CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

217347Orig1s000

PRODUCT QUALITY REVIEW(S)

MEMORANDUM: DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: 11-Jun-2024

TO: NDA 217347 File

FROM: Baoqing Ma
Senior Pharmaceutical Quality Assessor
OPQA II, DPQA VII

THROUGH: Nina Ni, Ph.D.
Supervisor
OPQA I, DPQA VII

SUBJECT: NDA 217347 - Resubmission and Update of CMC recommendation – Sofpironium tropical gel, 12.45% from Botanix SB Inc.

ACTION RECOMMENDATION: Approval

BACKGROUND/SUMMARY:
The CMC team recommended that all OPQ disciplines are adequate, but the application can not be approved due to pending labeling review, as documented in the IQA of 08/09/2023. The Office of Immunology and Inflammation sent a complete response letter to the applicant on 09/22/2023, due to inadequacy on human factors study for this product. The applicant submitted a Class 2 resubmission on 12/20/2023. This resubmission did not include any changes or new information with regard to the CMC parts of the application. Dr. Donna Christner reviewed the associated DMF# (b) (4) and found it adequate as of 01/05/2024. Dr. David Acevedo of the manufacturing review team confirmed in an electronic mail message on 6/11/2024 that all of the facilities in the application are still adequate in terms of compliance. In addition, all of the CMC-related labeling concerns have been addressed.

CONCLUSION:
From a CMC perspective, the application is now **recommended for approval.**

ATL: Baoqing Ma, 11-Jun-2024

Attachment: Facility Compliance Status

Hi,

Yes. I don't see any updates on the facilities compliance status associated to this application. The facilities remain acceptable.

Best regards,

David

From: Ranga, Rajani <Rajani.Ranga@fda.hhs.gov>
Sent: Tuesday, June 11, 2024 11:36 AM
To: Falabella, Christine <Christine.Falabella@fda.hhs.gov>; Acevedo, David <David.Acevedo@fda.hhs.gov>
Cc: Ma, Baoqing <Baoqing.Ma@fda.hhs.gov>
Subject: RE: NDA 217347 resubmission

Hello @Falabella, Christine and @Acevedo, David,

I see that for NDA-217347-ORIG-1-RESUB-24 (fda.gov), the OMIR task is complete and approved and your Facility task is NAI with no updates as of March 2024. We wanted to confirm whether the facility (facilities) for this NDA resubmission still remain adequate? PDUFA is 6/20/24.

Thank you for your assistance and we appreciate your response.

Warmly,

Rajani Ranga, Pharm.D., BCPS
Regulatory Business Process Manager
Division of Regulatory and Business Process Management I (DRBPMI)
Office of Program and Regulatory Operations (OPRO)
Office of Pharmaceutical Quality (OPQ)

From: Ma, Baoqing <Baoqing.Ma@fda.hhs.gov>
Sent: Tuesday, June 11, 2024 10:29 AM
To: Ranga, Rajani <Rajani.Ranga@fda.hhs.gov>
Subject: NDA 217347 resubmission

Hi Rajani,

Could you please reach out the OPMA reviewer to confirm that the facility for this NDA remains still adequate?

Thanks,

Baoqing

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

BAOQING MA
06/11/2024 03:33:36 PM

Memorandum

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

Date: **September 19, 2023**
From: **Nina Ni, Ph.D.**
Application Technical Lead, Branch 4
Division of New Drug Products 2
Office of New Drug Products

To: **To IQA Assessment of NDA 217347**

Subject: **Error Correction of the Proposed Indication in the IQA**

In the original IQA review, dated August 9, 2023, on page 3 of the executive summary, the proposed indication was mistakenly written as "For the treatment of people 9 years of age and older with (b) (4)". The correct indication is "For the treatment of **primary axillary hyperhidrosis** in adult and pediatric patients 9 years of age and older".

The correction of this error does not change the OPQ's recommendation of "Complete Response" in the original IQA review.

Nina Ni, Ph.D.
Branch 4/DNDP II/ONDP/OPQ

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/s/

NINA NI
09/19/2023 12:10:12 PM

RECOMMENDATION

☐ Approval
☐ Approval with Post-Marketing Commitment
☒ Complete Response

NDA 217347
Assessment 1

Drug Product Name	Tradename (sofpironium) tropical gel
Dosage Form	Gel
Strength	12.45%
Route of Administration	For topical use
Rx/OTC Dispensed	Rx
Applicant	Botanix SB Inc.
US agent, if applicable	NA

Submission(s) Assessed	Document Date	Discipline(s) Affected
Original Submission, eCTD SN 0001	09/23/2022	DS, DP, OPMA, and Micro
Amendment, SN 0006	01/25/2023	DP, OPMA
Amendment, SN 0007	01/31/2023	Micro

QUALITY ASSESSMENT TEAM

Discipline	Primary Assessor	Secondary Assessor
Drug Substance	Friedrich Burnett	Lawrence Perez
Drug Product	Caroline Strasinger	Nina Ni
Manufacturing	David Acevedo	Christine Falabella
Microbiology	Dacie Bridge	Yan Zheng
Biopharmaceutics	NA	NA
Regulatory Business Process Manager	Grafton Adams/Rajani Ranga	
Application Technical Lead	Nina Ni	
Laboratory (OTR)	NA	NA
Environmental	Caroline Strasinger	Nina Ni

QUALITY ASSESSMENT DATA SHEET

For more details about the items in this template, please see the Quality Assessment Data Sheet chapter of the NDA IQA Guide

1. RELATED/SUPPORTING DOCUMENTS

A. DMFs:

DMF #	Type	Holder	Item Referenced	Status	Date Assessment Completed	Comments
(b) (4)	II		(b) (4)	Adequate	12/02/2022	Reviewed by F. Burnett
	III			NA	NA	Adequate info provided in the NDA
	III			NA	NA	Adequate info provided in the NDA

B. OTHER DOCUMENTS: *IND, RLD, RS, Approved NDA*

Document	Application Number	Description
IND	121256	Conducted clinical studies

2. CONSULTS

Discipline	Status	Recommendation	Date	Assessor
Biostatistics	NA			
Pharmacology/Toxicology	NA			
CDRH	NA			
Clinical	NA			
Other	NA			

NDA Executive Summary

1. Application/Product Information

NDA Number.	217347
Applicant Name	Botanix SB Inc.
Drug Product Name	Tradename (sofpironium) tropical gel
Dosage Form.	Gel
Proposed Strength(s)	12.45%
Route of Administration	Topical
Maximum Daily Dose	144 mg sofpironium (equivalent to 174 mg sofpironium bromide)
Rx/OTC Dispensed	Rx
Proposed Indication	For the treatment of people 9 years of age and older with (b) (4)
Drug Product Description	The drug substance, sofpironium bromide, is a quaternary ammonium, anticholinergic drug, and ester analog of glycopyrrolate. TRADENAME (sofpironium) topical gel, 12.45%, is a combination product. It is a clear to translucent, colorless to pale yellow gel and packaged in an airless 50 mL bottle with a metered dose pump with applicator. The gel is an (b) (4) drug product with dissolved drug substance and compendial excipients. A single pump actuation dispenses 0.67 mL of gel containing 72 mg of sofpironium (equivalent to 87 mg of sofpironium bromide). Instructions for use call for one pump to each underarm per day.
Co-packaged product information	N/A
Device information:	N/A
Storage Temperature/ Conditions	The drug product is stored at 20ºC - 25ºC (68ºF - 77ºF); excursions permitted to 15ºC - 30ºC (59ºF - 86ºF) [See USP Controlled Room Temperature] with a proposed shelf-life of 36 months. Due to the high alcohol content in the formulation, drug product labeling also includes

	statements indicating that the drug product is flammable and to avoid (b) (4) flame, or smoking until the gel has dried.		
Review Team	**Discipline**	**Primary**	**Secondary**
	Drug Substance	Friedrich Burnett	Lawrence Perez
	Drug Product/ Labeling	Caroline Strasinger	Nina Ni
	Manufacturing	David Acevedo	Christine Falabella
	Biopharmaceutics	N/A	N/A
	Microbiology	Dacie Bridge	Yan Zheng
	Other (specify):	N/A	N/A
	RBPM	Grafton Adams/Rajani Ranga	
	ATL	Nina Ni	
Consults	N/A		

2. Final Overall Recommendation - Complete Response

2. Deficiencies

The CMC recommended changes for PI labeling as well as container and carton labels have been communicated to the Clinical Review Team. However, the labeling negotiation will not be pursued in this review cycle since this application will be given a complete response from the clinical perspective. All quality related label and labeling deficiencies discussed in this review should be reviewed again for accuracy in the next review cycle.

4. Basis for Recommendation:

a. Summary of Rationale for Recommendation:

OPQ recommends Complete Response of NDA 217347 for commercialization of Tradename (sofpironium) topical gel, 12.45% since the labeling negotiation is not pursued in this review cycle.

Based on our evaluation of the available information, the applicant provided sufficient information to support an approval recommendation from the product quality perspective. The applicant provided adequate chemistry, manufacturing, and controls (CMC) information to ensure the identity, strength, purity, and quality of the proposed drug product. The overall manufacturing inspection recommendation is approval for all the facilities associated with this application. However, the comments to the proposed labeling and labels have not been communicated to the applicant.

Thus, from the OPQ perspective this NDA is not ready for approval in its current form until the CMC labeling deficiencies and recommendations are appropriately addressed as per 21 CFR 314.125(b)(6). The CMC PI labeling as well as container and carton labels deficiencies are captured in the Labeling Review Chapter (Chapter IV) of this review.

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

Recommendation by Subdiscipline:

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

Environmental Assessment: Categorical Exclusion - Adequate
QPA for EA(s): Yes

5. Life-Cycle Considerations

Established Conditions per ICH Q12: No
Comments: N/A

Comparability Protocols (PACMP): No
Comments: N/A

Additional Lifecycle Comments: None

Nina Ni

Digitally signed by Nina Ni
Date: 8/09/2023 03:10:42PM
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CHAPTER IV: LABELING

Note: Applicant labeling discussions have been precluded due to clinical review issues. All quality related label and labeling deficiencies discussed below have been communicated to OND and should be reviewed again for accuracy in the next review cycle.

1.0 PRESCRIBING INFORMATION

Assessment of Product Quality Related Aspects of the Prescribing Information:

1.1 HIGHLIGHTS OF PRESCRIBING INFORMATION

(b) (4)

(b) (4)

[redacted]

Item	Items 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		
Established name(s)[1]	Inadequate	Change to sofpironium topical gel, 12.45%
Route(s) of administration	Adequate	
Dosage Forms and Strengths Heading in Highlights		
Summary of the dosage form(s) and strength(s) in metric system	Inadequate	Change to 12.45%, and include comment regarding parenthetical to the Applicant
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored".	N/A	

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

For injectable drug products for parental 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.	N/A	
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).	Inadequate	Labeling should be revised to be consistent with the USP salt policy. Convey comment to applicant.

1.2 FULL PRESCRIBING INFORMATION

1.2.1 Section 2 (DOSAGE AND ADMINISTRATION)

Item	Items 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, storage conditions needed to maintain the stability of the reconstituted or diluted product)	Adequate	Revised for clarity by other disciplines; no issues with proposed revisions from OPQ
Important administration instructions supported by product quality information (e.g., do not crush or chew extended-release tablets, instructions for mixing with food)	Adequate	Revised for clarity by other disciplines; no issues with proposed revisions from OPQ

For parenteral products: include statement: *"Parenteral drug products must be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit"*	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 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	

1.2.2 Section 3 (DOSAGE FORMS AND STRENGTHS)

3 DOSAGE FORMS AND STRENGTHS

(b) (4)

Item	Items 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	Inadequate	Revisions requested to be consistent with salt policy and mL of gel dispensed with each actuation.
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 (Tablets: 10 mg of drug-x hydrochloride).	Inadequate	Revisions requested to be consistent with salt policy
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	Revisions requested for clarity
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 parental 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.	N/A	

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QUALITY ASSESSMENT

Item	Items 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)	Inadequate	Established name changes requested
Dosage form(s) and route(s) of administration	Inadequate	Dosage form should include route (topical)
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)"	Inadequate	Revise for clarity and alignment with Salt Guidance
List names of all inactive ingredients. Use USP/NF names in alphabetical order. Avoid brand names.	Inadequate	List in alphabetical order
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.	N/A	
If alcohol is present, must provide the amount of alcohol in terms of percent volume of absolute alcohol	N/A	
Sterility statement (if applicable)	N/A	
Pharmacological/Therapeutic class	Inadequate	Revise to anticholinergic (confirmed by nonclinical)
Chemical name, structural formula, molecular weight	Adequate	
If radioactive, statement of important nuclear characteristics.	N/A	
Other important chemical or physical properties (such as pKa or pH)	Inadequate	Revise for clarity

Section 11 (DESCRIPTION) Continued

Item	Items 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 (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	

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Item	Items 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)	Inadequate	Revise to topical gel
Strength(s) in metric system	Inadequate	Revise to 12.45%
Available units (e.g., bottles of 100 tablets)	Adequate	
Identification of dosage forms (e.g., shape, color, coating, scoring, imprinting, and color and clarity of the solution, when applicable); Include NDC(s)	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 parental 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.	N/A	
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."	Inadequate	State pump actuation dispense amount

Section 16 (HOW SUPPLIED/STORAGE AND HANDLING) (Continued)

Item	Items 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)
Storage conditions. Where applicable, use USP storage range rather than storage at a single temperature.	Inadequate	Include C and F as appropriate
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."*	N/A	
Include information about child-resistant packaging	N/A	

1.2.6 Manufacturing Information After Section 17 (for drug products)

Item	Items 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)
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	

3.0 CONTAINER AND CARTON LABELING

3.1 Container Labels

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QUALITY ASSESSMENT

Item	Items in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments about Carton Labeling (If an item is Inadequate, provide more details on the issues, as appropriate)
Established name[2], (font size and prominence)	Inadequate	Revise the established name to "(sofpironinum) topical gel" or "(sofpironium topical gel)" and adjust the prominence
Strength(s) in metric system	Inadequate	Revise the strength to 12.45%
Route(s) of administration	Inadequate	Topical gel
If the active ingredient is a salt, include the equivalency statement per Salt Guidance and MAPP.	N/A	Revise [redacted] (b) (4) to read: Contains: Sofpironium……12.45% (equivalent to 15% sofpironium bromide)
Net contents (e.g., tablet count, volume of liquid)	Inadequate	Revise for clarity
"Rx only" displayed on the principal display	Inadequate	Revise for clarity
NDC	Inadequate	Revise for clarity
Lot number and expiration date	Inadequate	Revise for clarity
Storage conditions. If applicable, include a space on the carton labeling for the user to write the new beyond-use-date (BUD).	Inadequate	Revise for clarity
For injectable drug products for parental 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.	N/A	
For parenteral injectable dosage forms, include the name and quantities of all active and inactive ingredients in alphabetical order. For ingredients added to adjust the pH or make isotonic, include the name and statement of effect.	N/A	
If alcohol is present, must provide the amount of alcohol in terms of percent volume of absolute alcohol	N/A	
Linear Bar code	Adequate	

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

Item	Items in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments about Carton Labeling (If an item is Inadequate, provide more details on the issues, as appropriate)
Name of manufacturer/distributor /packer	Adequate	
If there is a Medication Guide, must include a statement about dispensing a Medication Guide to each patient.	N/A	
No text on Ferrule and Cap overseal, unless a cautionary statement is required.	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	
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.	N/A	
And others, if space is available.	N/A	

Assessment of Carton and Container Labeling: *INADEQUATE*

Note: DMEPA and OPQ comments have been combined to improve clarity and correctness of the carton and container labels as follows:

A. General Comments (Container labels & Carton Labeling)

1. Once a proprietary name is found conditionally acceptable, the placeholder "Tradename" must be replaced with the proprietary name on the container labels and carton labeling and the revised labels and labeling must be submitted to the Agency for review.
2. The established name is not at least half the size of the proprietary name. Revise the established name to be in accordance with 21 CFR 201.10(g)(2). Additionally, the established name lacks prominence on the principal display panel (PDP). We recommend increasing the prominence of the established name. Consider the use of different font type or size, bolding, color, or other means to achieve increased prominence. See Guidance for Industry: Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors (May 2022).

3. The strength statement lacks prominence. Lack of prominence of the strength statement may contribute to product selection medication errors. See 21CFR201.15(a)(6) which states a word, statement, or other information required by or under authority of the act to appear on the label may lack that prominence and conspicuousness required by section 502(c) of the act by reason, among other reasons, of: smallness or style of type in which such word, statement, or information appears, insufficient background contrast, obscuring designs or vignettes, or crowding with other written, printed, or graphic matter. Increase the prominence of the strength statement in accordance with 21 CFR 201.15(a)(6). Take into account all pertinent factors including font size, type, and color; background contrast; and statement location. If necessary, consider decreasing the prominence of other information that is not critical (e.g., net quantity statement, NDC code, etc.).

4. Revise the strength to 12.45% and the established name to "(sofpironinum) topical gel" or "(sofpironium topical gel)". Please see the below implications of each presentation and confirm the desired parenthetical presentation:
    - By utilizing "TRADENAME (sofpironium) topical gel" presentation you are indicating that the Proprietary Name can be used with any future sofpironium dosage form you may develop, for example TRADENAME (sofpironium) cream.
    - By utilizing TRADENAME (sofpironium topical gel) presentation you are indicating that the Proprietary Name can only be used with this topical gel dosage form of sofpironium and no other future dosage form you may choose to develop.

5. To ensure consistency with the Prescribing Information, revise the statement, [redacted] (b) (4) to read [redacted] (b) (4) Dosage: See prescribing information."

6. Revise the statement [redacted] (b) (4) to read: "Each pump actuation delivers 0.67 mL of gel containing 72 mg of sofpironium".

7. Relocate the statement "Multi-dose pump capable of dispensing 60 pump actuations" and place it underneath "each pump actuation delivers 0.67 mL of gel containing 72 mg of sofipironium".

8. Revise the net quantity to "50 mL" and relocate to the bottom of the principal display panel (PDP).

9. Remove [redacted] (b) (4) from the primary display panel.

10. Revise [redacted] (b) (4) to read:
    Contains:
    Sofpironium……12.45%
    (equivalent to 15% sofpironium bromide)

B. Container Labels

1. We recommend reorienting the linear barcode on the container label to a vertical position to improve the scannability of the barcode. Barcodes placed in a horizontal position may not scan due to container curvature. The bending of barcodes around a curved surface affects how light reflects off them, and, if it is distorted in such a way, scanners cannot capture the entire barcode. Consider orienting the linear barcode to a vertical position to improve the scannability of the barcode. Barcodes placed in a horizontal position may not scan due to vial curvature. [3]
2. Consider moving the statement: "Warnings: Gel is flammable. Avoid (b) (4) flame, or smoking until gel has dried" from the principal display panel to the side panel.

Overall Assessment and Recommendation:

The Labeling and Label of NDA 217347 are inadequate. Recommendations were communicated to OND March 23, 2023 and May 3, 2023 respectively. However, labeling discussions with the Applicant have been precluded due to clinical deficiencies as communicated in the Late Cycle Meeting Briefing Packet on 25-JUL-2023 and at the Late Cycle Meeting held 31-JUL-2023.

Excerpt from LCM Briefing Packet:

Major Labeling issues
As part of our ongoing review of your application, we have identified deficiencies that preclude discussion of labeling.

Primary Labeling Assessor Name and Date:
Caroline Strasinger, PhD
CDER/OPQ/ONDP/DNDP2
7/31/2023

Secondary Drug Product Assessor Name and Date:
Nina Ni, PhD
CDER/OPQ/ONDP/DNDP2
7/31/2023

Caroline Strasinger

Digitally signed by Caroline Strasinger
Date: 7/31/2023 02:04:38PM
GUID: 5051dfdd000013b995075b4d54108ed8

Nina Ni

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CHAPTER VII: MICROBIOLOGY

IQA NDA Assessment Guide Reference

Product Information	
NDA Number	217347
Assessment Cycle Number	01
Drug Product Name/ Strength	Sofpironium bromide gel, 15%
Route of Administration	Topical Gel
Applicant Name	Botanix SB Inc.
Therapeutic Classification/ OND Division	DDD
Manufacturing Site	(b) (4)
Method of Sterilization	Non-sterile drug product

Assessment Recommendation: **Adequate**

Assessment Summary:

Document(s) Assessed	Date Received
0001	**9/23/2022**
0007	**1/31/2023**

List Submissions being assessed (table):

Highlight Key Issues from Last Cycle and Their Resolution: Not appliable.

Remarks: Type-B Pre-NDA meeting minutes (dated 1/12/2022) were included with the submission. The following comments were communicated in the letter by Quality Microbiology:

(b) (4)

Concise Description of Outstanding Issues
(List bullet points with key information and update as needed): Not applicable

Supporting Documents: Not applicable

P.1 DESCRIPTION OF THE COMPOSITION OF THE DRUG PRODUCT

- **Description of drug product**
  (P.1: Description and Composition of the drug product)

  Sofpironium bromide gel, 15% is a clear to translucent, colorless to pale yellow gel. The combination drug-device product is non-sterile, (b) (4) and packaged in an airless 50 mL bottle with a metered dose pump/applicator that dispenses a nominal volume of 0.67 mL/actuation for topical administration. The product is multi-dose.

- **Drug Product Composition**
  (P.1: Description and Composition of the Drug Product)

Component	Function	Quantity (mg/g)	Quantity (% w/w)
Sofpironium Bromide (in house)	API	150.00	15.000
Hexylene glycol (USP/NF)	(b) (4)		
Isopropyl myristate (b) (4) IPM) (NF)			
Citric acid, (b) (4) (USP/EP)			
Hydroxypropyl cellulose (HPC) (b) (4) (NF/EP)			
Dehydrated alcohol (b) (4) (USP)			

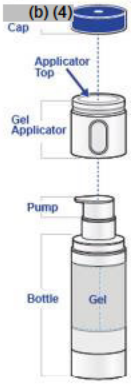
- **Description of Container Closure System**
  (P.7: Container Closure System).

  The proposed CCS contains a bottle, with a metered-dose pump, and cap. As the bottle and metered dose pump contain multiple components, respectively, a diagram of the CCS is provided for reference.

(b) (4)

Figure 1 **Primary Packaging Components for Sofpironium Bromide Gel, 15%**

(b) (4)



(b) (4)

Component		Description	Manufacturer
Bottle	(b) (4) Bottom Cover (b) (4)	(b) (4)	(b) (4)
Dispensing head subassembly: Metered dose pump (b) (4) that contains a specific applicator, actuator, (b) (4) snap on pump, and collar.	Specific Applicator and Collar Actuator (b) (4)		
Cap		Blue (b) (4) Cap	(b) (4)

Assessment: *Adequate*

P.2 PHARMACEUTICAL DEVELOPMENT

(b) (4)

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MICROBIOLOGY LIST OF DEFICIENCIES

Not Applicable

Primary Microbiology Assessor Name and Date*:* Dacie R. Bridge, Ph.D. February 2, 2023

Secondary Assessor Name and Date (and Secondary Summary, as needed)*:* Yan Zheng, Ph.D., February 2, 2023

Dacie Bridge

Digitally signed by Dacie Bridge
Date: 2/03/2023 06:48:13AM
GUID: 5a994d0c0051111bec366cf8880c9f85

Yan Zheng

Digitally signed by Yan Zheng
Date: 2/02/2023 04:35:13PM
GUID: 58ca9ce301e697996a209b08cf0d70b6

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