

OZGROW

The Australasian Paediatric Growth Hormone Database

ANNUAL REPORT

2006

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On behalf of:

**The OZGROW Committee of the
Australasian Paediatric Endocrine Group (APEG)**

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1. BACKGROUND INFORMATION REGARDING OZGROW

1.1 Introduction and rationale

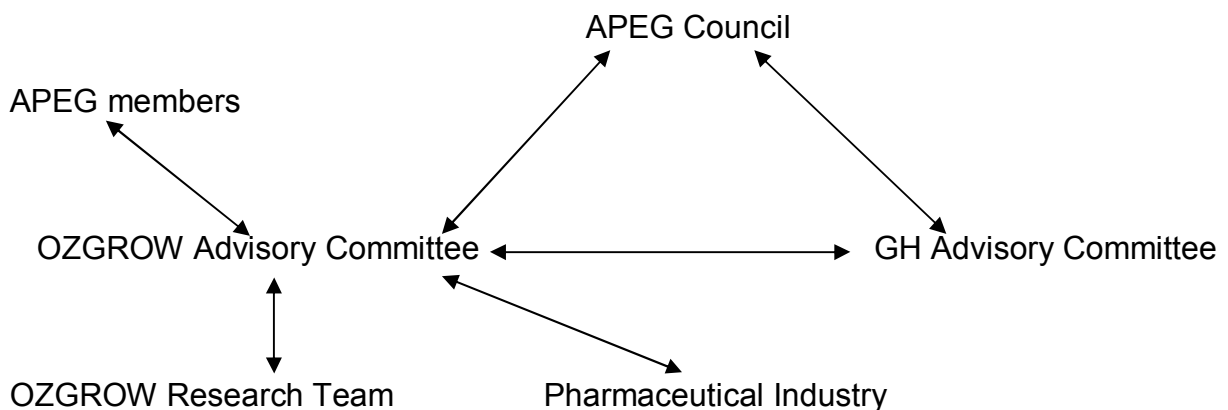
Throughout the world, thousands of height restricted children are treated with growth hormone (GH). Within Australia and New Zealand, nearly 2000 children with height restrictions currently receive GH treatment through government-funded programs. The main aim of GH treatment in children is to improve adult height. As with any medical intervention, it is important that children receiving GH treatment are regularly monitored at the local level to determine if the treatment has improved the targeted outcome (i.e. height gain). It is also important to look at trends in patient outcomes at the broader national and international level to assess the overall benefit of the treatment for improving outcomes for the target population.

‘OZGROW’ is the name given to the national database designed to prospectively collect outcome data on children receiving GH throughout Australia and New Zealand. The concept of OZGROW was an initiative of the Australasian Paediatric Endocrine Group (APEG).

In 2004, the OZGROW Advisory Committee of APEG appointed the position of OZGROW Research Team to the Children’s Nutrition Research Centre (CNRC), which is located on site at the Royal Children’s Hospital in Brisbane. The OZGROW Research Team consists of a 0.75 research position, currently shared by Pamela Dodrill and Lisa Atkin, and an overseeing role from the Director of the CNRC, A/Prof Peter S.W. Davies.

1.2 Structure of OZGROW

The current management structure of OZGROW is as follows:



1.3 OZGROW Database



- At the end of 2006, the OZGROW Database currently holds data on the growth outcomes of over 5000 children who have received GH treatment in Australia or New Zealand as part of a government-funded program.
- The OZGROW Research Team are able to use the OZGROW Database to provide detailed reports summarising diagnostic and auxological data on Australasian children who have received GH treatment.
- The OZGROW Research Team are also able to provide detailed reports on specific topics, such as adult height outcomes for children on GH, response to dosage of GH and complications of GH usage, as well as growth outcomes of children with specific disorders (e.g. Turner Syndrome, Russell Silver/ Prader Willi/ Noonan syndromes, chronic renal failure, or other indications for GH treatment).

1.4 Research opportunities

- The OZGROW Research Team is currently involved in several ongoing research projects, which have resulted in many presentations and publications.
- Further research projects are expected.
- Research undertaken by the using OZGROW Database has the potential to affect clinical practice in the area of paediatric endocrinology, both nationally and internationally.
- Collaboration between practicing endocrine clinicians and the OZGROW Research Team to investigate topics of clinical importance is encouraged.

The process for collaboration between practicing clinicians, the OZGROW Advisory Committee, and the OZGROW Research Team is outlined in the diagram overleaf.

1.5 Process for OZGROW research projects

<p style="text-align: center;">Clinician has suggestion for research topic</p> <p style="text-align: center;"></p>	<p style="text-align: center;">OZGROW Research Team has suggestion for research topic</p> <p style="text-align: center;"></p>
<p>The clinician contacts the OZGROW Advisory Committee with a brief outline of their suggested research topic.</p>	<p>The OZGROW Research Team contacts the OZGROW Advisory Committee with a brief outline of their suggested research topic.</p>
<p>The OZGROW Advisory Committee contacts the OZGROW Research Team to pass on the clinician's suggestion and contact details.</p>	<p>The OZGROW Advisory Committee forwards details of proposed project onto APEG members and asks if any clinicians are interested in being involved in the project.</p>
<p>The OZGROW Research Team contacts the clinician to discuss their suggested project. They agree on the level of involvement the clinician wishes to/ would be able to commit to (i.e. involvement in design, interpreting analysis, writing of papers, reviewing drafts of papers).</p>	<p>The interested clinician contacts the OZGROW Advisory Committee or the OZGROW Research Team directly.</p>
<p>The OZGROW Research Team and the clinician perform their allocated tasks, as agreed.</p>	<p>The OZGROW Research Team contacts the clinician to discuss the proposed project. They agree on the level of involvement the clinician wishes to/ would be able to commit to (i.e. involvement in design, interpreting analysis, writing of papers, reviewing drafts of papers).</p>
<p>The OZGROW Research Team and the clinician perform their allocated tasks, as agreed.</p>	<p>The OZGROW Research Team and the clinician perform allocated tasks, as agreed.</p>
<p>The OZGROW Advisory Committee are sent any draft papers to review prior to submission to journals.</p>	<p>The OZGROW Advisory Committee are sent any draft papers to review prior to submission to journals.</p>
<p>Both the OZGROW Research Team and the clinician are listed as authors on any papers arising from the project.</p>	<p>Both the OZGROW Research Team and the clinician are listed as authors on any papers arising from the project.</p>
<p>All papers are published on behalf of the OZGROW Advisory Committee of APEG.</p>	<p>All papers are published on behalf of the OZGROW Advisory Committee of APEG.</p>

2. ACKNOWLEDGEMENTS

The OZGROW Research Team would like to acknowledge the support and guidance of the OZGROW Advisory Committee of APEG:

- Dr Andrew Cotterill (Chair), Dr Cathy Choong, Dr Chris Cowell, Dr Wayne Cutfield, and Dr Kim Donaghue.

The OZGROW Research Team would also like to acknowledge the continuing financial support of the following companies:

- Eli-Lilly Australia Pty. Ltd.
- NovoNordisk Pharmaceuticals Pty. Ltd.
- Pfizer Australia Pty. Ltd.
- Sandoz Australia Pty. Ltd.
- SciGen Pty. Ltd.
- Serono Australia Pty. Ltd.

In addition, the OZGROW Research Team would also like to thank the clinical teams at the following growth centres for their time and effort spent in the collection and entering of patient data, and for their ongoing support of the work conducted by OZGROW:

- Adelaide Women's and Children's Hospital
- Dr Mike Thomsett's Private Clinic, Brisbane
- Liggins Institute, Auckland, New Zealand
- Mater Children's Hospital, Brisbane
- Monash Medical Centre, Melbourne
- Princess Margaret Hospital, Perth
- Royal Children's Hospital, Brisbane
- Royal Children's Hospital, Melbourne
- Royal Hobart Hospital
- Sydney Children's Hospital
- The Children's Hospital at Westmead
- The John Hunter Hospital, Newcastle
- Commonwealth Department of Health and Aging (DoHA), Canberra.

3. CURRENT STATUS OF THE OZGROW DATABASE

3.1 Access to data required for the OZGROW Database

History of data collection

Prior to 2000, data on children receiving GH treatment within Australia were collected on a purpose-built OZGROW Database, which operated on a DOS platform. Major growth centres throughout Australia entered data regarding their patients on GH treatment onto a local copy of the Database. Every month data were sent on disc to the national OZGROW Co-ordination Team, which, at that time, consisted of staff from the Children's Hospital at Westmead. The national OZGROW Database was then 'recreated' each month from the latest data sent from each centre.

Concerns regarding Y2K incompatibility resulted in the DOS database being abandoned. However, to their credit, most growth centres have since found other database platforms to use to enter and store their growth data. Some centres developed their own database platforms. Other centres chose to use a database developed by one of the pharmaceutical companies who supply GH.

Current data collection

Currently, OZGROW receives data from the following sources:

- The Children's Hospital at Westmead
 - Data supplied from a database unique to this hospital.
- Sydney Children's Hospital
 - Data supplied from a database unique to this hospital.
- Other major growth centres within Australia
 - Data supplied from a combination of database systems made available by various pharmaceutical companies (currently: KGS, MeGHA, Nordinet).
- Liggins Institute, New Zealand
 - Data supplied from a database developed by a pharmaceutical company (currently KGS).
- DoHA Canberra
 - Data supplied from a database unique to this department.

Data collection from growth centres

In 2006, the OZGROW Research Team has continued to work with growth centres across Australia and New Zealand to obtain updated patient data for the OZGROW Database.

Data retrieval from several of the Australasian growth centres has continued to be problematic for a number of reasons:

- Many centres have had problems entering data into their local database, and/or downloading information from their database to send to OZGROW.
- Many centres have recently changed, or are considering changing, to different local database platforms.
- Currently, some centres have patient data spread over different databases, or periods where patient data has not been entered into any database.
- Many of the database programs supplied by pharmaceutical companies are currently in the process of being updated/ redeveloped.

The OZGROW Research Team has spent much time liaising with the companies who supply GH patient databases to advocate for greater assistance for clinicians experiencing problems with their database, and for modified/ improved database functions to reflect the needs of Australian and New Zealand clinicians.

Data retrieval from Department of Health and Aging (DoHA) in Canberra

Throughout 2006, the OZGROW Research Team continued to invest much time and effort into obtaining access to the data stored by DoHA in Canberra from the *Application for Growth Hormone* and *Growth and Treatment* record forms submitted by clinicians. Special thanks are owed to Kim Oanh-Nguyen and Briar Carr from DoHA for their assistance with this task. This information has been used to augment information provided directly from centres.

Ongoing meetings/ visits with DoHA have been required to maintain and improve this source of data, in terms of:

- Information entered into the database and stored electronically by DoHA

- This information is limited to the data that Canberra currently requests on the *Application for Growth Hormone* and *Growth and Treatment* record forms.
 - This information is also limited by the amount of data from the forms that are entered onto the DoHA's electronic database, and the way in which the data are entered.
- Information requested on *Application for Growth Hormone* and *Growth and Treatment* record forms
 - To improve this data set, changes would be required to the forms that are sent to Canberra, as well as improvements in the way that DoHA enters and stores data.
 - The OZGROW Research Team have advocated that the OZGROW Advisory Committee and the APEG Council are consulted regarding any changes that DoHA plans to make to the information requested on these forms, or to the way that DoHA collects and stores GH patient data.

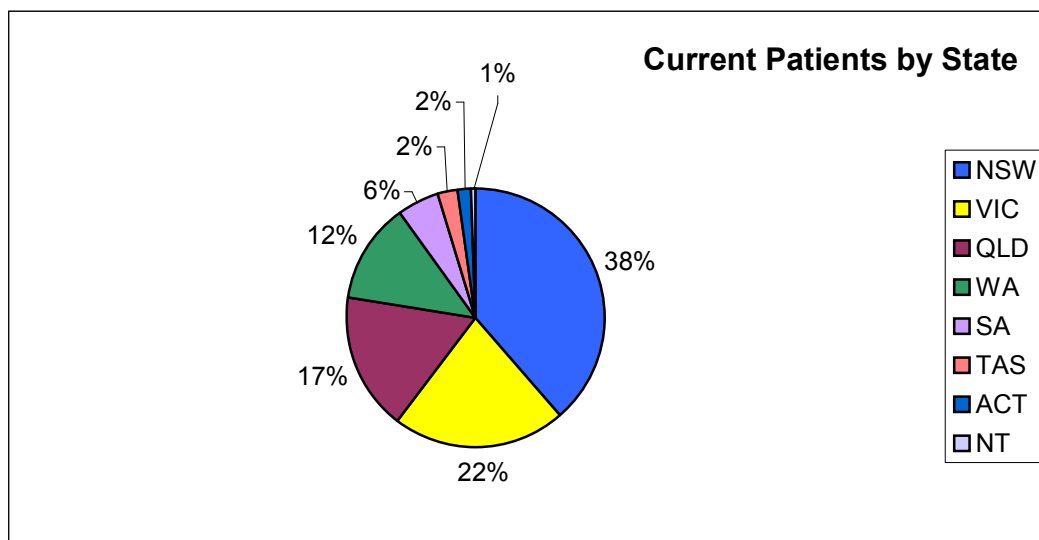
In addition, ongoing liaison with growth centres has been required to improve the quality of data sent into DoHA. For example:

- In 2005/06 it became apparent that many of the growth centres around Australia were no longer using OZGROW diagnosis codes on the DoHA record forms. To allow more accurate conclusions to be drawn from the DoHA data set, it was decided that it would be vital to re-establish a uniform set of diagnosis codes to be used across the various growth centres in Australia.
- The OZGROW Research Team was involved in mailing a paper copy of the OZGROW codes to all major growth centres to ensure that all sites have current access to the codes. In addition, an electronic copy of these codes has been made available on the APEG website at: www.racp.edu.au/apeg/ to assist clinicians to easily access this information.

A brief highlight of some of the key demographic information supplied by DoHA regarding patients currently on GH therapy in Australia is included overleaf.

Demographics of children currently receiving GH therapy in Australia through the government-funded PBAC program - 2006

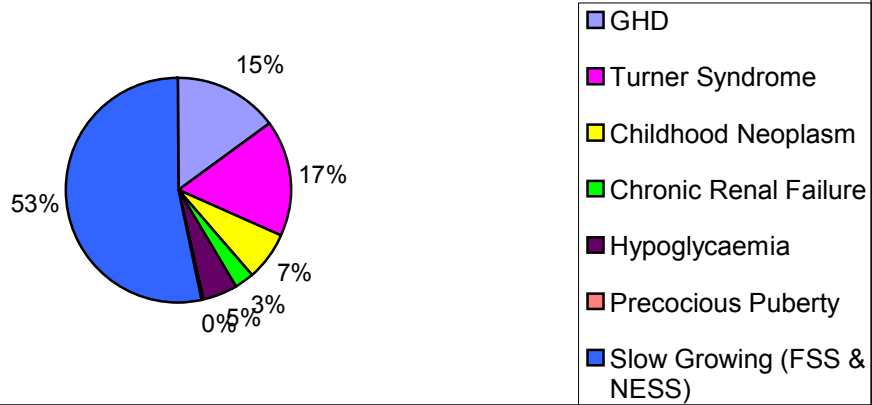
- Number of children currently receiving GH therapy in Australia = 1353.
- Gender of patients currently receiving GH therapy = 54% Male (M:F= 1.17:1)
- Average age (mean +/- SD) at commencement of GH therapy = 7.24 +/- 3.98 years (range 0-18).
- Within Australia, over 75% of patients currently receiving GH therapy originate from New South Wales, Victoria, and Queensland (see diagram). There are an increasing proportion of patients from Western Australia also.



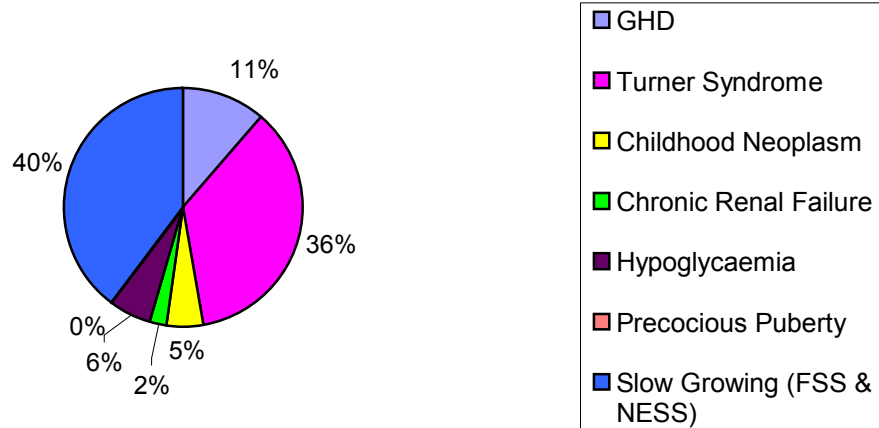
Reason for commencement of GH therapy in Australia

- Criteria for receiving GH therapy via the government funded GH program are listed in the DoHA document *Guidelines for the Availability of Human Growth Hormone (hGH) as a Pharmaceutical Benefit*.
- Greater than 50% of all current GH patients in Australia were commenced on GH therapy under the criterion of being 'slow growing' (i.e. height <1st percentile, according to CDC 2000 growth reference values) (see Figure).
- The 'slow growing' criterion is currently the most common treatment indication for males (65%). It is also the most common treatment indication for females (40%), closely followed by Turner Syndrome (36%).

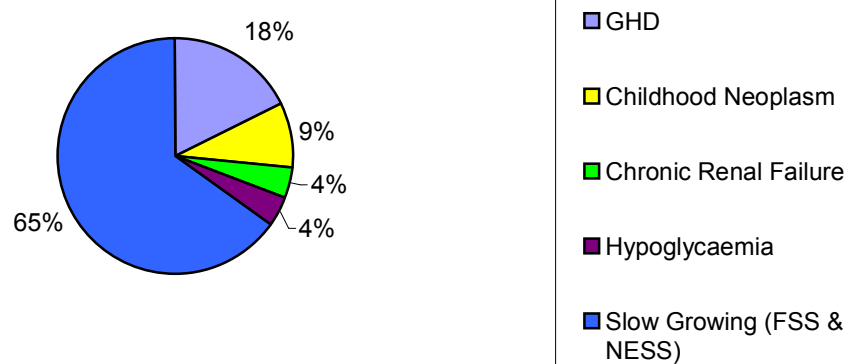
Reason for Commencement of GH Therapy



Reason for Commencement of GH Therapy (Females)



Reason for Commencement of GH Therapy (Males)



Average age (mean +/- SD) at commencement of GH therapy for patients meeting various criteria:

- GHD = 6.80 +/- 4.45 years
 - Females = 5.58 +/- 4.12 years
 - Males = 7.45 +/- 4.51 years*
- Turner syndrome = 7.03 +/- 3.70 years
- Childhood neoplasm = 10.06 +/- 3.10 years
 - Females = 9.92 +/- 3.23 years
 - Males = 10.12 +/- 3.05 years
- Chronic renal failure = 6.32 +/- 3.86 years
 - Females = 4.76 +/- 3.20 years
 - Males = 7.18 +/- 3.97 years*
- Hypoglycaemia = 1.15 +/- 1.42 years
 - Females = 1.06 +/- 1.23 years
 - Males = 1.26 +/- 1.60 years
- Slow growing = 7.69 +/- 3.59 years
 - Females = 7.92 +/- 3.52 years
 - Males = 7.58 +/- 3.62 years

*Gender difference statistically significantly different ($p < 0.001$)

Historical demographics of children who have received GH therapy in Australia as part of the government-funded PBAC program

- Average age (mean +/- SD) at commencement of GH therapy = 8.83 +/- 4.06 years (range 0-19)
 - Females = 8.80 +/- 3.93 years
 - Males = 8.85 +/- 4.17 years
- Average age (mean +/- SD) at cessation of GH therapy = 14.50 +/- 3.09 years (range 0-24)
 - Females = 14.37 +/- 2.65 years
 - Males = 14.61 +/- 3.40 years
- Average duration (mean +/- SD) of GH therapy = 4.91 +/- 3.11 years (range 0-17 years)
 - Females = 4.65 +/- 2.94 years
 - Males = 5.13 +/- 3.24 years

3.2 Data merging

Due to the diverse format of databases used for storing data across Australia and New Zealand, considerable time and effort was spent in 2006 in merging data from various data sources.

At present, the OZGROW data set exists in 2 platforms:

- i) A database of patient information supplied directly from the DoHA in Canberra
 - DoHA has data available on all Australian children receiving GH treatment as part of the government-funded program.
 - All data collected from DoHA are in a single format.
 - Currently, this information is used by the OZGROW Research Team in the primary stages of data analysis.

- ii) A collection of data obtained from the various growth centres throughout Australia and New Zealand
 - Data from various centres remain on separate systems. Therefore, at present, before any data analysis can occur, the relevant raw data need to be extracted from the various database platforms, synchronised, merged, and then stored. Clearly this is a labour-intensive and time-consuming process.
 - Currently, this information is used by the OZGROW Research Team in the later stages of data analysis, when additional information (beyond that collected by DoHA) is needed regarding specific patients, and/or to confirm data generated by the DoHA database.

Ongoing investigation into a more efficient way of collecting/ storing data will continue.

- One possible option would be to introduce a 'new' program in each centre for the specific collection of GH patient data. This would ensure that all data are in a single format (This is currently not a favourable option, due to problems that would be encountered transferring existing patient data onto any new system, but is an option that could be considered).

4. OTHER ACTIVITIES OF 2006

4.1 Presentations:

- Oral presentations
 - Conference posters:
 - Endocrine Society Conference, Boston, June 2006
 - Dodrill PMM, Atkin L-M, Davies PSW. *A comparison of published criteria for determining adult height in girls: Does the criteria used alter the determined height?*
 - Atkin L-M, Dodrill PMM, Davies PSW. *Variability in height response to growth hormone treatment across diagnostic groups.*
 - Conference presentations:
 - APEG Annual Scientific Meeting, Hobart, September 2006
 - Dodrill PMM, Atkin L-M, Davies PSW. *The OZGROW Database 2006.*
 - Other oral presentations:
 - Royal Children's Hospital Grand Rounds, Brisbane, October 2006
 - Davies PSW. *New Australian growth charts.*
 - Pfizer Clinical Nurse Symposium, Adelaide, March 2006
 - Davies PSW. *New Australian growth charts.*
 - Dodrill PMM. *The OZGROW Data Set 2005/06.*
- Written presentations
 - Articles (published):
 - Davies PSW (2007). *Growth charts for use in Australia.* Journal of Paediatrics and Child Health 43 (1-2), 4–5.
 - Articles (in preparation for publication):
 - Final Height
 - Dodrill PMM, Atkin L-M, Davies PSW (2007). *A comparison of published criteria for determining adult*

height in girls: Does the criteria used alter the determined height? (submitted)

- Atkin L-M, Dodrill PMM, Davies PSW. *Variability in height response to growth hormone treatment across diagnostic groups.*
- Cowell CT, Wang M, Bath LE, Werther GA, Dodrill PMM, Atkin L-M, Davies PSW. *Adult height after growth hormone therapy – The OZGROW experience.*
- Turner syndrome
 - Abbott RA, Atkin L-M, Dodrill PMM, Thompsett M, Davies PSW. *Growth hormone treatment in Turner syndrome: Effect of four years treatment in young girls.*
 - Atkin L-M, Abbott RA, Dodrill PMM, Thompsett M, Davies PSW. *Growth hormone treatment in Turner syndrome: Effect of dosage after three years of treatment.*
- APEG newsletter:
 - Dodrill PMM, Atkin L-M, Davies PSW. *Update on OZGROW 2006.*
- Other
 - Growth charts:
 - The development of 1st centile line for height for the new Australian growth charts, based on L, M, S data provided on the CDC website (analysis performed by P.S.W. Davies).
 - Clinician queries:
 - Four queries were received from clinicians. Relevant data were extracted from the OZGROW Database and provided to the requesting clinicians.

4.2 Liaison with Key Stakeholders:

- OZGROW Advisory Committee
 - Monthly meetings between the Chair of the OZGROW Advisory Committee and the OZGROW Research Team.
 - Quarterly teleconferences between the OZGROW Advisory Committee and the OZGROW Research Team.

- DoHA Canberra
 - 2 visits to Canberra for the purposes of:
 - (a) Negotiating access to data held by the DoHA relating to patients receiving GH therapy in Australia.
 - (b) Assisting DoHA to transition their existing database over to using the CDC 2000 growth reference data set.
 - (c) Liaising with DoHA regarding the establishment of a new DoHA database platform.

- Growth Centres
 - Visits to the Children's Hospital at Westmead and the Sydney Children's Hospital to organise access to data held on hospital databases relating to patients on GH therapy.

- Growth Hormone Advisory Committee (GHAC)
 - 2 meetings with representatives of GHAC and the OZGROW Advisory Committee to investigate ways in which the OZGROW Database can be utilised to inform decisions made by GHAC.

- Adverse Drug Reaction Advisory Council (ADRAC)
 - Correspondence to obtain adverse event data relating to the use of GH therapy held by ADRAC.

- Pharmaceutical Benefits Advisory Council (PBAC)
 - 1 visit to Sydney for the purpose of discussing possible GH treatment criteria to be used for patients with Prader Willi syndrome, if approval is given for this group to be eligible for GH treatment via the PBAC scheme (PSW Davies was involved in this consultative process in his

role as research advisor to the Australian GH Advisory Committee and Chair of the Prader Willi Association committee in New Zealand).

- Australasian Paediatric Endocrine Group (APEG) website
 - The OZGROW Research Team has been involved in organising the following links to be included on the APEG website:
 - DoHA website (to allow *Application for Growth Hormone* forms to be downloaded), and
 - TGA website (to allow ADRAC forms to be downloaded).
 - The OZGROW Research Team has also been involved in organising other relevant information to be included on the APEG website, including:
 - Copies of the new Australasian growth charts,
 - The raw values for the 1st centile for height organised by gender and age, and
 - Copies of the OZGROW diagnosis codes.

- Pharmaceutical companies
 - The OZGROW Research Team has spent much time liaising with the companies who supply GH patient databases to advocate for greater assistance for clinicians having problems with their database, and for modified/ improved database functions to reflect the needs of Australian clinicians (e.g. the ability to automatically generate reports suitable for sending to DoHA with *Application for Growth Hormone* and *Growth and Treatment* record forms).

5. DIRECTIONS FOR 2007

The major goals for the OZGROW Research Team in 2007 are:

- To continue to collect data for the OZGROW Database, both:
 - Directly from growth centres, and
 - Via DoHA, Canberra.

- To continue to work on merging patient data provided in different formats, while investigating more efficient options to allow data to be collected in the same format across the various growth centres.

- To continue with growth analyses on data within the OZGROW Database. Specifically to:
 - Complete research articles currently in preparation for publication.
 - Continue with growth studies recently commenced.
 - Commence new growth studies.

- To utilise the additional funding provided in the 2007 OZGROW budget for a 0.2 FTE administrative officer position to appoint a new staff member, Marea Fox, to take on administrative duties, and allow the OZGROW Research Team to focus on research activities.

- To utilise the additional funding provided in the 2007 OZGROW budget for a 0.2 FTE senior researcher position to appoint an experienced researcher and/or relevant Endocrine Fellows to assist with the completion of existing projects and manuscripts, and to assist with new upcoming projects.