

Alliance for Safe Biologic Medicines Docket Submission

The Honorable Edith Ramirez
Chairwoman, Federal Trade Commission
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Chairwoman Ramirez:

When it comes to biosimilars and the contentious issues of proprietary naming and state substitution laws, competitiveness and patient safety need not be mutually exclusive. They are, in fact, complimentary.

Product naming is an important element of patient safety. We firmly advocate that all biologics should receive distinct non-proprietary names to ensure products will be distinctly identified to facilitate accurate attribution of adverse events nationally as well as globally. The non-proprietary name of a reference product and each of its distinct biosimilar products, should have a common, shared root but have distinct and differentiating suffixes or prefixes as a means of facilitating clear adverse event identification and reporting with a preference towards suffixes.

Where FDA winds up on this issue -- nonproprietary names, nonproprietary names + identifier codes, unique names or somewhere in between – will significantly impact patients, providers, manufacturers, pharmacists, safety experts and others. We need to all side firmly with what's best for patients, in the United States as well as globally.

If you're for patient safety, you can't be against distinguishable naming. The WHO established the International Nonproprietary Names (INN) system in 1953 before biologics were even a figment of anyone's imagination. Through the INN system, innovators and generics that share the identical active ingredient also share the same generic name, also called the INN. It's worked pretty well for chemical compounds but, as has been acknowledged by WHO and regulatory bodies of every developed nation, biologics are not chemical compounds – they're infinitely more complicated and biosimilars are not the same as the biologic products they reference.

While the U.S. National Drug Code system will continue to serve a purpose for both small and large molecules, we can't count on it to be the be-all-end-all solution for safety monitoring for biologics. Not even close. Payers don't universally use NDC codes, they are rarely present in patient records and they are often inaccurately entered when they are. These codes are generally not available on the products patients take home so even if physicians started using them, patient reports of

product problems would still lack the information. Distinguishable names provide a necessary safeguard to maximize safety and credibility. It's really that simple.

When it comes to biosimilars, we need to be extremely thoughtful about how we set policy relating to these promising medicines and strike a balance that promotes health and safety, rather than forcing a binary response that is driven by profits instead of patients.

This is no trivial issue. It is a fact that no two biologic products produced by different manufacturers will be the same. A biosimilar can only resemble its reference product. Therefore, how biologics are named will directly impact clarity of information around which product a patient has been using. Greater clarity will obviously occur if biologics and biosimilars have distinguishable names, and that clarity will enable better safety monitoring, "adverse event" reporting and timeliness in managing adverse events if they occur, and can even help us better understand which products work better for certain patients.

If we go in the direction of non-unique names, and issues arise, we might not have the information we need to quickly understand which among similar products is causing the issue. That can unnecessarily affect trust across a class of drugs and biosimilars as a whole, and that could significantly affect uptake.

Biosimilars are already available in other parts of the world. This gives us a unique opportunity to learn from the experiences of those markets. In Europe, where biosimilars share the same non-proprietary names as the originator product, they have in place systems to direct physicians to prescribe biologics by brand name so that the product is specifically identified. In the US, a brand or trade name is not required, so prescribing by brand name doesn't solve the problem. Europe has also recently taken steps to improve their pharmacovigilance system, after recognizing that problems such as incorrect attribution or lack of identification made the existing reports problematic.

Thailand also uses nondistinguishable names and rapidly approved biosimilars to treat certain diseases, which has led to both a dramatic increase in the number of cases of life-threatening blood-related adverse events and near futility in efforts to track back to which products are causing the problems.

The Physician Perspective

Dr. Bert Petersen, a surgeon, is director of the Breast Surgery Clinic of St. Barnabas Hospital in New York City and an adjunct associate professor of surgery at New York University School of Medicine. Dr. Petersen is an advocate for the elimination of health disparities, particularly in terms of cancer and chronic diseases. Here are his thoughts on why the biologics naming issues matters for both him and his patients.

Q: What role do biologics play today in treating patients?

A: In my field, cancer – specifically breast cancer, we’ve seen great success in treatment for early and advanced stages with biologics. As we move toward more targeted therapies for chronic disease, they play an increasingly important role.

Q: Do you think there may be certain populations who are more at risk to an immunologic response from a biologic?

A: Yes. Any populations that may have a compromised immune system—specifically, many patients with chronic disease—can be impacted. These include at risk populations such as the elderly, immune deficient and chronic renal disease patients, etc. Additionally, at-risk populations tend to be patient populations that may lack quality insurance or access to healthcare. Furthermore, many of these chronic diseases disproportionately impact the poor. This makes access to biosimilars even more important for this population

Q: What value could biosimilars offer patients?

A: Two of the biggest reasons to look at biosimilars are cost and access. Can we offer the same effective treatment while controlling cost? My biggest concern is how we increase equal access to quality health care. We want to increase our reach in expanding healthcare, but it must be quality health care. Biosimilars offer a chance to meet the goals of affordable and quality treatment options.

Q: What is your view on the best approach FDA could take on biologics naming and how does distinguishable naming help keep our biologic supply safe?

A: Unlike any other field, medical decisions must be met with great scrutiny and thoughtfulness because any mistakes or missteps can be fatal. Patient safety should be the FDA’s overarching principal when it comes to approving biosimilars and any other drug.

In terms of distinguishable naming, I believe that biosimilars definitely should have different names, so you can determine if drugs are equal in their effectiveness. In my opinion, it’s unethical to treat patients with something pretending to be something else when it may or may not be. It’s also unsafe. I have a real problem with this as a practicing physician who treats patients with life threatening illnesses.

Q: Why is it important for patients and doctors to know what biologic is being, and has been put into, a patient’s body?

A: Much of how we practice is based on evidence-derived medicine. This is how we gather our evidence to know what is effective and what is not. Understanding which biologics patients have used will help us as we move toward the future to make any modifications that are found necessary.

Q: What impact would distinct naming have on trust in biosimilars?

A: I think if we could distinguish drugs, providers would have less hesitation in prescribing them. If providers are more educated and they have a clear pathway to

report adverse effects—they would be more motivated to trust and prescribe biosimilars and make the choice among those available to them.

Q: What role do biologics play in treating patients?

A: Biologics play an incredibly important role in treating patients, like me, who have multiple autoimmune conditions. My life really depends on biologic medications. And for so many thousands of other patients, our health, our productivity, and our ability to work and be with our families all are because we have access to biologic medications.

The Patient Perspective

There were no patient advocates asked to testify at the agency's February 4th hearing. Here is a brief Q&A from an actual life-long biologics user. Donna Cryer uses a mix of biologics and synthetic medicines for rheumatoid arthritis, inflammatory bowel disease, to preserve a transplanted liver she received nearly 20 years ago, and to deal with kidney issues that impair her body's ability to make red blood cells. Donna is a Harvard-trained health policy lawyer, a patient representative on an FDA advisory committee and the first patient to serve as Chairman of the American Liver Foundation. Here's Donna's perspective on why the right naming policy for biosimilars and all biologics matters for her and the millions of other biologics users like her.

Q: What value could biosimilars offer to patients like you?

A: Biosimilars often offer lower cost options, so that can provide more access to medications for more patients.

Q: Why is it important for patients and doctors to know which biologic is being and has been put into a patient's body?

A: It is essential that doctors and patients know exactly which medication, particularly with biologics, they are prescribing and using. Being able to manage a disease based on the reactions of your immune system is really tricky. You want to make sure that you are not suppressing the immune system so much that you are open to every infection, every cold, as well as more serious conditions like tuberculosis. Knowing exactly which biologic medication you're taking is absolutely vital because if there is a side effect, an adverse event, or just a change in your condition and your body's response, you want to be able to track it back to exactly the drug that you were prescribed, exactly the drug that you took.

Q: Since biologics are more complex than normal, chemical prescription medicines, how does that alter the conversation and relationship you have with your doctor?

A: The doctor/patient relationship is based on trust. In fact, the patient relationship within the entire healthcare system is based on trust, and a high degree of

confidence, that what we're being prescribed, what we rely on for our very lives, is safe and effective. We want to be able to know, and have confidence that our originator biologics and biosimilars medications are distinguishable, so that we can know what we're taking, how we're taking it, how it differs.

Q: From your view as a patient, what would be the best approach the FDA could take when creating a naming policy for biosimilars?

A: Well, the issue of biosimilars naming is really important, because unless FDA ensures that unique distinguishable names for biosimilars are given, patients and doctors really will be left without any recourse to track back and understand what medication might have caused their adverse event or their side effect. We want to be able to track back if there is an issue, a side effect, a serious adverse event, or just a change in our condition. We want to be able to know. We deserve the right to know what we have taken so that we can have recourse, if need be, about what has happened and what is happening to our bodies. As a patient, I'm not really sure why there is even an argument about having a distinguishable name for a biosimilar: it's such a simple solution to have a distinguishable name.

State Legislation, Competitiveness, & Patient Safety

On the state legislation front, more than a few speakers at the FTC hearing made the point that physician notification was anti-competitive because it somehow besmirches the reputation of generic drugs (and would do the same to biosimilars and interchangeables). Bruce Leicher (Senior Vice President & General Counsel for Momenta Pharmaceuticals) called physician notification a “tactic” to scare physicians. And Krystalyn Weaver (Director of Policy and State Relations, National Alliance of State Pharmacy Associations), pointed specifically at a Tennessee law that requires physician notification for pharmacy-based switching of epilepsy medications.

She cited data that showed that this requirement results in increased state spending for epilepsy medications (translation: increased physician insistence on innovator products). What she did not discuss was the fact that epilepsy drugs fall into the category of Narrow Therapeutic Index medications.

If there had been an FDA speaker, there might have been appropriate comments about the FDA's Pharmaceutical Science and Clinical Pharmacology Advisory Committee that debated and determined that the bioequivalence specifications should be tightened for, among other categories, generic versions of epilepsy medications – and that FDA officials presenting at that advisory committee signaled strong agency support for the move.

Mr. Leicher told FTC that the substitution principles are an effort to ask “states to join in a commercial marketing campaign to disparage interchangeable biologics.”

Notification requirements would “restrict substitution and provide notice to doctors to intervene and be concerned about FDA approved biologics,” he said. Leicher

accused supporters of the state legislation proposal of attempting to blur the distinction between biosimilars and interchangeable biologics. “The notification provisions are really designed to make the point that interchangeable biologics really aren’t interchangeable, they’re different,” he said.

What Leicher doesn’t seem to understand is that interchangeable biologics *are different* from their innovator progenitors – but bioequivalent enough to be therapeutically interchangeable (as per the FDA). That’s not a “scare tactic,” that’s just a fact.

Those who view physician notification and distinct naming as anti-competitive are addressing these issues through a single dimension.

Steven Miller (Senior Vice President & Chief Medical Officer, Express Scripts), said he had research showing that physicians don’t want information from pharmacists that tell which patients have filled a prescription – one of the key stumbling blocks to addressing the quagmire of adherence. (Miller was unable to cite the source of this data point.) Thus, according to Miller’s logic, physicians will not care to be notified about a pharmacy-level switch of an innovator biologic to a biosimilar (interchangeable or otherwise). In fact, we conducted a physician survey in the U.S. which was first presented at the FDA/DIA Biosimilars Conference in September 2012 that found that 86% of the more than 350 physicians who participated responded that they wanted to be notified BEFORE a patient is switched to a biologic other than the one prescribed.

It’s also important to mention that, in its 1979 report on generic drug substitution, the FTC concluded that, “increased communication (as well as lower prices) may explain why most pharmacists report that product selection laws have had a positive effect on their relations with patients”

(Or as Sumant Ramachandra, Senior Vice President & Chief Scientific Officer, Hospira, commented, “Communications fosters confidence.”)

The Generic Pharmaceutical Association (GPhA) has jumped into the biosimilars substitution debate, saying it prefers that doctors not be notified when a pharmacist substitutes a biosimilar for a name-brand biologic, and it is supporting legislative language that would implement that approach in states throughout the U.S. GPhA and other critics believe the physician notification provisions of the compromise will deter pharmacists from making substitutions.

Making sure that a patient gets the best treatment should never be viewed as “impeding access.” That’s a canard and shows the venality of a certain approach to biosimilars.

The GPhA supports Florida legislation. House and Senate lawmakers stripped physician notification from their bill. This doesn’t make sense — it ignores the most fundamental aspect of protecting the patient by cutting doctors out of the loop.

This change undermines patient safety. Biologics are incredibly complex — on average, they contain 1,000 times the number of atoms found in conventional chemical drugs. Doctors, especially those treating patients with multiple chronic or autoimmune conditions, need to know when their patients walk away from the pharmacy counter with a different medicine than the one they prescribed.

Rather than placing the burden of knowledge on physicians and pharmacists, this bill forces a patient (often a very ill patient) to demonstrate an advanced level of pharmaceutical sophistication. Is it plausible that patients are educated enough to know what a biosimilar is, let alone ask whether or not they are getting an originator biologic or a biosimilar? This is clearly not the case with small molecule generics – a much less complicated proposition. The fact that physicians have the ability to use "prescribe as directed" is good. But it is not enough.

A more practical Washington State bill offers a better, holistic and appropriate approach, specifically the language that reads:

If a biological product is dispensed, the pharmacist or the pharmacist's designee shall within a reasonable time but not to exceed ten days following the dispensing, record the name and manufacturer of the product dispensed in an interoperable health records system shared with the prescribing practitioner, to the extent such a system is available; or, in the case that an interoperable electronic health records system is not in place, communicate to the prescribing practitioner the name and the manufacturer of the biological product dispensed to the patient. No communication to the prescribing practitioner is required under this subsection where there is no interchangeable biological product for the prescribed biological product, or for a refill prescription that is not changed from the product originally dispensed.

This makes it much better legislation than the Florida version and a superior piece of "model legislation."

In conclusion, there are five key aspects of patient safety that the FTC must take into consideration as it drafts its report on biosimilars:

1. Track and trace of biologics is more challenging than with chemical drugs especially since adverse events may go unrecognized in patients for months.
2. Patient response must be traced to the correct manufacturer's product.
3. Multiple means of product identification avoid a single point of information failure.
4. Unique naming provides transparency and helps differentiate products for observing and reporting adverse events.
5. Accurate identification allows regulators to pool data early and identify issues that help physicians make informed, timely decisions for their patients.

When it comes to the need for proprietary naming and thoughtful state notification laws some see problems. At the ASBM we see opportunity. Working together, government, industry, patients, providers, payers, trade organizations and academics can devise thoughtful solutions that will enhance both competitiveness and patient safety.

In the words of Dr. Martin Luther King, Jr.,

“All progress is precarious, and the solution of one problem brings us face to face with another problem.”

It’s a universal reality: What’s in a name is a fundamental ability to tell things apart. Nothing more informs American competitiveness and informed consumer choice. No one more than the FTC should recognize that fact — and be its champion.

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