

## **EXHIBIT B**

### **FDA Chronology of Significant Activities**

**Chronology of Significant Activities Regarding IND 58,647 and NDA 21-476  
for LUNESTA™ (eszopiclone) Tablets**

**(July 22, 1999 to December 15, 2004)**



Date	Type	Activity
7-22-1999	IND	Original IND Submission (12 volumes)
7-28-1999	IND	Response to FDA Request for additional desk copies
7-29-1999	IND	General Correspondence: FDA communicates assignment of IND number 58,647.
7-30-1999	IND	FDA Letter acknowledging receipt of Original IND Submission.
8-17-1999	IND	FDA Request for clarification regarding Pharm Tox section
8-19-1999	IND	Response to FDA Request for clarification of Pharm Tox section: Vols. 5 & 6 resubmitted with pages reordered
8-25-1999	IND	FDA Request for information: reformatting TK information to tabular form
8-25-1999	IND	Response to FDA Request: reformatted to tabular form information regarding cause of death for animals in TK studies
8-30-1999	IND	FDA Request for information: clarification of data in table
8-30-1999	IND	Response to FDA Request: Corrections to table
9-13-1999	IND	FDA Communication granting permission to proceed with proposed clinical studies
10-13-1999	IND	Response to FDA Request: copy of labeling for ZIMOVANE distributed in the UK
12-7-1999	IND	Response to FDA Request for Information dated September 13, 1999, and Protocol Amendments: Change in Protocol (Amendments 1 and 2 to Protocol 190-001) and revised Protocol 190-001; New Protocol 190-002; and New Investigators (Ruckle and Stoltz) for Protocol 190-002
12-15-1999	IND	General Correspondence: Final toxicology reports (28-day mouse, rat, and dog studies) expected submission date; up-coming submission of a formal meeting request and information package
1-7-2000	IND	Protocol Amendments: Protocol 190-012, Amendment 1, and Modification Notice 1; New Protocol 190-026; and New Investigator (M. Cohn) for Protocol 190-012
1-18-2000	IND	General Correspondence: Proposed meeting with FDA regarding development of eszopiclone and intent to provide a pre-meeting package
1-27-2000	IND	Information Amendment: Pharm/Tox (study summaries and final reports for 1 pharmacology study and 12 toxicology studies submitted in draft in original IND, and study summaries and final reports for 6 drug metabolism studies provided as new information) (9 volumes)
2-7-2000	IND	Information Amendment: CMC (information for comparator drug)
2-10-2000	IND	General Correspondence: Meeting request by Sepracor to discuss development of eszopiclone with proposed outline information package
2-28-2000	IND	FDA Communication setting date of pre-NDA meeting: March 20, 2000
3-2-2000	IND	Protocol Amendment: New Investigators (B. Corser, M. Scharf, and J. Schwartz) for Protocol 190-026
3-7-2000	IND	Pre-Meeting Information Package for March 20, 2000 (hand-delivered to FDA)

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3-8-2000	IND	Teleconference with FDA regarding details of planned meeting to discuss clinical development and proposed NDA
3-15-2000	IND	FDA Request for an additional reviewer desk copy of Serial No. 003, Volume 6, and questions regarding Studies 516 and 505
3-15-2000	IND	Response to FDA Request: Provided additional reviewer desk copy of Serial No. 003, Volume 6
3-16-2000	IND	Protocol Amendments: New Protocol (Protocol 190-005), and New Investigator (R.Stoltz) for 190-005
3-20-2000	IND	General Correspondence: Provided list of attendees for Monday, March 20, 2000 meeting
3-20-2000	IND	Pre-NDA Meeting with the FDA
3-27-2000	IND	Teleconference with FDA: Discussion of FDA comments regarding Protocol 190-026
3-28-2000	IND	General Correspondence: Questions from Sepracor regarding Protocol 190-026
3-29-2000	IND	FDA Request for Information: Formally submit March 28, 2000 questions in hard copy with a 1571 Form
4-4-2000	IND	Response to FDA Request: Formal submission of March 28, 2000 questions
4-4-2000	IND	FDA Letter: Pharm/Tox review of the original IND submission completed
4-26-2000	IND	General Correspondence: Status inquiry review of submitted information
4-27-2000	IND	General Correspondence: Sepracor sent additional questions regarding Study 190-026
5-5-2000	IND	Protocol Amendment: New Investigator (eight new principal investigators) for Protocol 190-026
5-24-2000	IND	Sepracor Minutes of March 20, 2000 Meeting with FDA and Submission of Presentation Slides
5-30-2000	IND	Protocol Amendment: New Investigators (Black, Rosenberg, Vollmer, and Zammit) for Protocol 190-026
5-31-2000	IND	General Correspondence: Follow-up regarding Sepracor requests for comments for Protocol 190-026; timing for an End-of-Phase 2 meeting, Aug-Sept; FDA finalizing its minutes from March 20, 2000 meeting
6-6-2000	IND	General Correspondence: Sepracor status inquiry regarding FDA comments for Protocol 190-026, and scheduling of meeting with FDA.
6-20-2000	IND	General Correspondence: Status update from FDA re Sepracor's questions
6-23-2000	IND	FDA Minutes of March 20, 2000 meeting between FDA review team and Sepracor
6-30-2000	IND	Information Amendment: Chemistry, Manufacturing, and Controls (update for drug product and placebo/diluent; & additional comparator drug and placebo to the same)
7-7-2000	IND	Protocol Amendments: Changes in Protocol Objectives (Amendment 1 to Protocol 190-026); Administrative Change 1 to Protocol 190-005; and New Investigator (P.Leese) for Protocol 190-005

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7-11-2000	IND	General Correspondence: FDA called regarding status of review and circulating letter, and requested Sepracor provide preferred dates for End of Phase II meeting
7-18-2000	IND	General Correspondence: FDA scheduled End of Phase II meeting for September 21, 2000, and meeting package is due 3-4 weeks prior
7-19-2000	IND	Protocol Amendments: New Protocols; New Investigators for 190-010 (Abdou) and for 190-015 (Leese). Information Amendment: CMC alternate supplier of comparator and a new dosage form (film coated tablets)
8-18-2000	IND	Submission of draft Protocols 190-045 and 190-046 for FDA for Division review, advice, and comment. Protocol Amendment: New Protocol, New Investigator (N.Abdou) for Protocol 190-019
8-21-2000	IND	General Correspondence: informed FDA of August 18, 2000 submission and confirmed End of Phase II meeting for September 21, 2000
8-25-2000	IND	Submission of End of Phase II Pre-Meeting Information Package (1 volume)
8-28-2000	IND	General Correspondence: FDA confirmed receipt of End of Phase II Pre-Meeting Information Package.
9-1-2000	IND	Protocol Amendment: New Protocol (Protocol 190-045, Amendment 1); and New Investigator (B.Corser) for Protocol 190-045
9-5-2000	IND	General Correspondence: change in lab name for Protocols 190-010, 190-015, and 190-019
9-11-2000	IND	General Correspondence: FDA communicated that CMC portion of End of Phase II will be independent of and immediately following clinical/tox discussion
9-13-2000	IND	General Correspondence: FDA scheduled CMC portion of End of Phase II Meeting for September 26, 2000
9-15-2000	IND	General Correspondence: Discussion with FDA confirming issues to be discussed at the End of Phase II Meetings on September 21, 2000 (tox/clin/stats) and September 26, 2000 (CMC)
9-15-2000	IND	Protocol Amendment: New Protocols, New Investigators for Protocol 190-018 (T.Stock) and for Protocol 190-020 (P.Leese)
9-20-2000	IND	General Correspondence: FDA provides list of participants for End of Phase II meeting on September 21, 2000
9-20-2000	IND	General Correspondence: Sepracor provides Agenda, Sepracor attendees, and questions for FDA discussion for End of Phase II meeting on September 21, 2000
9-21-2000	IND	End of Phase II Meeting (tox/clin/stats) with FDA
9-22-2000	IND	FDA Request for Information: two desk copies of Protocol Amendments (Protocols 190-018 and 190-020)
9-26-2000	IND	End of Phase II Meeting (CMC) with FDA
9-27-2000	IND	Response to FDA Request: submission of two additional reviewer desk copies of Protocol Amendments (Protocols 190-018 and 190-020)
10-03-2000	IND	Protocol Amendment: New Protocol, New Investigator for Protocol 190-021 (N.Abdou)

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10-5-2000	IND	FDA Request for Information: Sepracor's minutes of End of Phase II Meetings on September 21 and 26, 2000.
10-10-2000	IND	FDA Request for Information: provide details of abuse liability assessment evaluation current procedure
10-13-2000	IND	FDA Request for Information: desk copy of Protocol Amendment submitted October 3, 2000
10-13-2000	IND	Response to FDA Request: submitted desk copy of October 3, 2000 Protocol Amendment
10-18-2000	IND	FDA communication regarding review of September 15, 2000 submission
10-19-2000	IND	Protocol Amendment: New Protocols, New Investigators. Protocols 190-014, 190-022, 190-023, and 190-046; Investigator information for these 4 protocols; and 2 new Investigators for Protocol 190-045
10-24-2000	IND	FDA Letter regarding notification of content and file date requirements for annual report of progress
10-26-2000	IND	FDA Request for Information: desk copy of PK Protocols 190-022 and 190-023, and all future PK protocols
10-26-2000	IND	Response to FDA Request: submitted desk copy of PK Protocols 190-022 and 190-023
10-27-2000	IND	FDA Request for Information: another desk copy of October 3, 2000 Protocol Amendment
10-27-2000	IND	Protocol Amendment: New Protocol, New Investigator for Protocol 190-013 (G.Bloomgren)
10-30-2000	IND	Response to FDA Request: desk copy of October 3, 2000 Protocol Amendment
11-29-2000	IND	General Correspondence: list of FDA attendees at End of Phase II meetings
12-1-2000	IND	Response to FDA Request: submitted Sepracor's End of Phase II Meetings Minutes and Statistical Rationale for Protocol 190-046
12-5-2000	IND	FDA Request for Information: electronic copies of Sepracor's End of Phase II Meetings Minutes submitted on December 1, 2000
12-5-2000	IND	Response to FDA Request: provided electronic files containing the End of Phase II Meetings Minutes submitted on December 1, 2000
12-7-2000	IND	Submitted Annual Report covering the period of August 25, 1999, through August 31, 2000 (1 volume)
12-8-2000	IND	Protocol Amendment: New Protocol for Protocol 190-049
12-22-2000	IND	Information Amendment: Pharm/Tox (study summaries and final reports for two pharm studies, nine tox studies, and five drug metabolism studies) (22 volumes)
1-3-2001	IND	Protocol Amendment: Change in Protocol (Amendment 1 to Protocol 190-010); New Investigator (J. Walsh) for Protocol 190-045; and New Investigators (10) for Protocol 190-046
1-9-2001	IND	FDA Request for Information: desk copy of January 3, 2001 Protocol Amendment
1-9-2001	IND	Response to FDA Request: provided desk copy of January 3, 2001 Protocol Amendment

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1-18-2001	IND	General Correspondence: Teleconference with initiated by FDA regarding status request for study 190-010 by Biopharmaceutics reviewer, & informing FDA study is complete
1-19-2001	IND	General Correspondence: Teleconference with initiated by FDA regarding status request for study 190-022 by Biopharmaceutics reviewer, & informing FDA study is complete. Also informed FDA that studies 190-011 and 190-048 will be submitted next week
1-25-2001	IND	General Correspondence: Sepracor status inquiry regarding End of Phase II Meetings Minutes and 190-046 statistical rationale, to which FDA indicated meeting minutes are within 2 weeks of finalization
1-25-2001	IND	FDA Communication providing comments and recommendations from the Biopharmaceutical reviewers regarding submissions of October 3, 19, & 27, 2000
2-22-2001	IND	FDA Final Minutes of End-of-Phase II meetings held September 21, 2000 (tox/clin/stats) and September 26, 2000 (CMC)
2-23-2001	IND	Information Amendment: CMC (additional film-coated tablet formulation)
3-1-2001	IND	General Correspondence: provided proposed format for presentation of Abuse Liability information section of NDA
3-9-2001	IND	General Correspondence: Notified FDA of up-coming two-volume submission that will include a request for review and comment
3-21-2001	IND	Sepracor requested FDA comments and advice on an IND and a request for a teleconference; Protocol Amendments: New Protocols (190-016 and 190-048); Change in Protocols (190-045, -046 and -049) and New Investigators for 190-046, -049 and -014
3-23-2001	IND	General Correspondence: Message from FDA regarding a new FDA medical reviewer and requesting recommendations for getting new reviewer up to speed
3-28-2001	IND	General Correspondence: Teleconference with FDA's new medical reviewer discussing general program
3-28-2001	IND	Response to FDA Request: send final FDA meeting minutes for the End of Phase II meetings held on September 21 and 26, 2000.
3-30-2001	IND	Protocol Amendment: New Protocol (Protocol 190-011); New Investigator (D.Morrison) for 190-011
4-9-2001	IND	Protocol Amendments: New Protocols (190-024 and 190-025); Revised Protocol (Amendment 1 and Revised Protocol for 190-049); New Investigators for 190-013, 190-024, 190-025, 190-046, and 190-049 (3 volumes)
4-12-2001	IND	Safety Reports: Event Nos. SU190049-010328.1.I and SU190049-010404.1.I
4-12-2001	IND	Information Amendment: CMC (3.0 mg film-coated tablet formulation and matching placebo; and over encapsulated active comparator drug (diazepam tablets) and matching placebo)
4-12-2001	IND	General Correspondence: FDA requesting results of the mutagenicity battery conducted with eszopiclone, and Sepracor responded that these assays were submitted in December 2000
4-19-2001	IND	General Correspondence: Teleconference with FDA Medical Reviewer for eszopiclone regarding teleconference scheduled for April 23, 2001

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4-24-2001	IND	Sepracor submitted Briefing documents for teleconference scheduled for April 25, 2001
4-25-2001	IND	Sepracor provided 1 replacement page and one additional page for briefing documents for teleconference scheduled for April 25, 2001
5-4-2001	IND	Information Amendment: Pharmacology/Toxicology: Sepracor Document Nos. 190-831 and 190-832.
5-9-2001	IND	General Correspondence: Sepracor status inquiry to FDA regarding statistical rationales submitted for Protocols 190-045 and 190-046
5-10-2001	IND	Telephone Report for the Status of 190-045 Review.
5-14-2001	IND	General Correspondence: FDA indicated their review of statistical rationales is nearly complete
5-14-2001	IND	Protocol Amendment: New Investigators (initial investigators for Protocols 190-016 and 190-048; new investigators for Protocols 190-011 and 190-946)
5-17-2001	IND	FDA Minute for April 25, 2001 teleconference discussing current status of carcinogenicity assessment for eszopiclone
5-31-2001	IND	FDA Request for Information: clarification of Sepracor Document No. 190-818-2000
6-6-2001	IND	Protocol Amendment: New Protocols for Protocols 190-024, -025, -046, -048, and -049
6-18-2001	IND	Response to FDA Request: information requested by FDA May 31, 2001
6-22-2001	IND	Response to FDA Request: Information Amendment (Pharmacology/ Toxicology)
6-25-2001	IND	General Correspondence: faxed copy of cover letter of Response to FDA Request submitted on June 22, 2001
6-26-2001	IND	Fax for Submission of Carcinogenicity Rationale: Telephone conversations were held on June 20, 22, 25 and 26, 2001
6-27-2001	IND	FDA Letter regarding statistical review and providing comments regarding Protocols 190-045 and -046
7-3-2001	IND	IND Safety Reports: Initial Reports for Event Nos. SUI90049-010418-1, SUI90049-010516-1, SUI90049-010529-1, SUI90049-010420-1, SUI90049-010510-1, and SUI90049-010514-1
7-3-2001	IND	Response to FDA Request: answers to FDA questions regarding Studies 190-045 and -046
7-5-2001	IND	General Correspondence: Sepracor status inquiry regarding FDA response to Sepracor's July 3, 2001 submission regarding Study 190-045
7-6-2001	IND	IND Safety Report: Initial Report for Event No. SUI90049-010622-1
7-6-2001	IND	FDA Response to Sepracor's July 3, 2001 submission regarding Protocol 190-046
7-10-2001	IND	Response to FDA Request: response to FDA's June 27, 2001 letter regarding Protocols 190-045 and -046
7-10-2001	IND	General Correspondence: Correction to July 3, 2001 submission
7-18-2001	IND	Response to FDA Request: information concerning Protocols 190-045 and -046; submitted for discussion during July 18, 2001 FDA teleconference
7-24-2001	IND	Information Amendment: New Investigators (6) for 190-048
7-31-2001	IND	IND Safety Report: Initial Report for Event No. SUI90049-010718-1
7-31-2001	IND	IND Safety Report: Initial Report for Event No. SUI90048-010723-1
7-31-2001	IND	FDA Request for Information: requesting clarification of information for investigator
8-1-2001	IND	IND Safety Report: Initial Report for Event No. SUI90049-010715-1
8-2-2001	IND	Response to FDA Request for Information: provided clarification of information for investigator
8-2-2001	IND	Response to FDA Request :Information Amendment: Pharmacology / Toxicology
8-7-2001	IND	IND Safety Report: Initial Report for Event No. SU190049-010616-1
8-7-2001	IND	IND Safety Report: Follow-up Report for Event No. SU190049-010529-1
8-10-2001	IND	Response to FDA Request: Overall Clinical Development Program, Submission of Draft Clinical Protocol for Review and Comment

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Date	Type	Activity
8-15-2001	IND	IND Safety Report: Initial Report for Event No. SU190048-010806-1
8-15-2001	IND	IND Safety Reports: Initial Report for Event No. SU190049-010726-1, and Follow-up Reports for Event Nos. SU190049-010514-1 and SU190049-010715-1.
8-21-2001	IND	IND Safety Reports: Initial Reports for Event Nos. SUI90049-0107222-1, SUI90049-010809-1, and SUI90049-010516-1
8-21-2001	IND	General Correspondence: Sepracor Request for Pre-NDA Meeting
8-23-2001	IND	General Correspondence: FDA Response to request for a Pre-NDA Meeting
8-23-2001	IND	General Correspondence: Sepracor's response to FDA's proposed date for Pre-NDA Meeting
8-24-2001	IND	IND Safety Report: Initial Report (Subject C-T/S002/R0313)
8-27-2001	IND	General Correspondence: Sepracor Request for separate CMC/Biopharm Pre-NDA Meeting
8-28-2001	IND	General Correspondence: Follow-up discussion regarding meeting request
9-4-2001	IND	General Correspondence: Scheduling requested CMC Pre-NDA Meeting
9-4-2001	IND	General Correspondence: Request for re-schedule CMC Pre-NDA Meeting due to religious holiday
9-5-2001	IND	General Correspondence: Rescheduled CMC Pre-NDA Meeting from September 27 to September 28, 2001
9-10-2001	IND	General Correspondence: Teleconference confirming CMC Pre-NDA Meeting details and number of Briefing Package copies needed
9-10-2001	IND	Submitted CMC Briefing Package for pre-NDA Type B Meeting
9-14-2001	IND	Response to FDA Request: Transmitted copy of Sepracor Minutes of March 20, 2000 Meeting with FDA and Submission of Presentation Slides originally sent May 24, 2000
9-17-2001	IND	IND Safety Reports: Follow-up Report (subject AAT/S003/R0099) and Follow-up Report (subject PGC/S013/R0672)
9-19-2001	IND	General Correspondence: Advise FDA of new Sepracor official correspondent for the eszopiclone IND, and Status Inquiry regarding two reviews currently underway by FDA
9-20-2001	IND	IND Safety Reports: Initial Reports (Subjects, MAD/S030/R0626 & MAM/S007/R0035)
9-20-2001	IND	Request for comments regarding the proposal for thyroid and estradiol levels in protocol 190-049
9-20-2001	IND	General Correspondence: Change of CMC Pre-NDA meeting venue from face-to-face to a teleconference
9-24-2001	IND	General Correspondence: Fax confirmation of teleconference details for CMC Pre-NDA meeting on September 28, 2001
9-25-2001	IND	General Correspondence: Requesting update on CMC Pre-NDA meeting and follow-up
9-26-2001	IND	General Correspondence: Update on CMC Pre-NDA Meeting participants and comments on carcinogenicity (CAC Meeting) and clinical study 190-047
9-28-2001	IND	General Correspondence: Facsimile to FDA regarding 2-Year mouse carcinogenicity study
9-28-2001	IND	CMC Pre-NDA Meeting with FDA (Teleconference)
10-01-2001	IND	General Correspondence: Teleconference regarding FDA's receipt of requested information from 2-Year mouse carcinogenicity study
10-3-2001	IND	Submission of Briefing Package for Pre-NDA Type B Meeting
10-9-2001	IND	General Correspondence: Submission of Sepracor's Pre-NDA CMC Meeting Minutes (Teleconference)
10-11-2001	IND	Protocol Amendments: Change in Protocols for 190-019, -018, and -020
10-12-2001	IND	IND Safety Report: Follow-up/Final Report (Subject ALL/S004/R0285)
10-12-2001	IND	IND Safety Reports: Follow-up Report (Subject C-T/S002/R0313), Amended Final Report (Subject KAH/S007/R0242), Follow-up Report (Subject SBK/S001/R0378), Initial Report (Subject KHM/S011/R0494), Initial & Follow-up Reports (Subject RPA/S033/R0616)

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10-18-2001	IND	General Correspondence: Sepracor request for information from FDA on Pre-NDA Meeting
10-23-2001	IND	Submission of Revised and Additional Questions for Pre-NDA Meeting
10-23-2001	IND	General Correspondence: Teleconference confirming FDA's receipt of Updated Questions for Pre-NDA Meeting
10-25-2001	IND	General Correspondence: Sepracor request for information regarding FDA's Pre-NDA Review Team Meeting
10-25-2001	IND	Fax of Minutes of the Executive CAC meeting.
10-26-2001	IND	Protocol Amendments: New Protocol, Change in Protocol, New Investigators (6) for 190-047
10-29-2001	IND	FDA Pre-NDA Type B Meeting
10-31-2001	IND	General Correspondence: Submitted FDA Pre-NDA Meeting Minutes from October 29, 2001
11-1-2001	IND	General Correspondence: Pre-NDA Meeting Minutes Fax
11-6-2001	IND	FDA Internal Meeting Regarding Pre-NDA Package – FDA Request for follow-up teleconference on November 27, 2001
11-7-2001	IND	IND Safety Reports: Initial Report subject DJS/S002/R0282, Final Follow-up Report subject FWR/S004/R0012, and Follow-up Report subject VLW/S008/R0666
11-14-2001	IND	General Correspondence: Sepracor request for input on eSub/eNDA
11-16-2001	IND	FDA Letter with comments referencing Sepracor's August 10, 2001 request for comments
11-19-2001	IND	FDA Letter with comments referencing Sepracor's March 21, 2001 request for comments
11-20-2001	IND	Fax from the FDA providing copies of FDA Letters issued November 16 & 19, 2001
11-20-2001	IND	General Correspondence: Informed the Division of upcoming teleconference with Dr. Levin (FDA-CDER electronic submissions)
11-21-2001	IND	IND Safety Reports: Final Follow-up Report (Subject SBK/S001/R0378), Initial Report (Subject LTJ/S009/R0471), and Initial Report (TID/S005/R0285)
11-27-2001	IND	Pre-NDA Meeting Follow-up Teleconference with FDA
11-28-2001	IND	Response to FDA Request: Information to support monitoring of Estradiol levels in clinical studies.
11-28-2001	IND	Protocol Amendment: New Investigators for 190-047 (28), and Information Amendment: Pharmacology/Toxicology (5 reports)
11-29-2001	IND	Response to FDA Request: copy of November 28, 2001 Response to FDA Request
11-30-2001	IND	General Correspondence: Teleconference with FDA regarding follow-up on Pre-NDA Discussions and Re-Submission of the Estradiol Monitoring Rationale Information
11-30-2001	IND	Response to FDA Request: Information Amendment: Pharmacology/Toxicology (new animal study to evaluate hormonal levels)
12-3-2001	IND	General Correspondence: Submitted Sepracor's Electronic Submission (eSub)/Electronic NDA (eNDA) Meeting Minutes (Teleconference)
12-6-2001	IND	FDA Request for Information: Pre-NDA Meeting Teleconference
12-6-2001	IND	Information Amendment: Chemistry, Manufacturing, and Controls
12-7-2001	IND	General Correspondence: provided list of attendees at the November 27, 2001 Pre-NDA Follow-Up Meeting teleconference
12-7-2001	IND	Response to FDA Request: submitted Sepracor's Pre-NDA Follow-up Meeting Minutes (Teleconference)
12-7-2001	IND	Protocol Amendment: New Investigator (Pellegrino) for 190-047
12-10-2001	IND	General Correspondence: Providing list of outstanding pre-NDA questions
12-10-2001	IND	General Correspondence: discussing new Sepracor contact person for eszopiclone
12-17-2001	IND	General Correspondence: Sepracor Request for information on Preclinical Study Design

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12-18-2001	IND	General Correspondence: Discussed outstanding questions with the FDA on Pre-NDA Meeting Package Questions
12-21-2001	IND	IND Safety Report: Initial Report (1)
1-3-2002	IND	General Correspondence: FDA notice pre-assigning NDA Number 21-476 to Eszopiclone NDA
1-4-2002	IND	Protocol Amendments: Change in Protocol, Revised Protocol 190-047
1-4-2002	IND	General Correspondence: Multiple teleconferences with FDA regarding Preclinical Study Design
1-8-2002	IND	General Correspondence: FDA responses to Preclinical Study Design & Pre-NDA Minutes
1-8-2002	IND	FDA Letter regarding FDA comments after review of IND for eszopiclone, and comments on the also on the November 30, 2001 Information Amendment
1-8-2002	IND	FDA Letter providing FDA's Minutes from October 29, 2001 Pre-NDA Meeting
1-9-2002	IND	General Correspondence: Follow-up with FDA on FDA's responses to Preclinical Study Design and Pre-NDA Minutes
1-24-2002	IND	General Correspondence: FDA stating that entire toxicology section must be duplicated in the NDA
2-21-2002	IND	IND Safety Report: Follow-Up Report (Subject LTJ/S009/R0471) for Study 190-049
2-26-2002	IND	General Correspondence: Discussion of 3 mg tablets
2-26-2002	IND	Protocol Amendments: Change in Protocol for 190-049 (Amendment 3), New Investigators (190-049-3, 190-013-2, 190-014-1, 190-026-1, 190-045-3, 190-046-3, 190-047-15, and 190-048-6)
2-27-2002	IND	IND Safety Report: Initial Report (JHD/S018/R0599) for Study 190-049
2-28-2002	IND	IND Safety Report: Initial Report (Subject S002/R0410/M-B) for Study 091-049
3-1-2002	IND	General Correspondence: Discussion of CMC stability data formatting, paper review copies for NDA, and new FDA Chemistry Team Leader
3-1-2002	IND	IND Safety Report: Initial Report (Subject D717/R0233/AAB) for Study 190-047
3-3-2002	IND	FDA Letter providing comments on Protocol Amendments submitted on October 26, 2001
3-4-2002	IND	General Correspondence: Follow-up discussion with FDA regarding CMC Review Aids and paper review copies
3-6-2002	IND	IND Safety Report: Initial Report (Subject DJB/S710/R0404) and Initial Report (Subject MAE/S014/R0694) for Protocols 190-047 and 190-049
3-7-2002	IND	General Correspondence: Proposal for providing CMC NDA Review aids per March 4, 2002 teleconference with FDA
3-11-2002	IND	Official FDA Meeting Minutes from the CMC End of Phase II meeting held on September 28, 2001
3-14-2002	IND	General Correspondence: USAN name eszopiclone adopted in place of previous chemical name (esopiclone)
3-15-2002	IND	IND Safety Report: Follow-up report (Subject TID/S005/R0285)
3-15-2002	IND	IND Annual Report for September 1, 2000, through August 31, 2001
3-26-2002	IND	General Correspondence: FDA called to follow-up on the content of the proposal for CMC NDA Review Aids Sepracor provided on March 7, 2002
3-29-2002	IND	IND Safety Reports: Initial report for 190-047 (Subject WTB/S173/R0103), 2 Follow up reports for 190-049 (RDA/S033/R0616 & DRH/S025/R0636)
3-29-2002	IND	Response to FDA Request: Information relating to Protocols 190-016 and -047
4-4-2002	IND	IND Safety Reports: 2 Follow up reports for 190-047 (Subjects AAB/S717/R0233 & DJB/S710/R0494). Two initial and one follow up reports for 190-049 (Subjects ETL/S011/R0008, TPH/S007/R0665, & MAE/S014/R0694)

**Chronology of Significant Activities Regarding IND 58,647 and NDA 21-476  
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**(July 22, 1999 to December 15, 2004)**

<b>Date</b>	<b>Type</b>	<b>Activity</b>
4-10-2002	IND	IND Safety Reports: Follow up report for 190-047 (Subject DJB/S710/R0494), three follow up reports for (Subjects TPH/S007/R0494, MAM/S007/R0035, and WTB/S714/R0103)
4-18-2002	IND	General Correspondence: Request for Type A Meeting to discuss plans to submit NDA with nonclinical data on mechanistic studies of hormonal changes per FDA's November 27, 2001 request
4-22-2002	IND	IND Safety Reports: Initial Report (Subject MTG/S714), Initial Report (Subject CAK/S022/R0660), Follow-Up Report (Subject CAK/S022/R0660) for Studies 190-047 and 190-049
4-25-2002	IND	General Correspondence: Request FDA's Endocrinology Review of Clinical Protocols
4-26-2002	IND	Protocol Amendment: New Investigators (190-046) and Other Investigators – Revised Forms FDA 1572 (190-024, -046, -047, & -049)
5-6-2002	IND	IND Safety Reports: Follow-up Report (Subject MTG/S714), Follow-up Report (Subject JHD/S018/R0599) for Studies 190-047 and 190-049
5-6-2002	IND	Protocol Amendments: Change in Protocol, Revised Protocol 190-049
5-9-2002	IND	IND Safety Reports: Initial Report (Subject GAR/S008/R0222), Initial Report (Subject L-H/S007/R0486) for Study 190-049
5-9-2002	IND	Information Amendment: Pharmacology/Toxicology Request to Attend the Carcinogenicity Peer Review meeting
5-10-2002	IND	General Correspondence: FDA acknowledged Sepracor's invitation to FDA to attend a Peer Review meeting
5-20-2002	IND	IND Safety Reports: Follow-up Report (Subject MTG/S714), and Follow-up Report (Subject ETL/S011/R0008) for Studies 190-047 and 190-049
5-21-2002	IND	General Correspondence: Teleconference with FDA regarding (1) report of Peer Review meeting; (2) FDA response on assessment of the design and collection of human hormone data; and (3) Sepracor's change of address
5-22-2002	IND	FDA Letter providing comments regarding Protocols 190-046, -048, and -049
5-30-2002	IND	Notification of change in sponsor's address and relocation downtime of phone and electronic systems
6-14-2002	IND	IND Safety Reports: Follow-up Report (Subject L-H/S007/R0486), and Final Follow-up Report (Subject S011/R0008/ETL)
6-24-2002	IND	IND Safety Reports: Initial Report (Subject S018/R0732/JLH), and Follow-up Report (Subject GAR/S007/R0222) for Study 190-049
7-10-2002	IND	General Correspondence: Teleconference with FDA regarding FDA's new Chemistry Team Leader and request for additional desk copy of CMC section of NDA
7-19-2002	IND	Protocol Amendment: New Investigator (190-049), IND Sponsor Responsibilities: Termination of Investigator Participation (B.Lewis)
7-23-2002	IND	IND Safety Report: Follow-up Report (Subject JLH/S018/R0732)
8-7-2002	IND	General Correspondence: Request for Type B Meeting to Discuss and Seek the Division's Input on Pharmacology/Toxicology Issues
8-8-2002	IND	General Correspondence: Teleconference with FDA confirming receipt of Type B Meeting Request Letter, and discussing possible meeting dates
8-8-2002	IND	IND Safety Report: Follow-up Report (Subject GAR/S007/R0222)

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<b>Date</b>	<b>Type</b>	<b>Activity</b>
8-20-2002	IND	General Correspondence: Follow-up on Type B Meeting Request proposed dates for the end of September/early October 2002
8-21-2002	IND	General Correspondence: FDA contacted Sepracor regarding its decision to deny Sepracor's request for a Type B Meeting at this time
8-26-2002	IND	General Correspondence: Teleconference with FDA regarding Request for Information relating to Pharmacology/Toxicology and clarification of the Type B Meeting request.
8-26-2002	IND	FDA Letter providing comments concerning Protocol 190-016
8-29-2002	IND	FDA Letter of confirmation of FDA denial to Sepracor's request for a Type B Meeting
9-4-2002	IND	FDA Request for Information: Requested full reports of studies 190-870, Pathology Working Group, and p53 <sup>+/+</sup> knockout mouse studies
9-5-2002	IND	Response to FDA Request: Provided by facsimile information requested by FDA on September 4, 2002
9-5-2002	IND	General Correspondence: Teleconference with FDA confirming FDA's receipt of information, and timing for submission of additional information
10-3-2002	IND	Response to FDA Request: Submission of Preclinical Package with requested information on Pharmacology/Toxicology and Type B Meeting Request (11 volumes)
10-10-2002	IND	General Correspondence: Teleconference with FDA confirming receipt of Sepracor's October 3, 2002 Preclinical Package
10-23-2002	IND	General Correspondence: FDA contacted Sepracor regarding logistics for eszopiclone NDA Meeting in December 2002, and guidelines for the length of briefing package and length of the meeting
10-24-2002	IND	General Correspondence: Fax to FDA memorializing October 23, 2002 teleconference discussion regarding the upcoming NDA Meeting
11-7-2002	IND	General Correspondence: FDA's list of FDA Attendees for December 17, 2002 meeting
11-20-2002	IND	General Correspondence: Teleconference with FDA on the meeting logistics and information package for December 17, 2002 meeting
11-22-2002	IND	Submission of Information Package for TYPE B Meeting to discuss issues relating to eszopiclone NDA Submission
11-25-2002	IND	Submitted fax revisions November 22, 2002 Information Package
12-3-2002	IND	General Correspondence: Request for specific attendee at NDA Meeting on December 17, 2002
12-6-2002	IND	General Correspondence: Teleconference to discuss request for particular attendee NDA Meeting on December 17, 2002
12-10-2002	IND	General Correspondence: Follow Up on the Request for particular attend and provision of additional information
12-12-2002	IND	Addendum to TYPE B Meeting Information Package: Pertinent review articles and presentation slides
12-13-2002	IND	Addendum II to TYPE B Meeting Information Package: Follow up to Addendum to the Meeting Information Package for December 17, 2002 Meeting
12-16-2002	IND	General Correspondence: Follow up regarding Addendum II to TYPE B Meeting Information Package

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<b>Date</b>	<b>Type</b>	<b>Activity</b>
12-17-2002	IND	Type B NDA Meeting with the FDA
12-23-2002	IND	General Correspondence: Queries regarding outstanding issues for eszopiclone NDA submission
1-8-2003	IND	General Correspondence: Teleconference with FDA regarding December 23, 2002 discussion of queries regarding outstanding issues for eszopiclone NDA
1-10-2003	IND	General Correspondence: Teleconference with FDA regarding provision of Sepracor's Meeting Minutes from the December 17, 2002 meeting
1-10-2003	IND	Submission of Sepracor's Meeting Minutes from December 17, 2002 Eszopiclone NDA meeting
1-10-2003	IND	General Correspondence: Teleconference with FDA regarding outstanding issues concerning the eszopiclone NDA
1-13-2003	IND	General Correspondence: FDA contacted Sepracor to discuss outstanding questions concerning the eszopiclone NDA
1-15-2003	IND	FIELD COPY REQUIREMENTS – New England District Office Requirements for Eszopiclone NDA Field Copy
1-16-2003	IND	Sepracor's Payment of User Fee (fee for original new drug application requiring clinical data)
1-17-2003	IND	General Correspondence: Notice to provide paper copies and/or CD-Rom copies in addition to the full electronic NDA (NDA 21-476)
<b>1-30-2003</b>	<b>NDA</b>	<b>Original NDA (eNDA) Submission</b>
1-30-2003	NDA	Original NDA Submission (Field Copy)
1-31-2003	NDA	General Correspondence: Teleconference with FDA confirming Sepracor's submission of eNDA on January 30, 2003
2-5-2003	NDA	General Correspondence: Multiple teleconferences with FDA to follow-up with FDA after the receipt of the eszopiclone NDA
2-10-2003	NDA	General Correspondence: Teleconference with FDA to answer questions concerning timing of NDA/IND Annual Reports
2-12-2003	IND	Official FDA Meeting Minutes from December 17, 2002 Eszopiclone Pre-NDA Meeting
2-12-2003	NDA	General Correspondence: FDA contacted Sepracor regarding eszopiclone's status as a new chemical entity (NCE)
2-27-2003	NDA	General Correspondence: FDA contacted Sepracor to advise that a new medical reviewer was assigned to the eszopiclone NDA
2-27-2003	NDA	General Correspondence: FDA contacted Sepracor to request Sepracor send the new medical reviewer historical information between FDA and Sepracor
3-6-2003	NDA	General Correspondence: Teleconference with FDA regarding FDA's response to the two proposed submissions for the NDA
3-10-2003	NDA	General Correspondence: Teleconference with FDA regarding format for eszopiclone NDA Amendment
3-11-2003	NDA	Response to FDA Request: Information concerning Aventis IND 19,258 withdrawal
3-12-2003	NDA	FDA Request for Information: additional information concerning studies for the eszopiclone NDA
3-12-2003	NDA	Submission: Amendment 1 to NDA - Preclinical Minor Amendment NDA Section 5J – Corrected Datasets for Studies 190-833 and 190-834

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**(July 22, 1999 to December 15, 2004)**

<b>Date</b>	<b>Type</b>	<b>Activity</b>
3-13-2003	NDA	Response to FDA Request: Information requested concerning Eszopiclone NDA
3-13-2003	NDA	Response to FDA Request: Facsimile sending requested nonclinical information concerning Eszopiclone NDA
3-13-2003	NDA	General Correspondence: Communication with FDA regarding clarification of the subject for the study reports recently submitted
3-17-2003	NDA	Submission: Electronic CMC Review Aid
3-17-2003	NDA	General Correspondence: FDA contacted Sepracor to set up a Teleconference for March 18, 2003 to discuss issues relating to Eszopiclone NDA
3-18-2003	NDA	Teleconference with the FDA discussing issues pertaining to Eszopiclone NDA
3-18-2003	NDA	Submission: PDF File Containing a List of Clinical Study Report ERRATA
3-19-2003	NDA	General Correspondence: Communication with the FDA regarding expected timing for receipt of requested package of clinical related queries from March 18, 2003 Teleconference
3-19-2003	NDA	Submission: Response to March 18, 2003 Request for information
3-21-2003	NDA	Information for further clarification of clinlab and ECG collections
3-24-2003	NDA	General Correspondence: Teleconference with the FDA to discuss the Clinical Study Reports that have separate files of errata
3-24-2003	NDA	Clarification of the Clinical Study Reports submitted on March 19, 2003
3-24-2003	NDA	General Correspondence: Follow-up to Teleconference of March 24, 2003
3-24-2003	NDA	Submission: Response to Request for Information - Clinical Information
3-25-2003	NDA	Response to Request for Information: Clinical Information
3-25-2003	NDA	General Correspondence: Teleconference with the FDA to discuss the potential fileability issues identified by the FDA
3-25-2003	NDA	Submission: Amendment 2 to NDA: Errata Incorporated in Clinical Study Reports for Studies 190-012, 190-023, 190-026, 190-045 and 190-048 and Revised ISS Dataset
3-26-2003	NDA	General Correspondence: Confirmation FDA's receipt of March 25, 2003 submission
3-27-2003	NDA	FDA Request for Information: copy of the Cover letter and 356h form from the March 25, 2003 submission
3-27-2003	NDA	Response to FDA Request: Provided copy of the cover letter and 356h form for the March 25, 2003 submission
3-27-2003	NDA	General Correspondence: Teleconference with FDA to discuss the Filing Date, PDUFA Date and 74-Day Letter for NDA 21-476.
3-31-2003	NDA	General Correspondence: Confirm the site of Eszopiclone Drug Substance Release and the Drug Product Release
4-1-2003	NDA	General Correspondence: Teleconference with FDA confirm receipt of FDA queries on BioPharm NDA Section 6
4-3-2003	NDA	General Correspondence: FDA request for information to initiate Good Clinical Practices (GCP's) audits at three (3) clinical study sites
4-14-2003	NDA	FDA Filing Review Letter
4-15-2003	NDA	Submission: Request for Division Comments on Additional ISS Analyses, and Outline for Consolidated Literature Review
4-16-2003	NDA	General Correspondence: electronic copy of FDA Filing Review Letter for eszopiclone

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<b>Date</b>	<b>Type</b>	<b>Activity</b>
4-18-2003	NDA	General Correspondence: FDA contacted Sepracor to clarify the FDA Biopharm Reviewers Request for Information
4-21-2003	NDA	Submission: Response to FDA Request - Information on three Clinical Study sites for Good Clinical Practices (GCPs) audits
4-22-2003	NDA	FDA BioPharm responses to the clarification on FDA queries
4-23-2003	NDA	General Correspondence: Clarification on the electronic submission of Eszopiclone NDA 21-476 format and content of 120-day Safety Update
4-28-2003	NDA	General Correspondence: Teleconference with FDA regarding follow-up on human endocrine study
5-2-2003	NDA	General Correspondence: FDA contacted Sepracor regarding reviewer for 120-day Safety Update eSUB Outline
5-2-2003	NDA	General Correspondence: FDA contacted Sepracor to follow-up on Pharm/Tox Study
5-5-2003	NDA	General Correspondence: Multiple communications concerning the teleconference on human endocrine study protocol
5-9-2003	NDA	General Correspondence: FDA-CDER Electronic Submission Specialist accepts Sepracor's NDA 21-476 120-day Safety Update Format Hierarchy
5-12-2003	NDA	General Correspondence: Sepracor request for a teleconference to discuss CMC issues and updates.
5-14-2003	NDA	General Correspondence: Communication with FDA to review attendees from both Sepracor and FDA for May 21, 2003 teleconference to discuss Protocols 190-041 and -042
5-15-2003	NDA	General Correspondence: Sepracor contacted FDA to follow-up on request for teleconference to discuss CMC issues and updates, and schedule the same
5-16-2003	NDA	General Correspondence: FDA contacted Sepracor to confirm the CMC issues and updates teleconference for May 19, 2003
5-19-2003	NDA	Teleconference between FDA and Sepracor regarding CMC issues and updates
5-19-2003	NDA	General Correspondence: FDA contacted Sepracor indicating that FDA's endocrine consultant will attend May 21, 2003 teleconference
5-21-2003	NDA	Teleconference between FDA and Sepracor regarding Protocols
5-21-2003	NDA	FDA Request For Information: complete address of vendor
5-23-2003	NDA	General Correspondence: Sepracor informed FDA the Full Response to the FDA BioPharm Review Team will be provided by June 2, 2003
5-28-2003	NDA	General Correspondence: FDA contacted Sepracor regarding timing for Sepracor's response to the 74-Day Letter
5-28-2003	NDA	Response to FDA Request: provided complete address for vendor
5-29-2003	NDA	Submission: Amendment to NDA - Clinical Amendment Submission of Amended Clinical Study Report 190-046
6-2-2003	NDA	General Correspondence: Sepracor contacted FDA regarding timing of the 120-Day Safety Update and responses to 74-Day Letter
6-5-2003	NDA	Submission: Sepracor's Meeting Minutes from May 19, 2003 CMC Teleconference
6-12-2003	NDA	General Correspondence: Sepracor contacted FDA to discuss response to BioPharm and Pharm/Tox queries by electronic submission
6-13-2003	NDA	Submission: Amendment to NDA - Response to Biopharmaceutical Queries

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<b>Date</b>	<b>Type</b>	<b>Activity</b>
6-16-2003	NDA	General Correspondence: FDA contacted Sepracor with questions regarding location of study file
6-18-2003	NDA	Submission: Response to Pharmacology/Toxicology Reviewer Request on Historical Control Data
6-23-2003	NDA	General Correspondence: FDA contacted Sepracor to discuss FDA's questions regarding the recent electronic submission on validation reports
6-24-2003	NDA	Submission: Plan for Response to Filing Review Letter
6-24-2003	NDA	Teleconference with FDA BioPharm Reviewer to clarify outstanding issues relating to submission of validation reports
6-30-2003	NDA	Submission: Amendment to NDA - 120-Day Safety Update
6-30-2003	NDA	General Correspondence: FDA contacted Sepracor to discuss FDA BioPharm response to Sepracor's Follow-Up relating to submission of validation reports
7-3-2003	NDA	General Correspondence: Communications with FDA transmitting BioPharm information on validation reports
7-8-2003	NDA	FDA Request for Information: additional Biopharm questions
7-8-2003	NDA	Submission: Additional Response to Biopharmaceutical Queries
7-9-2003	NDA	General Correspondence: FDA contacted FDA to follow-up Division of Neuropharmacological Drug Product questions
7-10-2003	NDA	General Correspondence: FDA contacted Sepracor to follow-up on inquiries of data files the Original NDA 21-476
7-10-2003	NDA	Response to FDA Request: providing response to July 8, 2003 BioPharm request
7-10-2003	NDA	General Correspondence: Sepracor presented questions to new FDA Regulatory Project Manager
7-11-2003	NDA	General Correspondence: providing FDA with additional information concerning study
7-15-2003	NDA	Submission: Amendment to NDA - Chemistry, Manufacturing and Controls (stability updates)
7-15-2003	NDA	Submission: Amendment to NDA: Chemistry, Manufacturing and Controls (stability updates) – FIELD COPY
7-16-2003	NDA	General Correspondence: Sepracor contacted FDA to follow up on Sepracor's queries and changes at the Division
7-17-2003	NDA	General Correspondence: FDA contacted Sepracor concerning supporting evidence in the Original NDA 21-476 annotated label under special population
7-18-2003	NDA	General Correspondence: Follow-up on discussions regarding Annotated Label – Special Population of original NDA
7-21-2003	NDA	General Correspondence: communications relating to code FDA used for SAS meta analysis
7-22-2003	NDA	General Correspondence: Communication relating to clarification on the use of the code for SAS meta analysis.
7-23-2003	NDA	General Correspondence: provided location of code for SAS meta analysis
7-24-2003	NDA	FDA Request: clarification of questions regarding assessment of postmarketing cancer reports provided in 120-day Safety Update
7-25-2003	NDA	Submission: Electronic CMC Review Aid and Paper Copy of CMC Amendment dated July 15, 2003

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<b>Date</b>	<b>Type</b>	<b>Activity</b>
7-29-2003	NDA	Response to FDA Request: Sepracor's plan of response to FDA's July 24, 2003 request, and submission of Sepracor questions regarding division changes
7-30-2003	NDA	General Correspondence: FDA correspondence referencing July 25, 2003 submission redirecting mailing of e-submissions
7-31-2003	NDA	General Correspondence: Request for teleconference from FDA Pharm/Tox Reviewer on upcoming nonclinical submissions
7-31-2003	NDA	FDA Response to July 29, 2003 questions regarding changes at the Neuropharm division and query on program/software used in data analysis.
8-4-2003	NDA	Response to FDA Request: provided information regarding study site audits
8-4-2003	NDA	General Correspondence: Questions for upcoming nonclinical submission teleconference.
8-6-2003	NDA	General Correspondence: teleconference scheduling with Pharm/Tox Reviewer on upcoming nonclinical submissions
8-6-2003	NDA	FDA Request for Information: pharm/tox sample collection times
8-7-2003	NDA	Response to FDA Request: provide clarification of sample collection times
8-7-2003	NDA	General Correspondence: scheduling of teleconference
8-7-2003	NDA	Response to informal observations made during Bioresearch Monitoring Inspection July 15-29, 2003
8-8-2003	NDA	General Correspondence: Clarification on use of SPSS software
8-14-2003	NDA	General Correspondence: confirmation of receipt of request for information
8-25-2003	NDA	General Correspondence: follow-up to requested re-analysis of bioequivalence study
8-27-2003	NDA	FDA Request for Information: clarification of USAN name for eszopiclone
8-27-2003	NDA	Response to FDA Request: provided USAN adoption letter for eszopiclone and print out of the official name listing
8-27-2003	NDA	FDA Request for Information: additional information on biostats, 120-day safety update, and pharm/tox teleconference issues
8-28-2003	NDA	Submission: Amendment to NDA: Pharmacology/Toxicology Amendment 6
8-28-2003	NDA	Submission: Amendment to NDA: Response to Filing Review Letter (74-Day Letter)
8-28-2003	NDA	General Correspondence: issues pertaining to the upcoming teleconference on September 3, 2003
8-28-2003	NDA	FDA Letter finding Sepracor to be compliant with applicable statutory requirements per FDA inspection (7/15-7/29/03)
8-28-2003	NDA	General Correspondence: Follow-up to confirming sufficiency bioequivalence analysis of 2 mg and 3 mg Clinical Service and Intended-for-Market Formulations
8-29-2003	NDA	Response to FDA Requests: regarding biostats, 120-day safety update, and pharm/tox issues
9-3-2003	NDA	Teleconference between FDA and Sepracor
9-4-2003	NDA	Response to questions regarding location of metabolic scheme for zopiclone
9-4-2003	NDA	Response to request minutes of eCAC meeting re: zopiclone
9-5-2003	NDA	Report encompassing communications from September 4-5, 2003
9-5-2003	NDA	Response to FDA Request: information requested during September 3, 2003 teleconference

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<b>Date</b>	<b>Type</b>	<b>Activity</b>
9-5-2003	NDA	Response to FDA Request: Follow-up on request for information on metabolic scheme for eszopiclone and drug-drug interactions
9-10-2003	NDA	General Correspondence: provided requested guidance regarding locating raw data original NDA
9-11-2003	NDA	Response to FDA Request: provide response to September 3, 2003 teleconference questions
9-12-2003	NDA	Response to FDA Request: complete response to queries on post marketing cancer reports in 120 day Safety Update
9-12-2003	NDA	FDA Request for Information: questions on Pharm/tox CAC data
9-12-2003	NDA	Response to FDA Request: regarding pharm/tox CACA data
9-15-2003	NDA	Request for further clarification on SAS code provided September 5, 2003
9-16-2003	NDA	FDA reply and comment on information to be sent to FDA by September 18, 2003
9-17-2003	NDA	Response to FDA Request: BioPharm query
9-18-2003	NDA	FDA Request for Information: regarding SAS programs
9-19-2003	NDA	General Correspondence: Action plan regarding mouse and rat carcinogenicity studies
9-22-2003	NDA	Response to FDA Request: supplied SAS program code per September 18, 2003 request
9-24-2003	NDA	General Correspondence: Sepracor request for teleconference with clinical/statistical reviewers
9-24-2003	NDA	General Correspondence: follow-up with FDA on action plan to respond to FDA queries
9-24-2003	NDA	General Correspondence: FDA agrees to a face-to-face meeting to discuss the evidentiary basis for longer term administration claim for and to confirm that no Advisory Committee is necessary
9-25-2003	NDA	General Correspondence: Follow-up with FDA on Action Plan submitted on September 19, 2003
9-30-2003	NDA	General Correspondence: FDA response to Sepracor's Action Plan regarding mouse and rat carcinogenicity studies
9-30-2003	NDA	General Correspondence: Sepracor's response to FDA request for all inquires to go through program director
9-30-2003	NDA	General Correspondence: FDA advised it will be delayed in sending questions from pharm/tox reviewers
9-30-2003	NDA	FDA Request for Information: Questions from FDA Controlled Substance Staff on Statistics
10-1-2003	NDA	FDA Request for Information: Question from FDA Pharm/Tox Reviewer
10-1-2003	NDA	FDA response to Sepracor's September 19, 2003 communication referencing resubmission of carcinogenicity data files for NDA 21-476
10-1-2003	IND	General Correspondence: FDA advises that eszopiclone IND 58,647 Transferred from the Division of Neuropharmacological Drug Products to the Division of Anesthetic, Critical Care and Addiction Drug Products
10-1-2003	IND	General Correspondence: Follow-up with FDA on teleconference scheduling with the Division of Neuropharmacological Drug Products for Phase 3b protocols and accompanying questions
10-1-2003	NDA	Discipline Review Letter: Outlining 28 deficiencies in the CMC section of the NDA

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<b>Date</b>	<b>Type</b>	<b>Activity</b>
10-2-2003	IND	Request for Type A Meeting to discuss matters relating to our pending application and new clinical trials
10-3-2003	IND	General Correspondence: Follow-up with FDA regarding October 2, 2003 request for Type A Meeting
10-6-2003	IND	FDA Notice that eszopiclone IND transfer is complete, and the Type A Meeting request is approved and will tentatively be held on January 14, 2004
10-7-2003	IND	FDA declines request for Type A Meeting (as requested October 2, 2003)
10-8-2003	IND	General Correspondence: Follow-up with Neuropharm on the e-mail response of October 7, 2003 to a request for a Type A Meeting
10-10-2003	IND	General Correspondence: Meeting Request to the Division of Neuropharmacological Drug Products
10-10-2003	NDA	Response to FDA Request: regarding FDA's October 1, 2003 question concerning pharm/tox
10-14-2003	NDA	Submission: Request for Teleconference in Response to CMC Discipline Review Letter
10-14-2003	NDA	Nonclinical Response: Datasets of mouse and rat carcinogenicity studies
10-16-2003	NDA	Submission: Amendment to NDA: Biopharmaceutical Information Submission of Amended Clinical Study Report
10-16-2003	NDA	Response to FDA Request: information regarding data analysis
10-22-2003	NDA	FDA Letter - Response to request for meeting with DNDP
10-22-2003	NDA	FDA Request for Information: additional request from pharm/tox reviewer
10-23-2003	NDA	Response to FDA Request: provided response to October 22, 2003 pharm/tox request
10-23-2003	IND	FDA Letter - Confirming Type C Meeting (teleconference) between DACCADP, DNDP and Sepracor on January 14, 2004
10-24-2003	NDA	General Correspondence: provide a copy of a new journal article and a corresponding editorial article
10-24-2003	NDA	General Correspondence: Follow-up with FDA Division of Neuropharm
10-24-2003	IND	General Correspondence: request for a teleconference/written feedback from the Division of Anesthetic, Critical Care and Addiction Drug Products
10-29-2003	IND	General Correspondence: Response from FDA to requests from Sepracor for Division of Anesthetics feedback
10-31-2003	IND	General Correspondence: Clarification of Request to Division for input
11-10-2003	NDA	General Correspondence: Follow-up with FDA (Division of Neuropharm) on Sepracor's request for information – ECAC meeting, proprietary name and PDUFA action letter logistics
11-11-2003	NDA	Submission: Plan for Response to Chemistry Discipline Review Letter
11-13-2003	Press Release	Stating that the FDA has extended the review timetable for eszopiclone, changing it from November 29, 2003 to February 29, 2004
11-13-2003	NDA	General Correspondence: Follow-up with FDA on PDUFA Extension
11-14-2003	NDA	General Correspondence: Request to submit certain e-mail communications (with attachments) to NDA in accordance with electronic submission guidance.
11-19-2003	IND	Submission: Type C Meeting Confirmation
11-19-2003	NDA	General Correspondence: Request information on logistics of NDA transfer from the Division of Neuropharm to the Division of Anesthetic

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<b>Date</b>	<b>Type</b>	<b>Activity</b>
11-24-2003	NDA	Submission: Nonclinical Studies Cross-Referenced to NDA 21-476
11-24-2003	NDA	General Correspondence: Proposed teleconference with FDA to Discuss CMC Issues on December 8, 2003
11-25-2003	NDA	Submission: Amendment to NDA Electronic (eNDA) Submission of Clinical and Pharmacology/Toxicology Data Currently under Review
11-26-2003	NDA	FDA Request for Information: Update on status of rat reproductive study
11-28-2003	NDA	FDA Letter: Review extension letter, extending from November 29, 2003 to February 29, 2004
12-3-2003	NDA	Response to FDA Request: response to November 26, 2003 request regarding rat reproductive study
12-3-2003	NDA	FDA Request For Information- list of questions to be discussed during CMC Teleconference on December 8, 2003
12-4-2003	NDA	Response to FDA Request: Proposed agenda, list of Sepracor attendees, and specific questions for CMC teleconference on December 8, 2003
12-8-2003	NDA	CMC Teleconference between FDA and Sepracor
12-16-2003	IND	Submission: Desk copies (5) of Type C Meeting Information Package for the IND
12-16-2003	NDA	Submission: Acknowledgement of Extension of PDUFA date
12-18-2003	NDA	General Correspondence: Pharm/Tox: Summary of rat reproductive study
12-18-2003	NDA	Submission: Summary of Key Findings for Study (rat reproductive study)
12-22-2003	NDA	Submission: Sepracor's Minutes of December 8, 2003 CMC Teleconference
12-23-2003	IND	IND Annual Report: September 1, 2002 through August 31, 2003
12-23-2003	IND	Protocol Amendment: New Investigators (190-050), Revised FDA form 1572 (190-050)
1-6-2004	IND	General Correspondence: Confirmation of location and time for Type C Meeting to be held at FDA on January 14, 2004
1-9-2004	IND	General Correspondence: Postponement of January 14 meeting between FDA and Sepracor
1-16-2004	IND	Protocol Amendment: New Protocol, New Investigators (190-052)
1-21-2004	NDA	General Correspondence: Communication regarding ECAC discussion and decision regarding trade name
1-23-2004	NDA	General Correspondence: inquiry regarding ECAC meeting, if any, and trade name review
1-23-2004	IND	Protocol Amendment: New Investigators (190-050)
1-27-2004	NDA	General Communication: FDA contacted Sepracor regarding transmittal of rat study to Pharm/Tox reviewer
2-2-2004	NDA	Letter to Field Office: Notification of Electronic Submission to CDER – Amendment to a Pending Application: Response to Chemistry Discipline Review Letter Dated October 1, 2003
2-6-2004	NDA	Submission: Response to CMC Discipline Review Letter
2-6-2004	NDA	Response to FDA Request: provided Pharm/Tox Report
2-6-2004	IND	Protocol Amendment: New Protocol, New Investigator (190-054 and 190-055)

**Chronology of Significant Activities Regarding IND 58,647 and NDA 21-476  
for LUNESTA™ (eszopiclone) Tablets**

**(July 22, 1999 to December 15, 2004)**

<b>Date</b>	<b>Type</b>	<b>Activity</b>
2-9-2004	NDA	General Correspondence: Provided desk copy of rat study and related papers
2-11-2004	NDA	Submission: Amendment to NDA: Submission of Audited Draft Report on Rat Reproductive Senescence
2-11-2004	NDA	General Correspondence: Follow-up communications regarding submission of audited draft report for rat reproductive study
2-12-2004	NDA	General Correspondence: Inquiry into unreturned messages by FDA
2-13-2004	IND	Protocol Amendment: Change in Protocol, New Investigators (190-052)
2-17-2004	NDA	General Correspondence: Communications discussing status of pending NDA action
2-20-2004	NDA	General Correspondence: Follow-up to February 17, 2004 conversation - package signed February 19, 2004 and will be delivered to Dr. Temple today, with expected PDUFA letter issuance February 27, 2004
2-23-2004	NDA	General Correspondence: Follow-up communications on delivery of PDUFA action letter package
2-24-2004	IND	Protocol Amendment: Revised FDA form 1572 (190-050)
2-24-2004	NDA	General Correspondence: Action Letter is with the ODE I Division Director and probably will not be processed and signed before February 27, 2004
2-24-2004	NDA	General Correspondence: Sepracor informed FDA of interim Sepracor contact person
2-25-2004	NDA	General Correspondence: FDA informed Sepracor that Action Letter will not go out before the afternoon of February 27, 2004
2-27-2004	NDA	General Correspondence: FDA contacted Sepracor to inform that Action Letter had been signed and was Approvable
2-27-2004	NDA	FDA Letter: Approvable letter for NDA 21-476
3-1-2004	NDA	General Correspondence: Communication to discuss NDA logistics, Request for End of Review Conference, and obtain name of Regulatory Project Manager assigned to the NDA
3-2-2004	NDA	Submission: Acknowledgement of Approvable Letter and Notification of Intent to File an Amendment per 21 CFR 314.110(a)(1)
3-3-2004	IND	General Correspondence: Request for Cancellation of Type C Meeting
3-5-2004	IND	Protocol Amendment: New Protocol, New Investigators (190-054 (48) and 190-055 (42))
3-5-2004	NDA	Submission: Request for End of Review Conference
3-8-2004	NDA	General Correspondence: Communications to discuss Sepracor's upcoming letter of intent to amend the NDA; to confirm FDA's receipt of request for end of review conference, and inform FDA that Sepracor expects conference to be a Type A Meeting
3-9-2004	NDA	Submission: Request for Final Report/Summary from the Executive Carcinogenicity Assessment Committee (Executive CAC)
3-10-2004	IND	Protocol Amendment: Revised Forms FDA 1572 (Protocol 190-029)
3-11-2004	NDA	General Correspondence: Follow-up with FDA concerning the End of Review Conference date and to confirm that FDA has received recent submissions

**Chronology of Significant Activities Regarding IND 58,647 and NDA 21-476  
for LUNESTA™ (eszopiclone) Tablets**

**(July 22, 1999 to December 15, 2004)**

<b>Date</b>	<b>Type</b>	<b>Activity</b>
3-12-2004	IND	Protocol Amendment: New Protocol, New Investigators (190-052 (25))
3-15-2004	NDA	General Correspondence: Inquiry to confirm that NDA will continue to reside at HFD-120 instead of being transferred to DACCADP (HFD-170)
3-16-2004	IND	IND Safety Report: Initial Report (MFR No. 2004SP000040)
3-16-2004	IND	Protocol Amendment: Change in Protocol 190-052 (Amendment 2)
3-18-2004	NDA	General Correspondence: Follow-up on date for end of review conference
3-19-2004	NDA	General Correspondence: FDA Response to submissions dated March 5 & 9, 2004 granting meeting request & scheduling for April 16, 2004.
3-19-2004	NDA	General Correspondence: Sepracor acceptance of April 16, 2004 meeting date, and Request to discuss the nomenclature issue
3-22-2004	NDA	FDA Letter: List of FDA attendees for April 16, 2004 Type B Meeting
3-24-2004	IND	IND Safety Report: Initial Report (MFR No. 2004SP000047, 2004SP000048)
3-29-2004	NDA	General Correspondence: Inquiry as to the number of meeting information packages needed by FDA for the April 16, 2004 Type B Meeting
3-31-2004	NDA	General Correspondence: Regarding list of FDA attendees for the Type B Meeting scheduled for April 16, 2004
3-31-2004	IND	IND Safety Report: Initial Report (MFR No. 2004SP000051)
4-1-2004	NDA	Submission: Type B Meeting Information Package
4-2-2004	NDA	General Correspondence: Request confirmation of FDA's receipt of Type B Meeting Information Package
4-2-2004	NDA	General Correspondence: Submission of Type B Meeting Information Package contained an audio CD not archivable at Central Document Room (No need to resubmit)
4-5-2004	IND	Protocol Amendment: New Investigators (190-054 and 190-055) 16 new Investigators
4-7-2004	NDA	General Correspondence: FDA communication changing meeting date to May 4, 2004, and indicating resubmission will be a Class II resubmission
4-12-2004	NDA	General Correspondence: Sepracor acceptance of new meeting date of May 4, 2004
4-13-2004	IND	IND Safety Report: Initial Report (MFR No. 2004SP000048-FU1)
4-13-2004	IND	Protocol Amendment: New Investigators Revised Forms FDA 1572(Protocol 190-052) 7 new investigators and 12 revised
4-14-2004	NDA	General Correspondence: Follow-up on Nomenclature; Classification of the Resubmission; and End of Review Meeting Logistics
4-20-2004	NDA	General Correspondence: Follow up request for FDA attendees for May 4, 2004 End of Review meeting, and to confirm contact information
4-20-2004	IND	IND Safety Reports: Initial Reports (MFR Nos. 2004SP000067, and 2004SP000068)
4-23-2004	IND	IND Safety Report: Initial Report (MFR No. 2004SP000070)

**Chronology of Significant Activities Regarding IND 58,647 and NDA 21-476  
for LUNESTA™ (eszopiclone) Tablets**

**(July 22, 1999 to December 15, 2004)**

<b>Date</b>	<b>Type</b>	<b>Activity</b>
4-30-2004	IND	IND Safety Reports: Initial Reports (MFR Nos. 2004SP000080, and 2004SP000082)
4-30-2004	NDA	General Correspondence: FDA attendee list for May 4, 2004 meeting
5-3-2004	NDA	General Correspondence: adding two people to the FDA attendee list for May 4, 2004 meeting
5-4-2004	NDA	General Correspondence: New FDA attendee list for May 4, 2004 meeting with new additions
5-4-2004	NDA	End of Review Meeting between FDA and Sepracor
5-6-2004	IND	Protocol Amendment: New Investigators (190-052 and 190-054) 4 new investigators
5-7-2004	IND	IND Safety Reports: Initial Report (MFR No. 2004SP000084), Follow-Up Report (MFR No. 2004SP000067-FU1)
5-10-2004	NDA	General Correspondence: Sepracor sent FDA a complete list of Sepracor attendees to May 4, 2004 meeting, and a request for clarification on the Biopharm Waiver
5-14-2004	NDA	General Correspondence: Communication to FDA relating to open issues
5-14-2004	IND	IND Safety Reports: Initial Report (MFR No. 2004SP000090)
5-17-2004	NDA	General Correspondence: FDA Response regarding the BioPharm bioequivalence waiver
5-20-2004	NDA	Submission: Sponsor Meeting Minutes for May 4, 2004 End of Review meeting
5-21-2004	IND	Protocol Amendment: Revised Forms FDA 1572 (190-029, 190-050)
5-21-2004	IND	IND Safety Reports: Follow-Up Report (MFR No. 2004SP000049-FU1)
5-24-2004	NDA	General Correspondence: Follow-up on proposed new trade name and Sepracor's request for a full waiver of pediatric studies
5-27-2004	IND	IND Safety Reports: 2 follow-up reports (MFR Nos. 2004SP000067-FU2, and 2004SP000084-FU1)
6-2-2004	NDA	General Correspondence: FDA Response regarding new trade name and pediatric studies
6-3-2004	NDA	General Correspondence: Inquire as to FDA's receipt of Sepracor's Meeting Minutes, and expected delivery date of FDA's Official Meeting Minutes
6-3-2004	IND	IND Safety Report Initial Report (MFR No. 2004SP000113)
6-4-2004	IND	Protocol Amendment: New Investigators (190-052, 190-054 and 190-055)
6-10-2004	NDA	General Correspondence: Communication informing FDA of resubmission timing, inquiring about meeting minutes, and need to submit draft promotional material in resubmission
6-14-2004	NDA	Submission: Complete response to Action Letter dated February 27, 2004
6-14-2004	IND	IND Safety Report: 7 Day Initial Report (MFR No. 2004SP000129)
6-15-2004	IND	IND Safety Report: 1st follow-up Report (MFR No. 2004SP000082), and 2nd follow-up report (MFR No. 2004SP000084)

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for LUNESTA™ (eszopiclone) Tablets**

**(July 22, 1999 to December 15, 2004)**

<b>Date</b>	<b>Type</b>	<b>Activity</b>
6-16-2004	NDA	Submission: Field Office notification that the Complete response to Action Letter dated February 27, 2004 has been submitted to FDA
6-16-2004	NDA	General Correspondence: Requesting confirmation of FDA Division receipt of resubmission
6-18-2004	IND	IND Safety Reports: Initial Report (MFR No. 2004SP000129), Follow-Up Report (MFR No. 2004SP000068-FU1)
6-22-2004	IND	Protocol Amendment: Revised Forms FDA 1572 (190-050)
6-25-2004	IND	IND Safety Report: Initial Report (MFR. No. 2004SP000130)
6-29-2004	IND	IND Safety Reports: Follow-up Reports (MFR. Nos. 2004SP000070, 2004SP000113, 2004SP000128, and 2004SP000129)
6-29-2004	NDA	General Correspondence: Follow-up on NDA Resubmission and inquire as to 14-day acknowledgement of full response, classification, and new 2nd cycle PDUFA due date for action on resubmission
6-30-2004	IND	Protocol Amendment: New Investigator 190-052
6-30-2004	NDA	General Correspondence: Informing FDA of temporary Sepracor contact person through July 6, 2004
7-9-2004	IND	IND Safety Report: 2004SP000139 – DRAFT Medwatch Form FDA 3500A.
7-12-2004	IND	IND Safety Report: Initial Report (MFR No. 2004SP000139)
7-13-2004	NDA	General Correspondence: Follow-up on NDA resubmission: Confirm receipt of resubmission, completeness, and new action date
7-15-2004	NDA	FDA Letter acknowledging receipt of Sepracor's complete response to the agency's Action Letter of 2/27/2004
7-15-2004	NDA	General Correspondence: Sepracor's acknowledges receipt of FDA Letter concerning the complete response to the agency's Action Letter of 2/27/2004
7-15-2004	IND	IND Safety Report: Initial Report (MFR No. 2004SP000151)
7-20-2004	NDA	General Correspondence: Follow-up with FDA regarding package on new proposed trade name
7-23-2004	NDA	General Correspondence: Follow-up with the Division of Neuropharmacological Drug Products: Status of alternate trade name
7-26-2004	NDA	General Correspondence: Informal update to CMC team leader at FDA providing quick update on Type-II DMF's for racemic zopiclone
7-26-2004	IND	IND Safety Report: Initial Report (MFR No. 2004SP000155), Initial Report (MFR No. 2004SP000156)
8-2-2004	IND	Protocol Amendment: New Investigators (190-050)
8-4-2004	NDA	FDA Request for Information: CMC inquiry
8-5-2004	NDA	Response to FDA Inquiry: CMC Inquiry
8-9-2004	NDA	FDA Request for Information: courtesy desk copies of CMC Submissions from 2/6/2004 and 6/14/2004
8-9-2004	NDA	General Correspondence: confirmation of temporary FDA contact person while primary contact is on vacation

**Chronology of Significant Activities Regarding IND 58,647 and NDA 21-476  
for LUNESTA™ (eszopiclone) Tablets**

**(July 22, 1999 to December 15, 2004)**

<b>Date</b>	<b>Type</b>	<b>Activity</b>
8-9-2004	NDA	General Correspondence: Review of proposed alternate trade name
8-9-2004	IND	IND Safety Report: Initial Report (MFR No. 2004SP000172)
8-10-2004	IND	Protocol Amendment: Revised Forms FDA 1572 for Protocol 190-052 (44 investigators)
8-10-2004	NDA	General Correspondence: Follow up on primary alternate trade name, and inform FDA of plans for submitting the secondary back-up trade name
8-10-2004	NDA	Submission-Response to FDA Request: providing paper desk copies of CMC Information dated February 6, 2004 and June 14, 2004
8-11-2004	NDA	Submission: Amendment to NDA: Submission of an Alternate Proprietary Trade Name
8-12-2004	NDA	FDA Request for Information: Desk copies (3) of electronic submission of August 11, 2004
8-12-2004	NDA	Submission: Response to FDA Request: providing desk copies (3) of August 11, 2004 Alternate Proprietary Trade Name submission.
8-17-2004	NDA	Response to FDA Request: providing response to August 5, 2004 request
8-18-2004	IND	IND Safety Report: Follow-Up Reports (MFR Nos. 2004SP000113-FU2, and 2004SP000156-FU1)
8-20-2004	NDA	Submission: Amendment to NDA: Response to FDA Request for Information regarding racemic zopiclone
8-23-2004	NDA	Submission: Field Office notification of Electronic Submission to CDER - Amendment to a Pending Application: Response to FDA Request for Information
8-25-2004	IND	IND Safety Report: Follow-Up Reports (MFR Nos. 2004SP000180, and 2004SP000139-FU1), Follow-Up Report (MFR No. 2004SP000090-FU1)
8-26-2004	NDA	Submission: Amendment to NDA: Chemistry, Manufacturing and Controls
8-27-2004	NDA	Submission: Field Office notification of Electronic Submission to CDER - Amendment to NDA: Chemistry, Manufacturing and Controls.
8-31-2004	NDA	General Correspondence: Notice to FDA regarding new contact person for eszopiclone tablets
8-31-2004	IND	General Correspondence: Notification to the FDA of new Sepracor contact person for eszopiclone matters
9-2-2004	IND	Protocol Amendment: New Investigator (1), Revised Form FDA 1572 (1)
9-7-2004	IND	IND Safety Reports: 3 Initial Reports (MFR Nos. 2004SP000188, 2004SP000195, and 2004SP000194)
9-9-2004	NDA	FDA Request for Information: regarding Sepracor's June 14, 2004 submission
9-13-2004	IND	IND Safety Reports: 1 Initial Report (MFR No. 2004SP000199)
9-14-2004	NDA	General Correspondence: Communication confirming FDA will receive information requested September 9, 2004 by no later than October 12, 2004, requesting teleconference to discuss upcoming CMC submission and pending trade name
9-23-2004	NDA	General Correspondence: Provide update on pending submissions to the NDA and status inquiry regarding proposed trade name review

**Chronology of Significant Activities Regarding IND 58,647 and NDA 21-476  
for LUNESTA™ (eszopiclone) Tablets**

**(July 22, 1999 to December 15, 2004)**

<b>Date</b>	<b>Type</b>	<b>Activity</b>
9-27-2004	NDA	General Correspondence: Notice informing FDA of new Sepracor CMC contact person for the NDA
9-29-2004	NDA	Submission: Amendment to NDA: Chemistry, Manufacturing and Controls
9-30-2004	NDA	General Correspondence: Fax of cover letter for the electronic submission to NDA 21-476 mailed to the Central Document Room on September 29, 2004
9-30-2004	NDA	Submission: Notification of Electronic Submission to CDER – Amendment to NDA: Chemistry, Manufacturing and Controls
9-30-2004	NDA	Submission: Desk copy of CMC Amendment submitted on September 29, 2004
9-30-2004	NDA	Submission: Amendment to NDA: Response to Medical Review Comments dated September 9, 2004
10-1-2004	NDA	General Correspondence: Fax of cover letter for the electronic submission to NDA 21-476 mailed to the Central Document Room on 9/30/2004
10-5-2004	IND	IND Safety Reports: 3 Follow-Up Reports (MFR Nos. 2004SP000172, 2004SP000180, and 2004SP000194)
10-6-2004	IND	IND Safety Report: 1 Initial Report (MFR No. 2004SP000213)
10-7-2004	NDA	General Correspondence: Follow-up with FDA regarding status of proposed trade name review and status of NDA review
10-8-2004	IND	IND Safety Report: Follow-Up Report (MFR No. 2004SP000155-FU1)
10-14-2004	IND	IND Safety Report: Follow-Up Report (MFR No. 2004SP000151-FU1)
10-15-2004	IND	Protocol Amendment: Revised Protocols (190-054 and 190-055)
10-20-2004	IND	IND Safety Reports: Follow-Up Report (MFR No. 2004SP000130), and Follow-Up Report (MFR No. 2004SP000213)
10-21-2004	NDA	General Correspondence: Notice informing FDA of new Sepracor contact person for NDA
10-27-2004	NDA	General Correspondence: Request FDA Division to review timelines
10-28-2004	NDA	General Correspondence: Notice informing FDA of temporary Sepracor contact person for NDA on 10/29/2004
11-1-2004	NDA	General Correspondence: Status inquiry regarding proposed trade name review
11-1-2004	NDA	FDA Request for Information: CMC Question
11-2-2004	NDA	Response to FDA Request: Follow-up to November 1, 2004 CMC question, and request for update on status of Label review
11-4-2004	NDA	General Correspondence: Status inquiry regarding proposed trade name
11-4-2004	IND	IND Annual Report (September 1, 2003, through August 31, 2004)
11-4-2004	IND	General Correspondence: Transfer of IND Responsibility
11-5-2004	IND	IND Safety Report: Follow-Up Report (MFR No. 2004SP000195)
11-5-2004	IND	IND Safety Reports: Follow-Up Report (MFR No. 2004SP000172)
11-5-2004	NDA	General Correspondence: Follow-up with FDA on Sepracor's response to CMC question
11-5-2004	NDA	Submission: Response to FDA Request: Response to FDA CMC Question of November 1, 2004

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for LUNESTA™ (eszopiclone) Tablets**

**(July 22, 1999 to December 15, 2004)**

<b>Date</b>	<b>Type</b>	<b>Activity</b>
11-8-2004	NDA	FDA Request: Provide alternative trade name for eszopiclone tablets
11-8-2004	NDA	FDA Request for Information: Additional CMC questions
11-8-2004	NDA	Response to FDA Request: provide information regarding additional CMC questions
11-8-2004	NDA	Submission: Amendment to NDA: Submission of an Alternate Proprietary Trade Name - Lunesta™
11-9-2004	NDA	General Correspondence: Sepracor Inquiry regarding any further actions Sepracor can take to assist FDA review team
11-9-2004	NDA	FDA Request for Information: CMC - updated stability data tables
11-9-2004	NDA	Response to FDA Request: Communication regarding CMC request for updated stability tables received November 9, 2004
11-9-2004	NDA	Submission: Amendment to NDA: Response to FDA Request for Information
11-9-2004	NDA	General Correspondence: Follow-up on Sepracor's response to CMC question November 1, 2004
11-9-2004	NDA	General Correspondence: Status Inquiry regarding new proposed trade name review, and review of NDA
11-10-2004	NDA	Submission: Notification of Electronic Submission to CDER: Amendment to NDA - Response to FDA Request for Information
11-11-2004	NDA	General Correspondence: Additional Status Inquiry regarding new proposed trade name review, and review of NDA
11-12-2004	NDA	General Correspondence: Communication inquiring if DMETS received alternate trade name submission of November 8, 2004
11-12-2004	NDA	General Correspondence: FDA Response to Sepracor's status inquiries
11-16-2004	NDA	General Correspondence: Follow up on Sepracor's November 8 & 9, 2004 responses to CMC requests
11-16-2004	NDA	Submission: e-mails stability update information for NDA 21-476
11-17-2004	NDA	FDA Request for Information: copies of most recent version of annotated labeling and location of same in previous submission
11-17-2004	NDA	Response to FDA Request: Submitted annotated labeling with track changes
11-17-2004	NDA	Response to FDA Request: provided information on where to find track changes labeling in a previous submission
11-18-2004	NDA	General Correspondence: Communication from FDA informing Sepracor review is underway for most recent trade name submission for eszopiclone tablets
11-18-2004	NDA	FDA Request for Information: Update carton and container labels
11-19-2004	NDA	General Correspondence: Sepracor acknowledges receipt of November 18, 2004 FDA request and inquires as to status of trade name review
11-19-2004	NDA	Submission: Amendment to NDA: Response to FDA Request for Information regarding updated carton and container labels
11-19-2004	NDA	Response to FDA Request: Follow up to request for updated container and carton labeling

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**(July 22, 1999 to December 15, 2004)**

<b>Date</b>	<b>Type</b>	<b>Activity</b>
11-22-2004	NDA	Submission: Amendment to NDA: Submission of an Alternate Proprietary Trade Name
11-23-2004	NDA	General Correspondence: Communication informing FDA of two recent submissions
11-23-2004	NDA	General Correspondence: Notice to FDA regarding temporary Sepracor contact person between November 24 and December 3, 2004
11-23-2004	NDA	FDA Communication forwarding proposed draft labeling for eszopiclone tablets, and indication of FDA's availability on November 24, 2004 to discuss any questions
11-23-2004	NDA	Response to FDA Request: Providing PDF versions of revised carton and container labeling
11-23-2004	IND	IND Safety Reports: 8 Follow-up reports relating to 190-052 unblinding, 1 Follow-up report relating to 190-050
11-24-2004	NDA	Submission: Amendment to a Pending Application: Response to FDA Request for Information
11-24-2004	NDA	Teleconference with FDA to discuss November 23, 2004 Draft Label
11-24-2004	IND	IND Safety Reports: Follow-up report (MFR No. 2004SP000188-FU1)
11-29-2004	NDA	Revised Label Update
11-29-2004	NDA	Revised Label Update Discussion with Controlled Substance Staff
11-29-2004	NDA	General Correspondence: Notice from FDA regarding temporary FDA contact person from November 30 to December 2, 2004
11-29-2004	NDA	General Correspondence: Exchange of Certificates to Establish Secure e-mail link between Sepracor and FDA
11-29-2004	NDA	Teleconference to discuss Draft label with the Controlled Substance Staff
12-1-2004	NDA	Submission: Notification of Electronic Submission to CDER: Amendment to NDA – Chemistry, Manufacturing and Controls
12-1-2004	NDA	Submission: Revised Draft Labeling
12-1-2004	NDA	Submission: Revised Draft Labeling
12-2-2004	NDA	General Correspondence: Continuing discussions with FDA concerning revised Draft Labeling and DDMAC submissions
12-6-2004	NDA	Notice regarding DMETS assessment and assignment of trade name Lunesta™
12-7-2004	NDA	Teleconference discussing proposed label changes for various sections
12-7-2004	NDA	Responses to FDA Requests: responses to FDA comments and requests of December 7, 2004
12-8-2004	NDA	General Correspondence: FDA transmittal of Draft Labeling as of 12/7/2004
12-8-2004	NDA	General Correspondence: Follow up with FDA on status of DEA notification that eszopiclone has been determined to be Class IV drug
12-8-2004	NDA	Teleconference with FDA regarding proposed Labeling/package insert

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**(July 22, 1999 to December 15, 2004)**

<b>Date</b>	<b>Type</b>	<b>Activity</b>
12-8-2004	NDA	General Correspondence: Teleconference regarding clarification of how FDA will communicate approved trade name; FDA agreed to send an e-mail with confirmation of the name Lunesta™
12-8-2004	NDA	General Correspondence: E-Mail Notification from FDA establishing Lunesta™ as approved trade name for eszopiclone
12-8-2004	NDA	General Correspondence: Sepracor Request that FDA provide WORD version of proposed Labeling from the approvable letter.
12-8-2004	NDA	General Correspondence: FDA response to Sepracor request for WORD version of proposed Labeling from approvable letter
12-8-2004	NDA	Submission: Revised draft Labeling as of 12/8/2004 after late afternoon discussions with FDA
12-8-2004	NDA	General Correspondence: Communication to FDA informing FDA of Sepracor's submission of revised draft Label after discussions with FDA
12-8-2004	NDA	Submission: Draft CMC blister labeling and request for FDA input
12-9-2004	NDA	General Correspondence: FDA sending December 6, 2004 draft Controlled Substance section of Labeling to Sepracor
12-10-2004	NDA	General Correspondence: Sepracor providing label comparison file to FDA
12-13-2004	NDA	Submission: Lunesta (eszopiclone) Press Release for DDMAC approval
12-13-2004	NDA	General Correspondence: Request for assignment of a DDMAC reviewer and expedited review of Lunesta (eszopiclone) press release
12-13-2004	NDA	Submission: Revised Draft Label, December 8, 2004
12-13-2004	IND	Protocol Amendment: Revised Forms FDA 1572 for Protocol 190-050 (71 investigators)
12-14-2004	NDA	General Correspondence: FDA transmitting proposed Final Labeling for NDA 21-476
12-14-2004	NDA	Submission: Revised Draft Labeling for NDA 21-476
12-14-2004	NDA	Teleconferences between FDA and Sepracor regarding clarification of Final Labeling wording for NDA 21-476
12-15-2004	IND	Protocol Amendment: New Investigator (1), Revised Forms FDA 1572 (1) for Protocol 190-050
12-15-2004	NDA	General Correspondence: Communication regarding carton label language
12-15-2004	NDA	General Correspondence: Multiple communications regarding latest version of revised carton and container labeling
12-15-2004	NDA	General Correspondence: FDA confirming receipt of latest version of carton label language
12-15-2004	NDA	Submission: Revised Draft Labeling (latest version requested by FDA)
12-15-2004	NDA	FDA Letter of approval for NDA 21-476