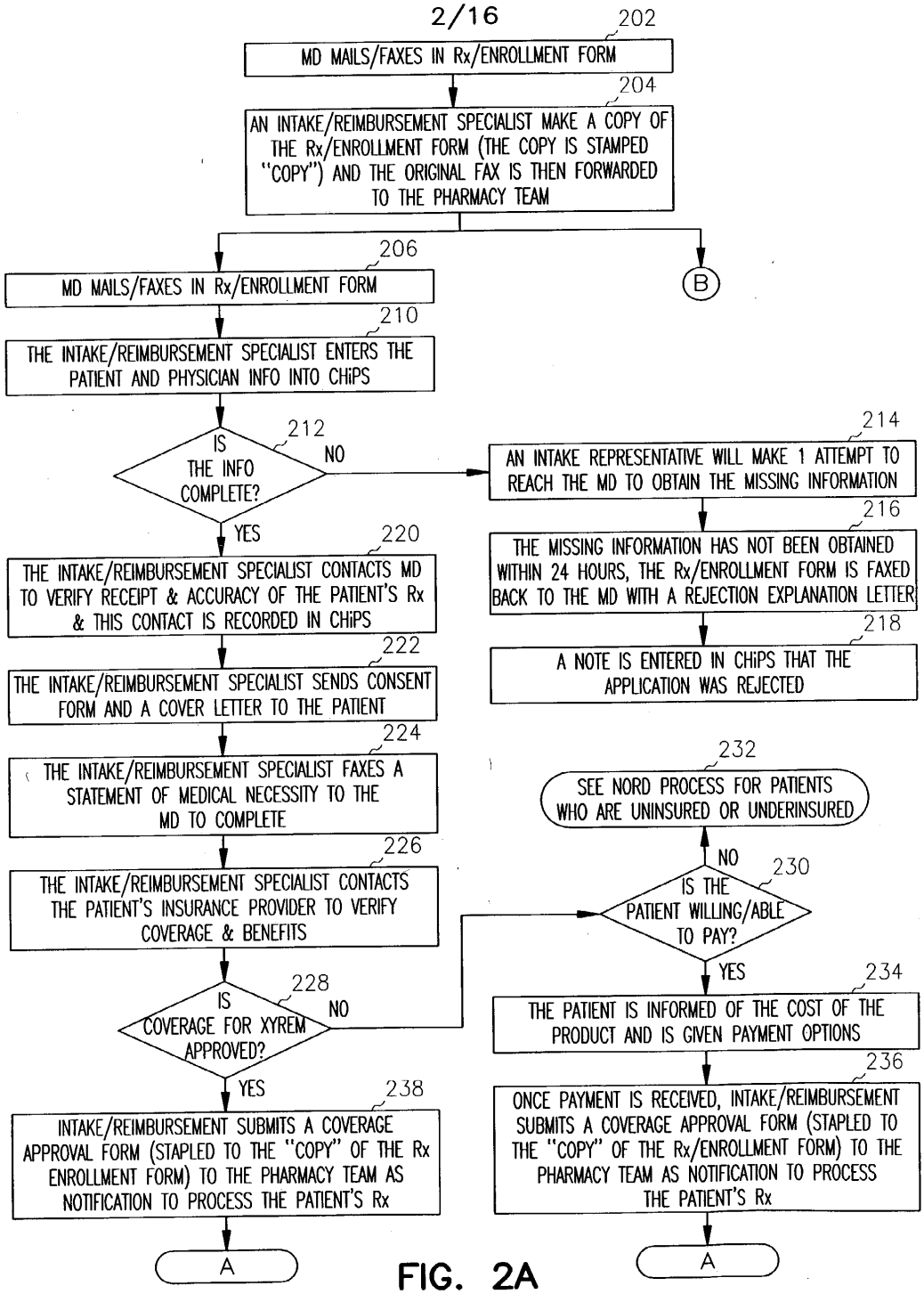

202
MD MAILS/FAXES IN Rx/ENROLLMENT FORM
204
AN INTAKE/REIMBURSEMENT SPECIALIST MAKE A COPY OF THE Rx/ENROLLMENT FORM (THE COPY IS STAMPED "COPY") AND THE ORIGINAL FAX IS THEN FORWARDED TO THE PHARMACY TEAM
206
MD MAILS/FAXES IN Rx/ENROLLMENT FORM
B
210
THE INTAKE/REIMBURSEMENT SPECIALIST ENTERS THE PATIENT AND PHYSICIAN INFO INTO CHiPS
212
IS THE INFO COMPLETE?
NO
214
AN INTAKE REPRESENTATIVE WILL MAKE 1 ATTEMPT TO REACH THE MD TO OBTAIN THE MISSING INFORMATION
216
THE MISSING INFORMATION HAS NOT BEEN OBTAINED WITHIN 24 HOURS, THE Rx/ENROLLMENT FORM IS FAXED BACK TO THE MD WITH A REJECTION EXPLANATION LETTER
218
A NOTE IS ENTERED IN CHiPS THAT THE APPLICATION WAS REJECTED
YES
220
THE INTAKE/REIMBURSEMENT SPECIALIST CONTACTS MD TO VERIFY RECEIPT & ACCURACY OF THE PATIENT'S Rx & THIS CONTACT IS RECORDED IN CHiPS
222
THE INTAKE/REIMBURSEMENT SPECIALIST SENDS CONSENT FORM AND A COVER LETTER TO THE PATIENT
224
THE INTAKE/REIMBURSEMENT SPECIALIST FAXES A STATEMENT OF MEDICAL NECESSITY TO THE MD TO COMPLETE
226
THE INTAKE/REIMBURSEMENT SPECIALIST CONTACTS THE PATIENT'S INSURANCE PROVIDER TO VERIFY COVERAGE & BENEFITS
228
IS COVERAGE FOR XYREM APPROVED?
NO
232
SEE NORD PROCESS FOR PATIENTS WHO ARE UNINSURED OR UNDERINSURED
NO
230
IS THE PATIENT WILLING/ABLE TO PAY?
YES
234
THE PATIENT IS INFORMED OF THE COST OF THE PRODUCT AND IS GIVEN PAYMENT OPTIONS
236
ONCE PAYMENT IS RECEIVED, INTAKE/REIMBURSEMENT SUBMITS A COVERAGE APPROVAL FORM (STAPLED TO THE "COPY" OF THE Rx/ENROLLMENT FORM) TO THE PHARMACY TEAM AS NOTIFICATION TO PROCESS THE PATIENT'S Rx
YES
238
INTAKE/REIMBURSEMENT SUBMITS A COVERAGE APPROVAL FORM (STAPLED TO THE "COPY" OF THE Rx ENROLLMENT FORM) TO THE PHARMACY TEAM AS NOTIFICATION TO PROCESS THE PATIENT'S Rx
A
A

FIG. 2A

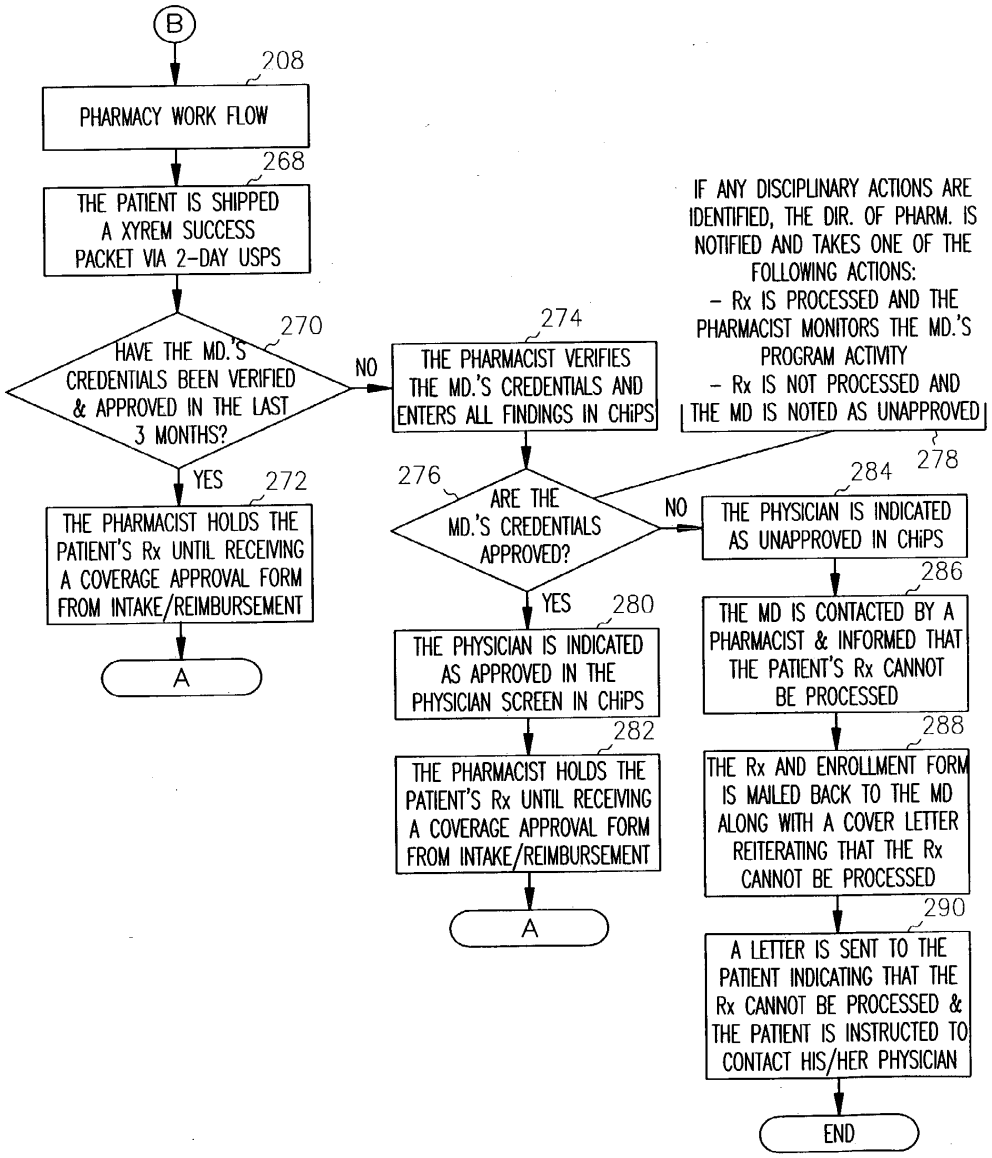

B
208
PHARMACY WORK FLOW
268
THE PATIENT IS SHIPPED A XYREM SUCCESS PACKET VIA 2-DAY USPS
270
HAVE THE MD.'S CREDENTIALS BEEN VERIFIED & APPROVED IN THE LAST 3 MONTHS?
NO
YES
272
THE PHARMACIST HOLDS THE PATIENT'S Rx UNTIL RECEIVING A COVERAGE APPROVAL FORM FROM INTAKE/REIMBURSEMENT
A
274
THE PHARMACIST VERIFIES THE MD.'S CREDENTIALS AND ENTERS ALL FINDINGS IN CHiPS
276
ARE THE MD.'S CREDENTIALS APPROVED?
YES
280
THE PHYSICIAN IS INDICATED AS APPROVED IN THE PHYSICIAN SCREEN IN CHiPS
282
THE PHARMACIST HOLDS THE PATIENT'S Rx UNTIL RECEIVING A COVERAGE APPROVAL FORM FROM INTAKE/REIMBURSEMENT
A
IF ANY DISCIPLINARY ACTIONS ARE IDENTIFIED, THE DIR. OF PHARM. IS NOTIFIED AND TAKES ONE OF THE FOLLOWING ACTIONS:
– Rx IS PROCESSED AND THE PHARMACIST MONITORS THE MD.'S PROGRAM ACTIVITY
– Rx IS NOT PROCESSED AND THE MD IS NOTED AS UNAPPROVED
278
NO
284
THE PHYSICIAN IS INDICATED AS UNAPPROVED IN CHiPS
286
THE MD IS CONTACTED BY A PHARMACIST & INFORMED THAT THE PATIENT'S Rx CANNOT BE PROCESSED
288
THE Rx AND ENROLLMENT FORM IS MAILED BACK TO THE MD ALONG WITH A COVER LETTER REITERATING THAT THE Rx CANNOT BE PROCESSED
290
A LETTER IS SENT TO THE PATIENT INDICATING THAT THE Rx CANNOT BE PROCESSED & THE PATIENT IS INSTRUCTED TO CONTACT HIS/HER PHYSICIAN
END

FIG. 2B

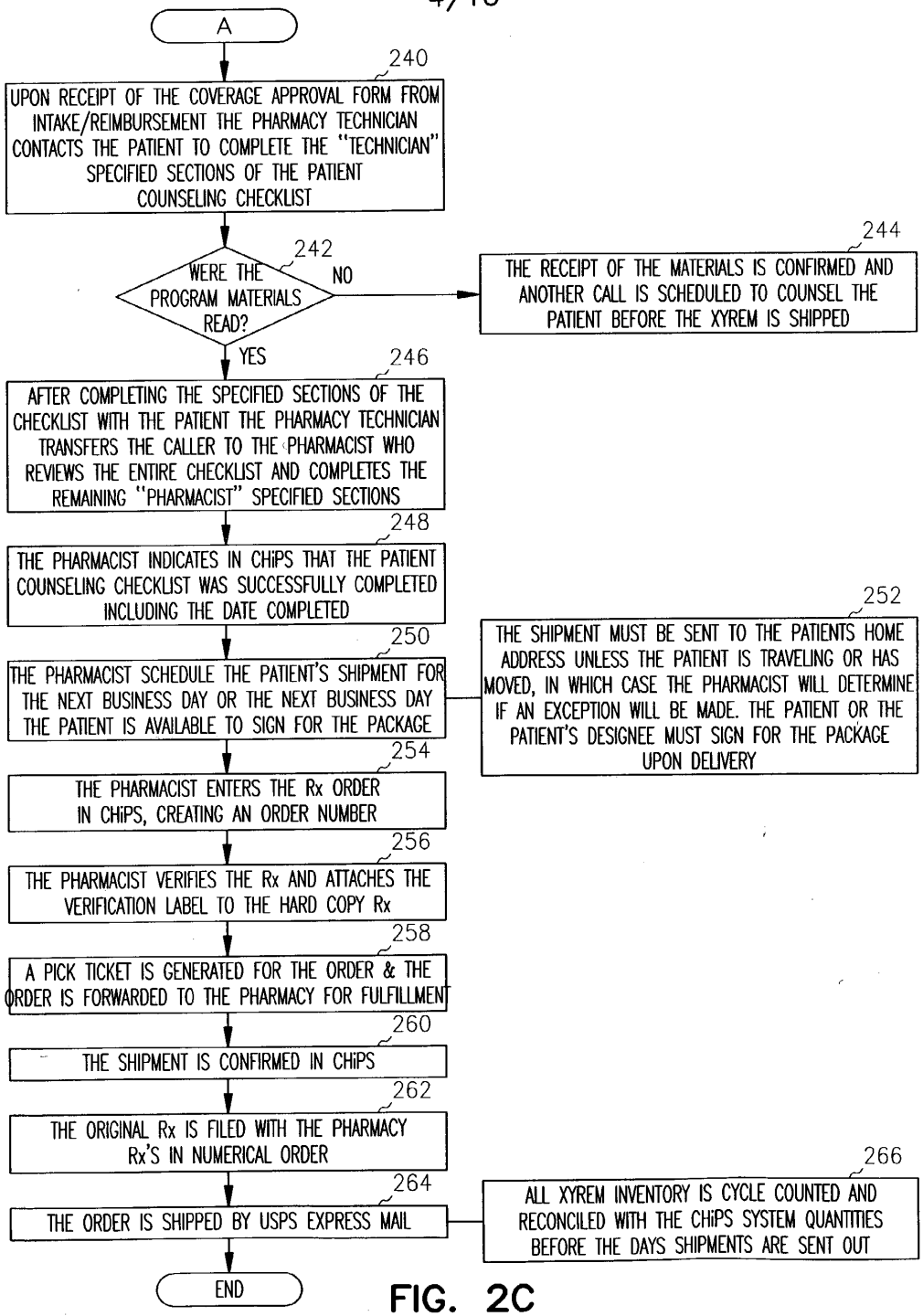

A
240
UPON RECEIPT OF THE COVERAGE APPROVAL FORM FROM INTAKE/REIMBURSEMENT THE PHARMACY TECHNICIAN CONTACTS THE PATIENT TO COMPLETE THE "TECHNICIAN" SPECIFIED SECTIONS OF THE PATIENT COUNSELING CHECKLIST
242
WERE THE PROGRAM MATERIALS READ?
NO
244
THE RECEIPT OF THE MATERIALS IS CONFIRMED AND ANOTHER CALL IS SCHEDULED TO COUNSEL THE PATIENT BEFORE THE XYREM IS SHIPPED
YES
246
AFTER COMPLETING THE SPECIFIED SECTIONS OF THE CHECKLIST WITH THE PATIENT THE PHARMACY TECHNICIAN TRANSFERS THE CALLER TO THE PHARMACIST WHO REVIEWS THE ENTIRE CHECKLIST AND COMPLETES THE REMAINING "PHARMACIST" SPECIFIED SECTIONS
248
THE PHARMACIST INDICATES IN CHiPS THAT THE PATIENT COUNSELING CHECKLIST WAS SUCCESSFULLY COMPLETED INCLUDING THE DATE COMPLETED
250
THE PHARMACIST SCHEDULE THE PATIENT'S SHIPMENT FOR THE NEXT BUSINESS DAY OR THE NEXT BUSINESS DAY THE PATIENT IS AVAILABLE TO SIGN FOR THE PACKAGE
252
THE SHIPMENT MUST BE SENT TO THE PATIENTS HOME ADDRESS UNLESS THE PATIENT IS TRAVELING OR HAS MOVED, IN WHICH CASE THE PHARMACIST WILL DETERMINE IF AN EXCEPTION WILL BE MADE. THE PATIENT OR THE PATIENT'S DESIGNEE MUST SIGN FOR THE PACKAGE UPON DELIVERY
254
THE PHARMACIST ENTERS THE Rx ORDER IN CHiPS, CREATING AN ORDER NUMBER
256
THE PHARMACIST VERIFIES THE Rx AND ATTACHES THE VERIFICATION LABEL TO THE HARD COPY Rx
258
A PICK TICKET IS GENERATED FOR THE ORDER & THE ORDER IS FORWARDED TO THE PHARMACY FOR FULFILLMENT
260
THE SHIPMENT IS CONFIRMED IN CHiPS
262
THE ORIGINAL Rx IS FILED WITH THE PHARMACY Rx'S IN NUMERICAL ORDER
264
THE ORDER IS SHIPPED BY USPS EXPRESS MAIL
266
ALL XYREM INVENTORY IS CYCLE COUNTED AND RECONCILED WITH THE CHiPS SYSTEM QUANTITIES BEFORE THE DAYS SHIPMENTS ARE SENT OUT
END

FIG. 2C

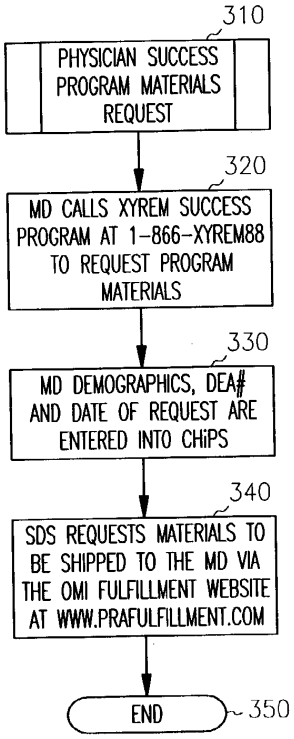

310
PHYSICIAN SUCCESS PROGRAM MATERIALS REQUEST
320
MD CALLS XYREM SUCCESS PROGRAM AT 1-866-XYREM88 TO REQUEST PROGRAM MATERIALS
330
MD DEMOGRAPHICS, DEA# AND DATE OF REQUEST ARE ENTERED INTO CHIPS
340
SDS REQUESTS MATERIALS TO BE SHIPPED TO THE MD VIA THE OMI FULFILLMENT WEBSITE AT WWW.PRAFULFILLMENT.COM
END
350

FIG. 3

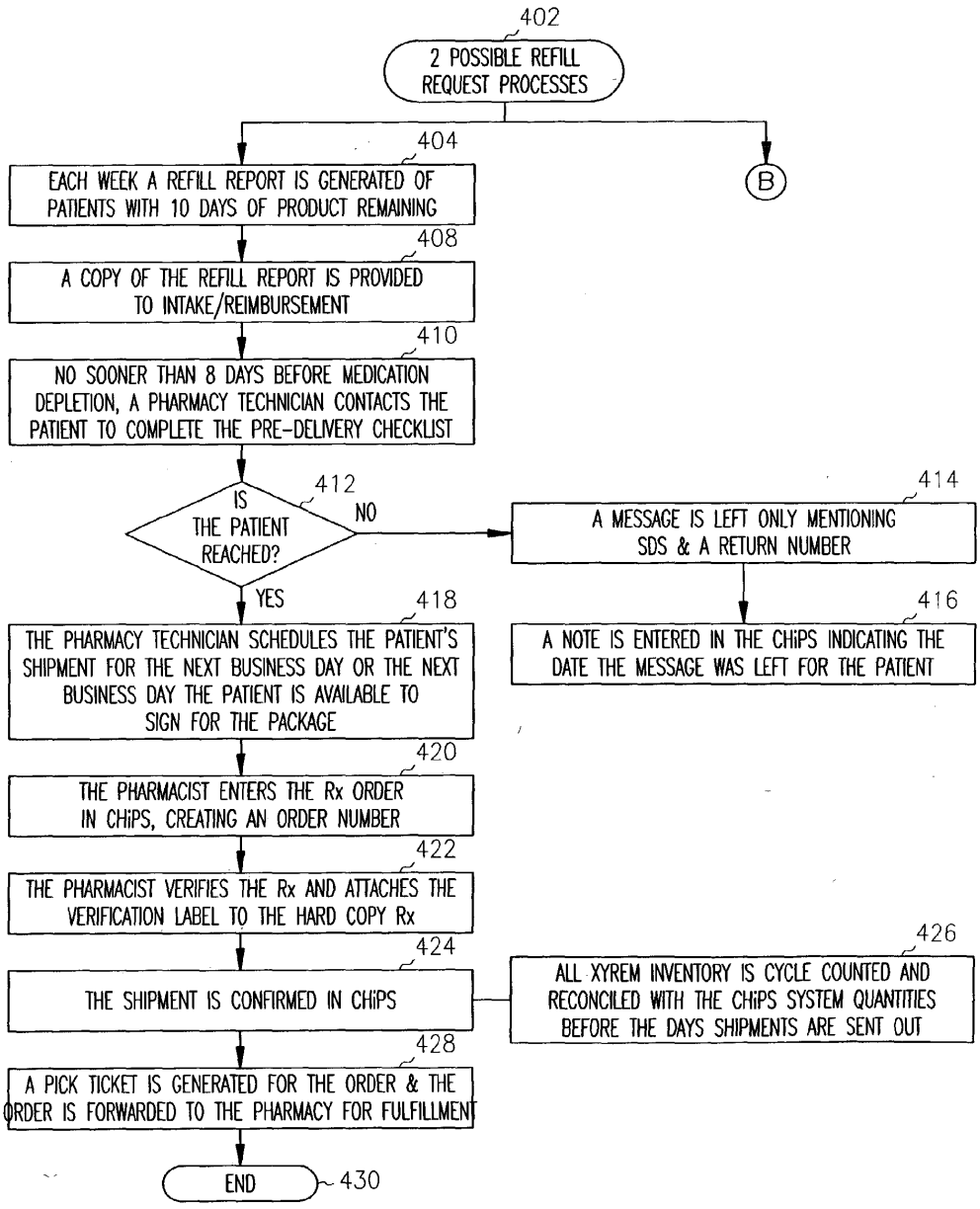

402
2 POSSIBLE REFILL REQUEST PROCESSES
404
EACH WEEK A REFILL REPORT IS GENERATED OF PATIENTS WITH 10 DAYS OF PRODUCT REMAINING
B
408
A COPY OF THE REFILL REPORT IS PROVIDED TO INTAKE/REIMBURSEMENT
410
NO SOONER THAN 8 DAYS BEFORE MEDICATION DEPLETION, A PHARMACY TECHNICIAN CONTACTS THE PATIENT TO COMPLETE THE PRE-DELIVERY CHECKLIST
412
IS THE PATIENT REACHED?
NO
414
A MESSAGE IS LEFT ONLY MENTIONING SDS & A RETURN NUMBER
416
A NOTE IS ENTERED IN THE CHiPS INDICATING THE DATE THE MESSAGE WAS LEFT FOR THE PATIENT
YES
418
THE PHARMACY TECHNICIAN SCHEDULES THE PATIENT'S SHIPMENT FOR THE NEXT BUSINESS DAY OR THE NEXT BUSINESS DAY THE PATIENT IS AVAILABLE TO SIGN FOR THE PACKAGE
420
THE PHARMACIST ENTERS THE Rx ORDER IN CHiPS, CREATING AN ORDER NUMBER
422
THE PHARMACIST VERIFIES THE Rx AND ATTACHES THE VERIFICATION LABEL TO THE HARD COPY Rx
424
THE SHIPMENT IS CONFIRMED IN CHiPS
426
ALL XYREM INVENTORY IS CYCLE COUNTED AND RECONCILED WITH THE CHiPS SYSTEM QUANTITIES BEFORE THE DAYS SHIPMENTS ARE SENT OUT
428
A PICK TICKET IS GENERATED FOR THE ORDER & THE ORDER IS FORWARDED TO THE PHARMACY FOR FULFILLMENT
END
430

FIG. 4A

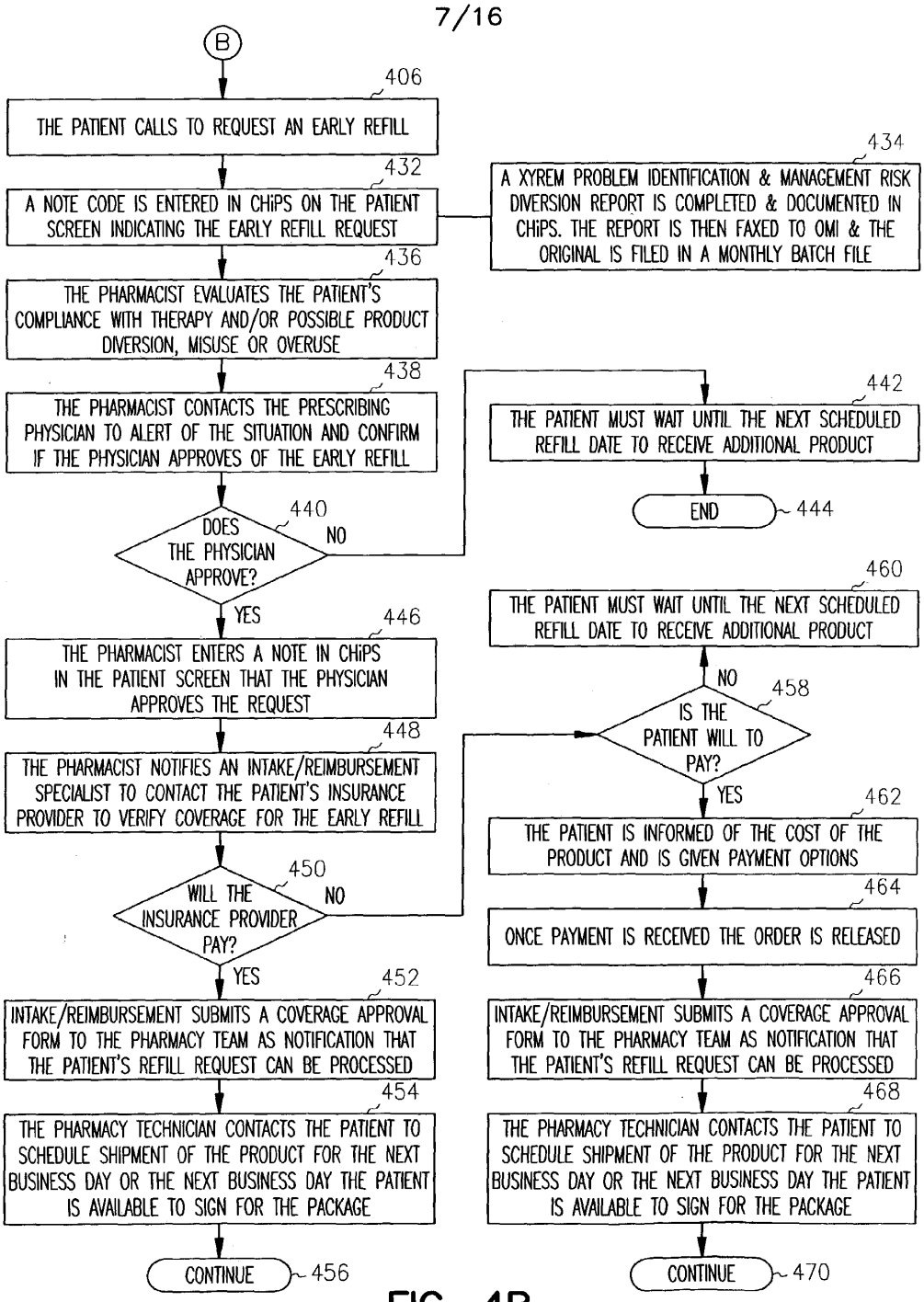

B
406
THE PATIENT CALLS TO REQUEST AN EARLY REFILL
432
A NOTE CODE IS ENTERED IN CHiPS ON THE PATIENT SCREEN INDICATING THE EARLY REFILL REQUEST
434
A XYREM PROBLEM IDENTIFICATION & MANAGEMENT RISK DIVERSION REPORT IS COMPLETED & DOCUMENTED IN CHiPS. THE REPORT IS THEN FAXED TO OMI & THE ORIGINAL IS FILED IN A MONTHLY BATCH FILE
436
THE PHARMACIST EVALUATES THE PATIENT'S COMPLIANCE WITH THERAPY AND/OR POSSIBLE PRODUCT DIVERSION, MISUSE OR OVERUSE
438
THE PHARMACIST CONTACTS THE PRESCRIBING PHYSICIAN TO ALERT OF THE SITUATION AND CONFIRM IF THE PHYSICIAN APPROVES OF THE EARLY REFILL
440
DOES THE PHYSICIAN APPROVE?
NO
442
THE PATIENT MUST WAIT UNTIL THE NEXT SCHEDULED REFILL DATE TO RECEIVE ADDITIONAL PRODUCT
END
444
YES
446
THE PHARMACIST ENTERS A NOTE IN CHiPS IN THE PATIENT SCREEN THAT THE PHYSICIAN APPROVES THE REQUEST
448
THE PHARMACIST NOTIFIES AN INTAKE/REIMBURSEMENT SPECIALIST TO CONTACT THE PATIENT'S INSURANCE PROVIDER TO VERIFY COVERAGE FOR THE EARLY REFILL
450
WILL THE INSURANCE PROVIDER PAY?
NO
YES
452
INTAKE/REIMBURSEMENT SUBMITS A COVERAGE APPROVAL FORM TO THE PHARMACY TEAM AS NOTIFICATION THAT THE PATIENT'S REFILL REQUEST CAN BE PROCESSED
454
THE PHARMACY TECHNICIAN CONTACTS THE PATIENT TO SCHEDULE SHIPMENT OF THE PRODUCT FOR THE NEXT BUSINESS DAY OR THE NEXT BUSINESS DAY THE PATIENT IS AVAILABLE TO SIGN FOR THE PACKAGE
CONTINUE
456
460
THE PATIENT MUST WAIT UNTIL THE NEXT SCHEDULED REFILL DATE TO RECEIVE ADDITIONAL PRODUCT
NO
458
IS THE PATIENT WILL TO PAY?
YES
462
THE PATIENT IS INFORMED OF THE COST OF THE PRODUCT AND IS GIVEN PAYMENT OPTIONS
464
ONCE PAYMENT IS RECEIVED THE ORDER IS RELEASED
466
INTAKE/REIMBURSEMENT SUBMITS A COVERAGE APPROVAL FORM TO THE PHARMACY TEAM AS NOTIFICATION THAT THE PATIENT'S REFILL REQUEST CAN BE PROCESSED
468
THE PHARMACY TECHNICIAN CONTACTS THE PATIENT TO SCHEDULE SHIPMENT OF THE PRODUCT FOR THE NEXT BUSINESS DAY OR THE NEXT BUSINESS DAY THE PATIENT IS AVAILABLE TO SIGN FOR THE PACKAGE
CONTINUE
470

FIG. 4B

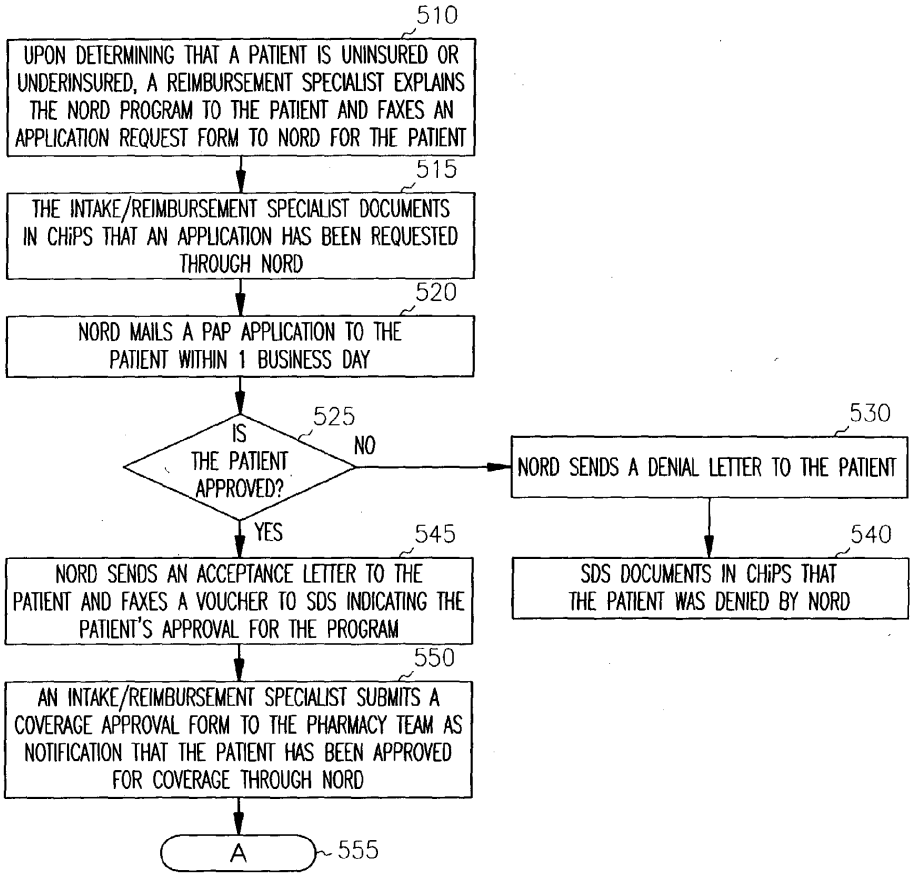

510
UPON DETERMINING THAT A PATIENT IS UNINSURED OR UNDERINSURED, A REIMBURSEMENT SPECIALIST EXPLAINS THE NORD PROGRAM TO THE PATIENT AND FAXES AN APPLICATION REQUEST FORM TO NORD FOR THE PATIENT
515
THE INTAKE/REIMBURSEMENT SPECIALIST DOCUMENTS IN CHIPS THAT AN APPLICATION HAS BEEN REQUESTED THROUGH NORD
520
NORD MAILS A PAP APPLICATION TO THE PATIENT WITHIN 1 BUSINESS DAY
525
IS THE PATIENT APPROVED?
NO
530
NORD SENDS A DENIAL LETTER TO THE PATIENT
YES
545
NORD SENDS AN ACCEPTANCE LETTER TO THE PATIENT AND FAXES A VOUCHER TO SDS INDICATING THE PATIENT'S APPROVAL FOR THE PROGRAM
540
SDS DOCUMENTS IN CHIPS THAT THE PATIENT WAS DENIED BY NORD
550
AN INTAKE/REIMBURSEMENT SPECIALIST SUBMITS A COVERAGE APPROVAL FORM TO THE PHARMACY TEAM AS NOTIFICATION THAT THE PATIENT HAS BEEN APPROVED FOR COVERAGE THROUGH NORD
A
555

FIG. 5

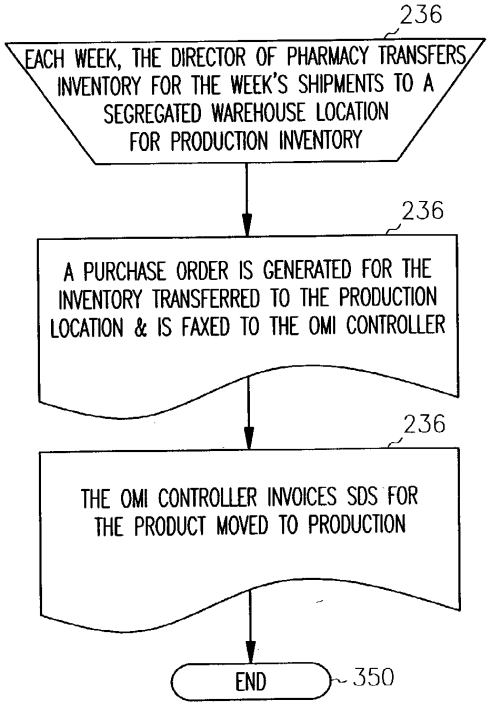


FIG. 6

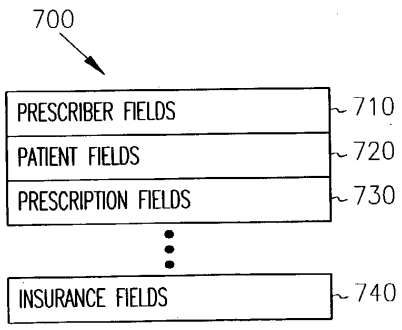


FIG. 7

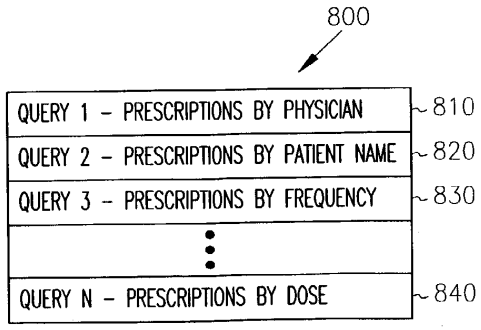


FIG. 8

900

PRESCRIPTION AND ENROLLMENT FORM

PRESCRIBER INFORMATION

PRESCRIBER'S NAME: _____ OFFICE CONTACT: _____
STREET ADDRESS: _____
CITY: _____ STATE: _____ ZIP: _____
PHONE: _____ FAX: _____
LICENSE NUMBER: _____ DEA NUMBER: _____
MD SPECIALTY: _____

PRESCRIPTION FORM

PATIENT NAME: _____ SS#: _____ DOB: _____ SEX M / F
ADDRESS: _____
CITY: _____ STATE: _____ ZIP: _____
Rx: XYREM ORAL SOLUTION (500 mg/mL) 180 Ml. BOTTLE QUANTITY: _____ MONTHS SUPPLY
SIG: TAKE _____ GMS P.O. DILUTED IN 60 mL WATER AT H.S. AND THEN AGAIN 2 1/2 TO 4 HOURS LATER
REFILLS (CIRCLE ONE): 0 1 2 (MAXIMUM OF 3 MONTH SUPPLY)
_____ DATE: ____/____/____
PRESCRIBER'S SIGNATURE

PHYSICIAN DECLARATION–PLEASE CHECK EACH BOX | TO BE COMPLETED AT INITIAL PRESCRIPTION ONLY

☐ I HAVE READ THE MATERIALS IN THE XYREM PHYSICIAN SUCCESS PROGRAM
☐ I VERIFY THAT THE PATIENT HAS BEEN EDUCATED WITH RESPECT TO XYREM PREPARATION, DOSING AND SCHEDULING.
☐ I UNDERSTAND THAT XYREM IS APPROVED FOR THE TREATMENT OF CATAPLEXY IN PATIENTS WITH NARCOLEPSY, AND THAT SAFETY OR EFFICACY HAS NOT BEEN ESTABLISHED FOR ANY OTHER INDICATION.
☐ I UNDERSTAND THAT THE SAFETY OF DOSES GREATER THAN 9gm/DAY HAS NOT BEEN ESTABLISHED

PATIENT INFORMATION

BEST TIME TO CONTACT PATIENT: ☐ DAY ☐ NIGHT
DAY #: _____ EVENING #: _____
INSURANCE COMPANY NAME: _____ PHONE #: _____
INSURED'S NAME: _____ RELATIONSHIP TO PATIENT: _____
IDENTIFICATION NUMBER: _____ POLICY/GROUP NUMBER: _____
PRESCRIPTION CARD: ☐ NO ☐ YES IF YES, CARRIER: _____ POLICY #: _____ GROUP: _____

PLEASE ATTACH COPIES OF PATIENT'S INSURANCE CARDS

FAX COMPLETED FORM TO XYREM SUCCESS PROGRAM (TOLL-FREE) 1-866-470-1744
FOR INFORMATION, CALL THE XYREM TEAM (TOLL FREE) AT 1-866-XYREM88 (1-866-997-3688)

FIG. 9

1000

PATIENT ASSISTANCE APPLICATION REQUEST FORM

DATE:

TO: PATIENT ASSISTANCE ORGANIZATION
FROM: SDS

FAX #: 203-798-2291

PLEASE SEND A XYREM PATIENT ASSISTANCE PROGRAM APPLICATION TO:

PATIENT NAME _____

ADDRESS _____

_____

_____

TELEPHONE: ( ) _____

PATIENT DOSAGE: _____ (GRAMS) TWICE NIGHTLY FOR A TOTAL DOSAGE OF _____ (GRAMS)

_____ BOTTLES (THREE MONTHS SUPPLY)

BACKGROUND INFORMATION:

_____

_____

_____

_____

_____

_____

FIG. 10

SENSITIVE DRUG PATIENT ASSISTANCE PROGRAM 1100

VOUCHER REQUEST FOR MEDICATION

PATIENT INFORMATION
<FIRST NAME><LAST NAME>
<ADDRESS 1>
<ADDRESS 2>
<CITY, STATE ZIP CODE>

PHONE: <123-456-7890
DOB: 01/01/1900
SSN: 123-45-6789
DRUG ALLOTMENT: 100%
LRD: 03/01/2001

CASE CODE: ********

PHYSICIAN INFORMATION
<PHYSICIAN NAME>
<ADDRESS 1>
<ADDRESS 2>
<CITY, STATE ZIP CODE>

PHONE: <123-456-7890

FIRST SHIPMENT THIS YEAR

DRUG	QUANTITY
XYREEM 180ml btl	1

VALIDATION DATE:	03/01/2001
EXPIRATION DATE:	05/31/2001
ISSUE DATE:	03/15/2001
APPROVED	_____

PHARMACY USE

NORD COPY

****

(DETACH HERE)

PATIENT INFORMATION
<FIRST NAME><LAST NAME>
<ADDRESS 1>
<ADDRESS 2>
<CITY, STATE ZIP CODE>

PHONE: <123-456-7890
DOB: 01/01/1900
SSN: 123-45-6789
DRUG ALLOTMENT: 100%
LRD: 03/01/2001

CASE CODE: ********

PHYSICIAN INFORMATION
<PHYSICIAN NAME>
<ADDRESS 1>
<ADDRESS 2>
<CITY, STATE ZIP CODE>

PHONE: <123-456-7890

FIRST SHIPMENT THIS YEAR

DRUG	QUANTITY
XYREM 180ml btl	1

VALIDATION DATE:	03/01/2001
EXPIRATION DATE:	05/31/2001
ISSUE DATE:	03/15/2001
APPROVED	_____

PHARMACY USE

FIG. 11

1200

SENSITIVE DRUG PHYSICIAN'S CERTIFICATE OF MEDICAL NEED

PATIENT INFORMATION

DATE: _____

NAME: _____
LAST FIRST M

DATE OF BIRTH: _____

DRUG BEING PRESCRIBED: XYREM

DIAGNOSIS/CONDITION FOR WHICH DRUG IS BEING PRESCRIBED: _____

ICD-9: _____

PHYSICIAN INFORMATION

PHYSICIAN'S NAME (PLEASE PRINT): _____

PHYSICIAN'S SIGNATURE: _____ DATE: _____

PLEASE FAX BACK TO SENSITIVE DRUG SUCCESS PROGRAM: (1-800-TOLL FREE NUMBER)

FIG. 12

ACTIVITY REPORTS

	REPORT FREQUENCY		
	WEEKLY	MONTHLY	QUARTERLY
SALES			
Rx BY ZIP (NEW AND TOTAL)	X	X	X
Rx BY PHYSICIAN BY ZIP	X	X	
$ BY ZIP	X	X	X
REGULATORY			
# OF PHYSICIAN REGISTRIES		X	
# OF DENIED PHYSICIAN REGISTRIES AND REASON		X	
# OF COMPLETED PATIENT REGISTRIES		X	
# OF PROBLEM IDENTIFICATION & MANAGEMENT RISK DIVERSION REPORTS COMPLETED	X		
# OF CYCLE COUNTS PERFORMED & ACCURACY OF EACH		X	
QUALITY ASSURANCE			
# OF PRODUCT DEFECTS/COMPLAINTS REPORTED, TYPE AND LOT #		X	
CALL CENTER			
# OF CALLS RECEIVED		X	
# OF CALLS INITIATED		X	
# OF CALLS ANSWERED IN 30 SECONDS, ETC.		X	
PERCENTAGE OF CALLS ANSWERED IN 30 SECONDS		X	
# OF ABANDONED CALLS		X	
% OF ABANDONED CALLS		X	
AVERAGE CALL LENGTH		X	
PHARMACY			
# OF FAXED Rx/ENROLLMENT FORMS		X	
# OF MAILED Rx/ENROLLEMENT FORMS		X	
# OF RxS SHIPPED W/IN 1, 2, 3, 4 ETC. DAYS (FROM THE TIME INITIAL RECEIPT TO SHIPMENT OF Rx)		X	
# OF PATIENT SUCCESS PACKETS SHIPPED		X	

FIG. 13A

ACTIVITY REPORTS

PHARMACY		X	
# OF PHYSICIAN SUCCESS PACKETS SHIPPED		X	
# OF COMPLETED SHIPMENTS		X	
# OF INCOMPLETE SHIPMENTS AND REASON		X	
# OF SHIPPING ERRORS		X	
# OF PAP SHIPMENTS		X	
# OF PAP APPLICATIONS		X	
# OF PAP APPROVALS		X	
# OF CANCELED ORDERS		X	
# OF USPS ERRORS		X	
INVENTORY		X	
# OF RETURNED PRODUCTS AND REASON		X	
# OF OUTDATED BOTTLES OF PRODUCT		X	
INVENTORY COUNTS OF CONSIGNMENT & PRODUCTION INVENTORY		X	
# OF UNITS RECEIVED		X	
LOTS RECEIVED		X	
REIMBURSEMENT		X	
# OF PENDED AND WHY		X	
# OF APPROVALS		X	
# OF DENIALS		X	
# OF REJECTIONS		X	
PAYOR TYPES		X	

FIG. 13B

ACTIVITY REPORTS

PATIENT CARE			
# OF ADVERSE EVENTS REPORTED AND TYPE		X	
# OF ADVERSE EVENTS SENT TO OMI		X	
# OF DOSING PROBLEMS AND TYPE		X	
# OF NONCOMPLIANCE EPISODES AND REASON		X	
# OF PATIENT COUNSELED AND REASON		X	
# OF PATIENTS DISCONTINUED AND REASON		X	
PATIENT CARE		X	
# OF PATIENTS REFERRED TO PHYSICIAN AND REASON		X	
# OF ACTIVE PATIENTS		X	
# OF NEW PATIENTS		X	
# OF RESTART PATIENTS		X	
# OF DISCONTINUED PATIENTS AND REASON		X	
DRUG INFORMATION		X	
# OF DRUG INFORMATION REQUESTS AND TYPE		X	
# OF CALLS TRIAGED TO OMI		X	

FIG. 13C

SCHWEGMAN ■ LUNDBERG ■ WOESSNER ■ KLUTH

United States Patent Application

COMBINED DECLARATION AND POWER OF ATTORNEY

As a below named inventor I hereby declare that: my residence, post office address and citizenship are as stated below next to my name; that

I verily believe I am the original, first and joint inventor of the subject matter which is claimed and for which a patent is sought on the invention entitled: **SENSITIVE DRUG DISTRIBUTION SYSTEM AND METHOD**.

The specification of which is attached hereto.

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to the patentability of this application in accordance with 37 C.F.R. § 1.56 (attached hereto). I also acknowledge my duty to disclose all information known to be material to patentability which became available between a filing date of a prior application and the national or PCT international filing date in the event this is a Continuation-In-Part application in accordance with 37 C.F.R. §1.63(e).

I hereby claim foreign priority benefits under 35 U.S.C. §119(a)-(d) or 365(b) of any foreign application(s) for patent or inventor's certificate, or 365(a) of any PCT international application which designated at least one country other than the United States of America, listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on the basis of which priority is claimed:

No such claim for priority is being made at this time.

I hereby claim the benefit under 35 U.S.C. § 119(e) of any United States provisional application(s) listed below:

No such claim for priority is being made at this time.

I hereby claim the benefit under 35 U.S.C. § 120 or 365(c) of any United States and PCT international application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT international application in the manner provided by the first paragraph of 35 U.S.C. § 112, I acknowledge the duty to disclose material information as defined in 37 C.F.R. § 1.56(a) which became available between the filing date of the prior application and the national or PCT international filing date of this application:

No such claim for priority is being made at this time.

[redacted]

I hereby appoint the following attorney(s) and/or patent agent(s) to prosecute this application and to transact all business in the Patent and Trademark Office connected herewith:

Anglin, J. Michael	Reg. No. 24,916	Haack, John L.	Reg. No. 36,154	Nama, Kash	Reg. No. 44,255
Arora, Suneel	Reg. No. 42,267	Harris, Robert J.	Reg. No. 37,346	Nelson, Albin J.	Reg. No. 28,650
Beekman, Marvin L.	Reg. No. 38,377	Jackson Huebsch, Katharine A.	Reg. No. 47,670	Nielsen, Walter W.	Reg. No. 25,539
Bianchi, Timothy E.	Reg. No. 39,610	Jurkovich, Patti J.	Reg. No. 44,813	Padys, Danny J.	Reg. No. 35,635
Billion, Richard E.	Reg. No. 32,836	Kalis, Janal M.	Reg. No. 37,650	Parker, J. Kevin	Reg. No. 33,024
Black, David W.	Reg. No. 42,331	Klima-Silberg, Catherine I.	Reg. No. 40,052	Perdok, Monique M.	Reg. No. 42,989
Brennan, Thomas F.	Reg. No. 35,075	Kluth, Daniel J.	Reg. No. 32,146	Peret, Andrew R.	Reg. No. 41,246
Chadwick, Robin A.	Reg. No. 36,477	Lacy, Rodney L.	Reg. No. 41,136	Peterson, David C.	Reg. No. 47,857
Clark, Barbara J.	Reg. No. 38,107	Lemaire, Charles A.	Reg. No. 36,198	Prout, William F.	Reg. No. 33,995
Clise, Timothy B.	Reg. No. 40,957	LeMoine, Dana B.	Reg. No. 40,062	Schumm, Sherry W.	Reg. No. 39,422
Cochran, David R.	Reg. No. 46,632	Lundberg, Steven W.	Reg. No. 30,568	Schwegman, Micheal L.	Reg. No. 25,816
Dahl, John M.	Reg. No. 44,639	Maki, Peter C.	Reg. No. 42,832	Speier, Gary J.	Reg. No. 45,458
Drake, Eduardo E.	Reg. No. 40,594	Malen, Peter L.	Reg. No. 44,894	Steffey, Charles E.	Reg. No. 25,179
Embretson, Janet E.	Reg. No. 39,665	Mates, Robert E.	Reg. No. 35,271	Stordal, Leif T.	Reg. No. 46,251
Forrest, Bradley A.	Reg. No. 30,837	McCrackin, Ann M.	Reg. No. 42,858	Terry, Kathleen R.	Reg. No. 31,884
Gamon, Owen J.	Reg. No. 36,143	McGough, Kevin J.	Reg. No. 31,279	Tong, Viet V.	Reg. No. 45,416
Gorrie, Gregory J.	Reg. No. 36,530	McTavish, Hugh E.	Reg. No. 48,341	Viksnins, Ann S.	Reg. No. 37,748
Gortych, Joseph E.	Reg. No. 41,791	Mehrle, Joseph P.	Reg. No. 45,535	Woessner, Warren D.	Reg. No. 30,440
Greaves, John N.	Reg. No. 40,362	Muller, Mark V.	Reg. No. 37,509		

I hereby authorize them to act and rely on instructions from and communicate directly with the person/assignee/attorney/firm/organization/who/which first sends/sent this case to them and by whom/which I hereby declare that I have consented after full disclosure to be represented unless/until I instruct Schwegman, Lundberg, Woessner & Kluth, P.A. to the contrary.

Please direct all correspondence in this case to **Schwegman, Lundberg, Woessner & Kluth, P.A.** at the address indicated below:

P.O. Box 2938, Minneapolis, MN 55402
Telephone No. (612)373-6900

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Full Name of joint inventor number 1 : **Dayton T. Reardan**
Citizenship: **United States of America** Residence: **Excelsior, MN**
Post Office Address: 22345 Bracketts Road
Excelsior, MN 55331

Signature: _____ Date: _____
Dayton T. Reardan

Full Name of joint inventor number 2 : **Patti Engel**
Citizenship: **United States of America** Residence: **Eagen, MN**
Post Office Address: 852 Basswood Lane
Eagen, MN 55123

Signature: _____ Date: _____
Patti Engel

X Additional inventors are being named on separately numbered sheets, attached hereto.

[redacted]

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Full Name of joint inventor number 3 : **Bob Gagne**
Citizenship: **United States of America** Residence: **St. Paul, MN**
Post Office Address: 202 So. Wheeler Street
St. Paul, MN 55015

Signature: _____ Date: _____
Bob Gagne

Full Name of inventor:
Citizenship: Residence:
Post Office Address:

Signature: _____ Date: _____

Full Name of inventor:
Citizenship: Residence:
Post Office Address:

Signature: _____ Date: _____

Full Name of inventor:
Citizenship: Residence:
Post Office Address:

Signature: _____ Date: _____

[redacted]

§ 1.56 Duty to disclose information material to patentability.

(a) A patent by its very nature is affected with a public interest. The public interest is best served, and the most effective patent examination occurs when, at the time an application is being examined, the Office is aware of and evaluates the teachings of all information material to patentability. Each individual associated with the filing and prosecution of a patent application has a duty of candor and good faith in dealing with the Office, which includes a duty to disclose to the Office all information known to that individual to be material to patentability as defined in this section. The duty to disclose information exists with respect to each pending claim until the claim is canceled or withdrawn from consideration, or the application becomes abandoned. Information material to the patentability of a claim that is canceled or withdrawn from consideration need not be submitted if the information is not material to the patentability of any claim remaining under consideration in the application. There is no duty to submit information which is not material to the patentability of any existing claim. The duty to disclose all information known to be material to patentability is deemed to be satisfied if all information known to be material to patentability of any claim issued in a patent was cited by the Office or submitted to the Office in the manner prescribed by §§ 1.97(b)-(d) and 1.98. However, no patent will be granted on an application in connection with which fraud on the Office was practiced or attempted or the duty of disclosure was violated through bad faith or intentional misconduct. The Office encourages applicants to carefully examine:

(1) prior art cited in search reports of a foreign patent office in a counterpart application, and

(2) the closest information over which individuals associated with the filing or prosecution of a patent application believe any pending claim patentably defines, to make sure that any material information contained therein is disclosed to the Office.

(b) Under this section, information is material to patentability when it is not cumulative to information already of record or being made of record in the application, and

(1) It establishes, by itself or in combination with other information, a prima facie case of unpatentability of a claim; or

(2) It refutes, or is inconsistent with, a position the applicant takes in:

(i) Opposing an argument of unpatentability relied on by the Office, or

(ii) Asserting an argument of patentability.

A prima facie case of unpatentability is established when the information compels a conclusion that a claim is unpatentable under the preponderance of evidence, burden-of-proof standard, giving each term in the claim its broadest reasonable construction consistent with the specification, and before any consideration is given to evidence which may be submitted in an attempt to establish a contrary conclusion of patentability.

(c) Individuals associated with the filing or prosecution of a patent application within the meaning of this section are:

(1) Each inventor named in the application:

(2) Each attorney or agent who prepares or prosecutes the application; and

(3) Every other person who is substantively involved in the preparation or prosecution of the application and who is associated with the inventor, with the assignee or with anyone to whom there is an obligation to assign the application.

(d) Individuals other than the attorney, agent or inventor may comply with this section by disclosing information to the attorney, agent, or inventor.

[redacted]

UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents
Washington, DC 20231
www.uspto.gov

APPLICATION NUMBER	FILING/RECEIPT DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NUMBER
10/322,348	12/17/2002	Dayton T. Reardan	101.031US1

CONFIRMATION NO. 5446

21186
SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.
P.O. BOX 2938
MINNEAPOLIS, MN 55402

FORMALITIES LETTER

OC000000009686927

Date Mailed: 03/24/2003

NOTICE TO FILE MISSING PARTS OF NONPROVISIONAL APPLICATION

FILED UNDER 37 CFR 1.53(b)

Filing Date Granted

Items Required To Avoid Abandonment:

An application number and filing date have been accorded to this application. The item(s) indicated below, however, are missing. Applicant is given **TWO MONTHS** from the date of this Notice within which to file all required items and pay any fees required below to avoid abandonment. Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a).

- The statutory basic filing fee is missing.
  Applicant must submit $ **375** *to complete the basic filing fee for a small entity.*
- The oath or declaration is unsigned.
- To avoid abandonment, a late filing fee or oath or declaration surcharge as set forth in 37 CFR 1.16(e) of $65 for a small entity in compliance with 37 CFR 1.27, must be submitted with the missing items identified in this letter.

Items Required To Avoid Processing Delays:

The item(s) indicated below are also required and should be submitted with any reply to this notice to avoid further processing delays.

- Additional claim fees of **$87** as a small entity, including any required multiple dependent claim fee, are required. Applicant must submit the additional claim fees or cancel the additional claims for which fees are due.

SUMMARY OF FEES DUE:

Total additional fee(s) required for this application is **$527** for a Small Entity

- **$375** Statutory basic filing fee.
- **$65** Late oath or declaration Surcharge.
- Total additional claim fee(s) for this application is **$87**
  - **$45** for **5** total claims over 20 .

- **$42** for **1** independent claims over 3 .

A copy of this notice MUST be returned with the reply.

Customer Service Center
Initial Patent Examination Division (703) 308-1202
PART 3 - OFFICE COPY

1743
3

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Dayton T. Reardan et al.

Title: SENSITIVE DRUG DISTRIBUTION SYSTEM AND METHOD

Docket No.: 101.031US1 Serial No.: 10/322,348
Filed: December 17, 2002 Due Date: N/A
Examiner: Unknown Group Art Unit: 1743

Commissioner for Patents
Washington, D.C. 20231

We are transmitting herewith the following attached items (as indicated with an "X"):

X A return postcard.
X An Information Disclosure Statement (1 pg.), Form 1449 (1 pg.), and copies of 7 cited documents.

Please consider this a PETITION FOR EXTENSION OF TIME for sufficient number of months to enter these papers and please charge any additional required fees or credit overpayment to Deposit Account No. 19-0743.

SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.
P.O. Box 2938, Minneapolis, MN 55402 (612-373-6900)

By: _____
Atty: Bradley A. Forrest
Reg. No. 30,837

CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: Commissioner for Patents, Washington, D.C. 20231, on this 8 day of April, 2003.

MEREDITH MESCHER
Name

Meredith Mescher
Signature

Customer Number 21186
SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A. P.O. Box 2938, Minneapolis, MN 55402 (612-373-6900)
(GENERAL)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Dayton T. Reardan Ph.D. et al.	Examiner:	Unknown
Serial No.:	10/322,348	Group Art Unit:	1743
Filed:	December 17, 2002	Docket:	101.031US
Title:	SENSITIVE DRUG DISTRIBUTION SYSTEM AND METHOD		

INFORMATION DISCLOSURE STATEMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

In compliance with the duty imposed by 37 C.F.R. § 1.56, and in accordance with 37 C.F.R. §§ 1.97 *et. seq.*, the enclosed materials are brought to the attention of the Examiner for consideration in connection with the above-identified patent application. Applicants respectfully request that this Information Disclosure Statement be entered and the documents listed on the attached Form 1449 be considered by the Examiner and made of record. Pursuant to the provisions of MPEP 609, Applicants request that a copy of the 1449 form, initialed as being considered by the Examiner, be returned to the Applicants with the next official communication.

Pursuant to 37 C.F.R. §1.97(b), it is believed that no fee or statement is required with the Information Disclosure Statement. However, if an Office Action on the merits has been mailed, the Commissioner is hereby authorized to charge the required fees to Deposit Account No. 19-0743 in order to have this Information Disclosure Statement considered.

The Examiner is invited to contact the Applicants' Representative at the below-listed telephone number if there are any questions regarding this communication.

Respectfully submitted,

DAYTON T. REARDAN PH.D. ET AL.

By their Representatives,

SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.
P.O. Box 2938
Minneapolis, MN 55402
612-373-6972

Date 4-8-2003 By _____
Bradley A. Forrest
Reg. No. 30,837

CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: Commissioner of Patents, Washington, D.C. 20231, on this 8 day of April, 2003

MEREDITH MESCHER
Name

Meredith Mescher
Signature

PTO/SB/08A(10-01)
Approved for use through 10/31/2002. OMB 851-0031
US Patent & Trademark Office: U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use as many sheets as necessary)

Sheet 1 of 1

Complete if Known	
Applicati n Number	10/322,348
Filing Date	December 17, 2002
First Nam d Invent r	Reardan Ph.D., Dayton
Group Art Unit	1743
Examiner Name	Unknown
Attorney Docket No: 101.031US1	

US PATENT DOCUMENTS						
Examiner Initial *	**USP Document Number**	**Publication Date**	**Name of Patentee or Applicant of cited Document**	**Class**	**Subclass**	**Filing Date If Appropriate**
	US-6,045,501	04/04/2000	Elsayed, Marc , et al			08/28/1998
	US-6,315,720	11/13/2001	Williams, Bruce A., et al			10/23/2000

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	**Foreign Document No**	**Publication Date**	**Name of Patentee or Applicant of cited Document**	**Class**	**Subclass**	**T²**

OTHER DOCUMENTS -- NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	**Cite No ¹**	**Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.**	**T²**
		NASCSA National Conference, (November 2000),8 pages	
		"Diversion Prevention Through Responsible Distribution", NADDI Regional Training, (May 2001),12 pages	
		"Diversion Prevention Through Responsible Distribution", NADDI Regional Training Tennessee, (June 2001),14 Pages	
		"Diversion Prevention Through Responsible Distribution", NADDI National Conference, (November 2001),15 pages	
		"Peripheral and Central Nervous System Drugs Advisory Committee", Department of Health and Human Services Food and Drug Administration Center for Drug Evaluation and Research, Holiday Inn, Bethesda, Maryland,(06/06/2001),7 pages	

EXAMINER **DATE CONSIDERED**

Substitute Disclosure Statement Form (PTO-1449)

* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ¹ Applicant's unique citation designation number (optional) ² Applicant is to place a check mark here if English language Translation is attached

NASCSA Nat'l Conference
November 2000

Orphan Medical, Inc.

Dedicated to patients with uncommon diseases

Xyrem®
(sodium oxybate) oral solution
Developmental History

- 1994: Orphan Medical begins development at request of NORD and FDA's Office of Orphan Product Development
- 1995-1996: Program design with FDA; formulation and toxicology
- 1997: Controlled trials begin
- 1998: Blind broken, efficacy and safety data confirm Xyrem's use in narcolepsy

2

GHB "Illicit Use" History

- 1990: FDA initiates voluntary removal from health food stores due to abuse by body builders/weight lifters
- 1996: reports of street use utilizing GHB-making kits obtained via Internet
- 1998: reports of GBL being utilized for "similar physical effect"
- 1999: reports of 1,4BD being utilized for "similar physical effect"
- 2000: PL 106-172 enacted "bifurcated" schedule of GHB
  - CI for illicit use
  - CIII for FDA approved NDA
- Orphan Medical responsibilities: Xyrem

3

Orphan Medical's Position

- Xyrem should be available for patients who could benefit from its medical properties
- Distribution and registries should be utilized to minimize/prevent/identify diversion
- Illicit use of GHB and its "chemical cousins" should be harshly penalized

Xyrem: Patient Success Program

- A comprehensive program designed to ensure the responsible distribution of Xyrem
- Provides
  - Appropriate physician and patient education
  - Minimization/prevention of diversion
  - Prosecution assistance

Xyrem: Patient Success Program

- Developed after extensive consultation with
  - •law enforcement
  - •forensics experts
  - •prosecutors
  - •consultants with DEA
  - •field law enforcement personnel
  - •drug diversion
  - •pharmaceutical distribution experts
- Draft program has been circulated and reviewed by key regulatory and enforcement officials for feedback

Xyrem Patient Success Program
Closed Loop Distribution

Bulk drug manufactured in PA (Lonza)

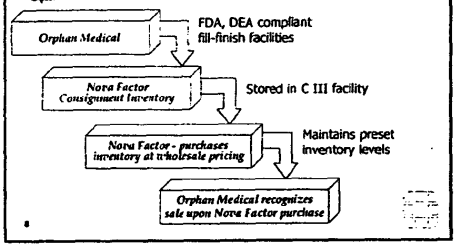
Drug product produced in NC (Catalytica)

Single pharmacy, Nova Factor, in TN

- Central location: all records and controls in one place
- Despite financial implications, Orphan will not place Xyrem in 63,000 retail pharmacy outlets nationally

7

Xyrem Patient Success Program
Inventory Management



8

Xyrem Patient Success Program
Prescription Process

- Potential physician targets identified through Provigil® IMS data
  - While 12,000 physicians have prescribed Provigil to date, only 4,000 have prescribed >X4, these become our "customer targets"
  - At launch, the Xyrem Physician Success Program is mailed to these 4,000 physicians (documentation of mailing)
  - Approx. 35 sales representatives "detail" target physicians, leaving behind the Xyrem Physician Success Program (signed documentation of receipt)
  - No Physician Sampling
  - Upon first Rx, "new prescriber" receives Xyrem Physician Success Program (documentation of mailing and follow up telephone call)

9

Xyrem Patient Success Program
Prescription Process

- Physician Success Program DOES NOT speak to efficacy and safety of Xyrem, but rather the prescription process, handling, reimbursement program, etc.
- Physician faxes Rx to Nova Factor
- Nova Factor verifies physician is "eligible"
  - Active DEA number
  - State on-line verification of pending actions
- Nova Factor calls physician, verifying Rx for given patient and obtains insurance information etc.

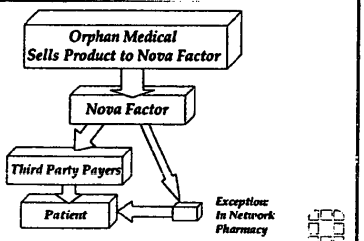
10

Xyrem Patient Success Program
Prescription Process

- Nova Factor contacts third party payor (insurance company) to obtain coverage
  - If necessary, obtains letter of medical necessity from physician
  - Obtains assignment of benefits from third party payor
  - Only if third party payor insists "in network" pharmacy be used will Nova Factor drop ship to "in network pharmacy", requiring patient information and all appropriate data for registry

11

Xyrem Patient Success Program
Distribution Process



12

Xyrem Patient Success Program Distribution Process

- Nova Factor contacts patient to inform them of insurance coverage and to determine patient availability for shipping
  - Xyrem shipped by overnight courier (FedX RapidTrac®) with real-time tracking
  - Xyrem delivered ONLY by authorized signature
  - If patient unavailable, Xyrem returned to Nova Factor
  - If product is lost, investigation begins regarding shipment's whereabouts

13

Xyrem Patient Success Program Distribution Process

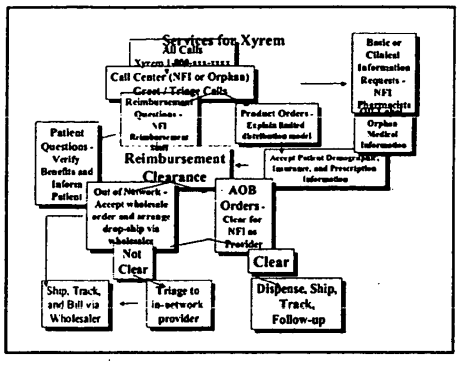
- If RapidTrac® shows Xyrem received, Nova Factor contacts patient within 24 hours to
  - Confirm receipt of prescription
  - Confirm receipt of Xyrem Patient Success Program
  - Offer counsel regarding Xyrem dosing and compliance
  - Confirm patient's understanding of contents of Xyrem Patient Success Program

14

Xyrem Patient Success Program Distribution Process

- If patient has not reviewed Xyrem Patient Success Program
  - Patient is instructed to review materials, and Nova Factor pharmacist will call again in 24 hours
  - After 2nd attempt, doctor will be contacted if pharmacist still uncomfortable
  - If pharmacist is still uncomfortable with patient's understanding, refill will be withheld until such time pharmacist is comfortable

15



Nova Factor Data Collection

- Physician/Patient Information
  - Prescriptions by physician specialty
  - Prescriptions by patient name
  - Prescriptions by volume (frequency)
  - Prescriptions by dose
- As a registered pharmacy and wholesaler, Nova Factor can and will share this information with appropriate state and federal authorities for investigation and prosecution

17

Xyrem Patient Success Program Closed Loop Distribution: Benefits

- All data in one location
- "Real time" data allows for verification prior to filling Rx
- Single location of data allows for rapid identification and prosecution
- Product ownership by Nova Factor allows for patient level data based on RPh/MD/Patient relationship

18

Xyrem Patient Success Program
Closed Loop Distribution: Benefits

- Data regarding educational materials gives law enforcement strong support in prosecution

19

Xyrem Physician Success Program
Educational Materials

- Video
- Success Program contact information
- Patient Education presentation
- Template medical record
- Template patient contract
- Patient reimbursement information

20

Xyrem Patient Success Program
Educational Materials

- Video
- Xyrem overview
- Patient Success Program contact information
- Tips for safe in-home storage & disposal
- Traveling tips
- Reimbursement information

21

Xyrem: Patient Success Program

- A comprehensive program which ensures the responsible distribution of Xyrem resulting in
  - Appropriate physician and patient education
  - Diversion minimization/prevention
  - Prosecution assistance

22

NADDI Regional Training
May 2001

Diversion Prevention Through Responsible Distribution

Orphan Medical, Inc.

Dedicated to patients with uncommon diseases

Who is Orphan Medical?

- Pharmaceutical company that specializes in development,marketing and distribution of medications to patients with rare diseases
  - Sucraid; congenital sucrase-isomaltase deficiency (n=1000 patients)
  - Cystadane; homocystinuria (n=100 patients)
  - Antizol; ethylene glycol poisoning (n<1000 patients)
- www.orphan.com

2

Xyrem®
(sodium oxybate) oral solution
Developmental History

- 1994: Orphan Medical begins development of "medical GHB" at request of NORD and FDA's Office of Orphan Product Development
- 1995-1996: Program design with FDA; formulation and toxicology
- 1997: Controlled trials begin
- 1998: Blind broken, efficacy and safety data confirm Xyrem's use in narcolepsy
- Oct. 2000: New drug application filed, FDA commits to "priority review"
- Mid 2001: Expect commercialization of Xyrem!

3

GHB "Illicit Use" History

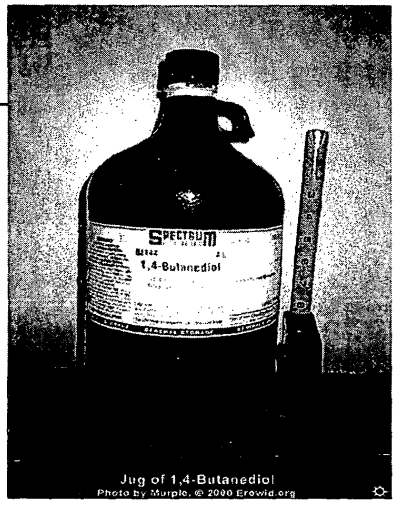
- 1990: FDA initiates voluntary removal of GHB from health food stores due to abuse by body builders/weight lifters
- 1996: reports of street use utilizing GHB-making kits obtained via Internet (home-made GHB)
- 1998: reports of GBL being utilized for "similar physical effect" ("chemical cousins")
- 1999: reports of 1,4-BD being utilized for "similar physical effect"
- No "medical GHB" ever been diverted from clinical trials for illicit use

4

The GHB Substitutes

- Convert to GHB in the body
- Identified as GHB by drug screens
- 725 million pounds of 1,4 BD produced
- 150 million pounds of GBL produced
  - Approx. $3,000 for 55 gallon drum ($250,000 profit?)
  - Easily obtainable with mailing address and credit card
- Few states have legislation which allows prosecution

5



Jug of 1,4-Butanediol
Photo by Murple, © 2000 Erowid.org

6

Orphan Medical's Position

- Xyrem should be available for patients who could benefit from its medical properties
- Distribution and registries should be utilized to minimize/prevent/identify diversion
- Illicit use of GHB and its "chemical cousins" should be harshly penalized

7

Legislative Success

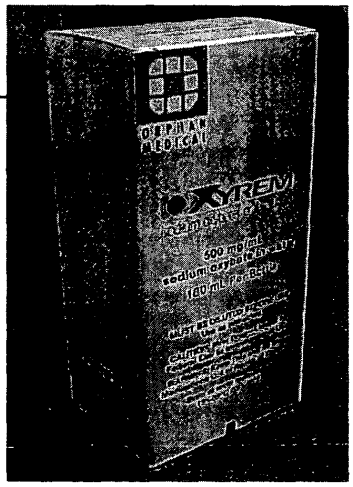
- February, 2000: PL 106-172 enacted
  - *CI for GHB*
  - *CIII for FDA approved GHB (Xyrem); CI penalties for illicit use*
  - *List I chemical status for GBL*
  - *Arcos-like reporting for Xyrem*
  - *Criminalize use of analogues in violent crime*
  - *Create model protocols for drug rape investigations*
  - *Create DEA unit to study drug rape*
  - *Underwrite development of GHB field test kit*
  - *Underwrite public education campaign*

8

Narcolepsy

- A chronic neurological disorder
- Affects approximately 135,000 Americans, only 75,000 who are identified/treated
- Symptoms
  - Excessive daytime sleepiness
  - Cataplexy attacks (loss of muscle control)
  - Hallucinations
  - Sleep paralysis
  - Fragmented nighttime sleep
- No viable alternatives which control cataplexy well
- Cost to society and to the patient
- Extreme day-to-day performance impairment
- Difficult to impossible to remain employed
- Substantially reduced quality of life

9



10

Xyrem: Patient Success Program

- A comprehensive program designed to ensure the responsible distribution of Xyrem to patients who need it
- Provides
  - Appropriate physician and patient education
  - Minimization/prevention of diversion
  - Prosecution assistance

11

Xyrem: Patient Success Program

- Developed after extensive consultation with
  - law enforcement
  - prosecutors
  - field law enforcement personnel
  - forensics experts
  - Ex-DEA officials
  - drug diversion investigators
  - pharmaceutical distribution experts
- Draft program has been circulated and reviewed by key regulatory and enforcement officials for feedback
- Copies will be available once finalized; call 1-888-8ORPHAN to obtain materials!

12

Xyrem Patient Success Program
Closed Loop Distribution

Bulk drug manufactured in PA (CI)

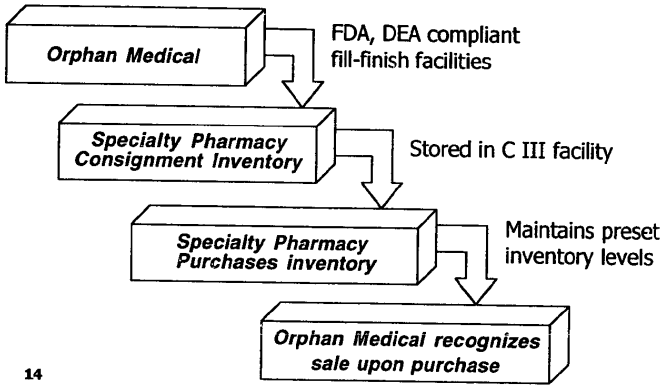
Drug product produced in NC (CIII)

Single pharmacy in TN

- Central location: all records and controls in one place
- Despite financial implications, Orphan Medical will not place Xyrem in all retail pharmacy outlets nationally

13

Xyrem Patient Success Program
Inventory Management



14

Xyrem Patient Success Program Prescription Process

- Potential physician prescribers identified and sent physician education materials
- Sales representatives call on physicians to educate regarding the benefits of Xyrem for narcolepsy patients
- If appropriate, physician prescribes Xyrem for patient, faxing prescription to Specialty Pharmacy

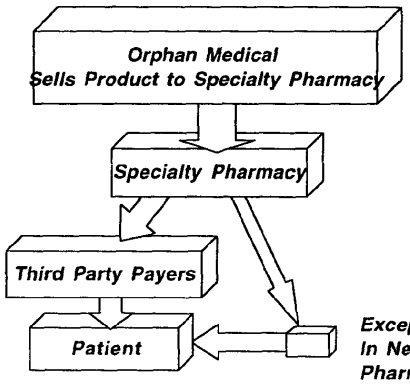
15

Xyrem Patient Success Program Prescription Process, Cont.

- Pharmacist verifies physician is "eligible"
  - Active licensed physician
  - Authorized to prescribe controlled substances
- Specialty Pharmacy calls physician, verifying Rx for given patient and obtains insurance information
- Specialty Pharmacy contacts third party payor (insurance company) to obtain coverage

16

Xyrem Patient Success Program
Distribution Process



17

Xyrem Patient Success Program
Distribution Process

- Pharmacist contacts patient to inform them of insurance coverage and to determine patient availability for shipping
  - Xyrem shipped by overnight courier with real-time tracking
  - First-time prescription for each patient is accompanied by the Xyrem Patient Success Program
  - Xyrem delivered ONLY by authorized signature
  - If patient unavailable, Xyrem returned to Specialty Pharmacy
  - If product is lost, investigation begins regarding shipment's whereabouts

18

Xyrem Patient Success Program
Distribution Process

- If on-line tracking system shows Xyrem received, Pharmacist contacts patient within 24 hours to:
  - Confirm receipt of prescription
  - Confirm receipt of Xyrem Patient Success Program
  - Offer counsel regarding Xyrem dosing and compliance
  - Confirm patient's understanding of contents of Xyrem Patient Success Program

19

Data Collection

- Physician/Patient Information which will be collected:
  - Prescriptions by physician specialty
  - Prescriptions by patient name
  - Prescriptions by volume (frequency)
  - Prescriptions by dose

20

Data Collection

- As a registered pharmacy and wholesaler, Specialty Pharmacy *can and will* share this information with appropriate state and federal authorities for investigation and prosecution
- Orphan Medical is working with NADDI to develop a central reporting mechanism for diversion investigators across the country to obtain the collected data

21

Xyrem Patient Success Program
Closed Loop Distribution: Benefits

- All data in one location, possibility of centralization of reporting to diversion investigators through NADDI
- "Real time" data allows for verification prior to filling Rx
- Single location of data allows for rapid identification and prosecution
- Product ownership by Specialty Pharmacy allows for patient level data based on RPh/MD/Patient relationship

22

Xyrem Patient Success Program

- A comprehensive program which ensures the responsible distribution of Xyrem resulting in
  - Appropriate physician and patient education
  - Diversion minimization/prevention
  - Prosecution assistance

23

NADDI Regional Training
June 2001 Tennessee

Diversion Prevention Through Responsible Distribution

Orphan Medical, Inc.

Dedicated to patients with uncommon diseases

Who is Orphan Medical?

- Pharmaceutical company who specializes in development,marketing and distribution of medications to patients with rare diseases
  - Sucraid; congenital sucrase-isomaltase deficiency (n=1000 patients)
  - Cystadane; homocystinuria (n=100 patients)
  - Antizol; ethylene glycol poisoning (n<1000 patients)
- www.orphan.com

2

Narcolepsy

- A chronic neurological disorder
  - Affects approximately 135,000 Americans, only 85,000 who are identified/treated
  - Symptoms
    - Excessive daytime sleepiness
    - Cataplexy attacks (loss of muscle control)
    - Hallucinations
    - Sleep paralysis
    - Fragmented nighttime sleep
  - No viable alternatives which control cataplexy well
  - Cost to society and to the patient
  - Extreme day-to-day performance impairment
  - Difficult to impossible to remain employed
  - Substantially reduced quality of life

3

Xyrem®
(sodium oxybate) oral solution
Developmental History

- 1994: Orphan Medical begins development of "medical GHB" at request of NORD and FDA's Office of Orphan Product Development
- 1995-1996: Program design with FDA; formulation and toxicology
- 1997: Controlled trials begin
- 1998: Blind broken, efficacy and safety data confirm Xyrem's use in narcolepsy
- Oct. 2000: New drug application filed, FDA commits to "priority review"
- Mid 2001: Expect commercialization of Xyrem!

4

GHB "Illicit Use" History

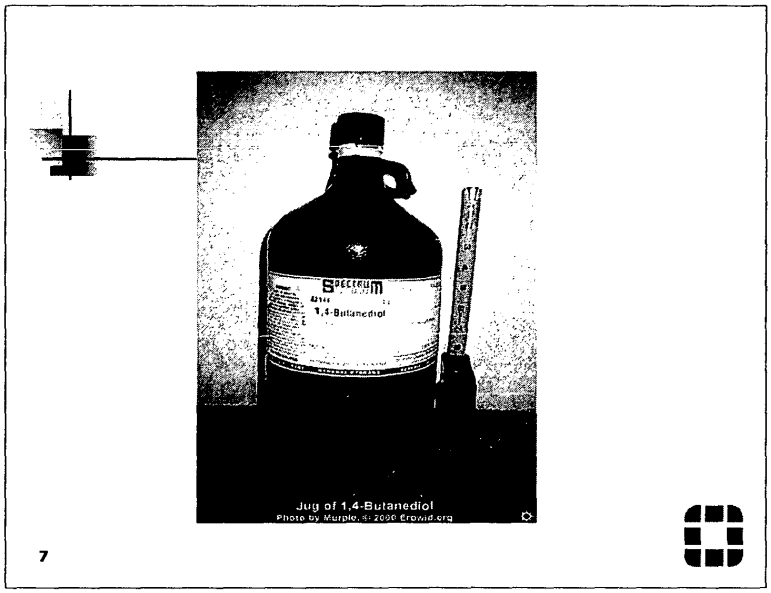
- 1990: FDA initiates voluntary removal of GHB from health food stores due to abuse by body builders/weight lifters
- 1996: reports of street use utilizing GHB-making kits obtained via Internet (home-made GHB)
- 1998: reports of GBL being utilized for "similar physical effect" ("chemical cousins")
- 1999: reports of 1,4 BD being utilized for "similar physical effect"
- No "medical GHB" ever been diverted from clinical trials for illicit use

5

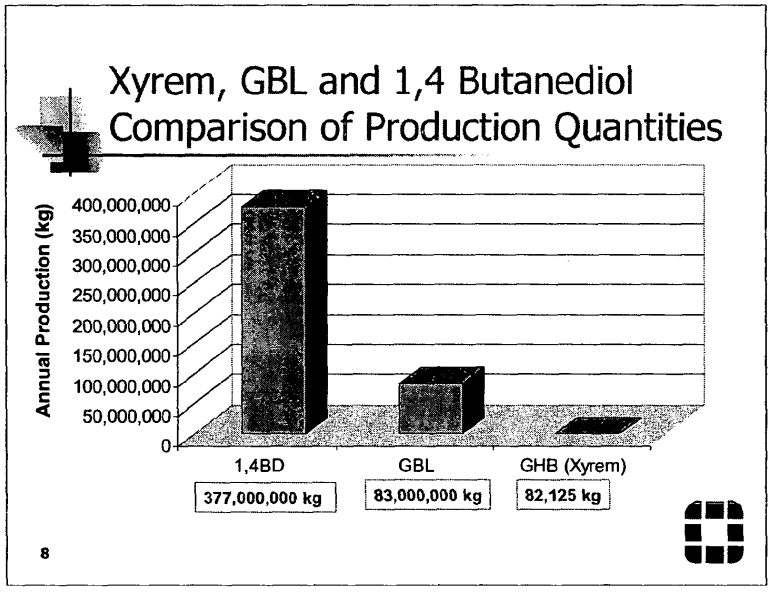
The GHB Substitutes

- Convert to GHB in the body
- Identified as GHB by drug screens
- 700 million pounds of 1,4 BD produced
  - Approx. $700 for 55 gallon drum ($250,000 profit?)
- 150 million pounds of GBL produced
  - Approx. $3,000 for 55 gallon drum
  - Easily obtainable with mailing address and credit card
- Few states have legislation which allows prosecution

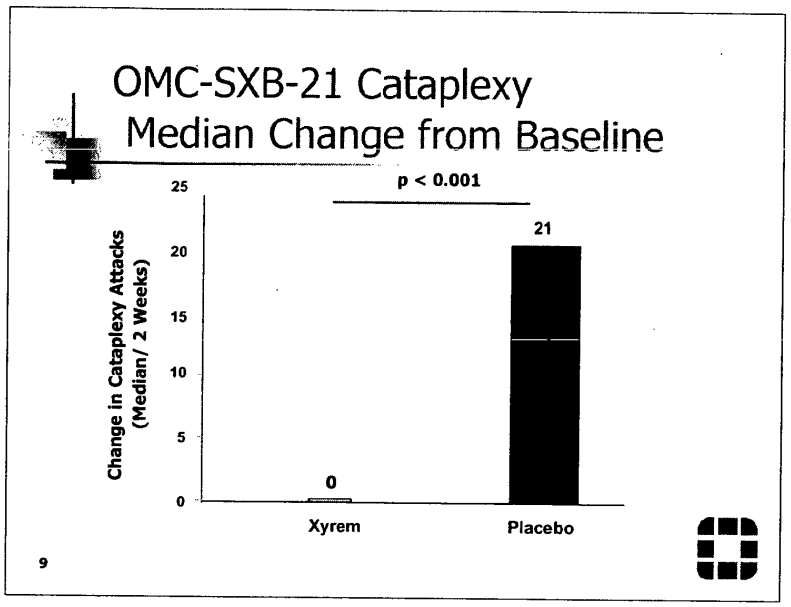
6

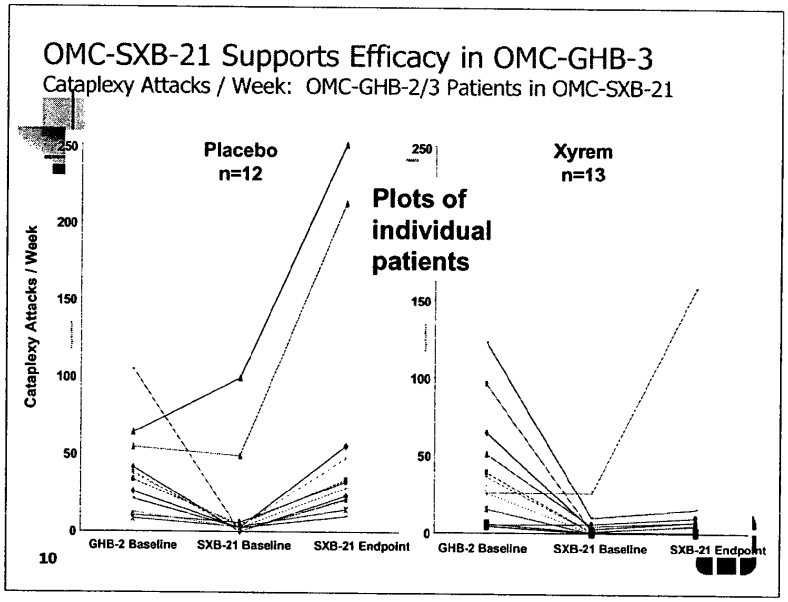

Spectrum
1,4-Butanediol
Jug of 1,4-Butanediol

7


Xyrem, GBL and 1,4 Butanediol
Comparison of Production Quantities
Annual Production (kg)
400,000,000
350,000,000
300,000,000
250,000,000
200,000,000
150,000,000
100,000,000
50,000,000
0
1,4BD
377,000,000 kg
GBL
83,000,000 kg
GHB (Xyrem)
82,125 kg

8


OMC-SXB-21 Cataplexy
Median Change from Baseline
p < 0.001
Change in Cataplexy Attacks (Median/ 2 Weeks)
25
20
15
10
5
0
21
0
Xyrem
Placebo
9


OMC-SXB-21 Supports Efficacy in OMC-GHB-3
Cataplexy Attacks / Week: OMC-GHB-2/3 Patients in OMC-SXB-21
Placebo
n=12
Xyrem
n=13
Plots of
individual
patients
Cataplexy Attacks / Week
250
200
150
100
50
0
GHB-2 Baseline
SXB-21 Baseline
SXB-21 Endpoint
10

OMC-SXB-21
Possible Withdrawal Associated AEs

COSTART Term	Placebo (n=29)	Xyrem (n=26)
Anxiety	2 (7%)	0
Dizziness	1 (3%)	0
Insomnia	1 (3%)	0
Sleep	1 (3%)	0
Somnolence*	1 (3%)	0

* Verbatim Term: Increased awakenings

11

Orphan Medical's Position

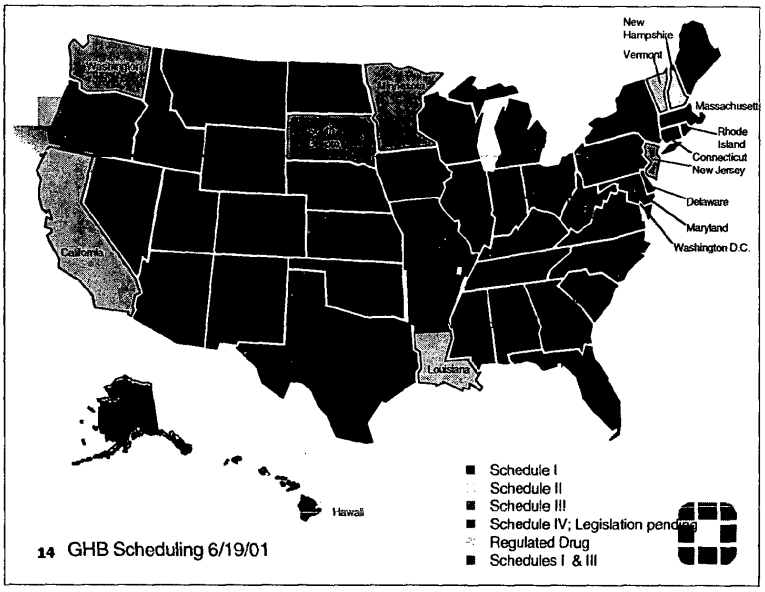
- Xyrem should be available for patients who could benefit from its medical properties
- Distribution and registries should be utilized to minimize/prevent/identify diversion
- Illicit use of GHB and its "chemical cousins" should be harshly penalized

12

Legislative Success

- February, 2000: PL 106-172 enacted
  - *CI for GHB*
  - *CIII for FDA approved GHB (Xyrem); CI penalties for illicit use*
  - *List I chemical status for GBL*
  - *Arcos-like reporting for Xyrem*
  - *Criminalize use of analogues in violent crime*
  - *Create model protocols for drug rape investigations*
  - *Create DEA unit to study drug rape*
  - *Underwrite development of GHB field test kit*
  - *Underwrite public education campaign*

13



14 GHB Scheduling 6/19/01

15

Xyrem: Patient Success Program

- A comprehensive program designed to ensure the responsible distribution of Xyrem to patients who need it
- Provides
  - Appropriate physician and patient education
  - Minimization/prevention of diversion
  - Prosecution assistance

16

Xyrem: Patient Success Program

- Developed after extensive consultation with
  - law enforcement
  - prosecutors
  - field law enforcement
  - pharmaceutical distribution experts
  - forensics experts
  - former DEA officials
  - drug diversion investigators
- Draft program has been circulated and reviewed by key regulatory and enforcement officials for feedback
- Copies will be available once finalized; call 1-888-8ORPHAN to obtain materials!

17

Xyrem Patient Success Program Closed Loop Distribution

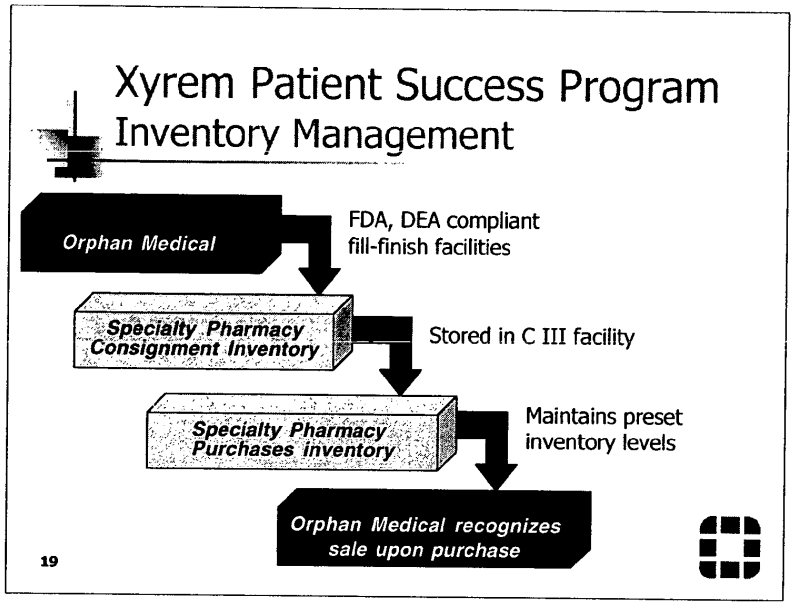
Bulk drug manufactured in PA (CI)

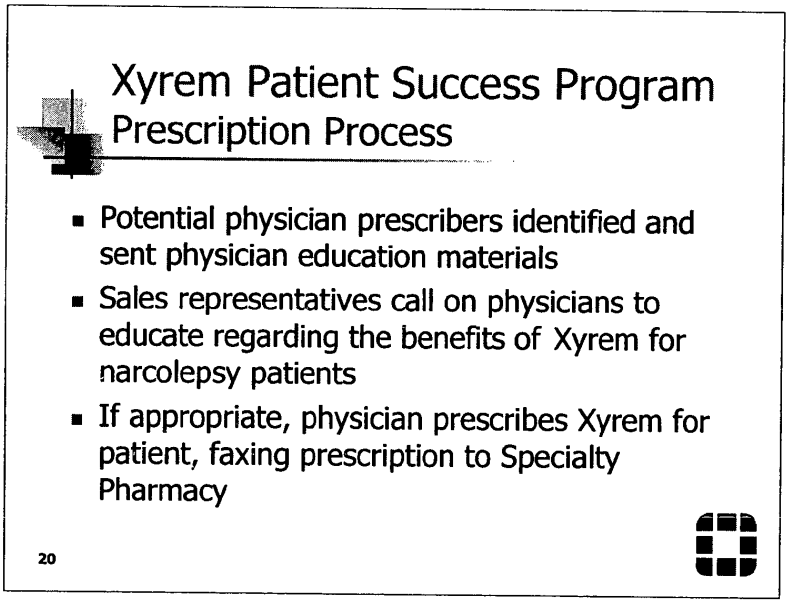
Drug product produced in NC (CIII)

Single pharmacy in TN

- Central location: all records and controls in one place
- Despite financial implications, Orphan Medical will not place Xyrem in all retail pharmacy outlets nationally

18


Xyrem Patient Success Program
Inventory Management
Orphan Medical
FDA, DEA compliant
fill-finish facilities
Specialty Pharmacy
Consignment Inventory
Stored in C III facility
Specialty Pharmacy
Purchases inventory
Maintains preset
inventory levels
Orphan Medical recognizes
sale upon purchase
19

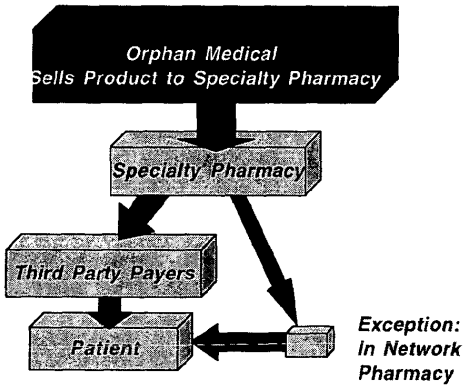

Xyrem Patient Success Program
Prescription Process
Potential physician prescribers identified and sent physician education materials
Sales representatives call on physicians to educate regarding the benefits of Xyrem for narcolepsy patients
If appropriate, physician prescribes Xyrem for patient, faxing prescription to Specialty Pharmacy
20

Xyrem Patient Success Program Prescription Process, Cont.

- Pharmacist verifies physician is "eligible"
  - Active licensed physician
  - Authorized to prescribe controlled substances
- Specialty Pharmacy calls physician, verifying Rx for given patient and obtains insurance information
- Specialty Pharmacy contacts third party payor (insurance company) to obtain coverage

21

Xyrem Patient Success Program Distribution Process



22

Xyrem Patient Success Program Distribution Process

- Pharmacist contacts patient to inform them of insurance coverage and to determine patient availability for shipping
  - Xyrem shipped by overnight courier with real-time tracking
  - First-time prescription for each patient is accompanied by the Xyrem Patient Success Program
  - Xyrem delivered ONLY by authorized signature
  - If patient unavailable, Xyrem returned to Specialty Pharmacy
  - If product is lost, investigation begins regarding shipment's whereabouts

23

Xyrem Patient Success Program Distribution Process

- If on-line tracking system shows Xyrem received, Pharmacist contacts patient within 24 hours to:
  - Confirm receipt of prescription
  - Confirm receipt of Xyrem Patient Success Program
  - Offer counsel regarding Xyrem dosing and compliance
  - Confirm patient's understanding of contents of Xyrem Patient Success Program

24

Data Collection

- Physician/Patient Information which will be collected:
  - Prescriptions by physician specialty
  - Prescriptions by patient name
  - Prescriptions by volume (frequency)
  - Prescriptions by dose
- As a registered pharmacy and wholesaler, Specialty Pharmacy *can and will* share this information with appropriate state and federal authorities for investigation and prosecution

25

Data Collection

- Orphan Medical is working with NADDI to develop a central reporting mechanism for diversion investigators across the country to obtain the collected data

26

Xyrem Patient Success Program Closed Loop Distribution: Benefits

- All data in one location, possibility of centralization of reporting to diversion investigators through NADDI
- "Real time" data allows for verification prior to filling Rx
- Single location of data allows for rapid identification and prosecution
- Product ownership by Specialty Pharmacy allows for patient level data based on RPh/MD/Patient relationship

27

Xyrem: Patient Success Program

- A comprehensive program which ensures the responsible distribution of Xyrem resulting in
  - Appropriate physician and patient education
  - Diversion minimization/prevention
  - Prosecution assistance

28

NADDI Nat'l Conference
November 20 1

Diversion Prevention Through Responsible Distribution

Pam Stahl
Vice President of Commercial Operations
Orphan Medical, Inc.

Company Profile

- Established as a public company in 1994
- Based in Minnetonka, MN
- 60 employees
- Pharmaceutical company that specializes in development, marketing and distribution of medications to patients with rare diseases

2

Strategy

- Strategic Therapeutic Market Segments
  - Congenital Diseases
  - Antidotes
  - Oncology Support
  - Sleep Disorders

3

Xyrem®

- A new treatment for narcolepsy
- Endogenous substance
  - Sodium oxybate or gamma hydroxybutyrate
- Developed at suggestion of FDA's Office of Orphan Products and National Organization for Rare Diseases (NORD) in 1994

4

Xyrem® Developmental History

- 1995-1996: Program design with FDA; formulation and toxicology
- 1997: Controlled trials begin
- 1998: Efficacy and safety data confirm Xyrem's use in narcolepsy
- Oct 2000: New drug application filed, FDA commits to "priority review"
- July 2001: Received Approvable letter
- Oct 9,2001: Submitted Response

5

Narcolepsy

- A chronic neurological disorder
- Affects approximately 180,000 Americans, only 75,000 who are identified/treated
- Symptoms
  - Excessive daytime sleepiness
  - Cataplexy attacks (loss of muscle control)
  - Hallucinations
  - Sleep paralysis
  - Fragmented nighttime sleep
- No viable alternatives which control cataplexy well
- Cost to society and to the patient
- Extreme day-to-day performance impairment
- Difficult to impossible to remain employed
- Substantially reduced quality of life

6

Orphan Medical's Commitments

- Patients with unmet medical needs
- Responsible distribution

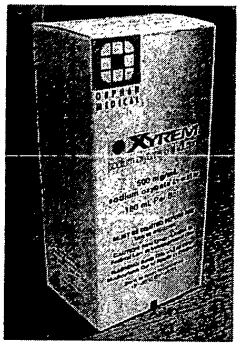
7

Xyrem®
Restricted Distribution Program

Judy S. Kelloway, Pharm.D.
Director of Patient and Professional Affairs

4

Xyrem: Medical Form of GHB



- For treatment of cataplexy
- About 90,000 potential patients
- Nightly 6 to 9 gm liquid dose
- Expect decision no later than April 9, 2002

9

Xyrem Restricted Distribution Program

- A comprehensive program designed to ensure the responsible distribution and safe use of Xyrem to patients who need it
- Developed after extensive consultation with
  - √ law enforcement
  - √ prosecutors
  - √ field law enforcement personnel
  - √ pharmaceutical distribution experts
  - √ forensics experts
  - √ ex-DEA officials
  - √ drug diversion investigators

10

Xyrem Restricted Distribution Program

- Provides
  - Central pharmacy for dispensing Xyrem via overnight delivery
  - System to proactively prevent diversion and to facilitate law enforcement investigations
  - Physician and patient education and monitoring
- Draft education materials are awaiting FDA review
- Final education materials will be accessible to NADDI members

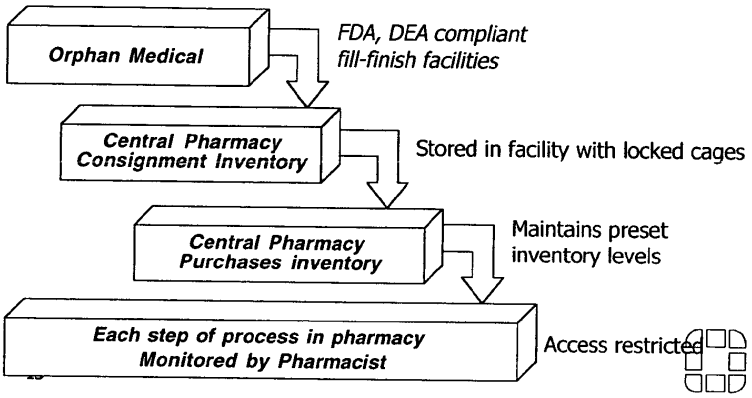
11

Closed Loop Distribution

- Xyrem dispensed from single-dedicated pharmacy in North Carolina
- Central pharmacy:
  - Is a secure, customized facility — security exceeds C-II requirements
  - Collects and maintains MD and patient registry
  - Reports prescription information to state authorities
- Xyrem will not be stocked in retail pharmacies

12

Xyrem Inventory Management Receipt/Storage and Shipping



Facility Security Measures

- There will be no signs on the building related to Xyrem
- Closed circuit TV monitoring maintained 24/7 for all areas
- Entire facility will be secured with motion detectors
- Consignment area inventory cage has unique construction (4" thick walls, internal wire cage on walls and ceilings all with 10 gauge steel)
- Consignment inventory area is padlocked
- Inventory checked daily

14

Pharmacy Personnel

- Selected, screened and trained according to set regulatory criteria.
- Access of Xyrem® holding, dispensing and shipping areas is secured by restricted access and is monitored.
- Use team concept with pharmacists trained in the disease and therapeutic aspects of Xyrem.

15

Xyrem Prescription Process

- Physician decides to prescribe Xyrem
- Physician receives Physician Success Program materials and verifies receipt
- Physician faxes a unique Rx form to central pharmacy
- Central pharmacy verifies physician is "eligible"

16

Physician Success Program

- Description of the prescription distribution process/video
- Special prescription requirements and unique Rx form
- Success Program contact information
- Patient reimbursement information
- Responsibilities of distribution

17

Physician Education and Verification

- Central pharmacy
  - At first Rx, verifies physician has read educational materials
  - With each new prescription (q 3 mo), verifies
    - Active DEA license
    - Active AMA number
    - No disciplinary actions via state medical board web site checked every six months

18

Patient Education and Verification at Central Pharmacy

- Sends educational materials to patient before dispensing Xyrem
- Verifies patient has read educational materials and provides additional information about
  - Xyrem therapy (dose preparation)
  - Safe storage and use
- Sets up time for Xyrem to be shipped via FedEx
- Rapid Trac® system will be used to track each shipment

19

Rapid Trac® System

- Detailed, real-time tracking
- Delivered ONLY by authorized signature
- If patient/designee unavailable, package returned to Specialty Pharmacy
- If not accounted, investigation begins regarding shipment's whereabouts
- If lost, law enforcement notified

20

Patient Success Program

- Video/Xyrem overview
- Patient Success Program contact information
- Medication guide
- Reimbursement information
- Tips for safe in-home storage and disposal
- Traveling tips
- Responsible use and consequences

21

Excerpt from Patient Success Program....

"Xyrem is classified as a schedule III medication which means that it is legal for you to use as prescribed. It is illegal for you to sell, distribute or give your Xyrem to anyone else, or to use your Xyrem for purposes other than it was prescribed. Failure to adhere to these rules may result in prosecution and fines as defined in Schedule I of the Controlled Substances Act.

Xyrem Patient Contacts

- Central pharmacy
  - Contacts patient within 24 hours of Xyrem delivery and confirms receipt
  - Provides additional patient counseling, if needed
  - Calls patient prior to each Xyrem shipment, tracks receipt, makes random calls to
    - Monitor use
    - Provide additional information
    - Assess patient compliance

23

Physician and Patient Registry

- Patient Information
  - Rx by name
  - Rx by social security number
  - Rx by date of birth
  - Rx by address
- Physician information
  - Rx by name, address and specialty
  - Prescriptions by volume
  - Prescriptions by dose

24

Data Availability

- As a registered pharmacy and wholesaler, central pharmacy will
  - Provide required reports to state and federal authorities
  - Provide information to law enforcement authorities upon request per applicable state/federal laws
  - Notify law enforcement of any lost prescriptions
  - Alert state medical board of any troubling physician activities

25

Benefits of Xyrem Restricted Distribution System

- Makes Xyrem available
  - To patients who need it
  - From one central pharmacy, not 37,000 retail pharmacies
- Education materials underscore responsible use of controlled substance
- Physician and patient verification conducted prior to filling Rx helps prevent diversion and illicit use
- Disciplined physicians identified and prescriptions stopped

26

Benefits of Xyrem Restricted Distribution System

- Doctor shopping identified, preventing multiple scrips for same person/address
- Patient "pharmacy-shopping" eliminated
- On-going monitoring and calls identify potential overuse of Xyrem
- All physician and patient data in one location and provided to authorities as required and upon request
- Fulfills commitment to support responsible distribution of Xyrem

27

Questions?

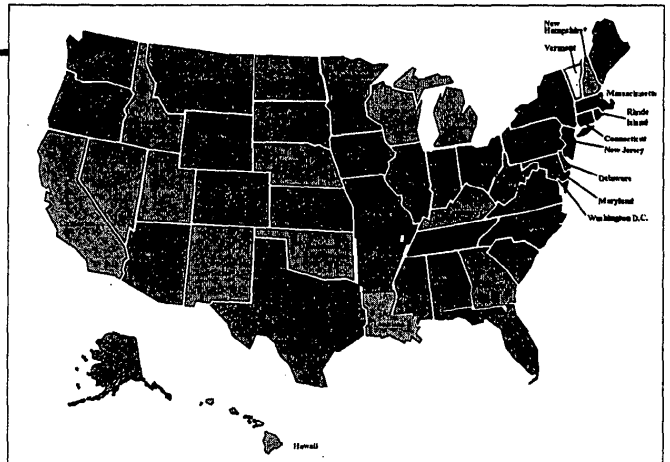
GAMMA-HYDROXYBUTYRATE (GHB) AND ITS ANALOGS: CURRENT LEGISLATIVE STATUS

NASCSA Nat'l Conference Nov. 2001

Engel PA, Hornfeldt CS. Orphan Medical, Inc., Minnetonka, MN

MAP LEGEND	
SCHEDULE I/III	**SCHEDULE I**
Alabama Alaska Arizona Arkansas Colorado Connecticut Florida Illinois Indiana Iowa Kansas Maine Maryland Massachusetts Mississippi Missouri Montana New York North Carolina North Dakota Ohio Oregon Pennsylvania Rhode Island South Carolina Texas Virginia West Virginia Wyoming	Delaware Georgia Hawaii Idaho* Kentucky* Michigan* Nebraska Nevada* New Hampshire* New Mexico* Oklahoma Utah Wisconsin
	SCHEDULE III
	Minnesota* New Jersey South Dakota Washington
	SCHEDULE IV
	Tennessee*
SCHEDULE II	**LEGEND DRUG**
California Louisiana	Vermont

*Will propose I/III schedule upon approval of Xyrem.
*The I/III Bill carried over to 2002 legislative session.



The current legislative status of GHB

Controlled Substance Analogues

"A new class of substances was created by the Anti-Drug Abuse Act of 1986. Controlled substance analogues are substances which are not controlled substances, but may be found in the illicit traffic. They are structurally or pharmacologically similar to Schedule I or II controlled substances and have no legitimate medical use. A substance which meets the definition of a controlled substance analogue and is intended for human consumption is treated under the CSA as if it were a controlled substance in Schedule I".

U.S. Department of Justice
Drug Enforcement Administration

Current Legislative Status of GHB Analogs

Arizona, California, Hawaii and Missouri have identified 1,4-BD and GBL as having similar structure OR similar effect as GHB and are regulating these as "listed chemicals", requiring special record keeping by manufacturers and industrial users.

Arkansas, Colorado and Kansas have adopted analog language as above adding GVL and including a "...and intended for human consumption" provision, making these Schedule I Controlled Substances.

Florida has classified GBL and 1,4-BD as Schedule I but not GVL; no general analog language. Similarly, New York has made all recognized analogs Schedule I but has not included any language defining what an analog is.

North Carolina has established a commission to study analogs and North Dakota has implemented penalties for analog trafficking. The remaining 39 states currently have no current laws recognizing or regulating GHB analogs.

Without such legislation illicit sales of analogs continue, putting consumers at risk. An example of an internet-marketed analog is found here, marketed as "Tranquili-G". While many states have addressed the issue of GHB abuse, abuse of GHB-like analogs will continue until rigorous and consistent legislative address of analogs exist nationwide. The bill passed by the Pennsylvania State Legislature, shown, demonstrates such a well written statute.

THE GENERAL ASSEMBLY OF PENNSYLVANIA
HOUSE BILL No. 1971 Session of 1999

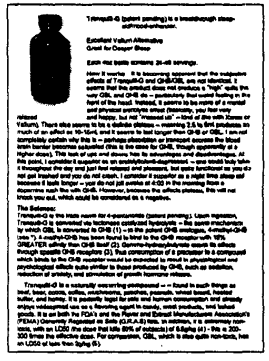
OCTOBER 18, 1999, AN ACT

Amending the act of April 14, 1972 (P.L.233, No.64), entitled "An act relating to the manufacture, sale and possession of controlled substances, other drugs, devices and cosmetics; conferring powers on the courts and the secretary and Department of Health, and a newly created Pennsylvania Drug, Device and Cosmetic Board; establishing schedules of controlled substances; providing penalties; requiring registration of persons engaged in the drug trade and for the revocation or suspension of certain licenses and registrations; and repealing an act," further defining "designer drug". The General Assembly of the Commonwealth of Pennsylvania hereby enacts as follows:

Section 1. The definition of "designer drug" in section 2(b) of the act of April 14, 1972 (P.L.233, No.64), known as The Controlled Substance, Drug, Device and Cosmetic Act, added December 22, 1989 (P.L.769, No.107), is amended to read:

Section 2. Definitions. As used in this act:

"Designer drug" means a substance other than a controlled substance that is intended for human consumption and that either has a chemical structure substantially similar to that of a controlled substance in Schedules I, II or III of this act or that produces an effect substantially similar to that of a controlled substance in Schedules I, II or III. Examples of chemical classes in which designer drugs are found include, but are not limited to, the following: Phenethylamines,N-substituted piperidines, morphinans, ecgonines, quinazolinones, substituted indoles and arylcycloalkylamines.



DEPARTMENT OF HEALTH AND HUMAN SERVICES

FOOD AND DRUG ADMINISTRATION

CENTER FOR DRUG EVALUATION AND RESEARCH

PERIPHERAL AND CENTRAL NERVOUS SYSTEM DRUGS

ADVISORY COMMITTEE

Wednesday, June 6, 2001

8:15 a.m.

Holiday Inn
Bethesda, Maryland

6/2001

As we contemplated the distribution of Xyrem and how to do this responsibly to meet the

178

prior stated goals, we determined that a closed distribution system would best fit everyone's needs for this product. The product is manufactured at one single manufacturing facility. It is sent to one single national specialty pharmacy. Eventually it goes by courier to patients with narcolepsy.

[Slide]

The benefits of this program are that not only is the product distributed from a central location, but all the controls and all the records are in one place.

[Slide]

So, how will this work? Because a number of doctors prescribe medicines for narcolepsy, we will focus our promotional effects on those physicians. They include such specialists as neurologists, pulmonologists, psychiatrists, internal medicine physicians and several primary specialties who practice sleep medicine.

[Slide]

Our small sales force will call on these physicians, communicating the clinical benefits of Xyrem in narcolepsy. At those calls, the sales representatives will also review with each physician something that we call the physician

179

Success Program. I will go into the details of this program in a more in depth fashion in just a moment. But it is important to know that each physician will sign that they have reviewed this program with the sales representative and understand the program. I should also note that at no time will we embark upon physician sampling.

[Slide]

I promised to come back to the components of the physician Success Program. I know that many of you received copies of this but I would like to highlight some of the main points. First, because we know individuals all learn differently -- some by hearing, some by reading, other methods -- we have made this a multi-faceted program which includes videos, brochures, pamphlets that describe four main areas.

The first is to highlight to physicians that the distribution process for Xyrem is different, that their patients won't be able to get this at the corner drugstore. The second important issue that this binder points out to physicians is the dosing and administration of Xyrem. The next important issue is that of home storage and secure handling. The fourth is an important module that

we call "doctor be wary" which is an educational module that educates doctors about the ways that drugs are commonly diverted in this country so they can be aware of patients who are attempting to illegitimately get a prescription from them for this product. Each of the kits will also contain a number of unique prescribing forms for Xyrem which will be necessary in order for the prescription to be filled. This is, in essence, a special prescription form. As well, contact information will be provided should the doctor have any questions at all about the program.

[Slide]

Once the physician decides to prescribe Xyrem the physician faxes this special prescription to the specialty pharmacy. Now, I am going to come back to how this prescription is verified. So, I will ask you to hold on that point for just one

moment. But, based on that prescription and based on the patient's geographic location, the pharmacy assigns that patient to a dedicated pharmacy team. So, each time that the patient deals with the system they are talking with the same pharmacist and the same reimbursement specialist.

[Slide] \

181

I mentioned that as the prescription comes to the specialty pharmacy there will be a number of checks to determine if the physician is, in fact, eligible to prescribe Xyrem. We will be utilizing DEA's NTIS or National Technical Information Services database to ensure that each physician has an active valid medical license, and also to ensure that that physician has current prescribing privileges which allow him or her to prescribe Schedule III medications in this country. As a backup check, the specialty pharmacy will also be checking with the appropriate state medical board to determine that there are no pending actions on the behalf of the state for that given physician.

[Slide]

As a secondary step, the specialty pharmacy will also do a check on the patient in essence. What they will do is when that prescription comes in they will call the prescribing physician's office to determine that, in fact, that patient is real and a prescription has, in fact, been written for that patient.

[Slide]

Once insurance reimbursement is obtained, the specialty pharmacy contacts the patient, first,

182

to determine the patient or the patient designee's location and availability for shipment, and also to describe to them the contents of the shipment. I

will come back to the details of this in just a moment, but it is important that you know that each patient, when they get their first prescription of Xyrem will receive a multi-faceted educational program called the Xyrem patient Success Program, and I will come back to the details of that in just a moment.

In that same shipment they will also receive their Xyrem, and that will look something like this, with child resistant closure not only on the primary container but also on the dosing cups which are provided by the company.

[Slide]

The shipment that goes to the patient is sent by a special system that has a special, unique tracking system called the Rapid Trac System. this system will allow detailed real-time tracking of that package which is delivered only by the authorized signature. If the patient or their designee is not available for receipt of the package at the time agreed upon with the specialty pharmacy, the package will be returned to the

specialty pharmacy after one delivery reattempt. So, a package will not sit on a delivery truck or in a hub for weeks at a time or anything like that. If the package is lost the system will allow an investigation to begin regarding the shipment's whereabouts at that point of loss.

[Slide]

I spoke a moment ago about the patient Success Program. Again, this is a multi-faceted program which includes video, brochures and pamphlets which deal with a number of important issues for patients. First addressed, of course, is the distribution process since it is so important that the patients understand that the

only way they will get Xyrem is through the special pharmacy and not at their corner drugstore.

There is information about Xyrem's dosing and administration because we feel that that is an important message to be delivered in an understandable and a very consistent manner.

There is information on home storage and secure handling, and we also are very clear with patients about the criminal and civil penalties that the public law assigns to any illicit use of Xyrem. So, if I were, as a valid narcolepsy

patient, to take my Xyrem prescription and use it to conduct a rape or in an assault situation, or if I were to sell it to someone for illicit use I would be penalized, I would be subject to C-I penalties. The patient Success Program also includes contact information for the specialty pharmacy should the patient have any questions at all, and also reimbursement information.

[Slide]

After the Rapid Trac System shows that the package has been received by the patient, the specialty pharmacist will call the patient within 24 hours not only to confirm receipt of that package but also to again reiterate certain important points with the patient. Those include the penalties for illicit use of Xyrem; Xyrem's dosing and administration; home storage and secure handling. The pharmacist will also take the opportunity to discuss with the patient the child-resistant features on the primary container as well as the child-resistant features on the dosing cups that are provided.

[Slide]

The central data repository designed for Xyrem really allows for identification of a number

of unusual types of behavior, including any duplicate prescriptions, any attempts of over-prescribing, or any attempts at over-use by patients. The benefit here is that that information is available prior to filling the prescription so appropriate pharmacist intervention can occur.

[Slide]

As you can see, the Xyrem Success Program is a comprehensive program which is designed to responsibly distribute this important medication in order that patients who need it have it available, and it is inaccessible for those who might abuse it. Thank you.

SCHWEGMAN ■ LUNDBERG ■ WOESSNER ■ KLUTH

United States Patent Application

COMBINED DECLARATION AND POWER OF ATTORNEY

As a below named inventor I hereby declare that: my residence, post office address and citizenship are as stated below next to my name; that

I verily believe I am the original, first and joint inventor of the subject matter which is claimed and for which a patent is sought on the invention entitled: **SENSITIVE DRUG DISTRIBUTION SYSTEM AND METHOD**.

The specification of which was filed on December 17, 2002 as application serial no. 10/322,348.

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to the patentability of this application in accordance with 37 C.F.R. § 1.56 (attached hereto). I also acknowledge my duty to disclose all information known to be material to patentability which became available between a filing date of a prior application and the national or PCT international filing date in the event this is a Continuation-In-Part application in accordance with 37 C.F.R. § 1.63(e).

I hereby claim foreign priority benefits under 35 U.S.C. §119(a)-(d) or 365(b) of any foreign application(s) for patent or inventor's certificate, or 365(a) of any PCT international application which designated at least one country other than the United States of America, listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on the basis of which priority is claimed:

No such claim for priority is being made at this time.

I hereby claim the benefit under 35 U.S.C. § 119(e) of any United States provisional application(s) listed below:

No such claim for priority is being made at this time.

I hereby claim the benefit under 35 U.S.C. § 120 or 365(c) of any United States and PCT international application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT international application in the manner provided by the first paragraph of 35 U.S.C. § 112, I acknowledge the duty to disclose material information as defined in 37 C.F.R. § 1.56(a) which became available between the filing date of the prior application and the national or PCT international filing date of this application:

No such claim for priority is being made at this time.

I hereby appoint the following attorney(s) and/or patent agent(s) to prosecute this application and to transact all business in the Patent and Trademark Office connected herewith:

Anglin, J. M	Reg. No. 24,916	Harris, Robert J	Reg. No. 37,346	Nielsen, Walter W	Reg. No. 25,539
Arora, Suneel	Reg. No. 42,267	Jackson Huebsch, Katharine A	Reg. No. 47,670	Padys, Danny J	Reg. No. 35,635
Beekman, Marvin L	Reg. No. 38,377	Jurkovich, Patti J	Reg. No. 44,813	Parker, J. K	Reg. No. 33,024
Bianchi, Timothy E	Reg. No. 39,610	Kalis, Janal M	Reg. No. 37,650	Peacock, Gregg A	Reg. No. 45,001
Billion, Richard E	Reg. No. 32,836	Klima-Silberg, Catherine I	Reg. No. 40,052	Perdok, Monique M	Reg. No. 42,989
Black, David W	Reg. No. 42,331	Kluth, Daniel J	Reg. No. 32,146	Peret, Andrew R	Reg. No. 41,246
Brennan, Thomas F	Reg. No. 35,075	Lacy, Rodney L	Reg. No. 41,136	Peterson, David C	Reg. No. 47,857
Chadwick, Robin A	Reg. No. 36,477	Lemaire, Charles A	Reg. No. 36,198	Prout, William F	Reg. No. 33,995
Clark, Barbara J	Reg. No. 38,107	Lundberg, Steven W	Reg. No. 30,568	Puckett, Ph. D., Craig L	Reg. No. 43,023
Clise, Timothy B	Reg. No. 40,957	Maki, Peter C	Reg. No. 42,832	Schumm, Sherry W	Reg. No. 39,422
Cochran, David R	Reg. No. 46,632	Malen, Peter L	Reg. No. 44,894	Schwegman, Micheal L	Reg. No. 25,816
Dahl, John M	Reg. No. 44,639	Mates, Robert E	Reg. No. 35,271	Speier, Gary J	Reg. No. 45,458
Drake, Eduardo E	Reg. No. 40,594	McCrackin, Ann M	Reg. No. 42,858	Steffey, Charles E	Reg. No. 25,179
Embretson, Janet E	Reg. No. 39,665	McGough, Kevin J	Reg. No. 31,279	Stordal, Leif T	Reg. No. 46,251
Forrest, Bradley A	Reg. No. 30,837	McTavish, Hugh E	Reg. No. 48,341	Terry, Kathleen R	Reg. No. 31,884
Gorrie, Gregory J	Reg. No. 36,530	Mehrle, Joseph P	Reg. No. 45,535	Tong, Viet V	Reg. No. 45,416
Gortych, Joseph E	Reg. No. 41,791	Muller, Mark V	Reg. No. 37,509	Viksnins, Ann S	Reg. No. 37,748
Greaves, John N	Reg. No. 40,362	Nama, Prakash	Reg. No. 44,255	Woessner, Warren D	Reg. No. 30,440
Haack, John L	Reg. No. 36,154	Nelson, A. J	Reg. No. 28,650		

I hereby authorize them to act and rely on instructions from and communicate directly with the person/assignee/attorney/firm/organization/who/which first sends/sent this case to them and by whom/which I hereby declare that I have consented after full disclosure to be represented unless/until I instruct Schwegman, Lundberg, Woessner & Kluth, P.A. to the contrary.

Please direct all correspondence in this case to **Schwegman, Lundberg, Woessner & Kluth, P.A.** at the address indicated below:

P.O. Box 2938, Minneapolis, MN 55402
Telephone No. (612)373-6900

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Full Name of joint inventor number 1 : **Dayton T. Reardan Ph.D.**
Citizenship: **United States of America** Residence: **Excelsior, MN**
Post Office Address: 22345 Bracketts Road
Excelsior, MN 55331

Signature: Dayton T. Reardan Date: April 3, 2003
Dayton T. Reardan Ph.D.

Full Name of joint inventor number 2 : **Patti ~~Engle~~ A. ENGEL**
Citizenship: **United States of America** Residence: **Eagan, MN**
Post Office Address: 852 Basswood Lane
Eagan, MN

Signature: Patti A. Engel Date: May 13, 2003
Patti ~~Engle~~
PATTI A. ENGEL

X Additional inventors are being named on separately numbered sheets, attached hereto.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Full Name of joint inventor number 3 : **Bob Gagne**
Citizenship: **United States of America** Residence: **St. Paul, MN**
Post Office Address: 202 So. Wheeler Street
St. Paul, MN 55015

Signature: Bob Gagne Date: 1 May 2003
Bob Gagne

§ 1.56 Duty to disclose information material to patentability.

(a) A patent by its very nature is affected with a public interest. The public interest is best served, and the most effective patent examination occurs when, at the time an application is being examined, the Office is aware of and evaluates the teachings of all information material to patentability. Each individual associated with the filing and prosecution of a patent application has a duty of candor and good faith in dealing with the Office, which includes a duty to disclose to the Office all information known to that individual to be material to patentability as defined in this section. The duty to disclose information exists with respect to each pending claim until the claim is canceled or withdrawn from consideration, or the application becomes abandoned. Information material to the patentability of a claim that is canceled or withdrawn from consideration need not be submitted if the information is not material to the patentability of any claim remaining under consideration in the application. There is no duty to submit information which is not material to the patentability of any existing claim. The duty to disclose all information known to be material to patentability is deemed to be satisfied if all information known to be material to patentability of any claim issued in a patent was cited by the Office or submitted to the Office in the manner prescribed by §§ 1.97(b)-(d) and 1.98. However, no patent will be granted on an application in connection with which fraud on the Office was practiced or attempted or the duty of disclosure was violated through bad faith or intentional misconduct. The Office encourages applicants to carefully examine:

(1) prior art cited in search reports of a foreign patent office in a counterpart application, and

(2) the closest information over which individuals associated with the filing or prosecution of a patent application believe any pending claim patentably defines, to make sure that any material information contained therein is disclosed to the Office.

(b) Under this section, information is material to patentability when it is not cumulative to information already of record or being made of record in the application, and

(1) It establishes, by itself or in combination with other information, a prima facie case of unpatentability of a claim; or

(2) It refutes, or is inconsistent with, a position the applicant takes in:

(i) Opposing an argument of unpatentability relied on by the Office, or

(ii) Asserting an argument of patentability.

A prima facie case of unpatentability is established when the information compels a conclusion that a claim is unpatentable under the preponderance of evidence, burden-of-proof standard, giving each term in the claim its broadest reasonable construction consistent with the specification, and before any consideration is given to evidence which may be submitted in an attempt to establish a contrary conclusion of patentability.

(c) Individuals associated with the filing or prosecution of a patent application within the meaning of this section are:

(1) Each inventor named in the application:

(2) Each attorney or agent who prepares or prosecutes the application; and

(3) Every other person who is substantively involved in the preparation or prosecution of the application and who is associated with the inventor, with the assignee or with anyone to whom there is an obligation to assign the application.

(d) Individuals other than the attorney, agent or inventor may comply with this section by disclosing information to the attorney, agent, or inventor.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Dayton T. Reardan et al.	Examiner:	Unknown
Serial No.:	10/322,348 ✓	Group Art Unit:	Unknown
Filed:	December 17, 2002	Docket No:	101.031US1
Title:	SENSITIVE DRUG DISTRIBUTION SYSTEM AND METHOD		

PRELIMINARY AMENDMENT

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Prior to taking up this application for examination, please enter the following amendments:

IN THE CLAIMS

1. (Original) A method of distributing a sensitive drug, the method comprising:

receiving prescription requests from a medical doctor containing information identifying the patient, the sensitive drug, and various credentials of the doctor;

entering the information into a central database for analysis of potential abuse situations;

checking the credentials of the doctor;

confirming with the patient that educational material has been read prior to shipping the sensitive drug;

confirming receipt of the sensitive drug; and

generating periodic reports via the central database to evaluate potential abuse patterns.

2. (Original) The method of claim 1 wherein receipt of the sensitive drug is confirmed by telephone call from the central pharmacy to the patient.

3. (Original) The method of claim 1 and further comprising launching an investigation of lost shipments.

4. (Original) The method of claim 1 and further comprising recording the confirmation with the patient that the educational material has been read in the central database.

5. (Original) The method of claim 1 and further comprising verifying the patient's home address.

6. (Original) The method of claim 1 and further comprising recording a designee identified by the patient to receive the sensitive drug.

7. (Original) The method of claim 1 and further comprising establishing a delivery date.

8. (Original) The method of claim 1 wherein prescription refills requested prior to an anticipated date are questioned by the pharmacist.

9. (Original) The method of claim 1 and further comprising shipping comprehensive printed materials to the physician if the physician is a first time prescriber of the sensitive drug.

10. (Original) The method of claim 1 wherein the credentials of the doctor comprise DEA (Drug Enforcement Agency) and state license numbers.

11. (Original) A method of monitoring potential abuse of a sensitive drug by use of an exclusive central database, the method comprising:

generating queries of prescription information from a database containing selected information for all prescriptions of the sensitive drug, wherein the queries comprise prescriptions by physician specialty, prescriptions by patient name, prescriptions by frequency and prescriptions by dose.

12. (Original) The method of claim 11 and further comprising running multiple predetermined reports based on data in the exclusive central database.

13. (Original) The method of claim 12 wherein such reports are selected from groups of reports consisting of sales, regulatory, quality assurance, pharmacy, inventory, reimbursement, patient care, and drug information.

14. (Original) The method of claim 13 wherein sales reports are selected from the group consisting of prescriptions by zip code, prescriptions by physician by zip code and total dollars by zip code.

15. (Original) The method of claim 13 wherein regulatory reports are selected from the group consisting of number of physician registries, number of denied physician registries and

reasons, number of completed patient registries, number of problem identification, number of cycle counts performed.

16. (Original) The method of claim 13 wherein inventory reports are selected from the group consisting of number of returned products and reasons, number of outdated bottles of product, inventory counts of consignment and production inventory, number of units received, and lots received.

17. (Original) The method of claim 13 wherein patient care reports are selected from the group consisting of number of adverse events, number of dosing problems and type, number of noncompliance episodes and reason, number of patients counseled and reason, number of discontinued and reason, number of patients referred to physician and reason, number of active patients, number of new patents, number of restart patients, and number of discontinued patients and reason.

18. (Original) The method of claim 13 wherein selected reports are run weekly, monthly or quarterly.

19. (Original) A method of obtaining FDA (Food and Drug Administration) approval for a sensitive drug, the method comprising:

determining current and anticipated patterns of potential abuse of the sensitive drug;

selecting multiple controls for distribution by an exclusive central pharmacy maintaining a central database, the controls selected from the group consisting of communicating prescriptions from a physician to the central pharmacy, identifying the physicians name, license and DEA (Drug Enforcement Agency) registration information, verifying the prescription; obtaining patient information, verifying the physician is eligible to prescribe the sensitive drug by consulting the National Technical Information Services to determine whether the physician has an active DEA number and check on whether any actions are pending against the physician, provide comprehensive printed materials to the physician, contacting the patient's insurance

company if any, verifying patient registry information, providing comprehensive education information to the patient, verifying the patient has reviewed the educational materials, verifying the home address of the patient, shipping via US postal service or similar shipping service, receiving the name of an at least 18 year old designee to receive the drug, confirming receipt of an initial shipment of the drug to the patient, returning the drug to the pharmacy after two attempts to deliver, launching an investigation when a shipment is lost, shipping to another pharmacy for delivery, requiring manufacture at a single location, releasing inventory in a controlled manner to the central pharmacy, questioning early refills, flagging repeat instances of lost, stolen, destroyed or spilled prescriptions, limiting the prescription to a one month supply, requiring rewriting of the prescription periodically, making the database available to the DEA for checking for abuse patterns in the data, cash payments, inappropriate questions; and

negotiating with the FDA by adding further controls from the group until approval is obtained.

20. (Original) The method of claim 19 wherein initially selected controls comprise communicating prescriptions from a physician to the central pharmacy, identifying the physicians name, license and DEA registration information, verifying the prescription; obtaining patient information, verifying the physician is eligible to prescribe the sensitive drug by consulting the National Technical Information Services to determine whether the physician has an active DEA number and check on whether any actions are pending against the physician, verifying patient registry information, providing comprehensive education information to the patient, verifying the patient has reviewed the educational materials, verifying the home address of the patient, shipping via US postal service, confirming receipt of an initial shipment of the drug to the patient releasing inventory in a controlled manner to the central pharmacy, flagging repeat instances of lost, stolen, destroyed or spilled prescriptions, and making the database available to the DEA for checking for abuse patterns in the data.

21. (Original) The method of claim 19 wherein the sensitive drug is a scheduled drug in Schedule II-V.

22. (Original) A method of distributing a sensitive drug, the method comprising:

determining current and anticipated patterns of potential abuse of the sensitive drug;

selecting multiple controls for distribution of the sensitive drug; and

adding additional controls to provide sufficient reassurance to a governmental regulatory body that the sensitive drug distribution can be adequately controlled in order to obtain marketing approval by the governmental regulatory body.

23. (Original) The method of claim 22 wherein the system allows marketing of a drug product pursuant to FDA subpart 4 regulation embodied in Title 21, CFR Part 314.

24. (Original) The method of claim 22 wherein distribution of the sensitive drug is controlled by a central distribution center sufficient to allow the DEA (Drug Enforcement Agency) to approve the central distribution center.

25. (Original) The method of claim 22 wherein the governmental regulatory body comprises a state regulatory agency that approves distribution of the sensitive drug in a state.

26. (New) A method to control abuse of a sensitive drug by controlling the distribution thereof via an exclusive central pharmacy that maintains a central database that tracks all prescriptions of said sensitive drug and analyzes for potential abuse situations, the method comprising:

determining current and anticipated patterns of potential prescription abuse of said sensitive drug from periodic reports generated by the central database based on prescription request data from a medical doctor, wherein said request data contain information identifying the patient, the drug prescribed, and credentials of the doctor; and

selecting multiple controls for distribution by said exclusive central pharmacy, the controls selected from the group consisting of communicating prescriptions from a physician to the central pharmacy; identifying the physicians name, license, and DEA (Drug Enforcement

Agency) registration information; verifying the prescription; obtaining patient information; verifying the physician is eligible to prescribe the sensitive drug by consulting the National Technical Information Services to determine whether the physician has an active DEA number and to check on whether any actions are pending against the physician; providing comprehensive printed materials to the physician; contacting the patient's insurance company if any; verifying patient registry information; providing comprehensive education information to the patient; verifying the patient has reviewed the educational materials; verifying the home address of the patient; shipping via US postal service or similar shipping service; receiving the name of an at least 18 year old designee to receive the drug; confirming receipt of an initial shipment of the drug to the patient returning the drug to the pharmacy after two attempts to deliver; launching an investigation when a shipment is lost; shipping to another pharmacy for delivery; requiring manufacture at a single location; releasing inventory in a controlled manner to the central pharmacy; questioning early refills; flagging repeat instances of lost, stolen, destroyed, or spilled prescriptions; limiting the prescription to a one month supply; requiring rewriting of the prescription periodically; and making the database available to the DEA for checking for abuse patterns in the data, for cash payments, and for inappropriate questions.

27. (New) The method of claim 26 wherein initially selected controls comprise communicating prescriptions from a physician to the central pharmacy; identifying the physicians name, license, and DEA registration information; verifying the prescription; obtaining patient information; verifying the physician is eligible to prescribe the sensitive drug by consulting the National Technical Information Services to determine whether the physician has an active DEA number and to check on whether any actions are pending against the physician; verifying patient registry information; providing comprehensive education information to the patient; verifying the patient has reviewed the educational materials; verifying the home address of the patient; shipping via US postal service; confirming receipt of an initial shipment of the drug to the patient; releasing inventory in a controlled manner to the central pharmacy; flagging repeat instances of lost, stolen, destroyed, or spilled prescriptions; and making the database available to the DEA for checking for abuse patterns in the data.

28. (New) The method of claim 26 which further comprises consulting a separate database to verify that the medical doctor is eligible to prescribe the drug.

29. (New) A method to control abuse of gamma hydroxy butyrate (GHB) by controlling the distribution of GHB via an exclusive central pharmacy that maintains a central database that tracks all prescriptions of GHB and analyzes for potential abuse situations, the method comprising:

determining current and anticipated patterns of potential prescription abuse of GHB from periodic reports generated by the central database based on prescription request data from a medical doctor, wherein said request data contain information identifying the patient, GHB as the drug prescribed, and credentials of the doctor; and

selecting multiple controls for distribution by said exclusive central pharmacy, the controls selected from the group consisting of communicating prescriptions from a physician to the central pharmacy; identifying the physicians name, license, and DEA (Drug Enforcement Agency) registration information; verifying the prescription; obtaining patient information; verifying the physician is eligible to prescribe the sensitive drug by consulting the National Technical Information Services to determine whether the physician has an active DEA number and to check on whether any actions are pending against the physician; providing comprehensive printed materials to the physician; contacting the patient's insurance company if any; verifying patient registry information; providing comprehensive education information to the patient; verifying the patient has reviewed the educational materials; verifying the home address of the patient; shipping via US postal service or similar shipping service; receiving the name of an at least 18 year old designee to receive the drug; confirming receipt of an initial shipment of the drug to the patient returning the drug to the pharmacy after two attempts to deliver; launching an investigation when a shipment is lost; shipping to another pharmacy for delivery; requiring manufacture at a single location; releasing inventory in a controlled manner to the central pharmacy; questioning early refills; flagging repeat instances of lost, stolen, destroyed, or spilled prescriptions; limiting the prescription to a one month supply; requiring rewriting of the

prescription periodically; and making the database available to the DEA for checking for abuse patterns in the data, for cash payments, and for inappropriate questions.

30. (New) The method of claim 29 wherein initially selected controls comprise communicating prescriptions from a physician to the central pharmacy; identifying the physicians name, license, and DEA registration information; verifying the prescription; obtaining patient information; verifying the physician is eligible to prescribe the sensitive drug by consulting the National Technical Information Services to determine whether the physician has an active DEA number and to check on whether any actions are pending against the physician; verifying patient registry information; providing comprehensive education information to the patient; verifying the patient has reviewed the educational materials; verifying the home address of the patient; shipping via US postal service; confirming receipt of an initial shipment of the drug to the patient; releasing inventory in a controlled manner to the central pharmacy; flagging repeat instances of lost, stolen, destroyed, or spilled prescriptions; and making the database available to the DEA for checking for abuse patterns in the data.

31. (New) The method of claim 29 which further comprises consulting a separate database to verify that the medical doctor is eligible to prescribe the drug.

REMARKS

By this amendment, Applicants have added new claims 26 to 31. No new matter has been added. Support for claim 26 appears in the specification at page 1(in the Summary of the Invention) and in original claim 19. Support for claim 27 appears in original claim 20. Support for claim 28 appears in the specification at page 2, line 1. Support for claim 29 appears at page 4, line 13, in the specification at page 1 (in the Summary of the Invention), and in original claim 19. Support for claim 30 appears at page 4, line 13 and in original claim 20. Support for claim 31 appears at page 4, line 13 and at page 2, line 1.

Conclusion

Applicants respectfully submit that the claims are in condition for allowance and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicants' attorney at (703) 239-9592 to facilitate prosecution of this application.

If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

Respectfully Submitted,

DAYTON T. REARDAN ET AL.

By their Representatives,

SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.
P.O. Box 2938
Minneapolis, MN 55402
(703) 239-9592

Date 9/30/2004 By _____
Bradley A. Forrest
Reg. No. 30,837

CERTIFICATE UNDER 37 CFR § 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelop addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 30th day of September 2004.

Name Dawn M. Pirle Signature _____

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Dayton T. Reardan et al.	Examiner:	Unknown
Serial No.:	10/322,348	Group Art Unit:	1743
Filed:	December 17, 2002	Docket:	101.031US1
Title:	SENSITIVE DRUG DISTRIBUTION SYSTEM AND METHOD		

INFORMATION DISCLOSURE STATEMENT

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

In compliance with the duty imposed by 37 C.F.R. § 1.56, and in accordance with 37 C.F.R. §§ 1.97 *et. seq.*, the enclosed materials are brought to the attention of the Examiner for consideration in connection with the above-identified patent application. Applicants respectfully request that this Information Disclosure Statement be entered and the documents listed on the attached Form 1449 be considered by the Examiner and made of record. Pursuant to the provisions of MPEP 609, Applicants request that a copy of the 1449 form, initialed as being considered by the Examiner, be returned to the Applicants with the next official communication.

Pursuant to 37 C.F.R. §1.97(b), it is believed that no fee or statement is required with the Information Disclosure Statement. However, if an Office Action on the merits has been mailed, the Commissioner is hereby authorized to charge the required fees to Deposit Account No. 19-0743 in order to have this Information Disclosure Statement considered.

The Examiner is invited to contact the Applicants' Representative at the below-listed telephone number if there are any questions regarding this communication.

Respectfully submitted,

DAYTON T. REARDAN ET AL.

By their Representatives,

SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.
P.O. Box 2938
Minneapolis, MN 55402
(703) 239-9592

Date 9/30/2004 By _____
Bradley A. Forrest
Reg. No. 36,530

CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 30th day of September, 2004.

Name _____ Signature _____

PTO/SB/08A(10-01)
Approved for use through 10/31/2002. OMB 651-0031
US Patent & Trademark Office: U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use as many sheets as necessary)

Sheet 1 of 2

Complete if Known	
Application Number	10/322,348
Filing Date	December 17, 2002
First Named Inventor	Reardan, Dayton
Group Art Unit	1743
Examiner Name	Unknown
Attorney Docket No: 101.031US1	

US PATENT DOCUMENTS

Examiner Initial *	USP Document Number	Publication Date	Name of Patentee or Applicant of cited Document	Class	Subclass	Filing Date If Appropriate
	US-2001/ 0001144	05/10/2001	Kapp, Thomas L.			12/22/2000
	US-2001/ 0042050	11/15/2001	Fletcher, Robert J., et al.			01/05/2001
	US-2001/ 0047281	11/29/2001	Keresman, III, Michael A., et al.			03/06/2001
	US-2002/ 0032581	03/14/2002	Reitberg, donald P.			06/01/2001
	US-2002/ 0032582	03/14/2002	Feeney, Jr., Robert J., et al.			08/15/2001
	US-2002/ 0042725	04/11/2002	Mayaud, Christian			08/30/2001
	US-2002/ 0042762	04/11/2002	McQuade, Richard , et al.			08/30/2001
	US-2002/ 0052762	05/02/2002	Kobylevsky, Paul , et al.			05/15/2001
	US-2002/ 0161607	10/31/2002	Subich, David C.			02/23/2001
	US-2003/ 0046110	03/06/2003	Gogolak, Victor			08/28/2002
	US-2003/ 0050802	03/13/2003	Jay, Richard , et al.			04/03/2002
	US-2003/ 0110060	06/12/2003	Clementi, William A.			12/12/2001
	US-2003/ 0127508	07/10/2003	Jones, William N.			01/21/2003
	US-2003/ 0144876	07/31/2003	Kosinski, Diana L., et al.			01/28/2002
	US-2003/ 0229519	12/11/2003	Eidex, Brian H., et al.			05/16/2003
	US-2003/ 0233256	12/18/2003	Cardenas, Rodolfo , et al.			06/13/2002
	US-2004/ 0019567	01/29/2004	Herceg, Michael J., et al.			07/23/2002
	US-2004/ 0019794	01/29/2004	Moradi, Ahmad , et al.			07/29/2002
	US-2004/ 0078237	04/22/2004	Kaafarani, William , et al.			08/28/2003
	US-2004/ 0107117	06/03/2004	Denny, Lawrence A.			11/25/2003

EXAMINER **DATE CONSIDERED**

Substitute Disclosure Statement Form (PTO-1449)

* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional) 2 Applicant is to place a check mark here if English language Translation is attached

PTO/SB/08A(10-01)
Approved for use through 10/31/2002. OMB 651-0031
US Patent & Trademark Office: U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use as many sheets as necessary)

Complete if Known	
Application Number	10/322,348
Filing Date	December 17, 2002
First Named Inventor	Reardan, Dayton
Group Art Unit	1743
Examiner Name	Unknown

Sheet 2 of 2

Attorney Docket No: 101.031US1

	US-2004/ 0117126	06/17/2004	Fetterman, Jeffrey E., et al.			11/25/2003
	US-2004/ 0122712	06/24/2004	Hill, Sr., Kenneth A., et al.			12/20/2002
	US-2004/ 0122713	06/24/2004	Hill, Sr., Kenneth A., et al.			12/20/2002
	US-2004/ 0162740	08/19/2004	Ericsson, Arthur D., et al.			02/14/2003
	US-2004/ 0176985	09/09/2004	Lilly, Ralph B., et al.			03/18/2004
	US-5,845,255	12/01/1998	Mayaud, C.	705	3	10/02/1997
	US-5,924,074	07/13/1999	Evans, J. A.	705	3	09/27/1996
	US-6,021,392	02/01/2000	Lester, Douglas D., et al.			12/08/1997
	US-6,055,507	04/25/2000	Cunningham, David W.			08/20/1998
	US-6,112,182	08/29/2000	Akers, William R., et al.			01/16/1996
	US-6,315,720	11/13/2001	Williams, Bruce A., et al.			10/23/2000
	US-6,347,329	02/12/2002	Evans, Jae A.			08/01/2000
	US-6,755,784	06/29/2004	Williams, Bruce A., et al.			03/07/2003

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Foreign Document No	Publication Date	Name of Patentee or Applicant of cited Document	Class	Subclass	T[2]

OTHER DOCUMENTS -- NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No [1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T[2]

EXAMINER **DATE CONSIDERED**

Substitute Disclosure Statement Form (PTO-1449)

* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional) 2 Applicant is to place a check mark here if English language Translation is attached

Appendix I
Copies of Prior Art References

The thirty-six (36) references include:

1. 5,845,255
2. 5,924,074
3. 6,347,329
4. 6,021,392
5. 6,055,507
6. 6,112,182
7. 6,315,720
8. 6,561,977
9. 6,755,784
10. 6,687,676
11. 2001/0001144
12. 2001/0042050
13. 2001/0047281
14. 2002/0032581
15. 2002/0032582
16. 2002/0042725
17. 2002/0042762
18. 2002/0052762
19. 2002/0161607
20. 2003/0046110
21. 2003/0050802
22. 2003/0093295
23. 2003/0110060
24. 2003/0127508
25. 2003/0144876
26. 2003/0229519
27. 2003/0233256
28. 2004/0019567
29. 2004/0019794

30. 2004/0078237
31. 2004/0107117
32. 2004/0117126
33. 2004/0122712
34. 2004/0122713
35. 2004/0162740
36. 2004/0176985

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Dayton T. Reardan et al.	Examiner:	
Serial No.:	10/322348	Group Art Unit:	
Filed:	December 17, 2002	Docket:	101.031US1
Title:	SENSITIVE DRUG DISTRIBUTION SYSTEM AND METHOD		

PETITION TO MAKE SPECIAL UNDER 37 C.F.R. § 1.102(d)

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Applicants hereby petition the Commissioner to advance the above-identified Application out of turn for accelerated examination under the provisions of 37 C.F.R. 1.102(d).

The Application meets the requirements of M.P.E.P. §708.02, section VIII. The petition fee of $130.00 as set forth in § 1.17(i), which is required pursuant to 37 C.F.R. § 1.102(d), is enclosed. The Application is a new application, not yet having received any examination. Applicants believe that all of the claims are directed to a single invention; however, if the Office shall determine that they do not obviously encompass only a single invention, Applicants agree to make a telephone election without traverse. An enclosed Statement avers that a pre-examination search has been carried out, lists the field of the search, and discusses the relevant references, pointing out how the claimed subject matter is patentable over these references with the particularity required by 37 C.F.R. 1.111(b) and (c). Copies of the references deemed most closely related to the subject matter are enclosed in the accompanying Information Disclosure Statement and Form 1449.

Respectfully submitted,

DAYTON T. REARDAN ET AL.

By their Representatives,

SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.
P.O. Box 2938
Minneapolis, MN 55402
(703) 239-9592

Date 9/30/2004 By _____
Bradley A. Forrest
Reg. No. 36,530

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on September 30th, 2004.

Name: Dawn M. Poole Signature Dawn M Poole

10/06/2004 MBELETE1 00000032 10322348

03 FC:1460 130.00 OP

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Dayton T. Reardan et al.	Examiner:	
Serial No.:	10/322348	Group Art Unit:	
Filed:	December 17, 2002	Docket:	101.031US1
Title:	SENSITIVE DRUG DISTRIBUTION SYSTEM AND METHOD		

PRE-EXAMINATION STATEMENT FOR PETITION TO MAKE SPECIAL UNDER 37 C.F.R. §1.102(d)

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

The undersigned Attorney for Applicant has caused a search to be made for the subject matter claimed in claims 1-31 of the above-identified Application.

The search was conducted in the USPTO classes/subclasses listed below:

Class	Subclasses	Description
700/		**DATA PROCESSING: GENERIC CONTROL SYSTEMS OR SPECIFIC APPLICATIONS**
	237	....Authorization (e.g., password, time usage limit, personal identification number (PIN)
705/		**DATA PROCESSING: FINANCIAL, BUSINESS PRACTICE, MANAGEMENT, OR COST/PRICE DETERMINATION**
	1	AUTOMATED ELECTRICAL FINANCIAL OR BUSINESS PRACTICE OR MANAGEMENT ARRANGEMENT
	2	. Health care management (e.g., record management, ICDA billing)
	3	.. Patient record management
707/		**DATA PROCESSING: DATABASE AND FILE MANAGEMENT OR DATA STRUCTURES**
	1	DATABASE OR FILE ACCESSING
	10	. Distributed or remote access
	104.1	. Application of database or data structure (e.g., distributed, multimedia, image)
709/		**ELECTRICAL COMPUTERS AND DIGITAL PROCESSING SYSTEMS: MULTICOMPUTER DATA TRANSFERRING OR PLURAL PROCESSOR SYNCHRONIZATION**
	200	MULTICOMPUTER DATA TRANSFERRING
	201	. Distributed data processing

217	. Remote data accessing
218	.. Using interconnected networks
219	.. Accessing a remote server

The references found to be relevant to claims 1-31 are listed on Form 1449 of the enclosed Information Disclosure Statement, and copies of each of these references are attached thereto. The following discussion sets forth with particularity the reasons why claims 1-31 are patentable over the relevant references.

In summary, the present claims relate to a new paradigm for controlling distribution of a sensitive drug. Heretofore, sensitive drug access has been restricted via a computer readable storage medium containing information on the patient, the prescriber, and the pharmacy. The computer readable storage medium evaluates risk parameters and generates an approval code to the pharmacy after determining that the degree of risk of contraindications to the patient is acceptable.

The new distribution model of the present system and method permits analysis and control of abuse of the sensitive drug and control of adverse reactions to the sensitive drug. It further permits obtaining FDA approval for the sensitive drug. The new model employs an exclusive central pharmacy that relies upon imposition of controls for distribution of a sensitive drug after a central database has analyzed for potential abuse situations and/or current and anticipated patterns of potential adverse reactions to the drug.

Patent 5,845,255 and related published application 2002/0042725 A1 to Mayaud provide for a **PRESCRIPTION MANAGEMENT SYSTEM.** Disclosed is a remote source database that may provide prescription abuse monitoring parameters. Multiple physicians and/or pharmacists may have access to a patient's prescription history record so that when a patient presents a problem or condition to more than one physician, it may be known. The system also allows for access to comprehensive drug information including scientific literature.

Instant claims 19 and 26 recite a feature that embodies the new distribution model, namely the distribution of a sensitive drug by an exclusive central pharmacy. This feature is not disclosed in Mayaud.

Patents 5,924,074 and 6,347,329 B1 to Evans provide for an **ELECTRONIC MEDICAL RECORDS SYSTEM.** Disclosed is reference database **104**, which includes

diagnosis module **300**, medication manager **302**, and procedure module **304**. A healthcare provider may use the reference database for assistance in diagnosing a patient's disease and prescribing medications to treat the disease. Medication manager **302** provides information on medications, such as proper dosages, allergies, contraindications, adverse interactions, and side effects. This system also provides instant access to a patient's electronic record by any authorized healthcare provider from any geographical location.

Instant claim 19 recites a feature that embodies the new distribution model, namely the distribution of a sensitive drug by an exclusive central pharmacy. This feature is not disclosed in Evans.

Patent 6,021,392 to Lester et al. provides for a **SYSTEM AND METHOD FOR DRUG MANAGEMENT**. Disclosed is a system for health care supply distribution from a central location.

Instant claim 1 recites features that embody the new distribution model. For example, among other distinctions recited in claim 1, checking the credentials of the doctor, patient education, analysis of potential abuse, and generating periodic reports are not discussed or suggested by Lester et al. These features do more than simply manage the distribution of health care supplies as in Lester et al. In contrast, the present model analyses for and determines potential abuse situations and current and anticipated patterns of potential adverse reactions.

Patent 6,055,507 to Cunningham provides for a **METHOD AND SYSTEM FOR DISPENSING TRACKING AND MANAGING PHARMACEUTICAL TRIAL PRODUCTS**. Disclosed is a centralized pharmaceutical sample distribution management system for controlling dispensing of samples among prescribers, patients, and pharmacies.

Instant claim 1 recites features that embody the new distribution model. For example, among other distinctions recited in claim 1, checking the credentials of the doctor, patient education, analysis of potential abuse, and generating periodic reports are not discussed or suggested by Cunningham. These features do more than simply manage the distribution of pharmaceutical samples as in Cunningham. In contrast, the present model analyses for and determines potential abuse situations and current and anticipated patterns of potential adverse reactions.

Patent 6,112,182 to Akers et al. provides for a **METHOD AND APPARATUS FOR**

INTEGRATED MANAGEMENT OF PHARMACEUTICAL AND HEALTHCARE SERVICES. Disclosed is a database for storing information on patients, doctors, drugs and prescriptions. Practice management system **102** checks for adverse interactions that the prescribed drug may have, and for possible adverse reactions of the patient to the drug due to allergies. The drug conflict information is maintained in conflict table **410**, and is displayed to the pharmacist. A prescription record is created and kept in the database for the practice management system **102** each time the drug is dispensed for reference.

Instant claims 19 and 26 recite a feature that embodies the new distribution model, namely the distribution of a sensitive drug by an exclusive central pharmacy. This feature is not disclosed in Akers et al.

Patents 6,315,720 B1, 6,561,977 B2, and 6,755,784 B2 to Williams et al. provide for **METHODS FOR DELIVERING A DRUG TO A PATIENT WHILE RESTRICTING ACCESS TO THE DRUG BY PATIENTS FOR WHOM THE DRUG MAY BE CONTRAINDICATED.** Disclosed is a computer readable storage medium in which the prescriber, pharmacy and patient may be registered. A storage medium is used to educate and reinforce the actions of patients who are taking a drug, as well as prescribers and pharmacies that distribute the drug. Based on information collected, patients are assigned to risk groups in order to limit unauthorized and inappropriate distribution of a drug.

Instant claims 19 and 26 recite a feature that embodies the new distribution model, namely the distribution of a sensitive drug by an exclusive central pharmacy. This feature is not disclosed in Williams et al.

Patent 6,687,676 B1 and related published application 2004/0107117 A1 to Denny provide a **PRESCRIPTION VERIFICATION SYSTEM.** Disclosed is a method for verifying/confirming prescription fulfillment, whereby a hosted database receives/provides prescription information including health care provider codes, patient codes, pharmacy system identification codes, and reports having prescription data summarized by patient name, social security numbers, the names of the prescribing health care providers, and the physician's Drug Enforcement Agency (DEA) number as means for minimizing fraud, abuse, and errors associated with prescription drugs.

Instant claim 1 recites features that embody the new distribution model. For example,

among other distinctions recited in claim 1, checking the credentials of the doctor, patient education, analysis of potential abuse, and generating periodic reports are not discussed or suggested by Denny. These features do more than simply verify and confirm fulfillment of prescriptions, as in Denny. In contrast, the present model analyses for and determines potential abuse situations and current and anticipated patterns of potential adverse reactions.

Published patent application 2001/0001144 A1 to Kapp provides for a **PHARMACY DRUG MANAGEMENT SYSTEM PROVIDING PATIENT SPECIFIC DRUG DOSING, DRUG INTERACTION ANALYSIS, ORDER GENERATION, AND PATIENT DATA MATCHING.** Disclosed is a pharmacy drug management system that includes drug interaction module **30**. Through the module, each drug to be prescribed will be examined for potential problems associated with other drugs and medical data of the patient such as the medical condition, allergy, and food of the patient. The module allows the input of medical history; allergies, diet, and prescribed drugs from all physicians being seen by the patient.

Instant claims 19 and 26 recite a feature that embodies the new distribution model, namely the distribution of a sensitive drug by an exclusive central pharmacy. This feature is not disclosed in Kapp.

Published patent application 2001/0042050 A1 to Fletcher et al. provides a **SECURE ELECTRONIC PROCUREMENT SYSTEM AND METHOD.** Disclosed is a secure, Internet-based electronic procurement system allowing a user (e.g., pharmacist) to order and confirm receipt of goods normally subject to a verifiable chain of custody (e.g., narcotics, controlled drugs and substances).

Instant claim 1 recites features that embody the new distribution model. For example, among other distinctions recited in claim 1, checking the credentials of the doctor, patient education, analysis of potential abuse, and generating periodic reports are not discussed or suggested by Fletcher et al. These features do more than simply facilitate the ordering and receipt of drugs as in Fletcher et al. In contrast, the present model analyses for and determines potential abuse situations and current and anticipated patterns of potential adverse reactions.

Published patent application 2001/0047281 A1 to Keresman et al. provides a **SECURE ON-LINE AUTHENTICATION SYSTEM FOR PROCESSING PRESCRIPTION DRUG FULFILLMENT**. Disclosed is a centralized database providing identity authentication over a

communication network, whereby network users/vendors are registered and provided with a uniquely defined identity as means for allowing ID authentication prior to closing a transaction. For doctors **40** and pharmacies **30**, the evaluation preferably includes a verification of their credentials and/or licenses by comparing collected registration data **114** corresponding to data made available from a government office or agency which issued the credentials and/or granted licenses.

Instant claim 1 recites features that embody the new distribution model. For example, among other distinctions recited in claim 1, checking the credentials of the doctor, patient education, analysis of potential abuse, and generating periodic reports are not discussed or suggested by Keresman et al. These features do more than simply authenticate identity as in Keresman et al. In contrast, the present model analyses for and determines potential abuse situations and current and anticipated patterns of potential adverse reactions.

Published patent application 2002/0032581 A1 to Reitberg provides **SINGLE-PATIENT DRUG TRIALS USED WITH ACCUMULATED DATABASE: RISK OF HABITUATION.** Disclosed is a method of predicting the abuse potential of a drug or substance when administered to an individual patient for chronic therapy or used habitually, and for gaining FDA approval and surveillance post-approval for new drugs which have been discovered for the treatment of chronic illnesses and conditions.

Instant claim 19 recites a feature that embodies the new distribution model, namely the distribution of a sensitive drug by an exclusive central pharmacy in order to obtain FDA approval. This feature is not disclosed in Reitberg.

Published patent application 2002/0032582 A1 to Feeney et al. provides for a **SYSTEM FOR MEDICATION DISPENSING AND INTEGRATED DATA MANAGEMENT.** Disclosed is a medical system for integrating data management with the process of controllably dispensing products including medications, and whereby a central server connected via a network to a prescription subsystem is configured to receive and process data including DEA, FDA, and drug interactions as means to determine whether the medication is appropriate for a patient.

Instant claim 1 recites features that embody the new distribution model. For example, among other distinctions recited in claim 1, checking the credentials of the doctor, patient education, analysis of potential abuse, and generating periodic reports are not discussed or

suggested by Feeney et al. These features do more than simply control dispensing of drugs at the point of care as in Feeney et al. In contrast, the present model analyses for and determines potential abuse situations and current and anticipated patterns of potential adverse reactions.

Published patent application 2002/0042762 A1 to McQuade et al. provides for **TRACKING THE DISTRIBUTION OF PRESCRIPTION DRUGS AND OTHER CONTROLLED ARTICLES**. Disclosed is a method for tracking the distribution of controlled articles from a central inventory.

Instant claim 1 recites features that embody the new distribution model. For example, among other distinctions recited in claim 1, checking the credentials of the doctor, patient education, analysis of potential abuse, and generating periodic reports are not discussed or suggested by McQuade et al. These features do more than simply control the distribution and inventory of pharmaceutical samples as in McQuade et al. In contrast, the present model analyses for and determines potential abuse situations and current and anticipated patterns of potential adverse reactions.

Published patent application 2002/0052762 A1 to Kobylevsky et al. provides for a **REMOTE PRESCRIPTION REFILL SYSTEM.** Disclosed is a central pharmacy system having software for automatically processing pharmacy orders.

Instant claim 1 recites features that embody the new distribution model. For example, among other distinctions recited in claim 1, checking the credentials of the doctor, patient education, analysis of potential abuse, and generating periodic reports are not discussed or suggested by Kobylevsky et al. These features do more than simply process refills automatically so as to relieve the burden on pharmacists as in Kobylevsky et al. In contrast, the present model analyses for and determines potential abuse situations and current and anticipated patterns of potential adverse reactions.

Published patent application 2002/0161607 A1 to Subich provides for a **PHARMACEUTICAL DRUG SAMPLE TRACKING AND CONTROL METHOD.** Disclosed is a pharmaceutical drug sample tracking and control method for storing patient information, adverse reaction information experienced by a patient, and patient recovery state, when a patient is treated with a drug sample.

Instant claim 1 recites features that embody the new distribution model. For example,

among other distinctions recited in claim 1, checking the credentials of the doctor, patient education, analysis of potential abuse, and generating periodic reports to evaluate potential abuse patterns are not discussed or suggested by Subich. These features do more than simply store prescription information so that interested parties may access the information.

Published patent application 2003/0046110 A1 to Gogolak provides for a **METHOD AND SYSTEM FOR CREATING, STORING, AND USING PATIENT SPECIFIC AND POPULATION-BASED GENOMIC DRUG SAFETY DATA.** Disclosed is drug safety database **10**, which may be accessed by users as a single virtual database. This source data covers three general areas: adverse event database **20**, drug information database **30**, and patient or genomic database **40**. Adverse event data are acquired by accessing, soliciting, or assembling data on patients experiencing adverse drug reactions, and comparing the data against data from a control set. This data may be provided from pharmaceutical corporations, hospitals, physicians, and government agencies.

Instant claim 1 recites features that embody the new distribution model. For example, among other distinctions recited in claim 1, checking the credentials of the doctor, patient education, analysis of potential abuse, and generating periodic reports are not discussed or suggested by Gogolak. These features do more than simply provide a database as in Gogolak. In contrast, the present model analyses for and determines potential abuse situations and current and anticipated patterns of potential adverse reactions.

Published patent application 2003/0050802 A1 to Jay et al. provides for a **MEDICAL SERVICE AND PRESCRIPTION MANAGEMENT SYSTEM.** Disclosed is point-of-care device **112**, which may connect to health plan database **104**. The system allows a doctor to search for drugs and perform drug interaction checking. It helps in dispensing of medication by presenting a warning message when the doctor selects a drug that is likely to cause drug-to-drug interactions or drug-allergy interactions for the patient. The drug interaction warnings may also include an analysis of the patient's family history and living habits.

Instant claim 1 recites features that embody the new distribution model. For example, among other distinctions recited in claim 1, checking the credentials of the doctor, patient education, analysis of potential abuse, and generating periodic reports are not discussed or

suggested by Jay et al. These features do more than simply allowing a doctor to search for drugs and perform drug interaction checking as in Jay et al. In contrast, the present model analyses for and determines potential abuse situations and current and anticipated patterns of potential adverse reactions.

Published patent application 2003/0093295 A1 to Lilly et al. provides a **CONTROLLED SUBSTANCE TRACKING SYSTEM AND METHOD.** Disclosed is a system and method for providing access to potential medication abuse information comprising identification of prescription duplications, potential drug interactions, multi-source interstate prescriptive medication abuse, and fraudulent prescriptive medications. Data storage **122** provides means for storing/receiving various types of data comprising: a doctor's name, DEA number, patient name, patient ID, patient address, patient phone number, drugs prescribed, dosage, frequency, start/end date, duration, quantity, number refills, whether substitution is allowed, generic allowed, notes, aberrant use flag, date prescription filed, location prescription was filled, pharmacist's name, phone number, and DEA number.

Instant claim 1 recites features that embody the new distribution model. For example, among other distinctions recited in claim 1, checking the credentials of the doctor, patient education, analysis of potential abuse, and generating periodic reports are not discussed or suggested by Lilly et al. These features do more than simply providing access to potential medication abuse information as in Lilly et al. In contrast, the present model analyses for and determines potential abuse situations and current and anticipated patterns of potential adverse reactions.

Published patent application 2003/0110060 A1 to Clementi provides for a **METHOD OF PROVIDING COMPREHENSIVE DRUG COMPLIANCE INFORMATION.** Disclosed is database **20**, which constructs patient report **12**. Patient **10** may access this report to see basic personal information, a record of all medicines being used, interactions between the medicines, and side effects of the medicine. The drug manufacturer **50** may also receive a number of such reports and note the side effect in a future product warning.

Instant claim 1 recites features that embody the new distribution model. For example, among other distinctions recited in claim 1, checking the credentials of the doctor, patient education, and analysis of potential abuse are not discussed or suggested by Clementi. These

features do more than simply provide information as in Clementi. In contrast, the present model analyses for and determines potential abuse situations and current and anticipated patterns of potential adverse reactions.

Published patent application 2003/0127508 A1 to Jones provides a **METHOD OF INDIVIDUALLY TRACKING AND IDENTIFYING A DRUG DELIVERY DEVICE.** Disclosed is a method and system for identifying an individual drug delivery device and for tracing its ownership, whereby a coded unique identifier is stored in a database for subsequent association/identification of distributing entities (e.g., transferee and a prescribing physician). Additional information added to the database may include the address of a patient, the RX number, the MD number, the identity of the prescribing physician, the DEA number, the pharmacy number, and the date of dispensation or transfer.

Instant claim 1 recites features that embody the new distribution model. For example, among other distinctions recited in claim 1, checking the credentials of the doctor, patient education, analysis of potential abuse, and generating periodic reports are not discussed or suggested by Jones. These features do more than simply track and identify a particular drug delivery device as in Jones. In contrast, the present model analyses for and determines potential abuse situations and current and anticipated patterns of potential adverse reactions.

Published patent application 2003/0144876 A1 to Kosinski et al. provides for an **APPARATUS AND METHOD FOR PROCESSING PHONE-IN PRESCRIPTION.** Disclosed is central or regional pharmacy **138** and prescription processing network **100,** whereby identification information including DEA data may be utilized as means to prevent prescription fraud.

Instant claim 1 recites features that embody the new distribution model. For example, among other distinctions recited in claim 1, checking the credentials of the doctor, patient education, analysis of potential abuse, and generating periodic reports are not discussed or suggested by Kosinski et al. These features do more than simply process audible, fax, or e-mail prescription requests as in Kosinski et al. In contrast, the present model analyses for and determines potential abuse situations and current and anticipated patterns of potential adverse reactions.

Published patent application 2003/0229519 A1 to Eidex et al. provides for **SYSTEMS**

AND METHODS FOR IDENTIFYING FRAUD AND ABUSE IN PRESCRIPTION CLAIMS. Disclosed is a system for identifying fraudulent prescription claims. The system monitors prescription transactions and returns appropriate notification messages to pharmacists or other health care providers. Database **105** may store data relating to pharmacies, doctors, and consumers. This may include typical doses filled by consumers, the likelihood indicators of fraud and abuse screening processes, and reports relating to the results of fraud and abuse screening processes. An example of a method of preventing drug abuse is a comparison of the distance between the pharmacy and the patient with the statistical average distance that has been previously computed.

Instant claims 19 and 26 recite a feature that embodies the new distribution model, namely the distribution of a sensitive drug by an exclusive central pharmacy. This feature is not disclosed in Eidex et al.

Published patent application 2003/0233256 A1 to Cardenas et al. provides **SECURE MEDICAL PRESCRIPTIONS.** Disclosed is a centralized method and system for producing a secure medical prescription by converting the physician's DEA number into an encrypted code for placement onto a medical prescription.

Instant claim 1 recites features that embody the new distribution model. For example, among other distinctions recited in claim 1, checking the credentials of the doctor, patient education, analysis of potential abuse, and generating periodic reports are not discussed or suggested by Cardenas et al. These features do more than simply producing secure medical prescriptions as in Cardenas et al. In contrast, the present model analyses for and determines potential abuse situations and current and anticipated patterns of potential adverse reactions.

Published patent application 2004/0019567 A1 to Herceg et al. provides for an **ELECTRONIC PRESCRIPTION ORDERING METHOD, SYSTEM, AND PROGRAM PRODUCT.** Disclosed is Web-based central pharmaceutical computer **12** having database **24** as means for providing electronic prescription ordering.

Instant claim 1 recites features that embody the new distribution model. For example, among other distinctions recited in claim 1, checking the credentials of the doctor, patient education, analysis of potential abuse, and generating periodic reports are not discussed or suggested by Herceg et al. These features do more than ordering prescriptions electronically. In

contrast, the present model analyses for and determines potential abuse situations and current and anticipated patterns of potential adverse reactions.

Published patent application 2004/0019794 A1 to Moradi et al. provides a **METHOD AND SYSTEM FOR DELIVERING PRESCRIPTION MEDICINE.** Disclosed is a system and method of distributing medicine, whereby the method provides for: accepting a prescription and a delivery address from a central server, wherein the prescription is for a medicine and wherein the delivery address is associated with a person; delivering the medicine to the delivery address; receiving a confirmation from the person that the medicine was delivered; and communicating the confirmation to the central server. In addition, the system provides for registering information relevant to the identification of a prescription issuing physician, patient, and fulfillment pharmacy.

Instant claim 1 recites features that embody the new distribution model. For example, among other distinctions recited in claim 1, checking the credentials of the doctor, patient education, analysis of potential abuse, and generating periodic reports are not discussed or suggested by Moradi et al. These features do more than prevent receipt of too much medicine as in Moradi et al. In contrast, the present model analyses for and determines potential abuse situations and current and anticipated patterns of potential adverse reactions.

Published patent application 2004/0078237 A1 to Kaafarani et al. provides for a **METHOD OF DISPENSING MEDICAL PRESCRIPTIONS.** Disclosed is a system which may protect against fraudulent or illegal re-use of a prescription. It includes steps of prompting the patient for personal information such as age, weight, telephone number, requested deliver time, and secret confirmation codes. Another method employs retaining a data slip with a mark of indelible ink or a patterned die cut.

Instant claims 19 and 26 recite a feature that embodies the new distribution model, namely the distribution of a sensitive drug by an exclusive central pharmacy. This feature is not disclosed in Kaafarani et al.

Published patent application 2004/0117126 A1 to Fetterman et al. provides a **METHOD OF ASSESSING AND MANAGING RISKS ASSOCIATED WITH A PHARMACEUTICAL PRODUCT.** Disclosed is method providing a continual and systematic assessment and management of the risks associated with the use of a pharmaceutical product as

means for gaining regulatory approval and physician adoption. In addition, a hazard assessment is utilized for creating interventions to be utilized in mitigating the risk of the pharmaceutical product, whereby educational materials may be continually evaluated and revised to achieve an expected level of effectiveness on a target audience.

Instant claim 19 recites a feature that embodies the new distribution model, namely the distribution of a sensitive drug by an exclusive central pharmacy in order to obtain FDA approval. This feature is not disclosed in Fetterman et al.

Published patent applications 2004/0122712 A1 and 2004/0122713 A1 to Hill et al. provide a **SYSTEM AND METHOD FOR PRESCRIPTION MANAGEMENT**. Disclosed is a prescription filling system for allowing physicians **102** and patients **104** to interact with pharmacy system **112** and central fill facility **124** to fill prescriptions. In addition, filled prescriptions may be delivered by central fill facility **124** to pharmacies **106** or home delivered for purchase by patient **104**.

Instant claim 1 recites features that embody the new distribution model. For example, among other distinctions recited in claim 1, checking the credentials of the doctor, patient education, analysis of potential abuse, and generating periodic reports are not discussed or suggested by Hill et al. These features do more than provide a prescription filling system to bypass manual filling as in Hill et al. In contrast, the present model analyses for and determines potential abuse situations and current and anticipated patterns of potential adverse reactions.

Published patent application 2004/0162740 A1 to Ericsson et al. provides for a **DIGITIZED PRESCRIPTION SYSTEM.** Disclosed is an apparatus comprising an electronic database containing a plurality of transaction records for transactions in which a prescription medicinal substance is dispensed to a patient. Additionally, a method is utilized in conjunction with FDA and DEA drug information to: obtain a patient's medication history comprising searching the electronic database by the patient's social security number; determine whether a proposed refill or remaining fill transaction is indicative of potential overuse; determine whether a medicinal substance in a proposed transaction will result in possible interactions with a patient's recently dispensed medicinal substances; and identify potential counterfeiting or illicit importation of prescription medicinal substances.

Instant claim 1 recites features that embody the new distribution model. For example,

among other distinctions recited in claim 1, patient education is not discussed or suggested by Ericsson et al. This feature does more than facilitate exchange of data as in Ericsson et al. In contrast, the present model analyses for and determines potential abuse situations and current and anticipated patterns of potential adverse reactions and uses patient education as a control on the distribution of a sensitive drug.

Published patent application 2004/0176985 A1 to Lilly et al. provides a **CONTROLLED SUBSTANCE TRACKING SYSTEM AND METHOD.** Disclosed is a method for tracking prescription medications, as means to address and control prescription drug abuse, whereby pharmaceutical information control organization **12** may be implemented as an independent information utility acting as a central service center for the management of prescriptive medication drugs.

Instant claim 1 recites features that embody the new distribution model. For example, among other distinctions recited in claim 1, checking the credentials of the doctor, patient education, analysis of potential abuse, and generating periodic reports are not discussed or suggested by Lilly et al. These features do more than generate a medication history for a particular purchaser as in Lilly et al. In contrast, the present model analyses for and determines potential abuse situations and current and anticipated patterns of potential adverse reactions.

In addition, instant claims 19 and 26 recite a feature that embodies the new distribution model, namely the distribution of a sensitive drug by an exclusive central pharmacy. This feature is not disclosed in Lilly et al.

Respectfully submitted,

DAYTON T. REARDAN ET AL.

By their Representatives,

SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.
P.O. Box 2938
Minneapolis, MN 55402
(703) 239-9592

Date: 9/30/2004

By _____
Bradley A. Forrest
Registration No. 36,530

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on **September 30th, 2004**.

Dawn M. Rode
Name:

Dawn M. Rode
Signature

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Dayton T. Reardan et al.

Title: SENSITIVE DRUG DISTRIBUTION SYSTEM AND METHOD

Docket No.:	101.031US1	Serial No.:	10/322,348
Filed:	December 17, 2002	Due Date:	N/A
Examiner:	Unknown	Group Art Unit:	1743

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

We are transmitting herewith the following attached items (as indicated with an "X"):

X A return postcard.
X Petition to Make Special Under 37 CFR 1.102(d) (1 Pg.).
X Appendix I (2 pgs.).
X An Information Disclosure Statement (2 pgs.), Form 1449 (2 pgs.). Documents NOT enclosed.
X A check in the amount of $140.00 to cover the fee for additional claims as calculated below.
X Preliminary Amendment (11 pgs.).
X Pre-Examination Statement For Petition To Make Special Under 37 CFR 1.102(d) (15 pgs.).
X A check in the amount of $130.00 to cover the Petition Fee.

If not provided for in a separate paper filed herewith, If an additional fee is required due to changes to the claims, the fee has been calculated as follows:

CLAIMS AS AMENDED						
	(1) Claims Remaining After Amendment		(2) Highest Number Previously Paid For	(3) Present Extra	Rate	Fee
TOTAL CLAIMS	31	-	25	6	x 9.00 =	$54.00
INDEPENDENT CLAIMS	6	-	4	2	x 43.00 =	$86.00
[]MULTIPLE DEPENDENT CLAIMS PRESENTED						$0.00
TOTAL						$140.00

Please consider this a PETITION FOR EXTENSION OF TIME for sufficient number of months to enter these papers and please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.
Customer Number 21186

By: _____
Atty: Bradley A. Forrest
Reg. No. 36,530

CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 30th day of September, 2004.

Dawn M. Poole
Name

Dawn M. Poole
Signature

SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.
(GENERAL)

Index of Claims

Application/Control No.	Applicant(s)/Patent under Reexamination
~~10/000,000~~ 10/322348	~~LIGHT~~
Examiner	Art Unit
~~***~~	1743

√	Rejected	–	(Through numeral) Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

Claim Final	Claim Original	Date	Claim Final	Claim Original	Date	Claim Final	Claim Original	Date
	(1)			51			101	
	2			52			102	
	3			53			103	
	4			54			104	
	5			55			105	
	6			56			106	
	7			57			107	
	8			58			108	
	9			59			109	
	10			60			110	
	(11)			61			111	
	12			62			112	
	13			63			113	
	14			64			114	
	15			65			115	
	16			66			116	
	17			67			117	
	18			68			118	
	(19)			69			119	
	20			70			120	
	21			71			121	
	(22)			72			122	
	23			73			123	
	24			74			124	
	25			75			125	
	~~(26)~~			76			126	
	27			77			127	
	28			78			128	
	(29)			79			129	
	30			80			130	
	31			81			131	
	32			82			132	
	33			83			133	
	34			84			134	
	35			85			135	
	36			86			136	
	37			87			137	
	38			88			138	
	39			89			139	
	40			90			140	
	41			91			141	
	42			92			142	
	43			93			143	
	44			94			144	
	45			95			145	
	46			96			146	
	47			97			147	
	48			98			148	
	49			99			149	
	50			100			150	

PATENT APPLICATION FEE DETERMINATION RECORD
Effective January 1, 2003

Application or Docket Number: 10/322348

CLAIMS AS FILED - PART I

	(Column 1)	(Column 2)
TOTAL CLAIMS	25	
FOR	NUMBER FILED	NUMBER EXTRA
TOTAL CHARGEABLE CLAIMS	25 minus 20=	* 5
INDEPENDENT CLAIMS	4 minus 3 =	* 1
MULTIPLE DEPENDENT CLAIM PRESENT		☐

* If the difference in column 1 is less than zero, enter "0" in column 2

SMALL ENTITY TYPE ☐			OR	OTHER THAN SMALL ENTITY	
RATE	FEE			RATE	FEE
BASIC FEE	$375		OR	BASIC FEE	$750
X$ 9=	45		OR	X$18=	
X42=	42		OR	X84=	
+140=			OR	+280=	
TOTAL	462		OR	TOTAL	

CLAIMS AS AMENDED - PART II

10.4.04

AMENDMENT A

	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA
Total	* 31	Minus	** 25	= 6
Independent	* 6	Minus	*** 4	= 2
FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM				☐

SMALL ENTITY			OR	OTHER THAN SMALL ENTITY	
RATE	ADDITIONAL FEE			RATE	ADDITIONAL FEE
X$ 9=	54		OR	X$18=	
~~X42=~~	86		OR	X84=	
+140=			OR	+280=	
TOTAL ADDIT. FEE	140		OR	TOTAL ADDIT. FEE	

AMENDMENT B

	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA
Total	*	Minus	**	=
Independent	*	Minus	***	=
FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM				☐

RATE	ADDITIONAL FEE		RATE	ADDITIONAL FEE
X$ 9=		OR	X$18=	
X42=		OR	X84=	
+140=		OR	+280=	
TOTAL ADDIT. FEE		OR	TOTAL ADDIT. FEE	

AMENDMENT C

	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA
Total	*	Minus	**	=
Independent	*	Minus	***	=
FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM				☐

RATE	ADDITIONAL FEE		RATE	ADDITIONAL FEE
X$ 9=		OR	X$18=	
X42=		OR	X84=	
+140=		OR	+280=	
TOTAL ADDIT. FEE		OR	TOTAL ADDIT. FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20."
*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3."
The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Dayton T. Reardan et al.

Title: SENSITIVE DRUG DISTRIBUTION SYSTEM AND METHOD

Docket No.: 101.031US1
Filed: December 17, 2002
Examiner: Unknown

Serial No.: 10/322,348
Due Date: N/A
Group Art Unit: 1743

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

We are transmitting herewith the following attached items (as indicated with an "X"):

X A return postcard.
X A Supplemental Information Disclosure Statement (2 pgs.), Form 1449 (2 pgs.), and copies of 33 cited documents.

If not provided for in a separate paper filed herewith, Please consider this a PETITION FOR EXTENSION OF TIME for sufficient number of months to enter these papers and please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.
Customer Number 21186

By: _____
Atty: Bradley A. Forrest
Reg. No. 30,837

CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 2nd day of November, 2004.

Dawn M. Rode
Name

Dawn M. Rode
Signature

SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.
(GENERAL)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Dayton T. Reardan et al.	Examiner:	Unknown
Serial No.:	10/322,348	Group Art Unit:	1743
Filed:	December 17, 2002	Docket:	101.031US1
Title:	SENSITIVE DRUG DISTRIBUTION SYSTEM AND METHOD		

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

MS Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

In compliance with the duty imposed by 37 C.F.R. § 1.56, and in accordance with 37 C.F.R. §§ 1.97 *et. seq.*, the enclosed materials are brought to the attention of the Examiner for consideration in connection with the above-identified patent application. Applicants respectfully request that this Supplemental Information Disclosure Statement be entered and the documents listed on the attached Form 1449 be considered by the Examiner and made of record. Pursuant to the provisions of MPEP 609, Applicants request that a copy of the 1449 form, initialed as being considered by the Examiner, be returned to the Applicants with the next official communication.

Pursuant to 37 C.F.R. §1.97(b), it is believed that no fee or statement is required with the Supplemental Information Disclosure Statement. However, if an Office Action on the merits has been mailed, the Commissioner is hereby authorized to charge the required fees to Deposit Account No. 19-0743 in order to have this Supplemental Information Disclosure Statement considered.

The Examiner is invited to contact the Applicants' Representative at the below-listed telephone number if there are any questions regarding this communication.

Respectfully submitted,

DAYTON T. REARDAN ET AL.

By their Representatives,

SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.
P.O. Box 2938
Minneapolis, MN 55402
(612) 373-6972

Date 11/2/2004 By _____
Bradley A. Forrest
Reg. No. 30,837

CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: MS Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 2nd day of November, 2004.

Name Dawn M. Poole

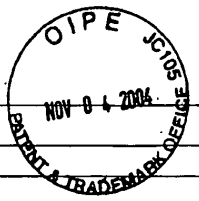
Signature _____

PTO/SB/08A(10-01)
Approved for use through 10/31/2002. OMB 651-0031
US Patent & Trademark Office: U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use as many sheets as necessary)



Sheet 1 of 2

Complete if Known	
Application Number	10/322,348
Filing Date	December 17, 2002
First Named Inventor	Reardan, Dayton
Group Art Unit	1743
Examiner Name	Unknown
Attorney Docket No: 101.031US1	

US PATENT DOCUMENTS

Examiner Initial *	USP Document Number	Publication Date	Name of Patentee or Applicant of cited Document	Class	Subclass	Filing Date If Appropriate
	US-2001/ 0,001,144	05/10/2001	Kapp, Thomas L.			12/22/2000
	US-2001/ 0,042,050	11/15/2001	Fletcher, Robert J., et al.			01/05/2001
	US-2001/ 0,047,281	11/29/2001	Keresman, III, Michael A., et al.			03/06/2001
	US-2002/ 0,032,581	03/14/2002	Reitberg, donald P.			06/01/2001
	US-2002/ 0,032,582	03/14/2002	Feeney, Jr., Robert J., et al.			08/15/2001
	US-2002/ 0,042,725	04/11/2002	Mayaud, Christian			08/30/2001
	US-2002/ 0,042,762	04/11/2002	McQuade, Richard , et al.			08/30/2001
	US-2002/ 0,052,762	05/02/2002	Kobylevsky, Paul , et al.			05/15/2001
	US-2002/ 0,161,607	10/31/2002	Subich, David C.			02/23/2001
	US-2003/ 0,046,110	03/06/2003	Gogolak, Victor			08/28/2002
	US-2003/ 0,050,802	03/13/2003	Jay, Richard , et al.			04/03/2002
	US-2003/ 0,110,060	06/12/2003	Clementi, William A.			12/12/2001
	US-2003/ 0,127,508	07/10/2003	Jones, William N.			01/21/2003
	US-2003/ 0,144,876	07/31/2003	Kosinski, Diana L., et al.			01/28/2002
	US-2003/ 0,229,519	12/11/2003	Eidex, Brian H., et al.			05/16/2003
	US-2003/ 0,233,256	12/18/2003	Cardenas, Rodolfo , et al.			06/13/2002
	US-2004/ 0,019,567	01/29/2004	Herceg, Michael J., et al.			07/23/2002
	US-2004/ 0,019,794	01/29/2004	Moradi, Ahmad , et al.			07/29/2002
	US-2004/ 0,078,237	04/22/2004	Kaafarani, William , et al.			08/28/2003
	US-2004/ 0,107,117	06/03/2004	Denny, Lawrence A.			11/25/2003

EXAMINER **DATE CONSIDERED**

Substitute Disclosure Statement Form (PTO-1449)

* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional) 2 Applicant is to place a check mark here if English language Translation is attached

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use as many sheets as necessary)

Sheet 2 of 2

Complete if Known

Application Number	10/322,348
Filing Date	December 17, 2002
First Named Inventor	Reardan, Dayton
Group Art Unit	1743
Examiner Name	Unknown
Attorney Docket No: 101.031US1	

	US-2004/ 0,117,126	06/17/2004	Fetterman, Jeffrey E., et al.			11/25/2003
	US-2004/ 0,122,712	06/24/2004	Hill, Sr., Kenneth A., et al.			12/20/2002
	US-2004/ 0,122,713	06/24/2004	Hill, Sr., Kenneth A., et al.			12/20/2002
	US-2004/ 0,162,740	08/19/2004	Ericsson, Arthur D., et al.			02/14/2003
	US-2004/ 0,176,985	09/09/2004	Lilly, Ralph B., et al.			03/18/2004
	US-5,845,255	12/01/1998	Mayaud, C.	705	3	10/02/1997
	US-5,924,074	07/13/1999	Evans, J. A.	705	3	09/27/1996
	US-6,021,392	02/01/2000	Lester, Douglas D., et al.			12/08/1997
	US-6,055,507	04/25/2000	Cunningham, David W.			08/20/1998
	US-6,112,182	08/29/2000	Akers, William R., et al.			01/16/1996
	US-6,315,720	11/13/2001	Williams, Bruce A., et al.			10/23/2000
	US-6,347,329	02/12/2002	Evans, Jae A.			08/01/2000
	US-6,755,784	06/29/2004	Williams, Bruce A., et al.			03/07/2003

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Foreign Document No	Publication Date	Name of Patentee or Applicant of cited Document	Class	Subclass	T[2]

OTHER DOCUMENTS -- NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No [1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T[2]

EXAMINER **DATE CONSIDERED**

Substitute Disclosure Statement Form (PTO-1449)

* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. [1] Applicant's unique citation designation number (optional). [2] Applicant is to place a check mark here if English language Translation is attached

UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents
United States Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450
www.uspto.gov

JUN 17 2005

Schwegman, Lundberg, Woessner
& Kluth, P.A.
P.O. Box 2938
Minneapolis, MN 55402-0938

In re application of : **DECISION ON PETITION**
Dayton T. Reardan, et al. : **TO MAKE SPECIAL**
Application No. 10/322,348 : **(ACCELERATED**
Filed: December 17, 2002 : **EXAMINATION)**
For: SENSITIVE DRUG DISTRIBUTION SYSTEM AND METHOD

This is in response to the renewed petition filed on October 4, 2004 to make the above-identified application special on the basis of special examining procedure for certain new applications - accelerated examination as set forth in MPEP § 708.02 VIII.

The requirements for granting special status under this section are: (A) a petition to make special accompanied by the fee set forth in 37 CFR 1.17(i); (B) all claims being directed to a single invention, or an election without traverse if the Office determines that all the claims are not directed to a single invention; (C) a statement that a pre-examination search was made listing the field of search; (D) one copy of each of the references deemed most closely related to the subject matter encompassed by the claims if said references are not already of record; and (E) a detailed discussion of how the claimed subject matter is patentable over the references in accordance with 37 CFR 1.111 (b) and (c).

Since all of the requirements for special status under MPEP § 708.02 VIII have been met, the petition is **GRANTED**.

The examiner is directed (1) to make an interference search for possible interfering applications, (2) to promptly examine this application out of turn, and (3) if any interfering application is discovered, to examine such application simultaneously and state in the first official letter of such application that it is being taken out of turn because of a possible interference.

Petitioner is advised that this application will continue to be special, throughout its entire prosecution and pendency, including interference or appeal, if any, only if petitioner makes a prompt ***bona fide*** effort, in response to each Office action, to place the application in condition for allowance, even if it is necessary to conduct an interview with the examiner to accomplish this purpose.

SUMMARY: Petition to Make Special **GRANTED.**

Randolph A. Reese
Special Programs Examiner
Technology Center 3600
571-272-6619

RAR/dcg: 6/1/05

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L12	37	(educational or printed) adj1 (material) same (prescriber or physician or doctor) same (new or first adj1 time or no adj1 experience or never adj1 before)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/21 14:53 looked at titles/abstracts
L15	22	(sensitive or controlled) and (drug or medication or medicine or prescription) same (first adj1 time) same (prescriber or doctor or physician) same (information or instruction or direction)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/21 14:57 Considered 1
L16	39	(drug or medication or medicine or prescription) same (first adj1 time) same (prescriber or doctor or physician) same (information or instruction or direction)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/21 15:19 Considered 1
S1	66586	(distribut$3 or provid$3 or supply$3 or deliver$3 or dispens$3) and ((sensitive or abuse or abusive or addictive) same (drug or medicine or medication or ointment or pharmaceutical or pill or agent) or (sodium adj1 oxybate or gamma adj1 hydroxy adj1 butyrate or narcotic or opium or pain adj1 killer))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/21 14:21
S2	4281	((705/2) or (705/3) or (600/300)).CCLS.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2005/06/17 13:13
S3	348	S1 and S2	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/17 13:14

S4	116	(data adj1 base or database or data adj1 bank or databank) and (enter$3 or submit$4 or input$4 or prompt) and (credential$3 or certif$7 or licens$3) and (refill or re adj1 fill) and (address or residence) and (educational adj1 (material or information or data) or brochure or pamphlet) and (pattern or track$3 or monitor$3) and (report or update) and (evaluat$3 or analy$4) and (doctor or physician or prescriber)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/17 13:35
S5	8	S1 and S4	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/17 13:19 looked at titles/ abstracts
S6	159939	(distribut$3 or provid$3 or supply$3 or deliver$3 or dispens$3) and ((sensitive or abuse or abusive or addictive or controlled) same (drug or medicine or medication or ointment or pharmaceutical or pill or agent) or (sodium adj1 oxybate or gamma adj1 hydroxy adj1 butyrate or narcotic or opium or pain adj1 killer))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/20 11:31
S7	14343	(distribut$3 or provid$3 or supply$3 or deliver$3 or dispens$3) and ((sensitive or abuse or abusive or addictive or controlled) adj1 (drug or medicine or medication or ointment or pharmaceutical or pill or agent) or (sodium adj1 oxybate or gamma adj1 hydroxy adj1 butyrate or narcotic or opium or pain adj1 killer))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/17 13:24
S8	8	S4 and S7	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/17 13:24 looked at titles/abstracts

S9	119	(data adj1 base or database or data adj1 bank or databank) and (enter$3 or submit$4 or input$4 or prompt) and (credential$3 or certif$7 or licens$3) and (refill or re adj1 fill or reorder or re adj1 order) and (address or residence) and (educational adj1 (material or information or data) or brochure or pamphlet) and (pattern or track$3 or monitor$3) and (report or update) and (evaluat$3 or analy$4) and (doctor or physician or prescriber)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/17 13:36
S10	41	(data adj1 base or database or data adj1 bank or databank) and (enter$3 or submit$4 or input$4 or prompt) and (credential$3 or certif$7 or licens$3) and (refill or re adj1 fill or reorder or re adj1 order) and (address or residence) and (educational adj1 (material or information or data) or brochure or pamphlet) and (pattern or track$3 or monitor$3) and (report or update) and (evaluat$3 or analy$4) and (doctor or physician or prescriber) and (patient)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/17 13:37
S11	8	(data adj1 base or database or data adj1 bank or databank) and (enter$3 or submit$4 or input$4 or prompt) and (credential$3 or certif$7 or licens$3) and (refill or re adj1 fill or reorder or re adj1 order) and (address or residence) and (educational adj1 (material or information or data) or brochure or pamphlet) and (pattern or track$3 or monitor$3) and (report or update) and (evaluat$3 or analy$4) and (doctor or physician or prescriber) and (patient) and ((sensitive or abuse or abusive or addictive) same (drug or medicine or medication or ointment or pharmaceutical or pill or agent) or (sodium adj1 oxybate or gamma adj1 hydroxy adj1 butyrate or narcotic or opium or pain adj1 killer))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/17 13:38

looked at titles/abstracts

looked at titles/abstracts

S12	32	(data adj1 base or database or data adj1 bank or databank) and (enter$3 or submit$4 or input$4 or prompt) and (credential$3 or certif$7 or licens$3) and (refill or re adj1 fill or reorder or re adj1 order) and (address or residence) and (educational adj1 (material or information or data) or brochure or pamphlet) and (pattern or track$3 or monitor$3) and (report or update) and (evaluat$3 or analy$4) and (doctor or physician or prescriber) and (patient) and ((sensitive or abuse or abusive or addictive or controlled) same (drug or medicine or medication or ointment or pharmaceutical or pill or agent) or (sodium adj1 oxybate or gamma adj1 hydroxy adj1 butyrate or narcotic or opium or pain adj1 killer))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/17 17:26
S54	4	S53 or S51	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/20 15:17

looked at titles/abstracts

Considered 1

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L12	37	(educational or printed) adj1 (material) same (prescriber or physician or doctor) same (new or first adj1 time or no adj1 experience or never adj1 before)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/21 14:53 looked at titles/abstracts
L15	22	(sensitive or controlled) and (drug or medication or medicine or prescription) same (first adj1 time) same (prescriber or doctor or physician) same (information or instruction or direction)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/21 14:57 looked at titles/abstracts
L16	39	(drug or medication or medicine or prescription) same (first adj1 time) same (prescriber or doctor or physician) same (information or instruction or direction)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/21 15:19 looked at titles/abstracts
S1	66586	(distribut$3 or provid$3 or supply$3 or deliver$3 or dispens$3) and ((sensitive or abuse or abusive or addictive) same (drug or medicine or medication or ointment or pharmaceutical or pill or agent) or (sodium adj1 oxybate or gamma adj1 hydroxy adj1 butyrate or narcotic or opium or pain adj1 killer))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/21 14:21
S2	4281	((705/2) or (705/3) or (600/300)). CCLS.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2005/06/17 13:13
S3	348	S1 and S2	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/17 13:14

S12	32	(data adj1 base or database or data adj1 bank or databank) and (enter$3 or submit$4 or input$4 or prompt) and (credential$3 or certif$7 or licens$3) and (refill or re adj1 fill or reorder or re adj1 order) and (address or residence) and (educational adj1 (material or information or data) or brochure or pamphlet) and (pattern or track$3 or monitor$3) and (report or update) and (evaluat$3 or analy$4) and (doctor or physician or prescriber) and (patient) and ((sensitive or abuse or abusive or addictive or controlled) same (drug or medicine or medication or ointment or pharmaceutical or pill or agent) or (sodium adj1 oxybate or gamma adj1 hydroxy adj1 butyrate or narcotic or opium or pain adj1 killer))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/17 17:26
S24	4	(data adj1 base or database or data adj1 bank or databank) and (enter$3 or submit$4 or input$4 or prompt) and (credential$3 or certif$7 or licens$3) and (refill or re adj1 fill or reorder or re adj1 order) and (address or residence) and (educational adj1 (material or information or data) or brochure or pamphlet) and (pattern or track$3 or monitor$3) and (report or update) and (evaluat$3 or analy$4) and (doctor or physician or prescriber) and (patient) and ((sensitive or abuse or abusive or addictive or controlled) same (drug or medicine or medication or ointment or pharmaceutical or pill or agent) or (sodium adj1 oxybate or gamma adj1 hydroxy adj1 butyrate or narcotic or opium or pain adj1 killer)) and (state adj1 licens$3)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/17 17:32

looked at titles/abstracts

looked at titles/abstracts

S25	8	(physician or doctor or medical adj1 professional or practitioner) same (request$3 or submit$4 or order$2) same (prescription or medication or medicine or drug or pill) and (central or main) adj1 (database or data adj1 base or databank or data adj1 bank) and (abuse or fraud or abusing or abusive) and (check$3 or verif$7 or confirm$5) same (credential$3 or certif$7 or licens$3) and (ship$4 or distribut$3 or supply$3 or deliver$3 or dispens$3) and (receiv$3 or receipt)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/20 11:20 looked at titles/abstracts
S26	118162	((sensitive or abuse or abusive or addictive) same (drug or medicine or medication or ointment or pharmaceutical or pill or agent) or (sodium adj1 oxybate or gamma adj1 hydroxy adj1 butyrate or narcotic or opium or pain adj1 killer or cocaine or marijuana))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/17 17:38
S27	5	S25 and S26	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/17 17:39 looked at titles/abstracts
S28	5	(physician or doctor or medical adj1 professional or practitioner or prescriber) same (request$3 or submit$4 or order$2 or enter$3 or input$4) same (prescription or medication or medicine or drug or pill or pharmaceutical) and (central or main) adj1 (database or data adj1 base or databank or data adj1 bank) and (abuse or fraud or abusing or abusive) and (check$3 or verif$7 or confirm$5) same (credential$3 or certif$7 or licens$3) and (ship$4 or distribut$3 or supply$3 or deliver$3 or dispens$3) and (generat$3 or creat$3) same (report or analy$3 or conclusion or summary or finding or document$5)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/21 12:59 looked at titles/abstracts

S29	24	(physician or doctor or medical adj1 professional or practitioner or prescriber) same (request$3 or submit$4 or order$2 or enter$3 or input$4) same (prescription or medication or medicine or drug or pill or pharmaceutical) and (central or main) adj1 (database or data adj1 base or databank or data adj1 bank) and (check$3 or verif$7 or confirm$5) same (credential$3 or certif$7 or licens$3) and (ship$4 or distribut$3 or supply$3 or deliver$3 or dispens$3) and (generat$3 or creat$3) same (report or analy$3 or conclusion or summary or finding or document$5)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/20 11:26
S30	19	(physician or doctor or medical adj1 professional or practitioner or prescriber) same (request$3 or submit$4 or order$2 or enter$3 or input$4) same (prescription or medication or medicine or drug or pill or pharmaceutical) and (central or main) adj1 (database or data adj1 base or databank or data adj1 bank) and (check$3 or verif$7 or confirm$5) same (credential$3 or certif$7 or licens$3) and (ship$4 or distribut$3 or supply$3 or deliver$3 or dispens$3) and (generat$3 or creat$3) same (report or analy$3 or conclusion or summary or finding or document$5) and (pharmacy)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/20 13:39
S31	63501	((sensitive or abuse or abusive or addictive or controlled) same (drug or medicine or medication or ointment or pharmaceutical or pill or agent) or (sodium adj1 oxybate or gamma adj1 hydroxy adj1 butyrate or narcotic or opium or pain adj1 killer)) same (pattern or finding or analy$3 or conclusion or result or track$3 or monitor$3)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/20 11:34
S32	4281	((705/2) or (705/3) or (600/300)). CCLS.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2005/06/20 11:33

looked at titles/abstracts

looked at titles/abstracts

S33	303	S31 and S32	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/20 11:33
S34	25010	((sensitive or abuse or abusive or addictive or controlled) same (drug or medicine or medication or ointment or pharmaceutical or pill or agent) or (sodium adj1 oxybate or gamma adj1 hydroxy adj1 butyrate or narcotic or opium or pain adj1 killer)) same (pattern or finding or analy$3 or track$3 or monitor$3)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/20 11:34
S35	25010	(((sensitive or abuse or abusive or addictive or controlled) same (drug or medicine or medication or ointment or pharmaceutical or pill or agent)) or (sodium adj1 oxybate or gamma adj1 hydroxy adj1 butyrate or narcotic or opium or pain adj1 killer)) same (pattern or finding or analy$3 or track$3 or monitor$3)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/20 11:34
S36	1028	(((sensitive or abuse or abusive or addictive or controlled) same (drug or medicine or medication or ointment or pharmaceutical or pill or agent)) or (sodium adj1 oxybate or gamma adj1 hydroxy adj1 butyrate or narcotic or opium or pain adj1 killer)) same (pattern or finding or analy$3 or track$3 or monitor$3) and (prescription or prescribing or medication adj1 order)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/20 11:35
S37	485	(((sensitive or abuse or abusive or addictive or controlled) same (drug or medicine or medication or ointment or pharmaceutical or pill or agent)) or (sodium adj1 oxybate or gamma adj1 hydroxy adj1 butyrate or narcotic or opium or pain adj1 killer)) same (pattern or finding or analy$3 or track$3 or monitor$3) and (prescription or prescribing or medication adj1 order) same (doctor or physician)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/20 11:36
S38	103	S32 and S37	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/20 11:35

S39	102	(((sensitive or abuse or abusive or addictive or controlled) adj2 (drug or medicine or medication or ointment or pharmaceutical or pill or agent)) or (sodium adj1 oxybate or gamma adj1 hydroxy adj1 butyrate or narcotic or opium or pain adj1 killer)) same (pattern or finding or analy$3 or track$3 or monitor$3) and (prescription or prescribing or medication adj1 order) same (doctor or physician)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/20 11:41
S40	97	(((sensitive abusive or addictive or controlled) adj2 (drug or medicine or medication or ointment or pharmaceutical or pill or agent)) or (sodium adj1 oxybate or gamma adj1 hydroxy adj1 butyrate or narcotic or opium or pain adj1 killer)) same (pattern or finding or analy$3 or track$3 or monitor$3) and (prescription or prescribing or medication adj1 order) same (doctor or physician)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/20 11:42
S41	97	(((sensitive or abusive or addictive or controlled) adj2 (drug or medicine or medication or ointment or pharmaceutical or pill or agent)) or (sodium adj1 oxybate or gamma adj1 hydroxy adj1 butyrate or narcotic or opium or pain adj1 killer)) same (pattern or finding or analy$3 or track$3 or monitor$3) and (prescription or prescribing or medication adj1 order) same (doctor or physician)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/20 11:45
S42	9	(((sensitive or abusive or addictive or controlled) adj2 (drug or medicine or medication or ointment or pharmaceutical or pill or agent)) or (sodium adj1 oxybate or gamma adj1 hydroxy adj1 butyrate or narcotic or opium or pain adj1 killer)) same (pattern or finding or analy$3 or track$3 or monitor$3) same (abuse or abusive or fraud) and (prescription or prescribing or medication adj1 order) same (doctor or physician)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/20 11:44

looked at titles/abstracts

S43	131	(((sensitive or abusive or addictive or controlled) adj2 (drug or medicine or medication or ointment or pharmaceutical or pill or agent or substance)) or (sodium adj1 oxybate or gamma adj1 hydroxy adj1 butyrate or narcotic or opium or pain adj1 killer)) same (pattern or finding or analy$3 or track$3 or monitor$3) and (prescription or prescribing or medication adj1 order) same (doctor or physician)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/20 11:57
S44	1072	(((sensitive or abusive or addictive or controlled) adj2 (drug or medicine or medication or ointment or pharmaceutical or pill or agent or substance)) or (sodium adj1 oxybate or gamma adj1 hydroxy adj1 butyrate or narcotic or opium or pain adj1 killer)) same (abuse or abusive or fraud$5)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/20 11:58
S45	143	(((sensitive or abusive or addictive or controlled) adj2 (drug or medicine or medication or ointment or pharmaceutical or pill or agent or substance)) or (sodium adj1 oxybate or gamma adj1 hydroxy adj1 butyrate or narcotic or opium or pain adj1 killer)) same (abuse or abusive or fraud$5) same (analy$4 or pattern or track$3 or monitor$3)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/20 12:00
S46	44	(((sensitive or abusive or addictive or controlled) adj2 (drug or medicine or medication or ointment or pharmaceutical or pill or agent or substance)) or (sodium adj1 oxybate or gamma adj1 hydroxy adj1 butyrate or narcotic or opium or pain adj1 killer)) same (abuse or abusive or fraud$5) same (analy$4 or pattern or track$3 or monitor$3) and (prescription or prescrib$3 or medication adj1 order)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/20 13:32

S48	8	(physician or doctor or medical adj1 professional or practitioner or prescriber) same (request$3 or submit$4 or order$2 or enter$3 or input$4) same (prescription or medication or medicine or drug or pill or pharmaceutical) and (central or main) adj1 (database or data adj1 base or databank or data adj1 bank) and (check$3 or verif$7 or confirm$5) same (credential$3 or certif$7 or licens$3) and (ship$4 or distribut$3 or supply$3 or deliver$3 or dispens$3) and (generat$3 or creat$3) same (report or analy$3 or conclusion or summary or finding or document$5) and (pharmacy) and (educational adj1 (material or information or data) or (brochure) or (pamphlet))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/20 13:44
S54	4	S53 or S51	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/20 15:17

looked at titles/abstracts

considered 2

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
S64	23	(confirm$3 or verif$7) same (prescription) same (read) same (instruction or advice)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/20 16:02 looked at titles/abstracts
S65	1	(call$3) same (patient) same (verif$7 or confirm$5) same (prescription or medication adj1 order) same (instructions or guidelines or education)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/20 16:08 looked at title/abstract
S66	275	(patient) same (verif$7 or confirm$5 or check$3) same (prescription or medication adj1 order) same (read or instructions or guidelines or education)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/20 16:10
S67	152	(patient) same (verif$7 or confirm$5 or check$3) same (prescription or medication adj1 order) same (instructions or guidelines or educational adj1 material)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/21 10:12
S68	36	(patient) same (verif$7 or confirm$5 or check$3) same (prescription or medication adj1 order) same (instructions or guidelines or educational adj1 material) same (database or data adj1 base or databank or data adj1 bank)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/21 10:17
S69	7	(patient) same (verif$7 or confirm$5 or check$3) same (prescription or medication adj1 order) same (instructions or guidelines or educational adj1 material) same (prior or before) same (ship$4 or dispens$3 or deliver$3 or send$3)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/21 10:20 looked at titles/abstracts
S70	29	(patient) same (verif$7 or confirm$5 or check$3) same (prescription or medication adj1 order or medication or pharmaceutical or drug or pill) same (instructions or guidelines or educational adj1 material) same (prior or before) same (ship$4 or dispens$3 or deliver$3 or send$3)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/21 10:28 looked at titles/abstracts

S71	53	(verif$7 or confirm$5 or check$3) same (prescription or medication adj1 order or medication or pharmaceutical or drug or pill) same (instructions or guidelines or educational adj1 material or prescription adj1 label) same (prior or before) same (ship$4 or dispens$3 or deliver$3 or send$3)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/21 12:21
S72	11	clark.inv. and (inform$2) adj1 consent	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/21 12:27 considered 1
S73	5	(educational adj1 material) same (prior or before) same (ship$4 or deliver$3 or dispens$3) same (medicine or medication or pharmaceutical or prescription or pill or drug)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/21 12:30
S74	15	(educational adj1 material) same (prior or before) same (ship$4 or deliver$3 or dispens$3)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/21 12:30 considered 1
S75	6	(educational adj1 material) same (prior or before) same (ship$4 or deliver$3 or dispens$3) and (medicine or medication or pharmaceutical or prescription or pill or drug)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/21 12:54
S83	98	(receipt or receiv$3 or deliver$3) same (confirm$5 or verif$7 or notif$7) same (call or phone or telephone) same (pharmacy)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/21 13:02
S84	91	(receipt or receiv$3 or deliver$3) same (confirm$5 or verif$7 or notif$7) same (call or phone or telephone) same (pharmacy) same (drug or prescription or medicine or medication)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/21 13:09
S85	16	(pharmacy) same (telephone or call or phone) same (patient) same (confirm$5 or verif$7) same (received or receipt or receiving) same (prescription or medication or medicine or drug or pharmaceutical)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/21 13:23 looked at titles/abstracts

S86	49	(pharmacy) same (telephone or call or phone) same (confirm$5 or verif$7 or ask or find adj1 out) same (received or receipt or receiving or delivered or sent) same (prescription or medication or medicine or drug or pharmaceutical)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/21 13:29
S87	31	(pharmacist) same (telephone or call or phone) same (confirm$5 or verif$7 or ask or find adj1 out) same (received or receipt or receiving or delivered or sent) same (prescription or medication or medicine or drug or pharmaceutical)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/21 13:32
S88	151	(pharmacist) same (confirm$5 or verif$7 or ask or find adj1 out) same (received or receipt or receiving or delivered or sent) same (prescription or medication or medicine or drug or pharmaceutical)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/21 13:32
S89	242	(pharmacist or pharmacy) same (confirm$5 or verif$7 or ask or find adj1 out) same (patient) same (received or receipt or receiving or delivered or sent) same (prescription or medication or medicine or drug or pharmaceutical)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/21 13:33
S90	162	(pharmacist or pharmacy) same (confirm$5 or verif$7 or ask or find adj1 out) same (patient) same (received or receipt or receiving or delivered or sent) same (prescription or medication or medicine or drug or pharmaceutical) and (phone or telephone or cellphone)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/21 13:33
S111	26	(investigat$3) same (lost) same (shipment or delivery or order) same (drug or medicine or medication or prescription or pharmaceutical)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/21 14:10
S118	105	(stolen or lost or missing) same (drug or medication or pharmaceutical or prescription) same (investigat$3)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/21 14:17

looked at titles/abstracts

looked at titles/abstracts

considered 1

S119	1066	(stolen or lost or missing) same ((sensitive or abuse or abusive or addictive) same (drug or medicine or medication or ointment or pharmaceutical or pill or agent) or (sodium adj1 oxybate or gamma adj1 hydroxy adj1 butyrate or narcotic or opium or pain adj1 killer))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/21 14:22
S120	37	(stolen or lost or missing) same ((sensitive or abuse or abusive or addictive) same (drug or medicine or medication or ointment or pharmaceutical or pill or agent) or (sodium adj1 oxybate or gamma adj1 hydroxy adj1 butyrate or narcotic or opium or pain adj1 killer)) same (shipment or delivery)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/21 14:23
S121	582	(stolen or lost or missing) same (drug or medicine or medication or pharmaceutical or prescription) same (shipment or delivery)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/21 14:23
S122	16	(stolen or lost or missing) same (drug or medicine or medication or pharmaceutical or prescription) same (shipment or delivery) same (investigat$3)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2005/06/21 14:23

Considered 1

Index of Claims

Application/Control No.	Applicant(s)/Patent under Reexamination
10/322,348	REARDAN ET AL.
Examiner	**Art Unit**
Lena Najarian	3626

√	Rejected	–	(Through numeral) Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

Claim		Date
Final	Original	6/21/05
	1	√
	2	√
	3	√
	4	√
	5	√
	6	√
	7	√
	8	√
	9	√
	10	√
	11	N
	12	N
	13	N
	14	N
	15	N
	16	N
	17	N
	18	N
	19	N
	20	N
	21	N
	22	N
	23	N
	24	N
	25	N
	26	N
	27	N
	28	N
	29	N
	30	N
	31	N
	32	
	33	
	34	
	35	
	36	
	37	
	38	
	39	
	40	
	41	
	42	
	43	
	44	
	45	
	46	
	47	
	48	
	49	
	50	

Claim		Date
Final	Original	
	51	
	52	
	53	
	54	
	55	
	56	
	57	
	58	
	59	
	60	
	61	
	62	
	63	
	64	
	65	
	66	
	67	
	68	
	69	
	70	
	71	
	72	
	73	
	74	
	75	
	76	
	77	
	78	
	79	
	80	
	81	
	82	
	83	
	84	
	85	
	86	
	87	
	88	
	89	
	90	
	91	
	92	
	93	
	94	
	95	
	96	
	97	
	98	
	99	
	100	

Claim		Date
Final	Original	
	101	
	102	
	103	
	104	
	105	
	106	
	107	
	108	
	109	
	110	
	111	
	112	
	113	
	114	
	115	
	116	
	117	
	118	
	119	
	120	
	121	
	122	
	123	
	124	
	125	
	126	
	127	
	128	
	129	
	130	
	131	
	132	
	133	
	134	
	135	
	136	
	137	
	138	
	139	
	140	
	141	
	142	
	143	
	144	
	145	
	146	
	147	
	148	
	149	
	150	

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/322,348	12/17/2002	Dayton T. Reardan	101.031US1	5446

21186 7590 06/29/2005

SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.
P.O. BOX 2938
MINNEAPOLIS, MN 55402-0938

EXAMINER	
NAJARIAN, LENA	
ART UNIT	**PAPER NUMBER**
3626	

DATE MAILED: 06/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 10/03)

Office Action Summary	Application No.	Applicant(s)	
	10/322,348	REARDAN ET AL.	
	Examiner	Art Unit	
	Lena Najarian	3626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 December 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *11-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 December 2002* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *20030414*, 15/4/04
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-10, drawn to a method of distributing a sensitive drug, classified in class 705, subclass 2.

II. Claims 11-18, drawn to a method of monitoring potential abuse of a sensitive drug by use of an exclusive central database, classified in class 707, subclass 3.

III. Claims 19-25, drawn to a method of obtaining FDA approval for a sensitive drug, classified in class 700, subclass 237.

IV. Claims 26-31, drawn to a method to control abuse of a sensitive drug, classified in class 705, subclass 4.

2. The inventions are distinct, each from the other because of the following reasons:

Inventions I, II, III and IV are related as subcombinations disclosed as usable together in a single combination. The subcombinations are distinct from each other if they are shown to be separately usable. In the instant case, invention I has separate utility such as a healthcare management system, invention II has separate utility such as query processing, invention III has separate utility such as authorization, and invention IV has separate utility such as an insurance processing system. See MPEP § 806.05(d).

3. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification and/or because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

4. During a telephone conversation with Richard Schwartz on 3/18/05 a provisional election was made without traverse to prosecute the invention of Group 1, claims 1-10. Affirmation of this election must be made by applicant in replying to this Office action. Claims 11-31 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

5. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Drawings

6. The drawings are objected to as failing to comply with 37 CFR 1.84(p)(5) because they include the following reference character(s) not mentioned in the description: items 232 & 238 (Fig. 2A), item 286 (Fig. 2B), items 262 & 264 (Fig. 2C), item 402 (Fig. 4A), item 434 (Fig. 4B), and item 1200 (Fig. 12). Corrected drawing sheets in compliance with 37 CFR 1.121(d), or amendment to the

specification to add the reference character(s) in the description in compliance with 37 CFR 1.121(b) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. Claims 1-10 recite the limitations for which there is no antecedent basis in the claims. In particular, the following passages lack or have vague antecedent basis:

(i) "the patient": claim 1, lines 3 & 6

claim 2, line 2

claim 4, line 2

claim 6, line 2

(ii) "the patient's": claim 5, line 1

(iii) "the central pharmacy": claim 2, line 2

(iv) "the pharmacist": claim 8, line 2

(v) "the physician": claim 9, line 2

(vi) Claims 3, 7, and 10 incorporate the deficiencies of claim 1, through dependency, and are also rejected.

Claim Rejections - 35 USC § 101

10. Claims 1-10 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The basis of this rejection is set forth in a two-prong test of:

(1) whether the invention is within the technological arts; and

(2) whether the invention produces a useful, concrete, and tangible result.

For a claimed invention to be statutory, the claimed invention must be within the technological arts. Mere ideas in the abstract (i.e., abstract idea, law of nature, natural phenomena) that do not apply, involve, use, or advance the technological arts fail to promote the "progress of science and the useful arts" (i.e., the physical sciences as opposed to social sciences, for example) and therefore are found to be non-statutory subject matter. For a process claim to pass muster, the recited process must somehow apply, involve, use, or advance the technological arts.

(A) In the present case, it is not clear whether or not the various elements of claims 1-10 clearly and definitely require technology. For example in exemplary claim 1, a database in its broadest sense, may simply be a paper-based table (e.g., chart) or paper files in a file cabinet. As such, the claims when given their broadest reasonable interpretation appear to be devoid of any technological device.

Additionally, for a claimed invention to be statutory, the claimed invention must produce a useful, concrete, and tangible result. In the present case, the claimed invention generates periodic reports to evaluate potential abuse patterns. Although the recited process produces a useful, concrete, and tangible result, since the claimed invention, as a whole, is not within the technological arts as explained above, claims 1-10 are deemed to be directed to non-statutory subject matter.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 1-2, 4-8, and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moradi et al. (US 2004/0019794 A1) in view of Lilly et al. (US 2004/0176985 A1) and further in view of Califano et al. (US 2003/0033168 A1).

(A) Referring to claim 1, Moradi discloses a method of distributing a drug, the method comprising (para. 3 of Moradi):

receiving prescription requests from a medical doctor containing information identifying the patient, the drug, and various credentials of the doctor (para. 35, para. 116, and para. 117 of Moradi);

checking the credentials of the doctor (para. 118 of Moradi); and

confirming receipt of the drug (see abstract of Moradi).

Moradi does not expressly disclose that the drug is a sensitive drug, entering the information into a central database for analysis of potential abuse situations, confirming with the patient that educational material has been read prior to shipping the sensitive drug, and generating periodic reports via the central database to evaluate potential abuse patterns.

Lilly et al. disclose that the drug is a sensitive drug, entering the information into a central database for analysis of potential abuse situations, and generating periodic reports via the central database to evaluate potential abuse patterns (para. 33, para. 69, para. 54, and para. 58 of Lilly; the Examiner interprets "controlled substance" to be a form of "sensitive drug").

At the time of the invention, it would have been obvious to a person of ordinary skill in the art to combine the features of Lilly within Moradi. The motivation for doing so would have been to ensure that prescribers have an accurate view of their patients' use of prescription drugs and to help protect professionals from lawsuits and other potential liabilities (para. 58 of Lilly).

Moradi and Lilly do not disclose confirming with the patient that educational material has been read prior to shipping the drug.

Califano et al. disclose confirming with the patient that educational material has been read prior to shipping the drug (para. 84 of Califano).

At the time of the invention, it would have been obvious to a person of ordinary skill in the art to combine the feature of Califano within Moradi and Lilly. The motivation for doing so would have been to ensure that the patient knows about the risks and dangers associated with the drug (para. 43 of Califano).

(B) Referring to claims 2 and 6, Moradi discloses wherein receipt of the drug is confirmed by telephone call from the central pharmacy to the patient (abstract, para. 42, para. 26, and para. 47 of Moradi) and recording a designee identified by the patient to receive the drug (para. 24 of Moradi; the Examiner interprets recipient's...name" to be a form of "designee").

Moradi does not expressly disclose that the drug is a sensitive drug.

Lilly et al. disclose that the drug is a sensitive drug (para. 33 of Lilly; the Examiner interprets "controlled substance" to be a form of "sensitive drug").

At the time of the invention, it would have been obvious to a person of ordinary skill in the art to combine the feature of Lilly within Moradi. The motivation for doing so would have been for the distribution method to be used primarily for drugs that are likely to be abused (para. 9 of Lilly).

(C) Referring to claim 4, Moradi and Lilly do not disclose recording the confirmation with the patient that the educational material has been read in the central database.

Califano discloses recording the confirmation with the patient that the educational material has been read in the central database (para. 120 of Califano).

At the time of the invention, it would have been obvious to a person of ordinary skill in the art to combine the feature of Califano within Moradi and Lilly. The motivation for doing so would have been to have documentation confirming that the patient knows about the risks and dangers associated with the drug (para. 43 of Califano).

(D) Referring to claim 5, Moradi discloses verifying the patient's home address (para. 43 of Moradi).

(E) Referring to claim 7, Moradi discloses establishing a delivery date (para. 46 of Moradi).

(F) Referring to claim 8, Moradi discloses wherein prescription refills requested prior to an anticipated date are questioned by the pharmacist (para. 42 of Moradi).

(G) Referring to claim 10, Moradi discloses wherein the credentials of the doctor comprise DEA (Drug Enforcement Agency) and state license numbers (para. 116 and para. 117 of Moradi).

13. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Moradi et al. (US 2004/0019794 A1) in view of Lilly et al. (US 2004/0176985 A1) in view of Califano et al. (US 2003/0033168 A1) as applied to claim 1 above, and further in view of Andreasson et al. (US 2003/0160698 A1).

(A) Referring to claim 3, Moradi, Lilly, and Califano do not disclose launching an investigation of lost shipments.

Andreasson discloses disclose launching an investigation of lost shipments (para. 79 of Andreasson).

At the time of the invention, it would have been obvious to a person of ordinary skill in the art to combine the feature of Andreasson within Moradi, Lilly, and Califano. The motivation for doing so would have been to reduce the risk of lost or stolen medical products by immediately notifying healthcare workers so that they may take appropriate action (para. 79 of Andreasson).

14. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Moradi et al. (US 2004/0019794 A1) in view of Lilly et al. (US 2004/0176985 A1) in view of Califano et al. (US 2003/0033168 A1) as applied to claim 1 above, and further in view of Mayaud (5,845,255).

(A) Referring to claim 9, Moradi, Lilly, and Califano do not disclose shipping comprehensive printed materials to the physician if the physician is a first time prescriber of the drug.

Mayaud discloses shipping comprehensive printed materials to the physician if the physician is a first time prescriber of the drug (col. 37, lines 6-31 of Mayaud).

At the time of the invention, it would have been obvious to a person of ordinary skill in the art to combine the feature of Mayaud within Moradi, Lilly, and Califano. The motivation for doing so would have been to reduce the reluctance

of physicians to prescribe new drugs by providing them with the latest information about the drugs (col. 37, lines 6-23 of Mayaud).

Mayaud does not expressly disclose that the drug is a sensitive drug.

Lilly et al. disclose that the drug is a sensitive drug (para. 33 of Lilly; the Examiner interprets "controlled substance" to be a form of "sensitive drug").

At the time of the invention, it would have been obvious to a person of ordinary skill in the art to combine the feature of Lilly within Mayaud, Moradi, and Califano. The motivation for doing so would have been for the distribution method to be used primarily for drugs that are likely to be abused (para. 9 of Lilly).

Conclusion

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lena Najarian whose telephone number is 571-272-7072. The examiner can normally be reached on 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Thomas can be reached on 571-272-6776. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

In
6-21-05

JOSEPH THOMAS
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 3600

Search Notes	Application/Control No.	Applicant(s)/Patent under Reexamination
	10/322,348	REARDAN ET AL.
	Examiner	Art Unit
	Lena Najarian	3626

SEARCHED			
Class	Subclass	Date	Examiner
705	2 3	6/17/2005	LN
600	300	6/17/2005	LN
705	2 3	6/20/2005	LN
600	300	6/20/2005	LN

INTERFERENCE SEARCHED			
Class	Subclass	Date	Examiner

SEARCH NOTES (INCLUDING SEARCH STRATEGY)		
	DATE	EXMR
East (see attached printout) USPAT; USOCR; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	6/17/2005	LN
East (see attached printout) USPAT; USOCR; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	6/20/2005	LN
East (see attached printout) USPAT; USOCR; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	6/21/2005	LN

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

Bib Data Sheet

CONFIRMATION NO. 5446

SERIAL NUMBER	FILING DATE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
10/322,348	12/17/2002 RULE	705	3626	101.031US1

APPLICANTS

Dayton T. Reardan, Excelsior, MN;

Patti A. Eneel, Eagan, MN;
Bob Gagne, St. Paul, MN;

** CONTINUING DATA **********

none LN 6-17-05

** FOREIGN APPLICATIONS **********

none LN 6-17-05

IF REQUIRED, FOREIGN FILING LICENSE GRANTED ** SMALL ENTITY **
** 03/21/2003

Foreign Priority claimed ☐ yes ☒ no 35 USC 119 (a-d) conditions met ☐ yes ☒ no ☐ Met after Allowance Verified and Acknowledged Examiner's Signature Initials	STATE OR COUNTRY MN	SHEETS DRAWING 16	TOTAL CLAIMS 25	INDEPENDENT CLAIMS 4

ADDRESS
21186
SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.
P.O. BOX 2938
MINNEAPOLIS , MN
55402-0938

TITLE
Sensitive drug distribution system and method

FILING FEE	FEES: Authority has been given in Paper	☐ All Fees
RECEIVED 667	No. _____ to charge/credit DEPOSIT ACCOUNT No. _____ for following:	☐ 1.16 Fees (Filing) ☐ 1.17 Fees (Processing Ext. of time) ☐ 1.18 Fees (Issue)

		☐ Other _____
		☐ Credit

Notice of References Cited	Application/Control No. 10/322,348	Applicant(s)/Patent Under Reexamination REARDAN ET AL.	
	Examiner Lena Najarian	Art Unit 3626	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
	A	US-2004/0019794 A1	01-2004	Moradi et al.	713/185
	B	US-2003/0033168 A1	02-2003	Califano et al.	705/3
	C	US-2004/0176985 A1	09-2004	Lilly et al.	705/002
	D	US-5,845,255 A	12-1998	Mayaud, Christian	705/3
	E	US-2003/0160698 A1	08-2003	Andreasson et al.	340/573.1
	F	US-			
	G	US-			
	H	US-			
	I	US-			
	J	US-			
	K	US-			
	L	US-			
	M	US-			

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	
	V	
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

PTO/SB/08A(10-01)
Approved for use through 10/31/2002. OMB 651-0031
US Patent & Trademark Office: U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use as many sheets as necessary)

Sheet 1 of 1

Complete if Known	
Application Number	10/322,348
Filing Date	December 17, 2002
First Named Inventor	Reardan Ph.D., Dayton
Group Art Unit	~~1743~~ 3626
Examiner Name	Unknown
Attorney Docket No: 101.031US1	

US PATENT DOCUMENTS

Examiner Initial *	USP Document Number	Publication Date	Name of Patentee or Applicant of cited Document	Class	Subclass	Filing Date If Appropriate
LN	US-6,045,501	04/04/2000	Elsayed, Marc , et al	600	300	08/28/1998
LN	US-6,315,720	11/13/2001	Williams, Bruce A., et al	600	300	10/23/2000

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Foreign Document No	Publication Date	Name of Patentee or Applicant of cited Document	Class	Subclass	T²

OTHER DOCUMENTS -- NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T²
LN		NASCSA National Conference, (November 2000),8 pages	
LN		"Diversion Prevention Through Responsible Distribution", NADDI Regional Training, (May 2001),12 pages	
LN		"Diversion Prevention Through Responsible Distribution", NADDI Regional Training Tennessee, (June 2001),14 Pages	
LN		"Diversion Prevention Through Responsible Distribution", NADDI National Conference, (November 2001),15 pages	
LN		"Peripheral and Central Nervous System Drugs Advisory Committee", Department of Health and Human Services Food and Drug Administration Center for Drug Evaluation and Research, Holiday Inn, Bethesda, Maryland,(06/06/2001),7 pages	

EXAMINER Lena Nafarian DATE CONSIDERED 6-17-05

Substitute Disclosure Statement Form (PTO-1449)

¹ EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ² Applicant's unique citation designation number (optional) ³ Applicant is to place a check mark here if English language Translation is attached

PTO/SB/08A(10-01)
Approved for use through 10/31/2002. OMB 651-0031
US Patent & Trademark Office: U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use as many sheets as necessary)

Sheet 1 of 2

Complete if Known	
Application Number	10/322,348
Filing Date	December 17, 2002
First Named Inventor	Reardan, Dayton
Group Art Unit	~~1743~~ 3626
Examiner Name	Unknown
Attorney Docket No: 101.031US1	

US PATENT DOCUMENTS

Examiner Initial*	USP Document Number	Publication Date	Name of Patentee or Applicant of cited Document	Class	Subclass	Filing Date If Appropriate
LN	US-2001/ 0001144	05/10/2001	Kapp, Thomas L.	705	3	12/22/2000
LN	US-2001/ 0042050	11/15/2001	Fletcher, Robert J., et al.	705	64	01/05/2001
LN	US-2001/ 0047281	11/29/2001	Keresman, III, Michael A., et al.	705	2	03/06/2001
LN	US-2002/ 0032581	03/14/2002	Reitberg, donald P.	705	2	06/01/2001
LN	US-2002/ 0032582	03/14/2002	Feeney, Jr., Robert J., et al.	705	2	08/15/2001
LN	US-2002/ 0042725	04/11/2002	Mayaud, Christian	705	2	08/30/2001
LN	US-2002/ 0042762	04/11/2002	McQuade, Richard , et al.	705	29	08/30/2001
LN	US-2002/ 0052762	05/02/2002	Kobylevsky, Paul , et al.	705	2	05/15/2001
LN	US-2002/ 0161607	10/31/2002	Subich, David C.	705	3	02/23/2001
LN	US-2003/ 0046110	03/06/2003	Gogolak, Victor	705	2	08/28/2002
LN	US-2003/ 0050802	03/13/2003	Jay, Richard , et al.	705	3	04/03/2002
LN	US-2003/ 0110060	06/12/2003	Clementi, William A.	705	2	12/12/2001
LN	US-2003/ 0127508	07/10/2003	Jones, William N.	235	375	01/21/2003
LN	US-2003/ 0144876	07/31/2003	Kosinski, Diana L., et al.	705	2	01/28/2002
LN	US-2003/ 0229519	12/11/2003	Eidex, Brian H., et al.	705	2	05/16/2003
LN	US-2003/ 0233256	12/18/2003	Cardenas, Rodolfo , et al.	705	3	06/13/2002
LN	US-2004/ 0019567	01/29/2004	Herceg, Michael J., et al.	705	64	07/23/2002
LN	US-2004/ 0019794	01/29/2004	Moradi, Ahmad , et al.	713	185	07/29/2002
LN	US-2004/ 0078237	04/22/2004	Kaafarani, William , et al.	705	2	08/28/2003
LN	US-2004/ 0107117	06/03/2004	Denny, Lawrence A.	705	2	11/25/2003

EXAMINER Lena Najarian DATE CONSIDERED 6-17-05

Substitute Disclosure Statement Form (PTO-1449)

* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional) 2 Applicant is to place a check mark here if English language Translation is attached

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use as many sheets as necessary)

Sheet 2 of 2

Complete if Known	
Application Number	10/322,348
Filing Date	December 17, 2002
First Named Inventor	Reardan, Dayton
Group Art Unit	1743
Examiner Name	Unknown
Attorney Docket No: 101.031US1	

LN	US-2004/0117126	06/17/2004	Fetterman, Jeffrey E., et al.	702	19	11/25/2003
LN	US-2004/0122712	06/24/2004	Hill, Sr., Kenneth A., et al.	705	2	12/20/2002
LN	US-2004/0122713	06/24/2004	Hill, Sr., Kenneth A., et al.	705	2	12/20/2002
LN	US-2004/0162740	08/19/2004	Ericsson, Arthur D., et al.	705	3	02/14/2003
LN	US-2004/0176985	09/09/2004	Lilly, Ralph B., et al.	705	2	03/18/2004
LN	US-5,845,255	12/01/1998	Mayaud, C.	705	3	10/02/1997
LN	US-5,924,074	07/13/1999	Evans, J. A.	705	3	09/27/1996
LN	US-6,021,392	02/01/2000	Lester, Douglas D., et al.	705	2	12/08/1997
LN	US-6,055,507	04/25/2000	Cunningham, David W.	705	3	08/20/1998
LN	US-6,112,182	08/29/2000	Akers, William R., et al.	705	2	01/16/1996
LN	US-6,315,720	11/13/2001	Williams, Bruce A., et al.	600	300	10/23/2000
LN	US-6,347,329	02/12/2002	Evans, Jae A.	709	202	08/01/2000
LN	US-6,755,784	06/29/2004	Williams, Bruce A., et al.	600	300	03/07/2003

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Foreign Document No	Publication Date	Name of Patentee or Applicant of cited Document	Class	Subclass	T[2]

OTHER DOCUMENTS -- NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T[2]

EXAMINER Lena Najarian DATE CONSIDERED 6-17-05

Substitute Disclosure Statement Form (PTO-1449)

* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. [1] Applicant's unique citation designation number (optional) [2] Applicant is to place a check mark here if English language Translation is attached

IN THE SPECIFICATION

Please amend the paragraph on page 6, starting at line 17 as follows:

If the information is complete at 212, the MD is contacted at 220 to verify receipt and accuracy of the patient's Rx. This contact is recorded in CHIPS. The intake and reimbursement specialist then sends a consent form and a cover letter to the patient at 224. The insurance provider is contacted at 226 to verify coverage and benefits. At 228, a determination is made regarding coverage for the drug. If it is not available, it is determined at 230 whether the patient is willing and able to pay. If not, a process 232 is performed for handling patients who are uninsured or underinsured. In one embodiment, the process is referred to as a NORD process.

Please amend the paragraph on page 6, starting at line 25 as follows:

If the patient is willing and able to pay at 230, the patient is informed of the cost of the product and is given payment options at 234. At 236, once payment is received, the intake reimbursement specialist submits a coverage approval form with the enrollment form to the pharmacy team as notification to process the patient's prescription. If coverage is approved at 228, the intake reimbursement specialist also submits the coverage ~~coveral~~ approval form at 238 with the enrollment form to the pharmacy team as notification to process the patient's prescription. Processing of the prescription is described below.

Please amend the paragraph on page 7, starting at line 18 as follows:

If any disciplinary actions are identified, as referenced at block 278, management of the pharmacy is notified and either approves processing of the prescription with continued monitoring of the physician, or processing of the prescription is not performed, and the physician is noted in the database as unapproved at 284. The MD is contacted by a pharmacist at 286, and informed that the patient's Rx cannot be processed. The enrollment form is then mailed back to the physician with a cover letter reiterating that the prescription cannot be processed at 288. The patient is also sent a letter at 290 indicating that the prescription cannot be processed and the patient is instructed to contact their physician.

Please amend the paragraph on page 8, starting at line 12 as follows:

At 254, the pharmacist enters the prescription order in the database, creating an order number. The pharmacist then verifies at 256 the prescription and attaches a verification label to the hard copy prescription. At 258, a pick ticket is generated for the order and the order is forwarded to the pharmacy for fulfillment. The shipment is confirmed in the database at 260, the original Rx is filed with the pharmacy Rx's in numerical order at 262, and the order is shipped by USPS Express Mail 264. Use of the US mail invokes certain criminal penalties for unauthorized diversion. Optionally, other mail services may be used. Potential changes in the law may also bring criminal penalties into play. Following shipment, the patient is called by the central pharmacy to confirm that the prescription was received.

Please amend the paragraph on page 8, starting at line 29 as follows:

A refill request process begins at ~~302~~ 402 in FIG.s 4A and 4B. There are two different paths for refills. A first path beginning at 404 involves generating a report from the central database of patients with a predetermined number of days or product remaining. A second path beginning at 406 is followed when a patient calls to request an early refill.

Please amend the paragraph on page 9, starting at line 12 as follows:

The second path, beginning at 406 results in a note code being entered into the database on a patient screen indicating an early refill request at 432. At 434, a sensitive drug problem identification and management risk diversion report may be completed, documented and distributed. The pharmacist evaluates the patient's compliance with therapy or possible product diversion, misuse or over-use at 436. In one embodiment, cash payers are also identified. The pharmacist then contacts the prescribing physician to alert them of the situation and confirm if the physician approves of the early refill at 438. If the physician does not approve as indicated at 440, the patient must wait until the next scheduled refill date to receive additional product as indicated at 442, and the process ends at 444.

Please amend the paragraph on page 12, starting at line 5 as follows:

FIG. 12 is a copy of one example voucher request 1200 for medication for use with the NORD application request form of FIG. 10. In addition to patient and physician information, prescription information and diagnosis information is also provided.

1FW 3626

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Dayton T. Reardan et al.	Examiner:	Unknown
Serial No.:	10/322,348	Group Art Unit:	3626
Filed:	December 17, 2002	Docket:	101.031US1
Title:	SENSITIVE DRUG DISTRIBUTION SYSTEM AND METHOD		

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

MS Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

In compliance with the duty imposed by 37 C.F.R. § 1.56, and in accordance with 37 C.F.R. §§ 1.97 *et. seq.*, the enclosed materials are brought to the attention of the Examiner for consideration in connection with the above-identified patent application. Applicants respectfully request that this Supplemental Information Disclosure Statement be entered and the documents listed on the attached Form 1449 be considered by the Examiner and made of record. Pursuant to the provisions of MPEP 609, Applicants request that a copy of the 1449 form, initialed as being considered by the Examiner, be returned to the Applicants with the next official communication.

Pursuant to 37 C.F.R. §1.97(c)(2), Applicants have included the fee of $180.00 as set forth in 37 C.F.R. §1.17(p). Please charge any additional fees or credit any overpayment to Deposit Account No. 19-0743.

10/04/2005 FMETEKI1 00000018 10322348
01 FC:1806 180.00 OP

The Examiner is invited to contact the Applicants' Representative at the below-listed telephone number if there are any questions regarding this communication.

Pursuant to 37 C.F.R. 1.98(a)(2), Applicant believes that copies of cited U.S. Patents and Published Applications are no longer required to be provided to the Office. Notification of this change was provided in the United States Patent and Trademark Office OG Notices dated October 12, 2004. Thus, Applicant has not included copies of any US Patents or Published Applications cited with this submission. Should the Office require copies to be provided, Applicant respectfully requests that notice of such requirement be directed to Applicant's below-signed representative. Applicant acknowledges the requirement to submit copies of foreign patent documents and non-patent literature in accordance with 37 C.F.R. 1.98(a)(2).

Respectfully submitted,

DAYTON T. REARDAN ET AL.

By their Representatives,

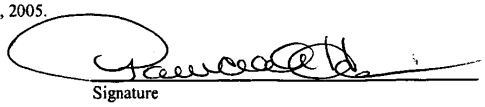
SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.
P.O. Box 2938
Minneapolis, MN 55402
(612) 373-6972

Date 9-29-2005 By 

Bradley A. Forrest
Reg. No. 30,837

CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: MS Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 29th day of September, 2005.

PATRICIA A. HULTMAN
Name

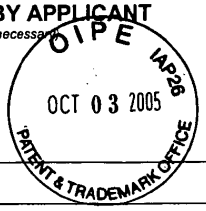

Signature

PTO/SB/08A(10-01)
Approved for use through 10/31/2002. OMB 651-0031
US Patent & Trademark Office: U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use as many sheets as necessary)



Sheet 1 of 1

Complete if Known

Application Number	10/322,348
Filing Date	December 17, 2002
First Named Inventor	Reardan, Dayton
Group Art Unit	3626
Examiner Name	Lena Najarian

Attorney Docket No: 101.031US1

US PATENT DOCUMENTS

Examiner Initial *	USP Document Number	Publication Date	Name of Patentee or Applicant of cited Document	Filing Date If Appropriate

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Foreign Document No	Publication Date	Name of Patentee or Applicant of cited Document	T[2]

OTHER DOCUMENTS -- NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No [1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T[2]
		Preliminary Amendment Pursuant to 37 CFR 1.115 filed with United States Patent and Trademark Office on June 17, 2005 in Application Serial No. 11/104,013 (3 pages).	

EXAMINER **DATE CONSIDERED**

Substitute Disclosure Statement Form (PTO-1449)

* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional) 2 Applicant is to place a check mark here if English language Translation is attached

REMARKS

This responds to the Office Action mailed on June 29, 2005, and the references cited therewith.

Claims 1, 2, 4, 8 and 9 are amended. Claims 1-10 are now pending in this application.

Affirmation of Election

Restriction to one of the following claims was required:

As provisionally elected by Applicant's representative, Richard Schwartz on March 18, 2005, Applicant elects to prosecute the invention of Group I, claims 1-10.

The claims of the non-elected invention, claims 11-31, are hereby canceled. However, Applicant reserves the right to later file continuations or divisions having claims directed to the non-elected inventions.

Drawing Objection

The drawings were objected to as containing reference numbers not identified in the description. The description has been amended to include such reference numbers. Any text added to the description is fully supported by the drawings.

§112 Rejection of the Claims

Claims 1-10 were rejected under 35 U.S.C. § 112, second paragraph, for indefiniteness. Amendments related solely to addressing antecedence have been made.

§101 Rejection of the Claims

Claims 1-10 were rejected under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter. The claims have been amended to clarify that the database is a computer database. Thus, the recited process clearly involves the technological arts.

§103 Rejection of the Claims

Claims 1-2, 4-8 and 10 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Moradi et al. (US 2004/0019794 A1) in view of Lilly et al. (US 2004/0176985 A1) and further in view of Califano et al. (US 2003/0033168 A1). Applicant reserves the right to swear behind each of the references at a later date. The rejection is respectfully traversed.

The Examiner has the burden under 35 U.S.C. § 103 to establish a *prima facie* case of obviousness. *In re Fine*, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988). To do that the Examiner must show that some objective teaching in the prior art or some knowledge generally available to one of ordinary skill in the art would lead an individual to combine the relevant teaching of the references. *Id.*

The *Fine* court stated that:

> Obviousness is tested by "what the combined teaching of the references would have suggested to those of ordinary skill in the art." *In re Keller*, 642 F.2d 413, 425, 208 USPQ 871, 878 (CCPA 1981)). But it "cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion supporting the combination." *ACS Hosp. Sys.*, 732 F.2d at 1577, 221 USPQ at 933. And "teachings of references can be combined *only* if there is some suggestion or incentive to do so." *Id.* (emphasis in original).

The M.P.E.P. adopts this line of reasoning, stating that

> In order for the Examiner to establish a *prima facie* case of obviousness, three base criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *M.P.E.P.* § 2142 (citing *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed.Cir. 1991)).

An invention can be obvious even though the suggestion to combine prior art teachings is not found in a specific reference. *In re Oetiker*, 24 USPQ2d 1443 (Fed. Cir. 1992). At the same time, however, although it is not necessary that the cited references or prior art specifically suggest making the combination, **there must be some teaching somewhere which provides the suggestion or motivation to combine prior art teachings and applies that combination to solve the same or similar problem which the claimed invention addresses** *(emphasis added)*.

One of ordinary skill in the art will be presumed to know of any such teaching. (See, e.g., *In re Nilssen*, 851 F.2d 1401, 1403, 7 USPQ2d 1500, 1502 (Fed. Cir. 1988) and *In re Wood*, 599 F.2d 1032, 1037, 202 USPQ 171, 174 (CCPA 1979)).

The suggestion to combine the reference in the Office Action is not directed to solving the same or similar problem which the claimed invention addresses. Further, there is no teaching in the prior art of application of the combination to solve the same or similar problems which the claimed invention addresses. The Office Action indicates that the motivation for combining the features of Lilly within Moradi would be "to ensure that prescribers have an accurate view of their patients' use of prescription drugs and to help protect professionals from lawsuits and other potential liabilities (para. 58 of Lilly)." The purpose of the presently claimed invention is to track sensitive drugs and reduce the potential for abuse. These are very different problems, and there is no suggestion to apply the combination to solve the same or similar problem which the claimed invention addresses.

Moradi is directed to "securely providing prescription medication to patients." Abstract. Prescriptions are validated, a pharmacy is selected, and the prescribed medicine is delivered to the patient, as described in the Abstract. As the Office Action indicates, Moradi does not disclose that the drug is a sensitive drug, does not disclose the use of a central database for analysis of potential abuse situations, does not confirm that the patient has read educational material and does not generate periodic reports via a central database to evaluate potential abuse patterns. As is evident from these statements, Moradi lacks quite a few elements of the claimed invention, and the suggestion provided to combine Moradi with Lilly is improper, since the purpose stated is not related to the same or similar problem addressed by the claimed invention. It would seem that a suggestion to combine the references, drawing several different elements from each of the references, should be a very strong suggestion. As indicated above, the suggestion does not even apply the combination to solve the same or similar problem, and thus is a very weak suggestion at best.

Even if one were to combine multiple selected elements from each of Moradi and Lilly, an element of the claimed invention is still lacking. The Office Action indicates that the combination does not disclose "confirming with the patient that educational material has been read prior to shipping the drug." Califano is cited as providing this missing element, and that the

motivation for doing so "would have been to ensure that the patient knows about the risks and dangers associated with the drug (para. 43 of Califano)." Califano is directed to obtaining consent for a clinical trial. Abstract. The cited motivation is very different from the purpose of the presently claimed invention, making it very unlikely that one of skill in the art would be motivated to combine the references. As a proper prima facie case of obviousness has not been established, the rejection should be withdrawn.

The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991); MPEP § 2143. The Examiner must avoid hindsight. *In re Bond*, 910 F.2d 831, 834, 15 USPQ2d 1566, 1568 (Fed. Cir. 1990). As indicated above, multiple elements from each of Moradi and Lilly were combined to make the rejection. Because multiple elements from each were used, there is no reasonable expectation of success in making the combination. Further, it points toward the improper use of hindsight, using the claims as a roadmap to make the combination.

A factor cutting against a finding of motivation to combine or modify the prior art is when the prior art teaches away from the claimed combination. A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path the applicant took. *In re Gurley*, 27 F.3d 551, 31 USPQ 2d 1130, 1131 (Fed. Cir. 1994); *United States v. Adams*, 383 U.S. 39, 52, 148 USPQ 479, 484 (1966); *In re Sponnoble*, 405 F.2d 578, 587, 160 USPQ 237, 244 (C.C.P.A. 1969); *In re Caldwell*, 319 F.2d 254, 256, 138 USPQ 243, 245 (C.C.P.A. 1963). Lilly describes the cooperative use of a database by multiple different pharmacies, prescribers and patients, to keep track of the prescription history for a patient. It would be an extremely daunting task to get the cooperation of all these parties. The presently claimed invention uses a central database for analysis of potential abuse situations for distribution of a sensitive drug, not to track all prescriptions for a patient. The ambitious path set forth in Lilly would discourage one of skill in the art from considering using it to solve the problems addressed in the presently claimed invention.

Claims 2, 4-8 and 10 depend from claim 1 and distinguish the references for at least the same reasons as claim 1. In addition, claim 2 recites a central pharmacy. The Office Action

states that Moradi discloses confirming receipt by a telephone call from the central pharmacy. Applicant has reviewed the cited sections of Moradi, and cannot find the concept of a central pharmacy. As the term is used in the present application, a central pharmacy is a pharmacy that exclusively controls the distribution of a sensitive drug. While it may have branches and affiliates, it uses the central database to keep track of all distribution of the sensitive drug. This enables a much improved ability to monitor abuse situations. Patients seeking prescriptions from different doctors will be detected, because the drug is tracked in the central database. Each pharmacy that distributes the sensitive drug also uses the central database. Practically, this is accomplished by obtaining FDA approval that requires the use of the central database. Since any entity that distributes the sensitive drug requires the FDA approval, all must use the same central database. The term central database is used to encompass any real or virtual manifestation of a central database that facilitates evaluation of potential abuse patterns for distribution of the sensitive drug.

Claim 3 was rejected under 35 U.S.C. § 103(a) as being unpatentable over Moradi et al. (US 2004/0019794 A1) in view of Lilly et al. (US 2004/0176985 A1) in view of Califano et al. (US 2003/0033168 A1) as applied to claim 1 above, and further in view of Andreasson et al. (US 2003/0160698 A1). Applicant further reserves the right to swear behind each of the references. This rejection is also respectfully traversed. Claim 3 depends from claim 1 and distinguishes from the references at least in the same manner as claim 1. Andreasson et al. describe monitoring distribution of medical products within a facility as indicated by the title. Claim 3 recites launching an investigation of lost shipments, which implies that the shipments have already left a facility. Monitoring within the facility would not address a lost shipment that has left the facility. As such, there is no showing of a reasonable likelihood of success in making the combination. As a proper prima facie case of obviousness has not been established, the rejection should be withdrawn.

Claim 9 was rejected under 35 U.S.C. § 103(a) as being unpatentable over Moradi et al. (US 2004/0019794 A1) in view of Lilly et al. (US 2004/0176985 A1) in view of Califano et al. (US 2003/0033168 A1) as applied to claim 1 above, and further in view of Mayaud (U.S. Patent

No. 5,845,255). Claim 9 depends from claim 1 and distinguishes from the references at least in the same manner as claim 1. The Office Action cites a motivation to combine the four references as "to reduce the reluctance of physicians to prescribe new drugs by providing them with the latest information about the drugs". This motivation has nothing to do with the problems addressed by the currently claimed invention as identified above. As a proper prima facie case of obviousness has not been established, the rejection should be withdrawn.

CONCLUSION

Applicant respectfully submits that the claims are in condition for allowance, and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicant's attorney at (612) 373-6972 to facilitate prosecution of this application.

If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

Respectfully submitted,
DAYTON T. REARDAN ET AL.
By their Representatives,
SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.
P.O. Box 2938
Minneapolis, MN 55402
(612) 373-6972

Date 9-29-2005 By _____
Bradley A. Forrest
Reg. No. 30,837

CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: Mail Stop Amendment, Commissioner of Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 29th day of September, 2005.

PATRICIA A. HULTMAN _____

Name Signature

IN THE CLAIMS

Please amend the claims as follows:

1. (Currently Amended) A method of distributing a sensitive drug, the method comprising:

receiving prescription requests from a medical doctor containing information identifying a ~~the~~ patient, the sensitive drug, and various credentials of the doctor;

entering the information into a central computer database for analysis of potential abuse situations;

checking the credentials of the doctor;

confirming with the patient that educational material has been read prior to shipping the sensitive drug;

confirming receipt of the sensitive drug; and

generating periodic reports via the central computer database to evaluate potential abuse patterns.

2. (Currently Amended) The method of claim 1 wherein receipt of the sensitive drug is confirmed by telephone call from a ~~the~~ central pharmacy to the patient.

3. (Original) The method of claim 1 and further comprising launching an investigation of lost shipments.

4. (Currently Amended) The method of claim 1 and further comprising recording the confirmation with the patient that the educational material has been read in the central computer database.

5. (Original) The method of claim 1 and further comprising verifying the patient's home address.

6. (Original) The method of claim 1 and further comprising recording a designee identified by the patient to receive the sensitive drug.

7. (Original) The method of claim 1 and further comprising establishing a delivery date.

8. (Currently Amended) The method of claim 1 wherein prescription refills requested prior to an anticipated date are questioned by a ~~the~~ pharmacist.

9. (Currently Amended) The method of claim 1 and further comprising shipping comprehensive printed materials to the doctor ~~physician~~ if the doctor ~~physician~~ is a first time prescriber of the sensitive drug.

10. (Original) The method of claim 1 wherein the credentials of the doctor comprise DEA (Drug Enforcement Agency) and state license numbers.

11. (Withdrawn) A method of monitoring potential abuse of a sensitive drug by use of an exclusive central database, the method comprising:

generating queries of prescription information from a database containing selected information for all prescriptions of the sensitive drug, wherein the queries comprise prescriptions by physician specialty, prescriptions by patient name, prescriptions by frequency and prescriptions by dose.

12. (Withdrawn) The method of claim 11 and further comprising running multiple predetermined reports based on data in the exclusive central database.

13. (Withdrawn) The method of claim 12 wherein such reports are selected from groups of reports consisting of sales, regulatory, quality assurance, pharmacy, inventory, reimbursement, patient care, and drug information.

14. (Withdrawn) The method of claim 13 wherein sales reports are selected from the group consisting of prescriptions by zip code, prescriptions by physician by zip code and total dollars by zip code.

15. (Withdrawn) The method of claim 13 wherein regulatory reports are selected from the group consisting of number of physician registries, number of denied physician registries and reasons, number of completed patient registries, number of problem identification, number of cycle counts performed.

16. (Withdrawn) The method of claim 13 wherein inventory reports are selected from the group consisting of number of returned products and reasons, number of outdated bottles of product, inventory counts of consignment and production inventory, number of units received, and lots received.

17. (Withdrawn) The method of claim 13 wherein patient care reports are selected from the group consisting of number of adverse events, number of dosing problems and type, number of noncompliance episodes and reason, number of patients counseled and reason, number of discontinued and reason, number of patients referred to physician and reason, number of active patients, number of new patents, number of restart patients, and number of discontinued patients and reason.

18. (Withdrawn) The method of claim 13 wherein selected reports are run weekly, monthly or quarterly.

19. (Withdrawn) A method of obtaining FDA (Food and Drug Administration) approval for a sensitive drug, the method comprising:

determining current and anticipated patterns of potential abuse of the sensitive drug;

selecting multiple controls for distribution by an exclusive central pharmacy maintaining a central database, the controls selected from the group consisting of communicating prescriptions from a physician to the central pharmacy, identifying the physicians name, license

and DEA (Drug Enforcement Agency) registration information, verifying the prescription; obtaining patient information, verifying the physician is eligible to prescribe the sensitive drug by consulting the National Technical Information Services to determine whether the physician has an active DEA number and check on whether any actions are pending against the physician, provide comprehensive printed materials to the physician, contacting the patient's insurance company if any, verifying patient registry information, providing comprehensive education information to the patient, verifying the patient has reviewed the educational materials, verifying the home address of the patient, shipping via US postal service or similar shipping service, receiving the name of an at least 18 year old designee to receive the drug, confirming receipt of an initial shipment of the drug to the patient, returning the drug to the pharmacy after two attempts to deliver, launching an investigation when a shipment is lost, shipping to another pharmacy for delivery, requiring manufacture at a single location, releasing inventory in a controlled manner to the central pharmacy, questioning early refills, flagging repeat instances of lost, stolen, destroyed or spilled prescriptions, limiting the prescription to a one month supply, requiring rewriting of the prescription periodically, making the database available to the DEA for checking for abuse patterns in the data, cash payments, inappropriate questions; and

negotiating with the FDA by adding further controls from the group until approval is obtained.

20. (Withdrawn) The method of claim 19 wherein initially selected controls comprise communicating prescriptions from a physician to the central pharmacy, identifying the physicians name, license and DEA registration information, verifying the prescription; obtaining patient information, verifying the physician is eligible to prescribe the sensitive drug by consulting the National Technical Information Services to determine whether the physician has an active DEA number and check on whether any actions are pending against the physician, verifying patient registry information, providing comprehensive education information to the patient, verifying the patient has reviewed the educational materials, verifying the home address of the patient, shipping via US postal service, confirming receipt of an initial shipment of the drug to the patient releasing inventory in a controlled manner to the central pharmacy, flagging

repeat instances of lost, stolen, destroyed or spilled prescriptions, and making the database available to the DEA for checking for abuse patterns in the data.

21. (Withdrawn) The method of claim 19 wherein the sensitive drug is a scheduled drug in Schedule II-V.

22. (Withdrawn) A method of distributing a sensitive drug, the method comprising:

determining current and anticipated patterns of potential abuse of the sensitive drug;

selecting multiple controls for distribution of the sensitive drug; and

adding additional controls to provide sufficient reassurance to a governmental regulatory body that the sensitive drug distribution can be adequately controlled in order to obtain marketing approval by the governmental regulatory body.

23. (Withdrawn) The method of claim 22 wherein the system allows marketing of a drug product pursuant to FDA subpart 4 regulation embodied in Title 21, CFR Part 314.

24. (Withdrawn) The method of claim 22 wherein distribution of the sensitive drug is controlled by a central distribution center sufficient to allow the DEA (Drug Enforcement Agency) to approve the central distribution center.

25. (Withdrawn) The method of claim 22 wherein the governmental regulatory body comprises a state regulatory agency that approves distribution of the sensitive drug in a state.

26. (Withdrawn) A method to control abuse of a sensitive drug by controlling the distribution thereof via an exclusive central pharmacy that maintains a central database that tracks all prescriptions of said sensitive drug and analyzes for potential abuse situations, the method comprising:

determining current and anticipated patterns of potential prescription abuse of said sensitive drug from periodic reports generated by the central database based on prescription

request data from a medical doctor, wherein said request data contain information identifying the patient, the drug prescribed, and credentials of the doctor; and

selecting multiple controls for distribution by said exclusive central pharmacy, the controls selected from the group consisting of communicating prescriptions from a physician to the central pharmacy; identifying the physicians name, license, and DEA (Drug Enforcement Agency) registration information; verifying the prescription; obtaining patient information; verifying the physician is eligible to prescribe the sensitive drug by consulting the National Technical Information Services to determine whether the physician has an active DEA number and to check on whether any actions are pending against the physician; providing comprehensive printed materials to the physician; contacting the patient's insurance company if any; verifying patient registry information; providing comprehensive education information to the patient; verifying the patient has reviewed the educational materials; verifying the home address of the patient; shipping via US postal service or similar shipping service; receiving the name of an at least 18 year old designee to receive the drug; confirming receipt of an initial shipment of the drug to the patient returning the drug to the pharmacy after two attempts to deliver; launching an investigation when a shipment is lost; shipping to another pharmacy for delivery; requiring manufacture at a single location; releasing inventory in a controlled manner to the central pharmacy; questioning early refills; flagging repeat instances of lost, stolen, destroyed, or spilled prescriptions; limiting the prescription to a one month supply; requiring rewriting of the prescription periodically; and making the database available to the DEA for checking for abuse patterns in the data, for cash payments, and for inappropriate questions.

27. (Withdrawn) The method of claim 26 wherein initially selected controls comprise:

communicating prescriptions from a physician to the central pharmacy; identifying the physicians name, license, and DEA registration information; verifying the prescription; obtaining patient information; verifying the physician is eligible to prescribe the sensitive drug by consulting the National Technical Information Services to determine whether the physician has an active DEA number and to check on whether any actions are pending against the physician; verifying patient registry information; providing comprehensive education information to the patient; verifying the patient has reviewed the educational materials; verifying the home address

of the patient; shipping via US postal service; confirming receipt of an initial shipment of the drug to the patient; releasing inventory in a controlled manner to the central pharmacy; flagging repeat instances of lost, stolen, destroyed, or spilled prescriptions; and making the database available to the DEA for checking for abuse patterns in the data.

28. (Withdrawn) The method of claim 26 which further comprises consulting a separate database to verify that the medical doctor is eligible to prescribe the drug.

29. (Withdrawn) A method to control abuse of gamma hydroxy butyrate (GHB) by controlling the distribution of GHB via an exclusive central pharmacy that maintains a central database that tracks all prescriptions of GHB and analyzes for potential abuse situations, the method comprising:

determining current and anticipated patterns of potential prescription abuse of GHB from periodic reports generated by the central database based on prescription request data from a medical doctor, wherein said request data contain information identifying the patient, GHB as the drug prescribed, and credentials of the doctor; and

selecting multiple controls for distribution by said exclusive central pharmacy, the controls selected from the group consisting of communicating prescriptions from a physician to the central pharmacy; identifying the physicians name, license, and DEA (Drug Enforcement Agency) registration information; verifying the prescription; obtaining patient information; verifying the physician is eligible to prescribe the sensitive drug by consulting the National Technical Information Services to determine whether the physician has an active DEA number and to check on whether any actions are pending against the physician; providing comprehensive printed materials to the physician; contacting the patient's insurance company if any; verifying patient registry information; providing comprehensive education information to the patient; verifying the patient has reviewed the educational materials; verifying the home address of the patient; shipping via US postal service or similar shipping service; receiving the name of an at least 18 year old designee to receive the drug; confirming receipt of an initial shipment of the drug to the patient returning the drug to the pharmacy after two attempts to deliver; launching an investigation when a shipment is lost; shipping to another pharmacy for delivery; requiring

manufacture at a single location; releasing inventory in a controlled manner to the central pharmacy; questioning early refills; flagging repeat instances of lost, stolen, destroyed, or spilled prescriptions; limiting the prescription to a one month supply; requiring rewriting of the prescription periodically; and making the database available to the DEA for checking for abuse patterns in the data, for cash payments, and for inappropriate questions.

30. (Withdrawn) The method of claim 29 wherein initially selected controls comprise:

communicating prescriptions from a physician to the central pharmacy; identifying the physicians name, license, and DEA registration information; verifying the prescription; obtaining patient information; verifying the physician is eligible to prescribe the sensitive drug by consulting the National Technical Information Services to determine whether the physician has an active DEA number and to check on whether any actions are pending against the physician; verifying patient registry information; providing comprehensive education information to the patient; verifying the patient has reviewed the educational materials; verifying the home address of the patient; shipping via US postal service; confirming receipt of an initial shipment of the drug to the patient; releasing inventory in a controlled manner to the central pharmacy; flagging repeat instances of lost, stolen, destroyed, or spilled prescriptions; and making the database available to the DEA for checking for abuse patterns in the data.

31. (Withdrawn) The method of claim 29 which further comprises consulting a separate database to verify that the medical doctor is eligible to prescribe the drug.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Dayton T. Reardan et al.	Examiner: Lena Najarian
Serial No.:	10/322,348	Group Art Unit: 3626
Filed:	December 17, 2002	Docket No.: 101.031US1
Title:	SENSITIVE DRUG DISTRIBUTION SYSTEM AND METHOD	

RESPONSE TO RESTRICTION REQUIREMENT AND AMENDMENT AND RESPONSE UNDER 37 CFR § 1.111

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

This responds to the Office Action mailed on June 29, 2005. Please amend the above-identified patent application as follows.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Dayton T. Reardan et al.

Title: SENSITIVE DRUG DISTRIBUTION SYSTEM AND METHOD

Docket No.: 101.031US1
Filed: December 17, 2002
Examiner: Lena Najarian

Serial No.: 10/322,348
Due Date: September 29, 2005
Group Art Unit: 3626

MS Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

We are transmitting herewith the following attached items (as indicated with an "X"):

X Return postcard.
X Response to Restriction Requirement and Amendment and Response Under 37 CFR 1.111 (19 pgs.).
X Supplemental Information Disclosure Statement (2 pgs.), Form 1449 (1 pg.), and copies of 1 cited document.
X Check in the amount of $180.00 to cover the fee for consideration of Information Disclosure Statement under 97(c).

If not provided for in a separate paper filed herewith, Please consider this a PETITION FOR EXTENSION OF TIME for sufficient number of months to enter these papers and please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.
Customer Number 21186

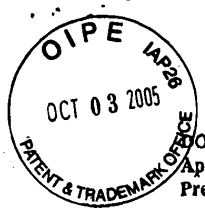
By: _____
Atty: Bradley A. Forrest
Reg. No. 30,837

CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: MS Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 29th day of September, 2005.

PATRICIA A.HULTMAN
Name

_____
Signature

SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.
(GENERAL)



DOCKET NO.: CELG-0471
Application No.: 11/104,013
Preliminary Amendment - First Action Not Yet Received

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Marc Elsayed and Bruce Williams

Confirmation No.: **Not yet assigned**

Application No.: **11/104,013**

Group Art Unit: **Not yet assigned**

Filing Date: **April 12, 2005**

Examiner: **Not yet assigned**

For: **Methods For Delivering A Drug To A Patient While Preventing The Exposure Of A Foetus Or Other Contraindicated Individual To The Drug**

DATE OF DEPOSIT: June 17, 2005

I HEREBY CERTIFY THAT THIS PAPER IS BEING DEPOSITED WITH THE UNITED STATES POSTAL SERVICE AS FIRST CLASS MAIL, POSTAGE PREPAID, ON THE DATE INDICATED ABOVE AND IS ADDRESSED TO THE COMMISSIONER FOR PATENTS, P.O. BOX 1450, ALEXANDRIA, VA 22313-1450.

Angela Verrecchio

TYPED NAME: Angela Verrecchio
REGISTRATION NO.: 54,510

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

PRELIMINARY AMENDMENT PURSUANT TO 37 CFR § 1.115

Preliminary to examination of the above-captioned patent application, please amend the application as follows:

☐ **Amendments to the Specification** begin on page of this paper.

☒ **Amendments to the Claims** are reflected in the listing of the claims which begins on page 2 of this paper.

☐ **Amendments to the Drawings** begin on page of this paper and include an attached replacement sheet.

☒ **Remarks** begin on page 3 of this paper.

DOCKET NO.: CELG-0471 **PATENT**
Application No.: 11/104,013
Preliminary Amendment - First Action Not Yet Received

REMARKS

Claims 1-10 have been canceled, and claims 11-14 added. Support for these claims can be found throughout the specification as originally filed. No new matter has been added. Consideration and allowance of all pending claims is respectfully requested.

Date: June 17, 2005

Angela Verrecchio
Registration No. 54,510

Woodcock Washburn LLP
One Liberty Place - 46th Floor
Philadelphia PA 19103
Telephone: (215) 568-3100
Facsimile: (215) 568-3439

DOCKET NO.: CELG-0471 **PATENT**
Application No.: 11/104,013
Preliminary Amendment - First Action Not Yet Received

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

Claims 1-10 (Canceled)

11. (New) A method of distributing a drug, comprising:

a. receiving data from a prescriber for the drug, said data comprising information identifying a patient, the drug, and the prescriber;

b. entering the data into a computer database;

c. confirming the ability of the prescriber to prescribe the drug;

d. confirming that patient educational materials have been read; and

e. generating periodic reports regarding distribution of the drug via the computer database.

12. (New) The method of claim 11, further comprising the step of recording the confirmation that the educational materials have been read in the database.

13. (New) The method of claim 11, further comprising the step of blocking inappropriate refill requests.

14. (New) The method of claim 11, further comprising the step of shipping educational materials to the prescriber.

PATENT APPLICATION FEE DETERMINATION RECORD
Effective January 1, 2003

Application or Docket Number: 10/322348

CLAIMS AS FILED - PART I

	(Column 1)	(Column 2)
TOTAL CLAIMS	25	
FOR	NUMBER FILED	NUMBER EXTRA
TOTAL CHARGEABLE CLAIMS	25 minus 20=	* 5
INDEPENDENT CLAIMS	4 minus 3 =	* 1
MULTIPLE DEPENDENT CLAIM PRESENT		☐

* If the difference in column 1 is less than zero, enter "0" in column 2

SMALL ENTITY TYPE ☐		OR	OTHER THAN SMALL ENTITY	
RATE	FEE		RATE	FEE
BASIC FEE	$375	OR	BASIC FEE	$750
X$ 9=	45	OR	X$18=	
X42=	42	OR	X84=	
+140=		OR	+280=	
TOTAL	462	OR	TOTAL	

CLAIMS AS AMENDED - PART II

10404

AMENDMENT A

	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA
Total	* 31	Minus	** 25	= 6
Independent	* 6	Minus	*** 4	= 2
FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM				☐

SMALL ENTITY		OR	OTHER THAN SMALL ENTITY	
RATE	ADDITIONAL FEE		RATE	ADDITIONAL FEE
X$ 9=	54	OR	X$18=	
X42=	86	OR	X84=	
+140=		OR	+280=	
TOTAL ADDIT. FEE	140	OR	TOTAL ADDIT. FEE	

DN 10/3/05

AMENDMENT B

	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA
Total	* 31	Minus	** 25	=
Independent	* 6	Minus	*** 4	= 1
FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM				☐

RATE	ADDITIONAL FEE		RATE	ADDITIONAL FEE
X$ 9=		OR	X$18=	
X42=	1	OR	X84=	1
+140=		OR	+280=	
TOTAL ADDIT. FEE		OR	TOTAL ADDIT. FEE	

AMENDMENT C

	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA
Total	*	Minus	**	=
Independent	*	Minus	***	=
FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM				☐

RATE	ADDITIONAL FEE		RATE	ADDITIONAL FEE
X$ 9=		OR	X$18=	
X42=		OR	X84=	
+140=		OR	+280=	
TOTAL ADDIT. FEE		OR	TOTAL ADDIT. FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20."
*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3."
The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.

Search Notes	Application/Control No.	Applicant(s)/Patent under Reexamination
	10/322,348	REARDAN ET AL.
	Examiner	Art Unit
	Lena Najarian	3626

SEARCHED			
Class	Subclass	Date	Examiner
	updated previous seaches	12/12/2005	LN

INTERFERENCE SEARCHED			
Class	Subclass	Date	Examiner

SEARCH NOTES (INCLUDING SEARCH STRATEGY)		
	DATE	EXMR

Index of Claims

Application/Control No.	Applicant(s)/Patent under Reexamination
10/322,348	REARDAN ET AL.
Examiner	**Art Unit**
Lena Najarian	3626

√	Rejected	–	(Through numeral) Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

Claim		Date
Final	Original	12/12/05
	1	√
	2	|
	3	|
	4	|
	5	|
	6	|
	7	|
	8	|
	9	|
	10	√
	11	-
	12	|
	13	|
	14	|
	15	|
	16	|
	17	|
	18	|
	19	|
	20	|
	21	|
	22	|
	23	|
	24	|
	25	|
	26	|
	27	|
	28	|
	29	|
	30	|
	31	-
	32	
	33	
	34	
	35	
	36	
	37	
	38	
	39	
	40	
	41	
	42	
	43	
	44	
	45	
	46	
	47	
	48	
	49	
	50	

Claim		Date
Final	Original	
	51	
	52	
	53	
	54	
	55	
	56	
	57	
	58	
	59	
	60	
	61	
	62	
	63	
	64	
	65	
	66	
	67	
	68	
	69	
	70	
	71	
	72	
	73	
	74	
	75	
	76	
	77	
	78	
	79	
	80	
	81	
	82	
	83	
	84	
	85	
	86	
	87	
	88	
	89	
	90	
	91	
	92	
	93	
	94	
	95	
	96	
	97	
	98	
	99	
	100	

Claim		Date
Final	Original	
	101	
	102	
	103	
	104	
	105	
	106	
	107	
	108	
	109	
	110	
	111	
	112	
	113	
	114	
	115	
	116	
	117	
	118	
	119	
	120	
	121	
	122	
	123	
	124	
	125	
	126	
	127	
	128	
	129	
	130	
	131	
	132	
	133	
	134	
	135	
	136	
	137	
	138	
	139	
	140	
	141	
	142	
	143	
	144	
	145	
	146	
	147	
	148	
	149	
	150	

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/322,348	12/17/2002	Dayton T. Reardan	101.031US1	5446

21186 7590 12/29/2005

SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH
1600 TCF TOWER
121 SOUTH EIGHT STREET
MINNEAPOLIS, MN 55402

EXAMINER	
NAJARIAN, LENA	
ART UNIT	**PAPER NUMBER**
3626	

DATE MAILED: 12/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 10/03)

Office Action Summary	Application No.	Applicant(s)	
	10/322,348	REARDAN ET AL.	
	Examiner	Art Unit	
	Lena Najarian	3626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 03 October 2005.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-10 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-10 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 20051003.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Notice to Applicant

1. This communication is in response to the amendment filed 10/3/05.

Claims 1-10 are pending. Claims 1, 2, 4, 8, and 9 have been amended.

Drawings

2. The objection to the drawings is hereby withdrawn due to the amendment filed 10/3/05.

Claim Rejections - 35 USC § 112

3. The rejection of claims 1-10 under 35 U.S.C. 112, second paragraph, is hereby withdrawn due to the amendment filed 10/3/05.

Claim Rejections - 35 USC § 101

4. The rejection of claims 1-10 under 35 U.S.C. 101 is hereby withdrawn due to the amendment filed 10/3/05.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1-2, 4-8, and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moradi et al. (US 2004/0019794 A1) in view of Lilly et al. (US 2004/0176985 A1) and further in view of Califano et al. (US 2003/0033168 A1).

(A) The amendments to claims 1, 2, 4, and 8 were apparently made to overcome 112, 2nd paragraph and/or 101 issues set forth in the prior Office Action. However, these changes do not affect the scope and breadth of the claims as originally presented and/or in the manner in which the claims were interpreted by the Examiner when applying prior art within the previous Office Action. As such, these claims are rejected under the same rationale given in the prior Office Action, and incorporated herein.

(B) Claims 5-7 and 10 have not been amended and are rejected for the same reasons given in the previous Office Action, and incorporated herein.

7. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Moradi et al. (US 2004/0019794 A1) in view of Lilly et al. (US 2004/0176985 A1) in view of Califano et al. (US 2003/0033168 A1) as applied to claim 1 above, and further in view of Andreasson et al. (US 2003/0160698 A1).

(A) Claim 3 has not been amended and is rejected for the same reasons given in the previous Office Action, and incorporated herein.

8. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Moradi et al. (US 2004/0019794 A1) in view of Lilly et al. (US 2004/0176985 A1)

in view of Califano et al. (US 2003/0033168 A1) as applied to claim 1 above, and further in view of Mayaud (5,845,255).

(A) The amendment to claim 9 was apparently made to overcome 112, 2nd paragraph issues set forth in the prior Office Action. However, these changes do not affect the scope and breadth of the claim as originally presented and/or in the manner in which the claim was interpreted by the Examiner when applying prior art within the previous Office Action. As such, this claim is rejected under the same rationale given in the prior Office Action, and incorporated herein.

Response to Arguments

9. Applicant's arguments filed 10/3/05 have been fully considered but they are not persuasive. Applicant's arguments will be addressed hereinbelow in the order in which they appear in the response filed 10/3/05.

(1) Applicant argues at page 15 that the suggestion to combine the reference in the Office Action is not directed to solving the same or similar problem which the claimed invention addresses.

(2) Applicant argues at page 16 that Califano is directed to obtaining consent for a clinical trial and that the cited motivation is very different from the purpose of the presently claimed invention, making it very unlikely that one of skill in the art would be motivated to combine the references.

(3) Applicant argues at page 16 that multiple elements from each of Moradi and Lilly were combined to make the rejection and that there is no reasonable

expectation of success in making the combination. Further, it points toward the improper use of hindsight, using the claims as a roadmap to make the combination.

(4) Applicant argues at page 16 that the prior art teaches away from the claimed combination. Lilly describes the cooperative use of a database by multiple different pharmacies, prescribers and patients, to keep track of the prescription history for a patient. It would be an extremely daunting task to get the cooperation of all these parties. The ambitious path set forth in Lilly would discourage one of skill in the art from considering using it to solve the problems addressed in the presently claimed invention.

(5) Applicant argues at page 17 that Applicant has reviewed the cited sections of Moradi and cannot find the concept of a central pharmacy. As the term is used in the present application, a central pharmacy is a pharmacy that exclusively controls the distribution of a sensitive drug.

(6) Applicant argues at page 17 that Andreasson et al. describe monitoring distribution of medical products within a facility as indicated by the title. Claim 3 recites launching an investigation of lost shipments, which implies that the shipments have already left a facility. Monitoring within the facility would not address a lost shipment that has left the facility. As such, there is no showing of a reasonable likelihood of success in making the combination.

(7) Applicant argues at page 18 that the Office Action cites a motivation to combine the four references "to reduce the reluctance of physicians to prescribe new drugs by providing them with the latest information about the drugs." This

motivation has nothing to do with the problems addressed by the currently claimed invention as identified above.

(A) As per the first argument, in response to applicant's argument that the suggestion to combine Moradi with Lilly is improper since the purpose stated is not related to the same or similar problem addressed by the claimed invention, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

In addition, the Examiner respectfully submits that Applicant has failed to fully consider the Lilly reference. At para. 12, Lilly discloses reducing misused and abused prescriptions and the need for better tracking and management of prescriptions. As such, it is readily apparent that Lilly and Applicant's invention solve the same or similar problem.

(B) As per the second argument, in response to applicant's argument that Califano is directed to obtaining consent for a clinical trial, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

In response to applicant's argument that the cited motivation is very different from the purpose of the presently claimed invention, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

(C) As per the third argument, in response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

(D) As per the fourth argument, whether or not the Lilly reference discloses tracking all prescriptions for a patient and not just sensitive drugs is immaterial to the issue at hand, especially since Lilly is directed to a tracking system for controlled substances. In addition, it is irrelevant whether the applied references contain elements in addition to or beyond those claimed by Applicant, and not required by Applicant, insofar as Applicant uses the word "comprising" at end of each preamble of the pending claims. The Examiner understands this claim language to mean "having at least". If Applicant desires to claim an invention that is exclusively limited to only those elements specifically recited in the claims,

the Examiner suggests that Applicant use the term "consisting of" rather than "comprising".

(E) As per the fifth argument, in response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., "a central pharmacy is a pharmacy that exclusively controls the distribution of a sensitive drug") are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

(F) As per the sixth argument, the Examiner respectfully submits that para. 79 of Andreasson discloses tracking the delivery of medical products and immediately notifying healthcare workers and/or administrators of any missing medical products so that they make take appropriate action to recover and/or investigate the missing medical products. Para. 43 discloses comparing the information of the medical products shipped to the healthcare facility with the information received from the pharmacy terminal to verify that all of the medical products shipped to the healthcare facility were received by the pharmacy. As such, it is readily apparent that Andreasson teaches launching an investigation of lost shipments.

(G) As per the seventh argument, in response to applicant's argument that the motivation to combine the four references has nothing to do with the problems addressed by the currently claimed invention, the fact that applicant has recognized another advantage which would flow naturally from following the

suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

Conclusion

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lena Najarian whose telephone number is 571-272-7072. The examiner can normally be reached on Monday - Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Thomas can be reached on 571-272-6776. The

fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

In
12-12-05

JOSEPH THOMAS
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER

PTO/SB/08A(10-01)
Approved for use through 10/31/2002. OMB 651-0031
US Patent & Trademark Office: U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use as many sheets as necessary)

Sheet 1 of 1

Complete if Known	
Application Number	10/322,348
Filing Date	December 17, 2002
First Named Inventor	Reardan, Dayton
Group Art Unit	3626
Examiner Name	Lena Najarian
Attorney Docket No: 101.031US1	

US PATENT DOCUMENTS				
Examiner Initial *	USP Document Number	Publication Date	Name of Patentee or Applicant of cited Document	Filing Date If Appropriate

FOREIGN PATENT DOCUMENTS				
Examiner Initials*	Foreign Document No	Publication Date	Name of Patentee or Applicant of cited Document	T[2]

OTHER DOCUMENTS -- NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No [1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T[2]
LN		Preliminary Amendment Pursuant to 37 CFR 1.115 filed with United States Patent and Trademark Office on June 17, 2005 in Application Serial No. 11/104,013 (3 pages).	

EXAMINER Lena Najarian DATE CONSIDERED 12-9-05

Substitute Disclosure Statement Form (PTO-1449)

* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional) 2 Applicant is to place a check mark here if English language Translation is attached

REQUEST FOR CONTINUED EXAMINATION (RCE) TRANSMITTAL		
Subsection (b) of 35 U.S.C. § 132, effective on May 29, 2000, provides for continued examination of an utility or plant application filed on or after June 8, 1995. See The American Inventors Protection Act of 1999 (AIPA).	*Application Number*	10/322,348
	Filing Date	December 17, 2002
	First Named Inventor	Dayton T. Reardan
	Group Art Unit	3626
	Examiner Name	Lena Najarian
	Attorney Docket Number	101.031US1
	Customer No.	21186

This is a Request for Continued Examination (RCE) under 37 CFR § 1.114 of the above-identified application entitled SENSITIVE DRUG DISTRIBUTION SYSTEM AND METHOD.
Submission required under 37 C.F.R. § 1.114

1. __ Consider the amendment(s)/reply under 37 C.F.R. § 1.116 previously filed on .

2. __ Consider the arguments in the Appeal Brief or Reply Brief previously filed on .

3. X Amendment Under 37 CFR § 1.116 (11 pages) is enclosed.

4. __ New power of attorney (pages) is enclosed.

5. X Information Disclosure Statement is enclosed (2 pages), with:
   a. Form 1449 (1 pages)
   b. Copies of IDS Citations (1)

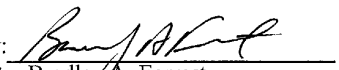
6. X Please charge Deposit Account 19-0743 in the amount of $395.00 to pay the RCE filing fee required under C.F.R. § 1.17(e).

7. X **The Commissioner is hereby authorized to credit overpayments or charge any fees set forth in 37 CFR §§ 1.16 through 1.18 to Deposit Account No. 19-0743.**

8. __ Petition for Extension of Time in the prior application (1 page) is enclosed along with authorization to charge Deposit Account 19-0743 in the amount of to pay the extension fee.

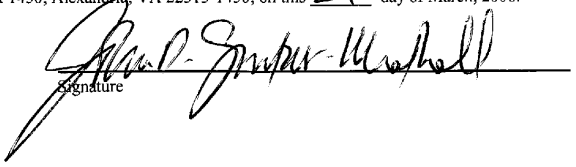
9. X Others: Communication Concerning Related Applications (2 pgs.).

SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.

By: 
Atty: Bradley A. Forrest
Reg. No. 30,837

CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being filed using the USPTO's electronic filing system EFS-Web, and is addressed to: Mail Stop RCE, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 24 day of March, 2006.

John Gustav-Wrathall
Name


Signature

EXPEDITED PROCEDURE – EXAMINING GROUP 3626

S/N 10/322,348 **PATENT**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Dayton T. Reardan et al.	Examiner: Lena Najarian
Serial No.:	10/322,348	Group Art Unit: 3626
Filed:	December 17, 2002	Docket No.: 101.031US1
Title:	SENSITIVE DRUG DISTRIBUTION SYSTEM AND METHOD	

AMENDMENT & RESPONSE UNDER 37 C.F.R. 1.116

Mail Stop RCE
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

In response to the Final Office Action mailed December 29, 2005, please amend the application as follows:

REMARKS

This responds to the Office Action mailed on December 29, 2005.

New claims 32 - 37 have been added. Claims 1-10 and 32-37 are now pending in this application.

New claims 32 - 37 distinguish the references for reasons similar to those provided below regarding claim 1. In addition, claim 32 recites the use of an exclusive central pharmacy and an exclusive central database to track distribution and potential diversion of the sensitive drug.

In paragraph E of the Response to Arguments section of the Final Office Action, it is stated that the then pending claims did not recite that a central pharmacy is a pharmacy that exclusively controls distribution of a sensitive drug. New claims 32 - 37 have been written based on claim 1 to include language that expressly addresses exclusivity of distribution. Such claims also address exclusivity of the central database. None of the references cited are believed to address such exclusivities. The original claims are also believed to describe aspects of centralization, as described in the previous response. The submission of new claims 32-37 is not an admission otherwise.

§103 Rejection of the Claims

Claims 1-2, 4-8 and 10 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Moradi et al. (US 2004/0019794 A1) in view of Lilly et al. (US 2004/0176985 A1) and further in view of Califano et al. (US 2003/0033168 A1).

The suggestion to combine the reference in the Office Action is not directed to solving the same or similar problem which the claimed invention addresses. Further, there is no teaching in the prior art of application of the combination to solve the same or similar problems which the claimed invention addresses. The Office Action indicates that the motivation for combining the features of Lilly within Moradi would be "to ensure that prescribers have an accurate view of their patients' use of prescription drugs and to help protect professionals from lawsuits and other

potential liabilities (para. 58 of Lilly)." As stated in the response to arguments section A of the Final Office Action, Lilly also describes reducing misused and abused prescriptions and the need for better tracking and management of prescription in Paragraph 12. However, the purpose for such reductions is related to abuse by the patient, and not abuse of a sensitive drug as claimed. The purpose of the presently claimed invention is to track sensitive drugs and reduce the potential for abuse, such as diversion of the sensitive drug.

Moradi is directed to "securely providing prescription medication to patients." Abstract. In other words, it is directed to making sure that the patient receives the medication, not preventing abuse, such as further distribution by the patient. Prescriptions are validated, a pharmacy is selected, and the prescribed medicine is delivered to the patient, as described in the Abstract. As the Office Action indicates, Moradi does not disclose that the drug is a sensitive drug, does not disclose the use of a central database for analysis of potential abuse situations, does not confirm that the patient has read educational material and does not generate periodic reports via a central database to evaluate potential abuse patterns. As is evident from these statements, Moradi lacks quite a few elements of the claimed invention, and the suggestion provided to combine Moradi with Lilly is improper, since the purpose stated is not related to the same or similar problem addressed by the claimed invention. It would seem that a suggestion to combine the references, drawing several different elements from each of the references, should be a very strong suggestion.

Even if one were to combine multiple selected elements from each of Moradi and Lilly, an element of the claimed invention is still lacking. The Office Action indicates that the combination does not disclose "confirming with the patient that educational material has been read prior to shipping the drug." Califano is cited as providing this missing element, and that the motivation for doing so "would have been to ensure that the patient knows about the risks and dangers associated with the drug (para. 43 of Califano)." Califano is directed to obtaining consent for a clinical trial. Abstract. It is not directed toward preventing abuse. The cited motivation is very different from the purpose of the presently claimed invention of distributing a sensitive drug in a manner that helps prevent abuse, making it very unlikely that one of skill in the art would be motivated to combine the references. As a proper prima facie case of obviousness has not been established, the rejection should be withdrawn.

The Response to Arguments section B of the Final Office Action, the Examiner states that the test for obviousness is what the combined teachings of the references would have suggested to those of ordinary skill in the art. This, however, does not address the fact that there is no proper suggestion to combine the references in the first place, since they are not directed towards the same or similar problems. Thus, one does not even arrive at the question of what the combination suggests if the combination is not proper.

Further in section B of the response to arguments in the Final Office Action, the Examiner states: "In response to applicant's argument that the cited motivation is very different from the purpose of the presently claimed invention, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious." No such recognition is being stated by Applicant. Applicant is merely trying to say that the art addresses a different problem than that of the invention as claimed, and thus, the references are not properly combinable. The language quoted from the Final Office Action appears to state that Applicant simply recognized new advantages flowing from the combination of the references. This statement is respectfully traversed, as Applicant is merely stating that the combination is improper, since the references are directed to problems that are not similar to those addressed by the claimed invention.

The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991); MPEP § 2143. The Examiner must avoid hindsight. *In re Bond*, 910 F.2d 831, 834, 15 USPQ2d 1566, 1568 (Fed. Cir. 1990). As indicated above, multiple elements from each of Moradi and Lilly were combined to make the rejection. Because multiple elements from each were used, there is no reasonable expectation of success in making the combination. Further, it points toward the improper use of hindsight, using the claims as a roadmap to make the combination.

The Final Office Action in section C, purports to address the above argument by reciting that reconstruction based on hindsight is proper so long as it takes into account only knowledge that was within the level of ordinary skill and does not include knowledge gleaned only from the applicant's disclosure. Section C does not state how only knowledge within the level of ordinary

skill was used, and further does not address the argument that a reasonable expectation of success in making the combination has not been shown.

A factor cutting against a finding of motivation to combine or modify the prior art is when the prior art teaches away from the claimed combination. A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path the applicant took. *In re Gurley*, 27 F.3d 551, 31 USPQ 2d 1130, 1131 (Fed. Cir. 1994); *United States v. Adams*, 383 U.S. 39, 52, 148 USPQ 479, 484 (1966); *In re Sponnoble*, 405 F.2d 578, 587, 160 USPQ 237, 244 (C.C.P.A. 1969); *In re Caldwell*, 319 F.2d 254, 256, 138 USPQ 243, 245 (C.C.P.A. 1963). Lilly describes the cooperative use of a database by multiple different pharmacies, prescribers and patients, to keep track of the prescription history for a patient. It would be an extremely daunting task to get the cooperation of all these parties. The presently claimed invention uses a central database for analysis of potential abuse situations for distribution of a sensitive drug, not to track all prescriptions for a patient. The ambitious path set forth in Lilly would discourage one of skill in the art from considering using it to solve the problems addressed in the presently claimed invention.

Claims 2, 4-8 and 10 depend from claim 1 and distinguish the references for at least the same reasons as claim 1. In addition, claim 2 recites a central pharmacy. The Office Action states that Moradi discloses confirming receipt by a telephone call from the central pharmacy. Applicant has reviewed the cited sections of Moradi, and cannot find the concept of a central pharmacy. As the term is used in the present application, a central pharmacy is a pharmacy that exclusively controls the distribution of a sensitive drug. While it may have branches and affiliates, it uses the central database to keep track of all distribution of the sensitive drug. This enables a much improved ability to monitor abuse situations. Patients seeking prescriptions from different doctors will be detected, because the drug is tracked in the central database. Each pharmacy that distributes the sensitive drug also uses the central database. Practically, this is accomplished by obtaining FDA approval that requires the use of the central database. Since any entity that distributes the sensitive drug requires the FDA approval, all must use the same central database. The term central database is used to encompass any real or virtual manifestation of a

central database that facilitates evaluation of potential abuse patterns for distribution of the sensitive drug.

Claim 3 was rejected under 35 U.S.C. § 103(a) as being unpatentable over Moradi et al. (US 2004/0019794 A1) in view of Lilly et al. (US 2004/0176985 A1) in view of Califano et al. (US 2003/0033168 A1) as applied to claim 1 above, and further in view of Andreasson et al. (US 2003/0160698 A1). Applicant further reserves the right to swear behind each of the references. This rejection is also respectfully traversed. Claim 3 depends from claim 1 and distinguishes from the references at least in the same manner as claim 1. Andreasson et al. describe monitoring distribution of medical products within a facility as indicated by the title. Claim 3 recites launching an investigation of lost shipments, which implies that the shipments have already left a facility. Monitoring within the facility would not address a lost shipment that has left the facility. As such, there is no showing of a reasonable likelihood of success in making the combination. As a proper prima facie case of obviousness has not been established, the rejection should be withdrawn.

In paragraph F of the Response to Arguments section of the Final Office Action, the Examiner indicates that para. 79 of Andreasson discloses tracking the delivery of medical products and immediately notifying healthcare workers of any missing medical product so they can investigate. Note that the start of para. 79 recites "..a closed-loop system for tracking and monitoring medical products within a healthcare facility,..." While Andreasson may describe launching an investigation, it lacks the concept of shipping drugs to a patient, and investigating lost shipments to the patient as claimed.

Claim 9 was rejected under 35 U.S.C. § 103(a) as being unpatentable over Moradi et al. (US 2004/0019794 A1) in view of Lilly et al. (US 2004/0176985 A1) in view of Califano et al. (US 2003/0033168 A1) as applied to claim 1 above, and further in view of Mayaud (U.S. Patent No. 5,845,255). Claim 9 depends from claim 1 and distinguishes from the references at least in the same manner as claim 1. The Office Action cites a motivation to combine the four references as "to reduce the reluctance of physicians to prescribe new drugs by providing them with the latest information about the drugs". This motivation has nothing to do with the problems

addressed by the currently claimed invention as identified above. As a proper prima facie case of obviousness has not been established, the rejection should be withdrawn.

In paragraph G of the Response to Arguments section of the Final Office Action, the Examiner again recites something about recognizing another advantage which would flow naturally from following the suggestion of the prior art, which as stated above, Applicant has not done. It is believed that such an argument incorrectly presupposes that the references are properly combinable, which Applicant believes they are not.

CONCLUSION

Applicant respectfully submits that the claims are in condition for allowance and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicant's attorney (612) 373-6972 to facilitate prosecution of this application.

If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

Respectfully submitted,

DAYTON T. REARDAN ET AL.

By their Representatives,

SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.
P.O. Box 2938
Minneapolis, MN 55402
(612) 373-6972

Date 3-29-2006

By _____
Bradley A. Forrest
Reg. No. 30,837

CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being filed using the USPTO's electronic filing system EFS-Web, and is addressed to: Mail Stop RCE, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 29 day of March, 2006.

JOHN D. GUSTAV-WRATHALL
Name

_____
Signature

IN THE CLAIMS

Please amend the claims as follows.

1. (Previously Presented) A method of distributing a sensitive drug, the method comprising:

receiving prescription requests from a medical doctor containing information identifying a patient, the sensitive drug, and various credentials of the doctor;

entering the information into a central computer database for analysis of potential abuse situations;

checking the credentials of the doctor;

confirming with the patient that educational material has been read prior to shipping the sensitive drug;

confirming receipt of the sensitive drug; and

generating periodic reports via the central computer database to evaluate potential abuse patterns.

2. (Previously Presented) The method of claim 1 wherein receipt of the sensitive drug is confirmed by telephone call from a central pharmacy to the patient.

3. (Original) The method of claim 1 and further comprising launching an investigation of lost shipments.

4. (Previously Presented) The method of claim 1 and further comprising recording the confirmation with the patient that the educational material has been read in the central computer database.

5. (Original) The method of claim 1 and further comprising verifying the patient's home address.

6. (Original) The method of claim 1 and further comprising recording a designee identified by the patient to receive the sensitive drug.

7. (Original) The method of claim 1 and further comprising establishing a delivery date.

8. (Previously Presented) The method of claim 1 wherein prescription refills requested prior to an anticipated date are questioned by a pharmacist.

9. (Previously Presented) The method of claim 1 and further comprising shipping comprehensive printed materials to the doctor if the doctor is a first time prescriber of the sensitive drug.

10. (Original) The method of claim 1 wherein the credentials of the doctor comprise DEA (Drug Enforcement Agency) and state license numbers.

11. – 31. (Cancelled)

32. (New) A method of distributing a sensitive drug under exclusive control of an exclusive central pharmacy, the method comprising:

receiving prescription requests from a medical doctor containing information identifying a patient, the sensitive drug, and various credentials of the doctor;

entering the information into an exclusive computer database associated with the exclusive central pharmacy for analysis of potential abuse situations;

checking the credentials of the doctor;

confirming with the patient that educational material has been read prior to shipping the sensitive drug;

confirming receipt by the patient of the sensitive drug; and

generating periodic reports via the exclusive computer database to evaluate potential diversion patterns.

33. (New) A method of distributing a sensitive drug under exclusive control of an exclusive central pharmacy, the method comprising:

receiving prescription requests from a medical doctor containing information identifying a patient, the sensitive drug, and various credentials of the doctor;

entering the information into an exclusive computer database associated with the exclusive central pharmacy for analysis of potential abuse situations;

checking the credentials of the doctor;

confirming receipt by the patient of the sensitive drug; and

generating periodic reports via the exclusive computer database to evaluate potential diversion patterns.

34. (New) The method of claim 33 wherein the exclusive central pharmacy controls the exclusive central database.

35. (New) The method of claim 33 and further comprising selectively blocking shipment of the sensitive drug to a patient.

36. (New) The method of claim 33 wherein an abuse pattern is associated with a patient, and shipment is blocked upon such association.

37. (New) The method of claim 33 wherein the sensitive drug comprises gamma hydroxy butyrate (GHB).

Electronic Acknowledgement Receipt

EFS ID:	1014264
Application Number:	10322348
Confirmation Number:	5446
Title of Invention:	Sensitive drug distribution system and method
First Named Inventor:	Dayton T. Reardan
Customer Number:	21186
Filer:	Gregg Alan Peacock/John Gustav-Wrathall
Filer Authorized By:	Gregg Alan Peacock
Attorney Docket Number:	101.031US1
Receipt Date:	29-MAR-2006
Filing Date:	17-DEC-2002
Time Stamp:	18:36:53
Application Type:	Utility
International Application Number:	

Payment information:

Submitted with Payment	yes
Payment was successfully received in RAM	$395.0
RAM confirmation Number	165
Deposit Account	190743
The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows: Charge any Additional Fees required under 37 C.F.R. Section 1.16 and 1.17	

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)	Multi Part	Pages
1		101031us1_rce.pdf	886051	yes	17

Multipart Description		
Doc Desc	**Start**	**End**
Request for Continued Examination (RCE)	1	1
Amendment After Final	2	12
Information Disclosure Statement (IDS) Filed	13	15
Miscellaneous Incoming Letter	16	17

Warnings:

Information:

2	NPL Documents	steps.pdf	20861586	no	103

Warnings:

Information:

3	Fee Worksheet (PTO-875)	fee-info.pdf	8169	no	2

Warnings:

Information:

Total Files Size (in bytes):	21755806

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Dayton T. Reardan et al.	Examiner:	Lena Najarian
Serial No.:	10/322,348	Group Art Unit:	3626
Filed:	December 17, 2002	Docket:	101.031US1
Title:	SENSITIVE DRUG DISTRIBUTION SYSTEM AND METHOD		

INFORMATION DISCLOSURE STATEMENT

MS RCE
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

In compliance with the duty imposed by 37 C.F.R. § 1.56, and in accordance with 37 C.F.R. §§ 1.97 *et. seq.*, the enclosed materials are brought to the attention of the Examiner for consideration in connection with the above-identified patent application. Applicants respectfully request that this Information Disclosure Statement be entered and the documents listed on the attached Form 1449 be considered by the Examiner and made of record. Pursuant to the provisions of MPEP 609, Applicants request that a copy of the 1449 form, initialed as being considered by the Examiner, be returned to the Applicants with the next official communication.

Pursuant to 37 C.F.R. §1.97(b), it is believed that no fee or statement is required with the Information Disclosure Statement. However, if an Office Action on the merits has been mailed, the Commissioner is hereby authorized to charge the required fees to Deposit Account No. 19-0743 in order to have this Information Disclosure Statement considered.

Pursuant to 37 C.F.R. 1.98(a)(2), Applicant believes that copies of cited U.S. Patents and Published Applications are no longer required to be provided to the Office. Notification of this change was provided in the United States Patent and Trademark Office OG Notices dated October 12, 2004. Thus, Applicant has not included copies of any US Patents or Published Applications cited with this submission. Should the Office require copies to be provided, Applicant respectfully requests that notice of such requirement be directed to Applicant's below-signed representative. Applicant acknowledges the requirement to submit copies of foreign patent documents and non-patent literature in accordance with 37 C.F.R. 1.98(a)(2).

The Examiner is invited to contact the Applicants' Representative at the below-listed telephone number if there are any questions regarding this communication.

Respectfully submitted,

DAYTON T. REARDAN ET AL.

By their Representatives,

SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.
P.O. Box 2938
Minneapolis, MN 55402
(612) 373-6972

Date 3-29-2006 By _____
Bradley A. Forrest
Reg. No. 30,837

CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being filed using the USPTO's electronic filing system EFS-Web, and is addressed to: Mail Stop RCE, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 29 day of March, 2006.

Name _____ Signature _____

PTO/SB/08A(10-01)
Approved for use through 10/31/2002. OMB 651-0031
US Patent & Trademark Office: U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use as many sheets as necessary)

Sheet 1 of 1

Complete if Known

Application Number	10/322,348
Filing Date	December 17, 2002
First Named Inventor	Reardan, Dayton
Group Art Unit	3626
Examiner Name	Najarian, Lena
Attorney Docket No:	101.031US1

US PATENT DOCUMENTS				
Examiner Initial *	**USP Document Number**	**Publication Date**	**Name of Patentee or Applicant of cited Document**	**Filing Date If Appropriate**

FOREIGN PATENT DOCUMENTS				
Examiner Initials*	**Foreign Document No**	**Publication Date**	**Name of Patentee or Applicant of cited Document**	**T[2]**

OTHER DOCUMENTS -- NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	**Cite No [1]**	**Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.**	**T[2]**
		"System for Thalidomide Education and Prescribing Safety (S.T.E.P.S.) Starter Kit", Celgene Corporation, (2001),103 pgs.	

EXAMINER **DATE CONSIDERED**

Substitute Disclosure Statement Form (PTO-1449)

* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional) 2 Applicant is to place a check mark here if English language Translation is attached

Electronic Patent Application Fee Transmittal	
Application Number:	10322348
Filing Date:	17-Dec-2002
Title of Invention:	Sensitive drug distribution system and method
First Named Inventor:	Dayton T. Reardan
Filer:	Gregg Alan Peacock/John Gustav-Wrathall
Attorney Docket Number:	101.031US1
Filed as Small Entity	

Utility Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
Request for continued examination	2801	1	395	395
		Total in USD ($)		**395**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Dayton T. Reardan et al.	Examiner: Lena Najarian
Serial No.:	10/322,348	Group Art Unit: 3626
Filed:	December 17, 2002	Docket: 101.031US1
Title:	SENSITIVE DRUG DISTRIBUTION SYSTEM AND METHOD	

COMMUNICATION CONCERNING RELATED APPLICATION(S)

MS RCE
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Applicants would like to bring to the Examiner's attention the following related application(s) in the above-identified patent application:

Serial/Patent No.	Filing Date/Issue Date	Attorney Docket	Title
10/979665	November 2, 2004	101.031US2	SENSITIVE DRUG DISTRIBUTION SYSTEM AND METHOD
11/097651	April 1, 2005	101.031US3	SENSITIVE DRUG DISTRIBUTION SYSTEM AND METHOD
11/097985	April 1, 2005	101.031US4	SENSITIVE DRUG DISTRIBUTION SYSTEM AND METHOD

Continuations and divisionals may be later filed on the cases listed above, or cited to the Examiner in any previous Communication Concerning Related Applications. Applicants request that the Examiner review all continuations and divisionals of the above-listed or previously-cited patent applications before allowing the claims of the present patent application.

Respectfully submitted,

DAYTON T. REARDAN ET AL.

By Applicants' Representatives,

SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.
P.O. Box 2938
Minneapolis, MN 55402
(612) 373-6972

Date 3-29-2006 By _____
Bradley A. Forrest
Reg. No. 30,837

CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being filed using the USPTO's electronic filing system EFS-Web, and is addressed to: Mail Stop RCE, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 29 day of March, 2006.

_____ _____
Name Signature

System for Thalidomide Education and Prescribing Safety (*S.T.E.P.S.*™)

Enhanced *S.T.E.P.S.*™ Materials! For use starting 7/30/01

- Pocket Guide to *S.T.E.P.S.*™ and Patient Surveys
- Patient Brochure
- *Your Contraceptive Choices* Brochure
- *Emergency Contraception* Brochure

To order additional Patient Resource Packs call 1-888-4-CELGENE (1-888-423-5436)

MOVING THEORIES INTO CLINICAL PRACTICE: THALIDOMIDE

Moving Theories Into Clinical Practice: Thalidomide
Enhanced S.T.E.P.S.™ Program

ENHANCED S.T.E.P.S.™ PROGRAM

WARNING: SEVERE, LIFE-THREATENING HUMAN BIRTH DEFECTS.
IF THALIDOMIDE IS TAKEN DURING PREGNANCY, IT CAN CAUSE SEVERE BIRTH DEFECTS OR DEATH TO AN UNBORN BABY. THALIDOMIDE SHOULD NEVER BE USED BY WOMEN WHO ARE PREGNANT OR WHO COULD BECOME PREGNANT WHILE TAKING THE DRUG. EVEN A SINGLE DOSE [1 CAPSULE (50 MG)] TAKEN BY A PREGNANT WOMAN DURING HER PREGNANCY CAN CAUSE SEVERE BIRTH DEFECTS.
BECAUSE OF THIS TOXICITY AND IN AN EFFORT TO MAKE THE CHANCE OF FETAL EXPOSURE TO THALOMID® (thalidomide) AS NEGLIGIBLE AS POSSIBLE, THALOMID® (thalidomide) IS APPROVED FOR MARKETING ONLY UNDER A SPECIAL RESTRICTED DISTRIBUTION PROGRAM APPROVED BY THE FOOD AND DRUG ADMINISTRATION. THIS PROGRAM IS CALLED THE "SYSTEM FOR THALIDOMIDE EDUCATION AND PRESCRIBING SAFETY (*S.T.E.P.S.™*)".
UNDER THIS RESTRICTED DISTRIBUTION PROGRAM, ONLY PRESCRIBERS AND PHARMACISTS REGISTERED WITH THE PROGRAM ARE ALLOWED TO PRESCRIBE AND DISPENSE THE PRODUCT. IN ADDITION, PATIENTS MUST BE ADVISED OF, AGREE TO, AND COMPLY WITH THE REQUIREMENTS OF THE *S.T.E.P.S.™* PROGRAM IN ORDER TO RECEIVE PRODUCT.

Goal

To educate pharmacists about:

- The pharmacology of thalidomide (THALOMID®)
- The enhanced System for Thalidomide Education, and Prescribing Safety *S.T.E.P.S.*™ program required for prescribing and dispensing thalidomide
- The management of side effects associated with thalidomide (THALOMID®) for the treatment of erythema

Objectives

At the end of this program, pharmacists should be able to:

- Outline the pharmacology (absorption, distribution, metabolism, elimination, drug interactions) of thalidomide (THALOMID®)
- Discuss the dosage and administration of thalidomide (THALOMID®) for the treatment of erythema nodosum leprosum
- Describe the elements of the enhanced *S.T.E.P.S.*™ program
- Understand the side effects related to thalidomide (THALOMID®) and management of these side effects

Target Audience

This program has been designed for pharmacists engaged in dispensing thalidomide (THALOMID®).

Thalidomide (THALOMID®) is indicated for the acute treatment of the cutaneous manifestation of moderate to severe erythema nodosum leprosum (ENL).

Accreditation

Extension Services in Pharmacy at the University of Wisconsin School of Pharmacy is approved by the American Council on Pharmaceutical Education as a provider of pharmacy continuing education.

This course is accredited for 1 continuing education hour (0.1 CEU). Statements of credit for continuing pharmaceutical education participation will be mailed within one month of completion of the course, based on successful completion (score of 70% or better) of the post-test and evaluation materials. ACPE Universal Program #073-999-01-022-H01. Expiration 4/9/04

This program is presented by Extension Services in Pharmacy at the University of Wisconsin School of Pharmacy, and is supported by an unrestricted educational grant from Celgene Corporation.

Acknowledgment

This program is supported through an unrestricted educational grant from Celgene Corporation.

Table of Contents

Introduction

In the 1950s and 60s, thalidomide gained widespread use as a nonbarbiturate sedative and antiemetic until it was discovered that it had teratogenic properties, forcing its withdrawal from worldwide markets.[1] (pp458,459),[2] (p1239) Thalidomide was associated with one of the most devastating tragedies of modern medicine; over 10,000 reports of children born with phocomelia (defective development of the limbs) or amely (absence of limbs).[2] (p1241) Thalidomide was never approved for marketing in the United States due to a medical reviewer's concern about reports of neuropathy associated with thalidomide use in Europe. Consequently, reports of phocomelia had become increasingly evident during this period. Nevertheless, the thalidomide experience prompted the FDA to implement even more stringent standards against potential future epidemics.[1] (p458) Closely monitored research on thalidomide's pharmacologic and immunologic actions has continued since the 1960s, in part to reveal the mechanism for its embryopathy, but also to exploit its significant potential for the treatment of other conditions.[3] (p469) Favorable results in the treatment of lepra reactions had already been published as early as 1965.[4] However, it was not until 1998 that thalidomide (THALOMID®, Celgene Corporation) was approved by the US Food and Drug Administration for the acute treatment of the cutaneous manifestations of moderate to severe erythema nodosum leprosum (ENL) and as maintenance therapy to suppress recurrence.

In accordance with the concerns over the teratogenic effects of this agent, a comprehensive program, the System for Thalidomide Education and Prescribing Safety (*S.T.E.P.S.*™), has been developed to control and monitor access to thalidomide.[5]

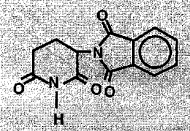
Pharmacology

Trade Name
THALOMID®

Generic Name
Thalidomide

Chemical Name
Alpha-N-(phthalimido)glutarimide

Chemical Structure
$C_{13}H_{10}N_2O_4$



Absorption

Thalidomide has a poor aqueous solubility, which has hampered development of an intravenous formulation and thereby the ability to assess the absolute bioavailability of oral thalidomide in humans. Absorption from the gastrointestinal tract takes 2.9-5.7 hours to achieve peak plasma concentrations (T_{max}). The influence of food on the rate or extent of thalidomide absorption has not been fully determined, but coadministration with a high-fat meal causes minor (<10%) changes in the extent of absorption (AUC) or peak concentration (C_{max}) and an increase in Tmax to 6.0 hours.[6]

Distribution

Human pharmacokinetic studies to date indicate that thalidomide has a large apparent volume of distribution. The extent of plasma protein binding is unknown. Animal studies have demonstrated that even and wide distribution occurs throughout most tissues and organs, including the placenta.[6] Thalidomide and/or its breakdown products have been found in semen following oral administration in rabbits[7] (p1019) and is also present in the ejaculate of human males.[8] Unlike some other sedative compounds, thalidomide does not accumulate in fatty tissue after chronic dosing.[9] (p395)

Metabolism

Thalidomide undergoes spontaneous and rapid nonenzymatic hydrolytic cleavage at physiologic pH into its 20+ metabolites in plasma. The exact metabolic route and fate are not known in humans. Overall, very little metabolism of thalidomide is thought to occur via the hepatic CYP P450 enzyme system.[6] Recent evaluation of single- and multiple-dose pharmacokinetic parameters of oral thalidomide (200 mg/day) in healthy female volunteers indicates that thalidomide does not inhibit or induce its own metabolism over a 21-day period.[10] (p488)

Elimination

Animal data suggest that thalidomide is quickly excreted in the urine with a nonabsorbed portion of the drug excreted unchanged in the feces.[9] (p395) The mean half-life of elimination ranges from approximately 5 to 7 hours following a single dose; at 48-hour levels, thalidomide is undetectable in the urine.[6] The renal clearance of thalidomide is 1.15 mL/min with less than 0.7% of the dose excreted in the urine as unchanged drug. When R- and S-isomers were measured separately in healthy male volunteers, their mean terminal half-lives were nearly identical with a mean of 4.7 hours.[11] The effects of renal or hepatic dysfunction on the clearance of thalidomide are not known, and additional studies are needed to determine if age-related physiologic changes affect clearance.

Drug Interactions

Systematic evaluation of drug-drug interactions with thalidomide has not been conducted except with oral contraceptives. The results of two clinical trials that evaluated the effect of thalidomide on the plasma pharmacokinetics of oral contraceptives suggest that the efficacy of hormonal contraceptives is unlikely to be affected by concomitant therapy.[10] (p489)[12]

An early pharmacology study in mice showed that thalidomide enhances the sedative effect of barbiturates and alcohol and the catatonic effects of chlorpromazine and reserpine.[6] Central nervous system stimulants (methylamphetamine, methylphenidate) counteracted the depressant effects of thalidomide.[13] (p8)

Medications known to be associated with peripheral neuropathy should be used with caution in patients receiving thalidomide.[6]

Dosage and Administration

Initial Use

For an episode of cutaneous ENL, thalidomide should be administered at an initial dose of 100 to 300 mg/day, administered once per day with water, preferably at bedtime and at least 1 hour after the evening meal. Patients weighing less than 50 kg should be started at the low end of the range. In the case of a severe cutaneous ENL reaction, a dose up to 400 mg/day can be given. Dosing with thalidomide should continue until signs and symptoms of active reaction have subsided, usually a period of at least 2 weeks. Patients may be tapered off medication in 50-mg increments every 2 to 4 weeks.[6]

Special Populations[6]

Geriatric Use

No systematic studies in geriatric patients have been conducted. Thalidomide has been used in clinical trials in patients up to 90 years of age. Adverse events in patients over the age of 65 did not appear to differ in kind from those reported for younger individuals.

Pediatric Use

Safety and effectiveness in pediatric patients below the age of 12 years have not been established.

Use in Nursing Mothers

It is not known whether thalidomide is excreted in human milk. Because many drugs are excreted in human milk and due to the potential for serious adverse reactions in nursing infants from thalidomide, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pregnancy Category X

Because of the known teratogenicity of thalidomide, thalidomide is contraindicated in women who are or may become pregnant and are not using the two required types of birth control or who are not continually abstaining from reproductive heterosexual sexual intercourse.

Patients With Renal Impairment

The pharmacokinetics of thalidomide in patients with renal dysfunction has not been determined.

Patients With Hepatic Impairment

The pharmacokinetics of thalidomide in patients with hepatic dysfunction has not been determined.

Patients With Hansen's Disease

Analysis of data from a small study in Hansen's disease patients suggests that these patients, relative to healthy patients, may have an increased bioavailability of thalidomide.

HIV-Seropositive Patients

There is no apparent significant difference in measured pharmacokinetic parameter values between healthy human patients and HIV-seropositive patients following single-dose administration of thalidomide capsules.

How Supplied

The product is supplied as hard gelatin, 50-mg, white opaque capsules, imprinted "Celgene" with a "do not get pregnant" logo. Cartons contain either ten (10) blister packs of 14 capsules each (140 capsules total) or ten (10) blister packs of 28 capsules each (280 capsules total).

Enhanced *S.T.E.P.S.*™ Program

System for Thalidomide Education and Prescribing Safety

Due to its removal from worldwide markets for causing life-threatening human birth defects, the current distribution of thalidomide is tightly controlled by the FDA in an attempt to avoid these predictable and preventable teratogenic effects. In compliance with the FDA's unprecedented requirements, Celgene Corporation developed an oversight system for stringent monitoring, including contraceptive counseling.[6] (p1721) This program—for patients, physicians, and pharmacists—is called the System for Thalidomide Education and Prescribing Safety (*S.T.E.P.S.*™) and its compliance requirements have been incorporated into the product labeling. The *S.T.E.P.S.*™ program has been specifically designed for THALOMID® (thalidomide), manufactured by Celgene Corporation, and does not currently apply to any other product.

The goal of *S.T.E.P.S.*™ is to prevent any fetal exposure to the drug through education and controlled access. Celgene Corporation and the FDA monitor compliance with all requirements of the program. The *S.T.E.P.S.*™ program has been revised utilizing state of the art technology. For example, the informed consent form and patient registration form have been combined and will be generated by the prescriber from a software application. The form is then signed by the patient and prescriber and faxed directly into Celgene Customer Care where optical character recognition (OCR) "reads" the form, thus minimizing human data entry errors. Patient and prescriber surveys as well as pharmacy calls will now be conducted via the telephone using integrated voice recognition (IVR) technology. In other words, questions will be answered via the telephone using the keypad to eliminate long delays. Prescribers will obtain an authorization number at the end of his/her survey that must be written on the prescription. As mentioned above, patients will be registered by their prescriber; therefore, the pharmacist is no longer responsible for collecting and filing the informed consent form. Each prescription for

Patient Procedures

To enhance their patient's safety during treatment with thalidomide, pharmacists and prescribers should be informed of the patient's requirements, in addition to their own. Patients are required to complete an informed consent form, which is provided by their prescriber. Before beginning treatment, all patients are required to receive contraceptive counseling from their prescriber, and female patients who are of childbearing potential must test negative on a pregnancy test. Once treatment has begun, patients can continue thalidomide treatment only if they agree to use appropriate contraceptive methods. Females of childbearing potential must agree to use two reliable forms of contraception or abstain from sex continuously during treatment and they must take regular pregnancy tests. Birth control must be initiated 4 weeks prior to thalidomide treatment and continued for 4 weeks after thalidomide is discontinued. Males must agree to use a latex condom each time they have sex with a woman. All patients must also agree not to share their thalidomide medication with anyone and they must participate in mandatory and confidential patient phone surveys.

Any patient, physician, or pharmacist with a question or concern regarding the new *S.T.E.P.S.*™ program should:

1. contact his/her immunology specialist/*S.T.E.P.S.*™ field coordinator
2. call 1-888-4CELGENE or
3. visit **www.stepsinfo.com**

Thalidomide in Clinical Practice

Thalidomide is currently approved for the treatment of erythema nodosum leprosum (ENL), an inflammatory complication of Hansen's disease.[6] Data on the efficacy of thalidomide in prevention of ENL relapse was derived from a retrospective evaluation of 102 patients treated under the auspices of the US Public Health Service. A subset of patients with ENL, controlled on thalidomide, demonstrated repeated relapses upon drug withdrawal and remission with reinstitution of therapy. Thirty-two other published studies involving over 1600 patients consistently report generally successful treatment of the cutaneous manifestation of moderate to severe ENL with thalidomide. Treatment with thalidomide can resolve lesions within 1 to 2 days and can also relieve other symptoms, such as headache, orchitis, myalgia, and hepatosplenomegaly, within a similarly short time.

Management of Side Effects

Side Effect Recognition and Management

Common side effects may include:

- Teratogenic effects
- Sedation/somnolence/fatigue
- Rash
- Neutropenia
- Orthostatic hypotension/dizziness
- Peripheral neuropathy
- Constipation
- Peripheral or dependent edema

Except for teratogenicity and some cases of peripheral neuropathy, each one of these side effects is temporary and reversible once thalidomide usage is discontinued. Because most of these side effects are dose-dependent, in many cases it may not be necessary to discontinue therapy, and dose reduction may result in resolution of the side effect.

Teratogenic Effects

Prevention of birth defects is the major focus of the *S.T.E.P.S.*™ program and patients are warned that even a single dose of thalidomide taken while pregnant can cause severe and life-threatening birth defects. The boxed warning that appears on the product label and in patient information brochures provided by Celgene Corporation is presented below.

WARNING: SEVERE, LIFE-THREATENING HUMAN BIRTH DEFECTS. IF THALIDOMIDE IS TAKEN DURING PREGNANCY, IT CAN CAUSE SEVERE BIRTH DEFECTS OR DEATH TO AN UNBORN BABY. THALIDOMIDE SHOULD NEVER BE USED BY WOMEN WHO ARE PREGNANT OR WHO COULD BECOME PREGNANT WHILE TAKING THE DRUG. EVEN A SINGLE DOSE [1 CAPSULE (50 MG)] TAKEN BY A PREGNANT WOMAN CAN CAUSE SEVERE BIRTH DEFECTS.

Phocomelia (defective shortened limbs) of the upper extremities is the most prominent thalidomide-associated congenital abnormality, but in addition, congenital heart disease, duodenal stenosis, esophageal fistulae, neural tube abnormalities, micro-ophthalmia, deformities of the ears, and mid-line hemangiomas have also been reported.[1] (pp458,461,462),[2] (pp1238-1241),[14] (pp491,492) Neither a safe level nor a window of opportunity for administration of thalidomide during pregnancy has been identified.[15] (p321)

Sedation/Somnolence/Fatigue

Signs and symptoms associated with this adverse event include weakness, fatigue, sedation, mood changes, decreased libido, confusion, and impaired memory. In patients experiencing excessive somnolence, the physician may use the following strategies to prevent or manage this side effect:

Preventive Strategies

- Recommend an evening dose to minimize the effects of daytime somnolence.
- Initiate thalidomide with a low dose and titrate gradually.

Management Strategies

- No action may be necessary at the beginning of treatment, as tolerance to the sedative effects may only develop after several weeks.
- Because the sedative effect is dose-related, lowering the patient's dose should be considered before discontinuing thalidomide therapy. Sedation is less frequent and more mild with daily doses ≤200 mg.
- Inform patient to avoid co-administration with alcohol, barbiturates, reserpine, chlorpromazine, and any other sedatives/tranquilizers, as thalidomide has been shown to enhance their depressant effect. Advise patient to avoid any other medications that cause drowsiness unless they have consulted their physician first.
- Consider that methylphenidate and methylamphetamine may antagonize the sedative effects of thalidomide.
- Situations in which drowsiness may be hazardous should be avoided.

Rash

The commonly described thalidomide-associated rash is characterized by generalized mild erythema, itching, and dryness of the skin, which occur over the trunk, back, and proximal extremities. Serious dermatologic reactions including Stevens-Johnson syndrome and toxic epidermal necrolysis (TEN), which may be fatal, have rarely been reported in association with thalidomide therapy. Patients who develop rash during therapy with thalidomide should have prompt medical evaluation. If clinically appropriate, thalidomide therapy should be discontinued. Evaluation and management should consider the following:

- The most common rashes associated with thalidomide are mild and transient and can be treated symptomatically.
- Patients who experience rash accompanied by systemic signs or symptoms may be at risk for the development of severe hypersensitivity reactions. These patients should permanently discontinue treatment and should not be rechallenged with thalidomide.
- Renal insufficiency may increase the risk for hypersensitivity reactions with erythroderma and eosinophilia.
- Patients with ENL may develop a transient, thalidomide-associated allergic dermatitis. This can generally be controlled with oral histamines, and thalidomide treatment can be continued. In addition, some patients have been successfully rechallenged with a lower dose of thalidomide. If treatment is discontinued, the rash will usually resolve within 24 hours.
- **If the rash is exfoliative, purpuric, or bullous, or if Stevens-Johnson syndrome or toxic epidermal necrolysis are suspected, use of thalidomide should not be resumed and the patient should not be rechallenged.**
- Be aware that the use of topical and systemic corticosteroids and antihistamine therapy for thalidomide-associated rashes has not been evaluated in controlled clinical trials.

Neutropenia

Neutropenia has been reported in association with thalidomide therapy in a variety of patient populations. Thalidomide has no known direct myelosuppressive effects. Effects of thalidomide on blood cell counts may occur indirectly through thalidomide's effects on tumor necrosis factor alpha (TNF-α) or other immunomodulatory and inflammatory cytokines, which influence blood cell regulation, recruitment, and activation. Depending on a patient's condition, baseline and monthly white blood cell (WBC) counts may be considered. For patients who may be prone to neutropenia, baseline and biweekly WBC counts should be taken for at least the first 3 months of treatment, then monthly thereafter if the counts are stable.

Thalidomide therapy should not be initiated in a patient who has an absolute neutrophil count (ANC) below 750/mm^3. Depending upon the severity of the neutropenia, consider the following management strategies:

- Consider decreasing the patient's dose or, if necessary, discontinuing thalidomide therapy.
- For patients whose ANC decreases below 750/mm^3, re-evaluate the patient's entire treatment regimen and consider discontinuing thalidomide, if clinically appropriate, until the neutropenia resolves.
- For patients whose ANC decreases below 500/mm^3, discontinue thalidomide until the neutropenia has resolved.
- The therapeutic administration of granulocyte colony stimulating factor (G-CSF) appears potentially to be safe and effective. The use of G-CSF to treat thalidomide-associated neutropenia has not been evaluated in controlled clinical trials.

Orthostatic Hypotension/Dizziness

This condition may be accompanied by bradycardia, weakness, unsteady gait, confusion, and blurred vision. Once recognized, management of this side effect includes:

- Advising the patient to sit upright for a few minutes before standing from a recumbent position.
- Re-evaluating the patient's treatment regimen and considering adjusting the dose(s) of any concomitant medications that may contribute to or exacerbate dizziness, hypotension, or bradycardia, including diuretics, vasodilators, phosphodiesterase type 5 (PDE5) inhibitors, anti-hypertensive agents, other cardiovascular medications, or agents for prostatic hypertrophy (alpha-adrenergic blockers).
- Adjusting the patient's dose of thalidomide or, if necessary, discontinuing treatment.

Constipation

Several measures can be taken to minimize and prevent the effects of this condition.

- When initiating thalidomide treatment, consider concurrent use of a stool softener.
- Patients can be advised to increase their daily intake of fluids as tolerated to approximately six to eight 8-ounce glasses per day, and increase dietary fiber as tolerated, including fresh fruits, vegetables, whole grain cereals, and breads.
- A bowel regimen should be considered in patients who will be titrated to higher doses.
- Start with a mild emollient/lubricant laxative such as docusate sodium 1 to 3 times daily as needed.
- If needed, add a stimulant such as senna-based laxative twice a day.
- If tolerated in patients who are adequately hydrated and have normal renal function, saline or hyperosmotic laxatives such as milk of magnesia or lactulose may be considered.
- If no stool within 4 days, try magnesium citrate or polyethylene glycol 3350 (Colyte®, Golytely®, Nulytely®).*
- Consider adjusting the thalidomide dose or, if necessary, discontinuing therapy. Be aware that concurrent use of thalidomide and laxatives, bowel evacuants, or gastrointestinal prokinetic agents has not been evaluated in controlled clinical studies.

Peripheral Neuropathy

This is a potentially severe, and sometimes irreversible, side effect of thalidomide treatment. The appearance and severity of peripheral neuropathy does not appear to be related to the dose or duration of thalidomide treatment and inter-individual patient susceptibility may be more relevant.[6] (p1238),[16] (p66),[17] (p266)

Symptoms are mainly sensory, especially in the lower limbs. They can include symmetrical, painful paresthesias of the hands and feet, hyperesthesia, pallor and coldness of the fingers and toes, and superficial sensory loss. In addition, less common symptoms that may still help identify this condition include muscle cramps, muscle weakness, postural tremor, decreased muscle stretch reflexes, palmar erythema, and brittle nails.[2] (pp1238-1241),[15] (p68),[17] (pp543-544)

Thalidomide treatment should be re-evaluated if it is determined that the neuropathy is drug-related. While sensory symptoms often improve after discontinuation, they may not resolve completely.[18] (p550) In addition, management strategies should include the following:

- Patients with HIV infection and underlying malignancies may be at higher risk for peripheral neuropathy malignancies.[19] (p1223)
- Patients should be regularly evaluated for signs or symptoms of peripheral neuropathy. Neurologic examinations should be performed every 30 days after starting treatment and periodically thereafter.[14] (p492)
- Measurement of sensory nerve action potentials at baseline and every 6 months during treatment may be useful in patients at risk for the development of neuropathy. If the amplitude decreases by more than 30%, electrophysiologic testing should be performed more frequently, and if the decrease is more than 50% from baseline, discontinuation of thalidomide therapy should be considered.[13] (p492)

Peripheral or Dependent Edema

- Intermittent elevation of the lower extremities is helpful to some patients and resting in a supine position may be necessary for several hours each day.
- Wearing elastic stockings may be helpful.
- Diuretics have been successful in some cases when used concomitantly with thalidomide, but be aware that this has not been evaluated in controlled clinical trials.[19] (p308)
- Consider adjusting the thalidomide dose or, if necessary, discontinuing therapy.

* Colyte® is a registered trademark of Schwarz Pharma; Golytely® and Nulytely® are registered trademarks of Braintree Laboratories, Inc.

THIS PAGE INTENTIONALLY LEFT BLANK

PROGRAM EVALUATION

Moving Theories Into Clinical Practice: Thalidomide
Enhanced *S.T.E.P.S.*™ Program
ACPE Program #073-999-01-022-H01

How to obtain Pharmacy CE Credit

To earn 1 hour (0.1 CEU) of pharmacy CE credit for completion of this program, record on the answer form your answers to the test questions found on pages 21-22; complete the other evaluation questions and send this program evaluation to Extension Services in Pharmacy. No payment is required. A statement of CE credit will be issued within one month of receipt of all evaluation materials; an exam score of 70% or greater is required to earn CE credits.
Mail or fax the evaluation form to:

Enhanced *S.T.E.P.S.*™ Program
Extension Services in Pharmacy
777 Highland Avenue
Madison, WI 53705-2222
Fax: 608-262-2431
Phone: 608-262-3130

Please circle the appropriate response for each evaluation component:

	Excellent			Good	Poor
Program content	5	4	3	2	1
Relevance of program content to my practice	5	4	3	2	1
Amount of new knowledge gained	5	4	3	2	1
Overall evaluation of this program	5	4	3	2	1

Additional Comments: _____

_____

_____

Was this program presented as a fair and balanced discussion, not commercial in nature?

_____ Yes _____ No If no, please explain: _____

_____

Indicate the total time (in hours) required to complete this program (include the time to complete the final examination and evaluation): _____ hours

Please print the following information:

Name: _____

Home Address: _____

City, State, Zip: _____

I certify that I have completed this program independently:

_____
(Signature)

Program Expiration Date is 4/9/04

Circle the correct (best) response:

1. a b c d e	6. a b c d e
2. a b	7. a b c d e
3. a b c d	8. a b c d e
4. a b	9. a b c d e
5. a b c	10. a b c d

POST-TEST

1. In 1998, thalidomide was approved by the US Food and Drug Administration for the acute treatment of:
   - a. hematologic tumors, including advanced refractory multiple myeloma.
   - b. cutaneous manifestations of moderate to severe erythema nodosum leprosum (ENL).
   - c. reduction of load from primary HIV infection, as adjunctive therapy.
   - d. b and c.
   - e. all of the above.

2. THALOMID® (thalidomide) is metabolized completely in the hepatic CYP P450 enzyme system.
   - a. True.
   - b. False.

3. Following a single dose of THALOMID® (thalidomide), the mean half-life of elimination is approximately:
   - a. 1 to 3 hours.
   - b. 5 to 7 hours.
   - c. 8 to 10 hours.
   - d. 12 hours.

4. The current distribution of thalidomide is tightly controlled by the FDA in an attempt to avoid its associated teratogenic effects, which are predictable and preventable.
   - a. True.
   - b. False.

5. Females of childbearing potential must agree to use _____ reliable form(s) of contraception or abstain from sex continuously during treatment.
   - a. one.
   - b. two.
   - c. three.

6. Among the changes of the enhanced *S.T.E.P.S.*™ program is:
   - a. the removal of the pharmacist's requirement to register patients.
   - b. the requirement for pharmacists to contact physicians if they are presented with an old prescription.
   - c. the requirement for the pharmacist to record the prescription confirmation number directly on the prescription.
   - d. none of the above.
   - e. all of the above.

7. Pharmacists can accept prescriptions for automatic refills ONLY when:
   a. they have a written informed consent form on file.
   b. Celgene Corporation has approved the prescription.
   c. the patient has completed his/her 28-day course of therapy.
   d. a and b.
   e. none of the above.

8. Side effects associated with thalidomide therapy include:
   a. sedation/somnolence/fatigue.
   b. orthostatic hypotension/dizziness.
   c. constipation.
   d. peripheral neuropathy.
   e. all of the above.

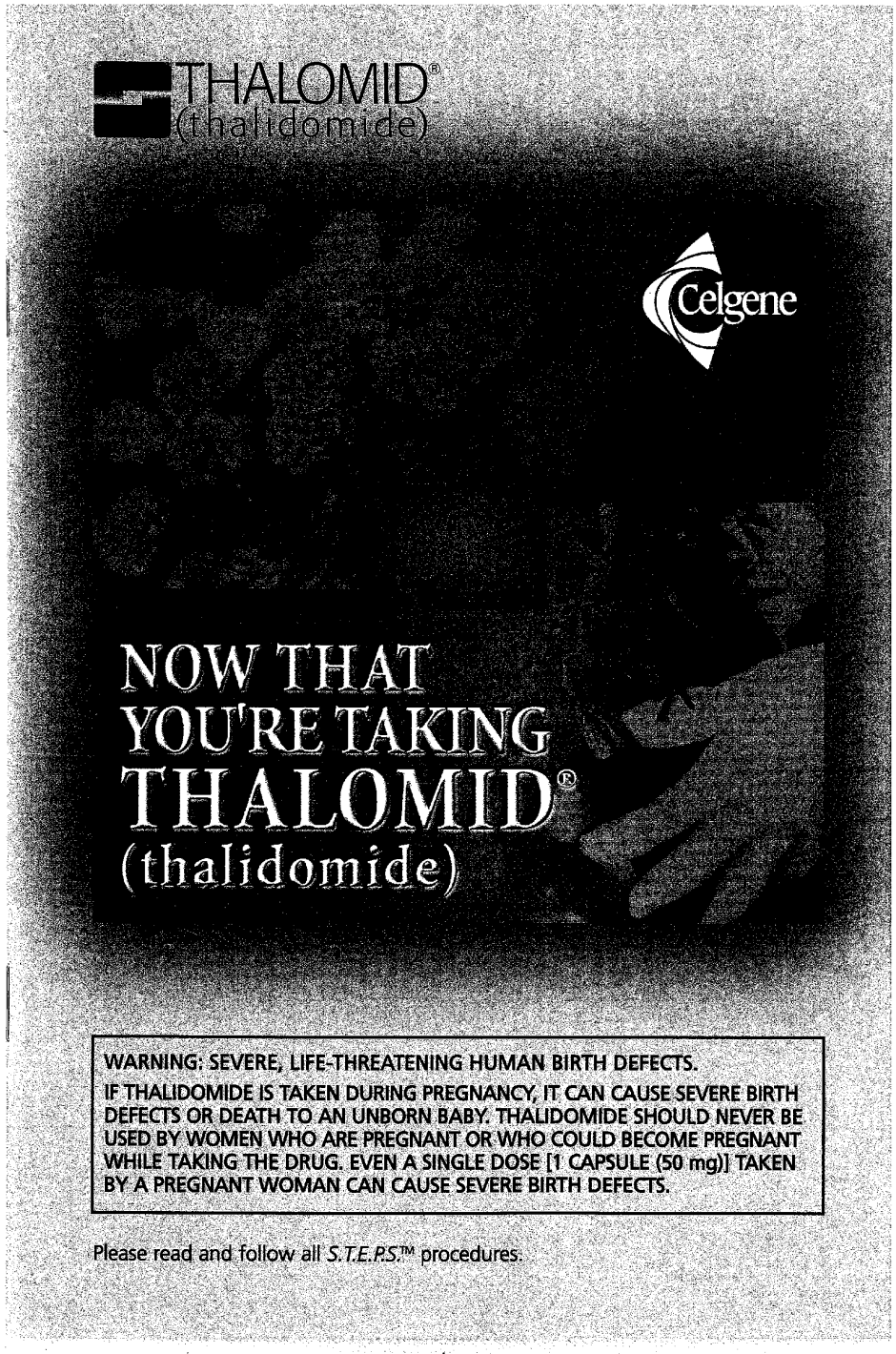
9. For patients with neutropenia, the physician should:
   a. re-evaluate the patient's treatment regimen and consider discontinuing THALOMID® (thalidomide) until the neutropenia resolves for any patient whose absolute neutrophil count (ANC) decreases below 750/mm^3.
   b. discontinue THALOMID® (thalidomide) until the neutropenia has resolved for any patient whose ANC decreases below 500/mm^3.
   c. consider decreasing dose, or if necessary, discontinuing THALOMID® (thalidomide) treatment.
   d. a and c, but not b.
   e. all of the above.

10. For ENL, THALOMID® (thalidomide) should be administered at an initial dose of 100 to 300 mg/day and up to 400 mg/day for severe reactions. In addition:
   a. it should be administered once per day with water, preferably at bedtime and at least 1 hour after the evening meal.
   b. it should be started at the low end of the range for patients weighing less than 50 kg.
   c. when tapering patients off medication, it should be done in 50-mg decrements every 2 to 4 weeks.
   d. all of the above.

REFERENCES

1. Sherman M, Strauss S. Thalidomide: a twenty-five year perspective. *Food Drug Cosmetic Law J.* 1986;41:458-466.
2. Mellin GW, Katzenstein M. The saga of thalidomide (concluded): neuropathy to embryopathy, with case reports of congenital anomalies. *N Engl J Med.* 1962;267:1238-1244.
3. Hales B. Thalidomide on the comeback trail. *Nature-Medi*1999; 5:469-470.
4. Sheskin J. Thalidomide in the treatment of lepra reactions. *Clin Pharmacol Ther.* 1965;6:303-306.
5. Keravich DP, Daniels CE. Challenges of thalidomide distribn in a hospital setting. *Am J Health-Syst Pharm.* 1999;56:1721-1725.
6. THALOMID® [thalidomide] Package Insert, Celgene Corporation.
7. Lutwak-Mann C, Schmid K, Keberle H. Pathology: Thalidomide in Rabbit Semen. *Nature.* 1967;214:1018-1020.
8. Data on file, Celgene Corporation
9. Faigle JW, Keberle H, Riess W, et al. The metabolic fate of thalidomide. *Experientia.* 1962;18:389-397.
10. Scheffler MR, Colburn W, Cook KA, et al. Thalidomide does not alter estrogen-progesterone hormone single-dose pharmacokinetics. *Clin Pharmacol Ther.* 1999;65:483-490.
11. Eriksson T, Bjorkman S, Roth B, et al. Stereospecific determination, chiral inversion in vitro and pharmacokinetics in humans of the enantiomers of thalidomide. *Chirality.* 1995;7:44-52.
12. Trapnell CB, Donahue SR, Collins JM, et al. Thalidomide does not alter the pharmacokinetics of ethinyl-estradiol and norethindrone. *Clin Pharmacol Ther.* 1998;64:597-602.
13. Stirling DI. Pharmacology of thalidomide. *Sem Hematol.* 2000;37:5-
14. Calabrese L, Fleischer AB. Thalidomide: current and potential clinical applications. *Am J Med.* 2000;108:487-495.
15. Zeldis JB, Williams BA, Thomas SD, et al. STEPSTM: A comprehensive program for controlling and monitoring access to thalidomide. *Clin Ther.* 1999;21:319-330.
16. Ochonisky S, Verroust J, Bastuji-Garin S, Gherardi R, Revuz J. Thalidomide neuropathy incidence and clinicoelectrophysiologic findings in 42 patients. *Arch of Dermat.* 1994;130: 66–69.
17. Scoville CD, Reading JC. Open trial of thalidomide in the treatment of rheumatoid arthritis. *J Clin Rheumatol.* 1999; 5:1–7.
18. Fullerton PM, O'Sullivan DJ. Thalidomide neuropathy: a clinical, electrophysiological, and histological follow-up study. *J Neurol Neurosurg Psychiat.* 1968;31:543-551.
19. Haslett P, Tramontana J, Burroughs M, Hempstead M, Kaplan G. Adverse Reactions to Thalidomide in Patients Infected with Human Immunodeficiency Virus. *Clin Infect Dis.* 1997;24:1223-7.
20. Cazort RJ, Song YK. A Trial of Thalidomide in Progressive Lepra Reactions. *Cur Ther Res.* 1966;8:299-311.

NOTES


THALOMID®
(thalidomide)
Celgene
NOW THAT
YOU'RE TAKING
THALOMID®
(thalidomide)
WARNING: SEVERE, LIFE-THREATENING HUMAN BIRTH DEFECTS.
IF THALIDOMIDE IS TAKEN DURING PREGNANCY, IT CAN CAUSE SEVERE BIRTH DEFECTS OR DEATH TO AN UNBORN BABY. THALIDOMIDE SHOULD NEVER BE USED BY WOMEN WHO ARE PREGNANT OR WHO COULD BECOME PREGNANT WHILE TAKING THE DRUG. EVEN A SINGLE DOSE [1 CAPSULE (50 mg)] TAKEN BY A PREGNANT WOMAN CAN CAUSE SEVERE BIRTH DEFECTS.
Please read and follow all S.T.E.P.S.™ procedures.

WHAT YOU SHOULD KNOW ABOUT THALOMID® (thalidomide) THERAPY

Work with your doctor

During treatment with THALOMID® (thalidomide), it is important to work closely with your doctor and the other members of your health care team to recognize and carefully monitor possible side effects associated with THALOMID® (thalidomide) therapy. You are in the best position to identify any changes and report them to your doctor. This brochure outlines side effects that may occur in some patients during treatment with THALOMID® (thalidomide) and offers suggestions to help manage these effects in order to help you obtain the benefit of THALOMID® (thalidomide) therapy.

Side effects, with the possible exception of numbness, tingling, pain or burning sensation in the feet or hands (peripheral neuropathy) —which in some cases is irreversible—are temporary and should resolve when you stop taking THALOMID® (thalidomide).

Birth Defects

WARNING: SEVERE, LIFE-THREATENING HUMAN BIRTH DEFECTS.

IF THALIDOMIDE IS TAKEN DURING PREGNANCY, IT CAN CAUSE SEVERE BIRTH DEFECTS OR DEATH TO AN UNBORN BABY. THALIDOMIDE SHOULD NEVER BE USED BY WOMEN WHO ARE PREGNANT OR WHO COULD BECOME PREGNANT WHILE TAKING THE DRUG. EVEN A SINGLE DOSE [1 CAPSULE (50 MG)] TAKEN BY A PREGNANT WOMAN CAN CAUSE SEVERE BIRTH DEFECTS.

Drowsiness

Signs and symptoms associated with this sedative effect may include:

- Dizziness, weakness, fatigue, incoordination, trembling, confusion, mood changes

WHAT TO DO

- Taking THALOMID® (thalidomide) in the evening may minimize daytime drowsiness
- Some patients are able to develop a tolerance to the sedative effect of THALOMID® (thalidomide), with a decrease in the drowsiness occurring after several weeks of treatment
- Ask your doctor about adjusting your dose before stopping THALOMID® (thalidomide)
- If you are drowsy, do not drive a car or operate machinery while taking THALOMID® (thalidomide)
- Avoid alcohol and medications that may cause drowsiness, such as sedatives or tranquilizers, unless directed by your doctor

Rash

WHAT TO DO

- Notify your doctor immediately if a rash develops during treatment with THALOMID® (thalidomide)
- If a rash occurs, do not take another dose of THALOMID® (thalidomide) until you have been evaluated and given instructions by your doctor

Sudden dizziness after standing from a reclining or sitting position (orthostatic hypotension)

WHAT TO DO

- Sit upright for a few minutes before standing up from a reclining position
- Be sure your doctor knows about all other medications you are taking before starting treatment with THALOMID® (thalidomide)
  — It is especially important for your doctor to know about any blood pressure medications, diuretics ("water pills"), or heart medications
- Ask your doctor about adjusting your dose before stopping THALOMID® (thalidomide)

Numbness, tingling, pain, or burning sensation in the feet or hands (peripheral neuropathy)

WHAT TO DO

Notify your doctor at the occurrence of symptoms that typically begin as numbness and tingling in the toes and fingertips

- Be sure you tell your doctor about all of the medications you are taking
  — Other medications can contribute to these symptoms
- Avoid tight-fitting shoes and socks
- Wear shoes and socks that offer good air circulation to avoid overheating of feet
- Keep feet uncovered in bed to avoid friction and overheating
- Maintain moderate activity (such as walking), as tolerated, to enhance blood circulation
- Massaging affected areas may improve circulation and temporarily dull pain
- Soaking affected areas in cool water may help

Constipation

WHAT TO DO

- During THALOMID® (thalidomide) therapy, drink plenty of fluids (six to eight 8-ounce glasses per day)
- Increase your daily intake of dietary fiber
  — Good sources of dietary fiber include fresh fruits (including prunes or prune juice) and vegetables, plus whole grain breads and cereals
- To help prevent constipation, ask your doctor if you might benefit from starting a mild laxative at the start of THALOMID® (thalidomide) therapy
- Ask your doctor about adjusting your dose before stopping THALOMID® (thalidomide)

Swelling or fluid retention in the feet, ankles, and legs (peripheral or dependent edema)

WHAT TO DO

- If swelling or fluid retention occurs while taking THALOMID® (thalidomide), consult your doctor before trying any prescription or over-the-counter medications (including diuretics or "water pills") or treatments for swelling, bloating, water weight gain
- For some patients, occasional elevation of the feet and legs is helpful
- Lying down to rest for several hours each day may be necessary
- Wearing elastic stockings may also be helpful
- Ask your doctor about adjusting your dose before stopping THALOMID® (thalidomide)

Please see full Prescribing Information behind flap.

Provided as a service of
Celgene Corporation
7 Powder Horn Drive
Warren, NJ 07059 U.S.A.

Printed in the U.S.A. 3/00 CG267B

"Seed & Soil..."
The Tumor and its Environment

An educational service developed by Celgene Corporation
in conjunction with Paul G. Richardson, MD, Dana-Farber Cancer Institute

Celgene Corporation
7 Powder Horn Drive
Warren, NJ 07059 USA

Printed in U.S.A. 6/00 CG312

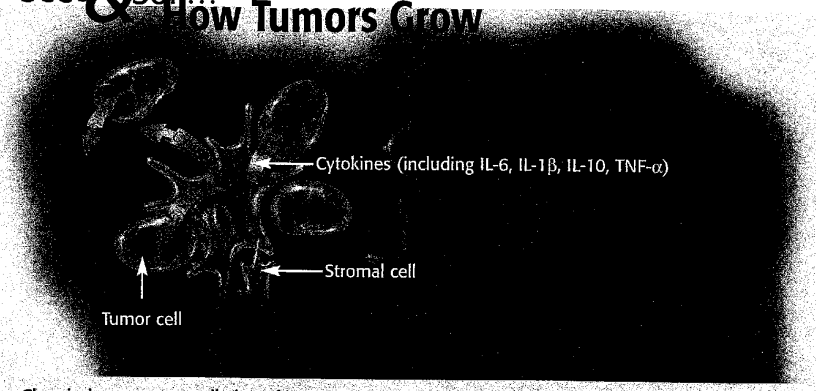
"Seed & Soil..." How Tumors Grow

When cancer cells multiply to form a growth, it is called a *tumor.* Tissue surrounds the tumor much like the way soil surrounds a seed. Seeds depend on soil to provide nutrients and other chemicals for growth. Similarly, tumors depend on surrounding tissue for certain chemicals to grow and survive. By changing the way some of these chemicals interact in the tissue surrounding tumors, it may be possible to slow, or even stop, tumor growth.

How Altering Its "Soil" May Stop a Tumor's Growth

A tumor depends greatly on its surrounding tissue for the chemicals it needs to grow. Changing the nature of this "soil" can create an environment that is hostile to tumor growth. Using certain drugs, a tumor's "soil" can be changed to:

- Interfere with the ability of specific chemicals to help tumors grow
- Make it harder for tumor cells to "stick" to body cells
- Boost the production of special cells that can attack tumors
- Block a tumor's ability to increase its blood supply



Chemical messengers called *cytokines* (including IL-6, IL-1β, IL-10, and TNF-α) are produced by stromal and/or tumor cells and help the tumor get the chemicals it needs for growth and survival.

Interfering With Chemical Messengers Called *Cytokines*

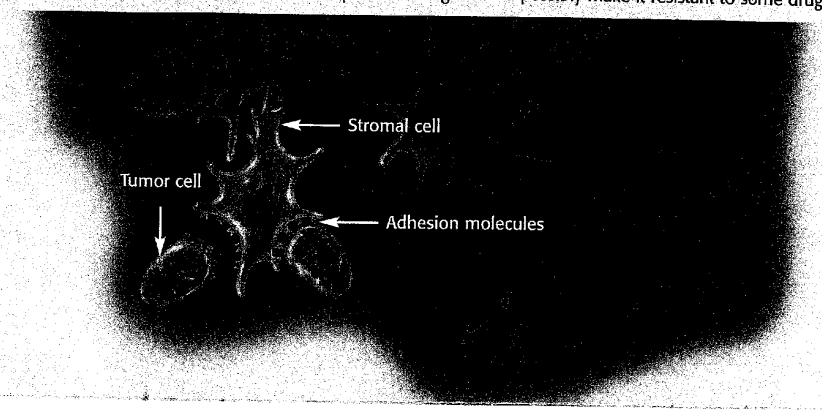
As a tumor develops in an organ of the body, the cells surrounding and supporting the organ (called *stromal cells*) produce a number of special proteins (called *cytokines*). Cytokines carry chemical "messages" between cells that help them receive nutrients and other chemicals needed for survival. The tumor uses cytokines to "request" more of the chemicals it needs to grow. It may also produce cytokines itself. The cytokines most involved with helping tumor cells grow include:

- Interleukin-6 (IL-6)
- Interleukin-1 beta (IL-1β)
- Interleukin-10 (IL-10)
- Tumor necrosis factor-alpha (TNF-α)

Certain drugs can interfere with the production of cytokines or their "message-carrying" ability. In this way, they deprive a tumor of the chemicals it needs for growth.

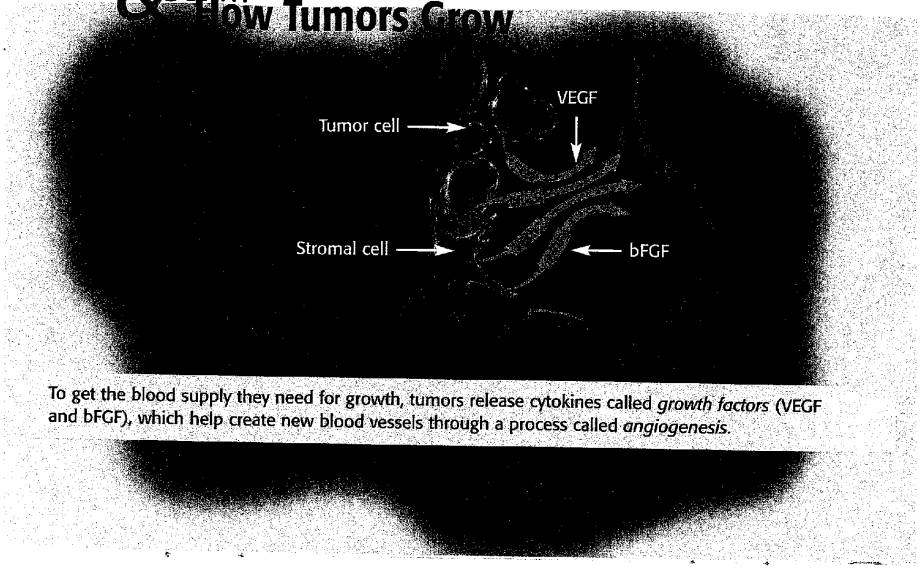
"Seed & Soil..." How Tumors Grow

Tiny antennae-like growths (called *adhesion molecules*) on tumor cells help them "stick" to an organ, which triggers the release of cytokines that help the tumor grow and possibly make it resistant to some drugs.



Making It Harder for Tumor Cells to "Stick" to Body Cells

To grow, tumor cells must first attach themselves to an organ in the body. Tiny antennae-like growths (called *adhesion molecules*) cover the tumor cells to help them "stick" to an organ. As tumor cells "stick," they trigger the release of cytokines from surrounding stromal cells. This helps the tumor grow and may even make it resistant to some drugs. Certain drugs can make tumor cells less "sticky" by changing the shape and arrangement of adhesion molecules on the surface of the tumor cell. This makes it harder for tumor cells to attach to, and grow on, body cells.

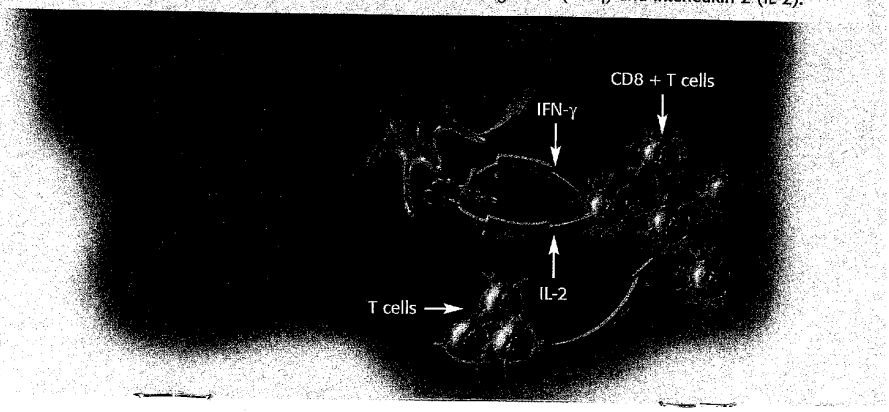


To get the blood supply they need for growth, tumors release cytokines called *growth factors* (VEGF and bFGF), which help create new blood vessels through a process called *angiogenesis*.

Stopping the Blood Supply to a Tumor

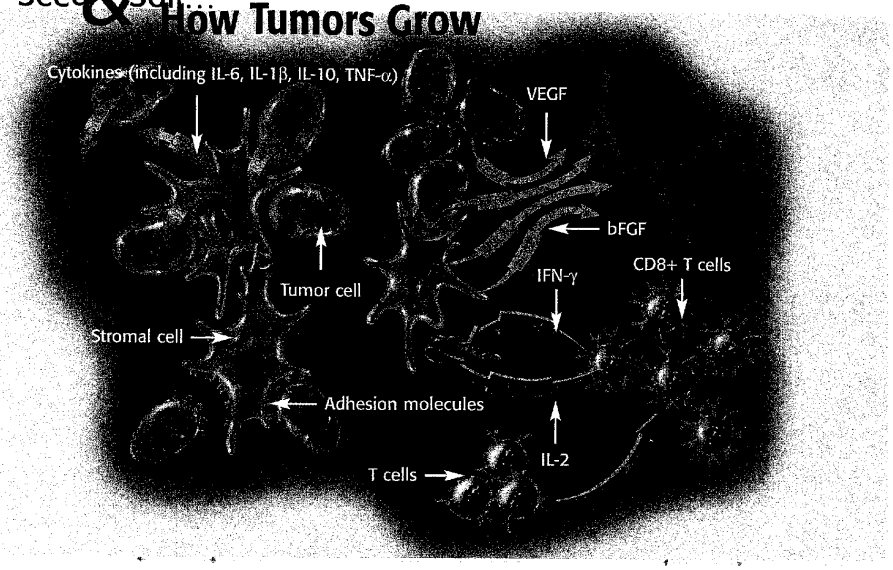
Like any other cells in the body, tumor cells need a blood supply to get the oxygen and nutrients they need to grow. To help a tumor "connect" with a blood supply, its cells release specific cytokines called *growth factors*. The two main growth factors involved are called *vascular endothelial growth factor* (VEGF) and *basic fibroblast growth factor* (bFGF). VEGF and bFGF help create new blood vessels (called *capillaries*) from existing vessels through a process called *angiogenesis*. Certain drugs can block the production of VEGF and bFGF, and they may also interrupt angiogenesis at different stages in its process. This slows or even stops the formation of new blood vessels, "starving" the tumor of the blood supply it needs to grow.

Specialized cells, the CD8+ T cells, are produced by the body's immune system and are designed to attack tumor cells with the help of two substances called interferon gamma (IFN-γ) and interleukin-2 (IL-2).



Boosting the Body's Ability to Attack Tumor Cells

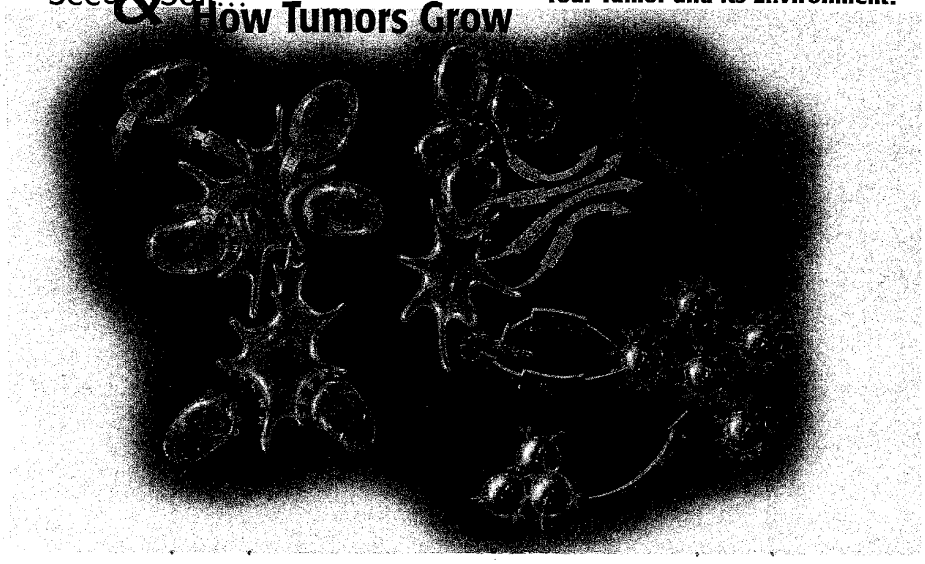
When bacteria and tumor cells are found in the body, they are recognized as "foreign" or "enemies" by the body's immune system. This triggers the release of different cells, called T cells, that are designed to attack foreign cells. One type of T cell, the CD8+ T cell, specializes in attacking tumor cells. To help it, the CD8+ T cell produces substances including *interferon gamma* (IFN-γ) and *interleukin-2* (IL-2). Drugs that help the immune system produce more CD8+ T cells significantly boost the body's ability to fight tumor cells.



Creating "Hostile Soil" Where Tumors Can't Grow

Like a seed, a tumor needs certain nutrients and other chemicals from its surrounding environment to grow and survive. By changing the chemical makeup of the tissue surrounding a tumor (its "soil"), it may be possible to stop, and even reverse, tumor growth. There are a number of different ways certain drugs can be used to create this "hostile soil."

- Certain drugs can interfere with the production of cytokines (such as IL-6, IL-1β, IL-10, and TNF-α) or with their "message-carrying" ability, depriving a tumor of the chemicals it needs for growth.
- Some drugs can make tumor cells less able to "stick" to organ cells by changing the shape and arrangement of adhesion molecules on the surface of the tumor cell. This makes it harder for tumor cells to attach to, and grow on, body cells.
- Drugs can be used to help the immune system produce more CD8+ T cells (and the IFN-γ and IL-2 they produce) to significantly boost the body's ability to fight tumor cells.
- Other drugs block the production of growth factors called VEGF and bFGF and may also interrupt angiogenesis. This slows or even stops the formation of new blood vessels, "starving" a tumor of the blood supply it needs to grow.



How Does "Seed and Soil" Relate to Your Tumor and Its Environment?

Research has shown that certain drugs can create a hostile environment for tumor growth and survival. Tumor growth and survival is threatened or even stopped.

Your doctor is informing you about the "seed and soil" theory to explain tumors and their environments because it may be involved in your illness. He or she will explain how your treatment may be related to the tumor's environment. Be sure to ask your doctor any questions you may have regarding your treatment.

Glossary of Terms

Adhesion molecules Small, antennae-like growths on the surface of some tumor cells that make it easier for them to "stick" to the extracellular matrix, stromal cells, or organ cells and begin to grow.

Angiogenesis A process by which new capillaries (the body's smallest blood vessels) form from existing capillaries.

Cytokines Proteins released by various types of cells that control the way the immune system responds. Cytokines carry chemical "messages" between cells that help them receive nutrients and other chemicals needed for survival.

Extracellular matrix A complex network of proteins to which cells anchor themselves. Most cells, including tumor cells, need to anchor to the extracellular matrix to survive. Alterations in the extracellular matrix may lead to cell death (apoptosis).

Growth factors Certain cytokines that stimulate the creation and growth of blood vessels.

Stromal cells Cells that make up the tissue surrounding and supporting an organ, but are not part of the organ itself.

T cells The general name for a variety of cells, triggered by the body's immune system, that are designed to attack foreign cells, such as bacteria.

Tumor A growth of cancerous tissue (tumor cells).

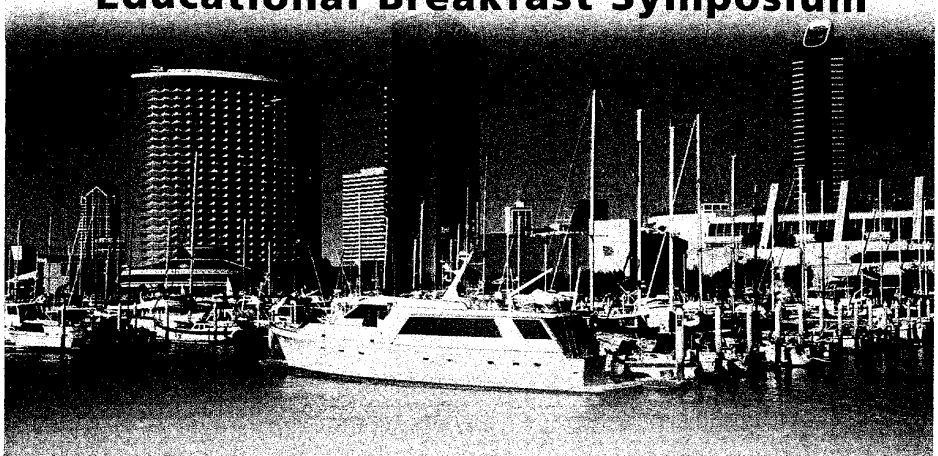
Questions to Ask Your Doctor

If you have any questions about your health condition, write them down here so you remember to ask your doctor.

Notes

Celgene Corporation
cordially invites you to attend an

Educational Breakfast Symposium



Targeting the Tumor Microenvironment

Symposium Management Symposium

Saturday, May 19, 2001

6:00AM — 8:00AM

San Diego Marriott Hotel & Marina,
Marriott Hall Ballroom
San Diego, CA
ONS 26th Annual Congress

Celgene

Agenda

6:00AM - 8:00AM

- ***Introduction***
  Melodie Thomas, RN, BSN, OCN®, CCRP
- ***Affecting Tumors in Their Microenvironment***
  James R. Berenson, MD
- ***Challenges in Managing Multiple Myeloma***
  Melodie Thomas, RN, BSN, OCN®, CCRP
- ***Effective Symptom Management***
  Jami Mayorga, RN, BSN, OCN®
- ***Prevention Strategies: The S.T.E.P.S. Program***
  Jami Mayorga, RN, BSN, OCN®
- ***Panel Q & A***
- ***Closing Remarks***
  Melodie Thomas, RN, BSN, OCN®, CCRP

Please register for this program using the enclosed Fax Registration Form and fax to: 1-800-544-8493.

The favor of a reply is requested by **April 23, 2001**.

Approval for contact hours by the Oncology Nursing Society (ONS) Department of Education is pending. The ONS is accredited as an approver of continuing education by the American Nursing Credentialing Center's Commission on Accreditation.

Celgene Corporation has been assigned meeting space to support an educational offering during the ONS 26th Annual Congress. The ONS' assignment of meeting space does not imply product endorsement nor does the ONS assume responsibility for the educational content.

Faculty

James R. Berenson, MD

Dr Berenson is currently the director for the multiple myeloma and bone metastasis programs at Cedars-Sinai Medical Center in Los Angeles, California. Recent publications include a review of the clinical use of oral bisphosphonates in metastatic bone disease in *Cancer* and germline *CDKN2A* mutations in multiple myeloma in *Blood*. In addition, Dr Berenson authored a chapter on the biology and treatment of myeloma bone disease in *Cancer and the Skeleton* (Martin Bunitz Ltd. Publishers, 2000).

Jami Mayorga, RN, BSN, OCN®

Ms Mayorga is a nurse clinician for the Department of Medical Oncology, Hematology, and Bone Marrow Transplant at the Arlington Cancer Center, Arlington, Texas. Recent presentations include a discussion of angiogenesis and metastatic disease at the Central Alabama Oncology Nursing Society Meeting and an update on management of outpatient allogeneic transplant patients at the Annual Meeting of the International Society for Experimental Hematology. Publications include a description of the effects of massive doses of CD34+ stem cells in matched sibling allogeneic transplants in the journal *Blood*.

Melodie Thomas, RN, BSN, OCN®, CCRP

Ms Thomas is the director of nursing research for The Sarah Cannon Cancer Center in Nashville, Tennessee. She has published extensively on the use of systemic therapy in a number of tumor types. Ms Thomas regularly presents at medical centers and for the Oncology Nursing Society and the American Cancer Society on topics such as management of treatment-related symptoms and the clinical research process.

OmegaMed Inc.
50 Dey Street
Jersey City, NJ 07306-9720

PRESORTED
FIRST CLASS
U.S. POSTAGE
PAID
NEW YORK, N.Y.
PERMIT NO. 6118

Targeting the Tumor Microenvironment

Symptom Management Symposium

Saturday, May 19, 2001, San Diego, CA

San Diego Marriott Hotel & Marina, Marriott Hall Ballroom

An educational symposium sponsored by Celgene

FAX-BACK REGISTRATION FORM

"Targeting the Tumor Microenvironment"
Symptom Management Breakfast Symposium
San Diego Marriott Hotel & Marina, Marriott Hall Ballroom
Saturday, May 19, 2001 6:00 AM - 8:00 AM

To register, simply complete this form and fax to: 1-800-544-8493
by April 23, 2001

On-site registration may be available, but advance registration is recommended.

☑ YES! I plan to attend. Please register me for this CE Breakfast Symposium.

Name and credentials:_____

RN#_____ONS#_____

Institution:_____

E-mail Address:_____

Work Fax:_____

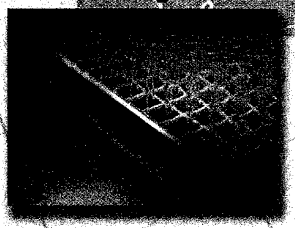
Work Phone:_____Date Faxed:_____

This educational event is sponsored by an unrestricted educational grant from Celgene

MULTIPLE MYELOMA RESEARCH FOUNDATION

MMRF Presents...

Global Advances in Multiple Myeloma



A CME activity on CD-ROM

PIM

cti
Making Cancer More Treatable

Sponsored by Postgraduate Institute for Medicine through unrestricted educational grants from Celgene Corporation and Cell Therapeutics, Inc.
This activity has been planned and produced in accordance with the ACCME Essential Areas and Policies.

Date of original release: July 2001
Expiration date: July 2002
Estimated time to complete activity: 2 hours

Celgene
Innovating Ltd

MULTIPLE MYELOMA RESEARCH FOUNDATION

Dear Doctor:

In May 2001, multiple myeloma's scientific elite gathered in Banff, Alberta, for the VIIIth International Myeloma Workshop. In a series of dazzling lectures, the participants poured out the state-of-the-art science on multiple myeloma, which has an annual incidence of more than 14,000 patients in the United States alone.

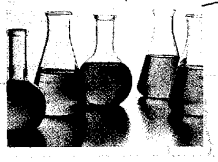
For oncologists and hematologists who need to know the evolving world of multiple myeloma, the Multiple Myeloma Research Foundation (MMRF) has developed ***Global Advances in Multiple Myeloma,*** a CME activity on CD-ROM, which focuses on these emerging treatment options, as they were discussed during the workshop.

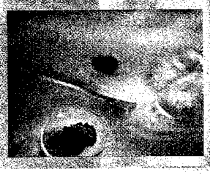
Each of the presentations featured on the Global Advances CD-ROM, together with related abstracts contained in the companion booklet, includes key findings about today's and tomorrow's approaches to therapies for multiple myeloma – the second most common hematologic malignancy and the third fastest growing cancer of any kind.

We invite you to participate in this compelling and engaging program which provides encouraging insight into therapeutic advances in multiple myeloma … MAIL or FAX your reply card TODAY!

Kathy Giusti, President
Multiple Myeloma
Research Foundation

Mohamad A. Hussein, MD
Director, Multiple Myeloma Program
Cleveland Clinic Taussig Cancer Center





Kenneth Anderson, MD
Dana-Farber
Cancer Institute

Bart Barlogie, MD, PhD
University of Arkansas
Cancer Research Center

Mohamad A. Hussein, MD
Cleveland Clinic
Taussig Cancer Center

S. Vincent Rajkumar, MD
Mayo Clinic

Featured Abstracts

Angiogenesis–
presentation by S. Vincent Rajkumar, MD

- Expression of Angiogenic Factors in Multiple Myeloma
- Interactions Between Myeloma Cells and Bone Marrow Microenvironment: Clues for the Biology and Management of the Disease
- Expression of VEGF and its Receptors in Myeloma
- Increasing Rationale for Targeting VEGF and Anti-Angiogenesis Approaches in Myeloma Therapy

Arsenic Trioxide in Multiple Myeloma: Rationale and Future Directions –
presentation by Mohamad A. Hussein, MD

- Background and Review of the Clinical Experience with Arsenic Trioxide
- Potential for Arsenic Trioxide as an Agent for Multiple Myeloma
- Preclinical Data with Arsenic Trioxide in Multiple Myeloma
- Role of Glutathione Depletion in Arsenic-based Treatment
- Arsenic Trioxide + Ascorbic Acid for the Treatment of Refractory/Relapsed Multiple Myeloma
- Arsenic Tri-Oxide in the Management of Advanced Multiple Myeloma Patients

Thalidomide: Mechanisms of Action and Clinical Outcomes –
presentations by Kenneth Anderson, MD and Bart Barlogie, MD, PhD

- Toward Curing Myeloma: Keeping the Pressure on Tumor Cells and the Microenvironment with High Dose Melphalan and Thalidomide
- Thalidomide Alone and in Combination for Previously Untreated Myeloma
- Angiogenesis and Anti-angiogenic Therapy with Thalidomide for Myeloma

New Therapies –
presentation by Kenneth Anderson, MD

- The Tumor Microenvironment: How it influences drug response and drug resistance in myeloma
- Vaults and Drug Resistance in Multiple Myeloma
- Results of a Phase I/II Trial with ^{166}Ho-DOTMP Plus High Dose Chemotherapy in Patients with Multiple Myeloma
- Antibody-Based Immunotherapy Against a Myeloma Cell-Specific Antigen HM1.24
- Novel Biologically Based Therapies for Myeloma

cti
Making Cancer More Treatable

PIM

Celgene
Innovating Life

Accreditation Statement

This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint sponsorship of Postgraduate Institute for Medicine and AOI Communications, Inc. The Postgraduate Institute for Medicine is accredited by the ACCME to provide continuing medical education for physicians and takes responsibility for the content, quality, and scientific integrity of this CME activity.

Designation Statement

The Postgraduate Institute for Medicine designates this educational activity for a maximum of 2 hours in category 1 credit toward the AMA Physician's Recognition Award. Each physician should claim only those hours of credit that he/she actually spent in the activity.

Faculty Disclosure Statement

All faculty participating in Continuing Medical Education activities sponsored by Postgraduate Institute of Medicine are expected to disclose to the audience any real or apparent commercial financial affiliations related to the content of their presentations/materials.

Support Statement

This CME activity is supported by unrestricted educational grants from Celgene Corporation and Cell Therapeutics, Inc.

To Receive Your **Complimentary** Copy of Global Advances in Multiple Myeloma:

- Complete and return the attached reply card by US Mail

OR

- Complete and fax the attached reply card to (203) 406-1726

For Further Information

- Please contact Lauren Fischer of AOI Communications, Inc. at (650) 321-6068 or via email at L.fischer@accessoncology.com

Global Advances in Multiple Myeloma

A CME activity on CD-ROM

Name_____

Affiliation_____

Address_____

City_____ State____ Zip_____

Phone_____ Fax_____

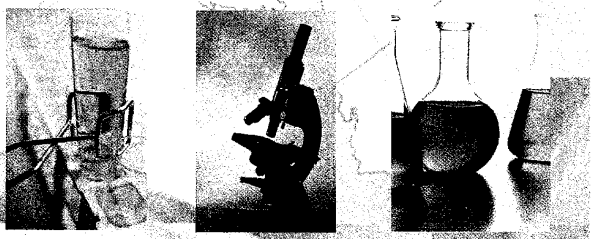
Sponsored by Postgraduate Institute for Medicine through unrestricted educational grants from Celgene Corporation and Cell Therapeutics, Inc.

(PLEASE PRINT CLEARLY)

The Multiple Myeloma Research Foundation (MMRF) is an international nonprofit organization dedicated to accelerating the search for a cure for multiple myeloma. The MMRF focuses on the following five goals: funding research, raising awareness, providing information, building collaboration and advocating optimal patient care.

Contact Information:

Web Address: www.multiplemyeloma.org
Email Address: themmrf@themmrf.org
Mailing Address: 3 Forest Street, New Canaan, CT 06840
Phone number: 203-972-1250



Global Advances in Multiple Myeloma
c/o **AOI Communications, Inc.**
405 El Camino Real, #131
Menlo Park, CA 94025-5240

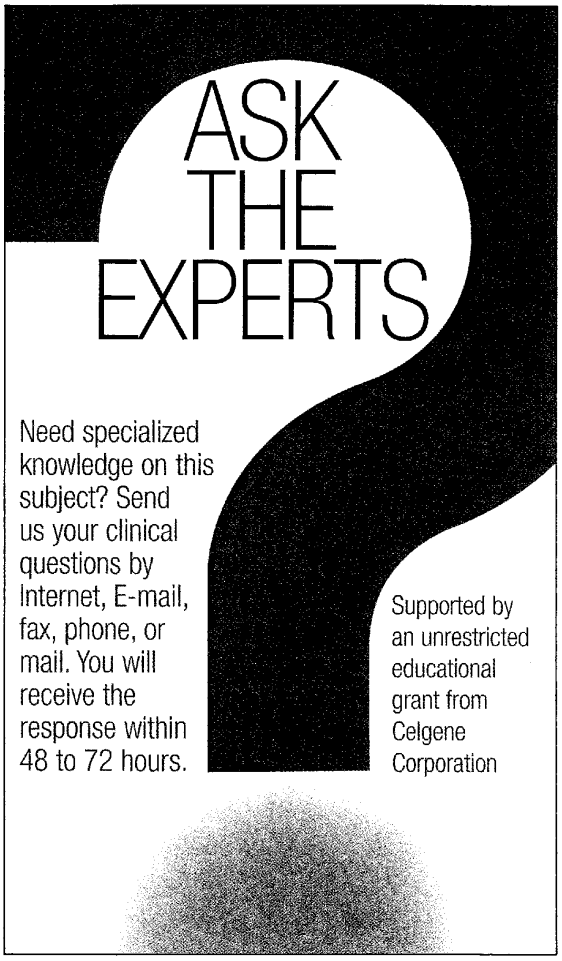
NO POSTAGE
NECESSARY
IF MAILED
IN THE
UNITED STATES

BUSINESS REPLY MAIL
FIRST CLASS MAIL PERMIT NO. 127 SAN FRANCISCO CA

POSTAGE WILL BE PAID BY ADDRESSEE

Global Advances in Multiple Myeloma
c/o **AOI Communications, Inc.**
405 El Camino Real, #131
Menlo Park, CA 94025-5240

ASK THE EXPERTS: Immunomodulatory Agents—New and Emerging Therapies



Meet the ASK THE EXPERTS Panel

SPECIALTY: ONCOLOGY/HEMATOLOGY

AREA OF INTEREST: MYELOMA

K. Raman Desikan, MD
Associate Professor
University of Arkansas for Medical Sciences
Little Rock, AR

Mohamad Hussein, MD
Director, Multiple Myeloma Program
Department of Hematology/ Medical Oncology
The Cleveland Clinic Foundation
Taussig Cancer Center
Cleveland, OH

AREA OF INTEREST: LEUKEMIA

Deborah Thomas, MD
Assistant Professor
Department of Leukemia
MD Anderson Cancer Center
Houston, TX

AREA OF INTEREST: RENAL CELL CARCINOMA

Robert Amato, DO
Associate Professor
Baylor College of Medicine
Scott Department of Urology
Houston, TX

Michael Gordon, MD
Associate Dean for Research
Associate Professor of Medicine
Department of Medicine
University of Arizona College of Medicine
Phoenix, AZ

AREA OF INTEREST: GASTROINTESTINAL MALIGNANCIES

Rangaswamy Govindarajan, MD
Assistant Professor of Medicine
University of Arkansas for Medical Sciences
Little Rock, AR

The ASK THE EXPERTS panel has vast clinical experience treating patients with immunomodulatory agents. Many panel members are also involved in clinical research of immunomodulatory agents in relation to their areas of interest.

AREA OF INTEREST: BRAIN TUMORS

Mark Kieran, MD, PhD
Director, Pediatric Medical Neuro-Oncology
Dana-Farber Cancer Institute
Children's Hospital
Boston, MA

AREA OF INTEREST: MELANOMA

Wen-Jen Hwu, MD, PhD
Associate Attending Physician
Melanoma Section
Clinical Immunology Service
Memorial Sloan-Kettering Cancer Center
New York, NY

AREA OF INTEREST: MYELODYSPLASIA

Alan List, MD
Associate Professor of Medicine
Section of Hematology/Oncology
Department of Medicine
University of Arizona College of Medicine
Director, Bone Marrow Transplant Program
University of Arizona Cancer Center
Tucson, AZ

AREA OF INTEREST: NURSING ISSUES

Lorraine Anderson, ANP
Multiple Myeloma Program
St. Vincents Comprehensive Cancer Center
New York, NY

SPECIALTY: GASTROENTEROLOGY

AREA OF INTEREST: INFLAMMATORY BOWEL DISEASE

Eric Vasiliauskas, MD
Associate Clinical Director
Inflammatory Bowel Disease Center
Cedars-Sinai Medical Center
Los Angeles, CA

SPECIALTY: RHEUMATOLOGY

Leonard Calabrese, DO
Head, Section of Clinical Immunology
Department of Rheumatic & Immunologic Disease
The Cleveland Clinic Foundation
Cleveland, OH

SPECIALTY: DERMATOLOGY

Joseph Jorizzo, MD
Professor and Chair
Department of Dermatology
Wake Forest University School of Medicine
Winston-Salem, NC

AREA OF INTEREST: LEPROSY

Samuel Moschella, MD
Senior Consultant
Department of Dermatology
Lahey Clinic
Clinical Professor
Dermatology
Harvard Medical School
Burlington, MA

Overview

The ASK THE EXPERTS program provides you with an opportunity to pose questions to a panel of physicians and nurses with considerable experience using immunomodulatory agents.

- Peer-to-peer communication
- Convenient access to current disease state information
- Practice-based responses to diagnostic and treatment challenges regarding immunomodulatory agents

Immunomodulatory Agents
Immunomodulatory agents have been shown to modulate specific components of the immune system that have been associated with major diseases.

These agents have been used to treat a variety of disease states with varying degrees of success. Currently, these agents are being studied and have shown great promise in many different forms of cancer, and in the fields of rheumatology and dermatology.

Mechanism of Action
The exact mechanism of action of immunomodulatory agents is not fully understood; however, they are

Present Your Question

Name _____

Specialty _____

Address _____

_____

Phone _____ Pager _____

Fax _____

E-mail _____

Would you like to receive your response by:

❑ E-mail ❑ Fax ❑ Phone ❑ Mail

If you would like to receive your response by telephone, please provide 2 call-back dates and times when you will be available to receive a response:

Date 1 _____ Date 2 _____

Time _____ AM/PM Time _____ AM/PM

Patient History

Age _____ Weight _____ Sex: ❑ Male ❑ Female

Symptoms/chief complaint _____

_____

Previous serious illness(es) _____

_____

Current medications _____

_____

Question _____

_____

_____

_____

_____

_____

_____

_____

Receive a response within 48 to 72 hours

Fax this form back to: (203) 359-2170

Overview *(continued)*

thought to regulate the production of the protein tumor necrosis factor-alpha (TNF-α), which is a cytokine. Overproduction of TNF-α has been linked to many chronic inflammatory and immunologic disorders, such as rheumatoid arthritis, inflammatory bowel disease, and Crohn's disease.

Another possible mechanism of action is the inhibition of the growth of blood vessels that feed tumors. This antiangiogenic effect of these agents has shown promise in treating a variety of cancers. Many clinical trials of immunomodulatory agents that have similar mechanisms of action are ongoing in a variety of disease states.

ASK THE EXPERTS

A great deal of interest on the part of practicing clinicians has surrounded this class of agents. However, much confusion exists about when and how immunomodulatory agents should be used. To address this problem, the ASK THE EXPERTS program has convened a multidisciplinary panel of experts, who have investigated and/or used immunomodulatory compounds, to serve as a resource for their peers with less experience with these agents.

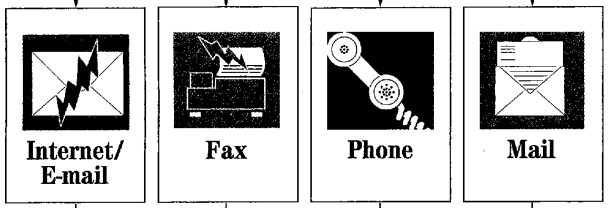
Disclaimer

Please note that answers provided by the ASK THE EXPERTS panel are for informational purposes only. Answers represent the experience and opinion of the responding physician/nurse and are not based on a full clinical evaluation of the patient. Health care professionals placing an inquiry are solely and fully responsible for the treatment of their patients and should fully evaluate and investigate all treatment options to determine optimal care.

This Is How It Works

Physician/nurse has an inquiry for the EXPERTS panel

Physician/nurse selects inquiry and response method



Inquiries are retrieved daily and distributed to the EXPERTS panel who will respond within 48 to 72 hours

Receive Your Reply Within 48 to 72 Hours

Contact the EXPERTS

Internet/E-mail
- Visit the www.immunoinfo.com Web site
- Complete the *Present Your Question* form
- Submit form electronically
- Or E-mail your question to expert@immunoinfo.com
- Panel member responds

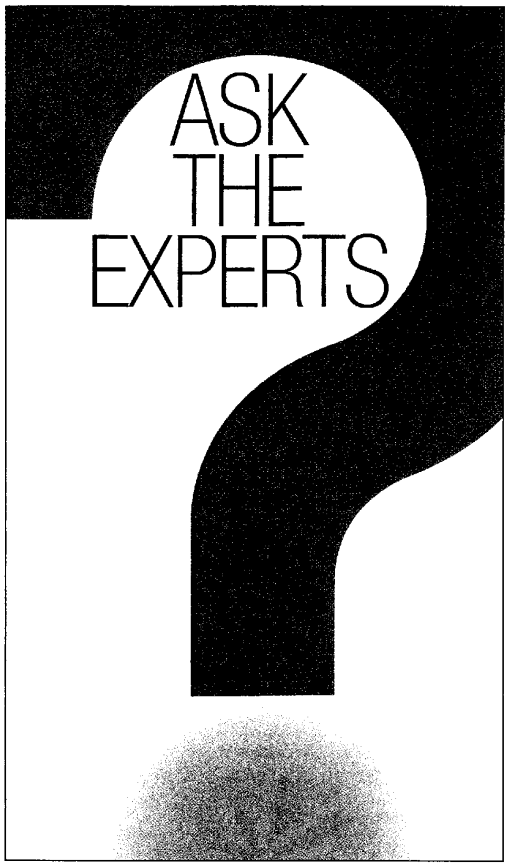
Fax
- Complete the *Present Your Question* form
- Fax the form to: (203) 359-2170
- Panel member responds

Telephone
- Call (888) 739-2191
- Answer the *Present Your Question* voice prompts
- Provide call-back dates and times
- Panel member responds during designated times
- If the expert is unsuccessful in reaching you, you will receive a written response

Direct mail*
- Complete the *Present Your Question* form
- Mail the form to: PharmaCom Group, Inc., 76 Progress Drive, Stamford, CT 06902
- Panel member responds

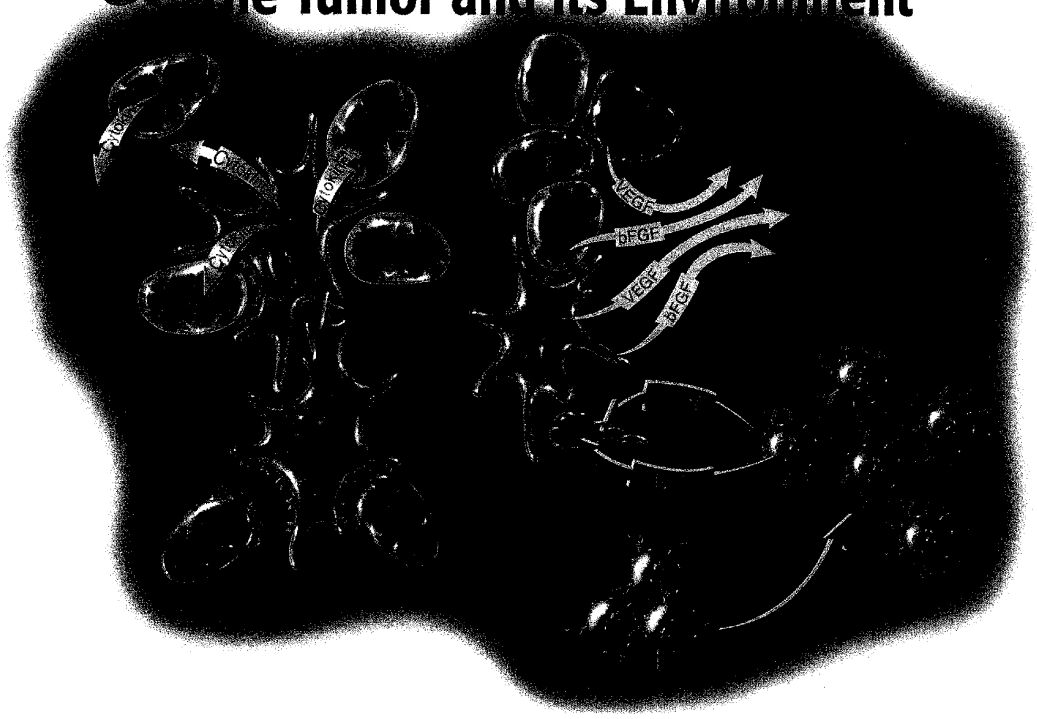
*Subject to the variables of direct mail delivery.

Inquiry and Response Options: Internet, E-mail, Fax, Phone, Mail

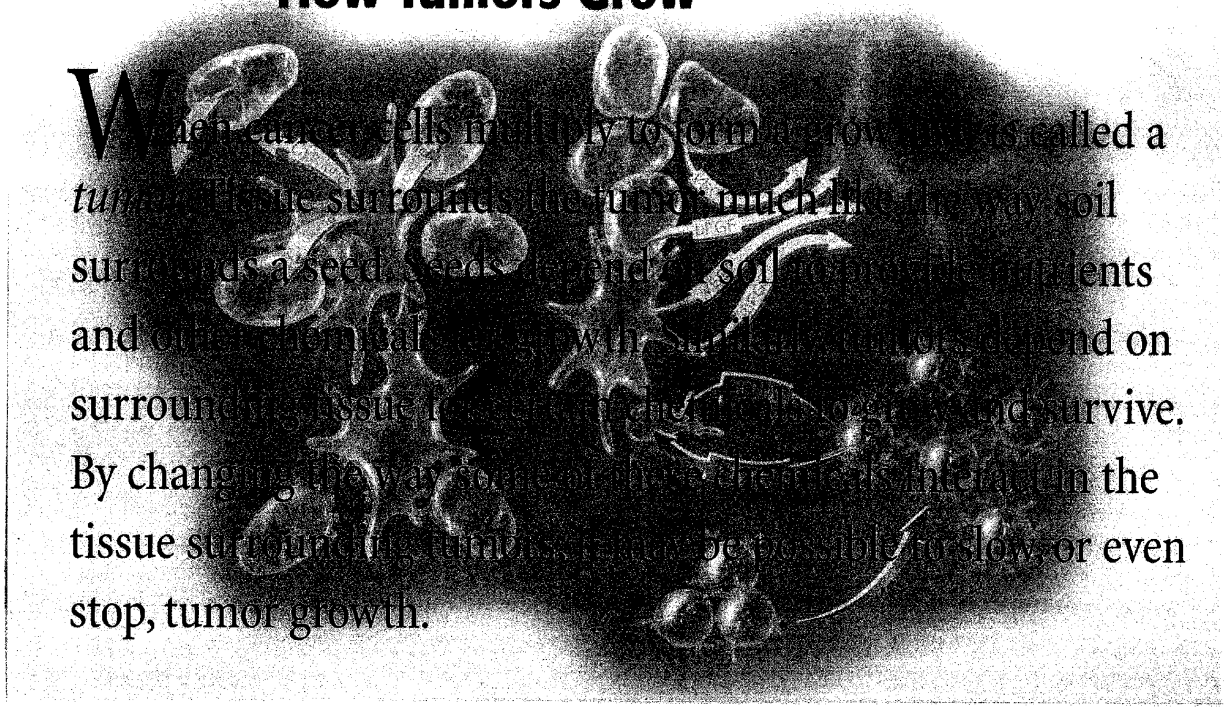

ASK
THE
EXPERTS

"Seed & Soil..."

The Tumor and Its Environment



"Seed & Soil..." How Tumors Grow



When cancer cells multiply to form a growth, it is called a *tumor*. Tissue surrounds the tumor, much like the way soil surrounds a seed. Seeds depend on soil to provide nutrients and other chemicals for growth. Similarly, tumors depend on surrounding tissue to provide the cells they need to grow and survive. By changing the way some of these chemicals interact in the tissue surrounding tumors, it may be possible to slow, or even stop, tumor growth.

How Altering Its "Soil" May Stop a Tumor's Growth

A tumor depends greatly on its surrounding tissue for the chemicals it needs to grow. Changing the nature of this "soil" can create an environment that is hostile to tumor growth. Using certain drugs, a tumor's "soil" can be changed to:

- Interfere with the ability of specific chemicals to help tumors grow
- Make it harder for tumor cells to "stick" to body cells
- Boost the production of special cells that can attack tumors
- Block a tumor's ability to increase its blood supply

An educational service developed by Celgene Corporation
in conjunction with Paul G. Richardson, MD, Dana-Farber Cancer Institute

Celgene Corporation
7 Powder Horn Drive
Warren, NJ 07059 USA

Printed in U.S.A. 10/00 CG312

System for Thalidomide Education and Prescribing Safety (*S.T.E.P.S.*™)

Patient Resource Pack

▼ Detach and affix to patient chart ▼

THALOMID®
(thalidomide)

Patient registration date: _____

Prescriber:

- Complete prescriber survey with every prescription
- Instruct the patient to complete a survey (check one):

❑ monthly ❑ every 6 months

Date of Visit	Date of Pregnancy Test (If applicable)	Prescriber Survey	Patient Survey*

*As indicated in Instructions for Prescribers.

 Printed in U.S.A. 6/01 542

 Printed in U.S.A. 6/01 543

System for Thalidomide Education and Prescribing Safety (S.T.E.P.S.™)

Important Information for Men and Women Taking

THALOMID® (thalidomide)

50 mg Capsules
in blister packs containing 28 or 14 capsules

WARNING: SEVERE, LIFE-THREATENING HUMAN BIRTH DEFECTS.
IF THALIDOMIDE IS TAKEN DURING PREGNANCY, IT CAN CAUSE SEVERE BIRTH DEFECTS OR DEATH TO AN UNBORN BABY. THALIDOMIDE SHOULD NEVER BE USED BY WOMEN WHO ARE PREGNANT OR WHO COULD BECOME PREGNANT WHILE TAKING THE DRUG. EVEN A SINGLE DOSE [1 CAPSULE (50 mg)] TAKEN BY A PREGNANT WOMAN CAN CAUSE SEVERE BIRTH DEFECTS.

WARNING: FOR YOUR HEALTH AND SAFETY, PLEASE READ THIS BOOKLET CAREFULLY. ALSO, BE SURE YOU UNDERSTAND WHAT YOUR DOCTOR HAS TOLD YOU ABOUT THALOMID (THALIDOMIDE) BEFORE STARTING TREATMENT.

Table of Contents

Before taking THALOMID® (thalidomide), you must:

- Understand that THALOMID® (thalidomide) can cause severe birth defects
- Know how to prevent pregnancy, if you are a woman
- Understand that you must use latex condoms EVERY TIME you have sexual contact with a woman, if you are a man
- Understand that you must NEVER share this drug with friends, relatives, or anyone else
- Know about other health problems called "side effects"
- Understand that you must NEVER donate blood or sperm while you are taking THALOMID® (thalidomide)

How to Use This Booklet

For easy reading, this booklet has four sections. If you are a woman, read all of Sections 1, 2, and 4. If you are a man, read all of Sections 1, 3, and 4.

This booklet contains important information about THALOMID® (thalidomide), but may not answer all of your questions about the drug. If you need more information, ask your doctor before starting treatment.

A video presentation of the information in this booklet is available from your doctor. You may borrow a copy to view at home.

When you see this symbol, it means the information nearby is an important reminder not to get pregnant. THALOMID® (thalidomide) can cause severe birth defects.

Section 1: Information for All Patients

General guidelines for taking THALOMID® (thalidomide)

- THALOMID® (thalidomide) MUST NEVER be used by pregnant women or women who are able to become pregnant and are not using the required two methods of birth control. Just ONE CAPSULE (50 mg) taken by a pregnant woman can cause severe birth defects.
- Men taking THALOMID® (thalidomide) must use latex condoms every time they have sexual contact with women since THALOMID® (thalidomide) is found in semen or sperm.
- This medicine is ONLY for you. DO NOT SHARE IT WITH ANYONE, even someone who has symptoms like yours. It must be kept out of the reach of children and should never be given to women who are able to become pregnant.
- Contact your doctor immediately if you have any strange or unusual reactions to THALOMID® (thalidomide).
- Keep THALOMID® (thalidomide) in a cool, dry place.
- THALOMID® (thalidomide) does not induce abortion of the fetus and should never be used for contraception.

Birth defects
READ THIS SECTION CAREFULLY!

If a woman taking THALOMID® (thalidomide) gets pregnant, her baby will almost certainly have severe birth defects—or may even die. Women taking THALOMID® (thalidomide) MUST NOT become pregnant, and men taking THALOMID® (thalidomide) must not have sexual contact with a woman without

using a latex condom. If you have sexual contact without birth control for any reason, stop taking THALOMID® (thalidomide) immediately and talk to your doctor. If your doctor is not available, call 1-888-668-2528 for information about emergency contraception.

THALOMID® (thalidomide) can cause severe birth defects, including missing or severely deformed legs and arms. These babies often have hands attached directly to their shoulders and feet attached directly to their hips. Photo reprinted by permission.

Other medical problems

Warnings for all patients:
THALOMID® (thalidomide) can cause other health problems called "side effects," including:

- **Drowsiness:**
  THALOMID® (thalidomide) often causes drowsiness. If you are drowsy, you should not operate machinery or drive a car while taking THALOMID® (thalidomide).

- **Nerve damage:**
  Nerve damage is a common and potentially severe side effect that may be irreversible. Arms, hands, legs, and feet may tingle, hurt, or feel numb. If so, stop taking THALOMID® (thalidomide) and call your doctor right away.

Precaution

Do not drink alcohol or take any other medicines that may make you sleepy without consulting your doctor.

- **Allergic reaction:**
  If you have a red, itchy rash, stop taking THALOMID® (thalidomide) and call your doctor right away. You may also have a fever or fast heartbeat.

- **Dizziness:**
  If you feel dizzy, sit upright for a few minutes prior to standing up from a lying down or sitting position.

ANY OF THESE SIDE EFFECTS SHOULD BE REPORTED TO YOUR DOCTOR IMMEDIATELY!

Ask your doctor about other side effects associated with THALOMID® (thalidomide).

Section 2: Facts for Women

WARNING: THALOMID® (thalidomide) can cause SEVERE BIRTH DEFECTS. It must not be taken if you are pregnant. If you are capable of becoming pregnant you will need to use TWO methods of birth control for 4 weeks before beginning THALOMID® (thalidomide) therapy. Your doctor must confirm that you are NOT PREGNANT with pregnancy tests. Please read and understand all warnings.

Before treatment:

- You must sign a form that says you understand the risk of birth defects, and that you agree not to become pregnant while taking THALOMID® (thalidomide).

- Remember that this medicine is ONLY for you. YOU MUST NOT SHARE IT with ANYONE, even someone who has symptoms like yours. It must be kept out of the reach of children and should never be given to women who are able to have children.

- If there is ANY chance that you can get pregnant you must begin TWO methods of birth control 4 weeks BEFORE you start taking THALOMID® (thalidomide).

- Your doctor must give you a pregnancy test within the 24 hours before you begin taking THALOMID® (thalidomide). **If you are pregnant,** you cannot take THALOMID® (thalidomide).

- You will have pregnancy tests before and during treatment, even if you agree not to have sexual contact.

- You will be given information about the following acceptable birth control methods:

Highly effective methods
- Intrauterine device (IUD)
- Hormonal (birth control pills, injections, or implants)
- Tubal ligation
- Partner's vasectomy

Additional effective methods
- Latex condom
- Diaphragm
- Cervical cap

Remember: You must use at least one highly effective method and one additional effective method AT THE SAME TIME. However, your doctor may recommend that you use two barrier methods for medical reasons.

REMEMBER THAT THE ONLY METHOD OF BIRTH CONTROL THAT IS 100% EFFECTIVE IS NOT HAVING SEXUAL CONTACT AT ALL.

During treatment:

- You must take part in a mandatory, confidential survey that will help make sure that everyone taking THALOMID® (thalidomide) receives, understands, and follows information designed to prevent birth defects.

- If you are able to have children, you must continue to use TWO methods of birth control, as discussed with your doctor.

- You must talk to your doctor before changing any birth control methods you have already agreed to use.

- You should have a pregnancy test done by your doctor every week during the first 4 weeks of treatment. You will then have a pregnancy test every 4 weeks if your menstrual cycles are regular, or every 2 weeks if your cycles are irregular. You may also need to have a pregnancy test if you miss your period or have unusual menstrual bleeding.

- You will receive no more than a 4-week (28-day) supply of THALOMID® (thalidomide) at a time. You will not receive any THALOMID® (thalidomide) capsules unless testing proves that you are not pregnant. Your THALOMID® (thalidomide) prescription cannot be refilled automatically.

- If you have sexual contact without birth control or if, for any reason, you think you may be pregnant, you must IMMEDIATELY stop taking THALOMID® (thalidomide) and tell your doctor. If your doctor is not available, call 1-888-668-2528 for information about emergency contraception.

- If you get pregnant, you must IMMEDIATELY stop taking THALOMID® (thalidomide). Contact your doctor immediately to discuss your pregnancy. If you do not have an obstetrician, your doctor will refer you to one for care and counseling.

- You must not breast-feed a baby while you are being treated with THALOMID® (thalidomide).

- You must NEVER donate blood while you are being treated with THALOMID® (thalidomide).

- You should be examined by your doctor for nerve damage every month for 3 months after beginning treatment and periodically thereafter. Tests for nerve damage are simple and are not painful.

After treatment:

- You must continue to use the same TWO methods of birth control for 4 weeks after you receive your last dose of THALOMID® (thalidomide).

Section 3:
Facts for Men

WARNING: THALOMID® (thalidomide) can cause SEVERE BIRTH DEFECTS if a woman receives the drug during pregnancy. Because THALOMID® (thalidomide) is present in semen or sperm, you must USE A LATEX CONDOM EVERY TIME you have sexual contact with a woman who is able to get pregnant.

Before treatment:

- You must sign a form that says you understand the risk of birth defects and that you agree to NEVER have sexual contact with a woman unless you use a latex condom (read Section 1).
- Remember that this medicine is ONLY for you. You CANNOT share it with ANYONE, even someone who has symptoms like yours. It must be kept out of the reach of children and should never be given to women who are able to have children.

During treatment:

- You must take part in a mandatory, confidential survey that will help make sure that everyone taking THALOMID® (thalidomide) receives, understands, and follows information in the survey designed to help prevent birth defects. Men must participate in the survey because having sexual contact with a woman without a latex condom or sharing THALOMID® (thalidomide) capsules could result in exposing an unborn baby to the drug.
- You must use a latex condom **every time** you have sexual contact with a woman while you are taking THALOMID® (thalidomide) and for 4 weeks after you stop taking the drug.

- You must tell your doctor if you have sexual contact with a woman without using a latex condom, or if you think for any reason that your partner may be pregnant. If your doctor is not available, call 1-888-668-2528 for information about emergency contraception.

REMEMBER THAT THE ONLY BIRTH CONTROL METHOD THAT IS 100% EFFECTIVE IS NO SEXUAL CONTACT AT ALL.

- You must NOT donate sperm or blood while you are taking THALOMID® (thalidomide) or for 4 weeks after you stop taking the drug.
- You should be examined by your doctor for nerve damage every month for 3 months after beginning treatment and periodically thereafter. Tests for nerve damage are simple and are not painful.

After treatment:

- You must use a latex condom EVERY TIME you have sexual contact with a woman for 4 weeks after receiving your last dose of THALOMID® (thalidomide).

THALIDOMIDE VICTIMS ASSOCIATION OF CANADA

Section 4:
Warning from Thalidomide Victims Association of Canada (TVAC)

Dear Doctor/Patient:

Have you ever met someone who was born disabled after exposure to thalidomide?

We have. In fact, we are *thalidomiders*—the name we have adopted to describe the surviving children of mothers who were prescribed thalidomide during their pregnancy as a sedative or for nausea and other symptoms of "morning sickness."

You've undoubtedly seen the **dramatic photographs of babies with severe birth defects** caused when thalidomide is taken EVEN ONCE by a pregnant woman. You know the risks!

The **Thalidomide Victims Association of Canada** (TVAC) was formed to meet the needs of the approximately 125 thalidomiders alive in Canada today, and to aid the surviving 10 thalidomiders living in the United States. Of the 10,000 to 12,000 children born with thalidomide deformities around the world in the early sixties, 5,000 survive today. No one will ever know how many children were miscarried or were stillborn because of thalidomide.

TVAC exists as a survivors group to determine and find solutions to the ongoing problems we face. TVAC has also undertaken a mandate of monitoring the responsible use of thalidomide and ensuring the tragedy of the past *never happens again.*

Because of our own personal traumas, and those of our families, we have always stated that we can never accept a world with thalidomide in it.

However, as we know first-hand how people may suffer, we also concede that no one should suffer needlessly. If thalidomide can extend a life, or offer a better quality of life to people with debilitating or chronic illnesses, then we are forced to accept the fact that thalidomide use may be their choice.

As well, we are forced to prefer the regulated use of thalidomide over the alternative:

> *One thalidomide baby born out of ignorance is far worse than one born out of a legitimate attempt to regulate and control the distribution process of this drug.*

Since you may soon be involved in prescribing or taking thalidomide, we need for you to be **fully aware of the power you have ...**

- the responsibility to see that you **fully understand the risks thalidomide poses ...**
- the **commitment** to do whatever it takes to make sure that NOT EVEN ONE woman loses a child due to thalidomide.

We were as surprised as anyone when the people at Celgene Corporation, makers of THALOMID® (thalidomide), sought the opinions and input of those of us at TVAC concerning the use of thalidomide in the United States. We felt it was a respectful step in the right direction that our feelings, opinions, and knowledge were being considered.

We are also consoled to know that Celgene Corporation has instituted a comprehensive program to help physicians and pharmacists inform patients about side effects and risks and ensure that they are aware of precautions they must take before, during and after therapy.

The **System for Thalidomide Education and Prescribing Safety** (***S.T.E.P.S.***™) is a multifaceted program developed to help ensure that fetal exposure to THALOMID® (thalidomide) does not occur. All of the materials you need to comply with this system are enclosed.

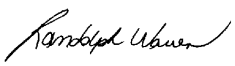
Meanwhile, we make you one promise:

> *The Thalidomide Victims Association of Canada will continue to watch the progression of events where thalidomide use is concerned.*

We have to!

For further information regarding the history of thalidomide or the status of survivors today, please feel free to contact us.

Sincerely,



Randolph Warren
Chief Executive Officer
Thalidomide Victims
Association of Canada

Giselle Cole
Past President
Thalidomide Victims
Association of Canada

Thalidomide Victims Association of Canada

P.O. Box 9061, Sub 40
London, Ontario N6E 1VO

Tel: (519) 681-0357

Fax: (519) 685-1518

[redacted]

Warning to patients taking THALOMID® (thalidomide)

50 mg Capsules in blister packs containing 28 or 14 capsules

Attention Women:
Do NOT take THALOMID® (thalidomide) if you are pregnant, if you are breast-feeding, or if you are able to become pregnant and are not using the required two forms of birth control.

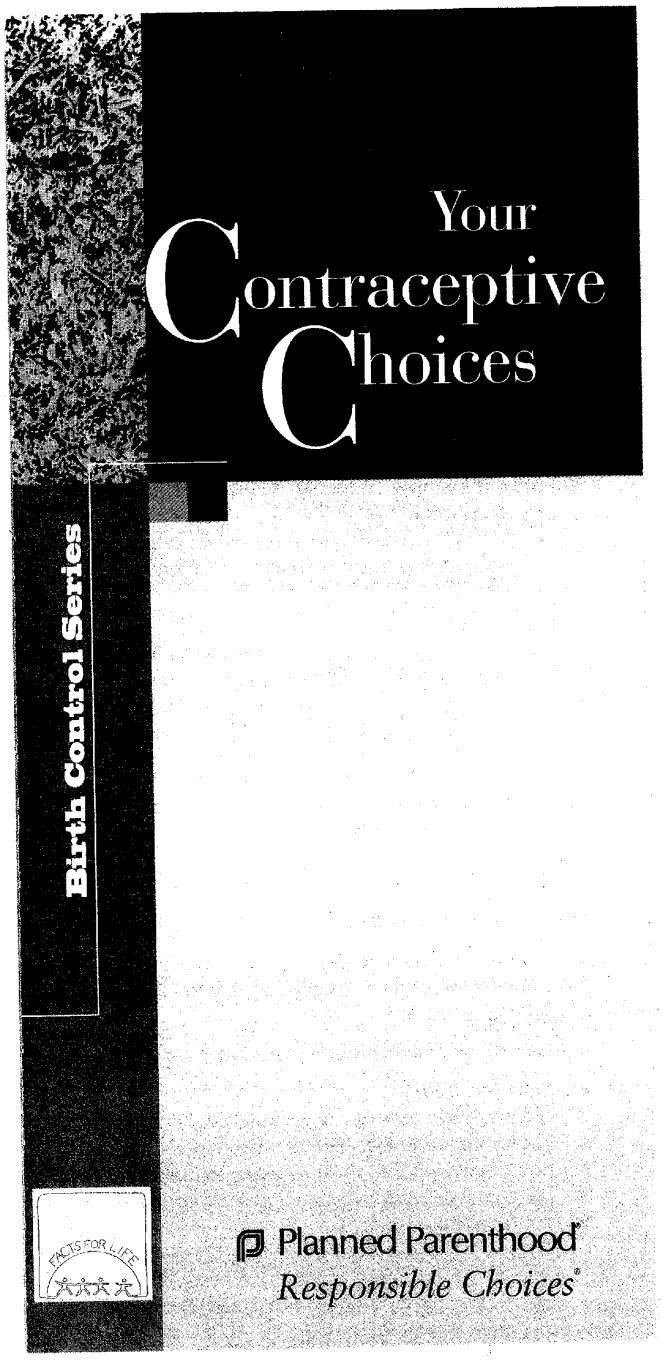
Attention Men:
You must use a latex condom EVERY TIME you have sexual contact with a woman.

If you have any questions, call 1-888-4-CELGENE

Celgene

Celgene Corporation
7 Powder Horn Drive
Warren, New Jersey 07059

 Printed in U.S.A. 6/01 541


Your
Contraceptive
Choices
Birth Control Series
FACTS FOR LIFE
Planned Parenthood
Responsible Choices®

If You Choose Continuous Abstinence...

... you will not have any sex play with a partner. This will keep sperm from joining egg.

EFFECTIVENESS
100%
- prevents sexually transmitted infections

ADVANTAGES
- no medical or hormonal side effects

POSSIBLE PROBLEMS
- difficult for many people to abstain from sex play for long periods
- forgetting to protect against pregnancy or sexually transmitted infections when abstinence ends

If You Choose Withdrawal...

... the man will pull his penis out of the vagina before he "comes" to keep sperm from joining egg.

EFFECTIVENESS
81–96%
nearly 100% with condom

- pregnancy is possible if sperm are spilled on the vulva
- not effective against sexually transmitted infections

ADVANTAGES
- can be used when no other method is available

POSSIBLE PROBLEMS
- requires great self-control, experience, and trust
- not for men who ejaculate prematurely
- not for men who don't know when to pull out
- not recommended for sexually inexperienced men
- not recommended for teens

If You Choose Outercourse...

... you will have sex play without vaginal intercourse. This will keep sperm from joining egg.

EFFECTIVENESS
nearly 100%

- pregnancy possible if sperm are spilled on the vulva
- effective against HIV and many other sexually transmitted infections — unless body fluids are exchanged through unprotected oral or anal intercourse

ADVANTAGES
- no medical or hormonal side effects
- can be used as safer sex if no body fluids are exchanged
- may prolong sex play and enhance orgasm
- can be used when no other methods are available

POSSIBLE PROBLEMS
- difficult for many people to abstain from vaginal intercourse for long periods
- people often forget to protect themselves against pregnancy or sexually transmitted infections if intercourse takes place

If You Choose Sterilization...

... you will have an operation to keep sperm from joining egg.

Tubal sterilization — intended to permanently block woman's tubes where sperm join egg
Vasectomy — intended to permanently block man's tubes that carry sperm

EFFECTIVENESS
99.5–99.9%
- not effective against sexually transmitted infections
- latex or female condoms can reduce risk of infection

ADVANTAGES
- permanent protection against pregnancy
- no lasting side effects
- no effect on sexual pleasure
- protects women whose health would be seriously threatened by pregnancy

POSSIBLE PROBLEMS
- mild bleeding or infection right after operation
- some people later regret not being able to have children
- negative reaction to anesthetic
- reversibility cannot be guaranteed
- rarely, tubes reopen, allowing pregnancy to occur
- pregnancies that rarely occur are more likely to be ectopic (in the fallopian tubes)

Tubal sterilization
- bruising where the incision is made
- very rare injury to blood vessels or bowel

Vasectomy
- infection or blood clot in or near the testicles
- temporary bruises, swelling, or tenderness of the scrotum
- sperm leakage may form temporary small lumps near testicles

COST
$1,000 – $2,500 for **tubal sterilization**.
$240 – $520 for **vasectomy**.
(Vasectomy costs less because it is a simpler procedure that can be done in the clinician's office.)

If You Choose Norplant®...

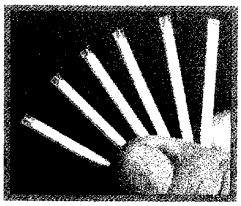
... your clinician will put six small capsules under the skin of your upper arm. Capsules constantly release small amounts of hormone that
- prevent release of egg
- thicken cervical mucus to keep sperm from joining egg

Removal must be done by clinician.

EFFECTIVENESS
99.95%
- not effective against sexually transmitted infections
- latex or female condom can reduce risk of infection

ADVANTAGES
- protects against pregnancy for five years
- no daily pill
- nothing to put in place before intercourse
- can use while breast-feeding starting six weeks after delivery
- can be used by some women who cannot take the Pill

POSSIBLE PROBLEMS



- side effects include irregular bleeding and other discomforts, including headaches, depression, and weight gain or loss
- possible scarring and/or discoloration of the skin at insertion site
- possibility that implants may be visible beneath the skin
- rarely, infection at insertion site
- pregnancies, which rarely occur, are more likely to be ectopic (in the fallopian tubes)
- removal is sometimes difficult, requiring more than one appointment

COST
$500 – $750 for exam, implants, and insertion.
$100 – $200 for removal.
Check with your local family planning clinic for information.

If You Choose
Depo-Provera®...

... your clinician will give you a shot of the hormone progestin in your arm or buttock every 12 weeks to

- prevent release of egg
- thicken cervical mucus to keep sperm from joining egg
- prevent fertilized egg from implanting in uterus

EFFECTIVENESS

99.7%

- not effective against sexually transmitted infections
- latex or female condoms can reduce risk of infection

ADVANTAGES

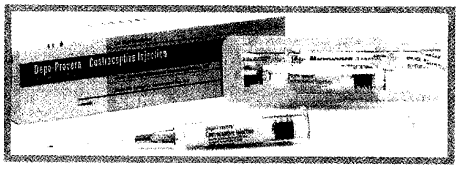
- protects against pregnancy for 12 weeks
- reduces menstrual cramps
- no daily pill
- nothing to put in place before intercourse
- can be used by some women who cannot take the Pill
- protects against cancer of the lining of the uterus and iron deficiency anemia
- can be used while breast-feeding immediately after delivery

POSSIBLE PROBLEMS

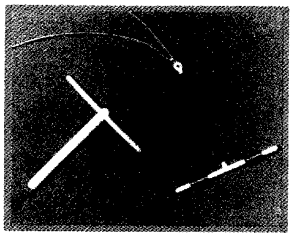
- side effects include loss of monthly period, irregular bleeding, increased appetite, headaches, depression, abdominal pain, and increased or decreased sex drive
- side effects not reversed until medication wears off (up to 12 weeks)
- may cause delay in getting pregnant after shots are stopped
- pregnancies, which rarely occur, are more likely to be ectopic (in the fallopian tubes)

COST

$20 – $40 for visits to a clinician.
$30 – $75 per injection. Some family planning clinics charge according to income.



If You Choose
The IUD
(Intrauterine Device)...



Progestasert® and ParaGard®

... your clinician will put a small plastic device in your uterus. The IUD contains copper or hormones that

- keep sperm from joining egg
- prevent fertilized egg from implanting in uterus

EFFECTIVENESS

97.4–99.2%

- not effective against sexually transmitted infections
- latex or female condoms can reduce risk of infection

ADVANTAGES

- nothing to put in place before intercourse
- copper IUDs may be left in place for up to 10 years
- no daily pill
- IUDs with hormones may reduce menstrual cramps and may be left in place for one year.

POSSIBLE PROBLEMS

- increase in cramps
- spotting between periods
- heavier and longer periods
- increased chance of tubal infection for women who contract a sexually transmitted infection, which may lead to infertility
- rarely, wall of uterus is punctured during insertion
- rarely, insertion can cause infection
- pregnancies, which rarely occur, are more likely to be ectopic (in fallopian tubes)

COST

$150 – $300 for exam, insertion, and follow-up visit.
Some family planning clinics charge according to income.

You May Want Emergency Contraception if...

His condom broke. You forgot to take your pill. He didn't pull out in time. You weren't using any birth control. He forced you to have unprotected sex.

Emergency Contraception (EC) ...
... is designed to prevent pregnancy *after* unprotected vaginal intercourse.
... is provided in two ways:

- **Emergency IUD insertion** within five days of unprotected intercourse is **99.9% effective.**
- **Emergency contraception pills** — two doses of hormonal pills taken 12 hours apart and started within 72 hours of unprotected sex — reduces the risk of pregnancy **75–89%**. The sooner a woman starts EC, the more effective it may be. Nausea, vomiting, and cramping are common side effects when combined hormones — estrogen and progestin — are used.

Don't use emergency hormonal contraception if you

- are pregnant
- are allergic to the medication

Consult your clinician about what kind of emergency contraception pills may be best for you.

Call toll-free
1-800-230-PLAN
for an appointment with the nearest Planned Parenthood center.

Planned Parenthood®
www.plannedparenthood.org
www.teenwire.com

2012 *Your Contraceptive Choices* 11/00-500 2.1
ISBN 0-934586-84-5

If You Choose Lunelle...

... your clinician will give you a shot with the hormones estrogen and progestin in your arm, buttock, or thigh every month to

- prevent release of egg
- thicken cervical mucus to keep sperm from joining egg
- prevent fertilized egg from implanting in uterus

EFFECTIVENESS

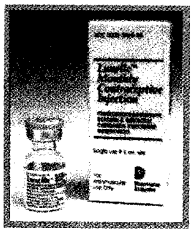
more than 99%

- not effective against sexually transmitted infections
- latex or female condoms can reduce risk of infection

ADVANTAGES

- protects against pregnancy for one month
- no daily pill
- nothing to put in place before intercourse

Although results of studies won't be available for some time, it is assumed that the advantages of Lunelle are similar to those of combination pills:



- periods become more regular
- less: menstrual cramping, acne, iron deficiency anemia, premenstrual tension, menstrual flow, and rheumatoid arthritis
- protects against ovarian and endometrial cancers, pelvic inflammatory disease, non-cancerous growths of the breasts, ovarian cysts, and osteoporosis (thinning of the bones)
- fewer tubal pregnancies

POSSIBLE PROBLEMS

- must receive injection once a month
- rare but serious health risks, including blood clots, heart attack, and stroke — women who are over 35 and smoke are at a greater risk
- other side effects include temporary irregular bleeding, loss of monthly period, weight gain or loss, depression, nausea, breast tenderness, and other discomforts

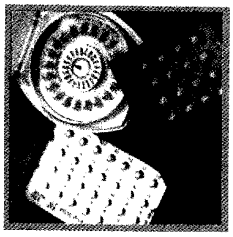
COST

$30 – $35. Some family planning clinics charge according to income.

If You Choose The Pill...

... your clinician will prescribe the right pill for you. Take one pill once a day. Complete one pill-pack every month. Combination pills contain estrogen and progestin. Others are progestin-only. Pills contain hormones that work in different ways.

- Combination pills prevent release of egg.
- Both types thicken cervical mucus to keep sperm from joining egg.
- Both types also may prevent fertilized egg from implanting in uterus.



EFFECTIVENESS

95–99.9%

- not effective against sexually transmitted infections
- latex or female condoms can reduce risk of infection

ADVANTAGES

- nothing to put in place before intercourse
- periods become more regular
- less: menstrual cramping, acne, iron deficiency anemia, premenstrual tension, menstrual flow
- protects against ovarian and endometrial cancers, pelvic inflammatory disease, non-cancerous growths of the breast, ovarian cysts, and may protect against osteoporosis (thinning of the bones)
- fewer tubal pregnancies

POSSIBLE PROBLEMS

- must be taken daily
- rare but serious health risks, including blood clots, heart attack, and stroke — women who are over 35 and smoke are at greater risk
- side effects include temporary irregular bleeding, loss of monthly period, weight gain or loss, depression, nausea, breast tenderness, and other discomforts

COST

$15 – $25 per monthly pill-pack at drugstores — often less at clinics.

$35 – $125 for exam. Some family planning clinics charge according to income.

If You Choose
The Condom...

... you will cover penis with a sheath before intercourse to keep sperm from joining egg.

The sheath may be made of thin latex, plastic, or animal tissue.

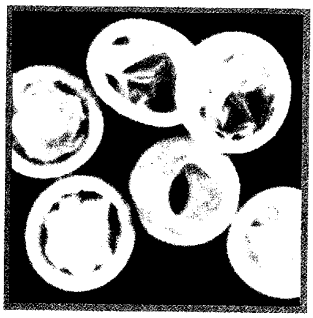
Lubricate condoms with spermicide to immobilize sperm and increase protection against pregnancy.

EFFECTIVENESS
86–98%
nearly 100% with withdrawal

Latex condoms are effective against many sexually transmitted infections — including HIV, the virus that can cause AIDS.

ADVANTAGES
- ❋ easy to buy in drugstores, supermarkets, etc.
- ❋ can help relieve premature ejaculation
- ❋ can be put on as part of sex play
- ❋ can be used with other methods to reduce risk of infection

POSSIBLE PROBLEMS
- ❋ uncooperative partners
- ❋ latex allergies
- ❋ loss of sensation
- ❋ breakage



COST
50¢ and up.
Some family planning centers give them away or charge very little.

If You Choose
The Diaphragm or Cervical Cap...

... your clinician will fit you with a shallow latex cup (**diaphragm**) or a thimble-shaped latex cap (**cervical cap**). Clinician also will show you how to coat **diaphragm** or **cap** with spermicide and put it in your vagina to keep sperm from joining egg.

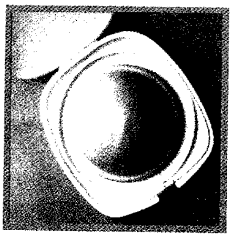
EFFECTIVENESS
80–94% — diaphragm
80–90% — cervical cap for women who have not had a child
60–80% — cervical cap for women who have had a child
- ❋ not effective against sexually transmitted infections
- ❋ latex or female condoms can reduce risk of infection

ADVANTAGES
- ❋ no major health concerns
- ❋ can last several years

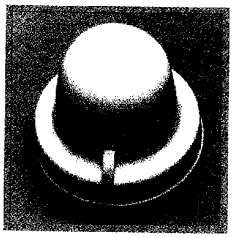
POSSIBLE PROBLEMS
- ❋ can be messy
- ❋ allergies to latex or spermicide
- ❋ should not be used during vaginal bleeding or infection

Diaphragm
- ❋ increased risk of bladder infection
- ❋ can only be left in place for up to 24 hours

Cervical Cap
- ❋ difficult for some women to use
- ❋ only four sizes — difficult to fit some women
- ❋ can only be left in place for up to 48 hours



Diaphragm



Cervical Cap

COST
$13 – $25 for diaphragm or cap.
$50 – $125 for examination.
Often costs less at family planning clinics.
$4 – $8 for supplies of spermicide jelly or cream.

If You Choose
The Female Condom or Spermicide...

... you will follow package instructions and insert **female condom** deep in your vagina to keep sperm from joining egg, or
... you will follow package instructions and insert **spermicide** — contraceptive foam, cream, jelly, film, or suppository — deep into your vagina shortly before intercourse to keep sperm from joining egg. Spermicides immobilize sperm.

Follow package instructions to remove **female condom**. **Spermicide** dissolves in vagina.

EFFECTIVENESS
79–95% female condom 72–94% spermicide

The **female condom** reduces the risk of sexually transmitted infections, including HIV. Use it or the latex condom with all other methods for protection against infection.

ADVANTAGES
- ❋ easy to buy in drugstores, supermarkets, etc.
- ❋ insertion may be part of sex play
- ❋ erection unnecessary to keep **female condom** in place
- ❋ **female condoms** can be used by people allergic to latex or **spermicide**
- ❋ external ring of **female condom** may stimulate clitoris

POSSIBLE PROBLEMS
Spermicide
- ❋ can be messy
- ❋ may irritate vagina or penis — which may increase risk of infection
- ❋ may set off allergies

Female condom
- ❋ may be noisy
- ❋ may irritate vagina or penis
- ❋ may slip into vagina during intercourse
- ❋ may be difficult to insert

COST
$2.50 for **female condom**.
$8 for applicator kits of **foam** and **gel**. $4 – $8 for refills.
Similar prices for **films** and **suppositories**.

If You Choose
Periodic Abstinence or FAMs
(Fertility Awareness Methods)...

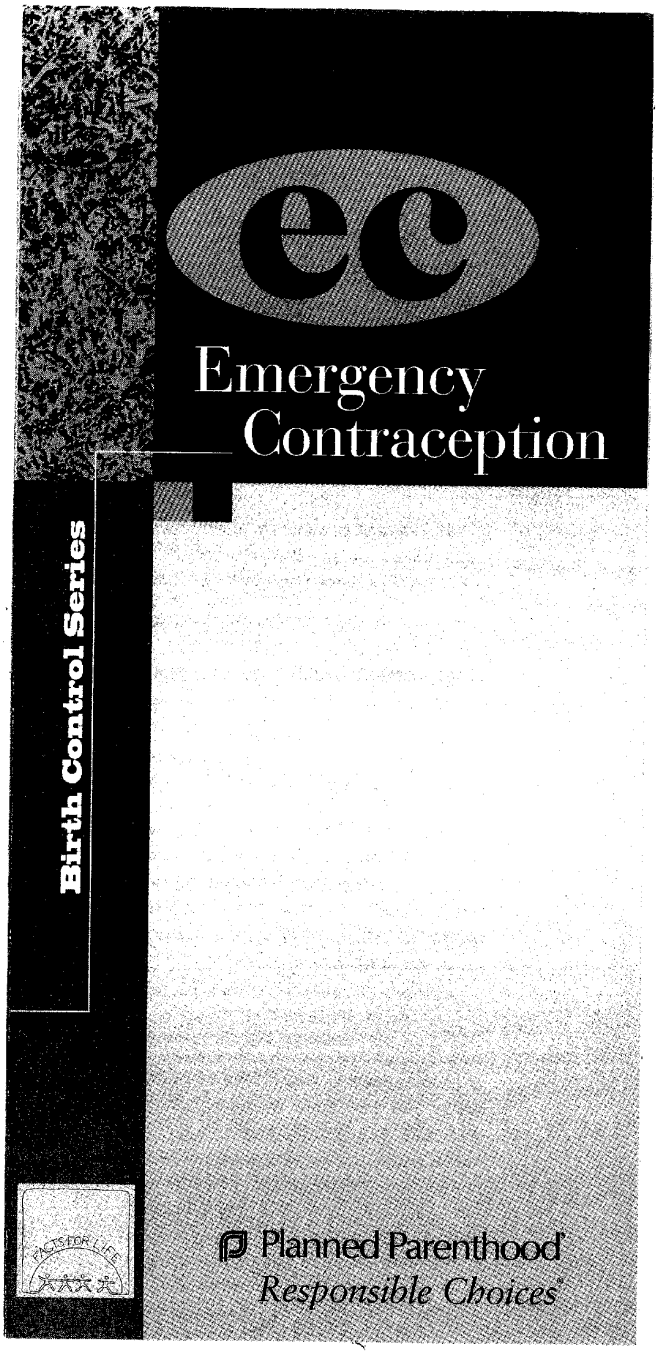
... a professional will teach you how to chart your menstrual cycle and to detect certain physical signs to help you predict fertility or "unsafe" days. Abstain from intercourse **(periodic abstinence)** or use condoms, diaphragms, cervical caps, or spermicide **(FAMs)** during nine or more "unsafe" days.
Predicting fertility includes
- ❋ checking temperature daily
- ❋ checking cervical mucus daily
- ❋ recording menstrual cycles on calendar

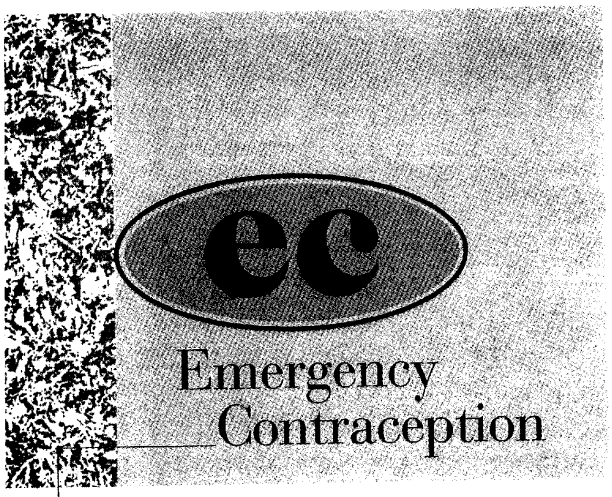
EFFECTIVENESS
75–99%
- ❋ not effective against sexually transmitted infections

ADVANTAGES
- ❋ no medical or hormonal side effects
- ❋ calendars, thermometers, and charts easy to get

POSSIBLE PROBLEMS
- ❋ requires months of training before effective use
- ❋ uncooperative partners
- ❋ taking risks during "unsafe" days
- ❋ poor record keeping
- ❋ illness and lack of sleep affect body temperature
- ❋ changes caused by vaginal infections and douches
- ❋ cannot use with irregular periods or temperature patterns

COST
$5 – $8 and up for temperature kits (drugstores).
Free classes often available in health and church centers.


ec
Emergency Contraception
Birth Control Series
Planned Parenthood
Responsible Choices



... can **prevent** pregnancy *after* unprotected vaginal intercourse. It is also called post-coital or "morning-after" contraception.

... is available from health care providers, Planned Parenthood health centers, and other women's health and family planning centers.

... is provided in two ways
- emergency contraceptive pills (ECPs)
- insertion of an IUD

... is used only if a woman is **not already pregnant** from a previous act of intercourse. It prevents pregnancy by stopping ovulation, fertilization, or implantation. It will not effect an existing pregnancy. And it will not cause an abortion.

ECPs

ECPs are given in two doses of hormonal pills. Some ECPs are "combination pills" with estrogen and progestin — synthetic hormones like the ones a woman's body makes. Others are progestin-only. Women who can't take estrogen may be able to take progestin-only pills.

Some clinicians review your medical history before they prescribe ECP. Some may want you to give informed consent by signature or over the telephone.

How to Use ECPs

ECPs are taken in two doses, 12 hours apart. They work best when the first dose is taken within 72 hours of unprotected vaginal intercourse. Some are designed specifically for emergency contraception — Plan B® (progestin-only) and Preven® (estrogen and progestin). Certain other birth control pills can be used for EC. Several brands have been shown to be effective. The number of pills in a dose depends on the brand. Use the same brand for both doses.

Pill Brand	Manufacturer	1st Dose
Alesse®	Wyeth-Ayerst	5 pink pills
Levlen®	Berlex	4 light orange pills
Levlite®	Berlex	5 pink pills
Levora®	Watson	4 white pills
Lo/Ovral®	Wyeth-Ayerst	4 white pills
LowOgestrel®	Watson	4 white pills
Nordette®	Wyeth-Ayerst	4 light orange pills
Ogestrel®	Watson	2 white pills
Ovral®	Wyeth-Ayerst	2 white pills
Ovrette®*	Wyeth-Ayerst	20 yellow pills
Plan B®*	Woman's Capital Corporation	1 white pill
PREVEN®	Gynétics	2 blue pills
Tri-Levlen®	Berlex	4 yellow pills
Triphasil®	Wyeth-Ayerst	4 yellow pills
Trivora®	Watson	4 pink pills

* Progestin-only

With a regular 28-pill birth control pack, use any of the first 21 pills for
Don't use the last seven pills in a 28-day pack. They are only reminder
hormones. With Triphasil or Tri-Levlen, use only the yellow ones. With

FIRST DOSE: Swallow the pills in the first dose within 72 hours — three days — after having unprotected sex. If you are not using progestin-only pills, you may want to eat saltines or soda crackers or drink a glass of milk 30 minutes before taking each dose to avoid vomiting. You can buy medication to reduce nausea, such as Dramamine® or Bonamine®.

SECOND DOSE: Swallow the second dose 12 hours after taking the first dose. If you threw up after the first dose, be sure to use an anti-nausea medication 30 minutes before taking the second one. Or you may want to take the second dose as a vaginal suppository by inserting the pills with your fingers as high into the vagina as you can reach. (The medication will be absorbed through the vaginal tissue.)

	2nd Dose (12 hours later)
	5 pink pills
ge pills	4 light orange pills
	5 pink pills
s	4 white pills
s	4 white pills
s	4 white pills
ge pills	4 light orange pills
s	2 white pills
s	2 white pills
ills	20 yellow pills
	1 white pill
	2 blue pills
lls	4 yellow pills
lls	4 yellow pills
	4 pink pills

ls for emergency contraception.
inder pills that contain no
With Trivora, use only the pink ones.

If you vomit the second dose, do not take any extra pills. They probably won't reduce the risk of pregnancy. But they will probably make you sick to your stomach.

After You Take the Pills

- Your next period may be earlier or later than usual.
- Your flow may be heavier, lighter, or more spotty than usual.
- If you see other health care providers before you get your period, remember to tell them that you have taken emergency contraception pills.
- Schedule a follow-up visit with your clinician if you do not have your period in three weeks or if you have symptoms of pregnancy.
- Be sure to use another method of contraception if you have vaginal intercourse any time before you get your period again.
- Continue using the birth control method of your choice for as long as you want to avoid pregnancy.

Side Effects

Side effects associated with the use of ECPs usually taper off one or two days after the second dose has been taken.

- Half of the women who take the combined pills feel sick to their stomachs, but only for about 24 hours.
- Up to one out of three women throw up with combined pills.
- The risk of nausea and vomiting is lower with progestin-only ECPs.
- Breast tenderness, irregular bleeding, fluid retention, dizziness, and headaches may also occur.

Frequent use of ECPs may cause periods to become irregular and unpredictable. The side effects of anti-nausea medication may include lightheadedness, dizziness, or feeling spacey. Please follow the precautions on the package insert.

Emergency contraception may not prevent ectopic pregnancy. An ectopic pregnancy is one that develops outside the uterus. It must be treated to prevent complications that may be fatal.

If you think you may have an ectopic pregnancy, get medical attention immediately. Signs of ectopic pregnancy include

- severe pain on one or both sides of the lower abdomen
- abdominal pain and spotting, especially after a very light or missed menstrual period
- feeling faint or dizzy

ECPs will not harm a fetus. Still, you should not use emergency contraception if you are pregnant.

Emergency IUD Insertion

A clinician can insert an IUD for emergency contraception within seven days of unprotected intercourse.
The Copper T 380A IUD (ParaGard®) is used for emergency contraception. It can be left in place for up to 10 years for very effective contraception. Or the IUD can be removed after your next menstrual period, when it is certain that you are not pregnant.

IUD insertion for emergency contraception is not recommended for

- women with more than one sex partner or whose partners have more than one partner
- women with new partners
- women who have been raped

Uterine cramping may occur during insertion. Some women feel a bit dizzy, and rarely a woman may faint.

If you have an IUD inserted, you may want to have someone with you to escort or drive you home. You may need to rest afterwards.

The side effects, advantages, and disadvantages of using IUDs for emergency contraception are the same as those associated with using IUDs for ongoing contraception.

continued over ➜

For more information about IUDs...

Ask your clinician for a copy of the Planned Parenthood pamphlet, *Understanding IUDs*, for more information about the advantages and disadvantages of the IUD as a regular method of birth control.

How Well Emergency Contraception Works

- **Combined ECPs reduce the risk of pregnancy by 75 percent.** For example, eight out of 100 women will become pregnant after having unprotected sex once during the second or third week of their cycles. But only two out of 100 will become pregnant after taking ECPs.
- **Progestin-only ECPs reduce the risk of pregnancy by 89 percent**. Only one woman out of 100 will become pregnant after taking progestin-only ECPs.

Timing is important

Timing affects how well ECPs work:

- ECPs work best taken as soon as possible after unprotected intercourse.
- The closer a woman is to ovulation at the time of unprotected intercourse, the greater her chances of pregnancy.

- **Emergency IUD insertion reduces the risk of pregnancy by 99.9 percent.** Only one out of 1,000 women will become pregnant after emergency IUD insertion.

Emergency contraception is meant for emergencies only. It is not as effective as the regular use of reversible contraception — Norplant®, Depo-Provera®, Lunelle®, the IUD, or the Pill.

ECPs do not continue to prevent pregnancy during the rest of the cycle. Other methods of birth control must be used.

Emergency contraception offers no protection against sexually transmitted infections. Consider testing for sexually transmitted infections if there is a possibility that unprotected sex put you at risk.

Where to Get Emergency Contraception

Emergency contraception is available at Planned Parenthood, college, public, and women's health centers; private doctors; and hospital emergency rooms — unless they are affiliated with religions that oppose the use of birth control.

Some clinics and clinicians will prescribe ECPs over the phone and call the prescription in to a pharmacy. ECPs are available directly from some pharmacists in Washington state.

You can get the names and phone numbers of five emergency contraception providers nearest you by calling, toll-free, the emergency contraception hotline — **1-888-NOT-2-LATE**. Or contact the nearest Planned Parenthood health center at **1-800-230-PLAN**.

Emergency Contraception to Go

Packs of ECPs are available from some women's health centers. Some may only provide them to women whose medical histories are well known to their clinicians. Take-home kits allow women to use ECPs in emergency situations without having to wait to see their clinicians.

Costs Vary Widely

Fees may be lesser at family planning clinics and health centers. Some use a sliding scale. Costs also depend on region and location and on which of the following services are needed. Here are some estimates:

ECP	Range of Costs
Plan B®	$8 – $20
PREVEN®	$8 – $20
one pack of combination pills	$20 – $35
two packs of progestin-only pills	$50
visit with health care provider (if needed)	$35 – $150
pregnancy test (if needed)	$10 – $20

IUD — The ParaGard® IUD costs about $400 for exam, IUD, and insertion. It lasts for 10 years. However, that amounts to only $40 a year if left in place.

Planned Parenthood®
Every child wanted and loved.
Every woman in charge of her destiny.

Nationwide, Planned Parenthood affiliates provide medical services and sexuality education for millions of women, men, and teenagers each year. Planned Parenthood also serves women and men around the world.

Call toll-free 1-800-230-PLAN for an appointment with the nearest Planned Parenthood center.

Support sexual and reproductive health and rights for women and men worldwide. Visit **www.plannedparenthood.org** and click on Responsible Choices.

For a free catalog of Planned Parenthood sexual health resources, call toll-free 1-800-669-0156 or visit **www.plannedparenthood.org/store**.

Written by Jon Knowles
Revised by Danielle Dimitrov

ISBN 0-934586-77-2

You May Want Emergency Contraception If

- His condom broke or slipped off, and he ejaculated inside your vagina.
- You forgot to take your birth control pills.
- Your diaphragm or cervical cap slipped out of place, and he ejaculated inside your vagina.
- You miscalculated your "safe" days.
- He didn't pull out in time.
- You weren't using any birth control.
- He forced you to have unprotected vaginal sex.

Contact your health care provider immediately if you have had unprotected intercourse and you think you might become pregnant. **Ask About Emergency Contraception.**

Planned Parenthood®
www.plannedparenthood.org
www.teenwire.com

EC — Emergency Contraception
2675 11/00-125 2.13.5
ISBN 0-934586-77-2

System for Thalidomide Education and Prescribing Safety (*S.T.E.P.S.*™)

Pocket Guide to *S.T.E.P.S.*™ and Patient Surveys

As a patient who is registered in the *S.T.E.P.S.*™ program for THALOMID® (thalidomide), you will need to complete a brief, confidential telephone survey before you can receive a prescription for the medication.

Patient Telephone Survey Frequency: Monthly

- Adult females who are able to become pregnant
- Female children
- Male patients

[redacted]

Patient Telephone Survey Frequency:
Every 6 Months

- Adult females who are not able to become pregnant

[redacted]

- Prior to filling your prescription, call the Celgene Customer Care Center at **1-888-4-CELGENE** (1-888-423-5436) PRESS "1" to complete the survey
- Be prepared with your Social Security Number

[redacted]

- Your doctor will write an authorization number on every prescription you receive for THALOMID® (thalidomide)
- After you have completed the phone survey, take the prescription to a registered *S.T.E.P.S.*™ pharmacy. To locate one, call **1-888-4-CELGENE** (1-888-423-5436)

 Printed in U.S.A. 6/01 546

Programa de información y prescripción segura de talidomida (*S.T.E.P.S.*™)

Guía de bolsillo sobre el programa *S.T.E.P.S.*™ y encuestas para el paciente

Todos los pacientes inscritos en el programa *S.T.E.P.S.*™ del fármaco THALOMID® (talidomida) deben completar una breve encuesta telefónica confidencial antes de poder recibir la receta para obtener dicho fármaco.

Frecuencia de la encuesta telefónica para el paciente:
Mensual

- Mujeres adultas que pueden quedar embarazadas
- Niñas
- Pacientes varones

Frecuencia de la encuesta telefónica para el paciente:
Cada 6 meses

- Mujeres adultas que no pueden quedar embarazadas

- Antes de obtener el medicamento, llame al Centro de Atención al Cliente de Celgene al teléfono **1-888-4-CELGENE** (1-888-423-5436). OPRIMA EL "1" para realizar la encuesta.
- Tenga a la mano su número del Seguro Social.

- Su médico escribirá un número de autorización en cada receta de THALOMID® (talidomida) que le entregue.
- Al finalizar su encuesta telefónica, lleve la receta a una farmacia participante en el programa *S.T.E.P.S.*™ Para averiguar cuáles son las farmacias participantes, llame al **1-888-4-CELGENE** (1-888-423-5436).

 Impreso en EE. UU. 6/01 546

S.T.E.P.S.™ At-A-Glance

Initial Prescription

- Counsel and perform pregnancy testing (if applicable)
- Provide mandatory contraception counseling
- Complete, print, and sign Patient Registration/Informed Consent Form
- Fax Patient Registration/Informed Consent Form to 1-888-432-9325
- Instruct patient to complete phone survey prior to filling prescription
- Complete a prescriber phone survey by calling 1-888-4-CELGENE (1-888-423-5436) and obtain a new authorization number for each prescription
  —Be prepared with:
  - Prescriber DEA number
  - Patient's Social Security Number
  - Date and result of patient's last pregnancy test (if applicable)
  - Average daily dose
  - Total number of days supplied
- Write the authorization number on the prescription

Subsequent Prescriptions

- Perform scheduled pregnancy testing (if applicable)
- Instruct patient to complete surveys **as scheduled,** prior to filling prescription
- Complete a prescriber phone survey
  —Be prepared with:
  - Prescriber DEA number
  - Patient's Social Security Number
  - Date and result of patient's last pregnancy test (if applicable)
  - Average daily dose
  - Total number of days supplied
- Obtain authorization number for each new prescription
- Write the authorization number on the new prescription

Please see complete **Instructions for Prescribers.**

THALOMID® (thalidomide)

Celgene

Printed in U.S.A. 6/01 547

Prescriber Guide to Fax Back Services
Call 1-888-423-5436

- For prescribers who do not have access to a computer or whose computer systems are not compatible with the MAC® or Windows® disks provided with *S.T.E.P.S.*™ program materials
- In 14 languages, to meet patient needs:
  - Patient Registration/Informed Consent Forms
  - Patient Brochure
  - Survey Forms
- Instructions in English for prescribers

Available languages:

Cambodian	French (France)	Japanese	Polish	Spanish
Chinese	German	Korean	Portugese	Vietnamese
English	Italian	Laotian	Russian	

The documents you request will be faxed directly to the number you indicate. Please be prepared to provide:

- Prescriber's
  - Name
  - DEA or Social Security number
  - Full address
- Patient's
  - Name
  - Full address
  - Phone number
  - Date of birth
  - Social Security number
  - Diagnosis
  - For female patients, whether the patient is menstruating, has had a hysterectomy, or has been without menses for at least 24 months

With this information, the Celgene Customer Care Center will generate the applicable form(s) and have them faxed to the number you request.

THALOMID®
(thalidomide)

Celgene

Printed in U.S.A. 6/01 837

Instructions for Prescribers

Review the *S.T.E.P.S.*™ Starter Kit

S.T.E.P.S.™ Prescriber Resources (1 per registered prescriber)

- Computer disks to generate Patient Registration/Informed Consent Forms (available for MAC® and Windows®)
- *S.T.E.P.S.*™ At-A-Glance
- Prescriber Guide to Fax Back Services
- Instructions for Prescribers
- *Emergency Contraception* Brochure
- THALOMID® (thalidomide) Patient Chart Sticker for each chart (located on Patient Resource Pack)
- Full Prescribing Information for THALOMID® (thalidomide)

S.T.E.P.S.™ Patient Resource Pack (1 per patient)

- Pocket Guide to *S.T.E.P.S.*™ and Patient Surveys
- Brochure entitled *Important Information for Men and Women Taking THALOMID® (thalidomide)*
  (A videotape presentation of this information is provided with the *S.T.E.P.S.*™ Starter Kit)
- *Your Contraceptive Choices* Brochure
- *Emergency Contraception* Brochure

S.T.E.P.S.™ System Set-up for Prescribers

- Insert appropriate computer software (disk)
- Install *S.T.E.P.S.*™ Patient Registration/Informed Consent Form Program
- Computer software (disk) is only installed once

THALOMID®
(thalidomide)

Celgene

Patient Registration

Before a patient can receive THALOMID® (thalidomide), he or she must understand and, along with the prescriber, sign a Patient Registration/Informed Consent Form (available on computer disk).

Prescribers who do not have access to a computer or whose computer systems are not compatible with the MAC® or Windows® disks provided with *S.T.E.P.S.*™ materials, should use the Prescriber Guide to Fax Back Services. These services provide Patient Registration/Informed Consent Forms, Patient Brochures, and Survey Forms in 14 languages, including English.

- Generate appropriate Patient Registration/Informed Consent Form
  - — Enter patient data
  - — Enter prescriber data
- Print and complete the Patient Registration/Informed Consent Form
  - — Patient and/or parent/legal guardian must be read the Patient Registration/Informed Consent Form in the language of their choice (available in 14 languages through the Celgene Customer Care Center at 1-888-423-5436)
  - — **Each statement must be initialed by the patient to indicate understanding**
  - — **The form must be completed and signed by both prescriber and patient**
  - — If the patient is under 18 years of age, his or her parent/legal guardian must read this material, initial the statements, sign the form, and agree to ensure compliance
- Fax the completed Patient Registration/Informed Consent Form to the Celgene Customer Care Center at 1-888-432-9325

Initial THALOMID® (thalidomide) Prescriptions

THALOMID® (thalidomide) is indicated for the acute treatment of the cutaneous manifestations of moderate to severe erythema nodosum leprosum (ENL). THALOMID® (thalidomide) is not indicated as monotherapy for such ENL treatment in the presence of moderate to severe neuritis.

THALOMID® (thalidomide) is also indicated as maintenance therapy for prevention and suppression of the cutaneous manifestations of ENL recurrence.

After the appropriateness of THALOMID® (thalidomide) therapy has been established, please refer to the following step-by-step guidelines:

Female Patients

- Provide comprehensive counseling on the benefits and risks of THALOMID® (thalidomide) therapy
  - — Patients must be counseled on the risk of birth defects, other side effects, and important precautions associated with THALOMID® (thalidomide) therapy
- Provide contraceptive counseling, including counseling on emergency contraception
  - — Use the patient education materials provided in the *S.T.E.P.S.*™ Patient Resource Pack

Female Patients (continued)

- Determine whether patient is of childbearing potential
  - — Female patients must thoroughly understand the need for two recommended forms of birth control beginning 4 weeks before therapy, all during therapy, and for at least 4 weeks after stopping therapy with THALOMID® (thalidomide)
  - — Contraceptive methods must include at least one highly effective method (e.g., intrauterine device [IUD], hormonal [birth control pills, injections, or implants], tubal ligation, or partner's vasectomy) **AND** one additional effective barrier method (e.g., latex condom, diaphragm, or cervical cap)
  - — If hormonal or IUD contraception is medically contraindicated, another highly effective method or two barrier methods must be used **AT THE SAME TIME**
- Continue selected birth control options for at least 4 weeks prior to initiating THALOMID® (thalidomide), all during therapy, and 4 weeks after discontinuing therapy
- Perform an in-office pregnancy test, even if continuous abstinence is the chosen method of birth control, in all female patients of childbearing potential:
  - — Pregnancy test must be performed, **with negative results in written form**, within the 24 hours before beginning THALOMID® (thalidomide) therapy
  - — Women of childbearing potential should also receive a pregnancy test every week for the first 4 weeks of therapy
  - — Then, every month if patient has regular menses; every 2 weeks if irregular menses
  - — Pregnancy test must be performed with a sensitivity of at least 50 mIU/mL
  - — Pregnancy testing and counseling should be performed if a patient misses her period or if there is any abnormality in menstrual bleeding
  - — If pregnancy does occur during treatment, THALOMID® (thalidomide) must be immediately discontinued. Any suspected fetal exposure to THALOMID® (thalidomide) must be reported immediately to the FDA via the MedWATCH number at 1-800-FDA-1088 and also to Celgene Corporation. The patient should be referred to an obstetrician/gynecologist experienced in reproductive toxicity for further evaluation and counseling

Male Patients

- Provide comprehensive counseling on the risks and benefits of THALOMID® (thalidomide) therapy
  - — Patients must be counseled on the risk of birth defects, other side effects, and important precautions associated with THALOMID® (thalidomide) therapy
- Provide contraceptive counseling, including counseling on emergency contraception
  - — Use the patient education materials provided in the *S.T.E.P.S.*™ Patient Resource Pack
  - — Male patients must be instructed to use a latex condom every time they have heterosexual sexual contact (e.g., sexual intercourse, oral sex, or anal sex), even if they have undergone a successful vasectomy, as THALOMID® (thalidomide) is present in semen

Issuing a THALOMID® (thalidomide) Prescription

Before issuing a prescription for THALOMID® (thalidomide), be sure that contraceptive counseling and pregnancy testing have been performed as required.

- Instruct the patient to complete a brief telephone survey
- Complete a brief prescriber telephone survey for every patient before each prescription is written
  — An authorization number will be issued upon completion of the survey and must be written on the prescription
- Provide prescription
  — Write authorization number on the prescription
  — Prescriptions cannot be issued by telephone
  — Prescribe no more than 4 weeks (28 days) of therapy, with no automatic refills
  — Inform the patient that all prescriptions must be filled within 7 days
  — It is recommended that female patients of childbearing potential initially receive no more than a 1-week supply for each of the first 4 weeks to coincide with weekly pregnancy testing requirements

Subsequent THALOMID® (thalidomide) Prescriptions

The prescriber must complete a brief phone survey and obtain a new authorization number *EVERY TIME* a prescription for THALOMID® (thalidomide) is written.

Female Patients

- Repeat patient counseling
- Female patients must complete a brief telephone survey, according to the following schedule:
  — Monthly
    - Adult females of childbearing potential
    - Female children
  — Every 6 months
    - Adult females not of childbearing potential
- Perform pregnancy test every 4 weeks if patient's menstrual cycles are regular, every 2 weeks if cycles are irregular
  — It is recommended that pregnancy tests be performed within the 24 hours before providing subsequent prescriptions
  — Pregnancy tests must be performed even if continuous abstinence is the chosen method of birth control
- If pregnancy test is negative, provide a prescription for no more than a 4-week (28-day) supply of THALOMID® (thalidomide) therapy
- Telephone prescriptions are not permitted

Male Patients

- Repeat patient counseling
- Male patients must complete a brief phone survey once monthly
- Provide a new prescription for no more than a 4-week (28-day) supply of THALOMID® (thalidomide)
- Telephone prescriptions are not permitted

Printed in U.S.A. 6/01

Emergency Contraceptive Pills: Medical and Service Delivery Guidelines

Consortium for Emergency Contraception

Printed on recycled paper
in Seattle, Washington, USA

Graphic design by Elizabeth Sanders

CONSORTIUM FOR EMERGENCY CONTRACEPTION

Emergency Contraceptive Pills: Medical and Service Delivery Guidelines

October 2000

CONTENTS

ACKNOWLEDGEMENTS

The Consortium's original guidelines were based on the service delivery guidelines of the International Planned Parenthood Federation, Pathfinder International, and PATH. The Consortium is grateful to Elizabeth Raymond, M.D., for updating the Consortium's guidelines to reflect the latest clinical information about ECP use. We also would like to thank the following individuals who reviewed these guidelines: Yusuf Ahmed, Sharon Camp, Marilyn Edmunds, Douglas Huber, Carlos Huezo-Toledo, Valerie Koscelnik, Suneeta Mittal, Jose David Ortiz, Karen Ostea, Khama Rogo, Jeff Spieler, James Trussell, Paul Van Look, and Helena von Hertzen.

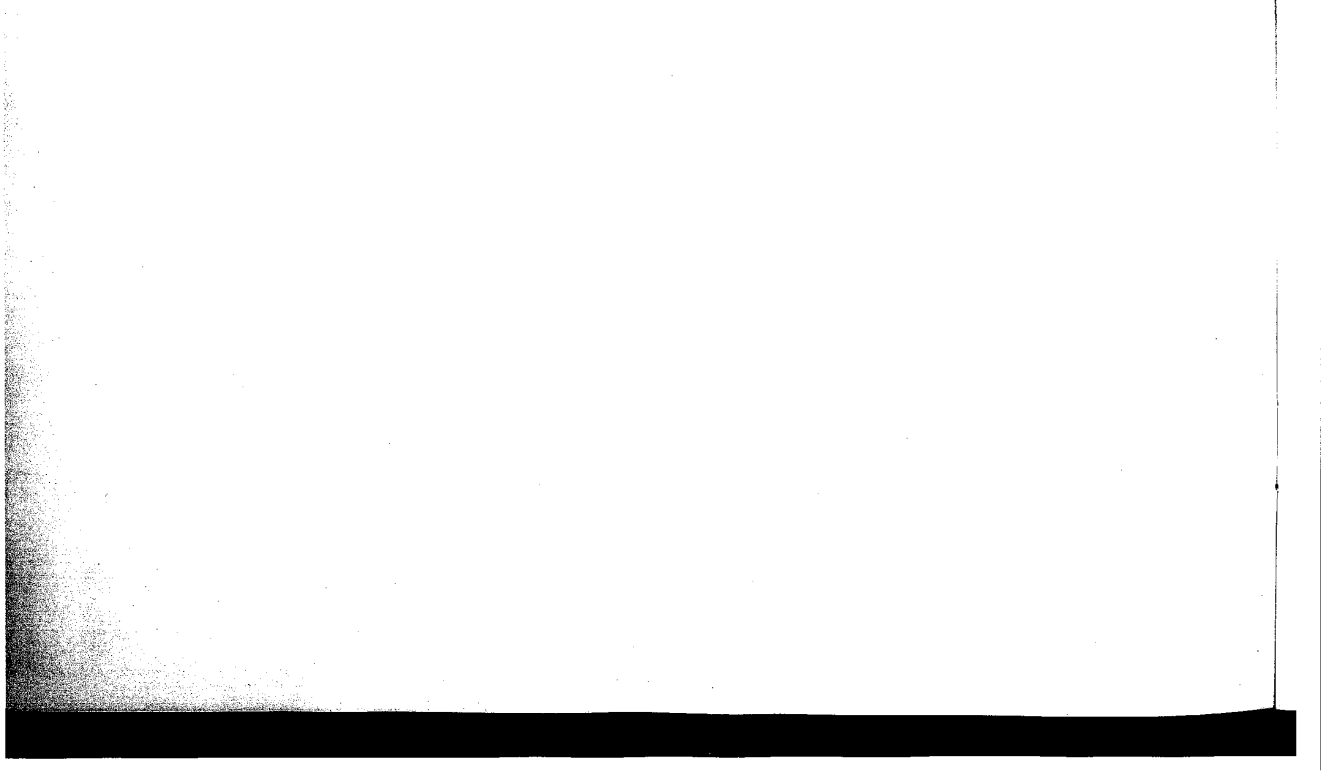
FOREWORD

Offering emergency contraception is an important way for family planning and reproductive health programs to improve the quality of their services and better meet the needs of their clients. Emergency contraception is needed because no contraceptive method is 100 percent reliable and few people use their method perfectly each time they have sex. Furthermore, emergency contraception is useful in cases of sexual assault.

Emergency contraceptive pills (ECPs), the most commonly used and most convenient form of emergency contraception, are not difficult to provide. Specially packaged ECPs or supplies of regular oral contraceptives that can be used for ECPs are readily available in most places. Providers can be trained easily in the correct use, counseling, and follow-up related to ECPs. Nevertheless, providing ECPs does entail unique service delivery issues, such as the need to ensure rapid access to the method to maximize efficacy and the importance of counseling clients about additional, ongoing methods to prevent both pregnancy and sexually transmitted infections after the ECPs are used.

An essential component of programs providing emergency contraception is informing women about this important option before they need it. Because the timeframe for seeking treatment is short, women need to be aware that emergency contraception is an option, know where they can seek services, and understand that services should be started as soon as possible, but optimally within three days (72 hours) of unprotected sex. Providing emergency contraceptive information and, if practical, supplies of ECPs at the time of a regular contraceptive visit is one way of ensuring that women have the resources they need to protect themselves from pregnancy in the event of unprotected intercourse or a contraceptive failure.

The organizations that make up the Consortium for Emergency Contraception have compiled these service delivery guidelines to give family planning and reproductive health programs the information they need to provide ECPs safely and effectively. The recommendations in these guidelines reflect the latest available research on emergency contraception, and have been reviewed by internationally recognized reproductive health experts. Local programs can adapt these guidelines as necessary to comply with national or other requirements.



SUMMARY SERVICE PROTOCOL FOR EMERGENCY CONTRACEPTIVE PILLS

Emergency contraceptive pills (ECPs) are an important option for women who recently have had unprotected intercourse or a contraceptive failure and who do not want to become pregnant. ECPs have been shown to be safe and effective in studies conducted over the past two decades. For further information, see relevant sections of this manual.

Indication

To prevent pregnancy after unprotected intercourse.

Regimens

Levonorgestrel-only regimen

0.75 mg levonorgestrel (or 1.5 mg norgestrel) as soon as possible but optimally within 72 hours after unprotected intercourse; repeat in 12 hours.

Combined estrogen-progestin (Yuzpe) regimen

100 mcg ethinyl estradiol plus 0.50 mg of levonorgestrel (or 1.0 mg norgestrel) as soon as possible, but optimally within 72 hours after unprotected intercourse; repeat in 12 hours.

Both regimens are available in some locations as products formulated and labeled specifically for use as ECPs, or they can be made up from a variety of regular oral contraceptive pills (see Table 1). The levonorgestrel-only regimen is preferred because it is more effective and is associated with a lower incidence of side effects.

Treatment should be initiated as soon as possible. Recent research has indicated that efficacy declines substantially over time after intercourse.

Mode of Action

The exact mode of action of ECPs is not known. In some studies, ECPs have been shown to prevent or delay ovulation. They also may prevent pregnancy through the following additional mechanisms, though these have not been proven:

- by affecting the movement of sperm through the cervical mucus;
- by altering transport of sperm, ovum, or embryo;
- by interfering with corpus luteum function;
- by preventing fertilization;
- by inhibiting implantation.

Which mechanism is active in a particular case may depend on the time in the cycle when the ECPs are taken. The two ECP regimens discussed in these guidelines do not disrupt an established (implanted) pregnancy.

Effectiveness

The levonorgestrel-only regimen reduces the risk of pregnancy by about 85 percent after a single act of intercourse. The combined regimen reduces the risk of pregnancy by about 74 percent. The levonorgestrel regimen is significantly and substantially more effective than the combined regimen. Both regimens appear to be more effective the sooner after sex they are used. ECPs are not as effective as consistent and correct use of most modern contraceptive methods.

Side Effects

Side effects of both regimens include nausea, vomiting, abdominal pain, fatigue, headache, dizziness, breast tenderness, and irregular vaginal spotting or bleeding. The levonorgestrel-only regimen is associated with a significantly lower risk of nausea and vomiting than the combined regimen. In most women, menses will come up to a week earlier or later than expected.

Prevention of Nausea and Vomiting

The incidence of nausea and vomiting in women using the levonorgestrel-only regimen is low enough that prophylactic treatment with antiemetic drugs is not warranted. However, antiemetics may be appropriate for women who use the combined regimen. Meclizine (50 mg, taken one hour before the first ECP dose) has been shown to significantly reduce the incidence of nausea and vomiting associated with the combined regimen. Patients should be warned that meclizine may cause drowsiness. Other antiemetic regimens also may be effective.

Management of Vomiting

If vomiting occurs within one hour after either dose, repeat the dose, if feasible. In cases of severe vomiting, vaginal administration of ECPs may be effective.

Precautions

The only medical condition in which ECPs should not be used is confirmed pregnancy. ECPs will not be effective

if pregnancy already is established. ECPs may be given when pregnancy status is unclear and pregnancy testing is not available, as there is no evidence suggesting harm to the woman or to an existing pregnancy.

There are no other known medical conditions in which ECPs should not be used. Since the pills are used for such a short time, experts believe that the precautions associated with continuous use of combined oral contraceptives and levonorgestrel-only pills do not apply to ECPs.

Screening

If possible, establish that the client is not pregnant by determining the time since her last normal menstrual period. Ascertain the date and time of unprotected intercourse. If intercourse occurred more than 72 hours before screening, counsel the client that the hormonal treatment may still have limited effectiveness. (IUD insertion may be a more effective option, if medically appropriate.) No pelvic exam or other tests are needed unless pregnancy is suspected.

Special Situations

Breastfeeding

ECPs may be used, as there is no evidence of danger to the woman or infant.

Unprotected act(s) more than 72 hours ago

ECPs may be used, but clients should be informed that efficacy will be low.

More than one prior unprotected act

One ECP regimen may be given to cover all unprotected acts, but clients should understand that efficacy to prevent pregnancy from acts more than 72 hours prior will be low.

Repeated ECP use

ECPs may be used as frequently as requested, but clients should be informed that ongoing, correct use of other contraceptive methods provides more effective protection over time.

Use of ECPs before intercourse

Clients should be discouraged from using ECPs before intercourse, since ECPs may not be as effective as other contraceptive methods, and no data exist on the effectiveness of this practice.

Unprotected sex during the "infertile period"

Because it often is difficult to define the infertile period with certainty, ECPs generally are recommended any time that unprotected sex occurs and the client is concerned that she is at risk for pregnancy.

Concurrent use of other drugs

Clients should be counseled about the possibility of drug interactions and managed accordingly (see Section 2.7).

Use of other formulations

Combined estrogen-progestin pill formulations containing the progestin norethindrone in place of levonorgestrel can be used when standard regimens are not available (see Section 2.7).

Counseling

Clients may feel stressed or embarrassed to talk about unprotected intercourse. Nonjudgmental counseling is crucial. Ideally, counseling should include a review of efficacy and possible side effects of ECPs, and clients should be given information about regular contraceptive methods to use after taking ECPs. Whenever possible, clients should be provided with a temporary method, such as condoms, for use in the immediate future. At a minimum, the following messages should be conveyed:

- The client should take the first dose of ECPs as soon as possible, and the second dose 12 hours after the first.
- Following ECP use, if the client's menstrual period is more than one week later than expected, she should seek evaluation and care for possible pregnancy.
- ECPs do not prevent pregnancy from sexual acts after treatment. Therefore, clients should use another form of contraception after using ECPs. ECPs are not suitable for ongoing contraception because the risk of pregnancy, the incidence of side effects, and the total hormone dose will be high.
- ECPs do not protect against HIV/AIDS or sexually transmitted infections (STIs). Clients who had unprotected intercourse should be counseled about evaluation for possible infection and risk-reduction techniques (particularly condom use), if appropriate.

Follow-up

Advise the client to see a health care provider if she has any questions or reason for concern.

EMERGENCY CONTRACEPTIVE PILLS: MEDICAL AND SERVICE DELIVERY GUIDELINES

1. Introduction

Despite the availability of highly effective methods of contraception, many pregnancies are unplanned and unwanted. These pregnancies carry a higher risk of morbidity and mortality, often due to unsafe abortion. Many of these unplanned pregnancies can be avoided using emergency contraception.

1.1 Definition

Emergency contraceptive pills (ECPs) are hormonal methods of contraception that can be used to prevent pregnancy after an unprotected act of sexual intercourse.

ECPs sometimes are referred to as "morning-after" or "post-coital" pills. The term "emergency contraceptive pills" is preferred because it conveys the important message that the treatment should not be used as an ongoing contraceptive method, and it avoids giving the mistaken impression that the pills must be taken on the morning after sex.

These guidelines deal with medical and service delivery issues related to two types of ECPs: (1) pills containing a progestin only (levonorgestrel or norgestrel), and (2) pills containing a combination of a progestin (levonorgestrel or norgestrel) and an estrogen (ethinyl estradiol).

A brief overview of the use of IUDs for emergency contraception is included in the Appendix.

1.2 Indications

ECPs are indicated to prevent pregnancy after unprotected sexual intercourse, including:

- when no contraceptive has been used;
- when there is a contraceptive failure or misuse, including:
  - condom breakage, slippage, or misuse
  - two or more consecutive missed oral contraceptive pills
  - more than 2 weeks late for a progestin-only contraceptive injection (depot medroxyprogesterone acetate or norethisterone enanthate)
  - more than 3 days late for a combined estrogen-plus-progestin injection (medroxyprogesterone acetate and estradiol cypionate)
  - diaphragm or cap dislodgment, breakage, tearing, or early removal
  - failed coitus interruptus (e.g., ejaculation in vagina or on external genitalia)
  - failure of a spermicide tablet or film to melt before intercourse
  - miscalculation of the periodic abstinence method or failure to abstain on fertile day of cycle
  - intrauterine device (IUD) expulsion
- in cases of sexual assault when the woman was not protected by a reliable contraceptive method.

2. Emergency Contraceptive Pills

2.1 ECP Regimens

Two ECP regimens are discussed in these guidelines:

Levonorgestrel-only regimen

0.75 mg levonorgestrel (or 1.5 mg norgestrel) as soon as possible, but optimally within 72 hours after unprotected intercourse; repeat in 12 hours.

Combined estrogen-progestin (Yuzpe) regimen

100 mcg ethinyl estradiol plus 0.5 mg of levonorgestrel (or 1.0 mg norgestrel) as soon as possible, but optimally within 72 hours after unprotected intercourse; repeat in 12 hours.

Both regimens are available in some locations as products formulated and labeled specifically for use as ECPs. They also can be made up from a variety of regular oral contraceptive pills (see Table 1). The levonorgestrel-only regimen is preferred because it is more effective and is associated with a lower risk of nausea and vomiting.[1]

Treatment should not be delayed unnecessarily, as efficacy appears to decline substantially with time.[2]

2.2 Mode of Action

The precise mechanism of action of ECPs in a particular case cannot be known and may depend on the time in the menstrual cycle when the intercourse occurred and when the ECPs were taken. Some studies have suggested that the combined regimen taken before ovulation can inhibit or delay ovulation.[3-5] Some studies have shown histologic or biochemical alterations in the endometrium after treatment with the regimen, leading to the suggestion that the regimens may act by impairing endometrial receptivity to implantation of a fertilized egg.[4,6] However, other studies

have found no such effects on the endometrium,[5] and it is not clear whether the endometrial changes that have been observed would be sufficient to inhibit implantation. Additional possible mechanisms include thickening of the cervical mucus resulting in trapping of sperm; alterations in the transport of sperm, egg, or embryo; interference with corpus luteum function; and direct inhibition of fertilization. No clinical data exist regarding these possibilities. Nevertheless, statistical evidence on the effectiveness of ECPs suggests that there must be a mechanism of action other than delaying or preventing ovulation.[7]

Data from studies of high-dose oral contraceptives indicate that the two ECP regimens described in these guidelines do not cause abortion; that is, they do not interrupt or damage a pregnancy, defined as beginning after implantation has occurred.[8,9]

2.3 Efficacy

Levonorgestrel-only regimen

The largest study of the efficacy of this regimen included 1,001 women using the regimen at 21 centers in 14 countries. The authors of this study concluded that the regimen prevents about 85 percent of the pregnancies that would occur if the treatment is not used.[1] For example, if 100 women had unprotected sex, about 8 would typically become pregnant. If all 100 women used the regimen, however, only 1 would become pregnant. Thus, use of the levonorgestrel-only regimen reduced the chance of pregnancy by about eight-fold.

Combined estrogen-progestin regimen

A meta-analysis of eight studies of the efficacy of the combined regimen including more than 3,800 women in eight studies concluded that the regimen prevents about 74 percent of expected pregnancies.[10] For example, if 100 women had unprotected sex without using the regimen, about 8 would become pregnant. If all 100 women had unprotected sex and used the regimen, only 2 would become pregnant. Thus, use of the combined regimen reduces the chance of pregnancy by about four-fold.

A large randomized trial that directly compared the two regimens showed that the levonorgestrel regimen is significantly more effective than the combined regimen. The relative risk of pregnancy in this study was 0.36, indicating that the chance of pregnancy among women who received the levonorgestrel regimen was about one third the chance among those who received the combined regimen.[1]

Three studies have suggested that the combined regimen is substantially more effective the sooner after sex the pills are taken.[1,11,12] The largest of these studies showed that the pregnancy risk was three times higher if the first ECP dose was taken on the third day after sex rather than on the first day. Older studies did not show this time effect,[13] but they may not have been as rigorously conducted as the more recent research. Two studies[1,11] have indicated that the efficacy of the levonorgestrel regimen also decreases with time after intercourse, but the numbers of pregnancies were smaller, and the trend was not statistically significant.

ECPs are inappropriate for regular use as an ongoing contraceptive method for several reasons. First, ECPs are less effective than most modern methods over the long term. Because the ECP pregnancy rates are based on a single use, they cannot be directly compared to failure rates of ongoing contraceptives, which represent the risk of failure during a prolonged period (e.g., one year) of use. However, if ECPs were used as an ongoing method, the cumulative risk of pregnancy during a full year of use would likely be higher than the risk associated with regular hormonal contraceptives, male condoms, and other barrier methods.[14] In addition, very frequent ECP use would result in more side effects and exposure to a higher total hormone dose than would regular use of either combined oral contraceptive pills or progestin-only pills. Data are not available on the incidence of serious medical complications in women who use ECPs frequently over a long period of time.

2.4 Side Effects, Prevention, and Management

Nausea and vomiting

Nausea occurs in approximately 23 percent of women and vomiting occurs in about 6 percent of women using levonorgestrel-only ECPs.[1] Nausea and vomiting occur in about 43 percent and 16 percent, respectively, of clients using the combined regimen.[15] In studies directly comparing the two regimens, the levonorgestrel regimen has been shown to cause significantly and substantially less nausea and vomiting than the combined regimen. If they occur, these symptoms are usually limited to the first three days after treatment.[16]

Prevention

The best way to minimize nausea and vomiting is to use the levonorgestrel-only regimen instead of the combined regimen whenever possible. Nausea and vomiting are uncommon enough with the levonorgestrel-only regimen that prophylactic administration of an antiemetic drug is not routinely warranted. However, if the combined regimen is used, antiemetic pretreatment may be considered, depending on program and client resources. Meclizine is the only drug that has been proven to be effective; a single

dose of 50 mg, taken one hour before the first dose of ECPs, reduces the risk of nausea by about 30 percent and the incidence of vomiting by about 60 percent. Clients who use meclizine should be warned that it may cause drowsiness. Lower doses of meclizine and other antiemetics also may prevent nausea and vomiting, but they have not been studied. It is not possible to predict which ECP users will have nausea or vomiting or which women will benefit from antiemetic pretreatment. No evidence exists that suggests that taking ECPs with food will alter the risk of nausea.[15,17]

Management

If vomiting occurs within one hour of taking either ECP dose, some experts believe that the dose should be repeated.[17] In cases of severe vomiting, ECPs can be administered vaginally. Studies of regular oral contraceptive pills administered by this route suggest that the hormones are absorbed through the vaginal mucosa.[18,19]

Irregular vaginal bleeding

A small number of women may experience irregular bleeding or spotting after taking ECPs.[11] Such irregular bleeding should not be confused with menses, which is the much-anticipated evidence of success of treatment. Clients should be informed that ECPs do not necessarily bring on menses immediately (a common misperception among ECP clients); most women will have their menstrual period within one week before or after the expected time.

Management

After using ECPs, if the menstrual period is more than a week later than expected, the possibility of pregnancy should be considered, and the client should be advised to seek appropriate evaluation (such as a pregnancy test) and care.

Other side effects of ECPs

Other side effects may include abdominal pain, breast tenderness, headache, dizziness, and fatigue. These side effects usually do not occur more than a few days after treatment, and they generally resolve within 24 hours.[16]

Management

A non-prescription pain reliever can be used to reduce discomfort due to headaches or breast tenderness.

Aside from these side effects, there are no known adverse medical effects to the woman from use of ECPs. There are also no known teratogenic effects on the fetus in the event of inadvertent ECP use during early pregnancy (see Section 2.5). ECPs do not appear to increase either the absolute risk of ectopic pregnancy or the chance that a pregnancy following ECP use will be ectopic.

2.5 Precautions

- ECPs should not be given to a woman who has a confirmed pregnancy because the treatment will not be effective.
- If, after evaluation, the woman wants ECPs and pregnancy cannot be ruled out with certainty, it is permissible to give ECPs if you explain that she could already be pregnant, in which case the regimen will not be effective. However, results from studies of high-dose oral contraceptives suggest that neither the pregnant woman nor the fetus will be harmed if ECPs are inadvertently used during early pregnancy.[8]
- There are no other known medical conditions in which ECPs should not be used. Since the pills are used for a short time, experts believe that the precautions associated with continuous use of combined oral contraceptives and levonorgestrel-only pills do not apply.[20] Women with previous ectopic pregnancy may use ECPs.

2.6 Screening

Screen the client for ECP use by:

- assessing the date of the last menstrual period and whether it was normal, to exclude the possibility that the client may already be pregnant. If the client has not had a recent menstrual period for a discernible reason other than pregnancy (for example, she has been using an injectable contraceptive, she has recently been pregnant, she is breastfeeding, or she often has irregular or prolonged cycles), or if the client cannot remember the date of her last menstrual period accurately, then ECPs may be administered, as long as the client understands that pregnancy has not been ruled out;
- determining how long ago the unprotected coital act occurred. If it occurred earlier than 72 hours previously, treatment may be given, but the client should be warned that efficacy may be limited (see Section 2.7).

Other health assessments (e.g., pregnancy test, blood pressure measurement, laboratory tests, pelvic exam) are not required but can be offered if medically indicated for other reasons and desired by the client. Providers also should ask if the client is currently using a regular method of contraception; this question can be a good starting point for a discussion of regular contraceptive use and how to use methods correctly.

2.7 Special Issues

Use in breastfeeding women

A woman who is exclusively breastfeeding and who has not had a menstrual period since delivery is unlikely to be ovulatory and therefore may not need ECPs. However, a woman who is providing supplemental feeding to her infant or who has had menses since delivery may be at risk for pregnancy. A single treatment with ECPs is unlikely to have an important effect on milk quantity or quality. Some hormones may pass into the breast milk, but they are unlikely to affect the infant adversely.

Use after unprotected act(s) more than 72 hours ago

Studies of efficacy of treatment given within 72 hours show a declining effectiveness as the 72 hours progress, but suggest that ECPs probably retain some limited efficacy even after that time.[2] Recent data looking at use beyond 72 hours suggest that ECPs retain some efficacy when taken more than 72 hours after intercourse.[17] Since ECPs apparently pose no danger either to the woman or to the embryo if the ECPs fail, it is reasonable to provide them if program and client resources permit and the client is fully counseled about the possibility of pregnancy. A more effective approach would be to insert a copper IUD (see Appendix), if the woman is otherwise a candidate for emergency IUD insertion.

Use after more than one unprotected act

ECPs should not be withheld if the client has had more than one unprotected act of intercourse, unless she is known to already be pregnant. However, clients should be informed that, as the interval between the earliest unprotected act and the use of the ECPs lengthens, the efficacy of the ECPs will be lower. Clients should be encouraged to use ECPs as promptly as possible after unprotected sex, and not to wait until they have had a series of unprotected acts. Only one ECP regimen should be given at a time, regardless of the number of prior unprotected acts.

Repeated use

ECPs are not intended for repeated use (see Section 2.3). However, given the low likelihood of harm from limited repeated use, ECPs should not be denied just because the woman has used them before, even within the same menstrual cycle. All women who use ECPs, especially those who use them repeatedly, should be given information about other forms of contraception and counseling about how to avoid future contraceptive failure.

Use of ECPs before intercourse

No data are available about how long the contraceptive effect of ECPs persists after the pills have been taken. Presumably ECPs taken immediately before intercourse are as effective as ECPs taken immediately afterwards. However, if a woman has the opportunity to plan to use a contraceptive method before intercourse, a method other than ECPs, such as condoms or another barrier method, is recommended.

Use of ECPs during the "infertile period"

Studies have shown that fertilization can result from intercourse only during a five- to seven-day interval around the time of ovulation.[21] Theoretically, ECPs should not be needed if unprotected intercourse occurs at other times of the cycle, because the chance of pregnancy even without ECPs would be zero. However, in practice, it often is difficult to determine for certain whether a specific act of intercourse occurred on a fertile or infertile cycle day. Therefore, ECPs generally should be provided any time unprotected sex occurs and the client is concerned that she is at risk for pregnancy. In situations when the unprotected act is extremely unlikely to result in pregnancy, the client's anxiety level and the availability of program and client resources should be taken into account in making the decision.

Drug interactions

No specific data are available about the interactions of ECPs with other drugs that the client may be taking. However, it seems reasonable that drug interactions would be similar to those with regular oral contraceptive pills. A full discussion of this matter is beyond the scope of these guidelines, but several excellent references on the subject are available.[22-25] Women taking drugs that may reduce the efficacy of oral contraceptives (including but not limited to rifampin, certain anticonvulsant drugs, and Saint John's wort) should be advised that the efficacy of ECPs may be reduced. Consideration may be given to increasing the amount of hormone administered in the ECPs, either by increasing the amount of hormone in one or both doses, or by giving an extra dose.

Use of other formulations

New research shows that combined estrogen-progestin pill formulations containing the progestin norethindrone in place of levonorgestrel can be used as emergency contraceptives where the levonorgestrel-only or standard combined regimens are not available. Norethindrone combination pills offer an efficacy and side effect profile similar to combined pills containing levonorgestrel.[17]

2.8 Counseling

As with any contraceptive method, ECPs should be provided in a manner that is respectful of clients and responsive to their needs for information and counseling. Clients may feel particularly anxious after unprotected intercourse due to fear of becoming pregnant, worry about missing the 72-hour window of opportunity for hormonal emergency contraception, embarrassment at failing to use contraception effectively, general embarrassment about sexual issues, rape-related trauma, concern about AIDS, or a combination of these factors. Providers should be as supportive as possible of the client's choices and refrain from making judgmental comments or indicating disapproval through body language or facial expressions while discussing ECPs with clients. Supportive attitudes will help set the stage for follow-up counseling about regular contraceptive use and prevention of STIs. Actively involving the client in the counseling process, for example, by asking her what she has heard about ECPs, discussing her experience with other contraceptive methods (particularly the incident that led to the ECP request), and exploring her current approach to protecting herself from STIs (especially condom use), and then validating or correcting her ideas as appropriate, may be more effective in ensuring compliance than simply providing her with information.

Whenever possible, ensure that counseling is conducted in private. In situations where privacy is inadequate (for instance, in many pharmacies), advise clients to contact a health care or family planning provider for additional information and counseling about regular contraceptive methods. Reassure all clients, regardless of age or marital status, that all information that they give to the provider, as well as the fact that they have received treatment, will be kept confidential.

When possible, give clients written as well as verbal instructions for taking the ECPs. Pictorial instructions may help clients whose literacy may be limited.

2.9 Information for the Client

Clients should be given information about efficacy, side effects, and mechanism of action of ECPs. In addition, counseling should be provided on how to prevent future contraceptive emergencies and on contraceptive options that they can use to prevent pregnancy after ECP use. However, care should be taken to avoid overwhelming clients with so much information that they cannot absorb it all. In addition, some clients may not want counseling on certain topics (such as information on other contraceptive methods or on the mechanism of action of ECPs) at the time they receive ECPs. Providers should not deny ECPs to women who refuse more than the minimum information needed to ensure that they use the ECPs correctly. The following key messages should be conveyed whenever possible:

- Clients should take the first dose of ECPs as soon as possible after sex to maximize efficacy. The second dose should be taken 12 hours after the first. Ensure that clients understand how to calculate the 12-hour interval. They should not take extra doses unless they vomit within one hour after a dose.
- After taking ECPs, if the next menstrual period is more than one week later than normally expected, the client should consider the possibility that she may be pregnant. Advise her where to obtain appropriate evaluation and care.
- ECPs do not prevent pregnancy from sexual acts after treatment, and they are not suitable for ongoing contraception because pregnancy rates, incidence of side effects, and total hormone dose will be high. Give clients information about other contraceptive methods or about where to obtain such information. If possible, provide a contraceptive method such as condoms that can be used in the immediate future.
- ECPs do not protect against HIV/AIDS or STIs. The act of unprotected intercourse that prompted the request for ECPs may have put her at risk for these infections. Advise her where to obtain evaluation and treatment for STIs, if appropriate, and how to reduce her risk of acquiring STIs in the future.

2.10 Follow-up

Clients should be advised to seek follow-up care if they:

- need ongoing contraceptive counseling or a contraceptive method;
- have menses more than a week later than expected;
- suspect they may be pregnant; or
- have other reasons for concern.

2.11 If the Client Becomes Pregnant

A woman who has used ECPs may later find herself to be pregnant because the ECPs have failed, because she was already pregnant before taking the ECPs, or because coital acts after taking the ECPs led to pregnancy. In any of these cases:

- Advise the client about all available options, and let her decide which is most appropriate for her situation. Her

decision should be respected and supported. Refer the client to other service providers as appropriate.

- If she decides to continue the pregnancy, reassure her that there is no evidence of any teratogenic effect following ECP use. Available data suggest that ECPs do not increase the likelihood that a subsequent pregnancy will be ectopic.

2.12 Starting or Resuming Regular Contraception After ECP Use

Whenever possible, clients receiving ECPs should be given contraceptive counseling and provided with an ongoing contraceptive method, such as condoms, for at least immediate future use. However, such counseling may not be appropriate in all situations or may not be desired by clients at the time of ECP provision, and it should not be a prerequisite for providing ECP services. Clients who need or desire counseling but who do not receive it at the ECP visit should be referred for a follow-up appointment at the earliest convenient time.

Clients may wish to restart their previous contraceptive method after taking ECPs, or they may prefer to initiate a new method. If the reason for requesting ECPs is because the regular contraceptive method failed (for example, the condom broke, or the client missed taking oral contraceptive pills), discuss with the client the reasons for failure and how it can be prevented in the future.

Women with risk factors for STIs, such as young age or residence in a location where STIs are especially prevalent, should receive special counseling on how to prevent STIs as well as pregnancy. Use of condoms in addition to or as the primary contraceptive method should be emphasized.

Guidelines for initiating or restarting contraceptive use after using ECPs follow:

Male or female condom

Can be used immediately.

Diaphragm or cervical cap

Can be used immediately.

Spermicidal foam, tablets, jelly, cream, or film

Can be used immediately.

Oral contraceptives

Two options are recommended:

a. The client may wait until the beginning of her next menstrual cycle and then start a new pack according to the package instructions for the pill brand being used. In this case, she should be advised to use a barrier contraceptive method or abstain from intercourse for the remainder of the current cycle.

b. The client may start oral contraceptives on the day after she takes the ECPs. She may begin a new pack of pills, or if she was using oral contraceptives before taking the ECPs (i.e., the ECPs were indicated because of missed pills), she may resume taking pills from the pack that she was previously using. She should use a barrier method for at least seven days after starting or restarting the oral contraceptive pills. She may have some irregular bleeding until the onset of menses.

Injectables

Initiate progestin-only injectables within 7 days after the beginning of the next menstrual cycle. Initiate combined injectables within 5 days after the beginning of the next menstrual cycle. The client should use a barrier contraceptive or abstain from intercourse until she receives the injection.

Implants (e.g., Norplant®)

Insert within 7 days after the beginning of next menstrual cycle. Use a backup method or abstain from intercourse until the implants are inserted.

IUD

Insert during the next menstrual period. The client should use a barrier contraceptive or abstain from intercourse until the IUD is inserted.

NOTE: If the client intends to use an IUD as a long-term method and meets IUD screening criteria, emergency insertion of a copper-bearing IUD may be an alternative to ECP use (see Appendix).

Natural family planning

Natural family planning may be initiated after the first normal menstrual period following ECP use. An alternate nonhormonal contraceptive method should be used in the interim.

Female or male sterilization

Perform the operation only after informed consent can be ensured. It is not recommended that clients make this decision under the stressful conditions that often surround ECP use. Defer female sterilization until after the client's first menstrual period, to ensure that she is not pregnant. Use a backup method or abstain from intercourse until the sterilization procedure is performed.

3. *ECP Service Delivery Systems*

ECPs can be distributed safely and effectively by a variety of trained personnel and through a variety of clinical and nonclinical service delivery systems. For instance, doctors, nurses, midwives, pharmacists, and other clinically trained personnel as well as community health workers and trained sexual assault counselors may be able to provide ECPs, depending on the local regulations and practices. Over-the-counter provision (without interaction with a provider) also has been suggested as a way to increase rapid access to ECPs.

All ECP providers should be given appropriate training and follow clear service delivery guidelines. Training should include information on indications for ECP use, recommended ECP regimens, mode of action, efficacy, side effects and their management, precautions and screening, client information and counseling needs, and follow-up procedures. In addition, since ECPs are a back-up method, the training also should include information about other contraceptive methods, if necessary for the audience. The training often is most effective if it is participatory in nature and includes exercises to build participant skills in the areas of screening, counseling, and follow-up. A provider training curriculum, *Emergency Contraceptive Pills, Module 5, A Comprehensive Training Course,* is available from Pathfinder International. (To request a copy, contact Pathfinder International, Medical Services, 9 Galen Street, Suite 217, Watertown, MA 02172 USA, or on the Internet at www.pathfind.org. A Spanish version also is available.)

Given that ECPs appear to be most effective when taken soon after unprotected intercourse, every effort should be made to ensure that women know about ECPs and have ready access to them. This can be accomplished by:

- routinely informing women about ECPs at the time of regular family planning visits;
- instituting mass-media informational campaigns and advertising ECP services;
- providing women with an advance supply of ECPs;
- providing ECPs through non-clinical settings, such as through community-based services, social marketing programs, and the commercial sector (e.g., pharmacies).

Programs also should attempt to make ECP services available to high-risk audiences, such as youth and victims of sexual assault.

3.1 Youth

Reaching adolescents with emergency contraceptive information and services poses special challenges to programs. Young women may find it difficult to access relevant information about and/or services for emergency contraception because they:

- are unaware of the availability of ECPs;
- lack confidence or are embarrassed to visit a family planning clinic;
- do not know of the existence of the clinic;
- find the clinic hours inconvenient;
- fear a pelvic examination; or
- are anxious about judgmental attitudes of the providers.

Programs should work to ensure that clinics serving adolescents are youth-friendly (for example, by ensuring privacy and confidentiality, accessible facilities, reasonably priced services, and flexible hours—particularly during evenings and weekends).

3.2 Sexual Assault Victims

Reaching women who have been forced to have sex also poses special challenges. ECP providers should be attentive to the possibility that these women may be:

- unaware that something can be done to prevent pregnancy after sexual assault;
- unwilling to report the assault and therefore unwilling to seek services;
- concerned they will be blamed for the assault by the medical provider; or
- also in need of diagnosis and treatment for STIs.

Program managers and providers should ensure that police stations, emergency health care centers, and other facilities where women may seek help after an assault can provide clients with ECPs, if appropriate, or at least with information about where to obtain ECPs as promptly as possible.

TABLE 1. ECP Formulations

	Formulation (per Pill)	Common Brand Names	First Dose (Number of Tablets)	Second Dose (Number of Tablets)
Levonorgestrel-only Regimen	LNG 0.75 mg	Levonelle-2, NorLevo, Plan B, Postinor-2, Vikela	1	1
	LNG 0.03 mg	Microlut, Microval, Norgeston	25	25
	LNG 0.0375 mg	Ovrette	20	20
Combined Regimen	EE 50 mcg + LNG 0.25 mg or EE 50 mcg + NG 0.50 mg	Eugynon 50, Fertilan, Neogynon, Noral, Nordiol, Ovidon, Ovral, Ovran, PC-4, Preven	2	2
	EE 30 mcg + LNG 0.15 mg or EE 30 mcg + NG 0.30 mg	Lo/Femenal, Microgynon 30, Nordette, Ovral L, Rigevidon	4	4

Abbreviations:
EE = ethinyl estradiol LNG = levonorgestrel NG = norgestrel

For all regimens, the first dose should be taken as soon as possible after intercourse, but optimally within 72 hours, and the second dose should be taken 12 hours after the first dose.

APPENDIX: USE OF IUDS FOR EMERGENCY CONTRACEPTION

Copper-bearing IUDs can be used as a method of emergency contraception. They are most appropriate for women in stable relationships who wish to retain the IUD for long-term contraception and who meet the screening requirements for regular IUD use. When inserted within five days of unprotected intercourse, copper-bearing IUDs are the most effective method of emergency contraception; they reduce the risk of pregnancy by more than 99 percent.[26]

However, emergency IUD insertion requires a much higher degree of training and clinical oversight than administration of ECPs, including screening to eliminate clients who are already pregnant (e.g., a pregnancy test, if the woman is not menstruating), who have pelvic inflammatory disease or another reproductive tract infection, or who are at high risk for STIs. In many instances, the act of unprotected intercourse that led to the request for emergency contraception might put the woman at increased risk of STIs, in which case the IUD is not an optimal contraceptive choice.

For further information about use of IUDs for emergency contraception, consult the *IPPF Medical and Service Delivery Guidelines* (the most recent edition, which contains information about emergency contraception, is available from IPPF, Regent's College, Inner Circle, Regent's Park, London NW1 4NS, England), or the World Health Organization publication *Emergency Contraception—A Guide for Service Delivery* (1998).

REFERENCES

1. Task Force on Postovulatory Methods of Fertility Regulation. Randomised controlled trial of levonorgestrel versus the Yuzpe regimen of combined oral contraceptives for emergency contraception. *Lancet* 1998;352:428–33.
2. Piaggio G, von Hertzen H, Grimes DA, Van Look PFA. Timing of emergency contraception with levonorgestrel or the Yuzpe regimen. Task Force on Postovulatory Methods of Fertility Regulation. *Lancet* 1999;353:721.
3. Rowlands S, Kubba AA, Guillebaud J, Bounds W. A possible mechanism of action of danazol and an ethinylestradiol/norgestrel combination used as postcoital contraceptive agents. *Contraception* 1986;33:539–45.
4. Ling WY, Robichaud A, Zayid I, Wrixon W, MacLeod SC. Mode of action of DL-norgestrel and ethinylestradiol combination in postcoital contraception. *Fertil Steril* 1979;32:297–302.
5. Swahn ML, Westlund P, Johannisson E, Bygdeman M. Effect of post-coital contraceptive methods on the endometrium and the menstrual cycle. *Acta Obstet Gynecol Scand* 1996;75:738–44.
6. Yuzpe AA, Thurlow HJ, Ramzy I, Leyshon JI. Post coital contraception—A pilot study. *J Reprod Med* 1974;13:53–8.
7. Trussell J, Raymond EG. Statistical evidence concerning the mechanism of action of the Yuzpe regimen of emergency contraception. *Obstet Gynecol* 1999;93:872–76.
8. US Department of Health and Human Services, Food and Drug Administration. Prescription Drug Products; Certain Combined Oral Contraceptives for Use as Postcoital Emergency Contraception. *Federal Register* 1997;62:8610–2.
9. Hughes EC (ed.), Committee on Terminology, The American College of Obstetricians and Gynecologists. *Obstetric-Gynecologic Terminology*. Philadelphia: F.A. Davis Co., 1972.
10. Trussell J, Rodriguez G, Ellertson C. Updated estimates of the effectiveness of the Yuzpe regimen of emergency contraception. *Contraception* 1999;59:147–51.
11. Ho PC, Kwan MS. A prospective randomized comparison of levonorgestrel with the Yuzpe regimen in post-coital contraception. *Hum Reprod* 1993;8:389–92.
12. Kane LA, Sparrow MJ. Postcoital contraception: a family planning study. *N Z Med J* 1989;102:151–3.
13. Trussell J, Ellertson C, Rodriguez G. The Yuzpe regimen of emergency contraception: how long after the morning after? *Obstet Gynecol* 1996;88:150–4.
14. Trussell J. Contraceptive efficacy. In: Hatcher RA, Trussell J, Stewart F, Cates W, Stewart GK, Guest F, Kowal D. *Contraceptive Technology*. 17th edition. New York: Ardent Media, Inc., 1998.
15. Raymond EG, Creinin MD, Barnhart KT, Lovvorn AE, Rountree RW, Trussell J. Meclizine for prevention of nausea associated with use of emergency contraceptive pills: a randomized trial. *Obstet Gynecol* 2000;95:271–7.
16. Van Santen MR, Haspels AA. Interception II: postcoital low-dose estrogens and norgestrel combination in 633 women. *Contraception* 1985;31:275–93.
17. Ellertson C et al. *Refining the Yuzpe Method of Emergency Contraception*. Population Council. Forthcoming, 2000.
18. Back DJ, Grimmer SF, Rogers S, Stevenson PJ, Orme ML. Comparative pharmacokinetics of levonorgestrel and ethinyloestradiol following intravenous, oral and vaginal administration. *Contraception* 1987;36:471–9.
19. Alvarez F, Faundes A, Johansson E, Coutinho E. Blood levels of levonorgestrel in women following vaginal placement of contraceptive pills. *Fertil Steril* 1983;40:120–3.
20. Vasilakis C, Jick SS, Jick H. The risk of venous thromboembolism in users of postcoital contraceptive pills. *Contraception* 1999;59:79–83.
21. Wilcox AJ, Weinberg CR, Baird DD. Timing of sexual intercourse in relation to ovulation. Effects on the probability of conception, survival of the pregnancy, and sex of the baby. *N Engl J Med* 1995;333:1517–21.
22. Breckenridge AM, Back DJ, Orme M. Interactions between oral contraceptives and other drugs. *Pharmacol Ther* 1979;7:617–26.
23. Shenfield GM. Drug interactions with oral contraceptive preparations. *Med J Aust* 1986;144:205–11.
24. Szoka PR, Edgren RA. Drug interactions with oral contraceptives: compilation and analysis of an adverse experience report database. *Fertil Steril* 1988;49:31S–38S.
25. Guerts TBP, Goorissen EM, and Sitsen JMA. *Summary of Drug Interactions with Oral Contraceptives*. Carnforth, England: Parthenon Publishing Group, Ltd., 1993.
26. Trussell J, Ellertson C. Efficacy of emergency contraception. *Fertility Control Reviews* 1995;4:8–11.

ABOUT THE CONSORTIUM FOR EMERGENCY CONTRACEPTION

The mission of the Consortium for Emergency Contraception is to expand access to and ensure safe and locally appropriate use of emergency contraception worldwide within the broader context of family planning and reproductive health, with emphasis on developing countries.

The seven founding members of the Consortium initially focused on introducing a dedicated emergency contraceptive pill product in selected "demonstration" countries. As interest in emergency contraception and the Consortium grew, the Consortium expanded its membership to include a wide range of organizations working to ensure that women have access to all forms of emergency contraception. The specific objectives of the expanded Consortium are to:

- serve as an authoritative source of information about emergency contraception;
- be a voice for expanded access to and safe and appropriate use of emergency contraception;
- serve as a strategic planning forum for emergency contraception service delivery and information, education, and communication efforts;
- set high-quality medical and service delivery guidelines for emergency contraception based on the most current information available;
- facilitate information sharing and networking among Consortium members and other groups working to broaden knowledge of and access to emergency contraception;
- encourage partnerships between public-sector organizations and private industry that are designed to make high-quality products for emergency contraception available to large numbers of women worldwide at an affordable price;
- seek and promote new emergency contraceptive methods that are safe and effective.

The Consortium welcomes applications for membership from non-commercial agencies that share the Consortium's overall goal of expanding access to emergency contraceptive products and services in developing countries. Interested applicants should contact the Consortium Coordinator. The Consortium and the American Society for Emergency Contraception also jointly produce an electronic update of emergency contraception activities worldwide. If you would like to subscribe or contribute an article to this update, please contact contact the American Society for Emergency Contraception at Amsocec@aol.com.

Elisa Wells, *Consortium Coordinator*
c/o PATH
(Program for Appropriate Technology in Health)
4 Nickerson Street
Seattle, WA 98109 USA
Email: ewells@path.org
Website: www.path.org/cec/

CONSORTIUM FOR EMERGENCY CONTRACEPTION

Asociación Colombiana para el Estudio e la Población
Asociación Para la PRevención de Embarazos No DEseados
AVSC International • British Pregnancy Advisory Service
The Concept Foundation* • CONRAD Program • DKT International
Family Health International • Institute for Reproductive Health
International Planned Parenthood Federation (and affiliates)*
International Planned Parenthood Federation/Western Hemisphere Region • Ipas
JSI Research and Training Center for Women's Health • Marie Stopes International
Meridian Development Foundation • Pacific Institute for Women's Health*
PATH (Program for Appropriate Technology in Health)* • Pathfinder International*
Population Council* • Population Services International • SHILO Pregnancy Advisory Service
World Health Organization Special Programme of
Research, Development and Research Training in Human Reproduction*

* Founding member, 1995.

EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
S2	18	pharmacy same (controlled or sensitive) adj1 (drug or medicine or medication or substance or agent) same (database or data adj1 base or databank or data adj1 bank)	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2006/06/01 17:12
S3	93	(controlled or sensitive) adj1 (drug or medicine or medication or substance or agent) same (database or data adj1 base or databank or data adj1 bank)	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2006/06/01 17:13
S4	39	(controlled or sensitive) adj1 (drug or medicine or medication or substance or agent) same (database or data adj1 base or databank or data adj1 bank) and (pattern)	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2006/06/01 17:13
S5	5	(controlled or sensitive) adj1 (drug or medicine or medication or substance or agent) same (database or data adj1 base or databank or data adj1 bank) and (gamma adj1 hydroxy adj1 butyrate)	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2006/06/01 17:14
S6	12	(controlled or sensitive) adj1 (drug or medicine or medication or substance or agent) and (gamma adj1 hydroxy adj1 butyrate)	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2006/06/01 17:14
S7	18	(gamma adj1 hydroxy adj1 butyrate) and computer	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2006/06/01 17:15
S8	67	(gamma adj1 hydroxy adj1 butyrate or gamma adj1 hydroxybutyrate) and computer	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2006/06/01 17:15
S9	9	(gamma adj1 hydroxy adj1 butyrate or gamma adj1 hydroxybutyrate) and computer and track$3	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2006/06/01 17:27
S10	379	(block$3 or prevent$3) same (ship$) same (drug or medicine or medication)	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2006/06/01 17:27

EAST Search History

S11	85	(block$3 or prevent$3) same (shipment) same (drug or medicine or medication)	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2006/06/01 17:28
S12	0	(block$3 or prevent$3) same (shipment) same (drug or medicine or medication) same abuse	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2006/06/01 17:28
S13	135	(block$3 or prevent$3) same (shipment) same (drug or medicine or medication or pharmaceutical)	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2006/06/01 17:28
S14	0	(block$3 or prevent$3) same (shipment) same (drug or medicine or medication or pharmaceutical) same abuse	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2006/06/01 17:28
S15	17	(block$3 or prevent$3) same (shipment) same (sensitive or controlled) same (substance or drug or medicine or medication or pharmaceutical)	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2006/06/01 17:29 title+abstracts

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/322,348	12/17/2002	Dayton T. Reardan	101.031US1	5446

21186 7590 06/19/2006

SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.
P.O. BOX 2938
MINNEAPOLIS, MN 55402

EXAMINER	
NAJARIAN, LENA	

ART UNIT	PAPER NUMBER
3626	

DATE MAILED: 06/19/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 10/03)

Office Action Summary	Application No.	Applicant(s)	
	10/322,348	REARDAN ET AL.	
	Examiner	Art Unit	
	Lena Najarian	3626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10 and 32-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10 and 32-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *20060329*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Notice to Applicant

1. This communication is in response to the request for continued examination (RCE) filed 3/29/06. Claims 1-10 and 32-37 are pending. Claims 11-31 have been cancelled. Claims 32-37 are newly added.

Double Patenting

2. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

3. Claims 1-10 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-10 of copending Application No. 10/979,665. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claim 34 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Claim 34 recites the limitation "the exclusive central database" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1-2, 4-8, 10, and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moradi et al. (US 2004/0019794 A1) in view of Lilly et al. (US 2004/0176985 A1) and further in view of Califano et al. (US 2003/0033168 A1).

(A) Referring to claim 1, Moradi discloses a method of distributing a drug, the method comprising (para. 3 of Moradi):

receiving prescription requests from a medical doctor containing information identifying a patient, the drug, and various credentials of the doctor (para. 35, para. 116, and para. 117 of Moradi);

checking the credentials of the doctor (para. 118 of Moradi); and

confirming receipt of the drug (see abstract of Moradi).

Moradi does not expressly disclose that the drug is a sensitive drug, entering the information into a central computer database for analysis of potential abuse situations, confirming with the patient that educational material has been read prior to shipping the sensitive drug, and generating periodic reports via the central computer database to evaluate potential abuse patterns.

Lilly et al. disclose that the drug is a sensitive drug, entering the information into a central computer database for analysis of potential abuse situations, and generating periodic reports via the central computer database to evaluate potential abuse patterns (para. 33, para. 69, para. 54, and para. 58 of Lilly; the Examiner interprets "controlled substance" to be a form of "sensitive drug").

At the time of the invention, it would have been obvious to a person of ordinary skill in the art to combine the features of Lilly within Moradi. The motivation for doing so would have been to ensure that prescribers have an accurate view of their patients' use of prescription drugs and to help protect professionals from lawsuits and other potential liabilities (para. 58 of Lilly).

Moradi and Lilly do not disclose confirming with the patient that educational material has been read prior to shipping the drug.

Califano et al. disclose confirming with the patient that educational material has been read prior to shipping the drug (para. 84 of Califano).

At the time of the invention, it would have been obvious to a person of ordinary skill in the art to combine the feature of Califano within Moradi and Lilly. The motivation

for doing so would have been to ensure that the patient knows about the risks and dangers associated with the drug (para. 43 of Califano).

(B) Referring to claims 2 and 6, Moradi discloses wherein receipt of the drug is confirmed by telephone call from a central pharmacy to the patient (abstract, para. 42, para. 26, and para. 47 of Moradi) and recording a designee identified by the patient to receive the drug (para. 24 of Moradi; the Examiner interprets "recipient's...name" to be a form of "designee").

Moradi does not expressly disclose that the drug is a sensitive drug.

Lilly et al. disclose that the drug is a sensitive drug (para. 33 of Lilly; the Examiner interprets "controlled substance" to be a form of "sensitive drug").

At the time of the invention, it would have been obvious to a person of ordinary skill in the art to combine the feature of Lilly within Moradi. The motivation for doing so would have been for the distribution method to be used primarily for drugs that are likely to be abused (para. 9 of Lilly).

(C) Referring to claim 4, Moradi and Lilly do not disclose recording the confirmation with the patient that the educational material has been read in the central computer database.

Califano discloses recording the confirmation with the patient that the educational material has been read in the central computer database (para. 120 of Califano).

At the time of the invention, it would have been obvious to a person of ordinary skill in the art to combine the feature of Califano within Moradi and Lilly. The motivation

for doing so would have been to have documentation confirming that the patient knows about the risks and dangers associated with the drug (para. 43 of Califano).

(D) Referring to claim 5, Moradi discloses verifying the patient's home address (para. 43 of Moradi).

(E) Referring to claim 7, Moradi discloses establishing a delivery date (para. 46 of Moradi).

(F) Referring to claim 8, Moradi discloses wherein prescription refills requested prior to an anticipated date are questioned by a pharmacist (para. 42 of Moradi).

(G) Referring to claim 10, Moradi discloses wherein the credentials of the doctor comprise DEA (Drug Enforcement Agency) and state license numbers (para. 116 and para. 117 of Moradi).

(H) Referring to claim 32, Moradi discloses a method of distributing a drug under exclusive control of an exclusive central pharmacy, the method comprising (para. 3 and para. 24 of Moradi):

receiving prescription requests from a medical doctor containing information identifying a patient, the drug, and various credentials of the doctor (para. 35, para. 116, and para. 117 of Moradi);

checking the credentials of the doctor (para. 118 of Moradi); and

confirming receipt by the patient of the drug (see abstract of Moradi).

Moradi does not expressly disclose that the drug is a sensitive drug, entering the information into an exclusive computer database associated with the exclusive central pharmacy for analysis of potential abuse situations, confirming with the patient that

educational material has been read prior to shipping the sensitive drug, and generating periodic reports via the exclusive computer database to evaluate potential diversion patterns.

Lilly et al. disclose that the drug is a sensitive drug, entering the information into an exclusive computer database associated with the exclusive central pharmacy for analysis of potential abuse situations, and generating periodic reports via the exclusive computer database to evaluate potential diversion patterns. (para. 33, para. 69, para. 54, para. 58, para. 61, para. 11, and para. 57 of Lilly; the Examiner interprets "controlled substance" to be a form of "sensitive drug").

At the time of the invention, it would have been obvious to a person of ordinary skill in the art to combine the features of Lilly within Moradi. The motivation for doing so would have been to ensure that prescribers have an accurate view of their patients' use of prescription drugs and to help protect professionals from lawsuits and other potential liabilities (para. 58 of Lilly).

Moradi and Lilly do not disclose confirming with the patient that educational material has been read prior to shipping the drug.

Califano et al. disclose confirming with the patient that educational material has been read prior to shipping the drug (para. 84 of Califano).

At the time of the invention, it would have been obvious to a person of ordinary skill in the art to combine the feature of Califano within Moradi and Lilly. The motivation for doing so would have been to ensure that the patient knows about the risks and dangers associated with the drug (para. 43 of Califano).

9. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Moradi et al. (US 2004/0019794 A1) in view of Lilly et al. (US 2004/0176985 A1) in view of Califano et al. (US 2003/0033168 A1) as applied to claim 1 above, and further in view of Andreasson et al. (US 2003/0160698 A1).

(A) Referring to claim 3, Moradi, Lilly, and Califano do not disclose launching an investigation of lost shipments.

Andreasson discloses disclose launching an investigation of lost shipments (para. 79 of Andreasson).

At the time of the invention, it would have been obvious to a person of ordinary skill in the art to combine the feature of Andreasson within Moradi, Lilly, and Califano. The motivation for doing so would have been to reduce the risk of lost or stolen medical products by immediately notifying healthcare workers so that they may take appropriate action (para. 79 of Andreasson).

10. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Moradi et al. (US 2004/0019794 A1) in view of Lilly et al. (US 2004/0176985 A1) in view of Califano et al. (US 2003/0033168 A1) as applied to claim 1 above, and further in view of Mayaud (5,845,255).

(A) Referring to claim 9, Moradi, Lilly, and Califano do not disclose shipping comprehensive printed materials to the doctor if the doctor is a first time prescriber of the drug.

Mayaud discloses shipping comprehensive printed materials to the doctor if the doctor is a first time prescriber of the drug (col. 37, lines 6-31 of Mayaud).

At the time of the invention, it would have been obvious to a person of ordinary skill in the art to combine the feature of Mayaud within Moradi, Lilly, and Califano. The motivation for doing so would have been to reduce the reluctance of physicians to prescribe new drugs by providing them with the latest information about the drugs (col. 37, lines 6-23 of Mayaud).

Mayaud does not expressly disclose that the drug is a sensitive drug.

Lilly et al. disclose that the drug is a sensitive drug (para. 33 of Lilly; the Examiner interprets "controlled substance" to be a form of "sensitive drug").

At the time of the invention, it would have been obvious to a person of ordinary skill in the art to combine the feature of Lilly within Mayaud, Moradi, and Califano. The motivation for doing so would have been for the distribution method to be used primarily for drugs that are likely to be abused (para. 9 of Lilly).

11. Claims 33-36 rejected under 35 U.S.C. 103(a) as being unpatentable over Moradi et al. (US 2004/0019794 A1) in view of Lilly et al. (US 2004/0176985 A1).
(A) Referring to claim 33, Moradi discloses a method of distributing a drug under exclusive control of an exclusive central pharmacy, the method comprising (para. 3 and para. 24 of Moradi):

receiving prescription requests from a medical doctor containing information identifying a patient, the drug, and various credentials of the doctor (para. 35, para. 116, and para. 117 of Moradi);

checking the credentials of the doctor (para. 118 of Moradi); and

confirming receipt by the patient of the drug (see abstract of Moradi).

Moradi does not expressly disclose that the drug is a sensitive drug, entering the information into an exclusive computer database associated with the exclusive central pharmacy for analysis of potential abuse situations, confirming with the patient that educational material has been read prior to shipping the sensitive drug, and generating periodic reports via the exclusive computer database to evaluate potential diversion patterns.

Lilly et al. disclose that the drug is a sensitive drug, entering the information into an exclusive computer database associated with the exclusive central pharmacy for analysis of potential abuse situations, and generating periodic reports via the exclusive computer database to evaluate potential diversion patterns. (para. 33, para. 69, para. 54, para. 58, para. 61, para. 11, and para. 57 of Lilly; the Examiner interprets "controlled substance" to be a form of "sensitive drug").

At the time of the invention, it would have been obvious to a person of ordinary skill in the art to combine the features of Lilly within Moradi. The motivation for doing so would have been to ensure that prescribers have an accurate view of their patients' use of prescription drugs and to help protect professionals from lawsuits and other potential liabilities (para. 58 of Lilly).

(B) Referring to claim 34, Moradi discloses wherein the exclusive central pharmacy controls the exclusive central database (para. 7 and para. 43 of Moradi).

(C) Referring to claim 35, Moradi discloses selectively blocking shipment of the drug to a patient (para. 45 and para. 46 of Moradi).

Moradi does not expressly disclose that the drug is a sensitive drug.

Lilly discloses that the drug is a sensitive drug (para. 2 of Lilly).

At the time of the invention, it would have been obvious to a person of ordinary skill in the art to modify Moradi to include Lilly's sensitive drug with the motivation of tracking and managing controlled substances in order to reduce abuse (para. 2 and para. 12 of Lilly)

(D) Referring to claim 36, Moradi discloses wherein abuse is associated with a patient, and shipment is blocked upon such association (para. 45 and para. 46 of Moradi).

Moradi does not expressly disclose an abuse pattern.

Lilly discloses detecting medication patterns (see para. 58 of Lilly).

At the time of the invention, it would have been obvious to a person of ordinary skill in the art to combine the feature of Lilly within Moradi. The motivation for doing so would have been to proactively deal with potential abuse problems (para. 58 of Lilly).

12. Claim 37 is rejected under 35 U.S.C. 103(a) as being unpatentable over Moradi et al. (US 2004/0019794 A1) in view of Lilly et al. (US 2004/0176985 A1), and further in view of Melker et al. (US 2002/0177232 A1)

(A) Referring to claim 37, Moradi and Lilly do not disclose wherein the sensitive drug comprises gamma hydroxy butyrate (GHB).

Melker teaches that gamma hydroxy butyrate (GHB) is an illicit substance (para. 3 of Melker).

At the time of the invention, it would have been obvious to modify Moradi and Lilly to include gamma hydroxyl butyrate. The motivation for doing so would have been to include drugs of recent concern, such as GHB (para. 3 of Melker).

Response to Arguments

13. Applicant's arguments filed 3/29/06 have been fully considered but they are not persuasive. Applicant's arguments will be addressed hereinbelow in the order in which they appear in the response filed 3/29/06.

(1) Applicant argues at pages 5-6 that the suggestion to combine the reference in the Office Action is not directed to the same or similar problem which the claimed invention addresses. Further, there is no teaching in the prior art of application of the combination to solve the same or similar problems which the claimed invention addresses. Lilly describes reducing misused and abused prescriptions and the need for better tracking and management of prescription in Paragraph 12. However, the purpose of such reductions is related to abuse by the patient, and not abuse of a sensitive drug as claimed. The purpose of the presently claimed invention is to track sensitive drugs and reduce the potential for abuse, such as diversion of the sensitive drug.

(2) Applicant argues at page 6 that Califano is directed to obtaining consent for a clinical trial. It is not directed toward preventing abuse. The cited motivation is very different from the purpose of the presently claimed invention of distributing a sensitive drug in a manner that helps prevent abuse, making it very unlikely that one of skill in the art would be motivated to combine the references.

(3) Applicant argues at page 7 that multiple elements from each of Moradi and Lilly were combined to make the rejection. Because multiple elements from each were used, there is no reasonable expectation of success in making the combination. Further, it points toward the improper use of hindsight, using the claims as a roadmap to make the combination.

(4) Applicant argues at page 8 that Lilly describes the cooperative use of a database by multiple different pharmacies, prescribers and patients, to keep track of the prescription history for a patient. It would be an extremely daunting task to get the cooperation of all these parties. The presently claimed invention uses a central database for analysis of potential abuse situations for distribution of a sensitive drug, not to track all prescriptions for a patient. The ambitious path set forth in Lilly would discourage one of skill in the art from considering using it to solve the problems addressed in the presently claimed invention.

(5) Applicant argues at page 8 that Applicant has reviewed the cited sections of Moradi, and cannot find the concept of a central pharmacy. As the term is used in the present application, a central pharmacy is a pharmacy that exclusively controls the distribution of a sensitive drug.

(6) Applicant argues at page 9 that while Andreasson may describe launching an investigation, it lacks the concept of shipping drugs to a patient, and investigating lost shipments to the patient as claimed.

(7) Applicant argues at pages 9-10 that the Office Action cites a motivation to combine the four references as "to reduce the reluctance of physicians to prescribe new drugs by providing them with the latest information about the drugs." This motivation has nothing to do with the problems addressed by the currently claimed invention as identified above. As a proper prima facie case of obviousness has not been established, the rejection should be withdrawn.

(A) As per the first argument, the Examiner fails to understand the distinction between the tracking and management of drugs to reduce misused and abused prescriptions, as taught by Lilly and "potential abuse," as claimed by Applicant. At para. 11, Lilly discloses that "abuse" includes reselling drugs on the street. As such, it is respectfully submitted that both Lilly and Applicant's invention are directed to the same or similar problem of diversion of sensitive drugs.

(B) In response to applicant's argument that Califano is directed to obtaining consent for a clinical trial and not directed toward preventing abuse, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined

teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

In addition, it is respectfully submitted that all of the applied references relate to health care management. As such, the references are combinable to a person of ordinary skill in the art.

(C) As per the third argument, the issue of obviousness is not determined by what the references expressly state but by what they would reasonably suggest to one of ordinary skill in the art, as supported by decisions in *In re DeLisle* 406 Fed 1326, 160 USPQ 806; *In re Kell, Terry and Davies* 208 USPQ 871; and *In re Fine*, 837 F.2d 1071, 1074, 5 USPQ 2d 1596, 1598 (Fed. Cir. 1988) (citing *In re Lalu*, 747 F.2d 703, 705, 223 USPQ 1257, 1258 (Fed. Cir. 1988)). Further, it was determined in *In re Lamberti et al*, 192 USPQ 278 (CCPA) that:

(i) obviousness does not require absolute predictability;

(ii) non-preferred embodiments of prior art must also be considered; and

(iii) the question is not express teaching of references, but what they would suggest.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a

reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

(D) As per the fourth argument, in response to applicant's argument that Lilly is nonanalogous art, it has been held that a prior art reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the applicant was concerned, in order to be relied upon as a basis for rejection of the claimed invention. See *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). In this case, the Examiner respectfully submits that Lilly is directed to the tracking and management of prescriptions to reduce misuse and abuse (para. 12 of Lilly). As such, Lilly is in the field of applicant's endeavor and is pertinent to the particular problem with which the applicant was concerned.

(E) As per the fifth argument, the Examiner respectfully submits that throughout Moradi reference is made to a pharmacy (note para. 24 and item 106 of Fig. 1). As such, it is respectfully submitted that the broadest reasonable interpretation of the term "central pharmacy" would include the pharmacy that is disclosed in Moradi. In addition, it is noted that the features upon which applicant relies (i.e., exclusively controls the distribution of a sensitive drug) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

(F) As per the sixth argument, the Examiner respectfully submits that para. 79 of Andreasson discloses tracking the delivery of medical products and immediately

notifying healthcare workers and/or administrators of any missing medical products so that they make take appropriate action to recover and/or investigate the missing medical products. Para. 43 discloses comparing the information of the medical products shipped to the healthcare facility with the information received from the pharmacy terminal to verify that all of the medical products shipped to the healthcare facility were received by the pharmacy. As such, it is readily apparent that Andreasson teaches launching an investigation of lost shipments.

(G) As per the seventh argument, the reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve a different problem. It is not necessary that the prior art suggest the combination to achieve the same advantage or result discovered by applicant. *In re Linter*, 458 F.2d 1013, 173 USPQ 560 (CCPA 1972).

Conclusion

14. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. The cited but not applied prior art teaches a system for dispensing drugs in health care institutions (4,847,764); a medicine dispensing apparatus (3,556,342); a system and method for tracking medical devices (US 2004/0008123 A1); a method and system for prescription distribution security (US 2003/0197366 A1); and a distribution system (US 2002/0010661 A1).

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lena Najarian whose telephone number is 571-272-7072. The examiner can normally be reached on Monday - Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Thomas can be reached on 571-272-6776. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

ln
6-2-06

C. LUKE GILLIGAN
PATENT EXAMINER

Index of Claims

Application/Control No.	Applicant(s)/Patent under Reexamination
10/322,348	REARDAN ET AL.
Examiner	**Art Unit**
Lena Najarian	3626

√	Rejected	–	(Through numeral) Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

Claim		Date
Final	Original	6/2/06
	1	√
	2	|
	3	|
	4	|
	5	|
	6	|
	7	|
	8	|
	9	|
	10	√
	~~11~~	-
	~~12~~	|
	~~13~~	|
	~~14~~	|
	~~15~~	|
	~~16~~	|
	~~17~~	|
	~~18~~	|
	~~19~~	|
	~~20~~	|
	~~21~~	|
	~~22~~	|
	~~23~~	|
	~~24~~	|
	~~25~~	|
	~~26~~	|
	~~27~~	|
	~~28~~	|
	~~29~~	|
	~~30~~	|
	~~31~~	-
	32	√
	33	|
	34	|
	35	|
	36	|
	37	√
	38	
	39	
	40	
	41	
	42	
	43	
	44	
	45	
	46	
	47	
	48	
	49	
	50	

Claim		Date
Final	Original	
	51	
	52	
	53	
	54	
	55	
	56	
	57	
	58	
	59	
	60	
	61	
	62	
	63	
	64	
	65	
	66	
	67	
	68	
	69	
	70	
	71	
	72	
	73	
	74	
	75	
	76	
	77	
	78	
	79	
	80	
	81	
	82	
	83	
	84	
	85	
	86	
	87	
	88	
	89	
	90	
	91	
	92	
	93	
	94	
	95	
	96	
	97	
	98	
	99	
	100	

Claim		Date
Final	Original	
	101	
	102	
	103	
	104	
	105	
	106	
	107	
	108	
	109	
	110	
	111	
	112	
	113	
	114	
	115	
	116	
	117	
	118	
	119	
	120	
	121	
	122	
	123	
	124	
	125	
	126	
	127	
	128	
	129	
	130	
	131	
	132	
	133	
	134	
	135	
	136	
	137	
	138	
	139	
	140	
	141	
	142	
	143	
	144	
	145	
	146	
	147	
	148	
	149	
	150	

Search Notes	Application/Control No.	Applicant(s)/Patent under Reexamination
	10/322,348	REARDAN ET AL.
	Examiner	Art Unit
	Lena Najarian	3626

SEARCHED			
Class	Subclass	Date	Examiner
	updated previous searches	6/1/2006	LN

INTERFERENCE SEARCHED			
Class	Subclass	Date	Examiner

SEARCH NOTES (INCLUDING SEARCH STRATEGY)		
	DATE	EXMR
East (see attached printout) USPAT;US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	6/1/2006	LN

PTO/SB/08A(10-01)
Approved for use through 10/31/2002. OMB 651-0031
US Patent & Trademark Office: U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use as many sheets as necessary)

Complete if Known	
Application Number	10/322,348
Filing Date	December 17, 2002
First Named Inventor	Reardan, Dayton
Group Art Unit	3626
Examiner Name	Najarian, Lena

Sheet 1 of 1

Attorney Docket No: 101.031US1

US PATENT DOCUMENTS				
Examiner Initial *	USP Document Number	Publication Date	Name of Patentee or Applicant of cited Document	Filing Date If Appropriate

FOREIGN PATENT DOCUMENTS				
Examiner Initials*	Foreign Document No	Publication Date	Name of Patentee or Applicant of cited Document	T[2]

OTHER DOCUMENTS -- NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T[2]
LN		"System for Thalidomide Education and Prescribing Safety (S.T.E.P.S.) Starter Kit", Celgene Corporation, (2001),103 pgs.	

EXAMINER Lena Najarian DATE CONSIDERED 5-30-06

Substitute Disclosure Statement Form (PTO-1449)

* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional) 2 Applicant is to place a check mark here if English language Translation is attached

Notice of References Cited	Application/Control No. 10/322,348	Applicant(s)/Patent Under Reexamination REARDAN ET AL.	
	Examiner Lena Najarian	Art Unit 3626	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
*	A	US-2002/0177232 A1	11-2002	Melker et al.	436/151
*	B	US-4,847,764	07-1989	Halvorson, Jerry L.	700/231
*	C	US-3,556,342	01-1971	Joseph S. Guarr	221/2
*	D	US-2004/0008123 A1	01-2004	Carrender et al.	340/825.49
*	E	US-2003/0197366 A1	10-2003	Kusterbeck, Shawn	283/69
*	F	US-2002/0010661 A1	01-2002	Waddington et al.	705/28
	G	US-			
	H	US-			
	I	US-			
	J	US-			
	K	US-			
	L	US-			
	M	US-			

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	
	V	
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

RECEIVED
CENTRAL FAX CENTER
JUL 28 2006

SCHWEGMAN ■ LUNDBERG ■ WOESSNER ■ KLUTH
PATENT, TRADEMARK & COPYRIGHT ATTORNEYS
P.O. Box 2938
Minneapolis, MN 55402
Telephone (612) 373-6900 Facsimile (612) 339-3061

July 28, 2006

Time: 5:37 p.m.
(Minneapolis, Minn.)

TO: Commissioner for Patents
Attn: Lena Najarian
Patent Examining Corps
Facsimile Center
P.O. Box 1450
Alexandria, VA 22313-1450

FAX NUMBER (571) 273-8300

FROM: Bradley A. Forrest
Reg. No. 30,837
OUR REF: 101.031US1

TELEPHONE: 571-272-7072

*** Please deliver to Examiner Lena Najarian in Art Unit 3626. ***

Document(s) Transmitted: **Proposed Claims for Examiner Interview (9 pages).**

Total pages of this transmission, including cover letter: 10 pgs.
If you do NOT receive all of the pages described above, please telephone us at 612-373-6900 or fax us at 612-339-3061.

In re. Patent Application of: Dayton T. Reardan et al.
Serial No.: 10/322,348
Filed: December 17, 2002
Title: SENSITIVE DRUG DISTRIBUTION SYSTEM AND METHOD

Examiner: Lena Najarian
Group Art Unit: 3626
Docket No.: 101.031US1

Please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

I hereby certify that this paper is being transmitted by facsimile to the U.S. Patent and Trademark Office on the date shown below.

John Gustav-Wrathall

7-28-06
Date of Transmission

RECEIVED
CENTRAL FAX CENTER
JUL 2 8 2006

Proposed claims for 101.031US1 (serial 10/322,348) fax to 571-273-8300

1. (Previously Presented) A method of distributing a sensitive drug, the method comprising:

receiving prescription requests from a medical doctor containing information identifying a patient, the sensitive drug, and various credentials of the doctor;

entering the information into a central computer database for analysis of potential abuse situations;

checking the credentials of the doctor;

confirming with the patient that educational material has been read prior to shipping the sensitive drug;

confirming receipt of the sensitive drug; and

generating periodic reports via the central computer database to evaluate potential abuse patterns.

2. (Previously Presented) The method of claim 1 wherein receipt of the sensitive drug is confirmed by telephone call from a central pharmacy to the patient.

3. (Original) The method of claim 1 and further comprising launching an investigation of lost shipments.

4. (Previously Presented) The method of claim 1 and further comprising recording the confirmation with the patient that the educational material has been read in the central computer database.

5. (Original) The method of claim 1 and further comprising verifying the patient's home address.

6. (Original) The method of claim 1 and further comprising recording a designee identified by the patient to receive the sensitive drug.

7. (Original) The method of claim 1 and further comprising establishing a delivery date.

8. (Previously Presented) The method of claim 1 wherein prescription refills requested prior to an anticipated date are questioned by a pharmacist.

9. (Previously Presented) The method of claim 1 and further comprising shipping comprehensive printed materials to the doctor if the doctor is a first time prescriber of the sensitive drug.

10. (Original) The method of claim 1 wherein the credentials of the doctor comprise DEA (Drug Enforcement Agency) and state license numbers.

11. – 31. (Cancelled)

32. (Previously Presented) A method of distributing a sensitive drug under exclusive control of an exclusive central pharmacy, the method comprising:

receiving prescription requests from a medical doctor containing information identifying a patient, the sensitive drug, and various credentials of the doctor;

entering the information into an exclusive computer database associated with the exclusive central pharmacy for analysis of potential abuse situations;

checking the credentials of the doctor;

confirming with the patient that educational material has been read prior to shipping the sensitive drug;

confirming receipt by the patient of the sensitive drug; and

generating periodic reports via the exclusive computer database to evaluate potential diversion patterns.

33. (Previously Presented) A method of distributing a sensitive drug under exclusive control of an exclusive central pharmacy, the method comprising:

receiving prescription requests from a medical doctor containing information identifying a patient, the sensitive drug, and various credentials of the doctor;

entering the information into an exclusive computer database associated with the exclusive central pharmacy for analysis of potential abuse situations;

checking the credentials of the doctor;

confirming receipt by the patient of the sensitive drug; and

generating periodic reports via the exclusive computer database to evaluate potential diversion patterns.

34. (Previously Presented) The method of claim 33 wherein the exclusive central pharmacy controls the exclusive central database.

35. (Previously Presented) The method of claim 33 and further comprising selectively blocking shipment of the sensitive drug to a patient.

36. (Previously Presented) The method of claim 33 wherein an abuse pattern is associated with a patient, and shipment is blocked upon such association.

37. (Previously Presented) The method of claim 33 wherein the sensitive drug comprises gamma hydroxy butyrate (GHB).

Additional limitations:

1 – only way to distribute sensitive drug is through use of the central database.

This differs significantly from Moradi et al., which selects a pharmacy based on the patient's location and ensures delivery of a prescription. There is no discussion in Maradi et al., of requiring use of the central database to distribute a sensitive drug. In other words, many different pharmacies may or may not use the system of Moradi et al. In the current claims, the use of a single central database is required for all distribution of the sensitive drug.

Lilly describes cooperative use of a database by multiple pharmacies to keep track of a prescription history for patients. This does not describe requiring the use of a central database for tracking all shipments of a sensitive drug. Thus, neither reference, alone or combined, suggests the requirement that all shipments of a sensitive drug be controlled through the use of a central database.

None of the references, alone or combined, suggest that a sensitive drug can only be distributed under control of a single source, or required to be tracked through the use of a single central database. It provides the ability to track potential abuse patterns with much greater accuracy, and may have been the basis for allowing the life improving drug Xyrem, to make it onto the market.

A progression of claims based off claim 32 and 33.

38. (Proposed) A method of distributing a sensitive drug, the method comprising:

receiving prescription requests from an authorized prescriber containing information identifying a patient, the sensitive drug, and various credentials of the authorized prescriber;

entering the information into an exclusive computer database for analysis of potential abuse situations, **wherein the use of the exclusive computer database is required for distribution of the sensitive drug**;

checking the credentials of the authorized prescriber;

confirming with the patient that educational material has been read prior to providing the sensitive drug to the patient;

confirming receipt by the patient of the sensitive drug; and

generating periodic reports via the exclusive computer database to evaluate potential diversion patterns.

Last element optional?

39. (Proposed) A method of distributing a sensitive drug, the method comprising:

receiving prescription requests **at a central pharmacy** from an authorized prescriber containing information identifying a patient, the sensitive drug, and various credentials of the authorized prescriber;

entering the information into **an exclusive computer database under exclusive control of the central pharmacy** for analysis of potential abuse situations, **wherein the use of the exclusive computer database is required for distribution of the sensitive drug;**

checking the credentials of the authorized prescriber;

confirming with the patient that educational material has been read prior to providing the sensitive drug to the patient;

confirming receipt by the patient of the sensitive drug; and

generating periodic reports via the exclusive computer database to evaluate potential diversion patterns.

40. (Proposed) A method of distributing a sensitive drug **under control of an exclusive central pharmacy**, the method comprising:

receiving prescription requests **at the central pharmacy** from an authorized prescriber containing information identifying a patient, the sensitive drug, and various credentials of the authorized prescriber;

entering the information into **an exclusive computer database under exclusive control of the central pharmacy** for analysis of potential abuse situations, **wherein the use of the exclusive computer database is required for distribution of the sensitive drug;**

checking the credentials of the authorized prescriber;

confirming with the patient that educational material has been read prior to providing the sensitive drug to the patient;

checking the exclusive central computer database for potential abuse associated with the patient;

providing the sensitive drug to the patient provided information in the exclusive computer database is not indicative of potential abuse;

confirming receipt by the patient of the sensitive drug; and

generating periodic reports via the exclusive computer database to evaluate potential diversion patterns.

41. (Proposed) A method of distributing a sensitive drug **under exclusive control of a central pharmacy**, the method comprising:

receiving prescription requests **at the central pharmacy** from an authorized prescriber containing information identifying a patient, the sensitive drug, and various credentials of the authorized prescriber;

entering the information into **an exclusive computer database under exclusive control of the central pharmacy** for analysis of potential abuse situations, **wherein the use of the exclusive computer database is required for distribution of the sensitive drug**;

checking the credentials of the authorized prescriber;

confirming with the patient that educational material has been read prior to providing the sensitive drug to the patient;

checking the exclusive central computer database for potential abuse associated with the patient or the authorized prescriber;

providing the sensitive drug to the patient under control of the exclusive central pharmacy provided information in the exclusive computer database is not indicative of potential abuse;

confirming receipt by the patient of the sensitive drug; and

generating periodic reports via the exclusive computer database to evaluate potential diversion patterns.

8

42. (Proposed) A method of distributing a sensitive drug **under an exclusive controlling entity**, the method comprising:

receiving prescription requests from an authorized prescriber containing information identifying a patient, the sensitive drug, and various credentials of the authorized prescriber;

entering the information into **an exclusive computer database under exclusive control of the exclusive controlling entity** for analysis of potential abuse situations, **wherein the use of the exclusive computer database is required for distribution of the sensitive drug**;

checking the credentials of the authorized prescriber;

confirming with the patient that educational material has been read prior to providing the sensitive drug;

checking the exclusive central computer database for potential abuse associated with the patient;

providing the sensitive drug to the patient provided information in the exclusive computer database is not indicative of potential abuse;

confirming receipt by the patient of the sensitive drug; and

generating periodic reports via the exclusive computer database to evaluate potential diversion patterns.

Proposed claims for 101.031US1 (serial 10/322,348) fax to 571-273-8300

1. (Previously Presented) A method of distributing a sensitive drug, the method comprising:

receiving prescription requests from a medical doctor containing information identifying a patient, the sensitive drug, and various credentials of the doctor;

entering the information into a central computer database for analysis of potential abuse situations;

checking the credentials of the doctor;

confirming with the patient that educational material has been read prior to shipping the sensitive drug;

confirming receipt of the sensitive drug; and

generating periodic reports via the central computer database to evaluate potential abuse patterns.

2. (Previously Presented) The method of claim 1 wherein receipt of the sensitive drug is confirmed by telephone call from a central pharmacy to the patient.

3. (Original) The method of claim 1 and further comprising launching an investigation of lost shipments.

4. (Previously Presented) The method of claim 1 and further comprising recording the confirmation with the patient that the educational material has been read in the central computer database.

5. (Original) The method of claim 1 and further comprising verifying the patient's home address.

6. (Original) The method of claim 1 and further comprising recording a designee identified by the patient to receive the sensitive drug.

7. (Original) The method of claim 1 and further comprising establishing a delivery date.

8. (Previously Presented) The method of claim 1 wherein prescription refills requested prior to an anticipated date are questioned by a pharmacist.

9. (Previously Presented) The method of claim 1 and further comprising shipping comprehensive printed materials to the doctor if the doctor is a first time prescriber of the sensitive drug.

10. (Original) The method of claim 1 wherein the credentials of the doctor comprise DEA (Drug Enforcement Agency) and state license numbers.

11. – 31. (Cancelled)

32. (Previously Presented) A method of distributing a sensitive drug under exclusive control of an exclusive central pharmacy, the method comprising:

receiving prescription requests from a medical doctor containing information identifying a patient, the sensitive drug, and various credentials of the doctor;

entering the information into an exclusive computer database associated with the exclusive central pharmacy for analysis of potential abuse situations;

checking the credentials of the doctor;

confirming with the patient that educational material has been read prior to shipping the sensitive drug;

confirming receipt by the patient of the sensitive drug; and

generating periodic reports via the exclusive computer database to evaluate potential diversion patterns.

33. (Previously Presented) A method of distributing a sensitive drug under exclusive control of an exclusive central pharmacy, the method comprising:

receiving prescription requests from a medical doctor containing information identifying a patient, the sensitive drug, and various credentials of the doctor;

entering the information into an exclusive computer database associated with the exclusive central pharmacy for analysis of potential abuse situations;

checking the credentials of the doctor;

confirming receipt by the patient of the sensitive drug; and

generating periodic reports via the exclusive computer database to evaluate potential diversion patterns.

34. (Previously Presented) The method of claim 33 wherein the exclusive central pharmacy controls the exclusive central database.

35. (Previously Presented) The method of claim 33 and further comprising selectively blocking shipment of the sensitive drug to a patient.

36. (Previously Presented) The method of claim 33 wherein an abuse pattern is associated with a patient, and shipment is blocked upon such association.

37. (Previously Presented) The method of claim 33 wherein the sensitive drug comprises gamma hydroxy butyrate (GHB).

Additional limitations:

1 – only way to distribute sensitive drug is through use of the central database.

This differs significantly from Moradi et al., which selects a pharmacy based on the patient's location and ensures delivery of a prescription. There is no discussion in Maradi et al., of requiring use of the central database to distribute a sensitive drug. In other words, many different pharmacies may or may not use the system of Moradi et al. In the current claims, the use of a single central database is required for all distribution of the sensitive drug.

Lilly describes cooperative use of a database by multiple pharmacies to keep track of a prescription history for patients. This does not describe requiring the use of a central database for tracking all shipments of a sensitive drug. Thus, neither reference, alone or combined, suggests the requirement that all shipments of a sensitive drug be controlled through the use of a central database.

None of the references, alone or combined, suggest that a sensitive drug can only be distributed under control of a single source, or required to be tracked through the use of a single central database. It provides the ability to track potential abuse patterns with much greater accuracy, and may have been the basis for allowing the life improving drug Xyrem, to make it onto the market.

A progression of claims based off claim 32 and 33.

38. (Proposed) A method of distributing a sensitive drug, the method comprising:

receiving prescription requests from an authorized prescriber containing information identifying a patient, the sensitive drug, and various credentials of the authorized prescriber;

entering the information into an exclusive computer database for analysis of potential abuse situations, **wherein the use of the exclusive computer database is required for distribution of the sensitive drug**;

checking the credentials of the authorized prescriber;

confirming with the patient that educational material has been read prior to providing the sensitive drug to the patient;

confirming receipt by the patient of the sensitive drug; and

generating periodic reports via the exclusive computer database to evaluate potential diversion patterns.

Last element optional?

39. (Proposed) A method of distributing a sensitive drug, the method comprising:

receiving prescription requests **at a central pharmacy** from an authorized prescriber containing information identifying a patient, the sensitive drug, and various credentials of the authorized prescriber;

entering the information into **an exclusive computer database under exclusive control of the central pharmacy** for analysis of potential abuse situations, **wherein the use of the exclusive computer database is required for distribution of the sensitive drug**;

checking the credentials of the authorized prescriber;

confirming with the patient that educational material has been read prior to providing the sensitive drug to the patient;

confirming receipt by the patient of the sensitive drug; and

generating periodic reports via the exclusive computer database to evaluate potential diversion patterns.

40. (Proposed) A method of distributing a sensitive drug **under control of an exclusive central pharmacy**, the method comprising:

receiving prescription requests **at the central pharmacy** from an authorized prescriber containing information identifying a patient, the sensitive drug, and various credentials of the authorized prescriber;

entering the information into **an exclusive computer database under exclusive control of the central pharmacy** for analysis of potential abuse situations, **wherein the use of the exclusive computer database is required for distribution of the sensitive drug**;

checking the credentials of the authorized prescriber;

confirming with the patient that educational material has been read prior to providing the sensitive drug to the patient;

checking the exclusive central computer database for potential abuse associated with the patient;

providing the sensitive drug to the patient provided information in the exclusive computer database is not indicative of potential abuse;

confirming receipt by the patient of the sensitive drug; and

generating periodic reports via the exclusive computer database to evaluate potential diversion patterns.

41. (Proposed) A method of distributing a sensitive drug **under exclusive control of a central pharmacy**, the method comprising:

receiving prescription requests **at the central pharmacy** from an authorized prescriber containing information identifying a patient, the sensitive drug, and various credentials of the authorized prescriber;

entering the information into **an exclusive computer database under exclusive control of the central pharmacy** for analysis of potential abuse situations, **wherein the use of the exclusive computer database is required for distribution of the sensitive drug;**

checking the credentials of the authorized prescriber;

confirming with the patient that educational material has been read prior to providing the sensitive drug to the patient;

checking the exclusive central computer database for potential abuse associated with the patient or the authorized prescriber;

providing the sensitive drug to the patient under control of the exclusive central pharmacy provided information in the exclusive computer database is not indicative of potential abuse;

confirming receipt by the patient of the sensitive drug; and

generating periodic reports via the exclusive computer database to evaluate potential diversion patterns.

42. (Proposed) A method of distributing a sensitive drug **under an exclusive controlling entity**, the method comprising:

receiving prescription requests from an authorized prescriber containing information identifying a patient, the sensitive drug, and various credentials of the authorized prescriber;

entering the information into **an exclusive computer database under exclusive control of the exclusive controlling entity** for analysis of potential abuse situations, **wherein the use of the exclusive computer database is required for distribution of the sensitive drug**;

checking the credentials of the authorized prescriber;

confirming with the patient that educational material has been read prior to providing the sensitive drug;

checking the exclusive central computer database for potential abuse associated with the patient;

providing the sensitive drug to the patient provided information in the exclusive computer database is not indicative of potential abuse;

confirming receipt by the patient of the sensitive drug; and

generating periodic reports via the exclusive computer database to evaluate potential diversion patterns.

SCHWEGMAN ■ LUNDBERG ■ WOESSNER ■ KLUTH
PATENT, TRADEMARK & COPYRIGHT ATTORNEYS
P.O. Box 2938
Minneapolis, MN 55402
Telephone (612) 373-6900 Facsimile (612) 339-3061

July 31, 2006

Time: 10:30 A.M.
(Minneapolis, Minn.)

TO: Commissioner for Patents
Attn: Lena Najarian
Patent Examining Corps
Facsimile Center
P.O. Box 1450
Alexandria, VA 22313-1450

FAX NUMBER (571) 273-8300

FROM: Bradley A. Forrest
Reg. No. 30,837
OUR REF: 101.031US1

TELEPHONE: 571-272-7072

*** Please deliver to Examiner Lena Najarian in Art Unit 3626. ***

Document(s) Transmitted: **Proposed Interview Agenda (1 page); Proposed Claims for Examiner Interview (9 pages).**

PLEASE NOTE: I neglected to send the proposed interview agenda with the proposed claims on Friday. Here is the agenda, with the proposed claims.

Total pages of this transmission, including cover letter: 11 pgs.
If you do NOT receive all of the pages described above, please telephone us at 612-373-6900 or fax us at 612-339-3061.

In re. Patent Application of: Dayton T. Reardan et al.	Examiner: Lena Najarian
Serial No.: 10/322,348	Group Art Unit: 3626
Filed: December 17, 2002	Docket No.: 101.031US1

Title: SENSITIVE DRUG DISTRIBUTION SYSTEM AND METHOD

Please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

I hereby certify that this paper is being transmitted by facsimile to the U.S. Patent and Trademark Office on the date shown below.

John D Gustav-Wrathall
John Gustav-Wrathall

7-31-06
Date of Transmission

RECEIVED
CENTRAL FAX CENTER
JUL 3 1 2006

Application No. 10/322,348
Filed: 12/17/2002

Interview Agenda
2PM August 2, 2006.
Attendees:
For Applicant: Brad Forrest; Felissa Cagan
For USPTO: Examiner Najarian and Supervisor Thomas

1. Objective of Interview
2. Problems associated with sensitive drug distribution
3. Discussion of the current claims and art used to reject the claims.
4. Propose new claims/claim limitations to place claims in condition for allowance.

PAGE 2/11 * RCVD AT 7/31/2006 11:52:51 AM [Eastern Daylight Time] * SVR:USPTO-EFXRF-3/11 * DNIS:2738300 * CSID:612 339 3061 * DURATION (mm-ss):03-24

Interview Summary	Application No.	Applicant(s)	
	10/322,348	REARDAN ET AL.	
	Examiner	Art Unit	
	Lena Najarian	3626	

All participants (applicant, applicant's representative, PTO personnel):

(1) *Lena Najarian*. (3)*Brad Forrest*.

(2) *Joseph Thomas*. (4)*Felissa Cagan*.

Date of Interview: *02 August 2006*.

Type: a)☐ Telephonic b)☐ Video Conference
c)☒ Personal [copy given to: 1)☐ applicant 2)☒ applicant's representative]

Exhibit shown or demonstration conducted: d)☐ Yes e)☒ No.
If Yes, brief description: _____.

Claim(s) discussed: ~~[illegible]~~ 1, in particular + proposed new claims

Identification of prior art discussed: Moradi + Lilly

Agreement with respect to the claims f)☐ was reached. g)☐ was not reached. h)☒ N/A.

Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments: _____.

(A fuller description, if necessary, and a copy of the amendments which the examiner agreed would render the claims allowable, if available, must be attached. Also, where no copy of the amendments that would render the claims allowable is available, a summary thereof must be attached.)

THE FORMAL WRITTEN REPLY TO THE LAST OFFICE ACTION MUST INCLUDE THE SUBSTANCE OF THE INTERVIEW. (See MPEP Section 713.04). If a reply to the last Office action has already been filed, APPLICANT IS GIVEN A NON-EXTENDABLE PERIOD OF THE LONGER OF ONE MONTH OR THIRTY DAYS FROM THIS INTERVIEW DATE, OR THE MAILING DATE OF THIS INTERVIEW SUMMARY FORM, WHICHEVER IS LATER, TO FILE A STATEMENT OF THE SUBSTANCE OF THE INTERVIEW. See Summary of Record of Interview requirements on reverse side or on attached sheet.

Discussed possible amendments to the claims. The Examiners will reconsider the applied references in light of any amendments + remarks to be made in response to the non-final rejection.

Joseph Thomas
JOSEPH THOMAS
SUPERVISORY PATENT EXAMINER

Examiner Note: You must sign this form unless it is an Attachment to a signed Office action.

Lena Najarian
Examiner's signature, if required

Summary of Record of Interview Requirements

Manual of Patent Examining Procedure (MPEP), Section 713.04, Substance of Interview Must be Made of Record
A complete written statement as to the substance of any face-to-face, video conference, or telephone interview with regard to an application must be made of record in the application whether or not an agreement with the examiner was reached at the interview.

Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews
Paragraph (b)
In every instance where reconsideration is requested in view of an interview with an examiner, a complete written statement of the reasons presented at the interview as warranting favorable action must be filed by the applicant. An interview does not remove the necessity for reply to Office action as specified in §§ 1.111, 1.135. (35 U.S.C. 132)

37 CFR §1.2 Business to be transacted in writing.
All business with the Patent or Trademark Office should be transacted in writing. The personal attendance of applicants or their attorneys or agents at the Patent and Trademark Office is unnecessary. The action of the Patent and Trademark Office will be based exclusively on the written record in the Office. No attention will be paid to any alleged oral promise, stipulation, or understanding in relation to which there is disagreement or doubt.

The action of the Patent and Trademark Office cannot be based exclusively on the written record in the Office if that record is itself incomplete through the failure to record the substance of interviews.

It is the responsibility of the applicant or the attorney or agent to make the substance of an interview of record in the application file, unless the examiner indicates he or she will do so. It is the examiner's responsibility to see that such a record is made and to correct material inaccuracies which bear directly on the question of patentability.

Examiners must complete an Interview Summary Form for each interview held where a matter of substance has been discussed during the interview by checking the appropriate boxes and filling in the blanks. Discussions regarding only procedural matters, directed solely to restriction requirements for which interview recordation is otherwise provided for in Section 812.01 of the Manual of Patent Examining Procedure, or pointing out typographical errors or unreadable script in Office actions or the like, are excluded from the interview recordation procedures below. Where the substance of an interview is completely recorded in an Examiners Amendment, no separate Interview Summary Record is required.

The Interview Summary Form shall be given an appropriate Paper No., placed in the right hand portion of the file, and listed on the "Contents" section of the file wrapper. In a personal interview, a duplicate of the Form is given to the applicant (or attorney or agent) at the conclusion of the interview. In the case of a telephone or video-conference interview, the copy is mailed to the applicant's correspondence address either with or prior to the next official communication. If additional correspondence from the examiner is not likely before an allowance or if other circumstances dictate, the Form should be mailed promptly after the interview rather than with the next official communication.

The Form provides for recordation of the following information:
- Application Number (Series Code and Serial Number)
- Name of applicant
- Name of examiner
- Date of interview
- Type of interview (telephonic, video-conference, or personal)
- Name of participant(s) (applicant, attorney or agent, examiner, other PTO personnel, etc.)
- An indication whether or not an exhibit was shown or a demonstration conducted
- An identification of the specific prior art discussed
- An indication whether an agreement was reached and if so, a description of the general nature of the agreement (may be by attachment of a copy of amendments or claims agreed as being allowable). Note: Agreement as to allowability is tentative and does not restrict further action by the examiner to the contrary.
- The signature of the examiner who conducted the interview (if Form is not an attachment to a signed Office action)

It is desirable that the examiner orally remind the applicant of his or her obligation to record the substance of the interview of each case. It should be noted, however, that the Interview Summary Form will not normally be considered a complete and proper recordation of the interview unless it includes, or is supplemented by the applicant or the examiner to include, all of the applicable items required below concerning the substance of the interview.

A complete and proper recordation of the substance of any interview should include at least the following applicable items:
1) A brief description of the nature of any exhibit shown or any demonstration conducted,
2) an identification of the claims discussed,
3) an identification of the specific prior art discussed,
4) an identification of the principal proposed amendments of a substantive nature discussed, unless these are already described on the Interview Summary Form completed by the Examiner,
5) a brief identification of the general thrust of the principal arguments presented to the examiner,
   (The identification of arguments need not be lengthy or elaborate. A verbatim or highly detailed description of the arguments is not required. The identification of the arguments is sufficient if the general nature or thrust of the principal arguments made to the examiner can be understood in the context of the application file. Of course, the applicant may desire to emphasize and fully describe those arguments which he or she feels were or might be persuasive to the examiner.)
6) a general indication of any other pertinent matters discussed, and
7) if appropriate, the general results or outcome of the interview unless already described in the Interview Summary Form completed by the examiner.

Examiners are expected to carefully review the applicant's record of the substance of an interview. If the record is not complete and accurate, the examiner will give the applicant an extendable one month time period to correct the record.

Examiner to Check for Accuracy

If the claims are allowable for other reasons of record, the examiner should send a letter setting forth the examiner's version of the statement attributed to him or her. If the record is complete and accurate, the examiner should place the indication, "Interview Record OK" on the paper recording the substance of the interview along with the date and the examiner's initials.