**THIRD DECLARATION OF LEONARD J. CHYALL, PH.D.**

I, the undersigned, **Dr. Leonard J. Chyall**, U.S. Passport No. 432624896, with a business address of Chyall Pharmaceutical Consulting LLC, 3000 Kent Avenue, Suite D1-105, West Lafayette, Indiana 47906, USA, having been warned that I must state the truth and that I shall be liable to the penalties prescribed by law should I fail to do so, hereby declare in writing as follows:

1. I am the same Leonard J. Chyall who submitted a declaration dated August 3, 2010 (**the "First Chyall Declaration"**) and a declaration dated March 7, 2012 (**the "Second Chyall Declaration"**), in support of the position of Teva Pharmaceutical Industries Ltd. (**"Teva"**) in the proceedings before the Honorable Deputy Registrar of Patents regarding Israel Patent Application No. 172563, filed by Merck & Co. Inc., U.S.A (**"Merck"**).

2. This declaration was prepared in response to the Affidavit of Prof. Jerry L. Atwood submitted on behalf of Merck regarding an experiment that Prof. Atwood conducted in August 2012 (**the "Second Atwood Affidavit"**). I was advised by Teva's counsel that Merck does not rely on paragraphs 3, 6, 7, 8 and 9 of the Second Atwood Affidavit.

3. The fact that I have not commented on any particular point in the Second Atwood Affidavit does not mean that I accept or agree with that point. There is nothing in the Second Atwood Affidavit that causes me to change the views that I expressed in the First and Second Chyall Declarations.

**Prof. Atwood's New Experiment**

4. In the Second Atwood Affidavit, Prof. Atwood describes a new experiment, in which he claims to have "repeated the procedure for making the 2:1 phosphate salt in isopropanol and water", which was described in Paragraphs 31 and 68 of his First Affidavit, this time with a "filtration and washing" step (**"the New Experiment"**). I shall refer below to the unwashed solids recovered by Prof. Atwood using the procedure described in Paragraphs 31 and 68 of his First Affidavit as "**the Atwood Unwashed Solids,**" and to the solids recovered by Prof. Atwood after his "filtration and washing step" as "**the Atwood Washed Solids**". Based on the elemental analysis of the Atwood Washed Solids, Prof. Atwood claims that his New Experiment shows that "the same 2:1 phosphate salt was obtained in all procedures, with or without Dr. Chyall's suggested work up" (paragraph 5 of Prof. Atwood's Second Affidavit). Prof. Atwood described his alleged "2:1 salt" as having a characteristic X-Ray Powder Diffraction ("**XRPD**") pattern that can be used to identify that alleged salt.

5. I note that Prof. Atwood's New Experiment attempts to rebut (but fails to do so, as explained below) only **one** of the criticisms that I raised in the Second Chyall Declaration with regard to Prof. Atwood's first set of experiments, *i.e.*, Prof. Atwood's failure to filter and wash the solid reaction products that he recovered. The New Experiment does not attempt to address any of the other criticisms I raised in the Second Chyall Declaration with regard to Prof. Atwood's experiments, such as Prof. Atwood's use of irregularly high reactant concentrations and lack of analytical data capable of proving that Prof. Atwood recovered any phosphate salts of sitagliptin other than the expected dihydrogenphosphate salt (**"DHP Salt"**). In

fact, Prof. Atwood's New Experiment is also fraught with these very same flaws, which are not remedied by his washing step.

6. In addition, Prof. Atwood's New Experiment attempts to rebut my criticism of his failure to filter and wash the reaction products with respect to only **one** of Prof. Atwood's experiments: his "procedure for making the 2:1 phosphate salt in isopropanol and water" (described in paragraphs 31 and 68 of his First Affidavit). Prof. Atwood did not present any experiment to rebut any of my criticisms, including his failure to filter and wash, with regard to any of the other preparations of alleged non-DHP Salts described in the First Atwood Affidavit.

7. There is nothing in the Second Atwood Affidavit that causes me to change the views that I expressed in the First and Second Chyall Declarations, *i.e.*, that the only pharmaceutically suitable stable salt that will result from a reaction of sitagliptin free base and phosphoric acid is the DHP Salt, a salt containing a 1:1 ratio of sitagliptin to phosphoric acid.

**Prof. Atwood Used Poor Experimental Techniques**

8. Based on my review of Prof. Atwood's Second Affidavit and laboratory notebook pages in which he describes the New Experiment, Prof. Atwood's protocol included at least the following steps that may have resulted in inadequate washing of the recovered solids:

A Prof. Atwood states that his reaction solution solidified. *See* Atwood Exhibit HH. In my experience, a reaction mixture that has solidified is more likely to contain entrapped impurities, such as unreacted starting materials, than a solid product that precipitated from the reaction solution.

B. Prof. Atwood states that he used a spatula to place his solidified material on a Büchner funnel fitted with an approximately 7 cm diameter piece of filter paper. *See* Atwood Exhibit HH. Prof. Atwood does not indicate whether he crushed or broke up his solidified reaction material before placing the solidified material on the Büchner funnel, a step that would have improved the effectiveness of Prof. Atwood's washing.

C. Prof. Atwood also does not indicate whether he evenly spread his recovered solids on the filter paper to minimize the possibility that washing solvent could pass through the filter with little or no contact with the solids to be washed. Any washing solvent that passed through the filter with little or no contact with the solids to be washed would not effectively wash the solids.

D. Prof. Atwood used filter paper with an approximate diameter of 7 cm (*see* Atwood Exhibit HH), meaning that the Büchner funnel that Prof. Atwood used also likely had a diameter of approximately 7 cm. If Prof. Atwood recovered 100% of his starting materials, he would only have recovered about 1.7 grams of solids. Depending on whether and/or how Prof. Atwood spread his recovered solids on the filter paper, the use of a filter with a 7 cm diameter with such a small amount of solids may leave parts of the filter bare, which would permit washing solvent to pass through the filter with little or no contact with the solids to be washed.

E. Prof. Atwood states that prior to the actual washing, he drew air through his recovered solids and the filter paper for 5 minutes. *See* Atwood Exhibit HH. If no liquid was extracted from the solids by this procedure, then it likely did little more than dry the solids. Drying the solids, including any impurities,

byproducts and/or unreacted sitagliptin base dissolved in the reaction solvent and trapped inside the recovered solids, would make it more difficult to remove those now solidified impurities, byproducts and/or unreacted sitagliptin base through subsequent washing.

F. Prof. Atwood states that he used 3 x 3 mL of isopropanol solvent to wash and filter the solids that he recovered. *See* Atwood Exhibit HH. This is a very small amount of solvent for washing Prof. Atwood's recovered solids when using a Büchner funnel with a diameter of approximately 7 cm. Using too little solvent for washing would result in ineffective removal of impurities, byproducts and unreacted starting materials.

9. Prof. Atwood's laboratory notebook, Exhibit HH of his Second Affidavit, by itself, does not provide enough detail to determine whether one or more of the above steps rendered Prof. Atwood's washing steps inadequate. Therefore, unlike my criticism of Prof. Atwood's previous experiments – which did not include **any** filtration and washing and therefore did not require that I conduct experiments to conclude that Prof. Atwood's assertions regarding the solids that he recovered were unreliable and without scientific merit – I could only prove the misleading nature of Prof. Atwood's New Experiment, which included a "filtration and washing" step, by conducting experiments.

**My Experiments Prove That Prof. Atwood's "Filtration And Washing" Was Ineffective**

10. I received from Teva a sample container labeled lot no. D6655070112, which I understand to contain Sitagliptin Free Base. The sample was assigned LIMS No. 308390, and I characterized the material using XPRD (see Exhibit A). The XRPD

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