United States Senate
WASHINGTON, DC 20510

March 1, 2019

The Honorable Dr. Scott Gottlieb
Commissioner
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Dear Commissioner Gottlieb:

On December 11, 2018, the U.S. Food and Drug Administration (FDA) issued several guidance documents aimed at facilitating the development of lower-cost biosimilar products by clarifying FDA's regulatory framework for biologics. We commend FDA for its efforts to "inspire competition that can help lower costs and broaden patient access."[1] However, we write to share our concerns with policies that may have the opposite effect for the 7.5 million Americans with diabetes who rely on a daily supply of insulin to survive.[2] To help expedite approval in the short term of desperately needed lower-cost biosimilar or "generic" insulin products, we urge FDA to quickly amend its recent guidance documents that pose unreasonable approval delays for insulin products that could help patients with diabetes.

The skyrocketing cost of insulin has made this life-saving medication unaffordable and has forced patients into alarming, and at times fatal, practice of rationing insulin.[3] There has been a six-fold increase in the price of their life-saving insulin over the past two decades. For example, the price of Eli Lilly's Humalog has increased from $21 for a 10-mL vial in 1996 to $275 today; Sanofi's Lantus has jumped from $35 per vial in 2001 to $270 today; and Novo Nordisk's Novolog has increased from $40 in 2001 to $289 today.[4] Notably, insulin was first discovered in 1921, and its patent and license terms were then sold for $1. We recognize there are myriad reasons for the significant insulin price increases, including limited competition, exploitation of the patent system, the opaque role of pharmacy benefit manager rebates, product improvements and variance over time, and a lack of transparency. However, it remains unacceptable that—nearly a century after insulin was first discovered—there are no approved, lower-cost insulin products that can be substituted at the pharmacy level.

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[1] FDA Commissioner Scott Gottlieb. Statement from FDA Commissioner Scott Gottlieb, M.D., on new actions advancing the agency's biosimilars policy framework, December 11, 2018.
[2] Cefalu, William T. et al. "Insulin Access and Affordability Working Group: Conclusions and Recommendations." *Diabetes Care*, American Diabetes Association, June 2018, 41(6): 1299-1311.
[3] Rosenthal E. When High Prices Mean Needless Death. *JAMA Intern Med.* Published online December 03, 2018. doi:10.1001/jamainternmed.2018.5007
[4] Stanley, Tiffany. "Life, Death and Insulin" *The Washington Post Magazine*, 7 January 2019

The December 2018 guidance documents will help FDA implement the Biologics Price Competition and Innovation Act (BPCIA) by transitioning certain biologics—which had previously been regulated as drugs under the FDA's Federal Food, Drug, and Cosmetics Act (FD&C)—to the biological product regulatory framework under the Public Health Service Act (PHSA). This is an important action to ease the approval pathway for lower-cost biosimilar products. However, there currently are no insulin reference products under the PHSA, which are required for the submission of "generic" or biosimilar insulin applications. The FDA guidance will facilitate the submission of applications for biosimilar insulin products for the first time. Although these changes will bring new insulin products into market in 2020, the current regulatory framework still introduces perverse incentives that could delay the introduction of low-cost insulin products into the market in the short-term, when they are needed most.

Our first concern is that approved insulin "follow-ons" under the FD&C will not transition to biosimilar licenses, meaning they cannot be substituted for brand name versions by pharmacists. Further, according to this guidance document, companies with 505 insulin applications in FDA's approval pipeline that are still pending or are tentatively approved on March 23, 2020, will be rejected by FDA and companies must then start over with a new application under a different pathway, and incur an additional user fee. It is concerning that an application to bring a new or follow-on insulin to market would be rejected and forced to submit a new application, while FDA provides flexibility by planning to "administratively convert" pending New Drug Application supplements to pending Biologics License Applications supplements. If FDA has the ability to offer flexibility in one domain, recognizing the cumbersome requirement to withdraw and re-submit an application, then FDA should offer similar flexibility for pending and/or tentatively approved 505 insulin applicants.

As a related consequence, FDA's implementation creates an application termination cliff and discourages new applicants. No potential applicant who is otherwise prepared to file today would sensibly choose to do so in face of the looming March 23, 2020, cut-off date—such applicants would instead wait over a year until they would submit under the biosimilar application pathway. While we recognize FDA's efforts to work with sponsors to prepare applications, we are concerned that potential applicants are being precluded from BPCIA's clear transition framework. To assist us in understanding FDA's transition plans, we respectfully request that FDA also provide an explanation on (1) the steps FDA is taking to expedite the approval of insulin follow-on applications prior to the March 23, 2020 deadline, (2) how many applications are currently pending, and (3) whether FDA anticipates approving any insulin follow-on applications prior to the March 23, 2020 deadline. We respectively request responses by March 15, 2019.

While we certainly support FDA's overall goals of bringing lower-cost biosimilar products to market, we remain concerned the Agency's 2018 guidance has flaws in the context of insulin products that must be quickly remedied. Most notably, the policy of effectively freezing all applications for lower-cost competitor insulin products, while penalizing those applicants that have already submitted FDA product reviews, must be corrected.

Under your leadership, FDA has taken important strides to help patients by speeding approval of generics—including a record-setting amount in 2018. On behalf of the millions of Americans who rely on insulin every single day, we urge you to promptly reconsider these policies so that lower-cost competitor insulin products can come to market sooner.

Sincerely,

Richard J. Durbin
United States Senator

Kevin Cramer
United States Senator

Tina Smith
United States Senator

Bill Cassidy, M.D.
United States Senator