

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

207131Orig1s000

OTHER REVIEW(S)

505(b)(2) ASSESSMENT

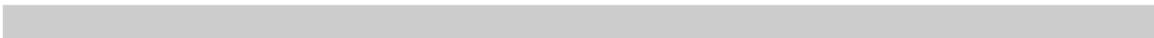
Application Information		
NDA # 207131	NDA Supplement #: S-	Efficacy Supplement Type SE-
Proprietary Name: N/A Established/Proper Name: Cefazolin Injection, USP Dosage Form: Sterile solution for Injection Strengths: 2 g/100 mL		
Applicant: Celerity Pharmaceuticals, LLC.		
Date of Receipt: 10/17/2014		
PDUFA Goal Date: 08/16/2015		Action Goal Date (if different):
RPM: Fariba Izadi		
Proposed Indication(s): Perioperative prophylaxis		

GENERAL INFORMATION

- 1) Is this application for a recombinant or biologically-derived product and/or protein or peptide product *OR* is the applicant relying on a recombinant or biologically-derived product and/or protein or peptide product to support approval of the proposed product?

YES NO

If "YES" contact the (b)(2) review staff in the Immediate Office, Office of New Drugs.



**INFORMATION PROVIDED VIA RELIANCE
(LISTED DRUG OR LITERATURE)**

- 2) List the information essential to the approval of the proposed drug that is provided by reliance on our previous finding of safety and efficacy for a listed drug by reliance on published literature, or by reliance on a final OTC monograph. *(If not clearly identified by the applicant, this information can usually be derived from annotated labeling.)*

Source of information* (e.g., published literature, name of listed drug(s), OTC final drug monograph)	Information relied-upon (e.g., specific sections of the application or labeling)
NDA 050779 Cefazolin for Injection USP and Dextrose Injection USP	FDA's previous finding of safety and effectiveness (clinical and nonclinical)

*each source of information should be listed on separate rows, however individual literature articles should not be listed separately

- 3) Reliance on information regarding another product (whether a previously approved product or from published literature) must be scientifically appropriate. An applicant needs to provide a scientific "bridge" to demonstrate the relationship of the referenced and proposed products. Describe how the applicant bridged the proposed product to the referenced product(s). (Example: BA/BE studies)

In accordance with 21 C.F.R. 320.24(b)(6) Celerity Pharmaceuticals, LLC requested a waiver for in-vivo bioavailability/bioequivalence requirements for Cefazolin Injection. This request was based on 21 CFR § 320.24(b)(6), which states that for certain drug products, the in-vivo bioavailability or bioequivalence of the drug product may be self-evident provided the drug product (1) is a parenteral solution intended solely for administration by injection, or an ophthalmic or otic solution; and (2) contains the same active and inactive ingredients in the same concentration as a drug product that is the subject of an approved full new drug application. The drug product's self-evident in-vivo bioavailability or bioequivalence is based on the fact that the drug product is a sterile solution intended solely for administration by intravenous infusion that has the same active ingredient in the same strength as the reference listed drug that is the subject of an approved NDA. Further, the dosage form, route of administration and dosing regimen for the proposed drug are the same as the RLD.

A biowaiver was granted on 3/13/15 for this submission..

RELIANCE ON PUBLISHED LITERATURE

- 4) (a) Regardless of whether the applicant has explicitly stated a reliance on published literature to support their application, is reliance on published literature necessary to support the approval of the proposed drug product (i.e., the application *cannot* be approved as labeled without the published literature)?

YES NO
If "NO," proceed to question #5.

- (b) Does any of the published literature necessary to support approval identify a specific (e.g., brand name) *listed* drug product?

YES NO
If "NO", proceed to question #5.
If "YES", list the listed drug(s) identified by name and answer question #4(c).

(c) Are the drug product(s) listed in (b) identified by the applicant as the listed drug(s)?
YES NO

RELIANCE ON LISTED DRUG(S)

Reliance on published literature which identifies a specific approved (listed) drug constitutes reliance on that listed drug. Please answer questions #5-9 accordingly.

5) Regardless of whether the applicant has explicitly cited reliance on listed drug(s), does the application **rely** on the finding of safety and effectiveness for one or more listed drugs (approved drugs) to support the approval of the proposed drug product (i.e., the application cannot be approved without this reliance)?
YES NO
If "NO," proceed to question #10.

6) Name of listed drug(s) relied upon, and the NDA #(s). Please indicate if the applicant explicitly identified the product as being relied upon (see note below):

Name of Listed Drug	NDA #	Did applicant specify reliance on the product? (Y/N)
Cefazolin for Injection USP and Dextrose Injection USP	NDA 050779	Y

Applicants should specify reliance on the 356h, in the cover letter, and/or with their patent certification/statement. If you believe there is reliance on a listed product that has not been explicitly identified as such by the applicant, please contact the (b)(2) review staff in the Immediate Office, Office of New Drugs.

7) If this is a (b)(2) supplement to an original (b)(2) application, does the supplement rely upon the same listed drug(s) as the original (b)(2) application?
N/A YES NO
*If this application is a (b)(2) supplement to an original (b)(1) application or not a supplemental application, answer "N/A".
If "NO", please contact the (b)(2) review staff in the Immediate Office, Office of New Drugs.*

8) Were any of the listed drug(s) relied upon for this application:
a) Approved in a 505(b)(2) application?
YES NO
If "YES", please list which drug(s).
Name of drug(s) approved in a 505(b)(2) application: NDA 050779 Cefazolin for Injection USP and Dextrose Injection USP

b) Approved by the DESI process?
YES NO
If "YES", please list which drug(s).

Name of drug(s) approved via the DESI process:

c) Described in a final OTC drug monograph?

YES NO
If "YES", please list which drug(s).

Name of drug(s) described in a final OTC drug monograph:

d) Discontinued from marketing?

YES NO
If "YES", please list which drug(s) and answer question d) i. below.
If "NO", proceed to question #9.

Name of drug(s) discontinued from marketing:

i) Were the products discontinued for reasons related to safety or effectiveness?

YES NO

(Information regarding whether a drug has been discontinued from marketing for reasons of safety or effectiveness may be available in the Orange Book. Refer to section 1.11 for an explanation, and section 6.1 for the list of discontinued drugs. If a determination of the reason for discontinuation has not been published in the Federal Register (and noted in the Orange Book), you will need to research the archive file and/or consult with the review team. Do not rely solely on any statements made by the sponsor.)

9) Describe the change from the listed drug(s) relied upon to support this (b)(2) application (for example, "This application provides for a new indication, otitis media" or "This application provides for a change in dosage form, from capsule to solution").

This application provides for a change in tonicity adjuster, pH adjuster, volume, concentration, and container closure system. Stability, instructions for use, and infusion rate are different from the RLD as well.

The purpose of the following two questions is to determine if there is an approved drug product that is equivalent or very similar to the product proposed for approval that should be referenced as a listed drug in the pending application.

*The assessment of pharmaceutical equivalence for a recombinant or biologically-derived product and/or protein or peptide product is complex. If you answered **YES to question #1**, proceed to question #12; if you answered **NO to question #1**, proceed to question #10 below.*

10) (a) Is there a pharmaceutical equivalent(s) to the product proposed in the 505(b)(2) application that is already approved (via an NDA or ANDA)?

(Pharmaceutical equivalents are drug products in identical dosage forms intended for the same route of administration that: (1) contain identical amounts of the identical active drug ingredient, i.e., the same salt or ester of the same therapeutic moiety, or, in the case of modified release dosage forms that require a reservoir or overage or such forms as prefilled syringes where residual volume may vary, that deliver identical amounts of the active drug ingredient over the identical dosing period; (2) do not necessarily contain the same inactive ingredients; and (3) meet the identical compendial or other applicable standard of identity, strength, quality, and purity, including potency and, where applicable, content uniformity,

disintegration times, and/or dissolution rates. (21 CFR 320.1(c), FDA's "Approved Drug Products with Therapeutic Equivalence Evaluations" (the Orange Book)).

Note that for proposed combinations of one or more previously approved drugs, a pharmaceutical equivalent must also be a combination of the same drugs.

YES NO

If "NO" to (a) proceed to question #11.
If "YES" to (a), answer (b) and (c) then proceed to question #12.

(b) Is the pharmaceutical equivalent approved for the same indication for which the 505(b)(2) application is seeking approval?

YES NO

(c) Is the listed drug(s) referenced by the application a pharmaceutical equivalent?

N/A YES NO

*If this application relies only on non product-specific published literature, answer "N/A"
If "YES" to (c) and there are no additional pharmaceutical equivalents listed, proceed to question #12.*

If "NO" or if there are additional pharmaceutical equivalents that are not referenced by the application, list the NDA pharmaceutical equivalent(s); you do not have to individually list all of the products approved as ANDAs, but please note below if approved approved generics are listed in the Orange Book. Please also contact the (b)(2) review staff in the Immediate Office, Office of New Drugs.

Pharmaceutical equivalent(s): Cefazolin for Injection USP and Dextrose Injection USP

11) (a) Is there a pharmaceutical alternative(s) already approved (via an NDA or ANDA)?

(Pharmaceutical alternatives are drug products that contain the identical therapeutic moiety, or its precursor, but not necessarily in the same amount or dosage form or as the same salt or ester. Each such drug product individually meets either the identical or its own respective compendial or other applicable standard of identity, strength, quality, and purity, including potency and, where applicable, content uniformity, disintegration times and/or dissolution rates. (21 CFR 320.1(d)) Different dosage forms and strengths within a product line by a single manufacturer are thus pharmaceutical alternatives, as are extended-release products when compared with immediate- or standard-release formulations of the same active ingredient.)

Note that for proposed combinations of one or more previously approved drugs, a pharmaceutical alternative must also be a combination of the same drugs.

YES NO

If "NO", proceed to question #12.

(b) Is the pharmaceutical alternative approved for the same indication for which the 505(b)(2) application is seeking approval?

YES NO

(c) Is the approved pharmaceutical alternative(s) referenced as the listed drug(s)?

N/A YES NO

If this application relies only on non product-specific published literature, answer "N/A"
If "YES" and there are no additional pharmaceutical alternatives listed, proceed to question #12.

If "NO" or if there are additional pharmaceutical alternatives that are not referenced by the application, list the NDA pharmaceutical alternative(s); you do not have to individually list all of the products approved as ANDAs, but please note below if approved generics are listed in the Orange Book. Please also contact the (b)(2) review staff in the Immediate Office, Office of New Drugs.

Pharmaceutical alternative(s): Cefazolin for Injection USP and Dextrose Injection USP

PATENT CERTIFICATION/STATEMENTS

- 12) List the patent numbers of all unexpired patents listed in the Orange Book for the listed drug(s) for which our finding of safety and effectiveness is relied upon to support approval of the (b)(2) product.

Listed drug/Patent number(s):

No patents listed proceed to question #14

- 13) Did the applicant address (with an appropriate certification or statement) all of the unexpired patents listed in the Orange Book for the listed drug(s) relied upon to support approval of the (b)(2) product?

YES NO

If "NO", list which patents (and which listed drugs) were not addressed by the applicant.

Listed drug/Patent number(s):

- 14) Which of the following patent certifications does the application contain? (Check all that apply and identify the patents to which each type of certification was made, as appropriate.)

No patent certifications are required (e.g., because application is based solely on published literature that does not cite a specific innovator product)

21 CFR 314.50(i)(1)(i)(A)(1): The patent information has not been submitted to FDA. (Paragraph I certification)

21 CFR 314.50(i)(1)(i)(A)(2): The patent has expired. (Paragraph II certification)

Patent number(s):

21 CFR 314.50(i)(1)(i)(A)(3): The date on which the patent will expire. (Paragraph III certification)

Patent number(s):

Expiry date(s):

21 CFR 314.50(i)(1)(i)(A)(4): The patent is invalid, unenforceable, or will not be

infringed by the manufacture, use, or sale of the drug product for which the application is submitted. (Paragraph IV certification). *If Paragraph IV certification was submitted, proceed to question #15.*

- 21 CFR 314.50(i)(3): Statement that applicant has a licensing agreement with the NDA holder/patent owner (must also submit certification under 21 CFR 314.50(i)(1)(i)(A)(4) above). *If the applicant has a licensing agreement with the NDA holder/patent owner, proceed to question #15.*
- 21 CFR 314.50(i)(1)(ii): No relevant patents.
- 21 CFR 314.50(i)(1)(iii): The patent on the listed drug is a method of use patent and the labeling for the drug product for which the applicant is seeking approval does not include any indications that are covered by the use patent as described in the corresponding use code in the Orange Book. Applicant must provide a statement that the method of use patent does not claim any of the proposed indications. (Section viii statement)

Patent number(s):
Method(s) of Use/Code(s):

15) Complete the following checklist **ONLY** for applications containing Paragraph IV certification and/or applications in which the applicant and patent holder have a licensing agreement:

- (a) Patent number(s):
- (b) Did the applicant submit a signed certification stating that the NDA holder and patent owner(s) were notified that this b(2) application was filed [21 CFR 314.52(b)]?
YES NO

If "NO", please contact the applicant and request the signed certification.

- (c) Did the applicant submit documentation showing that the NDA holder and patent owner(s) received the notification [21 CFR 314.52(e)]? This is generally provided in the form of a registered mail receipt.
YES NO

If "NO", please contact the applicant and request the documentation.

- (d) What is/are the date(s) on the registered mail receipt(s) (i.e., the date(s) the NDA holder and patent owner(s) received notification):

Date(s):

Note, the date(s) entered should be the date the notification occurred (i.e., delivery date(s)), not the date of the submission in which proof of notification was provided

- (e) Has the applicant been sued for patent infringement within 45-days of receipt of the notification listed above?

*Note that you may need to call the applicant (after 45 days of receipt of the notification) to verify this information **UNLESS** the applicant provided a written statement from the notified patent owner(s) that it consents to an immediate effective date of approval.*

YES NO Patent owner(s) consent(s) to an immediate effective date of approval

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

/s/

FARIBA IZADI
08/07/2015

Division of Anti-Infective Products

REGULATORY PROJECT MANAGER LABELING REVIEW

Application: NDA 207131

Name of Drug: Cefazolin Injection, USP, 2 g/100 mL

Applicant: Celerity Pharmaceuticals, LLC.

Labeling Reviewed

Submission Date: 10-16-14

Receipt Date: 10-16-14

Background and Summary Description: NDA) 207131 for Cefazolin Injection, USP in GALAXY Container (2 g/100 mL) was submitted October 16, 2014 (SEQ-0000). While Celerity had proposed (b) (4), the Division stated that the only indication approved for the 2 g dose of cefazolin is (b) (4).

Celerity communicated that due to electronic publishing deadlines and its desire to submit the original NDA by October, 2014; it was unable to revise the labeling prior to submission and wished to provide the revised labeling as an Amendment. The Division agreed that it was Celerity's decision to make the changes before submission or to submit as planned, but the labeling would need to be revised and resubmitted. The Division confirmed that Celerity could submit the NDA as planned and recommended amending the application to (b) (4) and provide updated labeling information. Celerity agreed to provide the updated labeling information and related documentation as an amendment to the application. The labeling amendment was provided to the NDA on July 10, 2015.

Review

This review is based on Celerity's submitted Word format of the prescribing information (PI). The proposed PI was reviewed in accordance with the labeling format requirements listed in the "Selected Requirements for Prescribing Information (SRPI).

Recommendations

The review of the prescribing information was reviewed and found to be acceptable

Fariba Izadi, PharmD	07-17-15
Regulatory Project Manager	Date
Frances V. LeSane	07-23-15
Chief, Project Management Staff	Date

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

/s/

FARIBA IZADI
07/24/2015

FRANCES V LESANE
07/24/2015

**FOOD AND DRUG ADMINISTRATION
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion**

*****Pre-decisional Agency Information*****

Memorandum

Date: June 30, 2015

To: Fariba Izadi, Pharm.D.
Regulatory Project Manager
Division of Anti-Infective Products (DAIP)

From: Adam George, Pharm.D.
Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

Through: Amy Toscano, Pharm.D, RAC, CPA
Team Leader
Office of Prescription Drug Promotion (OPDP)

Subject: **NDA 207131 Cefazolin injection, for intravenous use**

This consult review is in response to DAIP's April 15, 2015, request for OPDP's review of the draft package insert (PI) and carton/container labeling for Cefazolin injection, for intravenous use. OPDP's comments on the PI are based on the substantially complete version titled "207131 pi-draft-labeling-text-original-draft-v3" which was accessed via SharePoint on June 29, 2015. Our comments on the PI are included directly on the attached copy of the labeling, and were uploaded to the DAIP SharePoint site on June 29, 2015. We reviewed the version of the carton and container labeling sent via email from Dr. Izadi on June 30, 2015. OPDP does not have any comments on this version of the carton and container labeling.

OPDP appreciates the opportunity to provide comments on these materials. If you have any questions or concerns, please contact Adam George at 301-796-7607 or adam.george@fda.hhs.gov

11 Page(s) of Draft Labeling 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/

ADAM N GEORGE
06/30/2015

MEMORANDUM

REVIEW OF REVISED LABEL AND LABELING

Division of Medication Error Prevention and Analysis (DMEPA)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

Date of This Memorandum: June 11, 2015
Requesting Office or Division: Division of Anti- Infective Products (DAIP)
Application Type and Number: NDA 207131
Product Name and Strength: Cefazolin Injection, USP
2 g/100 mL in Galaxy Container
Product Type: Single ingredient
Rx or OTC: Rx
Applicant/Sponsor Name: Celerity Pharmaceuticals, LLC (Celerity)
Submission Date: 10/16/2014
OSE RCM #: 2014-2250
DMEPA Primary Reviewer: Sevan Kolejian, PharmD
DMEPA Team Leader: Vicky Borders-Hemphill, PharmD

1 PURPOSE OF MEMO

The Division of Anti –Infective Products (DAIP) requested that we review the revised container label and carton labeling (Appendix A) to determine if they are acceptable from a medication error perspective. The revisions are in response to recommendations that we made during a previous label and labeling review.¹

2 CONCLUSIONS

In a letters dated May 29, 2015 and June 11, 2015, Celerity Pharmaceuticals, LLC provided a rationale for the FDA recommendations that we made during a previous label and labeling review. We find their rationale and revisions made by Celerity acceptable from a medication error perspective. The revised container labels and carton labeling are acceptable from a medication error perspective.

¹ Kolejian S. Label and Labeling Review for Cefazolin injection, USP 2g/100ml in Galaxy container (NDA 207131). Silver Spring (MD): Food and Drug Administration, Center for Drug Evaluation and Research, Office of Surveillance and Epidemiology, Division of Medication Error Prevention and Analysis (US); 2015 May 5. 4 p. OSE RCM No.: 2014-2250.

APPENDIX A. LABEL AND LABELING SUBMITTED ON MAY 29, 2015

Container Label



(b) (4)

APPENDIX B. SPONSORS LABELING COMMENTS JUNE 11, 2015

FDA INFORMATION REQUEST RECEIVED MAY 29, 2015

Celerity requests that the Agency consider the responses below in relation to the amended carton and container labeling submitted to NDA 207131, via eCTD sequence number 0005, on May 29, 2015.

For ease of review, FDA comments are in **bold** followed by Celerity's responses.

1. Revise the statement "Each 100 ml contains..." to include the excipient "water for injection, USP".

Celerity agrees to incorporate "water for injection, USP" in the list of ingredients for the container and carton labeling.

2. Revise the statement "Single Dose Container" to read "single use only – discard unused portions"

Celerity proposes that the "Single Dose Container" statement be maintained on the container label to remain consistent with other drug products packaged in the GALAXY container closure system and agrees to incorporate "Discard unused portion" below the "Single Dose Container" statement. Celerity believes that the combination of these statements sufficiently indicate to the end-user that the drug product should only be used once and any unused drug product should be discarded.

Celerity believes this recommendation is no longer applicable to the carton label submitted in the May 29, 2015 amendment.

3. Revise the caution statement to read "No further dilution is necessary. Do not add supplementary medication or additives. Must not be used in series connections. Check for minute leaks and solution clarity. Contains no preservative."

Celerity proposes that "No further dilution is necessary" not be added to the caution statement of the container and carton labels. Celerity agrees with the Agency's guidance, described in *Guidance for Industry: Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors* April 2013 (hereafter referred to as FDA GUIDANCE), that affirmative statements (e.g. "Must Dilute Before Use"), as applicable, are essential information and be reserved for the immediate container label. Since Cefazolin (2g /100mL) Injection is a premixed, ready-to-use drug product that does not require further dilution, Celerity proposes that this statement be added to section 2.4,

Directions for Use of Cefazolin Injection, [REDACTED] (b) (4)
of the prescribing information (PI).

Celerity agrees with FDA GUIDANCE that statements (in either the affirmative or negative) on the addition of supplemental medication(s) and additive compatibility with the drug product are essential information for parenterals. “Do not add supplemental medication or additives” has been maintained in the caution statement of the amended container and carton labels; refer to the amendment submitted on May 29, 2015.

Celerity agrees with FDA GUIDANCE that the statements [REDACTED] (b) (4)
[REDACTED] (b) (4) communicate non-essential information. Celerity has removed this non-essential information from the container and carton labels to increase whitespace and readability of the labels. These changes are reflected in the amended labeling referenced above. Further, these statements are currently located in the PI and Celerity believes that the PI is the most appropriate location for this information.

Celerity proposes that “Contains no preservatives” not be added to the caution statement of the container and carton labels. Celerity believes that this is a statement related to the composition of the drug product and not a caution statement. Its potential relevance would be with respect to the list of ingredients indicated in the labeling. Further, since preservatives are not a component of the drug product, Celerity believes this is non-essential information for the container and carton labels to the end-user. Celerity proposes that this statement be added to section 11, *Description*, of the PI.

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

/s/

SEVAN H KOLEJIAN
06/11/2015

BRENDA V BORDERS-HEMPHILL
06/11/2015

REGULATORY PROJECT MANAGER PHYSICIAN'S LABELING RULE (PLR) FORMAT REVIEW OF THE PRESCRIBING INFORMATION

Complete for all new NDAs, BLAs, Efficacy Supplements, and PLR Conversion Labeling Supplements

Application: 207131

Application Type: NDA

Name of Drug/Dosage Form: Cefazolin Injection, USP, 2 g/100 mL

Applicant: Celerity Pharmaceuticals, LLC.

Receipt Date: 10-16-2014

Goal Date: 10-16-2015

1. Regulatory History and Applicant's Main Proposals

NDA) 207131 for Cefazolin Injection, USP in GALAXY Container (2 g/100 mL) was submitted October 16, 2014 (SEQ-0000). While Celerity had proposed (b) (4), the Division stated that the only indication approved for the 2 g dose of cefazolin is (b) (4).

Celerity communicated that due to electronic publishing deadlines and its desire to submit the original NDA by October 23, 2014; it was unable to revise the labeling prior to submission and wished to provide the revised labeling as an Amendment. The Division agreed that it was Celerity's decision to make the changes before submission or to submit as planned, but the labeling would need to be revised and resubmitted. The Division confirmed that Celerity could submit the NDA as planned and recommended amending the application to (b) (4) and providing updated labeling information. Celerity committed to providing the updated labeling information and related documentation as an amendment to the application.

Celerity provided updated labeling information and related documentation as a labeling amendment to NDA 2071 31.

2. Review of the Prescribing Information

This review is based on the applicant's submitted Word format of the prescribing information (PI). The applicant's proposed PI was reviewed in accordance with the labeling format requirements listed in the "Selected Requirements for Prescribing Information (SRPI)" checklist (see the Appendix).

2. Conclusions/Recommendations

The following comments were sent to the Sponsor in 74 day letter

Your proposed prescribing information (PI) does not conform to the content and format regulations found at 21 CFR 201.56(a) and (d) and 201.57.

We request that you resubmit labeling (in Microsoft Word 2010 format) that addresses these issues concerning content and format by **January 18, 2015**. The resubmitted labeling will be used for further labeling discussions. Use the SRPI checklist to correct any formatting errors to ensure conformance with the format items in regulations and guidances.

Selected Requirements of Prescribing Information

At the end of labeling discussions, use the SRPI checklist to ensure that the PI conforms with format items in regulations and guidances.

Appendix

The Selected Requirement of Prescribing Information (SRPI) is a 42-item, drop-down checklist of important format elements of the prescribing information (PI) based on labeling regulations (21 CFR 201.56 and 201.57) and guidances.

Highlights

See Appendix A for a sample tool illustrating the format for the Highlights.

HIGHLIGHTS GENERAL FORMAT

- NO** 1. Highlights (HL) must be in a minimum of 8-point font and should be in two-column format, with ½ inch margins on all sides and between columns.
***Comment:** Highlights are in two-column format, but the margin is not 1/2 inch on all sides and between columns.*
- YES** 2. The length of HL must be one-half page or less unless a waiver has been granted in a previous submission. The HL Boxed Warning does not count against the one-half page requirement.
***Instructions to complete this item:** If the length of the HL is one-half page or less, select “YES” in the drop-down menu because this item meets the requirement. However, if HL is longer than one-half page, select “NO” unless a waiver has been granted.*
Comment:
- YES** 3. A horizontal line must separate HL from the Table of Contents (TOC). A horizontal line must separate the TOC from the FPI.
Comment:
- NO** 4. All headings in HL must be **bolded** and presented in the center of a horizontal line (each horizontal line should extend over the entire width of the column as shown in Appendix A). The headings should be in UPPER CASE letters.
***Comment:** The headings are not centered*
- YES** 5. White space should be present before each major heading in HL. There must be no white space between the HL Heading and HL Limitation Statement. There must be no white space between the product title and Initial U.S. Approval. See Appendix A for a sample tool illustrating white space in HL.
Comment:
- YES** 6. Each summarized statement or topic in HL must reference the section(s) or subsection(s) of the Full Prescribing Information (FPI) that contain more detailed information. The preferred format is the numerical identifier in parenthesis [e.g., (1.1)] at the end of each summarized statement or topic.
Comment:
- YES** 7. Section headings must be presented in the following order in HL:

Selected Requirements of Prescribing Information

Section	Required/Optional
• Highlights Heading	Required
• Highlights Limitation Statement	Required
• Product Title	Required
• Initial U.S. Approval	Required
• Boxed Warning	Required if a BOXED WARNING is in the FPI
• Recent Major Changes	Required for only certain changes to PI*
• Indications and Usage	Required
• Dosage and Administration	Required
• Dosage Forms and Strengths	Required
• Contraindications	Required (if no contraindications must state "None.")
• Warnings and Precautions	Not required by regulation, but should be present
• Adverse Reactions	Required
• Drug Interactions	Optional
• Use in Specific Populations	Optional
• Patient Counseling Information Statement	Required
• Revision Date	Required

* RMC only applies to the BOXED WARNING, INDICATIONS AND USAGE, DOSAGE AND ADMINISTRATION, CONTRAINDICATIONS, and WARNINGS AND PRECAUTIONS sections.

Comment:

HIGHLIGHTS DETAILS

Highlights Heading

- YES** 8. At the beginning of HL, the following heading must be **bolded** and should appear in all UPPER CASE letters: "**HIGHLIGHTS OF PRESCRIBING INFORMATION**".

Comment:

Highlights Limitation Statement

- YES** 9. The **bolded** HL Limitation Statement must include the following verbatim statement: "**These highlights do not include all the information needed to use (insert name of drug product) safely and effectively. See full prescribing information for (insert name of drug product).**" The name of drug product should appear in UPPER CASE letters.

Comment:

Product Title in Highlights

- YES** 10. Product title must be **bolded**.

Comment:

Initial U.S. Approval in Highlights

- YES** 11. Initial U.S. Approval in HL must be **bolded**, and include the verbatim statement "**Initial U.S. Approval:**" followed by the **4-digit year**.

Comment:

Boxed Warning (BW) in Highlights

- N/A** 12. All text in the BW must be **bolded**.

Comment:

Selected Requirements of Prescribing Information

- N/A** 13. The BW must have a heading in UPPER CASE, containing the word “**WARNING**” (even if more than one warning, the term, “**WARNING**” and not “**WARNINGS**” should be used) and other words to identify the subject of the warning (e.g., “**WARNING: SERIOUS INFECTIONS and ACUTE HEPATIC FAILURE**”). The BW heading should be centered.

Comment:

- N/A** 14. The BW must always have the verbatim statement “*See full prescribing information for complete boxed warning.*” This statement should be centered immediately beneath the heading and appear in *italics*.

Comment:

- N/A** 15. The BW must be limited in length to 20 lines (this includes white space but does not include the BW heading and the statement “*See full prescribing information for complete boxed warning.*”).

Comment:

Recent Major Changes (RMC) in Highlights

- N/A** 16. RMC pertains to only the following five sections of the FPI: BOXED WARNING, INDICATIONS AND USAGE, DOSAGE AND ADMINISTRATION, CONTRAINDICATIONS, and WARNINGS AND PRECAUTIONS. RMC must be listed in the same order in HL as the modified text appears in FPI.

Comment:

- N/A** 17. The RMC must include the section heading(s) and, if appropriate, subsection heading(s) affected by the recent major change, together with each section’s identifying number and date (month/year format) on which the change was incorporated in the PI (supplement approval date). For example, “Warnings and Precautions, Acute Liver Failure (5.1) --- 9/2013”.

Comment:

- N/A** 18. The RMC must list changes for at least one year after the supplement is approved and must be removed at the first printing subsequent to one year (e.g., no listing should be one year older than revision date).

Comment:

Indications and Usage in Highlights

- YES** 19. If a product belongs to an established pharmacologic class, the following statement is required under the Indications and Usage heading in HL: “(Product) is a (name of established pharmacologic class) indicated for (indication)”.

Comment:

Dosage Forms and Strengths in Highlights

- YES** 20. For a product that has several dosage forms (e.g., capsules, tablets, and injection), bulleted subheadings or tabular presentations of information should be used under the Dosage Forms and Strengths heading.

Selected Requirements of Prescribing Information

Comment:

Contraindications in Highlights

- YES** 21. All contraindications listed in the FPI must also be listed in HL or must include the statement “None” if no contraindications are known. Each contraindication should be bulleted when there is more than one contraindication.

Comment:

Adverse Reactions in Highlights

- YES** 22. For drug products other than vaccines, the verbatim **bolded** statement must be present: “**To report SUSPECTED ADVERSE REACTIONS, contact (insert name of manufacturer) at (insert manufacturer’s U.S. phone number) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch**”.

Comment:

Patient Counseling Information Statement in Highlights

- YES** 23. The Patient Counseling Information statement must include one of the following three **bolded** verbatim statements that is most applicable:

If a product **does not** have FDA-approved patient labeling:

- “**See 17 for PATIENT COUNSELING INFORMATION**”

If a product **has** FDA-approved patient labeling:

- “**See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling**”
- “**See 17 for PATIENT COUNSELING INFORMATION and Medication Guide**”

Comment:

Revision Date in Highlights

- YES** 24. The revision date must be at the end of HL, and should be **bolded** and right justified (e.g., “**Revised: 9/2013**”).

Comment:

Selected Requirements of Prescribing Information

Contents: Table of Contents (TOC)

See Appendix A for a sample tool illustrating the format for the Table of Contents.

- YES** 25. The TOC should be in a two-column format.
Comment:
- YES** 26. The following heading must appear at the beginning of the TOC: “**FULL PRESCRIBING INFORMATION: CONTENTS**”. This heading should be in all UPPER CASE letters and **bolded**.
Comment:
- YES** 27. The same heading for the BW that appears in HL and the FPI must also appear at the beginning of the TOC in UPPER CASE letters and **bolded**.
Comment:
- YES** 28. In the TOC, all section headings must be **bolded** and should be in UPPER CASE.
Comment:
- YES** 29. In the TOC, all subsection headings must be indented and not bolded. The headings should be in title case [first letter of all words are capitalized except first letter of prepositions (through), articles (a, an, and the), or conjunctions (for, and)].
Comment:
- YES** 30. The section and subsection headings in the TOC must match the section and subsection headings in the FPI.
Comment:
- YES** 31. In the TOC, when a section or subsection is omitted, the numbering must not change. If a section or subsection from 201.56(d)(1) is omitted from the FPI and TOC, the heading “FULL PRESCRIBING INFORMATION: CONTENTS” must be followed by an asterisk and the following statement must appear at the end of TOC: “*Sections or subsections omitted from the full prescribing information are not listed.”
Comment:

Selected Requirements of Prescribing Information

Full Prescribing Information (FPI)

FULL PRESCRIBING INFORMATION: GENERAL FORMAT

- YES** 32. The **bolded** section and subsection headings in the FPI must be named and numbered in accordance with 21 CFR 201.56(d)(1) as noted below (section and subsection headings should be in UPPER CASE and title case, respectively). If a section/subsection required by regulation is omitted, the numbering must not change. Additional subsection headings (i.e., those not named by regulation) must also be **bolded** and numbered.

BOXED WARNING
1 INDICATIONS AND USAGE
2 DOSAGE AND ADMINISTRATION
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
5 WARNINGS AND PRECAUTIONS
6 ADVERSE REACTIONS
7 DRUG INTERACTIONS
8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
8.2 Labor and Delivery
8.3 Nursing Mothers
8.4 Pediatric Use
8.5 Geriatric Use
9 DRUG ABUSE AND DEPENDENCE
9.1 Controlled Substance
9.2 Abuse
9.3 Dependence
10 OVERDOSAGE
11 DESCRIPTION
12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
12.2 Pharmacodynamics
12.3 Pharmacokinetics
12.4 Microbiology (by guidance)
12.5 Pharmacogenomics (by guidance)
13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
13.2 Animal Toxicology and/or Pharmacology
14 CLINICAL STUDIES
15 REFERENCES
16 HOW SUPPLIED/STORAGE AND HANDLING
17 PATIENT COUNSELING INFORMATION

Comment:

- YES** 33. The preferred presentation for cross-references in the FPI is the section (not subsection) heading followed by the numerical identifier. The entire cross-reference should be in *italics* and enclosed within brackets. For example, “[*see Warnings and Precautions (5.2)*]” or “[*see Warnings and Precautions (5.2)*]”.

Comment:

- N/A** 34. If RMCs are listed in HL, the corresponding new or modified text in the FPI sections or

Selected Requirements of Prescribing Information

subsections must be marked with a vertical line on the left edge.

Comment:

FULL PRESCRIBING INFORMATION DETAILS

FPI Heading

- YES** 35. The following heading must be **bolded** and appear at the beginning of the FPI: “**FULL PRESCRIBING INFORMATION**”. This heading should be in UPPER CASE.

Comment:

BOXED WARNING Section in the FPI

- N/A** 36. In the BW, all text should be **bolded**.

Comment:

- N/A** 37. The BW must have a heading in UPPER CASE, containing the word “**WARNING**” (even if more than one Warning, the term, “**WARNING**” and not “**WARNINGS**” should be used) and other words to identify the subject of the Warning (e.g., “**WARNING: SERIOUS INFECTIONS and ACUTE HEPATIC FAILURE**”).

Comment:

CONTRAINDICATIONS Section in the FPI

- N/A** 38. If no Contraindications are known, this section must state “None.”

Comment:

ADVERSE REACTIONS Section in the FPI

- YES** 39. When clinical trials adverse reactions data are included (typically in the “Clinical Trials Experience” subsection of ADVERSE REACTIONS), the following verbatim statement or appropriate modification should precede the presentation of adverse reactions:

“Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.”

Comment:

- N/A** 40. When postmarketing adverse reaction data are included (typically in the “Postmarketing Experience” subsection of ADVERSE REACTIONS), the following verbatim statement or appropriate modification should precede the presentation of adverse reactions:

“The following adverse reactions have been identified during post-approval use of (insert drug name). Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.”

Comment:

PATIENT COUNSELING INFORMATION Section in the FPI

- N/A** 41. Must reference any FDA-approved patient labeling in Section 17 (PATIENT COUNSELING INFORMATION section). The reference should appear at the beginning of Section 17 and

Selected Requirements of Prescribing Information

include the type(s) of FDA-approved patient labeling (e.g., Patient Information, Medication Guide, Instructions for Use).

Comment:

- N/A** 42. FDA-approved patient labeling (e.g., Medication Guide, Patient Information, or Instructions for Use) must not be included as a subsection under section 17 (PATIENT COUNSELING INFORMATION). All FDA-approved patient labeling must appear at the end of the PI upon approval.

Comment:

Selected Requirements of Prescribing Information

Appendix A: Format of the Highlights and Table of Contents

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use [DRUG NAME] safely and effectively. See full prescribing information for [DRUG NAME].

[DRUG NAME (nonproprietary name) dosage form, route of administration, controlled substance symbol]
Initial U.S. Approval: [year]

WARNING: [SUBJECT OF WARNING]

See full prescribing information for complete boxed warning.

- [text]
- [text]

RECENT MAJOR CHANGES

[section (X.X)] [m/year]
[section (X.X)] [m/year]

INDICATIONS AND USAGE

[DRUG NAME] is a [name of pharmacologic class] indicated for [text]

DOSAGE AND ADMINISTRATION

- [text]
- [text]

DOSAGE FORMS AND STRENGTHS

[text]

CONTRAINDICATIONS

- [text]
- [text]

WARNINGS AND PRECAUTIONS

- [text]
- [text]

ADVERSE REACTIONS

Most common adverse reactions (incidence > x%) are [text].

To report SUSPECTED ADVERSE REACTIONS, contact [name of manufacturer] at [phone #] or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

- [text]
- [text]

USE IN SPECIFIC POPULATIONS

- [text]
- [text]

See 17 for PATIENT COUNSELING INFORMATION [and FDA-approved patient labeling OR and Medication Guide].

Revised: [m/year]

FULL PRESCRIBING INFORMATION: CONTENTS*

WARNING: [SUBJECT OF WARNING]

1 INDICATIONS AND USAGE

2 DOSAGE AND ADMINISTRATION

2.1 [text]

2.2 [text]

3 DOSAGE FORMS AND STRENGTHS

4 CONTRAINDICATIONS

5 WARNINGS AND PRECAUTIONS

5.1 [text]

5.2 [text]

6 ADVERSE REACTIONS

6.1 [text]

6.2 [text]

7 DRUG INTERACTIONS

7.1 [text]

7.2 [text]

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

8.2 Labor and Delivery

8.3 Nursing Mothers

8.4 Pediatric Use

8.5 Geriatric Use

9 DRUG ABUSE AND DEPENDENCE

9.1 Controlled Substance

9.2 Abuse

9.3 Dependence

10 OVERDOSAGE

11 DESCRIPTION

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

12.2 Pharmacodynamics

12.3 Pharmacokinetics

12.4 Microbiology

12.5 Pharmacogenomics

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

13.2 Animal Toxicology and/or Pharmacology

14 CLINICAL STUDIES

14.1 [text]

14.2 [text]

15 REFERENCES

16 HOW SUPPLIED/STORAGE AND HANDLING

17 PATIENT COUNSELING INFORMATION

*Sections or subsections omitted from the full prescribing information are not listed.

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

/s/

FARIBA IZADI
05/29/2015

LABEL AND LABELING REVIEW

Division of Medication Error Prevention and Analysis (DMEPA)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

***** This document contains proprietary information that cannot be released to the public*****

Date of This Review: May 5, 2015
Requesting Office or Division: Division of Anti- Infective Products (DAIP)
Application Type and Number: NDA 207131
Product Name and Strength: Cefazolin Injection, USP
2 g/100 mL in Galaxy Container
Product Type: Single ingredient
Rx or OTC: Rx
Applicant/Sponsor Name: Celerity Pharmaceuticals, LLC (Celerity)
Submission Date: 10/16/2014
OSE RCM #: 2014-2250
DMEPA Primary Reviewer: Sevan Kolejian, PharmD
DMEPA Team Leader: Vicky Borders-Hemphill, PharmD
Associate Director: Irene Chan, PharmD, BCPS

1 REASON FOR REVIEW

Celerity Pharmaceuticals submitted a 505(b)(2) new drug application for Cefazolin injection, USP. The proposed Cefazolin product is a frozen, premixed, iso-osmotic, sterile, non-pyrogenic solution packaged in Baxter’s Galaxy container system (2 g as Cefazolin /100 mL) and intended for intravenous use after thawing to room temperature.

This review evaluates the container label, carton labeling, and prescribing information (PI) for Cefazolin Injection, USP in Galaxy Container (2 g/100 mL). The Division of Anti-Infective Products (DAIP) requested that DMEPA review the labels and labeling for areas of vulnerability that may lead to medication errors.

2 MATERIALS REVIEWED

We considered the materials listed in Table 1 for this review. The Appendices provide the methods and results for each material reviewed.

Material Reviewed	Appendix Section (for Methods and Results)
Product Information	A
FDA Adverse Event Reporting System (FAERS)	B
Previous DMEPA Reviews	C
Human Factors Study	D (N/A)
ISMP Newsletters	E
Other	F
Labels and Labeling	G

N/A=not applicable for this review

3 OVERALL ASSESSMENT OF THE MATERIALS REVIEWED

Cefazolin is currently marketed as:

- Cefazolin injection 1 g/50 mL in the Baxter Galaxy bag container (ANDA 063002),
- Cefazolin for injection 2 g in the duplex drug delivery system by Braun (NDA 050779; reference listed drug),
- Cefazolin for injection 500 mg, 1 gram and 2 gram per vial,
- Cefazolin injection 10 gram (b) (4) dose vials/containers.

The proposed cefazolin Injection 2 g/100 mL product submitted by Celerity Pharmaceuticals contracted and packaged by Baxter, will use the Baxter Galaxy bag container system. This

container system is currently used to package Baxter's frozen premixed drug product line that includes Cefazolin (1 g/50 mL) as well as other antibiotics (ceftriaxone, cefotaxime, aztreonam, ceftazidime, oxacillin, nafcillin, vancomycin, and cefepime injection). We determined that use of the Galaxy bag container system for this proposed strength of cefazolin does not pose a safety concern from a medication error perspective.

Container Labels and Carton Labeling

We performed a risk assessment of the proposed label and labeling to identify deficiencies that may lead to medication errors and for areas of improvement. The container label and carton labeling for the proposed product uses Baxter's corporate trade dress making it similar in appearance to the labels and labeling of Baxter's currently marketed cefazolin Injection, USP 1 g/50 mL and other Baxter's products in the Galaxy bag container currently on the market (see Appendix G). We are concerned that the similar appearance of the labels and labeling poses the risk for product selection and wrong drug errors. Therefore, we provide recommendations in Section 4.2 below.

Prescribing Information (PI)

We performed a risk assessment of the proposed PI to identify deficiencies that may lead to medication errors and areas for improvement. Our review of the *Dosage and Administration* section of the full PI identified areas of improvement including removal of hazardous abbreviations, revisions for readability and clarity of important route of administration, storage, and how supplied information. In section 4.1, we provide recommendations to mitigate confusion and promote the safe use of this product.

ISMP Newsletters

We conducted a search of ISMP newsletters and identified 14 cefazolin reports. The details of these reports are provided in Appendix E. However, our search did not identify any medication errors that could inform our review of the currently proposed labels and labeling of cefazolin injection submitted by Celerity Pharmaceuticals.

FAERS

Our review of the data gathered from the FAERS database identified medication errors where, Baxter's Galaxy product line was implicated in several errors with trade dress being cited as a contributing factor. Based on this information we evaluated the labels and labeling for this product and have determined that additional changes should be implemented to minimize the risk for confusion with other Baxter Galaxy products and ensure identifying product information is prominent on the labels and labeling.

4 CONCLUSION & RECOMMENDATIONS

DMEPA concludes that the introduction of cefazolin Injection, USP in Baxter’s Galaxy containers has potential for mix up with Baxter’s other currently marketed frozen premixed drug products. To promote safe use of this product, we recommend that the sponsor revise the proposed labels and labeling of cefazolin Injection and implement the recommendations in Section 4.1 and section 4.2.

If you have further questions or need clarifications, please contact Karen Townsend, OSE Project Manager, at 301-796-5413.

4.1 RECOMMENDATIONS FOR THE DIVISION

DMEPA concludes that the proposed labels and labeling are vulnerable to confusion which poses a risk for medication errors. We have recommendations for the *Dosage and Administration* section and How Supplied section of the Full Prescribing Information (See Appendix F) and have provided a detailed summary below for review and consideration by DAIP. We advise the following recommendations be implemented prior to approval:

A. Full Prescribing Information (see Appendix F)

1. Remove all dangerous abbreviations, including “IV” from the prescribing information.
2. In Dosage and Administration Section 2.2:
 - a. Revise sentences from using text with all upper-case letters to appear in sentence or title case for improved readability.
 - b. Revise the (b) (4) to start with a positive statement such as “Bring to room temperature. Do not force thaw”. Additionally, we recommend using sentence case for improved readability.

4.2 RECOMMENDATIONS FOR THE CELERITY PHARMACEUTICALS

We recommend the following be implemented prior to approval of Cefazolin (2 g/100 mL) in 4% Dextrose in Galaxy Plastic Container, NDA 207131.

A. Container Label

1. We recommend revising the font color to another color other than (b) (4) to distinguish Cefazolin (2 g/100 mL) in 4% Dextrose in Galaxy Plastic Container (b) (4).

2. To increase the prominence of the product name and strength on the principal display panel, consider decreasing the size of the “Celerity Pharmaceuticals, LLC” logo that competes with more important information on the label.
3. To prevent misinterpretation of the Celerity logo as the product name, we recommend relocating “Celerity Pharmaceuticals, LLC” logo from line 1 to appear under the bottom of the principal display panel (similar to the referenced RLD container).
4. Revise the NDC numbers so that the carton labeling and bag label NDC numbers are different for these two package configurations.
5. Relocate the fill volume statement “100 ml” to appear next to the 2g so that the total quantity per total volume are represented in the strength statement for clarity and prominence of this important information similar to the referenced RLD container as follows:

2 g per 100 ml

6. Revise the statement [REDACTED] (b) (4) to read “For Intravenous Infusion Only” [REDACTED] (b) (4).
7. The proposed labels do not indicate where the lot number and expiration date will appear. Per 21CFR 201.17 and 21CFR 201.18, please indicate where the required lot number and expiration date will appear on the labels (or if the lot and expiration will be embossed on the bag).
8. We recommend, revising the [REDACTED] (b) (4) to start with a positive statement such as “Bring to room temperature. Do not force thaw”. Additionally, we recommend using sentence case for improved readability.

B. Carton labeling

1. See A.1 through A.8 above
2. Relocate “Rx only” statement from the side panel to the principle display above the quantity statement.
3. Revise the quantity statement from “[REDACTED] (b) (4)” to read “Contains 6 units of Single- Use bags. [REDACTED] (b) (4) [REDACTED] [REDACTED] 12 units per case).

APPENDICES: METHODS & RESULTS FOR EACH MATERIALS REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table 2 presents relevant product information for Cefazolin Injection that Celerity Pharmaceuticals submitted on October 16, 2014, and the listed drug (LD).

Table 2. Relevant Product Information for Cefazolin injection and the Listed Drug		
Product Name	Cefazolin (2 g/100 mL)[0.02 g/mL] in 4% Dextrose in GALAXY Plastic Container (premixed/frozen]	RLD: Cefazolin for Injection, USP and Dextrose Injection, USP In Duplex® Container, for intravenous use NDA 050779
Initial Approval Date	N/A	7/27/2000
Active Ingredient	Cefazolin injection	Cefazolin for Injection USP and Dextrose Injection USP
Indication	cephalosporin antibacterial indicated for [REDACTED] (b) (4)	Cephalosporin antibacterial indicated in the treatment of the Respiratory tract infections, urinary tract infections, skin and skin structure infections, biliary tract infections, bone and joint infections, genital infections, septicemia, endocarditis and perioperative prophylaxis.
Route of Administration	intravenous	intravenous
Dosage Form	Injection	Injection
Strength	2 g in 100 mL	1 g in 50 mL and 2 g in 50 mL
Dose and Frequency	1 to 2 gram IV administered 1/2 hour to 1 hour prior to the start of surgery.	1 [REDACTED] (b) (4) IV administered 1/2 hour to 1 hour prior to the start of surgery. For lengthy operative procedures (e.g., 2 hours or more), 500 mg to 1 gram IV during surgery (administration modified depending on the duration of the operative procedure). 500 mg to 1 gram IV every 6 to 8 hours for 24 hours postoperatively.

How Supplied	Premixed frozen iso-osmotic solution in 100 mL single dose GALAXY plastic containers (12/case)	DUPLEX® Drug Delivery System that has a flexible dual chamber container supplied in two concentrations. After reconstitution, the concentrations are equivalent to 1 g (b) (4) Cefazolin. The diluent chamber contains approximately 50 mL of Dextrose Injection USP.
Storage	Store at or below -20°C/-4°F	Store the unactivated unmixed unit at (b) (4) 25°C ((b) (4) 77°F). Excursions permitted to 15-30°C (59-86°F).
Container Closure	USP in GALAXY Container (PL 2040 Plastic)	Sterile and nonpyrogenic in the DUPLEX® Drug Delivery System Containers packaged 24 units per case.

APPENDIX B. FDA ADVERSE EVENT REPORTING SYSTEM (FAERS)

B.1 Methods

We searched the FDA Adverse Event Reporting System (FAERS) on February 26, 2015, using the criteria in Table 3, and then individually reviewed each case. We limited our analysis to cases that described errors possibly associated with the label and labeling. We used the NCC MERP Taxonomy of Medication Errors to code the type and factors contributing to the errors when sufficient information was provided by the reporter¹.

Table 3: FAERS Search Strategy	
Date Range	01/01/2000 to 02/01/2015
Product	CEFAZOLIN ;CEFAZOLIN SODIUM [active ingredient] CEFAZOLIN ;CEFAZOLIN SODIUM;CEFAZOLIN \DEXTROSE;ANCEF [product name]
Event (MedDRA Terms)	DMEPA Official FBIS Search Terms Event List: Medication Errors [HLGT] Product Packaging Issues [HLT] Product Label Issues [HLT] Product Adhesion Issue [PT] Product Compounding Quality Issue [PT] Product Difficult to Remove [PT] Product Formulation Issue [PT] Product Substitution Issue [PT] Inadequate (b) (4) Technique in Use of Product [PT]

B.2 Results

Our search identified 115 cases, after initial review, we excluded all cases not involving Baxter Galaxy bags. We identified six cases relevant to these review. We reviewed the cases to identify factors that contributed to the medication errors. If an error occurred, we reviewed the reports

¹ The National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) Taxonomy of Medication Errors. Website <http://www.nccmerp.org/pdf/taxo2001-07-31.pdf>.

to determine if the root cause could be associated with the labels or labeling of the product, and thus pertinent to this review.

- Wrong Route of Administration (n=1)

This case describes cefazolin inadvertently administered via patient's epidural line. cefazolin is approved for intravenous administration only. Therefore, DMEPA recommends that label and labeling clearly display a route statement that conveys that the product is to be administration via intravenous route.

- Hazardous conditions (n=3)

These hazardous condition cases describe the potential for wrong drug due to similarity in packaging or labeling. These cases report that Baxter's Galaxy bag corporate trade dress has contributed to near misses due to the similar appearance of vancomycin, albumin, oxacillin, clindamycin, ceftriaxone, cefotaxime labels and confusion with Cefazolin bags during preparation, dispensing or administration process. We reviewed Baxter's galaxy container product line and noted similar container labeling presentations (see label comparison in APPENDIX G). Therefore, we will conduct a post marketing signal review to determine if any further action is necessary to mitigate these errors.

- Wrong Drug (n=2)

One case from 2003 describes the patient receiving Baxter's Ancef 1 g instead of Mefoxin. Root cause and outcomes were not provided; Baxter's cefazolin and mefoxin are in similar Galaxy containers with similar labels. The second case describes 15 patients incorrectly receiving vancomycin instead of cefazolin in Baxter's Galaxy bags. The outcome was reported in one patient as renal failure. Since the proposed Cefazolin product will be packaged in Baxter Galaxy container and have Baxter corporate trade dress, we recommend Celerity revise the container label in such a manner that there is no potential for mix up with other Baxter's products. In section 4.2, we provide recommendations regarding revisions to the trade dress of the proposed product and strategies to minimize mix up between currently marketed Baxter's frozen premixed drug products.

B.3 List of FAERS Case Numbers

Below is a list of the FAERS case number and manufacturer control numbers for the cases relevant for this review.

FAERS Medication Error Cases Associated with Cefazolin in Baxter Galaxy bags (n=6)				
Case #	FDA Initial Recd Date	Narrative	Cause	Outcome
3916217	3/5/2003	Cefazolin (Kefzol) 1 gram/50 ml D5W (Baxter) was piggybacked into the patient's epidural line.	Y in with epidural line: knowledge deficit	Not reported
3441319	3/6/2000	Reporter states that 15 patients received the incorrect drug as a result of labeling mix up between VANCOMYCIN & CEFAZOLIN.	no sufficient information to determine what contributed to the label mix up.	Non Serious: 1 patient experienced adverse event related to the mix up.
3939563	4/25/2003	Nurse found ANCEF 1G IVPB hang on the patient instead of Mefoxin	mix up with Mefoxin not sufficient information provided to determine the cause	Not reported
3684814	4/18/2002	Reporter states that there are a number of pre-mixed, frozen IV bags, called Galaxy bags, manufactured by Baxter, that contain cefazolin, oxacillin, clindamycin, etc. that have similar labels. Reporter states that When the bags are stacked up, they all look the same and there is high potential for mixing up and administering the wrong medication.	label looks similar	Near miss
3967079	6/30/2003	Reporter states that there have been several medication errors due to Baxter labels for vancomycin and cefazolin are very similar.	look a like vancomycin with Cefazolin : baxter product	Not reported

FAERS Medication Error Cases Associated with Cefazolin in Baxter Galaxy bags (n=6)				
Case #	FDA Initial Recd Date	Narrative	Cause	Outcome
6033122	4/20/2006	Recently due to shortages a hospital has had to obtain albumin in bags (instead of vials) from Baxter. It was brought to the hospital's attention that the albumin bags appear very similar to several Baxter bags that contain antibiotics. Due to the fact that many of the Baxter antibiotic bags have been mistakenly confused (cefazolin and cefuroxime) due to similar bag appearances, the potential for albumin to be confused with one of these antibiotics is high.	Baxter pre-mixed Albumin similar to cefazolin and cefuroxime	Not reported

B.4 Description of FAERS

The FDA Adverse Event Reporting System (FAERS) is a database that contains information on adverse event and medication error reports submitted to FDA. The database is designed to support the FDA's postmarket safety surveillance program for drug and therapeutic biologic products. The informatic structure of the FAERS database adheres to the international safety reporting guidance issued by the International Conference on Harmonisation. FDA's Office of Surveillance and Epidemiology codes adverse events and medication errors to terms in the Medical Dictionary for Regulatory Activities (MedDRA) terminology. Product names are coded using the FAERS Product Dictionary. More information about FAERS can be found at:

<http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/default.htm>.

APPENDIX C. PREVIOUS DMEPA REVIEWS

C.1 Methods

We searched the L:Drive on February 10, 2015 using the terms, Cefazolin to identify reviews previously performed by DMEPA.

C.2 Results

Our search identified one previous review² RCM # 2011-423 submitted by Samson Medical Technologies for Cefazolin for Injection, USP 100 grams, 300 grams pharmacy bulk package products. However, the recommendation in previous review was not relevant to current review of Cefazolin injection label and labeling review submitted by Celerity Pharmaceuticals.

² Baugh, Denise, Label and Labeling Review for Cefazolin for Injection, USP 100 grams, 300 grams (ANDA 065141). Silver Spring (MD): Food and Drug Administration, Center for Drug Evaluation and Research, Office of Surveillance and Epidemiology, Division of Medication Error Prevention and Analysis (US); 2011 MAY 18. 32 p. OSE RCM No.: 2011-423.

APPENDIX E. ISMP NEWSLETTERS

E.1 Methods

We searched the Institute for Safe Medication Practices (ISMP) newsletters on February 10, 2015 using the criteria below, and then individually reviewed each newsletter. We limited our analysis to newsletters that described medication errors or actions possibly associated with the label and labeling.

ISMP Newsletters Search Strategy	
ISMP Newsletter(s)	Acute Care, Community, Nursing, ISMP Medication Safety Alert
Search Strategy and Terms	Match Exact Word or Phrase: Cefazolin

E.2 Results

Our search of ISMP newsletters resulted in fourteen newsletter articles related to errors with Cefazolin. We did not identify any results relevant for this review.

The following are the summary of the newsletter articles:

ISMP	Summary
ISMP Medication Safety Alert!™ Vol. 2, No. 20 October 8, 1997	Cefazolin labels were redesigned to distinguish between labels for Cefazolin 10 g bulk vial from the 1 g single use vial label. On the new label, no matter which way the vial is turned, the word "BULK" is prominently displayed.
ISMP Medication Safety Alert!™ Vol. 3, No. 1 January 14, 1998	
ISMP Medication Safety Alert!™ Vol. 3, No. 5 March 11, 1998	Describes an error where a faxed Cefazolin order was misinterpreted for "every 6 hours" instead of "every 8 hours".
ISMP Medication Safety Alert!™ Vol. 4, No. 6 March 24, 1999	The Cefazolin allergy was not listed on the MARs since they were generated from the pharmacy computer system. Thus, the nurse administering the drug did not detect the allergy. The patient became hypotensive and unresponsive.
ISMP Medication Safety Alert Vol. 7, No. 8 April 17, 2002	The order for Cefazolin 1 g IV q8h was overlooked during order entry of a large set of new orders because the pharmacist was repeatedly interrupted during the process.

ISMP Medication Safety Alert! Vol. 8, No. 19 September 18, 2003	A hospital reported that they accidentally purchased prefilled sodium chloride syringes with the short plunger rod instead of the conventional syringe. Nurses began using them to dilute vials of Cefazolin to 10 mL, draw the medication back into the syringes, and infuse the medication using a B. Braun Perfusor syringe pump. Then they began to notice that about 1 to 2 mL of antibiotic remained in the syringe after removal from the pump because the pump clamp blocked the plunger rod from completing the infusion.
ISMP Medication Safety Alert! Vol. 8, No. 20 October 2, 2003	Saline syringes (10 mL) with short-length plunger rods were used to dilute and administer Cefazolin via a syringe pump.
ISMP Medication Safety Alert! Vol. 12, No. 8 April 19, 2007	Cefazolin infusion with smart pump. Investigation revealed that, while the IV label stated to give the drug over 30 minutes, the drug library had been programmed to infuse the drug over 1 hour or more.
ISMP MSA; Vol. 13, No. 10 May 22, 2008	Tall man lettering Cefazolin
ISMP MSA; Vol. 13, No. 15 July 31, 2008	
ISMP MSA; Vol. 14, No. 14 July 16, 2009	ON-Q pump is designed to deliver local anesthetics to surgical sites for non-narcotic pain relief. The company's product information provides information regarding stability when various local anesthetics are mixed with dexamethasone, ketorolac, morphine sulfate and ketorolac, cefTRIAXone, or Cefazolin —implying that mixing the local anesthetics with other drugs is safe and perhaps even effective.
ISMP MSA; Vol. 15, No. 23 November 18, 2010	ISMP list of drug names with recommended tall man letters
ISMP MSA; Volume 17, No. 15 July 26, 2012	Prefilled Cefazolin syringe looks a like syringe of potassium chloride (KCl) injection concentrate 20 mEq. The syringe was the same size as the Cefazolin syringe, and both had red caps. Because of a shortage of KCl injection concentrate in vials and pharmacy bulk packages, a pharmacy technician purchased syringes of the product from an outsourcing company, Ameridose.
ISMP MSA; Volume 17, No. 20 October 4, 2012	

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

/s/

SEVAN H KOLEJIAN
05/05/2015

BRENDA V BORDERS-HEMPHILL
05/05/2015

IRENE Z CHAN
05/06/2015

RPM FILING REVIEW

(Including Memo of Filing Meeting)

To be completed for all new NDAs, BLAs, and Efficacy Supplements [except SE8 (labeling change with clinical data) and SE9 (manufacturing change with clinical data)]

Application Information		
NDA # 207131 BLA#	NDA Supplement #: S- BLA Supplement #: S-	Efficacy Supplement Category: <input type="checkbox"/> New Indication (SE1) <input type="checkbox"/> New Dosing Regimen (SE2) <input type="checkbox"/> New Route Of Administration (SE3) <input type="checkbox"/> Comparative Efficacy Claim (SE4) <input type="checkbox"/> New Patient Population (SE5) <input type="checkbox"/> Rx To OTC Switch (SE6) <input type="checkbox"/> Accelerated Approval Confirmatory Study (SE7) <input type="checkbox"/> Animal Rule Confirmatory Study (SE7) <input type="checkbox"/> Labeling Change With Clinical Data (SE8) <input type="checkbox"/> Manufacturing Change With Clinical Data (SE9) <input type="checkbox"/> Pediatric
Proprietary Name: N/A Established/Proper Name: Cefazolin Injection, USP Dosage Form: Sterile solution for Injection Strengths: 2 g/100 mL		
Applicant: Celerity Pharmaceuticals, LLC. Agent for Applicant (if applicable):		
Date of Application: 10/16/2014 Date of Receipt: 10/16/2014 Date clock started after UN:		
PDUFA Goal Date: 08/16/2015		Action Goal Date (if different): 08/16/2015
Filing Date: 12/15/2014		Date of Filing Meeting: 12/08/2014
Chemical Classification (original NDAs only) : <input type="checkbox"/> Type 1- New Molecular Entity (NME); NME and New Combination <input type="checkbox"/> Type 2- New Active Ingredient; New Active Ingredient and New Dosage Form; New Active Ingredient and New Combination <input type="checkbox"/> Type 3- New Dosage Form; New Dosage Form and New Combination <input type="checkbox"/> Type 4- New Combination <input checked="" type="checkbox"/> Type 5- New Formulation or New Manufacturer <input type="checkbox"/> Type 7- Drug Already Marketed without Approved NDA <input type="checkbox"/> Type 8- Partial Rx to OTC Switch		
Proposed indication(s)/Proposed change(s): (b) (4)		
Type of Original NDA: AND (if applicable) Type of NDA Supplement:		<input type="checkbox"/> 505(b)(1) <input checked="" type="checkbox"/> 505(b)(2) <input type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2)
<i>If 505(b)(2): Draft the "505(b)(2) Assessment" review found at:</i> http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/ImmediateOffice/UCM027499		

Type of BLA	<input type="checkbox"/> 351(a) <input type="checkbox"/> 351(k)
If 351(k), notify the OND Therapeutic Biologics and Biosimilars Team	
Review Classification:	<input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority
The application will be a priority review if:	<input type="checkbox"/> Pediatric WR <input type="checkbox"/> QIDP <input type="checkbox"/> Tropical Disease Priority Review Voucher <input type="checkbox"/> Pediatric Rare Disease Priority Review Voucher
<ul style="list-style-type: none"> • A complete response to a pediatric Written Request (WR) was included (a partial response to a WR that is sufficient to change the labeling should also be a priority review – check with DPMH) • The product is a Qualified Infectious Disease Product (QIDP) • A Tropical Disease Priority Review Voucher was submitted • A Pediatric Rare Disease Priority Review Voucher was submitted 	
Resubmission after withdrawal? <input type="checkbox"/>	Resubmission after refuse to file? <input type="checkbox"/>
Part 3 Combination Product? <input type="checkbox"/>	<input type="checkbox"/> Convenience kit/Co-package <input type="checkbox"/> Pre-filled drug delivery device/system (syringe, patch, etc.) <input type="checkbox"/> Pre-filled biologic delivery device/system (syringe, patch, etc.) <input type="checkbox"/> Device coated/impregnated/combined with drug <input type="checkbox"/> Device coated/impregnated/combined with biologic <input type="checkbox"/> Separate products requiring cross-labeling <input type="checkbox"/> Drug/Biologic <input type="checkbox"/> Possible combination based on cross-labeling of separate products <input type="checkbox"/> Other (drug/device/biological product)
If yes, contact the Office of Combination Products (OCP) and copy them on all Inter-Center consults	

<input type="checkbox"/> Fast Track Designation <input type="checkbox"/> Breakthrough Therapy Designation <i>(set the submission property in DARRTS and notify the CDER Breakthrough Therapy Program Manager)</i> <input type="checkbox"/> Rolling Review <input type="checkbox"/> Orphan Designation <input type="checkbox"/> Rx-to-OTC switch, Full <input type="checkbox"/> Rx-to-OTC switch, Partial <input type="checkbox"/> Direct-to-OTC Other:	<input type="checkbox"/> PMC response <input type="checkbox"/> PMR response: <input type="checkbox"/> FDAAA [505(o)] <input type="checkbox"/> PREA deferred pediatric studies (FDCA Section 505B) <input type="checkbox"/> Accelerated approval confirmatory studies (21 CFR 314.510/21 CFR 601.41) <input type="checkbox"/> Animal rule postmarketing studies to verify clinical benefit and safety (21 CFR 314.610/21 CFR 601.42)
--	--

Collaborative Review Division (if OTC product):

List referenced IND Number(s): NDA 50779

Goal Dates/Product Names/Classification Properties	YES	NO	NA	Comment
PDUFA and Action Goal dates correct in tracking system?	<input checked="" type="checkbox"/>	<input type="checkbox"/>		
<i>If no, ask the document room staff to correct them immediately. These are the dates used for calculating inspection dates.</i>				
Are the established/proper and applicant names correct in tracking system?	<input checked="" type="checkbox"/>	<input type="checkbox"/>		
<i>If no, ask the document room staff to make the corrections. Also, ask the document room staff to add the established/proper name to the supporting IND(s) if not already entered into tracking system.</i>				

Is the review priority (S or P) and all appropriate classifications/properties entered into tracking system (e.g., chemical classification, combination product classification, orphan drug)? <i>Check the New Application and New Supplement Notification Checklists for a list of all classifications/properties at:</i> http://inside.fda.gov:9003/CDER/OfficeofBusinessProcessSupport/ucm163969.htm <i>If no, ask the document room staff to make the appropriate entries.</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Application Integrity Policy	YES	NO	NA	Comment
Is the application affected by the Application Integrity Policy (AIP)? <i>Check the AIP list at:</i> http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm	<input type="checkbox"/>	<input checked="" type="checkbox"/>		
If yes, explain in comment column.				
If affected by AIP, has OC/OMPQ been notified of the submission? If yes, date notified:	<input type="checkbox"/>	<input type="checkbox"/>		
User Fees	YES	NO	NA	Comment
Is Form 3397 (User Fee Cover Sheet)/Form 3792 (Biosimilar User Fee Cover Sheet) included with authorized signature?	<input checked="" type="checkbox"/>	<input type="checkbox"/>		
<u>User Fee Status</u> <i>If a user fee is required and it has not been paid (and it is not exempted or waived), the application is unacceptable for filing following a 5-day grace period. Review stops. Send Unacceptable for Filing (UN) letter and contact user fee staff.</i>	Payment for this application (<i>check daily email from UserFeeAR@fda.hhs.gov</i>): <input checked="" type="checkbox"/> Paid <input type="checkbox"/> Exempt (orphan, government) <input type="checkbox"/> Waived (e.g., small business, public health) <input type="checkbox"/> Not required			
<i>If the firm is in arrears for other fees (regardless of whether a user fee has been paid for this application), the application is unacceptable for filing (5-day grace period does not apply). Review stops. Send UN letter and contact the user fee staff.</i>	Payment of other user fees: <input checked="" type="checkbox"/> Not in arrears <input type="checkbox"/> In arrears			
<u>User Fee Bundling Policy</u> <i>Refer to the guidance for industry, Submitting Separate Marketing Applications and Clinical Data for Purposes of Assessing User Fees at:</i> http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM079320.pdf	Has the user fee bundling policy been appropriately applied? <i>If no, or you are not sure, consult the User Fee Staff.</i> <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No			
505(b)(2) (NDAs/NDA Efficacy Supplements only)	YES	NO	NA	Comment
Is the application a 505(b)(2) NDA? (<i>Check the 356h form, cover letter, and annotated labeling</i>). If yes, answer the bulleted questions below:	<input checked="" type="checkbox"/>	<input type="checkbox"/>		

<ul style="list-style-type: none"> Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA? 	<input type="checkbox"/>	<input checked="" type="checkbox"/>																		
<ul style="list-style-type: none"> Is the application for a duplicate of a listed drug whose only difference is that the extent to which the active ingredient(s) is absorbed or otherwise made available to the site of action is less than that of the reference listed drug (RLD)? [see 21 CFR 314.54(b)(1)]. 	<input type="checkbox"/>	<input checked="" type="checkbox"/>																		
<ul style="list-style-type: none"> Is the application for a duplicate of a listed drug whose only difference is that the rate at which the proposed product's active ingredient(s) is absorbed or made available to the site of action is unintentionally less than that of the listed drug [see 21 CFR 314.54(b)(2)]? <p><i>If you answered yes to any of the above bulleted questions, the application may be refused for filing under 21 CFR 314.101(d)(9). Contact the 505(b)(2) review staff in the Immediate Office of New Drugs for advice.</i></p>	<input type="checkbox"/>	<input checked="" type="checkbox"/>																		
<ul style="list-style-type: none"> Is there unexpired exclusivity on another listed drug product containing the same active moiety (e.g., 5-year, 3-year, orphan, or pediatric exclusivity)? <p>Check the Electronic Orange Book at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm</p> <p>If yes, please list below:</p> <table border="1"> <thead> <tr> <th>Application No.</th> <th>Drug Name</th> <th>Exclusivity Code</th> <th>Exclusivity Expiration</th> </tr> </thead> <tbody> <tr><td> </td><td> </td><td> </td><td> </td></tr> <tr><td> </td><td> </td><td> </td><td> </td></tr> <tr><td> </td><td> </td><td> </td><td> </td></tr> </tbody> </table>	Application No.	Drug Name	Exclusivity Code	Exclusivity Expiration													<input type="checkbox"/>	<input checked="" type="checkbox"/>		
Application No.	Drug Name	Exclusivity Code	Exclusivity Expiration																	
<p><i>If there is unexpired, 5-year exclusivity remaining on another listed drug product containing the same active moiety, a 505(b)(2) application cannot be submitted until the period of exclusivity expires (unless the applicant provides paragraph IV patent certification; then an application can be submitted four years after the date of approval.) Pediatric exclusivity will extend both of the timeframes in this provision by 6 months. 21 CFR 314.108(b)(2). Unexpired, 3-year exclusivity may block the approval but not the submission of a 505(b)(2) application.</i></p>																				
Exclusivity	YES	NO	NA	Comment																
Does another product (same active moiety) have orphan exclusivity for the same indication? Check the Orphan Drug Designations and Approvals list at: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm	<input type="checkbox"/>	<input checked="" type="checkbox"/>																		
If another product has orphan exclusivity , is the product considered to be the same product according to the orphan drug definition of sameness [see 21 CFR 316.3(b)(13)]?	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>																	
<i>If yes, consult the Director, Division of Regulatory Policy II, Office of Regulatory Policy</i>																				
NDAs/NDA efficacy supplements only: Has the applicant requested 5-year or 3-year Waxman-Hatch exclusivity?	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>																	
If yes, # years requested:																				
<i>Note: An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.</i>																				
NDAs only: Is the proposed product a single enantiomer of a	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>																	

racemic drug previously approved for a different therapeutic use?				
If yes, did the applicant: (a) elect to have the single enantiomer (contained as an active ingredient) not be considered the same active ingredient as that contained in an already approved racemic drug, and/or (b): request exclusivity pursuant to section 505(u) of the Act (per FDAAA Section 1113)? <i>If yes, contact the Orange Book Staff (CDER-Orange Book Staff).</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	
BLAs only: Has the applicant requested 12-year exclusivity under section 351(k)(7) of the PHS Act? <i>If yes, notify Marlene Schultz-DePalo, OBP Biosimilars RPM</i> <i>Note: Exclusivity requests may be made for an original BLA submitted under Section 351(a) of the PHS Act (i.e., a biological reference product). A request may be located in Module 1.3.5.3 and/or other sections of the BLA and may be included in a supplement (or other correspondence) if exclusivity has not been previously requested in the original 351(a) BLA. An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	

Format and Content				
<i>Do not check mixed submission if the only electronic component is the content of labeling (COL).</i>	<input type="checkbox"/> All paper (except for COL) <input checked="" type="checkbox"/> All electronic <input type="checkbox"/> Mixed (paper/electronic)			
	<input type="checkbox"/> CTD <input type="checkbox"/> Non-CTD <input type="checkbox"/> Mixed (CTD/non-CTD)			
If mixed (paper/electronic) submission, which parts of the application are submitted in electronic format?				
Overall Format/Content	YES	NO	NA	Comment
If electronic submission, does it follow the eCTD guidance? ¹ If not, explain (e.g., waiver granted).	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Index: Does the submission contain an accurate comprehensive index?	<input type="checkbox"/>	<input type="checkbox"/>		
Is the submission complete as required under 21 CFR 314.50 (NDAs/NDA efficacy supplements) or under 21 CFR 601.2 (BLAs/BLA efficacy supplements) including: <input checked="" type="checkbox"/> legible <input checked="" type="checkbox"/> English (or translated into English)	<input checked="" type="checkbox"/>	<input type="checkbox"/>		

1

<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm072349.pdf>

<input checked="" type="checkbox"/> pagination <input checked="" type="checkbox"/> navigable hyperlinks (electronic submissions only)				
If no, explain.				
BLAs only: Companion application received if a shared or divided manufacturing arrangement?	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	
If yes, BLA #				
Forms and Certifications				
<i>Electronic forms and certifications with electronic signatures (scanned, digital, or electronic – similar to DARRTS, e.g., /s/) are acceptable. Otherwise, paper forms and certifications with hand-written signatures must be included. Forms include: user fee cover sheet (3397/3792), application form (356h), patent information (3542a), financial disclosure (3454/3455), and clinical trials (3674); Certifications include: debarment certification, patent certification(s), field copy certification, and pediatric certification.</i>				
Application Form	YES	NO	NA	Comment
Is form FDA 356h included with authorized signature per 21 CFR 314.50(a)? <i>If foreign applicant, a U.S. agent must sign the form [see 21 CFR 314.50(a)(5)].</i>	<input checked="" type="checkbox"/>	<input type="checkbox"/>		
Are all establishments and their registration numbers listed on the form/attached to the form?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Patent Information (NDAs/NDA efficacy supplements only)	YES	NO	NA	Comment
Is patent information submitted on form FDA 3542a per 21 CFR 314.53(c)?	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	No exclusivity periods in effect
Financial Disclosure	YES	NO	NA	Comment
Are financial disclosure forms FDA 3454 and/or 3455 included with authorized signature per 21 CFR 54.4(a)(1) and (3)? <i>Forms must be signed by the APPLICANT, not an Agent [see 21 CFR 54.2(g)].</i> <i>Note: Financial disclosure is required for bioequivalence studies that are the basis for approval.</i>	<input type="checkbox"/>	<input checked="" type="checkbox"/>		No clinical studies
Clinical Trials Database	YES	NO	NA	Comment
Is form FDA 3674 included with authorized signature? <i>If yes, ensure that the application is also coded with the supporting document category, "Form 3674."</i> <i>If no, ensure that language requesting submission of the form is included in the acknowledgement letter sent to the applicant</i>	<input checked="" type="checkbox"/>	<input type="checkbox"/>		

Debarment Certification	YES	NO	NA	Comment
<p>Is a correctly worded Debarment Certification included with authorized signature?</p> <p><i>Certification is not required for supplements if submitted in the original application; If foreign applicant, both the applicant and the U.S. Agent must sign the certification [per Guidance for Industry: Submitting Debarment Certifications].</i></p> <p><i>Note: Debarment Certification should use wording in FD&C Act Section 306(k)(1) i.e., “[Name of applicant] hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug, and Cosmetic Act in connection with this application.” Applicant may not use wording such as, “To the best of my knowledge...”</i></p>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Field Copy Certification (NDAs/NDA efficacy supplements only)	YES	NO	NA	Comment
<p>For paper submissions only: Is a Field Copy Certification (that it is a true copy of the CMC technical section) included?</p> <p><i>Field Copy Certification is not needed if there is no CMC technical section or if this is an electronic submission (the Field Office has access to the EDR)</i></p> <p><i>If maroon field copy jackets from foreign applicants are received, return them to CDR for delivery to the appropriate field office.</i></p>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	
Controlled Substance/Product with Abuse Potential	YES	NO	NA	Comment
<p><u>For NMEs:</u> Is an Abuse Liability Assessment, including a proposal for scheduling, submitted per 21 CFR 314.50(d)(5)(vii)?</p> <p><i>If yes, date consult sent to the Controlled Substance Staff:</i></p> <p><u>For non-NMEs:</u> <i>Date of consult sent to Controlled Substance Staff:</i></p>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	
Pediatrics	YES	NO	NA	Comment
<p><u>PREA</u></p> <p>Does the application trigger PREA?</p> <p><i>If yes, notify PeRC@fda.hhs.gov to schedule required PeRC meeting²</i></p> <p><i>Note: NDAs/BLAs/efficacy supplements for new active ingredients (including new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration trigger PREA. All waiver & deferral requests, pediatric plans, and</i></p>	<input type="checkbox"/>	<input checked="" type="checkbox"/>		Please check with clinical team

2

<http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/ImmediateOffice/PediatricandMaternalHealthStaff/ucm027829.htm>

Version: 10/20/2014

7

<i>pediatric assessment studies must be reviewed by PeRC prior to approval of the application/supplement.</i>				
If the application triggers PREA , is there an agreed Initial Pediatric Study Plan (iPSP)?	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	
<i>If no, may be an RTF issue - contact DPMH for advice.</i>				
If required by the agreed iPSP , are the pediatric studies outlined in the agreed iPSP completed and included in the application?	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	
<i>If no, may be an RTF issue - contact DPMH for advice.</i>				
<u>BPCA:</u>				
Is this submission a complete response to a pediatric Written Request?	<input type="checkbox"/>	<input checked="" type="checkbox"/>		
<i>If yes, notify Pediatric Exclusivity Board RPM (pediatric exclusivity determination is required)³</i>				
Proprietary Name	YES	NO	NA	Comment
Is a proposed proprietary name submitted?	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	
<i>If yes, ensure that the application is also coded with the supporting document category, "Proprietary Name/Request for Review."</i>				
REMS	YES	NO	NA	Comment
Is a REMS submitted?	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	
<i>If yes, send consult to OSE/DRISK and notify OC/OSI/DSC/PMSB via the CDER OSI RMP mailbox</i>				
Prescription Labeling	<input type="checkbox"/> Not applicable			
Check all types of labeling submitted.	<input checked="" type="checkbox"/> Package Insert (PI) <input type="checkbox"/> Patient Package Insert (PPI) <input type="checkbox"/> Instructions for Use (IFU) <input type="checkbox"/> Medication Guide (MedGuide) <input checked="" type="checkbox"/> Carton labels <input checked="" type="checkbox"/> Immediate container labels <input type="checkbox"/> Diluent <input type="checkbox"/> Other (specify)			
	YES	NO	NA	Comment
Is Electronic Content of Labeling (COL) submitted in SPL format?	<input type="checkbox"/>	<input checked="" type="checkbox"/>		Not yet
<i>If no, request applicant to submit SPL before the filing date.</i>				

3

<http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/ImmediateOffice/PediatricandMaternalHealthStaff/ucm027837.htm>

Version: 10/20/2014

8

Is the PI submitted in PLR format? ⁴	<input type="checkbox"/>	<input checked="" type="checkbox"/>		
If PI not submitted in PLR format , was a waiver or deferral requested before the application was received or in the submission? If requested before application was submitted , what is the status of the request? <i>If no waiver or deferral, request applicant to submit labeling in PLR format before the filing date.</i>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	
All labeling (PI, PPI, MedGuide, IFU, carton and immediate container labels) consulted to OPDP?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
MedGuide, PPI, IFU (plus PI) consulted to OSE/DRISK? (send WORD version if available)	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	
Carton and immediate container labels, PI, PPI sent to OSE/DMEPA and appropriate CMC review office (OBP or ONDQA)?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
OTC Labeling	<input checked="" type="checkbox"/> Not Applicable			
Check all types of labeling submitted.	<input type="checkbox"/> Outer carton label <input type="checkbox"/> Immediate container label <input type="checkbox"/> Blister card <input type="checkbox"/> Blister backing label <input type="checkbox"/> Consumer Information Leaflet (CIL) <input type="checkbox"/> Physician sample <input type="checkbox"/> Consumer sample <input type="checkbox"/> Other (specify)			
	YES	NO	NA	Comment
Is electronic content of labeling (COL) submitted? <i>If no, request in 74-day letter.</i>	<input type="checkbox"/>	<input type="checkbox"/>		
Are annotated specifications submitted for all stock keeping units (SKUs)? <i>If no, request in 74-day letter.</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
If representative labeling is submitted, are all represented SKUs defined? <i>If no, request in 74-day letter.</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
All labeling/packaging sent to OSE/DMEPA?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Other Consults	YES	NO	NA	Comment
Are additional consults needed? (e.g., IFU to CDRH; QT study report to QT Interdisciplinary Review Team) <i>If yes, specify consult(s) and date(s) sent:</i>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	
Meeting Minutes/SPAs	YES	NO	NA	Comment

4

<http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/ImmediateOffice/StudyEndpointsandLabelingDevelopmentTeam/ucm025576.htm>

End-of Phase 2 meeting(s)? Date(s): <i>If yes, distribute minutes before filing meeting</i>	<input type="checkbox"/>	<input checked="" type="checkbox"/>		
Pre-NDA/Pre-BLA/Pre-Supplement meeting(s)? Date(s): 05/30/2014 <i>If yes, distribute minutes before filing meeting</i>	<input checked="" type="checkbox"/>	<input type="checkbox"/>		
Any Special Protocol Assessments (SPAs)? Date(s): <i>If yes, distribute letter and/or relevant minutes before filing meeting</i>	<input type="checkbox"/>	<input checked="" type="checkbox"/>		

ATTACHMENT

MEMO OF FILING MEETING

DATE: October 16, 2014

BACKGROUND: (NDA) 207131 for Cefazolin Injection, USP in GALAXY Container (2 g/100 mL) was submitted October 16, 2014 (SEQ-0000). While Celerity had proposed (b)(4), the Division stated that the only indication approved for the 2 g dose of cefazolin is (b)(4). Celerity communicated that due to electronic publishing deadlines and its desire to submit the original NDA by October 23, 2014, it was unable to revise the labeling prior to submission and wished to provide the revised labeling as an Amendment. The Division agreed that it was Celerity's decision to make the changes before submission or to submit as planned, but the labeling would need to be revised and resubmitted. The Division confirmed that Celerity could submit the NDA as planned and recommended amending the application to withdraw (b)(4) and providing updated labeling information. Celerity committed to providing the updated labeling information and related documentation as an amendment to the application.

Celerity provided updated labeling information and related documentation as a labeling amendment to NDA 2071 31. In addition to the updated labeling information, and revised (b)(4)

- Module 1.12.12 Comparison of Generic Drug and Reference Listed Drug
 - Module I .12. 15 Request for Waiver of In Vivo Bioavailability Studies
 - Module 2.3 Quality Overall Summary Introduction
 - Module 2.5 Clinical Overview
- The content of labeling in structured product labeling (SPL) format is provided.

REVIEW TEAM:

Discipline/Organization	Names		Present at filing meeting? (Y or N)
Regulatory Project Management	RPM:	Fariba Izadi	
	CPMS/TL:	Frances LeSane	N
Cross-Discipline Team Leader (CDTL)	Thomas Smith		Y
Division Director/Deputy	Sumathi Nambiar		Y
Office Director/Deputy			
Clinical	Reviewer:	Peter Kim	Y
	TL:	Thomas Smith	Y
Social Scientist Review (<i>for OTC products</i>)	Reviewer:		NA
	TL:		

OTC Labeling Review (<i>for OTC products</i>)	Reviewer:		NA
	TL:		
Clinical Microbiology (<i>for antimicrobial products</i>)	Reviewer:	Kerian Grande Rosche	N
	TL:	Kerry Snow	N
Clinical Pharmacology	Reviewer:	Kunyi Wu	Y
	TL:	Kimberly Bergman	Y
Biostatistics	Reviewer:	Christopher Kadoorie	Y
	TL:	Thamban Valappil	Y

Nonclinical (Pharmacology/Toxicology)	Reviewer:	Amy Ellis	Y
	TL:	Wendelyn Schmidt	Y
Statistics (carcinogenicity)	Reviewer:		NA
	TL:		NA
Immunogenicity (assay/assay validation) <i>(for protein/peptide products only)</i>	Reviewer:		NA
	TL:		NA
Product Quality (CMC)	Reviewer:	Chunchun Zhang	Y
	TL:	Dorota Matecka	Y
Biopharmaceutics	Reviewer:	Kelly Kitchens	N
	TL:	Tapash Ghosh	N
Quality Microbiology	Reviewer:	Vinayak Pawar	N
	TL:	Ryan Riley	N
CMC Labeling Review	Reviewer:		
	TL:		
Facility Review/Inspection	Reviewer:		
	TL:		
OSE/DMEPA (proprietary name, carton/container labels))	Reviewer:		
	TL:		
OSE/DRISK (REMS)	Reviewer:		
	TL:		
OC/OSI/DSC/PMSB (REMS)	Reviewer:		
	TL:		

Bioresearch Monitoring (OSI)	Reviewer:		
	TL:		
Controlled Substance Staff (CSS)	Reviewer:		
	TL:		
Other reviewers/disciplines	Reviewer:		
	TL:		
Other attendees			

FILING MEETING DISCUSSION:

<p>GENERAL</p> <ul style="list-style-type: none"> • 505(b)(2) filing issues: <ul style="list-style-type: none"> ○ Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA? ○ Did the applicant provide a scientific “bridge” demonstrating the relationship between the proposed product and the referenced product(s)/published literature? <p>Describe the scientific bridge (e.g., BA/BE studies):</p>	<input type="checkbox"/> Not Applicable <input type="checkbox"/> YES <input checked="" type="checkbox"/> NO <input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
<ul style="list-style-type: none"> • Per reviewers, are all parts in English or English translation? <p>If no, explain:</p>	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
<ul style="list-style-type: none"> • Electronic Submission comments <p>List comments:</p>	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> No comments
<p>CLINICAL</p> <p>Comments:</p>	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input type="checkbox"/> Review issues for 74-day letter
<ul style="list-style-type: none"> • Clinical study site(s) inspections(s) needed? <p>If no, explain:</p>	<input type="checkbox"/> YES <input checked="" type="checkbox"/> NO

<ul style="list-style-type: none"> Advisory Committee Meeting needed? <p>Comments:</p> <p><i>If no, for an NME NDA or original BLA, include the reason. For example:</i></p> <ul style="list-style-type: none"> <i>this drug/biologic is not the first in its class</i> <i>the clinical study design was acceptable</i> <i>the application did not raise significant safety or efficacy issues</i> <i>the application did not raise significant public health questions on the role of the drug/biologic in the diagnosis, cure, mitigation, treatment or prevention of a disease</i> 	<input type="checkbox"/> YES Date if known: <input checked="" type="checkbox"/> NO <input type="checkbox"/> To be determined Reason:
<ul style="list-style-type: none"> If the application is affected by the AIP, has the division made a recommendation regarding whether or not an exception to the AIP should be granted to permit review based on medical necessity or public health significance? <p>Comments:</p>	<input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> YES <input type="checkbox"/> NO
<p>CONTROLLED SUBSTANCE STAFF</p> <ul style="list-style-type: none"> Abuse Liability/Potential <p>Comments:</p>	<input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input type="checkbox"/> Review issues for 74-day letter
<p>CLINICAL MICROBIOLOGY</p> <p>Comments:</p>	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input type="checkbox"/> Review issues for 74-day letter
<p>CLINICAL PHARMACOLOGY</p> <p>Comments:</p>	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input type="checkbox"/> Review issues for 74-day letter
<ul style="list-style-type: none"> Clinical pharmacology study site(s) inspections(s) needed? 	<input type="checkbox"/> YES <input checked="" type="checkbox"/> NO
<p>BIOSTATISTICS</p> <p>Comments:</p>	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input type="checkbox"/> Review issues for 74-day letter

<p>NONCLINICAL (PHARMACOLOGY/TOXICOLOGY)</p> <p>Comments:</p>	<p><input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE</p> <p><input type="checkbox"/> Review issues for 74-day letter</p>
<p>IMMUNOGENICITY (protein/peptide products only)</p> <p>Comments:</p>	<p><input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE</p> <p><input type="checkbox"/> Review issues for 74-day letter</p>
<p>PRODUCT QUALITY (CMC)</p> <p>Comments:</p>	<p><input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE</p> <p><input type="checkbox"/> Review issues for 74-day letter</p>
<p>New Molecular Entity (NDAs only)</p> <ul style="list-style-type: none"> Is the product an NME? 	<p><input type="checkbox"/> YES <input checked="" type="checkbox"/> NO</p>
<p><u>Environmental Assessment</u></p> <ul style="list-style-type: none"> Categorical exclusion for environmental assessment (EA) requested? <p>If no, was a complete EA submitted?</p> <p>If EA submitted, consulted to EA officer (OPS)?</p> <p>Comments:</p>	<p><input type="checkbox"/> YES <input type="checkbox"/> NO</p> <p><input type="checkbox"/> YES <input type="checkbox"/> NO</p> <p><input type="checkbox"/> YES <input type="checkbox"/> NO</p>
<p><u>Quality Microbiology</u></p> <ul style="list-style-type: none"> Was the Microbiology Team consulted for validation of sterilization? <p>Comments:</p>	<p><input type="checkbox"/> Not Applicable</p> <p><input checked="" type="checkbox"/> YES <input type="checkbox"/> NO</p>

<p><u>Facility Inspection</u></p> <ul style="list-style-type: none"> • Establishment(s) ready for inspection? ▪ Establishment Evaluation Request (EER/TBP-EER) submitted to OMPQ? <p>Comments:</p>	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> YES <input type="checkbox"/> NO
<p><u>Facility/Microbiology Review (BLAs only)</u></p> <p>Comments:</p>	<input type="checkbox"/> Not Applicable <input type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input type="checkbox"/> Review issues for 74-day letter
<p><u>CMC Labeling Review</u></p> <p>Comments:</p>	<input type="checkbox"/> Review issues for 74-day letter
<p>APPLICATIONS IN THE PROGRAM (PDUFA V) (NME NDAs/Original BLAs)</p> <ul style="list-style-type: none"> • Were there agreements made at the application's pre-submission meeting (and documented in the minutes) regarding certain late submission components that could be submitted within 30 days after receipt of the original application? • If so, were the late submission components all submitted within 30 days? 	<input type="checkbox"/> N/A <input type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> YES <input type="checkbox"/> NO
<ul style="list-style-type: none"> • What late submission components, if any, arrived after 30 days? 	t
<ul style="list-style-type: none"> • Was the application otherwise complete upon submission, including those applications where there were no agreements regarding late submission components? 	<input type="checkbox"/> YES <input type="checkbox"/> NO

<ul style="list-style-type: none"> • Is a comprehensive and readily located list of all clinical sites included or referenced in the application? 	<input type="checkbox"/> YES <input type="checkbox"/> NO
<ul style="list-style-type: none"> • Is a comprehensive and readily located list of all manufacturing facilities included or referenced in the application? 	<input type="checkbox"/> YES <input type="checkbox"/> NO
REGULATORY PROJECT MANAGEMENT	
<p>Signatory Authority: Sumathi Nambiar, MD</p> <p>Date of Mid-Cycle Meeting (for NME NDAs/BLAs in “the Program” PDUFA V):</p> <p>21st Century Review Milestones (see attached) (listing review milestones in this document is optional):</p> <p>Comments:</p>	
REGULATORY CONCLUSIONS/DEFICIENCIES	
<input type="checkbox"/>	The application is unsuitable for filing. Explain why:
<input checked="" type="checkbox"/>	The application, on its face, appears to be suitable for filing. <u>Review Issues:</u> <input checked="" type="checkbox"/> No review issues have been identified for the 74-day letter. <input type="checkbox"/> Review issues have been identified for the 74-day letter. <u>Review Classification:</u> <input checked="" type="checkbox"/> Standard Review <input type="checkbox"/> Priority Review
ACTIONS ITEMS	
<input checked="" type="checkbox"/>	Ensure that any updates to the review priority (S or P) and classifications/properties are entered into tracking system (e.g., chemical classification, combination product classification, orphan drug).
<input type="checkbox"/>	If RTF, notify everyone who already received a consult request, OSE PM, and Product Quality PM (to cancel EER/TBP-EER).
<input type="checkbox"/>	If filed, and the application is under AIP, prepare a letter either granting (for signature by Center Director) or denying (for signature by ODE Director) an exception for review.
<input type="checkbox"/>	351(k) BLA/supplement: If filed, send filing notification letter on day 60
<input type="checkbox"/>	If priority review:

	<ul style="list-style-type: none"> • notify sponsor in writing by day 60 (see CST for choices) • notify OMPQ (so facility inspections can be scheduled earlier)
<input checked="" type="checkbox"/>	Send review issues/no review issues by day 74
<input checked="" type="checkbox"/>	Conduct a PLR format labeling review and include labeling issues in the 74-day letter
<input type="checkbox"/>	Update the PDUFA V DARRTS page (for applications in the Program)
<input type="checkbox"/>	Other

Annual review of template by OND ADRAAs completed: September 2014

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

/s/

FARIBA IZADI
03/17/2015

FRANCES V LESANE
03/17/2015