

Appendix H

Chronological Listing of Significant Communications

Date 10/25/99

Time 12.32.51

Contact Tracking/FDA Review
All Corresp/Submission/Contacts To/From FDA
Product History Log From 01/01/80 To 10/22/99
HOE 901 INSULIN GLAR
NDA Number 21-081

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Submission Date	Log Number IND/NDA:Date	Origin/Type	Classification	Supp/Serial#	Description/Comments
99/04/09	21-081:990409	MMD Sub	Original		ORIGINAL NDA SUB. (479 VOLS)/ SUBMISSION LETTER DATED 4/9/99, BUT PICKED UP BY EMERY ON 4/22/99 AND DELIVERED TO FDA ON 4/23/99. LANTUS (INSULIN GLARGINE INJECTION) (479 VOLUME SUBMISSION) SUBMISSION DATE AND DATE OF LETTER DIFFERENT IN ORDER TO PROPERLY BURN CD
99/04/23	21-081:990423	MMD Sub	CMC		COPY OF SECTION 4 (CMC)/ PROVIDE FIELD COPY FOR NDA 21-081 AND COMPLETE AND ACCURATE COPY OF SECTION 4 (CMC) FOR NDA. PRODUCT MANUFACTURED IN GERMANY, THEREFORE, FIELD COPY SENT TO FDA KC DISTRICT OFFICE SINCE THE NORTH AMERICAN HEADQUARTERS FOR HMR IS IN KANSAS CITY.
99/04/26	21-081:990426	MMD Tel	ALL		CONFIRM AGENCY REC'D NDA/ TO CONFIRM THE AGENCY RECEIVED THE NDA AND TO LET JULIE KNOW I WOULD BE SENDING ADDITIONAL INFORMATION TO HER THIS WEEK. COPY OF DATA FROM 49,078:990426
99/04/27	21-081:990427	MMD Sub	ALL		DISKETTES AND COMPACT DISCS/ PROVIDE DISKETTES OF LABELING IN WORD 6; DISKETTES & PRINTED COPY CARCINOGENICITY DATA; SPECIFIC CLIN PHARM DATA SETS; SUPPORTING STAT ANAL PROGRAMS, DATASETS AND DOCUMENTATION; COMPACT DISCS OF COMPLETE NDA ELECTRONICALLY ALONG WITH USERS MANUAL (SAME CDS SUPPLIED WITH ORIG NDA).
99/04/29	21-081:990429	MMD Sub	Other		RESPONSE TO 4/29 REQUEST/ PER FDA REQUEST OF 4/29, PROVIDE DESK COPY OF THE FIRST VOLUME OF HOE 901 NDA.

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99/04/29	21-081:990429A	MMD Tel	ALL		QUESTIONS ON NDA SUBMISSION/ LAVONNE PATTON CONTACTED JULIE RHEE TO ASK ABOUT A NUMBER OF ITEMS RELATED TO THE HOE 901 NDA SUBMISSION. JULIE WAS NOT AVAILABLE SO LAVONNE LEFT A VOICEMAIL MESSAGE ASKING HER TO RETURN THE CALL. SHE CALLED BACK LATER THAT DAY. COPY OF DATA FROM 49,078:990429
99/05/03	21-081:990503	FDA Tel	CMC		CMC SECTION OF NDA/SITE REG./ DR. BERLIN CALLED TO SAY THAT HE HAD RECEIVED THE CMC SECTION OF THE NDA TODAY AND TO CLARIFY SITE REGISTRATION NUMBERS IN THE HOE901 NDA COPY OF DATA FROM 49,078:990503
	21-081:990503A	FDA Tel	Clinical		SUMMARY OF MAY 3/4/5 CONTACTS/ SUMMARY OF MAY 3/4/5. JULIE RHEE CALLED ON MAY 3 TO REQUEST 2 ADDITIONAL COPIES OF VOL.2 OF NDA. LAVONNE CONTACTED JULIE ON MAY 4 WITH ADDITIONAL QUESTIONS ABOUT SUBMISSION OF PEDIATRIC STUDY REPORT. COPY OF DATA FROM 49,078:990503A
99/05/04	21-081:990504	MMD Tel	CMC		MARBURG SITE REGISTRATION #/ SUE ZORDAN CALLED DR. BERLIN TO PROVIDE ADDITIONAL INFORMATION ABOUT THE SITE REGISTRATION NUMBER FOR THE MARBURG SITE COPY OF DATA FROM 49,078:990504
99/05/07	21-081:990507	FDA Tel	Clinical		PEDIATRIC STUDY - AGE RANGES/ JULIE RHEE CALLED TO SAY NOT TO SUBMIT THE PEDIATRIC STUDY UNTIL WE RECEIVE AGREEMENT FROM THE AGENCY REGARDING THE AGE RANGES FOR THE STUDY.
	21-081:990507A	MMD Tel	CMC		CONTACT: ULTRA-FILTERED WATER/ CONTACT: DSHAH/PCOONEY: USE OF ULTRA-FILTERED WATER IN RINSING VIALS/ AMPOULES. (EJS)
99/05/08	21-081:990508	MMD Tel	CMC		CONTACT: UFW/ CONTACT: DSHAH/RDABBAH: SEEK ADVICE ON USE OF UFW. (EJS)

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99/06/04	21-081:990604	MMD Sub	Labeling		PROPOSED LABELING DISKETTE/ PROVIDE FDA WITH A COPY OF DISKETTE CONTAINING PROPOSED TEXT OF LABELING FOR HOE 901 IN WORD 6.0, ORIGINALLY SUBMITTED ON 4/27/99.
	21-081:990604A	FDA Tel	Clinical		REQUEST PHASE III TRIALS INFO/ DR ROY BLAY FROM DIVISION OF SCIENTIFIC INVESTIGATIONS CALLED JUNE 4, 1999 TO REQUEST PHASE III TRIALS INFORMATION
	21-081:990604B	MMD Tel	Clinical		CLARIFY REQUESTS-PHASE III/ CONTACTED JULIE RHEE TO CLARIFY REQUESTS FROM STATISTICAL REVIEWER FOR PHASE III TRIALS & SEE IF REQUESTS FROM THE BIOPHARM REVIEWER HAD BEEN RECEIVED
99/06/07	21-081:990607	MMD Sub	Clinical		DESK COPY VOLS 1.23 AND 1.41/ PER FDA TELEPHONE REQUEST OF 6/7, PROVIDE DESK COPY OF VOLUME 1.23 AND VOLUME 1.41.
	21-081:990607A	FDA Tel	Clinical		REQUEST VOL 23 & 41 OF NDA/ JULIE RHEE CALLED ON JUNE 7 & LEFT A VOICEMAIL MESSAGE REQUESTING VOLUMES 23 AND 41 OF THE HOR 901 NDA SUBMISSION
99/06/09	21-081:990609	MMD Tel	Clinical		SUMMARY: JUNE 9, 10 & 11/ DISCUSS SUBMISSION OF UPDATED PACKAGE INSERT IN THE SAFETY UPDATE. SUMMARY OF JUNE 9, 10, 11.
99/06/10	21-081:990610	MMD Sub	ALL		REQUEST FOR MARKETING EXCLUS./ QUINTILES PROVIDED LETTER FROM HMR TO FDA REQUESTING EXTENDED MARKETING EXCLUSIVITY FOR INSULIN GLARGINE (NDA 21-081).
99/06/11	21-081:990611	FDA Tel	Clinical		2ND REQUEST FOR INFORMATION/ DR ROY BLAY FROM THE DIVISION OF SCIENTIFIC INVESTIGATIONS CALLED ON JUNE 11, 1999 AND ASKED WHEN HE COULD EXPECT TO RECEIVE THE PHASE III TRIALS INFORMATION HE REQUESTED ON JUNE 4

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99/06/24	21-081:990624	FDA Tel	Clinical		REQUEST INFO FOR P III AUDIT/ DR BLAY CALLED ON JUNE 24 TO REQUEST ADDITIONAL INFO IN PREPARATION OF HIS AUDIT OF THE HOE 901 PHASE III CLINICAL TRIALS
99/06/25	21-081:990625	MMD Tel	CMC		CONTACT: UFW/ CONTACT: DSHAH/RFRIEDMAN: FOLLOW UP TO PREVIOUS DISCUSSIONS RE: USE OF UFW AS FINAL RINSE TO VIALS. (EJS)
	21-081:990625A	MMD Tel	Clinical		FOLLOW-UP ON ELECTRONIC FILES/ DR. PATTON CALLED DR. WEI TO FOLLOW UP ON ELECTRONIC FILES SUBMITTED ON JUNE 18, 1999 & CHECK ON REVIEW AID
99/06/30	21-081:990630	MMD Sub	Clinical		RESP TO FDA REQ. OF 6/24/99^ PROVIDE THE FOLLOWING IN RESPONSE TO FDA REQUEST OF 6/24/99: 1) LIST OF DIFFERENCED BETWEEN PROTS 3001 & 3004; 2) COPY OF PROT 3001; 3) COPY OF PROT 3004; 4) LISTING BY SITE AND SUBJECT NUMBER FOR STUDIES 3001 & 3004 AND 4) A COPY OF APPLICATION SUMMARY.
99/07/01	21-081:990701	MMD Tel	CMC		CONTACT: PAIS/ CONTACT: DSHAH/JDIETRICK: DISCUSS NEED FOR PAIS FOR 3 NDAS/SUPPLEMENTS. (EJS)
	21-081:990701A	FDA Tel	Clinical		REQUESTED INFORMATION ON 6/24/ DR BLAY CALLED TO SEE IF WE HAD SENT THE INFORMATION HE REQUESTED ON 6/24/99
99/07/06	21-081:990706	FDA Tel	Clinical		RE: NORMAL RANGE GHB/ JULIE RHEE CALLED REQUESTING NORMAL RANGE FOR GHB AT DR. GOLDSTEIN'S LAB.
	21-081:990706A	MMD Sub	Clinical		SAFETY UPDATE REPORT (53 VOLS)/ SUBMITTED SAFETY UPDATE REPORT ON DAY 75 AS AGREED IN PRE-NDA MEETING WITH AGENCY (INSTEAD OF 120) AND CONTAINS NEW SAFETY INFO FROM THE TIME OF THE ORIGINAL SAFETY DATA CUTOFF THROUGH 4/22/99. INCLUDES FINAL REPORT 3002 AND ONGOING TRIALS 1019, 3101, 3011, 3012 & 3013.

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99/07/07	21-081:990707	FDA Tel	Clinical		RE: TELECONF. DR. SAHLROOT/ JULIE RHEE CALLED ABOUT TELECONFERENCE BETWEEN STATISTICIAN(S) AND DR. TODD SAHLROOT
99/07/12	21-081:990712	FDA Tel	CMC		SUM: 7/12&13-BIOASSAY TESTING/ SUMMARY OF 7/12 AND 7/13. DR BERLIN CALLED WITH INITIAL FEEDBACK REGARDING BIOASSAY TESTING FOR INSULIN GLARGINE.
99/07/14	21-081:990714	FDA Tel	CMC		BIOASSAY TESTING INFORMATION/ ADDITIONAL INFORMATION ON BIOASSAY TESTING FOR INSULIN GLARGINE.
	21-081:990714A	MMD Fax	CMC		OUTLINE FOR BIOASSAY TESTING/ PROVIDE OUTLINES FOR LOCATIONS OF SECTIONS RELEVANT TO BIOASSAY AND BIOIDENTITY TESTING OF INSULIN GLARGINE DRUG SUBSTANCE AND DRUG PRODUCT IN NDA 21-081.
99/07/15	21-081:990715	MMD Sub	Clinical		RESPONSE TO FDA--STATS DISKETTE/ PROVIDE TO FDA DISKETTE CONTAINING THE SUPPORTING STATISTICAL ANALYSIS PROGRAMS, DATASETS AND DOCUMENTATION FOR STATS REVIEWER FOR STUDIES 3002 & 3003.
99/07/19	21-081:990719	FDA Tel	Clinical		6-MONTH EXCLUSIVITY ON PEDI/ SUMMARY OF JULY 15 & 19: RE: 6-MONTH EXCLUSIVITY BASED ON PEDIATRIC STUDY GRANTED
99/07/20	21-081:990720	FDA Tel	Clinical		? ON PDF FILE TO MS WORD/ DR BERLIN INQUIRED HOW TO COPY A TABLE FROM THE PDF FILE TO MS WORD
	21-081:990720A	FDA Tel	Clinical		RE: INFO FOR 4 SITES FOR AUDIT/ SUMMARY OF JULY 20 & 21 CONTACTS: DR BLAY CALLED REQUESTING ADDITIONAL INFORMATION REGARDING THE FOUR SITES SELECTED FOR AUDITING THE HOE 901 NDA
99/07/26	21-081:990726	MMD Sub	Clinical		RESPONSE TO FDA REQUEST/ RESPONSE TO FDA REQUEST OF 7/20/99, PROVIDING INFORMATION FROM STUDY 3004 FOR SITES 16, 25, 44 AND 49 FOR UPCOMING AUDITS.
	21-081:990726A	MMD Tel	Clinical		ADVISE PROTOCOL 3004 INFO SENT/ ADVISE DR BLAY INFO REQUESTED ON PROTOCOL 3004 INVESTIGATORS SENT TODAY.
99/08/04	21-081:990804	MMD Tel	Clinical		DISCUSS STATUS OF NDA REVIEW/ CONTACTED JULIE RHEE TO DISCUSS REVIEW STATUS OF HOE 901 NDA SUBMISSION

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99/08/05	21-081:990805	MMD Tel	Clinical		FOLLOW-UP JULY 26 SUBMISSION/ FOLLOW-UP OF OUR SUBMISSION DATED JULY 26, 1999
99/08/06	21-081:990806	FDA Tel	CMC		CDRH CONSULT COMPLETED/ DR BERLIN CALLED TO SAY CDRH CONSULT WAS COMPLETED
	21-081:990806A	FDA Tel	ALL		CDRH REVIEW COMMENTS-OPTIPEN/ JULIE RHEE CALLED-FAXING CDRH REVIEW COMMENTS FOR THE OPTIPEN PRO DEVICE.
	21-081:990806B	FDA Fax	ALL		PART OF THE HOE 901 NDA CDRH REVIEW COMMENTS/ RECEIVED FROM JULIE RHEE THE FAXED CDRH REVIEW COMMENTS ON SUBMISSION DATED 4/9/99, ASKING FOR RESPONSE TO DR. SOLOMON SOBEL FOR FORWARDING TO CDRH
99/08/11	21-081:990811	FDA Tel	CMC		LANTUS TRADENAME ACCEPTABLE/ DR. BERLIN CALLED TO NOTIFY US THAT THE LANTUS TRADENAME WAS ACCEPTABLE.
99/08/13	21-081:990813	FDA Tel	CMC		CONTACT: FRANKFURT INSPECTION/ CONTACT: DSHAH/RKIMMEL: DISCUSS DATES FOR FRANKFURT INSPECTION (EJS).
	21-081:990813A	MMD Tel	CMC		CONTACT: FRANKFURT INSPECTION/ CONTACT: DSHAH/RKIMMEL: DISCUSS UPCOMING INSPECTION OF FRANKFURT FACILITY (EJS)
99/08/24	21-081:990824	MMD Sub	ALL		AMENDMENT-RESP TO CDRH QUES./ SUBMIT AMENDMENT IN RESPONSE TO CDRH QUESTIONS RECEIVED BY FAX FROM JRHEE ON 8/6/99. JULIE IS TO FORWARD ON TO CDRH FOR THEIR REVIEW.
	21-081:990824A	MMD Sub	CMC		PROVIDE COPY OF CMC SECTIONS/ PER TELEPHONE CONVERSATION BETWEEN DSHAH AND RKIMMEL A COPY OF THE CMC SECTIONS (FIRST 15 VOLUMES OF NDA) WAS SENT TO MS. TRACY RAMSEUR, FDA, CHARLOTTE, NORTH CAROLINA, IN PREPARA- TION FOR THE PRE-APPROVAL INSPECTION AT THE MANUFACTURING FACILITIES IN FRANKFURT, GERMANY IN SEPTEMBER.

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99/08/24	21-081:990824B	MMD Sub	CMC		PROVIDE COPY OF CMC SECTIONS/ PER TELEPHONE CONVERSATION BETWEEN DSHAH AND RKIMMEL A COPY OF THE CMC SECTIONS (FIRST 15 VOLUMES OF NDA) WAS SENT TO MR. PHILIP ISTAFANOS, FDA, BROOKLYN, NEW YORK, IN PREPARATION FOR THE PRE-APPROVAL INSPECTION AT THE MANUFACTURING FACILITIES IN FRANKFURT, GERMANY IN SEPTEMBER. CONTACT: INSPECTION/ CONTACT: DSHAH/RKIMMEL: DISCUSS PLANS FOR FRANKFURT INSPECTION. (EJS)
	21-081:990824C	FDA Tel	CMC		CONTACT: DISCUSS INSPECTION/ CONTACT: DSHAH/TRAMSEUR: DISCUSS PLANS FOR FRANKFURT INSPECTION. (EJS)
	21-081:990824D	MMD Tel	CMC		CONTACT: FOLLOW-UP/ CONTACT: DSHAH/RKIMMEL: FOLLOW UP ON PREVIOUS DISCUSSION ON ADVERSE REPORTING FILES. (EJS)
	21-081:990824E	MMD Tel	CMC		
99/08/25	21-081:990825	FDA Tel	Clinical		ELECTRONIC REVIEW AID QUESTION/ DR HERMAN RHEE CALLED REGARDING ELECTRONIC REVIEW AID FOR SECTION 5 OF HOE 901 NDA CONTACT: INSPECTION/ CONTACT: DSHAH/RKIMMEL: PROVIDE INFO REGARDING ARRANGEMENTS FOR THE FRANKFURT INSPECTION. (EJS)
	21-081:990825A	MMD Tel	CMC		
99/08/26	21-081:990826	MMD Tel	Clinical		RE: RESPONSE TO CDRH QUESTIONS/ NOTIFIED JULIE RHEE, WE SUBMITTED A RESPONSE TO QUESTIONS FROM CDRH. ALSO, ADOBE ACROBAT 4.0 NOW AVAILABLE WITHIN CDER FOR REVIEWERS FOR HOE 901 NDA.
99/08/31	21-081:990831	FDA Tel	Clinical		QUESTIONS ABOUT ACROBAT 4.0/ DR MA CALLED AT JULIE RHEE'S REQUEST TO ASK ABOUT ACROBAT 4.0
99/09/02	21-081:990902	MMD Sub	CMC		CMC AMENDMENT (2 VOLUMES)/ SUBMIT CMC AMENDMENT CONTAINING STERILIZATION VALIDATION REPORT FOR INSULIN GLARGINE CARTRIDGES AND A REVISED VERSION OF REPORT FOR VILAS WAS ALSO ATTACHED.

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99/09/02	21-081:990902A	MMD Sub	CMC		CMC AMEND FIELD COPY KC OFFICE/ SUBMIT TO KARA RODEN (FDA) KANSAS CITY DISTRICT OFFICE A FIELD COPY OF THE CMC AMENDMENT (2 VOLUMES) SUBMITTED ON 9/2/99 (21-081:990902).
99/09/08	21-081:990908	MMD Tel	CMC		PARTICULULATE/CLARITY 901 VIALS/ DISCUSSED PARTICULATES/CLARITY PROBLEM WITH HOE 901 VIALS WITH DR. BERLIN.
99/09/14	21-081:990914	FDA Tel	CMC		INSPECT. OF OPTIPEN FACILITIES/ DR BERLIN CALLED WITH SOME QUESTIONS RAISED BY THE OFFICE OF COMPLIANCE REGARDING INSPECTION OF THE OPTIPEN MANUFACTURING FACILITIES.
99/09/28	21-081:990928	MMD Tel	CMC		INSULIN GLARGINE IN-USE TESTS/ CALLED DR. BERLIN TO SEE IF HE HAD DISCUSSED THE INSULIN GLARGINE IN-USE TEST ISSUES WITH DR. MOORE.
99/10/04	21-081:991004	MMD Tel	CMC		FAX INFO PKS ON IN-USE CLARITY/ CALLED DR. BERLIN TO NOTIFY HIM OF FAX ON INFORMATION PACKAGE ABOUT INSULIN GLARGINE IN-USE CLARITY ISSUE.
	21-081:991004A	MMD Sub	CMC		CMC INFORMATION AMENDMENT/ SUBMIT CMC INFORMATION AMENDMENT RE: INFORMATION ABOUT THE IN-USE TESTING OF INSULIN GLARGINE INJECTION
99/10/06	21-081:991006	MMD Tel	Clinical		PHASE IIIB CLINICAL TRIAL/ PHONED J. RHEE TO DISCUSS THAT HMR PLANNED TO CONDUCT A PHASE IIIB CLINICAL TRIAL USING 3ML CARTRIDGES & OPTIPEN PROJ 1 INJECTION PEN DEVICE.
	21-081:991006A	MMD Tel	CMC		INSULIN GLARGIN IN-USE CLARITY/ CALLED DR. BERLIN TO SEE IF HE HAD LOOKED AT THE INFORMATION PACKAGE ABOUT INSULIN GLARGINE IN-USE CLARITY ISSUE YET
99/10/08	21-081:991008	FDA Tel	Clinical		RE: HOE 901 LABELING/ SUMMARY OF CALLS FROM DR. MISBIN & JULIE RHEE TO REQUEST A CHANGE TO THE HOE 901 LABELING.
99/10/12	21-081:991012	FDA Tel	Clinical		REQUEST FOR NDA, VOLS 16 & 21/ JULIE RHEE CALLED REQUESTING VOLUMES 16 & 21 OF THE HOE 901 NDA.

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Through 12/10/99

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99/10/04B	21-081:991004B	MMD Tel	CMC		FAX of hard copy (991004A) Provide via Fax a copy of the amendment to NDA 21-081 which is also being mailed today (991004A) re: in-use clarity issue with the insulin glargine vials.
99/10/18B	21-081:991018B	MMD Tel	Clinical		Summary of Oct. 18, 19 & 20 Summary of Oct. 18, 19 & 20 for HOE 901. Julie Rhee & Dr. MOH JEE NG requested some volumes of the NDA & to discuss the carcinogenicity data sets provided as part of the HOE 901 NDA.
99/10/20	21-081:991020	MMD Tel	Clinical		Retinopathy Data Package Julie Rhee called regarding retinopathy data package for HOE 901, sent to agency on Oct. 18, 1999.
99/10/26	21-081:991026	MMD Tel	Pre Clin		Dr. HRhee called LPatton to discuss carcinogenicity studies in HOE 901 NDA
99/10/28	21-081:991028	MMD Tel	CMC		JRhee called LPatton to advise she sending FAX containing microbiology reviewers pre-clin questions on HOE 901 NDA
99/10/28A	21-081:991028A	FDA FAX	Pre Clin		Received FAX from JRhee providing microbiology reviewers comments and questions.
99/11/04	21-081:991104	MMD Sub	Clinical Pre-Clin		Response to FDA Response to questions from HRhee, pre-clinical reviewer

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99/11/18	21-081:991118	MMD	Tel	Clinical	RE: 4002 & General Progress LPatton called JRhee to ask questions and inquire status of FDA review of Protocol 4002.
99/11/18A	21-081:991118A	FDA	Fax	Clinical	FAX from FDA Additional questions from JRhee/RMisbin
99/11/22	21-081:991122	MMD	Sub	Clinical CMC	Amendment: Microb deficiencies Response submitted to list of microbiology deficiencies received by FAX from JRhee on 10/28/99.
99/11/23	21-081:991123	MMD	Tel	Clinical	RE: FAX from CDRH Reviewer LPatton called JRhee to follow up on JRhee's FAX of 11/18/99.
99/12/02	21-081:991202	MMD	Sub	Clinical	Amend: additional clin information Response to request from JRhee received by FAX on 11/18/99

Aventis Pharmaceuticals Inc.
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LANTUS (insuline glardine injection)
HOE 901
NDA 021-081

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12/10/1999	021-081:19991210	FDA TEL	Preclinical		REQUEST INFORMATION Dr Ng called to ask if tumor code information, she requested on Oct. 19, 1999 had been submitted. It was sent on Oct. 21.
12/16/1999	021-081:19991216	QKAN TEL	Clinical		REQUEST INFORMATION Summary of Dec. 14 & 16: 1) Dr. Moh Jee Ng received submission of tumor codes in October. 2) CDRH reviewer agreed we could use info from his e-mail note to respond to questions from IRBs on protocol 4002 and can also refer the IRBs to 21 CFR Part 56. 3) Not anticipating questions over Christmas break.
12/17/1999	021-081:19991217	QKAN TEL	Clinical		REQUEST INFORMATION Questions regarding Dr. Sobels status as Director of the Division of Metabolism and Endocrine Drug Products.
12/21/1999	021-081:19991221	QKAN SUB	CMC		NDA AMENDMENT CMC Info amendment -- Provide data supporting the new sealing disc and updated stability reports as promised to FDA.
12/22/1999	021-081:19991222	QKAN SUB	Clinical		NDA AMENDMENT Two volume submission providing Final Safety Update, which includes new safety information on the seven ongoing clinical trials (data through November 24, 1999).
12/22/1999	021-081:19991222-A	QKAN TEL	CMC		RESPONSE TO FDA REQUEST Notified Julie Rhee that the NDA amendment containing the data for the new sealing disc for the insulin glargine vials was mailed Dec. 21.
12/27/1999	021-081:19991227	FDA TEL	Clinical Preclinical		REQUEST INFORMATION Summary of contacts on Dec. 23 & 27. Dr. Misbin had some questions on the metabolism of HOE 901 and wanted to speak with someone in the Biopharm or PK group to discuss them.
12/28/1999	021-081:19991228	QKAN TEL	Clinical Preclinical		RESPONSE TO FDA REQUEST Notified Agency that responses to his question of Dec. 27 have been faxed.

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12/28/1999	021-081:19991228-A	QKAN FAX	Preclinical		RESPONSE TO FDA REQUEST FAX to FDA in response to question raised by Dr. Misbin on 12/17/99. Will follow with paper submission.
12/29/1999	021-081:19991229	QKAN SUB	Preclinical		RESPONSE TO FDA REQUEST Follow up to FAX of 12/28 and in response to 12/27/99 FDA request from Dr. Misbin, regarding the metabolic activity of the HOE 901 metabolites, M1 and M2, in receptor binding assays and isolated cells.
01/04/2000	021-081:20000104	FDA TEL	Clinical		OTHER Julie requested 5 & 10mL vials and proposed labeling. They want to compare with other vials currently available on US market.
01/06/2000	021-081:20000106	QKAN LTR	Clinical		RESPONSE TO FDA REQUEST Provide FDA with three samples of the 5 mL and 10 mL vial packages as requested, along with copies of the labels.
01/06/2000	021-081:20000106-A	QKAN FAX	Labeling		OTHER Provide copy of updated Lantus labeling
01/06/2000	021-081:20000106-B	QKAN FAX	Preclinical		RESPONSE TO FDA REQUEST Response to FDA in answer to questions raised by Herman Rhee.
01/06/2000	021-081:20000106-C	QKAN LTR	Preclinical		RESPONSE TO FDA REQUEST Submit response to FDA with regard to question received 1/5/2000 by Hermann Rhee regarding incidence of hepatocellular adenomas in male NMRI mice
01/06/2000	021-081:20000106-D	FDA TEL	Preclinical		REQUEST INFORMATION Dr Herman Rhee, Preclinical Reviewer for HOE 901, requested additional information on the historical controls in NMRI mice for hepatocellular adenomas.
01/06/2000	021-081:20000106-E	FDA TEL	Labeling		REQUEST INFORMATION Dr Misbin called to request a clean copy of the updated Lantus labeling without the strikeouts and additions highlighted. He asked that this information be faxed to him.

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01/07/2000	021-081:20000107	QKAN FAX	Labeling		RESPONSE TO FDA REQUEST Provide documentation to address the two questions on ultralente in labeling
01/07/2000	021-081:20000107-A	QKAN LTR	Labeling		RESPONSE TO FDA REQUEST Provide copy of updated draft labeling submitted in the Final Safety Update on 12/22/99.
01/07/2000	021-081:20000107-B	FDA TEL	Clinical		REQUEST INFORMATION Dr. Misbin called to discuss statements in our label regarding Ultralente. Will fax supporting statements from the submission.
01/07/2000	021-081:20000107-C	FDA TEL	Labeling		REQUEST INFORMATION Julie Rhee requested I send her an Electronic copy (with password protection on the file) of the HOE 901 labeling that was provided to Dr. Misbin by fax.
01/11/2000	021-081:20000111	FDA TEL	CMC		REQUEST INFORMATION Dr Komanduri asked questions related to the CMC file: how synthesis goes from tons to kg quantities. More CMC questions coming 1/12.
01/11/2000	021-081:20000111-A	QKAN TEL	Clinical CMC		REQUEST INFORMATION I asked if she'd located 5 & 10ml vials we sent (not yet located). Asked her about the CMC questions Dr Komanduri said he would send.
01/12/2000	021-081:20000112	FDA FAX	CMC		REQUEST INFORMATION CMC review request from FDA
01/12/2000	021-081:20000112-A	FDA TEL	Clinical CMC		REQUEST INFORMATION Julie Rhee asked how the vials had been packaged. They cannot be located at FDA. Asked if we could send replacement samples to her today.
01/13/2000	021-081:20000113	QKAN LTR	Clinical		RESPONSE TO FDA REQUEST Response to questions raised by Dr. Robert Misbin on 12/28/99
01/14/2000	021-081:20000114	QKAN FAX	CMC		RESPONSE TO FDA REQUEST Response to questions raised by Dr. Pardha Komanduri which were received by FAX on 1/12/00.

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01/14/2000	021-081:20000114-A	QKAN LTR	CMC		RESPONSE TO FDA REQUEST Response to CMC questions from Dr. Komanduri received 1/12/00 via FAX.
01/17/2000	021-081:20000117	QKAN SUB	Other		OTHER Resending another set of vials (two samples of 5 mL and 10 mL as requested). Vials originally sent on 1/6/00; however, even though these vials reached the document control room, they did not reach Julie Rhee.
01/18/2000	021-081:20000118	QKAN FAX	CMC		RESPONSE TO FDA REQUEST Response to question raised by Dr. Komanduri on 1/11/00.
01/18/2000	021-081:20000118-A	QKAN LTR	CMC		RESPONSE TO FDA REQUEST Provide response to question raised by Dr. Pardha Komanduri in 1/11/2000 conversation.
01/18/2000	021-081:20000118-B	QKAN TEL	CMC		OTHER Clarification of his 011400 request to LPatton. Faxing document GPDA009/00 today.
01/18/2000	021-081:20000118-C	FDA TEL	Clinical Preclinical		REQUEST INFORMATION Has received sample vials. Needs to know what the maximum response was for figure 1, "lipogenesis in vitro on rat adipocytes."
01/18/2000	021-081:20000118-D	QKAN TEL	Clinical		OTHER Asked if she'd received sample vials (no), and ophthalmologic consult (e-mail received but no official response). Discussed strategy & timing of meeting with Misbin.
01/20/2000	021-081:20000120	QKAN FAX	Preclinical		RESPONSE TO FDA REQUEST Provide response to Dr. Robert Misbin's question of 1/18/00.
01/21/2000	021-081:20000121	QKAN TEL	Clinical		REQUEST INFORMATION Discussed encryption software and division's review meeting. Meeting has been rescheduled to 012700. Asked about meeting to discuss retinopathy.

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01/21/2000	021-081:20000121-A	FDA TEL	Clinical Preclinical		FDA ACKNOWLEDGEMENT Dr Misbin acknowledged receipt of preclinical response that was faxed to him on 012000.
01/27/2000	021-081:20000127	QKAN FAX	CMC		RESPONSE TO FDA REQUEST Provide response to question raised by Julie Rhee regarding the method of pooling centers in the ANCOVA model for 3001 and 3004.
01/27/2000	021-081:20000127-A	FDA TEL	Clinical		REQUEST INFORMATION Question on the HOE 901 file from the statistical reviewer.
02/01/2000	021-081:20000201	QKAN TEL	Clinical		REQUEST INFORMATION I told Julie we had not received the revised labeling. Julie will send on 020300. Asked whether Dr Misbin had considered our request for meeting on retinopathy. He doesn't think meeting is necessary.
02/03/2000	021-081:20000203	FDA FAX	Clinical		REQUEST INFORMATION FDA request via FAX for Phase IV study concerning the progression of retinopathy in patients with type 2 diabetes.
02/04/2000	021-081:20000204	QKAN FAX	Labeling		RESPONSE TO FDA REQUEST Provide via FAX labeling requested, and will follow with a hard copy.
02/04/2000	021-081:20000204-A	QKAN SUB	Labeling		RESPONSE TO FDA REQUEST Provide per FDA request, info for patient for Lantus vial, info for patient for Lantus cartridge, User Manuals for OptiPen Pro 1 and 2 as well as diskette with electronic format.
02/04/2000	021-081:20000204-B	QKAN TEL	Preclinical		REQUEST INFORMATION I told Julie I had not received the Phase IV request she mentioned Feb 1. More changes to labeling. Guidance on developing drugs for the treatment of diabetes has been put to sleep.
02/07/2000	021-081:20000207	FDA FAX	Labeling		GENERAL CORRESPONDENCE FDA provided comments on Physician PI (FDA revision #1).

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02/07/2000	021-081:20000207-A	QKAN EML	Other		GENERAL CORRESPONDENCE Provide JRhee with PGP Quintiles Public key for electronic file encryption.
02/07/2000	021-081:20000207-B	QKAN TEL	Clinical Preclinical		REQUEST INFORMATION I told Julie I received fax of the label and asked if she planned to send diskette. She's still evaluating the PGP software for sending label back and forth.
02/08/2000	021-081:20000208	QKAN EML	Labeling		GENERAL CORRESPONDENCE Provide draft labeling to FDA via encryption software, noting hand written comments on the faxed copy were not included in this draft.
02/08/2000	021-081:20000208-A	QKAN TEL	Clinical Preclinical		REQUEST INFORMATION Discuss labeling, issue of inadvertent mixing of Lantus with regular insulin, schedule teleconference to discuss same.
02/09/2000	021-081:20000209	QKAN FAX	Other		GENERAL CORRESPONDENCE Provide JRhee with background information for teleconference on 2/10/00.
02/09/2000	021-081:20000209-A	QKAN LTR	Other		GENERAL CORRESPONDENCE Provide hard copy of background document to JRhee for the telecon on 2/10/00 to discuss mixing of HOE901.
02/09/2000	021-081:20000209-B	QKAN EML	Other		GENERAL CORRESPONDENCE Provide JRhee call-in information for teleconference on 2/10, advising faxed background information.
02/10/2000	021-081:20000210	QKAN TEL	Clinical Preclinical		OTHER Summary of Feb 9 & 10 contacts. Faxing preclinical information for Feb. 11 teleconference & question about CV for Dr. Jackie See, an investigator in HOE 901 studies. Also checked to see if Julie had followed-up with Dr. Malozowski on Division guidance on the development of short-acting insulins.

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02/10/2000	021-081:20000210-A	FDA MTG	Clinical Labeling Preclinical		OTHER Teleconference with the FDA to discuss the statement made by the FDA as follows: Lantus cannot be mixed with regular insulin. Inadvertent mixing of Lantus with regular insulin could cause precipitation of the regular insulin. This could constitute a safety hazard. For this reason, the Agency recommends that only the cartridges should be approved for marketing.
02/11/2000	021-081:20000211	FDA FAX	Clinical		GENERAL CORRESPONDENCE Fax from FDA providing clinical recommendations.
02/11/2000	021-081:20000211-A	QKAN FAX	EntireApplication		GENERAL CORRESPONDENCE Provided via FAX a copy of the letter notifying Quintiles that the USAN Council adopted insulin glargine.
02/11/2000	021-081:20000211-B	FDA TEL	CMC		REQUEST INFORMATION Dr Komanduri called to inquire about the status of the approval of the USAN name for insulin glargine.
02/16/2000	021-081:20000216	FDA TEL	CMC		REQUEST INFORMATION Dr. Wu called and introduced himself as a new CMC reviewer for the HOE 901 file. He stated he had some questions and we discussed them.
02/22/2000	021-081:20000222	FDA TEL	CMC Labeling		REQUEST INFORMATION Summary of Feb. 11, 18 & 22 contacts. Feb. 11-PGP encryption program; Feb 18-Still receiving CMC questions on the file from Dr. Wu/Revised Labeling; Feb. 22-Faxing 5 more questions from CMC reviewers.
02/22/2000	021-081:20000222-A	FDA FAX	CMC		REQUEST INFORMATION Request from FDA via FAX for additional CMC information.
02/23/2000	021-081:20000223	QKAN TEL	CMC		REQUEST INFORMATION Requested information on CMC questions which were faxed on February 22 -- to get clarification.
02/24/2000	021-081:20000224	QKAN TEL	CMC		REQUEST INFORMATION Summary of several phone calls on February 23 and 24 regarding CMC questions faxed on February 22.

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02/24/2000	021-081:20000224-A	QKAN LTR	CMC		GENERAL CORRESPONDENCE Response to FDA questions received 2/16/2000 regarding a European Medicines Eval Agency report discussing isolated reports of leakage from 3.15 mL insulin cartridges.
02/24/2000	021-081:20000224-B	QKAN FAX	CMC		GENERAL CORRESPONDENCE FAX of 2/24/2000 letter in response to FDA inquiry of 2/16/2000
02/24/2000	021-081:20000224-C	QKAN SUB	Labeling		NDA AMENDMENT Submit packaging for the OptiPen Pro injection device, including draft label for the carton and diskette containing a PDF file of the OptiPen Pro User Manual.
02/24/2000	021-081:20000224-D	QKAN SUB	Preclinical		GENERAL CORRESPONDENCE Provide information with regard to carcinogenicity data for HOE 901 related to NMRI mice.
02/25/2000	021-081:20000225	FDA TEL	Clinical		REQUEST INFORMATION Summary of several contacts (Feb. 24 and Feb. 25) regarding the HOE 901 NDA submission.
02/25/2000	021-081:20000225-A	QKAN TEL	Clinical		REQUEST INFORMATION Glen Park (Aventis) and Lavonne Patton called Dr. Misbin to discuss their approach for responding to the changes suggested by the FDA regarding the Lantus Prescribing Information.
02/27/2000	021-081:20000227	FDA TEL	Clinical Labeling		REQUEST INFORMATION Requested names of participants in Feb. 10, 2000 teleconference and discussed OptiPen Pro 1 & 2 devices labeling
02/28/2000	021-081:20000228	QKAN SUB	CMC		NDA AMENDMENT Provide response to CMC questions from Dr. Stephen Moore received via FAX 2/22/2000.
02/28/2000	021-081:20000228-A	QKAN FAX	CMC		GENERAL CORRESPONDENCE FAX to FDA -- Response to CMC questions from Dr. Stephen Moore received via FAX 2/22/2000.

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02/28/2000	021-081:20000228-B	FDA FAX	CMC		GENERAL CORRESPONDENCE CDRH comments on 8/24/99 submission.
02/28/2000	021-081:20000228-C	QKAN TEL	CMC		RESPONSE TO FDA REQUEST Called Julie Rhee to let her know that the CMC responses to questions received February 22 were submitted.
02/29/2000	021-081:20000229	QKAN SUB	Labeling		INFORMATION AMENDMENT Provide revisions to proposed labeling, including diskettes.
03/01/2000	021-081:20000301	QKAN TEL	CMC		RESPONSE TO FDA REQUEST On Feb 28, called Pardha Komanduri to let him know that the CMC responses to questions received February 22 were submitted. On March 1, called Pardha again to confirm that he had received the faxed responses.
03/02/2000	021-081:20000302	QKAN LTR	CMC		RESPONSE TO FDA REQUEST Provide FDA two samples each of the OptiPen Pro 1 and OptiPen Pro 2 insulin injection device.
03/02/2000	021-081:20000302-A	QKAN SUB	Preclinical		RESPONSE TO FDA REQUEST Per FDA telecon request of 2/10/2000 for mixing study, providing preliminary report and data from the dog study.
03/02/2000	021-081:20000302-B	QKAN FAX	Preclinical		RESPONSE TO FDA REQUEST Provide via FAX preliminary results requested from the mixing study.
03/03/2000	021-081:20000303	FDA FAX	CMC		REQUEST INFORMATION FDA requested Aventis provide Phase IV CMC commitments.
03/03/2000	021-081:20000303-A	QKAN SUB	CMC		INFORMATION AMENDMENT NDA amendment providing information for the patient for Lantus cartridge and vial, as well as provide diskette containing data from the mixing study submitted 3/2/00.
03/03/2000	021-081:20000303-B	QKAN EML	Preclinical		RESPONSE TO FDA REQUEST Provide via e-mail data for the dog study provided in excel spreadsheet format.

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03/06/2000	021-081:20000306	QKAN LTR	CMC		RESPONSE TO FDA REQUEST Response to FDA request via FAX dated 3/3/00
03/06/2000	021-081:20000306-A	QKAN TEL	Clinical Labeling		REQUEST INFORMATION Summary of March 2, 3 & 6: March 2-Results of dog study received & would be fax to Julie Rhee; OPDRA replaced the Nomenclature Committee. March 3: FDA wants dog data in excel spreadsheet or SAS format; discussed OptiPen Pro 2 in US market. March 6: Checking on vial & cartridge patient info diskettes.
03/08/2000	021-081:20000308	QKAN SUB	Labeling Other		INFORMATION AMENDMENT In response to FDA request, providing changes re: the Optipen Pro User Manual. The manual was separated into two manuals: Optipen Pro 1 and OptiPen Pro 2. Also provided manuals on diskette, w/o figures. Enclosed carton label for OptiPen Pro 2 device.
03/09/2000	021-081:20000309	FDA TEL	Clinical CMC Labeling		REQUEST INFORMATION Summary of March 7 & 9: March 7-Julie unable to open electronic files sent on March 3; told Julie Phase IV CMC commitment sent. March 9-Discussed submitting Phase IV clinical commitment to conduct the retinopathy study after March 10; discussed withdrawing OptiPen Pro 2 from the NDA submission.
03/13/2000	021-081:20000313	FDA TEL	CMC		REQUEST INFORMATION Dr Wu called regarding an article that appeared on March 6, 2000 in the Pink Sheets.
03/13/2000	021-081:20000313-A	FDA TEL	Clinical Labeling Preclinical		OTHER Agency requested a teleconference for Friday, March 17, to discuss the results of the mixing study conducted in dogs. Electronic files we sent were MIME condensed files, coming across as ".txt" files not ".doc" files.
03/13/2000	021-081:20000313-B	QKAN LTR	Clinical CMC		INFORMATION AMENDMENT

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					Advise FDA that Aventis is withdrawing from consideration for approval the OptiPen Pro 2 injection device as part of HOE 901 NDA 21-081. The OptiPen Pro 1 device will remain in the file being reviewed.
03/13/2000	021-081:20000313-C	QKAN TEL	Preclinical		REQUEST INFORMATION Contacted Dr. Misbin to follow up on the Agency's concerns regarding the information we provided with the dog study on mixing HOE 901 with regular insulin.
03/14/2000	021-081:20000314	QKAN SUB	Clinical		RESPONSE TO FDA REQUEST Provide Phase IV Clinical Commitment
03/14/2000	021-081:20000314-A	QKAN FAX	Clinical		RESPONSE TO FDA REQUEST Provide via FAX phase IV clinical commitment for retinopathy study.
03/14/2000	021-081:20000314-B	QKAN SUB	Labeling		INFORMATION AMENDMENT Provide to FDA vial, cartridge and carton updated labels for the Lantus packaging.
03/14/2000	021-081:20000314-C	QKAN EML	Other		OTHER Provide via e-mail to JRhee information for telephone conference call for today (3/14/00)
03/14/2000	021-081:20000314-D	FDA MTG	Entire Application		REQUEST INFORMATION The FDA requested a teleconference to discuss the dog data we submitted on March 2, 2000 regarding mixing of HOE 901 with regular insulin. Involved Lavonne Patton, Ralf Rosskamp, Jeff Miller, Dalton Tomlinson, Sue Zordan, Tom Mecca, and Gerhard Seipke.
03/15/2000	021-081:20000315	QKAN SUB	Labeling		INFORMATION AMENDMENT Provide to FDA proposed precautionary statement for mixing of Lantus with regular insulin for labeling.
03/15/2000	021-081:20000315-A	QKAN SUB	Other		INFORMATION AMENDMENT Provide to FDA outline of the educational program for health care professionals and patients.

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03/15/2000	021-081:20000315-B	QKAN FAX	Other		GENERAL CORRESPONDENCE Provide a copy to Julie Rhee of three submissions: 1) 3/13/00B, OptiPen Pro 2 withdrawal; 2) 3/15/00, precautionary statement for mixing and 3) 3/15/00A, outline of educational program.
03/16/2000	021-081:20000316	QKAN SUB	Clinical CMC		RESPONSE TO FDA REQUEST Provide information regarding nocturnal hypoglycemia and proposed revisions to clinical efficacy tables.
03/16/2000	021-081:20000316-A	QKAN FAX	Clinical CMC		GENERAL CORRESPONDENCE Copy of 3/16/00 submission providing information re nocturnal hypoglycemia and proposed revisions to clinical efficacy tables.
03/16/2000	021-081:20000316-B	QKAN TEL	Clinical Labeling		RESPONSE TO FDA REQUEST Summary of March 15 & 16 contacts: Notify Julie Rhee that NDA amendments relating to mixing Lantus with other insulins was sent. Discussed amendment withdrawing OptiPen Pro 2; information on hypoglycemia; clarification of statement in Phase IV commitment letter for retinopathy study.
03/20/2000	021-081:20000320	QKAN TEL	Clinical Labeling		REVIEW STATUS Summary of March 17 & 20. Checked on receipt of submission on nocturnal hypoglycemia, teleconference, and next version of package insert.
03/21/2000	021-081:20000321	FDA FAX	Labeling		GENERAL CORRESPONDENCE FAX from FDA providing container/carton labeling recommendations:
03/22/2000	021-081:20000322	FDA TEL	Clinical Labeling		REQUEST INFORMATION Summary of March 21 & 22. FDA called to schedule a teleconference. Also, discussed using name OptiPen "One".
03/23/2000	021-081:20000323	FDA MTG	Clinical Labeling		REQUEST INFORMATION Teleconference (FDA requested) to discuss the information the Sponsor submitted on nocturnal hypoglycemia.

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03/24/2000	021-081:20000324	FDA TEL	Clinical Labeling		INTENT TO RESPOND Julie sending revised labeling to us.
03/27/2000	021-081:20000327	FDA TEL	Clinical Labeling		REVIEW STATUS Discussed labeling for the HOE 901 file she is sending and patient information leaflets for the vial & cartridge.
03/27/2000	021-081:20000327-A	FDA EML	Labeling		REQUEST INFORMATION Received via e-mail from JRhee Physician PI FDA revision 2.doc
03/27/2000	021-081:20000327-B	FDA EML	Labeling		REQUEST INFORMATION Received via e-mail from JRhee 1) Patient PI cartridge FDA 1.doc 2) Patient PI Vial FDA 1.doc 3) OptiPen user manual FDA 1.doc
03/28/2000	021-081:20000328	FDA TEL	Clinical Labeling		REVIEW STATUS RE: Labeling for HOE 901 file
03/30/2000	021-081:20000330	QKAN LTR	Labeling		RESPONSE TO FDA REQUEST Response to changes requested in labeling, providing revised labeling.
03/30/2000	021-081:20000330-A	QKAN EML	Labeling		RESPONSE TO FDA REQUEST E-mail in response to JRhee request for electronic copy of documents from 3/30/00 submission.
03/30/2000	021-081:20000330-B	QKAN EML	Labeling		RESPONSE TO FDA REQUEST E-Mail: resending electronic document for Cartridge-clean patient information provided in previous e-mail.
03/31/2000	021-081:20000331	QKAN LTR	Labeling		RESPONSE TO FDA REQUEST Provide revised OptiPen One User Manual. The only difference between 3/30 and 3/31 OptiPen user manual submission is that the work "One" was added to the device name in the 3/31 submission.
03/31/2000	021-081:20000331-A	QKAN EML	Labeling		RESPONSE TO FDA REQUEST

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03/31/2000	021-081:20000331-B	QKAN FAX	Labeling		Provide Julie Rhee electronic copy of revised OptiPen User Manual, with the work "One" added to the device name. RESPONSE TO FDA REQUEST Provide copy of "Tab" information (info behind tabs 1 thru 6) from 3/30/00 submission.
03/31/2000	021-081:20000331-C	QKAN TEL	Clinical Labeling		REVIEW STATUS Summary of March 29, 30 & 31 contacts about HOE 901 labeling.
04/03/2000	021-081:20000403	FDA TEL	Clinical Labeling		REVIEW STATUS Julie called regarding the HOE 901 labeling teleconference scheduled for Wednesday, April 5.
04/04/2000	021-081:20000404	FDA TEL	Clinical Labeling		REVIEW STATUS Attendees for teleconference scheduled for April 5 on HOE 901 labeling will be clinical, biopharm & statistics.
04/05/2000	021-081:20000405	QKAN EML	Other		OTHER Provide information for access to teleconference (4/5/00).
04/05/2000	021-081:20000405-A	FDA TEL	EntireApplication		REVIEW STATUS Julie called to update me with comments from Dr. Misbin on our proposed labeling. Julie called to tell me that Dr. Misbin was requesting the following two items be added to the tables in the efficacy section of the PI: 1) Change in dose of basal insulin 2) Episodes of asymptomatic hypoglycemia.
04/05/2000	021-081:20000405-B	FDA MTG	Clinical Labeling		PRE-NDA/BLA MEETING Meeting Minutes of teleconference with the FDA on Wed, April 5, 2000.
04/06/2000	021-081:20000406	QKAN TEL	EntireApplication		REVIEW STATUS This report summarizes contacts with Julie Rhee on April 5 and 6, 2000, regarding the labeling for HOE 901.
04/06/2000	021-081:20000406-A	FDA EML	Labeling		GENERAL CORRESPONDENCE Provide DDMAC's comments for User Manual (OptiPen Pro 1)

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04/06/2000	021-081:20000406-B	FDA FAX	Labeling		GENERAL CORRESPONDENCE FDA provided via FAX marked-up draft package insert (FDA revision #3 dated 4/5/00)
04/10/2000	021-081:20000410	QKAN SUB	Labeling		NDA AMENDMENT Response to FDA request, providing revisions to proposed labeling.
04/10/2000	021-081:20000410-A	FDA TEL	Clinical Labeling		REQUEST INFORMATION Regarding HOE 901 labeling.
04/10/2000	021-081:20000410-B	QKAN EML	CMC Labeling		RESPONSE TO FDA REQUEST Provide revised labeling for physicians package insert and a vial storage statement, as provided in 4/10/00 submission.
04/12/2000	021-081:20000412	QKAN TEL	Clinical Labeling		REVIEW STATUS Summary of April 11 & 12 contacts regarding labeling.
04/12/2000	021-081:20000412-A	QKAN SUB	CMC Labeling		RESPONSE TO FDA REQUEST Provide response to changes requested by FDA to OptiPen One User Manual.
04/12/2000	021-081:20000412-B	QKAN EML	CMC Labeling		RESPONSE TO FDA REQUEST E-mail to JRhee, providing electronic copy of OptiPen User Manual with all changes accepted (clean version).
04/12/2000	021-081:20000412-C	QKAN EML	CMC Labeling		RESPONSE TO FDA REQUEST E-mail to JRhee, providing electronic copy of OptiPen User Manual with all changes marked.
04/12/2000	021-081:20000412-D	QKAN EML	CMC Labeling		RESPONSE TO FDA REQUEST E-mail to JRhee, providing electronic copy of drawing requested by DDMAC for the OptiPen One User Manual.
04/17/2000	021-081:20000417	QKAN TEL	Clinical Labeling		REVIEW STATUS Summary of April 13, 14 & 17 contacts regarding the labeling for HOE 901.
04/17/2000	021-081:20000417-A	FDA FAX	Labeling		REVIEW STATUS

Aventis Pharmaceuticals Inc.
Contact Tracking To/From Agency
All Corresp/Submissions/Contacts
Product History Log From 12/10/1999 to 04/21/2000

LANTUS (insuline glardine injection)
 HOE 901
 NDA 021-081

Document Date	Log # (Application # & Date)	Origin & Comm Type	Classification	Supp #/ Serial#	Description Comments
04/18/2000	021-081:20000418	QKAN TEL	Clinical Labeling		FAX of FDA revisions (dated 4/17/00) to Physician PI as well as revisions to Patient PI for vial and cartridge. REVIEW STATUS Discussions on labeling for HOE 901.
04/18/2000	021-081:20000418-A	QKAN EML	Labeling		REVIEW STATUS Eight (8) e-mails to Julie Rhee on 4/18/00 sending each file in a separate e-mail as follows: 7:04 PM, PI clean dated 4 18 00.doc 7:07 PM, PI changes marked 4 18 00.doc 7:10 PM, PIL vial clean 4 18 00.doc 7:16 PM, PIL vial changes marked 4 18 00.doc 7:18 PM, PIL cartridge clean 4 18 00.doc 7:21 PM, PIL cartridge changes marked 4 18 00.doc 7:26 PM, Optipen user manual clean 4 18 00.doc 7:26 PM, Optipen user manual changes marked 4 18 00.doc
04/18/2000	021-081:20000418-B	QKAN SUB	Labeling		NDA AMENDMENT Provide FDA Revisions to Proposed Labeling (hard copy and on diskette), based on comments received on April 17 and April 18, 2000.
04/18/2000	021-081:20000418-C	FDA FAX	Labeling		REVIEW STATUS FAX from FDA of their revisions (dated 4/18/00) for OptiPen One Insulin Delivery Device User Manual.
04/19/2000	021-081:20000419	QKAN TEL	Clinical Labeling		REVIEW STATUS Discussions on labeling for HOE 901.
04/20/2000	021-081:20000420	FDA TEL	Clinical Labeling		REVIEW STATUS Summary of April 19 & 20 contacts regarding the labeling for HOE 901.
04/20/2000	021-081:20000420-A	QKAN EML	Labeling		REVIEW STATUS

Aventis Pharmaceuticals Inc.
Contact Tracking To/From Agency
All Corresp/Submissions/Contacts
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LANTUS (insuline glardine injection)
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04/20/2000	021-081:20000420-B	QKAN SUB	Labeling		Seven (7) E-mails to FDA on April 20, 2000, providing revised labeling in separate e-mails as follows: 10:15 AM, PI clean copy 4 20 00.doc 10:19 AM, PI changes marked 4 20 00.doc 12:43 PM, PIL vial changes marked 4 20 00.doc 12:43 PM, PIL vial clean 4 20 00.doc 12:45 PM, PIL cartridge clean 4 20 00.doc 12:45 PM, PIL cartridge changes marked 4 20 00.doc 2:45 PM, sending again, PI clean copy 4 20 00.doc
04/20/2000	021-081:20000420-C	QKAN FAX	Labeling		NDA AMENDMENT Provide regvisions to proposed labeling (hard copy and diskette), based on comments received on April 20, 2000.
04/20/2000	021-081:20000420-D	QKAN FAX	Labeling		OTHER Provide FDA via FAX copy of cover letter for 4/20 submission (21-081:20000420B), providing revisions to proposed labeling.
04/21/2000	021-081:20000421	FDA TEL	Clinical Labeling		OTHER Providing FDA via FAX copy of information sent via e-mail for: Physician PI (Sponsor revision #5)--clean copy and changes marked copy.
04/21/2000	021-081:20000421-A	QKAN FAX	EntireApplication		FDA APPROVAL LETTER Julie Rhee called regarding the action letter for HOE 901 which she was getting ready to fax to us.
04/21/2000	021-081:20000421-B	QKAN LTR	EntireApplication		GENERAL CORRESPONDENCE Provide via FAX a copy of AVENTIS letter agreeing that Quintiles can receive the action letter from the Div. of Metab & Endo for NDA 21-081.
04/21/2000	021-081:20000421-C	FDA FAX	EntireApplication		GENERAL CORRESPONDENCE Submit AVENTIS letter dated 4/21/00 agreeing that Quintiles, Inc. can receive the action letter from the Div of Metab & Endo on behalf of Aventis Pharmaceuticals Inc. for NDA 21-081.
					FDA APPROVAL LETTER

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LANTUS (insuline glardine injection)
HOE 901
NDA 021-081

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04/21/2000	021-081:20000421-D	QKAN FAX	EntireApplication		Received TWO (2)FAXES: 1) 9:49 AM, approval letter for NDA 21-081, noting a hard copy of letter will follow, and 2) 9:54 AM, correction to approval letter, first page only. Correcting dates in second paragraph to eliminate 4/21. FDA asked we acknowledge via FAX.
04/21/2000	021-081:20000421-E	QKAN LTR	EntireApplication		FDA APPROVAL LETTER Per FDA request, acknowledgement via FAX indicating receipt of FDA approval letter by two (2) faxes on 4/21/00 -- one fax of complete letter and the other fax correcting page one. FDA APPROVAL LETTER Confirm receipt by Agent of both faxes dated 4/21/00 from FDA regarding the approval of NDA 21-081 and the OptiPen One Insulin Delivery Device.