SUBMISSION

We are writing this submission as parents of our son, who was affected by Mucopolysachharide Type VI (Maroteaux Lamy). has received Naglazyme through the LSDP as his Enzyme Replacement Therapy. This submission is written from our experiences as parents, and our observations of other parents and children we have been in contact with, who are affected by MPS, or other Lysosomal Storage Disorders.

With two older brothers, it became very obvious to us that by the time was around 4 years old, that his development was not following the same path as theirs. He was very reluctant to walk any significant distance, and would usually be carried on any walk or extended outing. He tired very easily and would need to rest frequently, sleep in the afternoons after pre-school, or other activities. Both his brothers played sport, and in particular soccer, and when it came time to enroll in the Under 6 team, it was clear that he was not physically capable of joining in.

, was diagnosed with MPS VI at age 6. At the time of this diagnosis we were advised that there was no treatment available. We were made aware of the life limiting nature of his condition, and the unreliability of any attempt to assess the severity of his disorder.

The route to his diagnosis was typical of most MPS children. A continual stream of minor issues and observances had us visiting numerous doctors and specialists. Operations were carried out on his ears and throat, but the overall feeling that something was not right persisted. By chance we were referred to a specialist who also worked within the clinics at the Children's Hospital at Westmead, and who realized that there was a more serious underlying condition involved. After two years we finally received a diagnosis, and some relief that our concerns were recognized. There was no history of this disease within our family, and in an instant we opened a door to a world we never knew existed, but which was filled will many wonderful people who have now become a huge part of our lives.

From the ages of 6 to 9, we witnessed a steady decline in health. In this time period he had moved from pre-school to school, and life became progressively more difficult for him. His joints were becoming stiffer, and he would need a shower or bath most mornings to help ease out his joints. His days at school were very tiring, and he would often rest and sleep when he came home. Sitting at a desk, writing and moving around the school were all activities that he found difficult. He rarely complained, and just understood this to be his "normal". Although we were not aware, his sleeping was not providing his body with the rest he needed, and at age 9 he went onto using a CPAP machine. This provided a real positive benefit for him. In terms of other aides, had become increasingly reliant on the use of a wheelchair for any activity that required extended walking, or standing. While he resisted using it a school, he did take it on excursions so that he could manage the physical aspects and could keep up with the class and his friends. He needed assistance at school to help with taking notes, and later with exams and the like.

In 2002, at age 9, we felt like we had won the lottery when was enrolled into the Phase 2 trial for the use of Naglazyme as Enzyme Replacement Therapy, at a trial site in Adelaide. continued to receive weekly ERT throughout the trial, post-trial and following the eventual approval of the treatment on the LSDP. We will discuss these experiences below with regard to the Terms of Reference of the Review. Throughout the period of his life post 2002 he moved from primary school through to high school, and on to university. He transitioned from the Children's Hospital to Westmead Hospital. He gained his drivers license and became an engaged and active member of his community, and the world in general.

Having completed two years of his three year Arts degree, we (and he) had every expectation that he would have completed university, found a career and gone on to have as usual a life as those of his friends and peers. The experience of having a rare disease, and the great fortune to be on treatment made him a compassionate person, and very aware that not all people are in a situation of their choosing.

passed away unexpectedly in December 2013. The circumstances of his death in are still not clear to us, however, it appears that it was the result of a seizure (not commonly observed in MPS VI) that may have combined with his compromised airways. At that time was in the best health he had ever been.

We would now like to comment on the Terms of Reference for this review, with regard to our, and , experience of receiving treatment for a rare disorder.

CLINICAL EFFECTIVENESS - NAGLAZYME

was on ERT for over 11 years, and in that time missed only a handful of infusions. At no stage did he suffer any reaction to the treatment. This included progressing from the very slow initial doses during the trial phases, and then eventually quicker infusion rates in later years.

Having commenced on ERT as part of the Phase 2 trial, progress in a number of physical indicators was monitored by the trial's clinicians at regular intervals to monitor Naglazyme's effectiveness. We understand that it is difficult to quantitatively measure some of the outcomes of ERT, or that these measurements do not fully convey the significance of even small improvements on a patients quality of life. For the improvements in his health as a result of receiving ERT led to significant improvements in his quality of life and his confidence to more actively participate in everyday activities. In particular, we note the following improvements in quality of life as a result of receiving ERT with Naglazyme:

- Walking – Prior to commencing ERT, mobility had been steadily decreasing . and he had become increasingly reliant on a wheelchair for longer trips (>500m). After commencing ERT, felt much more capable of walking longer distances, and hadn't used his wheelchair in about half a decade. The ability to walk meant that could more fully participate in life, particularly in terms of his ability to attend university at Macquarie University where he could catch public transport and get around a large campus to his classes. Without ERT, it is likely that mobility issues would have continued to be a barrier for to the extent that university may not have been a viable option for
- Sleeping – A good nights sleep is critical to having the stamina to get through every day. Lack of sleep on an ongoing basis can be crippling to maintaining the energy and enthusiasm needed every day. While the ERT on it's own may not have helped his airways, we are certain that the combination of ERT and CPAP treatments gave the energy to get through a day, and meet the requirements of schooling, study and every day activities.
- Range of Motion – For most people, the ability to turn, lift, bend or reach for items is something that is taken for granted. These abilities are critical to getting through the activities of daily living that are essential. Putting on shoes and tying laces, being able to dress oneself, pick up dropped items, turn while driving to change lanes are all minor matters to most people. However these are all activities that many with MPS find increasingly difficult as joints become less mobile. Without ERT was reliant on us and his brothers to do many simple tasks . The continued improvement in his ROM

meant that he could be self sufficient in managing his activities of daily living, rather than relying on help. Again these may be small issues, however it cannot be underestimated how quickly these can become limiting factors to self-sufficiency and participation.

- Overall Quality of Life – In the years of the testing and measuring as part of the clinical trials and LSDP reporting, we found that the clinical measurements never fully explained just how important the treatment was to and our family. The progressive decline of most of his symptoms had been halted, and some symptoms had even improved. As a result the outlook for his health was quite positive, and whilst several elements of his health continued to require management, we all had the confidence that would be able to continue to live a fulfilling and meaningful life. Naglazyme was the most critical element in allowing to complete high school and go to university, and would have allowed him to go on to employment in the future. We are sure that this positive outlook for health, as a result of Naglazyme, gave him the drive to get up and go each day, and get on with things.

We understand that these treatments are expensive, and that some consideration needs to be given to their cost-effectiveness. However while to some observers these small improvements in markers may seem minor, they can be "tipping points" that may substantially affect the pathways and outcomes of an individual. We are concerned that with limited ability to apply empirical measurement, as the indirect impacts of these small changes could be undervalued in any benefit analysis.

EMERGING TREATMENTS

We have watched the steady progress of new treatments being developed as lessons learnt in one area of research are applied to other areas. We have no doubt that in the near future all forms of the group of MPS diseases will have an ERT developed and available if required. A more likely outcome, however, is that while some MPS are still waiting for ERT, the development of other forms of treatment (such as gene therapy which is already underway) will be developed and that current forms of therapy will eventually be replaced with more effective treatments, perhaps even before they are fully implemented.

This continuing development carries that hope that treatments will become:

- better able to target areas of need
- more efficient in delivery
- more cost effective, and
- closer to being a cure than a treatment

It's also likely that disease understanding and the utilization of technologies will also cross disease boundaries. Scientific progress in other fields of medical research will have flow-through benefits that will improve the quality of treatments for MPS patients and, likewise, further research to treat MPS patients will have benefits to other fields of medical research and diseases.

For this reason, and because of the clearly evident accelerating pace of research and discovery, we support that wherever possible existing treatments should be provided to patients in the hope that any possibility to halt or delay disease onset may keep patients in the best possible position for future treatments that will become available. Simply because a patient may not receive all the improvements a treatment can offer, should not exclude them from receiving any improvement.

This may also become important as better diagnostic tools will likely identify more sub-groups

within diseases, that were previously classified on the basis of fairly rudimentary clinical observations (which defined very early the different MPS disorders). With the identification of sub-groups will come debate about how effective treatments can be used on each group, and therefore a broad application of treatments will eliminate any dispute over whether a treatment is or is not worth using on a particular sub-group.

INTERNATIONAL COMPARISONS

We understand that almost every country has a different approach as to how these treatments are (or are not) provided. We do know from discussions with families in other countries that some governments automatically fund treatments as they become available, and do not screen patients for eligibility based on health thresholds. We would like this to be the situation in Australia.

The development of the LSDP has provided a mechanism for funding that enables some rigour to be applied to the decision to fund treatments. This is important in that there is a defined pathway to funding, and not just an ad-hoc approach on a case-by-case basis. This provides some certainty for both suppliers and patients.

However we believe that from a family perspective the following opportunities for improvement should be considered:

- Early treatment of MPS (and other LSD's) is critical to avoid deterioration, which may not be reversible. It is therefore critical that following diagnosis, treatment is able to be commenced as soon as possible, rather than having to wait for symptoms to appear in order to meet the thresholds to qualify for treatment under the LSDP (as seems to be the case for consideration of some disorders). Early treatment should be a default position until no benefit can be demonstrated, rather than the reverse.
- Interim funding / approval of treatments based on accepted overseas review: In some instances, very low patient numbers in Australia may deter suppliers from making applications for funding because of the costs involved in making such an application. This can significantly impede access to available treatments for patients. It should be possible to streamline approval for funding by adopting overseas approval, and thereby enabling treatments to be available in Australia earlier than if an application has to be lodged here, as is currently the case. This may also have some benefit in reducing supply price here by eliminating a substantial cost.

SUBSIDISATION

While we do not have access to the exact supply costs for treatment, we do understand that they are extremely expensive, and that a user-pays system is entirely unfeasible. We are extremely grateful to the Australian Government for its role as the supplying agent, as without it would not have had access to the treatment that so significantly benefited his life.

We note that the Government is well-positioned to be able to negotiate the supply cost as the sole Australian purchaser, providing it with a stronger market position to deal with pharmaceutical companies.

While some amount of patient contribution could be considered (such as with the PBS), in reality this would recover only a fraction of the supply cost, and would therefore not be an useful mechanism to recover or defray costs, or to deter use (the demand for treatment is not

a choice). The fact that these drugs are truly 'life saving' would also mean that the costs passed on to patients would have to be met, even where patients and their families are not necessarily able to do so. If any financial contributions by patients is required, this must be means-tested to ensure that financial barriers to not impede access to treatment.

In terms of subsidisation and pricing, we would only suggest, and support that:

- Supply costs provide for some initial recovery of research costs, but that this should fall as costs are recovered (ie at the end of a defined "orphan status").
- At this point competition should be allowed from "generic" suppliers, and perhaps supply could be tendered.

VALUE FOR MONEY / COST BENEFIT

As noted above, we understand that pricing of these treatments must make some provision for recovery of research costs, particularly as these can have accrued over long durations. We accept that the role of research has been effectively been shed by government in favour of market mechanisms. However we do not believe that treatments for rare disorders can be left soley to the markets, as there is simply not the demand base to drive research and treatment as there is for more widely applied treatments.

It is therefore unreasonable that life-saving treatments for rare diseases be considered purely on any cost benefit basis. As we mentioned in our introduction, and in this submission, seemingly small changes in patient health can have a huge affect on their quality of life, and these changes cannot be empirically measured or formulated.

Whilst we acknowledge, and are extremely grateful for, the significant financial costs incurred by the Australian Government in providing access to Naglazyme and other drugs under the LSDP, the benefits received by the government in return should not be undervalued. In particular, the benefits to the government as a result of providing this service should not be overlooked. In the case of and our family, we would note that:

- ERT treatment with Naglazyme had resulted in some substantial improvements in health, relieving symptoms that may otherwise have required serious and costly surgical procedures to be undertaken.
- Access to Naglazyme for meant that he had good prospects of going on to lead a productive life, and based on his strong performance at university we expect that he would have had good employment prospects. Based on the decline in his health prior to receiving Naglazyme, we are uncertain whether employment would have been a realistic option for without access to this treatment.
- The improvement in health also meant that he could be increasingly independent. As a result, was able to return to the workforce as a nurse after commenced university.
- As treatments progressed, opportunities to further reduce the costs of his treatment were also arising. For example, we had been in the process of arranging home infusions for prior to his passing, which would have reduced the cost of treatment compared to the hospital infusion setting.

In addition to financial benefits, we are quite certain that in case access to treatment meant that he, and the rest of our family, could more fully engage with and contribute to society. How could this ever be measured or costed? How could we measure the costs to all involved if he was not on treatment, and what the future costs of his care would be?

ADMINISTRATION / DATA COLLECTION

We understand that with such expensive treatments being used, that there should be some mechanism to ensure that the most benefit is being obtained. We do not object to annual reviews of patient health and progress. We would suggest that consideration be given to these reviews being done locally to help eliminate the need for travel that can be very difficult for patients and families in regional & remote areas. Surely technology can be utilised more effectively in this regard?

We would like to see some data being published to provide the public with some basic information such as numbers of patients, averages and ranges of measureable markers, such as is done with other health treatments / outcomes. There should be recognition that in this field, with such limited numbers of patients, with a wide variance in attenuation of their disease impacts that the data will be widely variable, and cannot be used as a sole determinant for treatment outcomes, patient improvement or continued access to treatment

CONCLUSION

Our son has now travelled the full MPS journey. From diagnosis, participation in clinical trails through to Enzyme Replacement Therapy. His unexpected passing at age 20 cut short what should have been an active, engaged and rewarding contribution to society, that, we believe was made possible due to timely access to treatment. We have witnessed the impact of MPS on him, and the ability for this impact to be halted and reversed such that . could enjoy a quality of life that was equal in most regards to his peers. We firmly believe that this was made possible through access to treatment funding by the LSDP, knowing that there is no chance that we could fund this treatment ourselves. These impacts as best summarised in the attached poster, which was presented at the 2014 International Symposium in his memory.

Having been through this experience, we would strongly urge that the LSDP be maintained, and broadened to provide access to a wider range of patients where benefits may not be so easily measured, and earlier access to treatment, even if only partially successful, so that patient health is maintained as best as possible for future improved treatments when they become available.

The role of the LSDP is a basic tenet of government in providing services to our population that we cannot individually afford, and which recognizes the dignity of each individual, and their right to a quality of life that we each expect.