# CENTER FOR DRUG EVALUATION AND RESEARCH

***APPLICATION NUMBER:***

# 210906Orig1s000

# PRODUCT QUALITY REVIEW(S)

**Recommendation: APPROVAL**

# NDA 210906

# Review # 1

| | |
|---|---|
| Drug Name/Dosage Form | Calcium gluconate injection |
| Strength | 20 mg/mL (1g/50 mL and 2g/100 mL) |
| Route of Administration | Intravenous Injection |
| Rx/OTC Dispensed | Rx |
| Applicant | HQ Specialty Pharma Corporation |

| SUBMISSIONS REVIEWED | DOCUMENT DATE |
|---|---|
| Original | 09/29/2017 |
| Quality Response to Information Request | 10/30/2017 |
| Quality Information | 12/11/2017 |
| Quality Response to Information Request | 12/15/2017 |
| Quality Response to Information Request | 02/05/2018 |
| Quality Response to Information Request | 02/09/2018 |
| Quality Response to Information Request | 03/23/2018 |
| Quality Response to Information Request | 04/05/2018 |
| Quality Response to Information Request | 06/22/2018 |
| Quality Response to Information Request | 08/23/2018 |

## Quality Review Team

| DISCIPLINE | PRIMARY REVIEWER | SECONDARY REVIEWER |
|---|---|---|
| Drug Substance | Friedrich Burnett | Donna Christner |
| Drug Product | Dhanalakshmi Kasi | Danae Christodoulou |
| Process | Brian Rogers | Yong Hu |
| Microbiology | Hemlata Tamta | Nandini Bhattacharya |
| Facility | Laurie Nelson | Vidya Pai |
| Biopharmaceutics | Hansong Chen | Haritha Mandula |
| Regulatory Business Process Manager | Anika Lalmansingh | |
| Application Technical Lead | Dhanalakshmi Kasi | |

# Quality Review Data Sheet

## 1. RELATED/SUPPORTING DOCUMENTS

### A. DMFs:

| DMF # | Type | Holder | Item Referenced | Status | Date Review Completed |
|---|---|---|---|---|---|
| (b) (4) | Type II | | (b) (4) | Adequate | 28 Apr 2018 |

### B. Other Documents:

| DOCUMENT | APPLICATION NUMBER | DESCRIPTION |
|---|---|---|
| NDA | 208418 | RLD |

## 2. CONSULTS

**N/A**

# Executive Summary

## I. Recommendations and Conclusion on Approvability

The final OPQ recommendation is for Approval.

## II. Summary of Quality Assessments

### A. Product Overview

This is a 505(b)(2) application for calcium gluconate injection relying on the safety and efficacy of the approved drug, calcium gluconate injection, USP 10% (NDA 208418) (see CDTL's review).

Calcium gluconate injection, 100 mg/mL is approved on June 15, 2017 under NDA 208418 and it is marketed by Fresenius Kabi. The referenced approved drug product is supplied in a single dose 10 mL or 50 mL vial and it is diluted in 5% dextrose or saline.

HQ Specialty Pharma's proposed calcium gluconate injection is a ready to infuse solution with a concentration of 20 mg/mL of calcium gluconate. The drug product is supplied in a 100 mL one port (b) (4) flexible bag. The drug product contains the same active (calcium gluconate monohydrate) and inactive ingredients (calcium D-saccharate, sodium hydroxide and hydrochloric acid) present in RLD's formulation. Sodium chloride is added as a tonicity agent and the drug product doesn't require further dilution. Each mL of calcium gluconate in sodium chloride injection contains 20 mg of calcium gluconate (equivalent to 18.8 mg of calcium gluconate and 0.9 mg of calcium saccharate tetrahydrate), hydrochloric acid and/or sodium hydroxide for pH adjustment (6.0 to 8.2) and sodium chloride 6.75 mg/mL as tonicity adjustor. Each mL of calcium gluconate injection contains 1.86 mg (0.093 mEq) of elemental calcium.

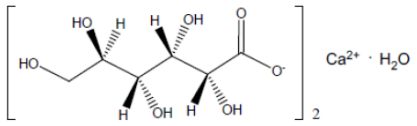
The Applicant provided adequate information to support the relative bioavailability of the proposed drug product to the reference listed drug. A scientific bridge has been established to the Agency's finding of safety and effectiveness to the reference listed drug. Thus, additional in vivo bioequivalence (BE) bridging study is not required.

The overall manufacturing cGMP recommendation is for approval as of 05/09/18.

## B. Quality Assessment Overview

### Drug Substance

Calcium gluconate monohydrate is [redacted] with a solubility of 3 [redacted]g/100 mL in water at [redacted]°C.




Molecular Formula: $C_{12}H_{22}CaO_{14} \cdot H_2O$
Molecular Weight: 448.39 g/mol

DMF [redacted] is referenced for all CMC information on the drug substance. DMF holder and the API supplier is [redacted] DMF [redacted] is currently adequate upon review as of 28 April 2018. The drug substance, calcium gluconate monohydrate, meets the current USP specifications and is adequate to ensure the quality of the drug substance as it relates to the safety and efficacy of the eventual drug product. The drug substance information is adequate to support approval of the NDA.

### Drug Product

HQ Specialty Pharma's proposed calcium gluconate injection is a ready to infuse solution with the concentration of 20 mg/mL. Each mL of calcium gluconate in sodium chloride injection contains 20 mg of calcium gluconate (equivalent to 18.8 mg of calcium gluconate and 0.9 mg of calcium saccharate tetrahydrate), hydrochloric acid and/or sodium hydroxide for pH adjustment (6.0 to 8.2) and sodium chloride 6.75 mg/mL as tonicity adjustor. Each mL of calcium gluconate injection contains 1.86 mg (0.093 mEq) of elemental calcium. Calcium gluconate injection (1g/50 mL and 2g/100 mL) is packaged in a single use 100 mL [redacted] bags, containing a pre-printed label. The bags contain single port closed with a twist off port. The bags are placed in a [redacted] aluminum overwrap with pre-printed labels using green and blue and black ink.

The manufacturing process [redacted] Critical quality attributes are established based on manufacturing experience.

The applicant is following USP monograph to test their drug product. The drug product is tested for appearance, identification, pH, calcium assay, chloride assay, weight loss, osmolality, and Al content. The proposed limit for Al content is [redacted] µg/L and the recommended allowed limit for small volume parenteral is [redacted] µg/L. HPIC method was developed during the review process for the separation and quantitation of gluconate and saccharate and to analyze their impurities/degradants present in the drug product. The sterile drug product is a single dose and antimicrobial effectiveness testing is not required. Batch analysis results are provided for 6 batches (50 ml: 5R010, 5R011, 5R012, 100 ml: 5R013, 5R014 and 5R015) and the test results are within the specified limits. The proposed shelf life is 24 months.

**C. Special Product Quality Labeling Recommendations:** None

**D. Final Risk Assessment:**

**Drug Product (Calcium gluconate injection)**

| Attribute/ CQA | Factors that can impact the CQA | Initial Risk Ranking | Risk Mitigation Approach | Final Risk Evaluation |
|---|---|---|---|---|
| Identity of Calcium | Method of manufacture, suitability of analytical methods | Low | (b) (4) | Low. Acceptable |
| Assay of Calcium | Method of manufacture, suitability of analytical methods | Low | | Low. Acceptable |
| Assay of gluconate and saccharate | Method of manufacture, suitability of analytical methods | Medium | | Low. Acceptable |
| pH | Formulation, method of manufacture | Low | | Low. Acceptable |
| Impurities | Suitability of analytical methods | Medium | | Low. Acceptable |
| Microbial Limits | Components, manufacturing process. | Low | | Low. Acceptable |
| Al content | API, excipients, container and closure | Low | | Low. Acceptable |

***E.* Life Cycle Knowledge Information:** None

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***Application Technical Lead Name and Date: Dhanalakshmi Kasi, Ph.D.***

# BIOPHARMACEUTICS

**Product Background:**

**NDA/ANDA:** NDA 210906

**Drug Product Name / Strength:** Calcium Gluconate Injection 1 g/50 mL and 2 g/100 mL (20 mg/mL)

**Route of Administration:** IV injection

**Applicant Name:** HQ Specialty Pharma Corporation

***Review Summary:***

The Listed Drug, Calcium Gluconate Injection, USP 10%., 100 mg/mL, developed by Fresenius Kabi USA, LLC. was approved by FDA under NDA 208418 on 06/15/2017. It is indicated for the treatment of acute symptomatic hypocalcemia.

HQ Specialty Pharma Corporation developed Calcium Gluconate Injection 1 g/50 mL and 2 g/100 mL (20 mg/mL) and submitted the application under NDA 210906 to seek approval from the Agency through 505(b)(2) pathway on 9/29/2017.

The Biopharmaceutics review focuses on the side-by-side comparison between the proposed product and the Listed Drug for the active and inactive ingredients including pH and osmolality, as well as the Applicant's waiver request on the in vivo BA/BE for its proposed drug product.

From the Biopharmaceutics perspective, NDA 210906 for Calcium Gluconate Injection 1 g/50 mL and 2 g/100 mL (20 mg/mL) was reviewed and found adequate, and the wavier for the proposed product is also granted. This NDA is, therefore, recommended for approval.

**List Submissions being reviewed (table):**

| SUBMISSION(S) REVIEWED | DOCUMENT DATE |
|---|---|
| 0000 | 9/29/2017 |
| 0005 | 12/15/2017 |

**Highlight Key Outstanding Issues from Last Cycle:** None.

**Concise Description Outstanding Issues Remaining:** N/A

***BCS Designation***

**Reviewer's Assessment:** Not reported.

**Solubility:**

The solubility of Calcium Gluconate in water at (b)(4)°C is 3 (b)(4)g/100 mL.

**Permeability:** not reported.

**Dissolution:** N/A

***Bridging of Formulations***

**Reviewer's Assessment: N/A**

***Biowaiver Request***

**Reviewer's Assessment:**

## 1. Background

HQ Specialty Pharma Corporation developed Calcium Gluconate Injection 1 g/50 mL and 2 g/100 mL (20 mg/mL) and submitted the application under NDA 210906 to seek approval through 505(b) (2) path. The Listed Drug is Calcium Gluconate Injection, USP 10%., 100 mg/mL. The proposed product and the Listed Drug have the same active ingredient. However, they do not have the same concentrations of active ingredients. In addition, it was not clear whether these two products have the same inactive ingredients. An information request was sent out to clarify it.

Table 1. Table 1. Components of Calcium Gluconate Injection, 1g/ 50 mL

| Name of Ingredients | Composition | |
|---|---|---|
| | Label Claim mg /mL | mg per 50 mL container |
| Calcium Gluconate Monohydrate (b) (4) | (b) (4) (18.8) | (b) (4) (940) |
| Calcium D saccharate (tetrahydrate) | 0.9 | 45 |
| Hydrochloric Acid and/ or sodium hydroxide | q.s. | q.s to pH |
| Sodium Chloride | 6.75 | 337.5 |
| (b) (4) | | |
| **Total** | **q.s 1 mL** | **q.s 50 mL** |

Table 2. Composition of Calcium Gluconate Injection, 2g/ 100 mL

| Name of Ingredients | Composition | |
|---|---|---|
| | Label Claim\ mg / mL | mg per 100 mL container |
| Calcium Gluconate monohydrate (b) (4) | (b) (4) (18.8) | (b) (4) (1880) |
| Calcium D saccharate (tetrahydrate) | 0.9 | 90 |
| Hydrochloric Acid and/ or sodium hydroxide | q.s. | q.s to pH |
| Sodium Chloride | 6.75 | 675 |
| (b) (4) | | |
| **Total** | **q.s 1 mL** | **q.s 100 mL** |

**2. Information Request**

A Biopharmaceutics IR was sent to the Applicant on 11/15/2017. On 12/15/2017, the Applicant responded to the IR. The following are the Biopharmaceutics IR, the Applicant's response, and this Reviewer's assessment of the Applicant's response.

**IR**

Submit a detailed side-by-side comparison of your proposed drug product and the Listed Drug along with comparative physicochemical properties (pH, viscosity, tonicity, and osmolality). Provide justification with supporting data (e.g., literature articles/data and/or your study results) to demonstrate that any differences between the two formulations in terms of inactive ingredients and in terms of physicochemical properties (e.g., pH, viscosity, tonicity, and osmolality) will not affect its In Vivo PK performance and clinical outcome in regards to efficacy/safety. Please be advised that the physico-chemical properties should be compared at the same concentration.

**The Applicant's response**

The Applicant stated that the proposed drug has the same active (b) (4) ingredients as the Listed Drug. (b) (4) The proposed drug is manufactured for ready to use, and in contrast, the Listed Drug needs to be diluted with normal saline before injection. Specifically, per the Listed Drug package insert, Calcium gluconate injection is diluted from 10 to 50 mg/mL for bolus administration and from 5.8 to 10 mg/mL for continuous infusion in 0.9% sodium chloride or 5% dextrose.

In order for comparison, the Listed Drug Calcium Gluconate Injection USP 10% (1g/10 mL) Fresenius Kabi Lot 6014339 was diluted in 0.9% NaCl to obtain a 50 mL of solution, which has the same concentration of calcium gluconate as the proposed drug (20 mg/mL). Tables 3, 4 and 5 show the side by side comparison in components and physicochemical properties between the proposed drug product and the Listed Drug, respectively.

Table 4 shows that the diluted Listed Drug and proposed product have the same concentrations of active (b) (4) ingredients except different concentrations of NaCl. The former is 0.72% NaCl, and the latter 0.675%.

Table 3. Comparison of components and composition between **the undiluted Listed Drug** and the proposed drug

| | ***Calcium gluconate injection, Fresenius Kabi Vial Concentrate*** *1 g/10 mL* | ***Calcium Gluconate Injection, USP HQ Ready to use*** *1g/50 mL* |
|---|---|---|
| Calcium Gluconate | 1 g/10 mL (94 mg/mL) | 1 g/50 mL (b) (4) |
| Diluent /tonicity Agent | Dilute in normal saline (0.9%) or 5% dextrose | Sodium chloride 0.675% |
| (b) (4) | 45 mg /10 mL Calcium D-saccharate | 45 mg/50 mL Calcium D-saccharate |
| pH Adjustor | Hydrochloric acid or sodium hydroxide | Hydrochloric acid or sodium hydroxide |
| (b) (4) | | |
| pH range | 6.0 – 8.2 | 6.0 – 8.2 |

Table 4. Comparison of components and composition between **the diluted Listed Drug** and the proposed drug

| | ***Calcium gluconate injection, Fresenius Kabi Vial*** *1 g/10 mL diluted to 50 mL* | ***Calcium Gluconate Injection, USP HQ Ready to use*** *1g/50mL* |
|---|---|---|
| Calcium Gluconate concentration | 1 g/50 mL (b) (4) | 1 g/50 mL |
| Diluent /tonicity Agent | Dilute in 40 mL normal saline (0.9%) (final 0.72% NaCl) | Sodium chloride 0.675% |
| (b) (4) | 45 mg /50 mL Calcium D-saccharate (0.9 mg/mL calcium D-saccarate tetrahydrate) | 45 mg/50 mL Calcium D-saccharate (0.9 mg/mL calcium D-saccarate tetrahydrate) |
| pH Adjustor | Hydrochloric acid or sodium hydroxide | Hydrochloric acid or sodium hydroxide |
| (b) (4) | | |

Table 5. Comparison of Physico-chemical Parameters between the diluted Listed Drug and the proposed drug

| Physico-chemical Parameters | Listed drug Fresenius Lot 60143391 (10mL diluted to 50 mL) | The Proposed drug HQ 5R010 | Specification |
|---|---|---|---|
| Osmolality (mOsmol/kg) | 314 | 300 | (b) (4) |
| pH | 6.6 | 6.3 | 6.0-8.2 |
| Viscosity (time flow, seconds) | 100 | 101 | |

Table 5 shows that the proposed product and the diluted Listed Drug have very similar osmolality, pH, and viscosity.

## 2. Biowaiver Request

The Applicant requested the waiver of the in vivo BA/BE for their proposed product by citing 21 CFR 320.22(b) (1). The Applicant stated that the diluted Listed Drug and the proposed drug have the same active ingredient and inactive ingredients in the same concentrations. In addition, the proposed product and the diluted Listed Drug have very similar physico-chemical properties, such as osmolality and pH.

**Reviewer's comment:**

*The criteria for a biowaiver under 21 CFR 320.22(b)(1) is fully met:*

1. *The proposed drug product and the listed Drug product are for intravenous use, and their bioavailability is self-evident.*
2. *The proposed drug product contains the same active* (b) (4) *ingredients in the same concentrations as the Listed Drug that has been approved by FDA under NDA 208418.*
3. *The tiny differences in pH and osmolality between two products do not bring any safety issues.*

**Conclusion**

As consistent with 21 CFR 320.24(b)(1), the Applicant provided adequate information to support the relative bioavailability of the proposed drug product to the Listed Drug and a scientific

bridge has been established to the Agency's finding of safety and effectiveness to the Listed Drug. Thus, additional in vivo bioequivalence (BE) bridging study is not needed. NDA 210906 for Calcium Gluconate Injection 1 g/50 mL and 2 g/100 mL (20 mg/mL) is adequate and recommended for approval from the Biopharmaceutics perspective.

**R Regional Information**

***Comparability Protocols: None***

**Reviewer's Assessment:**

***Post-Approval Commitments***

**Reviewer's Assessment:** N/A

***Lifecycle Management Considerations; N/A***

***List of Deficiencies:*** *N/A*

***Primary Biopharmaceutics Reviewer Name and Date:***

*Hansong Chen, PharmD., Ph.D.,4/13/2018*

*Biopharmaceutics reviewer,*

*Division of Biopharmaceutics/ONDP/OPQ*

***Secondary Reviewer Name and Date (and Secondary Summary, as needed):***

*Haritha Mandula, Ph.D., 6/7/2018*

*Acting Biopharmaceutics Lead,*

*Division of Biopharmaceutics/ONDP/OPQ*

Hansong Chen

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Haritha Mandula

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# MICROBIOLOGY

**Product Background:**

**NDA: 210906**

**Drug Product Name / Strength:** Calcium Gluconate Injection, 1 g/50 mL and 2 g/100 mL (20 mg/mL)

**Route of Administration:** Intravenous injection

**Applicant Name:** HQ Specialty Pharma Corporation
120 Route 17 North, Paramus, NJ 07652

**Manufacturing Site:** (b) (4)

**Method of Sterilization:** (b) (4)

***Review Recommendation:*** Adequate

***Review Summary:*** The submission is **recommended** for approval in the basis of sterility assurance.

**List Submissions Being Reviewed:**

| Submit | Received | Review Request | Assigned to Reviewer |
|---|---|---|---|
| 09/29/2017 | 09/29/2017 | N/A | 12/19/2017 |
| 03/23/2018 | 03/23/2018 | N/A | 03/23/2018 |

**Highlight Key Outstanding Issues from Last Cycle:** NA

**Remarks:** This is an eCTD submission. IR was conveyed to the applicant on 02/22/2018. The response to IR was received on 03/23/2018 and incorporated in the review.

**Concise Description Outstanding Issues Remaining:** None

**Supporting Documents: N/A**

**List Number of Comparability Protocols (ANDA only):** NA

## P.1 Description of the Composition of the Drug Product

- **Description of drug product** – Calcium gluconate injection (20 mg/mL) is a sterile (b) (4) ready to infuse solution filled in 100 mL (b) (4) bags in 2 different fill volumes (1 g/50 mL; 50 mL fill and 2 g/100 mL; 100 mL fill).
- **Drug product composition** –

| Components | Quality Standard | Function | Composition | |
|---|---|---|---|---|
| | | | 1g /50 mL | 2 g/100 mL |
| Calcium gluconate | USP | Active ingredient | (b) (4) | |
| Calcium D saccharate (tetrahydrate) | USP | (b) (4) | 45 mg | 90 mg |
| Hydrochloric acid and/ or Sodium hydroxide | NF | | q.s. to pH | q.s. to pH |
| Sodium chloride | USP | Tonicity agent | 337.5 mg | 675 |
| (b) (4) | | | | |

**Exhibit batches:**

| Batch Type | Batch Size | |
|---|---|---|
| | 1 g/50 mL | 2g/100mL |
| Exhibit batches | (b) (4) | |
| Proposed commercial batch | | |

- **Description of container closure system** –

| Container closure system | Component | Supplier |
|---|---|---|
| (b) (4) bags | (b) (4) 100 mL bag, (b) (4) (b) (4) | (b) (4) |
| (b) (4) | (b) (4) | |
| Twist off port | | |
| Overwrap | Each bag is over-wrapped (b) (4) (b) (4) Aluminum/ (b) (4) | |

**Reviewer's Assessment:** ***Adequate***

**The proposed container closure system and drug product composition were adequately described.**

## P.2 Pharmaceutical Development

## P.2.5 Microbiological Attributes

***Container/Closure and Package Integrity***

(3.2.P.2. Pharmaceutical Development.pdf; p35/46)

(b) (4)

## P.7 Container Closure

**Summary table of the container closure system proposed**

**Reviewer's Assessment:** Please refer to P.1.

## P.8 Stability

## P. 8.1 Stability Summary and Conclusion

(3.2.P.8.1.)

Proposed Expiry: 24 months

**Reviewer's Assessment:** ***Adequate***

**The stability data provided from the exhibit batches support the expiry dating of the drug product.**

## P. 8.2 Post-Approval Stability Protocol and Stability Commitment

(3.2.P.8.2. Post-approval Stability Protocol and Stability Commitment.pdf)

The product stability specification includes the following microbiological tests:

| Test | Test Method | Acceptance Criteria (b) (4) |
|---|---|---|
| Bacterial Endotoxins | USP <85> | |
| Container/Closure Integrity | Internal Method (pressure test) | |

Samples (1g/ 50mL and 2g/ 100mL) will be stored under long term conditions at 25± 2ºC/40 ± 5% RH in horizontal position. The testing schedule in the post-approval protocol is as follows:

| Stability Test | Time (Months) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | 0 | 3 | 6 | 9 | 12 | 18 | 24 | 36 |
| **Bacterial Endotoxins** | X | | | | X | | X | X |
| **Sterility (Container/closure Integrity)** | | | | | X | | X | X |

Proposed expiry: A tentative shelf life of 24 months is proposed. Stability testing will be conducted per protocol. If additional stability data is obtained beyond 24 months, which will support the extension of the expiration period, the expiration date will be extended accordingly. The extended stability data will then be reported to the Agency in an annual report in accordance with 21 CFR 314.70 (d)(5).

Post Approval Stability Commitment

(3.2.P.8.2; post-approval-stability commitment.pdf, p1/1)

HQ Specialty Pharma commits to placing the first three commercial lots of the subject drug product (1g/ 50mL and 2g/ 100mL) into their stability program. Thereafter, on an annual basis, one production lot will be added to the stability program.

**Note to reviewer**: Applicant proposed the container/closure integrity test (pressure test) in lieu of sterility test. The proposed pressure test method is reviewed and assessed above in section P.2.5.

**Reviewer's Assessment:** ***Adequate***

**The post approval protocol and stability commitment is adequate.**

## P.8.3 Stability Data

Stability data generated for the registration batches of 1g/ 50mL (5R010, 5R011 and 5R012) and 2g/ 100mL (5R013, 5R014, and 5R015) under accelerated conditions (40 ± 2 ºC /15 ± 5 % RH) until 6 months and long term conditions (25 ± 2 ºC/40 ± 5 % RH) until 12 month time point has been tested according to the stability schedule. The report was included in the submission. Bacterial endotoxins testing and sterility (container closure integrity) met the specifications at the initial (for both long term and accelerated stability), 6 month time point for accelerated stability studies, and 12 month time point for long term stability studies. The applicant states that long term stability studies are ongoing.

**Reviewer's Assessment:** ***Adequate***

**The stability data provided for long term storage conditions up to 9 months and accelerated storage conditions up to 6 months support the expiration dating of the drug product as proposed.**

## R Regional Information

***Executed Batch Records***

(3.2.R Regional Information.pdf)

Calcium Gluconate Injection 20 mg/mL batches manufactured for primary stability studies were manufactured (b) (4) The relationship between the bulk batch solution and final batch was provided and is summarized below.

| Dissolution Batch | Final Batch Number | Strength |
|---|---|---|
| 5R011 | 5R011 | 1 g/50 mL |
| | 5R014 | 2 g/100 mL |
| 5R015 | 5R012 | 1 g/50 mL |
| | 5R015 | 2 g/100 mL |
| 5R010 | 5R010 | 1 g/50 mL |
| | 5R013 | 2 g/100 mL |

Executed batch records for 1g/50mL (5R010, 5R011 and 5R012) and 2g/100mL (5R013, 5R014 and 5R015) are provided in Module 3.2.R. (b) (4)

**Reviewer's Assessment:** ***Adequate***

***Comparability Protocols***

No comparability protocol was included in the application.

**Reviewer's Assessment:** ***Adequate***

***2. REVIEW OF COMMON TECHNICAL DOCUMENT – QUALITY (CTD-Q) MODULE 1***

***2.A. Package Insert***

(R.1.14.1.3 Draft Carton and Container Labels)

Storage temperature: Controlled room temperature between 20 to 25 ºC (68 to 77ºF); Route of administration: Intravenous only; Container: Single dose

- **Post-dilution/constitution hold time- N/A**

***Post-Approval Commitments:*** **N/A**

***List of Deficiencies:***

NDA: 210906 APPLICANT: HQ Specialty Pharma Corporation

DRUG PRODUCT: Calcium Gluconate injection, 1g/50 mL and 2g/100mL

The Division of Microbiology Assessment has no comments at this time.

***Primary Microbiology Reviewer Name and Date:***
Hemlata Tamta, Ph.D.
Microbiologist
CDER/OPQ/OPF/DMA/BII
Date: 05/24/2018

***Secondary Reviewer Name and Date (and Secondary Summary, as needed):***
Nandini Bhattacharya, Ph.D.
Microbiologist
CDER/OPQ/OPF/DMA/BII
Date: 05/24/2018

Hemlata Tamta

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Nandini Bhattacharya

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Dhanalakshmi Kasi

Digitally signed by Dhanalakshmi Kasi
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