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Editor's introduction to the initial issue of the third volume of GaBI Journal

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As we begin the third volume of the *GaBI Journal* a growing number of follow-on biological products have been and will be approved (as discussed in the review of monoclonal products as a Commentary by Thorpe et al.) and discussions concerning biosimilars are becoming increasingly 'heated'. Unfortunately, this heat has often produced more smoke than light, as some of the articles in this issue demonstrate.

For example, it would appear logical to assume that the introduction of generics and biosimilars would make drug shortages less likely. However, as discussed in the first Editorial article on oncology drug shortages written by Dr Bea Perks, *GaBI Journal* editor, both the number and impact of drug shortages appear to be increasing instead. It is not yet clear how the increased availability of follow-on drug products has influenced these clinically important shortages or how or whether this problem can be resolved.

Drug nomenclature has not generally been considered a 'hot' topic yet the naming of biosimilars is discussed in a number of articles in this issue including Letters to the Editor, a Commentary, a Perspective, and a Guideline article. The naming of biosimilars has been and remains rather simple for easily characterized chemical generics for which the active ingredient can relatively easily be tested for identity to an original product and where simple, comparative bioavailability studies can exclude major differences in the pharmacokinetic behavior of products even if they contain different inactive ingredients and have different manufacturing processes, packaging, formulations, or dosage forms. However, both the issues involved and their potential impact on clinical performance are much greater for biological products for which the methods used to investigate bioequivalence are much less clear.

The International Nonproprietary Name (INN) of a product has always required the unequivocal identification of the substance named. Unfortunately, this is not possible to do for all or even most biological products. In addition, their clinical and toxicological profiles can be altered by minor changes in either their complex manufacturing processes, inactive components or characteristics such as pH, as well as packaging and storage conditions.

It has been proposed that the INN requirements be changed for biosimilars, but concerns have been expressed about the use of identical names for chemically different products. For example, effective post-marketing surveillance of biological products is required to assess the toxicity profiles of both originator and biosimilars. However, existing monitoring programmes are not always able to identify which products or batches were taken by which patients or how the products were shipped or stored prior to use. There are some potential advantages to changing the INN system to give the same, originator name to biosimilars but these must be weighed against the potential problems that would be created by this change.

This is an issue for originator companies as well as biosimilars. It could be argued that all biological products that are produced or packaged using even minimally different methods whether by originator or by biosimilars companies should also be given different INNs. Naming of biosimilars has major regulatory, clinical and economic implications, some of which can complicate the resolution of this issue. It is also important that patient perceptions are considered, as discussed in a Perspective article by a healthcare professional who is also one of the many patients who are affected by this issue.

The availability, approval, and pricing of biosimilars are all affected by the methods used to test and approve them. Testing methods and possible ways to improve them are discussed in two articles covering statistical approaches to this testing. The acceptance and potential impact of these suggested statistical methods depend on when, how, or if they are incorporated into regulatory guidelines.

Articles that discuss and compare current regulatory guidelines include a Meeting Report in this issue. The need to re-evaluate the regulatory guidelines used to evaluate non-biological complex drugs (NBCDs) was a major focus of this educational meeting organized and conducted by GaBI in Kuala Lumpur, Malaysia, in October 2013. As illustrated by the drug shortage and naming issues discussed above, the development, approval, marketing, use and monitoring of generic and follow-on biological products are already extremely complicated. The NBCDs including IV iron carbohydrate products, random amino acid polymers such as glatiramer, as well as liposomal and other nanoparticle products are making this even more complicated.

NBCDs are not simple chemical entities that can be managed using the generic drug paradigm. While they are not biological products their structures can be as or even more complicated than biological products. Also, their compositions as well as their clinical effects and toxicological properties are, like biologicals, altered in as yet unclear ways by even minor differences in production methods. The best practice, global approaches to the testing, approval, use, and post-approval monitoring of NBCDs are unclear. The regulators and clinicians who attended this meeting felt that in large part this was the result of a lack of understanding of NBCDs on the part of both clinicians and regulators.

In response to this perceived lack, the *GaBI Journal* will both publish a number of articles dealing with NBCDs and conduct additional educational conferences such as the one held in Kuala Lumpur designed to educate regulators and clinicians about NBCDs. We also encourage our readers to submit comments and manuscripts dealing with NBCDs.

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