CONSULTATION SUBMISSION COVER SHEET

This form accompanies a submission on:

TGA Medicine Labelling and Packaging Review Consultation Paper	
Name and designation:	David Tsui (Director, Regulatory Affairs)
Company/organisation name and address:	Shire Australia Pty Ltd, Level 6, 123 Epping Road, North Ryde, NSW, Australia 2113
Contact phone number:	
☐ Yes ☒ No	I would like the comments I have provided to be kept confidential: *(Please give reasons and identify specific sections of response if applicable)*
☐ Yes ☒ No	I would like my name to be removed from all documents prior to publication and not be included within the list of submissions on the TGA website.

It would help in the analysis of stakeholder comments if you provide the information requested below.

I am, or I represent, a: (*tick all that apply*)

Business in the therapeutics industry (please tick sector):

☒ Prescription Medicines ☐ OTC Medicines

☐ Complementary Medicines ☐ Medical Devices

☐ Blood/Tissues ☐ Other

☐ Sole trader ☐ Business with employee(s)

☐ Importer ☐ Manufacturer ☐ Supplier ☐ Industry organisation

☐ Government ☐ Researcher ☐ Professional body

☐ Consumer Organisation ☐ Institution *(eg. University, hospital)*

☐ Reg. Affairs Consultant ☐ Laboratory Professional

☐ Healthcare Practitioner - please indicate type of practice

☐ Other (please specify):

If you would like to be kept informed on TGA reform consultation activities, please subscribe to the TGA-UPDATE email list via
http://www.tga.gov.au/newsroom/subscribe-tga-consultations.htm

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23 August 2012

Therapeutic Goods Administration
Labeling and Packaging Review
PO Box 100
Woden, ACT 2606

Re: Shire Comments on the Therapeutic Goods Administration's (TGA) Medicine Labelling and Packaging Review Consultation Paper – Version 1.0, May 2012

Shire very much welcomes the opportunity to comment on the Therapeutic Goods Administration's (TGA) Medicine Labelling and Packaging Review Consultation Paper – Version 1.0, May 2012, and acknowledges the importance of the TGA's role in promoting and protecting the public health.

Shire is organized into three divisions each represented by Shire Australia Pty Ltd. Shire Human Genetic Therapies (HGT) is solely focused on researching, developing and marketing novel products and services that profoundly enhance the quality of life of patients suffering from rare diseases. Through its Specialty Pharmaceuticals division, Shire focuses on small-molecule medications within the therapeutic areas of Behavioral Health, where it maintains a leadership position, and gastrointestinal disease, among others. Shire Regenerative Medicine is a leader in providing regenerative medicine solutions for people with life-altering conditions. We aspire to harness the power of regenerative medicine to address society's unmet medical needs, and are focused on developing and delivering solutions that support the body's natural healing process.

With major operations in the US, UK and Switzerland, and a network of offices and distribution channels throughout Europe, South America, Canada, and the Pacific Rim, Shire employs over 5,000 people who continue to carry forward many of the original attributes of its founders—opportunistic thinking, transparent behavior, a deep commitment to doing what is right, and a prevailing concern for the patients and caregivers served by its well-differentiated product lines.

We are strongly supportive of TGA 's objective to develop appropriate regulatory solutions that effectively address the consumer safety and risks contained within "Medicine Labelling and Packaging Review Consultation Paper", and we offer the following general and section-specific comments listed below for your consideration.

General Comments:
Key points for prescription medicines:

- Recommended space dimensions are smaller than the standard dispensing label size in Australia according to the info in this consultation paper.
- Will TGA have a process to allow a company to submit names for assessment suitability prior to full regulatory submission of the MA?
- Requirement to have generic name in same font size as the brand name – (might present a challenge for multi active ingredient products).
- Proposals for products with multiple active ingredients are very burdensome and likely to take up a lot of space, impacting overall readability.
- The consultation paper should be sufficiently flexible to allow for alternative format leaflets such as Fixaform leaflets.

Section-specific Comments:

TGA's Medicine Labelling and Packaging Review Consultation Paper Version 1.0, May 2012	
TGA Proposed Regulatory Changes	**Shire Comments to TGA's Proposed Regulatory Changes**
Prominence of Active Ingredients on Medicine Labels	
Page 17, Figure 3 Illustration of the recommendations for active ingredient prominence and the warning statement for products containing paracetamol.	• Separation of the strength from the active ingredient might be unhelpful for combination products. • Guidance indicates that the standard dispensing label is 80mm x 40mm. Figure 3 displays size of 70mm x 30mm.
Page 18, Figure 4 Illustration for the recommendation for active ingredient prominence when there are multiple active ingredients.	• This example does not meet the requirements for font size in 1.2.2; please consider revising the words in 1.2.2 (the example is about 50% font size). • The ingredient text takes up lots of space on the front of this pack so that it detracts from what the medicine is used for - which is the key information for a consumer for products that can be bought without prescription. The UK PAGB Packaging Code provides some good insight on packaging for products that can be bought without prescription:

	http://www.pagbpackagingcode.com/guideline.cfm?gid=11
Page 18 – 1.2 On the front/main panel of the label, the active ingredient must have equal prominence with the brand name	There is no reference to any research findings to support the proposal that 'equal prominence' is necessarily better than proportional prominence; e.g.: half or 2/3 of the font size of the brand name. The lack of evidential basis for this proposal is of significant concern. Additionally, this proposal has not taken into account the following: • *Modified dosage forms* – these formulations confer a different pharmacokinetic profile to the active ingredient. The undue prominence given to the active ingredient could work against the objective of minimizing medication errors • *Biosimilars* – unlike small molecule generic medicines, the active ingredients are not identical in the conventional sense as different cell lines and manufacturing process can give rise to differences in glycosylation pattern and higher order structures. From a pharamacovigilance perspective, it would be important to distinguish these products by brand name rather than by the active ingredient name so adverse events can be correctly attributed to the right molecule.
Page 18 - 1.2.1 The intention of 'equal prominence' is for the active ingredient to be as easy to locate and identify on the label as the brand name.	• Active ingredients should be of sufficient prominence, so that they can be easily identified by the patient - however, making them the same size as the brand name will make packs very crowded.
Page 18 - 1.2.2 The font size of the active ingredient must be at least 100% of the font size of the medicine brand name on the main/front label.	• Inconsistent with the example presented as Figure 4 (illustration for the recommendation for active ingredient prominence when there are multiple active ingredients). The active ingredients are presented in font size approximately half that of the brand name "TG Pharmacist Day and Night". More important, it is not apparent from this example why the active ingredients have to be of the same font size as the brand name since all ingredients are adequately legible.

Page 18 - 1.3 Where there are more than 3 active ingredients, the most abundant ingredients must appear on the main label immediately below the brand name and the names, together with the quantities of every active ingredient, are to be included on a side panel/label or on a rear panel/label for the product. (This does not apply to day and night preparations.)	• Might cause confusion if the patient does not realize that the list of the active ingredients on the front is incomplete - better to have all or none on front and always list all actives together. • Font size of active ingredients may be adjusted to less then 100 % of the size of the brand name.
Page 19 - 1.4 For products containing day and night preparations that have different formulations, the composition of each tablet must be provided immediately below the brand name and the font size must be no less than 2mm in height on the main/front panel.	• Is "day and night" too specific? Should other multi content pack also be covered?
Page 19 - 1.5 The active ingredient must be included with, and of equal prominence as, the brand name on at least 3 non-opposing faces of a carton.	• It should only be necessary to have the active ingredients appearing with equal or due prominence on one (preferably the front) panel, due to the amount of space that will be taken up if this is done on multiple panels.
General Questions on the Proposed Regulatory Changes for the Prominence of the Active Ingredients on Medicine Labels (Page 19)	
What do you think will be the impact of increasing the prominence and standardizing the location of the active ingredient on the medicine label?	• Without results from research findings to backup this proposal, the outcome of this requirement on prescription medicines is unknown and one cannot be confident of its effectiveness in addressing consumer safety risks as applied to prescription medicines. • Moreover, no data are presented on the extent of medication errors due to manufacturers' current

	packaging and labelling practices and therefore there is no way to be able to quantify the effectiveness of any implemented changes which will add significant cost to the industry. • Although one of the objectives is to help patients recognise the same active ingredient in different generic medicines, it should be remembered that the active ingredient name itself can lead to confusion due to being long (and difficult to pronounce) and there is often a similarity in spelling of unrelated medicines (eg approx 20 prescription medicine active ingredients begin with "meth"). Furthermore, patients may incorrectly think the salt moiety (eg hydrochloride) is the "active" part and may be confused if a number of their medicines contain the same salt.
What do you think about the proposal warnings for paracetamol and ibuprofen containing products	• We are not providing comments on these specific active ingredients as they are not contained in any of the prescription products we have registered with the TGA.
If the active ingredient name is clear, directly below the brand name and in a large font, what are the additional benefits that you see by making it the same size as the brand name?	• Instead of gathering views and opinions, we believe this question should be answered by appropriately designed research with attention paid to whether the product is stored at the front of shop and sold as a self-selected OTC medicine or stored behind the counter and dispensed by a pharmacist according to a doctor's prescription.
What is the smallest size font that you consider readable?	• 6 Point.
Look- Alike and Sound-Alike Medicine Brand Names and Look-Alike Packaging Branding	
Page 22, Figure 5 An example of look-alike medicine branding.	• The example presented does not illustrate increased risk for the patient if they select the "wrong indication" - it's all ibuprofen 200mg.
General Questions on the Proposed Regulatory Changes for Look-Alike Sound-Alike Names and Look-Alike Packaging Medicine (Page 23)	

Do you think the proposed changes to address LASA names and LA packaging will improve medicine safety? Why/why not?	• The construction of a brand name is not just a random combination of alphabets but subject to the constraint of it being easily pronounceable and not overly long for ready recall by HCP and patients alike**.** With the ever expanding new medicinal products entering the market, it will be increasingly difficult for sponsors to develop a new brand name that is highly distinguishable from all other existing products on the market both in pronunciation and in appearance. This evolving situation will challenge the practicality and enduring nature of the proposed approach, and has the potential to delay timely availability of new medicines to patients until a name deemed acceptable by all stakeholders (including checking for non-infringement of trademark on a multi-country basis). From the perspective of dispensing errors, we believe it is important to consider alternative approaches. For example, prescribing software is used by the majority of doctors today in Australia. A different approach could be to incorporate in dispensing software the additional feature to print on the prescription a barcode unique to the prescribed medicinal product. The matching of this barcode against that printed on a product label by scanning should eliminate dispensing errors.
Page 23 - 3.1 Sponsors of new medicines will be required to submit evidence of risk assessment of the proposed labelling and packaging. The TGA will work with industry to develop guidance for this assessment, which may include consumer testing or risk assessment checklists similar to those used in other countries. The TGA is investigating methods to electronically screen proposed brand names against already existing brand names to identify	• What are considered "other" countries? • Is consumer testing referring to “Readability user testing” or something else? • Name assessment only? • What will be the criteria to know the undefined intentions can actually help?

potential LASA names.	
Page 23 – 3.2 In relation to applications to include a new medicine in the ARTG, if the proposed medicine brand name differs from another product included in the ARTG by three letters or fewer, the presentation of the proposed medicine label and packaging must use colours and designs that contrast with the medicine label and packaging of the existing product. During the implementation of this change, the TGA will work with the medicines industry to develop guidelines to provide clarity about these proposed requirements.	• In-process changes would create conflict and loss of time to retool.
Page 23 - 3.4 Products that are listed on the ARTG cannot be marketed under the same name as a registered medicine.	• Consider revising the ending text to: "...cannot be marketed under the same name as a medicine currently or previously registered on the ARTG."
Standardised Information Format: the Medicine Information Box	
Page 28 - 4.3 The Medicine Information Box must have a white background with black text. Headings must be highlighted or bolded so they are sufficiently emphasized.	• Figure 8 contains conflicting information as it displays white text in a black box.
Page 29 – Below Section 4.6 Where space restrictions do not allow for the required information to be provided in the Medicine Information Box, an alternative	• Consider more acceptable options. • Some products with small containers have pull-open labels. Is this acceptable? • Consider revising the existing sentence: "This may include breaking the information over more than one panel, or reduction in font size", to read: "This may

arrangement or formatting of information should be provided to the TGA for assessment and approval, together with a justification for non-standardised presentation. This may include breaking the information over more than one panel, or reduction in font size.	include breaking the information over more than one panel, reduction in font size, or fold out panels."
Dispensing Label Space	
Page 30 - Figure 9	• Are the displayed dimensions sufficient? The document states that the standard size of the label used in Australia is 80 x 40 mm.
Page 31 - 5.1 A designated space of 70 x 30 mm, consistent with international best practice11, must be provided to accommodate the dispensing label.	• See comment above.
General Question on the Proposed Regulatory Changes for Dispensing Label Space (Page 31)	
Do you support a designated space for the dispensing label on prescription medicines? Why/why not?	• Does this only allow for the sticker on the immediate package? • What about cartons that contain blisters? • Exemption should be allowed for small volume injectable dosage forms administered by or under supervision of a doctor.
Blister Strip Labeling	
Page 33 - Figure 10: 2. Segmented strips have all the critical information.	• Condition #2 is not met by the illustration in Figure 10. • Brand name, active ingredient and amount, expiry date and batch number are repeated every 2 units,

	however if perforation is made as illustrated (vertically), the entire right side is left without most of the information. Consider alternative print or perforation.
Page 34 - 6.3 A maximum of 3 active ingredients should be listed on each segment / each 2 units of a blister strip for registered medicines.	• A lot of text to accommodate on a blister in a usable way. • Although we can understand the benefit of repeating the brand and generic names, we are concerned that the requirement to repeat the batch number and expiry date is not achievable or only at considerable cost. This is because such variable information cannot be pre-printed and therefore is normally embossed at the time of packaging. Modifying tooling to perform multiple embossing on blister strips would be very costly if at all possible, noting the requirement for very accurate placement of the information due to the limited free space on the strips. Also, special attention is required not to compromise closure integrity around the tablets/capsules by the increased amount of embossing on the strips. This may require the blister strips to be increased in size, thereby leading to additional costs.
Page 34 – 6.4 Where there are more than 3 ingredients, for example multi-vitamins packaged this way, it may be sufficient to include a single list of active ingredients printed on the foil of each blister strip. Alternatively, the brand name, together with batch number and expiry date, should be repeated on the foil.	• Would this supplant the requirement for brand name?
Small Containers	
Page 35 - Figure 11	• Does not look like most of the text would be readable as the font size appears too small
Page 36 - Figure 12	• Would be better to include less text here and include a pack insert that is legible.

Page 36 – 7.1 The following requirements are proposed for medicine containers with a nominal capacity of 20 millilitres or less: • 7.1 These containers must be enclosed in a primary pack that fully complies with all labelling requirements and that includes a pack insert that provides detailed instructions for use.	• It is unclear why small containers need to be enclosed in a carton or why there is a specific need to include a pack insert providing detailed instructions considering CMIs may be provided separately or at the time of dispensing for other medicines. We are concerned that this requirement will lead to outlaying of significant cost (modification of tooling; additional packaging components) which may be seen as a waste, particularly as the consultation paper acknowledges that it is common for the outer packaging and package insert to be discarded by patients.
Page 37 - 7.3 A clear space should also be provided to allow a pharmacist to affix a dispensing sticker. This space need not be the size of a standard dispensing sticker (80 x 40 mm), but should allow a folded sticker to be attached like a flag without obscuring information.	• These dimensions are inconsistent with previous for dispensing label (page 31, section 5.1). See text below: o 5.1 A designated space of 70 x 30 mm, consistent with international best practice11, must be provided to accommodate the dispensing label.
General Question on the Proposed Regulatory Changes for Small Container Labelling (Page 37)	
To what extent do you support the proposed changes for small container labels? Please provide details. Do you have any further suggestions for how labelling of small containers could be improved?	• For small volume containers with a volume of less than 20 mL for an injectable dosage form, there should be exemption from Recommendation 7.3 when the product is administered by a health care professional who will refer to the package insert.
Pack Inserts	
Page 38 - 8.2	Please consider revising the existing sentence:

A pack insert must be in a form separate to the packaging; i.e. it cannot be printed on the inside of a carton.	• "A pack insert must be in a form separate to the packaging; i.e. it cannot be printed on the inside of a carton", to read "It cannot be printed on the inside of a carton."
General Question on the Proposed Establishment of a Labels and Packaging Advisory Committee (Page 39)	
To what extent do you think that a Labels and Packaging Advisory Committee will assist the TGA to manage consumer health risks associated with medicine labels and packaging?	• It is important for sponsors to know how the advisory body is going to be integrated in the TGA regulatory framework for evaluating and approval new medicine registration application. • At what point in the new medicine registration process will this advisory body insert itself, and how will issues be communicated to sponsors without affecting the established TGA review process and time line?

Thank you for the opportunity to comment on TGA's Medicine Labelling and Packaging Review Consultation Paper – Version 1.0, May 2012.

Please feel free to contact either of us should you have any questions.

Sincerely,

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