Submission
Consultation: Strengthening monitoring of medicines in Australia
May 2017
INTRODUCTION
The Generic and Biosimilar Medicines Association (GBMA) represents the manufacturers and suppliers of generic and biosimilar medicines in Australia. As a representative body, GBMA is making this submission on behalf of members and it is our intention to provide a balanced assessment of the reform proposals with specific comments on the commercial and operational implications for Australian sponsors.

GENERAL COMMENTS ON THE CONSULTATION
GBMA strongly supports the monitoring of medicines marketed in Australia and our members take their role in pharmacovigilance very seriously.

Overall, GBMA supports the need for a rigorous and efficient process for post-marketing monitoring of medicines. GBMA welcomes the opportunity to effect significant reforms to the current process.

The TGA takes a risk-based approach to the evaluation of all medicines. Post-approval, a process is in place for the ongoing monitoring of medicines that is broadly aligned with international practices and recognises the unique nature of the Australian market.

GBMA believes the current risk-based approach to the existing medicines vigilance tools are appropriate and takes the following position in response to this consultation:

- The Black Triangle would best be applied case-by-case;
- There is no rationale to apply a Black Triangle to biosimilar medicines;
- Reformatting the Product Information offers no obvious benefits to patients, prescribers or pharmacists, is unlikely to minimise the occurrence of adverse events and will impose a significant burden on industry;
- There is no evidence to support implementation of a PV inspection program which will impose an unacceptable burden on industry. As the pilot study conducted by the TGA indicated appropriate systems were in place in industry with no critical deficiencies, it is considered counter-productive to introduce a monitoring scheme for a system that should first be evaluated to determine its overall effectiveness;
- Enhancing medicines vigilance must not simply seek to increase the number of adverse event reports or increase the "white noise", but must provide useful data that can be linked and analysed to support our understanding of the medicine in the clinical setting;
- A study into the current program run by the TGA should be undertaken to determine the number of important adverse events reported compared to those of limited or no relevance, and the effectiveness of follow up actions taken by the TGA to improve patient safety; and
- An awareness and education program would strengthen monitoring of medicines in Australia.
ADVERSE EVENT REPORTING – BLACK TRIANGLE

GBMA understands the TGA proposes to introduce a Black Triangle Scheme to alert healthcare professionals and consumers to the fact a particular medicine is newly available, so they will be encouraged to report adverse events associated with that medicine.

GBMA takes the position that healthcare professionals and consumers should be encouraged to report adverse events associated with ALL medicines and a specific education and awareness initiative is required.

**GBMA opposes the proposal to introduce a Black Triangle for all new medicines.**

GBMA is concerned about the unintended consequences of a blanket approach to the application of the Black Triangle, such as:

- Being overused and becoming meaningless over time as it is simply viewed as an indication that a medicine is ‘new’;
- Confusion when a biosimilar has a Black Triangle and the reference medicine does not; and
- Causing heightened concern for consumers which may result in incorrect use of a medicine.

GBMA is also concerned that the effectiveness of the Black Triangle scheme has not yet been assessed in the European Union. It is understood that around 300 medicines are currently required to display the Black Triangle in the EU, but the scheme’s effectiveness in encouraging reporting of adverse events and enhancing pharmacovigilance is unknown. Prior to adopting this scheme in Australia, GBMA recommends an assessment of the EU experience is undertaken.

GBMA rejects the proposal to apply a Black Triangle on all new medicines. However, GBMA supports a mechanism to encourage enhanced medicines vigilance on a case-by-case basis where significant concerns may exist - such as a new class of medicine, medicine with specific safety concerns in a (sub-set) population, an orphan drug, or where a medicine is approved via a provisional pathway.

**GBMA opposes the application of a Black Triangle for biosimilar medicines.**
According to the TGA website:\(^1\)

A biosimilar medicine is a version of an already registered biological medicine (the reference medicine).

For a biosimilar to be registered in Australia, the reference medicine must be a biological medicine that has been registered in Australia based on full quality, safety and efficacy data (‘the Australian reference medicine’).

In addition, the Australian reference medicine must have been marketed in Australia for a substantial period and have a volume of marketed use so that there is likely to be a substantial body of acceptable data regarding the safety and efficacy for the approved indications.

Both the biosimilar and its reference medicine will have the following similar characteristics (demonstrated using comprehensive comparability studies):

- physicochemical
- biological
- immunological
- efficacy and safety.

Therefore, with no physicochemical, biological, immunological, or clinically significant differences, there is no basis for different monitoring requirements for a biosimilar compared to its reference product.

Considering the risk-based approach to medicines vigilance and the fact much is already known about the safety profile of the reference medicine, there is no rationale for applying a Black Triangle to biosimilar medicines.

**PRODUCT INFORMATION (PI) REFORMAT**

GBMA agrees in principle that prescribing information on the PI should be easily accessible. However, there is no evidence to suggest that the current PI format has not supported medicines vigilance or proper use of medicines.

While reformatting the PI may simplify prescribing and support quality use of medicines, it must be noted that most PIs are accessed electronically, and the consistent headings required in the PI enable the reader to quickly search for the desired information.

GBMA questions the statement in the consultation document that reformatting the PI with ‘minimise the occurrence of adverse events’ on the basis that there is no evidence to support this claim.

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\(^1\) https://www.tga.gov.au/publication/evaluation-biosimilars
GBMA believes there is no obvious benefit to patients, prescribers or pharmacists from reformatting the PI.

The consultation document provides very little information upon which to comment, and it does not outline the nature of the proposed format change. However, GBMA understands the intent is to move certain sections of the PI from the back to the front. This might include sections such as indications, dosage and administration, precautions and adverse effects.

It is expected the PI reformat will be administrative in nature, but the investment of sponsor time and resources into this exercise must not be underestimated. GBMA members report that reformatting a PI is not a simple ‘cut and paste’ exercise, but will require multiple steps including (and not limited to):

- version control and cross checking;
- internal local approval, possibly requiring international head office approval;
- completion of a TGA application for a post approval variation;
- validation of sequencing in eCTD or NeeS administration;
- printing of physical PI for pack inclusion for injectable medicines; and
- uploading onto Guildlink or other PI provision website.

This does not consider the TGA resources required to check, approve and upload the reformatted PI. Nor does take into account any communication between TGA and the sponsor if an error or omission is identified.

With thousands of medicines listed on the ARTG, GBMA members are concerned about the regulatory impost reformatting the PI will place on industry.

GBMA members estimate that reformatting one PI can take between two and eight hours of sponsor time, depending upon the complexity of the medicine. Extrapolating that out across a portfolio of generic medicines shows that a sponsor of 350 medicines would be required to invest at least 700 hours, and up to 2800 hours, on reformatting their PIs. This significant investment of time can only be supported if where there is a demonstrable patient benefit.

It is therefore vital that:

- the TGA provide evidence to demonstrate how the proposed changes benefit patient safety;
- the requirements for the new format are clearly communicated;
- fees for making PI changes are waived; and
- an appropriate implementation timeframe is provided.
Sponsors of generic medicines are required to update their PIs in line with any changes made to the innovator PI and at this point it is unclear if a generic medicine PI may be reformatted ahead of the innovator PI. GBMA has advocated over many years for a notification scheme of PI changes as this would significantly reduce disparity between PIs and reduce regulatory burden.

**GBMA proposes that introducing a PI change notification scheme would support sponsors to comply with the reformatting of PIs as it would enable several PI updates to occur simultaneously.**

**PHARMACOVIGILANCE (PV) INSPECTION PROGRAM**

GBMA members take their role in pharmacovigilance very seriously, noting that a condition of registration is that sponsors must collect and report on relevant adverse events. It is incumbent upon the sponsor to have robust processes in place for collecting, analysing and reporting on issues related to their products.

This is an effective requirement that sees vital PV data provided directly from the sponsor to the TGA.

GBMA understands the TGA undertook a pilot PV Inspection Program in 2016 across a wide range of sponsors, and involving an array of therapeutic goods. The purpose of this pilot was to verify Australian sponsors are complying with the existing PV requirements.

**As no critical deficiencies were identified as a result of the pilot, GBMA opposes the proposal to implement a system of inspection audits.**

For an evidence-based organisation to implement an inspection program where there is no evidence of a problem represents unnecessary compliance monitoring and an unacceptable burden on industry.

GBMA members are highly concerned that valuable TGA resources and personnel would be diverted to the inspection program, when effective use of data from the current program is yet to be evaluated. It is expected the program costs would be funded through sponsor fees and charges, and that there would be additional indirect costs and loss of productivity that would be imposed on sponsors during an audit.

**As the pilot program identified areas for improvement, GBMA believes education for the sponsor and TGA staff would enhance medicines vigilance and would result in a better use of TGA resources.**
It is unclear how efficiently and effectively the TGA currently utilises PV data to benefit patient safety. It is proposed that a first step in making improvements to the TGA PV system is to undertake an external and comprehensive evaluation of the current program. While the TGA seeks to enhance medicines vigilance through increasing the reporting of adverse events, a clear protocol for identifying significant events is required to ensure they are not lost in a sea of information, and to enable TGA to ensure appropriate action is taken to support patient safety.

ADVERSE EVENTS MANAGEMENT SYSTEM (ADRS)

GBMA is highly supportive of the implementation of a new IT system that will improve and streamline the way sponsors, health professionals, state and territory health departments and consumers submit adverse event reports.

Currently, the reporting of an adverse event requires certain contact details from the reporter. However, the reporter is only required to disclose the name of the suspected medicine.

GBMA believes that mandating several identifying characteristics of the suspected medicine would greatly enhance the monitoring of medicines, specifically the medicine's:

- Active ingredient/s;
- Brand name;
- Batch number; and
- Expiry date.

FURTHER CONSIDERATIONS

GBMA believes awareness and education is vital to enhance the monitoring of medicines in Australia.

Importantly, this awareness should focus on the importance of reporting adverse events to capture those of relevance to patient safety and minimising those that add nothing or even detract from the value of the overall system, and must be coupled with healthcare professional and consumer education on how and what to report.

GBMA supports the proposed improvements to analytics which will allow linking of existing datasets held by the Department of Health with those of the TGA. Simply increasing the reporting of adverse events, or adding to the “white noise” is not useful unless that information can provide meaningful insights.

GBMA also supports international information sharing to gather additional post-marketing data on medicines used in Australia.