CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

219776Orig1s000

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

IND 135058

MEETING MINUTES

BioCryst Pharmaceuticals, Inc.
Attention: Caroline Monkiewicz
Associate Director, Regulatory Affairs Strategy
4505 Emperor Boulevard
Nottingham Hall, Suite 200
Durham, NC 27703

Dear Caroline Monkiewicz:

Please refer to your Investigational New Drug Application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for berotralstat.

We also refer to the video conference between representatives of your firm and the FDA on January 23, 2025. The purpose of the meeting was to discuss the content and format of the planned NDA for berotralstat oral granules to expand the indication to include pediatric patients 2 to < 12 years of age with hereditary angioedema (HAE).

A copy of the official minutes of the video conference is enclosed for your information. Please notify us of any significant differences in understanding regarding the meeting outcomes.

If you have any questions, contact me at (301) 796-1648 or phuong.ton@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Phuong Nina Ton, PharmD
Senior Regulatory Project Manager
Pulmonology, Allergy, and Critical Care
Division of Regulatory Operations for Immunology and Inflammation
Office of Regulatory Operations
Office of New Drugs
Center for Drug Evaluation and Research

Enclosure:

- Meeting Minutes

MEMORANDUM OF MEETING MINUTES

Meeting Type:	B
Meeting Category:	Pre-NDA
Meeting Date and Time:	January 23, 2025; 12:00 – 1:00 PM ET
Meeting Location:	Video conference
Application Number:	IND 135058
Product Name:	Berotralstat
Indication:	Prophylaxis to prevent attacks of hereditary angioedema in pediatric patients 2 to < 12 years of age
Sponsor Name:	BioCryst Pharmaceuticals, Inc.
Regulatory Pathway:	505(b)(1) of the Federal Food, Drug, and Cosmetic Act
Meeting Chair:	Kelly Stone, MD, PhD
Meeting Recorder:	Nina Ton, PharmD

FDA ATTENDEES

Kelly Stone, MD, PhD, Associate Director for Therapeutic Review, Division of Pulmonology, Allergy, and Critical Care (DPACC), Office of Immunology and Inflammation (OII)
Miya Paterniti, MD, Clinical Team Leader, DPACC, OII
Diana Nichols Vinueza, MD, MHSc, Clinical Reviewer, DPACC, OII
Carol Galvis, PhD, Pharmacology/Toxicology Supervisor, Division of Pharm/Tox for Immunology and Inflammation (DPT-II), OII
Luqi Pei, PhD, Pharmacology/Toxicology Reviewer, DPT-II, OII
Yunzhao Ren, MD, PhD, Master Pharmacokineticist, Division of Inflammation and Immune Pharmacology (DIIP), Office of Clinical Pharmacology (OCP)
Amer Al-Khouja, PhD, MHS, Acting Team Leader, DIIP, OCP
James Mease, PharmD, Pharmacokineticist, DIIP, OCP
Yongman Kim, PhD, Biostatistics Team Leader, Division of Biometrics III (DBIII), Office of Biostatistics (OB)
Emily Shives, PhD, MS, Biostatistics Reviewer, DBIII, OB
Shirley Abraham, PharmD, Safety Evaluator, Division of Medication Error Prevention and Analysis (DMEPA), Office of Surveillance and Epidemiology (OSE)
Ameet Joshi, PharmD, Team Leader, Project Management Staff, OSE
Cristina Attinello, MPH, Safety Regulatory Project Manager, OSE
Nina Ton, PharmD, Senior Regulatory Project Manager, Division of Regulatory Operations for Immunology and Inflammation, Office of Regulatory Operations

SPONSOR ATTENDEES
William Sheridan, MB BS, Chief Development Officer
Phil Collis, PhD, Senior Vice President, Global Development
Heather Iocca, PhD, Vice President, Global Development and Product Team Leader
Douglas Johnston, DO, FAAAAI, Vice President, Clinical Development
Laurent Vernillet, PharmD, PhD, FCP, Vice President, Clinical Pharmacology
Scott Brantley, PhD, Associate Director, Clinical Pharmacology
Tatiana Khariton, PhD, Executive Director, Pharmacometrics
John Michael Sauer, PhD, Vice President, Nonclinical Development
Robbie Waites, PhD, Director, Toxicology
Yahya El-Kattan, PhD, Senior Vice President, Chemistry, Manufacturing, and Controls
Sharon Murray, PhD, Vice President, Biometrics
Michael DeSpirito, MS, Associate Director, Biometrics
Sylvia Dobo, MD, Senior Vice President, Global Drug Safety and Pharmacovigilance
Salisa Hauptmann, MPH, Chief Regulatory Officer and Head of Clinical Sciences
Nicole McMillan, BSN, Director, Global Regulatory Affairs Labeling
Caroline Monkiewicz, MS, Associate Director, Regulatory Affairs Strategy

1. BACKGROUND

BioCryst submitted a pre-NDA meeting request dated November 26, 2024, to the Division of Pulmonology, Allergy, and Critical Care. The purpose of the meeting was to discuss the content and format of the planned NDA for berotralstat oral granules to expand the indication to include pediatric patients 2 to < 12 years of age with HAE. The Division provided preliminary comments to BioCryst's questions via electronic correspondence dated January 21, 2025. Caroline Monkiewicz, Associate Director, Regulatory Affairs Strategy, communicated to the Division via email dated January 22, 2025, requesting to focus the meeting discussion on Questions 1 and 2. The Sponsor also provided a slide deck for discussion of Question 1, which is attached to the meeting minutes. The Sponsor's questions from the December 16, 2024, meeting package are provided below in italics, FDA's responses are in normal font, and the meeting discussion is in bold.

2. DISCUSSION

Nonclinical

Question 1
Based on recent general guidance from the Agency, BioCryst is conducting additional in vitro mammalian mutagenicity and human metabolism studies to support the negative enhanced Ames assay for (b) (4) *nitrosamine* (b) (4)*. Although the approach to the mammalian mutagenicity study is clear, BioCryst is seeking alignment with the Agency on the approach to the in vitro human metabolism assay.*
(b) (4)

(b) (4)

Does the Agency have additional guidance (b) (4)

FDA Response to Question 1

(b) (4)

(b) (4)

Meeting Discussion

BioCryst presented to the Agency their development program to comply with FDA guidance and nitrosamines requirements (slide 2). The following topics were discussed regarding their nitrosamines program:

(b) (4)

FDA responded that these are review issues. The review team also needs to consult the Nitrosamine Working Group prior to providing feedback on this proposal.

BioCryst proposed to submit the NDA in February 2025 with the available data (negative Ames assay) and to submit the two additional reports around June 2025. The Sponsor stated that there are challenges getting these studies initiated because the CRO test labs are overwhelmed with other sponsors requesting similar tests.

FDA noted that the Nitrosamine Working Group consultation response will take time. Submitting the additional reports 2 months prior to PDUFA goal date can cause additional delays. FDA advised BioCryst to work with the CROs to provide the reports earlier, if possible.

The Sponsor proposed to file the NDA and accept the risk for the delayed report submission [redacted] (b) (4)

FDA could not respond to this proposal at this time, but planned to provide additional feedback in a post-meeting comment. [redacted] (b) (4) **FDA clarified that acceptable intake would be a review issue and could not provide comments for the category until consulting the Nitrosamine Working Group.**

The Sponsor then asked whether the NDA submission without the required reports would constitute a Refusal to File action. FDA advised that an NDA submission should be complete with all the required reports. FDA added that guidance and additional information will be provided in a post-meeting comment when the meeting minutes are issued in 30 days. BioCryst proposed to submit a Type A meeting request to engage with members from the Nitrosamine Working Group. FDA advised the Sponsor to wait for the official meeting minutes since the Sponsor does not have the final reports and the discussion would be hypothetical.

Post-Meeting Comment

You may submit the NDA with the available information for nitrosamine risk assessment. If we determine that additional data are needed to support a proposed acceptable intake after our review and discussion with the Nitrosamine Working Group, we will communicate this and request the additional information for review. This additional information could constitute new data not previously submitted to or reviewed by the Agency and could be considered a major amendment.

Clinical Pharmacology

Question 2

Following up to Question 3 from the Type C Meeting Written Responses dated 08 May 2024, does the Agency agree with BioCryst's dosing selection approach using Study 304 data and simulated C_{trough} and C_{max}?

FDA Response to Question 2

In general, your proposed extrapolation approach for pediatric dose selection based on comparing steady state C_{trough}, steady state C_{max}, and other exposure parameters is reasonable.

We recommend that the doses and weight bands selected for labeling are those which have been evaluated in clinical trials and for which safety data are available. Based on the preliminary data you have provided from ongoing Study 304, it appears that pediatric subjects in Cohorts 2-4 (with body weight < 40 kg) had berotralstat exposure within the range of that observed for adults, while subjects in Cohort 1 (with body weight ≥ 40 kg) who received 150 mg capsules had exposure exceeding that observed in adults (Table 7 from your meeting package). Therefore, we agree that a lower dose is likely needed for patients ≥ 40 kg.

You have stated that potential berotralstat doses were simulated in (b) (4) to inform your proposed dosing regimens. In your NDA submission, to support dose selection for pediatric patients with higher body weight (i.e., ≥ 40 kg), we recommend you provide additional justifications (e.g., simulations of various doses) to support that your proposed dosing regimens are optimal, considering the exposure-response relationships for both efficacy (e.g., HAE attack rate) and safety (e.g., QT prolongation).

In addition, you have currently defined the adult reference ranges according to simulations based on data derived from adult and adolescent participants from phase 1, 2, and 3 studies. We have no objection to this approach. Although, you may also consider defining the adult exposure reference ranges using observed data, rather than simulated data, to assess whether this results in any meaningful differences in your conclusions.

The final determination of the acceptability of the proposed dosing will be a review issue.

Meeting Discussion

BioCryst stated that pediatric doses evaluated in Study 304 were safe, with similar exposures observed between pediatric patients and adults, except for the dose administered to the highest weight group. In addition, population PK modeling and simulation was used to support the proposed commercial weight-based dose selection (b) (4) The Sponsor agreed with FDA that a dose lower than 150 mg is needed for HAE patients with a body weight ≥ 40 kg, based on exposure observed in Study 304. The Sponsor indicated that the population PK modeling and simulation dosing selection approach was used to propose commercial pediatric weight-based doses and that simulation results showed that the new doses/weight bands result in exposures that are within the range of the ones administered in Study 304. The Sponsor predicts that the proposed doses will result in comparable C_{trough} values between pediatric patients aged 2 to 12 years and adult patients, while keeping C_{max} within the acceptable exposure reference range. The Sponsor indicated that the population PK modeling and simulation report will be included in the NDA submission. The Sponsor plans to

file the NDA globally, but wanted to align with FDA regarding the dose selection approach.

FDA noted that the Agency places greater emphasis on observed data over simulated data during the review, and that the proposed doses should ideally reflect the doses studied in clinical trials in order to rely on the observed safety and tolerability data. The FDA added that any deviation from doses studied in the trial will require adequate justification. The Sponsor inquired if simulation would be an adequate justification. FDA responded this would be a review issue and noted that it would be challenging to justify using commercial doses higher than doses studied in clinical trials. The Sponsor commented (b) (4) **and planned to provide a comparison between exposures from the simulated doses and new weight bands to the exposures observed in the study. FDA agreed that comparison would be helpful for the NDA review but could not comment on dosing at this time. FDA also suggested the Sponsor conduct simulations to evaluate doses** (b) (4) **and consider other possibilities. BioCryst indicated that they have this information in the modeling report and will submit it.**

Question 3

In the Type C Meeting Written Responses dated 08 May 2024, the Agency recommended to summarize observed pediatric concentrations and PK parameters and compare to reference ranges observed in adults. As such, BioCryst plans to provide a standalone report, BCX7353-MS-003, of a comparison of the observed concentrations and PK parameters in Study 304 to reference ranges observed in adult participants dosed with the approved 150 mg capsule to steady state in prior clinical studies. Summary outputs for the reference analysis adult population will be provided, along with the supportive analysis datasets, Analysis Dataset of Pharmacokinetic Parameters (ADPP) and Subject-Level Analysis Dataset (ADSL).

Does the Agency agree that BioCryst's proposal will satisfy the Agency's recommendation?

FDA Response to Question 3

Your proposal to furnish a standalone report to provide a comparison of observed PK data in pediatrics (Study 304) to adults dosed with 150 mg capsule at steady state from previous clinical studies is reasonable.

We note that you intend to include PK data obtained in adults from Study 106 and Study 116. Clarify whether Study 106 and Study 116 are the only two relevant studies from which adult berotralstat exposure data could be derived for comparison. If feasible, consider also deriving plasma concentration data from phase 2 and 3 studies in subjects with HAE.

Meeting Discussion
This question was not discussed.

Regulatory

Question 4
Does the Agency agree with the format and content of planned NDA 219,776?

FDA Response to Question 4
Generally, the planned format and content format is adequate. In Section 1.9, Pediatric Administrative Information, include the Proposed Pediatric Study Request (PPSR) and amendments as well as the attached Pediatric Exclusivity Determination Template, summarizing the final version of the Written Request (WR), and how the completed study addresses each section of the WR.

Meeting Discussion
This question was not discussed.

Question 5
BioCryst plans to market the oral granules and the capsule formulations under the same proprietary name, Orladeyo. The Proprietary Name Review (PNR) request submitted under NDA 214,094 will be cross-referenced in the planned NDA 219,776. No additional PNR request is planned.
Does the Agency agree?

FDA Response to Question 5
If you plan to market your proposed NDA 219776 under a proprietary name, a request for proprietary name should be submitted for our review.

We recommend you submit **A REQUEST FOR PROPRIETARY NAME REVIEW** at the time of your NDA 219776 submission. Note your submission should include your justification for using the same proprietary name for both formulations.

When submitting a proprietary name request for review to the Agency, it is crucial to:

a. Check “Request for Proprietary Name Review” in Box 21 of FDA form 356h.

b. Include the statement **"REQUEST FOR PROPRIETARY NAME REVIEW”** in bold capital letters, at the **top** of your cover letter **and** at the **top** of the first page of the main submission document (refer to the complete submission guidance link below).

c. Clearly state in the cover letter and supporting documentation the exact name you are requesting for review and include the phonetic spelling of the name.

d. If you have already submitted draft labels & labeling, add a link to them in the cover letter.

We refer you to the following guidances and information on submitting requests for proprietary name review or PDUFA performance goals associated with proprietary name reviews:

a. Guidance for Industry *Contents of a Complete Submission for the Evaluation of Proprietary Names*[2]

b. Draft Guidance for Industry *Best Practices in Developing Proprietary Names for Human Nonprescription Drug Products*[3]

c. Guidance for Industry *Best Practices in Developing Proprietary Names for Human Prescription Drug Products*[4]

d. PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2022 through 2027[5]

Meeting Discussion
This question was not discussed.

Question 6
BioCryst proposes to have 1 product label (prescribing information and patient package insert) that includes all required information for both berotralstat formulations (capsules and oral granules). The proposed indication under the product label is "Orladeyo is indicated for prophylaxis to prevent attacks of hereditary angioedema (HAE) in adults and pediatric patients 2 years of age and older".

Does the Agency agree?

FDA Response to Question 6
Your proposal to have one product label for both formulations appears reasonable; however, the acceptability of label and labeling is a review issue and will be assessed at the time of the NDA submission.

[2] We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database https://www.fda.gov/RegulatoryInformation/Guidances/default.htm
[3] When final, this guidance will represent the FDA's current thinking on this topic. For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/RegulatoryInformation/Guidances/default.htm
[4] We update guidances periodically. For the most recent version of a guidance, check the. FDA Guidance Documents Database https://www.fda.gov/RegulatoryInformation/Guidances/default.htm
[5] https://www.fda.gov/industry/prescription-drug-user-fee-amendments/pdufa-vii-fiscal-years-2023-2027

Meeting Discussion
This question was not discussed.

Question 7
With regard to administration information for the oral granules, BioCryst plans to update text in the prescribing information and patient package insert, as appropriate, and include images with text on the intermediate packaging. A patient Instructions for Use document is not planned.

Does the Agency agree with BioCryst's proposal?

FDA Response to Question 7
The structure, format and content of your proposed prescribing information and patient package insert will be a review issue. It is premature to comment on the necessity of an instructions for Use (IFU) at this time. The necessity of an IFU will be a review issue.

Meeting Discussion
This question was not discussed.

Question 8
Does the Agency agree that the planned NDA 219,776 for prophylaxis to prevent attacks of HAE in pediatric patients 2 to < 12 years of age meets the criteria for priority review?

FDA Response to Question 8
Yes, we agree. Any supplement to an application under section 505 of the FD&C Act that proposes a labeling change pursuant to a report on a pediatric study under this section shall be considered a priority review supplement per section 505A of the FD&C Act as amended by section 5(b) of the Best Pharmaceuticals for Children Act.

Meeting Discussion
This question was not discussed.

Question 9
Does the Agency agree that if BioCryst successfully complies with the conditions of the WR, pediatric exclusivity will be granted?

FDA Response to Question 9
Whether pediatric exclusivity will be granted will be a review issue, based on whether the submitted study reports fairly respond to the issued WR.

Meeting Discussion
This question was not discussed.

Question 10

With regard to product safety reporting requirements, does the Agency agree with the following:

- *Submission of a 90-day Safety Update Report in lieu of a 120-day Safety Update Report during NDA review*
- *Harmonization of the 3-month Periodic Adverse Drug Experience Reports (PADERs) to the International Birth Date (IBD) of 03 December*
- *Submission of 12-month PBRERs that include both dosage forms of the active substance to NDA 214,094*
- *Submission of 3 quarterly PADERs to NDA 219,776 and 1 annual PBRER to NDA 214,094 in lieu of the quarterly PADER covering the reporting period 03 September to 02 December for 3 years, followed by annual PBRER submissions to NDA 214,094*

FDA Response to Question 10

You may submit a 90-day Safety Update Report in lieu of a 120-day Safety Update Report during the NDA review.

Regarding the 3 questions, referencing PADERs and PBRERs, which pertain to a postmarketing safety reporting requirement under 21 CFR 314.80(c)(2) for an approved new drug application, FDA only grants postmarketing safety waiver requests following commencement of an applicant's safety reporting requirements under 21 CFR 314.80. These responsibilities start upon approval of the application. Thus, we do not agree to your proposals at this time.

If applicable, following a decision from FDA on the application, submit your postmarketing reporting waiver request(s) to each pertinent application (i.e., as a safety waiver request to NDA 219776 and as a waiver modification to NDA 214094) in the electronic common technical document (eCTD) format. If your waiver request is for several products, you can submit a single waiver request letter that references multiple applications.

Meeting Discussion

This question was not discussed.

Additional Comments

We note in Table 5 titled "Berotralstat Oral Granules Product Attributes" (Page 24 of your briefing document), you state that "*Dosage strengths are subject to change based on final analyses (see sponsor's position to Question 2)".* As you develop your proposed product in oral granules packets for pediatric patients ages 2 to 12 years of age, we

recommend that you ensure your product strengths are congruent with the dosage and administration of the product to avoid complicating the calculation, preparation, and administration of a dose which may lead to medication errors. It is not clear if your development plan considers the risk of medication errors due to usage of partial packet(s) to achieve one dose. We recommend you consider developing multiple strengths of your proposed oral granule packets to facilitate using one full packet to obtain each proposed dose (i.e.,72 mg, 96 mg, and 132 mg).

Meeting Discussion
These comments were not discussed.

3. OTHER IMPORTANT MEETING LANGUAGE SECTIONS

PREA REQUIREMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Please be advised that under the Food and Drug Administration Safety and Innovation Act (FDASIA), you must submit an Initial Pediatric Study Plan (iPSP) within 60 days of an End-of-Phase-2 (EOP2) meeting. In the absence of an EOP2 meeting, refer to the draft guidance below. The iPSP must contain an outline of the pediatric study or studies that you plan to conduct (including, to the extent practicable study objectives and design, age groups, relevant endpoints, and statistical approach); any request for a deferral, partial waiver, or waiver, if applicable, along with any supporting documentation, and any previously negotiated pediatric plans with other regulatory authorities. The iPSP should be submitted in PDF and Word format. Failure to include an Agreed iPSP with a marketing application could result in a refuse to file action.

For additional guidance on the timing, content, and submission of the iPSP, including an iPSP Template, please refer to the guidance for industry *Pediatric Study Plans: Content of and Process for Submitting Initial Pediatric Study Plans and Amended Pediatric Study Plans*.[6] In addition, you may contact the Division of Pediatric and Maternal Health at 301-796-2200 or email Pedsdrugs@fda.hhs.gov. For further guidance on pediatric product development, please refer to FDA.gov.[7]

[6] https://www.fda.gov/media/86340/download
[7] https://www.fda.gov/drugs/development-resources/pediatric-and-maternal-health-product-development

PRESCRIBING INFORMATION

In your application, you must submit proposed prescribing information (PI) that conforms to the content and format regulations found at 21 CFR 201.56(a) and (d) and 201.57 including the Pregnancy and Lactation Labeling Rule (PLLR) (for applications submitted on or after June 30, 2015). As you develop your proposed PI, we encourage you to review the labeling review resources on the PLR Requirements for Prescribing Information[8] and Pregnancy and Lactation Labeling Final Rule[9] websites, which include:

- The Final Rule (Physician Labeling Rule) on the content and format of the PI for human drug and biological products.
- The Final Rule (Pregnancy and Lactation Labeling Rule) on the content and format of information related to pregnancy, lactation, and females and males of reproductive potential.
- Regulations and related guidance documents.
- A sample tool illustrating the format for Highlights and Contents, and
- The Selected Requirements for Prescribing Information (SRPI) − a checklist of important format items from labeling regulations and guidances.
- FDA's established pharmacologic class (EPC) text phrases for inclusion in the Highlights Indications and Usage heading.

Pursuant to the PLLR, you should include the following information with your application to support the changes in the Pregnancy, Lactation, and Females and Males of Reproductive Potential subsections of labeling. The application should include a review and summary of the available published literature regarding the drug's use in pregnant and lactating women and the effects of the drug on male and female fertility (include search parameters and a copy of each reference publication), a cumulative review and summary of relevant cases reported in your pharmacovigilance database (from the time of product development to present), a summary of drug utilization rates amongst females of reproductive potential (e.g., aged 15 to 44 years) calculated cumulatively since initial approval, and an interim report of an ongoing pregnancy registry or a final report on a closed pregnancy registry. If you believe the information is not applicable, provide justification. Otherwise, this information should be located in Module 1. Refer to the draft guidance for industry *Pregnancy, Lactation, and Reproductive Potential: Labeling for Human Prescription Drug and Biological Products – Content and Format*.

Prior to submission of your proposed PI, use the SRPI checklist to ensure conformance with the format items in regulations and guidances.

[8] https://www.fda.gov/drugs/laws-acts-and-rules/plr-requirements-prescribing-information
[9] https://www.fda.gov/drugs/labeling/pregnancy-and-lactation-labeling-drugs-final-rule

MANUFACTURING FACILITIES

To facilitate our inspectional process, we request that you clearly identify *in a single location*, either on the Form FDA 356h, or an attachment to the form, all manufacturing facilities associated with your application. Include the full corporate name of the facility and address where the manufacturing function is performed, with the FEI number, and specific manufacturing responsibilities for each facility.

Also provide the name and title of an onsite contact person, including their phone number, fax number, and email address. Provide a brief description of the manufacturing operation conducted at each facility, including the type of testing and DMF number (if applicable). Each facility should be ready for GMP inspection at the time of submission.

Consider using a table similar to the one below as an attachment to Form FDA 356h. Indicate under Establishment Information on page 1 of Form FDA 356h that the information is provided in the attachment titled, "Product name, NDA/BLA 012345, Establishment Information for Form 356h."

Site Name	Site Address	Federal Establishment Indicator (FEI) or Registration Number (CFN)	Drug Master File Number (if applicable)	Manufacturing Step(s) or Type of Testing [Establishment function]
(1)				
(2)				

Corresponding names and titles of onsite contact:

Site Name	Site Address	Onsite Contact (Person, Title)	Phone and Fax number	Email address
(1)				
(2)				

To facilitate our facility assessment and inspectional process for your marketing application, we refer you to the instructional supplement for filling out Form FDA 356h[10] and the guidance for industry, *Identification of Manufacturing Establishments in*

[10] https://www.fda.gov/media/84223/download

Applications Submitted to CBER and CDER Questions and Answers[11]*.* Submit all related manufacturing and testing facilities in eCTD Module 3, including those proposed for commercial production and those used for product and manufacturing process development.

OFFICE OF SCIENTIFIC INVESTIGATIONS (OSI) REQUESTS

The Office of Scientific Investigations (OSI) requests that the items described in the draft guidance for industry, *Standardized Format for Electronic Submission of NDA and BLA Content for the Planning of Bioresearch Monitoring (BIMO) Inspections for CDER Submissions,* and the associated conformance guide, *Bioresearch Monitoring Technical Conformance Guide Containing Technical Specifications,* be provided to facilitate development of clinical investigator and sponsor/monitor/CRO inspection assignments, and the background packages that are sent with those assignments to the FDA ORA investigators who conduct those inspections. This information is requested for all major trials used to support safety and efficacy in the application (i.e., phase 2/3 pivotal trials). Please note that if the requested items are provided elsewhere in submission in the format described, the Applicant can describe location or provide a link to the requested information.

Please refer to the draft guidance for industry *Standardized Format for Electronic Submission of NDA and BLA Content for the Planning of Bioresearch Monitoring (BIMO) Inspections for CDER Submissions* (February 2018) and the associated *Bioresearch Monitoring Technical Conformance Guide Containing Technical Specifications*.[12]

4. ISSUES REQUIRING FURTHER DISCUSSION

There were no issues requiring further discussion.

5. ACTION ITEMS

There were no action items that were identify during the meeting.

6. ATTACHMENTS AND HANDOUTS

A copy of the presented slides is attached.

[11] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/identification-manufacturing-establishments-applications-submitted-cber-and-cder-questions-and
[12] https://www.fda.gov/media/85061/download

7 Page(s) have been Withheld in Full as b4 (CCI/TS) immediately following this page

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This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

PHUONG N TON
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