UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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MYLAN PHARMACEUTICALS INC.,
Petitioner,

v.

MERCK SHARP & DOHME CORP.,
Patent Owner.

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Case No. IPR2020-00040
U.S. Patent No. 7,326,708

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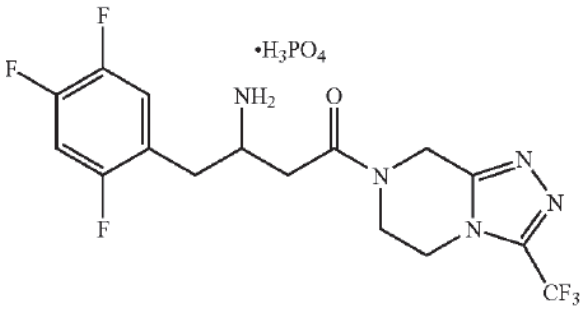
# DECLARATION OF VICKY K. VYDRA

I, Vicky K. Vydra, hereby declare as follows:

## I. INTRODUCTION

1. I am a named inventor of subject matter claimed in U.S. Patent No. 7,326,708 ("the '708 patent"). I understand that Merck Sharp & Dohme Corp. ("Merck") is the owner and assignee of the '708 patent.

2. In this declaration, I attest to certain facts related to the discovery of the dihydrogenphosphate ("DHP") salt of 4-oxo-4-[3-(trifluoromethyl)-5,6-dihydro[1,2,4] triazolo[4,3-a]pyrazine-7(8H)-yl]-1-(2,4,5-trifluorophenyl)butan-2-amine (also known as "sitagliptin") claimed in the '708 patent. The structural formula of the DHP salt of sitagliptin in a 1:1 stoichiometric ratio as claimed in the '708 patent as shown below:




## II. BACKGROUND

3. I received a Bachelor of Arts degree in chemistry from Rutgers, The State University of New Jersey, in 2001.

4. From June 2001 to June 2006, I was employed by Merck as a Staff Chemist in the Process Research Department of Merck Research Laboratories. My

work involved attempting to identify candidate salts and polymorphic forms of active pharmaceutical ingredients and other compounds of interest for further solid form and formulation development.

5. Since departing Merck in June 2006, I have held several positions at Bristol-Myers Squibb ("BMS"), where I am currently employed. My present title at BMS is Specialty Laboratories Category Manager, Clinical Laboratory Services, Global Procurement.

## III. SYNTHESIS AND CHARARACTERIZATION OF THE DIHYDROGENPHOSPHATE SALT OF SITAGLIPTIN

6. In or around December 2001, I began collaborating with the project team developing L-224715, the internal Merck designation for sitagliptin. I understood that sitagliptin had been identified by Merck as an inhibitor of the enzyme dipeptidyl peptidase IV ("DPP-IV") and that Merck was attempting to develop L-224715 into a dosage form for the treatment of type 2 diabetes.

7. As part of the project, I was asked to perform experiments in an attempt to synthesize one or more crystalline salts of L-224715. The intended purpose of my experiments was to attempt to identify crystalline salts of sitagliptin suitable for further development into a final formulated dosage form.

8. In accordance with Merck's policies and my own recordkeeping practices, I recorded the experiments I conducted in my lab notebook. Over the course of my career at Merck, I maintained many lab notebooks; my lab notebooks

are contemporaneous records based on my personal knowledge and kept in the course of my regularly conducted research activities on behalf of Merck. A true and correct copy of the relevant pages of the lab notebook where I recorded my experiments with L-224715 discussed herein is attached as Appendix A.

9. On December 12, 2001, I began conducting a set of experiments with L-224715 in an attempt to form one or more salts of the compound. As described on page 59 of my lab notebook, I conducted these experiments in a 96-well plate.

10. In column 4 of the 96-well plate, I dispensed solutions containing equimolar amounts of L-224715 freebase and phosphoric acid. I allowed the solvent in the wells to evaporate before proceeding further.

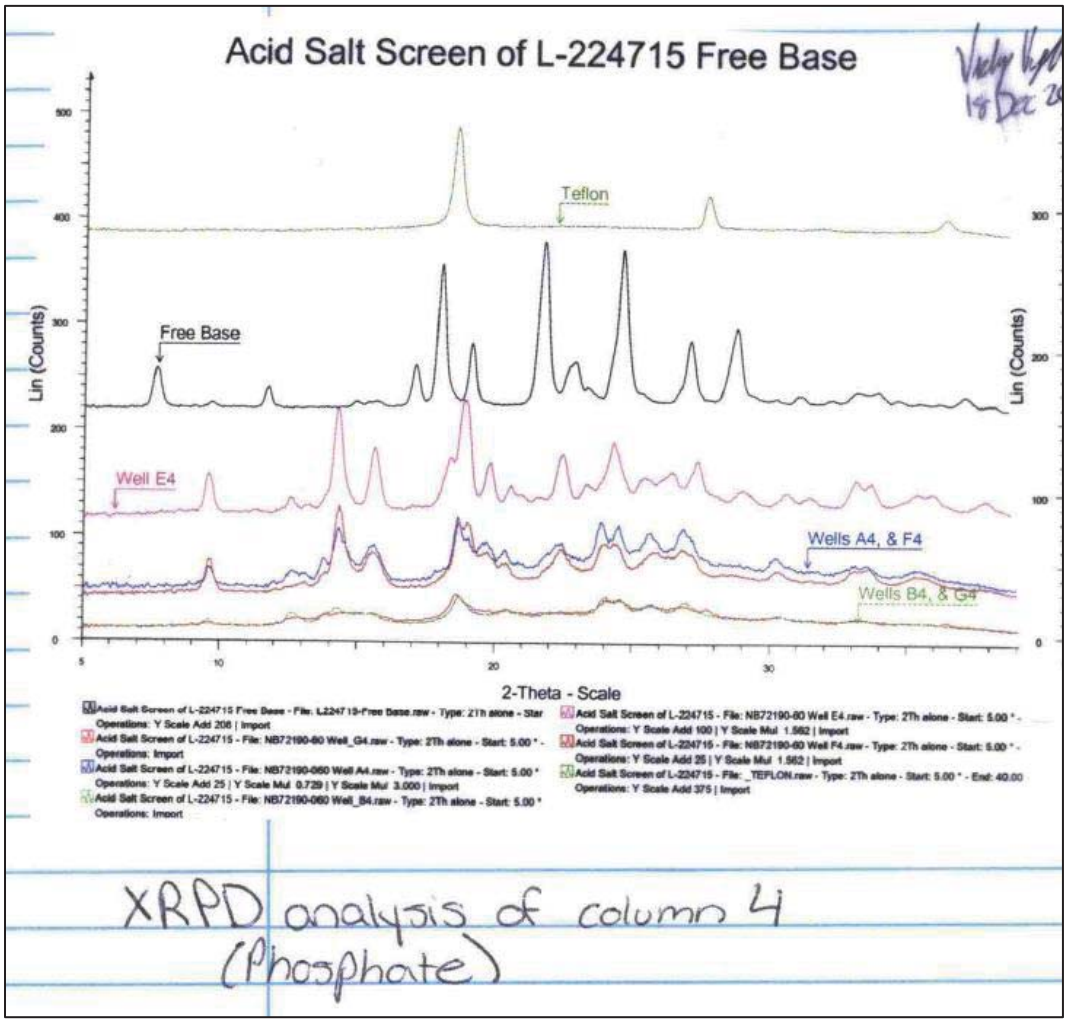
11. I then dispensed eight different recrystallization solvents, ethanol, 2-propanol, toluene, nitromethane, acetonitrile, 1,2-dimethoxyethane (or "1,2-DME"), isopropyl acetate, or methyl tert-butyl ether (or "MTBE"), one per row in rows 1 through 8 (or A through H), respectively, across the 96-well plate.

12. After adding the recrystallization solvents, I capped the 96-well plate, heated it to 70°C for one hour to dissolve any solids, and then lowered the temperature from 70°C to 10°C over the course of 8 hours.

13. On December 14, 2001, I analyzed the results of my experiments visually under a cross-polarized light microscope. I determined that solid material had precipitated in the wells of column 4 in which I had reacted L-224715 freebase

and phosphoric acid. I proceeded to isolate and prepare the solids for X-Ray Powder Diffraction ("XRPD") analysis.

14. On December 18, 2001, I obtained 2-theta patterns from XRPD (reflectance) analysis of the solid material I had been able to isolate and prepare in sufficient quantities on December 14. To analyze my results, I compared the patterns to a reference pattern for the crystalline freebase of L-224715, as well as a reference pattern for Teflon. The XRPD diffraction patterns that I compared are shown on page 62 of my lab notebook in Appendix A and below:



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