Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
4/9/1998	Facisimile	FDA	BB-IND 7616			

Re: list of Attendees of A-Gal conference call in which dosing schedule and clinical endpoints were discussed.

4/13/1998	Facisimile	FDA	BB-IND 7616			

Re: A-Gal Patient Accrual Schedule

4/14/1998	Phone Log	FDA	BB-IND 7616			

Re: Telephone call to Darin Weber re: Fast Track Status Review of A-Gal.

4/14/1998	Email to Team Members	FDA	BB-IND 7616			

Re: Conversation with Tom Eggerman, 4/14 regarding his having reviewed dosing schedule.

4/28/1998	Phone Log	FDA	BB-IND 7616			

Re: Telephone call to Tom Eggerman regarding Clinical Reviewer and scheduling conflicts with first patient.

4/29/1998	Facisimile	FDA	BB-IND 7616			

Fax regarding replacement trial and completion of first infusion for first two patients in the 0.3 mg/kg group. No drug-related adverse events in either of the first two.

4/29/1998	Phone Log	FDA	BB-IND 7616			

Re: Telephone call to Tom Eggerman regarding Clinical Reviewer and request from Christine Eng to infuse third patient after 24 hours instead of 48 hours.

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
5/8/1998	Phone Log	FDA	BB-IND 7616			
	Re: Telephone call to Darin Weber regarding Fast Track Status Review of A-GAL.					
5/8/1998	Correspondence Received	FDA	BB-IND 7616			
	Letter from FDA concluding that submittal of 6 March 1998 meets criteria for Fast Track designation.					
5/14/1998	Amendment	FDA	BB-IND 7616	001		001
	Amendment 1 to original submission of March 6, 1998. Revisions to Chemical, Manufacturing and Control Summary. IND Phase 1 Safety, Pharmacokinetic and Pharmacodynamic study in Fabry Population; Chemistry/Microbiology; dated May 14, 1998.;					
5/20/1998	Amendment	FDA	BB-IND 7616	002		002
	Amendment 002 to BB-IND No. 7616 - Revision to Clinical Protocol Pharmacokinetic and Pharmacodynamic Evaluation of Recombinant Human a-Galactosidase A (r-ha-GAL) Replacement in Patients with Fabry disease, Protocol No. FB9702-01.; Amendment to original submission of March 6, 1998, revised April 15, 1998					
6/25/1998	Amendment	FDA	BB-IND 7616			
	Re: BB-IND 7616 - Amendment 004 - Revisions to Chemistry, Manufacturing, and Controls Section					
6/29/1998	Request for Information	FDA	BB-IND 7616			
	Request for Additional Information on A-GAL.					
7/6/1998	Amendment	FDA	BB-IND 7616	003		003
	Re: Amendment 003 to BB-IND No. 7616, Recombinant Human a-Galactosidase (r-haGal) 0 Revisions to Chemistry, Manufacturing and Controls Section.					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
7/6/1998	Phone Log	FDA	BB-IND 7616			
	Re: Conference Call on Tuesday, 23 June 1998 with Tom Eggerman, regarding Phase I/II Clinical Trial.					
7/13/1998	Phone Log	FDA	BB-IND 7616			
	Re: Changes to CMC section of BB-IND 7616; request for a meeting to be set up with John Hill on afternoon of 9 July 1998.					
7/16/1998	Amendment	FDA	BB-IND 7616	004		004
	Re: Amendment 04 to BB-IND No. 7616 -- Serious Adverse Event - 15 day report.; This Submission Contains The Following: Initial Written Report					
7/21/1998	Amendment	FDA	BB-IND 7616	005		005
	Re: Amendment 005 to BB-IND No. 7616 - Revisions to Chemistry, Manufacturing and Controls Section.; Release data on drug substance 1ot AG812 and one month stability testing data on drug product 1ot AG812A.					
8/18/1998	Phone Log	FDA	BB-IND 7616			
	Re: Request for Meeting protocol					
9/10/1998	Phone Log	FDA	BB-IND 7616			
	Re: 320L scale up teleconference between John Hill, David Finbloom, and Genzyme					
9/11/1998	Phone Log	FDA	BB-IND 7616			
	Re: 320L scale up teleconference between John Hill, David Finbloom, and Genzyme - followup call.					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
9/14/1998	Phone Log	FDA	BB-IND 7616			
	Re: Follow up to 320L meeting request					
9/15/1998	Phone Log	FDA	BB-IND 7616			
	Re: Filing fees for A-Gal; discussion with Darin Weber regarding possible fees for A-Gal, specifically BLA. As Orphan Drug, A-Gal is exempt from standard PDUFA user fees, now $250,000 per application.					
10/1/1998	Amendment	FDA	BB-IND 7616	006		006
	FDA Request for Additional Information - Letter dated June 29, 1998					
10/1/1998	Amendment		BB-IND 7616	007		
	Amendment 007 - Revision to Clinical Protocol Pharmacokinetic and Pharmacodynamic Evaluation of A-GAL, Protocol No. FB9702--01					
10/7/1998	Amendment	FDA	BB-IND 7616	008		008
	Re: Amendment 008 to BB-IND No. 7616 - Request for end Phase III meeting. The purpose of this meeting to review clinical data and results of the initial analysis from our recently completely Phase I/II study "Pharmacokinetic and Pharmacodynamic Evaluation of Recombinant Human a-Galactosidase A (r-haGAL) Replacement In Patients With Fabry disease, Protocol No. FB9702-01. Includes cover fax from Carolyn McGarry dated 10/7/98.					
10/22/1998	USAN Application	FDA	BB-IND 7616			
	USAN (United States Adopted Names) application for A-Gal application, with a check for $5,000.00, and verification of absence of conflict.					
10/22/1998	Annual Report	FDA	ODD 86-152			
	Re: 86-152 - Annual Report of holder of Orphan Drug Designation - period of February 1997 through September 1998 for Orphan Drug designate # 86-152.					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
11/12/1998	Meeting Announcement	FDA	BB-IND 7616			
	Copy of FDA's announcement of meeting scheduled for Tuesday, 15 December 1998 at FDA in WOC1 Conference Room, 200S, from 1-2:30 p.m.; and internally on Friday, 11 December.					
11/23/1998	Amendment	FDA	BB-IND 7616	009		009
	Amendment 009 to BB-IND 7617 End of Phase I/II Meeting Briefing Package, in preparation for the upcoming End of Phase I/II Meeting, scheduled for December 15, 1998, to discuss Genzyme's recombinant human recombinant human a-galactosidase (r-HaGAL) progam.					
11/24/1998	Amendment	FDA	BB-IND 7616	009		009
	Re: Amendment 009 to BB-IND No. 7616 - End of Phase I/II briefing package. Please find color copies of the figures and graphs that were submitted on November 23, 1998 as part of the briefing packages for the End of Phase I/II meeting.					
12/1/1998	Amendment	BPA	BB-IND 7616	009		009
	Amendment 009 to BB-IND No. 7616 - Phase I/II briefing package. "Questions to Consider" which reference the briefing package for the End of Phase I/II briefing package that was submitted fo FDA on November 24, 1998.					
12/2/1998	Amendment	FDA	BB-IND 7616	009		009
	Amendment 009 to BB-IND 7616 - End of Phase I/II briefing package and Phase I/II draft report, with letter from Carolyn McGarry to Darin Weber (FDA) dated 2 December 1998.; Title of draft report: "Effect of Dose and Repeat Dosing on the Pharmacokinetics of r-haGAL in Man." ; NOTE: THERE ARE SEVERAL AMENDMENTS # 009 -- THIS IS OKAY					
12/15/1998	Presentation	FDA	BB-IND 7616			
	Draft of the End of Phase 1/2, Phase 3 Meeting Presentation (PowerPoint) MISSING DOCUMENT??					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
12/15/1998	Presentation Notes	FDA	BB-IND 7616	?		
	End of Phase 1/2 Phase 3 Meeting December 15, 1998 ; Introduction: David Schubert; Phase 1/2 Clinical Trial Results: David Meeker, M.D.; Histological Analysis: Michael O'Callaghan, D.V.M., Ph.D; Proposed Phase 3 Clinical Trial Protocol: David Meeker, M.D.					
12/21/1998	Meeting Minutes	FDA	BB-IND 7616			
	Draft of Meeting Minutes of 15 December 1998 meeting					
1/1/1999	Chart	FDA	BB-IND 7616			
	Page 7 of Process Scale up - 340 liter Bioreactor (proposed) - "Release Assays for Drug Substance" and "Release Assays for Drug Product"					
1/13/1999	Correspondence	FDA	BB-IND 7616			
	Re: Discussion of 340L process scale up. Attachment of summary document of process changes being proposed for the manufacture of a-gal.					
1/20/1999	Correspondence	FDA	BB-IND 7616			
	Re: Conference call scheduled for 21 January 1999 at 2 p.m.					
1/22/1999	Facsimile	FDA	BB-IND 7616			
	Fax to John Hill noting names of attendees at program (no date noted).					
1/25/1999	Amendment	FDA	BB-IND 7616	010		010
	Amendment 010 to BB-IND No. 7616, Recombinant Human a-Galactosidase (r-haGAL - Clinical Development Strategy. Response to FDA request for information.					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
1/27/1999	Phone Log	FDA	BB-IND 7616			

Re: Teleconference (no date noted, assuming of this date) to discuss 340 L scale up. Participants from FDA were John Hill, Earl Dye, and Blaire Fraser

2/3/1999	Facisimile	FDA	BB-IND 7616			

Re: copy of minutes of Pre-Phase 3 meeting that took place on 15 December 1998 for his review. Cover fax page included only from 7 page fax. Includes fax back to Caroline McGarry - FDA minutes of 15 December 1998, plus what seems to be a sheet from Genzyme's minutes, with their corrections on titles. What happened to Genzyme's minutes?

2/5/1999	Amendment	FDA	BB-IND 7616	011		011

Amendment 011 to BB-IND No. 7616, Recombinant Human a-Galactosidase (r-haGAL) - Phase 3 Clinical Protocol. "A Multi-Center, Placebo Controlled, Double Blind, Randomized Study of the Safety And Efficacy Of Recombinant Human a-Galactosidase A (r-haGAL) Replacement In Patients With Fabry Disease", Protocol -- No. AGAL-1-002-98

2/15/1999	Amendment	FDA	BB-IND 7616	013		013

Re: Amendment 013 to BB-IND No. 7616 - Repeat Dose Toxicity Study. Our initial proposal, as discussed with Dr. Martin Green during a conference call on August 21, 1998, was for a 3 month study with a 1 month interim wvaluation and interim study report.

2/18/1999	Amendment	FDA	BB-IND 7616	012		012

Amendment 012 to BB-IND No. 7616. This amendment provides details on a 340 liter bioreactor manufacturing process as well as release data on drug substance and drug product as manufactured via this process. Amendment contains: Amended CMC section to original IND 7616 incorporating all changes made to manufacturing process. Appendices 1-5. Two volumes.

2/22/1999	Amendment	FDA	BB-IND 7616	014		014

Re: Amendment 014 to BB-IND No. 7616 - Final Reports For Non-Clinical Studies. This amendment provides final versions of the draft reports that were provided in BB-IND 7617, submitted on March 6, 1998. StudyNo. 96001, 96002, 96003, 96004, 97056, 3-L68, 97044, 97043, and 97044a. Many attachments.

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
2/25/1999	Amendment	FDA	BB-IND 7616	015		015
	Re: Amendment 015 to BB-IND No. 7616 -- Revisions to Amendment 012 - Chemistry, Manufactring and Controls Section - Submitted February 18, 1999					
2/27/1999	Request for Information	FDA	BB-IND 7616			
	Re: questions regarding Amendment 012, Appendix 1					
3/2/1999	Responses to Questions	FDA	BB-IND 7616			
	Re: Responses to questions sent by Tom Eggerman.					
3/2/1999	Facisimile	FDA	BB-IND 7616			
	Re: Telecon Announcement -- scheduled for Tuesday, 9 March 1999, 3-4 p.m. at WOC1, DCTDA, Rm 236, to discuss Genzyme's strategy for validating surrogate endpoints.					
3/10/1999	Amendment	FDA	BB-IND 7616	016		016
	Re: Amendment 016 to BB-IND No. 7616 - Form 1572 for Phase 3 Protocol, CV of Principal Investigator, Meeting minutes from End of Phase I/2 Meeting					
3/12/1999	Amendment	FDA	BB-IND 7616	017		017
	An amended protocol for the Phase 3 clinical study "A Multi-Center, Placebo Controlled, Double Blind, Randomized Study of The Safety And Efficacy of Recombinant Human a-Galactosidase A (r-haGAL) Replacement In Patients With Fabry Disease", Protocol No. AGAL-1-002-98.					
3/22/1999	Phone Log	FDA	BB-IND 7616			
	Conversation between Carolyn McGarry and Tom Eggerman re: issues regarding Phase 3 clinical protocol for A-Gal.					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
3/26/1999	Facsimile	FDA	BB-IND 7616			

Re: Telecon Announcement -- Updated -- scheduled for Tuesday, 30 March 1999, 3-4 p.m., WOC1, DARP, Room 350, to discuss validating surrogate endpoints and proposed Phase 3 protocol.

3/26/1999	Amendment	FDA	BB-IND 7616	018		018

Facsimile to Thomas Eggerman with IND Amendment No. 018. Written response to issues discussed during conference call held March 24, 1999. Written response to Phase 3 protocol issues discussed at teleconference between Thomas Eggerman, MD, CBER and Genzyme on March 2, 1999. Issue #1. Measurement of alpha galactosidase protein levels at baseline. Are patients with some AGAL less likely to experience hypersensitivity reactions?

4/1/1999	Facsimile	FDA	BB-IND 7616

Attachment: list of participants of Genzyme employees who participated in teleconference of 30 March 1999.

4/1/1999	Email to Team Members	FDA	BB-IND 7616

Re: FDA Teleconference. Attached two electronic documents (not printed for file), first summarizing outcome of the surrogate endpoint validation discussion; second summarizing issues/responses from specific Phase 3 protocol questions.

4/1/1999	Phone Conference	FDA	BB-IND 7616

FDA Telephone Conference - March 30, 1999: Surrogate Endpoints Discusstion--Critical Issues

4/26/1999	Summary of Contact	FDA	BB-IND 7616

Re: Phase 3 Protocol Modifications

5/10/1999	Memorandum	FDA	BB-IND 7616

Re: End of Phase 2/Pre-Phase 3 teleconference with Genzyme, regarding the use of a-GAL for the treatment of Fabry's disease on March 30, 1999, 3-4:30 p.m., WOC I/Room 350

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
5/18/1999	Request for Information	FDA	BB-IND 7616			
	Acknowledgment of receipt of 15 February 1999 submission to IND, with questions.					
5/19/1999	Amendment	FDA	BB-IND 7616	020		020
	Re: Amendment 020 to BB-IND No. 7616 - Amendment No. 3 to Protocol AGAL - 1-002-98.					
5/19/1999	Amendment	FDA	BB-IND 7616	019		019
	Re: Amendment 019 to BB-IND No. 7616 - Amendment No. 2 Protocol AGAL 1-002-98. Indication Phase 3 Safety and Efficacy of Recombinant Human - Galactosidase a (r-haGAL) Replacement in Patients whith Fabry Disease.					
5/21/1999	Correspondence	USAN	BB-IND 7616			
	RE: USAN request for Alfa galactosidase, and request for a nonproprietary name, submitted on October 22, 1998. Need further information.					
5/25/1999	Correspondence	FDA	BB-IND 7616			
	Re: Cover letter for the meeting notes of the teleconference on March 30, 1999 between representatives of FDA and Genzyme. Note: The meeting notes mentioned are not attached.					
5/26/1999	Email	FDA	BB-IND 7616			
	Re: Inquiry regarding submission of Endpoint Proposal					
6/1/1999	Amendment	FDA	BB-IND 7616	021		021
	Re: BB-IND No. 7616, Amendment No. 021: Information Amendment. Please find information providing for the use of a liquid placebo in the clinical trial program. Reference is made to Amendment 012, dated February 18, 1999 in which the amended CMC section to the original IND.					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
6/4/1999	Amendment	FDA	BB-IND 7616	023		023

Re: BB-IND No. 7616 - Amendment 023 -- General Correspondence: Request for Meeting--Clinical.; Telephone conversation between Genzyme Corporation and CBER on March 30, 1999, and the provisions of Fast Track regulation,Genzyme requests a formal teleconference with CBER to discuss the revised analysis plan for Phase 3 Protocol No. AGAL-1-002-98 (originally submitted on February 5, 1999; amended on May 19, 1999, submission 020).

6/4/1999	Amendment	FDA	BB-IND 7616	022		022

Re: BB-IND No. 7616 - Amendment 022. General Correspondence--Request for Exemption and Meeting Request.

6/9/1999	Amendment / Annual Report	FDA	BB-IND 7616	024		024

Re: BB-IND No. 7616. Amendment 024 IND Annual Report. Pursuant to 21CFR312.33 enclosed please find the annual report to IND 7616. Annual Report Covering March 6, 1999 through April 9, 1999.

6/10/1999	Email	FDA	BB-IND 7616			

Re: Receipt of two meeting requests by Michael Noska at FDA. Original message from Nicole Brien to Dave, forwarded to Carol.

6/10/1999	Correspondence	FDA	ODD 86-152			

Re: requesting the presence of an Office of Orphan Products Development representative at a meeting to be held with CBER, date yet to be determined.

6/10/1999	Amendment	FDA	BB-IND 7616	025		025

Re: BB-IND No. 7616 - Amendment 025. Please find a copy of the correspondence to the office of Orphan Products Development (OPD) regarding OPD representation at the meeting with CBER regarding clinical endpoints.

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
6/11/1999	Amendment	FDA	BB-IND 7616	026		026

Re: BB-IND No. 7616 Amendment 026 -- New Investigators to Clinical Study. European investigators are being named to participate in study AGAL-1-002-98 entitled"A Multi-Center, Placebo Controlled, Double Blind, Randomized study of the safety and efficacy of Recombinant Human a-Galactosidase A (r-haGAL) Replacement in Patients with Fabry Disease"

6/16/1999	Amendment	FDA	BB-IND 7616	027		027

Re: BB-IND No. 7616 - Amendment 027 -- Initial IND Safety Report: Patient No. E08 - 008, Manufacturer Report # AGF003-S99FRA.

6/16/1999	Correspondence	FDA	BB-IND 7616

Re: Request for a copy of inspection report for BLA 98-0012, Centocor (Infliximab)

6/17/1999	Correspondence	FDA	BB-IND 7616

Re: receipt of Genzyme's request for records regarding Centocor - Infliximab BLA 98-0012

6/17/1999	email	FDA	BB-IND 7616

Re: FDA Contact. Mike Noska returned call regarding two meeting requests.

6/25/1999	Amendment	FDA	BB-IND 7616	028		028

Follow-up #1 to initial IND Safety report: Patient No. E008 - 008, Manufacturer Report # AGF003 - S99FRA

7/6/1999	Presentation	FDA	BB-IND 7616

Meeting at MCA July 6, 1999 a- galactosidase, Fabry Disease, Phase 1/2 Trial Design, Evaluations, Phase 1/2 Clinical Findings, Pharmacokinetics: First and Fifth Infusions, Percent GL - 3 Clearance in Plasma, Percent GL -3 Clearance in Liver, Liver Immunohistochemistry, Liver EM Endothelial Cells,GL - 3 Clearance (%) - Skin, Immunohistochemistry of Skin, Skin LM - Superficial Capillaries, Skin EM Superficial Capillary - Endothelium, and more. This is a printout of the presentation given at this meeting.

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
7/12/1999	Contact Report/Email	FDA	BB-IND 7616			
	FDA phone call: CMC methods plan submitted to FDA on June 4, 1999.					
7/12/1999	Contact Report	FDA	BB-IND 7616			
	Re: FDA phone call / follow up to conference call of 6/12/99.					
7/13/1999	Memorandum	FDA	BB-IND 7616			
	Re: list of participants in conference call of July 12, 1999					
7/14/1999	Facisimile	FDA	BB-IND 7616			
	Reminder to send in Annual Report, due in October 1999.					
7/15/1999	Contact Report	FDA	BB-IND 7616			
	Re: CMC Topics/Informal discussion with CMC reviewer - CONFIDENTIAL					
7/21/1999	Amendment	FDA	BB-IND 7616	029		029
	Re: Amendment 029 to BB-IND 7616 - Amendment No. 4 to Protocol AGAL-1-002-98. This amendment provides for the final infusion to occur at Visit 11, rather than at Visit 13, which reduces the trial length by two infusions or approximately four weeks.					
7/21/1999	Amendment	FDA	BB-IND 7616	030		030
	Volumes 1 and 2: Pre-Meeting Package; Volume 1: Letter to Michael Noska on July 21, 1999 Re: Amendment 030 to BB-IND No. 7616 - Meeting Request and Pre-Meeting Package. Meeting is requested to discuss and finalize the primary efficacy endpoints for the Phase 3 trial of r-haGAL in Fabry patients.; Volume 2: Appendix 4, continued from Volume 1.					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
7/29/1999	Contact Report	FDA	BB-IND 7616			
	Re: Discussion with CBER Medical Reviewer regarding a-GAL Amendment No. 4 to Phase 3 Protocol. CONFIDENTIAL					
7/30/1999	Correspondence	AMA	BB-IND 7616			
	Re: Responses to questions outlined in their communication of 21 May 1999 relating to the US Adopted Names application for A-GAL.					
8/3/1999	Amendment	FDA	BB-IND 7616	031		031
	Re: BB-IND 7616 - Amendment 031. Follow-up #1 to IND Safety Report: Patient No. E08-008, Manufacturer Report # AGF004 - S99FRA .					
8/9/1999	email	FDA	BB-IND 7616			
	Re: FDA endpoints call timing.					
8/11/1999	Correspondence	FDA	ODD 86-152			
	Re: Orphan Drug Designate 86-152; requesting presence of an OPD representative at a meeting with CBER on August 23, 1999.					
8/11/1999	Facisimile	FDA	BB-IND 7616			
	Re: Telecon Announcment of meeting on Monday, August 23, 1999 at 3-4 p.m. to discuss and finalize the primary efficacy endpoints for the Phase 3 trial.					
8/11/1999	Email to Team Members	FDA	BB-IND 7616			
	Re: FDA Contact regarding bulk sterility testing.					
8/11/1999	Correspondence	FDA	ODD 86-152			
	Re: requesting presence of an Office of Orphan Products Development representative at a meeting to be held with CBER on August 23, 1999, 3-4 p.m.					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
8/12/1999	Email to Team Members	FDA	BB-IND 7616			
	Re: FDA Contact # 2 on 8/12/99 regarding questions on endpoints proposal and global autonomic function.					
8/16/1999	Contact Report	FDA	BB-IND 7616			
	Re: Notation of contact with Eggerman at FDA about questions regarding endpoints proposal. Might be Dave Schubert's notes.					
8/16/1999	Contact Report	FDA	ODD 86-152			
	Re: Contact Report, 12:15 p.m. Endpoints discussion with FDA/Office of Orphan Drug Products Rep. Captain Melvin Lessing called to confirm the OPH had received meeting materials and confirmation for August 23rd telecon date.					
8/17/1999	Telecon	FDA	BB-IND 7616			
	Re: Telecon announcement of meeting set for Monday, 23 August 1999, 3-4 p.m.					
8/18/1999	Phone Log	FDA	BB-IND 7616			
	Re: Phase 3 Efficacy Endpoints Proposal - Discussion with Eggerman on Wednesday, August 18 regarding proposal and his specific questions.					
8/18/1999	Email	FDA	BB-IND 7616			
	Re: Time of contact set for August 18, 1999 at 3 p.m.					
8/18/1999	Amendment	FDA	BB-IND 7616	032		032
	Re: BB-IND No. 7616 - Amendment 032 -- Request for Type C Meeting.					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
8/19/1999	Amendment	FDA	BB-IND 7616	033		033
	Re: Amendment 033 to BB-IND No. 7616. Phase 3 Clinical Study Extension Protocol.					
8/19/1999	Phone Log	FDA	BB-IND 7616			
	Re: Phase 3 Efficacy Endpoints Proposal - Follow up.					
8/23/1999	Meeting Minutes	FDA	BB-IND 7616			
	Re: Genzyme's draft of Meeting minutes from FDA and Genzyme Teleconference discussion of Surrogate Endpoints, Phase 3 Protocol for A-GAL, August 23, 1999.					
8/24/1999	Facsimile	FDA	BB-IND 7616			
	Re: Type C Meeting set for September 9, 1999 at 10-10:30 a.m. - pre-read materials must be sent two weeks in advance.					
8/26/1999	Amendment	FDA	BB-IND 7616	034		034
	Re: IND Amendment No. 32 dated August 18, 1999; Pre-Meeting Package for Type C Meeting					
9/7/1999	Amendment	FDA	BB-IND 7616	035		035
	Re: BB-IND No. 7616 - Amendment 035. Additional Pre-Meeting Materials for Type C Meeting to be held September 9, 1999.					
9/8/1999	Contact Report	FDA	BB-IND 7616			
	Re: Confidential -- Discussion with Mike Noska re: bulk sterility testing.					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
9/8/1999	Memorandum	FDA	BB-IND 7616			
	Re: Type C Meeting about bulk sterility testing on September 9 at 10 a.m.					
9/13/1999	Correspondence	FDA	BB-IND 7616			
	Re: Minutes from meetng held between Genzyme and CBER on September 9, 1999.					
9/14/1999	Approval Letter	FDA	BB IND 7616			
	Re: BB IND 7616 - Approval Letter - Supplemental NDA dated 15 April 1999, received 16 April 1999; review completed and approved. "Supplement - Changes Being Effected in 30 Days".					
9/16/1999	Email	FDA	BB-IND 7616			
	Re: CALA Questionnaire attached by email					
9/22/1999	Proposal - Confidential	FDA	BB-IND 7616			
	Re: Phase 3 Study Efficacy Endpoints Proposal - CONFIDENTIAL - faxed to Tom Eggerman 9/22/99					
9/27/1999	Facisimile	FDA	BB-IND 7616			
	Re: Phase I/II Trial Scoares from Vascular Endothelium list					
10/4/1999	Facisimile	USAN	BB-IND 7616			
	Request to recheck response to Question 3 on Genzyme's preparred July 30th response to her letter of 21 May 1999.					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
10/5/1999	Approval Letter	FDA	BB IND 7616			

Re: BB IND 7616 - Approval Letter - Supplement new drug application (dated 4/7/99) provides for the use of the fill/finish area at the Allston, MA facility for filling and lyophilization of an additional product, recombinant human alphagalactosidase (rhaGAL), an investigational drug. March 9, 1999 is the implementation date for the change.

10/13/1999	Contact Report	FDA	BB-IND 7616			

Re: Confidential -- Informal teleconference with Michael Fontleroy, acting director, electronic submissions, CBER

10/13/1999	Teleconference Meeting Minutes	FDA/CBER	BB-IND 7616			

Re: BB-IND 7616 - Meeting minutes, Phase 3 Teleconference from August 23, 1999, 3-4 p.m. teleconference at W0C I/Conference Room 2.

10/13/1999	Correspondence	FDA	BB-IND 7616			

Re: Summary of telephone meeting held on August 23, 1999 between Genzyme and FDA.

10/15/1999	Amendment	FDA	BB-IND 7616	037		037

Re: BB-IND No. 7616 - Amendment 037 -- Initial IND Safety Report Patient No. 0111 MPH, Manufacturer Report No. AGF011-S99USA

10/15/1999	Amendment	FDA	BB-IND 7616	036		036

Re: Amendment 036 to BB-IND No. 7616 -- New Clinical Protocol.

10/15/1999	Correspondence	FDA	BB-IND 7616			

Re: Letter provides clarification requested in letter of October 4, 1999.

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
10/18/1999	Phone Log	FDA	BB-IND 7616			
	Re: Trademark Labeling of Investigational Drug.					
10/26/1999	Facisimile	FDA	BB-IND 7616			
	Re: Attached final version of the primary endpoints proposal for the Fabry clinical trial.					
10/26/1999	Phone Log	FDA	BB-IND 7616			
	Re: Phase 3 Efficacy Endpoints Proposal. Dr. James Kaiser will be new primary reviewer.					
11/3/1999	Amendment	FDA	BB-IND 7616	038		038
	Re: BB-IND No. 7616 - Amendment 038 -- Initial IND Safety Report: Patient No. 0801 B-O, Manufacturer Report No. AGF020-S99FRA.					
11/4/1999	email	FDA	BB-IND 7616			
	Re: Conversation with Dr. Eggerman re: endpoints proposal--reasonable, containing appropriate information that can go into a protocol amendment.					
11/16/1999	Amendment	FDA	BB-IND 7616	040		040
	Re: BB-IND No. 7616 - Amendment 040 R -- IND Safety Report No. 0703, Manufacturer Report # AGF022-S99FRA.					
11/16/1999	Amendment	FDA	BB-IND 7616	039		039
	Re: Amendment 039 to BB-IND No. 7616 - Amendment No. 5 to Protocol AGAL-1-002-98.; Phase 3 Safety and Efficacy of Recombinant Human Galactosidase A Replacement in Patients with Fabry Disease.					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
11/16/1999	Facisimile	FDA	BB-IND 7616			
	Re: Attached information relating to histology specimen collection and review incldulng definition/criteria for scoring, the description of data colletion and review, and the detail for handling discrepant scores between pathologists.					
11/22/1999	Amendment	FDA	BB-IND 7616	041		041
	Re: Study AGAL-005-99 entitled "A Multi-Center, Open-Label Extension Study of the Safety and Efficacy of Recombinant Human a-Galactosidase A (r-haGAL) Replacement in Patients with Fabry Disease" (protocol submitted on August 19, 1999, Submission No. 033).					
11/23/1999	Amendment	FDA	BB-IND 7616	042		042
	Re: BB-IND No. 7616 - Amendment 042 -- Response to FDA Request for Information and Request for Written Correspondence. Reference is made to Protocol No. AGAL - 1-002-98.					
11/23/1999	email	FDA	BB-IND 7616			
	Re: Secure Messaging Pilot.					
12/1/1999	Facisimile	USAN	BB-IND 7616			
	Re: USAN's recommendation to adopt "afgalsidase beta" for r-haGAL.					
12/2/1999	email	FDA	BB-IND 7616			
	Re: Briefs of FDA Contacts					
12/6/1999	email	FDA	BB-IND 7616			
	Re: USAN name assigned to a-gal; Barngrover's dissatisfaction with it.					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
12/7/1999	Amendment	FDA	BB-IND 7616	043		043
	Letter to Michael Noska December 7, 1999 RE: BB-IND 7616 - Amendment 043 ; Initial IND Safety Report: Patient No. 0602, Manufacturer Report # AGF024-S99UK; Initial IND Safety Report: Patient No. 0115, Manufacturer Report # AGF023-S99USA					
12/8/1999	Amendment	FDA	BB-IND 7616	043		043
	Additional Information to [FDA] Amendment No. 043 of November 23, 1999. (Genzyme Amendment 042).					
12/8/1999	Email	FDA	BB-IND 7616			
	Re: A-Gal FDA Contracts					
12/10/1999	Email to Team Members	FDA	BB-IND 7616			
	Re: A-Gal FDA Contracts - URGENT: Tom Eggerton received the IND submitted recently on 23 November; had specific questions.					
12/16/1999	Memorandum	FDA	BB-IND 7616			
	Re: Information Conference Call / Pathology Review Methods - call to be held December 17, 1999 at 10:45 a.m.					
12/17/1999	Amendment	FDA	BB-IND 7616	044		044
	Re: BB-IND 7616 - Amendment 044 -- Pathology Review Procedures and Training Manual.					
12/21/1999	Memorandum	FDA	BB-IND 7616			
	RE: Informal Conference Call / Pathology Review Methods - call to be held December 21, 1999 at 11 a.m.					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
12/21/1999	FDA Call Summary	FDA	BB-IND 7616			
	FDA Call Summary, describing events at teleconference held on December 21, 1999					
12/28/1999	Amendment	FDA	BB-IND 7616	045		045
	Re: BB-IND 7616 - Amendment 045 - IND Safety report Patient No. 0201, Manufacturer Report # AGF027-S99USA.					
1/4/2000	Memorandum	FDA	BB-IND 7616			
	Informal Conference Call / Discussion re: PIV and responses					
1/6/2000	Amendment	FDA	BB-IND 7616	046		046
	Re: BB-IND 7616 - Amendment 046 -- Clinical Amendment: New Investigators to Study AGAL-005-99 (Phase 3 Extension)					
1/7/2000	Contact Report	FDA	BB-IND 7616			
	Purpose of call was to further address some of the questions previously raised, Phase 4 and to discuss any additional info Genzyme can provide to assist with process.					
1/14/2000	Response to Request for Information	FDA	BB-IND 7616			
	Re: 11 pages, written response to questions under discussion with respect to primary endpoint agreed for Phase 3 clinical trial.					
1/17/2000	Correspondence	FDA	BB-IND 7616			
	Genzyme is in receipt of USAN communication dated December 1, 1999 recommending "afgalsidase beta" as the USAN name for A-GAL.					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
1/19/2000	Amendment	FDA	BB-IND 7616	047		047
	Re: BB-IND 7616 - Amendment 047 -- Response to FDA Request for Information: Strike-Through Version of Amended Protocol previously submitted on November 16, 1999. Faxed to Tom Eggerman on 1/18/00, fax receipt included.					
1/20/2000	Contact Report	FDA	BB-IND 7616			
	Re: Phone call to Dr. Gupta to inquire about a-GAL Phase 3 efficacy study statistical plan, citing protocol number.					
1/21/2000	Amendment	FDA	BB-IND 7616	048		048
	Re: BB-IND 7616 - Amendment 048 -- Response to FDA Request for Information--Phase 3 Study Questions and Responses					
1/27/2000	Facsimile	USAN	BB-IND 7616			
	Re: USAN Council Program Notice relative to her resignation from AMA with attached table identifying Genzyme's applications logged in through Nov 1999. Attached also USAN application LL-45, copy of the WHO application mailed to INN Committee Secretariat on January 27, 2000.					
1/27/2000	Email to Team Members	FDA	BB-IND 7616			
	Re: Discussion with Tom Eggerman about their not being ready to make a decision yet.					
1/27/2000	Contact Report	FDA	BB-IND 7616			
	Re: Contact with Dr. Gupta, statistical reviewer, at 2 p.m., to confirm his review of the Phase 3 Draft Statistical Plan submitted to IND on November 16, 1999.					
1/31/2000	email	FDA	BB-IND 7616			
	RE: Call to Dr. Hill to report plan to send him responses to May 1999 FDA questions.					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
2/3/2000	Amendment	FDA - CBER	BB-IND 7616	049		049
	Amendment 049 to BB-IND 7616, re: New Investigator to Phase 3 Extension Study					
2/10/2000	Correspondence	FDA	BB-IND 7616			
	Update of Information: Orphan Drug Listing. Includes change of designation date: 1/19/1988					
2/10/2000	Correspondence	FDA	BB-IND 7616			
	Re: update of information being submitted in order to update the Orphan Drug and Approvals database and web page.					
2/10/2000	Amendment	FDA	BB-IND 7616	051		051
	Request for Type A Meeting regarding BB-IND 7616 -- Amendment 051 - a copy of this letter is in ODD chron file as a cross rererence because it contains update of information as an Orphan Drug Listing.					
2/10/2000	Amendment	FDA	BB-IND 7616	050		050
	Amendment 050 to BB-IND 7616. Response to FDA Request for Information.					
2/10/2000	Correspondence	FDA	ODD 86-152			
	Update of Information: Orphan Drug Listing. Includes change of designation date: 1/19/1988					
2/11/2000	Amendment	FDA	BB-IND 7616	053		053
	RE: BB-IND 7616 -- re: BB-IND 7616 -- Amendment 053 -- Phase 4 Clinical Trial Proposal.					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
2/11/2000	Amendment	FDA	BB-IND 7616	052		052

Amendment 052 to BB-IND 7616 re: BLA Electronic Submission Demo and Questionnaire to Michael Fauntleroy and Michael Noska for review. Re: BLA Electronic Submission Demo and Questionnaire. Attached is Rachel Carle's letter of 28 January 2000 to Michael Fauntleroy attached to the CALA questionnaire form.

2/14/2000 Meeting Notes FDA BB-IND 7616

Notes from impromptu meeting with M. Fauntleroy re: delivering a copy of the aGal eSub demo CD to him in person.

2/17/2000 email FDA ODD 86-152

Re: Orphan Drug Office Contact Report; recent submission sent to Stephanie Donahoe's office updating the contact list for our orphan drug products did not have the orphan drug designations indicated in the text.

2/18/2000 Amendment FDA BB-IND 7616 055 055

Request for Type B Meeting to discuss content, timing and format of Alpha-GAL BLA, and two pre-BLA meeting requests. Amendment 055

2/18/2000 Amendment FDA BB-IND 7616 054 054

Request for Type C Meeting re: Amendment No. 054 to BB-IND 7616; to discuss issues related to the manufacturing facilities for Alpha-GAL.

2/22/2000 Phone Log FDA BB-IND 7616

Phone conversation with Tom Eggerman recgarding his questions from other reviewers.

2/22/2000 Amendment FDA BB-IND 7616 056 056

Response to FDA request for information re: replacement of original photomicrographs with scanned digitized copies; written comment on the difference in the resolution and/or sensitivity in LM and TEM. Amendment 056

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
2/23/2000	Annual Report	FDA	ODD 86-152			
	Re: Annual Report of holder of orphan-drug designation, # 86-152, for period of October 1998 through September 1999					
2/23/2000	Phone Log	FDA	BB-IND 7616			
	Re: Phone conversation with Marc Walton re: status and timing of providing assessment of Phase 3 endpoints.					
2/24/2000	Contact Report/email	FDA	BB-IND 7616			
	Email to Schubert regarding FDA phone contact with Tom Eggerman and Mike Noska regarding responses to two recent questions on Gruenfeld article and training meeting.					
2/24/2000	Amendment	FDA	BB-IND 7616	057		057
	Amendment 057. Agenda and a list of participants for Type C meeting.					
2/24/2000	Facsimile	FDA	BLA 99-2865 / STN BL 103979/0			
	Additional information requested related to the pre-BLA meeting, also submitted to the IND.					
2/25/2000	Contact Report	FDA	BB-IND 7616			
	Re: Phone Contact, Friday, February 25, 2000, 3 p.m.: Mike Noska and Nicole discussed plans for pathologist training meeting.					
2/25/2000	Contact Report	FDA	BB-IND 7616			
	Re: Phone contact, Friday, February 25, 2000, 4 p.m.: Schubert and Eggerman regarding outcome of the CBER internal meeting.					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
2/28/2000	Meeting Announcement	FDA	BB-IND 7616			
	Re: Meeting Announcment for Phase 3 Meeting on Tuesday, 14 March 2000, 3-4:30 p.m., with follow-up call notes in hand on bottom of page from talk with Walton & Weiss					
2/29/2000	Amendment	FDA	BB-IND 7616	058		058
	Amendment 058. Agenda, specific questions and a list of participants for Type B meeting.					
3/1/2000	Contact Report	FDA	BLA 99-2865 / STN BL 103979/0			
	Contact report re: discussion with Michael Fauntleroy re: eSUB, Question 1 on sponsor questions, etc.					
3/1/2000	Facisimile	FDA	BB-IND 7616			
	Re: Meeting information for Friday, March 24, 2000.					
3/2/2000	Facisimile	FDA	BB-IND 7616			
	Re: Responses to FDA communication dated 18 May 1999, also submitted to the IND. 10 pages.					
3/2/2000	email	FDA	BB-IND 7616			
	Re: C1-7; can the material form C1-7 run be used for commercial product -- FDA needs written information.					
3/3/2000	Contact Report	FDA	BB-IND 7616			
	Re: Electronic Submission Demo, Friday, 3 March 2000. Telephone conference with M. Fauntleroy to discuss his review of demo electronic submission sent to CBER on February 11, 2000.					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
3/3/2000	Facisimile	FDA	BB-IND 7616			
	Re: List of representatives who took part in telecon on 2/2/00.					
3/3/2000	Contact Report	FDA	BB-IND 7616			
	Re: Phone contacts with Eggerman, 2/24/00 re: responses to two recent questions; Noska, 2/24/00 re: training meeting.					
3/3/2000	Amendment	FDA	BB-IND 7616	059		059
	Amendment 059. Responses to FDA request for information dated 5-18-99 regarding Alpha-GAL product manufacturing and characterization.					
3/5/2000	Contact Report - Draft	FDA	BB-IND 7616			
	Re: March 2, 2000 Telecon with CBER Medical Reviewers; re-read proposal (followup to 2/29/00 telecon)					
3/8/2000	Amendment	FDA	BB-IND 7616	060		060
	Amendment # 060 to BB-IND 7616, New Protocol					
3/9/2000	Amendment	FDA	BB-IND 7616	061		061
	Amendment 061 to BB-IND 7616, Type C Meeting Package					
3/10/2000	Response to Request for Information	FDA	BB-IND 7616			
	RE: Written responses to questions raised by FDA on February 29, 2000.					
3/13/2000	Email to Team Members	FDA	BB-IND 7616			
	Re: FDA responses reviewed and sent to FDA on Friday, March 10, 2000. Attached Word doc.					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
3/16/2000	Facisimile	FDA	BB-IND 7616			
	RE: Change of conference room for March 24, 2000 meeting.					
3/17/2000	Amendment	FDA	BB-IND 7616	062		062
	Amendment 062 to BB-IND 7616, "A Multicenter, Open-Label Extension Study of the Safety and Efficacy of Recombinant Human a-Galactosidase A Replacement In Patients with Fabry Disease" (Study # AGAL-005-99)					
3/20/2000	Amendment	FDA	BB-IND 7616	063		063
	Amendment 063 to BB-IND 7616, response to request for information.					
3/23/2000	Amendment	FDA	BB-IND 7616	064		064
	Amendment 064, earlier submitted as IND Amendment 039 on November 16, 1999.					
3/24/2000	Amendment	FDA	BB-IND 7616	065		065
	Amendment 065 to BB-IND, a safety report for patient # 0015, R-S enrolled in the Open Label Phase 3 Extension study. "Although the event was not considered related to [Alpha-GAL], we are submitting this report for your information due to the nature of the event (suicide attempt)."					
3/26/2000	Contact Report	FDA	BB-IND 7616			
	Re: Phone contact report, Walton, 3/24/00; after speaking with Walton, called Eggerman to express surprise on fact that STAT plan was not agreed upon.					
3/29/2000	Amendment	FDA	BB-IND 7616	066		066
	Amendment 066 to BB-IND 7616, with responses to issues raised prior to the March 14, 2000 meeting.					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
3/31/2000	Amendment	FDA	BB-IND 7616	067		067
	Amendment 067 to BB-IND 7616, with Revised Statistical Analysis Plan and Histology Reread Procedure					
3/31/2000	Amendment	FDA	BB-IND 7616	068		068
	BLA Electronic Submission Demo # 2, with disk					
3/31/2000	Contact Report	FDA	BB-IND 7616			
	Re: Phone contact report, 3/30/00, Eggerman and Walton to inform them of latest verson of STAT plan and modificed proceedure t to re-read Histology.					
4/3/2000	Amendment	FDA	BB-IND 7616	069		069
	Amendment No. 069 to BB-IND 7616, Safety Report for Patient No. 0306.					
4/5/2000	Contact Report	FDA	BB-IND 7616			
	Re: Phone contact report, Walton/Eggerman - 4/4/00 - to discuss STAT plan for this week.					
4/6/2000	Contact Report	FDA	BB-IND 7616			
	Re: Phone contact report, Penny Dowd with Michael Fauntleroy re: Serial # 068, Electronic Submission Demo, 3/31/00. Error in CD submitted, sent corrected CD bgy Fedex, Tracking # 791					
4/9/2000	Contact Report	FDA	BB-IND 7616			
	Re: Phone log reports (Walton, 4/6/00, Eggerman, 4/7/00). CONFIDENTIAL					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
4/10/2000	Amendment	FDA	BB-IND 7616	070		070
	Amendment # 070 to BB-IND No. 7616 - General Correspondence regarding Phase 3 endpoints.					
4/12/2000	Facisimile	FDA	BB-IND 7616			
	Re: Participant list for teleconference set for April 11, 2000 to discuss Phase 3 Statistical Analysis Plan					
4/13/2000	Amendment	FDA	BB-IND 7616			
	Amendment # 05 to Protocol Number AGAL-1-002-98 - fifth draft					
4/13/2000	Amendment	FDA	BB-IND 7616	071		071
	Amendment 071: IND Safety Report, Patient No. 0805, Manufacturer Report # AGF050-S00FRA					
4/13/2000	Memorandum	FDA	BB-IND 7616			
	RE: Phase 3 meeting with Genzyme regarding use of A-Gal, March 14, 2000, 3-5:30 p.m.					
4/14/2000	Contact Report	FDA	BB-IND 7616			
	Phone Contact Reports, 4/14/00 and 4/17/00 with Tom Eggerman and Marc Walton regarding their comments on faxed revision to the STAT plan per the teleconference call on 4/11/00.					
4/17/2000	Amendment	FDA	BB-IND 7616	072		072
	Amendment 072: Phase 3 Protocol Revised Statistical Analysis Plan					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
4/18/2000	Meeting Minutes	FDA	BB-IND 7616			
	Meeting Minutes from FDA/Genzyme teleconference with Dr. Marc Walton and Dr. Tom Eggerman on April 11, 2000, 2-3:15 p.m.					
4/20/2000	Amendment	FDA	BB-IND 7616	073		073
	Re: Amendment 073: Investigation into Bioreactor Contamination and Disposition of Harvested Material, 27 pages					
4/21/2000	Meeting Minutes	FDA	BLA 99-2865 / STN BL 103979/0			
	Minutes of Genzyme-CBER meeting of 3-24-00.					
4/21/2000	Meeting Minutes	FDA	BB-IND 7616	062		
	Re: BB-IND 7616 - Copy of memorandum summarizing 24 March 2000 meetng with CBER.					
4/28/2000	Facsimile	FDA	BLA 99-2865 / STN BL 103979/0			
	Confirmation of teleconference scheduled for Monday, 1 May 2000 at 10 a.m. with Dr. Marc Walton and Dr. Tom Eggerman, and Alison Lawton, Dave Schubert, Nicole Brien, John McPherson, PK Tandon, and Rich Moscicki.					
5/1/2000	Contact Report	FDA	BB-IND 7616			
	Re: Teleconference 5/1/00 with Bill Purvis per Marc Walton's request for press release on Phase 3 data; 5/2/00 -- teleconference with Purvis regarding CBER comments faxed by BP. Attached: press release					
5/1/2000	Amendment	FDA	BB-IND 7616	074		074
	RE: Amendment 074: General Correspondence regarding Phase 3 Primary Efficacy and Pre-BLA Meeting Scheduling					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
5/1/2000	Contact Report	FDA	BLA 99-2865 / STN BL 103979/0			
	Contact report notes include current demo.					
5/3/2000	Contact Report	FDA	BB-IND 7616			
	FDA contacts of 5/3/00, 5/11/00 with Fauntleroy, Noska, and Eggerman re: Phase 4 plan					
5/4/2000	Amendment	FDA	BB-IND 7616	075		075
	Re: Amendment 075 - Initial Written and Follow-Up Safety Reports on Patients No. 0304, 0306, 0805					
5/5/2000	Amendment	FDA	BB-IND 7616	076		076
	Amendment 076					
5/8/2000	email	FDA	BB-IND 7616			
	Re: CD to Fauntleroy, eSub					
5/8/2000	email	FDA	BB-IND 7616			
	Re: Phone contact report with M. Fauntleroy requesting additional contact name for discussion about secure email with CBER.					
5/9/2000	Correspondence	FDA	ODD 86-152			
	Re: Request for OPD Representation at Pre-BLA Meetings with CBER Orphan Drug Designation # 86-152.					
5/9/2000	Draft	FDA	BB-IND 7616			
	Draft of Summary of Suspected Hypersensitivity-type Events					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
5/9/2000	Correspondence	FDA	BB-IND 7616			
	Press Release for Fabrazyme Phase 3 Clinical Trial Results					
5/11/2000	Telecon Confirmation	FDA	BLA 99-2865 / STN BL 103979/0			
	Facsimile re: teleconference confirmation with FDA for Tuesday, 30 May 2000, 1-3 p.m.					
5/12/2000	Email	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: Michael Fauntleroy's call regarding MAA demo CD receipt and the comments he received from Dr. Walsh on Part IV clinical content on Demo # 2.					
5/12/2000	Meeting Announcement	FDA	BLA 99-2865 / STN BL 103979/0			
	Meeting Announcement for Tuesday, 23 May 2000, 3-5 p.m., and Tuesday, 30 May 2000, 1-3 p.m.					
5/17/2000	Amendment	FDA	BB-IND 7616	077		077
	Amendment 077: Clinical Amendment: New Investigators to Study AGAL-005-99 (Phase 3 Extension); Clinical Amendment: Updated FDA Form 1572 for Phase 3 Study No. AGAL-002-98; Clinical Amendment: Updated FDA Form 1572 for Skin Test Study No. AGAL-004-99.					
5/18/2000	Amendment	FDA	BB-IND 7616	078		078
	RE: Amendment 078 - Supplemental Information for Pre-BLA CMC Meeting scheduled for Tuesday, 23 May 2000. Attached is letter from Herndon dated 31 August 1999.					
5/19/2000	Email	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: conversation with product reviewer and "moratorium" for the submission of BLAs, beginning on July 3, lasting for 2-3 weeks.					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
5/23/2000	Correspondence	AMA	BB-IND 7616			

Re: INN Expert Committee found linguistic difficulties in several languages with the f-g combination and has selected alternative designation, "agalsidase alfa" and subsequently "agalsidase beta". If the name is accepted by all parties, "agalsidase beta" can be adopted as USAN on June 28, 2000.

5/23/2000	Meeting Notes	FDA	BB-IND 7616			

Re: Phase 4 discussion with Dr. Kaiser: participants were PK, Sanj, Pedro, Mary, Rich, Alison, Dave, NB

5/25/2000	Phone Log	APLB	BB-IND 7616			

Re: Phone Log regarding conversation with Bill Purvis at Advertising & Promotion Branch about when to submit Fabrazyme trade name to branch for review, before BLA submission, or after.

5/25/2000	Facisimile	FDA	BB-IND 7616			

Fax to Michael Noska with participant list of pre-BLA CMC teleconference of 23 March 2000.

6/5/2000	Amendment	FDA	BB-IND 7616	080		080

Amendment 080 to BB-IND 7616 re: Protocol Amendments: Phase 1/2 Extension Study and Phase 3 Study. Genzyme is submitting Amendment No. 1 to Phase 1/2 Extension Study AGAL-006-99.

6/6/2000	Amendment	FDA	BB-IND 7616	079?		079?

Amendment 079 - MISSING

6/7/2000	Correspondence	AMA	LL-45			

USAN application for a-GAL, LL-45; receipt of USAN letter of 23 May 2000 recommending "agalsidase beta"

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
6/9/2000	Amendment	FDA	BB-IND 7616	081		081
	Amendment 081 re: Request for Trademark Review					
6/11/2000	TOC - BLA	FDA	BB-IND 7616			
	Item 1 (TOC) of the 356H of the a-GAL BLA, 23 pages.					
6/12/2000	Amendment	FDA	BB-IND 7616	082		082
	Amendment 082 - Annual Report to the IND covering period from April 9, 1999 through April 9, 2000.					
6/13/2000	Amendment	FDA	BB-IND 7616	083		083
	Amendment # 083 to BB-IND No. 7616 - Initial Written and Follow-Up Safety Reports: patient No. 0109, AAP, 0115					
6/13/2000	Contact Report	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: Noska will send information regarding BLA submissions; Jules Meisher, Mike Noska, Mike Fauntleroy need to be notified of the submission date of arrival, etc.					
6/14/2000	Facisimile	FDA	BB-IND 7616			
	DCC Procedure Guide # 4b from FDA CBER Document Control Center					
6/19/2000	Contact Report	FDA	BB-IND 7616			
	Phase 3 Extension LM Pathology Review Procedures					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
6/20/2000	Facisimile	FDA	BB-IND 7616			

List of participants in teleconference with Drs. Eggerman and Kaiser held on Friday, 16 June 2000.

6/21/2000	Project Notes	FDA	BB-IND 7616			

Nicole Brien's handwritten notes re: Jim Crim and Phil Noquchi.

6/21/2000	Memorandum	FDA	BB-IND 7616			

Re: Pre-BLA Teleconference with Genzyme, May 23, 2000, 3 p.m. Meeting Notes: purpose of teleconference was to discuss the manufacturing and facilities issues surrounding the Sponsor's proposed Biologics License Application (BLA) submission.

6/21/2000	Contact Report	FDA	BLA 99-2865 / STN BL 103979/0			

Re: told him we have 19 boxes, 2 full copies and 28 additions, etc.

6/23/2000	Original Submission	FDA	BLA 99-2865 / STN BL 103979/0			

Original BLA Submission, 81 volumes submitted to FDA on 23 June 2000. Electronic, except for two CDs, which are in Central Files on shelves in Binder #031. This is cross-referenced as separate document entry.

6/23/2000	Original Submission (CDs)	FDA	BLA 99-2865 / STN BL 103979/0			

CDs of Original BLA Submission, 81 volumes submitted to FDA on 23 June 2000, with Administrative corrections on 11 September 2000.

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
6/23/2000	Original Submission (CDs)	FDA	BLA 99-2865 / STN BL 103979/0			
	CDs of Original BLA Submission, 81 volumes submitted to FDA on 23 June 2000, with Administrative corrections on 11 September 2000.					
6/23/2000	Original Submission	FDA	BLA 99-2865 / STN BL 103979/0			
	Original BLA Submission, 81 volumes submitted to FDA on 23 June 2000. Electronic, except for two CDs, which are in Central Files on shelves in Binder #031. This is cross-referenced as separate document entry.					
6/26/2000	Amendment	FDA	BB-IND-7616	084		084
	Amendment 084 - Follow-up written Safety Report, Manufacturer Report No. AGF 054-S00USA. MedWatch report for Patient # 0304 RBB					
6/28/2000	Correspondence	FDA	BB-IND 7616			
	Re: Letter informing Genzyme that USAN council has adopted "agalsidase beta" US adopted name for a-GAL. Enclosed Statement of Adoption.					
6/29/2000	Memorandum	FDA	BB-IND 7616			
	Memorandum/Meeting Notes of Meeting held on May 30, 2000 at 1 p.m. Purpose of meeting was for the sponsor to present results of pivotal trial and for the Agency and the Sponsor to discuss and come to agreement on the format and content of the clinical, pharmacology and statistical portions of the proposed BLA.					
6/30/2000	Correspondence	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: Reference Number 99-2865 has been assigned to recent submission of BLA, received June 23, 2000.					
6/30/2000	Amendment	FDA	BB-IND 7616	085		085
	Amendment 085 to BB-IND 7616: Pathology Review Procedures for Phase 3 Extension Study					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
7/5/2000	Amendment	FDA	BB-IND 7616	086		086

Amendment # 086 to BB-IND No. 7616 - IND Safety Report for Patient No. 0202, Manufacturer Control No. AGF061-S00USA.

7/10/2000 Correspondence FDA BB-IND 7616

Re: Attached is Amendment 067 from 3/31/00, IND submission of the Final Procedure for the Kindey Pathology Review

7/10/2000 Facisimile FDA BLA 99-2865 / STN BL 103979/0

Re: IND submission of the Final Procedure for the Kidney Pathology Review, as submitted to the IND on March 31, 2000.

7/11/2000 Contact Report FDA BB-IND 7616

Attached pathology review process descriptions for the Phase 3 trial. Included are entire documents and cover letters to the respective IND submissions.

7/12/2000 Contact Report FDA BB-IND 7616

Re: Initial questions and responses and further questions on adjudication process, TEM, statistical plan, CRFs, Kidney, etc. - internal meeting

7/14/2000 Case Report FDA BB-IND 7616

Re: Case report for kidney, skin and heart attached, as per his request, Protocol AGAL-005-99.

7/14/2000 Facisimile FDA BB-IND 7616

Attached Skin CRF with the IHC removed. Version represents the proposed pathology review process.

7/14/2000 Contact Report FDA BB-IND 7616

Re: Record of call with Tom Eggerman on adjudication process, TEM, Statistical Plan, CFFs, Kidney

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Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
7/17/2000	Contact Report	FDA	BB-IND 7616			
	Re: Eggerman called with a few questions, I.e., wants to ensure we address adjudication in the propsal for how to cover the full range of scores, in particular 1, 2, 3.					
7/18/2000	Amendment	FDA	BB IND 7616	087		
	Re: Proposal for Submission of Phase 3 Extension Data During BLA Review Period					
7/18/2000	Amendment	FDA	BB-IND 7616	087		087
	Proposal for Submission of P3 Extension Data during BLA review period					
7/18/2000	Responses to Questions	FDA	BB-IND 7616			
	RE: Responses to questions regarding the pathology review for the Phase 3 Extension Study.					
7/20/2000	Contact Report	FDA	BB-IND 7616			
	Re: Request for Tradename Review" to Reviewing Division, OTRR; Fabrazyme name					
7/20/2000	Contact Report	FDA	BB-IND 7616			
	Re: Conversation with Noska re: additional BLA copies to be sent to FDA; submissions to IND/BLA					
7/21/2000	Correspondence Sent	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: General Correspondence regarding Official Contacts and Phase 3 Extension Plans					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
7/24/2000	Amendment	FDA	BB-IND 7616	088		088
	Amendment # 088 to BB-IND No. 7616 - Phase 3 Extension Pathology Review Procedures - Response to FDA Requests for Information					
7/26/2000	Amendment	FDA	BB-IND 7616	089		089
	Amendment # 089 to BB-IND No. 7616 - General Correspondence Regarding Meeting Minute Clarifications (BB IND 7616 and BLA Ref. No. 99-2865)					
7/26/2000	Correspondence Sent	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: Meeting Minute Clarifications regarding CMC issues associated with pending BLA.					
7/31/2000	Contact Report	FDA	BB-IND 7616			
	Re: Kaiser's technical questions regarding navigability within the electronic submission.					
8/1/2000	Contact Report	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: Dr. Kaiser phoned with questions regarding content of BLA submission					
8/2/2000	Correspondence Sent	FDA	BLA 99-2865 / STN BL 103979/0			
	Facsimile included: Phase 3 Study AGAL-1-002-98 Final Statistical Analysis Plan; Phase 3 Study AGAL-1-002-98 Procedure for quantitation of glycolipid inclusions in the kidney.					
8/2/2000	Contact Report	FDA	BB-IND 7616			
	Re: Dr. Kaiser has no pre-requests or questions at the moment.					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
8/3/2000	Contact Report - MISSING	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: teleconference between Nicole, Richard Moscicki, Dr. Kaiser, in follow-up to teleconference with CBER on Phase 4 study.					
8/8/2000	Amendment	FDA	BLA 99-2865 / STN BL 103979/0	001		001
	Amendment 001 - Response to Medical Reviewer Request for Information. CD attached; sent by Fedex.					
8/8/2000	Meeting Minutes	FDA	BB-IND 7616			
	Teleconference with Jim Kaiser, minutes of that meeting. Purpose of meetng was to review the proposed plan for submitting Phase 3 extension efficacy data to the BLA and the 120 day safety update.					
8/9/2000	Amendment	FDA	BB-IND 7616	090		090
	Amendment # 090 to BB-IND No. 7616 - Phase 4 Draft Protocols for CBER Review and Teleconference Request					
8/10/2000	Correspondence Sent	FDA	BLA 99-2865 / STN BL 103979/0			
	Facsimile of 63 pages (not included) "as requested - P3 X protocol"					
8/11/2000	Amendment	FDA	BB-IND 7616	091		091
	Amendment # 091 to BB-IND No. 7616 - Clinical Amendment: New Investigators to Study AGAL-005-99 (Phase 3 Extension); and AGAL-006-99 (Phase 1/2 Extension).					
8/14/2000	Correspondence Sent	FDA	BLA 99-2865 / STN BL 103979/0			
	Summary of efficacy assessments to be represented in upcoming submissions.					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
8/16/2000	Email	FDA	BB-IND 7616			
	Re: FDA Contact - Site Inspection -- production schedules must clearly outline relevant activities. FDA called to request the schedules for the facilities.					
8/16/2000	Contact Report	FDA	BB-IND 7616			
	Re: Whether the Phase 4 protocol must be submitted to the IND and or the BLA. Resolution: submit the protocol to the IND and copy the cover letter to BLA file.					
8/16/2000	Email to Team Members	FDA	BB-IND 7616			
	Re: FDA Clinical Site Inspections -- audit of data at the French sites participating in the AGAL-1-002-98 study, Cochet/Lyon and Germain/Paris, primary auditor Lourdes Valentin.					
8/17/2000	Amendment	FDA	BB-IND 7616	092		092
	Amendment # 092 to BB-IND No. 7616 - Initial Written Safety Report, Manufacturer Report No. AGF064-S00UK					
8/18/2000	Contact Report	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: Dr. Kaiser's receipt of fax dated 8/18/00 prepared by E. Singer. It needs to be submitted to the BLA so a future review would have access to it.					
8/18/2000	Contact Report	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: Dr. Kaiser's receipt of fax dated 8/18/00 prepared by E. Singer.					
8/18/2000	Correspondence Sent	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: Attached information referred to in earlier phone call on AGAL 1-002-98, Description of Slide Analysis Datasets					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
8/21/2000	Correspondence Received	FDA	BLA 99-2865			
	FAX received regarding inspection of Clinical Site Participating in Study AGAL-1-002-98 Confirmation of Dates Planned					
8/21/2000	Email	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: Attached PAI Schedule and Fabryzyme Manufacturing Schedule sent originally to Nicole by Mark Hayes; Nicole emailed back to Mark that it has been faxed to Mike Noska and that she will submit it to the BLA tomorrow.					
8/21/2000	Correspondence Sent	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: Attached Fabrazyme Production Schedule.					
8/22/2000	Correspondence Sent	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: September Amendment to the BLA will include data in the same formats as provided in the original BLA submission, except where noted below.					
8/23/2000	Amendment	FDA	BLA 99-2865 / STN BL 103979/0	002		002
	Amendment 002; Response to Medical Reviewer Request for Information. CD attached					
8/23/2000	Articles	FDA	BB-IND 7616			
	Attached three articles referred to in open label study protocol to be discussed on the 25th of April.					
8/24/2000	Amendment	FDA	BB-IND 7616	093		093
	Amendment # 093 to BB-IND No. 7616 - IND Safety Reprot for Patient No. 0605, Manufacturer Control No. AGF065-S00UK.					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
8/24/2000	Article		BB-IND 7616			
	Article: Fabry Disease: Robert J. Desnick and David F. Bishop, no date - APPROXIMATE DATE					
8/24/2000	Contact Report	FDA	BB-IND 7616			
	Re: FDA contact on GCP Inspections and action items regarding hotels, transportation, etc.					
8/24/2000	Email	CAS	BB-IND 7616			
	Re: Discussion with CAS on more information regarding the registry and cost of the process					
8/25/2000	Correspondence Sent	FDA - CDER	BLA 99-2865			
	List of experts to consider for the December 8, 2002 Advisory Committee Meeting					
8/29/2000	Correspondence Sent	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: List of participants in Phase 4 telecon on August 25, 2000.					
8/30/2000	Contact Report	FDA	BB-IND 7616			
	Re: Compassionate Use Request for Mr. Cordell					
8/30/2000	Contact Report	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: Phase 4 Planning and Compassionate Use Request - Teleconference					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
8/30/2000	Amendment	FDA	BB-IND 7616	094		094
	Amendment # 094 to BB-IND No. 7616 - Compassionate Use Request for patient CAC under care of Dr. Thomas M. Bashore at Duke University Medical Center.					
9/1/2000	Teleconference Notes	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: Fabrazyme BLA electronic submission					
9/1/2000	Contact Report	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: Fabrazyme BLA GCP Inspections of French Sites					
9/5/2000	Correspondence	CAS	104138-64-9			
	Re: Update to CAS Registry No. 104138-64-9.					
9/5/2000	Facisimile	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: GCP inspections, Hotels in France					
9/5/2000	Correspondence Sent	FDA	BLA 99-2865			
	Hotels in France for Fabrazyme BLA 99-2865 GCP Inspections					
9/6/2000	Contact Report	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: Various BLA and IND (Compassionate Use and Clinical Material)					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
9/6/2000	Contact Report	FDA	BLA 99-2865 / STN BL 103979/0			

Re: Telecontact between Michael Fauntleroy and Nicole Brien, Darlene Stevens, Andy Siegel, Shy Kumar regarding the BLA electronic submission in a followup to the telecon of 1 Sept 2000 during which Fauntleroy described the usability issue.

9/6/2000	Contact Report	FDA	BLA 99-2865 / STN BL 103979/0			

Re: PAI planning; participants were Nicole, Mark Hayes, Dale Audet; Walt Lange, Kevin O'Brien, M. Noska

9/6/2000	Contact Report	FDA	BB-IND 7616			

Various BLA and IND items (Comp. Use and clinical material, etc.)

9/7/2000	Amendment	FDA	BB-IND 7616	095		095

Amendment # 095 to BB-IND No. 7616 - request for compassionate use of Fabrazyme was made for patient CAC at the Duke University Medical Center.

9/7/2000	General Correspondence	FDA	BB-IND 7616			

Re: BB-IND 7616 - Receipt of supplemental new drug application dated April 7, 1999, received April 8, 1999. Completed review and approved it.

9/8/2000	Correspondence Sent	FDA	BLA 99-2865			

Modified manufacturing schedule for Fabrazyme around the week of November 13-17, 2000.

9/11/2000	Correspondence Sent	FDA	BLA 99-2865 / STN BL 103979/0			

Re: BLA 99-2865 / STN BL 103979/0 - Administrative Correction to Original BLA Electronic Media submitted on 23 June 2000. Pursuant to recent discussions with Michael Fauntleroy, Genzyme is now providing an administrative amendment to BLA 99-2865 to make improvements to the Original BLA electronic media that will enhance usability. Includes two CDs.

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
9/11/2000	Meeting Minutes	FDA	BB-IND 7616			
	Global meeting (participants: Arlene, Canada; Pauline, Europe; Konomi, Japan; Dave Hymes, Int'l; Kimberlee, RACME; Rumana, US; Nicole, Global)					
9/12/2000	Teleconference Notes	FDA	BLA 99-2865 / STN BL 103979/0			
	Various BLA and IND (CBER action dates, nanofiltration, etc.)					
9/12/2000	Correspondence Received	FDA	BLA 99-2865			
	CBER has completed an initial review of the June 23, 2000 application for agalsidase beta, for the treatment of Fabry disease, to determine its acceptablility for filing					
9/12/2000	Facisimile	FDA	BLA 99-2865 / STN BL 103979/0			
	Commercial Use Request					
9/12/2000	Facisimile	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: Hotel confirmations of the hotel in Lyon and Paris					
9/12/2000	Correspondence Sent	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: Travel information during visit to France.					
9/12/2000	Correspondence	FDA	BB-IND 7616			
	Re: Attached is summary of changes to the phase 4 double blind study (Study No. AGAL-008-00)					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
9/12/2000	Contact Report	FDA	BB-IND 7616			
	Re: Various BLA and IND items (CBER action dates, nanofiltration, etc)					
9/13/2000	Facisimile	FDA	BB-IND 7616			
	Re: Representatives participating in the call on Friday, September 8, 2000 regarding the Phase 4 protocol.					
9/13/2000	Teleconference Notes	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: Submission directory structure; participant from FDA was Joseph Montgomery, CBER					
9/14/2000	Correspondence Sent	FDA	BLA 99-2865 / STN BL 103979/0			
	General Correspondence / Modified Manufacturing Schedule					
9/14/2000	Correspondence Sent	FDA	BLA 99-2865			
	Information to share on the travel situation in France					
9/14/2000	Correspondence Received	FDA	BLA 99-2865			
	FDA received FOIA request for records regarding THomas Acki, Henry Bone, Jaime Davison, etc. - CV Reference number - 00017927					
9/18/2000	FDA Site Visit Report	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: FDA Audit De-Brief (Report) - Protocol AGAL 1-002-98. Site Number 7 (Lyon) Attached are emails from Lisa Becker to Nicole Brien and others regarding this FDA audit.					

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Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
9/18/2000	Facisimile	FDA	BB-IND 7616			
	Re: Phase 4 Protocol, Revised description of Cardiac Events					
9/18/2000	Amendment	FDA	BB-IND 7616	096		096
	Amendment # 096 to BB-IND No. 7616 - IND Safety Report for Patient No. 0506, Manufacturer Control No. AGF064-S00UK					
9/21/2000	Teleconference Notes	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: BLA questions regarding slide Ids, IHC, FDA slide review plans					
9/22/2000	Contact Report	FDA	BB-IND 7616			
	Re: Cardiac endpoints, datasets and the slide Ids; conversation with Dr. Kaiser.					
9/22/2000	Contact Report	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: attached summary of recent changes to the draft protocol AGAL-008-00.					
9/22/2000	Email	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: Urgent follow-up FDA; Amendment # 2 of the Protocol includes the May 14th version of the "summary of changes"					
9/26/2000	Amendment	FDA	BB-IND 7616	097		097
	Amendment 097, Follow-up written safety report for Patient No. 0605, Manufacturer Control No. AGF065-S00UK					
9/26/2000	Correspondence Sent	FDA	BLA 99-2865			
	explanation of the Slide ID topic that Dr. Kaiser brought to Genzyme's attention					

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Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
9/28/2000	Contact Report	FDA	BLA 99-2865			
	Contact Report Regarding Technical Reviews, Tradename Letter, GMP Inspection, Phase 3 Extension Efficacy Report, Filability Letter, Advisory Committee, STN Number and Follow-up Voicemail to Mike Noska					
9/29/2000	Contact Report	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: Request for Slides, question about vendor error					
9/29/2000	Request for Slides	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: Request for slides to be sent to CBER (trial AGAL-1-002-98)					
9/29/2000	CAS Registry Confirmation	FDA	BB-IND 7616			
	Re: BB-IND 7616 - CAS registration confirmation from Sabine Kuhn, CAS, American Chemical Society; attached is Rumana Rahman's letter by fax to CAS with a request for the update to CAS Registry No. 104138-64-9.					
10/2/2000	Amendment	FDA	BLA 99-2865 / STN BL 103979/0	003		
	Amendment 003 to BLA 99-2865, Phase 3 Extension Study, Interim Efficacy Report, with CD, 4 volumes (2 volumes on the shelves)					
10/3/2000	Facsimile	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: Hotel recommendations in Cambridge and Framingham					
10/3/2000	Amendment	FDA	BB-IND 7616	098		098
	Amendment 098: Initial Written Report; Manufacturer Report No. AGF067-S00USA.					

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Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
10/5/2000	Contact Report	FDA	BLA 99-2865			
	Contact Report regarding various BLA items: *Request for additional data listings, new requests from Dr. Kaiser, vendor question and question regarding stat plan and blind status, histology slides to be sent to FDA*					
10/5/2000	Amendment	FDA	BB-IND 7616	099		099
	Amendment 099: Final Phase 4 Protocol (Study AGAL-008-00)					
10/10/2000	Correspondence Sent	FDA	BLA 99-2865 / STN BL 103979/0			
	Fleiss Statistics (tables, listing, page from programming spe, pages from textbook)					
10/11/2000	Amendment	FDA	BLA 99-2865 / STN BL 103979/0	004		004
	Amendment 004; HVAC Classification modifications					
10/11/2000	Correspondence Sent	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: STN BL103979/0 (BLA Reference No. 99-2865, General Correspondence), Phase 3 Study Original LM Slides					
10/12/2000	Correspondence	USAN	BB-IND 7616			
	Re: LL-45, Update to CAS Registry No. 104138-64-9					
10/13/2000	Correspondence Received	FDA	BLA 99-2865 / STN BL 103979/0			
	BLA Information request letter per phone message (BL 103979/0 replaces 99-2865)					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
10/14/2000	Correspondence Sent	FDA	BLA 99-2865 / STN BL 103979/0			

Description of errors in the study treatment allocation.

10/14/2000	Contact Report	FDA	BLA 99-2865			

Contact Report regarding various items related BLA requests that are pending and new requests. Vendor error description, submission of additional analyses, change in GFR, product preparation, Urinary GL-3, antibody titer table versus kidney scores, and baseline leukocyte.

10/17/2000	Correspondence Sent	FDA	BLA 99-2865 / STN BL 103979/0			

Sensitivity Analysis

10/18/2000	Correspondence	FDA	BB-IND 7616			

Copies of vials and labels (Study Agal-1-002-98)

10/18/2000	Correspondence Sent	FDA	BLA 99-2865 / STN BL 103979/0			

Copies of vials and lables (Study Agal-1-002-98) - documentation on the labels for patients that were affected by errors in kit assignment. 30 pages

10/19/2000	Contact Report	FDA	BLA 99-2865 / STN BL 103979/0			

Re: Discussion with Dr. Kaiser regarding various items related BLA request that are pending and new requests. Vendor error description, information about urinary GL-3 for patient 307, Table 11-31 in the Phase 3 Study Report, Additional Analyses, new request from 10/18, new request from 10/19

10/20/2000	Correspondence Sent	FDA	BLA 99-2865 / STN BL 103979/0			

Fax with attached analyses requested by Dr. Kaiser re: Change in GFR as Treated; Kidney LM stratified by age; Conconmitant meds - 45 pages

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
10/20/2000	Contact Report	FDA	BLA 99-2865 / STN BL 103979/0			

Re: Advisory Panel. Discussion with Kathleen Reedy, Executive Secretary of the Endocrinologic and Metabolic Drugs Advisory Committee re: December 8th committee meeting to review Fabrazyme.

10/20/2000	Correspondence Sent	FDA	BLA 99-2865 / STN BL 103979/0			

With Fabrazyme P3 trial abstract presented at ASHG earlier in October.

10/20/2000	Correspondence Received	FDA	BLA 99-2865 / STN BL 103979/0			

Copy of letter to Lourdes Valentin from Dominique Germain in Paris re: observations featured on the 483 form she issued following her inspection on 22, 25, 26 September 2000.

10/24/2000	Correspondence Sent	FDA	BLA 99-2865 / STN BL 103979/0			

Analysis and data listing related to the Fleiss statistic. (8 pages)

10/24/2000	Contact Report	FDA	BLA 99-2865 / STN BL 103979/0			

BLA various items: discussion with Dr. Kaiser. He requested additional information: AEs that are laboratory abnormalities, tables showing whether the abnormalities were above or below the norm, conconmitant med listing that shows only the pain meds

10/25/2000	Facisimile	FDA	BLA 99-2865 / STN BL 103979/0			

Re: BB-IND 7616 - List of suggestions for experts during EMDAC panel meeting on 12/8/00.

10/25/2000	Facisimile	FDA	BLA 99-2865 / STN BL 103979/0			

Attachment of requested analyses: listing of infusions for P3 Extension; Summary of All AEs by Preferred Term; Listing of Renal Assessments; 15 pages

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
10/27/2000	Contact Report	FDA	BLA 99-2865 / STN BL 103979/0			

Re: BB-IND 7616 - Contact Report of Telephone Conference with CBER requested by Genzyme to clarify CBER expectations to responses to questions issued by CBER on 10/13/00.

10/27/2000	Correspondence	FDA	BLA 99-2865 / STN BL 103979/0			

Letter from FDA to Dr. Eng regarding their conduct of a clinical study entitled "A Multicenter, Placebo-Controlled, Double-Blind, Randomized, Study of the Safety and Efficacy of Recombinant Human aGalactosidase A (r-aGAL) Replacement in Patients with Fabry Disease", conducted at Mount Sinai School of Medicine in New York. The letter was faxed to Nicole by Dr. Desnick at Mt. Sinai.

10/30/2000	Facisimile	FDA	BLA 99-2865 / STN BL 103979/0			

Fax to Dr. Marc Walton re: attached press release that Genzyme plans to release.

10/31/2000	Contact Report	FDA	BLA 99-2865 / STN BL 103979/0			

Contact report re: Safety Update and Vendor Error - reports to be submitted to FDA

10/31/2000	Correspondence Sent	FDA	BLA 99-2865 / STN BL 103979/0			

Phase 3 extension plasma and urine GL-3 report; finalized and to be submitted to the BLA with safety update later in week. Faxed.

11/2/2000	Correspondence Sent	FDA	BLA 99-2865 / STN BL 103979/0			

Attached analyses requested by Dr. Kaiser: Summary of conconmitant pain medications (P3 Trial, As Treated); Summary of AEs that are lab abnormalities (P3 Trial, As Treated); Summary of Shifted Laboratory Values (P3 Trial, As Treated); 10 pages

11/3/2000	Amendment	FDA/CBER	BLA 99-2865 / STN BL 103979/0	005		

Safety Update: Plasma and Urinary GL-3; Faxed communications. 9 volumes, one CD-ROM.

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
11/6/2000	Amendment	FDA	BB-IND 7616	100		100
	Amendment 100 to IND 7616 - Revisions to Phase 1/2 Extension Protocol (Study AGAL-006-00)					
11/7/2000	Amendment	FDA	BB-IND 7616	101		101
	Re: BB-IND 7616 - Amendment 101, Initial Written Report, Manufacturer Report No. AGF066-S00USA, in reference to AGAL-008-99 Study.					
11/9/2000	Facisimile	FDA	BLA 99-2865 / STN BL 103979/0			
	Fax with three attachments: directions to Allston Landing from Logan; Directions to NY Avenue from Cambridge or Logan; Manufacturing Schedule					
11/10/2000	Correspondence	FDA	BLA 99-2865 / STN BL 103979/0			
	Letter from Alison Lawton to Marc Walton re: pending BLA for Fabrazyme; appeal letter; 42 pages					
11/15/2000	Amendment	FDA/CBER	BLA 99-2865 / STN BL 103979/0	006		
	Response to Request for Clinical Information (original labels), STN BL103979/0					
11/17/2000	Report	FDA	BLA 99-2865 / STN BL 103979/0			
	Pre-approval inspection Day 5 report and attached original FDA notification of inspection.					
11/17/2000	Correspondence	FDA	BLA 99-2865 / STN BL 103979/0			
	General Correspondence re: Phase 4 multi-center, randomized, double-blind, placebo-controlled trial. STN BL103979/0					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
11/17/2000	Correspondence Received	FDA	BLA 99-2865			

FDA 483. Fabrazyme CBER Pre-License Inspection Final Close-Out November 17, 2000 re: inspection from Inspection November 13-17, 2000. Includes 51 New York Avenue Facility Introduction, organization charts, floor maps. Includes Allston Quality Assurance Operations,Allston Quality Control and Fill Finish Department Overviews.

11/20/2000	Contact Report	FDA	BLA 99-2865 / STN BL 103979/0			

Contact report re: discussion with Marc Walton of FDA regarding Phase 4 Trial and when we can have a conversation about end point for the trial.

11/20/2000	Correspondence Sent	FDA	BB IND 7616			

Fax of Letter to Elaine Cole, FDA-CBER, from Mt Sinai School of Medicine regarding Inspection of Mount Sinai School of Medicine, Fabrazyme Study BB-IND 7616.

11/28/2000	Contact Report	FDA	BLA 99-2865 / STN BL 103979/0			

Follow-up voice mail to Phase 4 telecon with Dr. Kaiser,

12/4/2000	Amendment	FDA	BB-IND 7616	102		102

Responses to request for information regarding Phase 4 Clinical Study.

12/4/2000	Correspondence/Fax	FDA	BLA 99-2865 / STN BL 103979/0			

Letter re: Inspection of Mount Sinai School of Medicine, Fabrazyme Study. Fax is dated 12/4/00; original letter is dated 11/20/00.

12/5/2000	Correspondence Sent	FDA	BB IND 7616	102		

RE: BLA 99-2865 and IND BB-7616. This is a copy of Amendment 102 to BB-7616 submitted on December 5, 2000, faxed to Dr. Jim Kaiser by Nicole Brien.

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
12/6/2000	Email	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: BB-IND 7616 - FDA answers to recent questions. 483 submit to OCBQ; not required to request an exemption from lot release					
12/7/2000	Amendment	FDA	BB-IND 7616	103		103
	Clinical protocol amendment: Phase 4 study AGAL-008-00					
12/8/2000	Correspondence Sent	FDA/CBER	STN BL103979/0 BLA 99-2865			
	Pre License Inspection *Response to FDA 483* *Genzyme's 51, 76, 80 New York Avenue and Allston Landing Facilities*					
12/8/2000	Amendment	FDA	BLA 99-2865 / STN BL 103979/0	007		
	Response to CBER Request for Information for the CMC section of the Fabrazyme BLA. STN BL 103979/1. 1 CD for CF, 1 for Archives					
12/13/2000	Amendment	FDA	BB-IND 7616	104		104
	Protocol Amendment (Study AGAL005-99): New investigators and updated 15725); Protocol Amendment (Study AGAL006-99): Change of principal investigator; Updated investigator's brochure					
12/14/2000	Correspondence	FDA	BLA 99-2865 / STN BL 103979/0			
	General Correspondence regarding Phase 4 Clinical Study AGAL-008-00, including Attachment 1, IND Amendment 102 of December 4, 2000 and Attachment 2, IND Amendment 103 of December 7, 2000					
12/14/2000	Amendment	FDA	BLA 99-2865 / STN BL 103979/0	008		
	Correction to Amendment 007 - Response to CBER Request for Information for the CMC section of the Fabrazyme BLA. STN BL 103979/0					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
12/19/2000	Contact Report	FDA	BLA 99-2865 / STN BL 103979/0			

Re: Call between Nicole Brien and Michael Noska about CBER Complete Response letter for Fabrazyme.

12/22/2000	Correspondence Received	FDA	BLA 99-2865 / STN BL 103979/0			

Re: BB-IND 7616 - Request for clarification concerning the BLA license application dated 23 June 2000, FDA information request letter dated 13 October 2000, and to telcon on 27 October 2000. Fax sent by Michael Noska, letter from Dr. Amy Rosenberg and Dr. Karen Weiss. Faxed copy and orginal letter from FDA included. Archive copy submitted.

12/22/2000	Contact Report	FDA	BLA 99-2865			

Teleconference between Nicole Brien and Mike Noska of the FDA regarding the Phase 3 LM slides at the FDA.

12/28/2000	Correspondence Sent	FDA	BLA 99-2865 / STN BL 103979/0			

Re: BLA 99-2865 / BL 103979 - Letter to Michael Noska at FDA from Alison Lawton regarding Intent to Amend BLA for the purposes of addressing the FDA's comments, responding to their questions, and submitting the requested information as described in their December 22, 2000 letter.

12/28/2000	Correspondence	FDA	BLA 99-2865 / STN BL 103979/0			

Re: BB-IND 7616 - Letter with Intent to Amend BLA. Re: BL 103979/0

1/4/2001	Correspondence/Fax	FDA	BB-IND 7616			

Re: BB-IND 7616 - Advice letter from FDA regarding AGAL-008-00 study with cross reference to BLA responses. Sent by fax to team members; fax cover sheet included. Attached is Memo from Nicole to Team of same date.

1/4/2001	Response Lettter	FDA	BB-IND 7616			

Re: BB-IND 7616 - January 4, 2001 letter from FDA to Nicole Brien regarding their review of the October 6, 2000 submission to our IND for Fabrazyme. Attached is memo from Nicole Brien to team stating that majority of items have been addressed in protocol. A copy of this doc may be in binder # 025 also.

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
1/4/2001	Meeting Minutes/Draft	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: BLA 99-2865 - Letter from FDA to Nicole Brien regarding their review of the October 6, 2000 submission to our IND for Fabrazyme.					
1/9/2001	Facisimile	FDA	BLA 99-2865 / STN BL 103979/0			
	Fax to Michael Noska from Nicole Brien with confirmation regarding agenda and participants to the call scheduled at 3 p.m., on 1/9/01.					
1/9/2001	Contact Report	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: BB-IND 7616 - Contact Report on teleconference concerning BLA action letter informal discussion with medical reviewers.					
1/9/2001	Correspondence Sent	FDA	BLA 99-2865			
	list of Genzyme participants and meeting agenda for general discussion on 1/9/01 at 3pm					
1/17/2001	Facisimile	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: BB-IND 7616 - Draft 2, final of press release for review RE: ATU and Registry; sent to Bill Purvis with discussed changes, with Form 2253;					
1/17/2001	Facisimile	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: BB-IND 7616 - PR/Part I Form 2253 used with review of press release. *Revise as suggested. OK to go final*					
1/18/2001	Facisimile	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: BB-IND 7616 - Final of press release sent to Bill Purvis with discussed changes, with Form 2253					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
1/18/2001	Facisimile	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: BLA 99-2865 - Fax regarding various CMC issues and topics to be discussed at 1/19/01 teleconference, and a list of Genzyme participants.					
1/19/2001	Amendment	FDA	BB-IND 7616	105		105
	Re: BB-IND 7616 - New protocol: Amendment 105 - Natural history study; archive copy submitted					
1/19/2001	Contact Report	FDA	BB-IND 7616			
	Re: BB-IND 7616 - phone report between Nicole Brien and Dr. James Kaiser regarding a death in P3X study. Patient No. 0506 participating in Phase 3 Extension Trial at London site.					
1/22/2001	Facisimile	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: BB-IND 7616 - Fax from Michael Noska to Nicole Brien with a list of likely participants from CBER to the telecon on 1/24/01.					
1/23/2001	Correspondence Sent	FDA	BLA 99-2865			
	DIaling instructions for January 24 conference call regarding CMC					
1/23/2001	Facisimile	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: BLA 99-2865 - Fax of original letter from Chris Harris to Mercedes Serabian regarding telecon scheduled for 1/25/01 discussing two preclinical studies to support reproductive and developmental toxicology.					
1/24/2001	Advertising and Promotion	FDA				
	Re: Fabry Disease Collateral Materials: "Understanding Fabry Disease"; "The Medical Family Tree"; Disease Monograph - stored in Ad Prom file cabinets					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
1/24/2001	Amendment	FDA	BB-IND 7616	106		106

Re: BB-IND 7616 - Amendment 106 - Transfer of obligations for study AGAL-008-00 Protocol Amendment: new investigators for studies AGAL-005-00 and AGAL-006-00. With three attachments. Archive copy submitted.

1/24/2001	Correspondence Sent	FDA	BLA 99-2865 / STN BL 103979/0			

Re:BLA 99-2865 - Fax from Chris Harris to Mercedes Serabian with list of participants of 1/25/01 telecon, and draft outline for proposed 6-month repeat dose study in monkeys to support reproductive and developmental toxicology. 4 pages

1/25/2001	Facisimile	FDA	BLA 99-2865 / STN BL 103979/0			

Re: BLA 99-2865 - Fax to Mercedes Serabian with dial-in instructions for scheduled telecon on 1/25/01. Topic: reproductive and developmental toxicology.

1/25/2001	Contact Report	FDA	BB-IND 7616			

Re: BB-IND 7616 - Teleconference report regarding Dr. Kaiser's call on 1/25/01 to discuss various issues: 12/7/00 protocol submission/study AGAL-008-00 Amendment 2 vs. the items in the "Advice" letter from FDA dated 1/4/01. Also "Case Report Form" and "Sample Information Consent Form." Also applies to BLA 99-2865.

1/25/2001	Contact Report	FDA	BLA 99-2865 / STN BL 103979/0			

Re: BLA 99-2865 - Teleconference report regarding Dr. Kaiser's call on 1/25/01 to discuss various issues: 12/7/00 protocol submission/study AGAL-008-00 Amendment 2 vs. the items in the "Advice" letter from FDA dated 1/4/01. Also "Case Report Form" and "Sample Information Consent Form."

1/25/2001	Facisimile	FDA	BLA 99-2865 / STN BL 103979/0			

Re: BLA 99-2865 - Mark Hayes fax to Mike Noska regarding list of participants to the telecon on 1/24/01 and a copy of the table in the BLA that contains the relevant data.

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
1/25/2001	Facisimile	FDA	BB-IND 7616			
	Re: BB-IND 7616 - Dial-in instructions for telecon to be held on 26 January 2001 at 11 a.m. to 12 noon regarding issues concerning study AGAL-008-00.					
1/25/2001	Response to Request	FDA	BB-IND 7616			
	Re: BB-IND 7616 - Attached "information consent template for Phase 4 Study" requested by Dr. Jim Kaiser. Sent by fax to Dr. Kaiser.					
1/26/2001	Amendment	FDA	BB-IND 7616	108		108
	Re: BB-IND 7616 - Amendment 108: Initial Written Report, Manufacturer Report No. AGF074-S00UK, concerning expiration of Patient No. 0506 JSP on 12 January 2001.					
1/26/2001	Change of Contacts	FDA	BB-IND 7616	107		107
	Re: BB-IND 7616 - Amendment 107: General Correspondence - Change of primary and alternate contacts. Archive submitted.					
1/26/2001	Telecon Minutes	FDA	BB-IND 7616			
	RE: BB-IND 7616 - Minutes from Telecon on 1/26/01 regarding Phase 4 Study Interim Analysis					
1/30/2001	Correspondence Sent	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: BLA 99-2865 - C. Harris faxed M. Serabian the draft version of meeting minutes of telecon of 1/25/01 concerning Question 15 of FDA letter received on 12/22/00.					
1/31/2001	Correspondence Sent	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: BLA 99-2865 - Notice of Change of Primary and Alternate Contacts. Archive submitted.					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
2/1/2001	Telecon Minutes	FDA	BB-IND 7616			
	RE: BB-IND 7616 - Minutes from Telecon on 1/26/01 regarding Phase 4 Protocol submitted on 12/7/00 and FDA/IND Advice Letter dated 1/4/01.					
2/5/2001	Amendment	FDA	BB-IND 7616	109		109
	Re: BB-IND 7616 - Amendment 109 - Compassionate Use Study (AGAL-013-01) to provide A-Gal to treat patients with severe Fabry disease. Two attachments. Archive copy submitted.					
2/5/2001	IND/BLA	FDA	BB-IND 7616/BLA 103979	109		
2/7/2001	Contact Report	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: BLA 99-2865 / BL 103979 - Christine Harris spoke to M. Serabian regarding meeting minutes draft on meeting concerning Question 15.					
2/8/2001	Contact Report	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: BLA 99-2865 (BL 103979) - Christine Harris spoke to M. Serabian regarding Question 15 (two preclinical reproactive toxicity studies) of FDA's letter of 12/22/01.					
2/14/2001	Contact Report	FDA	IND 7616 / BL 103979 (BLA 99-286			
	Re: IND 7616 / BL 103979 (BLA 99-2865) - Christine Harris phoned Dr. Kaiser to follow up on Natural History Protocol submitted on 1/19/01. Cross reference in BLA chron file.					
2/14/2001	Contact Report	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: BLA 99-2865 / BL 103979 - C. Harris phoned Dr. Kaiser to follow up on natural history protocol submitted on 1/19/01.					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
2/14/2001	Contact Report	FDA	IND 7616 / BL 103979 (BLA 99-286			

Re: IND 7616 / BL 103979 (BLA 99-2865) - Christine Harris phoned Dr. Kaiser to follow up on Natural History Protocol submitted on 1/19/01. Cross reference in IND chron file.

2/14/2001	Contact Report	FDA	BB-IND 7616			

Re:BB-IND 7616 - C. Harris phoned Dr. Kaiser to follow up on natural history protocol submitted on 1/19/01.

2/26/2001	Contact Report	FDA	BLA 99-2865 / STN BL 103979/0			

Re: BLA 99-2865 - C. Harris phoned Dr. Kaiser to follow up on the natural history protocol submitted on 1/19/01. The protocol is under review.

2/26/2001	Contact Report	FDA	BB-IND 7616			

Re: BB-IND 7616 - C. Harris phoned Dr. Kaiser to follow up on the natural history protocol submitted on 1/19/01. The protocol is under review.

2/27/2001	Contact Report	FDA	BLA 99-2865 / STN BL 103979/0			

Re: BLA 99-2865 / BL 103979 - Telecon with Dr. Kaiser - follow-up on submission of Natural History Protocol on 1/19/01. No comments for now, but review process in motion.

3/5/2001	Amendment	FDA	BB-IND 7616	110		110

Re: BB-IND 7616 - Amendment 110 - Initial written safety report: manufacturer's report no. AGF078-S01FRA (AGAL-005-99). Patient number 0804.

3/7/2001	Contact Report	FDA	BLA 99-2865 / STN BL 103979/0			

Re: BLA 99-2865 - Chris Harris faxed Dr. Kaiser with dial-in information for the conference call scheduled for 3/9/01 to discuss historical data and compassionate use protocols.

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
3/7/2001	Contact Report	FDA	BLA 99-2865 / STN BL 103979/0			

Re: BLA 99-2865 - Dennis Bucceri spoke with Dr. Walton concerning collection of comprehensive historical data and arrangement of a conference call with Dr. Kaiser. Report submitted by Chris Harris.

3/7/2001	Contact Report	FDA	BB-IND 7616			

Re:BB-IND 7616 / BL103979/0 - Chris Harris faxed Dr. Kaiser with dial-in information for the conference call scheduled for 3/9/01 to discuss historical data and compassionate use protocols.

3/7/2001	Contact Report	FDA	BB-IND 7616			

Re: BB-IND 7616 - Contact Report of Dennis Bucceri's conversation with Dr. Walton concerning collection of comprehensive historical data and arrangement of a conference call with Dr. Kaiser

3/8/2001	Contact Report	FDA	BB-IND 7616			

Re:BB-IND 7616 / BL103979/0 - Chris Harris faxed Dr. Kaiser with dial-in information for the conference call scheduled for 3/9/01 to discuss historical data and compassionate use protocols.

3/9/2001	Contact Report	FDA	BB-IND 7616			

Re:BB-IND 7616 / BL103979/0 - Chris Harris faxed Dr. Kaiser list of Genzyme participants for 3/9/01 telecon regarding Phase 4 study.

3/9/2001	Contact Report	FDA	BLA 99-2865 / STN BL 103979/0			

Re: BLA 99-2865 - Chris Harris faxed Dr. Kaiser list of Genzyme participants for 3/9/01 telecon regarding Phase 4 study.

3/9/2001	Contact Report	FDA	BLA 99-2865 / STN BL 103979/0			

Re: BLA 99-2865 - Teleconference Report from 9 March 2001 telecon with FDA Marc Walton and Dr. Kaiser to discuss Fabrazyme Compassionate Use protocol and the natural history protocols for Fabrazyme and Pompe.

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
3/9/2001	Contact Report	FDA	BB-IND 7616			
	Re: BB IND 7616 - Teleconference Report from 9 March 2001 telecon with FDA Marc Walton and Dr. Kaiser to discuss Fabrazyme Compassionate Use protocol and the natural history protocols for Fabrazyme and Pompe.					
3/14/2001	Adverse Event	FDA	BB-IND 7616	111		111
	Re: BB IND 7616 - Amendment 111 - Safety Report - Initial Written Report; manufacturer number AGF079-S01UK. Study: AGAL-005-99					
3/22/2001	Amendment	FDA	BB-IND 7616	112		112
	Re: BB-IND 7616 - Serial # 112 - Withdrawal of Serial # 109, Protocol No., AGAL-013-01, for compassionate use program, submitted on 2/5/01.					
4/10/2001	Advertising and Promotion					
	Fabry disease postcard mailing *Objective: disease awareness for earlier diagnosis, promote Fabry Registry, drive interest In clinical trial participation*					
4/18/2001	Amendment	FDA	BLA 99-2865 / STN BL 103979/0	009		
	Re: BLA 99-2865 - Amendment 009 - STN BL 103979/0 - Response to CBER's Complete Review Letter, dated December 22, 2000. Response to Request for Information. Includes CD, disk .001					
4/21/2001	Memorandum / Minutes	FDA/CBER	BB-IND 7616			
	Re: BB-IND 7616 - Memorandum to Amendment 062 - Meeting Minutes between CBER and Genzyme - Alpha-GAL 005. Cover letter only is scanned.					
4/26/2001	Annual Report	FDA	ODD 86-152			
	Re: ODD 86-152 - Annual Report of holder of orphan-drug designation (ODD). Reporting period of October 1999 through September 2000.					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
5/2/2001	Protocol Amendment	FDA	BB-IND 7616	114		114
	Re: BB-IND 7616 - Amendment 114 - Change in Protocol - New Investigators for Study					
5/4/2001	Request	FDA	BB-IND 7616			
	Re: BB-IND 7616 - Request for Clinical Telecon - Expanded Access					
5/9/2001	Contact Report	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: BLA 103979 - Christine Harris phoned Dr. Kaiser regarding request for clinical teleconference - expanded access. Cross-referenced in BB IND 7616.					
5/9/2001	Contact Report	FDA	BB IND 7616			
	Re: BB IND 7616 - Christine Harris phoned Dr. Kaiser regarding request for clinical teleconference - expanded access. Cross-referenced in STN BB 103979.					
5/10/2001	Correspondence Sent	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: STN BL103979 - Christine Harris faxed General Correspondence Amendment: Change of Contact submitted on 01/31/01 to Dr. James Crim.					
5/11/2001	Acknowledgement of Receipt	FDA	BB-IND 7616			
	Re: BB-IND 7616 - Acknowledgement of receipt of 18 April 2001 resubmission to license application for Fabrazyme.					
5/11/2001	Letter	FDA	BB-IND 7616			
	Re: BB-IND 7616 - Letter from FDA regarding acknowledgement of receipt on April 20, 2001 of resubmission to license application Fabrazyme containing additional information in response to complete response letter received from FDA on Dec. 22, 2001.					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
5/14/2001	Letter of Authorization	FDA	BB-IND 7616			

Re: BB-IND 7616 - Letter of Authorization for Kaiser-Permanente, Los Angeles, CA - authorization is granted to support an investigator-sponsored IND for the treatment of a single patient with r-haGAL. Contact is Rebecca Mardach, M.D.

5/15/2001	Advertising and Promotion	FDA	BLA 99-2865 / STN BL 103979/0			

Re: Fabrazyme - Fabry Registry Physician Brochure

5/18/2001	Amendment	FDA	BB-IND 7616	115		115

BB-IND 7616 - Amendment 115 - Addition of Nanofiltration to 340L process for ongoing clinical trials. Five attachments.

6/4/2001	Letter	FDA	BLA 99-2865 / STN BL 103979/0			

Re: STN BL 103979/0 - Letter from Alison Lawton to Dr. Haffner requesting a meeting to discuss the Orphan Drug Fabrazyme. Cross-reference in ODD.

6/4/2001	Amendment	FDA	BB-IND 7616	116		116

Re: BB-IND 7616 - Amendment 116 - Teleconference request concerning upcoming CMC changes

6/4/2001	Correspondence Sent	FDA	ODD 86-152			

Re: ODD 86-152 - Letter from Alison Lawton to Dr. Haffner requesting a meeting to discuss the Orphan Drug Fabrazyme. Cross-reference in STN BL 103979/0.

6/5/2001	Contact Report	FDA	IND 7616			

Telephone Contact Report
Review of IND Amendment 115 - addition of nanofiltration to the 340L process in the manufacture of clinical trial material recombinant human a-galactosidase. Was what our estimated viral load was on the 340L process relative to the viral removal we had demonstrated in the validation?

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
6/11/2001	Adverse Event	FDA	BB-IND 7616	117		117
	Re: BB-IND 7616 - Amendment 117 - Initial 15 Day Adverse Event Report: AGF076-S01FRA, Patient 0806 M-D, positive skin test					
6/18/2001	Advertising and Promotion	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: Fabrazyme - Powerpoint slides - Overview of Fabry Disease					
6/18/2001	Contact Report	FDA - CBER	BLA 99-2865			
	Telephone Contact Report regarding Advisory Committee Meeting date tentatively scheduled in September, 2001					
6/21/2001	Adverse Event	FDA	BB-IND 7616	118		118
	Re: BB-IND 7616 - Amendment 118 - Initial 15 day report; Phase 4 trial (AGAL-008-00) AGF087-S01USA. Positive IgE serum test. Patient withdrawn from study.					
6/28/2001	Amendment	FDA	BB-IND 7616	119		119
	Follow-up report 1 to Serious Adverse Event AGF074-S00UK. The patient died. Cause of death was Fabry Disease. Autopsy information included.					
	Note that this is indexed and filed in Livelink as an Amendment, though the cover letter does not state that it is an Amendment, nor carry an Amendment number.					
6/28/2001	Advertising and Promotion	N/A	N/A			
	Re: Ad Prom materials : NOT required for submission to the FDA. Powerpoint slides on overview of Fabry disease - available on CD-Rom.					
7/2/2001	Amendment	FDA	BB-IND 7616	120		120
	Re: BB-IND 7616 - Amendment 120 - P4 SAE AGF087-S01USA (Folow-up Report # 1)					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
7/5/2001	Correspondence Sent	FDA - CBER	BLA 99-2865			
	FAX - final press release issued regarding publication of the recent results of out Phase 3 extension study in the New England Journal of Medicine					
7/6/2001	Contact Report	FDA - CBER	IND 7616			
	Update on Amendment 116 that was submitted on June 4, 2001 *CBER would like to have an internal discussion about this amendment before having a teleconference with Genzyme.*					
7/11/2001	Amendment	FDA	BB-IND 7616	121		121
	Re: BB-IND 7616 - Amendment 121 - New Investigators Named to Participate In Phase 4 trial.					
7/12/2001	Facsimile	FDA	BB IND 7616			
	Re: BB IND 7616 - In response to Chris Harris' call to Dr. Kaiser on 9 May 2001 and her follow-up call to Dr. Crim on 12 July 2001, she is providing a summary of IND activities related to expanded access and is requesting a teleconference to discuss these activities.					
7/12/2001	Contact Report	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: STN BL 1039079 - Contact Report regarding draft press release - Fabrazyme European Approval. Request to revise press release per attached comments.					
7/17/2001	Advertising and Promotion	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: STN BL 103979 - Fabrazyme Ad Prom Materials - Fax from Carole Broadnax at FDA regarding draft press release on Fabrazyme European approval. Request to revise press release per attached comments.					
7/17/2001	Press Release (draft)	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: STN BL 1039079 - Draft press release - Fabrazyme European Approval. Revised by FDA Carole Broadnax.					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
7/26/2001	Contact Report	FDA	BLA 99-2865 / STN BL 103979/0			

Re: STN BL 1039079 - Contact Report regarding request for guidance from FDA on need to submit safety update to BLA within 4 months of April submission date. Contact: Mike Noska.

7/31/2001	Advertising and Promotion	N/A	N/A			

Re: Ad Prom materials : NOT required for submission to the FDA. (Revised) Program Advertisement to be placed in ASHG annual meeting official program and abstracts guidebook.

7/31/2001	Advertising and Promotion	N/A	N/A			

Re: Ad Prom materials : NOT required for submission to the FDA. Program Advertisement to be placed in ASHG annual meeting official program and abstracts guidebook.

8/2/2001	Contact Report	FDA	BLA 99-2865 / STN BL 103979/0			

Re: BLA 99-2865 / STN BL 103979/0 - Contact Report regarding follow-up to message of 26 July asking Mike Noska for guidance from FDA on need to submit a safety update to BLA within 4 months of our April submission. Contact: Mike Noska.

8/3/2001	Contact Report	FDA	BLA 99-2865 / STN BL 103979/0			

Re: STN BL 1039079 - Contact Report regarding safety update. Dr. Kaiser would like the MedWatch form and follow-up data.

8/3/2001	Contact Report	FDA	BB-IND 7616			

Re: BB-IND 7616 - Contact report regarding upcoming CMC changes (IND Amendment 116)

8/3/2001	Facsimile	FDA	BLA 99-2865 / STN BL 103979/0			

Re: STN BL 103979 - Fax to Mike Noska with dial-in information for CMC telecon on 8/3/01.

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
8/14/2001	Facsimile	FDA	STN BL 103979			

Re: STN BL 103979 - Fax to Jeff Fritsch from Christine Harris with a list of Genzyme attendees to meeing on 8/16/01. Agenda of meeting, special issues raised by "Ultra Orphan Drug." Questions and Discussions.

8/20/2001	Correspondence Sent	FDA	BB IND 7616			

Chris Harris faxed Dr. Kaiser with regards to Draft Study Safety Report. And patient exparation AGF149-S01USA who particpated in study AGAL-008-00

8/20/2001	Facsimile	FDA	BLA 99-2865 / STN BL 103979/0			

Re: STN BL 103979 - Safety Update, Phase 4 Study Update - Fax to Dr. Kaiser regarding report submitted to the BLA of the safety data available for Fabrazyme and an update of the status of the AGAL-08-00 study progress.

8/20/2001	Facsimile	FDA	BB-IND 7616			

Re: BB-IND 7616 - C. Harris faxed J. Kaiser regarding submitted Safety Update Report available for Fabrazyme to the BLA and Phase 4 Study Update. AGAL-088-00.

8/20/2001	Amendment	FDA	BLA 99-2865 / STN BL 103979/0	010		010

Re: BLA 99-2865 / STN BL103979/0 - Safety Update - Amendment 010 - URLs below are cover fax dated 8/20/01 and the amendment dated 7/16/01. Both in Archive box 3374204

8/21/2001	Adverse Event	FDA	BB-IND 7616		123	

Re: BB-IND 7616 - Amendment 123 - Initial 15 Day Report : SAE reported in the French ATU Program - Mfr Report Number AGF112-ATU01FRA - Myocardial Infarction

8/24/2001	Advertising and Promotion	N/A	N/A			

Ad Prom Materials - NOT required for submission to FDA. Fabry disease overview brochure. Describes the disease, signs, symptoms, diagnosis and medical management of Fabry disease. NOT on rolling shelves; electronic and Ad Prom files only.

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
8/27/2001	Advertising and Promotion					

CD Rom with Powerpoint slides on Fabry Phase 1-3 extension data. To distribute CD Rom via medical information and clinical group to physicians upon request from MD.

8/27/2001	Advertising and Promotion	N/A	N/A			

Re: Ad Prom materials : NOT required for submission to the FDA. 2nd reprint of Fabry disease monograph

8/29/2001	Advertising and Promotion					

Ad/Prom materials
Not required for submission to FDA
Ads to go in program book for ISONG, NORD & NSGC Conferences

9/4/2001	Contact Report	FDA	BLA 99-2865 / STN BL 103979/0			

Re: STN BL 103979/0 - Dr. Kaiser contacted Chris Harris regarding the navigation in the .xpt files in our BLA amendment.

9/7/2001	Contact Report	FDA	BLA 99-2865 / STN BL 103979/0			

Re: STN BL 103979/0 - Alison Lawton contacted Dr. Walton concerning status of Fabrazyme BLA review, dialog prior to BLA action letter, clinical development program, extension of review clock, changes in P4 clinical program.

9/10/2001	Advertising and Promotion	N/A	N/A			

Re: Ad Prom materials : NOT required for submission to the FDA. Panels for ASHG booth - October 2001 (commercial booth, GLC booth, med Info booth.

9/12/2001	Amendment	FDA	BB-IND 7616	124		124

Re: BB-IND 7616 - Phase 4 SAE - Initial 15 day report - AGF 116-S01USA. Upgraded to a serious medical event. With fax to Michael Noska of same date.

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
9/20/2001	Amendment	FDA	BB IND 7616	125		125
	Re: BB IND 7616 - Annual Report for the period of 9 April 200 through 31 May 2001 - Amendment 125					
9/24/2001	Amendment	FDA	BB-IND 7616	126		126
	Re: BB-IND 7616 - Protocol Amendment 126 - New Investigators Named to Particiate in the following Genzyme Studies: Phase 1/2 Extension, Phase 3 Extension, Phase 4, Natural History. Updated 1572 Form provided for one investigator in the Phase 4 study.					
9/28/2001	Amendment/Initial 15 Day Report	FDA	BB IND 7616	127		127
	Re: BB IND 7616 - Amendment # 127 / Initial 15 Day Report. Special Access Program in Canada. AGF027-CU01CAN.					
10/2/2001	Advertising and Promotion	N/A	N/A			
	Re: Ad Prom materials : NOT required for submission to the FDA. Order form for new genetic counselor patient education tool.					
10/4/2001	Amendment	FDA	BB-IND 7616	128		
	Re: BB-IND 7616 - Amendment 128 : Change in Protocol for the Phase 3 Extension					
10/4/2001	Amendment	FDA	BB IND 7616	128		128
	Re: BB IND 7616 - Phase 3 Extension Protocol Amendment 128					
10/4/2001	Contact Report	FDA	BB-IND 7616			
	Re: BB-IND 7616 - Dr. Kaiser left message requesting fax of a copy of most recent informed consent document for our current placebo controlled trial and to call him when received message.					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
10/10/2001	Advertising and Promotion	N/A	N/A			
	Re: Ad Prom materials : NOT required for submission to the FDA. Brochure: "Understanding Fabry Disease" .					
10/15/2001	Contact Report	FDA	BB IND 7616			
	Re: BB IND 7616 - Dr. Kaiser left message requesting faxed copy of informed consent form. C. Harris called back to inform Dr. Kaiser that the informed consent had not changed since submission in May 2001 Amendment 3 to the protocol.					
10/19/2001	Facsimile	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: STN BL 103979/0 - "Complete Response Letter" from the FDA to Christine Harris regarding the BLA application.					
10/22/2001	Pre-Meeting Package	FDA	BLA 99-2865 / STN BL 103979 / 0			
10/22/2001	Pre-Meeting Package	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: BLA 99-2865 / STN BL 103979/0 - Pre-meeting package for Type C meeting with FDA on 8 November 2001 for the Fabrazyme 2000L facilities transfer.					
10/24/2001	Amendment	FDA	BB IND 7616			129
	Mfr. Report number AGF129-CU01CAN. Initial 15-day report					
10/24/2001	Correspondence Sent	FDA	STN BL 103979/0			
	General Correspondence: Intent to Amend BLA					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
11/5/2001	Correspondence Sent	FDA	ST: BL 103979/0			
	List of participants to Oct. 30, 2001 Teleconference					
11/6/2001	Correspondence Sent	FDA	STN: BL 103979/0			
	Attached list of participants to telcon regarding patient death in study AGAL-008, and attached revised consent from P3X					
11/9/2001	Amendment	FDA	BB IND 7616			130
	General Correspondence: Change of contacts					
11/9/2001	Correspondence Sent	FDA	STN: BL 103979/0			
	General Correspondence: Change of Contacts					
11/14/2001	Correspondence Sent	FDA	BB-IND 7616			
	General Correspondence: Type A meeting request					
11/15/2001	Correspondence Sent	FDA	BB IND 7616			
	Desk copy of the meeting request submitted by Genzyme for the Fabrazyme BLA					
11/15/2001	Correspondence Sent	FDA	BB IND 7616			
	Desk copy of a meeting request filed to the BLA today					
11/15/2001	Contact Report	FDA	BB-IND 7616			
	Re: BB-IND 7616 - Reports of Patients' Deaths - contacts with Dr. Kaiser between 11/15/01 and 11/19/01					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
11/19/2001	Contact Report	FDA	STN: 103979/0			
	BLA Type A Meeting request. Change of responsibilities to Dr. Crim					
11/20/2001	Correspondence Sent	FDA	BB IND 7616			
	Fax to Dr. Kaiser with the Draft MedWatch Report for patient deaths.					
11/20/2001	Contact Report	FDA	BB IND 7616			
	Dr. Kaiser called C. Harris again regarding patient deaths and Phase 4 meeting request.					
11/20/2001	Contact Report	FDA	BB IND 7616			
	Patient deaths in study. Mfg #:AGF064-S00UK, AGF111-ATU01FRA, AGF104-CU1JAP					
11/21/2001	Amendment	FDA	BB-IND 7616	131		
	Re: BB-IND 7616 - Amendment # 131 - Investigation into Nanofilter Recovery Loss, Reprocessing, and Disposition of Reprocessed Lot					
11/28/2001	Meeting Request	FDA	BLA STN 103979			
	Re: BLA STN 103979 - Meeting request with Dr. Chu, FDA statistician to seek clarifications on Question in the BLA and IND regarding the interim analysis for the proposed post-marketing study, AGAL-008. Cross-referenced in BB-IND 7616.					
11/28/2001	Meeting Request	FDA	BB-IND 7616			
	Re: BB-IND 7616 - Meeting request with Dr. Chu, FDA statistician to seek clarifications on Question in the BLA and IND regarding the interim analysis for the proposed post-marketing study, AGAL-008. Cross-referenced in BLA STN 103979.					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
11/29/2001	Amendment	FDA	BB-IND 7616	132		

Re: BB-IND 7616 - Amendment # 132 - Correction to Annual Report (Amendment 125)

12/4/2001 Advertising and Promotion

Protocol Description for Veritas Website.
Patient Recruitment Tool - Fabrazyme Phase IV Clinic Trial

12/4/2001	Amendment	FDA	BB-IND 7616	133		

Re: BB-IND 7616 - Amendment # 133 - CMC Revision - Scale-up from 340L to 2000 liter bioreactor working volume

12/7/2001	Meeting Minutes	FDA	BLA 99-2865 / STN BL 103979/0			

Re: BLA 99-2865 / STN BL 103979/0 - Official FDA Meeting Minutes from Type C Meeting re: Fabrazyme 2000L Facilities Transfer held on 8 November 2001.

12/13/2001	Fax	FDA	BLA STN:103979			

Re: BLA STN:103979 - Fax with Genzyme participant list for conference call to be held 12/14/01 plus dial-in info. Cross-reference with BB-IND 7616

12/13/2001	Fax	FDA	BB-IND 7616			

Re: BB-IND 7616 - Fax with Genzyme participant list for conference call to be held 12/14/01 plus dial-in info. Cross-reference with BLA STN:103979

12/13/2001	Fax	FDA	BB-IND 7616			

Re: BB-IND 7616 - Letter from FDA regarding study AGAL-008-00 to confirm surrogate endpoint, results dependent upon results of interim report, etc. and regarding the consent form and the "Possible Risk and Discomforts" section.

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
12/13/2001	Amendment/Initial 15 Day Report	FDA	BB-IND 7616	134		
	Re: BB-IND 7616 - Amendment 134, Initial 15 Day Report - P3X SAE AGF153-S01FRA					
12/17/2001	Meeting Package	FDA	BLA 99-2865/STN BL 103979/0			
	Re: BLA 99-2865/STN BL 103979/0 - General Correspondence/Type A Meeting Package - Volume 1 of 1 - for meeting scheduled for 8 January 2001 to discuss the 19 October 2001 "complete response" letter from the Agency.					
12/28/2001	Amendment	FDA	BB-IND 7616	135		
	Re: BB-IND 7616 - Amendment 135 - SAE Germany (post-marketing) FABR-10001, Initial 15-day report					
1/4/2002	Pre-meeting Information	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: BLA 99-2865 / STN BL 103979/0 - Pre-Meeting Information - Type A Meeting, January 8, 2002 - List of attendees. Faxed to Dr. Crim, Karen Weiss, Amy Rosenberg, Diane Sartor; fax cover sheets included.					
1/7/2002	Letter of Authorization	FDA	BB-IND 7616			
	Re: BB-IND 7616 - Letter of Authorization : Genzyme Corp. grants permission to the FDA to reference confidential information supplied within IND application to Dr. Ellen Boyd at Fullerton Genetics Center, Asheville, NC.					
1/10/2002	General Correspondence	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: BLA 99-2865 / STN BL 103979/0 - Addendum to Pre-Meeting Information, December 17, 2001 - Type A Meeting, January 8, 2002. Two attachments included.					
1/18/2002	Faxed Document to FDA	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: GP-AG_015/01 Receipt, Masking and Tracking of "post" Fabry Samples (effective 12/07/99). Procedure now obsolete.					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
1/22/2002	Response to Request from FDA	FDA	BLA 99-2865 / STN BL 103979/0			

Re: BLA 99-2865 / STN BL 103979/0 - Modification to the File advrse_0.xpt from BLA Amendment 005, submitted November 2000. In response to Dr. Kaiser's inquiry to C. Harris on 16 January 2002. 2 CDs submitted, one for CF shelves, one for archive copy.

2/7/2002	Advertising and Promotion	N/A	N/A			

Re: Ad Prom materials : NOT required for submission to the FDA. Phase 4 study briefing document.

2/11/2002	Advertising and Promotion	N/A	N/A			

Re: Ad Prom materials : NOT required for submission to the FDA. Registry article.

2/20/2002	Advertising and Promotion					

Genzyme Treatment Support
Support patients in obtaining insurance reimbursement

2/21/2002	Advertising and Promotion	N/A	N/A			

Re: Ad Prom materials : NOT required for submission to the FDA. Fabrazyme reimbursement letters for clinical study investigators.

2/22/2002	Letter of Authorization	FDA	BB-IND 7616			

Re: BB-IND 7616 - Letter of Authorization - Physician-sponsor IND - Dr. Robert Steiner (Oregon Health Sciences University)

2/22/2002	Contact Report	FDA	BLA 99-2865 / STN BL 103979/0			

Re: BLA 99-2865 / STN BL 103979/0 - C. Harris returned call from Dr. Kaiser. Dr. Kaiser has reviewed the 6 and 12 month safety updates in the BLA and has questions about discrepancies in the reported data relating to the preferred term "tremors". He sorrted data from the export file provided in our complete response.

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
2/25/2002	Response to Request	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: BLA 99-2865 / STN BL 103979/0 - Fax to Dr. Kaiser in response to his request for procedure for the evaluation of TEM. Includes: ND submission 3/20/00, draft of clinical protocol for AGAL-1-002-98.					
2/28/2002	Letter	FDA	BLA 99-2865 / STN BL 103979/0			
	Re: BLA 99-2865 / STN BL 103979/0 - CBER Type A Meeting Summary of 8 January 2002. This constitutes official record of meeting.					
2/28/2002	Amendment	FDA/CBER	BB-IND 7616	136		
	Re: BB-IND 7616 - Amendment 136 - Follow-Up to Amendment 133: Comparison of the MWCB used for 340L and 2000L Process.					
3/5/2002	Letter of Authorization	FDA	BB-IND 7616			
	Re: BB-IND 7616 - Letter of Authorization for Dr. Neal Weinreb					
3/6/2002	Amendment	FDA	BLA 99-2865 / STN BL 103979/0	011		
	Re: BLA 99-2865 / STN BL 103979/0 - First Part Response to 19 Oct 2001 - Complete Response Letter. Form FDA 356h. 10 volumes plus 1 CD in 6 binders.					
3/7/2002	Amendment	FDA	BB-IND 7616	137		
	RE: BB-IND 7616 - Amendment # 137 - Follow-up # 1 - Phase 3 Extension SAE - AGF078-S01FRA - Nephrotic Syndrome					
3/14/2002	Amendment	FDA	BLA 99-2865 / STN BL 103979 / 0	011		
	Re: Reissue - Administrative correction to BLA Amendment 011: First Part Response to October 19, 2001 Complete Response Letter, 6 March 2002.					

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
3/15/2002	Contact Report	FDA	BLA 99-2865 / STN BL 103979/0			

Re: BLA 99-2865 / STN BL 103979/0
Alison Lawton called Dr. Walton to inform him that the first part of the two-part submission responding to the Fabrazyme CR letter had been sent on 3/14/2002.

3/18/2002	Amendment/Initial 15 Day Report	FDA	BB-IND 7616	138		138

Re: BB-IND 7616 - Amendment 138 - Initial 15 Day Report - Post Marketing SAE - FABR-10028 - Important medical event.

3/20/2002	Protocol Amendment	FDA	BB-IND 7616	139		139

Re: BB-IND 7616 - Protocol Amendment # 139: Change in Protocol; new protocol; new investigators named to participate in Genzyme studies.

3/22/2002	Fax	FDA	BLA 99-2865; STN BL 103979 / 0			

Re: BLA 99-2865; STN BL 103979 / 0 - Facsimile from Harris to Reedy with recommendations for Advisory Committee/Fabry Panel

3/26/2002	Advertising and Promotion	N/A	N/A			

Re: Advertising and Promotional Material. NOT required for submission to FDA. Letter to managed care medical directors. Used to educate physicians about outgoing Fabry trial.

3/29/2002	Response to Request	FDA	BLA 99-2865 / STN BL 103979 / 0			

Re: BLA 99-2865 / STN BL 103979 / 0 - Clarification of the AE data in response to FDA request.

4/2/2002	Contact Report	FDA	BLA 99-2865-STN: BL 103979/0			

Alison Lawton called Dr. Walton to inform him that a proposed list of experts for the July AC had been faxed on 3/26/02 to Kathleen Reedy, and that the second part of the two part submission with data of 400 patients is on schedule.

Chronology Report for Fabrazyme (Alpha-GAL)

Date	Document Type	Agency	Agency Ref #	Amd	Suppl	Ser
4/3/2002	Amendment	FDA	BB-IND 7616	140		

Re: BB-IND 7616 - Protocol Amendment 140: Change in Phase 4 Study (Genzyme Study AGAL-008-00) Protocol and Sample Patient Information and Consent Form). General Correspndence - Update on the status of the Phase 4 study.

4/8/2002	Contact Report	FDA	BB-IND 7616			

Re: BB-IND 7616
Documentation of Dr. Kaiser's request to convert all physician INDs under 1 protocol under Genzyme's IND.

Public Health Service

Food and Drug Administration

5629 '03 AUG 29 P1:29

Memorandum

Date: August 28. 2003

From: Claudia Grillo, Paralegal Specialist
Office of Regulatory Policy (HFD-013)

Subject: Patent Term Restoration Application
for Fabrazime

To: Dockets Management (HFA-305)

Attached please find a copy of the Application for Extension of Patent Term Under 35 U.S.C. § 156 for the above-referenced human biological product, together with the cover letter from the Patent and Trademark Office. The applicant is Genzyme and the product's trade name is Fabrazime. Please assign a docket number to this application for patent extension and advise me of same.

If you have any questions, please contact me at 240 453-6699. Thank you for your assistance.

Attachment