

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

210933Orig1s000

ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS



IND 117192

MEETING MINUTES

Kala Pharmaceuticals, Inc.
Attention: Michele La Russa
SVP, Global Head of Regulatory Affairs and Quality Assurance
100 Beaver Street, #201
Waltham, MA 02453

Dear Ms. La Russa:

Please refer to your Investigational New Drug Application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for KPI-121 (loteprednol etabonate ophthalmic suspension), 0.25%.

We also refer to the teleconference between representatives of your firm and the FDA on August 16, 2017. The purpose of the meeting was to discuss the statistical analysis plan for the ongoing Phase 3 trials and format and content of the nonclinical and clinical modules of the upcoming NDA submission.

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

If you have any questions, call Judit Milstein, Chief, Project Management Staff at (301) 796- 0763.

Sincerely,

{See appended electronic signature page}

Wiley A. Chambers, MD
Deputy Director
Division of Transplant and Ophthalmology Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Enclosure: Meeting Minutes



FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

MEMORANDUM OF MEETING MINUTES

Meeting Type: B
Meeting Category: Pre-NDA

Meeting Date and Time: August 16, 2017, 2:00 PM to 3:00 PM
Meeting Location: Teleconference

Application Number: 117192
Product Name: KPI-121 (loteprednol etabonate ophthalmic suspension), 0.25%
Indication: Temporary relief of the signs and symptoms of dry eye disease
Sponsor/Applicant Name: Kala Pharmaceuticals, Inc.

Meeting Chair: Wiley A. Chambers, M.D.
Meeting Recorder: Judit Milstein

FDA ATTENDEES

Renata Albrecht, Director, Division of Transplant and Ophthalmology Products (DTOP)
Wiley A. Chambers, Deputy Director, DTOP
William M. Boyd, Clinical Team Leader, DTOP
Lucious Lim, Clinical Reviewer, DTOP
Martin Nevitt, Clinical Reviewer, DTOP
Jennifer Harris, Clinical Reviewer, DTOP
Andrew McDougal, Pharmacology/Toxicology Reviewer, DTOP
Lori Kotch, Pharmacology/Toxicology Team Leader, DTOP
Yunfan Deng, Biometrics Reviewer, Division of Biometrics IV (DBIV)
Daphne Lin, Deputy Director, DBIV
Amit Somani, Clinical Pharmacology Reviewer, Division of Clinical Pharmacology IV
Chunchun Zhang, Acting Pharmaceutical Assessment Lead, Office of Product Quality
Judit Milstein, Chief, Project Management Staff, DTOP

KALA PHARMACEUTICALS, INC. ATTENDEES

Kim Brazzell, CMO, Kala Pharmaceuticals
Susan Coultas, VP, Clinical Operations, Kala Pharmaceuticals
(b) (4) Statistical Consultant
Michele La Russa, SVP, Regulatory Affairs and QA, Kala Pharmaceuticals
(b) (4) Statistical Consultant
(b) (4) Statistical Consultant

BACKGROUND

Kala Pharmaceuticals, Inc. (the Sponsor) is developing KPI-121 (loteprednol etabonate ophthalmic suspension), an ester corticosteroid for the temporary relief of the signs and symptoms of dry eye. Kala claims the new formulation of loteprednol etabonate enhances penetration through the mucous layer of the tear film allowing [REDACTED] (b) (4) [REDACTED] (b) (4) increased drug penetration into ocular tissues [REDACTED] (b) (4).

On June 26, 2017, Kala submitted a meeting request for a Pre-NDA meeting to discuss the statistical analysis plan for the ongoing Phase 3 trials and the format and content of the nonclinical and clinical modules of the upcoming NDA submission. The meeting was granted for August 16, 2017. FDA issued Meeting Preliminary Comments on August 8, 2017, in response to questions included in the July 13, 2017, Meeting Package. On August 15, 2017, the Sponsor sent an e-mail with clarification on the proposed statistical analysis plan for further discussion during the meeting (see Attachment).

DISCUSSION

For the purposes of these minutes, the questions submitted in the DATE, Meeting Package are in **bold** font, FDA preliminary responses are in *italics* font, and the meeting discussions are in normal font.

Regulatory

- 1. The phase 3 pivotal trials (KPI-121-C-006 and KPI-121-C-007) for Kala's proposed NDA are in patients with dry eye disease. Assuming the data are supportive, we will be requesting approval of the indication of the temporary relief of the signs and symptoms of dry eye disease utilizing a 505(b)(2) pathway.**

Does the Agency agree?

FDA Response: There is not enough information to make this determination. Labeling is a review issue. The specific language to be included in the Indication Section of the labeling will be determined after review of the NDA.

Meeting Discussion: None.

Clinical

- 2. Kala has conducted a number of clinical trials with KPI-121. In the ISS for the temporary relief of the signs and symptoms of dry eye disease NDA (for KPI-121 0.25%), Kala proposes to describe the safety results from all completed trials of KPI-121 0.25%, regardless of the indications studied in these trials (i.e., Protocols KPI-121-C-001, KPI-121-C-002, KPI-121-C-006, KPI-121-C-007, and KPI-121-C-009). See Table 3 for a complete list of Kala's studies of KPI-121.**

The primary focus of the ISS for the NDA is proposed to be on the safety results from the 2 phase 3 pivotal studies (Protocols KPI-121-C-006 and KPI-121-C-007) and the phase 2 trial (Protocol KPI-121-C-002), which will be described based on summary tables derived both from each individual protocol dataset and from an integrated dataset from the 3 trials. The safety results from the KPI-121 0.25% arm of Protocol KPI-121-C-001 (a phase 3 trial in the treatment of postoperative inflammation and pain) and the safety results from Protocol KPI-121-C-009 (a PK trial of KPI-121 0.25% conducted in healthy adults), will also be summarized, separately.

The text summary of all safety data is expected to meet the Agency's definition of "small" and is proposed to be included in Module 2.7.4 (Summary of Clinical Safety). Does the Agency agree with the plan for the trials to be included in the ISS and in the manner described?

FDA Response: Agree.

Meeting Discussion: None.

3. For the integrated (i.e., pooled) data presentations in the ISS, Kala proposes to include tabular summaries of demographics, disposition, exposure, adverse events (AEs), and IOP data for the pooled safety population of Protocols KPI-121-C-006, KPI-121-C-007, and KPI-121-C-002.

Does the Agency agree with the plan for the pooled analyses to be included in the ISS?

FDA Response: Agree.

Meeting Discussion: None.

4. Medical Dictionary for Regulatory Activities (MedDRA) version 19.0 was used to code all AE data for Protocols KPI-121-C-006 and KPI-121-C-007, and version 16.1 was used for Protocol KPI-121-C-002. The pooled AE analyses for the integrated dataset from Protocols KPI-121-C-006, KPI-121-C-007, and KPI 121 C 002 trials are proposed to be presented using MedDRA version 19.0.

Does the Agency agree that the pooled AE data can use MedDRA version 19.0?

FDA Response: Agree. The Agency also expects presentation of AE data for each individual trial.

Meeting Discussion: None.

5. Kala proposes to include the following for all trials submitted in Module 5:
 - patient narratives for all deaths and other SAEs, all severe ocular AEs, and all discontinuations (from treatment or after randomization) due to AEs.
 - case report forms (CRFs) for all patients for whom a narrative is submitted, plus all patients who discontinued early (from treatment or after randomization) for any reason.

Does the Agency agree with the proposals for narratives and CRFs?

FDA Response: Agree.

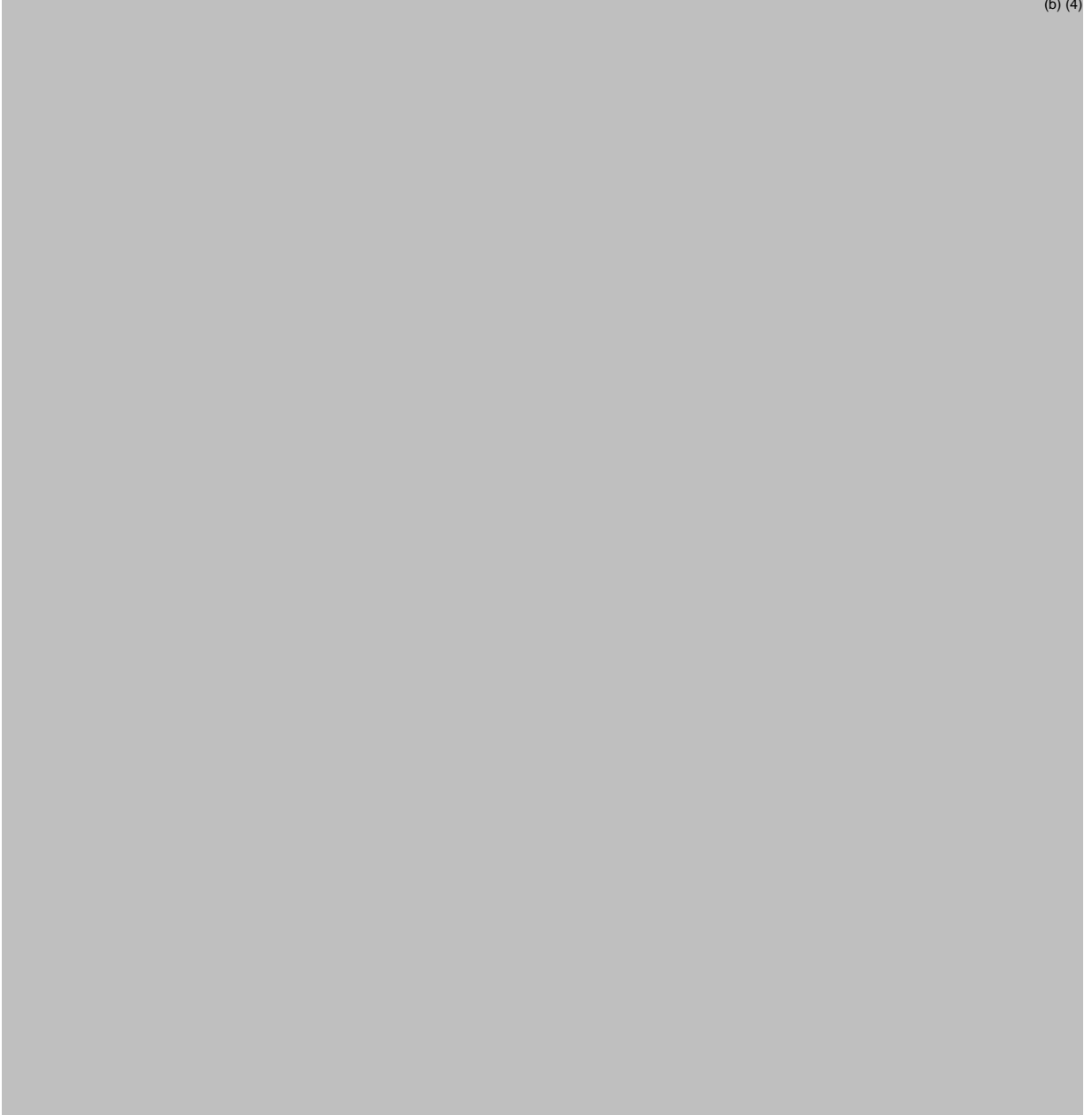
Meeting Discussion: None.

- 6. Kala proposes to utilize the following statistical analyses of the primary endpoints for the ongoing Phase 3 trials (as described in the draft guidance entitled ‘Multiple Endpoints in Clinical Trials Guidance for Industry’ dated Jan 2017)**

All primary endpoint comparisons will be performed between KPI-121 0.25% ophthalmic suspension group and the vehicle group using sequentially rejective multiple testing as described below.

Primary Efficacy Endpoints:

(b) (4)



Does the Agency agree with the statistical plan?

FDA Response: No.

(b) (4)

The Agency may have further comments when the complete protocol and statistical analysis plan are submitted to the IND.

Meeting Discussion: The Sponsor provided clarification on the proposed statistical plan, as described in the enclosed attachment. The Division stated that it understood the statistical theory involved, but remained concerned about the strength of the finding regarding the proposal for (b) (4). The Division stated that the strength of the findings on the signs and symptoms will determine the adequacy of the data submitted in support of the NDA submission.

- 7. After locking the database and reviewing unmasked tabulated data and statistical analyses from the first completed Phase 3 pivotal trial (either Protocol KPI-121-C-006 or KPI-121-C-007), Kala may choose to modify the Statistical Analysis Plan for the second ongoing phase 3 trial (prior to unmasking the database of the second trial) based on the results and statistical analyses from the first pivotal trial. Any change to the Statistical Analysis Plan would be clearly documented before the database is unmasked for the second trial.**

Does the Agency agree?

FDA Response: Agree.

Meeting Discussion: None.

- 8. Kala proposes to present the efficacy results from Protocols KPI-121-C-006, KPI-121-C-007, and KPI-121-C-002 in Module 2.7.3 (Summary of Clinical Efficacy), by protocol. No pooled analysis of an integrated dataset is proposed, to allow the reviewer to compare and contrast the outcomes of the independent trials in subjects with dry eye disease.**

A summary of the pharmacokinetic data from Protocol KPI-121-C-009 will also be included.

The text summary of all efficacy data is expected to meet the Agency's definition of "small" and is proposed to be included in Module 2.7.3 (Summary of Clinical Efficacy). This is the same strategy as proposed for planned NDA 210565, for KPI-121 1% (for the treatment of postoperative inflammation and pain following ocular surgery), as noted in the briefing document submitted on 29 Mar 2017.

Does the Agency agree with the plan for the presentation of efficacy data?

FDA Response: Agree.

Meeting Discussion: None.

9. **During the conduct of Protocol KPI-121-C-006, it was discovered that 1 site (Alexandra Kostick, MD-Site 170) initiated subjects' treatment with study product at Visit 1, without first completing the protocol-mandated 2-week run-in period with vehicle, and prior to randomization. Eighteen subjects received study product for up to 2 weeks. Upon discovery of this issue, Kala discontinued all of the affected subjects from the trial and closed the site. None of the eighteen subjects had adverse events while on study product. They were only seen at screening and early termination. For the handling of these subjects' data in the study report, Kala proposes for simplicity that these patients not be included.**

Does the Agency agree?

FDA Response: The events that occurred at that site and the action taken should be included in the study report, but the data does not otherwise need to be included.

Meeting Discussion: None.

10. **For the clinical data presentation, Kala proposes to produce and submit SDTM compliant datasets and documentation for the 2 phase 3 pivotal trials (KPI-121-C-006 and KPI-121-C-007), phase 2 trial (KPI-121-C-002), and the phase 1 pharmacokinetic trial (KPI-121-C-009), which were conducted in support of the proposed indication for the temporary relief of the signs and symptoms of dry eye disease. Kala proposes to also produce and submit SDTM compliant datasets and documentation for KPI-121-C-001 (phase 3 trial in postoperative inflammation and pain), as it enrolled subjects in a 0.25% arm. Kala proposes that SDTM compliant datasets will not be submitted for the supportive trials (b) (4) (KPI-121-C-003) and DME/RVO (KPI-121-C-004); these datasets will be submitted in legacy format.**

Does the Agency agree?

FDA Response: Acceptable, if there will not be any reliance on Study KPI-121-C-003 for a determination of efficacy or for any other labeling claims.

Meeting Discussion: None.

11. **Kala proposes to produce and submit ADaM compliant datasets for the pooled analyses only (inclusive of study ID), and for the small pharmacokinetic studies in healthy adult subjects, KPI-121-C-008 and KPI-121-C-009.**

Analysis datasets and documentation used for the outputs prepared for the individual CSRs are proposed to be submitted as non-standard legacy (i.e., SAS) datasets (i.e., raw CRF data and programs on which the individual CSR tables and listings were based) that are not ADaM compliant.

This is the same strategy as proposed for planned NDA 210565, for KPI-121 1% (for the treatment of postoperative inflammation and pain following ocular surgery), as noted in the briefing document submitted on 29 Mar 2017.

Does the Agency agree?

FDA Response: Please also submit the SAS program codes along with their define documents you use to generate the efficacy and safety results in the study reports.

Meeting Discussion: None.

Nonclinical

12. Kala believes that the company has sufficient nonclinical information to support a 505(b)(2) NDA for the temporary relief of the signs and symptoms of dry eye disease with KPI-121 0.25% QID, including the publicly available nonclinical toxicology data contained in the Lotemax package inserts, published loteprednol etabonate nonclinical data, Kala's GLP 28-day ocular toxicity study in rabbits conducted with KPI-121 1%, and ocular pharmacokinetic studies in rabbits conducted with KPI-121.

This is the same strategy as proposed for planned NDA 210565, for KPI-121 1% (for the treatment of postoperative inflammation and pain following ocular surgery), as noted in the briefing document submitted on 29 Mar 2017.

Does the Agency agree?

FDA Response: Your approach appears appropriate. The adequacy of the data will be a review issue.

Meeting Discussion: None.

13. In Module 2.4 of the proposed NDA, Kala proposes to make reference to publicly available data including but not limited to: Lotemax package inserts and literature to support the nonclinical summary for KPI-121 0.25%, in addition to the results from a 28-day toxicity study in rabbits conducted with topically administered KPI-121 1%.

Does the Agency agree?

FDA Response: We concur with your approach. The following general advice is the same as was conveyed for the May 2, 2017 meeting. It is included here for completeness of record:

- a. All recommended nonclinical elements should be provided, either directly (original studies or published literature) or by relying on the FDA's findings of safety and effectiveness for a listed drug. If literature is being relied upon to support the NDA, published literature relevant to your product should be considered, and relevant data should be summarized in the NDA.
 - i. Include a summary of all published nonclinical literature being relied upon and a copy of all publications cited.

- ii. *The nonclinical summary is typically organized to address each of the nonclinical elements (e.g. pharmacology, pharmacokinetics, ocular toxicity, systemic toxicity, genotoxicity, reproductive toxicity, carcinogenicity, etc.).*
 - iii. *A copy of each cited article should be provided. Please note that review articles cannot be relied upon to support an application; the source articles which contain full study data should be provided or incorporated by reference.*
 - iv. *Published data is viewed at the same level of scrutiny as original data and expected to be of comparable/sufficient quality to support an NDA. In your integrated summary, provide discussion of the potential impact of study shortcomings (e.g. insufficient animal numbers, insufficient endpoint analyses, formulation differences, inadequate test article characterization, etc.), if applicable.*
 - v. *Please also identify any listed drug(s) described in the published literature (e.g., trade name(s)). Reliance on published literature describing a listed drug(s) is considered to be reliance on FDA's finding of safety and/or effectiveness for the listed drug(s).*
- b. *Please note that non-US labeling or non-US regulatory authority assessments may not be relied upon as they are neither FDA's findings related to a listed drug, nor are they published literature. If the studies upon which the non-US conclusions are based have been published, you may be able to rely upon that literature.*
 - c. *FDA discipline reviews cannot be relied upon to support an 505(b)(2) NDA application. FDA finding of safety and efficacy is captured in the product labeling, and may include findings that can be inferred from fact of approval. If you intend to rely on FDA's finding of safety and/or effectiveness for a listed drug, you must establish that such reliance is scientifically appropriate. You should establish a "bridge" (e.g., via comparative pharmacokinetic data) between your proposed formulation and the listed drug. If exposure levels using your proposed formulation are less than or equal to that of the listed drug (at approved dose) following ocular administration, then reliance upon the listed drug would be considered scientifically justified. If exposure levels using your formulation exceed those of the listed drug, then additional toxicity studies may be needed to support the increased exposure.*
 - d. *You should ensure that all nonclinical data needed to support your application are either provided directly, or are adequately bridged if you opt to rely on the FDA's findings of safety and effectiveness for a listed drug(s). A detailed description regarding how you intend to bridge data that you don't own or have right of reference to should be provided in the NDA.*
 - e. *Impurity specifications that exceed qualification limits specified in the ICHQ3 guidances should be adequately qualified and the supporting safety data should be provided in the NDA submission. Ensure that ocular and systemic safety are addressed.*
 - f. *Novel excipients should be qualified, and safety data provided.*
 - g. *For the NDA, labeling should comply with the Pregnancy and Lactation Labeling Rule (PLLR). For more information, please see the final rule.*
<https://www.fda.gov/drugs/developmentapprovalprocess/developmentresources/labeling/ucm093307.htm>

Meeting Discussion: None.

Additional discussion:

The Sponsor indicated that they have more than 50K images on the hyperemia and inquired about how many of those the Division will like to be submitted. The Division indicated that a representative sample of 10% of the patients, i.e. full patient sets of 10% of patients, will be adequate.

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.

We acknowledge your submissions dated May 25, 2016, containing your initial Pediatric Study Plan (iPSP) and November 22, 2016, containing your agreed iPSP respectively. We also note the Division's acknowledgment of your agreed iPSP dated December 16, 2016.

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](#) and [Pregnancy and Lactation Labeling Final Rule](#) 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.

The application should include a review and summary of the available published literature regarding drug use in pregnant and lactating women, a review and summary of reports from your pharmacovigilance database, and an interim or final report of an ongoing or closed pregnancy registry (if applicable), which 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* (<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM425398.pdf>).

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

SUBMISSION FORMAT REQUIREMENTS

The Electronic Common Technical Document (eCTD) is CDER and CBER’s standard format for electronic regulatory submissions. Beginning **May 5, 2017**, the following submission types: **NDA, ANDA, BLA** and **Master Files** must be submitted in eCTD format. **Commercial IND** submissions must be submitted in eCTD format beginning **May 5, 2018**. Submissions that do not adhere to the requirements stated in the eCTD Guidance will be subject to rejection. For more information please visit: <http://www.fda.gov/ectd>.

SUBMISSION FORMAT REQUIREMENTS

The Electronic Common Technical Document (eCTD) is CDER and CBER’s standard format for electronic regulatory submissions. As of **May 5, 2017**, the following submission types: **NDA, ANDA, and BLA** must be submitted in eCTD format. **Commercial IND** and **Master File** submissions must be submitted in eCTD format beginning **May 5, 2018**. Submissions that do not adhere to the requirements stated in the eCTD Guidance will be subject to rejection. For more information please visit: <http://www.fda.gov/ectd>.

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.				

505(b)(2) REGULATORY PATHWAY

The Division recommends that sponsors considering the submission of an application through the 505(b)(2) pathway consult the Agency’s regulations at 21 CFR 314.54, and the draft guidance for industry, *Applications Covered by Section 505(b)(2)* (October 1999), available at <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>. In addition, FDA has explained the background and applicability of section 505(b)(2) in its October 14, 2003, response to a number of citizen petitions that had challenged the Agency’s interpretation of this statutory provision (see Docket FDA-2003-P-0274-0015, available at <http://www.regulations.gov>).

If you intend to submit a 505(b)(2) application that relies for approval on FDA’s finding of safety and/or effectiveness for one or more listed drugs, you must establish that such reliance is scientifically appropriate, and must submit data necessary to support any aspects of the proposed drug product that represent modifications to the listed drug(s). You should establish a “bridge” (e.g., via comparative bioavailability data) between your proposed drug product and each listed drug upon which you propose to rely to demonstrate that such reliance is scientifically justified.

If you intend to rely on literature or other studies for which you have no right of reference but that are necessary for approval, you also must establish that reliance on the studies described in the literature or on the other studies is scientifically appropriate. You should include a copy of such published literature in the 505(b)(2) application and identify any listed drug(s) described in the published literature (e.g. by trade name(s)).

If you intend to rely on the Agency's finding of safety and/or effectiveness for a listed drug(s) or published literature describing a listed drug(s) (which is considered to be reliance on FDA's finding of safety and/or effectiveness for the listed drug(s)), you should identify the listed drug(s) in accordance with the Agency's regulations at 21 CFR 314.54. It should be noted that 21 CFR 314.54 requires identification of the "listed drug for which FDA has made a finding of safety and effectiveness," and thus an applicant may only rely upon a listed drug that was approved in an NDA under section 505(c) of the FD&C Act. The regulatory requirements for a 505(b)(2) application (including, but not limited to, an appropriate patent certification or statement) apply to each listed drug upon which a sponsor relies.

If FDA has approved one or more pharmaceutically equivalent products in one or more NDA(s) before the date of submission of the original 505(b)(2) application, you must identify one such pharmaceutically equivalent product as a listed drug (or an additional listed drug) relied upon (see 21 CFR 314.50(i)(1)(i)(C), 314.54, and 314.125(b)(19); see also 21 CFR 314.101(d)(9)). If you identify a listed drug solely to comply with this regulatory requirement, you must provide an appropriate patent certification or statement for any patents that are listed in the Orange Book for the pharmaceutically equivalent product, but you are not required to establish a "bridge" to justify the scientific appropriateness of reliance on the pharmaceutically equivalent product if it is scientifically unnecessary to support approval.

If you propose to rely on FDA's finding of safety and/or effectiveness for a listed drug that has been discontinued from marketing, the acceptability of this approach will be contingent on FDA's consideration of whether the drug was discontinued for reasons of safety or effectiveness.

We encourage you to identify each section of your proposed 505(b)(2) application that is supported by reliance on FDA's finding of safety and/or effectiveness for a listed drug(s) or on published literature (see table below). In your 505(b)(2) application, we encourage you to clearly identify (for each section of the application, including the labeling): (1) the information for the proposed drug product that is provided by reliance on FDA's finding of safety and/or effectiveness for the listed drug or by reliance on published literature; (2) the "bridge" that supports the scientific appropriateness of such reliance; and (3) the specific name (e.g., proprietary name) of each listed drug named in any published literature on which your marketing application relies for approval. If you are proposing to rely on published literature, include copies of the article(s) in your submission.

In addition to identifying the source of supporting information in your annotated labeling, we encourage you to include in your marketing application a summary of the information that supports the application in a table similar to the one below.

List the information essential to the approval of the proposed drug that is provided by reliance on the FDA's previous finding of safety and effectiveness for a listed drug or by reliance on published literature

Source of information (e.g., published literature, name of listed drug)	Information Provided (e.g., specific sections of the 505(b)(2) application or labeling)
<i>1. Example: Published literature</i>	<i>Nonclinical toxicology</i>
<i>2. Example: NDA XXXXXX “TRADENAME”</i>	<i>Previous finding of effectiveness for indication A</i>
<i>3. Example: NDA YYYYYY “TRADENAME”</i>	<i>Previous finding of safety for Carcinogenicity, labeling section B</i>
<i>4.</i>	

Please be advised that circumstances could change that would render a 505(b)(2) application for this product no longer appropriate. For example, if a pharmaceutically equivalent product were approved before your application is submitted, such that your proposed product would be a “duplicate” of a listed drug and eligible for approval under section 505(j) of the FD&C Act, then it is FDA’s policy to refuse to file your application as a 505(b)(2) application (21 CFR 314.101(d)(9)). In such a case, the appropriate submission would be an Abbreviated New Drug Application (ANDA) that cites the duplicate product as the reference listed drug.

ISSUES REQUIRING FURTHER DISCUSSION

None

ACTION ITEMS

The Division will issue the minutes of the meeting within 30 days.

ATTACHMENTS AND HANDOUTS

E-mail dated August 15, 2017, with clarification on statistical considerations.

2 Page(s) have been Withheld in Full as B4 (CCI/TS) immediately following this page

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

WILEY A CHAMBERS
08/29/2017