NDA 218316

NDA APPROVAL

Novo Nordisk Inc.
Attention: Devraj Chakravarty
Director, Regulatory Affairs
800 Scudders Mill Road
P.O. Box 846
Plainsboro, NJ 08536

Dear Devraj Chakravarty:

Please refer to your new drug application (NDA) received February 28, 2025, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Wegovy (semaglutide) tablets.

This NDA provides for the use of Wegovy (semaglutide) tablets in combination with a reduced calorie diet and increased physical activity:

- To reduce the risk of major adverse cardiovascular (CV) events (CV death, non-fatal myocardial infarction, or non-fatal stroke) in adults with established CV disease and either obesity or overweight.
- To reduce excess body weight and maintain weight reduction long term in adults with obesity or overweight in the presence of at least one weight-related comorbid condition.

APPROVAL & LABELING

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling with minor editorial revisions listed below and reflected in the enclosed labeling:

- Revised the Subsection Heading 14.4 to reflect (emphasis added) “Noncirrhotic Metabolic Dysfunction-associated Steatohepatitis with Moderate to Advanced Liver Fibrosis in Adults Treated with WEGOVY Injection”
- Revised the Table of Contents to reflect the revisions discussed above.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at

FDA.gov.[1] Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information and Medication Guide) as well as annual reportable changes not included in the enclosed labeling. Information on submitting SPL files using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As.*[2]

The SPL will be accessible via publicly available labeling repositories.

CARTON AND CONTAINER LABELING

Submit final printed carton and container labeling that are identical to the enclosed carton and container labeling, as soon as they are available, but no more than 30 days after they are printed. Please submit these labeling electronically according to the guidance for industry *SPL Standard for Content of Labeling Technical Qs & As.* For administrative purposes, designate this submission "**Final Printed Carton and Container Labeling for approved NDA 218316**." Approval of this submission by FDA is not required before the labeling is used.

DATING PERIOD

Based on the stability data submitted to date, the expiry dating period for Wegovy (semaglutide) tablets shall be 36 months from the date of manufacture when stored at at temperatures between 20°C to 25°C (68°F to 77°F).

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Cardiovascular Risk Reduction:

We are waiving the pediatric study requirement for this application because necessary studies are impossible or highly impractical. Atherosclerotic cardiovascular disease is on FDA's list of adult-related conditions that qualify for a waiver because they rarely or never occur in pediatrics (dated September 30, 2024).

Weight Reduction:

[1] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm
[2] We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

We are waiving the pediatric studies requirement for ages under 6 years old because the product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in this age group **and** is not likely to be used in a substantial number of pediatric patients in this group.

Both the FDA and the American Academy of Pediatrics propose that studies of weight-management products are limited to children who are 7 years or older with age- and sex-matched BMIs ≥95th percentile. The European Medicines Agency (EMA) guideline on the clinical evaluation of medicinal products used in weight management in children recommends that weight loss should be attained through lifestyle modification only for children aged 2 years to 6 years, and recommends enrollment of children aged 6 years to 18 years in clinical trials. As the pediatric study plan is a global program, the EMA guideline will be applied.

We are deferring submission of your pediatric studies for ages 6 to less than 18 years for this application because this product is ready for approval for use in adults and the pediatric studies have not been completed.

Your deferred pediatric studies required by section 505B(a) of the FDCA are required postmarketing studies. The status of these postmarketing studies must be reported annually according to 21 CFR 314.81 and section 505B(a)(4)(C) of the FDCA. These required studies are listed below.

4954-1 Conduct population pharmacokinetic (PK) and exposure-response analyses to evaluate the efficacy and safety of oral semaglutide (25 mg tablet) for the treatment of long-term weight reduction in pediatric patients with obesity ages 12 to less than 18 years.

Final Protocol Submission: June 2026
Study Completion: September 2026
Final Report Submission: January 2027

4954-2 Conduct population pharmacokinetic (PK) and exposure-response analyses to evaluate the efficacy and safety of semaglutide to support the 25 mg tablet for the treatment of long-term weight reduction in pediatric patients with obesity ages 6 to less than 12 years.

Final Protocol Submission: June 2027
Study Completion: September 2027
Final Report Submission: January 2028

FDA considers the term *final* to mean that the applicant has submitted a protocol, the FDA review team has sent comments to the applicant, and the protocol has been revised as needed to meet the goal of the study or clinical trial.[3]

Submit the protocols to your IND 151138, with a cross-reference letter to this NDA. Reports of these required pediatric postmarketing studies must be submitted as an NDA or as a supplement to your approved NDA with the proposed labeling changes you believe are warranted based on the data derived from these studies. When submitting the reports, please clearly mark your submission "**SUBMISSION OF REQUIRED PEDIATRIC ASSESSMENTS**" in large font, bolded type at the beginning of the cover letter of the submission.

POSTMARKETING REQUIREMENTS UNDER 505(o)

Section 505(o)(3) of the FDCA authorizes FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute.

We have determined that an analysis of spontaneous postmarketing adverse events reported under subsection 505(k)(1) of the FDCA will not be sufficient to identify an unexpected serious risk of maternal, fetal, and infant adverse outcomes or to assess a signal of a serious risk of medullary thyroid carcinoma.

Furthermore, the active postmarket risk identification and analysis system as available under section 505(k)(3) of the FDCA will not be sufficient to assess these serious risks.

Therefore, based on appropriate scientific data, FDA has determined that you are required to conduct the following studies:

4954-3 Conduct a prospective, registry-based observational exposure cohort study that compares the maternal, fetal, and infant outcomes of women exposed to semaglutide during pregnancy to an unexposed reference population. The registry will detect and record major and minor congenital malformations, spontaneous abortions, stillbirths, elective terminations, small for gestational age, preterm birth, and any other adverse pregnancy outcomes. These outcomes will be assessed throughout pregnancy. Infant

[3] See the guidance for Industry *Postmarketing Studies and Clinical Trials—Implementation of Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act (October 2019).* https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

outcomes, including effects on postnatal growth and development, will be assessed through at least the first year of life.

The timetable you submitted on December 18, 2025, states that you will conduct this study according to the following schedule:

Draft Protocol Submission:	June 2026
Final Protocol Submission:	June 2027
Interim Report Submission:	August 2028
	August 2029
	August 2030
	August 2031
	August 2032
	August 2033
	August 2034
Study Completion:	August 2034
Final Report Submission:	August 2035

4954-4 Conduct an additional pregnancy study that uses a different observational design from the Pregnancy Exposure Registry, using claims or electronic medical record data, to assess the associations between semaglutide exposure during pregnancy with pregnancy outcomes and infant outcomes, including but not limited to major congenital malformations, spontaneous abortions, stillbirths, and small for gestational age, preterm birth and postnatal growth and development.

The timetable you submitted on December 18, 2025, states that you will conduct this study according to the following schedule:

Draft Protocol Submission:	June 2026
Final Protocol Submission:	June 2027
Interim Report Submission:	August 2028
	August 2029
	August 2030
	August 2031
	August 2032
	August 2033
	August 2034
Study Completion:	August 2034
Final Report Submission:	August 2035

4954-5 Conduct a medullary thyroid carcinoma registry-based case series of at least 15 years duration to systematically monitor the annual incidence of medullary thyroid carcinoma in the United States and to identify any

increase related to the introduction of semaglutide tablet for the treatment of obesity into the marketplace. This study will also establish a registry of incident cases of medullary thyroid carcinoma and characterize their medical histories related to the use of semaglutide for the treatment of obesity/overweight.

The timetable you submitted on December 18, 2025, states that you will conduct this study according to the following schedule:

Draft Protocol Submission:	June 2026
Final Protocol Submission:	December 2026
Interim Report Submission:	March 2027
	March 2028
	March 2029
	March 2030
	March 2031
	March 2032
	March 2033
	March 2034
	March 2035
	March 2036
	March 2037
	March 2038
	March 2039
	March 2040
	March 2041
Study Completion:	February 2041
Final Report Submission:	February 2042

FDA considers the term *final* to mean that the applicant has submitted a protocol, the FDA review team has sent comments to the applicant, and the protocol has been revised as needed to meet the goal of the study or clinical trial.[4]

Finally, we have determined that only a clinical trial (rather than a nonclinical or observational study) will be sufficient to assess the known serious risk of of pulmonary aspiration in patients receiving GLP-1 RA products undergoing elective surgeries or procedures requiring general anesthesia and deep sedation or to inform potential mitigation recommendations including whether modifying preoperative fasting recommendations or temporarily discontinuing semaglutide could reduce the incidence of retained gastric contents in these patients.

[4] See the guidance for Industry *Postmarketing Studies and Clinical Trials—Implementation of Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act (October 2019).* https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

Therefore, based on appropriate scientific data, FDA has determined that you are required to conduct the following trials:

4954-6 Conduct a clinical pharmacology trial that uses ultrasound to measure the effect of both temporary withholding of semaglutide 25 mg tablets and fasting duration on retained gastric contents to evaluate delayed gastric emptying associated with glucagon-like peptide-1 receptor agonist (GLP-1 RA) use and inform potential recommendations to mitigate the serious risk of pulmonary aspiration.

The timetable you submitted on December 18, 2025, states that you will conduct this study according to the following schedule:

Trial Completion:	August 2026
Final Report Submission:	November 2026

FDA considers the term *final* to mean that the applicant has submitted a protocol, the FDA review team has sent comments to the applicant, and the protocol has been revised as needed to meet the goal of the study or clinical trial.[5]

Submit clinical protocol(s) to your IND 151138 with a cross-reference letter to this NDA. Submit nonclinical and chemistry, manufacturing, and controls protocols and all final report(s) to your NDA. Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission, as appropriate: **REQUIRED POSTMARKETING PROTOCOL UNDER 505(o) , REQUIRED POSTMARKETING FINAL REPORT UNDER 505(o), REQUIRED POSTMARKETING CORRESPONDENCE UNDER 505(o).**

Submission of the protocol(s) for required postmarketing observational studies to your IND is for purposes of administrative tracking only. These studies do not constitute clinical investigations pursuant to 21 CFR 312.3(b) and therefore are not subject to the IND requirements under 21 CFR part 312.

Section 505(o)(3)(E)(ii) of the FDCA requires you to report periodically on the status of any study or clinical trial required under this section. This section also requires you to periodically report to FDA on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Section 506B(a)(1) of the FDCA, as well as 21 CFR 314.81(b)(2)(vii) requires you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

FDA will consider the submission of your annual report under section 506B(a)(1) and 21 CFR 314.81(b)(2)(vii) to satisfy the periodic reporting requirement under section

[5] See the guidance for Industry *Postmarketing Studies and Clinical Trials—Implementation of Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act (October 2019).* https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

505(o)(3)(E)(ii) provided that you include the elements listed in 505(o) and 21 CFR 314.81(b)(2)(vii). We remind you that to comply with 505(o), your annual report must also include a report on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Failure to submit an annual report for studies or clinical trials required under 505(o) on the date required will be considered a violation of FDCA section 505(o)(3)(E)(ii) and could result in enforcement action.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. For information about submitting promotional materials, see the final guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format—Promotional Labeling and Advertising Materials for Human Prescription Drugs.*[6]

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the Prescribing Information, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at FDA.gov.[7] Information and Instructions for completing the form can be found at FDA.gov.[8]

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

COMPENDIAL STANDARDS

A drug with a name recognized in the official United States Pharmacopeia or official National Formulary (USP-NF) generally must comply with the compendial standards for strength, quality, and purity, unless the difference in strength, quality, or purity is plainly stated on its label (see FD&C Act § 501(b), 21 USC 351(b)). FDA typically cannot share application-specific information contained in submitted regulatory filings with third parties, which includes USP-NF. To help ensure that a drug continues to comply with compendial standards, application holders may work directly with USP-NF to revise official USP monographs. More information on the USP-NF is available on USP's website[9].

[6] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/media/128163/download.
[7] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[8] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf
[9] https://www.uspnf.com/

If you have any questions, call Martin White, Regulatory Project Manager, at 240-402-6018.

Sincerely,

{See appended electronic signature page}

John Sharretts, M.D.
Deputy Director
Division of Diabetes, Lipid Disorders, and Obesity
Office of Cardiology, Hematology,
Endocrinology, and Nephrology
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Medication Guide
- Carton and Container Labeling

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/

JOHN M SHARRETTS
12/22/2025 04:54:49 PM