

# American Autoimmune Related Diseases Association

Report on the September 17, 2015 Hearing on Biosimilars.

On September 17, 2015, the U.S. Senate Committee on Health, Education, Labor, and Pensions (HELP) conducted a hearing to assess the progress of the Food and Drug Administration (FDA) in implementing biosimilars. Below is a summary of the hearing and key topics addressed by the Committee Members and the hearing's one witness, Dr. Janet Woodcock, who serves as Director of FDA's Center for Drug Evaluation and Research.

**Hearing Title:** "Biosimilars Implementation: A Progress Report from FDA"

**Witness:** Janet Woodcock, M.D. (Director of the Center for Drug Evaluation and Research, FDA)

## **Opening Remarks and Overall Tenor of the Hearing**

- **Cost of Biologics:** Senators Cassidy and Murphy opened the hearing by commenting on the rapidly growing costs of healthcare, and the costs of biologics in particular. Specifically, Sen. Murphy remarked that the United States spent \$374 billion on prescription drugs in 2014, which represents a 13% increase above what was spent in 2013, due, in part, to the increasing use of biologics and the costs associated with those products. Sen. Warren underscored these comments later in the hearing, noting that the costs of biologics represented 28% of all drug spending in 2013 and that just eight biologic drugs account for over 40% of all Medicare Part B spending.
  - In light of the high costs associated with biologics, several senators noted that biosimilars, provided for by Congress with the passage of the Biologics Price Competition and Innovation Act (BPCIA) in 2010, represent an opportunity to increase access to life-saving treatments while lowering the cost of healthcare. In this regard, Sen. Murphy stated that biosimilars are expected to be 15-30% cheaper than innovator biologic products, and Sen. Warren noted that a RAND analysis projected that the use of biosimilars could save \$44 billion over the next ten years.
- **Need for FDA to Issue Critical Guidance Related to Biosimilars:** Several senators expressed concern about the about the lack of industry guidance with respect to the development of biosimilars despite the fact that the BPCIA was passed more than five years ago. Indeed, Sen. Cassidy noted at the outset of the hearing that the industry is still waiting for draft and/or final guidance in several key areas including: (1) interchangeability, (2) naming, (3) labeling, and (4) data extrapolation.
  - Sen. Murphy noted that the industry is not willing to invest the significant resources required to develop biosimilars without clearer guidance. Similarly, Sen. Warren stated that the healthcare system cannot realize the significant cost savings associated with biosimilars until two or more competitors of the underlying innovator products enter the market, which they are not willing to do without clearer "rules of the road" for how to develop competitor biosimilars.

## FDA's Efforts to Publish Guidance for the Industry and Healthcare Providers

- Interchangeability: Several senators, including Sen. Cassidy and Sen. Murphy, identified the development of regulatory standards for interchangeability as critical to the industry's development of biosimilars and expressed concerns about FDA's lack of guidance in this area.
  - Citing the statutory language from the BPCIA, Dr. Woodcock explained that the standard for interchangeability among biologics is a particularly "high bar," and stated that FDA is actively working to establish a scientific framework for demonstrating interchangeability.
  - Dr. Woodcock further explained that the "interchangeability" framework is difficult to develop due to the concerns associated with human immune response and the risk of developing heightened immunity to certain proteins or hormones potentially associated with a patient's therapy switching between a biosimilar and innovator product. Dr. Woodcock expressed the concern that switching between an innovator biologic and a biosimilar may produce an unexpected immune response and could cause a patient's immune system to attack its own hormones/proteins. Nevertheless, she stated that FDA "believe[s] that getting to interchangeability is feasible and we will get there."
  - Despite direct questions from several senators about whether FDA was "on track" to release its interchangeability guidance in 2015 as expected, Dr. Woodcock did not give a concrete answer, stating that FDA is working very hard to develop the guidance, but that it requires multiple levels of clearance and the timing is "out of [her] hands."
  - Dr. Woodcock clarified that even if a biosimilar is determined to be interchangeable with the innovator biologic, state laws will govern if and when a pharmacist can substitute the biosimilar for the biologic.
- Scientific Analytical Framework for Establishing Bioequivalence: Sen. Cassidy noted that, according to the industry, FDA's lack of guidance on statistical approaches to determining analytical similarity is highly problematic with respect to the development of follow-on products, which is compounded by the FDA's lack of transparency regarding the requirements for establishing biosimilarity and the ongoing evolution of FDA's position on the matter.
  - Dr. Woodcock acknowledged that the lack of guidance in this area is problematic for the industry, but noted that FDA is working directly with 16 different manufacturers on the development of 57 new biosimilar products. She noted that while FDA is still working to draft and issue guidance clearly describing the analytical framework for bioequivalence, the Agency is providing direct consultation on this matter to manufacturers with biosimilars under development.
  - Dr. Woodcock noted that the "analytical chemistry and statistics" of an innovator drug can vary between different lots/batches of the same innovator drug, and, for this reason, the FDA does not think that "rigid limits for bioequivalence are appropriate." Dr. Woodcock indicated that a more flexible standard for demonstrating biosimilarity, such as the use of "confidence intervals," is necessary.

- In response to a direct question from Sen. Cassidy, Dr. Woodcock again stated that she is unsure when these confidence intervals will be released but hopes that it will be within the next six months.
- Labeling: Sen. Scott expressed concern about FDA's lack of guidance on the requirements for appropriate biosimilar labeling. In particular, Sen. Scott noted that, in light of the amount of pressure already on physicians with the development of new billing codes and the burden of electronic healthcare records, it seems costly with respect to patient safety to approve biosimilars without clear guidance on the labeling requirements for those products.
  - Dr. Woodcock explained FDA will issue guidance that explicitly addresses labeling requirements in the near future, and noted that the Agency has received a citizen petition from AbbVie that it is evaluating as it develops the guidance.
  - Dr. Woodcock stated that there are significant trade-offs in the labeling decisions and noted that it is important to select a labeling convention that maintains the trust of clinicians and clearly describes the appropriate indications and uses for biosimilars.
  - Dr. Woodcock did not give a time estimate on when the industry can expect to see draft labeling guidance from the FDA, but she said FDA plans to do so "as soon as possible."
- Naming: Sen. Hatch noted that when the FDA approved the first biosimilars product, it approved a suffix that indicated the name of the manufacturer, but the draft guidance provides for a "random letter suffix convention." Sen. Hatch inquired about FDA's shift in thinking on this issue.
  - Dr. Woodcock explained that there are "lots of trade-offs" in selecting an appropriate naming convention for biosimilar products. For example, Dr. Woodcock stated that it is crucial that the naming convention allow FDA to track adverse events and clearly determine what products patients were given. She added, however, that the use of the "company contraction" as a suffix may inhibit switching once interchangeability becomes a reality and may become complicated if the product is acquired by another company post FDA-approval, which is why FDA proposed the four-letter random (or "non-meaningful") suffix. Nonetheless, Dr. Woodcock noted that, ultimately, FDA is not sure what the most appropriate approach is, which is why the Agency explicitly solicited comments from the industry on this issue in the proposed rule it released last month.
  - Dr. Woodcock noted that the FDA is working closely with the World Health Organization (WHO) to develop a "global solution" to the naming convention for biosimilar products in light of the current situation in the European Union (EU), in which prescribers must list both the brand name of the product and the lot number because the EU did not develop a clear naming convention for how to distinguish among biosimilars.
- Reimbursement: Sen. Murphy noted CMS' recent proposal with respect to reimbursement of biosimilars and inquired about the impact that would have on FDA's activities. In particular, a CMS proposed rule released in July 2015 would assign all biosimilars of a single reference

product one code and would reimburse biosimilars with the same code based on a weighted average of their average sales price under Medicare Part B.

- Dr. Woodcock explained that FDA often uses CMS' billing codes for tracking drug products. She said that, if the proposed rule is made final, FDA and CMS plan to develop an approach to use sub-codes or coding modifiers to distinguish among products if there are multiple biosimilars within the same billing code.

### **FDA's Plans to Educate the Public and Healthcare Professionals**

- **Education Campaign:** Several senators, including Sens. Murphy and Warren, expressed concern about the uptake of biosimilars and asked Dr. Woodcock how FDA plans to address this issue.
  - Dr. Woodcock said she thinks the responsibility for educating clinicians and the public about the safety and efficacy of biosimilars “fall[s] on FDA’s shoulders.” She said FDA plans to launch an active public education campaign and also plans to offer CMEs to individual physicians and focus targeted educational efforts on sub-specialty groups (such as rheumatology) that primarily tend to use biologics. She also noted that some state legislators have approached FDA about collaborating on joint educational efforts.
  - Sen. Murphy stated that Congress must be sure it provides FDA with the resources it needs to perform these educational activities. He suggested that such activities are needed in order to combat the negative marketing that the manufacturers of innovator products will roll out as more biosimilars enter the market.
- **State Laws:** Sen. Murphy stated that, to date, 31 states have considered passing state laws addressing how biosimilars would be provided to patients and expressed concern that some state laws may operate as “barriers to the utilization” of these products as more are approved. Dr. Woodcock stated that some proposed state laws the FDA has seen would limit patient access to biosimilars. To counteract such laws, Dr. Woodcock reiterated the importance of earning and continuing to maintain the trust of the clinical community. She also noted that the FDA has an intergovernmental affairs office that interacts with state legislatures and helps answer any questions that these lawmakers may have about the impact of biosimilars.