THERAPEUTIC GOODS ADMINISTRATION

2016 ORPHAN DRUGS PROGRAM PROPOSAL

SUBMISSION
November 2016

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Our Credo

We believe our first responsibility is to the doctors, nurses and patients, to mothers and fathers and all others who use our products and services. In meeting their needs everything we do must be of high quality. We must constantly strive to reduce our costs in order to maintain reasonable prices. Customers' orders must be serviced promptly and accurately. Our suppliers and distributors must have an opportunity to make a fair profit.

We are responsible to our employees, the men and women who work with us throughout the world. Everyone must be considered as an individual. We must respect their dignity and recognise their merit. They must have a sense of security in their jobs. Compensation must be fair and adequate, and working conditions clean, orderly and safe. We must be mindful of ways to help our employees fulfil their family responsibilities. Employees must feel free to make suggestions and complaints. There must be equal opportunity for employment, development and advancement for those qualified. We must provide competent management, and their actions must be just and ethical.

We are responsible to the communities in which we live and work and to the world community as well. We must be good citizens - support good works and charities and bear our fair share of taxes. We must encourage civic improvements and better health and education. We must maintain in good order the property we are privileged to use, protecting the environment and natural resources.

Our final responsibility is to our stockholders. Business must make a sound profit. We must experiment with new ideas. Research must be carried on, innovative programs developed and mistakes paid for. New equipment must be purchased, new facilities provided and new products launched. Reserves must be created to provide for adverse times. When we operate according to these principles, the stockholders should realise a fair return.

Submission Information & Company Overview

Organisation: Johnson & Johnson Pty Ltd
Type of Organisation: Proprietary Limited Company

[redacted]

Johnson & Johnson Pty Ltd is a subsidiary of Johnson & Johnson, the world's most comprehensive and broadly based healthcare company. In Australia we provide products and services including medical devices, diagnostics, pharmaceuticals and consumer healthcare products.

The Johnson & Johnson Family of Companies in Australia consists of:

- Johnson & Johnson Pacific Pty Limited – consumer health brands;
- Johnson & Johnson Medical Pty Limited – medical devices and related technology; and
- Janssen-Cilag Pty Limited – pharmaceuticals.

We employ approximately 1,500 Australians who bring innovative ideas, products and services to advance the health and well-being of the patients we serve. We recognise the impact of serious conditions on people's lives, and we aim to empower people through disease awareness, education and access to quality care. Our research and development focuses on identifying medical needs and harnessing the best science, whether from our own laboratories or through strategic relationships and collaborations.

Johnson & Johnson Pacific is a provider of consumer health and wellbeing products, offering families more than 650 trusted solutions for their most common health and wellbeing needs. Many of our brands have earned consumers' trust over generations.

Johnson & Johnson Medical produces a range of innovative products and solutions used primarily by healthcare professionals in the fields of orthopaedics, neurological disease, vision care, diabetes, infection prevention, diagnostics, cardiovascular disease, and aesthetics. We are the largest medical technology provider in Australia working across public and private sectors.

Janssen is dedicated to addressing unmet medical needs in oncology, immunology, neuroscience, infectious diseases and vaccines, and cardiovascular and metabolic diseases. Janssen has a long-standing history in making a meaningful difference in global public health, dating back to Dr Paul Janssen's pioneering work in mental health and pain medications, as well as the development of more than 80 medicines.

Comments on the 2016 Orphan Drugs Program Proposal

Overall Comment
We note that under the current proposals it is anticipated that the system will be overall more restrictive and, therefore, patients who would have previously benefited from medicines in orphan program, could be impacted. Given the intention of the orphan program is to encourage sponsors to file applications for rare diseases, is it appropriate to restrict the program in order seek to control costs? The existing cost recovery approach to application fees should mean any proposed changes in orphan designations should not impact on Therapeutic Goods Administration (TGA) costs. Therefore cost should not be a consideration in amending the orphan drug program. The existing fee structure for all applications (non-orphan) would cover any fluctuations resulting from orphan fee waivers.

Question 1: Do you support Criterion One?
Criterion 1 – Rare disease threshold or lack of financial viability and seriousness of the condition.
We support the first limb of the proposed first threshold test in Criterion 1 but not the proposed second limb. We support the proposed increase in the numeric threshold from the current less than 2,000 to the 5 in 10,000 threshold. We do not support the inclusion of the additional restriction that the rare disease must be life-threatening or chronically debilitating because the meaning of this terminology is unclear. For example, what is meant by "chronically debilitating"? How would this be assessed objectively? Furthermore what is meant by life-threatening"? We would require greater clarity in terminology before being able to determine support for the whole of the first threshold test.
We do not support the proposed alternative (second) threshold test in Criterion 1. Similarly with the first threshold test we note this second test introduces the broad concepts of 'seriously debilitating' and 'serious and chronic' without definition. The uncertainty in relation to these terms potentially rules out conditions which have a significant impact on a sufferer's quality of life and are truly rare but may not be deemed to meet the unstated requirements of those terms. It is also unclear how either term would interact with the first threshold test concept of 'chronically debilitating'. The additional requirement, to demonstrate a 'lack of commercial viability' introduces yet more undefined uncertainty. We note this is similar to the existing requirements in the current orphan drug designation program. The drawback with the existing and proposed requirement is that it would appear to necessitate the provision of company confidential financial information and this type of financial assessment would appear to be beyond the traditional expectation of the TGA. In our experience the existing criteria is very rarely used. We would require greater clarity in terminology before being able to determine support for the second threshold test.

Question #2: Do you support criterion two?
Criterion two: Alternate methods of diagnosis prevention or treatment
We do not support the first alternative method ("no existing therapy") on the basis that the

existence of one, individual therapy does not remove the need for the availability of alternative treatments for reasons of: tolerability, resistance, individual response, etc. This orphan program is intended to help make medicines available to patients with rare diseases, and is important this includes options for more than one treatment per disease.

If the TGA decides to implement this requirement, we would request greater clarity in terminology. For example, the concept of 'existing therapy' is not defined. A product may be registered for a given condition but not currently marketed.

We do not support the second alternative method ("for existing therapy, product represents significant benefit") on the basis it may impose a requirement that is particularly difficult to meet for orphan diseases. The nature of orphan disease means that clinical trials are more likely to be limited by: the smaller subject patient population and the economics of drug development and thus are less likely in their design to incorporate a comparator arm. Therefore it is less likely that a given treatment for an orphan condition will be able to demonstrate a significant benefit over an existing therapy. It appears the limitation may require a comparative assessment. Any limitation should be assessed pragmatically and should not require detailed comparative data for example, phase 3 clinical studies with comparator arms.

Question 3: Do you agree with criteria three and four?

Criteria three and four: Medical plausibility / Justification.

We understand the intent of these proposed criteria. We have concerns as to the level of detail that would be required to meet the proposed criteria for subsets. The process of developing new medicines requires decisions to be made at various time points to narrow the field of investigation. The current wording of the criteria may not clearly recognise the practical considerations (for example, a particular subgroup may be selected for medicine development based on the *in vitro* science or an unmet clinical need and hence may not be possible to show the product cannot be used in a broader disease group).

Question 4: Do you support the proposed consideration of paediatric indications?

We strongly oppose the TGA's proposed changes regarding paediatric indications. TGA is proposing to limit orphan designations to instances where: "the prevalence of a paediatric indication is met in relation to the whole disease, or where the disease is different in a paediatric subgroup, or specific to a paediatric subgroup". This proposed approach risks denying applications for necessary treatments and better use of medicines for paediatric patients. Under the proposed changes, even if the prevalence of the paediatric population falls below the orphan drug designation threshold, it will be ineligible (as a subgroup) for orphan status as TGA will require the prevalence to be met for the whole disease. Requiring the prevalence of the whole disease population is likely to reduce eligibility for paediatric designation. It is certainly our understanding that there would be a very small number of diseases that would be specific to or different in the paediatric subgroup.

By way of example, products for HIV in paediatric patients may not be eligible such as PREZISTA® (darunavir) which was previously granted orphan designation in 2008. The prevalence of HIV as a whole in Australia would be above the prevalence threshold and therefore PREZISTA for paediatric

use would no longer qualify for orphan designation.

For a range of reasons (including population size and financial viability) the development of paediatric medicines can be more limited than that of medicines for the general population. There are currently no specific incentives in Australia to encourage sponsors to register new medicines, indications, dosage information or presentations for paediatric patients, whereas comparable jurisdictions such as the United States, the European Union and Canadian regulatory systems all have specific incentives in place for some time, including in the form of data exclusivity. In this regard, the Australian system appears already to be lagging behind and the proposed changes would not improve the system. We suggest that the orphan drug program should allow paediatric subgroups to qualify for orphan designation. In addition, to encourage quality use of medicines for paediatric patients, we propose that this should be extended even further in the form of a TGA waiver of fees for all applications for new medicines, indications, dosage information or presentations for paediatric patients, regardless of the prevalence in Australia.

Question 5: Do you support the proposed changes to the designation process and the timing of automatic lapsing?

We do not support the proposed 3-6 month time line to file after designation. We suggest 12 months as a more reasonable time in light of the practical requirements associated. In some cases the decision to file is dependent on designation and the time to assemble a dossier may be longer than 6 months. This also would not allow time for the sponsor to meet TGA under proposed expedited process (6 to 7 months pre-submission meeting prior to filing). TGA have noted on page 15 on the consultation that 57% of applications were lodged within 12 months, further supporting this proposed 12 month timeline.

The given patient population is not likely to alter significantly in the suggested 12 month period.

We seek further clarification in relation to the proposal of a designation being cancelled by TGA if criteria are no longer met at any time. In particular, whether this would only apply prior to filing a Category 1 application. We propose this would not be appropriate to be revoked once the evaluation of the Category 1 application has commenced. We would also seek advice as to consideration of a retrospective application of the proposed lapsing.

Question 6: Are there any other key issues that should be considered in developing the changes to the orphan drugs program?

We note that under the current proposals it is anticipated that the system will be overall more restrictive and, therefore, that patients who would have previously benefited from medicines in orphan program, could be impacted. Given the intention of the orphan program is to encourage sponsors to file applications for rare diseases, is it appropriate to restrict the program in order seek to control costs? The existing cost recovery approach to application fees should mean any proposed changes in orphan designations should not impact on TGA costs. Therefore cost should not be a

consideration in amending the orphan drug program. The existing fee structure for all applications (non-orphan) would cover any fluctuations resulting from orphan fee waivers.

Comments Regarding Box 4

Janssen notes that the consultation document (Box 4, p18) presents an analysis of PBS sales for six drugs (not identified). The analysis utilized the number of services and then calculated the cost of providing these services by multiplying the services by the dispensed price for maximum quantity (DPMQ). This analysis is inappropriate as the benefits paid by the PBAC for these services do not need to be calculated this way but can be seen by selecting services rather than benefit. The benefit paid is likely to be overestimated in Box 4 because it fails to take into account that not all patients will receive the maximum quantity particularly if any of the drugs used as examples are dosed according to weight. Furthermore, the analysis fails to consider that there may be Special Pricing Arrangements or rebates provided through commercial in confidence Deeds of Agreement with the Commonwealth that do means the benefits paid not reflect the real price.

It is unclear why the TGA would comment on the sales associated with orphan drugs. This is not the TGA's remit and the price of a drug should not factor into the determination of whether a drug receives orphan status. The price of a drug on the PBS is the result of a comparative cost-effectiveness assessment and is not determined by consideration of commercial returns.