Therapeutic Goods Administration
PO Box 100
WODEN ACT 2606

21st March 2019

Dear Sir/Madam,

Re: Consultation Paper – Reforms to the generic medicine market authorisation process

Solve Consulting would like to thank the TGA for the opportunity to comment on the proposed reforms to the generic medicines market authorisation process. Solve Consulting are actively involved in supporting the preparation of generic product applications, both in Australia and in other markets such as the US and EU, and provide input based on their experience of these processes.

Solve believes that the proposed generic reforms present a great opportunity to improve the generic medicines registration process and help assure patient access to more cost-effective treatments. The TGA document offers some good proposals on how this may be achieved but we believe there are a number of additional activities that could be included in the generic reforms consultation in order to achieve a more efficient and harmonised process and these are presented in detail at the end of our attached response.

Some key considerations that must be taken into account during the generic reforms consultation are;

(i) There are very few truly global generic pharmaceutical companies. Hence it would be an uncommon practice that applications for generic drug registration will take place at the same time in multiple markets by the same company.

(ii) Generic pharmaceutical companies predominantly source products through licensing activities. As a result, their product portfolios are sourced from numerous companies, located in multiple countries using multiple manufacturing sites. There is also a great deal of crossover in the manufacturing sites utilised by generic companies, often for the same product.

(iii) In order to maintain supply in such a competitive environment, there is a need for generic manufacturers to include additional or replacement finished product and API manufacturers to their product registrations. The amount of effort and time taken to register these additional sites should not be overlooked during reform consultation.

(iv) Generic pharmaceutical companies generally operate at far lower operating margins than our counterparts in the innovative pharmaceutical space. Therefore, the cost of maintaining product registrations in Australia must be taken into account to maintain a reliable supply of generic pharmaceuticals.

Please find our feedback on each of the questions posed in the consultation paper on the following pages. Should you require clarification of any of the points raised or wish to discuss anything, please feel free to contact me on [redacted]

Yours Sincerely

[redacted]

[redacted]

Feedback to Questions:

1. ***Would changes to our requirements for demonstrating that Australian and overseas reference products are identical reduce barriers for applicants seeking to register new generic medicines?***

The requirement to demonstrate that Australian and overseas references products are identical is a significant barrier to entry for new generic medicines.

According to the guidance it should in theory be possible to demonstrate that the Australian reference product is identical to an overseas reference product based on the available documentation. However, our experience is that this is very rarely achievable due to the lack of information available in the public domain.

At a minimum, physical and chemical comparative testing therefore needs to be undertaken to confirm 'essential similarity' which is often costly and difficult to conduct. The time required to conduct this testing means that there is almost always a time lag between the product being submitted in Australia, subsequent to other markets.

TGA's proposal to align with the approach of comparable overseas regulators bioequivalence requirements is welcomed and Solve would suggest that as a first step the TGA Guidance 15.6 *Choice of reference product for bioequivalence of generic medicines* be revised. This document lists many attributes that have to be addressed to justify that an overseas product is identical to the reference product. The requirements of this guidance could be simplified for supple generic formulations such as immediate release solid dose product and some injectable products.

US FDA have recently introduced product specific guidance's for generic products with complex formulations, where the approach for demonstration of bioequivalence is less clear. A similar approach would be beneficial for the registration of more complex products in Australia. Upfront publication of the requirements for these products would result in the need for less consultation with the agency, would speed up the time to submission and would potentially result in fewer product rejections due to a lack of suitable data.

TGA should also consider ways in which bioequivalence studies from other markets can be used to support registration in Australia. Often generic manufacturers have already conducted successful bioequivalence studies for the European or US markets. The cost of conducting an additional bioequivalence study for Australia is often not justified by the local market value and as a consequence many products are not put forward for registration. In seeking to accept the results of studies from other markets, TGA could potentially broaden the range of generic products to be registered in Australia, thereby increasing competitiveness and helping to secure supply.

Solve would also like TGA to provide guidance on situations where the Australian innovator product is no longer on the market or is difficult to obtain. US FDA have a process whereby an alternate product is designated as the reference for the purposes of generic comparison and this works well in these instances.

2. ***Are there any potential unintended consequences of changing the data requirements when using an overseas reference product in a bioequivalence study submitted to the TGA?***

Solve are not aware of any unintended consequences of changing the data requirements when using an overseas reference product in a bioequivalence study.

3. ***Are there any other ways that we could reduce barriers through increased international alignment in the processes for obtaining market authorisation for generic medicines?***

Solve believes that significant opportunities still exist for increased international alignment.

Whilst the comparable overseas regulatory authority (COR) pathway was introduced in 2018, it is as yet unclear whether this offers any significant benefit to sponsors. It would appear that applications are still undergoing an almost full review by TGA. There is currently no reduction in approval time or data requirements for sponsors who utilise this pathway.

Solve would suggest that this pathway could be significantly improved to allow simple generic products with approvals from other CORs to receive an expedited review which follows a risk based approach. Solve believe that with the permission of the sponsor, TGA should be able to access assessment reports from other markets. This would allow the TGA to focus in on aspects of the application which are most critical.

Solve also believes that there is the potential to streamline and reduce the number of Therapeutic Goods Orders that impact quality aspects of the products, such as TGO 78. These TGOs place an additional unnecessary burden on the manufacturer and applicants when there are pharmacopoeial monographs (specific and general) already recognised and referred to in the Therapeutic Goods Act, Regulations and Orders that provide guidance on the acceptable quality and testing of the dosage forms. These Australia specific requirements create additional burden for manufacturers and mean that modifications are required to existing product dossiers before they can be submitted in Australia.

The TGA's GMP Clearance process is another aspect of the product submission and approval process which has significant scope for streamlining and international alignment. The current process is one of the most onerous around the world and requires significant coordination by sponsors who have extensive global sourcing networks. Solve encourage increased collaboration between agencies to reduce the burden in this area.

4. ***Would early advice from the TGA on biowaiver justifications be useful in compiling a dossier?***

Solve believes that early advice from the TGA on the acceptability of biowaiver justifications would be extremely useful, particularly whether a bioequivalence study based on a foreign reference product would be acceptable. This advice should be in writing and be binding.

As mentioned in a previous response, US FDA have introduced product specific guidances for generic products with more complex formulations and this have been extremely helpful in clarifying the requirements for manufacturers. These guidances also include instances where in vitro bioequivalence studies are not required.

Transparency from TGA on instances where bioequivalence studies are not required could potentially result in an increased number of product applications in Australia where the need for a study may have been cost prohibitive.

5. ***In what other ways can we increase transparency and clarity of regulatory requirements for generic medicine applications?***

Solve believes that there are a number of ways in which TGA could improve transparency and clarity of the regulatory requirements for generic medicine applications. These are summarised below:

- Restructuring and simplification of the TGA website. The current TGA website is not easy to navigate and it is not easy to find all of the information relevant to generic medicines as it is not all consolidated in one place.
- Ensuring consistency in review practices and avoiding the escalation of issues which are an individual reviewers' preference. It is clear that there are points raised during S31 deficiencies which relate to a style or way of presenting data which don't seem to be applied consistently. Improved consistency across evaluators would help sponsors to understand more clearly what are truly mandatory requirements.
- Improved processes for seeking clarification on data requirements. The current email system is inefficient and can lead to delays for sponsors.

6. ***Will adopting these international templates improve opportunities for joint submissions to multiple agencies and hence work sharing?***

Solve believes that the use of the use of international templates may improve opportunities for joint submissions and provide clarity around the information required. However, this approach will only work if country specific requirements can be minimised or eliminated.

7. ***Are there other ways of improving the generic medicines market authorisation process to support work sharing?***

As mentioned above, work sharing will only be successful if country specific requirements can be minimised or eliminated.

8. ***Is it appropriate to offer incentives to medicine sponsors to bring more generic medicines to Australia?***

Solve believes that there are two instances where additional incentives could be used to help increase the number generic products to Australia. These are:

i. For products where data exclusivity and patents have expired and there is no generic product on the market.

ii. For products which are sole supply, or which have been subjected to shortages.

In offering additional incentives to sponsors for products which meet these criteria TGA could help to assure product supply and improve competitiveness. This could potentially work in a similar way to the *US FDA's Competitive Generic Therapies* program which was introduced in 2018. This program offers 180-day exclusivity to products and has been well received by manufacturers. This program has also encouraged sponsors to look at the development of more niche products where there is less competition.

9. ***Should we offer incentives to medicine sponsors to address medicine shortages and medicine expenditure?***

Solve believes that the best way for TGA to incentivise sponsors to address medicine shortages is through the pathway described in response to Question 8 above.

More broadly, the best way for TGA to assist in containing the costs of medicines is by making the product submission and approval process as efficient as possible. Given that the margins in generic products are much lower than those of innovative medicines, any delay to the product approval process has the potential to impact the viability of any product. This can at times result in a product being approved and never launched which is a situation that is not beneficial to TGA or the sponsor.

10. ***Are there any other examples where a more robust supply of generic medicines may be beneficial to patients and the Australian health system?***

The manufacturer and supply of generic medicines is a complex business which relies on the efficiency of a large number of suppliers. Despite extensive planning, interruptions in supply are sometimes unavoidable due to equipment failures, material shortages and other unforeseen issues.

The S19a process in Australia allows sponsors to bring alternative sources of product into the country on a short term basis and this is very beneficial for helping to avoid supply issues especially for sole supply products.

Solve believes that there could be the potential for TGA to look at developing an expedited pathway for products which have been supplied under Section 19a on a more long term basis where the original Australian product can no longer be sourced. This would help to avoid interruptions to supply and presents a low risk to TGA.

TGA could also look at expedited post approval pathways to support the introduction of new manufacturer or active substances in the event of supply issues.

11. ***What incentives should we pursue in order to create a more robust supply of medicines?***

Solve believes that adoption of the ideas presented in the previous sections of this document would assist in creating a more robust supply of medicines.

12. ***Are there any other options for improvements to generic medicines market authorisation process that would:***

- **reduce regulatory barriers through greater international alignment with comparable overseas regulators**
- **increase clarity and transparency of regulatory requirements**
- **support international work sharing for generic medicines**
- **support a more robust supply of medicines?**

In addition to the ideas presented previously, Solve believes that there is scope to improve collaboration between TGA and industry to support continuous improvement of the submission and approval process. Increased transparency on the measures adopted to address the issues raised by industry would help to address many of the day to day issues experienced by sponsors.

Some more specific procedurals issues would improve efficiency are as follows:

- Consideration that additional strengths of registered products with no change to dosage requirements on the PI should be considered as Category 3 applications, instead of Category 1 applications.
- TGA should consider the acceptance of additional stability data during S31 questions. This is managed effectively by other agencies who also have a timetabled review process such as that followed by TGA. US FDA allow the submission of stability data to support the shelf life. This would facilitate earlier generic submissions into Australia.