

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

***APPLICATION NUMBER:***

**209347Orig1s000**

**ADMINISTRATIVE and CORRESPONDENCE  
DOCUMENTS**

# ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION <sup>1</sup>		
NDA # 209347 BLA #	NDA Supplement # BLA Supplement #	If NDA, Efficacy Supplement Type: <i>(an action package is not required for SE8 or SE9 supplements)</i>
Proprietary Name: Established/Proper Name: GANCICLOVIR INJECTION Dosage Form: Intravenous		Applicant: Exela Pharma Sciences, LLC Agent for Applicant (if applicable):
RPM: Garrette Martin-Yeboah, PharmD, BCGP, PMP		Division: DAVP
NDA Application Type: <input type="checkbox"/> 505(b)(1) <input checked="" type="checkbox"/> 505(b)(2) Efficacy Supplement: <input type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2)		<b><u>For ALL 505(b)(2) applications, two months prior to EVERY action:</u></b> <ul style="list-style-type: none"> <li>• Review the information in the 505(b)(2) Assessment and submit the draft<sup>2</sup> to CDER OND IO for clearance.</li> <li>• Check Orange Book for newly listed patents and/or exclusivity (including pediatric exclusivity)</li> </ul> <p style="margin-top: 10px;"> <input checked="" type="checkbox"/> No changes  <input checked="" type="checkbox"/> New patent/exclusivity (<i>notify CDER OND IO</i>)          Date of check: 1/26/17       </p> <p style="margin-top: 10px;"><i>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.</i></p>
<b>❖ Actions</b> <ul style="list-style-type: none"> <li>• Proposed action</li> <li>• User Fee Goal Date is <u>2/19/17</u></li> </ul>		<input checked="" type="checkbox"/> AP <input type="checkbox"/> TA <input type="checkbox"/> CR
• Previous actions ( <i>specify type and date for each action taken</i> )		<input checked="" type="checkbox"/> None
<b>❖</b> 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 <a href="http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf">http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf</a> ). If not submitted, explain _____		<input type="checkbox"/> Received
<b>❖ Application Characteristics</b> <sup>3</sup>		

<sup>1</sup> 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.

<sup>2</sup> 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).

<sup>3</sup> 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 <i>(approvals only)</i>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
❖ Public communications <i>(approvals only)</i>	
<ul style="list-style-type: none"><li>Office of Executive Programs (OEP) liaison has been notified of action</li><li>Indicate what types (if any) of information were issued</li></ul>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No  <input checked="" type="checkbox"/> None <input type="checkbox"/> FDA Press Release <input type="checkbox"/> FDA Talk Paper <input type="checkbox"/> CDER Q&As <input type="checkbox"/> Other
❖ Exclusivity	
<ul style="list-style-type: none"><li>Is approval of this application blocked by any type of exclusivity (orphan, 5-year NCE, 3-year, pediatric exclusivity)?</li><li>If so, specify the type</li></ul>	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes
❖ Patent Information (NDAs only)	
<ul style="list-style-type: none"><li>Patent Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought.</li></ul>	<input checked="" type="checkbox"/> Verified <input type="checkbox"/> 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 <i>(approvals only)</i>	<input checked="" type="checkbox"/> Included
Documentation of consent/non-consent by officers/employees	<input checked="" type="checkbox"/> Included

<b>Action Letters</b>	
❖ Copies of all action letters ( <i>including approval letter with final labeling</i> )	Action(s) and date(s) Approval, 2/17/17
<b>Labeling</b>	
❖ Package Insert ( <i>write submission/communication date at upper right of first page of PI</i> ) <ul style="list-style-type: none"> <li>• Most recent draft labeling (<i>if it is division-proposed labeling, it should be in track-changes format</i>)</li> <li>• Original applicant-proposed labeling</li> </ul>	<input checked="" type="checkbox"/> Included
❖ Medication Guide/Patient Package Insert/Instructions for Use/Device Labeling ( <i>write submission/communication date at upper right of first page of each piece</i> ) <ul style="list-style-type: none"> <li>• Most-recent draft labeling (<i>if it is division-proposed labeling, it should be in track-changes format</i>)</li> <li>• Original applicant-proposed labeling</li> </ul>	<input type="checkbox"/> Medication Guide <input type="checkbox"/> Patient Package Insert <input type="checkbox"/> Instructions for Use <input type="checkbox"/> Device Labeling <input checked="" type="checkbox"/> None
❖ Labels ( <b>full color carton and immediate-container labels</b> ) ( <i>write submission/communication date on upper right of first page of each submission</i> ) <ul style="list-style-type: none"> <li>• Most-recent draft labeling</li> </ul>	<input checked="" type="checkbox"/> Included
❖ Proprietary Name <ul style="list-style-type: none"> <li>• Acceptability/non-acceptability letter(s) (<i>indicate date(s)</i>)</li> <li>• Review(s) (<i>indicate date(s)</i>)</li> </ul>	Under review
❖ Labeling reviews ( <i>indicate dates of reviews</i> )	RPM: <input checked="" type="checkbox"/> PLR Format Review 6/30/16 DMEPA: <input checked="" type="checkbox"/> 9/22/16; 12/6/16, 1/30/17 DMPP/PLT (DRISK): None OPDP: <input checked="" type="checkbox"/> 1/23/17 SEALD: None CSS: None Product Quality <input checked="" type="checkbox"/> 1/17/17 (see integrated quality assessment; drug product/labeling review) and 1/26/17 (standalone labeling review not included in integrated quality assessment) Other: None
<b>Administrative / Regulatory Documents</b>	
❖ RPM Filing Review <sup>4</sup> /Memo of Filing Meeting ( <i>indicate date of each review</i> )	7/1/16
❖ All NDA 505(b)(2) Actions: Date each action cleared by 505(b)(2) Clearance Committee	2/2/17
❖ NDAs/NDA supplements only: Exclusivity Summary ( <i>signed by Division Director</i> )	<input checked="" type="checkbox"/> Completed <b>(Do not include)</b>
❖ Application Integrity Policy (AIP) Status and Related Documents <a href="http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm">http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm</a>	

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

<ul style="list-style-type: none"> <li>• Applicant is on the AIP</li> <li>• This application is on the AIP <ul style="list-style-type: none"> <li>○ If yes, Center Director's Exception for Review memo (<i>indicate date</i>)</li> <li>○ If yes, OC clearance for approval (<i>indicate date of clearance communication</i>)</li> </ul> </li> </ul>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Not an AP action
<b>❖ Pediatrics (approvals only)</b> <ul style="list-style-type: none"> <li>• Date reviewed by PeRC <u>11/9/16</u> If PeRC review not necessary, explain: _____</li> </ul>	
<b>❖ Breakthrough Therapy Designation</b> <ul style="list-style-type: none"> <li>• Breakthrough Therapy Designation Letter(s) (granted, denied, an/or rescinded)</li> <li>• CDER Medical Policy Council Breakthrough Therapy Designation Determination Review Template(s) (<i>include only the completed template(s) and not the meeting minutes</i>)</li> <li>• 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>)</li> </ul> <p><i>(completed CDER MPC templates can be found in DARRTS as clinical reviews or on the <a href="#">MPC SharePoint Site</a>)</i></p>	<input checked="" type="checkbox"/> N/A
<b>❖ Outgoing communications:</b> 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> )	<ul style="list-style-type: none"> <li>• Info Request- Patent Certification, 2/14/17</li> <li>• Info Request-Labeling, 1/24/17</li> <li>• Info Request-Carton and Container, 1/23/17</li> <li>• Info Request-Proprietary Name, 1/6/17</li> <li>• Info Request, CMC, 1/5/17</li> <li>• Proprietary Name Ack. Letter, 1/4/17</li> <li>• Information Request-Labeling, 12/15/16</li> <li>• Info Request-NDA Hyperlinks, 11/28/16</li> <li>• Information Request-Labeling, 11/23/16</li> <li>• Info Request, CMC, 10/28/16</li> <li>• Info Request, Carton and Container 10/5/16</li> <li>• Info Request, CMC, 9/2/16</li> <li>• Info Request, CMC, 7/8/16</li> <li>• Filing Letter, 6/30/16</li> <li>• Info Request, Labeling, Ped. Waiver, 6/6/16</li> <li>• Info Request, Ped. Waiver, 6/3/16</li> <li>• Info Request, Label, Ped Waiver 6/3/16</li> <li>• Info Request Proprietary Name, PREA 5/4/16</li> <li>• NDA Acknowledgement Letter, 5/3/16</li> <li>• Info Request, Debarment Cert., 4/27/16</li> </ul>
<b>❖ Internal documents:</b> 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)	2/2/17, 505(b)(2) assessment 2/16/17, Exclusivity Board Memo
<b>❖ Minutes of Meetings</b> <ul style="list-style-type: none"> <li>• If not the first review cycle, any end-of-review meeting (<i>indicate date of mtg</i>)</li> <li>• Pre-NDA/BLA meeting (<i>indicate date of mtg</i>)</li> <li>• EOP2 meeting (<i>indicate date of mtg</i>)</li> <li>• Mid-cycle Communication (<i>indicate date of mtg</i>)</li> <li>• Late-cycle Meeting (<i>indicate date of mtg</i>)</li> </ul>	<input checked="" type="checkbox"/> N/A or no mtg <input checked="" type="checkbox"/> No mtg <input checked="" type="checkbox"/> No mtg <input checked="" type="checkbox"/> N/A <input checked="" type="checkbox"/> N/A

<ul style="list-style-type: none"> <li>Other milestone meetings (e.g., EOP2a, CMC focused milestone meetings) (indicate dates of mtgs)</li> </ul>	
<ul style="list-style-type: none"> <li>Advisory Committee Meeting(s)</li> </ul>	<input checked="" type="checkbox"/> No AC meeting
<b>Decisional and Summary Memos</b>	
<ul style="list-style-type: none"> <li>Office Director Decisional Memo (indicate date for each review)</li> </ul>	<input checked="" type="checkbox"/> None
<ul style="list-style-type: none"> <li>Division Director Summary Review (indicate date for each review)</li> </ul>	<input checked="" type="checkbox"/> 2/16/17
<ul style="list-style-type: none"> <li>Cross-Discipline Team Leader Review (indicate date for each review)</li> </ul>	<input checked="" type="checkbox"/> 1/27/17
<ul style="list-style-type: none"> <li>PMR/PMC Development Templates (indicate total number)</li> </ul>	<input checked="" type="checkbox"/> None
<b>Clinical</b>	
<ul style="list-style-type: none"> <li>Clinical Reviews <ul style="list-style-type: none"> <li>Clinical Team Leader Review(s) (indicate date for each review)</li> <li>Clinical review(s) (indicate date for each review)</li> <li>Social scientist review(s) (if OTC drug) (indicate date for each review)</li> </ul> </li> </ul>	<input checked="" type="checkbox"/> No separate review-see CDTL review 1/27/17 1/12/17 <input checked="" type="checkbox"/> None
<ul style="list-style-type: none"> <li>Financial Disclosure reviews(s) or location/date if addressed in another review OR If no financial disclosure information was required, check here <input checked="" type="checkbox"/> and include a review/memo explaining why not (indicate date of review/memo)</li> </ul>	CDTL Review 1/27/17 (page 7) MO Disclosure 2/10/17
<ul style="list-style-type: none"> <li>Clinical reviews from immunology and other clinical areas/divisions/Centers (indicate date of each review)<sup>5</sup></li> </ul>	<input checked="" type="checkbox"/> None
<ul style="list-style-type: none"> <li>Controlled Substance Staff review(s) and Scheduling Recommendation (indicate date of each review)</li> </ul>	<input checked="" type="checkbox"/> N/A
<ul style="list-style-type: none"> <li>Risk Management <ul style="list-style-type: none"> <li>REMS Documents and REMS Supporting Document (indicate date(s) of submission(s))</li> <li>REMS Memo(s) and letter(s) (indicate date(s))</li> <li>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)</li> </ul> </li> </ul>	<input checked="" type="checkbox"/> None
<ul style="list-style-type: none"> <li>OSI Clinical Inspection Review Summary(ies) (include copies of OSI letters to investigators)</li> </ul>	<input checked="" type="checkbox"/> None requested
<b>Clinical Microbiology</b>	<input type="checkbox"/> None
<ul style="list-style-type: none"> <li>Clinical Microbiology Team Leader Review(s) (indicate date for each review)</li> </ul>	<input checked="" type="checkbox"/> No separate review
<ul style="list-style-type: none"> <li>Clinical Microbiology Review(s) (indicate date for each review)</li> </ul>	<input checked="" type="checkbox"/> 12/13/16
<b>Biostatistics</b>	<input checked="" type="checkbox"/> None
<ul style="list-style-type: none"> <li>Statistical Division Director Review(s) (indicate date for each review)</li> </ul>	<input type="checkbox"/> No separate review
<ul style="list-style-type: none"> <li>Statistical Team Leader Review(s) (indicate date for each review)</li> </ul>	<input type="checkbox"/> No separate review
<ul style="list-style-type: none"> <li>Statistical Review(s) (indicate date for each review)</li> </ul>	<input type="checkbox"/> None

<sup>5</sup> 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).

<b>Clinical Pharmacology</b>		<input type="checkbox"/> None
❖ Clinical Pharmacology Division Director Review(s) ( <i>indicate date for each review</i> )		<input checked="" type="checkbox"/> No separate review
Clinical Pharmacology Team Leader Review(s) ( <i>indicate date for each review</i> )		<input checked="" type="checkbox"/> No separate review
Clinical Pharmacology review(s) ( <i>indicate date for each review</i> )		<input checked="" type="checkbox"/> 1/13/17
❖ OSI Clinical Pharmacology Inspection Review Summary ( <i>include copies of OSI letters</i> )		None requested
<b>Nonclinical</b>		<input type="checkbox"/> None
❖ Pharmacology/Toxicology Discipline Reviews		
• ADP/T Review(s) ( <i>indicate date for each review</i> )		<input checked="" type="checkbox"/> No separate review
• Supervisory Review(s) ( <i>indicate date for each review</i> )		<input checked="" type="checkbox"/> No separate review
• Pharm/tox review(s), including referenced IND reviews ( <i>indicate date for each review</i> )		<input checked="" type="checkbox"/> None 1/12/17
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer ( <i>indicate date for each review</i> )		<input checked="" type="checkbox"/> None
❖ Statistical review(s) of carcinogenicity studies ( <i>indicate date for each review</i> )		<input checked="" type="checkbox"/> No carc
❖ ECAC/CAC report/memo of meeting		<input checked="" type="checkbox"/> None Included in P/T review, page
❖ OSI Nonclinical Inspection Review Summary ( <i>include copies of OSI letters</i> )		<input checked="" type="checkbox"/> None requested
<b>Product Quality</b>		<input type="checkbox"/> None
❖ Product Quality Discipline Reviews <sup>6</sup>		
• Tertiary review ( <i>indicate date for each review</i> )		<input checked="" type="checkbox"/> None
• Secondary review (e.g., Branch Chief) ( <i>indicate date for each review</i> )		<input checked="" type="checkbox"/> None
• Integrated Quality Assessment (contains the Executive Summary and the primary reviews from each product quality review discipline) ( <i>indicate date for each review</i> )		<ul style="list-style-type: none"> <li>• Executive Summary 1/19/17</li> <li>• Drug Substance Review 1/4/17</li> <li>• Drug Product/Labeling Review 1/17/17</li> <li>• Process Review 10/5/16</li> <li>• Facilities Review 12/16/16</li> <li>• Biopharmaceutics Review 10/13/16</li> <li>• Microbiology Review 11/3/16</li> <li>• Final Risk Assessment 1/19/17</li> </ul>
❖ Reviews by other disciplines/divisions/Centers requested by product quality review team ( <i>indicate date of each review</i> )		<input checked="" type="checkbox"/> None

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

❖ Environmental Assessment (check one) (original and supplemental applications)	
<input checked="" type="checkbox"/> Categorical Exclusion ( <i>indicate review date</i> ) ( <i>all original applications and all efficacy supplements that could increase the patient population</i> )	1/10/17; see page 70-71 of integrated quality assessment
<input type="checkbox"/> Review & FONSI ( <i>indicate date of review</i> )	
<input type="checkbox"/> Review & Environmental Impact Statement ( <i>indicate date of each review</i> )	
❖ Facilities Review/Inspection	
<input checked="" type="checkbox"/> Facilities inspections ( <i>indicate date of recommendation; within one week of taking an approval action, confirm that there is an acceptable recommendation before issuing approval letter</i> ) ( <i>only original applications and efficacy supplements that require a manufacturing facility inspection(e.g., new strength, manufacturing process, or manufacturing site change)</i> )	<input checked="" type="checkbox"/> Acceptable 12/16/17 <input type="checkbox"/> Withhold recommendation <input type="checkbox"/> Not applicable

Day of Approval Activities	
❖ For all 505(b)(2) applications: <ul style="list-style-type: none"><li>Check Orange Book for newly listed patents and/or exclusivity (including pediatric exclusivity)</li></ul>	<input checked="" type="checkbox"/> No changes <input type="checkbox"/> New patent/exclusivity ( <i>Notify CDER OND IO</i> ) <i>Check once more on approval date</i>
• Finalize 505(b)(2) assessment	<input checked="" type="checkbox"/> Done
❖ For Breakthrough Therapy (BT) Designated drugs: <ul style="list-style-type: none"><li>Notify the CDER BT Program Manager</li></ul>	<input checked="" type="checkbox"/> N/A ( <i>Send email to CDER OND IO</i> )
❖ For products that need to be added to the flush list (generally opioids): <a href="#">Flush List</a> <ul style="list-style-type: none"><li>Notify the Division of Online Communications, Office of Communications</li></ul>	<input checked="" type="checkbox"/> N/A
❖ Send a courtesy copy of approval letter and all attachments to applicant by fax or secure email	<input checked="" type="checkbox"/> Done
❖ If an FDA communication will issue, notify Press Office of approval action after confirming that applicant received courtesy copy of approval letter	<input checked="" type="checkbox"/> N/A
❖ 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	<input checked="" type="checkbox"/>
❖ Ensure Pediatric Record is accurate	<input checked="" type="checkbox"/> Done
❖ Send approval email within one business day to CDER-APPROVALS	<input checked="" type="checkbox"/> Done

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

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/s/

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GARRETTE F MARTIN-YEBOAH

02/21/2017

**DEPARTMENT OF HEALTH & HUMAN SERVICES**  
**Public Health Service**  
**Food and Drug Administration**  
**Center for Drug Evaluation and Research**



**DATE:** February 16, 2017

**TO:** Ganciclovir injection 500mg/250ml (NDA 209347) File  
Valganciclovir Hydrochloride (HCl) (NDAs 22257 and 21304) File

**FROM:** CDER Exclusivity Board

**SUBJECT:** Whether the 3-year exclusivity for Valcyte (valganciclovir HCl, NDAs 22257 and 21304) blocks the approval of Ganciclovir injection 500mg/250ml (NDA 209347)

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This memorandum addresses whether the unexpired 3-year exclusivity recognized by the Food and Drug Administration (FDA or the Agency) for Valcyte (valganciclovir HCl, new drug applications (NDAs) 22257 (for oral solution) and 21304 (tablets)) (Valcyte) blocks the approval of ganciclovir injection 500mg/250ml (NDA 209347) (Exela Pharma Sciences, LLC's (Exela's) Ganciclovir). For the reasons discussed below, the Exclusivity Board (Board) within the Center for Drug Evaluation and Research (CDER), in consultation with the Division of Antiviral Products (DAVP or Division), has determined that Exela's 505(b)(2) application for Ganciclovir should not be blocked by any unexpired 3-year exclusivity for Valcyte.

**I. Factual Background**

**A. Valcyte**

Valcyte contains a single active ingredient, valganciclovir HCl, and a single active moiety, ganciclovir.<sup>1</sup> Valcyte, which was first approved in 2001, has indications for both adult and pediatric populations. In adults, it is indicated for: (1) the treatment of cytomegalovirus (CMV) retinitis in patients with acquired immunodeficiency syndrome (AIDS), and (2) prevention of CMV disease in kidney, heart, and kidney-pancreas transplant patients at high risk (donor CMV

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<sup>1</sup> Valganciclovir HCl is “a hydrochloride salt of the L-valyl ester of ganciclovir that exists as a mixture of two diastereomers.” See Valcyte Labeling, Section 11.

seropositive/recipient CMV seronegative). In pediatric populations, it is indicated for the prevention of CMV disease in kidney and heart transplant patients at high risk.<sup>2</sup>

On April 23, 2015, FDA approved supplement 11 to NDA 21304 and supplement 5 to NDA 22257. The supplements “expand the Indications and Usage to include heart transplant patients from 1 month to 4 months of age and . . . extend the duration of dosing regimen from 100 days to 200 days post-transplantation for the prevention of CMV disease in pediatric kidney transplant patients 4 months to 16 years of age.”<sup>3</sup> FDA previously determined that the supplements qualified Valcyte for 3-year exclusivity, which expires on April 23, 2018. The 3-year exclusivity is denoted in FDA’s *Approved Drug Products with Therapeutic Equivalence Evaluations* (the Orange Book) by two exclusivity codes: (1) D-148 (“extended the duration of the dosing regimen from 100 days to 200 days post-transplantation for the prevention of CMV disease in pediatric kidney transplant”), and (2) NPP, new patient population. The D-148 exclusivity code relates to the extension of the dosing regimen from 100 days to 200 days post-transplantation for the prevention of CMV diseases in pediatric kidney transplant patients aged 4 months to 16 years. The NPP exclusivity code relates to the expansion of the heart transplant indication for pediatric patients 1 month to 4 months of age.

#### B. Ganciclovir

On April 16, 2016, Exela submitted a 505(b)(2) NDA for ganciclovir injection. The Prescription Drug User Fee Act (PDUFA) goal date is February 19, 2017. The applicant is seeking approval for its ganciclovir injection product for the treatment of CMV retinitis in immunocompromised adult patients, including patients with AIDS, and prevention of CMV disease in adult transplant recipients at risk for CMV disease. The product contains ganciclovir as its single active ingredient and ganciclovir as its single active moiety.

### II. Legal and Regulatory Overview

The statute and regulations for 3-year exclusivity describe which original NDAs and supplements are eligible for 3-year exclusivity and which are barred or blocked from approval by that exclusivity.

For original NDAs, section 505(c)(3)(E)(iii) of the Federal Food, Drug & Cosmetic (FD&C) Act states:

*If an application submitted under subsection (b) [of this section] for a drug, which includes an active ingredient (including any ester or salt of the active ingredient) that has been approved in another application approved under subsection (b) [of this section], is approved after [September 24, 1984,] and if such application contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted*

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<sup>2</sup> See Valcyte Labeling, Section 1.

<sup>3</sup> Letter from FDA to Roche Palo Alto, LLC, available on drugs@fda at [http://www.accessdata.fda.gov/drugsatfda\\_docs/appletter/2015/021304Orig1s011,022257Orig1s005ltr.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/appletter/2015/021304Orig1s011,022257Orig1s005ltr.pdf).

*or sponsored by the applicant, the Secretary may not make the approval of an application submitted under subsection (b) [of this section] for the conditions of approval of such drug in the approved subsection (b) application effective before the expiration of three years from the date of the approval of the application under subsection (b) [of this section]* if the investigations described in clause (A) of subsection (b)(1) [of this section] and relied upon by the applicant for approval of the application were not conducted by or for the applicant and if the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted.<sup>4</sup>

The first clause (italicized) in section 505(c)(3)(E)(iii), often referred to as the eligibility clause, describes the applications eligible for 3-year exclusivity. In the 5-year new chemical entity (NCE) exclusivity context, FDA has interpreted the term “active ingredient” in the phrase “active ingredient (including any ester or salt of the active ingredient)” to mean active moiety. Under the eligibility clause in section 505(c)(3)(E)(iii), applications for single-entity drugs that are not eligible for 5-year NCE exclusivity (because they contain an active moiety “that has been approved in another application”) are eligible for 3-year exclusivity if they include new clinical investigations (other than bioavailability studies), essential to approval of the application, that were conducted or sponsored by or on behalf of the applicant. FDA’s implementing regulations further interpret certain aspects of the statutory language regarding eligibility for 3-year exclusivity.<sup>5</sup>

The second clause in section 505(c)(3)(E)(iii) (underlined), often referred to as the bar clause, describes which 505(b)(2) NDAs will be barred or blocked from approval by the 3-year exclusivity and thus describes the scope of 3-year exclusivity. The Agency’s interpretation of the bar clause and thus a determination of the scope of 3-year exclusivity under section 505(c)(3)(E)(iii) generally involves two aspects. One aspect of the scope inquiry focuses on the drug at issue. The phrase “such drug in the approved subsection (b) application” in the bar clause refers to the earlier use of the term “drug” in the eligibility clause. The “drug” in the eligibility clause refers to “a drug, which includes an active ingredient (including any ester or salt of the active ingredient) that has been approved in another application,” that is, the drug which includes a previously approved active moiety. FDA interprets this cross reference to mean that, for a single-entity drug to be potentially barred by 3-year exclusivity for another single-entity drug, the drug must contain the same active moiety as the drug with 3-year exclusivity.<sup>6</sup> Another aspect of the scope inquiry focuses on the new clinical investigations essential to approval conducted or sponsored by the applicant. Under this aspect of the inquiry, the scope of the new clinical investigations essential to approval conducted or sponsored by the applicant informs the “conditions of approval” relevant to 3-year exclusivity.

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<sup>4</sup> See Section 505(c)(3)(E)(iii) of the FD&C Act (emphasis added); see also 21 CFR 314.108(b)(4)(iv).

<sup>5</sup> See generally, 21 CFR 314.108.

<sup>6</sup> See Letter from Janet Woodcock, M.D., Director, CDER, FDA to William H. Carson, M.D., President & CEO, Otsuka Pharmaceutical Development & Commercialization, Inc. and Ralph S. Tyler, Esq., Venable L.L.P. (Oct. 5, 2015) (Docket No. FDA-2015-P-2482), aff’d *Otsuka Pharmaceutical Co., Ltd., et al v. FDA*, Case No. 1:15-cv-01688-KBJ (D.D.C. July 28, 2016) (upholding FDA’s interpretation of section 505(c)(3)(E)(iii) that, for a single-entity drug to be potentially barred by 3-year exclusivity for another single-entity drug, the drug must contain the same active moiety as the drug with 3-year exclusivity) (currently pending appeal).

For supplements to approved NDAs, section 505(c)(3)(E)(iv) of the FD&C Act states:

*If a supplement to an application approved under subsection (b) [of this section] is approved after [September 24, 1984,] and the supplement contains reports of new clinical investigations (other than bioavailability [sic] studies) essential to the approval of the supplement and conducted or sponsored by the person submitting the supplement, the Secretary may not make the approval of an application submitted under subsection (b) [of this section] for a **change approved in the supplement** effective before the expiration of three years from the date of the approval of the supplement under subsection (b) [of this section] . . . . [(emphasis added)].*

Although the statute and regulations use different words to describe 3-year exclusivity for an original NDA and a supplement to an NDA, FDA has taken a consistent approach to both types of applications in determining eligibility for 3-year exclusivity and scope. The eligibility clause in section 505(c)(3)(E)(iv) (italicized) corresponds to the eligibility clause in section 505(c)(3)(E)(iii) of the FD&C Act, except, among other things, in section 505(c)(3)(E)(iv), the word “supplement” is substituted for the word “application” in section 505(c)(3)(E)(iii). As with an original NDA, a supplement may be eligible for 3-year exclusivity if it contains reports of new clinical investigations (other than bioavailability studies) essential to approval of the supplement that were conducted or sponsored by the applicant submitting the supplement.

The bar clause of section 505(c)(3)(E)(iv) (underlined) describes 3-year exclusivity as blocking approval of a 505(b)(2) application for “a change approved in the supplement.” Although this language is not identical to the phrase “conditions of approval of such drug in the approved subsection (b) application” used in section 505(c)(3)(E)(iii), in determining the scope of exclusivity and which applications are barred, there are likewise two aspects of the inquiry. One aspect of the inquiry focuses on the drug at issue. Under FDA’s interpretation of section 505(c)(3)(E)(iv) of the FD&C Act, for a single-entity drug to be potentially barred by 3-year exclusivity for another single-entity drug, the drug must contain the same active moiety as the drug with 3-year exclusivity. If the 505(b)(2) application for a single-entity drug seeks approval for the same drug (active moiety) to which exclusivity has attached, then the second aspect of the scope inquiry applies. This aspect of the scope inquiry focuses on the exclusivity-protected change approved in the supplement. FDA examines the conditions of approval supported by the new clinical investigations (other than bioavailability studies) that were essential to approval of the supplement. If the 505(b)(2) application for a single-entity drug is for the same drug for the same exclusivity-protected change approved in the supplement, it will be blocked. However, 3-year exclusivity does not block a 505(b)(2) application for the same drug that does not seek approval for the exclusivity-protected change approved in the supplement.

### **III. Discussion and Conclusion**

At issue here is whether the 3-year exclusivity for Valcyte blocks the approval of Exela’s 505(b)(2) application for Ganciclovir.

Although Valcyte and Exela's Ganciclovir have different active ingredients—valganciclovir HCl and ganciclovir, respectively—the products have the same active moiety, ganciclovir. Because the two products at issue contain the same active moiety, Exela's Ganciclovir could potentially be barred by Valcyte's unexpired 3-year exclusivity.

The Board must therefore consider whether the 505(b)(2) applicant is seeking approval for the exclusivity-protected changes approved in the supplements for Valcyte. The Board concludes that Exela is not seeking approval for the exclusivity-protected changes approved in the supplements. Valcyte's 3-year exclusivity relates to the new pediatric uses approved in the supplements. Exela is seeking approval of Ganciclovir for only adult indications: the treatment of CMV retinitis in immunocompromised adult patients, including patients with AIDS, and prevention of CMV disease in adult transplant recipients at risk for CMV disease. Exela is not seeking approval of Ganciclovir for any pediatric uses, and therefore, the conditions of approval for Ganciclovir are clearly outside the scope of Valcyte's 3-year exclusivity.

The Board recommends that any unexpired 3-year exclusivity for Valcyte should not block the approval of Exela's Ganciclovir injection 500mg/250ml (NDA 209347).

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/s/

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GARRETTE F MARTIN-YEBOAH

02/16/2017



DEPARTMENT OF HEALTH AND HUMAN SERVICES

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Food and Drug Administration  
Silver Spring MD 20993

NDA 209347

**INFORMATION REQUEST  
PATENT CERTIFICATION OR VERIFICATION**

Exela Pharma Sciences, LLC  
Attention: Phanesh Koneru, PhD, JD, LLM  
President and CEO  
1245 Blowing Rock Road  
Lenoir, NC 28645

Dear Dr. Koneru:

Please refer to your New Drug Application (NDA) dated April 18, 2016, received April 19, 2016, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA), for Ganciclovir Injection, 2mg/mL, 500mg/250mL.

We also refer to your amendments dated December 15, 2016, December 20, 2016, December 28, 2016, January 24, 2017 and January 25, 2017. These amendments do not comply with 21 CFR 314.60(f), which was added by the final rule on Abbreviated New Drug Applications and 505(b)(2) Applications; Final Rule, 81 FR 69580 (October 6, 2016). The final rule became effective on December 5, 2016.

Section 314.60(f) requires that an amendment to an unapproved 505(b)(2) application contain an appropriate patent certification or statement described in 21 CFR 314.50(i), or a “recertification” for a previously submitted paragraph IV certification, if approval is sought for changes described in any of the following types of amendments:

- To add a new indication or other condition of use;
- To add a new strength;
- To make other than minor changes in product formulation; or
- To change the physical form or crystalline structure of the active ingredient.

If an amendment to the 505(b)(2) application does not contain a patent certification (or recertification) or statement, the applicant must verify that the proposed change described in the amendment is not one of the types of amendments described above.

We recommend that the cover letter for your response to this information request and for future amendments to your unapproved 505(b)(2) application either: 1) states that the amendment contains a patent certification (or recertification) or statement required by 21 CFR 314.60(f)(1); or 2) verifies that the proposed change described in the amendment is not one of the types of

amendments described in 21 CFR 314.60(f)(1), as appropriate. Your response to this information request must clearly reference your amendments dated December 15, 2016, December 20, 2016, December 28, 2016, January 24, 2017 and January 25, 2017.

If you have any questions, contact me at (240) 402-2567.

Sincerely,

*{See appended electronic signature page}*

Garrette Martin-Yeboah, PharmD, BCGP, PMP  
Regulatory Project Manager  
Division of Antiviral Products  
Office of Antimicrobial Products  
Center for Drug Evaluation and Research

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/s/

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GARRETTE F MARTIN-YEBOAH

02/14/2017

## Martin-Yeboah, Garrette

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**From:** Martin-Yeboah, Garrette  
**Sent:** Tuesday, January 24, 2017 3:23 PM  
**To:** phanesh@exela.us  
**Cc:** Martin-Yeboah, Garrette; Thompson, Elizabeth  
**Subject:** NDA 209347 GANCICLOVIR INJECTION Proposed Labeling: Response Date of January 27, 2017  
**Attachments:** NDA 209347 Label to Sponsor with Track Changes\_1.24.17.pdf; NDA 209347 Label to Sponsor Clean Copy\_1.24.17.docx; NDA 209347 Label to Sponsor with Track Changes\_1.24.17.docx

Dear Dr. Koneru,

The Division's proposed labeling changes for the NDA 209347 (GANCICLOVIR INJECTION) label, submitted on December 20, 2016, are included in the attached PDF document. Two courtesy word copies of the document are also attached.

Please review the documents and provide a response by **Friday, January 27, 2017**.

**Note: If you have changes for the label, we request that you please make these changes in the clean Word copy of the document and be sure to show your edits in track changes.**

Please confirm receipt of this correspondence and contact me with any questions.

Kind regards,

Garrette Martin-Yeboah, PharmD, BCGP, PMP  
LCDR, USPHS Commissioned Corps  
Regulatory Project Manager  
Food and Drug Administration  
Center for Drugs Evaluation and Research  
Office of New Drugs/Office of Antimicrobial Products  
Division of Anti-Viral Products  
10903 New Hampshire Avenue  
WO22-RM6334  
Silver Spring, Maryland 20993  
Phone: 240-402-2567  
Fax: 301-796-9883

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23 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

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/s/

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GARRETTE F MARTIN-YEBOAH

01/24/2017

**DEPARTMENT OF HEALTH & HUMAN SERVICES**

Public Health Service

Division of Antiviral Products  
Food and Drug Administration  
Silver Spring MD 20993

**ELECTRONIC MAIL CORRESPONDENCE  
NDA ADVICE/INFORMATION REQUEST****NDA:** 209347**Drug:** Ganciclovir Injection**Date:** January 23, 2017**To:** **Phanesh Koneru, PhD, JD, LLM, President and CEO****Sponsor:** Exela Pharma Sciences**From:** Garrette Martin-Yeboah, PharmD, CGP, PMP, Regulatory Project Manager, DAVP**Subject: Comments to Applicant regarding Carton and Container Labeling**

Please refer to your NDA 209347 submission which contained proposed labeling for the product bag and overwrap. We recommend the following changes to the carton and container labeling at this time:

**A. Carton Labeling and Container Label**

- 1) Un-capitalize the first letter of each component and delete “USP” and “NF” for each component (active and inactives).
- 2) Revise storage to: Store at 20-25°C (68°-77°F).

We are providing the above information via electronic mail correspondence for your convenience. Please confirm receipt of this correspondence. If you have any questions regarding the contents of this transmission, please contact me at 240-402-2567 or 301-796-1500.

*{See appended electronic signature page}*

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Garrette Martin-Yeboah, PharmD, BCGP, PMP  
Regulatory Project Manager  
Division of Antiviral Products  
Office of Antimicrobial Products  
Center for Drug Evaluation and Research

1 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

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/s/

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GARRETTE F MARTIN-YEBOAH

01/23/2017

**From:** [Chaudhry, Danyal](#)  
**To:** [Phanesh Koneru](#); [Tracie Watkins](#)  
**Cc:** [Chaudhry, Danyal](#)  
**Subject:** RE: NDA 209347; Proprietary Name Review: Inforamtion Request  
**Date:** Friday, January 06, 2017 8:08:46 AM

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Thank you for the prompt response, Dr. Koneru. Kindly submit your response as a formal amendment to your application also.

Danyal

**From:** Phanesh Koneru [mailto:[phanesh@exela.us](mailto:phanesh@exela.us)]  
**Sent:** Thursday, January 05, 2017 9:33 PM  
**To:** Chaudhry, Danyal; Tracie Watkins  
**Subject:** Re: NDA 209347; Proprietary Name Review: Inforamtion Request

Dear Dr. Chaudhry:

Thank you for contacting me. I see the inconsistency as you noted. Even though we intended to pronounce as " [REDACTED] (b) (4)", it is more appropriate to pronounce it as " [REDACTED] (b) (4)". Please consider this communication as our request to change the pronunciation to " [REDACTED] (b) (4)".

If you like us to submit a formal response in addition to this email response, please let us know and we would do so promptly.

Sincerely, and best regards  
Phanesh

Phanesh Koneru, Ph.D., J.D., LL.M.  
President & CEO  
Exela Pharma Sciences, LLC  
1245 Blowing Rock Blvd  
Lenoir, NC 28645  
(828) 750-2436

On Thu, Jan 5, 2017 at 8:03 PM, Chaudhry, Danyal <[Danyal.Chaudhry@fda.hhs.gov](mailto:Danyal.Chaudhry@fda.hhs.gov)> wrote:  
Dear Dr. Koneru:

Reference is made to your request for proprietary name review submitted to NDA 209347 on December 16, 2016.

Clarification is needed on the intended pronunciation of the proposed proprietary name [REDACTED] (b) (4). You state "[REDACTED] (b) (4)" is the intended pronunciation; however, in regards to the name [REDACTED] (b) (4), is inconsistent with the sound made by [REDACTED] (b) (4). Additionally, you state [REDACTED] (b) (4)

The pronunciation of "[REDACTED] (b) (4)", appears to be consistent with how "[REDACTED] (b) (4)" in [REDACTED] (b) (4) would be pronounced. Please clarify if you intend for us to use the intended pronunciation submitted on December 16, 2016 or if you would like to submit a different pronunciation for us to consider during our review.

We request a response by Monday January 9, 2017 or sooner if possible.

Regards,

Danyal Chaudhry  
Safety Regulatory Project Manager  
OSE/CDER

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/s/

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GARRETTE F MARTIN-YEBOAH

02/02/2017



## DEPARTMENT OF HEALTH & HUMAN SERVICES

Sent: 01/05/2017 10:29:31 AM  
To: twatkins@exela.us  
CC: luz.e.rivera@fda.hhs.gov  
BCC:  
Subject: INFORMATION REQUEST NDA 209347

Food and Drug Administration  
Silver Spring, MD 20993

Good morning Ms. Watkins,

Please refer to your New Drug Application (NDA) 209347. We request additional information in order to continue our evaluation.

The following request is conveyed on behalf of the Product Quality review team:

- Provide two bag sample and overwrap of your proposed labeling

Provide the sample by Wednesday, January 11, 2017.

Submit the sample to the following address:

LCDR Luz E Rivera  
Food and Drug Administration  
Center for Drug Evaluation and Research  
White Oak Building 75, Room: 4649  
10903 New Hampshire Avenue  
Silver Spring, Maryland

Use 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).

Please acknowledge the receipt of this request.

Thank you,  
LCDR Luz E Rivera, Psy.D.  
Quality Assessment Lead (Acting), Div. I, Branch I  
Office of Program and Regulatory Operations

**Office of Pharmaceutical Quality  
Center for Drug Evaluation and Research**



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration  
Silver Spring MD 20993

NDA 209347

**PROPRIETARY NAME  
ACKNOWLEDGEMENT**

Exela Pharma Sciences, LLC.  
P.O. Box 818  
1245 Blowing Rock Blvd.  
Lenoir, NC 28645

ATTENTION: Phanesh Koneru, Ph.D, L.L.M  
President & CEO

Dear Dr. Koneru:

Please refer to your New Drug Application (NDA) dated April 18, 2016, received April 19, 2016, submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Ganciclovir Injection, 2 mg per mL.

We acknowledge receipt of your December 16, 2016, correspondence, received December 19, 2016, requesting a review of your proposed proprietary name, (b) (4).

The target date is March 19, 2017.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Danyal Chaudhry, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-3813. For any other information regarding this application, contact Garrette Martin-Yeboah, Regulatory Project Manager, in the Office of New Drugs at (240) 402-2567.

Sincerely,

*{See appended electronic signature page}*

Danyal Chaudhry, M.P.H.  
Safety Regulatory Project Manager  
Office of Surveillance and Epidemiology  
Center for Drug Evaluation and Research

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/s/

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AZEEM D CHAUDHRY

01/04/2017

## Martin-Yeboah, Garrette

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**From:** Martin-Yeboah, Garrette  
**Sent:** Thursday, December 15, 2016 10:28 PM  
**To:** phanesh@exela.us  
**Cc:** Martin-Yeboah, Garrette; Thompson, Elizabeth; Tyson, Victoria  
**Subject:** NDA 209347 GANCICLOVIR INJECTION Proposed Labeling: Response Date of December 20, 2016  
  
**Attachments:** Martin-YeboahG\_NDA 209347\_GANCICLOVIR INJECTION\_Label with Division Comments\_15DEC2016F.docx; Martin-YeboahG\_NDA 209347\_GANCICLOVIR INJECTION\_Label with Division Comments\_15DEC2016F.pdf

Dear Dr. Koneru,

The Division's proposed labeling changes for the NDA 209347 (GANCICLOVIR INJECTION) label, submitted on November 28, 2016, are included in the attached PDF document. A courtesy word copy of the document is also attached. Please review the documents and provide a response by **Tuesday, December 20, 2016**.

Please confirm receipt of this correspondence and contact me with any questions.

Kind regards,

Garrette Martin-Yeboah, PharmD, BCGP, PMP  
LCDR, USPHS Commissioned Corps  
Regulatory Project Manager  
Food and Drug Administration  
Center for Drugs Evaluation and Research  
Office of New Drugs/Office of Antimicrobial Products  
Division of Anti-Viral Products  
10903 New Hampshire Avenue  
WO22-RM6334  
Silver Spring, Maryland 20993  
Phone: 240-402-2567  
Fax: 301-796-9883

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GARRETTE F MARTIN-YEBOAH

12/15/2016

**From:** Tyson, Victoria  
**To:** ["phanesh@exela.us"](mailto:phanesh@exela.us)  
**Cc:** [Martin-Yeboah\\_Garrette](mailto:Martin-Yeboah_Garrette)  
**Subject:** NDA 209347/SDN 10-Ganciclovir Injection-NDA Problem-Hyperlinks  
**Date:** Monday, November 28, 2016 2:32:00 PM  
**Importance:** High

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Good afternoon Dr. Koneru,

Please note, the response to our request for information, SDN 10, dated 11/11/16 and received 11/14/16, contains hyperlinks that are not opening (Mod 1, 1.3.6.2). Also, there seems to be a missing page with responses to Q5 and 6 (Mod 1, 1.3.6.1) and no response in (Mod 1, 1.3.6.2).

Please check the hyperlinks and resubmit your response to this request as soon as possible. Thanks Vicky

*Victoria Tyson*  
Senior Regulatory Health Project Manager  
FDA/CDER/OAP/DAVP  
10903 New Hampshire Ave  
Bldg # 22, Room 6392  
Silver Spring, MD 20993-0002  
☎ 301-796-0827  
☎ 301-796-9883 (fax)  
✉ [victoria.tyson@fda.hhs.gov](mailto:victoria.tyson@fda.hhs.gov)

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/s/

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VICTORIA L TYSON

11/28/2016

## Martin-Yeboah, Garrette

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**From:** Martin-Yeboah, Garrette  
**Sent:** Wednesday, November 23, 2016 8:12 AM  
**To:** phanesh@exela.us  
**Cc:** Martin-Yeboah, Garrette; Tyson, Victoria; Thompson, Elizabeth  
**Subject:** NDA 209347 GANCICLOVIR INJECTION Proposed Labeling: Response Date of December 1, 2016  
**Attachments:** Martin-YeboahG\_NDA 209347\_Label with Division Comments\_23NOV2016.docx; Martin-YeboahG\_NDA 209347\_Label with Division Comments\_23NOV2016.pdf

Dear Dr. Koneru,

The Division's proposed labeling changes for the NDA 209347 (GANCICLOVIR INJECTION) label, submitted on August 1, 2016, are included in the attached PDF document. A courtesy word copy of the document is also attached.

Please review the documents and provide a response by **Thursday, December 1, 2016**.

Please confirm receipt of this correspondence and contact me with any questions. **Note:** Ensure that you copy both Victoria Tyson and Elizabeth Thompson on your response.

Kind regards,

Garrette Martin-Yeboah, PharmD, BCGP, PMP  
LCDR, USPHS Commissioned Corps  
Regulatory Project Manager  
Food and Drug Administration  
Center for Drugs Evaluation and Research  
Office of New Drugs/Office of Antimicrobial Products  
Division of Anti-Viral Products  
10903 New Hampshire Avenue  
WO22-RM6334  
Silver Spring, Maryland 20993  
Phone: 240-402-2567  
Fax: 301-796-9883

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GARRETTE F MARTIN-YEBOAH

11/23/2016



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration  
Silver Spring MD 20993

NDA 209347

**INFORMATION REQUEST**

Exela Pharma Sciences, LLC

Attention: Jonathan E. Sterling, Vice President of Quality and Regulatory Affairs  
P.O. Box 818  
1245 Blowing Rock Blvd.  
Lenoir, NC 28645

Dear Mr. Sterling:

Please refer to your New Drug Application (NDA) dated and received April 18, 2016, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Ganciclovir Injection.

We are reviewing the Chemistry Manufacturing and Controls section of your submission and have the following comments and information requests. We request a written response by **Thursday, November 10, 2016**, in order to continue our evaluation of your NDA.

1. Please revise the acceptance criteria for the visible particulates under the test of physical appearance and description to meet requirements of USP <790>.
2. Your specification for the pH is expressed as 7.5 (b) (4) but in the label and composition/ comparison a target of (b) (4) specified. Please make consistent.
3. You have stated in the NDA both that formulation is (b) (4) (3.2.P.8.1) and that it is (b) (4) (3.2.P.2.4). Your stability conclusions are to (b) (4) based on increased total impurities for one lot (b) (4), hence aluminum overpouch and labeling statements. Please reconcile 3.2.P.2.4 in NDA and provide data results from the other two lots.
4. In your summary table of extracted compounds (3.4 Extractables and Leachable section 3.2.P.7) you report that extractables in (b) (4) are not detected above the reporting limit. You further state that "no migration can be detected", although no migratory study (also referred to as leachable) report has been provided. If this information has been provided, please indicate the location. This drug product specific study was requested at Pre-IND/Pre-NDA meeting in 2013. We acknowledge your extractable testing of the raw material components and that they were found to be in

conformance to vendor's specification for extractables (these are potential leachable components that are extracted from the container closure and may migrate in the drug product). Please provide the leachable study results (actual components that migrate into the drug product) at the end of your proposed shelf life as determined for your drug product.

5. Additionally, we are unable to locate any of the approximately ten documents that are referenced by hyperlinks in the Container-Closure section (3.2.P.7). Provide copies of these reports as soon as possible, or indicate where they are located in your NDA submissions.
6. Please provide a stability update to include the 24 month time period.

If you have questions, call me at (240) 402-2691.

Sincerely,  
*{See appended electronic signature page}*

*LCDR Luz Rivera For*  
Florence Aisida, Pharm.D, BCPS  
Regulatory Business Process Manager  
Office of Program and Regulatory Operations  
Office of Pharmaceutical Quality  
Center for Drug Evaluation and Research



Luz  
Rivera

Digitally signed by Luz Rivera  
Date: 10/28/2016 01:25:33PM  
GUID: 502abbaa000025b89fdb52a977a3d336



## DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration  
Silver Spring, MD 20993

Sent: 10/28/2016 01:43:08 PM  
To: jsterling@exela.us  
CC: luz.e.rivera@fda.hhs.gov  
BCC:  
Subject: INFORMATION REQUEST NDA 209347

### NDA 209347 INFORMATION REQUEST

Exela Pharma Sciences, LLC  
Attention: Jonathan E. Sterling, Vice President of Quality and Regulatory Affairs  
P.O. Box 818  
1245 Blowing Rock Blvd.  
Lenoir, NC 28645

Dear Mr. Sterling:

Please refer to your New Drug Application (NDA) dated and received April 18, 2016, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Ganciclovir Injection.

Please find attached our Information Request.

Please acknowledge receipt of this request.

If you have any questions, please call me at (301) 796-4013 or email  
[luz.e.rivera@fda.hhs.gov](mailto:luz.e.rivera@fda.hhs.gov)

Sincerely,  
LCDR Luz E Rivera, Psy.D.  
Quality Assessment Lead (Acting)  
Office of Program and Regulatory Operations

Office of Pharmaceutical Quality  
Center for Drug Evaluation and Research

**DEPARTMENT OF HEALTH & HUMAN SERVICES**

Public Health Service

Division of Antiviral Products  
Food and Drug Administration  
Silver Spring MD 20993

**ELECTRONIC MAIL CORRESPONDENCE  
NDA ADVICE/INFORMATION REQUEST****NDA:** 209347**Drug:** Ganciclovir Injection**Date:** October 5, 2016**To:** Jonathan E. Sterling, Vice President of Quality and Regulatory Affairs**Sponsor:** Exela Pharma Sciences**From:** Garrette Martin-Yeboah, PharmD, CGP, PMP, Regulatory Project Manager, DAVP**Subject:** Comments to Applicant regarding Carton and Container Labeling

Please refer to your April 19, 2016, NDA 209347, submission which contained proposed labeling for the product bag and overwrap. We recommend the following changes to the carton and container labeling at this time:

**A. Carton Labeling and Container Label**

1. The presentation of the strength is missing from both the overwrap and container label as required per 21 CFR 201.15(a)(6). Present the strength as the amount of drug in the specified volume below the established name as follows: “500 mg per 250 mL (2 mg per mL)” per USP General Chapter <1> Injections.
2. Include the route of administration on the principal display panel (PDP) per 21 CFR 201.100(b)(3); and in addition include the statement, “Discard unused portion” as follows: “Single-dose for intravenous use only, discard unused portion of drug”
3. The strength of ganciclovir and sodium chloride in the equivalency statement are expressed with the use of a terminal zero, 2.0 mg and 8.0 mg, respectively. Remove all terminal zeros. The use of terminal zeros can lead to tenfold dosing errors when the decimal point goes unseen (e.g., 2.0 mL is seen as 20 mL).<sup>1</sup>
4. Adjust manufacturers name to be less prominent (font size) than the established name.

- Revise the principal display panel (PDP) to read:

Ganciclovir injection  
500 mg ganciclovir per 250 mL 0.8% sodium chloride solution  
(2 mg per mL)  
Single-dose for intravenous use only, discard unused portion of drug

#### **B. Container Label**

- The expiration date is required on the immediate container per 21 CFR 201.17 Add to the lower left hand corner of PDP.
- Similarly, add the lot number to the lower left corner on the immediate container.

#### **C. Carton (overwrap) Label**

- Include the statement “Leave bag in overwrap until use”
- Include recycling code symbol.

<sup>1</sup> ISMP—2014-15 Targeted Medication Safety Best Practices for Hospitals. Accessed: September 2016 at <http://www.ismp.org/tools/bestpractices/TMSBP-for-Hospitals.pdf>.

We are providing the above information via electronic mail correspondence for your convenience. Please confirm receipt of this correspondence. If you have any questions regarding the contents of this transmission, please contact me at 240-402-2567 or 301-796-1500.

*{See appended electronic signature page}*

---

Garrette Martin-Yeboah, PharmD, CGP, PMP  
Regulatory Project Manager  
Division of Antiviral Products  
Office of Antimicrobial Products  
Center for Drug Evaluation and Research

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

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/s/

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GARRETTE F MARTIN-YEBOAH

10/05/2016



## DEPARTMENT OF HEALTH & HUMAN SERVICES

---

Sent: 09/02/2016 11:19:41 AM

To: jsterling@exela.us

CC: Garrette.Martin-Yeboah@fda.hhs.gov

BCC: Bamidele.aisida@fda.hhs.gov

Subject: INFORMATION REQUEST NDA 209347

Food and Drug Administration  
Silver Spring, MD 20993

Please see attached and confirm receipt.

Florence Aisida, Pharm.D,BCPS

RBPM, Office of Program and Regulatory Operations

Office of Pharmaceutical Quality/CDER/FDA.

(240) 402-2691 |Bamidele.aisida@fda.hhs.gov



DEPARTMENT OF HEALTH AND HUMAN SERVICES

---

Food and Drug Administration  
Silver Spring MD 20993

NDA 209347

**INFORMATION REQUEST**

Exela Pharma Sciences, LLC

Attention: Jonathan E. Sterling, Vice President of Quality and Regulatory Affairs  
P.O. Box 818  
1245 Blowing Rock Blvd.  
Lenoir, NC 28645

Dear Mr. Sterling:

Please refer to your New Drug Application (NDA) dated and received April 18, 2016, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Ganciclovir Injection.

We are reviewing the Chemistry Manufacturing and Controls section of your submission and have the following comments and information requests. We request a written response in order to continue our evaluation of your NDA by Sept 14, 2016.

1. Please provide microbial ingress test data that validates integrity of the container closure system, including the bag and port. Include a description of challenge organism, number of bags tested, how positive control was breached and growth promotion results.
2. With regards to performance qualification of the [REDACTED] (b) (4)  
[REDACTED]  
studies is acknowledged. Please provide data for the [REDACTED] (b) (4)  
[REDACTED].
3. Please state the maximum length of time that the bulk drug solution may be held [REDACTED] (b) (4)  
[REDACTED].
4. With regards to endotoxin testing, please provide the dilution used for routine testing of the drug product.

5. Provide the hold time chemical stability data to support the proposed instructions  
stating (b) (4)

6. You stated that the (b) (4)

7. According to the (b) (4)

Clarify the discrepancy and revise appropriate sections in the proposed commercial master production record accordingly.

8. An instruction is noted in the (b) (4)

Revise the commercial batch

record to reflect the instruction.

If you have questions, call me at (240) 402-2691.

Sincerely,

Bamidele F.  
Aisida -A

Digital signature of Bamidele F. Aisida -A  
DN: c=US, o=U.S. Government, ou=HHS,  
ou=FDA, ou=People,  
0.92342.19200300.100.1.1=2001703308,  
cn=Bamidele F. Aisida -A  
Date: 2016.09.02 11:11:32 -04'00'

Florence Aisida, Pharm.D, BCPS  
Regulatory Business Process Manager  
Office of Program and Regulatory Operations  
Office of Pharmaceutical Quality  
Center for Drug Evaluation and Research



## DEPARTMENT OF HEALTH & HUMAN SERVICES

---

Sent: 07/08/2016 01:07:23 PM

To: jsterling@exela.us

CC: Garrette.Martin-Yeboah@fda.hhs.gov

BCC: Bamidele.aisida@fda.hhs.gov

Subject: NDA INFORMATION REQUEST

Food and Drug Administration  
Silver Spring, MD 20993

Please see attached and confirm receipt.

Florence Aisida, Pharm.D,BCPS

RBPM, Office of Program and Regulatory Operations

Office of Pharmaceutical Quality/CDER/FDA.

(240) 402-2691 |Bamidele.aisida@fda.hhs.gov



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration  
Silver Spring MD 20993

NDA 209347

**INFORMATION REQUEST**

Exela Pharma Sciences, LLC

Attention: Jonathan E. Sterling, Vice President of Quality and Regulatory Affairs  
P.O. Box 818  
1245 Blowing Rock Blvd.  
Lenoir, NC 28645

Dear Mr. Sterling:

Please refer to your New Drug Application (NDA) dated and received April 18, 2016, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Ganciclovir Injection.

We are reviewing the Chemistry Manufacturing and Controls section of your submission and have the following comments and information requests. We request a written response in order to continue our evaluation of your NDA by July 27, 2016.

1. With regards to the

(b) (4)

following:

addressing the

(b) (4)

2. The submitted biowaiver request is based on 21CFR§320.22(b), however, your proposed drug product (Ganciclovir Injection) does not contain the same concentration of active ingredient and same volume administered compared to the listed drug product (CYTOVENE-IV).

For example, based on the labeling of the listed drug product, the recommended initial dosage is 5 mg/kg for a 70 kg patient with normal renal function. Based on the labeling, a vial of 500 mg listed drug product will be reconstituted in 10 mL of sterile water to give a 50 mg/mL concentrated solution.

(b) (4)

(b) (4)

In order to evaluate the biowaiver request based on 21 CFR§320.24(b)(6), you need to provide the following supporting data/information:

- a. Physiochemical characteristics (i.e. pH and osmolality) of the reconstituted diluted infusion solution of the listed drug product compared to your proposed drug product. Justify any differences;
- b. Information indicating whether the differences (e.g. worst case scenario) in concentration of the active ingredient, administered volume, and infusion rate between the listed drug product and your proposed drug product do or do not affect the safety and efficacy of your proposed drug product.
3. Please note that (b) (4) was incorrectly described as an active ingredient in Description of 2.0 Batch Composition under 3.2.P.3.2 Batch Formula. Please state whether there are any other associated errors in NDA 209347.
4. We note that in the information submitted on June 10 (our Submission Number 4) there is a no document titled Control-Critical Steps.docx. Instead within the (b) (4) folder there is only “(b) (4).docx” which cannot be opened. Did you intend to resubmit the Control-Critical Steps document on June 10?
5. We also note that two documents within the June 10 submission have filenames so long that they cannot be copied to our PCs. For example:  
Pages from (b) (4).pdf  
Please keep filenames about 7 characters shorter than this example in the future.

If you have questions, call me at (240) 402-2691.

Sincerely,

Bamidele F.  
Aisida -A

  
Digitally signed by Bamidele F. Aisida -A  
DN: cn=US, o=U.S. Government, ou=HHS,  
ou=FDA, ou=People,  
0.9.2342.19200300.100.1.1=2001703308,  
cn=Bamidele F. Aisida -A  
Date: 2016.07.08 12:59:46 -04'00'

Florence Aisida, Pharm.D, BCPS  
Regulatory Business Process Manager  
Office of Program and Regulatory Operations  
Office of Pharmaceutical Quality  
Center for Drug Evaluation and Research



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration  
Silver Spring MD 20993

NDA 209347

**FILING COMMUNICATION -  
FILING REVIEW ISSUES IDENTIFIED**

Exela Pharma Sciences, LLC  
Attention: Jonathan Sterling  
Vice President of Quality and Regulatory Affairs  
1245 Blowing Road Blvd  
Lenoir, NC 28645

Dear Mr. Sterling:

Please refer to your New Drug Application (NDA) dated April 18, 2016, received April 19, 2016, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA), for Ganciclovir Injection, 2 mg/mL (500 mg/250 mL).

We also refer to your amendments dated May 4, 2016, May 6, 2016, June 10, 2016, and June 16, 2016.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, in accordance with 21 CFR 314.101(a), this application is considered filed 60 days after the date we received your application. The review classification for this application is **Standard**. Therefore, the user fee goal date is February 19, 2017.

We are reviewing your application according to the processes described in the Guidance for Review Staff and Industry: Good Review Management Principles and Practices for PDUFA Products. Therefore, we have established internal review timelines as described in the guidance, which includes the timeframes for FDA internal milestone meetings (e.g., filing, planning, mid-cycle, team and wrap-up meetings). Please be aware that the timelines described in the guidance are flexible and subject to change based on workload and other potential review issues (e.g., submission of amendments). We will inform you of any necessary information requests or status updates following the milestone meetings or at other times, as needed, during the process. If major deficiencies are not identified during the review, we plan to communicate proposed labeling and, if necessary, any postmarketing commitment requests by January 22, 2017.

During our filing review of your application, we identified the following potential review issues:

**Clinical/Nonclinical**

The label provided in your June 10, 2016 submission for ganciclovir (NDA 209347) is not

in requested format and structure of the Pregnancy and Lactation Labeling Rule (PLLR) (79 FR 72063) and you have not provided adequate information to support the labeling content for subsection 8.1 (Pregnancy), 8.2 (Lactation) and 8.3 (Females and Males of Reproductive Potential). Thus, your proposed PLLR labeling changes cannot be agreed upon until this information request is fulfilled. In this respect, 8.1 Pregnancy should have category classification removed, a risk summary describing human use recommendations should be presented followed by a comparison of animal studies to potential human exposure, and a data section that explains the animal data in detail. Section 8.2 Lactation should be added: this section should include an adequate risk summary similar to the current nursing mother's section, and should be followed with any publically available (human or animal) data. Section 8.3 Females and Males of Reproductive Potential should be added: this section should include any requirement or recommendation for pregnancy testing and/or contraception.

Your prescribing information (PI) must comply with the Pregnancy and Lactation Labeling Rule (PLLR) content and format requirements [see *Content and Format of Labeling for Human Prescription Drug and Biological Products, Requirements for Pregnancy and Lactation Labeling* (79 FR 72063, December 4, 2014), codified at 21 CFR 201.56 and 201.57(c)(9)]. Therefore, resubmit labeling in PLLR format by **August 1, 2016**. The submission should include a review and summary of the available published literature regarding drug use in pregnant and lactating women, a review and summary of reports from your pharmacovigilance database, and an interim or final report of an ongoing or closed pregnancy registry (if applicable), which should be located in Module 1. Refer to the *draft guidance for industry – Pregnancy, Lactation, and Reproductive Potential: Labeling for Human Prescription Drug and Biological Products – Content and Format* (<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM425398.pdf>).

1. Please submit with the updated label the following information (if it is not included in the Cytovene® - IV label):
  - A review and summary of the available published literature regarding ganciclovir use in pregnant and lactating women
  - A review and summary of relevant cases reported in your pharmacovigilance database.

We are providing the above comments to give you preliminary notice of potential review issues. Our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our review. Issues may be added, deleted, expanded upon, or modified as we review the application. If you respond to these issues during this review cycle, we may not consider your response before we take an action on your application.

## **PREScribing INFORMATION**

Your proposed prescribing information (PI) must conform 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\*](#) and [\*Pregnancy and Lactation Labeling Final Rule\*](#) websites, which include:

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

During our preliminary review of your submitted labeling, we have identified the following labeling issues and have the following labeling comments or questions:

1. 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:** Dosage and administration section contains no numerical identifiers in parentheses.*
2. The BW must have a title in UPPER CASE, following the word “WARNING” and other words to identify the subject of the warning. Even if there is more than one warning, the term “WARNING” and not “WARNINGS” should be used. For example: “**WARNING: SERIOUS INFECTIONS and ACUTE HEPATIC FAILURE**”. If there is more than one warning in the BW title, the word “and” in lower case can separate the warnings. The BW title should be centered.  
***Comment:** Other words to identify the subject of the warning are not present.*
3. The BW must always have the verbatim statement “See full prescribing information for complete boxed warning.” This statement must be placed immediately beneath the BW title, and should be centered and appear in italics.  
***Comment:** The statement "See full prescribing information for complete boxed warning" is not present.*

4. 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 which should be a toll-free number) or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).”**  
*Comment: Sponsor's listed phone number is not a toll-free number.*
5. The same title 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: The title for the BW that appears in HL and the FPI do not appear at the beginning of the TOC.*
6. 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 (for, of, to) and articles (a, an, the), or conjunctions (or, and)].  
*Comment: The word “in” for Section 8.6 needs to be capitalized “Use In Patients With Renal Impairment”*
7. The section and subsection headings in the TOC must match the section and subsection headings in the FPI.  
*Comment: Section 5.4 Laboratory Testing does not appear in the TOC.*
8. All text in the BW should be **bolded**.  
*Comment: The BW is not included in the FPI section.*
9. The BW must have a title in UPPER CASE, following the word “**WARNING**” and other words to identify the subject of the warning. (Even if there is more than one warning, the term, “**WARNING**” and not “**WARNINGS**” should be used.) For example: “**WARNING: SERIOUS INFECTIONS and ACUTE HEPATIC FAILURE**”. If there is more than one warning in the BW title, the word “and” in lower case can separate the warnings.  
*Comment: The BW is not included in the FPI section.*
10. When clinical trials adverse reactions data are included (typically in the “Clinical Trials Experience” subsection), the following verbatim statement (or appropriate modification) should precede the presentation of adverse reactions from clinical trials:

“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: The above statement was not included.*
11. When postmarketing adverse reaction data are included (typically in the “Postmarketing Experience” subsection), 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:** *The following statement is not included. The statement should be included verbatim with drug name inserted.*

We request that you resubmit labeling (in Microsoft Word format) that addresses these issues by **August 1, 2016**. 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.

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

Please respond only to the above requests for information. While we anticipate that any response submitted in a timely manner will be reviewed during this review cycle, such review decisions will be made on a case-by-case basis at the time of receipt of the submission.

## **PROMOTIONAL MATERIAL**

You may request advisory comments on proposed introductory advertising and promotional labeling. Please submit, in triplicate, a detailed cover letter requesting advisory comments (list each proposed promotional piece in the cover letter along with the material type and material identification code, if applicable), the proposed promotional materials in draft or mock-up form with annotated references, and the proposed package insert (PI). Submit consumer-directed, professional-directed, and television advertisement materials separately and send each submission to:

OPDP Regulatory Project Manager  
Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Prescription Drug Promotion (OPDP)  
5901-B Ammendale Road  
Beltsville, MD 20705-1266

Alternatively, you may submit a request for advisory comments electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft Guidance for Industry (available at:

<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf>.

Do not submit launch materials until you have received our proposed revisions to the package insert (PI), and you believe the labeling is close to the final version.

For more information regarding OPDP submissions, please see <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>. If you have any questions, call OPDP at 301-796-1200.

### **REQUIRED PEDIATRIC ASSESSMENTS**

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

We acknowledge receipt of your request for a full waiver of pediatric studies for this application. Once we have reviewed your request, we will notify you if the full waiver request is denied and a pediatric drug development plan is required.

If you have any questions, call Garrette Martin-Yeboah, PharmD, CGP, PMP, Regulatory Project Manager, at (240) 402-2567.

Sincerely,

*(See appended electronic signature page)*

Debra Birnkrant, MD  
Director  
Division of Antiviral Products  
Office of Antimicrobial Products  
Center for Drug Evaluation and Research

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

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/s/

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JEFFREY S MURRAY

06/30/2016

## **Martin-Yeboah, Garrette**

---

**From:** Martin-Yeboah, Garrette  
**Sent:** Monday, June 06, 2016 4:07 PM  
**To:** jsterling@exela.us  
**Cc:** Martin-Yeboah, Garrette; Thompson, Elizabeth  
**Subject:** NDA 209347 Telecon Summary

Dear Mr. Sterling,

It was a pleasure speaking with you and your colleague Tracy regarding NDA 209347. As stated during the teleconference, based on the issues noted during our review of the application, the Division requests that you please submit the following:

1. **Provide a written statement (by 6/10/16) to the Division stating that Exela will submit the labeling in SPL format** prior to the Action Date (2/19/17) for this NDA. All new NDA labeling is required to be submitted in SPL format.
2. **Provide the label in PLR/PLLR format** and forward a courtesy PDF copy via email.
3. **Complete Form 3542a** regarding patent information. This form was provided to Exela via email on 6/3/16. Although Exela states that no patents are pending at this time for the product, this form is required.
4. **Submit the full pediatric waiver request** and understand that mere submission of the waiver request will not satisfy all PREA requirements. A committee external to our office will review the waiver request and may recommend/require additional pediatric studies during their review. Exela states that a full pediatric waiver request will be submitted. The guidance regarding this submission was provided to Exela on 6/3/16 via email.
5. **Officially submit the sterilization/validation section for the CMC review** and forward a courtesy PDF copy via email.
6. Please follow-up regarding the nonfunctional hyperlinks in the submission.

The Division requests submission of the above items by **Friday, June 10, 2016**. Please confirm receipt of this correspondence and contact me with any questions.

Best regards,

Garrette Martin-Yeboah, PharmD, CGP, PMP  
LT, USPHS Commissioned Corps  
Regulatory Project Manager  
Food and Drug Administration  
Center for Drugs Evaluation and Research  
Office of New Drugs/Office of Antimicrobial Products  
Division of Anti-Viral Products  
10903 New Hampshire Avenue  
WO22-RM6391  
Silver Spring, Maryland 20993  
Phone: 240-402-2567  
Fax: 301-796-9883

### **NOTICE:**

*Secure email between CDER and sponsors is useful for informal communications when confidential information may be included in the message (for example, trade secrets or patient information). If you have not already established secure email with the FDA and*

would like to set it up, send an email request to [SecureEmail@fda.hhs.gov](mailto:SecureEmail@fda.hhs.gov). Please note that secure email may not be used for formal regulatory submissions to applications (except for 7-day safety reports for INDs not in eCTD format).

THIS MESSAGE IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED FROM DISCLOSURE UNDER LAW. If you are not the addressee, or a person authorized to deliver the document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please immediately notify the sender by e-mail or phone.

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/s/

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GARRETTE F MARTIN-YEBOAH

06/06/2016

## **Martin-Yeboah, Garrette**

---

**From:** Martin-Yeboah, Garrette  
**Sent:** Friday, June 03, 2016 2:22 PM  
**To:** jsterling@exela.us  
**Cc:** Martin-Yeboah, Garrette; Thompson, Elizabeth  
**Subject:** NDA 209347 Summary of 6/2/16 conversation and information request  
**Attachments:** Form FDA 3542a.pdf

Dear Mr. Sterling,

Thank you for speaking with me on 6/2/16. During our discussion, you confirmed the following:

- The revised label will be submitted in PLR/PLLR format on 6/2/16
- The sponsor does not plan to submit a proprietary name at this time
- No additional literature searches have been performed to determine new safety data since the approval of the reference listed drug.
- The sponsor plans to request a full pediatric study waiver and will amend the labeling for use of the Ganciclovir Injection only in adults.

### **Comments/Information Request**

Please do the following:

1. Submit the labeling in SPL format. Please refer to the language from the acknowledgement letter. This is a requirement and may be this may be a refuse to file issue.
  - If you have not already done so, promptly submit the content of labeling [21 CFR 314.50(l)(1)(i) in structured product labeling (SPL) format as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. Failure to submit the content of labeling in SPL format may result in a refusal-to-file action under 21CFR 314.101(d)(3). The content of labeling must conform to the content and format requirements of revised 21 CFR 201.56-57.
2. Submit your patent information per 21 CFR 314.53 on the appropriate form 3542a (attached above). The submitted patent information pertains to the reference listed drug which is required for 505 (b)(2) NDAs. However, no patent information was submitted related to Exela's proposed product and this is required for all NDA submissions (505 (b)(1) and 505 (b)(2)).
3. Clarify when the label in PLR/PLLR format will be submitted.

Please confirm receipt of this email and contact me with any questions.

Best regards,

Garrette Martin-Yeboah, PharmD, CGP, PMP  
LT, USPHS Commissioned Corps  
Regulatory Project Manager  
Food and Drug Administration  
Center for Drugs Evaluation and Research  
Office of New Drugs/Office of Antimicrobial Products  
Division of Anti-Viral Products

10903 New Hampshire Avenue  
WO22-RM6391  
Silver Spring, Maryland 20993  
Phone: 240-402-2567  
Fax: 301-796-9883

**NOTICE:**

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GARRETTE F MARTIN-YEBOAH

06/03/2016

## Martin-Yeboah, Garrette

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**From:** Martin-Yeboah, Garrette  
**Sent:** Friday, June 03, 2016 2:30 PM  
**To:** jsterling@exela.us  
**Cc:** Martin-Yeboah, Garrette; Thompson, Elizabeth  
**Subject:** NDA 209347 Pediatric Waiver Request Information

Dear Mr. Sterling,

The Pediatric Study Plan Guidance document states that “Sponsors seeking a full waiver of pediatric studies should complete only sections 1, 2, 4, and 12 of the iPSP template (see Appendix 1).” <http://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm360507.pdf>

The submission of a full waiver request with sections 1, 2, 4, and 12 of the iPSP template completed will be sufficient for your application.

Please confirm receipt of this email and note that the waiver request must be received prior to the filing date of June 18, 2016.

Best regards,

Garrette Martin-Yeboah, PharmD, CGP, PMP  
LT, USPHS Commissioned Corps  
Regulatory Project Manager  
Food and Drug Administration  
Center for Drugs Evaluation and Research  
Office of New Drugs/Office of Antimicrobial Products  
Division of Anti-Viral Products  
10903 New Hampshire Avenue  
WO22-RM6391  
Silver Spring, Maryland 20993  
Phone: 240-402-2567  
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GARRETTE F MARTIN-YEBOAH

06/03/2016



## DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Division of Antiviral Products  
Food and Drug Administration  
Silver Spring MD 20993

### ELECTRONIC MAIL CORRESPONDENCE NDA ADVICE/INFORMATION REQUEST

**NDA:** 209347

**Drug:** Ganciclovir Injection

**Date:** May 4, 2016

**To:** James Sterling, Vice President of Quality and Regulatory Affairs

**Sponsor:** Exela Pharma Sciences, LLC

**From:** Garrette Martin-Yeboah, PharmD, CGP, PMP, Regulatory Project Manager, DAVP

**Subject:** Request for Information-Labeling, PREA, and Proprietary Name submission

Please refer to your submission dated April 18, 2016, received April 19, 2016, which provided a new NDA for Ganciclovir Injection, 2 mg/mL (500 mg/250 mL) for the treatment of CMV retinitis in immunocompromised patients, including patients with AIDS, and for the prevention of CMV disease in transplant recipients at risk for CMV disease. Upon initial review of your submission, we have the following comments/requests for information: **(Please provide the requested materials prior to June, 3, 2016)**

#### Labeling/Prescribing Information

##### **1. Re-submit the proposed prescribing information (PI) in PLR/PLLR format.**

Your proposed prescribing information (PI) must conform 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 visit the labeling review resources websites [PLR Requirements for Prescribing Information](#) and [PLLR Requirements for Prescribing Information](#). Specifically, we refer your attention to:

- The Final Rule (Physician Labeling Rule) on the content and format of the PI for human drug and biological products
- The Final Rule (Pregnancy and Lactation Labeling Rule) on the content and format of information in the PI on pregnancy, lactation, and females and males of reproductive potential

- Regulations and related guidance documents
- A sample tool illustrating the format for Highlights and Contents
- The Selected Requirements for Prescribing Information (SRPI) – a checklist of important format items from labeling regulations and guidances and
- FDA's established pharmacologic class (EPC) text phrases for inclusion in the Highlights Indications and Usage heading.

## **PREA Requirements**

### **2. Submit an Initial Pediatric Study Plan (iPSP)**

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

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

For additional guidance on the timing, content, and submission of the PSP, including a PSP Template, please refer to the draft guidance for industry, Pediatric Study Plans: Content of and Process for Submitting Initial Pediatric Study Plans and Amended Pediatric Study Plans at: <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM360507.pdf>. In addition, you may contact the Division of Pediatric and Maternal Health at 301-796-2200 or email [pdit@fda.hhs.gov](mailto:pdit@fda.hhs.gov). For further guidance on pediatric product development, please refer to: <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/ucm049867.htm>.

## **Proprietary Name**

### **3. We did not note a proprietary name request with the initial submission.** If you intend to have a proprietary name for this product, we recommend that you submit a request for a proposed proprietary name review. (See the guidance for industry *Contents of a Complete Submission for the Evaluation of Proprietary Names*, available at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/uc>

[m075068.pdf](#) and “PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2008 through 2012”.)

We are providing the above information via electronic mail correspondence for your convenience. Please reply by email to acknowledge receipt and **provide the requested materials prior to the filing date of June 3, 2016**. If you have any questions regarding the contents of this transmission, please contact me at 240-402-2567 or 301-796-1500.

*{See appended electronic signature page}*

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Garrette Martin-Yeboah, PharmD, CGP, PMP  
Regulatory Project Manager  
Division of Antiviral Products  
Office of Antimicrobial Products  
Center for Drug Evaluation and Research

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GARRETTE F MARTIN-YEBOAH

05/04/2016



DEPARTMENT OF HEALTH AND HUMAN SERVICES

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Food and Drug Administration  
Silver Spring MD 20993

NDA 209347

**NDA ACKNOWLEDGMENT**

Exela Pharma Sciences, LLC  
Attention: Jonathan Sterling  
Vice President of Quality and Regulatory Affairs  
P.O. Box 818  
1245 Blowing Road Blvd  
Lenoir, NC 28645

Dear Mr. Sterling:

We have received your New Drug Application (NDA) submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

Name of Drug Product: Ganciclovir Injection, 2 mg/mL (500 mg/250 mL)

Date of Application: April 18, 2016

Date of Receipt: April 19, 2016

Our Reference Number: NDA 209347

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on June 18, 2016, in accordance with 21 CFR 314.101(a).

If you have not already done so, promptly submit the content of labeling [21 CFR 314.50(l)(1)(i) in structured product labeling (SPL) format as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. Failure to submit the content of labeling in SPL format may result in a refusal-to-file action under 21 CFR 314.101(d)(3). The content of labeling must conform to the content and format requirements of revised 21 CFR 201.56-57.

You are also responsible for complying with the applicable provisions of sections 402(i) and 402(j) of the Public Health Service Act (PHS Act) [42 USC §§ 282 (i) and (j)], which was amended by Title VIII of the Food and Drug Administration Amendments Act of 2007 (FDAAA) (Public Law No, 110-85, 121 Stat. 904).

The NDA number provided above should be cited at the top of the first page of all submissions to this application. Send all submissions, electronic or paper, including those sent by overnight mail or courier, to the following address:

Food and Drug Administration  
Center for Drug Evaluation and Research  
Division of Antiviral Products  
5901-B Ammendale Road  
Beltsville, MD 20705-1266

Secure email between CDER and applicants is useful for informal communications when confidential information may be included in the message (for example, trade secrets or patient information). If you have not already established secure email with the FDA and would like to set it up, send an email request to [SecureEmail@fda.hhs.gov](mailto:SecureEmail@fda.hhs.gov). Please note that secure email may not be used for formal regulatory submissions to applications.

If you have any questions, call Garrette Martin-Yeboah, PharmD, CGP, PMP, Regulatory Project Manager, at (240) 402-2567--.

Sincerely,

*{See appended electronic signature page}*

Garrette Martin-Yeboah, PharmD, CGP, PMP  
Regulatory Project Manager  
Division of Antiviral Products  
Office of Antimicrobial Products  
Center for Drug Evaluation and Research

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GARRETTE F MARTIN-YEBOAH

05/03/2016

## **Martin-Yeboah, Garrette**

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**From:** Martin-Yeboah, Garrette  
**Sent:** Wednesday, April 27, 2016 12:55 PM  
**To:** 'jsterling@exela.us'  
**Cc:** Martin-Yeboah, Garrette; Thompson, Elizabeth; Tyson, Victoria  
**Subject:** NDA 209347 Ganciclovir Injectable

Dear Mr. Sterling,

We acknowledge receipt, on April 19, 2016, of NDA 209347 for Ganciclovir Injectable. The current Debarment Certification states:

“As required by the Generic Drug Enforcement Act of 1992, Exela Pharma Sciences, LLC., certifies that we have not nor will we use in any capacity the service.) of any person debarred under subsections (a) or (b) [section 306 (a) or (b)] of the Act, in connection with this application.

There have been no convictions of crimes (as specified in section 306 (a) and (b) of the Act) within the previous five years of any Exela Pharma Sciences, LLC., employees, or affiliated company, or employees of the affiliated companies responsible for the development or submission of this application.”

Please revise the Debarment Certification in accordance with the FD&C Act Section 306(k)(1), as follows:

“[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.”

Please confirm receipt of this email and **submit the revised Debarment Certification by Thursday, May 5, 2016.** You may contact me with any questions.

Best regards,

Garrette Martin-Yeboah, PharmD, CGP, PMP  
LT, USPHS Commissioned Corps  
Regulatory Project Manager  
Food and Drug Administration  
Center for Drugs Evaluation and Research  
Office of New Drugs/Office of Antimicrobial Products  
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GARRETTE F MARTIN-YEBOAH

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