UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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MYLAN INSTITUTIONAL LLC,
Petitioner,

v.

NOVO NORDISK A/S,
Patent Owner.

_____

Case IPR2020-00324
Patent 8,114,833

_____

DECLARATION OF DORTHE KOT ENGELUND

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I, Dorthe Kot Engelund, hereby declare as follows:

I. INTRODUCTION

1. I am an inventor named in U.S. Patent No. 8,114,833 (the "'833 patent") owned by Novo Nordisk A/S ("Novo Nordisk"), which I understand is currently the subject of *Inter Partes* Review No. 2020-00324.

2. I am currently the Scientific Director in the CMC Drug Product Development Division at Novo Nordisk, a position I have held since 2015. As the Scientific Director, I am a scientific drug product and process specialist within the areas of injectable protein formulations for diabetes and biopharmaceutical projects.

3. I received my M.Sc. in Pharmacy in 1989 from The Royal Danish School of Pharmacy. After I received my M.Sc. in 1989, I joined Novo Nordisk as a Research Scientist in the Health Care Group, Diabetes Care Division. I was involved in research related to drug product formulation and manufacturing processes for marketed insulin products. From 1995 to 2000, I was a Research Scientist in the Health Care D&D, Biologics Development Division and was involved in the development of drug product formulation and manufacturing processes of soluble and crystalline injectable insulin analogues. From 2000 to 2004, I was a Research Scientist in the Protein Drug Delivery Division, where I worked on development of the liraglutide drug product and other ready-to-use liquid formulations.

4. In 2004, I was promoted to Principal Scientist in the Biopharm Formulation Development Division, where I was a specialist regarding the drug production formulation of liraglutide and other ready-to-use liquid formulations. In 2015, I was promoted again and assumed my current position as the Scientific Director in the CMC Drug Product Development Division.

5. I am a full-time employee of Novo Nordisk, and I am not being separately compensated for my work preparing this declaration.

6. I have personal knowledge of all information set forth in this declaration unless I specifically note otherwise.

II. SUMMARY

7. I make this declaration in support of Novo Nordisk's Patent Owner Response, including to establish an invention date for the claimed subject matter of the '833 patent.

8. I also make this declaration to show that propylene glycol unexpectedly and surprisingly reduced clogging and deposits compared to mannitol. Mannitol was known to act as an isotonic agent in formulations, whereas propylene glycol was not known for chronic, subcutaneous use as an isotonic agent. However, as described below, it was surprising and unexpected that mannitol presented problems when used in a formulation containing liraglutide, a GLP-1 agonist, whereas propylene glycol did not present any of those problems. Thus, it was surprising and

unexpected that propylene glycol, an excipient that was not known for chronic, subcutaneous use as an isotonic agent, demonstrated an optimal collection of properties related to: (a) reducing deposits on production equipment during production; (b) reducing the clogging of injection devices and deposits on needles; (c) physical and chemical stability; and (d) antimicrobial preservative efficacy.

III. THE '833 PATENT

9. I understand that all claims (claims 1-31) are at issue in this proceeding. Claims 1-15 are directed to pharmaceutical formulations having a pH from about 7 to 10 and containing a GLP-1 agonist, a disodium phosphate buffer, and propylene glycol. Claims 16-22 are directed to methods of preparing such formulations. The remainder of the claims are directed to methods of reducing deposits on the production equipment (claims 23-25), reducing deposits in the final product (claims 26-28), and reducing clogging of injection devices (claims 29-31) by "replacing the isotonicity agent previously utilized" in a GLP-1 agonist formulation with propylene glycol.

10. For the initial phase 1 and 2 clinical trials, we made small scale batches containing liraglutide, a mixture of disodium phosphate and sodium phosphate buffer, phenol, and mannitol at a pH of 7.4. Since we only made these as small scale batches, we did not see any issues related to deposits on production equipment. In early development, we found that the liraglutide formulations were not physically

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