CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

211759Orig1s000

PRODUCT QUALITY REVIEW(S)

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Office of Pharmaceutical Quality

New Drug Application (NDA)
Integrated Quality Assessment Template

NDA Executive Summary

1. Application/Product Information

NDA Number	211759		
Applicant Name	codaDOSE, Inc.		
Drug Product Name	Celecoxib Oral Suspension		
Dosage Form	Suspension		
Proposed Strength(s)	10 mg/mL		
NDA Classification	Type 3 - New Dosage Form		
Route of Administration	Oral		
Maximum Daily Dose	400 mg		
Rx/OTC Dispensed	Rx		
Proposed Indication	Osteoarthritis (OA)		
Drug Product Description	White, opaque, (b) (4) suspension packaged in (b) (4) amber bottle with (b) (4)		
Co-packaged product information	N/A		
Device information	N/A		
Storage Temperature/ Conditions	25 ºC		
Review Team	**Discipline**	**Primary**	**Secondary**
	Drug Substance	Brian Cawrse	Sam Bain
	Drug Product/ Labeling	Mariappan Chelliah	Valerie Amspacher/ Julia Pinto
	Manufacturing	Raeann Wu	Nathan Davis
	Biopharmaceutics	Bryan Ericksen	Ta-Chen Wu

	Microbiology	Peggy Kriger	Elizabeth Bearr
	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: A shelf-life 36 months may be granted, when stored at controlled room temperature 20°C to 25°C.

b. Additional Comments for Action

4. Basis for Recommendation:

a. Summary of Rationale for Recommendation:

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

This is a resubmission received 30 Sep 2024. This applicant was sent a refuse-to-file letter dated 30 April 2018. The refuse-to-file issues were clinical and non-clinical. This was fileable from a CMC perspective when originally submitted.

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 - Adequate
Microbiology - Adequate

Environmental Assessment: Categorical Exclusion - 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: N/A

Submission(s) Assessed	Document Date	Discipline(s) Affected
Supporting Document 7; eCTD 0006	30 Sep 2024	All, resubmission after RTF (no CMC refuse-to-file issues)
Supporting Document 16; eCTD 0015	19 Mar 2025	Biopharmaceutics
Supporting Document 17; eCTD 0016	31 Mar 2025	Process/facilities
Supporting Document 18; eCTD 0017	2 Apr 2025	Drug Product
Supporting Document 19; eCTD 0018	9 Apr 2025	Biopharmaceutics
Supporting Document 20; eCTD 0019	11 Apr 2025	Drug product
Supporting Document 21; eCTD 0020	5 May 2025	Drug substance
Supporting Document 22; eCTD 0021	15 May 2025	Microbiology

47 Page(s) have been Withheld in Full as b4 (CCI/TS) immediately following this page

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	211759
Assessment Cycle Number	1
Drug Product Name	Celecoxib Oral Suspension

Assessment Recommendation: Choose an item.

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

Brief Description of Outstanding Issues:

Submissions being reviewed:

Document Reviewed (eCTD #, SDN #)	Date Received	Information Provided

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)

1.1 HIGHLIGHTS OF PRESCRIBING INFORMATION

Shown below is the copy *of the proposed text* (SN0011/SDN12):

(b) (4)

[redacted]

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	
Route(s) of administration	Adequate	Because ROA is used as part of the dosage form, (b) (4) [redacted] at the end of the title was deleted.
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)]		
Dosage form(s)[4] and strength(s) in metric system[5]	Adequate	Edited per the recommendation of labeling review tool

[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).

[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>

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)
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	
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored."[7]	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]	N/A	

Assessment: *Adequate*

1.2 FULL PRESCRIBING INFORMATION

1.2.1 Section 2 (DOSAGE AND ADMINISTRATION)[9]

Shown below is the copy *of the proposed text* (SN0011/SDN12):

[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>
[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)

(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).	N/A	

[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)
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	
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]	N/A	
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	
For radioactive products, include radiation dosimetry for the patient and healthcare practitioner(s) who administer the drug	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	

Assessment: *Adequate*
No edit was made to this section.

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

[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)

Shown below is the copy *of the proposed text* (SN0011/SDN12):

(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 FORMS AND STRENGTHS section		
Available dosage form(s)	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	
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.	Adequate	Edited per the recommendation of labeling review tool
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 type terms include pharmacy bulk package and imaging bulk package (see USP <659>).	N/A	

Assessment: Choose an item.

(Provide any revision, if applicable, e.g., different color font, strikethrough, etc.) ***Any issues should be listed at the end in "OUTSTANDING ISSUES AND RECOMMENDATIONS"***

1.2.3 Section 11 (DESCRIPTION)[14]

Shown below is the copy *of the proposed text* (SN0011/SDN12):

(b) (4)

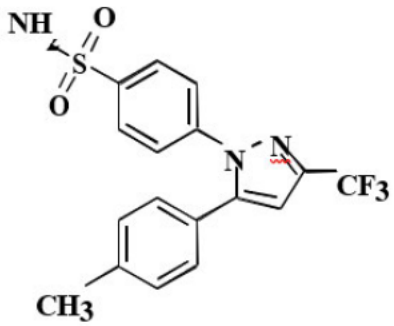
[redacted]

This section was rewritten as follows:

[14] See § 201.57(c)(12); Labeling Review Tool (March 2022, page 56)

11. DESCRIPTION

VYSCOXA contains celecoxib, a nonsteroidal anti-inflammatory agent. . The chemical name of celecoxib is 4-[5-(4-methylphenyl)- 3-(trifluoromethyl)-1H-pyrazol-1-yl] benzenesulfonamide. Celecoxib has a molecular weight of 381.38 g/mol, a molecular formula of $C_{17}H_{14}F_3N_3O_2S$, and the following structural formula:



Celecoxib is a white to off-white powder with a pKa of 11.1 (sulfonamide moiety). Celecoxib is hydrophobic (log P is 3.5) and is practically insoluble in aqueous media at physiological pH range.

The inactive ingredients in VYSCOXA oral suspension include: anhydrous citric acid, glycerin, magnesium aluminometasilicate, methylparaben, propylparaben, purified water, sucralose, trisodium citrate dihydrate, and xanthan gum. Sodium hydroxide and hydrochloric acid may be used to adjust the pH to 4.5 – 5.5.

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)].	Adequate	
Dosage form(s) and route(s) of administration [§ 201.57(c)(12)(i)(B)].	Adequate	
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	Adequate	

[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)
of drug-x hydrochloride)" [§ 201.57(c)(12)(i)(C)].		
List inactive ingredients (not required for oral use, except for colorant) by the USP/NF names in alphabetical order.[16] Avoid brand names. [§ 201.57(c)(12)(i)(C)].	Adequate	Edited per the recommendation of labeling review tool
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)].	N/A	
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	
Sterility statement (if applicable) [§ 201.57(c)(12)(i)(D)].	N/A	
Pharmacological/Therapeutic class[17] [§ 201.57(c)(12)(i)(E)].	Adequate	
Chemical name[18], structural formula, molecular weight [§ 201.57(c)(12)(i)(F)].	Adequate	

[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)
If radioactive, statement of important nuclear characteristics [§ 201.57(c)(12)(i)(G)].	N/A	
Other important chemical or physical properties (such as pKa or pH) [201.57(c)(12)(ii)].	Choose an item.	
For oral prescription drug products, include gluten statement[19] (if applicable).	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*

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

Shown below is the copy *of the proposed text* (SN0011/SDN12):

(b) (4)

[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)].	Adequate	
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)].	Adequate	
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>).	N/A	

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	Included the following statement: "Shake well before use"
Storage conditions. Where applicable, use USP storage range rather than storage at a single temperature. (see USP <659>).	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	
Include information about child-resistant packaging[22] (if chosen by manufacturer).	N/A	

Assessment: *Adequate*

[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.

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	This information is currently missing. The labeling was edited to include the following information: Manufactured for: codaDOSE, Inc. 5659 Southfield Drive, Flowery Branch, Georgia, 30542

Assessment: *Adequate*

2.0 PATIENT LABELING

Assessment of Product Quality Related Aspects of Patient Labeling (e.g., Medication Guides, Instructions for Use, Patient Information):

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

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments about Labeling (If an item is Inadequate, provide more details on the issues, as appropriate)
Established name[24]	Choose an item.	
Special preparation instructions (if applicable).	Choose an item.	
Storage and handling information (if applicable).	Choose an item.	
If the product contains a desiccant, ensure the desiccant has a warning (e.g., "Do not eat.") and the size and shape of the desiccant differ from the dosage form.	Choose an item.	
Active ingredient(s) (if applicable).	Choose an item.	
Alphabetical listing of inactive ingredients (if applicable).	Choose an item.	
Name and location of business (street address, city, state, and zip code) of manufacturer, distributor, and/or packer.	Choose an item.	

Assessment: *Adequate*
The medication Guide at the end of the PI discusses the general NSAIDs – not specifically the proposed drug product. This section will likely get revised to make it specific to this product as the labeling edits starts. Any appropriate edit will be made at that time.

3.0 CONTAINER AND CARTON LABELING[25]

3.1 Container Labels[26]

Copy of the container label (SN006/SDN7):

[24] Established name = [Drug] [Route of Administration] [Dosage Form]
[25] Carton and Container Labeling Resources
[26] Per § 201.10(h)(2)(i)(1), if the drug container is too small to bear all labeling information required by section 502(e)(1)(A)(ii) and (B) of the FD&C Act, the container label should bear: proprietary name, established name, lot number, the name of the manufacturer, packer, or distributor of the drug.

(b) (4)

3.2 Carton Labeling

There is no carton label.

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[27], (font size and prominence) [§ 201.10(g)(2)].	N/A	Adequate	
Strength(s) in metric system [§ 201.100(b)(4) & 201.100(d)].[28]	N/A	Adequate	
Route(s) of administration, not required for oral use [§ 201.100(b)(3)].	N/A	Adequate	

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

[28] 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)

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)
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	N/A	
Net contents (e.g., tablet count, volume of liquid) [§ 201.51(a)].[29]	N/A	Adequate	
"Rx only" displayed on the principal display [§ 201.100(b)(1)].	N/A	Adequate	
NDC (requested, but not required for all labels or labeling) [§ 201.2 & 207.35].	N/A	Adequate	
Lot number and expiration date [§ 201.18 & 201.17].	N/A	Adequate	
Storage conditions. If applicable, include a space on the carton labeling for the user to write the beyond-use-date (BUD).	N/A	Adequate	
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>).	N/A	N/A	
Name of all inactive ingredients, in alphabetical order [§ 201.10(a)] [except for oral drug per § 201.100(b)(5)	N/A	Adequate	Inactive ingredients are not listed. Acceptable for oral drug products.

[29] § 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)
or limited space per § 201.10(i)(2)].			
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)].	N/A	N/A	
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	
Linear Bar code [§ 201.25(c)(2)].[30]	N/A	Inadequate	Linear bar code is currently missing. We will ask the Applicant to include it.
Adequate directions for use: "Recommended Dosage: See Prescribing Information" [§ 201.5 & 201.55].	N/A	Adequate	
Name of manufacturer/distributor /packer [§ 201.1(a), 201.1(h)(5)].	N/A	Adequate	
"Keep out of reach of children" statement, optional for Rx, required for OTC [§ 201.66(c)(5)(x)].	N/A	Adequate	
If there is a Medication Guide, must include a statement about dispensing a Medication Guide to each patient.	N/A	N/A	
No text on Ferrule and Cap overseal of a vial of injectable	N/A	N/A	

[30] 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)
products unless a cautionary statement is required. (USP <7>).			
If there is a USP monograph for the drug product and it contains a labeling requirement, ensure the labeling requirement is fulfilled.	N/A	N/A	
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 criteria set forth in the relevant compendium, its difference shall be plainly stated on its label.[31]	N/A	N/A	
And others if space is available.	N/A	N/A	

Assesssment of Carton Labels and Container Labeling: *Adequate*

4. OUTSTANDING ISSUES AND RECOMMENDATIONS

Assess consistency of product-quality information in prescription drug labeling (PI, c/c labeling, and FDA-approved patient labeling). See Carton/Container Labeling Specific Resources for a presentation about inappropriate inconsistencies of product quality information between labeling. If there are inappropriate inconsistencies between the labeling (e.g., established name, strength(s), package type term, discard statement, identifying characteristics, storage, reconstitution/dilution instructions), please list these issues in this section.

[31] USP General Notices 3.20 Indicating Conformance

Suggested Edits for Carton Label (pending DMEPA concurrence):

1) The proposed container label is missing a linear bar code. In accordance with 21 CFR 201.25(c)(2), include a linear bar code.
2) The statement (b) (4) in the container label is not required. We recommend deleting it.
3) Include the following statement at the end of the storage statement in the container label: Shake well before use. Discard 21 days after opening.

Primary Labeling Assessor Name: Mariappan Chelliah

Secondary Assessor Name: Julia Pinto

Mariappan Chelliah

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Date: 6/04/2025 03:29:06PM
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Julia Pinto

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FDA U.S. FOOD & DRUG ADMINISTRATION

CHAPTER VI: BIOPHARMACEUTICS

NDA Number	NDA-211759-ORIG-1-RESUB-7
Assessment Cycle Number	1
Drug Product Name/ Strength	Vyscoxa (Celecoxib) Oral Suspension/10 mg/mL
Route of Administration	Oral
Applicant Name	codaDOSE, Inc.
Therapeutic Classification/ OND Division	CDER/OND/ON/DAAP
LD/RS Number	NDA 020998
Proposed Indication	Osteoarthritis (OA), Rheumatoid Arthritis (RA), Juvenile Rheumatoid Arthritis (JRA) in patients 2 years and older, and Ankylosing Spondylitis (AS)
Primary Reviewer	Bryan Ericksen, Ph.D.
Secondary Reviewer	Okponanabofa Eradiri, Ph.D.

Assessment Recommendation: **Adequate**

Background:
The Applicant is seeking approval of Vyscoxa (Celecoxib) Oral Suspension, 10 mg/mL, indicated for osteoarthritis. The Listed Drug (LD) for Vyscoxa is Celebrex® immediate-release capsules (NDA 020998). The initial NDA was received by FDA on March 9, 2018, but FDA determined that the submission was not sufficiently complete to permit a substantive review. Therefore, FDA issued a Refuse to File (RTF) letter dated April 30, 2018. As advised by the FDA in IND 122698 written response, the Applicant conducted a relative bioavailability study to bridge the proposed product and the LD, which is a different dosage form (capsules). The usual dose range of the oral suspension is as follows for the four indications: OA: 200 mg (20 mL) once daily or 100 mg (10 mL) twice daily; RA: 100 mg (10 mL) to 200 mg (20 mL) twice daily; JRA: 50 mg (5 mL) twice daily in patients 10 kg to 25 kg or 100 mg (10 mL) twice daily in patients more than 25 kg; AS: 200 mg (20 mL) once daily single dose or 100 mg (10 mL) twice daily, and if no effect is observed after 6 weeks, a trial of 200 mg (20 mL) twice daily may be of benefit.

In the current 505(b)(2) application, the Applicant reformulated Celecoxib Oral Suspension to be bioequivalent to the LD Celebrex, 200 mg, for chronic indications. A pharmacokinetic study was conducted using the reformulated Celecoxib Oral Suspension, which showed bioequivalence to the LD, Celebrex, in all clinically relevant measurements.

The Biopharmaceutics review was focused on the evaluation of the adequacy of the overall information/data supporting the proposed dissolution method and acceptance criterion. A summary of key findings is presented below.

Assessment Summary:

1) Dissolution Method and Acceptance Criterion

Solubility results indicate that the solubility of celecoxib would be too low in the physiologic pH range for a dissolution method to work with adequate sink conditions. Therefore, pH values above the physiologic range were tested. The Applicant developed an in-house dissolution method: Apparatus 2, 75 RPM, 1000 mL 0.04 M sodium phosphate tribasic, pH adjusted to 11.1 with H_3PO_4, with an SDS concentration of 0.5%. The discriminating ability of the dissolution method was tested using modified formulations that either had two parameters varied at once, had drastic changes, or involved replacing one excipient with another. A dissolution acceptance criterion of Q=(b) (4)% in 45 minutes was proposed, which is adequate.

2) Bridging of Formulations

Only one formulation is listed in the drug product development report that was selected for use in clinical trials. Therefore, bridging of formulations is not necessary.

3) Request for Biowaiver

No request for biowaiver was submitted. There is only one strength.

Recommendation:

From a biopharmaceutics perspective, NDA-211759-ORIG-1 for Vyscoxa (Celecoxib Oral Suspension), 10 mg/mL is deemed adequate and recommended for APPROVAL.

FDA-approved dissolution method and acceptance criterion for the proposed Celecoxib Oral Suspension at batch release and on stability:

Apparatus	Medium	Speed (rpm)	Volume (mL)	Acceptance Criterion
2 (Paddle)	0.04 M sodium phosphate tribasic, pH 11.1 + 0.5% SDS	75	1000	Q=(b) (4)% in 45 minutes

Submissions Being Assessed:

Document(s) Assessed	Date Received
NDA 211759/Sequence 0006/ Original Submission	**09/29/2024**
NDA 211759/Sequence 0015/ Response to Information Request	**03/19/2025**
NDA 211759/Sequence 0018/ Response to Information Request	**04/09/2025**

Concise Description of Outstanding Issues *(list bullet points with key information and update as needed)*: None

B.1 BCS DESIGNATION

The Applicant did not request a BCS biowaiver.

Solubility:

Aqueous solubility data in buffers across the physiological pH range are presented in the Dissolution Method Development Report provided in Module 3.2.P.2 in Sequence 0015. Celecoxib drug substance is not soluble in (b) (4) Therefore, solubility determinations were performed with the addition of (b) (4) and (b) (4)

The highest daily dose of Celecoxib Oral Suspension, 10 mg/mL, is 200 mg Celecoxib, or 20 mL. For the solubility studies, the equivalent of 200 mg of Celecoxib API was transferred into a 250 mL volumetric flask containing media. The samples were placed in a 40ºC chamber and stirred with magnetic stir bars on a stir plate for up to 24 hours. Samples were allowed to cool to room temperature and then filtered through 0.45 µm syringe filters with about 2 mL to waste. The pH 1.2 buffer was made using 0.085 M HCl and 0.05 M KCl. The pH 4.2 Acetate Buffer was made using 0.028 M Acetic Acid and 0.02 M Sodium Acetate Trihydrate. The pH 6.8 Phosphate Buffer was made using 0.05 M Potassium Phosphate Monobasic and 0.0225 M NaOH. The pH 7.4 Phosphate Buffer was made using 0.5 M potassium phosphate monobasic and 0.04 M NaOH.

(b) (4)

Table 1: Solubility Studies, Physiological pH

Media	mg/mL Celecoxib
Water	0.0005
pH 1.2 Buffer	0.0014
pH 4.5 Acetate Buffer	0.0005
pH 6.8 Phosphate	0.0003
pH 7.4 Phosphate Buffer	0.0002

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Permeability:

The Applicant did not submit permeability data. However, permeability of celecoxib was measured in a published study.[1] Harvested Caco-2 cells were counted with trypan blue and seeded at 100,000 cells/well on 12-well inserts having a pore size of 0.4 µm, and incubated in an incubator (Sanyo, Osaka, Japan) under 5% CO^2 atmosphere at 37 °C. For 21 days, the medium was changed every other day. The integrity of the Caco-2 cell monolayer was assessed at the conclusion of the incubation period by measuring Transepithelial Electrical Resistance (TEER) with a Millicell-ERS voltameter (Millipore Sigma, Burlington, VT, USA). The permeability result of pure celecoxib powder in drug suspension was $0.52 \pm 0.15 \times 10^{-6}$ cm/s. This result classifies celecoxib as high permeability. Therefore, celecoxib is a BCS Class II (low solubility, high permeability) drug substance.

Dissolution:

Dissolution was essentially complete in 45 minutes using the QC method, as shown in Figure 24, below.

B.2 DISSOLUTION METHOD AND ACCEPTANCE CRITERION

Assessment: Adequate

The dissolution method development report can be found by following this hyperlink: \\CDSESUB1\evsprod\NDA211759\0015\m3\32-body-data\32p-drug-prod\celecoxib-os\32p2-pharm-dev\32p2-solub-dissol-assess-report.pdf
The tests of discriminating ability of the dissolution method can be found by following this hyperlink: \\CDSESUB1\evsprod\NDA211759\0018\m3\32-body-data\32p-drug-prod\celecoxib-os\32p2-pharm-dev\32p2-disso-method-optim-report.pdf

The dissolution method development study included trials of different dissolution media as shown in Table 6. The trials incorporated (b) (4)

(b) (4)

(b) (4)

[1] Pharmaceutics. 2023 Jan 20;15(2):363. doi: 10.3390/pharmaceutics15020363

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Table 7: Dissolution Test Method

Media	0.04M Sodium Phosphate Tribasic, pH adjusted to 11.1 with H3PO4, with an SDS concentration of 0.5%
Media Volume	1000 mL
Paddle Speed	75 rpm
Media Temperature	37°C
Dispensing	(b) (4)
Pull Start Time	
Sampling	
Sampling points	5, 10, 15, 20, 30, 45, 60, and 90 minutes*

* Samples at these time points were performed during the initial assessment included in this report. Future studies post approval will include only 15, 30, and 45 minutes sampling times.

Complete dissolution data are shown for one lot of oral suspension in Table 8.

Table 8: Complete dissolution data, Test Product Celecoxib Oral Suspension (10 mg/1 mL), Lot 2207449

Vessel#	Time (min)							
	5	10	15	20	30	45	60	90
1	(b) (4)							
2								
3								
4								
5								
6								
7								
8								
9								
10								
11								
12								
Avg.	15	29	50	70	90	101	102	102
SD	8.94	8.14	9.26	8.56	4.37	1.29	0.52	0.52
%RSD	61	27	18	12	5	1	1	1
Min	(b) (4)							
Max								

The Applicant tested the discriminating ability of the dissolution method.

Critical Bioavailability Attributes (CBAs) including critical material attributes (CMAs), critical formulation variables (CFVs) and critical process parameters (CPPs) were defined as follows.

Celecoxib exhibits low aqueous solubility over the physiologic pH range but exhibits high permeability. Therefore, factors that affect the celecoxib solubility and rate of dissolution may be anticipated to impact the bioavailability. For the Celecoxib Oral Suspension, the API is (b) (4) The only aspect of the processing that is critical is (b) (4) but no effects of processing on solubility and/or rate of dissolution are anticipated. The Celecoxib API that is utilized in the oral suspension is Celecoxib polymorphic (b) (4) with a particle size of about (b) (4) Other polymorphic forms have been described with (b) (4) but there is no transition to these polymorphic forms during (b) (4) over the shelf-life of the product, as detailed in Section 5.2.1 of the Product Development Report RPT-0069 V5.0. The particle size of the API obtained from (b) (4) is controlled as part of the API specifications.

Regarding the (b) (4) utilized in the Celecoxib Oral Suspension drug product, the amounts of each of the (b) (4) are the critical formulation variables that are likely to affect the rate of dissolution. The (b) (4) .

Lab-scale batches were manufactured to evaluate the discriminating power of the method with changes to the (b) (4) for (b) (4) The changes to the formulations are provided in Table 9.

Table 9: Lab-Scale Batches, f2 Values versus Lot 2207449

Lot	F2 Value	Difference in Formulation from Registration Batches
2024CEL060	+	(b) (4)
2024CEL061	71	
2025CEL062	9	
2025CEL063	25	
2025CEL064	68	
2025CEL066	75	

(b) (4)

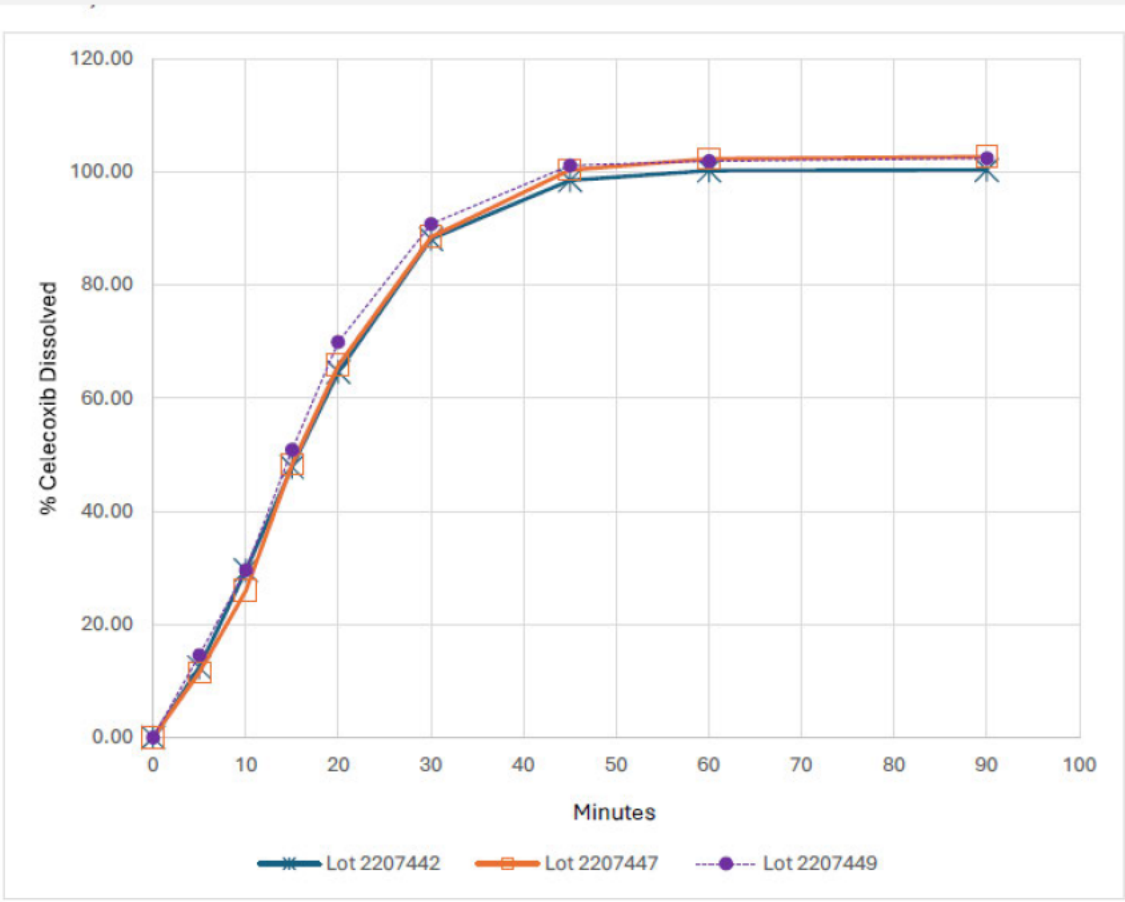
A similarity factor (f2) value greater than or equal to 50 indicates a sufficiently similar dissolution profile. Lot 2024CEL060, 2025CEL062, and 2025CEL063 demonstrate dissolution profiles which are significantly different from Registration Batch (Biobatch) lot 2207449, and lots 2024CEL061, 2025CEL064 and 2025CEL066 are similar to Registration (Biobatch) 2207449. Dissolution profiles of batches 2024CEL060, 2025CEL062, and 2025CEL063 different markedly from the unaltered control.

The dissolution profiles obtained with the proposed dissolution method for the critical formulation variables indicate that the type or concentration of the (b) (4) (b) (4) on the rate of dissolution for the celecoxib oral suspension.

The proposed dissolution method utilizes similar dissolution media as the original method. The original method utilized 0.04M Sodium Phosphate Tribasic Anhydrous buffer pH (b) (4) with (b) (4) SDS. The supporting validation data for the previous method are provided in Module 3.2.P.5.3. The proposed discriminative dissolution media will utilize 0.04M Sodium Phosphate Tribasic Anhydrous, pH 11.1 with 0.5% SDS. Use of the same buffer with a slight change in pH from pH (b) (4) o 11.1 and the same surfactant at a lower concentration (0.5% versus (b) (4) %) is not anticipated to require additional extensive validation studies for the analytical HPLC method. Robustness of the Dissolution Parameters will be addressed during the transfer to the CMO (b) (4)

Dissolution test results for Registration Batches, lots 2207442, 2207447, and 2207449, using the proposed optimized method, are shown in Figure 8. Each test sample was taken from separate bottles and administered according to the dosing instruction in the proposed labeling. The three lots show a similar dissolution profile.

Figure 8: Dissolution Results for Lots 2207442, 2207447, and 2207449 (Average of 12 Vessels)



The individual vessel dissolution profile data for the three Registration Batches is presented in Table 8, Table 10, and Table 11.

Table 10: Complete Dissolution Results, Lot 2207442

Vessel#	Time (min)							
	5	10	15	20	30	45	60	90
1	(b) (4)							
2								
3								
4								
5								
6								
7								
8								
9								
10								
11								
12								
Avg.	12	30	48	65	88	99	100	100
SD	3.31	6.80	6.75	3.72	3.63	3.27	1.83	1.98
%RSD	27	23	14	6	4	3	2	2
Min	(b) (4)							
Max								

Table 11: Complete Dissolution Results, Lot 2207447

Vessel#	Time (min)							
	5	10	15	20	30	45	60	90
1	(b) (4)							
2								
3								
4								
5								
6								
7								
8								
9								
10								
11								
12								
Avg.	11	26	48	66	89	100	102	103
SD	2.02	4.74	9.57	6.55	5.26	1.44	0.51	0.85
%RSD	18	18	20	10	6	1	0	1
Min	(b) (4)							
Max								

Dissolution Acceptance Criterion

The Applicant proposed Q=(b) (4)% in 45 minutes as the dissolution acceptance criterion.

Reviewer Assessment

Solubility results indicate that the solubility of celecoxib would be too low in the physiologic pH range for a dissolution method to work with adequate sink conditions, (b) (4). Therefore, pH values above the physiological range were tested. The 75 RPM paddle speed was adequately justified by the data in Figure 6. The discriminating ability of the dissolution method was investigated using modified formulations that either had two parameters varied at once, had drastic changes, or involved replacing one excipient with another. However, resulting changes were substantial, suggesting that more modest perturbations of the formulation would also have resulted in meaningful differences in dissolution profiles. Studies of the discriminating ability of the dissolution method are adequate. The dissolution acceptance criterion of Q (b) (4)% in 45 minutes adequately reflects the time taken to achieve complete dissolution (See Figure 8) and is adequate.

B.12 BRIDGING OF FORMULATIONS

Only one formulation is listed in the drug product development report that was selected for use in clinical trials. Therefore, bridging of formulations is not necessary.

B. 13 BIOWAIVER REQUEST

No request for biowaiver was submitted. There is only one strength.

BIOPHARMACEUTICS LIST OF DEFICIENCIES

None.

Primary Biopharmaceutics Assessor's Name and Date:
Bryan Ericksen, Ph.D. May 28, 2025

Secondary Assessor Name and Date (and Secondary Summary, as needed):
Okponanabofa Eradiri, Ph.D. June 17, 2025

Bryan Ericksen

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Date: 6/18/2025 08:52:39AM
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Okponanabofa Eradiri

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U.S. FOOD & DRUG ADMINISTRATION

CHAPTER VII: MICROBIOLOGY

Product Information	Indicated for osteoarthritis
NDA Number	211759
Assessment Cycle Number	1
Drug Product Name/Strength	Celecoxib Oral Suspension (VYSCOXA (proposed)/ 10 mg/mL
Route of Administration	Oral
Applicant Name	codaDOSE, Inc.
Therapeutic Classification/ OND Division	Non-Narcotic Analgesics/ OND/ON/DAAP
Manufacturing Site	(b) (4)
Method of Sterilization	N/A, product is non-sterile

Assessment Recommendation: **Adequate**

Assessment Summary: After (b) (4) (b) (4)

List Submissions being assessed:

Document(s) Assessed	Date Received
0006 (7), 0011 (12)[a], 0016 (17)[b]	9/30/24, 12/26/24, 3/31/25
0017 (18)[c], 0021 (22)[c]	4/2/25, 5/15/25

[a] Updated Labeling/PI, [b] Latest MBRs, [c] Updated specification

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

Remarks: The submission is in the eCTD format and was resubmitted after a Refuse to File decision. Some tables were copied from the submission. Amendments dated 10/1/24 (SD 8), 10/17/24 (9) and 10/23/24 (10) were administrative. Amendments dated 11/12/24 (11), 12/26/24 (12), 1/27/25 (13) and 2/18/25 (15) were submitted with Information Request (IR) responses for Clinical, Non-Clinical, and ClinPharm. Amendment 2/6/25 (14) was related to inspection of a CRO. Responses for P/F and DP IRs were submitted in amendments 3/31/25 (17), 4/2/25 (18), and 4/11/25 (20). Amendments 3/19/25 (16) and 4/9/25 (19) were IR responses for BioPharm. The 5/15/25 amendment provides a response to the Microbiology IR sent to the applicant on 5/9/25.

Concise Description of Outstanding Issues: None
Supporting Documents: N/A

P.1 DESCRIPTION OF THE COMPOSITION OF THE DRUG PRODUCT

- **Description of drug product –** Non-sterile, (b) (4) white, opaque, (b) (4) aqueous liquid suspension, pH 4.5-5.5, filled into multi-dose bottles.

- **Drug product composition –**

Ingredient	Content (mg/mL)	Function
Celecoxib	10.0	Active
Xanthan Gum	(b) (4)	
Citric Acid Anhydrous		
Methylparaben		
Propylparaben		
Sodium Citrate Dihydrate		
Glycerin		
Sucralose		
Magnesium Aluminometasilicate (b) (4)		
Sodium Hydroxide	q.s.	pH adjustment
Hydrochloric Acid	q.s.	pH adjustment
Purified Water	q.s. to 1 mL	Diluent

- **Description of container closure system –**
  Container: 16 oz (b) (4) (b) (4) amber (b) (4) (b) (4) (b) (4) bottle
  Closure: child resistant (b) (4) foil induction seal (b) (4) (b) (4)

Assessment: ***Adequate***

The description of the drug product composition and container closure system is satisfactory.

P.2 PHARMACEUTICAL DEVELOPMENT

(b) (4)

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/s/

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