



**Title: Preparation of Amendments to a Type V Facilities Electronic Master
File (eCTD Format)**

SOP Number: 24410

Revision Number: 04

Supersedes: Revision 03

Effective Date: JUN 26 2020

Originator/Date:

Approval/Date:

Approval/Date:

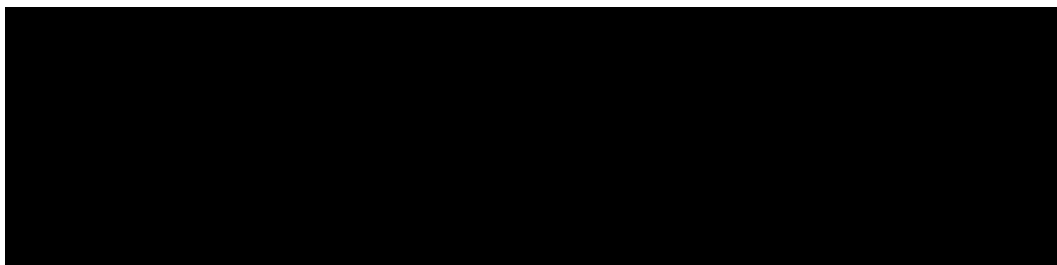


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1.0 Purpose

This procedure defines the process by which amendments to the Biopharmaceutical Development Program's (BDP's) an eCTD (electronic Common Technical Document) Type V Facilities Master File (MF) are created for submission to the Center for Biologics Evaluation and Research (CBER) / Food and Drug Administration (FDA) in electronic format.

2.0 Scope

This procedure applies to Biopharmaceutical Development Program (BDP) personnel that are involved in the preparation, review, and approval of amendments to a Type V Facilities MF (Master File) for the Frederick National Laboratory for Cancer Research (FNLCR) / National Cancer Institute (NCI) at Frederick. The most common amendments to the BDP Facilities Master File include the Annual Update and Letters of Authorization (LOA).

3.0 Authority and Responsibility

- 3.1 The Director, Biopharmaceutical Quality Assurance (BQA) has the authority to define this procedure.
- 3.2 BQA Regulatory Affairs (RA) (or designee) is responsible for the preparation, review, archiving, and submission of amendments to Type V Facilities eMFs. They ensure amendments have the appropriate bookmarks and hypertext links, are correctly paginated, and follow the table of contents. RA has the responsibility for ensuring the documents are prepared according to FDA guidelines.
- 3.3 The BDP Technical Operations Director, the Process Analytics Director, the BDP Program and Technical Director, the BQA Director, and the NCI/Biological Branch (BRB) Chief (or designee) are responsible for review and approval of amendments to a Type V Facilities eCTD MF. Those approving the document can be changed or other approvals can be added at the discretion of the RA Director.
- 3.4 Additional BDP personnel may also be asked to review specific amendments to a Type V Facilities eMF for accuracy.
- 3.5 The BQA RA director (or designee) is responsible for ensuring that amendments to a Type V Facility eMF are prepared according to Standard Operating Procedures and are organized properly following FDA established guidelines prior to document submission to the FDA.

4.0 General Guidelines for Amendments to the eMF

NOTE: This SOP contains text in blue font and screen shots shown in color. This SOP has been scanned in color and should be printed on a color printer for the most accurate results.

NOTE: Adobe Acrobat instructions provided throughout the SOP are given for Adobe Acrobat Professional DC. Consult the Adobe Acrobat Help Menu if a different version of the program is used.

- 4.1 A description of general formatting requirements applicable to the preparation of amendments to the Type V Facilities eMF (eMF) and Letters of Authorization (LOA) in Microsoft Word is included in **SOP 24408 – Preparation of Regulatory Documents**.
- 4.2 This SOP uses the eCTD software Omnicia for creating the submission to the FDA. See **SOP 24414 - Submitting Documents to the FDA Using BDPs eCTD Software**.
- 4.3 Create a folder in the DMF6298 Source folder () to save all of the source documents for the submission. The folder will be named with the next sequential four-digit serial number. For example, if folder “0019” is already created then create folder “0020”.

5.0 Letter of Authorization Amendment

- 5.1 Draft a letter of authorization (LOA) using Microsoft Word and save the letter in the Source folder created in Step 4.3. An example LOA is included in Attachment 1, and an FDA LOA template can be found at <https://www.fda.gov/drugs/drug-master-files-dmfs/drug-master-file-dmf-templates>. A LOA includes the following information (if available):
- 5.1.1 The date of the LOA submission
 - 5.1.2 DMF number
 - 5.1.3 DMF holder's name
 - 5.1.4 Name of person(s) authorized to incorporate information in the MF by reference
 - 5.1.5 Specific product(s) covered by the MF
 - 5.1.6 Submission date(s) of specific product(s) covered by the MF, if applicable.
 - 5.1.7 Section numbers and/or page numbers in the MF to be referenced
 - 5.1.8 Statement of commitment that the MF is current and that the MF holder will comply with the statements made in it
 - 5.1.9 Signature of authorizing official
 - 5.1.10 Typed name and title of official authorizing reference to the MF.
- 5.2 Prepare a pdf copy of the LOA on Leidos Biomedical Research letterhead by converting the Microsoft Word version to pdf using the Acrobat tab and choose "create pdf". The letter should be digitally signed (Refer to **SOP 24408 – Preparation of Regulatory Documents** for details on applying digital signatures).
- 5.2.1 The file name for the pdf copy of the LOA should be "00SN_LOA followed by the IND holder name or PI name. For example: "0020_loaconfer" would go in the source folder "0020". File names must be all lower case with no spaces. Avoid using special characters or hyphens. Underscores can be used in file names in place of a space.
 - 5.2.2 In situations where multiple LOAs will be submitted for the same sponsor, additional descriptors may be included following the sponsor's name, i.e., the product name or a meaningful number.
- 5.3 Draft a cover letter for the LOA amendment in Microsoft Word and save the document in the Source folder created in step 4.3.
- 5.3.1 Include the name of the MF holder, the MF number, and the identity of the sponsor authorized to incorporate information from the MF by reference in the cover letter. An example cover letter for a LOA amendment is included in Attachment 2.
 - 5.3.2 Prepare a pdf copy of the cover letter on Leidos Biomedical Research letterhead by converting the Microsoft Word version to pdf using the Acrobat tab and choose "create pdf". The letter should be digitally signed (Refer to **SOP 24408 - Preparation of Regulatory Documents**). Save the pdf copy of the cover letter

as "00SN_coverlet" in the source folder created in Step 4.3. For example: "0020_coverlet" would go in the source folder "0020". File names must be all lower case with no spaces. Avoid using special characters and hyphens, underscores can be used in place of a space in file names.

- 5.4 After a pdf copy of the cover letter and LOA are available, the submission needs to be put into eCTD format using the Omnicia software, refer to **SOP 24414 - Submitting Documents to the FDA using BDPs eCTD Software.**

6.0 eCTD MF Annual Report

- 6.1 The Biopharmaceutical Development Program's Type V Facilities Master File (MF) is updated if changes are made to the BDP GMP facility. Master File annual reports are required by the FDA on the anniversary date of the original submission. The annual report should contain the following:
- 6.1.1 Cover Letter
 - 6.1.2 A statement of commitment signed by the MF holder stating that the MF is current and that the holder will comply with the statements made in the MF. This statement can be included in eCTD section 1.2 and referenced in the annual report.
 - 6.1.3 An updated list of everyone authorized to incorporate information in the MF by reference.
 - 6.1.4 A list of parties whose authorization has been withdrawn and the dates of withdrawal.
 - 6.1.5 Dates of any amendments reporting changes since the last annual report.
- 6.2 Refer to the annual report template and subsequent submissions cover letter template on the FDA website (<https://www.fda.gov/drugs/forms-submission-requirements/drug-master-files-dmfs>) for additional information.

7.0 Changes to BDP'S Facility MF: Amendment

- 7.1 Individual Microsoft Word files that are prepared for a BDP Facility MF Amendment are accompanied by an approval signature page. One file includes lot release and characterization data for gene therapy products that had Certificates of Analysis issued since the last MF Amendment was submitted (refer to the MF File/Correspondence List for the date of the last submission). The other files include changes made to the text of the MF sections and appendices (included in the cover letter). Gene Therapy Product Lot Release and Characterization Data for the amendment are discussed in Step 7.2.3.
- 7.2 Preparation of MF Text for an Amendment
- 7.2.1 The Amendment to the MF is prepared using the previous MF files as the source documents:
 - Create a folder for the new amendment described in step 4.3 with the next sequence number.
 - Copy the Microsoft Word files from the previous Amendment to the [REDACTED] folder for the new sequence number for the Amendment. This includes Sections 1-4, Appendices 1-3, the table of contents, cover letter, cover approval page, and information statement.

- Facility Diagram files and the table of major equipment (Appendix 2) are also copied to the [REDACTED] folder.

7.2.2 Open each Microsoft Word file copied to the MF Amendment source folder and make any revisions known. The font used for text is Arial 12pt. If a file is revised, make sure the headers and footers are updated. Headers and footers remain unchanged if no revisions are made.

7.2.2.1 The header format for each Microsoft Word file appears in Arial 10-point font on each page of each section as follows:

BDP MF BB-MF 00XXXX

2019 Amendment

Leidos Biomedical Research, Inc. [REDACTED]

3.2.A.1 Facilities and Equipment

Section 1.0 Introduction

7.2.2.2 Update the year on the first line of the header to reflect the current year of the Amendment.

7.2.2.3 Confirm the "####" entry on the first line of the header reflects the MF FDA identification number.

7.2.2.4 The second line of the header is the company name: Leidos Biomedical Research Inc. [REDACTED].

7.2.2.5 Confirm the third line and fourth lines of the header reflect the title of the section being updated. The FDA suggested the BDP Facility Type V Master File be submitted under Section 3.2.A.1 Facilities and Equipment using the eCTD format.

7.2.2.6 The footer format for each Microsoft Word file appears in Arial 10-point font on each page of each section and has the following format. The number 1 represents the sequential page number, and the word "Confidential" appears in bold with all capital letter font.

1

CONFIDENTIAL

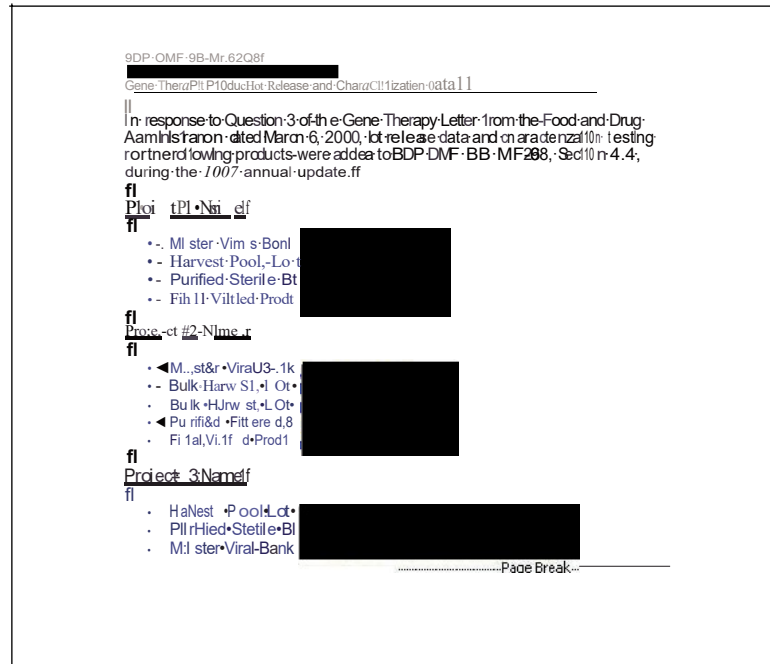
7.2.2.7 Appendix 2 contains approximately 20 separate facility diagrams and one table. The facility diagrams are each separate figures so if one is updated than only that figure needs to be replaced in the amendment. Figures may have a slightly different header that does not include the third line of "3.2.A.1 Facilities and Equipment" to get the information to fit. The words "Appendix 2 – [REDACTED]" are included.

7.2.2.8 Save and close each file when revisions are complete and update the file name to the appropriate sequence number and year of the amendment.

7.2.3 BQA RA (or designee) is responsible for updating and revising Section 4.0 (Response to March 6, 2000, FDA Letter to Sponsors of INDs or Master Files Manufacturing Gene Therapy Products). Section 4.0 consists of an introduction and responses to seven questions from the FDA Letter. RA reviews the response to each question, investigates the current status, and updates/edits the response to the question to provide the most current information.

This procedure is made available through federal funds from the National Cancer Institute, NIH, under contract [REDACTED].

7.2.3.1 Include a list (in blue font) of the COAs found in the update (grouped by product). An example is shown in the following screen shot.



7.2.3.2 Insert the COA's for each of the products as a jpeg file (refer to **SOP 24408 - Preparation of Regulatory Documents**). Include a title preceding each COA indicating the product, lot number, and date of manufacture for that COA. For example:

Date of Manufacture: August 25, 2006

7.2.4 A copy of all of the Microsoft Word files (and pdf Figures and table in Appendix 2) for the MF Amendment are placed in a shared network folder for review. The following BOP individuals (or their designee's) review each of sections relevant to their areas. Reviews are performed using the track changes feature of Microsoft Word.

- Director, Manufacturing Operations
- Director, Biopharmaceutical Process Analytics/Quality Control (PA/QC)
- Director, Biopharmaceutical Quality Assurance (BQA)
- BOP Facility Manager
- BQA, Quality Engineering Validation Manager
- BQA Auditing Manager

NOTE: The list of reviewers in Step 7.2.4 can be modified at the discretion of the Regulatory Affairs Director.

7.2.5 As the reviews are completed:

7.2.5.1 Resolve all reviewer comments and save the final file versions in the appropriate sequence Source folder.

NOTE: The version sent to the FDA will not have the tracked changes on it. It will be the final approved version.

- 7.2.5.2 Any editing required for facility diagrams requires that the date of each diagram is updated in the header to reflect the current status.
- 7.2.5.3 Compile a list of significant changes using Microsoft Word in the cover letter. Be sure to include section numbers, page numbers, paragraph, etc., as applicable to indicate the location and nature of the change. Title the file "coversigpage2019.docx". Where the number "2019" is changed to the year of the amendment.

7.3 Approval of the MF Amendment

- 7.3.1 Once the reviews are complete and any revisions are finished, place copies of the revised files along with the cover letter listing the changes on a shared BDP network drive for final approval. In addition, include the following two files:
 - 7.3.1.1 The table of contents should be included for final review. Update the table of contents to include a date beside each section title if it is not included in the revised Amendment being prepared, so the last date the section was updated and provided to the FDA is included. For example: "3.3 Materials Management and Inventory Control (provided in 2017 Annual Report)". This indicates the current Section 3.3 was last updated and provided in the 2017 Annual Report.
 - 7.3.1.2 An approval page should also be provided to obtain approval of the amendment (refer to **SOP 24408 - Preparation of Regulatory Documents** for how to add digital signature blocks). The previous annual report approval page can be used and updated as needed (appropriate date, reviewers, etc.). Approvers should include at a minimum the following individuals:
 - Director, Manufacturing Operations
 - Director, Biopharmaceutical Process Analytics/Quality Control (PA/QC)
 - Director, Biopharmaceutical Quality Assurance (BQA)
 - BQA, Quality Engineering/Validation Manager
 - BDP Program and Technical Director
 - BRB Branch Chief
- 7.3.1.2 Once all approval signatures are obtained, the files on the shared network drive can be deleted.

7.4 Preparation of the MF Amendment for eCTD FDA Submission

- 7.4.1 After all sections are approved the submission needs to be put into eCTD format using the Omnicia software.
- 7.4.2 Before using the Omnicia software, make sure all references in the text to appendices, figures, and tables are in blue font ([Blue 255](#)).
- 7.4.3 All links should be inserted in Microsoft Word before moving files to **Omnifile**. Apply appropriate links to the hyperlink destinations listed in blue font per Step 7.4.2.

- 7.4.3.1 In Microsoft Word, create a bookmark to the destination where you want the link to go.
 - 7.4.3.1.1 Highlight the document title where the bookmark will be placed.
 - 7.4.3.1.2 Go to the Search Tool on the top of Microsoft Word.
 - 7.4.3.1.3 Type Insert a Bookmark.
 - 7.4.3.1.4 Click on the Insert a Bookmark Link.
 - 7.4.3.1.5 Name the bookmark in all lowercase with no space marks.
 - 7.4.3.1.6 Select Add.
- 7.4.3.2 Highlight the reference, right click and choose link. The insert hyperlink box appears. Click on Place in This Document. Click on the bookmark created in 7.4.3.1.
- 7.4.3.3 Links can also be created in Microsoft Word in the Omnicia Software on the virtual server using the Omnicia plug in tab. Click the tab and then choose the OmniWord drop down. See the Omnicia Software manual and **SOP 24408 – Preparation of Regulatory Documents** for details.

- 7.4.4 Draft a cover letter for the MF Amendment in Microsoft Word. Save the document in the Source folder created in Step 4.3. An example of a cover letter is included in Attachment 3 and includes:
 - The identification of the submission (amendment, the DMF number, type of DMF, and the subject of the amendment);
 - The sponsors (IND number if know, IND title or product name, sponsor, and name of sponsor's representative) authorized to incorporate information contained in the DMF by reference;
 - A certification statement as follows: "We certify that the information contained in BB-MF ##### is current and that the Biopharmaceutical Development Program complies with the statements made therein."
 - A confidentiality statement as follows: "Please note the information contained in our BB-MF ##### is proprietary and confidential and may not be distributed to anyone without the written consent of the Biopharmaceutical Development Program / Leidos Biomedical Research, Inc./NCI at Frederick. The legal protection of such confidential material is hereby claimed under applicable provisions of 21 CFR 601.51 and 21 CFR 314.430.";
 - Signature, typewritten name, and title of the holder or the authorized representative.

- 7.4.4.1 The final cover letter should be digitally signed if possible. Refer to Step 5.3.2.

8.0 Submission and Archiving

8.1 Letter of Authorization Amendment Submission and Archiving.

- 8.1.1 Submission to the FDA is completed by the BDP's Regulatory Affairs department using the FDA Electronic Submissions Gateway according the **SOP 24302 –**

This procedure is made available through federal funds from the National Cancer Institute, NIH, under contract XXXXXXXXXX

Establishment and Use of an FDA Electronic Submissions Gateway (ESG) Account.

- 8.1.2 Provide a copy of the LOA to the sponsor. This may be completed by filling out a distribution form according to ***SOP 21417 – Distribution of Documents to External Recipients to electronically provide a copy***, or by providing the copy as an attachment to the Chemistry, Manufacturing, and Controls information/Manufacturing Report for the IND sponsor.
- 8.1.3 Merge individual pdf files including the signed distribution form, memo, virus statement, LOA, and FDA final receipt into a single pdf file according to ***SOP 24408 – Preparation of Regulatory Documents***. Follow ***SOP 24414 - Submitting Documents to the FDA Using BDPs eCTD Software*** for making sure hyperlinks and bookmarks are appropriately set.
- 8.1.4 The electronic copy of the eCTD submission for the LOA Amendment created in Step 8.1.3 (specifically the contents of the ESG Submission folder created in Step 4.3 is stored on the BDP network drive. A link to the document (distribution form, cover letter, virus statement and LOA) on the BDP network is placed in the Regulatory Affairs correspondence file for the MF.

8.2 eMF Amendment and Annual update Submission and Archiving

- 8.2.1 Submission to the FDA is completed by the BDP's RA department using the FDA Electronic Submissions Gateway according to ***SOP 24302 - Establishment and Use of an FDA Electronic Submissions Gateway (ESG) Account***.
- 8.2.2 Merge individual pdf files into a single pdf file including the signed approval page, memo, virus statement, Master File Sections, and FDA final receipt according to ***SOP 24408 – Preparation of Regulatory Documents***. Follow ***SOP 24414 - Submitting Documents to the FDA Using BDPs eCTD Software*** for making sure hyperlinks and bookmarks are appropriately set.
- 8.2.3 The electronic copy of the eCTD submission for the Annual Update or Amendment created is stored on the BDP network drive.
- 8.2.4 Generate a paper copy of the eMF Annual Update or Amendment created by printing the pdf files found in the Source folder including the cover letter and information statement. Convert any Microsoft Word file to pdf if needed using the "Convert to PDF" command from the Adobe PDF pull down menu in Microsoft Word. Add the printed document to the Regulatory Affairs correspondence file for the MF.
- 8.2.5 Add a copy of the final combined pdf MF Annual Update file to [REDACTED]. Delete the previous year's DMF Annual Update File BB-MF ##### so that only the most current version is available on the [REDACTED].

9.0 Definitions

- 9.1 **Amendments** – Amendments are additional electronic documents submitted to the existing Type V Facilities electronic Master Files (eMFs). There are three types of amendments submitted to the BDP's Type V Facilities eMFs. These include a Letter of Authorization (LOA) Amendment, the Annual Update Amendment, and an Amendment for any changes to the MF. These types of amendments are discussed in this SOP.

- 9.1.1 **Administrative Amendments** – These types of amendments include but are not limited to the following changes:
- 9.1.1.1 Name changes, acquisitions, or transfers of ownership
 - 9.1.1.2 Changes to the DMF subject
 - 9.1.1.3 Changes to the DMF type
- 9.1.2 **Quality Amendments** – Any changes to technical information should be submitted in a quality amendment.
- 9.2 **Annual Reports** – Annual reports should not be used to report changes in the DMF. If it is necessary to submit an amendment and an annual report, they must be submitted under separate eCTD sequence numbers. Annual reports help assure FDA that the statement of commitment is current. Failure to submit a report annually may result in the termination of a DMF.
- 9.3 **Bookmark** – A bookmark is a function in the pdf document. Bookmarks consist of a tree-structured hierarchy, which serves as a visual table of contents for a document. Bookmarks allow the document user to navigate to the targeted place within the document by selecting the bookmarked item.
- 9.4 **Digital Signature** – A process that can be used to attach a digital code to an electronic message that is unique to the individual signing the message. A digital signature results from the use of a “Private Key” to apply a signature to an electronic message. The “Public Key” on the file with the recipient of the electronic message can be used to verify whether or not the digital signature is valid and whether the message has been altered since it was signed.
- 9.5 **Master File (MF)** – A MF is a submission of information to the FDA that may be used to provide confidential detailed information about facilities, processes, or articles used in the manufacturing, processing, packaging, and storing of human drugs and biological products. The BDP maintains a Type V Master File on file with the FDA/CBER that describes the manufacturing facilities and operational responsibilities of the BDP at the NCI at Frederick’s CGMP biopharmaceutical manufacturing facilities.
- 9.6 **eCTD Master Files eMF)** – In this SOP the term eMF refers to any Type V Facilities MF organized into a format that is compliant with FDA’s eCTD electronic submission guidelines. The eMF is comprised of the initial submission and each subsequent amendment. When the term eMF is used in this SOP, the meaning is a Type V Facilities MF in eCTD format.
- 9.7 **eMF Changes Amendment** – Significant changes that may impact products (such as the addition of a new water system) are submitted to the FDA electronically in the form of an amendment to the eMF.
- 9.8 **Letter of Authorization (LOA)** – A LOA permits the FDA to access and review a document in their files, such as a MF, or portions thereof, on behalf of the person or company making reference to the document in their submission. The BDP provides LOAs to their MF on file at CBER in the form of an amendment to the eCTD Master File.
- 9.9 **Link or Hyperlink** – Links (also known as hyperlinks and hypertext links) within a document allow the user convenient access to other locations within the same document, to other electronic documents, or to websites. By selecting the hyperlinked text, the user has immediate access to the information in the linked location.

- 9.10 Portable Document Format (PDF)** – The page description language used in the Adobe Acrobat document exchange system. The eMF is created using numerous individual pdf files.
- 9.11 Serial Number (eCTD Sequence Number)** – A four-digit number assigned to each submission to the electronic Drug Master File. Serial numbers are assigned sequentially beginning with the serial number 0000 (assigned to the initial submission of the electronic Master File). For example, the first amendment has the serial number 0001). Serial numbers are abbreviated as 00SN throughout this document. Refer to the MF Regulatory File-Correspondence List to determine the next sequential serial number.
- 9.12 Subsequent Submissions** – Amendments and additions or deletions of information in the DMF including LOAs must be submitted to the DMF. These subsequent submissions should contain a cover letter and updated administrative and technical information as needed. DMF holder name changes and acceptance notifications should also include the statement of commitment.

10.0 References and Related Documents

- 10.1 SOP 21417** *Distribution of Documents to External Recipients*
- 10.2 SOP 24302** *Establishment and Use of an FDA Electronic Submissions Gateway (ESG) Account*
- 10.3 SOP 24408** *Preparation of Regulatory Documents*
- 10.4 SOP 24409** *Preparation of a Type V Facilities Electronic Drug Master File (CBER Format)*
- 10.5 SOP 24414** *Submitting Documents to the FDA Using BDP's eCTD Software*
- 10.6** FDA Draft Guidance for Industry: Providing Regulator Submissions to CBER in Electronic Format – General Considerations, October 2003
- 10.7** FDA Draft Guidance for Industry: Drug Master Files, October 2019
- 10.8** FDA Guidance for Industry: Providing Regulatory Submissions to CBER in Electronic Format – Investigational New Drug Application (INDs), March 2002
- 10.9** FDA Electronic Submissions Gateway (ESG) User Guide, <http://www.fda.gov/ForIndustry/ElectronicSubmissionsGateway/ucm334359.htm>
- 10.10** FDA Electronic Submissions Gateway (ESG), <http://www.fda.gov/esg/default.htm>

11.0 Attachments

- 11.1 Attachment 1** Example Letter of Authorization
- 11.2 Attachment 2** Example Cover Letter for LOA Amendment
- 11.3 Attachment 3** Example Cover Letter for eMF Amendment

Attachment 1

Example Letter of Authorization

leidos

Leidos Biomedical Research, Inc.

November6, 2019

Food and Drug Administration
Center for Biologics Evaluation and Research
Document Control Center

Subject: BB-MF... , Type V Master File
Letter of Authorization to Cross Reference BOP Master File

To Whom It May Concern:

This authorization letter is in reference to a Type V Master File BB-MF- [REDACTED] entitled

[REDACTED]
submitted by [REDACTED]

[REDACTED]. The most recent update to the Master File was submitted electronically in eCTD format to the FDA/CSER in [REDACTED]

We authorize the institution listed below to cross-reference the Master File (BB-MF- [REDACTED]) as described below in support of their Investigational New Drug Application (IND). The entire Master File may be referenced for the buildings, equipment, utilities, and flows of personnel, raw materials, product, process, components, and waste.

Institution:**Product:****IND Number :****IND/Study Title:****Institution Address:****Institution Representative:**

Frederick National Laboratory for Cancer Research

Attachment 1 (continued)

Institution Representative
Phone Number/Email:

[REDACTED]

We certify that the information contained in BB-MF--is current and that the- complies with the statements made therein.

Please note that information contained in BB-MF-- is proprietary and confidential and may not be distributed to anyone without the written consent of the [REDACTED]. The legal protection of such confidential material is hereby claimed under applicable provisions of 21 CFR 601.51 and 21 CFR 314.430.

Please feel free to contact me at [REDACTED] should you have any questions or require additional information.

Sincerely ,

[REDACTED]

Cc:

[REDACTED]

Frederick Nation::/ Laboratory for Cancer Research

This procedure is made available through federal funds from the National Cancer Institute, NIH, under contract--

UNCONTROLLED COPY FOR TRAINING AND REFERENCE PURPOSES ONLY

Attachment 2
Example Cover Letter for LOA Amendment

leidos

Leidos Biomedical Research, Inc.

November 6, 2019

Food and Drug Administration
Center for Biologics Evaluation and Research
Document Control Center

[REDACTED]

Subject : BB-MF.. Type V Master File
Letter of Authorization to Cross Reference - Master File

To Whom It May Concern:

This amendment is in reference to the [REDACTED]

[REDACTED] Type V Master File, BB-MF- [REDACTED]
entitled [REDACTED]
[REDACTED]

This amendment contains an electronic copy of a cross-reference letter authorizing the Food and Drug Administration (FDA) to refer to the Master File BB-MF-- [REDACTED] in support of [REDACTED] - sponsored by:

[REDACTED]

If you have any questions regarding this submission please feel free to contact me

Sincerely,

[REDACTED]

Frederick National Laboratory for Cancer Research

[REDACTED]

Attachment 3

Example Cover Letter for eDMF Annual Update Amendment

leidos

Leidos Biomedical Research, Inc.

Frederick National Laboratory for Cancer Research

August 22, 2019

Food and Drug Administration
Center for Biologics Evaluation and Research
Document Control Center
[REDACTED]

Subject: BB-MF [REDACTED] J:n?! v Biologics Master File
Serial Number: -
2019 Annual Report
Original Electronic Submission Date: [REDACTED]
First eCTD Submission Date: [REDACTED]

To Whom it Concerns:

This annual report is in reference to the [REDACTED]

[REDACTED] Type V Master File, BB-MF-[REDACTED], entitled [REDACTED]

This annual report contains an eCTD format copy of the revised sections of the 2018 MF for the 2019 Annual Report. As suggested by [REDACTED] FDA/CDER MF expert, this MF is being provided under Module 3 Section 32A1. A detailed list of the changes included is attached to this letter (pages 5-9).

The IND Sponsors listed on pages 3-4 of this letter are authorized to incorporate information in BB-MF - [REDACTED] reference. IND's or MF's referencing products manufactured at the closed [REDACTED] location should refer to MF versions dated 2011 or prior to 2011.

We certify that the information contained in BB-MF - [REDACTED] is current and that the [REDACTED] complies with the statements made therein.

Please note the information contained in our BB-MF - [REDACTED] is proprietary and confidential and may not be distributed to anyone without the written consent of the [REDACTED]

The legal protection of such confidential material is hereby claimed under applicable provisions of 21 CFR 601.51 and 21 CFR 314.430.

Leidos Biomedical Research, Inc., operating as the Frederick National Laboratory for the National Cancer Institute.

Attachment 3 (Continued)**Example Cover Letter for eDMF Annual Update Amendment**

If you have any questions regarding this submission, please feel free to contact me at

Sincerely,

A large black rectangular redaction box covering the signature and name of the sender.

Froaer/clf National Laboratory for cancer Research

IND Number	IND Title/Product Name	Manufacturing Location'	IND Sponsor	Sponsor's Representative
[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
[REDACTED] [REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]

1The location was closed between the summer of 2012 and 2013. Therefore, all ND's referencing this location should refer to DMF versions dated 2011 or prior 2011.

NOTE: A letter of authorization was also issued authorizing CSER and CDER to reference 88-
of _____ Type II Drug Master File

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Revisions to BB-MF - (to 2018 Version)

The following is a list of changes that were made during the 2018 port update of the [REDACTED] DMF--.

References were changed to reflect the new annual report date of 2019 for sections with revisions and only reference Master file (MF, not DMF).

Introduction, Section 1.0

[REDACTED]

Operational Layout, Department Responsibilities, Section 2.2

[REDACTED]

[REDACTED] Section 3.1 (other than some minor grammatical or typographical corrections, the following changes were made)

[REDACTED]

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[REDACTED]

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Quality Control. Section 3.2



Response to FDA Letter to Sponsors of IND's or Master Files
Manufacturing Gene Therapy Products. Section 4.2:

- The following sentence was added to the first paragraph: "There are no new gene therapy products added for the 2019 annual update."

Response to FDA Letter to Sponsors of IND's or Master Files
Manufacturing Gene Therapy Products. Section 4.3:



IND	IND Title/Product Name	IND Sponsor	Sponsor's Representative
None	[Redacted]	[Redacted]	[Redacted]
	[Redacted]	[Redacted]	[Redacted]



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[REDACTED]

Response to [REDACTED] FDA Letter to Sponsors of IND's or Master Files
Manufacturing Gene Therapy Products, Section 4.4:

[REDACTED]

Response to [REDACTED] FDA Letter to Sponsors of IND's or Master Files
Manufacturing Gene Therapy Products, Section 4.5:

[REDACTED]

Response to [REDACTED] FDA Letter to Sponsors of IND's or Master Files
Manufacturing Gene Therapy Products, Section 4.6:

[REDACTED]

Building A/B Facility Diagrams and Process Equipment List, Appendix 2:

[REDACTED]

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