CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

215256Orig1s000

PRODUCT QUALITY REVIEW(S)

QUALITY ASSESSMENT

Recommendation: Approval

NDA 215256
Review 1

Drug Name/Dosage Form	Wegovy™ (semaglutide) injection
Strength	0.25 mg/0.5 mL, 0.5mg/0.5mL, 1.0 mg/0.5mL, 1.7 mg/0.75mL, and 2.4 mg/0.75mL
Route of Administration	Subcutaneous injection
Rx/OTC Dispensed	Rx
Applicant	Novo Nordisk Inc.
US agent, if applicable	-

SUBMISSION(S) REVIEWED	DOCUMENT DATE	DISCIPLINE(S) AFFECTED
Pre-submission, Original submission, and amendments	Original submission: 12/4/2020 Amendments: 1/8/2021, 2/04/2021, 2/25/2021, 3/18/2021, 3/25/2021 (device), 4/6/2021, 4/9/2021 (device), 4/15/2021, 4/16/2021, 4/21/2021, 4/23/2021, 4/27/2021, and 5/4/2021	Quality modules 3, 1.14, and 1.11

Quality Review Team

Discipline	Reviewer/Secondary	Branch/division
Drug Substance	Daniel Jansen/ Suong Tran	Branch III/Division of New Drug Active pharmaceutical
Drug Product	Ali Mohamadi / David J Claffey	Branch V/New Drug Products III
Process/ Facility	Suresh Dadiboyena/ Sudipan Karmakar	Branch II/ Office of Pharmaceutical Manufacturing Assessment (OPMA)
Microbiology	Helen Ngai/ Elisabeth Bearr/Paul Dexter	OPMA
Regulatory Business Process Manager	Hamet Toure	Branch I/Regulatory Business Process Management I
Application Technical Lead	Muthukumar Ramaswamy	Branch V/New Drug Products III
Environmental Analysis (EA)	Ali Mohamadi/ David J Claffey	Branch V/New Drug Products III of New Drug Products

Quality Review Data Sheet

1. RELATED/SUPPORTING DOCUMENTS

A. DMFs:

DMF #	Type	Holder	Item Referenced	Status	Date Assessment Completed	Comments
(b) (4)	V		(b) (4)	adequate	6/8/2020[a]	LOA dated 4/2/2020
	III			Active	-	LOA dated 9/24/2020
	III			adequate	1/29/2020[a]	LOA dated 3/17/2021
	V			adequate	3/19/21[a]	LOA dated 3/17/2021
	V			adequate	3/2/2020[a]	LOA dated 3/17/2021
	III			Active	b	LOA dated 3/17/2021

[a] Please refer to microbiology review dated 4/16/2021 in Panorama under NDA 215256; [b] Sufficient information provided in the NDA

B. Other Documents: *IND, RLD, or sister applications*

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
IND	126360	Semaglutide injection
NDA	209637	Ozempic (semaglutide) injection for CMC information related to drug substance (Section 3.2.S)

2. CONSULTS: None

DISCIPLINE	STATUS	RECOMMENDATION	DATE	REVIEWER
Pharm. Tox. (impurities & leachables)	Complete	Adequate via email dated 4/26/21. Refer to Pharm. Tox. review for NDA 215256 in DARRTS	4/26/2021	Elena Braithwaite
Device related information	Complete	Adequate. Refer to CDRH review in DARRTS 4/30/2021	4/30/2021	Dunya Karimi

Executive Summary

I. Recommendations and Conclusion on Approvability

The recommendation from the Office of Pharmaceutical Quality (OPQ) for NDA 215256 is approval. This approval recommendation includes acceptable recommendation for all the facilities listed in the application. At present, there are no outstanding deficiencies associated with drug substance, drug product, environmental assessment, process, and microbiology sections of this application.

II. Summary of Quality Assessments

A. Product Overview

Semaglutide (NN9536) is an analog of the human glucagon-like peptide-1, GLP-1 (7-37). Semaglutide is a long-acting GLP-1 receptor agonist. This NDA is a 505(b)(1) application for Wegovy™ (semaglutide) injection. The proposed drug product, Wegovy (semaglutide) injection is intended for chronic weight management indication. Wegovy™ (semaglutide) injection is a clear, colorless, (b) (4) sterile aqueous solution provided as a single dose injector in five strengths (0.25 mg/0.5 mL, 0.5mg/0.5mL, 1.0 mg/0.5mL, 1.7 mg/0.75mL, and 2.4 mg/0.75mL).

The five different strengths differ primarily in semaglutide content and the excipient composition remains the same. Each mL of Wegovy contains 1.42 mg of disodium phosphate dihydrate (b) (4) 8.25 mg of sodium chloride (b) (4) and water for injection. The product pH is adjusted to 7.4 with hydrochloric acid or sodium hydroxide. The five different strength Wegovy pen injectors are differentiated through labelling and packaging design.

Previously, a related product, Ozempic (semaglutide) injection, 1.34 mg/mL was approved for the treatment of type 2 diabetes (NDA 209637). Ozempic injection is a (b) (4) formulation provided in single patient use pen injectors for delivering 0.25 or 0.5mg, and 1mg doses.

Wegovy should be stored at 2°C to 8°C (36°F to 46°F) for up to 24 months protected away from light in the carton. During shelf-life, each Wegovy single dose pen may be stored unrefrigerated at 8°C to 30°C (46 F to 86F) for 28 days in the commercial packaging.

Wegovy is a drug-device combination product. CDER OPQ review covers the product quality aspects of the drug-device combination product. CDRH review covers the device aspects of the combination product. CDRH recommendation for this application is adequate. For additional details, please refer to CDRH consult review filed in DARRTS dated 4/30/2021 under NDA 215256.

Proposed Indication(s) including Intended Patient Population	Chronic weight management
Duration of Treatment	Chronic
Maximum Daily Dose	2.4 mg dose (intended for once weekly use)
Alternative Methods of Administration	Not applicable

B. Quality Assessment Overview

Drug Substance

Semaglutide is a recombinant analogue of GLP-1 (7-37). In comparison to GLP-1 (7-37), the semaglutide has two amino acid substitutions (Ala8 to Aib8 (2-aminoisobutyric acid), Lys34 to Arg34) and also the lysine 26 is acylated at with a fatty diacid moiety. The Chemical name for semaglutide is N6.26-{18-[N-(17-carboxyheptadecanoyl)-L-γ-glutamyl]-10-oxo-3,6,12,15-tetraoxa-9,18-diazaoctadecanoyl}-[8-(2-amino-2-propanoic acid), 34-L-arginine] human glucagon-like peptide 1 (7-37).

This NDA cross-references approved NDA 209637 (also filed by Novo-Nordisk) for all drug substance information including drug substance and impurities characterization, manufacturing process and control, methods, drug substance specification, reference standard, and stability. The drug substance is stored (b) (4) (b) (4). Dr. Daniel Jansen reviewed the drug substance information. Dr. Jansen' s recommendation for this application is adequate. For additional details, please refer to Dr. Jansen' s CMC review for drug substance dated 2/11/2021 in Panorama under NDA 215256. See also NDA 209637 drug substance review dated 7/28/17 in Panorama.

Drug Product

Drug Product Formulation: The proposed product, Wegovy (semaglutide) injection, is a clear, colorless, sterile, aqueous, (b) (4) solution packaged in a (b) (4) mL single-dose pre-filled syringe assembled in a pen injector for delivering 5 different strengths (0.25 mg/0.5 mL, 0.5mg/0.5mL, 1.0 mg/0.5mL, 1.7 mg/0.75mL, and 2.4 mg/0.75mL). The five different strengths differ only in semaglutide content. The excipient concentration in the five strengths is the same. Each mL of Wegovy contains 1.42 mg of disodium phosphate dihydrate (b) (4) 8.25 mg of sodium chloride (b) (4) (b) (4) and water for injection. The product pH is adjusted to 7.4 with hydrochloric acid or sodium hydroxide. The Phase 2 and 3 clinical studies utilized a (b) (4) formulation containing (b) (4) and the drug product was packaged in (b) (4) mL pen injector. The composition of the proposed commercial product is the same as the one used during BE studies. The proposed commercial single dose pen injector is the same as the one was used in BE studies.

The primary container closure system consists of a (b) (4) Type I (b) (4) (b) (4) glass syringe fitted with a (b) (4) needle and (b) (4)

on one end and a [redacted] plunger on the other end. The primary container closure system (pre-filled syringe) is integrated with the secondary packaging components [redacted] to generate the single dose prefilled pen injector. The finished product is packaged in a carton. The product is light sensitive. Storage of the product in the carton is recommended to prevent exposure to light. The container closure components proposed for use in the product are known for use in approved products and the applicant provided leachable study assessment to assure the safety of the proposed container closure system. Pharmacology Toxicology Reviewer was consulted on the safety of impurities and leachables present in the product.

Dr. Mohamadi reviewed the drug product information including drug product composition, drug product specification, excipient information, analytical methods, container closure system, compatibility/analytical comparability information, and stability data. The compatibility of the active ingredient with excipients and the container closure components is supported by drug product stability data. The stability of drug products used in clinical trials was comparable to the stability of the proposed product intended for market.

The drug product is tested for visual appearance (color), identity, sub-visible particulate matter, pH, content of semaglutide, [redacted], sum of impurities, high molecular weight proteins, dose accuracy, endotoxin content, and sterility. Dr. Mohamadi's review concluded that the proposed specification is adequate to support the quality of the proposed product. Please refer to the drug product review dated 5/4/2021 for additional information.

Manufacturing Process and Controls: The manufacturing process and controls for the drug product was reviewed by Dr. Dadiboyena. The drug products corresponding to 0.25mg/0.5mL, 0.5mg/0.5mL and 1mg/0.5 mL strengths are manufactured [redacted] at [redacted] scale. The drug products corresponding to 1.7 mg/0.75mL and 2.4 mg/0.75mL are manufactured Novo Nordisk A/S Bagsværd at [redacted] scale. The manufacturing process performed at the two sites differ [redacted]

The applicant is proposing via a comparability protocol to add [redacted] an additional manufacturing facility to manufacture semaglutide injection 1.7 mg/0.75 mL and 2.4 mg/0.75 mL at [redacted] batch scale. Three consecutive production scale batches of semaglutide 2.27 mg/mL and semaglutide 3.2 mg/mL will be manufactured, release tested under per approved specification and will be placed on long term and accelerated stability. The comparability data supporting this change will be complied and reported in a comparability report and submitted to the agency for approval with proposed reporting category of CBE-30. Dr. Ngai and Dadiboyena reviewed the protocol and agreed with the proposal.

The proposed manufacturing process involves (b) (4) (b) (4)

The applicant is using batch record instructions and the following (b) (4) tests (b) (4) (b) (4) (b) (4). Fill volumes of each strength product is controlled (b) (4) (b) (4)

The essential performance requirements of the combination product (activation force, needle extension test, injection time, and dose accuracy) are controlled through (b) (4) acceptance, (b) (4) control, and/or release testing. Dose accuracy is included as a (b) (4) control for the final product. For information related manufacturing process and controls for the finished product, please refer to CDRH review dated 4/30/29021 in DARRTS and OPMA process review dated 5/4/2021 in Panorama. The process review also covers manufacturing process risk assessment for critical quality attributes and the review concluded that the overall risk is low.

The composition of the drug product, the drug product manufacturing process, and the packaging system used to manufacture the drug product used in BE studies and the registration stability studies are the same as that proposed for commercial use. The batch size of registration stability batches ranged from (b) (4). The proposed commercial batch size is (b) (4)

(b) (4)
For detailed information on the manufacturing process and process controls, refer to process review dated 5/4/2021 in Panorama. The process reviewer concluded that the proposed drug product manufacturing process controls are adequate to support the NDA.

Microbiological control information: Microbiology reviewer, Dr. Ngai reviewed the microbiological controls used in the drug product manufacturing process (b) (4) (b) (4)

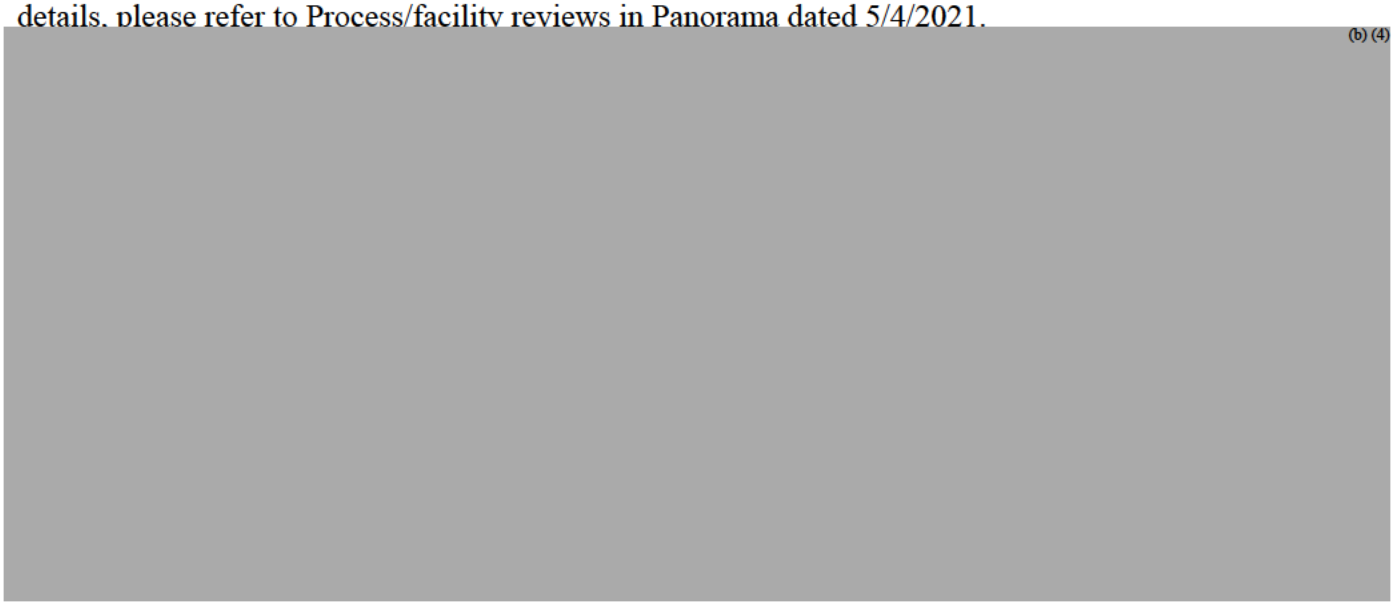
Ngai also reviewed the (b) (4) validation information provided (b) (4) (b) (4). Dr. Ngai's review concluded that the proposed microbiological controls are adequate to support the NDA. Refer to CMC (Microbiology) review by Dr. Ngai dated 4/16/2021 in Panorama.

Control Strategy: The critical quality attributes of the product are controlled through batch records instructions, process design including excipient specifications including bioburden and endotoxin control, drug substance specification, specifications for incoming container closure components, (b) (4) controls limits, hold time, bioburden, product pH, fill volume, (b) (4) device related controls (b) (4) and adequate finished product specification including semaglutide content, dose accuracy and sterility.

The proposed control strategy is adequate to assure the quality of the product. For additional information, please refer to the following CMC reviews in Panorama: drug substance review dated 2/11/2021, Dr. Ngai 's microbiology review dated 4/16/2021, Dr. Mohamadi's drug product review dated 5/4/2021, and Dr. Dadiboyena's process review dated 5/4/2021.

Facility compliance information: The facility compliance information for the drug product and drug substance manufacturing and testing facilities was reviewed by OPMA reviewer, Dr. Dadiboyena in consultation with ORA and CDRH reviewer, Dunya Karimi. This review concluded that the facilities associated with the application are adequate to support the application based on profile history or district recommendation. Thus, the overall manufacturing inspection recommendation (OMIR) from the Office of Process Manufacturing Assessment (OPMA) for this NDA is approve. Panorama screen shot of the submission facility status recorded on 5/10/2021 is shown below. For additional details, please refer to Process/facility reviews in Panorama dated 5/4/2021.

(b) (4)



(b) (4)

[redacted]

Based on DRH post-approval inspection is recommended for Novo Nordisk Pharmaceutical Industries, Clayton (FEI # 1000158576) and (b) (4) [redacted] (b) (4)

Environmental assessment: The applicant sought exemption from environmental impact analysis per 21CFR 25.31(b) and 25.21 as the action on this NDA may not significantly affect the quality of the human environment. The estimated concentration of the drug substance at the point of entry into the aquatic environment would be below 1 part per billion (1 ppb). Dr. Mohamadi granted categorical exclusion from submitting environmental assessment. Please refer to drug product review dated 5/4/2021 for additional information.

Expiration Date & Storage Conditions: The application contains 12 -18 months of long-term stability data (25°C/60% RH) and 6 months of accelerated stability data (25°C/60% RH) for 15 primary stability batches and 5 finished product batches (prefilled pen assembled in pen injector) manufactured at (b) (4) [redacted] scale. In addition, the NDA contains 3 months of long-term and accelerated stability data for 10 process validation batches manufactured at (b) (4) [redacted] scale. The applicant also provided photostability and in-use stability results. The product is sensitive to light. Dr. Mohamadi reviewed the stability information.

Based on available stability data, an expiration period of 24 months is granted when stored at 2°C to 8°C (36°F to 46°F) in original carton protected away from light. Each Wegovy single dose pen can be stored unrefrigerated for 28 days between 8 to 30°C (77°F). Please refer to the drug product review dated 5/4/2021 in Panorama for additional information.

Container and Carton Label Review: The drug product reviewer completed review of the container and carton label. Comments related to the carton and container label will be resolved during OND labeling review. Refer to the Dr. Mohamadi's labeling review dated 5/4/2021 for additional information.

OVERALL ASSESSMENT AND SIGNATURES:

At present, there are no outstanding deficiencies related to the drug substance, drug product, process, facility, microbiology, and environmental analysis sections of this NDA. The OPQ overall recommendation for NDA *215256 is approval.*

Muthukumar Ramaswamy, Ph.D. 5/10/2021

Application Technical Lead Name and Date:

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CHAPTER IV: LABELING

IQA NDA Assessment Guide Reference

1.0 PRESCRIBING INFORMATION

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

1.1 HIGHLIGHTS OF PRESCRIBING INFORMATION

Item	Information Provided in the NDA	Assessor's Comments
Product Title in Highlights		
Proprietary name	Tradename (semaglutide) injection.	Adequate DMEPA found 'Wegovy' acceptable.
Established name(s)	semaglutide injection	Adequate
Route(s) of administration	Subcutaneous Injection	Adequate
Dosage Forms and Strengths Heading in Highlights		
Summary of the dosage form(s) and strength(s) in metric system.	single-dose pen-injector that delivers doses of 0.25 mg, 0.5 mg, 1 mg, 1.7 mg or 2.4 mg.	Adequate
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored"	N/A	Adequate
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.	Single-dose	Adequate

1.2 FULL PRESCRIBING INFORMATION

1.2.1 Section 2 (DOSAGE AND ADMINISTRATION)

Item	Information Provided in the NDA	Assessor's Comments
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)	N/A	

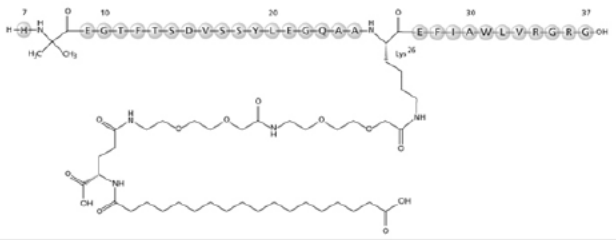
1.2.2 Section 3 (DOSAGE FORMS AND STRENGTHS)

<table>
<tr><th>Item</th><th>Information Provided in the NDA</th><th>Assessor's Comments</th></tr>
<tr><td colspan="3">DOSAGE FORMS AND STRENGTHS section</td></tr>
<tr><td>Available dosage form(s)</td><td>Injection</td><td>Adequate</td></tr>
<tr><td>Strength(s) in metric system</td><td><table><tr><th>Dose per Injection</th><th>Total Strength per Total Volume</th></tr><tr><td>0.25 mg</td><td>0.25 mg/ 0.5 mL</td></tr><tr><td>0.5 mg</td><td>0.5 mg/ 0.5 mL</td></tr><tr><td>1 mg</td><td>1 mg/ 0.5 mL</td></tr><tr><td>1.7 mg</td><td>1.7 mg/ 0.75 mL</td></tr><tr><td>2.4 mg</td><td>2.4 mg/ 0.75 mL</td></tr></table></td><td>Adequate</td></tr>
<tr><td>If the active ingredient is a salt, apply the USP Salt Policy per FDA Guidance</td><td>N/A</td><td>Adequate</td></tr>
<tr><td>A description of the identifying characteristics of the dosage forms, including shape, color, coating, scoring, and imprinting</td><td>N/A</td><td></td></tr>
<tr><td>Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored"</td><td>N/A</td><td>Adequate</td></tr>
<tr><td>For injectable drug products for parental administration, use appropriate labeling term (e.g., single-dose, multiple-dose, single-patient-use). Other package type terms include pharmacy bulk package and imaging bulk package.</td><td>Single-dose</td><td>Adequate</td></tr>
</table>

1.2.3 Section 11 (DESCRIPTION)

APPEARS THIS WAY ON ORIGINAL

Item	Information Provided in the NDA	Comments
DESCRIPTION section		
Proprietary and established name(s)	TRADENAME (semaglutide) injection	Adequate
Dosage form(s) and route(s) of administration	Injection, subcutaneous injection	Adequate
If the active ingredient is a salt, apply the USP Salt Policy and include the equivalency statement per FDA Guidance.	N/A	Adequate
List names of all inactive ingredients. Use USP/NF names. Avoid Brand names.	disodium (b) (4) phosphate dihydrate, sodium chloride, and water for injection	Adequate
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.	TRADENAME contains disodium (b) (4) phosphate dihydrate, 1.42 mg; sodium chloride, 8.25 mg; and water for injections. Hydrochloric acid or sodium hydroxide may be added to adjust pH.	Adequate after revision: Each (b) (4) mL of TRADENAME contains disodium (b) (4) phosphate dihydrate, 1.42 mg; sodium chloride, 8.25 mg; and water for injections. Hydrochloric acid or sodium hydroxide may be added to adjust pH.
If alcohol is present, must provide the amount of alcohol in terms of percent volume of absolute alcohol	N/A	Adequate

Statement of being sterile	Sterile	Adequate
Pharmacological/ therapeutic class	A human GLP-1 receptor agonist (or GLP-1 analog)	Adequate
Chemical name, structural formula, molecular weight	The molecular formula is $C^{187}H_{291}N_{45}O_{59}$ and the molecular weight is 4113.58 g/mol. 	Adequate
If radioactive, statement of important nuclear characteristics.	N/A	Adequate
Other important chemical or physical properties (such as pKa or pH)	TRADENAME has a pH of approximately 7.4.	Adequate

Section 11 (DESCRIPTION) Continued

Item	Information Provided in the NDA	Assessor's Comments
For oral prescription drug products, include gluten statement if applicable	N/A	Adequate
Remove statements that may be misleading or promotional (e.g., "synthesized and developed by Drug Company X," "structurally unique molecular entity"	N/A	Adequate

1.2.4 Section 16 (HOW SUPPLIED/STORAGE AND HANDLING)

<table>
<tr><th>Item</th><th>Information Provided in the NDA</th><th>Assessor's Comments</th></tr>
<tr><td colspan="3">HOW SUPPLIED/STORAGE AND HANDLING section</td></tr>
<tr><td>Available dosage form(s)</td><td>Injection</td><td>Adequate</td></tr>
<tr><td>Strength(s) in metric system</td><td>
<table>
<tr><th>Total Strength per Total Volume</th><th>Dose per Pen</th><th>Carton Contents</th><th>NDC</th></tr>
<tr><td>0.25 mg/0.5 mL</td><td>1 dose of 0.25 mg</td><td>4 pens</td><td>0169-4525-14</td></tr>
<tr><td>0.5 mg/0.5 mL</td><td>1 dose of 0.5 mg</td><td>4 pens</td><td>0169-4505-14</td></tr>
<tr><td>1 mg/0.5 mL</td><td>1 dose of 1 mg</td><td>4 pens</td><td>0169-4501-14</td></tr>
<tr><td>1.7 mg/0.75 mL</td><td>1 dose of 1.7 mg</td><td>4 pens</td><td>0169-4517-14</td></tr>
<tr><td>2.4 mg/0.75 mL</td><td>1 dose of 2.4 mg</td><td>4 pens</td><td>0169-4524-14</td></tr>
</table>
</td><td>Adequate</td></tr>
<tr><td>Available units (e.g., bottles of 100 tablets)</td><td>4 pens</td><td>Adequate</td></tr>
</table>

<table>
<tr><td>Identification of dosage forms, e.g., shape, color, coating, scoring, imprinting, NDC number</td><td><table>
<tr><th>Total Strength per Total Volume</th><th>Dose per Pen</th><th>Carton Contents</th><th>NDC</th></tr>
<tr><td>0.25 mg/0.5 mL</td><td>1 dose of 0.25 mg</td><td>4 pens</td><td>0169-4525-14</td></tr>
<tr><td>0.5 mg/0.5 mL</td><td>1 dose of 0.5 mg</td><td>4 pens</td><td>0169-4505-14</td></tr>
<tr><td>1 mg/0.5 mL</td><td>1 dose of 1 mg</td><td>4 pens</td><td>0169-4501-14</td></tr>
<tr><td>1.7 mg/0.75 mL</td><td>1 dose of 1.7 mg</td><td>4 pens</td><td>0169-4517-14</td></tr>
<tr><td>2.4 mg/0.75 mL</td><td>1 dose of 2.4 mg</td><td>4 pens</td><td>0169-4524-14</td></tr>
</table></td><td>Adequate</td></tr>
<tr><td>Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state “functionally scored”</td><td>N/A</td><td>Adequate</td></tr>
<tr><td>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.</td><td>Single-dose</td><td>Adequate</td></tr>
</table>

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

Item	Information Provided in the NDA	Assessor’s Comments

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.)	Do not freeze. Protect TRADENAME from light. TRADENAME must be kept in the original carton until time of administration. Discard the TRADENAME pen after use.	Adequate
If the product contains a desiccant, ensure the size and shape differ from the dosage form and desiccant has a warning such as "Do not eat."	N/A	Adequate
Storage conditions. Where applicable, use USP storage range rather than storage at a single temperature.	Store the TRADENAME single-dose pen in the refrigerator at 36°F to 46°F (2°C to 8°C). If needed, (b) (4) (b) (4) prior to cap removal, can be kept (b) (4) (b) (4)	Adequate after revision: Store the TRADENAME single-dose pen in the refrigerator from 2°C to 8°C (36°F to 46°F). If needed, prior to cap removal, the pen can be kept (b) (4) (b) (4) (b) (4) up to 28 days.
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	Adequate
Include information about child-resistant packaging	N/A	Adequate

1.2.5 Manufacturing Information After Section 17 (for drug products)

Item	Information Provided in the NDA	Assessor's Comments
Manufacturing Information After Section 17		
Name and location of business (street address, city, state and zip code) of the manufacturer, distributor, and/or packer	Manufactured by: Novo Nordisk A/S DK-2880 Bagsvaerd Denmark	Adequate

2.0 PATIENT LABELING

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

3.0 CARTON AND CONTAINER LABELING

10 Pages of Draft Labeling have been Withheld in Full as B4 (CCI/ TS) Immediately Following this Page

Item	Information Provided in the NDA	Assessor's Comments about Carton Labeling
Proprietary name, established name, and dosage form (font size and prominence	Wegovy	Adequate
Dosage strength	0.25 mg / 0.5 mL 0.5 mg / 0.5 mL 1 mg / 0.5 mL 1.7 mg / 0.75 mL 2.4 mg / 0.75 mL	Adequate
Route of administration	Injection	Adequate
If the active ingredient is a salt, include the equivalency statement per FDA Guidance	N/A	Adequate
Net contents (e.g. tablet count)	4 single-dose prefilled pens	Adequate
"Rx only" displayed on the principal display	Rx Only	Adequate
NDC number	Included	Adequate
Lot number and expiration date	Included	Adequate
Storage conditions. If applicable, include a space on the carton labeling for the user to write the new BUD.	(b) (4)	Adequate after revision: 2 °C to 8 °C (36 °F to 46 °F), and 8 °C to 30 °C (46 °F to °86 °F)
For injectable drug products for parental administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use)	Single-dose	Adequate after revision: (b) (4) 0.25 mg semaglutide
Other package terms include pharmacy bulk package and imaging bulk package which require "Not for direct infusion" statement.	N/A	Adequate

If alcohol is present, must provide the amount of alcohol in terms of percent volume of absolute alcohol	N/A	Adequate
Bar code	Included	Adequate

Item	Information Provided in the NDA	Assessor's Comments about Carton Labeling
Name of manufacturer/distributor	Manufactured by: Novo Nordisk A/S DK-2880 Bagsvaerd, Denmark	Adequate
Medication Guide (if applicable)	**Use as directed by your healthcare professional.** **Recommended Dosage: See prescribing information.** **Subcutaneous use only** **Not a child resistant container. Keep out of reach of children.** If the seal is broken before first use, contact your pharmacist.	Adequate
No text on Ferrule and Cap overseal	N/A	Adequate
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	Adequate

And others, if space is available	(b) (4)	Adequate after the revision: (b) (4)

Assessment of Carton and Container Labeling: *Adequate*

ITEMS FOR ADDITIONAL ASSESSMENT

None

Overall Assessment and Recommendation:

Adequate

Ali Mohamadi, Ph.D., 5/04/2021

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CHAPTER VII: MICROBIOLOGY

IQA NDA Assessment Guide Reference

Product Information	505(b)(1)
NDA Number	215256
Assessment Cycle Number	1
Drug Product Name/ Strength	Semaglutide; 0.25 mg/0.5ml, 0.5 mg/0.5ml, 1.0 mg/0.5ml, 1.7 mg/0.75ml, 2.4 mg/0.75ml
Route of Administration	Injection / subcutaneous
Applicant Name	Novo Nordisk Inc.
Therapeutic Classification/ OND Division	Obesity / CDER/ OCHEN/ DDLO
Manufacturing Site	(b) (4)
Method of Sterilization	

Assessment Recommendation: **Adequate**

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

List Submissions being assessed (table):

Document(s) Assessed	Date Received
New / Original	12/4/2020
General correspondence *	1/8/2021
Amendment	3/18/2021
Quality / Response to Information request	4/6/2021
Quality / Response to Information request	4/15/2021

* Provides an updated 356H form that is indicative of all facilities (drug substance, drug product and all testing facilities) supporting the NDA submission.

Highlight Key Issues from Last Cycle and Their Resolution: none

Remarks:

1. The same applicant, Novo Nordisk, has received FDA approval for NDA 209637, drug product Ozempic; semaglude injection approved on 12/5/2017. It is a 1.34 mg/mL concentration, packaged as 0.25 mg/ (b) (4), 0.5 mg (b) (4) and 1 mg/ (b) (4) fill volumes in cartridges. It is formulated with phenol (b) (4) and intended for multi-dose use.
2. The drug product for NDA 215256 is indicated for weight management. Per Panorama: Tropical disease priority voucher – Received. The NDA was granted priority review status.

3. The drug product in NDA 215256 is formulated (b) (4), packaged as 0.25 mg/0.5ml, 0.5 mg/0.5ml, 1.0 mg/0.5ml, 1.7 mg/0.75ml, 2.4 mg/0.75ml fill volumes in syringes; single use. The DMA reviewer took over primary review of the Priority NDA one week before the Mid-Cycle meeting. Microbiology comments were issued with chemistry and manufacturing on 3/5/2021; response received 3/18/2021. A second IR was issued 4/5/2021; response received 4/6/2021. A third IR was issued 4/7/2021; response received 4/15/2021.

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

Supporting Documents:

NDA 209637 and associated microbiology review N209637MR01.pdf (adequate) dated 7/26/2017. NDA 209637 supplement 5 and associated microbiology reviews N209637S005MR01.doc (not adequate) dated 2/2/2021 and N209637S005MR02.docx (adequate) dated 3/29/2021. The NDA is from the same applicant (Novo Nordisk), same API (semaglutide) but different strengths. The reviews are referenced for the same API, similar drug product description, same manufacturing facility (Denmark), (b) (4) similar (b) (4) validation studies, (b) (4) (b) (4) (b) (4) similar endotoxins, sterility test suitability studies. **Note**: 1. This drug product is filled in a cartridge/ plunger and formulated with phenol (b) (4). 2. The applicant references Type V DMF (b) (4) validation information at Novo Nordisk A/S, Novo Alle, 2880 Bagsvaerd, Denmark.

(b) (4)

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(b) (4)

Assessment: Adequate. The package insert supports adequate instructions for storage of the drug product. In use stability studies support the maintenance of microbiological quality of the drug product over 28 days when stored (b) (4) (b) (4).

Post-Approval Commitments – Two (b) (4) drug product manufacturing facilities. (b) (4) (b) (4)

Assessment: Adequate.

MICROBIOLOGY DEFICIENCIES: None

Primary Microbiology Assessor Name and Date: Helen Ngai, Ph.D., 4/16/2021
Secondary Assessor Name and Date (and Secondary Summary, as needed): Elizabeth Bearr, Ph.D., 4/16/2021.

Helen Ngai

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Elizabeth Bearr

Digitally signed by Elizabeth Bearr
Date: 4/16/2021 01:15:32PM
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/s/

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