Georgia Senator Introduces *The Combination Product Regulatory Fairness Act of 2015*

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On July 17, 2015, Georgia's U.S. Senator Johnny Isakson (R-GA), along with co-sponsors, Robert Casey (D-PA), and Pat Roberts (R-KS), introduced a Senate bill entitled, "*The Combination Product Regulatory Fairness Act of 2015*." The bill is intended to streamline device / drug combination approvals at the Food and Drug Administration (FDA) by implementing several new procedures, including letting the agency rely on previously approved premarket approval applications (PMAs) and new drug applications (NDAs) to help support new combination product approvals.

Senator Isakson released a statement characterizing the bipartisan legislation as a major improvement of an outdated and inefficient regulatory process for innovative products that currently do not fall under a single categorization for approval by FDA. "The *Combination Product Regulatory Fairness Act of 2015* will eliminate the high level of uncertainty in approval standards that currently exists for innovative companies, both small and large, when deciding to invest in a new product," said Isakson. "This bill creates a clear regulatory pathway for products to come to market that will directly translate to greater access and more innovative medical products for patients who will benefit most."

Isakson's legislation would implement a transparent, innovation-friendly and risk-based approach to regulation while improving efficiency through greater certainty in the interpretation of regulatory standards in the approval pathway for combination products. Of greatest significance, the proposed legislation provides an opportunity for manufacturers and the FDA to rely on existing safety and efficacy data to prevent a duplicative regulatory process from stalling combination products' accessibility to patients.

The proposed legislation will likely be considered as part of the Senate's broader focus as it crafts its own health innovation initiatives in response to the House of Representatives recent passage of the 21st Century Cures Act (H.R. 6). The 21st Century Cures Act aims to speed the development and approval of drugs and devices; provide more financial incentives for making products for small patient populations; and stabilize federal funding for basic biomedical research.

The Combination Product Regulatory Fairness Act of 2015 incorporates these key features:

1. Determination of a Product's Regulatory Status

The proposed legislation provides that when FDA determines that a combination product does not meet the definition of device in the Federal Food, Drug, and Cosmetic Act (FDCA), the agency must provide the sponsor of the product with both a "competent and reliable scientific rationale" that supports such a determination and citations to any scientific evidence relied upon by FDA to support that rationale. The sponsor is allowed to propose a nonclinical or clinical study to establish the significance, if any, of the chemical action in achieving in achieving the primary intended purpose of the combination product, and the FDA and the sponsor are obligated to collaborate in good faith to reach agreement on the design of such a study within a reasonable time, not to exceed 90 days. Finally, the proposed bill provides that the data resulting from the study shall inform the classification of the product.

2. Assigning a FDA Center to Regulate Combination Products

Under the current FDA regulatory procedures, sponsors are sometimes left with uncertainty as to what regulatory center will ultimately be charged with review of their application. This proposed legislation would formalize the normal practice of FDA's Office of Combination Products by requiring FDA to assign a leader center to address whether a product will be reviewed as a drug, device, or biologic, based on the primary intended use of the product. For example, if the primary mode of action (the single mode of action that provides the most important therapeutic action of the combination product) is that of a drug (other than a biological product), the Center for Drug Evaluation and Research would have primary jurisdiction. The proposed legislation goes on to provide that FDA, in assigning the lead center, may not determine the primary mode of action is that of a drug or biologic solely because the combination product has any chemical action within or on the human body. The proposed legislation further requires FDA to provide a competent and reliable scientific rationale to support its classification decision in cases where the agency disagrees with the conclusions of the sponsor regarding the primary mode of action.

3. Combination Product Review Plan

The proposed bill allows a sponsor of a combination product to submit a Combination Product Review Plan (CPRP) for the combination product and to request a meeting with FDA before submission of the CPRP to establish clarity and certainty regarding the standards and requirements applicable to establish safety and effectiveness, or substantial equivalence, of the combination product. This pre-submission meeting may also cover postmarket modifications to a combination product and good manufacturing practices for the combination product. Not later than 60 days following the submission of the CPRP, including a revision of a previously proposed or approved CPRP, FDA must take action to:

- approve the CPRP, and
- issue to the sponsor a response indicating such approval, or
- if FDA finds that the CPRP is not adequate to establish safety and effectiveness of the combination product, it may decline to approve the CPRP, but the agency must provide the sponsor with an explanation of the deficiencies in the CPRP.
- When FDA declines to approve a CPRP, it must within 30 days meet with the sponsor to discuss the CPRR unless the sponsor determines such a meeting is not necessary. At this meeting, FDA will be obligated to include any necessary experts from the relevant agency centers. Not later than 30 days from the date of the meeting, the sponsor must prepare minutes of the meeting, which are to be made available to FDA. Any agreement reached between FDA and the sponsor through this process shall be reduced to writing by the sponsor and once approved by FDA, made a part of the administrative record. Such agreements may not be modified except with the written consent of the sponsor, or in situations where FDA subsequently finds that a substantial issue essential to determining the safety or effectiveness, or substantial equivalence of the combination exists. In such a situation, FDA must provide notice within 2 days of the decision and allow for another meeting with the sponsor within 14 days.

4. Ability to Consider Prior Findings of Safety and Effectiveness

Currently, when approving products, the FDA does not take into account prior findings of safety and effectiveness of components of a combination product. *The Combination Product Regulatory Fairness Act of 2015* will allow FDA under certain prescribed conditions to rely on prior findings of safety and efficacy for a previously approved drug component and rely on previously-approved pre-market approvals.

5. Future FDA Guidance

The proposed legislation requires FDA to issue final guidance within 2 years after the date of enactment to describe the responsibilities of each FDA center regarding its review of combination products, including each center's role in evaluating evidence development and review under a risk-based approach, dispute resolution, labeling, product usability assessments, and human factors testing.

A copy of T*he Combination Product Regulatory Fairness Act of 2015* is available here[1].

1 https://www.pharmamedtechbi.com/~/media/Supporting%20Documents/The%20Gray%20Sheet/41/30/S1767.pdf

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