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**NDA SUBMISSION LOGBOOK**

**NDA No. 21-468**

**Title: FOSRENOL™ (Lanthanum Carbonate Hydrate)**

**Submission to FDA**

Submission No	Type of Submission	To/From	Date
095	General Correspondence: Final Draft Labels and Labeling	To: Dr. Stockbridge Fm: L. Wittmer	10/20/04
094	General Correspondence: Request for Type C Meeting	To: Dr. Stockbridge Fm: L. Wittmer	10/21/04
Regcon	To discuss timings and plan for submission of launch materials to DDMAC	To: L. McLeroy & M. Kiester Fm: D. Ahern	10/19/04
Regcon	To discuss the status of the Agency's feedback on the optimized formulation, and to confirm the upcoming Nov. 16 FDA meeting	To: D. Hinton Fm: L. Wittmer	10/18/04
093	General Correspondence: Final Draft Labeling (revised)	To: EDR Fm: D. Ahern	10/14/04
Email	Fosrenol labeling: final draft labeling with deletions as agreed by FDA, and corrected misspelled word of "administered"	To: D. Hinton Fm: L. Wittmer	10/12/04
092	General Correspondence: Final Draft Labeling	To: EDR Fm: D. Ahern	10/11/04
Email	Bottle label revisions	To: D. Hinton Fm: L. Wittmer	10/8/04
Email	Revised sample bottle label (250mg) for patient sample to match commercial labels	To: D. Hinton Fm: L. Wittmer	10/8/04
Email	Fosrenol labeling: supportive data packet for reference	To: D. Hinton Fm: L. Wittmer	10/6/04
Email	Fosrenol labeling: updated PI to reflect FDA's comments; alternative presentation of the AE section	To: D. Hinton Fm: L. Wittmer	10/6/04

**NDA SUBMISSION LOGBOOK**

**NDA No. 21-468**

**Title: FOSRENOL™ (Lanthanum Carbonate Hydrate)**

**Submission to FDA (continued)**

Submission No.	Type of Submission	To/From	Date
091	CMC Amendment: Withdrawal of optimized formula, 250, 500, 750, and 1000mg.	To: Dr. Stockbridge Fm: L. Wittmer	10/1/04
Email	Updated PI with tentative agreements made with the Agency	To: D. Hinton Fm: L. Wittmer	10/1/04
Email	Feedback on FDA's proposed wording for PI	To: Dr. Stockbridge Fm: L. Wittmer	9/20/04
Email	Additional revision to Fosrenol PI (change to line 64)	To: D. Hinton Fm: L. Wittmer	9/15/04
Email	Proposed package insert for Fosrenol in Word, and side-by-side comparison of the wording (FDA vs. Shire)	To: Dr. Raman Fm: L. Wittmer	9/13/04
090	General Correspondence: CMC (commitment to place first 3 validation/production batches on stability per SN086)	To: Dr. Stockbridge Fm: L. Wittmer	9/10/04
Email	Additional information wrt the proposed commercial pack (500mg/100count)	To: Dr. Raman Fm: L. Wittmer	9/10/04
Email	Information on double-blind studies for PI	To: D. Hinton Fm: L. Wittmer	9/7/04
089	CMC Amendment: Updated lanthanum carbonate specification and test methods for 250mg and 500mg current formula to support the use of Apparatus 2 dissolution method	To: Dr. Stockbridge Fm: L. Wittmer	9/2/04
088	General Correspondence: Meeting Minutes (CMC and Biopharm Teleconference 27-Aug-04)	To: Dr. Stockbridge Fm: L. Wittmer	9/2/04

**NDA SUBMISSION LOGBOOK**

**NDA No. 21-468**

**Title: FOSRENOL™ (Lanthanum Carbonate Hydrate)**

**Submission to FDA (continued)**

Submission No.	Type of Submission	To/From	Date
087	General Correspondence: Pharmacovigilance Risk Management Plan Supplement	To: Dr. Stockbridge and Desk Copy Hinton Fm: L. Wittmer	9/1/04
Regcon	To discuss an email sent to FDA on 8/19/04 regarding Biopharm and CMC issues	To: D. Hinton Fm: L. Wittmer	8/26/04
Regcon	Discuss Fosrenol Pharmacovigilance Risk Management Plan with FDA	To: D. Hinton and FDA Fm: D. Ahern and Team	8/19/04
086	Response to Request for Information – CMC Section (Cumulative Revisions)	To: Dr. Stockbridge and FIELD OFFICE COPY Fm: L. Wittmer	8/18/04
085	Response for Request for Information – Revised Labels and Labeling	To: FDA Central Document Room/EDR Fm: L. Wittmer	8/11/04
084	General Correspondence: CMC Correction to Zirconium specification	To: Dr. Stockbridge Fm: L. Wittmer	8/06/04
Letter	Desk copies of ISE Submission No. 000 Volume 1.78, ISE 15-month submission No. 066 (Volumes 17-36) and ISS 25-month No. 074 (Volumes 1-3)	To: D. Hinton Fm: L. Wittmer	7/29/04
083	Response to Request for Information (Updated current formulation specs)	To: Dr. Stockbridge Fm: L. Wittmer	7/26/04
082	Response to Request for Information (Dissolution data and update specifications; Pharmacodynamic equivalence – responses to inspection items; Sample bottle labels)	To: Dr. Stockbridge Fm: L. Wittmer	7/23/04
Email	Response to request for AEs treatment emergent by age group	To: D. Hinton Fm: L. Wittmer	7/22/04
Email	Error on pack size of 250cc instead of 300cc; will forward new artwork with correct dimensions	To: D. Hinton Fm: L. Wittmer	7/22/04
Email	Confirmed that USP names of inactives should be used for bottle labels	To: Dr. Raman Fm: L. Wittmer	7/21/04
Email	Current formulation bottle labels	To: D. Hinton Fm: L. Wittmer	7/21/04

### NDA SUBMISSION LOGBOOK

NDA No. 21-468

Title: FOSRENOL™ (Lanthanum Carbonate Hydrate)

Submission to FDA (continued)

Submission No	Type of Submission	To/From	Date
Email (regcon)	FDA agreed with API specs proposal	To: Dr. Raman Fm: J. Ferdinando	7/19/04
Email	Response to clinical questions (safety and efficacy analyses on subpopulation of patients over 65 years old; fracture analysis for 25-month ISS dataset)	To: D. Hinton Fm: L. Wittmer	7/19/04
Regcon	To let Denise know to expect one bottle each of 250 mg and 500 mg tablets	To: D. Hinton Fm: K. Epperly	7/19/04
Letter	Samples of 250 mg and 500 mg tablets	To: D. Hinton Fm: L. Wittmer	7/19/04
Email	More info on 250 mg current formulation dissolution testing using Apparatus 2	To: Dr. Raman Fm: J. Ferdinando	7/19/04
Email	Updated lanthanum oxide specification	To: Dr. Raman Fm: J. Ferdinando	7/19/04
Email	SPD405-116 Inspections (Shire's response to the 483s issues to vendors) updated scanned copies	To: D. Hinton Fm: L. Wittmer	7/16/04
Email	Crushed tablet dissolution data	To: Dr. Raman Fm: J. Ferdinando	7/15/04
Email	Raw data for the other dissolution media to the data provided to Dr. Dorrantes	To: D. Hinton Fm: L. Wittmer	7/15/04
Email	SPD405-116 Inspections (Shire's response to the 483s issues to vendors)	To: D. Hinton Fm: L. Wittmer	7/14/04
Email	Expanded dissolution data as requested on the current formulation	To: Dr. Raman Fm: J. Ferdinando	7/14/04
Email	Fracture rates (updated tables to respond to Dr. Williams' concerns that the fracture rates by exposure category may be misleading due to patients with minimal lanthanum exposure were included in the analysis)	To: Dr. Williams Fm: L. Wittmer	7/13/04
Email	Current formulation dissolution profiles (individual profiles for 250mg and 500mg tablets)	To: D. Hinton Fm: L. Wittmer	7/13/04

### NDA SUBMISSION LOGBOOK

NDA No. 21-468

Title: FOSRENOL™ (Lanthanum Carbonate Hydrate)

Submission to FDA (continued)

Submission No	Type of Submission	To/From	Date
081	Uremic Rat Bone - Pathology report	To: Dr. Stockbridge Fm: L. Wittmer	7/12/04
080	CMC Amendment (Updated metal specification, including scandium and indium; Updated hardness specifications; Commitment that blend uniformity will be an in-process test; Lanthanum hydroxycarbonate LOQs)	To: Dr. Stockbridge Fm: L. Wittmer	7/12/04
Regcon	To reconcile FDA's requests for information with what has been submitted; To request feedback on biopharm review, specifically feedback on the inspection results; To request update from FDA's internal labeling meeting; To confirm scheduled labeling discussion on 7/15/04	To: D. Hinton Fm: L. Wittmer	7/9/04
Email	Updated tablet spec which include the tightened hardness limits	To: Dr. Raman Fm: J. Ferdinando	7/9/04
Email	Statement from Shire committing to test scandium and indium with safety justifications for the limits; authorized revised specs to reflect new levels of metals in the API	To: Dr. Raman Fm: J. Ferdinando	7/9/04
Email	GI and MS AE event tables	To: D. Hinton Fm: L. Wittmer	7/9/04
079	CMC Amendment (Dissolution Data Update and Biowaiver Report)	To: Dr. Stockbridge Fm: L. Wittmer	7/8/04
Email	Fracture tables adjusted for discontinuations	To: D. Hinton Fm: L. Wittmer	7/8/04
Email	Confirmation regarding adding Indium and Scandium to API specs	To: Dr. Raman Fm: J. Ferdinando	7/8/04
Email	Blend uniformity; chewability and hardness; metal impurity testing of API; XRD method	To: Dr. Raman Fm: J. Ferdinando	7/7/04
078	Table outlining studies in which healthy volunteer have received lanthanum	To: Dr. Stockbridge Fm: L. Wittmer	7/6/04
Email	Clarification on LOQ values and specifications for tablets	To: D. Hinton Fm: J. Ferdinando	7/2/04

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**NDA No. 21-468**

**Title: FOSRENOL™ (Lanthanum Carbonate Hydrate)**

**Submission to FDA (continued)**

Submission No.	Type of Submission	To/From	Date
Regcon	Telecon to discuss ongoing CMC issues	To: Dr. Raman Fm: Jo Ferdinanco	6/29/04
Email	Proposed Packaging Configurations	To: D. Hinton Fm: R. Lilley	6/25/04
Email	Response to CMC Review Questions from 17-Jun-04 meeting	To: Dr. Raman Fm: R. Lilley	6/25/04
077	General Correspondence: Response to FDA Request for Information (summary of fracture data)	To: Dr. Stockbridge Fm: L. Wittmer	6/24/04
076	General Correspondence: Meeting Summary from 17-Jun-2004 (with attachments on GI AE outcomes adjusted, clarification of mortality analysis, reviewer's guide to GI AE data, and guide to bone fracture data)	To: Dr. Stockbridge Fm: L. Wittmer	6/21/04
Email	Line-numbered annotated labeling (Word and PDF versions)	To: D. Hinton Fm: L. Wittmer	6/21/04
Email	Response to Dr. Williams' request for info on number of patients with diabetes in studies, and patients who had bone biopsies	To: D. Hinton Fm: L. Wittmer	6/15/04
Email	Bone histology	To: Dr. Williams Fm: L. Wittmer	6/11/04
075	Briefing Package for FDA Meeting on 11-Jun-2004	To: Dr. Stockbridge Fm: L. Wittmer	6/2/04
074	General Correspondence: Request for Information (Safety Update for LAM-IV-307)	To: Dr. Stockbridge Fm: L. Wittmer	6/1/04
073	CMC Amendment (Dissolution Method Devt, Updated Stability Reports for API, Optimized Formulation and Current Formulation)	To: Dr. Stockbridge Fm: L. Wittmer	5/28/04
Email	Overview of Risk Management Plan	To: D. Hinton Fm: L. Wittmer	5/24/04

### NDA SUBMISSION LOGBOOK

NDA No. 21-468

Title: FOSRENOL™ (Lanthanum Carbonate Hydrate)

Submission to FDA (continued)

Submission No.	Type of Submission	To/From	Date
<b>Regcon</b>	To request an update from FDA's internal review meeting	To: D. Hinton Fm: L. Wittmer	5/18/04
<b>Email</b>	Request clarification regarding Dr. Williams' statement referring to slides/study of bone histology data	To: Dr. Williams Fm: L. Wittmer	5/6/04
<b>071</b>	General Correspondence: Bioanalytical Reports for the plasma/urine lanthanum assays	To: Dr. Throckmorton Fm: L. Wittmer	5/6/04
<b>072</b>	General Correspondence: Response to Information Request Letter (bone histological slides)	To: Dr. Throckmorton Fm: L. Wittmer	5/5/04
<b>Email</b>	Copy of Shire's internal tracking of correspondence/submission to FDA	To: D. Hinton Fm: L. Wittmer	4/20/04
<b>Email</b>	Follow-up on request for bone biopsy reference	To: D. Hinton Fm: L. Wittmer	4/14/04
<b>Email</b>	Propose an incremental safety update (ISS)	To: Dr. Throckmorton Fm: L. Wittmer	4/14/04
<b>Email</b>	Follow-up on proposal to provide 18-mos stability data on Boots tablet batches at the end of May	To: Dr. Raman Fm: L. Wittmer	4/13/04
<b>Email</b>	Follow-up on 1) FDA request for survival data for patients excluded from lanthanum carbonate clinical studies; 2) feedback on justification for examining bone toxicities using histomorphometry (SN068); 3) adequacy of PD equivalence data	To: Dr. Throckmorton Fm: L. Wittmer	4/8/04
<b>070</b>	Response to Request for Information (CMC)	To: Dr. Throckmorton Fm: L. Wittmer	4/1/04
<b>069</b>	Response to Request for Information (Gastrointestinal AE)	To: Dr. Throckmorton Fm: L. Wittmer	4/1/04
<b>Regcon</b>	- To discuss the timeframe for submission of the stability and safety updates; and - To discuss the timing of receipt of the request for information letter	To: D. Hinton Fm: L. Wittmer	3/29/04
<b>Email</b>	Outlines Shire's actions resulting from our recent telephone conference with the Biopharmaceutics and Chemistry reviewers on 10 March 2004	To: D. Hinton Fm: L. Wittmer	3/23/04

**NDA SUBMISSION LOGBOOK**

**NDA No. 21-468**

**Title: FOSRENOL™ (Lanthanum Carbonate Hydrate)**

**Submission to FDA (continued)**

Submission No	Type of Submission	To/From	Date
068	Response to FDA Request for Information (rationale for histomorphometric interpretation of bone biopsy data; fracture analysis; mortality data)	To: Dr. Throckmorton Fm: L. Wittmer	3/22/04
Email	Follow-up re: Dr. Williams' comment about patient profiles not readable	To: D. Hinton Fm: L. Wittmer	3/16/04
Email	Clinical mass balance study	To: D. Hinton Fm: L. Wittmer	3/16/04
Email	To provide response timings of FDA request for info from the resubmission filing, and to request a letter from the Division in order to address specific questions raised	To: D. Hinton Fm: L. Wittmer	3/11/04
Email	Preliminary response to Dr. Dorantes' question regarding fecal excretion data from orally-dosed subjects	To: D. Hinton Fm: L. Wittmer	3/8/04
Email	Will respond to request for number of patients in each group with at least one GI event with duration >28 days/unresolved	To: V. Freidlin Fm: L. Wittmer	3/5/04
Email	Table 1 of resolution of GI AE, source tables and SAS program	To: D. Hinton Fm: L. Wittmer	3/3/04
Email	Mortality analyses update (for discussion during teleconference with FDA on 3/2/04)	To: D. Hinton Fm: L. Wittmer	3/1/04
Email	Table 2 of proposed package insert with incidence of AE adjusted for exposure	To: D. Hinton Fm: L. Wittmer	3/1/04
Email	General inquiry regarding review time and feedback on bioequivalence data for study SPD405-116	To: D. Hinton Fm: L. Wittmer	2/23/04
Email	Provide official address of additional analytical testing lab (RSSL), as requested	To: Dr. Raman Fm: L. Wittmer	2/17/04
Email	Additional documents that were not included in the resubmission: - LAM-IV-307 (2nd interim report) - Patient listings - LAM-IV-301e (report addendum) - Case report forms for SAEs and	To: D. Hinton Fm: L. Wittmer	2/4/04

	<b>study discontinuations</b>		
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NDA No. 21-468

Title: FOSRENOL™ (Lanthanum Carbonate Hydrate)

Submission to FDA (continued)

Submission No.	Type of Submission	To/From	Date
067	Resubmission of Electronic Component of New Drug Application	To: Dr. Throckmorton Fm: L. Wittmer	2/2/04
066	Resubmission of New Drug Application (89 volumes on shelf)	To: Dr. Throckmorton Fm: L. Wittmer	1/26/04
Regcon	<ol style="list-style-type: none"> <li>1) Ask questions regarding the format and content of the resubmission,</li> <li>2) Confirm receipt of protocol 312 and the accompanying CMC amendment, and</li> <li>3) Request feedback on bioequivalence.</li> </ol>	To: D. Hinton Fm: L. Wittmer	1/14/04
Email	Follow-up items from 3-Dec-2003 FDA meeting	To: D. Hinton Fm: L. Wittmer	12/9/03
Email	Updated list of Shire attendees for FDA meeting on 3-Dec-2003	To: D. Hinton Fm: G. Miller	12/2/03
Regcon	To request a meeting confirmation and preliminary feedback from FDA regarding the briefing package for the 3 December 2003 meeting.	To: D. Hinton Fm: L. Wittmer	11/25/03
065	Clinical Amendment: Final Clinical Study Report SPD405-116	To: Dr. Throckmorton Fm: L. Wittmer	11/25/03
064	Pre-resubmission Briefing Package (to be held on 3-Dec-2003)	To: Dr. Throckmorton Fm: L. Wittmer	11/10/03
Email	Additional bone lanthanum and histomorphometry data that will be included in the briefing package for the upcoming 3 December 2003 meeting.	To: D. Hinton Fm: L. Wittmer	10/28/03
Email	Additional information on the SPD405-116 study to fulfil FDA's request for retrospective power estimation for the 116 study (per the teleconference on 21 October 2003).	To: D. Hinton Fm: L. Wittmer	10/28/03
Regcon	To provide the preliminary results of the analysis of additional biopsies (bone lanthanum levels) to FDA so that they are prepared to receive the briefing package next week and able to give us some feedback of impact on ongoing activities, particularly the 3b program.	To: D. Hinton Fm: L. Wittmer	10/27/03

**NDA SUBMISSION LOGBOOK**

**NDA No. 21-468**

**Title: FOSRENOL™ (Lanthanum Carbonate Hydrate)**

**Submission to FDA (continued)**

Submission No.	Type of Submission	To/From	Date
Email	Bioequivalence (Optimized Formulation) PK Data Preliminary PK data from 116 study	To: D. Hinton Fm: L. Wittmer	10/15/03
Regcon	Inquire about the acceptability of urinary phosphate in healthy volunteers as a measure of bioequivalence (FDA feedback on submission #062).	To: D. Hinton Fm: L. Wittmer	10/15/03
063	General Correspondence: Copy of USAN Letter	To: Dr. Throckmorton Fm: L. Wittmer	9/5/03
062	General Correspondence: BE Study Justification	To: Dr. Throckmorton Fm: L. Wittmer	8/27/03
061	General Correspondence: Meeting summary from 7-Aug-03 FDA meeting	To: Dr. Throckmorton Fm: L. Wittmer	8/27/03
060	Meeting Information Package (Revision)	To: Dr. Throckmorton Fm: L. Wittmer	8/4/03
Email	Additional dissolution figure (for meeting info package)	To: D. Hinton Fm: L. Wittmer	8/4/03
059	Meeting Information Package (CMC meeting on 7-Aug-03)	To: Dr. Throckmorton Fm: L. Wittmer	7/21/03
Email	To inform CSO the CMC briefing packet will be hand-delivered tomorrow morning.	To: D. Hinton Fm: L. Wittmer	7/21/03
058	General Correspondence: Meeting summary from 3-Jul-03 FDA meeting	To: Dr. Throckmorton Fm: L. Wittmer	7/14/03
057	General Correspondence: Meeting summary from 26-Jun-03 CMC teleconference	To: Dr. Throckmorton Fm: L. Wittmer	7/14/03
Email	Bioequivalence question – 500 mg and optimized formulations of lanthanum carbonate	To: D. Hinton Fm: L. Wittmer	7/1/03
Regcon	FDA CMC teleconference meeting regarding stability requirements for optimized formulation	To: Denise Hinton, Patrick Marroum, Angelica Dorrantes, Chris Raman, Dr. Srinivasachar Fm: L. Wittmer & Jo Ferdinando	6/26/03

**NDA SUBMISSION LOGBOOK**

**NDA No. 21-468**

**Title: FOSRENOL™ (Lanthanum Carbonate Hydrate)**

**Submission to FDA (continued)**

Submission No	Type of Submission	To/From	Date
<b>Email</b>	Optimized formulation (lanthanum carbonate) – stability question (background information for discussion on 26-Jun-03 with Drs. Raman and Srinivasachar)	To: D. Hinton Fm: L. Wittmer	6/25/03
<b>056</b>	General Correspondence: Request for Type C Meeting	To: Dr. Throckmorton Fm: L. Wittmer	6/25/03
<b>Email</b>	Draft CMC Meeting Request	To: D. Hinton Fm: L. Wittmer	6/18/03
<b>Email</b>	Optimized formulation (lanthanum carbonate) – stability question	To: D. Hinton Fm: L. Wittmer	6/18/03
<b>Email</b>	Open issues re: 1) API water spec agreement, 2) feedback on 3b study synopsis and 3) feedback on biostudy (SPD405-116)	To: D. Hinton Fm: L. Wittmer	5/23/03
<b>Regcon</b>	Inquire about the process and timing of responding to the action letter.	To: D. Hinton Fm: L. Wittmer	5/12/03
<b>Email</b>	Questions on optimized formulation of Fosrenol	To: D. Hinton Fm: L. Wittmer	5/6/03
<b>055</b>	General Correspondence – CMC (Response to FDA Questions: Factorization agreement)	To: Dr. Throckmorton Fm: L. Wittmer	5/2/03
<b>054</b>	General Correspondence – Request for Feedback on BE Study Synopsis (SPD405-116)	To: Dr. Throckmorton Fm: L. Wittmer	5/2/03
<b>053</b>	General Correspondence – CMC (Response to FDA Questions on factorization issue - revised)	To: Dr. Throckmorton Fm: L. Wittmer	4/24/03
<b>Regcon</b>	Inquire about the Agency's response to our question regarding the use of factorization in the manufacture of lanthanum carbonate.	To: Denise Hinton Fm: L. Wittmer	4/22/03
<b>052</b>	General Correspondence – CMC (Response to FDA Questions on factorization issue)	To: Dr. Throckmorton Fm: L. Wittmer	4/11/03
<b>051</b>	General Correspondence – Meeting Summary (27 March 03)	To: Dr. Throckmorton Fm: L. Wittmer	4/10/03

**NDA SUBMISSION LOGBOOK**

**NDA No. 21-468**

**Title: FOSRENOL™ (Lanthanum Carbonate Hydrate)**

**Submission to FDA (continued)**

Submission No	Type of Submission	To/From	Date
<b>Regcon</b>	<ul style="list-style-type: none"> <li>• To discuss whether Shire may use factorization in the manufacture of production batches of lanthanum carbonate.</li> <li>• To request feedback on our proposal to apply for a bio-waiver for the 500 mg tablet</li> <li>• To discuss whether a disintegration method could be use during long-term QC analysis of drug product batches</li> </ul>	<p>To: Denise Hinton, Kris Raman (CMC Reviewer), Kasturi Srinivasachar (CMC Reviewer) and Patrick Marroum (Biopharmaceutics Reviewer)</p> <p>Fm: Lisa Wittmer and Jo Ferdinando</p>	4/2/03
<b>Regcon</b>	1) To confirm CMC teleconference scheduled for 2 April 2003 to discuss factorization. 2) To request a teleconference with Dr. Dorantes (Clin Pharm & Biopharmaceutics) and at least one of the Pharmacology reviewers to discuss bio-waiver/bio-study options for supporting approval of the 500 mg tablet.	<p>To: Denise Hinton Fm: L. Wittmer</p>	3/31/03
<b>050</b>	General Correspondence – CMC Response to FDA Questions (analytical method and validation reports in response to 1/16/03 FDA letter)	<p>To: Dr. Throckmorton Fm: L. Wittmer</p>	3/31/03
<b>Regcon</b>	1) To request that the CMC reviewers provide an answer to Shire's question regarding the use of factorisation to achieve a fully potent product, and request a teleconference, if necessary. 2) To discuss follow-up items from the March 27 <sup>th</sup> meeting.	<p>To: Denise Hinton Fm: L. Wittmer</p>	3/28/03
<b>049</b>	General Correspondence - Pre Meeting Briefing Documents (hard copies of slides)	<p>To: Dr. Throckmorton Fm: Mark McLoudrey</p>	3/24/03
<b>Email</b>	To clarify a question for Chemistry reviewer with regard to factorization issue	<p>To: Denise Hinton Fm: M. McLoudrey</p>	3/24/03
<b>048</b>	General Correspondence - Notice of Intent to File an Amendment and Request for Teleconference in Response to FDA Approvable Action Letter Dated	<p>To: Dr. Throckmorton Fm: Mark McLoudrey</p>	3/07/03

	02/28/03		
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**NDA No. 21-468**

**Title: FOSRENOL™ (Lanthanum Carbonate Hydrate)**

**Submission to FDA (continued)**

Submission No	Type of Submission	To/From	Date
Email	To seek clarification on approvable letter dated 28-Feb-03	To: Denise Hinton Fm: M. McLoudrey	3/3/03
Email	FDA's request for Word version of ISE/ISS (from original NDA submission file)	To: Denise Hinton Fm: M. McLoudrey	2/21/03
Email	Call-in information for conference call on 21-Feb-03	To: Denise Hinton Fm: M. McLoudrey	2/20/03
047	General Correspondence – Response to Statistical Reviewer's Request for Information (fracture-related AEs)	To: Dr. Throckmorton Fm: G. Miller	2/12/03
Email	Response to Statistical Reviewer's Request for Information (via email on 2/11/03) (note: this set is comprised of 6 related email messages – 2/11/03-2/13/03).	To: Dr. Freidlin Fm: G. Miller	2/12/03
Regcon	To inquire the status of teleconference to discuss the contents of the action letter for the NDA.	To: Denise Hinton Fm: G. Miller	2/12/03
Regcon	Request for early issuance of action letter	To: Denise Hinton Fm: M. McLoudrey	1/28/03
Email	Further clarification on Subm 045 (response to statistical reviewer's request) sent via email by Dr. Freidlin on 1/28/03 @ 10:06am	To: Dr. Freidlin Fm: G. Miller	1/28/03
046	General Correspondence: Response to CMC Information Request (reference to conversation on 1/15/03 between Ms. Hinton and Dr. Wittmer)	To: Dr. Throckmorton Fm: L. Wittmer	1/28/03

**NDA SUBMISSION LOGBOOK**

**NDA No. 21-468**

**Title: FOSRENOL™ (Lanthanum Carbonate Hydrate)**

**Submission to FDA (continued)**

Submission No	Type of Submission	To/From	Date
045	General Correspondence: Response to Statistical Reviewer's Request (clarification of data representing death rate; CD-ROM incl.)	To: Dr. Throckmorton Fm: L. Wittmer	1/27/03
044	General Correspondence: Response to Medical Reviewer's Request (summary of cause of death based on latest available retrospective analysis of mortality)	To: Dr. Throckmorton Fm: L. Wittmer	1/23/03
Regcon	1) To get an update regarding topics that were discussed during the internal FDA meeting on Monday, January 6, 2003 to discuss the review of the NDA. 2) Had Fosrenol™ been approved as the brand name for lanthanum carbonate?	To: Denise Hinton Fm: L. Wittmer	1/7/03
Regcon	To get an update on the NDA review for Fosrenol	To: Denise Hinton Fm: L. Wittmer	1/2/03
Email	Bone fracture data by study	To: Dr. Pelayo Fm: L. Wittmer	12/24/02
043	General Correspondence: Response to Statistical Reviewer's and Medical Reviewer's Requests (changes in QTc, SAS programs, clarifications on ECG analysis report, summary of ECG data in Phase 2-3)	To: Dr. Throckmorton Fm: L. Wittmer	12/23/02
Email	ECG data available from Phase 2-3 studies	To: Dr. Pelayo Fm: L. Wittmer	12/23/02

**NDA SUBMISSION LOGBOOK**

**NDA No. 21-468**

**Title: FOSRENOL™ (Lanthanum Carbonate Hydrate)**

**Submission to FDA (continued)**

Submission No	Type of Submission	To/From	Date
042	General Correspondence – Clinical Information (mortality analysis, AE profile and bone fracture analysis)	To: Dr. Throckmorton Fm: L. Wittmer	12/20/02
041	General Correspondence – Response to CMC Reviewer's Request for Information	To: Dr. Throckmorton Fm: L. Wittmer	12/20/02
Email	NDA 21-468, Study 307, Visit 21, No. of patients (ECG Tables for 205, 204, 302)	To: Dr. Freidlin Fm: L. Wittmer	12/19/02
040	General Correspondence – Meeting Minutes (from the CMC teleconference held on December 12, 2002 to discuss the review of the NDA for lanthanum carbonate hydrate)	To: Dr. Throckmorton Fm: L. Wittmer	12/18/02
Email	NDA 21-468, Study 307, Visit 21, No. of patients (Response to statistical reviewer's request for ECG analysis report, table 2 for 307)	To: Dr. Freidlin Fm: L. Wittmer	12/18/02
Email	NDA 21-468, Study 307, Visit 21, No. of patients (QTc data from study 308)	To: Dr. Freidlin Fm: L. Wittmer	12/17/02
Email	Meeting Minutes for CMC meeting (held on 12 Dec 2002)	To: Denise Hinton Fm: L. Wittmer	12/16/02
039	General Correspondence – Response to Statistical Reviewer's Request	To: Dr. Throckmorton Fm: L. Wittmer	12/16/02
038	Amendment – Chemistry Manufacturing and Controls (packaging of lanthanum carbonate chewable tablets)	To: Dr. Throckmorton Fm: L. Wittmer	12/13/02
037	Electronic Submission - Fosrenol Bottle Labels for the 250 and 500 mg tablets	To: Dr. Throckmorton Fm: L. Wittmer	12/13/02
Email	Update to Table 2 of ECG Analysis Report of Protocol LAM-IV-307 (using 4-month safety database)	To: Dr. Freidlin Fm: L. Wittmer	12/13/02
Email	Bottle labels	To: Denise Hinton Fm: L. Wittmer	12/09/02
036	General Correspondence-Meeting Minutes from Dec 3	To: Dr. Throckmorton Fm: L. Wittmer	12/06/02

**NDA SUBMISSION LOGBOOK**

**NDA No. 21-468**

**Title: FOSRENOL™ (Lanthanum Carbonate Hydrate)**

**Submission to FDA (continued)**

Submission No.	Type of Submission	To/From	Date
<b>Email</b>	Deficiency list	To: Denise Hinton Fm: L. Wittmer	12/06/02
<b>Regcon</b>	To ask for clarification on the findings of the CAC review for Fosrenol	To: Denise Hinton Fm: L. Wittmer	12/04/02
<b>Email</b>	Clarification of calculation of patients exposed in Phase 2/3 studies (4 month safety update)	To: Denise Hinton Fm: L. Wittmer	12/03/02
<b>Email</b>	SAS program for calculating QTc changes	To: Dr. Freidlin Fm: L. Wittmer	12/03/02
<b>035</b>	General Correspondence – CMC Information (dissolution method redevelopment report)	To: Dr. Throckmorton Fm: L. Wittmer	11/27/02
<b>034</b>	Electronic File (Proposed package insert)	To: Central Doc Room Fm: L. Wittmer	11/27/02
<b>033</b>	General Correspondence – CMC Information (stability data to support shelf-life)	To: Dr. Throckmorton Fm: L. Wittmer	11/27/02
<b>Email</b>	General Correspondence – CMC Information (stability data to support shelf-life)	To: Denise Hinton Fm: L. Wittmer	11/27/02
<b>Regcon</b>	To confirm that a separate IND was not required for studies conducted with the optimized formulation (same dose form)	To: Denise Hinton Fm: L. Wittmer	11/27/02
<b>Email</b>	Package insert for Fosrenol (Word file)	To: Denise Hinton Fm: L. Wittmer	11/27/02
<b>Email</b>	Package insert for Fosrenol (pdf file)	To: Dr. Freidlin Fm: L. Wittmer	11/22/02
<b>032</b>	Electronic File (with paper copy) – SAS Program used to calculate phosphate levels in LAM-IV-307	To: Central Doc Room Fm: L. Wittmer	11/22/02
<b>031</b>	Electronic File (with paper copy) – ECG datasets for studies 204, 205, 302 and 308 - ECG dataset for study 307 with changes as requested by Biostat reviewer - Results of ECG for 307	To: Central Doc Room Fm: L. Wittmer	11/22/02

**NDA SUBMISSION LOGBOOK**

**NDA No. 21-468**

**Title: FOSRENOL™ (Lanthanum Carbonate Hydrate)**

**Submission to FDA (continued)**

Submission No	Type of Submission	To/From	Date
030	General Correspondence – Clinical Information (up-to-date mortality analyses)	To: Dr. Throckmorton Fm: L. Wittmer	11/21/02
029	Electronic File (Response to FDA Request for Additional Clinical Data for Changes from Baseline in Phosphate Levels and p-Values)	To: Central Document Room Fm: L. Wittmer	11/15/02
028	Electronic File (Response to FDA Request for ECG Dataset of Study 307)	To: Central Document Room Fm: R. Lilley	11/11/02
RegCon	To follow-up on the internal agency meeting	To: Denise Hinton Fm: S. Krishnan	11/05/02
027	General Correspondence – Additional CMC Information and response to questions raised at 90-day meeting	To: Dr. Throckmorton Fm: R. Lilley	11/04/02
026	General Correspondence – Response to FDA Request (assessment of potential interaction with concomitant meds)	To: Dr. Throckmorton Fm: R. Lilley	11/01/02
025	General Correspondence – Response to Preclinical Questions at teleconference on 10/23/02 with Dr. Joseph	To: Dr. Throckmorton Fm: R. Lilley	10/28/02

**NDA SUBMISSION LOGBOOK**

NDA No. 21-468

Title: FOSRENOL™ (Lanthanum Carbonate Hydrate)

Submission to FDA (continued)

Submission No.	Type of Submission	To/From	Date
024	General Correspondence – Response to Preclinical Request (Tumor data for CD-1 mouse)	To: Dr. Throckmorton Fm: R. Lilley	10/24/02
RegCon	Teleconference with Dr. Joseph to discuss progress of the preclinical review	To: Dr. Xavier Joseph Fm: Suma Krishnan, Steve Damment, Isobel Webster, Mike Burkin	10/23/02
023	General Correspondence – Response to FDA Question (Discrepancy in the no. of liver tumours in male rats)	To: Dr. Throckmorton Fm: R. Lilley	10/22/02
022	General Correspondence – Response to FDA Request (Time to event analysis related to fractures)	To: Dr. Throckmorton Fm: S. Krishnan	10/08/02
RegCon	To request for a teleconference to discuss gene toxicity concerns.	To: Dr. Xavier Joseph Fm: S. Krishnan	10/04/02
RegCon	To inform the Agency on the status of their requested information for time to event analysis on GI and AEs	To: Dr. Valeria Friedman Fm: S. Krishnan	10/04/02
021	General Correspondence – Response to FDA Request (Statistical time to event analysis)	To: Dr. Throckmorton Fm: S. Krishnan	10/03/02
020	General Correspondence – Response to FDA Request (Nonclinical Pharm and Tox on missing page in SPD /88/C)	To: Dr. Throckmorton Fm: S. Krishnan	09/25/02
019	General Correspondence – CMC Copy of DMF authorization letter)	To: Dr. Throckmorton Fm: S. Krishnan	09/18/02
018	General Correspondence – Response to FDA Request (CMC request for DMF#)	To: Dr. Throckmorton Fm: S. Krishnan	09/16/02
017	General Correspondence – Ninety Day Meeting Minutes from 9/5/02 meeting	To: Dr. Throckmorton Fm: S. Krishnan	09/13/02
016	<b>Resubmission of Electronic Files</b> for Four Month Safety Update – Integrated Summary of Safety	To: CDR Fm: S. Krishnan	09/10/02
015	General Correspondence – Response to FDA Request (NonClinical Pharmacology and Toxicology for statistical analysis report on carcino studies)	To: Dr. Throckmorton Fm: S. Krishnan	08/30/02

**NDA SUBMISSION LOGBOOK**

NDA No. 21-468

Title: FOSRENOL™ (Lanthanum Carbonate Hydrate)

Submission to FDA (continued)

Submission No	Type of Submission	To/From	Date
014	Electronic Files for Four Month Safety Update – Integrated Summary of Safety	To: Dr. Throckmorton Fm: S. Krishnan	08/30/02
013	Four Month Safety Update – Integrated Summary of Safety (32 acco volumes on shelf)	To: Dr. Throckmorton Fm: S. Krishnan	08/30/02
012	General Correspondence – CMC on updated specs and test method for drug substance and tablets	To: Dr. Throckmorton Fm: S. Krishnan	08/29/02
Letter	General Correspondence – Change of Address (note to file: audit 4/16/2003-letter is unsigned & plain bond)	To: Dr. Throckmorton Fm: S. Krishnan	08/29/02
011	General Correspondence – Briefing Package (Ninety Day Meeting on 9/5/02)	To: Dr. Throckmorton Fm: S. Krishnan	08/27/02
010	General Correspondence – Response to FDA request (Biopharmaceutics on dissolution method justification)	To: Dr. Throckmorton Fm: S. Krishnan	08/27/02
RegCon	Enquire about the status of the NDA review	To: D. Henton Fm: S. Krishnan	08/23/02
009	General Correspondence – Response to FDA Request (Nonclinical Pharmacology and Toxicology for rationale and justification for excluding beryllium from list of specified metal contaminants, and selection of maximum tolerated dose for long term carcino studies)	To: Dr. Throckmorton Fm: S. Krishnan	08/14/02
008	Resubmission of Electronic Files for Study Reports 202, 204, 301, 302, 307 and Carcinogenicity Studies	To: Electronic Doc. Rm Fm: S. Krishnan	08/05/02
007	General Correspondence-Response to FDA Request for Additional Information (list of countries that Calcium Carbonate was approved for treatment of hyperphosphatemia)	To: Dr. Throckmorton Fm: S. Krishnan	07/30/02
Desk Copy	Request for 2 additional copy of Investigator's Brochure	To: D. Henton Fm: S. Krishnan	07/25/02
Electronic Files	Electronic copies of Study Reports, Protocols, and Statistical Plans for 202, 204, 301, 302, 307, and	To: Electronic Document Room Fm: S. Krishnan	07/25/02

	<b>Carcinogenicity Studies</b>		
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### NDA SUBMISSION LOGBOOK

NDA No. 21-468

Title: FOSRENOL™ (Lanthanum Carbonate Hydrate)

Submission to FDA (continued)

Submission No.	Type of Submission	To/From	Date
Desk Copy	Request for Blank CRF, Protocol and Protocol Amendments for LAM-IV-307	To: Dr. R. Shibuya Fm: S. Krishnan	07/25/02
RegCon	Request for ninety-day meeting	To: D. Henton Fm: S. Krishnan	07/11/02
006	General Correspondence – Ninety-day Meeting Request	To: Dr. Throckmorton Fm: S. Krishnan	07/11/02
RegCon	To enquire about the progress of the NDA review.	To: Dr. J. C. Pelayo Fm: S. Krishnan	07/02/02
Electronic File	Request for electronic copy of preclinical data sets for carcinogenicity studies in mice [SPD/87/C and SPD/88/C]), information regarding criteria test results in the in vitro chromosomal aberration studies and the historical control data for gene mutation and chromosomal aberration frequency in the CHO cells, and bone expert report. (note to file: audit 4/16/03-no paper or elec copy in work file)	To: Electronic Document Room Fm: S. Krishnan	06/28/02
E-Mail	Per RegCon requested dated 06/26/02 for Information on CMC: Lot Numbers of Drug Substance and Drug Product that were and will be tested by TGA and ICP at Quintiles respectively. And the Certificate of Analysis of Drug Substance lots tested at Quintiles, Kansas and included in NDA. (note to file: email is customarily filed in Correspondence log only)	To: S. Berryman Fm: S. Krishnan	06/27/02
Response to Div. Sci. Inv.	Response to FDA Request	To: Dr. R. Shibuya Fm: S. Krishnan	06/25/02
Desk Copy	Request for 1 additional copy of Vol. 1.1 & Vol. 1.2	To: Dr. Throckmorton Fm: S. Krishnan	06/21/02
005	General Correspondence – NonClinical Pharmacology and Toxicology (additional study reports for SPD0130, R00081-LAM-IIIQ and R00182-LAM-IIIQ)	To: Dr. Throckmorton Fm: S. Krishnan	06/19/02
004	General Correspondence (Bone Expert Report)	To: Dr. Throckmorton Fm: S. Krishnan	06/14/02

**NDA SUBMISSION LOGBOOK**

**NDA No. 21-468**

**Title: FOSRENOL™ (Lanthanum Carbonate Hydrate)**

**Submission to FDA (continued)**

Submission No	Type of Submission	To/From	Date
Desk Copy	Resubmission of electronic copy of preclinical data sets for carcinogenicity studies in mice [SPD/87/C and SPD/88/C], information regarding criteria test results in the in vitro chromosomal aberration studies and the historical control data for gene mutation and chromosomal aberration frequency in the CHO cells, and bone expert report.	To: Dr. Xavier Joseph (PharmTox Reviewer) Fm: S. Krishnan	06/14/02
Fax	CMC documentation pages of original NDA pertaining to testing performed at Quintiles in Kansas City. (note to file: audit 4/16/03, Missing in file)	To: Shirley Berryman Fm: S. Krishnan	06/13/02
Desk Copy	Request for 1 additional copy of Vol. 1.1	To: Dr. Throckmorton Fm: S. Krishnan	06/12/02
003	General Correspondence (Per regcon request dated 6/3/02 for additional CMC information on manufacturing and testing contact info, clarify ID test performed on HCl, and update flow diagram to reflect use of Nitrogen).	To: Dr. Throckmorton Fm: S. Krishnan	06/07/02
Desk Copy	Request for 2 additional copies of CMC Section (Vol. 1.3, 1.4)	To: Dr. Throckmorton Fm: S. Krishnan	06/04/02
002	General Correspondence (Per regcon request dated 5/13/02 for information regarding criteria test results in the in vitro chromosomal aberration studies and the historical control data for gene mutation and chromosomal aberration frequency in the CHO cells).	To: Dr. Throckmorton Fm: S. Krishnan	05/22/02
001	General Correspondence (Per regcon request dated 5/13/02 for additional copies of draft package insert, and e-copy of preclinical data sets for carcinogenicity studies in mice [SPD/87/C and SPD/88/C]).	To: Dr. Throckmorton Fm: S. Krishnan	05/21/02
Volume 1.1-1.762	Original NDA Submission (762 acco binders on shelf) (note to file: audit 4/16/2003 – volume #117 out to Y. Zhang on 2/25/03).	To: CDR Fm: R. Lilley	04/30/02

## NDA SUBMISSION LOGBOOK

NDA No. 21-468      FOSRENOL® (Lanthanum Carbonate)

### Submissions to FDA

Submission No.	Type of Submission	To/From	Date
095	General Correspondence: Final Draft Labels and Labeling	To: Dr. Stockbridge Fm: L. Wittmer	10/20/04
094	General Correspondence: Request for Type C Meeting	To: Dr. Stockbridge Fm: L. Wittmer	10/21/04
093	General Correspondence: Final Draft Labeling (revised)	To: EDR Fm: D. Ahern	10/14/04
092	General Correspondence: Final Draft Labeling	To: EDR Fm: D. Ahern	10/11/04
091	CMC Amendment	To: Dr. Stockbridge Fm: L. Wittmer	10/1/04
090	General Correspondence: CMC	To: Dr. Stockbridge Fm: L. Wittmer	9/10/04
089	CMC Amendment: Updated lanthanum carbonate specification and test methods	To: Dr. Stockbridge Fm: L. Wittmer	9/2/04
088	General Correspondence: Meeting Minutes (CMC and Biopharm Teleconference 27-Aug-04)	To: Dr. Stockbridge Fm: L. Wittmer	9/2/04
087	General Correspondence: Pharmacovigilance Risk Management Plan Supplement	To: Dr. Stockbridge and Desk Copy D. Hinton Fm: L. Wittmer	9/1/04
086	Response to Request for Information – CMC Section (Cumulative Revisions)	To: Dr. Stockbridge and FIELD OFFICE COPY Fm: L. Wittmer	8/18/04
085	Response for Request for Information (Revised Labels and Labeling)	To: FDA Central Document Room/EDR Fm: L. Wittmer	8/11/04
084	General Correspondence: CMC	To: Dr. Stockbridge Fm: L. Wittmer	8/06/04
083	Response to Request for Information (Updated current formulation specs)	To: Dr. Stockbridge Fm: L. Wittmer	7/26/04
082	Response to Request for Information (Dissolution data and updated specifications; Pharmacodynamic equivalence – responses to inspection items; Sample bottle labels)	To: Dr. Stockbridge Fm: L. Wittmer	7/23/04
081	Pathology report	To: Dr. Stockbridge Fm: L. Wittmer	7/12/04
080	CMC Amendment	To: Dr. Stockbridge Fm: L. Wittmer	7/12/04

079	CMC Amendment	To: Dr. Stockbridge Fm: L. Wittmer	7/8/04
078	Table outlining studies in which healthy volunteer have received lanthanum	To: Dr. Stockbridge Fm: L. Wittmer	7/6/04
077	General Correspondence: Response to FDA Request for Information	To: Dr. Stockbridge Fm: L. Wittmer	6/24/04
076	General Correspondence: Meeting Summary from 17-Jun-2004	To: Dr. Stockbridge Fm: L. Wittmer	6/21/04
075	Briefing Package for FDA Meeting on 11-Jun-2004	To: Dr. Stockbridge Fm: L. Wittmer	6/2/04
074	General Correspondence: Request for Information (Safety Update for LAM-IV-307)	To: Dr. Stockbridge Fm: L. Wittmer	6/1/04
073	CMC Amendment	To: Dr. Stockbridge Fm: L. Wittmer	5/28/04
071	General Correspondence: Bioanalytical Reports	To: Dr. Throckmorton Fm: L. Wittmer	5/6/04
072	General Correspondence: Response to Information Request Letter	To: Dr. Throckmorton Fm: L. Wittmer	5/5/04
070	Response to Request for Information (CMC)	To: Dr. Throckmorton Fm: L. Wittmer	4/1/04
069	Response to Request for Information (AE)	To: Dr. Throckmorton Fm: L. Wittmer	4/1/04
068	Response to FDA Request for Information	To: Dr. Throckmorton Fm: L. Wittmer	3/22/04
067	Resubmission of Electronic Component of New Drug Application	To: Dr. Throckmorton Fm: L. Wittmer	2/2/04
066	Resubmission of New Drug Application	To: Dr. Throckmorton Fm: L. Wittmer	1/26/04
065	Clinical Amendment: Final Clinical Study Report SPD405-116	To: Dr. Throckmorton Fm: L. Wittmer	11/25/03
064	Pre-resubmission Briefing Package (to be held on 3-Dec-2003)	To: Dr. Throckmorton Fm: L. Wittmer	11/10/03
063	General Correspondence: Copy of USAN Letter	To: Dr. Throckmorton Fm: L. Wittmer	9/5/03
062	General Correspondence	To: Dr. Throckmorton Fm: L. Wittmer	8/27/03
061	General Correspondence: Meeting summary from 7-Aug-03 FDA meeting	To: Dr. Throckmorton Fm: L. Wittmer	8/27/03
060	Meeting Information Package (Revision)	To: Dr. Throckmorton Fm: L. Wittmer	8/4/03
059	Meeting Information Package (CMC meeting on 7-Aug-03)	To: Dr. Throckmorton Fm: L. Wittmer	7/21/03
058	General Correspondence: Meeting summary from 3-Jul-03 FDA meeting	To: Dr. Throckmorton Fm: L. Wittmer	7/14/03

057	General Correspondence: Meeting summary from 26-Jun-03 CMC teleconference	To: Dr. Throckmorton Fm: L. Wittmer	7/14/03
056	General Correspondence: Request for Type C Meeting	To: Dr. Throckmorton Fm: L. Wittmer	6/25/03
055	General Correspondence – CMC	To: Dr. Throckmorton Fm: L. Wittmer	5/2/03
054	General Correspondence – Request for Feedback	To: Dr. Throckmorton Fm: L. Wittmer	5/2/03
053	General Correspondence – CMC	To: Dr. Throckmorton Fm: L. Wittmer	4/24/03
052	General Correspondence – CMC	To: Dr. Throckmorton Fm: L. Wittmer	4/11/03
051	General Correspondence – Meeting Summary (27 March 03)	To: Dr. Throckmorton Fm: L. Wittmer	4/10/03
050	General Correspondence – CMC Response to FDA Questions	To: Dr. Throckmorton Fm: L. Wittmer	3/31/03
049	General Correspondence - Pre Meeting Briefing Documents	To: Dr. Throckmorton Fm: M. McLoudrey	3/24/03
048	General Correspondence - Notice of Intent to File an Amendment and Request for Teleconference in Response to FDA Approvable Action Letter Dated 02/28/03	To: Dr. Throckmorton Fm: M. McLoudrey	3/07/03
047	General Correspondence – Response to Statistical Reviewer's Request for Information	To: Dr. Throckmorton Fm: G. Miller	2/12/03
046	General Correspondence: Response to CMC Information Request (reference to conversation on 1/15/03 between Ms. Hinton and Dr. Wittmer)	To: Dr. Throckmorton Fm: L. Wittmer	1/28/03
045	General Correspondence: Response to Statistical Reviewer's Request	To: Dr. Throckmorton Fm: L. Wittmer	1/27/03
044	General Correspondence: Response to Medical Reviewer's Request	To: Dr. Throckmorton Fm: L. Wittmer	1/23/03
043	General Correspondence: Response to Statistical Reviewer's and Medical Reviewer's Requests	To: Dr. Throckmorton Fm: L. Wittmer	12/23/02
042	General Correspondence – Clinical Information	To: Dr. Throckmorton Fm: L. Wittmer	12/20/02
041	General Correspondence – Response to CMC Reviewer's Request for Information	To: Dr. Throckmorton Fm: L. Wittmer	12/20/02
040	General Correspondence – Meeting Minutes (from the CMC teleconference held on December 12, 2002)	To: Dr. Throckmorton Fm: L. Wittmer	12/18/02

039	General Correspondence – Response to Statistical Reviewer's Request	To: Dr. Throckmorton Fm: L. Wittmer	12/16/02
038	Amendment – Chemistry Manufacturing and Controls	To: Dr. Throckmorton Fm: L. Wittmer	12/13/02
037	Electronic Submission - Fosrenol Bottle Labels for the 250 and 500 mg tablets	To: Dr. Throckmorton Fm: L. Wittmer	12/13/02
036	General Correspondence-Meeting Minutes from Dec 3	To: Dr. Throckmorton Fm: L. Wittmer	12/06/02
035	General Correspondence – CMC Information	To: Dr. Throckmorton Fm: L. Wittmer	11/27/02
034	Electronic File (Proposed package insert)	To: Central Doc Room Fm: L. Wittmer	11/27/02
033	General Correspondence – CMC Information	To: Dr. Throckmorton Fm: L. Wittmer	11/27/02
032	Electronic File – SAS Program for study LAM-IV-307	To: Central Doc Room Fm: L. Wittmer	11/22/02
031	Electronic File – ECG datasets for studies 204, 205, 302 and 308 - ECG dataset for study 307 with changes as requested by Biostat reviewer - Results of ECG for 307	To: Central Doc Room Fm: L. Wittmer	11/22/02
030	General Correspondence – Clinical Information	To: Dr. Throckmorton Fm: L. Wittmer	11/21/02
029	Electronic File (Response to FDA Request for Additional Clinical Data)	To: Central Document Room Fm: L. Wittmer	11/15/02
028	Electronic File (Response to FDA Request)	To: Central Document Room Fm: R. Lilley	11/11/02
027	General Correspondence – Additional CMC Information and response to questions raised at 90-day meeting	To: Dr. Throckmorton Fm: R. Lilley	11/04/02
026	General Correspondence – Response to FDA Request	To: Dr. Throckmorton Fm: R. Lilley	11/01/02
025	General Correspondence – Response to Preclinical Questions at teleconference on 10/23/02 with Dr. Joseph	To: Dr. Throckmorton Fm: R. Lilley	10/28/02
024	General Correspondence – Response to Preclinical Request	To: Dr. Throckmorton Fm: R. Lilley	10/24/02
023	General Correspondence – Response to FDA Question	To: Dr. Throckmorton Fm: R. Lilley	10/22/02
022	General Correspondence – Response to FDA Request	To: Dr. Throckmorton Fm: S. Krishnan	10/08/02
021	General Correspondence – Response to FDA Request	To: Dr. Throckmorton Fm: S. Krishnan	10/03/02

020	General Correspondence – Response to FDA Request	To: Dr. Throckmorton Fm: S. Krishnan	09/25/02
019	General Correspondence – CMC	To: Dr. Throckmorton Fm: S. Krishnan	09/18/02
018	General Correspondence – Response to FDA Request	To: Dr. Throckmorton Fm: S. Krishnan	09/16/02
017	General Correspondence – Ninety Day Meeting Minutes from 9/5/02 meeting	To: Dr. Throckmorton Fm: S. Krishnan	09/13/02
016	Resubmission of Electronic Files for Four Month Safety Update – Integrated Summary of Safety	To: Central Document Room Fm: S. Krishnan	09/10/02
015	General Correspondence – Response to FDA Request (NonClinical Pharmacology and Toxicology for statistical analysis report)	To: Dr. Throckmorton Fm: S. Krishnan	08/30/02
014	Electronic Files for Four Month Safety Update – Integrated Summary of Safety	To: Dr. Throckmorton Fm: S. Krishnan	08/30/02
013	Four Month Safety Update – Integrated Summary of Safety	To: Dr. Throckmorton Fm: S. Krishnan	08/30/02
012	General Correspondence – CMC	To: Dr. Throckmorton Fm: S. Krishnan	08/29/02
Letter	General Correspondence – Change of Company Address	To: Dr. Throckmorton Fm: S. Krishnan	08/29/02
011	General Correspondence – Briefing Package (Ninety Day Meeting on 9/5/02)	To: Dr. Throckmorton Fm: S. Krishnan	08/27/02
010	General Correspondence – Response to FDA request	To: Dr. Throckmorton Fm: S. Krishnan	08/27/02
009	General Correspondence – Response to FDA Request (Nonclinical Pharmacology and Toxicology)	To: Dr. Throckmorton Fm: S. Krishnan	08/14/02
008	Resubmission of Electronic Files for Study Reports 202, 204, 301, 302, 307 and Carcinogenicity Studies	To: Electronic Doc. Rm Fm: S. Krishnan	08/05/02
007	General Correspondence-Response to FDA Request for Additional Information	To: Dr. Throckmorton Fm: S. Krishnan	07/30/02
006	General Correspondence – Ninety-day Meeting Request	To: Dr. Throckmorton Fm: S. Krishnan	07/11/02
005	General Correspondence – NonClinical Pharmacology and Toxicology	To: Dr. Throckmorton Fm: S. Krishnan	06/19/02
004	General Correspondence	To: Dr. Throckmorton Fm: S. Krishnan	06/14/02

003	General Correspondence (FDA request for additional CMC information on manufacturing and testing contact info)	To: Dr. Throckmorton Fm: S. Krishnan	06/07/02
002	General Correspondence (FDA request for information)	To: Dr. Throckmorton Fm: S. Krishnan	05/22/02
001	General Correspondence (FDA request for additional copies of draft package insert, and e-copy of preclinical data sets)	To: Dr. Throckmorton Fm: S. Krishnan	05/21/02
000 (Volume 1.1-1.762)	Original NDA Submission	To: Central Document Room Fm: R. Lilley	04/30/02

## IND SUBMISSION LOGBOOK

**IND 55,054 Lanthanum Carbonate (FOSRENOL®)**

### Submissions to FDA

IND Serial No	Description of Document	To/From	Date
170	Other (Change of Company Name/Address)	To: Dr. Stockbridge Fm: C. LaPree	11/18/04
169	Protocol Amendment: New Investigator (Updated Form 1572 for SPD405-309)	To: Dr. Stockbridge Fm: L. Wittmer	11/16/04
168	Protocol Amendment: New Protocol (SPD405-310)	To: Dr. Stockbridge Fm: D. Ahern	11/2/04
167	Follow-up to 15-Day Safety Report - Protocol SPD405.309	To: Dr. Throckmorton Fm: L. Wittmer	8/11/04
166	Protocol Amendment: New Investigator (SPD405-312)	To: Dr. Stockbridge Fm: L. Wittmer	7/27/04
165	Protocol Amendment: New Investigator	To: Dr. Throckmorton Fm: L. Wittmer	6/18/04
164	Follow-up to 15-Day Safety Report - Protocol SPD405.309	To: Dr. Throckmorton Fm: L. Wittmer	6/8/04
163	15-Day Safety Report - Protocol SPD405.309	To: Dr. Throckmorton Fm: L. Wittmer	5/18/04
162	Annual Report (Reporting period 2/14/03-2/13/04)	To: Dr. Throckmorton Fm: L. Wittmer	4/20/04
161	Protocol Amendment: Change in Protocol (SPD405-312, Amendment 1)	To: Dr. Throckmorton Fm: L. Wittmer	4/15/04
160	Protocol Amendment: New Investigator	To: Dr. Throckmorton Fm: L. Wittmer	3/22/04
159	Protocol Amendment: New Investigator	To: Dr. Throckmorton Fm: L. Wittmer	3/22/04
158	New Protocol (SPD405-312) and CMC Amendment	To: Dr. Throckmorton Fm: L. Wittmer	12/29/03
157	Protocol Amendment: New Investigator	To: Dr. Throckmorton Fm: L. Wittmer	12/17/03
156	Protocol Amendment: New Investigator	To: Dr. Throckmorton Fm: L. Wittmer	12/17/03
155	Protocol Amendment: Investigator Update	To: Dr. Throckmorton Fm: L. Wittmer	12/17/03
154	Protocol Amendment: Investigator Update	To: Dr. Throckmorton Fm: L. Wittmer	12/17/03
153	Protocol Amendment: Change in Protocol (SPD405.309, Amendment 2)	To: Dr. Throckmorton Fm: L. Wittmer	11/13/03
152	Clinical Study Report LAM-IV-205, Amendment 1	To: Dr. Throckmorton Fm: L. Wittmer	11/07/03
151	Protocol Amendment: New Investigator	To: Dr. Throckmorton Fm: L. Wittmer	09/09/03
150	Investigator's Brochure (Version 10)	To: Dr. Throckmorton Fm: L. Wittmer	09/09/03

149	Protocol Amendment: New Investigator	To: Dr. Throckmorton Fm: L. Wittmer	07/09/03
148	Annual Report (Reporting period 2/14/02-2/13/03)	To: Dr. Throckmorton Fm: L. Wittmer	06/11/03
147	Protocol Amendment: Change in Protocol (LAM-IV-307, Amendment 8)	To: Dr. Throckmorton Fm: L. Wittmer	05/23/03
146	General Correspondence: Protocol Synopsis for Comment (SPD405-312)	To: Dr. Throckmorton Fm: L. Wittmer	04/25/03
145	Protocol Amendment: New Investigator Update	To: Dr. Throckmorton Fm: M. McLoudrey	03/28/03
144	Protocol Amendment: New Investigator	To: Dr. Throckmorton Fm: M. McLoudrey	03/28/03
143	Protocol Amendment: New Investigator	To: Dr. Throckmorton Fm: M. McLoudrey	02/03/03
142	Protocol Amendment: New Investigator Update	To: Dr. Throckmorton Fm: L. Wittmer	01/02/03
141	Protocol Amendment: New Investigator	To: Dr. Throckmorton Fm: L. Wittmer	01/02/03
140	Protocol Amendment: New Investigator	To: Dr. Throckmorton Fm: R. Lilley	11/08/02
139	Protocol Amendment: New Investigator	To: Dr. Throckmorton Fm: S. Krishnan	10/10/02
138	Protocol Amendment: New Investigator	To: Dr. Throckmorton Fm: S. Krishnan	10/04/02
137	Change of Company Address	To: Dr. Throckmorton Fm: R. Lilley	08/29/02
136	Annual Report (2/01-2/02)	To: Dr. Throckmorton Fm: S. Krishnan	07/17/02
135	Protocol Amendments: New Protocol and Change in Protocol (Amendment 1) to SPD 405.309	To: Dr. Throckmorton Fm: S. Krishnan	6/14/02
134	Follow-up to 15-Day Safety Report	To: Dr. Lipicky Fm: Rick Lilley	6/6/02
133	Other-Request for Waiver of Pediatric Studies (for Fosrenol NDA 21-468)	To: Dr. Throckmorton Fm: S. Krishnan	4/26/02
132	Protocol Amendment: New Investigator	To: Dr. Throckmorton Fm: S. Krishnan	3/19/02
131	Protocol Amendment: New Investigator	To: Dr. Throckmorton Fm: S. Krishnan	3/5/02
130	Protocol Amendment: New Investigator	To: Dr. Throckmorton Fm: S. Krishnan	3/5/02
129	Protocol Amendment: New Investigator	To: Dr. Throckmorton Fm: S. Krishnan	3/4/02
128	Protocol Amendment: New Investigator	To: Dr. Throckmorton Fm: S. Krishnan	3/4/02
127	Protocol Amendment: New Investigator	To: Dr. Lipicky Fm: S. Krishnan	3/4/02
126	Protocol Amendment: New Investigator	To: Dr. Lipicky Fm: S. Krishnan	2/18/02

125	Protocol Amendment: New Investigator	To: Dr. Lipicky Fm: S. Krishnan	2/13/02
124	Notice of Termination of Clinical Investigator	To: Dr. Lipicky Fm: S. Krishnan	2/11/02
123	Follow-up to 15-Day Safety Report	To: Dr. Lipicky Fm: S. Krishnan	1/29/02
122	Follow-up to 15-Day Safety Report	To: Dr. Lipicky Fm: S. Krishnan	1/14/02
121	15-Day Safety Report (LAM-IV-307)	To: Dr. Lipicky Fm: S. Krishnan	1/3/02
120	Information Amendment: Clinical (Revised IB)	To: Dr. Lipicky Fm: S. Krishnan	12/17/01
119	Protocol Amendment: Change in Protocol (LAM-IV-307 Amend #6 & #7)	To: Dr. Lipicky Fm: S. Krishnan	12/17/01
118	General Correspondence (Meeting Minutes from 10/23/01)	To: Dr. Lipicky Fm: S. Krishnan	11/13/01
117	Protocol Amendment: New Investigator	To: Dr. Lipicky Fm: S. Krishnan	11/12/01
116	General Correspondence: Pre-NDA Clinical/Nonclinical Meeting Minutes from 9/18/01	To: Dr. Lipicky Fm: S. Krishnan	10/4/01
115	Protocol Amendment: New Investigator	To: Dr. Lipicky Fm: S. Krishnan	10/2/01
114	Protocol Amendment: New Investigator	To: Dr. Lipicky Fm: S. Krishnan	9/28/01
113	General Correspondence: Follow-up information from the Pre-NDA meeting	To: Dr. Lipicky Fm: S. Krishnan	9/19/01
112	General Correspondence: Pre-NDA Briefing Information Package	To: Dr. Lipicky Fm: S. Krishnan	9/4/01
111	Protocol Amendment: New Investigator	To: Dr. Lipicky Fm: S. Krishnan	7/25/01
110	Protocol Amendment: New Investigator	To: Dr. Lipicky Fm: S. Krishnan	7/19/01
109	Protocol Amendment: New Investigator	To: Dr. Lipicky Fm: S. Krishnan	7/16/01
108	Protocol Amendment: New Investigator	To: Dr. Lipicky Fm: S. Krishnan	7/19/01
107	General Correspondence: Request for Type B Meeting	To: Dr. Lipicky Fm: S. Krishnan	7/6/01
106	Protocol Amendment: New Investigator	To: Dr. Lipicky Fm: S. Krishnan	6/28/01
105	Protocol Amendment: New Investigator	To: Dr. Lipicky Fm: S. Krishnan	6/28/01
104	Follow-up to 15-Day Safety Report	To: Dr. Lipicky Fm: S. Krishnan	6/27/01
103	Protocol Amendment: Change in Protocol (307 Amend #5)	To: Dr. Lipicky Fm: S. Krishnan	6/11/01
102	Annual Report (2/00-2/01)	To: Dr. Lipicky Fm: S. Krishnan	5/29/01

101	Protocol Amendment: New Investigator	To: Dr. Lipicky Fm: S. Krishnan	5/17/01
100	Protocol Amendment: New Investigator	To: Dr. Lipicky Fm: S. Krishnan	5/4/01
099	Protocol Amendment: New Investigator	To: Dr. Lipicky Fm: T. Martin	4/23/01
098	Protocol Amendment: New Investigator	To: Dr. Lipicky Fm: T. Martin	3/26/01
097	15-Day Safety Report (LAM-IV-301)	To: Dr. Lipicky Fm: T. Martin	3/12/01
096	Protocol Amendment: Change in Protocol (307 Amend #4)	To: Dr. Lipicky Fm: T. Martin	3/5/01
095	Protocol Amendment: New Investigator	To: Dr. Lipicky Fm: T. Martin	3/5/01
094	15-Day Safety Report (LAM-IV-307)	To: Dr. Lipicky Fm: T. Martin	3/5/01
093	Protocol Amendment: New Investigator	To: Dr. Lipicky Fm: T. Martin	2/15/01
092	Protocol Amendment: New Investigator	To: Dr. Lipicky Fm: T. Martin	2/2/01
091	Protocol Amendment: Change in Protocol (LAM-IV-111 Amend #2)	To: Dr. Lipicky Fm: T. Martin	1/31/01
090	Protocol Amendment: New Investigator	To: Dr. Lipicky Fm: T. Martin	1/17/01
089	General Correspondence: Protocol LAM-IV-303	To: Dr. Lipicky Fm: T. Martin	1/15/01
088	Protocol Amendment: New Investigator	To: Dr. Lipicky Fm: T. Martin	1/10/01
087	Protocol Amendment: New Investigator	To: Dr. Lipicky Fm: T. Martin	1/8/01
086	General Correspondence: Draft Protocol LAM-IV-113	To: Dr. Lipicky Fm: T. Martin	1/4/01
085	Protocol Amendment: New Investigator	To: Dr. Lipicky Fm: T. Martin	1/3/01
084	CMC Amendment to the IND Application	To: Dr. Lipicky Fm: R. Kishore	11/27/00
083	Protocol Amendment: New Investigator	To: Dr. Lipicky Fm: T. Martin	11/21/00
082	Protocol Amendment: Change in Protocol (111 Amend #1)	To: Dr. Lipicky Fm: T. Martin	11/20/00
081	Follow-up #2 to 15-Day Safety Report (Protocol LAM-IV-307)	To: Dr. Lipicky Fm: T. Martin	11/17/00
080	Protocol Amendment: New Investigator	To: Dr. Lipicky Fm: T. Martin	11/8/00
079	Protocol Amendment: New Protocol (LAM-IV-111)	To: Dr. Lipicky Fm: T. Martin	10/19/00
078	Protocol Amendment: New Investigator	To: Dr. Lipicky Fm: T. Martin	10/19/00
077	15-Day Safety Report Protocol (LAM-IV-303)	To: Dr. Lipicky Fm: T. Martin	10/17/00
076	Protocol Amendment: New Investigator	To: Dr. Lipicky Fm: T. Martin	10/10/00

075	Protocol Amendment: New Investigator	To: Dr. Lipicky Fm: T. Martin	10/2/00
074	Annual Report (2/99-2/00)	To: Dr. Lipicky Fm: T. Martin	9/28/00
073	General Correspondence: Trade Name Evaluation	To: Dr. Lipicky Fm: T. Martin	9/28/00
072	Protocol Amendment: New Protocol (LAM-IV-112)	To: Dr. Lipicky Fm: T. Martin	9/28/00
071	General Correspondence (ongoing program of IND and ensure the parameters chosen are acceptable)	To: Dr. Lipicky Fm: T. Martin	9/22/00
070	Information Amendment: Tox Report	To: Dr. Lipicky Fm: T. Martin	9/19/00
069	General Correspondence (Bone assessments; response to FDA questions)	To: Dr. Lipicky Fm: T. Martin	8/22/00
068	Follow-up 15-Day Safety Report	To: Dr. Lipicky Fm: T. Martin	8/18/00
067	Protocol Amendment: Change in Protocol (308 Amend #1 & 2)	To: Dr. Lipicky Fm: T. Martin	8/11/00
066	Protocol Amendment: Change in Protocol (307 Amend #2 & 3)	To: Dr. Lipicky Fm: T. Martin	8/11/00
065	15-Day Safety Report	To: Dr. Lipicky Fm: T. Martin	7/31/00
064	Protocol Amendment: New Investigator	To: Dr. Lipicky Fm: T. Martin	7/28/00
063	Protocol Amendment: New Investigator	To: Dr. Lipicky Fm: T. Martin	6/26/00
062	General Correspondence	To: Dr. Lipicky Fm: T. Martin	6/7/00
061	15-Day Safety Report	To: Dr. Lipicky Fm: T. Martin	6/5/00
060	Protocol Amendment: New Investigator	To: Dr. Lipicky Fm: T. Martin	5/10/00
059	Follow-up 15-Day Safety Report	To: Dr. Lipicky Fm: T. Martin	5/8/00
058	Protocol Amendment: New Investigator	To: Dr. Lipicky Fm: T. Martin	4/27/00
057	General Correspondence (revised draft LAM-IV-111)	To: Dr. Lipicky Fm: T. Martin	4/17/00
056	General Correspondence	To: Dr. Lipicky Fm: T. Martin	4/4/00
055	15-Day Safety Report	To: Dr. Lipicky Fm: T. Martin	3/29/00
054	15-Day Safety Report	To: Dr. Lipicky Fm: T. Martin	3/20/00
053	General Correspondence (draft protocol LAM-IV-111)	To: Dr. Lipicky Fm: T. Martin	3/20/00
052	Protocol Amendment: New Investigator	To: Dr. Lipicky Fm: T. Martin	3/17/00
051	15-Day Safety Report	To: Dr. Lipicky Fm: T. Martin	3/15/00

050	Protocol Amendment: New Investigator	To: Dr. Lipicky Fm: S. Geroux	3/1/00
049	Protocol Amendment: New Investigator	To: Dr. Lipicky Fm: S. Geroux	2/17/00
048	Protocol Amendment: New Investigator	To: Dr. Lipicky Fm: S. Geroux	2/4/00
047	Protocol Amendment: New Investigator	To: Dr. Lipicky Fm: S. Geroux	1/12/00
046	General Correspondence: Amendment to IB	To: Dr. Lipicky Fm: S. Geroux	1/6/00
045	Protocol Amendment: New Protocol (LAM-IV-308)	To: Dr. Lipicky Fm: S. Geroux	12/21/99
044	Follow-up 15-Day Safety Report	To: Dr. Lipicky Fm: T. Martin	12/21/99
043	Protocol Amendment: New Investigator	To: Dr. Lipicky Fm: S. Geroux	12/16/99
042	General Correspondence (IC)	To: Dr. Lipicky Fm: S. Geroux	12/14/99
041	Follow-up 15-Day Safety Report	To: Dr. Lipicky Fm: S. Geroux	12/3/99
040	Protocol Amendment: New Investigator	To: Dr. Lipicky Fm: S. Geroux	11/18/99
039	Information Amendment: Pharm/Tox	To: Dr. Lipicky Fm: S. Geroux	11/16/99
038	Information Amendment: Clinical (Final study report LAM-IV-204)	To: Dr. Lipicky Fm: S. Geroux	10/27/99
037	General Correspondence	To: Dr. Lipicky Fm: S. Geroux	10/20/99
036	Protocol Amendment: New Investigator	To: Dr. Lipicky Fm: S. Geroux	10/19/99
035	Protocol Amendment: Change in Protocol (LAM-IV-307 Amend #1)	To: Dr. Lipicky Fm: S. Geroux	10/18/99
034	Protocol Amendment: New Investigator	To: Dr. Lipicky Fm: S. Geroux	10/7/99
033	Protocol Amendment: New Protocol (LAM-IV-302)	To: Dr. Lipicky Fm: S. Geroux	9/28/99
032	General Correspondence (Response to FDA request for information)	To: E. Fromm Fm: S. Geroux	9/8/99
031	Follow-up 15-Day Safety Report	To: Dr. Lipicky Fm: S. Geroux	8/30/99
030	Protocol Amendment: New Investigator	To: Dr. Lipicky Fm: S. Geroux	8/30/99
029	Protocol Amendment: New Investigator	To: Dr. Lipicky Fm: T. Martin	8/19/99
028	General Correspondence (copy of telecon on 8/12/99)	To: Dr. Lipicky Fm: T. Martin	8/17/99
027	General Correspondence (Response to FDA request for information) IB Version 8, IC for 205 & 307	To: Dr. Lipicky Fm: T. Martin	8/17/99

026	15-Day Safety Report	To: Dr. Lipicky Fm: S. Geroux	8/17/99
025	15-Day Safety Report	To: Dr. Lipicky Fm: S. Geroux	8/10/99
024	Protocol Amendment: New Investigator	To: Dr. Lipicky Fm: S. Geroux	8/9/99
023	15-Day Safety Report	To: Dr. Lipicky Fm: S. Geroux	8/3/99
022	Protocol Amendment: New Investigator	To: Dr. Lipicky Fm: S. Geroux	7/30/99
021	Protocol Amendment: New Protocol (LAM-IV-110) and Change in Protocol (LAM-IV-109 Amend #1)	To: Dr. Lipicky Fm: S. Geroux	7/27/99
020	Protocol Amendment: New Protocol (LAM-IV-302)	To: Dr. Lipicky Fm: S. Geroux	7/20/99
019	Protocol Amendment: New Protocol (LAM-IV-307) and New Investigators	To: Dr. Lipicky Fm: S. Geroux	7/20/99
018	15-Day Safety Report	To: Dr. Lipicky Fm: S. Geroux	7/9/99
Regcon	7-Day Safety Report	To: Colleen LoCicero & Dr. Pelayo	6/28/99
017	General Correspondence (Press Release)	To: Dr. Lipicky Fm: T. Martin	6/24/99
016	General Correspondence (Draft Protocol LAM-IV-307)	To: Dr. Lipicky Fm: S. Geroux	6/16/99
015	Protocol Amendment: New Investigator	To: Dr. Lipicky Fm: S. Geroux	5/14/99
014	End of Phase II Meeting Clinical Briefing Pack	To: Dr. Lipicky Fm: S. Geroux	4/27/99
013	End of Phase II Meeting CMC Briefing Pack	To: Dr. Lipicky Fm: S. Geroux	4/26/99
012	Information Amendment: Response to FDA's request for Information	To: Dr. Lipicky Fm: S. Geroux	4/19/99
011	Annual Report (2/98-2/99)	To: Dr. Lipicky Fm: S. Geroux	4/19/99
010	Protocol Amendment: Change in Protocol (LAM-IV-205 Amend #2 and #3)	To: Dr. Lipicky Fm: S. Geroux	3/22/99
009	Protocol Amendment: New Investigator	To: Dr. Lipicky Fm: S. Geroux	3/8/99
008	Protocol Amendment: New Investigator	To: Dr. Lipicky Fm: S. Geroux	2/2/99
007	Protocol Amendment: Change in Protocol (LAM-IV-204 Amend #2, LAM-IV-205 Amend #1)	To: Dr. Lipicky Fm: S. Geroux	10/5/98
006	Protocol Amendment: New Protocol (LAM-IV-205)	To: Dr. Lipicky Fm: T. Martin	9/9/98
005	Protocol Amendment: New Investigator	To: Dr. Lipicky Fm: S. Geroux	8/19/98

<b>004</b>	Protocol Amendment: New Investigator	To: Dr. Lipicky Fm: S. Geroux	7/31/98
<b>003</b>	Protocol Amendment: Change in Protocol (LAM-IV-204 Amend #1) and New Investigator	To: Dr. Lipicky Fm: S. Geroux	5/6/98
<b>002</b>	General Correspondence (Request for alternative frequency reporting of AE's)	To: Dr. Lipicky Fm: T. Martin	4/16/98
<b>001</b>	Information Amendment (Mutagenicity Reports)	To: Dr. Lipicky Fm: S. Geroux	2/5/98
<b>000</b>	Initial IND Submission	To: Dr. Lipicky Fm: E. Rudnic	1/14/98
<b>Pre-IND</b>	Pre-IND Meeting minutes	To: Dr. Lipicky Fm: S. Geroux	7/23/97
<b>Letter</b>	Pre-IND Meeting Request	To: Dr. Lipicky Fm: S. Geroux	7/07/97

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re United States Patent No. 4,927,814

Inventors: Gall et al.

Issue Date: May 22, 1990

For: DIPHOSPHONATE DERIVATIVES, PHARMACEUTICAL COMPOSITIONS  
AND METHODS OF USE

**TRANSMITTAL LETTER FOR SECOND SUPPLEMENT TO APPLICATION FOR  
EXTENSION OF PATENT TERM UNDER 35 U.S.C. §156, FILED ON JULY 14, 2003**

Nutley, New Jersey 07110  
January 6, 2005

Mail Stop Patent Ext.  
Commissioner for Patents  
P.O. Box 1450  
Arlington, VA 22313-1450

Sir:

Transmitted herewith are: (a) Second Supplement to Application for Extension of Patent Term under 35 U.S.C. §156, filed on July 14, 2003; and (b) Second Revised Calculation of Patent Term Extension for Boniva. The undersigned certifies that the Second Supplement and Second Revised Calculation are submitted in their original form, and three other original duplicate copies of all papers filed are being provided for the convenience of the patent office. One additional original duplicate copy of all papers is being submitted directly to the FDA separately for the convenience of the patent office.

No fee for this submission is believed to be due. However, if any fees are in fact due for this submission, the Commissioner is authorized to charge any such fees, or credit any overpayments to Account No. 08-2525.

U.S. Patent No. 4,927,814  
Issue Date: May 22, 1990

A duplicate copy of this cover sheet is enclosed.

Respectfully submitted,



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Attorney for Applicant  
Patricia Rocha-Tramaioni  
Reg. No. 31,054  
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Nutley, New Jersey 07110-1199  
Telephone: (973) 235-2441  
Telefax: (973) 235-2363

149372

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re United States Patent No. 4,927,814

Inventors: Gall et al.

Issue Date: May 22, 1990

For: DIPHOSPHONATE DERIVATIVES, PHARMACEUTICAL  
COMPOSITIONS AND METHODS OF USE

**SECOND SUPPLEMENT TO APPLICATION FOR EXTENSION OF  
PATENT TERM UNDER 35 U.S.C. § 156, FILED ON JULY 14, 2003**

Nutley, New Jersey 07110  
January 6, 2005

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

Dear Sir:

Pursuant to 35 U.S.C. §156 and in accordance with 37 C.F.R. §1.740, Applicant hereby supplements the Application for Extension of Patent Term Under 35 U.S.C. §156 dated July 11, 2003 ("Application"), which was filed on July 14, 2003, as well as the Supplement to Application for Extension of Patent Term Under 35 U.S.C. §156, which was filed on September 24, 2003 ("First Supplement").

In its First Supplement filed September 24, 2003, Applicant requested a patent term extension of 1,713 days, from July 9, 2007 to and including an extension date of February 16, 2012, for the above-captioned patent. While the requested number of days of extension is correct, namely 1,713 days, Applicant just became aware that the extension date requested was not correct. The addition of 1,713 days to the end of the original patent term of July 9, 2007 results in a date of March 17, 2012, not the originally requested date of February 16, 2012. This was an inadvertent miscalculation of a

calendar date. This Second Supplement does not change the calculated periods of time for the testing phase, application phase, regulatory review period or the requested extension of 1,713 days.

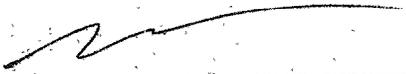
In support of Applicant's Second Supplement, Applicant submits herewith a Second Revised Calculation of Patent Term Extension for Boniva (formerly submitted as Exhibit I).

Applicant relies on its Application, as hereby supplemented, for its request for a patent term extension of 1,713 days, resulting in an extension date of March 17, 2012.

Revised Request for Extension

In view of the foregoing, Applicant respectfully requests (i) an extension of the patent term of U.S. Patent No. 4,927,814 for 1,713 days from July 9, 2007 to and including March 17, 2012, by reason of its claims encompassing the approved product and its salts and esters as a single entity or in combination with another active ingredient and (ii) certification that it is entitled to the rights derived from this patent as set forth in 35 U.S.C. § 156 (b).

Respectfully submitted,  
HOFFMANN-LA ROCHE INC.



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Patricia S. Rocha-Tramaloni  
Senior Counsel and Manager  
Reg. No. 31,054  
Date: January 6, 2005

CERTIFICATION

The undersign certifies that this Second Supplement to Application for Extension of Patent Term Under 35 U.S.C. §156, filed on July 14, 2003, including a Second Revised Calculation of Patent Term Extension for Boniva, and three other original duplicate copies of all papers (as a total of four copies), are being submitted herein. One further original duplicate copy of this Second Supplement, and Second Revised Calculation, is being submitted directly to the FDA at the following address: Mr. David T. Reed, Acting Director Health Assessment Policy Staff, CDER, Food and Drug Administration, 1451 Rockville Pike, HFD-7, Rockville, MD 20852.

Respectfully submitted,  
HOFFMANN-LA ROCHE INC.



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Patricia S. Rocha-Tramaloni  
Reg. No. 31,054  
Date: January 6, 2005

cc: Mr. David T. Reed, FDA

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