IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

PFIZER INC. and UCB PHARMA GMBH
Plaintiffs

vs.
C.V. No. 13-1110(GMS)

ALKEM LABORATORIES LTD., CONSOLIDATED
Et al.
Defendants.

CONFIDENTIAL ATTORNEYS EYES ONLY

Videotaped Deposition of Claus Meese

Vol 1

Taken at the offices of:

McDermott Will & Emery
Avenue des Nerviens 9-31
1040 Brussels

Tuesday, 20th January 2015

At 9.49 a.m.

A P P E A R A N C E S :

ON BEHALF OF PLAINTIFFS and THE WITNESS:

WHITE & CASE LLP
1155 Avenue of the Americas
New York, New York 10036-2787
212.819.8255
JAMES S. TRAINOR, ESQ.
jtrainor@whitecase.com
JURGEN HASSA
jurgen.hassa@ucb.com
REBECCA McCULLOUGH

ON BEHALF OF DEFENDANT, APOTEX, INC.:

RAKOCZY MOLINO MAZZOCHI SIWIK LLP
Six West Hubbard Street
Suite 500
Chicago, Illinois 60654
312.527.2157
BY PHONE: ERIN FORBES
eforbes@rmmslegal.com

ON BEHALF OF DEFENDANTS, HETERO USA INC. and HETERO LABS LIMITED:

AXINN, VELTROP & HARKRIDER LLP
114 West 47th Street
New York, New York 10036
212.728.2200
BY PHONE: MATT MURPHY ESQ.
mmurphy@axinn.com

A P P E A R A N C E S (contd)

ON BEHALF OF DEFENDANTS, SANDOZ INC.

McDERMOTT WILL & EMERY
227 West Monroe Street
Chicago, Illinois 60606-5096
312.984.5810
slo@mwe.com
WAN-SHON LO

ON BEHALF OF DEFENDANTS, WOCKHARDT BIO AG and WOCKHARDT USA, LLC:

KNOBBE, MARTENS, OLSON & BEAR, LLP
2040 Main Street
14th Floor
Irvine, California 92614
949.760.0404
KAREN CASSIDY, ESQ.
karen.cassidy@knobbe.com

Also Present:

Kay Hendrick - Court Reporter

Simon Rutson - Videographer

Andrea Boyer - Interpreter

I N D E X

E X H I B I T S

Tuesday, 20th January 2015

THE VIDEOGRAPHER: Good morning, this is the beginning of Tape One, Volume One in the deposition of Dr Claus Meese taken on 20th January 2015 at 9.49 am, as indicated on the video screen. This deposition is being taken in the matter of Pfizer Inc. and UCB Pharma GMBH, Plaintiffs, versus Alkem Laboratories Limited et al, Defendant's, case number CA13-1110 (GMS) Consolidated, being heard in the United States District Court for the District of Delaware.

The deposition is taking place at the offices of McDermott Will & Emey in Brussels, Belgium.

The videographer is Simon Rutson. The Court Reporter is Kay Hendrick on behalf of Henderson Legal Services.

Would counsel in the room please introduce themselves and state whom they represent?

MS CASSIDY: Karen Cassidy from Knobbe, Martens, Olson & Bear representing the Wockhardt Defendant's.

MS LO: Wan-Shon Lo representing the

Defendants Sandoz Inc.

MR HASSA: Jurgen Hassa European Patent Attorney, representing UCB.

MR TRAINOR: Jim Trainor from White & Case in New York on behalf of the Plaintiffs Pfizer, UCB, also on behalf of the witness. With me today is my colleague Rebecca McCullough.

THE VIDEOGRAPHER: Would counsel appearing telephonically please introduce yourselves and state who you represent?

MR MURPHY: Matt Murphy on behalf of Axinn Veltrop & Harkrider on behalf of the Hetero Defendant's.

MS FORBES: Good morning. This is Erin Forbes from Rakoczy Molino Mazzochi Siwik representing Apotex Inc.

THE VIDEOGRAPHER: Anyone else on the line?

Interpreter affirmed.

CLAUS MEESE

having been duly sworn,

testified as follows:

Examination by Ms Cassidy:

Q. Good morning, Dr Meese. Could you

please state your name and address for the record?

A. My name is Claus Meese and my address is -- my name is Claus Meese, Kreuzberger 50, 40748 Monheim, possibly 789 Monheim.

Q. Dr Meese, are you represented by counsel today?

MR TRAINOR: I represent to you that we are representing the witness if he is confused by that but ...

MS CASSIDY: Dr Meese, have you ever been deposed before?

A. No, never.

Q. Alright. Are you aware of any reason you would be unable to give full and accurate testimony today?

A. No.

Q. So a few ground rules for how we are going to run this deposition. I will ask you questions. The Court Reporter is here to take down the questions and your answers. Please make sure to give verbal responses so that the Court Reporter can take down your response and please wait until the question has been completed before you answer it?

A. Yes.

Q. If you do not understand a question please let me know otherwise I will assume that you understand?

A. Okay.

Q. Your attorney may object, please answer the question unless you are instructed not to answer by your attorney?

A. Okay.

Q. And if you need to take a break just let me know and we can take a break at any time but if there is a question pending please answer before we take a break?

A. Okay, yes.

Q. Did you do anything to prepare for this deposition?

A. We have had some discussions with our lawyers, and I had a look at previous document from the patent literature and our own work in order to recall everything, because some time has passed since that time.

Q. Did you meet with anyone aside from your attorney to prepare for the deposition?

A. No.

Q. And did you review any documents while you were preparing for this deposition?

A. Yes, as I mentioned before the patent literature and our own documents, the patent which we have filed in order to recall this world.

Q. We are going to start with a little bit of your background. Could you please describe your education history since after high school?

A. Yes, I started organic chemistry and as well as pharmaceutical chemistry and pharmacy and made my diploma and Doctor of thesis at the university of Hamburg. And afterwards, do you want me to tell what I did later on?

Q. Yes, actually that was going to be my next question, so you could explain after you finished your formal education what your first job was?

A. I have had a job at the University of Hamburg. I was a so-called assistant for the advanced chemistry student. And after that time it changed to the administration authorities of Hamburg, the Department of Environmental Affairs, and I specialized on the analytics of water, that means any kinds of water, tap water and bath water, swimming and so on. After a time I changed.

I moved to Stuttgart and used to work in the Institute of Clinical Pharmacology, Dr Margarete Fischer-Bosch, that is a private institution sponsored by the Robert Bosch Foundation in Stuttgart. And I used to work there for 14 years and I established a chemistry department at this Institute and primarily made studies on drugs, drug metabolism, in-vitro as well as animal studies, analytics, and after that time, which ended in 1993, I moved to a pharmaceutical company, Schwarz Pharma, at that time in Monheim, Germany, and I was responsible for the Chemistry Department of this Company.

In this Company I was involved in the development of new drugs and all chemistry affairs which occur in a pharmaceutical company until 2007. And during that time there was a time where very many papers were published and patents were made on different issues. This is well documented.

Q. And after 2007 were you employed anywhere else or did you retire at that time?

A. After 2007 when I left the Company I retired.

Q. Thank you.

A. And the reason was simply that my Company was merged with UCB Pharma GMBH from Belgium, and it was clear that many changes would occur there due to process, so I decided to leave the Company. It was a smooth goodbye from this Company, so I said yes. Any more questions?

Q. Are you familiar with a compound called festoterodine fumarate?

A. Yes, yes. I can say yes, I know this compound.

Q. Did you work with festoterodine fumarate anywhere besides your employment at Schwarz?

A. No, never. Never.

Q. And do you understand that the r-enantiomer of the festoterodine fumarate may also be referred to as SPM 8272?

A. Yes, I know that.

Q. Okay. And are you familiar with the festoterodine freebase?

A. Yes, I am.

Q. Did you work with that anywhere besides at Schwarz Pharma?

A. No, never.

Q. And do you understand that the

r-enantiomer of the freebase may also be referred to as SPM 8224?

A. Yes, it's the freebase. It's freebase. 8272 is the salt.

Q. And are you familiar with a compound called tolterodine?

A. Yes.

Q. Did you work with tolterodine anywhere besides in your employment at Schwarz?

A. No, never.

Q. And are you familiar with a compound called 5-hydroxymethyl tolterodine?

A. Yes.

Q. And are you comfortable if we refer to this as 5-HMT throughout the deposition, will you understand what I am referring to?

A. Yes.

Q. And did you work with 5-HMT anywhere besides in your employment at Schwarz?

A. No, never.

Q. How many patents are you listed as an inventor on?

A. I only remember the major patents, the priority patent which was filed in May 1998 the first one. And I remember, please correct me

if I am wrong, in total six patents. Yeah.

Q. And the six patents that you are referring to, are these all related to derivatives of the 5-HMT metabolite?

MR TRAINOR: Objection.

A. Yes.

MS CASSIDY: I am going to hand you a document which will be marked as Meese Exhibit 1, and it bears Bates numbers PT 00000001 through PT 00000019.

(Exhibit 1 marked for identification)

A. Yes, okay. Thank you.

Q. Dr Meese, do you recognize this document?

A. Yes.

Q. And can you tell me what this document is?

A. It describes new salt, stable salt and suitable salt, often metabolite they are talking of.

Q. And this document is a patent bearing the number US 6858650; is that correct?

A. That is right.

Q. Dr Meese, you are named as a sole inventor on this patent?

A. Yes.

Q. Do you recall whether you drafted any portions of this patent?

A. Yes, together with the Patent Department of Schwarz Pharma.

Q. So we are going to read through a couple of sections of this patent. I will read them out loud so that we can have the translator translate the sections as well to make it a little bit easier on you. The first section we are going to look at is column one, lines 15 through 21?

MR TRAINOR: May I assist the witness with understanding the line numbers?

MS CASSIDY: Please.

A. I need a magnifying glass. It is too small. Sorry.

MR TRAINOR: Do you have it? Can we go off-the-record for a moment?

THE VIDEOGRAPHER: Off-the-record at 10.09.

(off-the-record)

THE VIDEOGRAPHER: Back on the record at 13 minutes past 10.

MS CASSIDY: In column one of the 650 patent, starting at lines 15 through 21, it reads:

"From document PCT/EP 99/03212 novel derivatives of 3,3-dipenylpropylamine. These are valuable prodrugs for the treatment of urinary incontinence and other spasmodics complaints which overcome the disadvantage of the active substances available to date, namely inadequate absorption of the active substance by biological membranes or the unfavorable metabolism of these."?

A. Yes.

MS CASSIDY: Dr Meese, did you help draft that paragraph?

MR TRAINOR: If you remember.

A. Most primarily, as far as I remember written by the Patent Department people and the pharmacologists which gave some advice, because I just want to recall I am a chemist, and this is my focus on the whole issue.

MS CASSIDY: And do you recall the time this was drafted do you agree with the statement that essentially the derivatives of the 3,3-dipenylpropylamines were known?

A. Derivatives were known since the 1960s.

MS CASSIDY: And do you recall who the pharmacologists who assisted in the drafting of

this patent were?

MR TRAINOR: Objection.

A. I can't say the name but it must be a pharmacologist from the project team.

MS CASSIDY: Now, if you will look at column one, starting at line 63 through column one or column two, line 3 where it says:

"Surprisingly, it has now been found that the above mentioned disadvantages can be avoided if compounds with a structure of general formula A once they have been prepared under a special reaction process are converted with a physiologically compatible inorganic or organic acid with the general formula HX in which X represents the respective acid residue into their respective salt with the general formula I."?

A. Yes.

MS CASSIDY: If I could direct your attention to figure one of the 650 patent, I believe it will be one page over on your copy, back towards the front of the document?

A. Yes.

MS CASSIDY: Is the reaction depicted in figure one the special reaction process that was referred to in the section from column one of the

patent that we just read?

MR TRAINOR: Objection.

A. Yes, it's a abbreviated depiction of the transition from 1 to 2.

MS CASSIDY: And for this abbreviated figure why were these particular steps selected for the abbreviated figure 1?

A. Just to give an overview how we got compound 6 from 3 and then following steps from 3 to 2A or 2B they are essential, and they are again shown in the following columns.

MS CASSIDY: When you say that these steps are essential, do you recall whether in the full synthesis there are other essential steps as well?

MR TRAINOR: Objection.

A. Yes, certainly. The Regio specific acylation giving a compound of the formula A is certainly a crucial step, and salt formation again is a crucial step formula. We have 1, yes, on column 2.

MR TRAINOR: That is "R-E-G-I-O selective".

A. Yes, Regio selective because the precursor compound Number 6 in figure 1 has two

hydroxy groups and really it was to our experience surprising that only the phenolic hydroxy groups react under certain conditions with the respective acylation agent.

MR TRAINOR: That is A-C-Y-L-A-T-I-O-N. I am just helping her.

MS CASSIDY: Why was it surprising that only the phenolic hydroxy groups reacted under certain conditions?

A. We didn't expect that before, because there are two hydroxy groups available and molecule and we didn't expect a high degree of specificity.

MS CASSIDY: Was this because you expected both hydroxy groups to be equally reactive?

A. Yes, or less or more, but this way.

Q. I am going to hand you a document that has been previously marked as Sparf Exhibit 11 and it is bearing Bates numbers PT 00000020 through PT 00000052. Actually I think we are going to mark that, if you hand that back to the Court Reporter. We will mark this as Meese Exhibit 2.

(Exhibit 2 marked for identification)

Dr Meese, if you can take a minute to look at this document and let me know if you recognize it?

A. Yes.

Q. Dr Meese, what is this document that I have handed you?

A. A document the American translation of our priority patent from May 12th 1998.

Q. And this bears US patent Number 7384980; is that correct?

A. This paper here, yes.

Q. Yes?

A. 980.

Q. And you are listed as a co-inventor with Bengt Sparf; is that correct?

A. That is correct.

Q. And who is Bengt Sparf?

A. Bengt Sparf is a pharmacologist from Sweden who was familiar with anti-muscarinic drugs for many years and at that time he was kind of consultant for Schwarz Pharma, because this -- no, no.

Q. Do you recall how Dr Sparf became involved in this project, in this patent?

MR TRAINOR: Objection.

A. Well, we researched CEO of Schwarz Pharma, we needed external input. At that time the whole project was initiated at Schwarz Pharma, so this expert was willing to give support.

MS CASSIDY: Do you recall whether you had started work on this project prior to Dr Sparf becoming involved?

A. No, we haven't done anything on this field before.

MS CASSIDY: What do you understand Dr Sparf's contribution to the invention described in the 980 patent to be?

MR TRAINOR: Objection.

A. Well, his contribution was primarily in the field of pharmacology and handling of anti-muscarinic drugs in human and animal studies. There was no contribution in the field of chemistry, no significant contribution.

MS CASSIDY: And what do you understand your contribution to the invention described in this patent to have been?

MR TRAINOR: Objection.

A. I was responsible for the chemistry, for all chemical aspects.

MS CASSIDY: What do you understand the

difference between the 650 patent, the inventions described in the 650 patent and the invention in the 980 patent to have been?

MR TRAINOR: Objection.

A. 650 patent, this and this one?

MS CASSIDY: Yes.

A. The focus in the 650 patent clearly was on the formation of stable salts, as the title says. And the 980 is a more general patent on many more aspects of drug development.

Q. I am going to hand you a document which will be marked as Meese Exhibit 3, bearing Bates numbers PT 00000053 through PT 00000085.

(Exhibit 3 marked for identification)

A. Does that mean we are done with these for now?

Q. You can set them aside for now, we may come back to them. Do you recognize this document, Dr Meese?

A. Give me a second, yes. Okay.

Q. Do you recognize this document?

A. Yes.

Q. And if you look in the top right corner this document is bearing the US patent number 7855230; is that correct?

A. Yes.

Q. And you and Dr Sparf are named as co-inventors on this patent, correct?

A. Yes.

Q. And if you could please turn to the last page, the page ending in Bates Number 085 with the column top 56?

MR TRAINOR: The last page or column 56?

MS CASSIDY: Column 56 which should be on the last page.

MR TRAINOR: 57, 58 -- sorry, I have the wrong Exhibit. I apologize.

A. Column 56 and which number there?

THE INTERPRETER: Which line number?

MS CASSIDY: Starting at line number 17 right after it says "The invention claimed is," then the Number 1?

A. Yeah.

MS CASSIDY: And looking at Claim 1 what do you understand the difference between the 230 patent and the 980 patent, Exhibit 2, that we were just looking at to be?

MR TRAINOR: Objection. If you have an understanding.

A. Yeah. There is a clear difference

because the focus of this claim is clearly the transdermal application of the novel derivatives, and that was absolutely new and nobody thought of that before. Not oral, but transdermal.

MS CASSIDY: And what was your contribution to the invention described in this patent?

MR TRAINOR: Objection.

A. Simply spoken nobody thought of this transdermal application of this kind of normal compounds. Never before. And I was convinced that transdermal application has considerable advantages over oral, orally administered drug.

MS CASSIDY: Okay. I am handing you a document that will be marked as Meese Exhibit 4. It is a document bearing Bates numbers PT 00000086 through PT 00000117.

(Exhibit 4 marked for identification)

Do you recognize this document, Dr Meese?

A. Sorry. Yes, I remember it.

Q. And do you understand this document to be a patent bearing the US patent Number 7985772?

A. Yes.

Q. You are a co-inventor on this patent with Dr Sparf; is that correct?

A. Yes.

Q. And what do you understand your contribution to this, to the invention in this patent to have been?

MR TRAINOR: Objection. I just object to this whole line of questioning. These are about questions of law. This man is here to answer questions about facts. Interpreting patent documents, understanding what claims mean, what the difference between what one document is and another, legal documents, examine as you wish but I object to this question.

A. I just want to emphasise my initial command that I was responsible for the chemistry and not for other aspects.

MS CASSIDY: Okay. And based on your recollection do you understand -- what is your understanding is the difference between the 772 patent and the 230 patent that we just discussed?

MR TRAINOR: Objection.

A. There is one big difference. It's column 53 -- I go back again. Sorry. Sorry, but it's a couple of years ago so I have to.

MR TRAINOR: Can we give him the question back and can you please translate it?

MS CASSIDY: Before you do, Dr Meese, I can clarify, this is just based on your recollection, if you recall what the difference was?

A. First I see novel derivatives prepared by other methods, some experiments make polymers loaded with active drug. I can't find it now but I know there was a section for benzylic esters.

Q. Dr Meese, this is just based on your recollection. I understand it has been some time since you have looked at this, you don't need to analyze the entire document if you don't want to, based on your recollection what you have told us should be sufficient?

A. Okay. I just remember novel methods and novel variance, and one of them, an enzymetic process to get the benzylic esters which could not be obtained by other methods. It was completely new, and that's what I remember right now.

Q. Dr Meese, I am handing you a document bearing -- marked as Exhibit Number 5 bearing Bates numbers PT 00000118 through PT

00000149.

(Exhibit 5 marked for identification)

Dr Meese, do you recognize this document?

A. I will have to have a look at it first. Sorry. Yes.

Q. And do you recognize this document to be a US patent bearing patent Number 8338478?

A. Yes.

Q. And you are listed as co-inventor on this patent along with Dr Sparf; is that correct?

A. Yes.

Q. And if you recall what was your contribution to this patent?

MR TRAINOR: Objection. Talking about the patent, the claims?

MS CASSIDY: Sorry, to the invention disclosed in this patent?

A. Well, basically the processes, and I mean the chemical processes necessary to make novel derivatives but -- and I want to emphasise this, only until 2012, after that it was no longer Schwarz but UCB that was updating them.

Q. Dr Meese, do you receive any benefit, do employees at Schwarz receive any

benefit for being named as inventors on patents?

A. Not in financial terms, no. It is appreciated but that's all.

Q. I am going to hand you a document which bears the Bates number -- we will be marking as Meese Exhibit 6 bearing Bates numbers PT -- sorry, Exhibit 6?

MR TRAINOR: Five?

MS CASSIDY: Six. Exhibit 6 bearing the Bates numbers PT 02019287 through PT 02019292.

(Exhibit 6 marked for identification)

I am also handing you an English, a certified English translation of the same document which we will be marking as Meese Exhibit 7.

(Exhibit 7 marked for identification)

A. But this is not a copy for me, right, this is part of the document. I have never seen this translation before.

Q. This translation is one that we made. It is a copy that was translated of the German version so that we could understand what the document said?

A. Okay. I never have seen it, yeah.

Q. Dr Meese, if I could direct your attention to Exhibit 6, the German version of this

document?

A. Yes.

Q. If you could please take a look at this and let me know if you recognize the document?

A. Well, yes, I signed it.

Q. And this is an agreement relating to an inventor's bonus; is that correct?

A. Yes.

Q. If you could please turn to page 2 of the agreement. And if you look at Section 1 relating to international patent application W099/58478?

A. Where exactly is that.

Q. If you look on page 2 there is a bold 1 and underneath it a non bold 1?

A. Okay.

Q. Underneath unbolded 1 is where you will see International Patent Application W099/58478?

A. Yes.

Q. And underneath that do you see that there is a line labeled "inventors" with your name and Dr Sparf's name?

A. Yes.

Q. And next to your name is an 80%?
A. Yes.
Q. Do you have any recollection as to what the 80% represents?
MR TRAINOR: Objection.
A. That's what the two inventors agreed to.
MS CASSIDY: And when you say it is what the two inventors agreed to, do you mean agreed to as in a representation of their share of the work?
MR TRAINOR: Objection.
A. Yes.
MS CASSIDY: Okay. And if you could turn to page 4 of the agreement which has in the bottom right corner a Bates number PT 02019290.
A. Yes.
Q. And if you look at the paragraph with the bold number 5 next to it, it should be the last paragraph on the page?
A. Yes.
Q. And in this paragraph Schwarz Pharma agreed to pay you a one time flat rate inventor's bonus in the amount of 1m Euros; is that correct?
A. Yes.
Q. And if you turn to the next page,

looking next to the paragraph with the bold Number 6 next to it, Schwarz Pharma also agreed to pay an additional flat rate bonus in the amount of 200,000 Euros per year from March 31st 2007 until 2016; is that correct?

A. Yes.

Q. And you previously testified that Schwarz normally does not pay bonuses for being named as an inventor on their patent?

A. This is not a bonus. No, this is not considered a bonus. This is an obligation under the German law which protects inventors.

MR TRAINOR: For the record I would like to designate the entire transcript highly confidential pursuant to the terms of the Protective Order.

COURT REPORTER: Was yesterday's confidential as well?

MR TRAINOR: For the record yes and we will make that clear between the parties off-the-record.

MS CASSIDY: Aside from payments under this contract are you currently receiving any other payments from Schwarz?

A. My company pension.

Q. Okay. And are you receiving any payment from Pfizer at this time?

A. No, none.

Q. Are you receiving any payments from UCB?

A. Well, yes, to the extent that UCB is the successor of what was Schwarz Pharma and that would then again be my company pension.

Q. Dr Meese, are you being paid for your time here today?

A. No.

Q. We have been going about a little over an hour, so is this a good time to take a break?

MR TRAINOR: Yes, please.

A. Yes, that would be okay.

THE VIDEOGRAPHER: Going off-the-record at 11.06.

(Short Recess)

THE VIDEOGRAPHER: This is the beginning of Tape Two, Volume One and a continuation in the deposition of Dr Claus Meese. On the record at 11.24.

MS CASSIDY: Dr Meese, I am going to hand you a document that will be marked as Meese

Exhibit 8, bearing Bates numbers PT 02075767 through PT 02075771.

(Exhibit 8 marked for identification)

Dr Meese, if you could take a minute and review this document and then once you have finished reviewing please let me know if you recognize it?

A. There is a blank page in here.

Q. Yes, there should be a blank page in there?

A. Okay.

MR TRAINOR: The question is do you recognize this?

A. Yes.

MS CASSIDY: Did you participate in the drafting of this document?

A. Yes, each member of the early team meetings gave always a sheet of paper to the project manager with some brief notes about the contribution which are planned for the team meetings.

Q. And if I can direct your attention to the very first line of the chart on the left-hand column in the column labeled date?

A. Are you referring to the first line?

Q. Yes, do you see where it says CW 34?

A. I wasn't part of that. It is Lars Ekman and Peter Ney here. I am not a member of this meeting, of this first meeting.

Q. Okay. Do you have any understanding what CW 34 stands for?

A. Calendar week.

Q. Do you see under events and topics in the first line where it says:

"Discussion of research proposal on prodrug of tolterodine metabolite DD 01 made by BS."?

A. Yes, that was the meeting that I didn't attend, as I said.

Q. Although you didn't attend the meeting did you ever see the letter from Dr Sparf that's referenced in this event topic?

A. I can't see that.

Q. If you move to the second line dated August 28th, 1997?

A. Yes.

Q. In this August 28th 1997 meeting was

this the initial project discussion, the very first project discussion that you were involved in?

A. Exactly.

Q. And who are the others in attendance at this meeting?

A. Primarily Bengt Sparf and for a few couple of minutes at the beginning Peter Ney.

Q. I am going to hand you another set of two documents but if you could keep this chart off to the side we will likely be referring back to it again?

A. Umm hmm.

Q. I am going to be handing you a document bearing Bates, marked as Meese Exhibit 8 Bates numbers PT -- marked as Meese Exhibit 9, bearing Bates numbers PT 01855861.

(Exhibit 9 marked for identification)

And also I am handing you what has been marked as Exhibit 10 which is an English translation of PT 01855861.

(Exhibit 10 marked for identification)

MR TRAINOR: The English translation of the Exhibit?

MS CASSIDY: Of Exhibit 9. I am also

going to be handing you a document marked as Exhibit 11 bearing Bates numbers PT 01856445. through PT 01856447

(Exhibit 11 marked for identification)

THE INTERPRETER: Dr Meese, is asking in the English translation what does SCL mean?

A. Yes, it is a typing error, it should be SIL which was the name of our chemistry department at the time.

MS CASSIDY: Thank you. I was actually going to be asking you what SCL stood for?

A. Now it's clear. Thank you.

MS CASSIDY: I am also going to hand you a document marked as Meese Exhibit 12 which is the English translation of pages PT 01856445 of Exhibit 11.

(Exhibit 12 marked for identification)

THE INTERPRETER: There is mistakes in this too but I guess it is because it was translated from a handwritten document where it case grams and that should be milligrams.

MR TRAINOR: If we could wait until she asks a question.

MS CASSIDY: If you could start by looking at Exhibit 11, and Dr Meese you can refer

to the German version.

A. Yes.

Q. If you look in the top left-hand corner do you see the date?

A. Yes, of the first meeting on the topic or brainstorming.

Q. And this was that first meeting we were discussing in Exhibit 8, the chart?

A. Yes.

Q. And was this the first time that you had met with Dr Sparf?

A. Exactly.

Q. And during this meeting you have a note regarding P4502D6, do you recall what that refers to?

A. It means the formation of the metabolite if catalyzed by a cytochrome P450 type 2D6 enzyme and generically polymorph. That means a few percent of the population do not have this enzyme and this is always in the focus of the pharmacologist because a new drug which is metabolized by cytochrome P450 2D6 cannot metabolize via this polymorphic cytochrome enzyme, that means the new drug does not form the respective metabolite.

Q. And right underneath the reference to P450 2D6 references the hydroxy metabolite, is this a reference to 5-HMT?

A. Yes.

Q. Was this the first time that you had heard the term that you had been introduced to the hydroxy metabolite?

A. Yes, exactly.

Q. Did Dr Sparf provide you with any written information during this meeting?

A. No, no. No. He informed me about the previous publications and congress reports, abstracts on this issue, and then we looked at the literature, patent literature and scientific literature and found indeed a couple of disclosures.

Q. When you say you found a couple of disclosures, do you recall what those disclosures were related to?

MR TRAINOR: Objection.

A. In very general terms metabolization of tolterodine.

MS CASSIDY: In the left-hand column, the handwriting towards the top where it says:

"Only 10% bioavailability."

Do you recall is that referring to the bioavailability of the 5-HMT metabolite?

A. I don't know. I don't recall right now. It could be but, no, I really don't want to speculate.

MS CASSIDY: Would that information have been provided during this meeting by Dr Sparf?

MR TRAINOR: Objection.

A. Again I would have to speculate. I can't say.

MS CASSIDY: And do you see underneath the chemical drawings there is a line that says:

"(N+) tolterodine: Is now being licensed." Underneath that "(tartrate) (R)!?" exclamation point question mark."?

A. Umm hmm.

MS CASSIDY: Do you recall was that the form of tolterodine that was being sold on the market?

MR TRAINOR: Objection. Is your question whether it was sold on the market at that time or was --

MS CASSIDY: At that time?

MR TRAINOR: Same objection.

A. All I can see is this question mark.

MS CASSIDY: Would the r-enantiomer of tolterodine metabolize into the r-enantiomer of the active metabolite?

MR TRAINOR: Objection. Did he answer and you didn't get it.

THE INTERPRETER: There has been no answer.

MR TRAINOR: You can answer.

THE INTERPRETER: The first part in German was R is the absolute configuration for both the parent drug and the metabolite. Then you added in English.

A. It doesn't change during metabolization.

MS CASSIDY: Did the note that tolterodine may be licensed in the r-enantiomer form suggest anything to you in 1997 about the form a prodrug salt, a prodrug of the active metabolite salt should take when you developed your prodrug?

MR TRAINOR: Objection.

A. No, at the time I had no documents whatsoever concerning how it would be licensed. That was still Pharmacia back then.

MS CASSIDY: If you could turn now to

Exhibit 9. Do you recognize this document?

A. Yes.

MS CASSIDY: Is that your handwriting?

A. Yes.

MS CASSIDY: And do you see where it is dated 28th August 1997, is this a summary of your understanding of the August 28th, 1997 meeting?

A. Yes, exactly.

MR TRAINOR: I just object, there appears to be more than one date on this document, so ...

MS CASSIDY: I will clarify that for the record.

A. This was one month after the original first meeting.

MS CASSIDY: Okay. Dr Meese, if I could direct your attention up into the top left-hand corner, there is a date of September 26th, 2000, do you see that?

A. Well, yes, one month after the first meeting as far as I can tell. I can't see it here. It is missing here. It should be here.

Q. And your first meeting occurred on August 28th, 1997, correct?

A. Yes, that's right.

Q. Okay?

A. Oh, and this is 2000. I don't remember that.

Q. Based on the date of September 26th, 2000 in the top right-hand corner, does this appear to be a summary of your understanding of the August 28th, 1997 meeting as you recalled it on September 26th, 2000?

A. Yes, that is what it looks like.

Q. And during that August 28th, 1997 meeting Dr Sparf had suggested developing a prodrug form of the active metabolite; is that correct?

A. Umm hmm. Yes. Yes.

Q. And it was your understanding in 1997 that the active metabolite DD 01 had already been described in the literature as being biologically active?

A. Yes, there is several publications on that.

Q. Prior to your work on the development of festoterodine had you ever been involved in the development of a prodrug before?

A. No.

Q. Do you recall whether prodrugs of

active metabolites were being developed regularly in 1997?

MR TRAINOR: Objection.

A. No.

MS CASSIDY: You noted that the suggestion of derivatization of the benzylic hydroxy group, do you recall why derivatization of the benzyl active group was suggested first?

A. Yes, there are early reports from the Karolinska institute and some people from Pharmacia that for the anti-muscarinic specificity, specificity of similar drugs, the phenolic hydroxy group has to be free, it must not be blocked by derivatization. There are several reports in the patent literature and abstracts from congresses. It was advised phenolic hydroxy group has to be free to elicit this anti-muscarinic activity.

MR TRAINOR: I think there was "advised", not it was a bias. It was advised.

A. Exactly.

MS CASSIDY: Did Dr Sparf provide you with that information?

A. Yes, but I found it at the same time by a literature search. It is freely available

for everybody, but he knew these publications, was clear that phenolic hydroxy group has to be free to be effective.

MS CASSIDY: So if you perform the derivatization at the phenolic hydroxy group you would expect the compound to be inactive?

MR TRAINOR: Objection.

A. That was the belief back then.

MS CASSIDY: Could you please turn back to Exhibit 8?

A. Yeah.

Q. And if you look at the third row dated September 19th, 1997?

A. Yes.

Q. Do you see the events first team meeting?

A. Yes.

Q. Do you recall what, if anything, occurred between the August 28th, 1997 initial discussion and the first team meeting on September 19th, 1997?

A. The whole chemistry was started.

Q. When you say the whole chemistry was started, what do you mean?

A. Everything which is necessary to

initiate a project. We ordered the chemicals. We completed the literature and references and patent literature and we started to prepare precursors in order to get the necessary steps ready.

Q. During that time period between August 28th, 1997 and September 19th, 1997 would you also have begun drafting potential syntheses for --

A. Not me, it was somebody else.

Q. Do you recall who was drafting the potential syntheses of 5-HMT?

A. No, I found here under major points and decisions it was proposed that Bengt Sparf write a draft.

Q. So is your recollection that Dr Sparf prepared the first draft of potential synthesize of the 5-HMT metabolite?

A. No, that was not what I meant. It was his job to draft a mock patent.

Q. Okay. If you look under the row dated August 28th, 1997 under major points and decisions, that second row, the last sentence says: "COM to prepare first development plan."?

A. Yes.

Q. Does COM in this sentence refer to

you?

A. That is me, COM, yes.

Q. And what is the first chemical development plan? Let me rephrase that. What in general is a chemical development plan in Shorts?

MR TRAINOR: Objection. At this time?

MS CASSIDY: At this time?

A. Members of the team wanted to get some information how we intend to proceed.

MS CASSIDY: I am going to hand you a document which was previously marked as Sparf Exhibit 12 which we will mark as Meese Exhibit 13.

(Exhibit 13 marked for identification)

MR TRAINOR: Do you need him to make reference to any of these Exhibits?

MS CASSIDY: For now the timetable, the rest can get set aside.

MR TRAINOR: I am trying to help him out.

MS CASSIDY: Dr Meese, we have handed you what was previously marked as Sparf Exhibit 12 and has been marked in this case as Meese Exhibit 13, a document bearing Bates numbers PT 02075781 through PT 02075809. If you could please look through this Exhibit and then let me know if you

recognize this document?

A. I am losing track with so much paper on the table.

MR TRAINOR: She has asked you to look through it and see if you recognize it.

A. These are slides with intentions or proposed ways to proceed saying like we could do something.

MS CASSIDY: So for now looking just at the very first page labeled PT 02075781?

A. Okay.

Q. This is a document labeled: The first team meeting, correct?

A. I don't know here. We have got it here, yes, 19th September obviously. That is what it says here too.

Q. And did you attend this meeting, Dr Meese?

A. Yes, I was mentioned here so I think I attended it.

Q. And were team meeting minutes prepared in the regular course of business at Schwarz?

MR TRAINOR: Objection. If you understand it.

A. This wasn't really a team yet at the time. It's really what we would have called a pre-team. A pre-team doesn't become a team until you actually have a project that is approved by the Executive Board with the appropriate funding and everything, so this is what we would have called a pre-team meeting.

MS CASSIDY: And in 1997 was it the regular practice to take meeting minutes of pre-team meetings?

MR TRAINOR: Objection.

A. Well, usual. Schwarz had no experience with such early phase development and there was no usual. Sometimes yes and sometimes no.

MS CASSIDY: Dr Meese, do you recall what your role was in this first meeting on September 19th, 1997?

A. Well, generally it was my responsibility to inform the team on the progress that had been made in chemistry.

Q. Do you see where it says AD 3?

A. Yes.

Q. It states that synthesis in-house started September 15th. Do you recall what

synthesis was started on September 15th?

A. Priority of product confirmed (talking to himself).

That's something we would have to check up on in the laboratory journals. I don't recall.

Q. Okay. The next sentence states:

"Two starting chemicals outsourced available September 24th."

Do you recall which two chemicals, starting chemicals were outsourced?

A. No, I really can't remember which two that might have been.

Q. Okay. If you can turn to the next page, it is the one bearing Bates number PT 02075783, it is two pages?

MR TRAINOR: 63?

MS CASSIDY: 783. Do you see the second paragraph beginning:

"Structure similar to a compound already in approval process."

MR TRAINOR: The question is did you see it?

A. I don't know who would have made that statement here.

MS CASSIDY: Okay. Actually but you see

where the statement is?

A. Yes, of course.

MS CASSIDY: And underneath it it states: "Defined chemical strategy."

Do you know what defined chemical strategy it might refer to?

A. No, no.

MS CASSIDY: And in the third bullet point it states that there is a low development risk. Do you know how the development risk was determined for this product?

MR TRAINOR: Objection.

A. No, no I really don't know who wrote this and I can't tell you. You would have to ask the person who wrote this.

MS CASSIDY: And if you could turn to page PT 02075789, it is a page titled: Chemical Development Plan. Dr Meese, did you draft this chemical development plan?

A. Yes.

Q. And if you look at the first line where it says:

"Aim synthesis of a key intermediate (semi-protected hydroxy metabolite)".

Do you see that?

A. Yes.

Q. Is the semi-protected hydroxy metabolite the only key intermediate that you were trying to synthesize?

MR TRAINOR: Objection.

A. I need to look for something.

MR TRAINOR: Is your question at this time or at any time?

MS CASSIDY: At this time.

A. I can't find it here. There were a lot of people involved in this back then and it was always very busy and hectic and I know it was the team who asked me because they wanted to know what the current status was, and that was why I provided this report.

Q. Also in that section related to -- called "Aim" it goes on to say:

"Ready to give new prodrugs in two simple steps."

What was meant by -- strike that.

Were there already two simple steps that you had in mind for synthesizing the prodrug from the semi-protected hydroxy metabolite?

A. I am still looking for the structure which pertains to 9. At this time it was

primarily paper chemistry, just to signify the team members because otherwise as present they ask each week several times, so ...

Q. With the understanding that at this time it was primarily paper chemistry, do you recall why you believe the two steps to the new prodrug would be characterized as simple?

MR TRAINOR: Objection.

A. Well, we are still talking about paper chemistry based on our experience up until then.

MS CASSIDY: When you say "based on our experience up until then", are you referring to the knowledge that you had based on publications that were available to you prior to September 19th, 1997?

A. Yes, both, all experience in chemistry in general.

MS CASSIDY: If you go to the next line where it says "Prequisite", it then says:

"Cut down the number of steps from 9 (Pharmacia-Upjohn) to 3 to 5 (Shorts Pharma), design of a new patent- free route."

MR TRAINOR: Hold on, there was no question yet.

A. The answer was yes, that was the point.

MS CASSIDY: And why were you trying to cut down the number of the steps in the Pharmacia Upjohn process?

MR TRAINOR: Objection. Go ahead.

A. It is always general in chemistry and pharmaceutical chemistry favorable to have short processes because long processes are lengthy during the production, expansive and there is no word -- and if it's possible to cut down the number of steps during a certain route, that's progress.

MS CASSIDY: Was this listed as a prequisite because the intent was to develop that shortened synthesis prior to developing new prodrugs?

A. Well, it was a concession to the executives who said that everything was taking too long.

MS CASSIDY: And if you jump down to the section in bold where it says "timelines", at the third point you proposed that the first set of prodrugs would be available November 14th?

A. Yes.

Q. And you expected the first set of prodrugs, you would have greater than three prodrugs; is that correct?

A. No, that was a suggestion.

Q. A suggestion?

A. Yes. The whole material was racemic at that time. That should be noted.

Q. Had you been involved in the development of a new drug product before?

A. Yes, but on completely different indications.

Q. Based on your prior experience was the two month timeframe from when this chemical development plan was prepared to November 14th, when you had the expectation of a first set of prodrugs a fast period of time to prepare that first set of prodrugs for the pharmacology department?

MR TRAINOR: Objection.

A. Yes, it was ambitious.

MS CASSIDY: Was there a particular reason for the ambitious schedule in this project?

MR TRAINOR: Objection.

A. I could only speculate on that. All I can make statements on is chemistry. I don't

know.

MR TRAINOR: How are you doing, okay?

A. Yes, I am okay. Thank you.

MS CASSIDY: Dr Meese, if you need a break feel free to let me know and stop whenever you need.

A. No, no, we can proceed. If you reach a certain stage here.

MS CASSIDY: If you could please turn to PT 02075791.

A. Yes.

Q. In the top right-hand corner -- sorry top left-hand corner?

A. This one?

Q. Yes, that one. In the top left-hand corner the chemical structure depicted is tolterodine, correct?

A. Yes.

Q. And the middle structure depicted where it says "active metabolite", that is referring to 5-HMT; is that correct?

A. Yes, that is true. Still racemic shown on these schemes.

Q. Okay. What are the structural differences between tolterodine and 5-HMT?

MR TRAINOR: Objection.

THE INTERPRETER: He indicated the left groups of both.

A. Methyl group is replaced by hydroxymethyl group.

MS CASSIDY: In 1997 at the start of this project based on the public information that you had discussed with Dr Sparf and the structures of tolterodine and 5-HMT, what conclusions, if any, could you draw about the differences between 5-HMT and tolterodine's chemical properties?

MR TRAINOR: Objection.

A. There was no chemical characterization of these. They weren't available.

MS CASSIDY: And in 1997 did you have any understanding as to the clinical significance of the added benzyl hydroxy group on 5-HMT?

MR TRAINOR: Objection.

A. No.

MS CASSIDY: Okay. And looking at the structures of tolterodine and 5-HMT based on the knowledge that you had in 1997 as you were beginning work on this project, what did you anticipate would be the easiest way to derivatize

5-HMT?

MR TRAINOR: Objection.

A. We had no information concerning the chemical reaction or properties of any of these then. No information at all.

MS CASSIDY: In 1997 had you begun to develop a method of derivatizing 5-HMT yet?

A. I would have to look it up in the lab journals. I just don't know off the top of my head. Not that exactly, no.

Q. Can you turn to PT 02075797?

A. Yes, the first one.

Q. Could you take a minute to review the pages starting on 797 through the end of the document at PT 02075809?

A. Okay. I would like to suggest that we don't spend too much time going into this. These were just mind games, concepts that I was playing around with together with the chemists in the team that I was discussing these options with, but there was no experimental indication for any of these.

Q. So for each of these seven concepts these were the paper chemistry that we were talking about earlier?

A. Yes.

Q. Do you recall whether there was an attempt to reduce any of these seven concepts to actual chemistry at any point?

A. Yes, but at that time we were under extreme time constraints, we didn't have much time for a slow systematic development so we decided to develop this paper chemistry and to look at the potential key steps and to proceed if one of the potential key steps is available and it works, we would focus on that. And as soon as one of the concepts fail you different reasons, and this was actually the case, both of them failed. Then we will skip it and proceed with the most promising route.

MS CASSIDY: We have been going a little bit over an hour and I am about to switch documents, do you want to take a break now?

MR TRAINOR: Yes. Should we break for lunch?

MS LO: Yes, it should be set up outside.

THE VIDEOGRAPHER: Off the record at 12.43. This is the end of Tape Two in the deposition of Dr Claus Meese.

(The Lunch Recess)

THE VIDEOGRAPHER: This is the beginning of Tape Three, Volume One and a continuation in the deposition of Dr Claus Meese. On-the record at 1.33.

MS CASSIDY: Dr Meese, I am going to hand you what has been marked as Exhibit 14 bearing Bates numbers PT 02075813.

(Exhibit 14 marked for identification).

Do you recognize this document, Dr Meese?

A. Probably yes.

Q. Did you draft this document, Dr Meese?

A. Yes.

Q. And this was an update to the chemical development plan from October 3rd, 1997, correct?

A. Yes.

Q. In the update section you noted that the vacations of collaborators in training of an apprentice were postponed and work of academics was extended on weekends and holidays, was this due to the extreme priority of the project that we discussed earlier?

A. Yes, the boss made extreme pressure and the time constraint was irrational.

Q. Were you aware of any concerns that another company was also attempting to develop a prodrug from 5-HMT at the same time?

A. Yes, everybody feared that there were some signs for a Japanese company and another one, but I haven't the data on that, so it was a very competing fear of research, this sector on incontinence. That's true. In the field of incontinence research.

Q. Was there any concern that Pharmacia Upjohn was also pursuing a 5-HMT prodrug?

A. Yes, both companies were mentioned in this context.

Q. And the Pharmacia Upjohn, Pharmacia Upjohn had already patented a method of synthesizing 5-HMT; is that correct?

A. Yes, yes.

Q. And that was the method that you were modifying in order to develop your own synthesis of 5-HMT?

A. That's right, yes.

Q. Once you have 5-HMT, starting from 5-HMT did you expect the synthesis of a prodrug

from 5-HMT to be difficult?

A. We haven't had excellent experience and practice, but my experience from organic chemistry in different projects it was that there will be a way to get a stable derivative which can serve as an intermediate, and once we have an intermediate which is relatively stable the intermediates can mostly modify it in one to two steps to give a new compound. This is possible. Maybe it might not be the ideal new compound but it is new anyway.

Q. In the intermediate that you were referring to would that be the 5-HMT intermediate?

A. Yes.

Q. I am going to hand you a document which will be marked as Exhibit 15 and it bears Bates numbers PT 02075817 through PT 02075849.

(Exhibit 15 marked for identification)

If you can take a look at the first page of the document. This document is titled: The second team meeting NCE incontinence. Dr Meese, for now we are just going to talk about the minutes, if you want to a look at the first page and we will talk about the synthesis in a little bit.

A. I think so, yes. It cannot contain much information. When the project was started on September 28th this is one month later, what should happen during that time, its ...

Q. If I can direct your attention to the section labeled AD 2 on the very first page?

A. Yeah.

Q. The second paragraph states:

"First choice prodrugs will be the acetyl or benzyl derivatives."

Do you recall why these were the first choice prodrug derivatives?

A. This was simply because benzyl compound was starter material, an ester was one step so it was -- we haven't got the time to be ingenious, we took what was on the shelf.

Q. Because an ester was one step.

A. I wouldn't hesitate to call it an ester. If you mind go ahead and call it acetate but I wouldn't have a problem calling it an ester, no.

Q. To clarify, these are first choice prodrugs because the ester would have been a one step derivatization?

MR TRAINOR: Objection.

A. Yes, for chemical reasons it was simple.

MS CASSIDY: And if you turn to page PT 02075819, this is the update two to the chemical development plan. Did you draft this update to the chemical development plan?

A. Yes, and normally there was a copy was forwarded to this pre-team that came together.

Q. And if you go down to where it says "first goal"?

A. Yes.

Q. "The first goal includes making the hydroxy metabolite available for BA (chemically and enzymatically)"?

A. Yes.

Q. What was the difference between the chemical and enzymetic process of obtaining the hydroxy metabolite?

A. The chemical synthesis was not developed at this very early time and the enzymetic was expected to be more rapid. It is a simple incubation that's suitable with microsomes preparations or enzyme, incubation with microsomes, mostly S9 supernatant microsomes were used or liver, whole liver microsomes. They have

a high activity to metabolize suitable drugs, so in a subsequent step it is possible to isolate the metabolism products. However, only a very, very low amount, but mostly it is suitable for the bio-analytics, they don't need much. They just need a few microgram or nanogram, even as a reference for the development of the analytics which was not made at this time point. Chemistry is more efficient but it is more time consuming.

Q. If you turn to the page PT 02075821 and this goes through PT 02075849?

A. Yes.

Q. The concept, the chemical synthesis concepts that are disclosed in these pages, at this stage were these still paper chemistry concepts?

A. Yes, and several weeks later we noted that this doesn't work. This is just a brief comment to give you the information. We got a black tar which it's funny it landed in the west, so that's chemistry. It can happen.

Q. When you say this doesn't work you were referring to the Shorts Pharma concept one?

A. This one, yes. Yes, I have a feeling what the reason might be but it is just a

speculation. I never would repeat that reaction. I will never forget the flask of black syrup that was there in the chromatographic serums gave us hundreds of side products so it was not a very -- but that's typical for paper chemistry. It can be splendid but it can be a disaster.

Q. At the time of the second team meeting, October 24th 1997, you had not performed any of these concepts yet?

A. Well, I don't have these details in hands, but maybe there was a hard when we switched, chemistry which has been published by the Upjohn patents because I have the feeling this really might actually work, it is not ideal but it might work. It is better than erection. It looks theoretically splendid but it doesn't work.

Q. When you were testing the concepts throughout the development of festoterodine did you run the syntheses yourself or did you have someone else perform the actual chemical testing?

A. Both. It depends on the capacity that we have in our labs. If possible we do it in our labs, but in several cases people were all busy and so we have had so-called Contract Research Organisations, external CROs which got

some data and information that we have and we agreed that they work for a given time until they have a result, positive or not. It was to compensate the poor, let me say, amount of co-workers that we had. We didn't have enough people to quickly work on that, so...

Q. Were there any other -- sorry, were you finished?

A. As far as I see now the other proposals didn't work at all so we shouldn't look too much into details of projects or ideas that died very early.

Q. I am going to hand you a document that will be marked as Meese Exhibit 16. It's been previously marked as Sparf Exhibit 13 and bears the Bates number PT 02075853 through PT 02075865.

(Exhibit 16 marked for identification).

Dr Meese, do you recognize this document?

A. Yes, I do recognize it. It's from me. It's the same story, these are ideas which have not been publicly realized or investigated, elucidated. It is bio-analytics, yes, I know that.

MR TRAINOR: Let's wait for a question. Let's wait for her to ask a question, okay?

A. Okay.

MS CASSIDY: If you could turn to the first page that's titled "Third team meeting". And did you attend this meeting, Dr Meese?

A. Obviously I find my name there, yes.

Q. And if you look at AD 2 in bold there is a sentence:

"Post meeting note H. Boekens C. Meese, P. Ney and B. Sparf decided that the acetyl isobutyryl and ethylcarbonate prodrugs of the metabolite should be synthesized first."?

A. That describes some progress.

Q. Do you recall why you selected these three for the synthesis of the first prodrugs?

A. Where does it say that -- oh, down there. I think simply because some initial experiment showed the compounds can be made. It was a very practical reason at that time. We knew we can do work with these compounds and so we decided to take them for the animal studies in order to investigate the metabolic stability. Yes, I think that's it at that time.

Q. When you say "we knew we can do work

with these compounds", did you mean you knew you could synthesize those compounds?

A. Yes.

Q. And you knew that based on your knowledge of chemistry?

A. Yes.

MR TRAINOR: Hold on, let her finish the question.

MS CASSIDY: Based on your knowledge of chemistry leading up to 1997?

MR TRAINOR: Objection.

MS CASSIDY: Let me rephrase that. You knew this based on your knowledge of chemistry available to the public up to 1997?

A. Yes, we already made those compounds in small amounts and if it was possible we can, of course, make a resynthesis to provide even more for the animal studies and additional bio-analytical studies of in-vitro incubations.

MS CASSIDY: So as of December 2nd, 1997 you had already synthesized prodrugs of the metabolite based on the acetyl isobutyryl and ethyl carbonate derivatizations?

MR TRAINOR: Objection.

A. Yes, that's right.

MS CASSIDY: Do you recall when you first synthesized each of those prodrugs?

A. I imagine material was racemic. Material was, the chiral material was obtained later, optical, pure. We are learning a lot.

MS CASSIDY: If you look in AD 2 it states: "Enantiomer separation will be done on the final product."

Were you anticipating that separating the enantiomers would be a difficult process?

A. Yes, sure, because we have tried it before and we failed, so we were frightened that a failure might occur again.

MS CASSIDY: If you look at the line labeled AD 6 it states that: "The first draft of the mock patent distributed and discussed." What is a mock patent?

MR TRAINOR: Objection.

A. At that time I didn't know what it is. And I was told it is a draft of a patent just to write it -- kind of like writing a fictional type patent that can then be amended by others as soon as facts are found.

MS CASSIDY: I am going to hand you a document marked as Meese Exhibit 17 bearing Bates

numbers PT 02075871 through PT 02075889.

(Exhibit 17 marked for identification)

Do you recognize this document, Dr Meese?

A. Yes, yes.

Q. Did you draft any portions of this document?

A. Yes, yes, all of it and some of it was already distributed at earlier pre-project team meetings. This basically served to help people remember what developments had taken place since the beginning.

Q. If you could please turn to PT 02075875?

MR TRAINOR: Just wait for the question. We are just getting you there.

MS CASSIDY: The synthesis that's depicted on this page, is this the Pharmacia Upjohn method that you were modifying?

A. Yes. Essentially yes.

MS CASSIDY: At this time in the synthesis depicted on this page does it already include the Shorts Pharma modifications to the original Pharmacia Upjohn route?

A. Yes.

MR TRAINOR: Objection.

A. Again, paper chemistry ideas.

MS CASSIDY: So as of January 2nd, 1998 you had not begun actual synthesis of this Shorts Pharma modification of the Pharmacia Upjohn route?

MR TRAINOR: Objection.

A. I don't remember exactly, but I have the feeling -- none of the schemes represent a route which is very close to the final process. These are all experimental, descriptions and observations as far as I see now. It is still paper chemistry, and in practice most of them failed. It is frustrating but it is normal in science. It is normal.

MS CASSIDY: Could you please turn to PT 02075881?

A. You are faster.

MR TRAINOR: I am faster? Not always.

A. Thank you.

MS CASSIDY: If you look under the conclusion it states:

"In the given system the phenolic hydroxy group shows a higher reactivity than the benzylic hydroxy group."?

A. Yes.

MS CASSIDY: Was this a surprise that the phenolic hydroxy group was more reactive than the benzylic hydroxy group?

MR TRAINOR: Objection.

A. That was.

MS CASSIDY: And why was that surprising?

MR TRAINOR: Objection. To him?

MS CASSIDY: To you?

A. Yes, yes. The whole system for hydroxy benzyl alcohol, as I mentioned initially, is a very strange, very strange from a point of chemistry, and the benzyl alcohol can react in very strange ways. It depends on the activating function of the phenolic hydroxy group, that is what I initially mentioned as push pull effect. So everything is surprising. It depends on the whole structure of the molecule. Nobody can predict anything here, but we learn from this. It was very useful to make these experiments.

In this here, the scheme, a potential solution to the problems with this remarkable in respect to the enzymetic approach which demonstrated that we can solve the problems which are addressed and observed before by this

approach, but it actually works.

MR TRAINOR: The record should just reflect that the witness is looking at the page ending in 83 for that last bit of testimony.

A. 83, yes. This is a remarkable result because we met the required compounds and this leads to the result of that, what we hoped benzylic modification might be helpful clearly proved that it didn't work. So that's part of the whole invention, even if we have on this way many failures.

MS CASSIDY: Dr Meese, earlier you mentioned a push pull effect with regard to the two hydroxy groups, can you explain what you mean by the push pull effect?

MR TRAINOR: Are you asking him generally or referring to something in this document, just so we can have it?

MS CASSIDY: Generally he mentioned it. I don't believe it was mentioned in the document.

MR TRAINOR: Sorry.

A. I don't have the scheme here. If we look at the four hydroxy benzyl structure, and the benzyl alcohol has 1 OH group, and this OH group is modified, for example, by an acyl group to give

an ester. And the phenolic hydroxy group, the para sub situation loses one proton, then we have phenolate in the para subset, para position to the benzyl position. And the negative charge of the phenolate presses electron density in the benzyl group if there is a good leaving group which is capable of absorbing electron density so we will have a cleavage of this group.

In other cases we have even observed that normal benzyl derivatives can be alkylating agents. It is a species where a positive charge is at a common better. And this species is reactive and in many cases forms carbon, carbon ponds, what is not so easy in our case. So it became clearer and clearer with these experiments. Yes, I think we have that. So it was a frustrating presentation of many experiments that did not work.

With the expectation of the first synthesis of benzyl esters in this system, which was mentioned before are not stable, and the physiological conditions rapidly cleaved, and we have from the Bio-analytical Department extensive data on the cleavage rate and that's also NPH dependence, but this is all not useful for the

development of pharmaceuticals with only findings that demonstrate the limitations of certain routes. Okay. That is what we can say to this paper.

MS CASSIDY: Are you saying that you observed that the phenolic OH group was more reactive than the benzylic OH group?

MR TRAINOR: Objection. Can you translate that, please?

A. Yes, in respect to the ester formation under the usual esterification conditions.

MS CASSIDY: Can you turn to 02075855, and under the comment it is stated:

"It is obvious to try to take full advantage of the higher reactivity of the phenolic hydroxy group of the hydroxy metabolite."?

MR TRAINOR: Could you translate that, please?

MS CASSIDY: And when you say it is obvious to take full advantage of the higher reactivity was that based off of your knowledge, your chemical knowledge prior to 1997?

MR TRAINOR: Objection.

A. It is hard to say. I cannot

actually really not remember. These observations came up time and again and all the details of our work, and they were observed many times throughout the course of process. I can't put a date to it really.

MS CASSIDY: Can you please turn to PT 02075889?

A. Thank you.

MS CASSIDY: Under the conclusion it states:

"The reaction conditions are well documented in the chemical literature."

Were the reaction conditions for converting to prodrugs -- strike that. Were the reaction conditions for all of the derivation to prodrugs that you were attempting well documented in the chemical literature?

MR TRAINOR: Objection.

A. Yes. This page rules out extensive literature research worldwide, and I found a number of papers which dealt with the strange behavior of the structure for hydroxy benzyl alcohol, and from one of the papers, I remember it was a Japanese paper, showed that silylation S-I-L-Y-L might be Regio selective and the

cleavage of the silyl groups might be also chemo selective. It depends on the nature of the silyl group and the reagents used for the cleavage.

And again it could be differentiated in the system for hydroxy benzyl alcohol is the newly introduced silyl group on the phenolic side or the benzylic side. It looked brilliant but as we had a closer look we recognized that this has only academic interest, and I doubted that we will never can develop an industrial process on the basis of the different selectivities. So it is typical for this kind of chemistry, you find fascinating alternatives and then we investigate it, the practice, the reality that we had to recognize that this was not --

THE INTERPRETER: It wasn't the greatest idea of all times.

A. Fine, fine.

MS CASSIDY: I am going to hand you what will be marked as Exhibit 18, a document bearing Bates numbers PT 02075893 through PT 02075903.

(Exhibit 18 marked for identification)

Dr Meese, do you recognize this document?

A. Yes. Yes.

MS CASSIDY: And did you draft this document?

A. Yes. It is a very early report as you see. At the beginning of 1998 this was the attempt to inform the pre-project team of the status. Pre-project team.

MR TRAINOR: Just wait for the question.

MS CASSIDY: And at this time 17 prodrugs had been prepared; is that correct?

A. We have a table here. Yes. As far as I remember all compounds which have been prepared were racemic in structure. Yes.

Q. And if you look at page PT 02075895?

A. Exactly, that is the table which gives the status, yes of August '98, yes. Yes.

Q. And if you look at SPM number 7475, it's about six rows down?

A. Yes.

Q. It has a structure of HO-/-IBUT correct?

A. Exactly. This is racemic festoterodine based. 7475, yes, that's right. Yes. Yes.

Q. I am going to hand you a document which will be marked as Exhibit 19 which bears

Bates numbers PT 02075909.

(Exhibit 19 marked for identification)

A. Thank you.

MR TRAINOR: Since she's looking for something can we take a short break?

MS CASSIDY: Yes.

THE VIDEOGRAPHER: Going off-the-record at 2.36.

(Short Recess)

THE VIDEOGRAPHER: Back on the record at 2.57.

MS CASSIDY: Dr Meese, I am also going to hand you a document that is a translation of Exhibit 19. You should note for the record that this translation states that it is a translation of Bates number PT 02050579, however that is a typo and it should state that it is a translation of PT 02075909.

(Exhibit 20 marked for identification)

MR TRAINOR: For the record Exhibit 20 is the translation of Exhibit 19.

MS CASSIDY: Yes, that is correct.

A. Thank you.

MS CASSIDY: Dr Meese, if you would like to direct your attention to Exhibit 19, that is

the German version of Exhibit 20. Do you recognize this document?

A. Yes, I do.

Q. Is this your handwriting?

A. Yes, it is.

Q. And if you look there is a line through the middle of the page, if you look below that line on the left-hand side there is a table of five compounds, do you see that?

A. Yes.

Q. And if you look at compound Number 5?

A. Yes.

Q. This is the HO/IBUT formulation?

A. Exactly.

Q. Is this formulation the racemic of the festoterodine drug?

A. Yes, if it comes from February 1998 it must be racemic.

Q. Okay. There is an arrow next to it?

A. Yes.

Q. And underneath that a statement that it says:

"Excellent +++ to moderate ++ liberation of HYDR.MET form prodrug."

Is this referencing the fact that there was -- that this metabolizes into the 5-HMT?

MR TRAINOR: Objection.

A. Exactly. The liberation or the formation of the free HMT metabolite, yes, that's right, metabolite. It is very early data, yes, on a qualitative basis.

MS CASSIDY: Dr Meese, I am going to hand you a document which will be marked as Meese Exhibit 21 bearing Bates numbers PT 02075907.

(Exhibit 21 marked for identification)

Do you recognize this document?

A. Yes.

Q. Did you draft this document?

A. Yes.

Q. Under update five it states that an in-vitro assay with human liver homogenate was conducted?

A. Yes, that's right.

Q. Were you involved in the connection of this assay?

MR TRAINOR: Objection.

A. That was with the exception of the preparation of the starting materials, the prodrugs I was not involved. It was of the

Bio-analytical Department, Hilmar Boekens. That's his name there. He got a copy, of course.

MR TRAINOR: I think that is B-O-E-K-E-N-S.

MS CASSIDY: Underneath that it also states: "Efficient liberation of hydroxy metabolite."

A. Yes.

MS CASSIDY: And lists three compounds including HO/OI-BUT?

A. Yes.

MS CASSIDY: HO/OI-BUT that is referring to the racemate of the festoterodine; is that correct?

A. Yes, that is correct.

MS CASSIDY: And what did knowing that there was efficient liberation of the hydroxy metabolite from these compound tell you?

MR TRAINOR: Objection. Can you translate that question, please?

A. As I mentioned before these are qualitative data. Later on we got more precise qualitative data, but efficient means that significant amounts of the hydroxy metabolite were observed in the HPLC chromatograms after

incubation of the racemic prodrugs which are shown here. So the concept, this was very important for the Board. We showed them, we offered a compound which is a potential prodrug and we showed that it is a prodrug and it is cleaved, because again in this field we have had just this one sentence, a strange bias. In German this is a dogma. That by bulky phenolic ester are not, or are very difficult cleaved by human esterases or lipases. This was almost a fatal bias because the CEO said if the prodrugs are not cleaved the whole project will die, or will be killed by him personally.

So we could demonstrate that even bulky, that means very, very big constitutes, B-U-L-K-Y constitutes they hinder the esterases and lipase to cleave phenolic esters. That is true but it is not a disaster as should further investigations and precise qualitative data will follow.

Q. Do you recognize the handwriting that's on this document?

A. Yes.

Q. Is that your handwriting?

A. That's mine, yes.

Q. I am going to hand you what's been marked as Exhibit 22, which is a translation of

the handwriting in Exhibit 21.

(Exhibit 22 marked for identification)

MR TRAINOR: You keep this because you read the German.

A. Okay. If you want me to compare this.

MR TRAINOR: Let's wait for a question.

MS CASSIDY: In the handwriting that's a little right underneath "next challenge" which starts "patent concept".

MR TRAINOR: For the record this is the handwriting that is more to the right of the page. Here. This is your writing, this is German. Just don't worry about that.

MS CASSIDY: And underneath "patent concept" there is a dash and it says:

"HYDR.METAV is better."

A. That is an attempt to quantitate the qualitative data which was shown on the meetings by Dr Boekens. That means the word good cleavage is around 10%. That means 10% of the prodrug are observed in the HPC chromatograms, at least our very early and preliminary data.

MS CASSIDY: And if you recall when we were talking about your August 28th, 1997 meeting,

we discussed the bioavailability of the hydroxy metabolite as being 10%, and if we need to refer back to that Exhibit we can?

A. Yes, I remember that.

MS CASSIDY: Was that why -- in view of that was the bioavailability aim from the prodrug aimed to be higher than 10% in order to improve over the hydroxy metabolite that was already known?

MR TRAINOR: Objection.

A. I think this is different. This means the formation of the hydroxy metabolite after the administration of the racemic prodrugs, that is what this data means, and the 10% which appeared there is a completely different 10%, and I mean administration of the hydroxy metabolite that is the 5-hydroxymethyl tolterodine to any animal, and I don't have any more data, so these are information that came up on some of the congresses during posters and discussions, and these data are completely different 10%.

That means administration of the metabolite shows only small amounts of a metabolite in any animal. I don't even know what kind of animal. I don't want to speculate here.

But these are data under good analytical practice generated by the Bio-analytical Department, qualitive data, but it is a good basis to proceed.

Q. Okay. So the BA insufficient 10%, the 10% was data that was generated off of the prodrugs themselves?

A. Exactly.

Q. I am going to hand you a document which will be marked as Meese Exhibit 23, bearing Bates numbers PT 02075945 through PT 02075947.

(Exhibit 23 marked for identification)

A. Thanks.

Q. Dr Meese, do you recognize this document?

A. Yes, I know that. Yes, it comes from Peter Ney.

Q. And this document is the June 25th, 1998 team meeting minutes, correct?

A. Yes.

Q. Did you attend this meeting?

A. Yes.

Q. If you look at the line AD 1 you state that:

"It is obvious that the availability of pure enantiomers of the prodrugs is critical."?

MR TRAINOR: Can you just give me the line number?

MS CASSIDY: The second line under AD 1.

A. Yes, I see. Yes.

Q. How did you determine that the availability of the pure enantiomers of the prodrugs would be critical?

A. Simply in drug development most regulatory institutions such as the FDA or EMEA expect that the individual enantiomers of a drug which is under development have to be elucidated and given and presented. It is a state of the art that the enantiomers have to be available for all in-vitro and later for the in-vivo studies, so we have to have those enantiomers in substantial amounts, especially if we go in human studies later.

Q. If you turn to the next page, PT 02075947. Do you recognize this document?

A. Yes.

Q. Did you draft this update to the chemical development plan?

A. Yes, yes, I wrote that.

Q. And if you look at the third major point where it says "synthesis"?

A. Yes.

Q. And you have two option, the P&U route and underneath that it says "alternatives"?

A. Yes.

Q. Does this indicate that as of June 25th, 1998 when this chemical development plan was updated you were still developing the chemical synthesis route to 5-HMT?

A. Yes, in parallel.

Q. Since you were developing in parallel were you purchasing 5-HMTl to use as a starting point for the prodrugs synthesis?

MR TRAINOR: Objection.

A. I have to think it over, it's a long time ago. I remember we developed some activities to involve our own company in France, a company Siloc SR, to embark on a programme to support us as with raw materials. Then we contacted Dynamite Nobel, which was located very close to Schwarz Pharma, so we had an easy communication.

MS CASSIDY: Dr Meese, I just want to clarify for the record, first when you said yes, you were working in parallel, when you said in parallel were you referring to the two synthesis routes, or to the synthesis route and the prodrug

development?

MR TRAINOR: Objection. There is more than two routes referenced in this paper.

A. The metabolite or intermediate that was our primary goal. That is what we wanted to have, the hydroxymethyl. We got the complete documentation and started the work.

MS CASSIDY: And when you were working on the synthesis route you were working on the P&U route and the Heck-Cuprate route, H-E-C-K C-U-P-R-A-T-E?

A. Yes.

Q. And Reformatski, R-E-F-O-R-M-A-T-S-K-I, in parallel?

A. Yes, the most advanced route for the production on a larger scale was with the P&U route, Pharmacia Upjohn. Yes. And the other variance Heck-Cuprate route was on a laboratory scale at the Max Planck Institute in Mullheim. And we have had the chemistry under control, but what we were -- where we were without any success was the separation of the enantiomers corresponding to Pharmacia Upjohn patents. They didn't work. In order to get -- do I have questions to this point?

In order to get the enantiomers even in small amounts we contacted, for example, the University of the Munster. They have a chiral -- they have chiralstation there in phases, columns that are capable of separating the enantiomers, however on a small scale.

Q. Dr Meese, can you please turn back to Exhibit 19 for a minute?

A. Yes.

Q. In Exhibit 19 underneath the line on the left-hand side there are the five prodrugs that we discussed?

A. Yes.

Q. That had been tested for their metabolic activity?

A. Yes.

Q. What was the source of the starting material to synthesize the prodrugs that were used in the experiment summarized in this table?

MR TRAINOR: Objection.

A. You mean the chiralty?

MS CASSIDY: No, what was the source of the starting material to synthesize the prodrug?

A. A precise autwat would be if I have the laboratory journal and look at February 17th,

but I think it is perhaps in our lab. At that time we haven't had any significant scaleout.

MS CASSIDY: So as of February 17th, you had not synthesized the 5-HMT metabolite using one of the syntheses that you were developing in-house; is that correct?

MR TRAINOR: Objection. Can you retranslate that question back, please? It is syntheses.

THE INTERPRETER: That is why I am having problems reading this, sorry.

A. We have made it but the racemic material. No, no, we have racemic material made February because we file out patent, and the first patent in May 1998 in May, and we showed a number of derivatives and a number of biological data in this year, in this first priority patent, so I have to look, of course, at the laboratory journal but I think February was the time where we have had the metabolite in the racemic form. Yes. You can see it here in this handwritten text in the middle here. What we are doing right now di-hydroxy, the metabolite and the synthesis of a substance. Di-hydroxy is a compound we are talking about, yes. It was made in-house, yes.

MS CASSIDY: For the record, Dr Meese, you are looking at Exhibit?

A. 19.

Q. Thank you?

A. The upper part. In the lower part beyond the line there already shows some of the compounds that can only be made if you make the metabolite, and I am convinced we made it. The compound, chiral compounds were only used, I think it was in 1999.

Q. Dr Meese, I am going to hand you a document marked as Exhibit 24, bearing Bates numbers PT 02075955 through PT 02075967.

(Exhibit 24 marked for identification)

A. Yes.

Q. Do you recognize this document?

A. Yes.

Q. And this document are the team meeting minutes from August 10th, 1998, correct?

A. Yes, right.

Q. And did you attend this meeting?

A. Yes.

Q. If you would look at the third point AD 3, it states that:

"After intense discussions it was

decided to move forward the OH-/-OCOR compounds?

A. Yes.

Q. Were you involved with this decision?

A. No. It was some other members of the team.

Q. Do you know which members of the team were involved in that decision?

A. No, I could only speculate and I don't want to do that. I was not involved in the decision.

Q. The compounds of the general structure OH-/-OCOR that would include the festoterodine compounds; is that correct?

MR TRAINOR: Objection.

A. Yes, I have not written this text because that is chemically not precise what you find under AD 3, but definitely festoterodine, yes. And I mean freebase.

MS CASSIDY: And do you see the line: "It is expected that further modifications of the ester-moiety may lead to bioavailability of about 50%."?

MR TRAINOR: Can you translate that, please?

A. Yes, I don't know who made the statement but it was not me, but I presume by our Analytical Department or Mr Peter Ney. This is a statement, again not from me.

MS CASSIDY: Were you involved in discussions of what further modifications of the ester-moiety may be pursued at the time?

MR TRAINOR: Can you translate that?

A. Yes, of course. Also it was exactly the time I was on holidays with my family, so I was absent for some weeks but it is true, we were currently in discussion on this important issue, yes.

MS CASSIDY: And do you recall what types of modifications you were discussing at that time?

A. No, we have had some examples already in the first patent on the racemic skeleton. I was more interested at that time to get the enantiomers available in sufficient amounts because that was the urgent, very urgent exactly for the development.

Q. If you could turn the page to PT 02075959?

A. Okay, then I was back from holidays.

Q. Do you recognize this chemical plan update?

A. Yes.

Q. And did you draft this?

A. This, exactly this paper here?

Q. Yes, I will clarify. Did you draft this --

A. 959, yes, it is from me. Yes. August 10th, yes, that's from me.

Q. Thank you. And if you look at the very last sentence on the page above the date and your name starting, stating:

"Intrinsic instability of a phenolic monoester has been detected after four months at room temperature."?

A. Yes.

Q. "(Interconversion to di-ester and hydroxy metabolite)."?

A. Yes.

Q. Which phenolic monoesters were experiencing --

A. I can see which one.

MR TRAINOR: Let's just listen to the question that she asks. Did you finish the question?

MS CASSIDY: No, I will start over.
MR TRAINOR: Thank you.
MS CASSIDY: Which phenolic monoesters were found to have intrinsic instability?
MR TRAINOR: Objection.
A. I don't have any data here. This data from the Bio-analytic Department, which I wish I was informed after, as I told you I was on my holidays, I didn't know which were -- but whatever this phenolic monoesters at that time were all freebases and no salts. A very, very great difference. (Speaking in German).
MS CASSIDY: Why -- does it make a difference that these were freebases versus salt formations of the compounds?
MR TRAINOR: Objection.
A. Because it is expected that salt formation is capable of stabilizing a compound, and we have a compound which on the one side is an ester and on the other side is still an alcohol, and it is known that interconversions can occur, in particular if these are oils in pure compound and over such a long time. I think I wouldn't say this is a restriction to the further development. It was just an observation which some people make

in the company.

MS CASSIDY: I am going to hand you what will be marked as Meese Exhibit 25, a document bearing Bates numbers PT 01932087 through PT 01932089.

(Exhibit 25 marked for identification)

Dr Meese, have you seen this document before?

A. Yes, I have. Yes.

Q. And this is the team meeting notes from October 1st 1998; is that correct?

A. October 1st, yes, that's right.

Q. And did you attend this meeting?

A. Yes, I did.

Q. Under the section AD 1 on the first line states:

"Improvements in the synthesis i.e., reduction of the steps of the P&U route have been achieved."?

A. Yes.

Q. And how long had you been working on -- strike that. You had been working on reducing the number of steps in the P&U route since the beginning of the incontinence project; is that correct?

A. Yes, yes.

Q. So it took you a little over a year to finalize that synthesis?

A. Yes, exactly. It was one of the biggest problems which came up.

Q. And if you look down at the second full paragraph from the bottom of the page stating:

"The following substances will be studied in receptor binging assays."

B-I-N-G-I-N-G?

A. Yes.

Q. Probably binding is what it meant to say. Then it lists five substances, do you see that?

A. Yes.

Q. How were these five substances selected?

A. I don't know, that was a decision of some of the people here Ney, Arth, Boekens. I was not involved in this section.

Q. Do you know whether Dr Sparf was involved in the selection of those five substances?

A. I see his name here, he seems to be

he was a participant. I don't know.

Q. And we are running short on video time so if you want to take a short break right now?

A. Yes, okay.

THE VIDEOGRAPHER: Going off-the-record at 3.48. This is the end of Tape Three, Volume One of Dr Meese.

(Short Recess).

THE VIDEOGRAPHER: This is the beginning of Tape Four, Volume One and a continuation in the deposition of Dr Claus Meese. On-the record at 4.07.

MS CASSIDY: Dr Meese, I am going to hand you what will be marked as Meese Exhibit 26, it is a copy of European application number 0957073A1.

(Exhibit 26 marked for identification)

A. Thank you.

Q. Dr Meese, do you recognize this document?

A. Yes, it is.

Q. And I can represent to you that this is the European priority application for the 980 patent that was filed on May 12th, 1998?

A. Yes.

Q. And as of May 12th, 1998 you had not developed an enantiomeric specific synthesis of 5-HMT; is that correct?

MR TRAINOR: Objection.

A. That is correct.

MS CASSIDY: And as of May 12th, 1998 you also had not developed an enantiomeric specific synthesis of any prodrugs of 5-HMT; is that correct?

MR TRAINOR: Objection.

A. That is correct.

MS CASSIDY: And if you look at Table 1 on the first page of this European application, the prodrugs that are depicted in the table, each of those were the racemic versions of the prodrugs; is that correct?

A. That is correct.

Q. And if you could look at paragraph 58, which is on page 19?

A. Yes.

Q. In paragraph 58 each of the prodrugs depicted in that paragraph are examples of racemic prodrugs; is that correct?

A. Yes.

MR TRAINOR: Objection.

A. Yes, it is right.

MS CASSIDY: Dr Meese, could a chemist following the instructions and procedures in this European application make an enantiomerically pure version of festoterodine?

MR TRAINOR: Objection. Can you please translate that, and pay careful attention, Dr Meese.

A. No.

MR TRAINOR: I objected, but you can answer if you could know that answer.

A. There is no description given of the chiral material given here.

MS CASSIDY: Dr Meese, I am going to hand you what will be marked as Meese Exhibit 27, which is a document bearing Bates numbers PT 01931871 through PT 01931883.

(Exhibit 27 marked for identification)

Dr Meese, do you recognize this document to be the January 29th, 1999 team meetings for the NCE incontinence team?

A. I think so, yes.

Q. And did you attend this meeting?

A. Yes, I did. Yes.

Q. If you look at bullet point four, milestone decision, it states:

"After intense discussions it was decided to move forward with the following prodrugs."

And lists four prodrugs?

A. Yes.

Q. "Including HO/OIBUT (R)."?

A. Yes.

Q. And were you involved with the decision to move forward with those four prodrugs?

A. No, I can't remember.

Q. Do you recall who else may have been involved in this decision?

MR TRAINOR: Objection.

A. I can only speculate.

MS CASSIDY: And if you could please turn to page PT 01931875?

A. Yes, yes.

Q. And do you recognize this to be the eighth update to the chemical development plan dated January 29th, 1999?

A. Yes.

Q. And did you draft this document?

A. Yes, I am.

Q. And if you could please turn to page PT 01931879, this document states that it is the present process as of January 29th, 1999 of the SP modification of the P&U route?

A. Yes.

Q. And I am going to ask you now to get Exhibit 1, the 680 patent out -- sorry, 650. And in Exhibit 1 if you could please turn to figure one?

A. Yes.

Q. And if you look at figure one can you please compare that to the process on -- in Exhibit 27, and can you please point out which, if any, of the steps in Exhibit 27 correspond to step 3 in figure one of the 650 patent?

MR TRAINOR: Little (iii) or?

MS CASSIDY: Non (iii), the bolded three, that first compound.

MR TRAINOR: At the top?

MS CASSIDY: At the top, yes.

A. Is that Roman, I don't understand which with three.

MR TRAINOR: Can you retranslate the original question with -- that includes step three just so he understands.

A. Okay, so this is Exhibit 27.

MR TRAINOR: This is 27 and this is 1.

A. Exactly.

MR TRAINOR: And I object to the question.

A. These are all the same reactions.

THE INTERPRETER: So Exhibit 27.

A. Compound 10 to 11 corresponds to compound 4 to compound 6.

MS CASSIDY: So it is your understanding that compound 4 in the 650 patent corresponds to compound 10 in Exhibit 27?

A. Could you repeat that, please?

Q. So does compound 4 in the 650 patent correspond to compound 10 in Exhibit 27?

A. That's right.

Q. And compound 6 in the 650 patent corresponds to compound 11 in Exhibit 27?

A. That's right.

Q. And does compound 3 in the 650 patent correspond to compound 9 on PT 01931879?

A. Yes, that's right.

Q. And to your knowledge is the SP modification of the P&U route the method of synthesis that was used by Schwarz for the

synthesis of the 5-HMT metabolite throughout the remainder of the festoterodine project?

MR TRAINOR: Objection. Can I just get a clarification, so this is the last Exhibit?

MS CASSIDY: 27.

MR TRAINOR: Your question is whether the synthesis route on the page ending 879 in Exhibit 27 is the process used after January 29th, 1999?

MS CASSIDY: Yes.

MR TRAINOR: Maybe you could read that?

A. I really would have to check that up, it's been so many years, 16 years already.

MS CASSIDY: I am going to hand you a document.

A. Well, this --

MR TRAINOR: Hold on, there is no question pending.

MS CASSIDY: You can finish what you were saying?

A. Well, there is an underlying difference which is significant. For example, Exhibit 27 is a different kind of resolution in contrast to the P&U process, and Exhibit 27 the resolution is done from step two to step three.

MS CASSIDY: I am going to hand you what will be marked as Exhibit 28, a document bearing Bates numbers PT 01932319.

(Exhibit 28 marked for identification)

Dr Meese, do you recognize this to be the ninth update to the chemical development plan dated February 24th, 1999?

A. Yes.

Q. And did you draft this update?

A. Yes.

Q. If you look at the section labeled "prodrugs", the statement that:

"Chiral hydrochloride salts are available on a gram scale for toxicology, bioavailability S9 incubation stability."

Do you recall whether hydrochloride salts were the first salts that you used for the prodrugs?

MR TRAINOR: Objection.

A. I must look at documents. I actually don't know. I can only speculate but I don't like speculations.

MS CASSIDY: I am going to hand you what will be marked as Exhibit 29, which bears Bates numbers PT 01932091 through 01932093.

(Exhibit 29 marked for identification)

Do you recognize these to be the NCE incontinence meeting minutes from May 28th, 1999?

A. Yes.

Q. And did you attend this meeting?

A. Yes.

Q. And do you recall at this meeting presenting a route of synthesis?

A. Should be this one. I think it is this one here, is it, PT 2093?

Q. So you are looking at the synthesis on PT 01932093; is that correct?

A. Yes, that is correct.

Q. And the synthesis is the SP modification of the P&U route, this time dated May 28th, 1999; is that correct?

A. Yes.

Q. And to your recollection does that mean that this was the current process that Schwarz Pharma was pursuing with regards to synthesis of the enantiomeric prodrugs?

A. Umm hmm.

MR TRAINOR: Objection.

A. Yes.

MS CASSIDY: If you could turn back to

PT 01932091?

A. Yes.

Q. Do you recognize the handwriting on this document?

A. Yes.

Q. Is that your handwriting?

A. Yes, it is.

Q. And in this you are referring in this handwritten section, you are referring to SPM 8228, the statement that X is chloride; is that correct?

A. Yes.

Q. Does that mean that this was the hydrochloride salt that you were looking at?

A. Yes.

Q. And you state that this salt is amorph us and hagioscopic; is that correct?

A. It is not precise. Once a salt is formed it is highly crystalline, but if it is exposed to moisture, traces of water, it is hagioscopic, yes. Let me say it gives a syrup.

Q. And so you proposed looking at roughly 20 other salts to improve the physiochemical properties; is that correct?

A. Yes.

Q. And did you have specific salts in mind already when you made this proposal?

A. No, not yet. That was on top of our salt screening programme at that time.

Q. Were you involved in the salt screening programme?

A. Yes.

Q. What was your role?

A. First of all I gave the co-workers the description for the initial experiments on a lab scale such as solvent concentrations, solvent mixtures in order to get precipitations matching time and temperatures.

Q. Anything else?

A. I involved a number of external CROs, among them the University of Wuppertal, Germany, and we needed simply manpower because it's laborious to make all those experiments.

Q. Anything else?

A. And there was a brief involvement of the University of Groningen in the Netherlands, Holland. That is also in order to make some experiments. And I told them which acids should be tested first, so the necessities or which assay should be used and with what are the solvents, and

some of the reaction conditions also were given to the partners. They started the work for us.

Q. And which acids did you think should be tested first?

A. A large variety of inorganic acids, but also organic acids such as citric acid or tartaric risk acid, of course mendelic acid. And I remember I have to look at more than 100 acids.

Q. Right. I am going to hand you a document that will be marked as Meese Exhibit 30, bearing Bates numbers PT 01718486 through PT 01718498.

(Exhibit 30 marked for identification)

A. Thank you.

Q. Dr Meese, do you understand these to be the minutes of the CMC sub team taken on October 8th, 1999?

A. Umm hmm.

Q. And did you attend this meeting?

A. Yes, I did.

Q. What does CMC sub team mean?

A. That means that the project was pretty far developed and this sub team takes care primarily of chemistry. Yes, it seems CMC is clear.

Q. If you could turn to page PT 01718494?

MR TRAINOR: 495?

MS CASSIDY: 494.

A. Yes, okay.

MS CASSIDY: And is it your understanding that as of September 30th, 1999 this SP modification of the P&U route was the current synthesis route that Shorts Pharma was following in the synthesis of their prodrugs salt?

A. Yes, absolutely.

MR TRAINOR: Objection.

A. Because it has significant advantages over all alternatives. This was the way we made the product and enantiomers.

MS CASSIDY: Dr Meese, I am going to hand you a document that will be marked as Meese Exhibit 31, a document which bears Bates numbers PT 01932079 through PT 01932081.

(Exhibit 31 marked for identification)

Dr Meese, have you seen this document before?

A. I must have a look at that. I can't remember and I don't find my name on the paper, not as addressee or in a footnote. It looks like

a technical report from Mr -- Dr Arth.

Q. If you can look under section 2 do you see where it begins:

"By August 31st 1999 stable crystals of SPM 8224 hydrogen fumarate named SPM 8272 was available for the first time with a melting point of about 84 degrees Celsius."

A. Yes, that's right.

Q. And do you recall whether stable crystals of SPM 8224 had been formed -- strike that.

Do you recall whether prior to August 31st, 1999 any stable salt forms of festoterodine had been formed?

MR TRAINOR: Right now the question is just any stable salt forms?

MS CASSIDY: Any stable salt forms?

A. Yes, we made bromide and hydrochloride, monohydrate, at least those two besides the hydrogen fumarate here. This is all mentioned in the patent to stable salts.

MS CASSIDY: Earlier we discussed a salt screening programme, why is it necessary to conduct a salt screening programme?

MR TRAINOR: Objection.

A. For chemical process and the pharmaceutical operation it is absolutely necessary to have stable salts which are chemically and thermally stable on the shelf and in the formulation of the drug product, and that's the compound is not allowed to be hydroscopic. It must be crystalline, highly crystalline. That is really a must. Therefore, we made much efforts to have success here in this field.

Q. Dr Meese, I am going to hand you an Exhibit marked as Meese Exhibit 32. This document bears Bates numbers PT 01931905 through PT 01931917.

(Exhibit 32 marked for identification)

A. Thank you.

Q. Dr Meese, do you recognize these as the January 5th, 2000 meetings of the project team meeting for NCE incontinence?

A. It is 2000. Yes.

Q. And did you attend this meeting?

A. Yes, I did.

Q. And if you could please turn to page PT 01931909?

A. This one, yes. Okay.

Q. This attachment is titled: CMC

update January 5th, 2000. Did you participate in the drafting of this document?

A. Yes. Yes.

Q. And at point bullet point 4 it states that:

"Alternative synthesis route from step 5 to step 6 via amid showed reduced amount of impurities by increasing total yield."

Do you recall whether this alternative synthesis route was an alternative within the SP modification to the P&U route?

MR TRAINOR: Objection.

A. No, the Isotyric route is not shown here in this attachment. I am irritated that the synthetic scheme, the complete synthetic scheme with the numbers which are mentioned here step 5 to 6 is not shown. That is unusual. Normally I attach the chemistry. I have problems to remember this actually paper because I am irritated that improvement steps should be demonstrated and documented. Yes, of course, we have it in Monheim in the archives.

MS CASSIDY: I am going to hand you a document which will be Meese Exhibit 33 bearing Bates numbers PT 01717920.

(Exhibit 33 marked for identification)

Dr Meese, do you see your name in the to line of this e-mail?

A. Yes, I see my name.

Q. And this e-mail was sent to you from Andrea Schutz; is that correct?

A. That's right.

Q. What was Andrea Schutz's role in the development of festoterodine?

A. The -- once the final project, meeter or manager, after the pre-project has been finished the boss decided that this project will be a company project, as mentioned before, and as of that time she was the project leader and no longer Peter Ney stopped his activities on this field, or Christoph Arth, he was the intermediate manager for the sub team.

Q. If you look at the sentence beginning in the fourth line from the bottom, it states:

"This current route of synthesis is working well, therefore Claus Meese will leave the project team from now on."

What was your role in the festoterodine project after this e-mail dated June 8th, 2001?

A. As internal political reasons. (speaking to counsel).

MR TRAINOR: If you understand and know. The question is what was your role after, so can you just answer that question?

A. The question was that we have some organizational changes at that time. Linda Hakes came to Schwarz Pharma and was responsible for the preclinical development and it was decided to involve our Company in Ireland much more strongly than before. At my role to answer on your specific question, should be an internal act as internal consultant for Schwarz Pharma and the project. There were several personnel changes in the following weeks and months.

Q. So -- sorry, were you finished? So after this date did your day-to-day involvement with the festoterodine project decrease?

A. Yes, that's true, and part of my work was done by another man, and I can't see him here. No, he is just missing. The rest of the people who work in the project team of festoterodine.

Q. Do you recall who that was?

A. Pardon?

Q. Do you recall what his name was?

A. Yes, yes, Joerg Hamann. Dr Joerg Hamann, H-A-M-A-N-N.

MS CASSIDY: I think we have been going about an hour and I am at a good breaking point if you want to take a short break?

MR TRAINOR: Okay.

MS CASSIDY: Or break for the night.

THE VIDEOGRAPHER: Off-the-record at 5.08.

(Short Recess)

THE VIDEOGRAPHER: Back on the record at 5.19.

MS CASSIDY: We will now break for the night and reconvene tomorrow morning.

THE VIDEOGRAPHER: This is the end of Tape Four and concludes Tape Four, Volume One of Dr Claus Meese's deposition.

------ooo------

CERTIFICATE OF DEPONENT

I, Claus Meese, hereby certify that I have read the foregoing pages of my deposition of testimony taken in these proceedings on Tuesday, 20th January 2015 and, with the exception of the changes listed on the next page and/or corrections, if any, find them to be a true and accurate transcription thereof.

Signed: .....

Name: Claus Meese

CERTIFICATE OF COURT REPORTER

I, Kay Hendrick, an Accredited Court Reporter, hereby certify that the testimony of the witness, Claus Meese, in the foregoing transcript taken on Tuesday, 20th January, 2015 was recorded by me in machine shorthand and was thereafter transcribed by me; and that the foregoing transcript is a true and accurate verbatim record of the said testimony.

I further certify that I am not a relative, employee, counsel or financially involved with any of the parties to the within cause, nor am I an employee or relative of any counsel for the parties, nor am I in any way interested in the outcome of the within cause.

Signed: .....
KAY HENDRICK
Dated: .....

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

PFIZER INC. and UCB PHARMA GMBH
Plaintiffs

vs.
C.V. No. 13-1110(GMS)

ALKEM LABORATORIES LTD., CONSOLIDATED
Et al.
Defendants.

CONFIDENTIAL ATTORNEYS EYES ONLY

Videotaped Deposition of Claus Meese

Vol 2

Taken at the offices of:

McDermott Will & Emery
Avenue des Nerviens 9-31
1040 Brussels

Wednesday, 21st January 2015

At 9.36 a.m.

A P P E A R A N C E S :

ON BEHALF OF PLAINTIFFS and THE WITNESS:

WHITE & CASE LLP
1155 Avenue of the Americas
New York, New York 10036-2787
212.819.8255
JAMES S. TRAINOR, ESQ.
jtrainor@whitecase.com
JURGEN HASSA
jurgen.hassa@ucb.com

ON BEHALF OF DEFENDANT, APOTEX, INC.:

RAKOCZY MOLINO MAZZOCHI SIWIK LLP
Six West Hubbard Street
Suite 500
Chicago, Illinois 60654
312.527.2157
BY PHONE: KEVIN BURKE

ON BEHALF OF DEFENDANTS, SANDOZ INC.

McDERMOTT WILL & EMERY
227 West Monroe Street
Chicago, Illinois 60606-5096
312.984.5810
slo@mwe.com
WAN-SHON LO

ON BEHALF OF DEFENDANTS, WOCKHARDT BIO AG and WOCKHARDT USA, LLC:

KNOBBE, MARTENS, OLSON & BEAR, LLP
2040 Main Street
14th Floor
Irvine, California 92614
949.760.0404
KAREN CASSIDY, ESQ.
karen.cassidy@knobbe.com

Also Present:

Kay Hendrick - Court Reporter

Simon Rutson - Videographer

Andrea Boyer - Interpreter

I N X E X

E X H I B I T S

Wednesday, 21st January 2015

THE VIDEOGRAPHER: This is the beginning of Tape One, Volume 2 and a continuation in the deposition of Dr Claus Meese. Dr Meese is still under oath from yesterday and we are on-the record.

DR CLAUS MEESE

having been duly Previously sworn,

testified as follows:

Examination by Ms Cassidy:

Q. Good morning, Dr Meese. Have you discussed the content of your testimony with anyone since this deposition was ended last night?

A. No, no.

Q. I am going to hand you a document which will be marked as Meese Exhibit 34, bearing Bates numbers PT 01742062 through PT 01742110.

(Exhibit 34 marked for identification)

Dr Meese, do you recognize that this is a document from a festoterodine brainstorming meeting held on September 12th, 2003. This is part one of the meeting?

A. Yes.

Q. Did you attend this meeting?

A. Yes, I did.

Q. And if you could turn to page PT 01742064. In section 1.0 general introduction there are two bullet points. The first states that you are discussing improvements to the current festoterodine process?

A. Yes.

Q. Why was it believed that there were improvements needed to the current festoterodine process?

MR TRAINOR: Objection.

A. We agreed that the process was too lengthy, too many steps and we also had the feeling that with not too much work significant improvements can be made.

MS CASSIDY: And what was the concern with the process being too lengthy?

MR TRAINOR: Objection.

A. The price of the by products substances.

MR TRAINOR: By product substances?

THE INTERPRETER: Bulk drug substance was too high.

MR TRAINOR: I'm sorry.

A. Was too high, the price of the bulk

drug substance was too high as compared to some competing compounds on the market so we wanted to reduce that.

MR TRAINOR: When you answer in English try to keep your voice up a little bit so she can hear you.

A. Okay.

MS CASSIDY: Were there any other concerns with the process being too lengthy?

A. Yes, there were some. In some steps there were safety concerns. There was one step where the reaction is extremely exothermic and this is on a large scale a risk, a risk of an explosion. We fully agreed on all points. It was a very nice brainstorming meeting.

Q. If you could turn to PT 01742066?

A. Yes.

Q. As of this meeting in September 2003 is the process depicted on this page the current process that was being used?

A. Yes.

MR TRAINOR: Objection.

A. Yes.

MS CASSIDY: In this process can you tell me which step was the extremely exothermic

reaction that had safety concerns?

MR TRAINOR: Objection.

A. Yes, they don't have simple numbers here. It is the process for SPM 7699 to SPM 7642. You see the third row of structures, if you see the scheme the left compound and the compound in the middle, that means that bromine, aromatic bromine compound converted into a Grignard intermediate and this is extremely reactive. This Grignard reacts with carbon dioxide or another carbon dioxide analogue to give the methyl ester which has the internal code SPM 7642. This is an extremely exothermic step.

MS CASSIDY: Do you recall which of the bulk drug substances were expensive and that you were trying to reduce costs on?

A. I don't think it is a singular reagent or intermediate or raw material. It is simply the problem is the number of steps. For industrial processes very short routes are wanted such as four or five, but not 11, that's too much.

Another point which was discussed on that excellent meeting is that it is a linear synthesis. This is always a problem. That means if we have a low yield at the beginning of the

process this will have direct consequences for the yield, total yield of the final product. In industrial processes it's more favorable to have convergent synthesis. That means two products were connected to give another product which is very close to the final product, so any losses in yield can be compensated more easily.

Q. I am going to hand you a document that will be marked as Meese Exhibit 35, it bears Bates numbers PT 01742114 through PT 01742144.

(Exhibit 35 marked for identification)

Dr Meese, do you recognize this to be part two of the documents related to festoterodine brainstorming meeting held on September 12th, 2003?

A. Yes, yes.

Q. If you could please turn to page PT 01742124?

A. Yes.

Q. Actually make that PT 01742126. And in this section it appears that during this meeting you discussed alternative approaches to SPM 7605?

A. That's right. The scheme shown here is exactly the hazardous process which I mentioned

before.

Q. Okay. And if you can review the page you are on, the one ending in 2126 through the page ending in 2140?

A. 40?

MR TRAINOR: She's asking that he looks through them.

A. Sorry, I can't find it.

MS CASSIDY: If it is easier we can walk through these one page at a time and it will be fairly quick on each page. Why don't you turn to page PT 01742128?

A. Yes.

MS CASSIDY: And do you see the reaction labeled Scheme 9, it is the reaction at the top of the page, most of the page?

A. Yes.

MS CASSIDY: And was this proposed as an alternative approach to SPM 7605?

A. Yes.

MR TRAINOR: Objection.

A. Yes, it has been discussed as an alternative, yes.

MS CASSIDY: And if you could look back to page PT 01742118?

A. Yes.

MS CASSIDY: Does Scheme 9 -- will Scheme 9 still include the intermediates SPM 7642, SPM 7604 and SPM 7605 -- let me break that up. Does Scheme 9 still include the intermediate SPM 7642?

MR TRAINOR: Objection. Can you clarify what you mean by "still include".

MS CASSIDY: Does the intermediate with the structure of SPM 7642 appear in Scheme 9?

MR TRAINOR: I think to answer this question he needs to reference the Scheme 9. Let me help him.

MS CASSIDY: That's fine.

MR TRAINOR: Do you remember the question?

A. No.

MS CASSIDY: Does the intermediate with the structure of SPM 7642 appear in Scheme 9 on page PT 01742128?

MR TRAINOR: Objection.

A. Well, some structures are missing here in Scheme 9, so it is hard to answer. Some structures are identical to the survey scheme here but, you see this double arrow, that always means

there are potentially several steps in between which are not depicted. So I think this was a brainstorming meeting and these are some ideas which were discussed in the meeting. It is more important to look at the present process, which is shown in Scheme 1 at the beginning.

MS CASSIDY: And if you could turn the page to PT 01742130?

A. Yes.

MS CASSIDY: Which has -- is labeled Scheme 10 on it?

A. Yes.

MS CASSIDY: Was this also an alternative synthesis to make SPM 7605?

MR TRAINOR: Objection.

A. Yes, I remember the proposal. It is again an idea to supplement the critical Grignard process, which is Greek, a Grignard process, which is a very critical process because of the high reactivity of these intermediates, and the reaction is extremely exothermic, as I said. So it is unwanted to have these processes on an industrial scale. And this is an alternative but it was still during the brainstorming proposal, and I forget, this is not the place to discuss

whether this is feasible or not.

Q. If you could turn to PT 01742132?

A. Okay.

Q. And there are two schemes on this page, Scheme 11 and Scheme 12, do you see the two schemes?

A. Yes, yes.

Q. Was Scheme 11 also proposed as an alternative synthesis of SPM 7605?

A. Yes, I remember this discussion, or this here --

Q. And if you look at --

A. Sorry.

Q. If you look at the arrows in Scheme 11, since these are not double arrows does that mean they are not intermediates that are not shown on this?

A. Yes. It took quite a long time. I like that scheme here, Scheme 11. It is my personal opinion. It is the attempt to introduce re-chirality and this step, less, of course, a good idea but the problem is that it is extremely difficult to make an antio-selective hydrogenations which are shown here. That means that you need a big team which works for, let me

say, half a year or two years on this only step. That was clear to the team. In theory it's great. Yes. Chirality, that's okay.

And the process shown in Scheme 12 is addressed to the same problem chiral hydrogenation to introduce the chiral center in a more intelligent way. What we made was a resolution, that means primarily 50% of the material was going to be resolved as waste unless another step allows a resolution in order to recycle the waste which contains 50% of the r-enantiomer which is wanted. This is again a good idea, and I don't know who introduced this idea but it is again like Scheme 11, a process which requires basic work. And it was a result of this meeting that the Company was not willing to invest too much manpower and money into basic work.

MS CASSIDY: And if you turn the page to PT 01742134. Was Scheme 13 also an alternative to creating SPM 7605?

MR TRAINOR: Objection.

A. Yes, that's right. It is a simple idea because we have two reductive processes in the production of SPM 7605. The first step is the deep protection of the benzoyl protective groups

of a compound shown in Scheme 13 on the left side. And the second step is the reduction of a methyl ester, and this might be done in one step with one reagent. That is what I suggest. That is more realistic than the other alternatives.

MS CASSIDY: And in Scheme 13 the single arrow again means that there are no missing intermediates?

A. That is right. So two steps with one reagent. Maybe switch to the next scheme, Scheme 14.

MS CASSIDY: Scheme 14, was that also an alternative --

A. Yes.

MS CASSIDY: -- synthesis to make SPM 7605?

MR TRAINOR: Objection.

A. Well, it is a proposal to save at least one step.

MS CASSIDY: And if you could please turn to PT 01742136. And was Scheme 15 also an alternative synthesis of SPM 7605?

MR TRAINOR: Objection.

A. Scheme 15? Yes, it reminds me of the very, very early syntheses of

3,3-diphenylpropylamine compounds which have been made in the 1960s by others. It is one of the many alternatives which might be checked, but -- do you want me to comment on this? It is just to mention that I know this propyl was made. Yes.

MS CASSIDY: And if you turn the page to PT 01742138, there are two schemes. The first one is Scheme 16?

A. Yes.

MS CASSIDY: Was Scheme 16 also proposed as an alternative synthesis to make SPM 7605?

MR TRAINOR: Objection. Counsel, can you explain the relevance of this line of questioning? These are actions taken by the Company years after the Patents-in-Suit were filed. I really would appreciate an explanation of how any of this is relevant?

MS CASSIDY: We think it is relevant to whether they think this synthesis was -- the current synthesis in the patent was a good one and we wanted to see if they had some other alternatives. Just exploring his work on the synthesis.

MR TRAINOR: Objection. Go ahead. Could you please read back the question for him,

Madam Translator?

A. Okay, yes, it's here. These are variances to introduce the isopropyl group at the amino group of the lower side chain, this by reductive elimination. Well, I won't go into details, it takes too much time. The isopropyl group, isopropyl, diisopropyl amino group in one step because the starting material is very cheap and available in unlimited amounts. I think I can't see any advantage.

MR TRAINOR: Diisopropyl, one word. D-I-S-O-P-R-O-P-Y-L.

MS CASSIDY: Was Scheme 17 also proposed as an alternative synthesis to make SPM 7605?

A. Yes.

MR TRAINOR: Objection. Just wait for me.

A. Okay, I wait.

MS CASSIDY: And if you turn to page PT 01742140?

A. Yes, okay.

MS CASSIDY: There is a route labeled the ultra short lactone route. L-A-C-T-O-N-E?

A. Yes.

MS CASSIDY: Was the ultra short lactone

route on this page also an alternative synthesis of SPM 7605?

A. Yes.

MR TRAINOR: Objection.

A. Yes, it is a proposal I made several years ago. It is certainly one of the shortest routes, but again the opinion was the process is too far progress, we can not switch over to a completely new process.

MS CASSIDY: And if you turn to page PT 01742142?

A. Yes, okay.

MS CASSIDY: Above the conclusion there is a statement:

"Any of these routes if successful would provide a very short route to SPM 7605 and should be investigated thoroughly."

A. Yes, I remember the summary.

MS CASSIDY: And following this meeting did you believe that these routes would provide an improvement over the current 2000 -- September 2003 route of synthesis of SPM 7605?

MR TRAINOR: Objection.

A. Yes.

MS CASSIDY: Dr Meese, if you could turn

back to Exhibit 34?

A. Yes.

MS CASSIDY: And specifically to page PT 01742090?

MR TRAINOR: Sorry, did you say 34?

MS CASSIDY: Exhibit 34, the part one of the 2003 meetings.

MR TRAINOR: Thank you.

MS CASSIDY: And if look under the section labeled: "Proposal (fumarate salt formation)."

And specifically bullet point five which states:

"Factors influencing crystallization need to be investigated, particularly with regard to the formation of amorphous versus crystalline material. Solubility curve to be established."

In the September 2003 process that was being discussed during these meetings were you still experiencing crystallization problems with that process?

A. Yes.

MR TRAINOR: Objection. Go ahead.

A. Well, this is a summary what has been done. For instance, the individual steps

were discussed in detail and some critical point where some potential improvements which can be made.

MS CASSIDY: And during this meeting what factors influencing crystallization were investigated?

MR TRAINOR: Objection.

A. No, these are proposals, what should be done to get really a process improvement. That was the aim of the whole meeting. This is a summary of it.

MS CASSIDY: Were you involved in any later investigations of the factors influencing crystallization?

MR TRAINOR: Objection. Later than 2003?

MS CASSIDY: Later than 2003.

A. No, at that time I was involved in other projects and the responsibility for the whole project in respect to chemistry was transferred to Dr Jorg Hamann, my deputy.

MS CASSIDY: During the September 2003 meeting what, if any, potential factors influencing crystallization were discussed?

MR TRAINOR: Objection.

A. I remember that all potential factors were discussed in detail. Many details are in these few lines and this proposal was to study this in detail. It was a brilliant meeting, I repeat that.

MS CASSIDY: In the manufacturing process at this time were seed crystals used to make festoterodine fumarate?

MR TRAINOR: Objection. And again this is 2003?

A. No, during the development of the industrial process we learned that the reaction to obtain crystalline material, final product, can be run without seed crystals, because you know we were expected to work under GMB conditions which restricts the use of foreign material in those processes. So we get crystalline material without seed crystals. That was a great advantage.

MS CASSIDY: At what point in the development process did you learn that the reaction could obtain the final product without seed crystals?

MR TRAINOR: Objection.

A. It's the last point, fumarate salt formation, the salt formation process.

MS CASSIDY: Let me clarify, at what point in time during the development of the industrial process did you learn that you could develop, make the festoterodine fumarate formulation without the use of seed crystals?

MR TRAINOR: Objection.

A. During the development, the production of the final material a salt was made in several batches of about several kilograms and up to 40-80 kilogram, and we found that several factors influencing the crystallization process such as purity of starting material, reaction time concentration of the solvents, I think this was an empirical research for improvements which led to the final process which was discussed in 2003.

MS CASSIDY: What solvent system was used to crystalize festoterodine fumarate during the manufacturing process?

MR TRAINOR: During the manufacturing process? Objection.

A. Yes, it was methyl ethyl ketone which we abbreviate in the lab slang MEK, methyl ethyl ketone. This was the solvent system to dissolve the material which reacts together, and as an anti-solvent which makes the whole mixture

less polar we used cyclohexane. We used both solvents due to laboratory experience and to toxicological process because traces of this compounds are critical. The toxicology to humans of both solvents is well known and investigated, and very low. So that was an advantage for the process.

THE INTERPRETER: What I said was methyl ethyl ketone, and I also said cyclohexane and I said that we had a term we used in the lab for methyl ethyl ketone which is MEK, M-E-K.

MS CASSIDY: Dr Meese, could you turn back in Exhibit 34 to PT 01742066?

A. Yes.

MS CASSIDY: And if you could just stay on that page I am going to hand you a document which will be marked as Meese Exhibit 36, a document bearing Bates numbers PT 01282901 through PT 01282930.

(Exhibit 36 marked for identification).

Dr Meese, this is a festoterodine due diligence covering October 2005 to February 2006. If you could please turn to PT 01282913?

MR TRAINOR: Just note for the record that I don't know how the Defendants can represent

what this document is, it came from Schwarz's files. But you can proceed.

MS CASSIDY: I will clarify or represent that it is a document titled: The festoterodine technical Due Diligence from October 2005 to February 2006.

Do you see where it says Scheme 1: Summary of the Schwarz synthesis of festoterodine fumarate highlighting the isolated solid intermediates?

MR TRAINOR: And I just in addition, I am not waiving any other objections but I just want to note that this doesn't indicate that Dr Meese was at this meeting or had anything to do with this document. You have not established that he knows anything about this.

A. No.

MR TRAINOR: But with that objection, without waiving others you can proceed with the questioning.

A. I never have seen this paper.

MS CASSIDY: That's fine. I am not going to ask you about the contents of the meeting. Dr Meese, if you could look at Scheme 1 in Exhibit -- in the festoterodine technical

document?

A. Yes.

MS CASSIDY: And if you could please compare that to Exhibit 34, page PT 01742066, which states the introduction to the current process?

MR TRAINOR: Can you translate that, please?

MS CASSIDY: Do these two documents depict the same synthesis process?

MR TRAINOR: Objection.

A. Yes, at the first glance but it should be checked very carefully. It looks at least similar or even identical, yes.

MS CASSIDY: And, Dr Meese, I will note that in Scheme 1 on PT 01282913 the synthesis begins at SPM 7578, which appears to be the fourth structure on PT 01742066, if that helps you with your comparison?

MR TRAINOR: And the question?

MS CASSIDY: Same question, do these appear to be the same synthesis?

MR TRAINOR: Objection.

A. I have to really take quite a lot of time to give an answer on this question because

I have to study each structure from both schemes and then I can answer. Parts of the process are identical but I can't say the whole process from the beginning to the final product is depicted here, because if you see the first row in the document.

MS CASSIDY: Which document?

A. Exhibit 36. There are many reactions summarized for the first two structures. As you see these are the different processes that take place above and below the reaction arrow in the first Scheme. Similarly, you have it here. Some of the reactions are actually identical. I can't see many basic differences in both processes. Yes.

MS CASSIDY: Thank you. You can set that aside.

A. Yes.

MS CASSIDY: And Dr Meese, if you can turn back to Exhibit 12 that we discussed yesterday?

MR TRAINOR: Do you want him to read the German one? Twelve is the translation, so maybe 11.

MS CASSIDY: Eleven. Exhibit 11

reflects your notes from your first meeting regarding this project held on August -- regarding the incontinence project held on August 28th, 1997, correct?

A. Yes, that's right.

MS CASSIDY: And do you see in the center of the document there are four chemical structures depicted?

A. Yes, that's right.

MS CASSIDY: And the first one is an ester; is that correct?

A. That is correct, yes.

MS CASSIDY: And what was the purpose of drawing these chemical structures during this meeting?

MR TRAINOR: Objection.

A. During that meeting with Bengt Sparf we discussed what can be modified within the molecule, the modification should be a cleaved able. It was already the concept of a prodrug synthesis at the very beginning, and there are many examples which clearly show that esters are under certain circumstances can be cleaved endogenously, in the organism, and the same is true for carbonates. And there are also examples

that certain ethers are also cleaved, which is an oxidative metabolism in contrast to the lipolysis or hydrolysis. So these are some proposals that are made on how we could start to get suitable derivatives.

MS CASSIDY: Why don't we take a short break?

A. Yes.

THE VIDEOGRAPHER: Off-the-record at 10.33.

(Short Recess) brainstorming

THE VIDEOGRAPHER: Back on the record at 10.53.

MS CASSIDY: Dr Meese, I am going to hand you a document which will be marked as Meese Exhibit 37, bearing Bates numbers PT 01931529 through PT 01931531.

(Exhibit 37 marked for identification)

A. Thank you.

Q. Take a look at this document and let me know if you recognize it?

A. Yes, I know that.

Q. And if you could please turn to page PT 01931531?

A. Yes.

Q. Is that your name and signature at the bottom right of the page?

A. Yes, it is.

Q. And Dr Meese, did you author this document?

A. Yes, together with Dr Peter Ney.

Q. If you could please turn back to page PT 01931529?

A. Yes. Umm hmm.

Q. The second paragraph lists several publications, do you see that?

A. Yes. Yes.

Q. Were these publications provided to you by Dr Sparf?

MR TRAINOR: Objection.

A. Maybe that he gave me one or two references, I can't remember. We make our own literature at patent research, of course.

MS CASSIDY: Dr Meese, why did you draft this document?

MR TRAINOR: Objection.

A. Well, Dr Linda Hakes came into the Company and got responsibility for research and development work in the preclinical area, and at the beginning of her work she asked me to briefly

summarize the onset, the beginning of this project, and so I wrote this paper.

MS CASSIDY: And why was Dr Schact copied on this document?

MR TRAINOR: Objection. If you know. It is over here.

A. He was at that time the head of the Patent Department, Legal Department. Dietrich Schact. Yes, he gave some input.

MR TRAINOR: Hold on. Do not provide any communications that Dr Schact may have provided to you and your colleagues, any legal advice.

A. Okay.

MR TRAINOR: So I would instruct you not to provide any input that he provided.

A. Okay.

MR TRAINOR: Do you understand?

A. Okay.

MS CASSIDY: So Dr Schact was copied on this because he provided input on the document, and please just say yes or no without disclosing any information that you received from him?

MR TRAINOR: Objection.

A. Maybe he provided one or two

references, so I think it is fair that he is informed.

MS CASSIDY: We have no further questions at this time.

A. Okay.

MR TRAINOR: No questions for the witness. Thank you.

THE VIDEOGRAPHER: Going off-the-record at 10.59. This is the end of Tape One, Volume 2 and concludes the deposition of Dr Claus Meese.

------ooo------

CERTIFICATE OF DEPONENT

I, Claus Meese, hereby certify that I have read the foregoing pages of my deposition of testimony taken in these proceedings on Wednesday, 21st January 2015 and, with the exception of the changes listed on the next page and/or corrections, if any, find them to be a true and accurate transcription thereof.

Signed: .....

Name: Claus Meese

CERTIFICATE OF COURT REPORTER

I, Kay Hendrick, an Accredited Court Reporter, hereby certify that the testimony of the witness, Claus Meese, in the foregoing transcript taken on Wednesday, 21st January, 2015 was recorded by me in machine shorthand and was thereafter transcribed by me; and that the foregoing transcript is a true and accurate verbatim record of the said testimony.

I further certify that I am not a relative, employee, counsel or financially involved with any of the parties to the within cause, nor am I an employee or relative of any counsel for the parties, nor am I in any way interested in the outcome of the within cause.

Signed: .....

KAY HENDRICK

Dated: .....