

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

208083Orig1s000

**ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS**

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION¹

NDA # 208083 BLA #	NDA Supplement # BLA Supplement #	If NDA, Efficacy Supplement Type: (an action package is not required for SE8 or SE9 supplements)
Proprietary Name: N/A Established/Proper Name: Clindamycin in 0.9 Sodium Chloride Injection in GALAXY Container Dosage Form: Injection		Applicant: Celerity Pharmaceuticals, LLC Agent for Applicant (if applicable):
RPM: Naseya Minor		Division: DAIP
NDA Application Type: ☐ 505(b)(1) ☒ 505(b)(2) Efficacy Supplement: ☐ 505(b)(1) ☐ 505(b)(2) BLA Application Type: ☐ 351(k) ☐ 351(a) Efficacy Supplement: ☐ 351(k) ☐ 351(a)		For ALL 505(b)(2) applications, two months prior to EVERY action: - Review the information in the 505(b)(2) Assessment and submit the draft² to CDER OND IO for clearance. - Check Orange Book for newly listed patents and/or exclusivity (including pediatric exclusivity) ☒ No changes ☐ New patent/exclusivity (notify CDER OND IO) Date of check:
Note: If pediatric exclusivity has been granted or the pediatric information in the labeling of the listed drug changed, determine whether pediatric information needs to be added to or deleted from the labeling of this drug.		
Actions		
- Proposed action - User Fee Goal Date is <u>April 30, 2017</u>		☒ AP ☐ TA ☐ CR
Previous actions (specify type and date for each action taken)		☒ None
❖ If accelerated approval or approval based on efficacy studies in animals, were promotional materials received? Note: Promotional materials to be used within 120 days after approval must have been submitted (for exceptions, see http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf). If not submitted, explain _____		☐ Received
❖ Application Characteristics ³		

¹ The **Application Information** Section is (only) a checklist. The **Contents of Action Package** Section (beginning on page 2) lists the documents to be included in the Action Package.

² For resubmissions, 505(b)(2) applications must be cleared before the action, but it is not necessary to resubmit the draft 505(b)(2) Assessment to CDER OND IO unless the Assessment has been substantively revised (e.g., new listed drug, patent certification revised).

³ Answer all questions in all sections in relation to the pending application, i.e., if the pending application is an NDA or BLA supplement, then the questions should be answered in relation to that supplement, not in relation to the original NDA or BLA.

Review priority: ☒ Standard ☐ Priority

Chemical classification (new NDAs only):

(confirm chemical classification at time of approval)

- ☐ Fast Track
☐ Rolling Review
☐ Orphan drug designation
☐ Breakthrough Therapy designation

- ☐ Rx-to-OTC full switch
☐ Rx-to-OTC partial switch
☐ Direct-to-OTC

(NOTE: Set the submission property in DARRTS and notify the CDER Breakthrough Therapy Program Manager; Refer to the "RPM BT Checklist for Considerations after Designation Granted" for other required actions: [CST SharePoint](#))

NDAs: Subpart H

- ☐ Accelerated approval (21 CFR 314.510)
☐ Restricted distribution (21 CFR 314.520)

Subpart I

- ☐ Approval based on animal studies

- ☐ Submitted in response to a PMR
☐ Submitted in response to a PMC
☐ Submitted in response to a Pediatric Written Request

BLAs: Subpart E

- ☐ Accelerated approval (21 CFR 601.41)
☐ Restricted distribution (21 CFR 601.42)

Subpart H

- ☐ Approval based on animal studies

- REMS: ☐ MedGuide
☐ Communication Plan
☐ ETASU
☐ MedGuide w/o REMS
☐ REMS not required

Comments:

❖ BLAs only: Is the product subject to official FDA lot release per 21 CFR 610.2 (approvals only)	☐ Yes ☐ No
❖ Public communications (approvals only)	
• Office of Executive Programs (OEP) liaison has been notified of action	☐ Yes ☒ No
• Indicate what types (if any) of information were issued	☒ None ☐ FDA Press Release ☐ FDA Talk Paper ☐ CDER Q&As ☐ Other
❖ Exclusivity	
• Is approval of this application blocked by any type of exclusivity (orphan, 5-year NCE, 3-year, pediatric exclusivity)?	☒ No ☐ Yes
• If so, specify the type	
❖ Patent Information (NDAs only)	
• Patent Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought.	☐ Verified ☐ Not applicable because drug is an old antibiotic.
CONTENTS OF ACTION PACKAGE	
Officer/Employee List	
❖ List of officers/employees who participated in the decision to approve this application and consented to be identified on this list (approvals only)	☒ Included
Documentation of consent/non-consent by officers/employees	☒ Included

Action Letters	
❖ Copies of all action letters (including approval letter with final labeling)	Action(s) and date(s) April 20, 2017
Labeling	
❖ Package Insert (write submission/communication date at upper right of first page of PI)	
• Most recent draft labeling (if it is division-proposed labeling, it should be in track-changes format)	☒ Included
• Original applicant-proposed labeling	☒ Included
❖ Medication Guide/Patient Package Insert/Instructions for Use/Device Labeling (write submission/communication date at upper right of first page of each piece)	☐ Medication Guide ☐ Patient Package Insert ☐ Instructions for Use ☐ Device Labeling ☒ None
• Most-recent draft labeling (if it is division-proposed labeling, it should be in track-changes format)	☒ Included
• Original applicant-proposed labeling	☒ Included
❖ Labels (full color carton and immediate-container labels) (write submission/communication date on upper right of first page of each submission)	
• Most-recent draft labeling	☒ Included
❖ Proprietary Name	N/A
• Acceptability/non-acceptability letter(s) (indicate date(s))	
• Review(s) (indicate date(s))	
❖ Labeling reviews (indicate dates of reviews)	RPM: ☒ September 13, 2016 DMEPA: ☒ April 3, 2017 DMPP/PLT (DRISK): ☒ None OPDP: ☒ None March 13, 2017 SEALD: ☒ None CSS: ☒ None Product Quality ☒ None Other: ☐ None
Administrative / Regulatory Documents	
❖ RPM Filing Review ⁴ /Memo of Filing Meeting (indicate date of each review)	August 31, 2016
❖ All NDA 505(b)(2) Actions: Date each action cleared by 505(b)(2) Clearance Committee	☐ Not a (b)(2) April 5, 2017
❖ NDAs/NDA supplements only: Exclusivity Summary (signed by Division Director)	☒ Completed (Do not include)
❖ Application Integrity Policy (AIP) Status and Related Documents http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm	
• Applicant is on the AIP	☐ Yes ☒ No

⁴ Filing reviews for scientific disciplines are NOT required to be included in the action package.

- This application is on the AIP - If yes, Center Director's Exception for Review memo <i>(indicate date)</i> - If yes, OC clearance for approval <i>(indicate date of clearance communication)</i>	☐ Yes ☒ No ☐ Not an AP action
❖ Pediatrics <i>(approvals only)</i> - Date reviewed by PeRC _____ - If PeRC review not necessary, explain: <u>N/A</u>	N/A
❖ Breakthrough Therapy Designation	☒ N/A
Breakthrough Therapy Designation Letter(s) (granted, denied, an/or rescinded)	
CDER Medical Policy Council Breakthrough Therapy Designation Determination Review Template(s) <i>(include only the completed template(s) and not the meeting minutes)</i>	
CDER Medical Policy Council Brief – Evaluating a Breakthrough Therapy Designation for Rescission Template(s) <i>(include only the completed template(s) and not the meeting minutes)</i> <i>(completed CDER MPC templates can be found in DARRTS as clinical reviews or on the MPC SharePoint Site)</i>	
❖ Outgoing communications: letters, emails, and faxes considered important to include in the action package by the reviewing office/division (e.g., clinical SPA letters, RTF letter, Formal Dispute Resolution Request decisional letters, etc.) <i>(do not include OPDP letters regarding pre-launch promotional materials as these are non-disclosable; do not include Master File letters; do not include previous action letters, as these are located elsewhere in package)</i>	
❖ Internal documents: memoranda, telecons, emails, and other documents considered important to include in the action package by the reviewing office/division (e.g., Regulatory Briefing minutes, Medical Policy Council meeting minutes)	
❖ Minutes of Meetings	
If not the first review cycle, any end-of-review meeting <i>(indicate date of mtg)</i>	☒ N/A or no mtg
Pre-NDA/BLA meeting <i>(indicate date of mtg)</i>	☐ No mtg February 9, 2015
EOP2 meeting <i>(indicate date of mtg)</i>	☒ No mtg
Mid-cycle Communication <i>(indicate date of mtg)</i>	☒ N/A
Late-cycle Meeting <i>(indicate date of mtg)</i>	☒ N/A
Other milestone meetings (e.g., EOP2a, CMC focused milestone meetings) <i>(indicate dates of mtgs)</i>	
❖ Advisory Committee Meeting(s)	☒ No AC meeting
Date(s) of Meeting(s)	
Decisional and Summary Memos	
❖ Office Director Decisional Memo <i>(indicate date for each review)</i>	☒ None
Division Director Summary Review <i>(indicate date for each review)</i>	☐ None April 20, 2017
Cross-Discipline Team Leader Review <i>(indicate date for each review)</i>	☐ None April 20, 2017
PMR/PMC Development Templates <i>(indicate total number)</i>	☒ None
Clinical	

❖ Clinical Reviews	
• Clinical Team Leader Review(s) (indicate date for each review)	☒ No separate review
• Clinical review(s) (indicate date for each review)	March 15, 2017
• Social scientist review(s) (if OTC drug) (indicate date for each review)	☒ None
❖ Financial Disclosure reviews(s) or location/date if addressed in another review OR If no financial disclosure information was required, check here ☒ and include a review/memo explaining why not (indicate date of review/memo)	No clinical information for 505(b)(2)
❖ Clinical reviews from immunology and other clinical areas/divisions/Centers (indicate date of each review) ⁵	☒ None
❖ Controlled Substance Staff review(s) and Scheduling Recommendation (indicate date of each review)	☒ N/A
❖ Risk Management • REMS Documents and REMS Supporting Document (indicate date(s) of submission(s)) • REMS Memo(s) and letter(s) (indicate date(s)) • Risk management review(s) and recommendations (including those by OSE and CSS) (indicate date of each review and indicate location/date if incorporated into another review)	☒ None
❖ OSI Clinical Inspection Review Summary(ies) (include copies of OSI letters to investigators)	☒ None requested
Clinical Microbiology ☐ None	
❖ Clinical Microbiology Team Leader Review(s) (indicate date for each review)	☒ No separate review
Clinical Microbiology Review(s) (indicate date for each review)	☐ None April 10, 2017
Biostatistics ☐ None	
❖ Statistical Division Director Review(s) (indicate date for each review)	☒ No separate review
Statistical Team Leader Review(s) (indicate date for each review)	☒ No separate review
Statistical Review(s) (indicate date for each review)	☐ None April 18, 2017
Clinical Pharmacology ☐ None	
❖ Clinical Pharmacology Division Director Review(s) (indicate date for each review)	☒ No separate review
Clinical Pharmacology Team Leader Review(s) (indicate date for each review)	☒ No separate review
Clinical Pharmacology review(s) (indicate date for each review)	☐ None March 27, 2017
❖ OSI Clinical Pharmacology Inspection Review Summary (include copies of OSI letters)	☒ None requested

⁵ For Part 3 combination products, all reviews from the reviewing Center(s) should be entered into the official archive (for further instructions, see "Section 508 Compliant Documents: Process for Regulatory Project Managers" located in the CST electronic repository).

Nonclinical ☐ None	
❖ Pharmacology/Toxicology Discipline Reviews	
• ADP/T Review(s) (indicate date for each review)	☒ No separate review
• Supervisory Review(s) (indicate date for each review)	☒ No separate review
• Pharm/tox review(s), including referenced IND reviews (indicate date for each review)	☐ None April 14, 2017
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer (indicate date for each review)	☒ None
❖ Statistical review(s) of carcinogenicity studies (indicate date for each review)	☒ No carc
❖ ECAC/CAC report/memo of meeting	☒ None Included in P/T review, page
❖ OSI Nonclinical Inspection Review Summary (include copies of OSI letters)	☒ None requested
Product Quality ☐ None	
❖ Product Quality Discipline Reviews ⁶	
• Tertiary review (indicate date for each review)	☒ None
• Secondary review (e.g., Branch Chief) (indicate date for each review)	☒ None
• Integrated Quality Assessment (contains the Executive Summary and the primary reviews from each product quality review discipline) (indicate date for each review)	☐ None April 20, 2017
❖ Reviews by other disciplines/divisions/Centers requested by product quality review team (indicate date of each review)	☒ None
❖ Environmental Assessment (check one) (original and supplemental applications)	
☐ Categorical Exclusion (indicate review date)(all original applications and all efficacy supplements that could increase the patient population)	
☐ Review & FONSI (indicate date of review)	
☐ Review & Environmental Impact Statement (indicate date of each review)	
❖ Facilities Review/Inspection	
☐ Facilities inspections (indicate date of recommendation; within one week of taking an approval action, confirm that there is an acceptable recommendation before issuing approval letter) (only original applications and efficacy supplements that require a manufacturing facility inspection(e.g., new strength, manufacturing process, or manufacturing site change)	☒ Acceptable ☐ Withhold recommendation ☐ Not applicable

⁶ Do not include Master File (MF) reviews or communications to MF holders. However, these documents should be made available upon signatory request.

Day of Approval Activities

❖ For all 505(b)(2) applications: • Check Orange Book for newly listed patents and/or exclusivity (including pediatric exclusivity)	☐ No changes ☒ New patent/exclusivity (<i>Notify CDER OND IO</i>)
• Finalize 505(b)(2) assessment	☒ Done
❖ For Breakthrough Therapy (BT) Designated drugs: • Notify the CDER BT Program Manager	☐ Done (<i>Send email to CDER OND IO</i>)
❖ For products that need to be added to the flush list (generally opioids): <u>Flush List</u> • Notify the Division of Online Communications, Office of Communications	☐ Done
❖ Send a courtesy copy of approval letter and all attachments to applicant by fax or secure email	☐ Done
❖ If an FDA communication will issue, notify Press Office of approval action after confirming that applicant received courtesy copy of approval letter	☐ Done
❖ Ensure that proprietary name, if any, and established name are listed in the <i>Application Product Names</i> section of DARRTS, and that the proprietary name is identified as the “preferred” name	☐ Done
❖ Ensure Pediatric Record is accurate	☐ Done
❖ Send approval email within one business day to CDER-APPROVALS	☐ Done

From: Minor, Naseya
To: ["John Oberholtzer"](#)
Cc: [Amber Sheriff](#)
Subject: RE: NDA 208-083 Clindamycin in 0.9% Sodium Chloride Injection-Labeling Comment Clarification Request
Date: Monday, September 19, 2016 4:10:00 PM

Hi John,

It will not be acceptable to state that you are relying on the safety and efficacy of the listed drug or something to that effect alone. The comments contained in the letter were to identify areas where the labeling did not meet the PLR regulatory requirements per 21 CFR 201.57 and the corresponding guidance's provided in the filing letter. Additional clarifications are provided below:

Comment 14: Our comment states "if applicable" which means we not are asking you to provide source data but to make the information relevant to this section. For example, If this information is not specifically dosage-related as per the regulatory requirements for this section (i.e. 21 CFR 201.57 (c)(3)) then consider what section of labeling may be more appropriate.

Comment 17: Our comment was made for you to organize the content included in the section. Please re-organize the section as recommended in the letter. This does not require a review any source data.

Comment 19: We are asking you to review publicly available information and add "if appropriate" per the regulations.

Comment 21: If possible please delineate whether adverse reactions were experienced during Clinical Trials and/or Post Marketing Experience.

Comments 26, 27, 28, 29 are all regulatory requirements from the PLLR regulations and guidance

Comment 30 is a regulatory requirement further clarified in the pediatric labeling guidance

As requested in your September 18th email, please amend your application with revised labeling that addresses the issues described in the filing communication by **October 17, 2016**. The resubmitted labeling will be used for further labeling discussions. Please note that we may have additional labeling comments and edits during the application review.

Please let me know if you have any questions or need additional clarifications.
Thanks,

Naseya

From: John Oberholtzer [mailto:joberholtzer@celeritypharma.com]
Sent: Friday, September 16, 2016 11:13 AM
To: Minor, Naseya
Cc: Amber Sheriff
Subject: FW: NDA 208-083 Clindamycin in 0.9% Sodium Chloride Injection-Labeling Comment Clarification Request

Dear Ms. Minor,

We need clarification in regards to the Filing Communication dated September 12, 2016 for NDA 208-083 Clindamycin in 0.9% Sodium Chloride Injection. This application was filed as a 505 (b)(2)

where we are relying on the safety and toxicology information of the Listed Drug CLEOCIN. The only difference between the Listed Drug and our proposed product is that 0.9% Sodium Chloride is added as a diluent. A 505 (b)(2) application is allowed for this type of product. For the following comments, the information is not available since we don't have access to the Clinical Study.

A14

A17

A19

A21

A26

A27

A28

A29

A30

Would it be an acceptable response to say that we are relying on the safety and efficacy of the listed drug or something to the effect?

We look forward to your feedback and would appreciate a quick response so that we can maintain the deadline for submitting no later than October 3, 2016.

Thanks and Best Regards,

John Oberholtzer

John Oberholtzer, J.D.

Senior Regulatory Affairs Manager

9450 W. Bryn Mawr Ave.

Suite 640

Rosemont, IL 60018

Direct/Fax/SMS: + (847) 999-0816

Email: joberholtzer@celeritypharma.com

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/s/

NASEYA N MINOR
09/29/2016

Minor, Naseya

From: Sharma, Khushboo
Sent: Wednesday, April 05, 2017 12:27 PM
Subject: Minor, Naseya
Goldstein, Beth A (Duvall); Holovac, Mary Ann; Schumann, Katherine
NDA 208083 - clindamycin in 0.9% sodium chloride injection - cleared for action

Dear Naseya,

We discussed the subject application at Monday's 505(b)(2) clearance meeting. The application is cleared for action from a 505(b)(2) perspective.

Please make the following changes to the draft assessment before archiving in DARRTS, assuming you are heading towards an approval. If you are not approving this cycle, please make the changes below but defer archiving in DARRTS until you are headed towards approval (in which case you would need to have the application cleared again). If that's the case, please let us know when the RS arrives so that we can add it anew to our clearance queue.

- *Q11c: Please change to NO. The listed drug (NDA 50639) is pharmaceutical equivalent.*

Please let Mary Ann know if you have any questions.

Thanks,

Khushboo Sharma, MBA, RAC

Team Leader – Regulatory Affairs Team

Center for Drug Evaluation and Research

Office of New Drugs

U.S. Food and Drug Administration

Tel: 301-796-1270 Cell: (b) (6)

Khushboo.sharma@fda.hhs.gov



Minor, Naseya

From: Minor, Naseya
t: Thursday, March 30, 2017 12:12 PM
'John Oberholtzer'
Cc: Amber Sheriff
Subject: RE: NDA 208083 Clindamycin (b) (4) IR

Hi John,

Thank you for your response.

Some of the pending carton and container labeling recommendations (b) (4)

As a reminder for the NDA (b) (4), both Celerity and Baxter will be required to submit letters of (b) (4) of the NDA.

Thanks,

Naseya

From: John Oberholtzer [<mailto:joberholtzer@celeritypharma.com>]
Sent: Wednesday, March 29, 2017 6:14 PM
To: Minor, Naseya
Cc: Amber Sheriff
Subject: NDA 208083 Clindamycin (b) (4) IR

Hi Naseya,

(b) (4)

Naseya Minor, MPH*Regulatory Health Project Manager***Center for Drug Evaluation and Research****Office of Antimicrobial Products | Division of Anti-Infective Products****White Oak Building 22, Room 6219**

Tel: 301-796-0756

Naseya.Minor@fda.hhs.gov

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Minor, Naseya

From: Minor, Naseya
Subject: Tuesday, March 14, 2017 5:03 PM
'John Oberholtzer'
Cc: Amber Sheriff
Subject: RE: NDA 208083 Clindamycin Carton and Container Recommendations-Celerity Requests

Hi John,

Thank you for the response. For review purposes please submit mocked up versions of your proposed carton and container revisions.

Please include justification for not implementing any of our container label and carton labeling recommendations.

Please submit mocked up versions labels as soon as possible and please let me know if you have any additional questions or need clarification.

Thanks,

Naseya

From: John Oberholtzer [mailto:joberholtzer@celeritypharma.com]
Sent: Monday, March 13, 2017 6:02 PM
To: Minor, Naseya
Cc: Amber Sheriff
Subject: RE: NDA 208083 Clindamycin Carton and Container Recommendations-Celerity Requests

Hi Naseya,

Thank you for looking into this. I copied and pasted the requests in your email, which are in **bolded blue text below followed by** Celerity's responses in black. For greater clarity, the order of the 1st two questions and responses are switched.

You state that "The films for all three configurations of the Clindamycin in 0.9% Sodium Chloride Injection have been already ordered with current label printed on it due to the long printing lead time." Clarify if the "current" carton labeling and container labels you have ordered are the same as the labels and labeling that are referred to in the Agency's February 22, 2017 Container Labels and Carton Labeling recommendations.

Celerity's Response

(b) (4)



All Container and Carton Labeling

1- Celerity agrees to change the font color of the 300 mg strength statement (b) (4) to black on a white background with a black outline around the white box. When making this change for the 300 mg film, other recommendations as explained below will be included for the container and carton on the 300 mg strength. These changes will be submitted in the labeling amendment in response to the Agency's February 22, 2017 Container Labels and Carton Labeling recommendations. (b) (4)

[REDACTED]

[REDACTED]

2- See email to the FDA dated February 24, 2017 requesting clarification (Change statement to "Intravenous Infusion Only" and remove "Not for rapid injection or Intravenous Push").

3- The location of the expiration date and lot number will be depicted on the new labeling in the response to the February 22, 2017 Container Labels and Carton Labeling recommendations.

4- The middle 3 digits of the NDC numbers in the new labeling are non-sequential. For Celerity's new labeling submitted for approval, the NDC numbers are non-sequential (306, 612, and 918 for 300 mg, 600 mg, and 900 mg strengths, respectively). (b) (4)

[REDACTED]

[REDACTED]

(b) (4)

Container Label

1- See email to the FDA dated February 24, 2017 requesting clarification (prominence of drug product name in the principal display panel).

2- [REDACTED] (b) (4)

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

3- See email to the FDA dated February 24, 2017 requesting clarification (Move the cautions statement to precede the statement "Each 50 mL contains: ...").

4- [REDACTED] (b) (4)

[REDACTED]

[REDACTED]

[REDACTED]

cartons are all 24 to correspond with the number of units per carton. See Table 1 summarizing NDC numbers below.

Table 1. Summary of NDC Numbers on the Labeling-Middle Digits			
Packaging Configuration	NDC No. on Celerity's Current Proposed Labeling referred to 02/27/2017	NDC No. on Celerity's Revised Proposed Labeling	(b) (4)
300 mg/50 mL container	(b) (4)	67798-306-05	(b) (4)
300 mg/50 mL carton		67798-306-24	
600 mg/50 mL container		67798-612-05	
600 mg/50 mL carton		67798-612-24	
900 mg/50 mL container		67798-918-05	
900 mg/50 mL carton		67798-918-24	

Carton Labeling

1- The new carton labeling for the 900 mg strength will be revised so that a comma is added between clindamycin and 9 mg and will be submitted in the response to the February 22, 2017 Container Labels and Carton Labeling recommendations. (b) (4)

2- To provide clarification, the carton label information is printed two (2) times on one (1) adhesive label and is separable along a perforation. During production, the perforated adhesive label is placed so that it connects two (2) very small cartons (VSCs). Each VSC contains twelve (12) 50 mL GALAXY containers for the 300 mg/50 mL, 600 mg/50 mL, and 900 mg/50 mL strengths. When the VSCs are separated during use, one full label with complete information remains with each VSC. However, orders are placed twenty-four units (24) at a time for the 300 mg/50 mL, 600 mg/50 mL, and 900 mg/50 mL strengths. Two (2) VSCs make up a carton and cartons are one unit of sale. Thus, the How Supplied section of the package insert lists twenty-four (24) units for the 300 mg/50 mL, 600 mg/50 mL, and 900 mg/50 mL strengths and the carton labels list twelve (12) units.

3- The carton labeling for the 300 mg, 600 mg and 900 mg strength already includes this change. The last two digits are the same for each strength. See Table 1 for Response 4 under Container Label.

From: Minor, Naseya [<mailto:Naseya.Minor@fda.hhs.gov>]
Sent: Friday, March 10, 2017 10:49 AM
To: John Oberholtzer <joberholtzer@celeritypharma.com>
Cc: Amber Sheriff <asheriff@celeritypharma.com>
Subject: RE: NDA 208083 Clindamycin Carton and Container Recommendations-Celerity Requests

Hi John,

I have an information request for you. Please provide clarification for the following:

We note that your email request specifically addresses three of our twelve Container Labels and Carton Labeling recommendations. What are your plans regarding our additional nine Container Labels and Carton Labeling recommendations?

You state that "The films for all three configurations of the Clindamycin in 0.9% Sodium Chloride Injection have been already ordered with current label printed on it due to the long printing lead time." Clarify if the "current" carton labeling and container labels you have ordered are the same as the labels and labeling that are referred to in the Agency's February 22, 2017 Container Labels and Carton Labeling recommendations.

What is the quantity of films for all three configurations of the Clindamycin in 0.9% Sodium Chloride Injection that you have already ordered? How does this translate into expected product use (b) (4) once on the market?

When do you expect to print new labels and labeling with the implemented Agency revisions? In addition, when would you expect this product with the updated container label and carton labeling to be shipped?

Given our review timelines, we request a response no later than Monday, March 13, 2017.

Thanks,

Naseya

From: John Oberholtzer [mailto:joberholtzer@celeritypharma.com]

Sent: Friday, February 24, 2017 12:48 PM

To: Minor, Naseya

Cc: Amber Sheriff

Subject: NDA 208083 Clindamycin Carton and Container Recommendations-Celerity Requests

Dear Naseya,

The container label text for Celerity's Clindamycin in 0.9% Sodium Chloride Injection product is printed on an interior layer of the GALAXY container film. The films for all three configurations of the Clindamycin in 0.9% Sodium Chloride Injection have been already ordered with current label printed on it due to the long printing lead time and to facilitate an expeditious launch of the proposed product following anticipated FDA approval (PDUFA goal date April 30, 2017). Also three (3) batches of the 900 mg strength have been manufactured as

(b) (4) Based on this, Celerity is respectfully requesting quick feedback on the following recommendations.

FDA's recommendations of 02/22/2017 are provided in **bold** followed by Celerity's requests.

All Container Labels and Carton Labeling

2. To provide clarity and decrease the potential of wrong technique or rate of administration medication errors, revise all of the statements "For Intravenous Use" to read "For Intravenous Infusion Only". We also recommend that you consider moving this statement, "For Intravenous Infusion Only", up prior to the container size (50 mL) and description (Single-Dose Container) or increase the prominence of this important information. In addition, we recommend removing the statement "Not for rapid injection or Intravenous push" due to post-marketing reports that negative statements (e.g., do not) may have the opposite of the intended meaning because the word "not" can be overlooked and misinterpret the warning as an affirmative action.

Celerity's Request

Since the recommended changes for the statements (b) (4) are also currently present in the RLD labeling (CLEOCIN; NDA 50639), would it be acceptable for Celerity to defer the change for the 300 mg, 600 mg and 900 mg container and carton labeling at this point? Celerity acknowledges the Agency's recommendation and commits to implement the change

immediately upon completion of manufacturing of the first three (b) (4) batches of each 300 mg, 600 mg and 900 mg strength (b) (4)

Container Label

to help decrease the potential of wrong drug medication errors, we recommend increasing the prominence of the product name, "Clindamycin in 0.9% Sodium Chloride Injection", so that it is the most prominent information on the principal display panels for all three strength presentations.

Celerity's Request

Celerity assessed this recommendation with respect to the width of the container die line. We concluded that it adds more clutter as the product name with the current font size and is a perfect fit within the die line. If we increase the font size, part of the product name will shift to the next line. As a result, it will not allow space for remaining text to fit appropriately within the die line. Hence, we would propose to not implement this change for all three strengths as the current font is the maximum size text that allows the product name to fit on the same line.

3. To increase the prominence of this information and align with the Reference Listed Drug (RLD) container label consider moving the statements "Cautions: Do not add supplementary medication. Must not be used in series connections. Check for minute leaks and solution clarity." to precede the statement "Each 50 mL contains: Clindamycin phosphate, USP..."

Celerity's Request

Celerity prefers to keep the Cautions statement after the Dosage information based on our interpretation of the guidance document titled "Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors". Per the guidance, the first portion of the statement "Do not add supplementary medication." is essential. The second portion "Must not be used in series connections. Check for minute leaks and solution clarity." is considered less essential. Therefore, we prefer to keep this Cautions statement after the Dosage information to make it easier for the physician to read. We acknowledge the Agency comment; however, we believe this would not affect the safety of the product in its current state. If the Agency does not agree with this proposal, would it be acceptable if we implement the change immediately upon completion of manufacturing of first three (b) (4) batches of each 300 mg, 600 mg and 900 mg strengths and also commit to submit the change to the Agency in a subsequent annual report?

Please provide feedback as soon as possible. Your consideration of our requests will greatly help us. We look forward to hearing from you.

Best Regards,

From: Minor, Naseya [mailto:Naseya.Minor@fda.hhs.gov]
Sent: Wednesday, February 22, 2017 10:57 AM
To: John Oberholtzer <joberholtzer@celeritypharma.com>
Subject: NDA 208083 Clindamycin Carton and Container Recommendations

John,

We have reviewed the carton and container labels and have concluded there are areas in the labels which can be improved to minimize the risk of medication errors. We have the following recommendations:

All Container Labels and Carton Labeling

1. The font of the strength statement “300 mg per 50 mL (6 mg/mL)” appears to be a (b) (4) font which is difficult to read. To aid in readability and help to decrease the potential for wrong strength medication errors, we recommend changing the text “300 mg per 50 mL (6 mg/mL)” to more prominent font and/or color that does not overlap with that used for the proprietary name and differentiates compared to the 600 mg and 900 mg/50 mL strengths.
2. To provide clarity and decrease the potential of wrong technique or rate of administration medication errors, revise all of the statements “For Intravenous Use” to read “For Intravenous Infusion Only”. We also recommend that you consider moving this statement, “For Intravenous Infusion Only”, up prior to the container size (50 mL) and description (Single-Dose Container) or increase the prominence of this important information. In addition, we recommend removing the statement “Not for rapid injection or Intravenous push” due to post-marketing reports that negative statements (e.g., do not) may have the opposite of the intended meaning because the word “not” can be overlooked and misinterpret the warning as an affirmative action.
3. The location for the lot number and expiration date is not provided on the proposed container label and carton labeling that was submitted. The lot number statement and expiration date are required on the immediate container and carton labeling per 21 CFR 201.10(i)(1) and 21 CFR 201.17, respectively. Include the intended location for the lot number and expiration date on the container label and carton labeling.
4. Our post-marketing experience indicates that similarity of the product code (middle 3-4 digits) of the National Drug Code (NDC) has led to selecting and dispensing of the wrong strength and wrong drug. The middle digits are traditionally used by healthcare providers to check the correct product, strength, and formulation. Therefore, assignment of sequential numbers for the middle digits is not an effective differentiating feature (e.g., (b) (4)). If these numbers cannot be revised, increase the prominence of the middle digits by increasing their font size in comparison to the remaining digits and putting them in bold type. As an example: (b) (4).
5. To provide clarity, revise the Storage statement by inserting the Centigrade symbol (C) after the 20° and Fahrenheit symbol (F) after the 68°, to read: “Store at 20°C to 25°C (68°F to 77°F)[see USP Controlled Room Temperature]. Avoid temperatures above 30°C.”

Container Label

1. To help decrease the potential of wrong drug medication errors, we recommend increasing the prominence of the product name, “Clindamycin in 0.9% Sodium Chloride Injection”, so that it is the most prominent information on the principal display panels for all three strength presentations.
2. To provide (b) (4)
3. To increase the prominence of this information and align with the Reference Listed Drug (RLD) container label consider moving the statements “Cautions: Do not add supplementary medication. Must not be used in series connections. Check for minute leaks and solution clarity.” to precede the statement “Each 50 mL contains: Clindamycin phosphate, USP...”
4. The currently assigned NDC package codes (last 1-2 digits) are different (3, 6, and 9). As the last 1-2 digits are intended to represent the container size, we recommend that you consider revising these numbers to be the same for all three strengths in representing their identical (50 mL) container size.

Carton Labeling

1. To improve readability of the statement “...USP equivalent to 900 mg clindamycin 9 mg sodium...” that currently appears on the Right Panel of the 900 mg/50 mL carton labeling, we recommend inserting a comma

between "clindamycin" and "9 mg" on the Right Panel of the proposed 900 mg carton label so that it reads "...900 mg clindamycin, 9 mg sodium..."

2. The carton labeling indicates inclusion of 12 containers per carton, however Section 16, How Supplied/Storage and Handling, of your proposed Full Prescribing Information indicates 24 containers per carton. This information will need to be clarified and appropriate changes submitted.
3. The currently assigned NDC package codes (last 1-2 digits) are different (4, 5, and 7). As the last 1-2 digits are intended to represent the carton size, we recommend that you consider revising these numbers to be the same for all three strengths in representing their identical (12 count) carton size. In addition, we recommend that this package code be different than the container label as the container label of one unit and the carton labeling of 12 units should have different NDC numbers.

Please submit revised carton and container labels by March 8, 2017.

Thanks,

Naseya Minor, MPH

Regulatory Health Project Manager

Center for Drug Evaluation and Research
Office of Antimicrobial Products | Division of Anti-Infective Products
White Oak Building 22, Room 6219
Tel: 301-796-0756
Naseya.Minor@fda.hhs.gov



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Minor, Naseya

From: Minor, Naseya
t: Friday, March 10, 2017 11:49 AM
'John Oberholtzer'
Cc: Amber Sheriff
Subject: RE: NDA 208083 Clindamycin Carton and Container Recommendations-Celerity Requests

Hi John,

We have an information request for you. Please provide clarification for the following:

We note that your email request specifically addresses three of our twelve Container Labels and Carton Labeling recommendations. What are your plans regarding our additional nine Container Labels and Carton Labeling recommendations?

You state that "The films for all three configurations of the Clindamycin in 0.9% Sodium Chloride Injection have been already ordered with current label printed on it due to the long printing lead time." Clarify if the "current" carton labeling and container labels you have ordered are the same as the labels and labeling that are referred to in the Agency's February 22, 2017 Container Labels and Carton Labeling recommendations.

What is the quantity of films for all three configurations of the Clindamycin in 0.9% Sodium Chloride Injection that you have already ordered? How does this translate into expected product use (b) (4) once on the market?

When do you expect to print new labels and labeling with the implemented Agency revisions? In addition, when would you expect this product with the updated container label and carton labeling to be shipped?

In our review timelines, we request a response no later than Monday, March 13, 2017.

Thanks,

Naseya

From: John Oberholtzer [mailto:jobertoltzer@celeritypharma.com]
Sent: Friday, February 24, 2017 12:48 PM
To: Minor, Naseya
Cc: Amber Sheriff
Subject: NDA 208083 Clindamycin Carton and Container Recommendations-Celerity Requests

Dear Naseya,

The container label text for Celerity's Clindamycin in 0.9% Sodium Chloride Injection product is printed on an interior layer of the GALAXY container film. The films for all three configurations of the Clindamycin in 0.9% Sodium Chloride Injection have been already ordered with current label printed on it due to the long printing lead time and to facilitate an expeditious launch of the proposed product following anticipated FDA approval (PDUFA goal date April 30, 2017). Also three (3) batches of the 900 mg strength have been manufactured as (b) (4). Based on this, Celerity is respectfully requesting quick feedback on the following recommendations.

FDA's recommendations of 02/22/2017 are provided in **bold** followed by Celerity's requests.

All Container Labels and Carton Labeling

2. To provide clarity and decrease the potential of wrong technique or rate of administration medication errors, revise all of the statements “For Intravenous Use” to read “For Intravenous Infusion Only”. We also recommend that you consider moving this statement, “For Intravenous Infusion Only”, up prior to the container size (50 mL) and description (Single-Dose Container) or increase the prominence of this important information. In addition, we recommend removing the statement “Not for rapid injection or Intravenous push” due to post-marketing reports that negative statements (e.g., do not) may have the opposite of the intended meaning because the word “not” can be overlooked and misinterpret the warning as an affirmative action.

Celerity’s Request

Since the recommended changes for the statements “For Intravenous Use” and “Not for rapid injection or Intravenous push” are also currently present in the RLD labeling (CLEOCIN; NDA 50639), would it be acceptable for Celerity to defer the change for the 300 mg, 600 mg and 900 mg container and carton labeling at this point? Celerity acknowledges the Agency’s recommendation and commits to implement the change immediately upon completion of manufacturing of the first three (b) (4) batches of each 300 mg, 600 mg and 900 mg strength and also commits to submit the change to the Agency in a subsequent annual report.

Container Label

1. To help decrease the potential of wrong drug medication errors, we recommend increasing the prominence of the product name, “Clindamycin in 0.9% Sodium Chloride Injection”, so that it is the most prominent information on the principal display panels for all three strength presentations.

Celerity’s Request

Celerity assessed this recommendation with respect to the width of the container die line. We concluded that it adds more clutter as the product name with the current font size and is a perfect fit within the die line. If we increase the font size, part of the product name will shift to the next line. As a result, it will not allow space for remaining text to fit appropriately within the die line. Hence, we would propose to not implement this change for all three strengths as the current font is the maximum size text that allows the product name to fit on the same line.

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Celerity’s Request

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Please provide feedback as soon as possible. Your consideration of our requests will greatly help us. We look forward to hearing from you.

Best Regards,

From: Minor, Naseya [mailto:Naseya.Minor@fda.hhs.gov]
Sent: Wednesday, February 22, 2017 10:57 AM
To: John Oberholtzer <joberholtzer@celeritypharma.com>
Subject: NDA 208083 Clindamycin Carton and Container Recommendations

Hi John,

We have reviewed the carton and container labels and have concluded there are areas in the labels which can be improved to minimize the risk of medication errors. We have the following recommendations:

All Container Labels and Carton Labeling

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2. To provide clarity and decrease the potential of wrong technique or rate of administration medication errors, revise all of the statements "For Intravenous Use" to read "For Intravenous Infusion Only". We also recommend that you consider moving this statement, "For Intravenous Infusion Only", up prior to the container size (50 mL) and description (Single-Dose Container) or increase the prominence of this important information. In addition, we recommend removing the statement "Not for rapid injection or Intravenous push" due to post-marketing reports that negative statements (e.g., do not) may have the opposite of the intended meaning because the word "not" can be overlooked and misinterpret the warning as an affirmative action.
3. The location for the lot number and expiration date is not provided on the proposed container label and carton labeling that was submitted. The lot number statement and expiration date are required on the immediate container and carton labeling per 21 CFR 201.10(i)(1) and 21 CFR 201.17, respectively. Include the intended location for the lot number and expiration date on the container label and carton labeling.
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5. To provide clarity, revise the Storage statement by inserting the Centigrade symbol (C) after the 20° and Fahrenheit symbol (F) after the 68°, to read: "Store at 20°C to 25°C (68°F to 77°F)[see USP Controlled Room Temperature]. Avoid temperatures above 30°C."

Container Label

1. To help decrease the potential of wrong drug medication errors, we recommend increasing the prominence of the product name, "Clindamycin in 0.9% Sodium Chloride Injection", so that it is the most prominent information on the principal display panels for all three strength presentations.

3. To increase the prominence of this information and align with the Reference Listed Drug (RLD) container label consider moving the statements "Cautions: Do not add supplementary medication. Must not be used in series connections. Check for minute leaks and solution clarity." to precede the statement "Each 50 mL contains: Clindamycin phosphate, USP..."
4. The currently assigned NDC package codes (last 1-2 digits) are different (3, 6, and 9). As the last 1-2 digits are intended to represent the container size, we recommend that you consider revising these numbers to be the same for all three strengths in representing their identical (50 mL) container size.

Carton Labeling

1. To improve readability of the statement "...USP equivalent to 900 mg clindamycin 9 mg sodium..." that currently appears on the Right Panel of the 900 mg/50 mL carton labeling, we recommend inserting a comma between "clindamycin" and "9 mg" on the Right Panel of the proposed 900 mg carton label so that it reads "...900 mg clindamycin, 9 mg sodium..."
2. The carton labeling indicates inclusion of 12 containers per carton, however Section 16, How Supplied/Storage and Handling, of your proposed Full Prescribing Information indicates 24 containers per carton. This information will need to be clarified and appropriate changes submitted.
3. The currently assigned NDC package codes (last 1-2 digits) are different (4, 5, and 7). As the last 1-2 digits are intended to represent the carton size, we recommend that you consider revising these numbers to be the same for all three strengths in representing their identical (12 count) carton size. In addition, we recommend that this package code be different than the container label as the container label of one unit and the carton labeling of 12 units should have different NDC numbers.

Please submit revised carton and container labels by March 8, 2017.

Thanks,

Naseya Minor, MPH

Regulatory Health Project Manager

Center for Drug Evaluation and Research
Office of Antimicrobial Products | Division of Anti-Infective Products
White Oak Building 22, Room 6219
Tel: 301-796-0756
Naseya.Minor@fda.hhs.gov



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communication does not reflect an intention by the sender to conduct a transaction or make any agreement by electronic means.

Minor, Naseya

From: Minor, Naseya
Sent: Thursday, December 15, 2016 3:02 PM
To: joberholtzer@celeritypharma.com
Subject: NDA 208083 Clindamycin Information Request

Hi John,

We have an information request for you for NDA 208083 Clindamycin

Please provide three samples of each of the following components:

Baxter's 50 mL single-port PL 2501 Plastic Bag (GALAXY)

A copy of the proposed container label (actual label)

A copy of the proposed carton label (actual label)

If the label is printed directly on the container, please provide a sample of the container (bag) with the printed label.

Please submit the samples directly to me by January 5, 2017.

Naseya Minor
Food and Drug Administration
Center for Drug Evaluation and Research
White Oak Building 22, Room: 6219
10903 New Hampshire Avenue
Silver Spring, Maryland
20903 zip code 20903 if shipping via United States Postal Service (USPS).
Use zip code 20993 if sending via any carrier other than USPS (e.g., UPS, DHL, FedEx).

Thanks,

Naseya Minor, MPH
Regulatory Health Project Manager

Center for Drug Evaluation and Research
Office of Antimicrobial Products | Division of Anti-Infective Products
White Oak Building 22, Room 6219
Tel: 301-796-0756
Naseya.Minor@fda.hhs.gov





Pre-NDA 208083

MEETING MINUTES

Celerity Pharmaceuticals, LLC
Attention: John Oberholtzer, J.D.
Senior Regulatory Affairs Manager
9450 W. Bryn Mawr Ave., Suite 640
Rosemont, IL 60018

Dear Mr. Oberholtzer:

Please refer to your Pre New Drug Application (NDA) meeting request dated November 21, 2014, for Clindamycin Injection in 0.9% Sodium Chloride in GALAXY container.

We also refer to the teleconference between representatives of your firm and the FDA on February 9, 2015. The purpose of the meeting was to discuss the bioequivalence plan, stability plan, and submission strategy for filing your NDA.

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

If you have any questions, call Naseya Minor, Regulatory Project Manager at (301) 796-0756.

Sincerely,

{See appended electronic signature page}

Sumathi Nambiar, MD, MPH
Director
Division of Anti-Infective Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Enclosure:
Meeting Minutes



FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

MEMORANDUM OF MEETING MINUTES

Meeting Type: Type B
Meeting Category: Pre-NDA

Meeting Date and Time: February 9, 2015, 9:00 a.m.– 10:00 a.m.
Meeting Location: Teleconference

Application Number: NDA 208083
Product Name: Clindamycin Injection in 0.9% Sodium Chloride in GALAXY Container
Indication: Treatment of serious infections caused by susceptible anaerobic bacteria

Sponsor/Applicant Name: Celerity Pharmaceuticals, LLC

Meeting Recorder: Naseya Minor

FDA ATTENDEES

Office of Antimicrobial Products

David Roeder, MS Associate Director of Regulatory Affairs

Division of Anti-Infective Products

Sumathi Nambiar, MD, MPH	Director
Katherine Laessig, MD	Deputy Director
Joseph Toerner, MD, MPH	Deputy Director for Safety
Thomas Smith, MD	Clinical Team Lead
Maria Allende, MD	Medical Officer
Kimberly Bergman, Pharm D	Clinical Pharmacology Team Lead
Kunyi Wu, Pharm D	Clinical Pharmacology Reviewer
Seong Jang, PhD	Clinical Pharmacology Reviewer
Kerry Snow, MS	Clinical Microbiology Team Lead
Jalal Sheikh, PhD	Clinical Microbiology Reviewer
Elsbeth Chikhale, PhD	Biopharmaceutics Team Lead
Maziar Kakhi, PhD	Biopharmaceutics Reviewer
Wendelyn Schmidt, PhD	Pharmacology Toxicology Team Lead
Amy Ellis, PhD	Pharmacology Toxicology Reviewer

Thamban Valappil, PhD
Mushfiqur Rashid, PhD
Balajee Shanmugam, PhD
Naseya Minor, MPH

Statistical Team Lead
Statistical Reviewer
CMC Team Lead
Regulatory Project Manager

Celerity Pharmaceuticals, LLC

Daniel Robins, PhD
Ambareen Sheriff
John Oberholtzer
George Monen
Gordon Johnston, RPh
Glenn Dennis

President
Vice President, Regulatory Affairs and Quality Assurance
Senior Regulatory Affairs Manager
Senior Product Development Manager
Regulatory Consultant
Manager, Global Regulatory Affairs

BACKGROUND

On November 21, 2014 Celerity submitted a pre-NDA Meeting Request for Clindamycin Injection in 0.9% Sodium Chloride in GALAXY container which was granted on December 29, 2014. The meeting purpose was to discuss the bioequivalence plan and stability plan including the timeline and filing strategy for the NDA.

FDA sent preliminary comments to the Sponsor on February 4, 2015. The Sponsor was in agreement with the Division's responses to questions 1, 2, 5, and 7. The meeting discussion consists of clarifications of the additional meeting responses. The Division's preliminary responses are in bold followed by the meeting discussion in italics.

DISCUSSION

**Chemistry, Manufacturing, and Controls
Question 3**

At the time of the submission of the 505(b)(2) application there will be 6 months room temperature ($25^{\circ}\text{C} \pm 2^{\circ}\text{C}/40\% \pm 5\%\text{RH}$), 3 months accelerated ($40^{\circ}\text{C} \pm 2^{\circ}\text{C}/20\% \pm 5\%\text{RH}$) stability data, 6 months intermediate ($30^{\circ}\text{C} \pm 2^{\circ}\text{C}/35\% \pm 5\%\text{RH}$) and 12 months data on the developmental batches. Celerity intends to file with this data and provide the 12 month data from the registration/stability batches as soon as it is available around March 2016 (3 months after the planned date of submission, December 2015). Celerity feels that

(b) (4)

data from the development batches. The list of batches on the development study is provided in [Table 4](#) below. There are no known stability issues with the Clindamycin Injection in 0.9% Sodium Chloride in a 50 mL plastic GALAXY container.

Stability data up to 6 months from the development study has been complete. The available data is provided as Attachment C. Twelve (12) months data from these batches will be provided in the original submission, as appropriate.

As can be seen from the provided data below in [Table 5](#) below, at the six (6) month time point, the stability data from the development study remains stable on all strengths (300 mg, 600 mg and 900 mg) when stored under room temperature conditions and trends similarly to the listed drug. The stability registration batch will be manufactured using the same equipment/process as was used for the development batches. The same equipment (b) (4) will be used for commercial production.

Under accelerated conditions, at the 3 month time point, the assay values for all strengths and the assays on the listed drug experienced a significant drop (b) (4) indicating that neither the listed drug nor the proposed product is able to withstand accelerated conditions. Therefore, in addition to the samples stored at accelerated conditions and long term conditions being tested, samples stored at intermediate conditions will also be tested on the stability/registration batches. The listed drug trended similarly also at the accelerated conditions.

Following ICH Q1A R2, does the Agency agree that providing stability data on 3 months accelerated, 6 months intermediate, 6 months long term on the registration batches and 12 months long term on development batches be an acceptable stability strategy to support filing of the NDA?

FDA Response: No we do not agree. At the time of submission, the NDA should provide complete CMC information including 12-months long-term stability data and 6-months accelerated stability data from three registration batches. Any available additional stability information can be provided as supportive data. Please note that we will not be able to accept any updates to the CMC section during review of the NDA.

(b) (4)

Clindamycin Injection in 0.9% Sodium Chloride is being introduced as an effort to improve safety and to provide for specific patient populations (e.g., diabetics, trauma patients, stroke victims and burn patients).

FDA Response: The review classification of the application will be determined once the NDA is filed.

Meeting discussion:

(b) (4)

Clinical Pharmacology

Question 6

In accordance with 21 CFR § 320.22(a), Celerity intends to request a waiver of the requirement to submit in vivo bioavailability/bioequivalence data for the proposed premixed Clindamycin Injection in 0.9% Sodium Chloride (300 mg/50 mL, 600 mg/50 mL, and 900 mg/50 mL) in a plastic GALAXY container drug product. This request is based on 21 CFR § 320.22(b), which states that for certain drug products, the in vivo bioavailability or bioequivalence of the drug product may be self-evident provided:

- (1) The drug product:
 - i. Is a parenteral solution intended solely for administration by injection, or an ophthalmic or otic solution; and
 - ii. 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 or abbreviated new drug application.

The proposed drug product's self-evident in vivo bioavailability/bioequivalence is based on the fact that the product is a sterile solution intended solely for intravenous administration 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 listed drug. The proposed product contains a different tonicity agent (Celerity's product has 0.9% Sodium Chloride vs. Pfizer's 5% Dextrose), which is not expected to lead to clinical differences. Data on product osmolality, pH, and total related substances are similar between the listed drug and Celerity's product. [Table 5](#) demonstrates the analytical similarities between Celerity's product and the listed drug CLEOCIN PHOSPHATE IV Solution. The data on Celerity's proposed product in [Table 5](#) is obtained from the test articles, listed in [Table 4](#), during the Clindamycin Injection in 0.9% Sodium Chloride development study. The

CLEOCIN data is obtained from the Clindamycin Injection in 5% Dextrose development study.

In addition to 21 CFR 320.22(b), Celerity cites 21 CFR 320.22(e), which allows for waivers of bioequivalence for products that are considered safe by the FDA (i.e., compatible with the public health). The agency's guidance on the most appropriate legal basis for the waiver is requested.

Does the Agency agree with this position?

FDA Response: We agree that your position to request a biowaiver of the requirement to conduct a bioequivalence study for your proposed drug product seems reasonable. As part of the biowaiver request, you should provide a justification in the NDA, with supporting data (e.g., published literature, study data, etc.), demonstrating that the differences in excipients (including, but not limited to, differences in drug-excipient chemical and physical interactions), pH, and osmolality between your proposed drug product and the listed drug product will not have any impact on the stability, pharmacokinetics, efficacy, and safety of your proposed product, as compared to those of the listed drug product. For ease of review, we recommend (where possible) a side-by-side comparison of the relevant data for your proposed and the listed drug products to support your biowaiver request.

Meeting discussion: The Sponsor plans to submit the biowaiver request under 21 CFR 320.22(e). The Division agreed to review the request at the time of NDA submission.

PRESCRIBING INFORMATION

In your application, you must submit proposed prescribing information (PI) that conforms to the content and format regulations found at 21 [CFR 201.56\(a\) and \(d\)](#) and [201.57](#). As you develop your proposed PI, we encourage you to review the labeling review resources on the [PLR Requirements for Prescribing Information](#) website including:

- The Final Rule (Physician Labeling Rule) on the content and format of the PI for human drug and biological products
- Regulations and related guidance documents
- A sample tool illustrating the format for Highlights and Contents, and
- The Selected Requirements for Prescribing Information (SRPI) – a checklist of 42 important format items from labeling regulations and guidances.

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

MANUFACTURING FACILITIES

To facilitate our inspectional process, we request that you clearly identify in a single location, either on the Form FDA 356h, or an attachment to the form, all manufacturing facilities

associated with your application. Include the full corporate name of the facility and address where the manufacturing function is performed, with the FEI number, and specific manufacturing responsibilities for each facility.

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

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

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

Corresponding names and titles of onsite contact:

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

505(b)(2) REGULATORY PATHWAY

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

If you intend to submit a 505(b)(2) application that relies for approval, in part, on FDA's finding of safety and/or effectiveness for one or more listed drugs, you must establish that such reliance is scientifically appropriate, and must submit data necessary to support any aspects of the

proposed drug product that represent modifications to the listed drug(s). You should establish a “bridge” (e.g., via comparative bioavailability data) between your proposed drug product and each listed drug upon which you propose to rely to demonstrate that such reliance is scientifically justified.

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

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

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

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

In addition to identifying in your annotated labeling the source(s) of information essential to the approval of your proposed drug that is provided by reliance on FDA’s previous finding of safety and efficacy for a listed drug or by reliance on published literature, we encourage you to also include that information in the cover letter for your marketing application in a table similar to the one below.

List the information essential to the approval of the proposed drug that is provided by reliance on the FDA’s previous finding of safety and efficacy for a listed drug or by reliance on published literature
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Source of information (e.g., published literature, name of listed drug)	Information Provided (e.g., specific sections of the 505(b)(2) application or labeling)
<i>1. Example: Published literature</i>	<i>Nonclinical toxicology</i>
<i>2. Example: NDA XXXXXX “TRADENAME”</i>	<i>Previous finding of effectiveness for indication X</i>
<i>3. Example: NDA YYYYYY “TRADENAME”</i>	<i>Previous finding of safety for Carcinogenicity, labeling section XXX</i>
<i>4.</i>	

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

There were no attachments or handouts during the teleconference meeting. The meeting concluded and the Sponsor thanked the Division for their feedback and useful comments.

POST MEETING NOTE

With regard to submitting the NDA

(b) (4)

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

/s/

SUMATHI NAMBIAR
03/03/2015