



The Australia New Zealand Therapeutic Products Authority (ANZTPA)

Regulation of Human Cellular and Tissue Therapies (HCTs)

May 2007



Presentation Outline

Welcome

Overview of ANZTPA and the Joint Regulatory Scheme

Regulation of HCTs

Next Steps

Questions for the panel



ANZTPA Consultation

Phase 1 23 May 2006

- Medicines Rule
- Medical Devices Rule
- parts Administration and Interpretation Rule



ANZTPA Consultation

Phase 2 18 October 2006

- Medicines Scheduling Provisions
- consultation paper on regulation of Blood
- consultation paper on Post-market Product Vigilance
- Advertising Rule
- consultation paper on regulation of Clinical Trials



ANZTPA Consultation

Phase 3 4 April 2007

- release 3 ANZTPA Orders for Medical Devices
- IVD Rule incorporated in Medical Devices Rule
- consultation paper on Human Cellular and Tissue Therapies (HCTs)



Australia New Zealand Therapeutic Products Authority – Structure and Governance



ANZTPA objectives:

- Establish as a world-class regulatory agency to be responsible for the effective and efficient administration of the Scheme and to be accountable to both Parties
- Safeguard public health and safety in Australia and New Zealand
- Regulate the quality, safety, and efficacy or performance of medicines, medical devices, blood and tissue products
- Avoid barriers to trade except where necessary
 - to safeguard public health or safety, or
 - to fulfill' international obligations



PEST Analysis of ANZTPA

Political

- CER and TTMRA

Economic

- Duplication of work, cost-effectiveness

Social

- Similarities of regulatory culture

Technical

- Same standards, same decisions



Australian Government
Department of Health and Ageing
Therapeutic Goods Administration



Australian Government
Department of Health and Ageing
Therapeutic Goods Administration



Consultation Paper

The Regulation of Human Cellular and Tissue Therapies under the Australia New Zealand Therapeutic Products Authority (ANZTPA)

<http://www.anztpa.org/consult/hct.pdf>

Types of therapeutic goods

Biologicals

- Historically, therapeutic goods have been defined through their *mode of action*
- This has led to a classification based on *medicines* and devices
- As therapeutic goods have been sourced from living tissues, the concept of a new type of therapeutic goods – *biologicals* – has evolved internationally
- Biologicals include blood and related products, biotechnology products, vaccines and cell and tissue products
- The ANZTPA will include a new *Office of Biologicals*, charged with overseeing these products, under a *separate Rule*



Current regulation of cells and tissues

- With some exceptions, cells and tissue derived therapeutic goods are already regulated in Australia and New Zealand
- As only medicines and devices are currently defined and recognised in regulatory frameworks, this means that cells and tissues are regulated as such
- A number of factors make this inappropriate



Regulation and emerging biological therapies

- Cellular and tissue therapies possess crucial differences from conventional pharmaceuticals
- Despite these differences, new regulatory paradigms have been developed for these for these therapies in North America and Europe
- These paradigms hinge on
 - Infectious disease risk
 - Intensity of processing
 - Promotional claims



Background

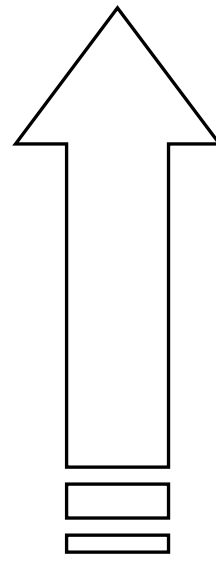
- Australian Health Ministers Conference requested TGA to develop new framework in June 2002
- Public consultations in 2003 and 2004
- Australian Health Ministers Advisory Council and Australian Health Ministers Conference agreed framework for Classes 2, 3 and 4 in 2006
- Incorporated into the ANZTPA proposal in March 2006
- To be incorporated into framework for Biologicals in ANZTPA



a proposed regulatory scheme

Increasing regulatory review and compliance

| |
|--|
| <p>Class 4</p> <ul style="list-style-type: none"> • Banked & processed, non-homologous function |
| <p>Class 3</p> <ul style="list-style-type: none"> • Banked & processed, homologous function |
| <p>Class 2</p> <ul style="list-style-type: none"> • Banked & unprocessed |
| <p>Class 1</p> <ul style="list-style-type: none"> • Unbanked & unprocessed • Hospital based manufacture |



Increasing risk/benefit ratio

- Regulation related to level of risk
- Factors determining risk level:
 1. Level of processing - manipulation
 2. Environment – manufacturing vs medical
 3. Usage – homologous vs non-homologous

- **Class 1**
 - Unbanked & unprocessed/unmanipulated
 - Solid organs (CURRENTLY SUBJECT TO CONSIDERATION BY GOVERNMENTS)
 - Hospital manufacture
 - HPCs for autologous/directed transplant by BMT units (IRRESPECTIVE OF SOURCE)
- **Class 2**
 - Banked & unprocessed/unmanipulated
 - Banked tissues – bone, skin etc
- **Class 3**
 - Banked & processed/manipulated, homologous function
 - Pancreatic islets
- **Class 4**
 - Banked & processed/manipulated, non-homologous function
 - MSCs
 - Cellular vaccines
 - All xenotransplantation products

HCTs may only be imported,
exported or supplied with a

Product Licence

It is proposed that HCTs may only be:

- imported into Australia and New Zealand; or
- exported to a third country from Australia and New Zealand; or
- supplied in Australia and New Zealand

by, or with the consent of, the holder of a **product licence** issued by the Authority, unless specifically exempted.



EXEMPTIONS AND EXCEPTIONS

Single surgical procedures

It is proposed that the following procedures would be exempt from regulation by the Authority:

- single surgical procedures performed on one patient (autologous transplant) such as bone grafts and vein transplants; and
- single surgical procedures involving two patients (non-autologous or allotransplant) such as organ donation from a live donor within the same facility as the transplant recipient.



Exemptions and Exceptions

Special Access

Where HCTs are subject to a product licence, the supply of unapproved (as distinct from non-compliant) product may be done under special access provisions similar to medicines, blood products and medical devices.

Clinical trials

It is proposed that clinical trials utilising HCTs be regulated in a manner consistent with clinical trials for other types of products. <http://www.anztpa.org/consult/clintrials.htm>



Application for Product Licence – Class 1

Applicants will be required to attest to compliance with relevant Standards as agreed through the submission to the Authority of a Declaration.

The proposed Declaration would require the applicant to

- specify the Class 1 HCT for which approval is sought,
- specify the Standard to be applied in relation to the Class 1 HCT and
- specify the testing laboratory to be used.

By completing the declaration the organisation would be acknowledging the implementation of the Standard.

The Standard for HCTs would be based on the appropriate parts of standards already in place for these products.

Class 1 HCT Product Licence

- The application for a Class 1 HCT Product Licence would include the submitting of an appropriately completed Declaration attesting compliance with the relevant Class 1 Standard(s).
- The Class 1 HCT Product Licence would detail the types of HCTs for which the licence has been issued and the Standards that must be complied with.



Application for Product Licence – Class 2

Applicants will be required to demonstrate compliance with:

- (a) Manufacturing Principles; and
- (b) relevant Standards for each tissue type



Currently licenced tissue banks

- Banks that are *currently* in compliance will *not* require another initial audit in order to demonstrate compliance.
- Banks will however be responsible for ensuring, that the Manufacturing Principles are observed.
- A new cGMP for banked tissues will guide the Authority and the sector's ongoing compliance level with the manufacturing principles



Compliance with HCT Standards

Tissue Banks will also need to demonstrate compliance with relevant Standards for each tissue type through the submission to the Authority of a ***Standards file*** for each tissue type.

Applicants will be required to:

- (a) demonstrate compliance with Manufacturing Principles (as for Class 2) – as evidenced by the Authority issuing a Manufacturing Licence in respect of the facility in which the cells or tissue will be manufactured; and
- (b) demonstrate that the particular HCT is safe, efficacious and of high quality. This will require the applicant to submit a **Dossier** to the Authority.



Product Licence – Class 3 Data requirements - Dossier

- The Dossier will need to show evidence of compliance with relevant Standards and that the HCT is ***safe, efficacious and of high quality.***
- The Dossier will need to include all manufacturing, pre-clinical and clinical information to support the product.



Application for Product Licence – Class 4

- Same requirements as Class 3
AND
- More detailed and relevant clinical data and analysis
- This data will include clinical trials as described in the Clinical Trial consultation paper – CTA path
- Detailed data requirements will be agreed with sponsors, depending on the nature of the product
- Guidance will be developed with the input of industry and independent experts



ADVERSE EVENT REPORTING

- Reportable events - occurrences that are contrary to the principles of the mandated Standards, or the quality, safety and efficacy requirements relevant to the therapy.
- A Guideline will be developed regarding reporting procedures and responsibilities in relation to the different classes of HCTs.
- Principles similar to those proposed in the Consultation Paper on Product Vigilance in the ANZTPA.
<http://www.anztpa.org/consult/consdocs2.htm>



Summary – the old and the new

| | Current Aus + NZ (current) | ANZTPA (proposed) | Comments |
|------------|---|--|---|
| Class 2 | <p><u>Aus + NZ</u> Manufacturers licensed under code of GMP for human blood and tissues</p> <p><u>Aus</u> Product quality documentation subject to auditor review</p> | <p>Product license as with all therapeutic goods under ANZTPA oversight:</p> <ul style="list-style-type: none"> ●Manufacturers licensed under quality system principles ●Product approval subject to standards file review aligning product quality and safety to specific product standards | <ul style="list-style-type: none"> ●cGMP for blood and tissues removed as manufacturing principle at the request of the industry (cGMP for blood and tissues was developed primarily for the ARCBS) ●Product standards chosen and developed by the industry ●Product licensing process will allow approval and withdrawal from the market of specific tissues without the need to suspend license to manufacture (as at present) |

| | Current Aus + NZ (current) | ANZTPA (proposed) | Comments |
|------------|--|---|---|
| Class 3 | <p><u>Aus only</u> Full pre-market review for safety, quality and efficacy, manufacturing licensure and product registration.</p> <p><u>Aus +NZ</u> Different codes of GMP and manufacturing principles, depending on whether tissue has a drug or device action</p> | <ul style="list-style-type: none"> • Same level of oversight. Manufacturing principles guided by cGMP. • Assessment of efficacy will be on a case by case basis depending on the risk benefit profile | <ul style="list-style-type: none"> • No significant change in level of regulation. • Change in manufacturing principle requested by industry as products do not fall comfortably into drug or device categories. • New framework will allow a more flexible approach to efficacy assessment for eg small patient numbers |



| | <p>Current Aus + NZ (current)</p> | <p>ANZTPA (proposed)</p> | <p>Comments</p> |
|-----------------|---|--|---|
| <p>•Class 4</p> | <p><u>Aus + NZ</u> Full pre-market review for safety, quality and efficacy, manufacturing licensure and product registration.</p> <p><u>Aus + NZ</u> Different codes of GMP and manufacturing principles, depending on whether tissue has a drug or device action</p> | <ul style="list-style-type: none"> •Same level of oversight. •Manufacturing principles guided by cGMPs. •Full assessment of efficacy and therapeutic claims | <ul style="list-style-type: none"> •No change in level of regulatory oversight. • All these products are currently regulated as medicines with full clinical trial and registration requirements. |

| Aspects | Current Aus + NZ (current) | ANZTPA (proposed) | Comments |
|---|---|---|-----------------------------------|
| Clinical development (for Classes 3 & 4) | <p><u>Aus</u> CTN and CTX scheme, according to institution choice, except for genetic manipulation where CTX is mandatory</p> <p><u>NZ</u> Section 30 exemption if defined as a medicine SCOTT +/- GTAC</p> | CTA & CTC system | All Class 4 HCTs will require CTA |
| Advice | <p>Australian Drug Evaluation Committee (ADEC), Medical Device Evaluation Committee (MDEC)</p> <p>Therapeutic Goods Committee (TGC)</p> | Specialist biologicals committee (Expert Advisory Committee on Biologicals) – risk management, evaluation standards | External input from specialists |



Next Steps

The Australia New Zealand Therapeutic Products Authority (ANZTPA)



Next Steps

Process

- **New Zealand Bill introduced to Parliament 5/12/2006. Public consultation occurs through Select Committee process**
- **Australian Bill exposure draft released for consultation 2/4/2007, prior to later commencement of Parliamentary process**



Next Steps

Process

Following passage of legislation in both countries

- Agreement ratified**
- ANZTPA and Ministerial Council established**
- Managing Director and Board members appointed**
- Rules and Orders signed and tabled in both Parliaments**
- Rules and Orders come into effect**
- Joint regulatory scheme commences**



Next Steps

Phase 3 Consultation on

- Draft IVD Rule
- Consultation paper on HCTs

closes 13 June 2007



Next Steps

For further information

Go to: www.anztpa.org

Email submissions and/or queries to:

consultation@anztpa.org



Questions for the Panel