# Fourth and final issue of GaBI Journal's sixth volume

*Professor Philip D Walson, MD*


Change is inevitable but often resisted, including or even especially in medicine. Hand washing is still neglected 170 years after Semmelweis' work, misuse of antibiotics persists 72 years after Fleming warned about it, and use of generics and biosimilars remains suboptimal. This final 2017 issue of the *GaBI Journal* deals with many of the barriers to one of these changes – the increased use of generic and biosimilar medicines.

The first Letter to the Editor by Azevedo et al. claims that the World Health Organization biosimilar naming system 'will help physicians and regulators to keep patients safe', and that 'Distinct naming ensures accurate tracking'. Unfortunately, there is little evidence to support these optimistic claims. In fact, physicians' lack of recognition and under-reporting of adverse events suggest otherwise. Actual data are needed on the effectiveness of this and all other attempts to improve pharmacovigilance, both for biosimilars as well as for new batches of originator products. The ability to track does not ensure that it will actually occur. Perhaps incentives, punishments, or both are needed to ensure that tracking actually occurs. Payments to manufacturers, prescribers and/or even patients could be linked to reporting, for example. It is also important that tracking includes data on product handling, storage and administration since these also affect product performance. Finally, there is no evidence reference for, or even a discussion of how these names will be used in countries 'without accurate pharmacovigilance'. Naming is likely to be useful but unlikely to be sufficient to 'keep patients safe'.

The second Letter to the Editor by Dr Karthik Bodhinathan concerns errata in a previously published non-biological complex drug (NBCD) paper. One such erratum concerns whether a non-originator NBCD should be called a 'generic.' Actually, 'generic' is in my view inappropriate to use for either a biological or an NBCD, and that 'follow-on' is a more accurate term to use.

Substitution and switching are important reasons for accurate product identification and pharmacovigilance. The Commentary by Dr Thijs J Giezen offers comments on the Original Research manuscript that follows it and calls for 'an exchange of (accurate) electronic information on product use'. In my view, this call should be expanded to include data on adverse events, storage and administration.

An Original Research manuscript by Larkin et al. presents interesting global survey data collected by Pfizer employees concerning the multitude of policies in 82 countries that control 'pharmacy mediated' substitution of biosimilars. While the validity of such survey data might be questioned, the fact is that manufacturers are incentivized to obtain accurate 'market research' data. Also, the authors provide an excellent summary of potential weaknesses of their study. It would be interesting to know if other biological manufacturers have collected any similar or conflicting data.

Interesting insight into the uptake of biosimilars is provided in a Review Article by Mr Michael Sarshad that chronicles events related to the US launch and marketing of the first Food and Drug Administration approved biosimilar – the filgrastim Zarxio. The author presents an in-depth discussion of Sandoz's marketing approach over time after introduction and the economic 'drivers' of acceptance of this biosimilar in the US market. This should be of great interest to manufacturers as well as payers, prescribers and patients even if this is not really the start of a 'biosimilar revolution' as promised by the title.

The moral and ethical aspects of suboptimal use of follow-on products are raised in a Perspective by Bashaar et al. in which issues that have prevented patients' access to needed medicines are explored, and a call is made for increased access to 'essential medicines'. The responsibility to provide access is shared between governments, international bodies, non-profits, charities, payers and patients. However, the effectiveness of the author's 18 proposed, non-prioritized actions including 'eliminate duties and taxes' is unclear. The authors present no data on either their actual or relative effectiveness. For many reasons, our current profit and patent-based pharmaceutical systems are failing to provide adequate access to 'essential medicines'. Moral and ethical appeals can be useful but may not be sufficient. More drastic 'disruptor' approaches may be necessary such as those being used in Cuba and Iran in response to economic sanctions – even if such sanctions were not supposed to interfere with sale of food or medical supplies. Perhaps if other low-resource governments acting alone or in collaboration produced their own lower cost generics, biologicals (including vaccines) and NBCDs, then more patients would have access to essential medicines.

In Guidelines, a biosimilar guidance paper from the Drug Commission of the German Medical Association summarizes a number of issues including quality, efficacy and safety, use of biosimilars to initiate treatment of naïve patients, switching patients from initial to other products, extrapolation of indications, pharmacovigilance, clinical and insurance considerations, and patient involvement. The authors, Professor Wolf-Dieter Ludwig and Dr Stanislava Dicheva, review some of the challenges to greater use (including 'unfounded fears and concerns') and propose approaches that they feel might increase uptake of biosimilars in Germany. One claim is that assisting physicians in becoming 'acquainted with biosimilars could effectively and consistently deliver the best health care for patients while retaining physicians' freedom to prescribe'. Unfortunately, the effectiveness of educational attempts to 'acquaint physicians' has not been well demonstrated. I wonder how long governments that provide universal

health care, as well as the patients who expect the care to be available and affordable, can wait for results before switching to more punitive or controlling approaches?

The first Special Report by Assistant Professor Gianluca Trifirò presents a summary of a session discussing how to build stakeholder confidence in biosimilar medicines presented at a recent European Commission stakeholder meeting. Professor Trifirò presented data collected from a survey questionnaire completed by 816 Italian physicians and which was coordinated by *Cittadinanzattiva*. The survey questionnaire was developed in a roundtable with representatives of several Italian scientific societies and patient and physicians organizations. Data included physicians' views on how regional/national drug policies affect their prescribing.

The second Special Report summarizes differences between USA and Europe approaches to interchangeability of biosimilar medicines. It should be noted that the US has not yet approved any product for such interchangeability and European Union (EU) decisions about this are left to individual EU Member States.

A Meeting Report by Gascón et al. summarizes the content of an international webcast that discussed pegfilgrastim and pegfilgrastim biosimilar treatment of chemotherapy-induced neutropenia. The webcast content, speakers and attendees were selected by Cinfa Biotech, the biosimilars company of the Cinfa Group. Figure 1 in this report for example is claimed to show no differences in absolute neutrophil count (ANC) responses to daily filgrastrim versus weekly pegfilgrastim in healthy volunteers. While the differences were not statistically different, this does not mean that they were not clinically meaningful. Readers should note that the log scale used could obscure differences. Figure 2 is more convincing since it compares the incidences of febrile neutropenia in actual patients. Clinical meaning, statistical differences, superiority versus non-inferiority, population studied, and potential causes of bias must all be considered when deciding whether, 'pegfilgrastim provides many medical advantages over filgrastim as a neutropenia treatment'.

A Research News presents a summary of a survey study of 66 Irish HIV patients concerning their views of generic HIV drug substitution. The authors concluded that 'generics substitution would be acceptable to the majority of HIV patients in Ireland'. These data and the very successful use of lower cost generics in many resource-poor countries suggest that factors other than patient resistance are responsible for the incomplete uptake of generic HIV drugs worldwide.

The first Abstracted Scientific Content summarizes recently reported studies of infliximab biosimilars. The NOR-SWITCH randomized clinical trial found no major efficacy or safety concerns in Crohn's or Colitis patients and the PLANETRA and PLANETAS studies found no major differences between infliximab and CT-P13 when patients with rheumatoid arthritis and ankylosing spondylitis, respectively were switched. Perhaps the authors are right when they predicted 'that we are only at the very beginning of the biosimilar era and that switching between an ever-growing number of biosimilar medicines will become more prevalent'. Hopefully studies such as these will be able to reverse the skepticism expressed by physicians and patients in previously published, often innovator supported, studies reporting physicians' and patients' concerns.

The second Abstracted Scientific Content abstracts the pre-print of a comparison of European and US generic drug markets based on 2013 data from 13 European countries with different generic drug policies that was recently accepted for publication in the *Milbank Quarterly*. The authors conclude their policy evaluation with a discussion of the obstacles preventing effective generic drug use policies. This part of the discussion will be abstracted in a future *GaBI Journal* edition.

As the end of the year approaches, one can only hope for progress towards a more peaceful world in which people everywhere will have more equitable access to 'essentials' including shelter, security, food, a healthy environment and medications.

I would like to take this opportunity to thank all of our staff, readers and supporters for helping GaBI strive to promote 'worldwide efficient use of high quality and safe medicines at an affordable price, thus advancing and supporting the idea of accessible, affordable and sustainable health care'.

Professor Philip D Walson, MD
Editor-in-Chief, GaBIJournal

DOI: 10.5639/gabij.2017.0604.030