# CENTER FOR DRUG EVALUATION AND RESEARCH

***APPLICATION NUMBER:***

# 220482Orig1s000

# PRODUCT QUALITY REVIEW(S)

# Table of Contents

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| Document ID: | OPQ-TEM-0016 |
| Effective Date: | 26 Sep 2023 Revision: 00 |
| Total Pages: | 4 |

*Template Revision: 03*

# Office of Pharmaceutical Quality

## New Drug Application (NDA)
## Integrated Quality Assessment Template

# NDA Executive Summary

## 1. Application/Product Information

| | | | |
|---|---|---|---|
| **NDA Number** | 220482 | | |
| **Applicant Name** | Haisco-USA Pharmaceuticals, Inc | | |
| **Drug Product Name** | cipepofol | | |
| **Dosage Form** | Injection | | |
| **Proposed Strength(s)** | 2.5 mg/mL | | |
| **NDA Classification** | Type 1 - NME | | |
| **Route of Administration** | Intravenous | | |
| **Maximum Daily Dose** | 36 mg | | |
| **Rx/OTC Dispensed** | Rx | | |
| **Proposed Indication** | Induction of general anesthesia in adults undergoing surgery | | |
| **Drug Product Description** | White to off-white emulsion | | |
| **Co-packaged product information** | N/A | | |
| **Device information** | N/A | | |
| **Storage Temperature/ Conditions** | 2 to 25 $^{o}$C | | |
| **Review Team** | **Discipline** | **Primary** | **Secondary** |
| | *Drug Substance* | Zhixing Shan | Donna Christner |
| | *Drug Product/ Labeling* | Grace Chiou | Valerie Amspacher/ Julia Pinto |
| | *Manufacturing* | Miral Patel | Shu-Wei Yang |
| | *Biopharmaceutics* | N/A | N/A |
| | *Microbiology* | Koushik Paul | Jesse Wells |

| | | | |
|---|---|---|---|
| | *Other (specify)* | N/A | N/A |
| | *RBPM* | Teicher Agosto | |
| | *ATL* | Valerie Amspacher | |
| **Consults** | N/A | | |

**2. Final Overall Recommendation - Approval**

**3. Action Letter Information**

**a. Expiration Dating: Based on the data provided, the proposed shelf life of 36 months is granted when stored at 2 to 25 ºC.**

**b. Additional Comments for Action**

**4. Basis for Recommendation:**

**a. Summary of Rationale for Recommendation:**

*The CMC recommendation is approval for this NDA based on reviews by drug substance, drug product, process/facilities and microbiology.*

**b. Is the overall recommendation in agreement with the individual discipline recommendations?** Yes

**Recommendation by Subdiscipline:**

**Drug Substance - Adequate**
**Drug Product - Adequate**
**Quality Labeling - Adequate**
**Manufacturing - Adequate**
**Biopharmaceutics - N/A**
**Microbiology - Adequate**

**Environmental Assessment:** Review & EI Statement - Adequate
**QPA for EA(s):** No

**5. Life-Cycle Considerations**

**Established Conditions per ICH Q12: No**
**Comments**:

**Comparability Protocols (PACMP): No**
**Comments:**

**Additional Lifecycle Comments:**

| Submission(s) Assessed | Document Date | Discipline(s) Affected |
|---|---|---|
| Supporting document 1 (eCTD 0001) | 30 May 2025 | All, original submission |
| Supporting document 6 (eCTD 0006) | 27 Aug 2025 | Process |
| Supporting document 10 (eCTD 0010) | 12 Sep 2025 | Microbiology |
| Supporting document 14 (eCTD 0014) | 8 Oct 2025 | Drug product |
| Supporting document 22 (eCTD 0022) | 24 Nov 2025 | Process |
| Supporting document 24 (eCTD 0024) | 17 Dec 2025 | Drug product |

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# CHAPTER IV: LABELING

For more details about the items in this template, please see Chapter IV (Labeling) of the NDA IQA Guide (OPQ-ALL-WI-0006)

| | |
|---|---|
| **NDA Number** | 220482 |
| **Assessment Cycle Number** | 1 |
| **Drug Product Name** | Cypsedo (cipepofol injectable emulsion) |

**Assessment Recommendation:** Choose an item.

| Item | Assessment Conclusion | SDN # where labeling is adequate ("N/A" otherwise) |
|---|---|---|
| Prescribing Information Labeling | Choose an item. | **0001** |
| Patient Information | Choose an item. | **NA** |
| Instruction for Use (IFU) | Choose an item. | **NA** |
| Container Labels | Choose an item. | **0001** |
| Carton Labeling | Choose an item. | **0001** |

**Brief Description of Outstanding Issues:**

**Submissions being reviewed:**

| Document Reviewed (eCTD #, SDN #) | Date Received | Information Provided |
|---|---|---|
| 0001 | 05/30/2025 | Prescribing Information, Carton/Container labels |
| 0029 | 02/26/2026 | Carton/Container labels |

## 1.0 PRESCRIBING INFORMATION[1]

**Assessment of Product Quality Related Aspects of the Prescribing Information:**

[1] Labeling Review Tool (LRT) (March 2022), including use of consistent terminology for dosage form and unit of measure for strength in the product title and DOSAGE FORMS AND STRENGTHS heading in Highlights, in the DOSAGE AND ADMINISTRATION, DOSAGE FORMS AND STRENGTHS, DESCRIPTION, and HOW SUPPLIED/STORAGE AND HANDLING sections (see page 2 of LRT)


| Item | Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A") | Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate) |
|---|---|---|
| **Product Title in Highlights[2] [21 CFR 201.57(a)(2)]** | | |
| Established name(s)[3] | Adequate | Adequate |
| Route(s) of administration | Adequate | |
| Controlled drug substance symbol (if applicable) | N/A | |
| Initial U.S. Approval [§201.57(a)(3)] | Adequate | |
| **Dosage Forms and Strengths Heading in Highlights [§ 201.57(a)(8)]** | | |

[2] Draft guidance: *Product Title and Initial U.S. Approval in the Highlights of Prescribing Information for Human Prescription Drug and Biological Products — Content and Format* (January 2018)

[3] Established name = [Drug] [Route of Administration] [Dosage Form]. Do use not "USP" descriptor in the product title or within the Highlights (see page 3 of LRT).

| Item | Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A") | Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate) |
|---|---|---|
| Dosage form(s)[4] and strength(s) in metric system[5] | Adequate | Adequate |
| If the drug product contains an active ingredient that is a salt, clearly state whether the strength is based on the active moiety (e.g., Tablets: 10 mg of drug-x) or active ingredient (e.g., Tablets: 10 mg of drug-x hydrochloride).[6] | N/A | Not salt |
| Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored."[7] | N/A | N/A |
| For injectable drug products for parenteral administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use). Other package terms include pharmacy bulk package and imaging bulk package.[8] | Inadequate | The Applicant intends to market the product as "single-patient-use." "Single-patient-use" should be revised to "single-dose." |

**Assessment:** *Adequate*

[4] Draft guidance: *Product Title and Initial U.S. Approval in the Highlights of Prescribing Information for Human Prescription Drug and Biological Products — Content and Format* (January 2018); USP <1151>; USP Nomenclature Guideline
[5] Labeling Review Tool (March 2022, page 13), include limited packaging information; USP <7>
[6] Guidance: *Naming of Drug Products Containing Salt Drug Substances* (June 2015); MAPP 5021.1
[7] Guidance: *Tablet Scoring: Nomenclature, Labeling, and Data for Evaluation* (March 2013)
[8] Guidance: *Selection of the Appropriate Package Type Terms and Recommendations for Labeling Injectable Medical Products Packaged in Multiple-Dose, Single-Dose, and Single-Patient-Use Containers for Human Use* (October 2018); USP <659>

## 1.2 FULL PRESCRIBING INFORMATION

### 1.2.1 Section 2 (DOSAGE AND ADMINISTRATION)[9]

(b) (4)

| Item | Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A") | Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate) |
|---|---|---|
| **DOSAGE AND ADMINISTRATION section** | | |
| Special instructions for product preparation (e.g., reconstitution and resulting concentration, dilution, compatible diluents and/or soft food[10], storage conditions needed to maintain the stability of the reconstituted or diluted product). | Adequate | The Applicant states it should not be diluted. |
| Important administration instructions supported by product quality information (e.g., do not crush or chew extended-release tablets, instructions for mixing with food). | N/A | N/A |

[9] See § 201.57(c)(3); draft guidance: *Dosage and Administration Section of Labeling for Human Prescription Drug and Biological Products — Content and Format* (January 2023); Labeling Review Tool (March 2022, page 25)

[10] Draft Guidance: Use of Liquids and/or Soft Foods as Vehicles for Drug Administration: General Considerations for Selection and In Vitro Methods for Product Quality Assessments

| Item | Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A") | Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate) |
|---|---|---|
| For parenteral products: include statement: *"Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit."*[11] | Adequate | Statement present |
| If there is a USP monograph for the drug product and it contains a labeling requirement, ensure the labeling requirement is fulfilled.[12] Note the labeling requirement may be applicable to another section of the PI (e.g., Section 11). | N/A | No USP monograph. |
| For radioactive products, include radiation dosimetry for the patient and healthcare practitioner(s) who administer the drug | N/A | N/A |
| For hazardous products, include the statement *"DRUG X is a hazardous drug. Follow applicable special handling and disposal procedures.*[x]*"* with x numerical citation to "OSHA Hazardous Drugs." | N/A | N/A |

**Assessment:** *Adequate*

### 1.2.2 Section 3 (DOSAGE FORMS AND STRENGTHS)[13]

(b) (4)

[redacted]

[11] §201.57(c)(3)(iv)
[12] USP General Notices 2.30 Legal Recognition
[13] See § 201.57(c)(4); Labeling Review Tool (March 2022, page 29)

| Item | Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A") | Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate) |
|---|---|---|
| **DOSAGE FORMS AND STRENGTHS section** | | |
| Available dosage form(s) | Adequate | Adequate |
| Strength(s) in metric system | Adequate | |
| If the active ingredient is a salt, apply the USP Salt Policy per FDA Guidance. Clearly state whether the strength is based on the active moiety (e.g., Tablets: 10 mg of drug-x) or active ingredient (e.g., Tablets: 10 mg of drug-x hydrochloride). No equivalency statement. | N/A | N/A |
| A description of the identifying characteristics of the dosage forms, including shape, color, coating, scoring, imprinting, and color and clarity of the solution, when applicable. | Inadequate | Revise to include identifying characteristic. (e.g., "white or off-white emulsion") |
| Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored." | N/A | N/A |
| For injectable drug products for parenteral administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use). Other package type terms include pharmacy bulk package and imaging bulk package (see USP <659>). | Inadequate | "Single-patient-use" should be revised to "single-dose." |

**Assessment:** *Adequate*

Adequate, pending revisions highlighted in red font.

### 1.2.3 Section 11 (DESCRIPTION)[14]

(b) (4)

| Item | Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A") | Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate) |
|---|---|---|
| **DESCRIPTION section** | | |
| Proprietary and established name(s)[15] [§ 201.57(c)(12)(i)(A)]. | Inadequate | Revise to "CYPSEDO (cipepofol injectable emulsion)" as only proprietary name is included and dosage form is missing. |
| Dosage form(s) and route(s) of administration [§ 201.57(c)(12)(i)(B)]. | Inadequate | |
| If the active ingredient is a salt, apply the USP Salt Policy and include the equivalency statement per Salt Guidance and MAPP. For example: "TRADENAME contains 100 mg of drug-x (equivalent to 123.7 mg of drug-x hydrochloride)" [§ 201.57(c)(12)(i)(C)]. | N/A | N/A |
| List inactive ingredients (not required for oral use, except for colorant) by the USP/NF names | Inadequate | Revise to include list of inactive ingredients in alphabetical order and include quantities. |

[14] See § 201.57(c)(12); Labeling Review Tool (March 2022, page 56)
[15] Use of "USP" descriptor is not required to be included next to the established name throughout Prescribing Information (PI) labeling. If an applicant wants to use the "USP" descriptor next to the established name in the PI, recommend limiting its use to the product quality sections of the Full Prescribing Information (FPI) (i.e., DOSAGE FORMS AND STRENGTHS, DESCRIPTION, HOW SUPPLIED/STORAGE AND HANDLING) (see page 3 of LRT).

| Item | Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A") | Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate) |
|---|---|---|
| in alphabetical order.[16] Avoid brand names. [§ 201.57(c)(12)(i)(C)]. | | |
| For parenteral injectable dosage forms, include the name and quantities of all inactive ingredients. For ingredients added to adjust the pH or make isotonic, include the name and statement of effect. [§ 201.100(b)(5)(iii)]. | Inadequate | |
| If alcohol is present, must provide the amount of alcohol in terms of percent volume of absolute alcohol at 60 °F. (15.56 °C) [§ 201.10(d)(2)]. | N/A | N/A |
| Sterility statement (if applicable) [§ 201.57(c)(12)(i)(D)]. | Adequate | Adequate |
| Pharmacological/Therapeutic class[17] [§ 201.57(c)(12)(i)(E)]. | Adequate | Adequate |
| Chemical name[18], structural formula, molecular weight [§ 201.57(c)(12)(i)(F)]. | Adequate | Revise to include chemical name. Structural formula and molecular weight are correct. |
| If radioactive, statement of important nuclear characteristics [§ 201.57(c)(12)(i)(G)]. | N/A | N/A |
| Other important chemical or physical properties (such as pKa or pH) [201.57(c)(12)(ii)]. | Inadequate | Revise to include physical properties (i.e., solubility, pKa, etc.) |

[16] Per § 201.100(b)(5)(i) and (ii), flavoring and colorants may be designated as such without naming their components except for FD&C Yellow No 5 and FD&C Yellow No 6, which must be listed per § 201.20. Per § 201.100(b)(5)(iii), trace amounts of harmless substances added solely for individual product identification need not be named. If an applicant wants to use the National Formulary (NF) descriptor next to excipients, recommend limiting its use to the product quality sections of the FPI (see page 3 of LRT). Do not list brand names, e.g., Opadry, Eudragit, Polistirex, etc.

[17] Listed before "indicated for" in INDICATIONS AND USAGE of Highlights section [§ 201.57(a)(6)]; can also search the term "FDA EPC Text Phrases" in FDA's Labeling Resources for Human Prescription Drugs for the most recent EPC list.

[18] Chemical names do not need to be capitalized unless it appears at the beginning of a sentence (see *Preferred IUPAC Names Provisional Recommendation*, September 2004; Chapter 1, par. 16 Name writing, p.80-90).

| Item | Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A") | Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate) |
|---|---|---|
| For oral prescription drug products, include gluten statement[19] (if applicable). | N/A | N/A |
| Remove statements that may be misleading or promotional (e.g., "synthesized and developed by Drug Company X," "structurally unique molecular entity"). | N/A | |
| If there is a USP monograph for the drug product and it contains a labeling requirement, ensure the labeling requirement is fulfilled. Note the labeling requirement may be applicable to another section of the PI (e.g., Section 2). | N/A | |

**Assessment:** *Adequate*

Revise to include all pending revisions in red.

### 1.2.4 Section 16 (HOW SUPPLIED/STORAGE AND HANDLING)[20]

**16 HOW SUPPLIED/STORAGE AND HANDLING**

(b) (4)

[redacted]

[19] Draft guidance: *Gluten in Drug Products and Associated Labeling Recommendations* (December 2017)
[20] See § 201.57(c)(17); Labeling Review Tool (March 2022, page 70). Consider including proprietary name and established name.

| Item | Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A") | Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate) |
|---|---|---|
| **HOW SUPPLIED/STORAGE AND HANDLING section** | | |
| Available dosage form(s) [§ 201.57(c)(17)]. | Inadequate | Revise to include nonproprietary name and dosage form. |
| Strength(s) in metric system. [§ 201.57(c)(17)(i)] If the active ingredient is a salt, apply the USP Salt Policy per FDA Guidance. Clearly state whether the strength is based on the active moiety. No equivalency statement. | Adequate | |
| Available units (e.g., bottles of 100 tablets) [§ 201.57(c)(17)(ii)]. | Adequate | |
| Identification of dosage forms (e.g., shape, color, coating, scoring, imprinting, and color and clarity of the solution, when applicable); Include NDC(s) [§ 201.57(c)(17)(iii)]. | Choose an item. | Revise to include NDC and identification of dosage form. |
| Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored." | N/A | |
| For injectable drug products for parenteral administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use). Other package terms include pharmacy bulk package and imaging bulk package (see USP <659>). | Inadequate | Revise to "single-dose" per previous comment. |

| Item | Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A") | Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate) |
|---|---|---|
| Special handling about the supplied product (e.g., protect from light, refrigerate). If there is a statement to "Dispense in original container," provide reason why (e.g., to protect from light or moisture, to maintain stability, etc.). For hazardous drugs, state "DRUG X is a hazardous drug. Follow applicable special handling and disposal procedures.[x]" with x numerical citation to "OSHA Hazardous Drugs." [§ 201.57(c)(17)(iv)] | Adequate | Adequate |
| Storage conditions. Where applicable, use USP storage range rather than storage at a single temperature. (see USP <659>). | Adequate | Adequate |
| Latex: If product does not contain latex and manufacturing of product and container did not include use of natural rubber latex or synthetic derivatives of natural rubber latex, state: *"Not made with natural rubber latex. Avoid statements such as "latex-free."*[21] | N/A | N/A |
| Include information about child-resistant packaging[22] (if chosen by manufacturer). | N/A | |

**Assessment:** *Adequate*

Adequate, pending revisions highlighted in red.

[21] Guidance: *Recommendations for Labeling Medical Products to Inform Users that the Product or Product Container is not Made with Natural Rubber Latex* (December 2014)
[22] Guidance: *Child-Resistant Packaging Statements in Drug Product Labeling* (August 2019)

### 1.2.5 Other Sections of Labeling

There may be other sections of labeling that contain product-quality related information. For example, there are specific required/recommended warnings for certain inactive ingredients [e.g., aspartame, aluminum in large and small volume parenterals, sulfites, FD&C Yellow Number 5 (tartrazine), and benzyl alcohol]. Please notify the prescription drug review division if the product contains any of these inactive ingredients.

Please include your comments about other sections of labeling if they contain product quality information.

Manufactured for:

Haisco-USA Pharmaceuticals, Inc.

1200 US Highway 22E

Suite 2000

Bridgewater, New Jersey 08807

Made in Italy

### 1.2.6 Manufacturing Information After Section 17 (for drug products)[23]

| Item | Item in Proposed Labeling (choose "Adequate" or "Inadequate") | Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate) |
|---|---|---|
| **Manufacturing Information After Section 17** | | |
| Name and location of business (street address, city, state, and zip code) of the manufacturer, distributor, and/or packer. | Adequate | Adequate |

**Assessment:** *Adequate*

### 3.0 CONTAINER AND CARTON LABELING[24]

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

[23] § 201.1(h)(5) and 201.1(i); Labeling Review Tool (March 2022, page 74)
[24] Carton and Container Labeling Resources

| Item | Item in Proposed Carton Labeling (choose "Adequate", "Inadequate", or "N/A") | Is item in Container Labels same as that of Carton Labeling? | Assessor's Comments about Container Labels and Carton Labeling (If an item is Inadequate or different, provide more details, as appropriate) |
|---|---|---|---|
| Proprietary name and established name[26], (font size and prominence) [§ 201.10(g)(2)]. | Adequate | Yes | N/A |
| Strength(s) in metric system [§ 201.100(b)(4) & 201.100(d)].[27] | Adequate | Yes | |
| Route(s) of administration, not required for oral use [§ 201.100(b)(3)]. | Adequate | Yes | |
| If the active ingredient is a salt, include the equivalency statement per Salt Guidance and MAPP [§ 201.10(d)(1) & 201.100(b)(4), USP <1121>]. | N/A | Yes | |
| Net contents (e.g., tablet count, volume of liquid) [§ 201.51(a)].[28] | Inadequate | Yes | Revise "Each vial contains: CYPSEDO 50 mg/20 mL" to "Each vial contains: 50 mg of cipepofol (2.5 mg/mL)." |
| "Rx only" displayed on the principal display [§ 201.100(b)(1)]. | Adequate | Yes | N/A |
| NDC (requested, but not required for all labels or labeling) [§ 201.2 & 207.35]. | Adequate | Yes | |
| Lot number and expiration date [§ 201.18 & 201.17]. | Inadequate | Yes | Revise to "YYYY-MMM" instead of "MMM-YYYY" per FDA Guidance "Safety Considerations for Container Labels and Carton Labeling Design to |

[26] Established name = [Drug] [Route of Administration] [Dosage Form]

[27] Express as " XX mg per tablet" or "XX mg per capsule" for strength of professional samples of solid oral dosage form with small net quantities per container (e.g., 5 or less) or blister pack/carton. See Guidance: *Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors* (May 2022)

[28] § 201.51(h): A drug shall be exempt from compliance with the net quantity declaration required by this section if it is an ointment labeled "sample", "physician's sample", or a substantially similar statement and the contents of the package do not exceed 8 grams.

| Item | Item in Proposed Carton Labeling (choose "Adequate", "Inadequate", or "N/A") | Is item in Container Labels same as that of Carton Labeling? | Assessor's Comments about Container Labels and Carton Labeling (If an item is Inadequate or different, provide more details, as appropriate) |
|---|---|---|---|
| | | | Minimize Medication Errors" |
| Storage conditions. If applicable, include a space on the carton labeling for the user to write the beyond-use-date (BUD). | Adequate | Yes | Says "Store between 2°C to 25 °C (35.6 °F to 77 °F). |
| For injectable drug products for parenteral administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use). Other package terms include pharmacy bulk package and imaging bulk package, and these products require a "Not for direct infusion" statement. (See USP <659>). | Inadequate | Yes | Revise to "single-dose" |
| Name of all inactive ingredients, in alphabetical order [§ 201.10(a)] [except for oral drug per § 201.100(b)(5) or limited space per § 201.10(i)(2)]. | Inadequate | Yes | Revise to put in alphabetical order |
| For parenteral injectable dosage forms, include quantities of all inactive ingredients. For ingredients added to adjust the pH or make isotonic, include the name and statement of effect. [§ 201.100(b)(5)(iii)]. | Adequate | No | Inactive ingredients only listed on carton, not on container. This is acceptable because there is no room on the vial label. |
| If alcohol is present, must provide the amount of alcohol in terms of percent volume of absolute alcohol at 60 °F. (15.56 °C) [§ 201.10(d)(2)]. | N/A | Yes | |

| Item | Item in Proposed Carton Labeling (choose "Adequate", "Inadequate", or "N/A") | Is item in Container Labels same as that of Carton Labeling? | Assessor's Comments about Container Labels and Carton Labeling (If an item is Inadequate or different, provide more details, as appropriate) |
|---|---|---|---|
| Linear Bar code [§ 201.25(c)(2)].[29] | Adequate | Yes | |
| Adequate directions for use: "Recommended Dosage: See Prescribing Information" [§ 201.5 & 201.55]. | Adequate | Yes | |
| Name of manufacturer/distributor /packer [§ 201.1(a), 201.1(h)(5)]. | Adequate | Yes | |
| "Keep out of reach of children" statement, optional for Rx, required for OTC [§ 201.66(c)(5)(x)]. | N/A | Yes | There is no statement. |
| If there is a Medication Guide, must include a statement about dispensing a Medication Guide to each patient. | N/A | Yes | No medication guide. |
| No text on Ferrule and Cap overseal of a vial of injectable products unless a cautionary statement is required. (USP <7>). | N/A | Yes | N/A |
| If there is a USP monograph for the drug product and it contains a labeling requirement, ensure the labeling requirement is fulfilled. | N/A | Yes | No USP monograph. |
| When a drug product differs from the relevant USP standard of strength, quality, or purity, as determined by the application of the tests, procedures, and acceptance | N/A | Yes | |

[29] See § 201.25(b)(1)(i) for a list where bar code is not required, e.g., prescription drug samples, medical gases, radiopharmaceuticals, etc.

| Item | Item in Proposed Carton Labeling (choose "Adequate", "Inadequate", or "N/A") | Is item in Container Labels same as that of Carton Labeling? | Assessor's Comments about Container Labels and Carton Labeling (If an item is Inadequate or different, provide more details, as appropriate) |
|---|---|---|---|
| criteria set forth in the relevant compendium, its difference shall be plainly stated on its label.[30] | | | |
| And others if space is available. | N/A | Yes | N/A |

**Assessment of Carton Labels and Container Labeling:** *Adequate*
**Adequate, pending revisions in red.**

## 4. OUTSTANDING ISSUES AND RECOMMENDATIONS

***None***

*Primary Labeling Assessor Name and Date: Grace Chiou, Ph.D.*

*Secondary Assessor Name and Date (and Secondary Summary, as needed): Julia Pinto, Ph.D.*

[30] USP General Notices 3.20 Indicating Conformance

Grace Chiou

Digitally signed by Grace Chiou
Date: 3/06/2026 10:35:18AM
GUID: 5c5df155002b1863abe42e6c00c2780f

Julia Pinto

Digitally signed by Julia Pinto
Date: 3/06/2026 10:56:20AM
GUID: 5050dbcb00001294a888a4bdc20a3a58

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# CHAPTER VII: MICROBIOLOGY

IQA ANDA Assessment Guide Reference

| | |
|---|---|
| **Product Information** | Induction of general anesthesia in adults undergoing surgery. |
| **NDA Number** | 220482 |
| **Assessment Cycle Number** | MR01 |
| **Drug Product Name / Strength** | Cipepofol (50 mg per 20 mL); single dose. |
| **Route of Administration** | Intravenous. |
| **Applicant Name** | Haisco-USA Pharmaceuticals, Inc. |
| **Manufacturing Site** | (b) (4) |
| **Method of Sterilization** | (b) (4) |

***Assessment Recommendation:*** **Adequate**

***Theme:***

| | |
|---|---|
| ☐ N/A | ☐ Depyrogenation Validation Data |
| ☒ Product Sterility Assurance | ☐ Product Release and/or Stability Specifications |
| ☐ Media Fill Data | ☐ Validation for Product Release and/or Stability Test Method |
| ☐ Validation of Product Test | ☐ Other (Requires Division Director Approval) |
| ☐ Due to Consult | |

***Justification:*** *view justification statements found at:* **Justification Statements**

| |
|---|
| N/A |
| Other (Requires Division Director Approval) – *Assessor writes-in justification here if "other" selected as theme.* |

***Assessment Summary:*** (b) (4)

**List Submissions Being Assessed (table):**

| Document(s) Assessed | Date Received |
|---|---|
| eCTD Seq #0001 | 05/30/2025 |
| eCTD Seq #0010 | 09/12/2025 |

**Highlight Key Issues from Last Cycle and Their Resolution:** N/A

**Remarks:** The submission is **recommended** for approval on the basis of sterility assurance.

**Concise Description of Outstanding Issues:** None.

**Supporting Documents:** A211574MR01.doc, dated 06/27/2019, A 212857MR01.doc, dated 12/11/2019 and N213407MR01_3.25.20.docx, dated 3/25/2020 and D10953M64R01.docx, dated 08/08/2024.

**Select Number of Approved Comparability Protocols: 0**

## S Drug Substance- Not Applicable.

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

- **Description of the Composition of the Drug Product**
  (*description-and-composition.pdf and container-closure-system-1.pdf)*

The Cipepofol injectable emulsion drug product (DP) is presented as a small volume injection at 2.5 mg/mL, with a 20 mL fill volume in each 20mL vial. The DP is non-preserved and administered via intravenous (IV) route. The overall formulations used for the drug product are summarized below:

**Table 1: Composition of Cipepofol Injectable Emulsion**

| Formulation Components | Quantity (per 20 mL Fill Volume) | Concentration % (w/v) | Function | Quality Grade |
|---|---|---|---|---|
| Cipepofol[1] | 50 mg | 0.25 (2.5 mg/mL) | Active pharmaceutical ingredient | In-house |
| Soybean oil[2] | 1000 mg | 5 | (b) (4) | USP |
| Medium-chain triglycerides | 1000 mg | 5 | | NF |
| Egg phospholipids[3] | 240 mg | 1.2 | | NF |
| Glycerin[4] | 450 mg | 2.25 | | USP |
| Sodium oleate | 6 mg | 0.03 | | In-house |
| Edetate disodium[5] | 1.1 mg | 0.0055[6] | | USP |
| (b) (4) | | | | NF |
| Water for injection | q.s. to 20 mL | q.s. to target DS concentration | | USP |
| (b) (4) | | | | NF |

DS = drug substance; NF = National Formulary; q.s.= quantity sufficient; USP = United States Pharmacopeia; w/v = weight/volume

[1]Also known as HSK3486, HPF, or ciprofol (formerly approved drug name in China).

(b) (4)

- **Description of container closure system –**

The following container-closure systems are used for the production:

**Table 1: Primary Packaging Components for Cipepofol DP**

(b) (4)

**Reviewer's Assessment:** Based on the above information the reviewer has concluded that applicant has provided adequate description of the drug product composition and the container closure system designed to maintain product sterility.

**Acceptable**

## P.2 Pharmaceutical Development

(b) (4)



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**Acceptable**

## P.7 Container Closure

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

## P.8 Stability

## P. 8.1 Stability Summary and Conclusion

*(postapproval-stability.pdf)*

Stability Protocol:

| Stability Test* | Initial | 3M | 6M | 12M | 24M | 36M | 48M |
|---|---|---|---|---|---|---|---|
| Bacterial Endotoxin | X | - | - | X | X | X | X |
| Sterility | X | - | - | - | - | - | - |
| CCIT | X | - | - | X | X | X | X |

**: The above table captures stability schedule at 25°C ± (b)(4)°C/60% RH ± 5% RH (long-term) storage condition.*

*Proposed Expiry*: Appears to be (b) (4) months.

**Reviewer's Assessment:** Based on the above information the reviewer concluded that the applicant has provided satisfactory stability protocol information to support the (b) (4) manufacturing process for the drug product.

**Acceptable**

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

Post Approval Stability Commitment:

The applicant commits to placing the first three full-scale commercial lots of the subject drug product into their long-term stability program. Thereafter on an annual basis, one production lot will be added to the ongoing stability program. The updated stability data will be shared with the agency in annual reports.

**Reviewer's Assessment:** The applicant confirms the sensitivity of the CCIT via IR.

**Acceptable**

## P.8.3 Stability Data

[*stability-data.pdf]*

Stability testing have been performed for three batches [V002B20, V004B20, and V005B20]. At least 36 months of data were provided at 25°C ± (b)(4)°C/60% RH ± 5% RH (long-term storage condition) for bacterial endotoxin and sterility and CCIT. Note that even though the CCIT appears to be performed *in lieu of sterility* test on stability, sterility test appears to be performed in the inverted position as well. The results from long-term stability were reviewed, and all the results met the minimum acceptance criteria for bacterial endotoxin and sterility and CCIT.

**Reviewer's Assessment:** The applicant provided adequate stability data to support the (b) (4) manufacturing process for the drug product. Note that the post approval stability protocol does not include sterility testing. Sterility testing only stated to be performed at the release and the CCIT is scheduled to be performed *in lieu of sterility* test on stability at the initial, 12-, 24-, 36- and 48-months' time point.

**Acceptable**

# A Appendices

## A.2 Adventitious Agents Safety Evaluation

**Reviewer's Assessment:** Not applicable

## A.2.1 Materials of Biological Origin

**Reviewer's Assessment:** Not applicable

## A.2.2 Testing at Appropriate Stages of Production

**Reviewer's Assessment:** Not applicable

## A.2.3. Viral Testing of Unprocessed Bulk

**Reviewer's Assessment:** Not applicable

## A. 2.4 Viral Clearance Studies

**Reviewer's Assessment:** Not applicable

# R Regional Information

***Executed Batch Records***

The batch records confirm that validated (b) (4) manufacturing processes were used for the manufacture of all three batches. Batch records also comply with minimum bacterial endotoxin and sterility and CCIT specifications.

**Reviewer's Assessment:** Based on the information provided the reviewer has concluded that the applicant has provided adequate executed batch record data to support the (b) (4) manufacturing process for the drug product.

**Acceptable**

***Comparability Protocols***

**Reviewer's Assessment:** Not provided for this application.

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

### *2. A. Package Insert*

*Storage temperature*: CYPSEDO vials are stored at 2-25°C (35.6-77°F). Do not freeze. Shake well before use.

*Dilution*: This product should be given as an undiluted intravenous injection.

*In-use period and supporting hold-time study*: Based on the information provided in the 2.3.P *drug-product-cipepofol* (b) (4) *.pdf, page 25/56;* an *in-use period* for up to 12 hours is proposed during the dose administration. The proposed DP is administered directly through the drug delivery system without dilution. The drug delivery components for administration include syringe, needle, syringe cap (optional), extension set (optional, a tubing that connects delivery components to facilitate the dose administration), 3-way stopcock (optional), and IV catheter (see the Table 9 for details). Hence to simulate the clinical use and support the proposed 12 hours *in-use period*, microbial proliferation effect has been evaluated.

The proposed DP three separate batches (R001B22A, V002B20A and V005B20A) were inoculated with USP <51> compendial organism and incubated at 30-35°C protected from light. The final concentration of the inoculum size in the test product was $\geq 10^5$ CFU/mL. Microbial enumeration (*S. aureus, P. aeruginosa, E. coli, C. albicans, and A. brasiliensis*) was performed as per USP <61> (Pour plate method) at 0, 2, 4, 6, 8, 10, 12, and 14 hours respectively. Based on the data there was no increase in $\log_{10}$ values (increased by $<0.5$ $\log_{10}$ at 14-hours compared to 0 hour) for any of the organism tested at 14-hours compared to 0 hour. Hence, DP *in-use period* for up to 12 hours is supported by the study.

**Reviewer's Assessment:** Based on the information provided the reviewer has concluded that the applicant has provided adequate labelling information.

**Acceptable**

***Post-Approval Commitments:***

**Reviewer's Assessment:** Not applicable

***Lifecycle Management Considerations***

**Reviewer's Assessment:** Changes to the container closure system, component, and equipment sterilization/ depyrogenation process, and vial filling line could affect microbiological quality of the subject drug product.

***List of Deficiencies:*** *None.*

***Primary Microbiology Reviewer Name and Date:***

Koushik Paul, Ph.D. and 09/22/2025

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

Jesse Wells, Ph.D. and 09/22/2025

Jesse Wells

Digitally signed by Jesse Wells
Date: 9/22/2025 09:32:25AM
GUID: 508da70b00028ea901ac6652677f7d00

Koushik Paul

Digitally signed by Koushik Paul
Date: 9/22/2025 08:30:42AM
GUID: 5600522e0069b02f59c7bd85b6b54742

Valerie Amspacher

Digitally signed by Valerie Amspacher
Date: 3/26/2026 10:32:25AM
GUID: 5714dbd10078d2d3d9b60a0ceb819fc3

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/s/

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