Department of Pediatrics
Ian M. Burr Division of
Pediatric Endocrinology and Diabetes

VANDERBILT UNIVERSITY
School of Medicine

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May 26, 2021

Re: Application to add long-acting insulin analogues to the WHO Model List of Essential Medicines

Dear Members of the Expert Committee,

I am writing as a pediatric endocrinologist and as a person living with Type 1 diabetes for over 45 years to support the inclusion of long-acting insulin analogues on the WHO EML. I have read with interest the application and the various responses and discussion around the issue in both 2017 and 2019. I have also noted with interest the wide range of new and expensive medications that are up for consideration across a variety of indications at your upcoming meeting. I find myself variously perplexed, flummoxed, and appalled that long-acting insulin analogues and indeed additional insulin analogues that have been widely available for more than 25 years have not already moved onto the EML.

I am surely grateful to the availability of the original animal insulins; they kept me alive in my youth. I was thrilled in my later childhood when in the early 80's human insulin became available for the first time with its greater consistency. I will concede here at the outset that it is possible to manage diabetes with injected human insulin; it is possible to obtain a decent A1c on these regimens; it is unlikely that anyone is doing or will do a study to show an improvement in A1c across large numbers of individuals. At the same time, an A1c is an average of tens of thousands of little moments that go in to being a person living with T1D. And those moments are profoundly impacted by the type of insulin they are provided.

In living with diabetes treated with insulin, you quickly learn that kinetics dictates life. When your insulin reaches its maximum efficacy, you had better have food on board or you will risk a substantial low blood sugar. This means planning out each day of your life around a strict schedule and food availability when you are on human insulin. If you are living in a situation where food access is uncertain or limited, the mix of NPH and regular is not the right insulin for you as these insulins force you to eat at specific times ***after*** taking them. This necessity distinguishes them from regimens built around long-acting insulin like glargine, detemir, and others that provide a level basal rate that demands little mandated food intake or timing. We are not even discussing here the addition of faster acting analogues that further improve this decision-making process and allow rapid treatment of food intake and hyperglycemia. The risk of human insulins is borne out in the increased rates of hypoglycemia associated with taking them, which often results from timing mismatches between insulin intake and food availability. In addition, these low blood sugars, which can be life-threatening, likely enable the attainment of a "good" A1c (since A1c is an average) but at a clear cost to the patient. Indeed, the use of human

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insulin moves a great deal of costs onto the patient including their need for stricter management of time, loss of flexibility, and an increase in frequency and severity of low blood sugars. These costs in turn may provide disincentives for individuals in these circumstances to be fully adherent with their diabetes regimen, given that they may not be able to afford going low in many circumstances, such as work, loss of access to food/shelter, or other life challenges. Thus, while human insulin is capable of providing acceptable long-term measures under optimal, controlled circumstances, it is not evident that it will achieve these outcomes for the individuals we are trying to serve. As far as I am aware, well-designed studies for outcomes and quality of life with long-acting analogues vs human insulin have not been performed in low resource countries, which is the population we are serving.

As a pediatric endocrinologist, I do not place any of my patients on NPH/regular regimens. Even though these regimens often involve only two doses a day of injected insulin compared to the 4+ doses of lantus plus insulin aspart that I routinely prescribe. If it were equally effective in terms of overall management and quality of life, surely I and the large diabetes communities in highly resourced countries would manage all our patients with this less invasive regimen. We of course do not do that as broad measures of 'equivalence' at population levels in terms of A1c do not portend equivalence for all individuals or in their day-to-day lives.

I hope that you will consider the impact of insulin therapy and selection on the lives of individuals with diabetes. Your choices and endorsements have profound impacts on how these individuals experience their day-to-day lives and can either compound or alleviate their struggles. I hope that the full weight of the WHO behind the importance of insulin analogues would facilitate bringing long-acting insulin to places where it can provide incredible, albeit immeasurable, benefit to persons living with T1D.

Sincerely,

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