**Submission to review of Life Saving Drugs Program.**

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This submission relates to my experience with administrative aspects of the Life Saving Drugs Program (LSDP):

For almost 20 years Australians with certain rare inherited disorders of metabolism have received subsidised life-saving therapy with ultra-expensive orphan drugs through the Federal Health Department's Life Saving Drugs Program (LSDP). Decisions regarding guidelines for therapy, consideration of therapy initiation and subsequent monitoring schedules and dosage alterations have been managed by Disease Advisory Committees (DAC). When these orphan drugs first became available in the 1990s, as president of the Human Genetics Society of Australasia I approached the Federal Health Department with a suggestion for establishing a central process for management of these individuals with rare disorders by committees of experts. Since the inception of the DACs I have served as chairman of the Gaucher Disease DAC and on the committees of the Fabry, Infantile Pompe and MPS DACs. This process established to gate-keep and rationally control the use of these drugs, and facilitate the development of expertise in the management of individuals with rare disorders, has had international recognition. Australia's small population (with resulting small numbers of patients with very rare life-threatening conditions) and the geographical distribution of these patients, presents particular challenges in linking these patients with expert care. The Australian process, whereby funded access to expensive orphan drugs for inherited metabolic disorders is centrally administered through the LSDP, has the major advantage of concentrating expertise, and developing experience, in managing these rare disorders by facilitating all the Australian patients being treated under the aegis of the DACs. The concentration of clinical expertise, and centralisation of management and data collection, in

the LSDP, has facilitated ongoing review of quality, optimisation of dosing schedules and equity of access for treatment of individuals with rare disorders of metabolism requiring extremely expensive replacement therapy. Regarding the future of the LSDP, the Federal Health minister announced a review of the LSDP and that the DACs would be dissolved from May 1st 2014. Of particular concern is that while the review is being conducted patients will no longer be managed through the DAC process. Clinical trials for orphan drugs for these extremely rare genetic conditions are complicated by factors including: there are limited numbers of patients available to treat which also limits matching, the conditions often manifest variable phenotypes with features developing over decades, the natural course of the untreated patients is variable and not well documented, the clinical trials are limited in time and usually involve patients with irreversible manifestations, the trials do not test drug schedules for the various therapeutic phases, such as maintenance therapy following initial "debulking". Thus, even after these drugs receive marketing approval following assessment by the TGA of clinical safety and efficacy, there are still many unanswered questions regarding their optimal usage. Issues still to be clarified include: when and in whom to start therapy, optimal individualised dosage at initiation to "debulk" and subsequent maintenance, monitoring schedules relevant to assessing continued response and safety, specific protocols for treating various organ manifestations. These issues would be extremely difficult to assess by specialists managing limited numbers of patients in geographically dispersed individual clinics. The concentration of patients, data and expertise in a national centralised program, coordinating the management of all Australian patients, has facilitated the ongoing development of revised therapeutic strategies for optimal use of these expensive resources. As an example, the Gaucher Disease DAC has used a titrated schedule of dosage that has resulted in patients having comparative clinical therapeutic outcomes to those managed internationally but with much lower doses, thus saving the health budget 10's of millions of

dollars over the life of the program. Dosage fine tuning of this nature would not be possible if individual physicians each manage few patients. Furthermore, centralisation of investigation protocols has allowed for standardisation of complex tests and, for instance, centralised reading of digitised imaging procedures by a single radiologist. The membership of the DACs has been relatively stable for many years and hence the concern that this accumulated experience will be lost with therapeutic decisions being made by physicians with limited experience in these rare disorders interacting with LSDP administrative staff.

Considering the success of the LSDP in optimising therapy for these rare disorders, and the absence of any overt concern from treaters and patients about the DAC process, it is difficult to understand why the DACs would be disbanded with loss of a considerable amount of expertise. For the majority of these conditions there is no other therapy available to reverse the inherited metabolic abnormality and this vulnerable group of individuals will thus potentially be denied optimal therapy for conditions with considerable morbidity and which will progress to premature death if untreated.

The explanation that the DACs were disbanded to facilitate the members making submissions to the review is illogical and spurious. The LSDP was reviewed in 2009 without disbanding the DACs during the review and I felt no constraint in interacting with the 2009 reviewer. I took part in a lengthy telephone interview with the reviewer and submitted a written report. The review made no mention of any problems with the DAC process nor made any suggestion to disband the DACs. Any concern that the DAC process adds to the red tape involved in the LSDP process of facilitating patient access to drugs is also contrary to the facts. The DACs have been incredibly timely in their reviews, which are rapidly done by email or teleconference, and this has facilitated rather than hindered the process. Delays have

occurred in the administrative processes within the LSDP and Federal Department of Health rather than by the DAC involvement. The DACs also add minimal costs to the LSDP and for about the first decade the members of the DACs received no payment for the many hours of reviews. As chairman of the Gaucher Disease committee I was contacted almost weekly by the LSDP staff for clinical advice which was always provided in detail, in a timely manner and for free. I would urge the committee undertaking the current review to urgently recommend the LSDP resurrect the DAC process to rationally manage access to funded therapy for rare disorders of metabolism in Australia.