Comments from the Alliance for Safe Biologic Medicines on FDA Guidance:

"Promotional Labeling and Advertising Considerations for Prescription Biological Reference and Biosimilar Products-Questions and Answers; Draft Guidance for Industry; Availability"

Docket Number: FDA-2019-D-5473

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(Adapted from oral testimony given at the March 9, 2020 FDA/FTC Workshop on a Competitive Biosimilar Marketplace)

I. Comments from Madelaine Feldman, MD, FACR; Chair, Alliance for Safe Biologic Medicines.

Good afternoon. My name is Madelaine Feldman. I am a rheumatologist in private practice in New Orleans, Louisiana. I am also President of the Coalition of State Rheumatology Organizations, founder of the Rheumatology Alliance of Louisiana, and Chair of Alliance for Safe Biologic Medicines.

ASBM is an organization composed of more than 140 patient advocacy groups and physician societies. Since 2010 we've worked to make sure that patients remain at the center of policy discussions regarding biosimilars. This work includes sharing the perspectives of patients, physicians, and pharmacists with regulators and other policymakers at the state, national and international level.

Today I'd like to speak to some issues that occur in discussions about biosimilars. The first is that "misinformation" continues to be spread affecting the objectivity of prescribers and creating an anti-biosimilar bias among physicians, slowing the uptake of the biosimilar market. In a meeting I ran last week with rheumatologists from around the country, when asked if anyone felt that biosimilars were in anyway inferior to originators, not one person raised their hand.

The reality is - It takes time for confidence to emerge among health care professionals, including physicians, with any new drug… including when generics were first introduced.

The Hippocratic Oath states: "First Do No Harm." By nature, clinicians are generally more cautious and conservative regarding starting new treatments and are hesitant to

change without sufficient experience, clinical data and independent recommendations. This is particularly true when physicians are asked to switch medications on a stable patient.

It can take years to adequately control the disease activity in a rheumatoid arthritis patient. And rheumatologists have been sensitized to non-medical switching by payers wherein we are told that the medicine that finally stabilized our patient… will no longer be paid for.

By changing formularies payers can legally switch our patients' medications every 6 months. This could involve switching back and forth not only among various biosimilars but even switching patients to an entirely different biologic. So yes, physicians are leery of The Great American switching experiment..

ASBM disagrees with procurement practices and payer policies giving advantage to one product over another through incentives that benefit the physician monetarily. These do nothing to help the patient afford the drug and could actually undermine patient's trust and confidence in their physician. Consequently if there are to be incentives they should be directed to cost considerations for the patient.

And finally considering the perception, that the US is somehow "behind" the advanced countries in Europe with respect to building our biosimilars market, it should be noted that our biosimilars pathway, the BPCIA, was adopted well after the EU began creating its own process for approving biosimilars.

Five years after the EMA approved its first biosimilar, it had approved 11 products. In the 5 years since the US' first biosimilar approval we have 26 biosimilars approved; and keep in mind that this total actually understates the growth in our biosimilar market. Many of the products counted as "biosimilars" in Europe are on the market here as well, but currently they are classified as "follow-on biologics" because they predate the BPCIA.

The FDA deserves credit their support in building of a biosimilar market so quickly, and without compromising on safety and efficacy standards. Physicians are enthusiastic about biosimilars and the benefits they can bring in terms of therapeutic choices that can offer cost savings to our patients and to the larger health system.

The most important strategies to continue this process in the US are strong FDA educational programs for health care professionals and patients along with pharmacovigilance programs, *particularly in light of payers' ability to so frequently switch our patient's medications through formulary changes.* This will allow clinicians the opportunity to learn from the real-world experience with biosimilars- and continue to gain confidence in using them.

Thank you for the opportunity to comment.

II. Comments from Philip Schneider, MS FASHP; Professor, Ohio State University College of Pharmacy; Advisory Board Chair, Alliance for Safe Biologic Medicines.

Good afternoon. My name is Philip Schneider. I am a professor of pharmacy at the Ohio State University. I also currently serve as Chair of the Advisory Board for the Alliance for Safe Biologic Medicines. Since its founding in 2010, ASBM has sought to empirically document the perspectives of healthcare providers around the world regarding biosimilars.

Today, I'd like to focus my comments on addressing what we at ASBM believe to be incorrect assumptions underlying these proceedings today - that biosimilar uptake in the U.S. is strongly linked to low physician confidence levels in biosimilars, and physician confidence has been depressed because of anti-competitive practices. First, we are unaware of either negative physician sentiment, or any anticompetitive practices. Second, we know that physicians have confidence in biosimilars.

Last year ASBM conducted a survey[1] of 579 physicians in 6 Western European countries - France, Germany, Italy, Spain, Switzerland, and the UK. We surveyed physicians in 10 different areas of practice including rheumatology, gastroenterology, oncology, dermatology, and neurology. All of these physicians prescribe biologics in their practice.

What we found was that these physicians were very familiar with and confident in biosimilars. This is perhaps not surprising since European physicians have had 13 years of experience with biosimilars. Depending on country, between 82% and 93% of prescribers considered themselves familiar or very familiar with biosimilars. Between 80% and 99% would feel comfortable prescribing a biosimilar to a new treatment-naïve patient. Between 46-76% would be comfortable switching a patient from a reference product to a biosimilar, even if they're stable on their current medicine.

But, if the premise behind today's proceedings is valid - that biosimilar uptake is strongly tied to physician confidence, the high physician confidence in biosimilars across the board should correlate with a consistently high uptake across the board.

Yet if we look at the biosimilar market shares across the six countries we surveyed, we can see that in fact there is a very wide variation, and a variation between biosimilars in different product classes. (Data here is taken from an IQVIA report "The Impact of Biosimilar Competition[2], September 2018")

- Biosimilar Epoetin market share ranged from 6-84%

[1] https://safebiologics.org/wp-content/uploads/2019/09/ESMO-Poster_2019-FINAL.pdf
[2] https://ec.europa.eu/docsroom/documents/31642/attachments/1/translations/en/renditions/native

- Biosimilar (G-CSF): 62-99%
- Biosimilar Anti-TNF: 7-69%
- Biosimilar Follitropin alfa : 0-30%
- Biosimilar insulin : 1-8%
- Biosimilar rituximab : 2-29%

Clearly there are other factors besides physician confidence, which is uniformly high across the countries. These factors likely include differences between each country's payer policies, differences in the length of time a biosimilar has been on the market, the number of biosimilars in a given product class, the discount of each product relative to the originator product, and other factors.

In March 2020, ASBM had a whitepaper published in the Journal of the Generics and Biosimilars Initiative (GaBI Journal[3]) which identified six policy requirements that we consider "must have" to create a sustainable biosimilar market. Two of them include:

(1) **Procurement practices must provide for multiple suppliers.** Competition creates downward pressure on prices, and greater savings for the health system. We are beginning to see this happen here in the US when we get multiple biosimilars in a given product class.

(2) **Policies with a potential to undermine sustainability, such as measures which induce biosimilar uptake or promote preferential treatment, thereby limiting physician choice, should be avoided.** There should be an even playing field that fosters competition among both reference products and biosimilars.

Healthcare professionals here in the US, as in Europe, are not anti-biosimilar. It is inaccurate to suggest that negative perceptions are holding up biosimilar development and commercialization. We are enthusiastic about biosimilars and want to see more of them as much as anyone, and we are pleased at how far the US has come in a few short years. We urge the FDA and FTC to continue their work to build a strong and sustainable biosimilar market.

Thank you for the opportunity to comment.

[3] Policy recommendations for a sustainable biosimilars market: lessons from Europe; GaBI Journal, Volume 9 / Year 2020 / Issue 2

III. Comments from Andrew Spiegel, Executive Director of the Global Colon Cancer Association; ASBM Steering Committee Member

Good afternoon. My name is Andrew Spiegel, Executive Director of the Global Colon Cancer Association. Today I am proud to also represent the Alliance for Safe Biologic Medicines, an organization of which I am a founding member. ASBM is comprised of many patient and physician groups and since 2010 we have advocated for patient centered policies regarding biosimilars. To that end I have testified numerous times before the FDA in support of approving biosimilars, and before state legislatures nationwide in support of updating pharmacy practice acts to facilitate biosimilar substitution. I also recently participated in a series of three joint meetings with the FDA, Health Canada, and the World Health Organization with the goal of advancing a harmonized international standard for biologic nomenclature to improve global pharmacovigilance for all biologics and biosimilars.

It has also been my privilege to serve in leadership roles in international patient organizations including the International Association of Patients Organizations (IAPO) and the World Patients Alliance. These organizations allow the global community of patients to work together to increase our shared understanding of biosimilars, how to improve access to these treatments, and to share best practices about their use.

We know that biologic medicines have helped more than 800 million people worldwide. In the case of colorectal cancer, these medications have help triple the life expectancy of the most advanced CRC patients, and we expect biosimilars to bring tremendous benefits to U.S. patients- not only offering new treatment options, but doing so at a reduced cost, and hopefully expanding access to these therapies.

With respect to the U.S. market, first and foremost, speaking as the head of an international patient organization let me be clear that I am unaware of any attempt to undermine confidence in biosimilars- either in the minds of the public, the patient community, or among physicians. To the contrary, I am encouraged by the extremely positive reception biosimilars have had in the US thus far among patients, physicians, and other health care providers. They recognize what an important tool they can be in containing health costs. Just a few days ago, I chaired a panel at a biologics conference in San Diego which included one of the largest reference companies as well as one of the largest biosimilar manufacturers. Both agreed the US biosimilar market thus far is very much a success story and both agreed the future looks very positive.

This great enthusiasm and confidence surrounding biosimilars is due in no small part to the phenomenal work the FDA has done in approving so many biosimilars in a relatively short time, and doing so without compromising on its standards for safety and efficacy.

The U.S. health system, like that of any country, has its own unique challenges- different

from those of the EU, or Canada, or Australia. Nevertheless, there ARE things we can learn from other countries' successes- particularly those of European countries, who enjoy robust biosimilar markets.

One thing we've seen across Europe is that as more and more biosimilars are launched in a given product class, competition drives prices downward, discounts increase substantially, and biosimilar market share goes up. So we know what to expect, and what things to look for.

Thankfully we are seeing this happening in the US. Here we have a biosimilar filgrastim that launched with a relatively low 15% discount over its reference product. Today, with increased competition, that product has attained a majority share of the US market in its class with 55%. [4] Late last year we saw the first rituximab biosimilar launch at a 10% discount[5] over the reference product, and only a few months later the second launched at a larger, 24% discount[6].

We have every reason to believe this pattern will continue as we see it becoming routine for 3, 4, or 5 biosimilars approved for a reference product, and as these come on the market, manufacturers will continue to compete on price- moving from low discounts, to higher discounts.

Speaking as a representative of the broader patient community, we of course want more biosimilars approved and available. But our enthusiasm is tempered by the understanding that as with anything of this scale and where people's lives and health are at stake, it's not an instantaneous process. Simply put, the system is working- if a little slower than some have hoped. But just as we don't want biosimilars or any other medicine rushed through approval, we urge our regulators to be mindful not to unnecessarily (and possibly counterproductively) interfere with a young - but steadily growing - biosimilars market right as it's getting started. We'd rather get it right than fast.

Thank you for the opportunity to comment.

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[4] https://www.pacificresearch.org/wp-content/uploads/2019/07/BiosimilarsCompetition_F.pdf

[5] https://pharmaintelligence.informa.com/resources/product-content/teva-debuts-us-rituximab-at-a-10-discount

[6] https://generics.pharmaintelligence.informa.com/GB149550/Pfizers-US-Rituximab-Launched-At-A-24-Discount