nature biotechnology

The INN crowd

Moves to give biosimilars nonproprietary names different from brand products are more than a wrangle about words—they could mean biosimilars arrive stillborn to the market.

In recent months, a tussle has emerged between industry trade groups representing brand manufacturers and those representing generics on how biosimilars should be named. Specifically, innovator companies are pressing for the World Health Organization (WHO) to give biosimilars International Nonproprietary Names (INNs) that are different from their brand counterparts. Changing INNs in such a manner goes against several decades of naming convention in the industry, and will likely compromise the ability of biosimilars to succeed in the marketplace.

The WHO established the INN system in 1953 to ensure the "clear identification, safe prescription and dispensing of medicines to patients, and for communication and exchange of information among health professionals and scientists worldwide." Every new drug is named according to a standardized procedure, which avoids conflict with existing names and attempts to provide an INN that informs as to the active ingredient of a drug. These INNs—otherwise known as 'generic' names—are not subject to proprietary trademark rights and are published in the public domain.

In addition to this INN, companies that commercialize a drug also choose their own trademarked 'brand' name to differentiate their products from competitors' products. Thus, Advil and Motrin are different brand names of the INN ibuprofen; Genotropin, Biotropin and Humatrope are different brands of somatropin.

At the end of October, WHO convened its 57th INN Consultation and discussed the potential revision of its naming system for biosimilars. Currently, WHO divides biosimilars into two different categories for the purposes of naming: those products that are nonglycosylated, and those that are glycosylated. Because the former have post-translational modifications highly similar to the brand counterpart's, they receive the same INN as the brand; in contrast, biosimilars that are glycosylated are distinguished from their originator products by qualifying their INN name with a Greek letter suffix. Thus, the INN for the Retacrit biosimilar version of the erythropoietin Eprex (epoetin alfa) is epoetin zeta.

At WHO's most recent meeting, discussion centered on a new scheme in which biosimilars would have two-part names, the first part including the INN of the originator biologic, the second part clarifying that the product is a biosimilar and providing a specific name. One approach discussed for such a qualifier would be to use a three-letter code or "fantasy suffix" to distinguish between biosimilars. This is a radical departure from the WHO's naming conventions for generic small molecules, where the INN designated is nearly always the same as the originator product.

So why does it matter whether a biosimilar's INN is different from its corresponding brand's? First, clinicians who prescribe drugs—and the patients who receive them—will assume the naming difference indicates the biosimilar has a different mechanism of action from the brand drug. In other words, it introduces uncertainty in the mind of the prescriber and provides a disincentive to use a cheaper biosimilar. Second, changing the INN due to small differences between an original biologic and that same biologic produced using a slightly different process runs counter to years of naming practice for brand products (a fact that seems to have been conveniently forgotten by innovator companies).

Every now and then, drugmakers of an original biologic make changes to the way they manufacture their product. Such changes can be as trivial as changing their supplier of culture materials or as fundamental as changing the cell line or manufacturing site. When this happens the product may change (a process termed 'drift' in the industry) and regulators require that manufacturers demonstrate that the new product shows physiochemical characteristics, biologic activity and clinical outcomes comparable to those of the original. Importantly, when regulators determine the new product produced by the different process is indeed comparable to the original, the brand manufacturer gets to use the same INN.

The logical inconsistency of arguing for a different INN for a biosimilar (which is deemed by regulators as comparable to an originator product) but keeping the same INN for a brand biologic produced by a different process (which is deemed by regulators as comparable to an originator product) seems to have escaped the Biotechnology Industry Organization (BIO). Responding to the controversy, BIO states that the US Congress should "ensure that follow-on biologics will be assigned a nonproprietary name readily distinguishable from that of the innovator's version." According to BIO, giving follow-on biologics the same INN as a brand "would be confusing and misleading to patients, physicians and pharmacists, could result in inadvertent substitution of the products, and would make it difficult to quickly trace and address adverse events…." It is unclear why BIO argues that the INN is important for tracking adverse events when another system—the National Drug Code—is already in use and works independently of the INN.

Fortunately for those who think that 'logical' is a good place for drug regulation to be, the US Food and Drug Administration is not (yet) persuaded of these minority apartheid industry arguments. FDA's 2006 Briefing on Biosimilars says that, INNs should not be used "to differentiate products with the same active ingredient(s)" unless there is credible scientific data either way.

BIO and its brand manufacturer members need to realize they cannot have their cake and eat it, too. If they are demanding modified INNs for biosimilars, then originator products produced using a new process should also be given modified INNs. If such a scenario were adopted, physicians would likely end up having to discombobulate reams of different INNs for brands and biosimilars alike. It is difficult to understand how such a situation would be helpful to prescribing physicians.

What it would mean is doubts sown in minds, impaired competition and ultimately limited patient access to medicines at competitive prices. In the end, the push for a different name really amounts to one thing: let's give biosimilars a bad name.