



INTERNATIONAL GENERIC AND
BIOSIMILAR MEDICINES ASSOCIATION

15 September 2017

Biologics Science Section
Therapeutic Goods Administration
PO Box 100
Woden ACT 2606

Consultation: Nomenclature of Biological Medicines

Dear Sir/Madam,

The International Generic and Biosimilar Medicines Association (IGBA) is a non-profit association of international generic medicines associations, as well as their specific biosimilar medicines sector groups. Our vision is to promote the widest possible access to generic and biosimilar medicines with high quality, safety and efficacy, support international harmonized pathways for the registration of those medicines, and a strong commitment by members to standards, agreed by the International Council for Harmonization (ICH) and the World Health Organization (WHO). A number of the companies our Associations represent are developing or have already developed and have been marketing biosimilar products in several parts of the world, including Australia, for more than 10 years.

IGBA therefore welcomes the opportunity to review the consultation document on the naming of biological medicines in Australia. We believe that the Therapeutic Goods Administration's (TGA's) outreach to stakeholders on this important topic provides a meaningful dialogue to the benefit of this consultation. Furthermore, IGBA appreciates that the Australian Government is committed to implementing a biosimilar medicines uptake policy and to supporting a viable and competitive market for biological medicines in Australia. It also appreciates the **Biosimilar Awareness Initiative** that was announced in May 2015 with the aim to support awareness of, and confidence in, the use of biosimilar medicines for healthcare professionals and consumers.



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Generic and Biosimilar Medicines Association (GBMA/Australia) is an associate member of IGBA. Like in the rest of the world, we endorse the GBMA Members in their commitment to enhance pharmacovigilance activities and the need to collect accurate and complete information regarding a suspected adverse event. IGBA also supports GBMA's opinion that changing how biological medicines are named today in Australia will not enhance pharmacovigilance, but would:

- Increase regulatory burden;
- Act as a barrier to market entry;
- Undermine healthcare professional and consumer confidence in biosimilar medicines;
- Create confusion in prescribing and dispensing software; and
- Undermine the government's policy to increase the uptake of biosimilar medicines.

In this letter, IGBA provides comments on the options posed by TGA. In short, IGBA strongly supports **option 2** and would welcome a **move towards option 3**, provided the inclusion of a consultation period involving all stakeholders, and allowing sufficient time for a smooth transition.

IGBA does **not support option 4** because we believe educating all stakeholders about observing biologic, including biosimilar medicines, in the real world and encouraging them on the proper reporting of adverse events is a much better approach than applying different names or adding a meaningless, unique identifier. Denmark, with one of the highest number of biosimilar medicines' penetration in the world, can serve as an example in this respect. Denmark has indeed enhanced the framework for pharmacovigilance for all biologics, including biosimilar medicines, facilitating the reporting and involving all stakeholders. In order to increase traceability, in case of ADR reports, physicians shall make records of the brand name and the batch number in patient records and provide those data when reporting ARDs, whenever possible. The consumer ADR reporting forms also include a field for the batch number. Additionally important are, information and education on biosimilar medicines, developed together with patients, an open dialogue with all stakeholders, and regular publication of pharmacovigilance data are an integral part of the biosimilar medicines policy in Denmark.

Comments on Option 1

In principle, IGBA supports the status quo where the Approved Biological Name (ABN) is used to identify the active ingredient in both, the originator reference product and all subsequent biosimilars, and that identification is enabled through other existing unique characteristics including the product's Australian Registration (AUST R) number and proprietary trade name.

The European Union has demonstrated that identification of biologics, including biosimilar medicines, in case of adverse reaction reports, is possible with a shared INN. However, as outlined in the consultation paper on page 7, TGA's adverse event reporting system gives prominence to reporting of a medicine's non-proprietary name, **with or without the trade name or batch number**, although all three are encouraged to be reported for all medicines. Normal TGA practice is to follow up with the reporter to obtain any missing information so that the actual medicine, and batch number where relevant, can be specifically identified.

Therefore, maintaining the current system with no improvements to the adverse event reporting system, as described just above, would be an unsatisfactory outcome and **is not supported**.

Comments on Option 2

IGBA supports GBMA in their opinion in supporting the status quo provided it is combined with activities to increase the public reporting of adverse events. This will enhance what is already in place without increasing

regulatory burden or adversely impacting the government's policy to support the increased uptake of biosimilar medicines.

A unique product name with the combination of batch specific details would give the required specificity and meet the objective for improving the adverse event reporting system; and as such, would enable the tracking and tracing of any medicinal product, including biological medicines – originator products and biosimilar medicines. Therefore, as suggested in the paper, mechanisms should be put in place to enhance the reporting of product and batch specific information. For example, through mandating this information as a field in the on-line reporting form, including the product's trade name, AUST R and the batch number.

Based on their vast experience with biological medicines, including biosimilar medicines, the European Medicines Agency (EMA) has adopted a guideline to enhance pharmacovigilance for biological medicines.¹ To ensure traceability of biological medicines throughout the supply chain, product packaging includes the product name and batch information, which facilitates the inclusion of this information throughout the supply chain, from manufacturer to patient including at the time of prescribing, dispensing and patient administration.

EMA's actions have resulted in the implementation of a thoughtful and risk-based approach to biologic pharmacovigilance that emphasizes the successful international naming system. An analysis of adverse drug reaction reports in the EU revealed clear identification of more than 90% of the affected biopharmaceuticals.² In this context, and striving for a harmonisation of the packaging requirements globally, we would like to stress the fact that the AUST R number should not replace the need for the inclusion of the batch number. The use of the batch number is the most important part of any adverse event reporting system across all highly-regulated regions in the world.

Additionally, increasing education activities for healthcare professionals and for the public to report suspected adverse events properly for all medicines would be a very important and powerful tool to increase the adverse event reporting system.

There is indeed no rationale for treating the post-market surveillance of biological, including biosimilar medicines, any differently to other medicines. These awareness activities must not be specific to biological medicines and by no means specific only to biosimilar medicines.

Finally, referring to the potential concerns that may arise from switching from the reference medicine to the biosimilar medicine, which "have largely not been evident", it is important to note that concerns regarding the need to change the naming requirements have only been raised after the development and commercialization of biosimilar medicines. These concerns or requests for changes did not come up prior to that time. Tellingly, there are no concerns that we are aware of that pharmacovigilance is impaired for the many biological medicines that already share international non-proprietary names, nor are there calls that there is a need to revise the naming of such products.³

In this regard, Europe has the largest experience with biosimilar medicines; and therefore, the viewpoint of the European Regulators is very relevant here. A recent scientific publication entitled *Interchangeability of biosimilars: A European Perspective*⁴ states "Because of the high similarity, there is no reason to believe that the body's immune system would react differently to biosimilars compared with the original biological medicine upon a switch. This view is supported by the current experience with biosimilars on the market and by literature data. In our opinion, switching from the original to a biosimilar medicine and vice versa can be considered safe."

¹ EMA. Guideline on good pharmacovigilance practices (GVP): Product- or Population-Specific Considerations II: Biological medicinal products, August 4, 2016. Accessed on August 21, 2017 at:

http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2016/08/WC500211728.pdf

² NS Vermeer et al. *Drug Safety* (2013) 36:617–625

³ McCamish, Gallaher, Orloff. "Biosimilar by Name and Biosimilar by Nature", RPM Report, June 28, 2013. Accessed on August 21, 2017 at: <https://www.pharmamedtechbi.com/publications/rpm-report/9/7/biosimilar-by-name-and-biosimilar-by-nature>

⁴ Kurki P. et al. *Interchangeability of Biosimilars: A European Perspective*. *BioDrugs*. 2017 Apr;31(2):83-91



Comment on Option 3

IGBA also offers **support** to move towards a barcode system similar to the one used in the European Union (EU).

IGBA agrees with the benefits of introducing a barcode as a future packaging requirement for all medicines, not just biological medicines. A bar code on all medicines would support the Government's broader e-prescribing and dispensing initiatives, linking with the My Health record to improve pharmacovigilance and quality use of medicines.

On 9 February 2016, the European Commission (EC) introduced two safety features to be placed on the packaging of most human medicines: a unique identifier (UDI, a 2-dimension barcode) and an anti-tampering device (ATD) to be implemented no later than 9 February 2019.

In light of the increase of falsified medicines on the market, IGBA in general supports a track and trace system that guarantees medicine authenticity for the benefit of patients and businesses. IGBA believes this will strengthen the security of the medicine supply chain, from manufacturers to distributors to pharmacies and hospitals – throughout the supply chain. Thereby, guaranteeing medicine authenticity from manufacturer to patient.

Since the implementation of a UDI, a track-and-trace system, and an ATD are additional feature on the packaging of the medicinal product, IGBA suggests a system of targeted education and training of health care professionals to improve information flow, facilitate medicine recall, and medicine return procedures.

IGBA supports aligning with requirements in the EU, wherever possible, as this is consistent with the TGA's current practice of adopting EMA guidelines, with respect to biosimilar medicines' evaluation. As biosimilar medicines are generally developed for the global market, it may be possible for Australian packaging to mirror that of the EU, including the 2-dimensional bar code. However, serialization should be implemented without primary package serialization. This would enable a straightforward implementation and minimise the financial burden on companies to implement this scheme.

Since the medicine packaging requirements have only recently been updated in Australia, the regulatory burden and cost of introducing another requirement cannot be ignored. IGBA supports GBMA in their call for TGA to consult on a structured implementation plan, outlining the regulatory requirements (especially concerning the label) and timelines. A transition phase of at least 3 years should be allowed, especially for existing marketing authorizations.

Comments on Option 4

IGBA **strongly opposes** the option to introduce suffixes to the naming of biological medicines. A suffix is very unlikely to enhance pharmacovigilance but would cause confusion among stakeholders. Additionally, it would seriously undermine the biosimilarity scientific concept; as well as, the government's policy of increased biosimilar uptake.

Europe has largely demonstrated that proper identification can be ensured without a suffix. Ignoring this reality is unconceivable. Furthermore, Australia has adopted the EU biosimilar guidelines; and hence, the logical and scientific consequence is to be consistent and to stay aligned with the EU naming policy for biosimilars.

A biosimilar medicine is a biological medicine that is highly similar to the reference medicine, notwithstanding natural variability inherent to all biological medicines. It also has to be demonstrated that there are **no clinically meaningful differences** between the biosimilar and the reference medicine in terms of safety, quality and efficacy. After all, biosimilar medicines contain a version of the active substance of an already authorised original reference product, and the originator company has had many versions of the same active



substance on the market following manufacturing changes of the original version of the reference product during its life cycle.

IGBA also opposed the WHO Biological Qualifier proposal, because any identifier may act as an additional barrier to market entry to biosimilar medicines and thereby hamper patient access.

As changes to prescribing software are introduced to enable active ingredient prescribing, applying a suffix to a biosimilar would make the reference product and any subsequent biosimilar appear as different drugs. This has the potential to undermine the Government's policy objective to increase uptake, and it may act as a market entry barrier, particularly if not applied retrospectively.

We understand from our member GBMA that those in favour of introducing a suffix are concerned that currently unknown adverse events may, in theory, arise from switching between a reference biological and a biosimilar medicine. Such concerns must also apply as a result of variability between batches of the same biological medicine, especially since significant batch-to-batch variability has been documented after significant changes to the production methods.⁵ It would logically follow, therefore, that if a suffix is to be applied to a biosimilar, a unique suffix must also be applied to the reference product after every significant manufacturing change.

While the desire for TGA to harmonise nomenclature with international practices is understood, we note that such a suffix (-xxx) to the INN consisting of four random letters has been adopted in the United States (U.S.) and that this has only been applied to biosimilar medicines up to now (see U.S. Food and Drug Administration (FDA's) Purple Book).

There is no information available that confirms that the added suffix offers any benefit to the U.S. pharmacovigilance system, although it is known that it will be very expensive to implement the new U.S. biologics naming convention throughout the U.S. healthcare system.⁶ Therefore, we are of the opinion that the introduction of suffixes to the non-proprietary names of biologics is unnecessary and may even cause more problems than it resolves. For example, changing non-proprietary names will cause additional burden for companies, providers (hospitals, clinics, healthcare professionals, pharmacies, etc.), pharmacovigilance systems, databases, and compendia. The revision of the Australian naming convention will not necessarily create a safer system but it will increase uncertainty, create confusion, and entail a significant financial burden on many stakeholders well beyond product sponsors.

Finally, the adoption of an FDA naming approach would be inconsistent with the TGA's current practice of harmonising with the EMA and adopting EMA guidelines with respect to biosimilar evaluation. We welcome TGA's recognition that any changes to the current naming convention should be applied equally and concurrently to all biological medicines.

Conclusion

We appreciate the opportunity to provide comments on this important topic. As described above, we **strongly support option 2**. IGBA believes improving the current system with increased public adverse events reporting, with the mandatory inclusion of the product's trade name, and batch number - in line with the EU guideline on pharmacovigilance for biologics, is the most prudent approach.

Additionally, we also offer **support for a move towards options 3, provided** the inclusion of a separate consultation on the packaging requirements with the EU - involving all stakeholders, allowing sufficient time for the transition, and being applicable to all medicines, including biological medicines.

⁵ M Schiestl, T Stangler, C Torella et al. Nature Biotech 29: 310-312

⁶ Comment from the National Council for Prescription Drug Programs to OMB Control No. 0910 and Docket No. FDA-2013-D-1543, dated 7 February 2017.; Comment from Wolters Kluwer Health to OMB Control No. 0910 and Docket No. FDA-2013-D-1543, dated 9 February 2017.



We **strongly oppose option 4** which would cause a change of the existing and reliable international non-proprietary naming convention. We also strongly believe that adding another unique characteristic will be expensive and is unnecessary because of the reasons mentioned above. Additionally, a number of unique characteristics already exist that will enable the identification of a medicine for the purpose of good pharmacovigilance practises.

We thank you very much for taking these comments into consideration. Please do not hesitate to contact us in case you should require further information.

Yours sincerely,

Ingrid Schwarzenberger,

A handwritten signature in blue ink, which appears to read 'Ingrid Schwarzenberger', is positioned below the typed name.

Chair of the IGBA Biosimilars Committee