PATENT
ATTORNEY DOCKET NO.: **056291-5004-01**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re PATENT APPLICATION of:	)	Confirmation No. **2093**
EVANS et al.	)	
Application No.: **10/872,784**	)	Group Art Unit: **1617**
Filed: **June 22, 2004**	)	Examiner: **Hui, San-ming R**
FOR: **FORMULATION**	)	
	)	Date: **August 21, 2008**

AMENDMENT AND RESPONSE

This is in response to the Action mailed March 17, 2008, the time for responding to which has been extended to and including September 17, 2008 by Petition and authorization for payment of fees submitted herewith. Please amend the claims as presented below.

Table of Contents is presented on page 2 of this paper.
Table of References discussed is presented on page 3 of this paper.
Amendments to the Claims begin on page 4 of this paper.
Remarks/Arguments begin on page 6 of this paper.

Applicants wish to express their appreciation to the Examiner for taking the time for the personal interview on July 15, 2008, with the undersigned, Dr. Gellert and two other representatives of Applicants' assignee, which interview will also be discussed further below.

The Examiner's attention is called to the accompanying Declaration of Dr. Paul Richard Gellert and Attachments thereto (hereinafter "the **Gellert Declaration**"), portions of which were presented at the interview, and additional portions of which provide further factual and documentary support for the patentability arguments presented during the interview.

It is believed that arguments presented in this response and the factual and documentary support provided by the Gellert Declaration establish the patentability of the amended claims presented below and should place this application in condition for allowance. Therefore early and favorable consideration is respectfully requested. However, if any outstanding issues nevertheless remain, it is respectfully requested that the Examiner telephone the undersigned to expedite the resolution of such issues and the allowance of this application.

For convenience of reference, the Remarks will be presented under the section headings listed in the following Table of Contents, beginning on the page noted:

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TABLE OF REFERENCES

Tab	Author/Inventor	Reference Citation/Patent
1	Cornelius (US '863)	US Patent 4,212,863
2	Dukes (EP '014)	EP 0 346 014 A1 (corresponds to US Patent 5,183,814)
3	Dukes (US '814)	US Patent 5,183,814 (corresponds to EP 0 346 013 A1)
4	Gupta (1999)	P.K. Gupta and G.A. Brazeau (eds). *Injectable Drug Development:Techniques to Reduce Pain and Irritation.* Chapters 11 & 17 Interpharm Press, Denver, Colorado (1999)
5	Huber (US '520)	US Patent 3,164,520
6	Lopatin (1972)	P.V. Lopatin, V. P. Safonov, T. P. Litvinova and L. M. Yakimenko. Use of nonaqueous solvents to prepare injection solutions. *Pharm. Chem. J.* ***6***:724-733 (1972)
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8	Nema (1997)	S. Nema, R.J. Washkuhn, and R.J. Brendel. Excipients and their use in injectable products. *PDA J. Pharm. Sci. Technol.* **51**:166-71 (1997)
9	PDR (1973)	*Physicians' Desk Reference (27th edition).* 1277-1278, 1350-1354, 1391-1392 Medical Economics Company, Oradell, NJ (1973)
10	Powell (1998)	M. F. Powell, T. Nguyen, and L. Baloian. Compendium of excipients for parenteral formulations. *PDA J. Pharm. Sci. Technol.* **52**:238–311 [pages 238-255 provided] (1998)
11	Riffkin (1964)	C. Riffkin, R. Huber and C.H. Keysser. Castor oil as a vehicle for parenteral adminstation of steroid hormones. *J.Pharm.Sci.* **53**: 891-5 (1964)
12	Strickley I (1999)	R. G. Strickley. Parenteral formulations of small molecule therapeutics marketed in the United States (1999) -Part I. *PDA J. Pharm. Sci. Technol.* **53**:324–349 (1999)
13	Strickley II (2000)	R. G. Strickley. Parenteral formulations of small molecule therapeutics marketed in the United States (1999) - Part II *PDA J. Pharm. Sci. Technol.* **54**:69–96 (2000)
14	Strickley III (2000)	R. G. Strickley. Parenteral formulations of small molecule therapeutics marketed in the United States (1999) - Part III. *PDA J. Pharm. Sci. Technol.* **54**:152–169 (2000)
15	Wang (1980)	Y.C. J. Wang and R. R. Kowal. Review of excipients and pH's for parenteral products used in the United States. *J. Parenteral Drug Assoc.* **34**:452–462 (1980).

IN THE CLAIMS:

This listing of claims will replace all prior versions and listing of claims in the application.

Listing of the claims:

Claims 1-34 **(cancelled)**.

Claim 35 **(new)**: A method of treating a hormonal dependent benign or malignant disease of the breast or reproductive tract by administration to a human in need of such treatment an intra-muscular injection of a pharmaceutical formulation comprising fulvestrant, a mixture of from 10 to 30 % weight of a mixture of ethanol and benzyl alcohol per volume of formulation and from 10 to 25 % weight of benzyl benzoate per volume of formulation and a sufficient amount of a castor oil vehicle, whereby a therapeutically significant blood plasma fulvestrant concentration of at least 2.5ngml^{-1} is attained for at least 2 weeks after injection.

Claim 36 **(new)**: A method of treating a hormonal dependent benign or malignant disease of the breast or reproductive tract by administration to a human in need of such treatment an intra-muscular injection of a pharmaceutical formulation comprising fulvestrant, a mixture of from 10 to 30 % weight of a mixture of ethanol and benzyl alcohol per volume of formulation and from 10 to 25 % weight of benzyl benzoate per volume of formulation and a sufficient amount of a castor oil vehicle, whereby the formulation comprises at least 45mgml^{-1} of fulvestrant.

Claim 37 **(new)**: The method as claimed in claim 35 or 36 wherein the formulation comprises a mixture of from 15 to 25 % weight of a mixture of ethanol and benzyl alcohol per volume of formulation and from 12 to 20 % weight of benzyl benzoate per volume of formulation.

Claim 38 **(new)**: The method as claimed in claim 35 or 36 wherein the formulation comprises a mixture of from 8.5 to 11.5 % weight of ethanol per volume of formulation, from 8.5 to 11.5 % weight of benzyl alcohol per volume of formulation and 12 to 18 % weight of

benzyl benzoate per volume of formulation.

Claim 39 (**new**): The method as claimed in claim 35 wherein the blood plasma fulvestrant concentration is attained for at least 3 weeks after injection.

Claim 40 (**new**): The method as claimed in claim 35 wherein the blood plasma fulvestrant concentration is attained for at least 4 weeks after injection.

Claim 41 (**new**): The method as claimed in claim 35 wherein a therapeutically significant blood plasma fulvestrant concentration of at least $3ngml^{-1}$ is attained for at least 2 weeks after injection.

Claim 42 (**new**): The method as claimed in claim 35 wherein a therapeutically significant blood plasma fulvestrant concentration of at least $8.5ngml^{-1}$ is attained for at least 2 weeks after injection.

Claim 43 (**new**): The method as claimed in claim 35 wherein a therapeutically significant blood plasma fulvestrant concentration of at least $8.5ngml^{-1}$ is attained for at least 4 weeks after injection.

Claim 44 (**new**): The method as claimed in claim 35 or 36 wherein the total volume of the formulation administered to said human is 6ml or less, and the concentration of fulvestrant in said formulation is at least $45mgml^{-1}$.

Claim 45 (**new**): The method as claimed in claim 35 or 36 wherein the total volume of the formulation administered to said human is 6ml or less, and the total amount of fulvestrant in said volume of formulation is 250mg or more.

Claim 46 (**new**): The method as claimed in claim 35 or 36 wherein the benign or malignant disease is breast cancer.

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