25 November 2016

Biological Science Section
Therapeutic Goods Administration
136 Narrabundah Lane
Symonston ACT 2609

Re: Report prepared for Submission on: TGA Consultation on Orphan drug program - *2015 consultation outcomes and 2016 orphan drug program proposal*

To whom it may concern:

ERA Consulting (Australia) Pty Ltd hereby submits comments on the *Consultation: Orphan drug program - 2015 consultation outcomes and 2016 orphan drug program proposal* released for consultation in October 2016.

If there are any questions regarding this submission, please do not hesitate to contact me [redacted]

[redacted]

Enclosures

This Cover Letter

[redacted]

ERA Consulting Submission to the TGA Consultation: Orphan Drugs Program - 2015 consultation outcomes and 2016 orphan drug program proposal

COMMENTS ON TGA PUBLIC CONSULTATION: ORPHAN DRUGS PROGRAM - 2016

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Reference/Page	**Issue**	**Comments**
Page 14 of 22	**Criterion one: Rare disease threshold or lack of financial viability and seriousness of the condition**	
Question 1: Do you support criterion one?	EITHER threshold of 5/10,000 (*less restrictive than status quo, more diseases may qualify as rare*) AND life threatening /chronically debilitating (*more restrictive than status quo*) OR life threatening /seriously debilitating or serious and chronic condition AND that without incentives it is unlikely that marketing would generate sufficient return to justify the necessary investment5 *(more restrictive than status quo*)	*Consistent with our previous recommendation (to the 2015 discussion paper) to follow the EU model of determining orphan designation, ERA agrees with the use of disease prevalence as a measure of patient threshold and considers the proposed threshold ratio of 5/10,000 to be appropriate. This prevalence threshold closely, if not identically, aligns with the major international standards.* *The new criterion proposed relating to the seriousness of the condition again follows the EU Regulation EC No141/2000 criteria when designation is based on prevalence. Removing the prior option for a designation to be sought in Australia for a rare disease that was a "serious" condition (rather than a life-threatening or chronically debilitating one) raises the question as to how to define a condition that is chronically debilitating and distinguish this from one that is serious. Will a clinical judgement made by the treating physician be considered as the starting point or will TGA decide on a case-by-case basis? The patients suffering from a rare and [only] serious condition will have their own view.* *Please note: ERA as a regulatory consultancy cannot provide input on the financial impact of the proposed criteria.*

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Page 14 of 22	**Criterion two: Alternative methods of diagnosis, prevention or treatment**	
Question 2: Do you support criterion two?	There is no existing therapy (*more restrictive than status quo*) OR if there is existing therapy, the product represents a significant benefit over existing therapies (*more restrictive than status quo*)	*To complement the harmonisation steps (in particular with the EU) proposed in Criterion one, and to mitigate the likely increase in orphan designations brought by the change in threshold, ERA considers the proposed Criterion two (adopted from Regulation EC No141/2000, EC No 847/2000) to be appropriate. The incentives of an Orphan Drug program should be supportive of development of potential new methods of diagnosis, prevention or treatment in the first instance or of potentially improved methods of diagnosis, prevention or treatment otherwise.*
Page 14 of 22	**Criteria three and four: Medical plausibility**	
Question 3: Do you support criteria three and four?	A justification for medical plausibility is required to support the orphan indication and to support subgrouping of indications.	*The proposal to maintain the concept of medical plausibility in the context of a designation request is considered reasonable.* *Consistent with our previous recommendation (to the 2015 discussion paper), ERA recognises that the current Orphan Drug definition in Australia is largely consistent with that of international regulators and agrees that the* status quo *be retained to allow subgrouping of indications upon justification.*
Page 14 of 22	**Paediatric populations**	
Question 4: Do you support the proposed consideration of	Paediatric indications will continue to be considered for orphan designation, where the prevalence criterion is met in relation to the whole of the disease, or where the disease is different in the	*ERA considers it is very important that paediatric indications should continue to be considered for orphan designation and agrees with this proposal.* *With regard to subgrouping within the paediatric population, the distinctions between diseases being deemed different amongst subgroups or specific to certain subgroups may be challenging to establish. Presumably the acceptance of such distinctions would require*

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paediatric indications?	paediatric subgroup, or specific to the paediatric subgroup. The change in the rare disease threshold in isolation could increase the number of paediatric conditions that classify as rare.	*justification based on medical plausibility, clinical practice and other relevant features of each scenario, and be determined on a case-by-case basis.* *We suggest that clarification on these issues should be considered, to support potential applicants.*
Page 16 of 22	**Modified designation process**	
Question 5: Do you support the proposed changes to the designation process and the timing of automatic lapsing?	Proposed modifications to the EMA process reflecting adaptation to the Australian context 1. Changes to the designation process: – the orphan designation will lapse within a set period if no registration application is made – the designation can be withdrawn by the sponsor or cancelled by the TGA if any of the criteria are demonstrably no longer satisfied at any time 2. No changes to the TGA incentives: – The current 100% waiver is proposed to be retained.	*The modifications to the EMA model might be reasonable, in principle, if the automatic lapse in designation period was significantly longer than suggested. A period of 3-6 months is NOT desirable or feasible in our view:* *i. This "lapsing" rule would not be supportive of Orphan Drug development programs in general. Even for larger companies this rule could be an impediment and negatively impact global strategies for registration of a product and possibly delay such products reaching the Australian market and patients.* *ii. This "lapsing" rule will be a particular disincentive and impediment to smaller entities that are pursuing development of diagnostics or therapies for rare diseases if they cannot keep a designation as they move (often slowly) through development towards a registration. Gaining Orphan Drug designation in an SME environment can be a significant advantage with high potential impact, as it is evidence of progress and can be a means to leverage financial support. <u>The case of SMEs in Australia seeking Orphan Drug designation should be re-considered in regard to this proposal,</u> so as to avoid the risk of stifling innovation or impeding the continuing development of products to potentially benefit Australian patients.*

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		iii. If an entity were prepared to re-apply under this proposed "lapsing" rule, how many times would a re-application be accepted? In principle, this could occur a number of times if the lapse period were to be short. We see such a scenario as a likely disincentive and an unnecessary use of resources from both the applicant and the TGA. *iv. Even assuming that an entity would be willing to risk the resources to re-apply under a short term "lapsing" rule, the justification for this being required so an application could be based on the most current information still seems dubious. It is unlikely that the prevalence data on an orphan disease would change significantly so as to preclude the product from being considered for orphan status within a 3 to 6 month period.* *ERA therefore counter-proposes that if a lapse rule is to be introduced, the period that a designation would stay in force should be significantly longer – perhaps a period of 2 years.* *Alternatively, if it is deemed necessary to place this kind of restriction on the scope of the Orphan Drug program in Australia, has it been considered that a requirement for a brief "Annual" Report might be easier for all parties than a lapse/re-application process? A simple form could be provided to capture the key up-to-date information.* *We agree that the sponsor or TGA should be able to withdraw a designation if the relevant criteria are no longer met.* *Retaining the* status quo *regarding the 100% fee waiver was the preferred option from the 2015 paper, and is supported by ERA.*