CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

208418Orig1s001

Trade Name:	Calcium Gluconate Injection, USP
Generic or Proper Name:	calcium gluconate
Sponsor:	Fresenius Kabi USA LLC
Approval Date:	December 22, 2017
Indication:	Calcium Gluconate Injection is a form of calcium indicated for pediatric and adult patients for the treatment of acute symptomatic hypocalcemia

CENTER FOR DRUG EVALUATION AND RESEARCH

208418Orig1s001

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

208418Orig1s001

APPROVAL LETTER

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

NDA 208418/S-001

SUPPLEMENT APPROVAL

Fresenius Kabi USA LLC
Attention: Raul Salmeron
Regulatory Affairs Specialist
Three Corporate Drive
Lake Zurich, IL 60047

Dear Mr. Salmeron:

Please refer to your Supplemental New Drug Application (sNDA) dated July 18, 2017, received July 18, 2017, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Calcium Gluconate Injection.

This "Changes Being Effected" supplemental new drug application provides for revision of the 'proper use of pharmacy bulk package' section of the vial and tray label of NDC 63323-360-61 (product code: 360161)

We have completed our review of this supplemental application. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling (text for the prescribing information) with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eLIST may be found in the guidance for industry titled *SPL Standard for Content of Labeling Technical Qs and As* at http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes, and

annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and immediate container labels that are identical to , as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry *Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (May 2015, Revision 3).* For administrative purposes, designate this submission "**Product Correspondence – Final Printed Carton and Container Labels for approved NDA 208418/S-001.**" Approval of this submission by FDA is not required before the labeling is used.

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.

Because none of these criteria apply to your application, you are exempt from this requirement.

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Teicher Agosto, PharmD, RPh, Regulatory Business Process Manager, at (240) 402 - 3777.

Sincerely,

{See appended electronic signature page}

Ramesh Raghavachari, Ph.D.
Branch Chief
Division of Post-Marketing Activities I
Office of Lifecycle Drug Products
Office of Pharmaceutical Quality
Center for Drug Evaluation and Research

Enclosure:
Carton and Container Labeling

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

208418Orig1s001

LABELING

NDC 63323-360-61

Calcium Gluconate
Injection, USP

10,000 mg per 100 mL
(100 mg per mL)

PHARMACY BULK PACKAGE –
NOT FOR DIRECT INFUSION

Preservative free.

20 x 100 mL
Vials

Rx only

Sterile.

Each mL contains: Calcium gluconate 94 mg;
calcium saccharate (tetrahydrate) 4.5 mg;
water for injection, q.s. Hydrochloric acid and/or
sodium hydroxide may have been added for pH adjustment.

0.465 mEq/mL **276 mOsmol/L**

Contains no more than 400 mcg/L of aluminum.

Preparation of Pharmacy Bulk Package:
This pharmacy bulk package (PBP) is intended for dispensing of single doses to multiple patients in a pharmacy admixture program. Penetrate the container closure only one time with a suitable sterile transfer device or dispensing set that allows measured dispensing of the contents. Use the PBP only in a suitable ISO Class 5 work area such as a laminar flow hood (or an equivalent clean air compounding area). Complete dispensing from the pharmacy bulk package vial within **4 hours** after the container closure is penetrated.

Dispensed aliquots must be used immediately and cannot be stored. See insert for further details.

Supersaturated solutions are prone to precipitation. See insert for further details.

STORE AT: 20° to **25°**C (**68°** to **77°**F) [see USP Controlled Room Temperature]. Do not freeze. Use only if solution is clear and seal intact. The container closure is not made with natural rubber latex.

Fresenius Kabi Lake Zurich, IL 60047

(01)

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LOT/EXP

LIFT HERE

Calcium Gluconate
Injection, USP

10,000 mg per 100 mL (100 mg per mL)

PHARMACY BULK PACKAGE – NOT FOR DIRECT INFUSION

Preservative free.

100 mL

Rx only

Sterile.

Each mL contains: Calcium gluconate 94 mg; calcium saccharate (tetrahydrate) 4.5 mg; water for injection, q.s. Hydrochloric acid and/or sodium hydroxide may have been added for pH adjustment.

0.465 mEq/mL 276 mOsmol/L

Contains no more than 400 mcg/L of aluminum.

Preparation of Pharmacy Bulk Package: This pharmacy bulk package (PBP) is intended for dispensing of single doses to multiple patients in a pharmacy admixture program. Penetrate the container closure only one time with a suitable sterile transfer device or dispensing set that allows measured dispensing of the contents.

Use the PBP only in a suitable ISO Class 5 work area such as a laminar flow hood (or an equivalent clean air compounding area). Complete dispensing from the pharmacy bulk package vial within **4 hours** after the container closure is penetrated.

Dispensed aliquots must be used immediately and cannot be stored. See insert for further details.

Supersaturated solutions are prone to precipitation. See insert for further details.

STORE AT: 20° to **25°**C (**68°** to **77°**F) [see USP Controlled Room Temperature]. Do not freeze. Use only if solution is clear and seal intact. The container closure is not made with natural rubber latex.

Fresenius Kabi Lake Zurich, IL 60047

VIAL ENTRY:

Date _____

Time _____

4031130A

LOT

EXP

3 63323-360-05 4

Calcium Gluconate Injection, USP 10,000 mg per 100 mL (100 mg per mL) **0.465 mEq/mL**

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

208418Orig1S001

OTHER REVIEW(S)

LABEL AND LABELING REVIEW

Division of Medication Error Prevention and Analysis (DMEPA)

Office of Medication Error Prevention and Risk Management (OMEPRM)

Office of Surveillance and Epidemiology (OSE)

Center for Drug Evaluation and Research (CDER)

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

Date of This Review:	October 18, 2017
Requesting Office or Division:	Division of Metabolism and Endocrinology Products (DMEP)
Application Type and Number:	NDA 208418/S-001
Product Name and Strength:	Calcium Gluconate injection, 10,000 mg per 100 mL (100 mg per mL)
Product Type:	Single Ingredient
Rx or OTC:	Rx
Applicant/Sponsor Name:	Fresenius Kabi USA, LLC
Submission Date:	July 18, 2017
OSE RCM #:	2017-1490
DMEPA Safety Evaluator:	Susan Rimmel, PharmD
DMEPA Team Leader:	Hina Mehta, PharmD

1 REASON FOR REVIEW

The Division of Metabolism and Endocrinology Products (DMEP) consulted DMEPA to evaluate the revised container labels and carton labeling for calcium gluconate injection 10,000 mg per 100 mL (100 mg per mL) submitted by Fresenius Kabi USA, LLC on July 18, 2017, under NDA 208418/S-001. The Changes Being Effected (CBE-0) labeling supplement revises the *proper use/preparation of pharmacy bulk package* sections of the container labels (vial) and carton labeling (tray) to ensure that administration instructions are identical to that of the Prescribing Information.

1.1 REGULATORY HISTORY

Calcium gluconate injection NDA 208418 was approved on June 15, 2017, (previously marketed without NDA approval since 1941) for the treatment of acute symptomatic hypocalcemia in pediatric and adult patients.

2 MATERIALS REVIEWED

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

Table 1. Materials Considered for this Label and Labeling Review

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

N/A=not applicable for this review
*We do not typically search FAERS for our label and labeling reviews unless we are aware of medication errors through our routine postmarket safety surveillance

3 OVERALL ASSESSMENT OF THE MATERIALS REVIEWED

Fresenius Kabi USA, LLC submitted a CBE-0 labeling supplement for calcium gluconate injection 10,000 mg per 100 mL (100 mg per mL). We performed a risk assessment of the container labels and carton labeling to identify deficiencies that may lead to medication errors and other areas of improvement. We find the revisions to the carton label and carton labeling acceptable from a medication error perspective.

4 CONCLUSION & RECOMMENDATIONS

DMEPA concludes that the revised carton label and carton labeling for calcium gluconate injection 10,000 mg per 100 mL (100 mg per mL) is acceptable from a medication error perspective. We have no further recommendations at this time.

APPENDICES: METHODS & RESULTS FOR EACH MATERIALS REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table 2 presents relevant product information for calcium gluconate that Fresenius Kabi USA, LLC submitted on July 18, 2017.

Table 2. Relevant Product Information for Calcium Gluconate

Initial Approval Date	06/15/2017 (marketed without NDA approval since 1941)
Active Ingredient	calcium gluconate
Indication	treatment of acute symptomatic hypocalcemia in pediatrics and adults
Route of Administration	intravenous (infusion)
Dosage Form	solution for injection
Strength	1,000 mg per 10 mL (100 mg per mL) 5,000 mg per 50 mL (100 mg per mL) 10,000 mg per 100 mL (100 mg per mL)
Dose and Frequency	Administer intravenously (bolus or continuous infusion) via a secure intravenous line. Dilute prior to use in 5% dextrose or normal saline and assess for potential drug or IV fluid incompatibilities. Individualize the dose within the recommended range in adults and pediatric patients depending on the severity of symptoms of hypocalcemia, the serum calcium level, and the acuity of onset of hypocalcemia.

Patient Population	**Initial Dose**	**Subsequent Doses (if needed)**	
		Bolus	**Continuous Infusion**
Neonate (≤ 1 month)	100 – 200 mg/kg	100 - 200 mg/kg every 6 hours	Initiate at 17-33 mg/kg/hour
Pediatric (> 1 month to < 17 years)	29 - 60 mg/kg	29 - 60 mg/kg every 6 hours	Initiate at 8-13 mg/kg/hour
Adult	1000 - 2000 mg	1000 - 2000 mg every 6 hours	Initiate at 5.4 - 21.5 mg/kg/hour

For bolus administration, DO NOT exceed an infusion rate of:
- 200 mg/minute in adult patients
- 100 mg/minute in pediatric patients

For continuous infusions, adjust rate as needed based on serum calcium levels

For patients with renal impairment, initiate Calcium Gluconate Injection at the lowest dose of the recommended dose ranges for all age groups and

<table>
<tr><td></td><td>monitor serum calcium levels every 4 hours.
Measure serum calcium during intermittent infusions every 4 to 6 hours and during continuous infusion every 1 to 4 hours.</td></tr>
<tr><td>How Supplied</td><td>
<table>
<tr><th>NDC</th><th>Strength/Vial Size (mL)</th></tr>
<tr><td>63323-360-19</td><td>1,000 mg calcium gluconate per 10 mL (100 mg per mL), in a 10 mL plastic, single-dose vial, packaged in a tray of 25.</td></tr>
<tr><td>63323-360-59</td><td>5,000 mg calcium gluconate per 50 mL (100 mg per mL), in a 50 mL plastic, single-dose vial, packaged in a tray of 25.</td></tr>
<tr><td>63323-360-61</td><td>10,000 mg calcium gluconate per 100 mL (100 mg per mL), in a 100 mL plastic, Pharmacy Bulk Package vial, packaged in a tray of 20.</td></tr>
</table>
</td></tr>
<tr><td>Storage</td><td>Store at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature]. Do not freeze.
Preservative Free. Discard any unused portion in the single-dose vial immediately or the Pharmacy Bulk Package vial within 4 hours after initial closure puncture.
Each dose dispensed from the Pharmacy Bulk Package vial must be used immediately.
The diluted solution must be used immediately.</td></tr>
<tr><td>Container Closure</td><td>tray containing 20 plastic 100 mL vials</td></tr>
</table>

APPENDIX B. PREVIOUS DMEPA REVIEWS

On October 17, 2017, we searched DMEPA's previous reviews using the terms, calcium gluconate. Our search identified two previous reviews,[a] and we confirmed that our previous recommendations were implemented or considered.

[a] Vee, S. Label and Labeling Review for Calcium Gluconate NDA 208418. Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2016 NOV 21. RCM No.: 2016-1264.

Vee, S. Label and Labeling Review for Calcium Gluconate NDA 208418. Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2017 Jan 09. RCM No.: 2016-1264-1.

APPENDIX D. ISMP NEWSLETTERS

D.1 Methods

On October 17, 2017, we searched the Institute for Safe Medication Practices (ISMP) newsletters using the criteria below, and then individually reviewed each newsletter. We limited our analysis to newsletters that described medication errors or actions possibly associated with the label and labeling.

ISMP Newsletters Search Strategy	
ISMP Newsletter(s)	Acute Care, Community, and Nursing
Date Range	06/15/2017 – 10/17/2017
Search Strategy and Terms	Match Exact Word or Phrase: calcium gluconate

D.2 Results

Our search identified one case relevant for this review,[b] which was originally cited in the April 6, 2017, Acute Care newsletter[c] and is summarized below.

A nurse administered a cloudy calcium gluconate and potassium phosphate infusion, which led to fatal pulmonary emboli. The patient had no previous cardiac or pulmonary disease. A bag of calcium gluconate and potassium phosphate mixed with saline in the pharmacy appeared cloudy prior to administration, but the nurse still started the infusion. About an hour later, the patient was found in respiratory distress, which quickly progressed to a fatal cardiac arrest. A different nurse had previously abandoned an attempt to administer the same solution due to its cloudy appearance, although she had not yet contacted the pharmacy. The nurse who then administered the solution decided to hang it after referencing a flawed hospital protocol that stated products with precipitates could be infused under "close observation" due to the risk of "sudden death." An autopsy showed scattered pulmonary emboli. The death was determined to be accidental and related to the infusion of the precipitated electrolyte infusion.

Our review of the container label, tray labeling, and Prescribing Information confirms there are appropriate warnings regarding the possibility of precipitation, which comply with current FDA regulations. Therefore, no further action is required at this time.

[b] Institute for Safe Medication Practices. Quarterly Action Agenda: Administration of a product with a precipitate. ISMP Med Saf Alert Acute Care. 2017; 22(15): QAA 2.

[c] Institute for Safe Medication Practices. Safety Alert: Administration of a product with a precipitate. ISMP Med Saf Alert Acute Care. 2017; 22(7): 1-2.

APPENDIX E. FDA ADVERSE EVENT REPORTING SYSTEM (FAERS)

E.1 Methods

On October 17, 2017, we searched FAERS using the criteria in the table below and identified one (n = 1) case. We individually reviewed the cases, and limited our analysis to cases that described errors possibly associated with the label and labeling. We used the NCC MERP Taxonomy of Medication Errors to code the type and factors contributing to the errors when sufficient information was provided by the reporter.[d] We excluded the one case identified because it described an error involving a concomitant medication.

Criteria Used to Search FAERS	
Initial FDA Receive Dates:	06/15/2017 – 10/01/2017
Product Name:	Calcium Gluconate
Event:	SMQ *Medication errors* (Narrow)
Country (Derived):	USA

E.2 Results

Our search identified one case, which is not relevant for this review.

E.4 Description of FAERS

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

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

APPENDIX G. LABELS AND LABELING

G.1 List of Labels and Labeling Reviewed

Using the principles of human factors and Failure Mode and Effects Analysis,[e] along with postmarket medication error data, we reviewed the following calcium gluconate labels and labeling submitted by Fresenius Kabi USA, LLC on July 18, 2017.

- Container Label
- Carton Labeling

G.2 Label and Labeling Images

Container Label

Carton Labeling (tray)

[e] Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

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/s/

SUSAN RIMMEL
10/18/2017

HINA S MEHTA
10/18/2017

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

208418Orig1S001

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION

TO *(Division/Office)*: **Mail: OSE**			FROM: OPQ/OPRO Laya Keyvan 240-402-4598	
DATE August 18, 2017	IND NO. N/A	NDA NO. NDA 208418/S-001	TYPE OF DOCUMENT Labeling CBE-0 Supplement	DATE OF DOCUMENT July 18, 2017
NAME OF DRUG Calcium Gluconate Injection	PRIORITY CONSIDERATION CBE-0		CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE October 18, 2017
NAME OF FIRM: FRESENIUS KABI USA LLC				

REASON FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ MANUFACTURING CHANGE/ADDITION
- ☐ MEETING PLANNED BY
- ☐ PRE--NDA MEETING
- ☐ END OF PHASE II MEETING
- ☐ RESUBMISSION
- ☐ SAFETY/EFFICACY
- ☐ CONTROL SUPPLEMENT
- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING
- ■ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- ☐ MEDICATION ERRORS
- ☐ OTHER *(SPECIFY BELOW)*:

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
☐ TYPE A OR B NDA REVIEW ☐ END OF PHASE II MEETING ☐ CONTROLLED STUDIES ☐ PROTOCOL REVIEW ☐ OTHER (SPECIFY BELOW):	☐ CHEMISTRY REVIEW ☐ PHARMACOLOGY ☐ BIOPHARMACEUTICS ☐ OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILTY STUDIES
- ☐ PHASE IV STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL-BIOPHARMACEUTICS
- ☐ IN-VIVO WAIVER REQUEST

IV. DRUG EXPERIENCE

- ☐ PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- ☐ DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- ☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
- ☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP
- ☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

- ☐ CLINICAL
- ☐ PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS:
Changes Being Effected (CBE-0) to revise the proper use of the pharmacy bulk package section of the vial and tray label of NDC 63323-360-61 (product code 306161– 100 cc vial), to ensure that administration of the drug product is identical in the label, carton, and package insert.

SIGNATURE OF REQUESTER Laya Keyvan, MS, MBA	METHOD OF DELIVERY (Check all that apply) ☐ MAIL ■ DARRTS ☐ HAND
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

06/18/2013

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

/s/

LAYA KEYVAN
08/18/2017

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION

TO *(Division/Office)*: **Mail: OSE**			FROM: OPQ/OPRO Laya Keyvan 240-402-4598	
DATE July 26, 2017	IND NO. N/A	NDA NO. NDA 208418/S-001	TYPE OF DOCUMENT Labeling CBE-0 Supplement	DATE OF DOCUMENT July 18, 2017
NAME OF DRUG Calcium Gluconate Injection	PRIORITY CONSIDERATION CBE-0		CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE October 18, 2017

NAME OF FIRM: FRESENIUS KABI USA LLC

REASON FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ MANUFACTURING CHANGE/ADDITION
- ☐ MEETING PLANNED BY
- ☐ PRE--NDA MEETING
- ☐ END OF PHASE II MEETING
- ☐ RESUBMISSION
- ☐ SAFETY/EFFICACY
- ☐ CONTROL SUPPLEMENT
- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING
- ■ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- ☐ MEDICATION ERRORS
- ☐ OTHER *(SPECIFY BELOW)*:

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
☐ TYPE A OR B NDA REVIEW ☐ END OF PHASE II MEETING ☐ CONTROLLED STUDIES ☐ PROTOCOL REVIEW ☐ OTHER (SPECIFY BELOW):	☐ CHEMISTRY REVIEW ☐ PHARMACOLOGY ☐ BIOPHARMACEUTICS ☐ OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILTY STUDIES
- ☐ PHASE IV STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL-BIOPHARMACEUTICS
- ☐ IN-VIVO WAIVER REQUEST

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- ☐ PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- ☐ DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- ☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
- ☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP
- ☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

☐ CLINICAL	☐ PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS:
Changes Being Effected (CBE-0) to revise the proper use of the pharmacy bulk package section of the vial and tray label of NDC 63323-360-61 (product code 306161– 100 cc vial), to ensure that administration of the drug product is identical in the label, carton, and package insert.

SIGNATURE OF REQUESTER Laya Keyvan, MS, MBA	METHOD OF DELIVERY (Check all that apply) ☐ MAIL ■ DARRTS ☐ HAND
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

06/18/2013

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/s/

LAYA KEYVAN
07/26/2017