



**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)**

**April 2007**

## HOW TO MAKE A SUBMISSION

You are invited to provide written comment on this consultation paper. Submissions can be sent by post or e-mail and, where possible, should be cross-referenced to specific sections set out in this consultation paper. In addition, we encourage you to provide other comments that may assist in the development of the draft Rule for the regulation of human cellular, tissue and emerging biological therapies under the Australia New Zealand Therapeutic Products Authority (ANZTPA).

### Content of submissions

Your submission should include:

- your name and full contact details including: address, telephone number, and if applicable, facsimile and e-mail address;
- the particular issue being addressed;
- relevant evidence and/or examples to support the views expressed; and
- in the case of organisations, the level at which the submission was authorised.

### Confidentiality of submissions

If you wish any information contained in a submission to be treated as confidential, please clearly identify the information and outline the reasons you wish it to be treated as confidential.

### Address for submissions

Electronic submissions should be e-mailed to: [consultation@anztpa.org](mailto:consultation@anztpa.org)

Hardcopy submissions should be addressed to either of the addresses below:

The Project Officer  
c/- Joint Agency Establishment Group  
Therapeutic Goods Administration  
PO Box 100  
WODEN ACT 2606  
AUSTRALIA

The Project Officer  
c/- Joint Agency Establishment Group  
Ministry of Health  
PO Box 5013  
WELLINGTON  
NEW ZEALAND

### Questions relating to submissions

Any questions relating to submissions should be directed to the Project Officer, by e-mail at: [consultation@anztpa.org](mailto:consultation@anztpa.org)

### Deadline for submissions

The deadline for receipt of submissions is **13 June 2007**.

## TABLE OF CONTENTS

|   |    |
|---|----|
| Abbreviations .....   | 4  |
| Part A: Introduction and Purpose of this document.....                        | 6  |
| Part B: Current regulation of HCTs in Australia.....                          | 7  |
| Part C: Current regulation of HCTs in New Zealand .....                       | 9  |
| Part D: Summary of the proposed trans-tasman regulatory framework ...         | 10 |
| Part E: Summary of the proposed new framework for the regulation of HCTs..... | 11 |
| Part F: Classes of HCTs .....   | 15 |
| Part G: Standards.....  | 17 |
| Part H: Types of Product Licences.....  | 18 |
| Part I: Applications for a Product Licence.....                               | 20 |
| Part J: Conditions and other particulars on a Product Licence .....           | 26 |
| Part K: Variation, suspension and revocation of Product Licence.....          | 28 |
| Part L: Manufacture of HCTs .....   | 31 |
| Part M: Advertising and Consumer Information .....                            | 32 |
| Part N: Adverse event reporting .....   | 33 |
| Part O: Exemptions and Exceptions.....  | 35 |
| Part P: Fees and charges .....  | 37 |
| Part Q: Transition provisions .....   | 38 |

## ABBREVIATIONS

|                |   |
|----------------|---|
| AATB           | American Association of Tissue Banks        |
| AHMC           | Australian Health Ministers' Conference     |
| ARTG           | Australian Register for Therapeutic Goods   |
| cGMP           | Code of Good Manufacturing Practice         |
| CTA            | Clinical Trial Assessment                   |
| CTC            | Clinical Trial Certification                |
| HCT            | Human Cellular and Tissue Therapies         |
| OTC            | Over-the-counter                            |
| SAS            | Special Access Scheme (operated by the TGA) |
| TGA            | Therapeutic Goods Administration            |
| TG Act         | <i>Therapeutic Goods Act 1989</i>           |
| TG Regulations | Therapeutic Goods Regulations 1990          |

## Technical terms specific to Human Cellular and Tissue Therapies (HCTs)

|                          |   |
|--------------------------|---|
| Dossier                  | A Dossier is the documentation that applicants will be required to provide to the Authority in support of an application for approval of a Class 3 or Class 4 HCT. The Dossier would include all scientific and technical information to support the design and production of the Class 3 or 4 HCT. Where there are applicable standards, the Dossier will also incorporate information regarding compliance with relevant standards (a Standards File).  |
| HCT                      | All articles containing or consisting of, or derived from, human cells or tissues that are intended for implantation, transplantation, infusion or transfer into a human recipient. (This definition does not include secreted products such as hormones, proteins, urine or milk, but only products consisting of processed or unprocessed whole cells or tissues).  |
| HCT Product Licence      | Under the proposed new trans-Tasman arrangements, a Certificate of Registration or Certificate of Listing will be replaced with a "Product Licence". An organisation will be eligible for an HCT Product Licence (an HCT Product Licence) if they have met the prescribed requirements in relation to safety (as demonstrated by compliance with Standards or technical information) and in the case of Class 2-4 HCTs only, a Manufacturing Licence (as demonstrated by compliance with Manufacturing Principles). |
| Manufacturing Principles | Manufacturing Principles will outline the manufacturing requirements necessary for the manufacture of HCTs. Applicants for Class 2, 3 and 4 HCTs will need to demonstrate compliance with the Principles for the manufacture of the HCTs.   |
| Standards                | The Authority proposes to adopt a number of Standards detailing technical features of specific HCT groups. These standards will be developed in partnership with the sector.  |
| Standards File           | A Standards File is technical information that demonstrates compliance with Standards applicable to the relevant HCT. It is proposed that a Standards File would need to be submitted in support of all applications for approval of Class 2 HCTs and that a Standards File would also form part of the Dossier (as described below) that will be required in support of Class 3 and 4 HCTs.  |

## **PART A: INTRODUCTION AND PURPOSE OF THIS DOCUMENT**

On 10 December 2003 the Australian and New Zealand Governments signed an agreement to establish a joint scheme for the regulation of therapeutic products in the two countries (the Treaty).

The joint regulatory scheme will be administered by a single, bi-national authority, the Australia New Zealand Therapeutics Products Authority (ANZTPA) (the Authority). The Authority will replace the Therapeutic Goods Administration (TGA) in Australia and the Medicines and Medical Devices Safety Authority (Medsafe) in New Zealand and will be accountable to both the Australian and New Zealand Governments.

A framework, comprising Acts in both countries, Rules and Orders, will replace the existing Australian *Therapeutic Goods Act 1989* (the Therapeutic Goods Act), its Regulations and Orders and the existing New Zealand *Medicines Act 1981* (the Medicines Act) and its Regulations.

The purpose of this document is to provide an explanation of the proposed means by which human cell and tissue therapies (HCTs) will be regulated by the new Authority. It is intended that the matters detailed in this document will be included in Rules relating to “Biologicals” of which HCTs will be a part – this is discussed in more detail in the following parts.

Please note that this document is indicative only of the types of matters likely to be addressed in the proposed Biologicals Rules in relation to HCTs.

## **PART B: CURRENT REGULATION OF HCTS IN AUSTRALIA**

The *Therapeutic Goods Act 1989* (the TG Act) currently provides that all devices of human, animal, bacterial or recombinant origin for use in, or on, the body of a person, must be included on the Australian Register of Therapeutic Goods (ARTG). This means that they must have pre-market approval from the TGA and that the manufacturer of such devices must be licensed by the TGA.

However, there are a number of exemptions to this requirement:

- whole organs for transplant are excluded from regulation;
- human tissue for implantation in the human body that is obtained, stored and supplied without any deliberate alteration to its biological or mechanical properties is exempt from the requirements for entry on the Register provided that the Australian institution complies with the current Code of Good Manufacturing Practice – Human Blood and Tissues (cGMP for Human Blood and Tissues). This effectively means that banked tissue (such as heart valves, skin, corneas and bone) is exempt from inclusion on the Register provided that the Australian tissue bank complies with cGMP for Human Blood and Tissues;
- medicines (other than medicines for gene therapy) that are dispensed, or extemporaneously compounded, for a particular person for therapeutic application to that person are exempt from the requirements for entry on the ARTG. Similarly those people that have traditionally developed such medicines are also exempt from the TGA's requirements for licensing of manufacturers – for example:
  - medical practitioners and health care workers are exempt from licensing requirements (and therefore compliance with the cGMP) provided that the “manufacture” of the cell or tissue therapy is for a patient under his or her care (and the medical practitioner himself/herself is developing the therapy); and
  - biomedical engineers, radiochemists and pharmacists in public hospitals are also exempt from licensing requirements provided that the goods produced are for supply in hospitals or public institutions in the same State or Territory.

The TGA has, to date, interpreted the legislation to require that:

- tissue banks are licensed by the TGA and demonstrate compliance with cGMP for Human Blood and Tissues; and

- all people who are “manufacturing and supplying” human tissue or cellular therapies are required to be licensed as manufacturers and the therapy entered on the ARTG. There are, however, a number of exemptions or exceptions to this requirement:
  - if the tissue is an organ – excluded from the legislation;
  - if the tissue is reproductive tissue – excluded from the legislation;
  - if the HCT is custom made (or extemporaneously compounded) for a particular person – no requirement for entering on ARTG;
  - if the “manufacturer” is a medical practitioner, health care worker, pharmacist etc – no requirement to be licensed;
  - if the HCT is for use in the treatment of a particular patient with special needs – patient must be notified to the TGA and supply for the particular case approved (Special Access Scheme - SAS) but no requirement for licensing or registration; and
  - if the HCT is for use in a clinical trial – schemes relating to clinical trials apply (either CTX or CTN).

The existing framework is not currently well adapted to cell and tissue therapies and the main drivers for change have been identified:

- the need to minimise infectious disease risk associated with the use of tissues;
- the need for greater regulatory certainty;
- the desirability of international harmonisation of regulatory requirements;
- the need for greater flexibility to respond to changes in technology; and
- the desirability of adopting a risk based approach to regulation.

Recognising these issues, the Australian Health Ministers’ Conference (AHMC) recommended in July 2002 that the TGA develop a proposal for a new regulatory framework for HCTs.

Since that time the TGA has been developing a proposal for implementation through the new trans-tasman regulatory framework. Extensive consultation on the proposed model has been undertaken in Australia. As noted in the following Part, New Zealand has also been progressing the issue and consulting with stakeholders in New Zealand.

## **PART C: CURRENT REGULATION OF HCTS IN NEW ZEALAND**

Currently the requirements for the safety of whole organs for transplantation are set out in the *Guidelines for Organ and Tissue Donation*. These Guidelines have no legal status. The Guidelines cover the criteria used to identify a potential donor and the criteria that exclude a potential donor (for example, fungal or viral infections or HIV).

Tissue banking providers currently operate under voluntary codes of practice and standards. Most agencies in New Zealand, from national organisations to local hospitals, appear to have adapted or followed the American Association of Tissue Banks (AATB) standard. The lack of formal regulation of tissue-based therapies is unusual internationally.

Public consultation in 2004 on proposals to regulate human cells and tissues for therapeutic use raised the follow issues:

- the lack of formal requirements impacts on the ability to assure the safety of therapeutic products, such as whole organs for transplantation and the ability to track the use of a product should an adverse event occur;
- the lack of formal international harmonisation which has implications for the sharing of whole organs between Australia and New Zealand;
- ongoing developments in new technology and changes to therapies. For example, xenotransplantation or stem cell technology present new ethical and safety challenges; and
- ethical consideration of research and innovative practice proposals is a core part of the health and disability sector. However ethical issues have arisen, for example, in relation to the commercial use of tissue.

As a result of this consultation process, the New Zealand Government has proposed that the therapeutic uses of human tissue would be regulated under the Joint Therapeutic Products scheme to be administered by the ANZTPA.

This means that tissue-based therapies would be regulated under a risk-based system where the level of regulatory control of a therapeutic product is based on the relative safety of the product and the seriousness of the condition for which it would be used. The auditing and licensing of tissue banking services and high-risk tissue-based therapies are essential public health activities that will ensure safety requirements are met.

Where a cellular therapy has been used in a clinical trial, Medsafe has regulated the product as a medicine and required the manufacturing site to be audited and licensed to cGMP.

## PART D: SUMMARY OF THE PROPOSED TRANS-TASMAN REGULATORY FRAMEWORK

The new Authority will regulate the import of therapeutic products into Australia and/or New Zealand, export of therapeutic products from Australia and/or New Zealand and the supply, manufacture and promotion of therapeutic products in Australia and/or New Zealand, and associated activities.

The new regime will be based around a system of licensing whereby a licence holder will be the person or entity in Australia or New Zealand with the legal responsibility for a therapeutic product that is imported into, supplied in or exported from Australia and/or New Zealand.

Article 1 of the Treaty defines 'therapeutic product' for the purposes of the joint scheme. This definition includes the following, all of which will be regulated under the joint scheme:

- prescription medicines;
- over-the-counter (OTC) medicines (including most sunscreens);
- complementary medicines;
- human blood and blood components;
- cellular and tissue therapies;
- medical devices (including in vitro diagnostic devices, sterilants and instrument grade disinfectants); and
- other products meeting the definition of therapeutic product (or declared in the Rules to be therapeutic products).

A framework, comprising Acts in both countries, Rules and Orders, will replace the existing Australian Therapeutic Goods Act, its Regulations and Orders and the existing New Zealand Medicines Act and its Regulations.

**Acts** in both countries will contain the broad regulatory matters and obligations that must be contained in primary legislation, including criminal offences and penalties. Each Act will recognise the Authority as the regulator of therapeutic products for that country, and will give effect to the regulatory decisions of the Authority made through its Managing Director.

A Ministerial Council, comprising the Australian and New Zealand Ministers of Health, will make a single set of **Rules** (analogous to regulations in the current Australian and New Zealand systems). These Rules will contain much of the detail of the regulatory requirements. The requirements for medicines, medical devices, biologicals and therapeutic products that are not medicines, medical devices or biologicals will be set out in separate parts of the Rules.

The Managing Director of the Authority will make **Orders** in relation to technical matters such as standards, manufacturing principles and packaging and labelling requirements.

# **PART E: SUMMARY OF THE PROPOSED NEW FRAMEWORK FOR THE REGULATION OF HCTS**

## **Classification of HCTs**

It is intended that:

- there be four classes of HCTs with varying levels of regulation applying, based on a risk benefit analysis of the types of HCTs;
- the four classes be defined as follows:

### ***Class 1***

It is proposed that Class 1 HCTs be defined to include HCTs which are:

- (a) unbanked and unprocessed; and
- (b) produced in hospital units for direct transfer to patients other than through a single surgical procedure.

The issue of the types of HCTs that should be included in Class 1 (including whether organs and reproductive tissue should be regulated under Class 1) is subject to further consideration and agreement by governments in Australia and New Zealand.

### ***Class 2***

A tissue or cell that is stored, maintained or preserved for future use and:

- (a) is not a Class 3 or 4 HCT; and
- (b) is not for direct transfer from donor to recipient.

### ***Class 3***

A cell or tissue processed in a manner that may alter the structure and properties of the cell or tissue but does not purposefully alter the biological activity.

### ***Class 4***

A cell or tissue processed:

- (a) so that the biological properties are deliberately manipulated; or
- (b) for a purpose for which the cell or tissue is intended to be used is not its usual biological function.

## **Level of regulation to be applied to each class**

It is proposed that the level of regulation applied to HCTs will be as follows:

- ***Class 1: Proposed declaration of compliance with relevant Standards***

This is subject to further discussion and agreement with all jurisdictions. One option is that an applicant be required to attest to compliance with relevant mandatory Standards relating to infectious disease risk, through the submission to the Authority of a Declaration. The Standards will be based on existing industry Standards.

- ***Class 2: Compliance with Standards and Manufacturing Principles***

Applicants for a Class 2 HCT Product Licence will be required to:

- (a) demonstrate compliance with Manufacturing Principles. Compliance will be evidenced by the Authority issuing a Manufacturing Licence in respect of the facility in which the tissue will be banked; and
- (b) demonstrate compliance with relevant Standards for each tissue type, through submissions to the Authority of a Standards File.

If both of these requirements are met, the Authority will issue a Class 2 HCT Product Licence for the relevant tissue type to the applicant.

- ***Class 3: Compliance with Standards and Manufacturing Principles and demonstration of safety, quality and efficacy***

Applicants for a Class 3 HCT Product Licence will be required to:

- (a) demonstrate compliance with Manufacturing Principles (as per 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.

If the applicant meets both of these requirements the Authority will issue a Class 3 HCT Product Licence to the applicant for the particular HCT.

- ***Class 4 – As for Class 3 except more detailed data required***

As for Class 3 except that the Dossier will also need to contain relevant clinical data and analysis.

## Exemptions and exceptions

It is proposed that the legislation include exemptions from the regulatory requirements described above for:

- single medical procedures. It is proposed that the following medical 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;
  - 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.
- exceptional release/acceptance. It is proposed that the Authority will set standards that must be complied with by organisations proposing exceptional release/acceptance of HCTs (for example, HCTs that show evidence of an infectious disease but no alternative is available for the treatment of a life-threatening condition).

## Adverse events reporting

It is proposed that the Authority will require each licence holder to have an appropriate system of product vigilance in place to assure licence holder responsibility and liability for its products on the market and to ensure that appropriate action can be taken when necessary.

Specific guidance will be developed in relation to HCTs to define what events will need to be reported to the Authority (with advice on a voluntary or mandatory basis) and the timeframes for reporting.

## Clinical Trials

It is proposed that the clinical trial regulatory arrangements in relation to HCTs will be based on the same risk-managed principles that are also proposed to apply to the medicines and medical devices. As with the current Australian and New Zealand schemes for clinical trials, the proposed ANZTPA Clinical Trial Assessment (CTA) and Clinical Trial Certification (CTC) schemes will continue to require all clinical trials conducted in either country to adhere to relevant ethical standards, as well as meet international standards of Good Clinical Practice. It is intended that trials with Class 4 human cells or tissues will normally follow the CTA route. Further information regarding the proposed clinical trial regulatory arrangements under ANZTPA is outlined in the Consultation Paper *Proposed clinical trial regulatory arrangements under the Australia New Zealand Therapeutic Products Authority*, a copy of which is available on the ANZTPA website at <http://www.anztpa.org/consult/clintrials.htm>.

## **Implementation**

It is proposed that the new regulatory framework for HCTs be implemented as part of ANZPA.

## **PART F: CLASSES OF HCTS**

### **Basis for classes of HCTS**

In summary, it is proposed that:

- HCTs will be a type of “Biological” (separate to medicines and medical device but a separate class of therapeutic product);
- the level of regulation imposed will be commensurate with the risks posed by the therapies to the individual and the community;
- there will be various classes of HCTs.

### **Classes of HCTS**

The types of HCTs proposed to fall into each class are as follows.

#### Class 1

HCTs which are:

- (a) unbanked and unprocessed; and
- (b) produced in hospital units for direct transfer to patients other than through a single surgical procedure.

#### Class 2

A tissue or cell that is stored, maintained or preserved for future use; and

- (a) is not a Class 3 or 4 HCT; and
- (b) is not for direct transfer from donor to recipient.

Example:

- Banked bone, skin
- Banked cord blood

#### Class 3:

A cell or tissue processed in a manner that may alter the structure and properties of the cell or tissue but does not purposefully alter the biological activity.

Examples:

- Islet cells disaggregated from the pancreas
- Autologous chondrocyte implants

#### Class 4:

A cell or tissue that is processed so that the biological property(ies) is/are deliberately manipulated or used for a purpose that is not the usual biological function of the cell or tissue.

Examples:

- Cells subject to genetic manipulation
- Xenotransplantation where permitted
- Blood stem cells when used for myocardial repair

## **PART G: STANDARDS**

It is proposed that the Authority may determine Standards for Biologicals (including HCTs) and that these will be set out in Orders. Advice on Standards will be sought from an Expert Advisory Committee on Biologicals.

All Biologicals must conform to all relevant Standards except with the written consent of the Authority. For example, HCTs must conform to:

- a core set of standards relating to infectious disease risk – all classes of HCTs will be expected to comply with these Standards;
- additional subject specific Standards. Such subject specific standards may be based partly or wholly on existing industry standards or international standards;
- Standards relating to quality management systems for the manufacture of HCTs.

## **PART H: TYPES OF PRODUCT LICENCES**

### **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 written approval of, the holder of a product licence issued by the Authority, unless specifically exempted.

### **Other types of Product Licence**

In addition to the four broad categories of product licence, the Authority may issue (in relation to any class of HCT):

a provisional product licence - Provisional product licences may be granted for HCTs to be used in the prevention or treatment of significant or life-threatening illnesses and where, based on the data provided, the Managing Director is satisfied that the HCT is likely to provide meaningful therapeutic benefits to patients over existing treatments. This allows limited access to an HCT where the potential benefit is considered greater than the risk of non-treatment.

- an export only product licence - An applicant intending only to export a product from Australia and/or New Zealand to a third country may obtain a special type of product licence, an 'export only product licence', in respect of the product; or
- a licence applying only to one country - A licence with a condition of supply for only one country will be issued only in those exceptional circumstances where the Authority deems such a restriction necessary.

In all cases, a product licence for an HCT will only be granted on the basis of an application submitted to the Authority which demonstrates that the potential risks are outweighed by the therapeutic benefit of the HCT. In general, the licence issued will be for supply in both countries.

As part of its assessment of the application, the Authority will also need to approve product information documents, labelling and in some cases certifications by the applicant before a product licence can be granted.

## **Separate and distinct products**

Generally, a separate product licence will be issued for each HCT. The circumstances in which an HCT is a new product (i.e. separate and distinct from other therapeutic products and requiring a new licence), will depend on the classification of the HCT and the nature of the difference or change.

## ***Grouping of HCTs on a product licence***

In certain circumstances it will be possible to 'group' more than one HCT on the same product licence. The circumstances in which HCTs can be grouped will vary depending on the type of product and will be set out in Orders.

## ***Ancillary products***

It is proposed that the safety and quality of a medical device or a medicine ancillary to the HCT be verified in accordance with the requirements for medical devices or medicines, and the ancillary action of the device or medicine must be verified having regard to the intended purpose of the HCT before a product licence can be issued.

## **PART I: APPLICATIONS FOR A PRODUCT LICENCE**

To obtain a licence for any Biological (including HCTs), the applicant will be required to submit an application to the Authority. The application is to be in a form approved by the Authority and accompanied by the prescribed fee. The application must not contain any false or misleading information.

While the general process for obtaining a product licence will be the same for all Biologicals, the data requirements will differ depending on the type of Biological (for example, HCTs compared to Blood) and the classification of the product (i.e. Class 1 HCT compared to Class 2, 3 or 4).

### **A. Applications for Class 1 HCTs**

If the option of attesting to a Standard is chosen, then applicants will be required to attest to compliance with relevant Standards as agreed with the Authority relating to infectious disease risk, through the submission to the Authority of a Declaration.

The proposed declaration would be a very simple document, requiring 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 simply be acknowledging the implementation of the standard and attesting that the required processes for minimising infectious disease risk are being followed.

#### Standard for Class 1 HCTs

The Standard for HCTs would be based on the appropriate parts of standards already in place for these products. As the focus of regulatory oversight for Class 1 HCTs will focus on infectious disease risk, it may be that the Standard mandated by the ANZTPA would be part of broader standards for professional practice with 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.

## **B. Applications for Class 2 HCTs**

Applicants for a Class 2 HCT Product Licence (tissue banks) will be required to demonstrate compliance with:

- (a) Manufacturing Principles. Compliance will be evidenced by the Authority issuing a Manufacturing Licence in respect of the facility in which the tissue will be banked; and
- (b) relevant Standards for each tissue type through the submission of an appropriate Standards File.

### Compliance with Manufacturing Principles

The Manufacturing Principles will cover:

- the standards to be maintained in the manufacture of the HCTs;
- the premises and the equipment to be used;
- procedures for quality assurance and quality control;
- the qualifications and experience required of people employed in the manufacture of the HCTs;
- the manufacturing practices to be employed; and
- other manufacturing matters relevant to the quality, safety and efficacy of the HCT.

A new manufacturer will be required to lodge an application for a Manufacturing Licence to the Authority and must be able to demonstrate compliance with the Manufacturing Principles. The Authority will also audit the site at which the activity will be occurring in order to assure compliance with the Principles.

Tissue banks that are currently in compliance with the current cGMP for Human Blood and Tissues will not require another initial audit in order to demonstrate compliance. The tissue banks will however be responsible for ensuring, on an ongoing basis, that the Manufacturing Principles are observed.

### 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.

### Class 2 HCT Product Licence

Once the Authority is satisfied that application requirements are met and that the applicant has demonstrated compliance with the Manufacturing Principles and the relevant HCT Standards, the Authority will issue to the applicant a Class 2 HCT Product Licence for the relevant tissue type.

### **C. Applications for Class 3 HCTs**

Applicants for a Class 3 HCT Product Licence 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.

#### 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 scientific and technical information to support the product. Where there are applicable Standards, the Dossier would also include detail regarding compliance with relevant Standards.

#### Class 3 HCT Product Licence

Once the Authority is satisfied that the application requirements have been met and that the applicant has demonstrated compliance with the Manufacturing Principles and that the HCT is safe, efficacious and of high quality, the Authority will issue the applicant with a Class 3 HCT Product Licence for the relevant HCT product.

### **D. Applications for Class 4 HCTs**

Applicants for a Class 4 HCT Product Licence will be required to:

- (a) demonstrate compliance with Manufacturing Principles (as per Class 3) 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.

If the applicant meets both of these requirements and application requirements are satisfied, the Authority will issue the applicant with a Class 4 HCT Product Licence for the relevant HCT product.

The only difference between the requirements in relation to Class 3 HCTs and Class 4 HCTs is that the Dossier in respect of a Class 4 HCT will also need to contain relevant clinical data and analysis.

## **E. Applications for Export Only HCTs**

In order to obtain a licence for HCTs intended only for export from Australia and/or New Zealand to a third country, the person will be required to submit to the Authority an application in a form approved by the Authority.

In the application, the applicant will be required to make certifications in relation to the HCTs.

These will be set out in the legislation and will include certifications that:

- the HCT is intended only for export from Australia and/or New Zealand to a third country and will not be supplied in Australia or New Zealand;
- the HCT is safe for the purposes for which it is to be used;
- the HCT conforms to Standards (if any) applicable to the HCT;
- the HCT complies with prescribed criteria for quality and safety;
- if the HCT has been manufactured in Australia or New Zealand, each step in the manufacture of the HCT has been carried out by a person who is the holder of a licence or approved to carry out that step (unless the HCT or manufacturer is exempt from this requirement);
- the applicant holds information or evidence to support any claim that the applicant makes relating to the HCT other than where a contract exists between the exporter and the overseas importer which states that the exporter is not responsible for substantiation of these claims;
- the applicant holds data to demonstrate that the product specifications will continue to be met for the period of the shelf life under the nominated storage conditions other than where a contract exists between the exporter and the overseas importer which states that the exporter is not responsible for nominating the shelf life of the HCT;
- the applicant holds product specifications and draft or actual labels for the HCT;
- where licensed for export from:
  - Australia – the HCT does not contain a substance the exportation of which is prohibited under Australian Customs legislation; or
  - New Zealand – the HCT does not contain a substance the exportation of which is prohibited under New Zealand Customs legislation; and
- the information included in, or with, the application is correct.

In certain circumstances, it will also be necessary for the applicant to obtain certifications from the Authority, prior to submitting the application. These circumstances will be set out in the legislation and include, for example:

- if a step in the manufacture of the HCT has been carried out outside Australia or New Zealand, the Authority must have certified that the manufacturing and quality control procedures used in each such step are acceptable (unless the HCT or manufacturer is exempt from this requirement); and

- if an export-only HCT contains any ingredient of human or animal origin in respect of which the Authority considers that there is a safety risk associated with its use, the applicant must have obtained from the Authority, before the application is lodged, a certificate that the ingredient is acceptable to the Authority (subject to any specified condition) for use in an HCT.

As for other product licences, at any time after a product licence has been issued for an export only HCT, the Authority may undertake an audit, evaluate the quality, safety and efficacy of the HCT or conduct a risk assessment of the HCT.

## **F. Timeframes for Assessment**

The timeframes for the granting of product licences for Class 1, Class 2, Class 3 and Class 4 HCTs are still under consideration. They will be similar to the timeframes used to review products of a similar level of complexity in the medical devices and medicines frameworks.

It is proposed that applications for product licences for Class 3 and 4 HCTs will be accepted or rejected for evaluation within 40 working days of receipt. If the application is accepted for evaluation, a decision to grant or to refuse a product licence will be made within 255 working days of receipt of the application.

An applicant will be notified within 20 working days of a decision to grant a licence.

These timeframes are maximum timeframes and it is anticipated that in the majority of cases timeframes would be considerably shorter.

The penalty to the Authority for not completing applications within statutory timeframes will be a forfeit of 25% of the evaluation fee to the applicant.

It is proposed that the Authority will have the facility to give priority to the evaluation of licence applications for important novel HCTs where it is in the interest of public health to do so.

The circumstances in which priority status may be assigned will include when a new HCT is intended for the treatment or diagnosis of a life-threatening or otherwise severely debilitating disease, disorder or condition or there is a need for supply in urgent situations (e.g. public health emergency).

Priority will only be given if the treatment potentially offers a major advance on currently available therapies.

## **G. Data Protection**

It is proposed that provisions will be included to protect data from “unfair commercial use” or disclosure. In practical terms, data submitted with an application to licence a new therapeutic product should be protected from use by a third party for a period of five years.

When evaluating a Biological for a product licence, the Authority must not use information regarding another Biological if that information is protected.

## **PART J: CONDITIONS AND OTHER PARTICULARS ON A PRODUCT LICENCE**

### **A. General particulars**

The product licence document will provide a summary of the particulars of the product that is/are the subject of the licence and set out or refer to the conditions, subject to which the licence has been granted. The product licence will include:

- the product licence identifier;
- the date the product licence was issued;
- the dates and details of variations to the licence (if applicable);
- the country(ies) in which the product licence is valid;
- particulars about:
  - the licence holder;
  - the product;
  - the manufacture of the product;
  - the intended use of the product;
- the conditions subject to which the product licence is granted; and
- other information relevant to the issuing of the licence.

### **B. Product Licence conditions**

As is the case with all product licences, conditions may be imposed by the Authority.

It is proposed that there will be some statutory conditions that will apply to all licensed Biologicals and some conditions that will apply only to HCTs or to specific classes of HCT.

In addition to statutory conditions, the Authority will also have the capacity to impose conditions on a case by case basis.

It is proposed that the following types of conditions will apply to all licensed HCTs (and may also apply to all Biologicals).

Licence holders must:

- allow authorised persons to enter premises where the licence holder or any other person deals with the HCT;
- where relevant supply samples of the HCT, on request, to the Authority for testing purposes;
- notify the Authority if they become aware of adverse effects relating to their products (including becoming aware of new information that contradicts previously supplied information, information that the product may have a harmful effect and information that the product may not be as effective as suggested in the original licence application);
- keep records relating to the products in order to expedite recall if necessary of any batch of the products; and identify the manufacturer(s)

of each batch of the products ensure that advertising material is consistent with the intended purpose of the product;

- retain records of the distribution for a minimum period of fifteen years;
- notify the Authority about any product recall or any other similar regulatory action taken overseas; and
- hold information or evidence to support any claims.

In addition to the statutory conditions, the Authority may impose specific conditions as part of the decision to issue a product licence. Conditions may relate to:

- the manufacture of the HCT;
- the custody, use, supply, disposal or destruction of the HCT;
- testing of the HCT;
- the presentation of the HCT;
- the keeping of records relating to the HCT;
- matters dealt with in Standards applicable to the HCT (or additional matters); or
- other matters relating to the HCT, which the Authority thinks appropriate.

The Authority may also:

- by a notice given in writing, impose specific conditions on an existing product licence or vary or remove existing conditions. If the imposition or variation of the condition is necessary to prevent imminent risk of death, serious illness or serious injury, it will have immediate effect. In any other case, it will take effect no earlier than 20 working days after a notice is given to the licence holder; or
- impose or vary conditions on a product licence, with immediate effect, if the Authority is satisfied that there is a potential risk of death, serious illness or serious injury if the HCT continues to be licensed and that, by the imposition of conditions, it is likely that the HCT would not cause a potential risk of death, serious illness or serious injury. This is in addition to the power to suspend the product licence if the Authority is satisfied that there is a potential risk of death, serious illness or serious injury if the HCT continues to be licensed and it is likely that the licence holder can take action to address the problem.

## **PART K: VARIATION, SUSPENSION AND REVOCAION OF PRODUCT LICENCE**

### **A. Variation**

It is proposed that the Authority may vary the terms of the product licence:

- on the Authority's own initiative – for example, if the particulars on a product licence are incomplete or incorrect; and
- on application by the licence holder. This may include where the particulars on a product licence are incomplete or incorrect or where a more substantial change is required. For example, the licence holder must apply to vary the product licence if the particulars on a product licence change or if there are changes to:
  - information contained in the product licence application or any subsequent product licence variation applications, being information that would have been relevant to a decision to licence the HCT or to vary the licence for the HCT, including information on the formulation or composition of the HCT and information on the manufacture of the HCT;
  - the approved product information for the HCT; or
  - the labels for the HCT.

Where the applicant seeks to vary a product licence to the extent that the change results in a new HCT product (i.e. a separate and distinct product) the applicant will be required to submit an application for a new product.

It is proposed that the Rules will describe periods within which applications to vary product licences must be accepted or rejected for evaluation and within which product licence variations are to be completed. Applications, where clinical, toxicological or bioequivalence data are not required to support the variation, will be decided within 45 working days from the date of acceptance of the application.

In this case, if the Authority has not made a decision within 45 days, the application is deemed to have been approved.

### **B. Suspension and Revocation of Product Licences**

It is proposed that the Authority will be able to suspend or revoke a product licence in the event that the licence holder fails to comply with its obligations, or the Authority receives new information on the safety, quality or efficacy of an HCT which makes such an action necessary.

Appropriate safeguards will be put in place to ensure that licence holders are informed and given adequate opportunity to respond to concerns and to seek a review of any decision to suspend or revoke a product licence, where appropriate.

### **C. Revocation with immediate effect**

It is proposed that, in certain circumstances, the Authority may revoke a product licence with immediate effect, in which case the licence holder must immediately cease import, supply or export of the product. In certain circumstances, the product may also be recalled.

Examples of circumstances in which a licence may be revoked with immediate effect include:

- if there is imminent risk of death, serious illness or serious injury if the HCT continues to be licensed;
- if the product has been misrepresented and accordingly misclassified in a particular class;
- if the product has become exempt from product licensing;
- where the licence holder requests in writing that the product licence be revoked; and
- if the product contains substances that are prohibited imports for the purposes of the Australian and/or New Zealand Customs legislation.

### **D. Revocation after notice of proposal to revoke**

If the Authority decides that a product licence should be revoked and the legislation does not provide for the licence to be revoked with immediate effect, the Authority must advise the licence holder of the intention to revoke the licence and give the licence holder the opportunity to respond to the proposed action.

In this case, the licence holder may continue to import, supply or export the product until such time as the Authority decides to revoke the product licence.

Examples of circumstances in which the Authority may revoke a product licence for an HCT (following a notice of proposal to revoke) include:

- if the product has changed so that it has become separate and distinct from the product that was licensed;
- the licence holder has refused to comply with a condition on the product licence;
- the product does not conform to a standard applicable to the product; or
- the classification for determining the level of assessment of the product changes.

## **E. Suspension**

Suspension of a product licence will stop further import, supply or export of a product pending provision of additional information by the licence holder to enable the Authority to determine whether or not the product licence should remain valid or be revoked. The Authority may suspend a product licence for an HCT if the Authority is satisfied that, for example:

- there is a potential risk of death, serious illness or serious injury if the HCT continues to be licensed and it is likely that, within the period of the suspension, the licence holder will be able to take the action necessary to ensure that the HCT would not cause a potential risk of death, serious illness or serious injury if it were to continue to be licensed; or
- it is likely there are grounds for revoking the product licence.

It is proposed that the period of suspension will not exceed 6 months but this may be extended by up to an additional 6 months if the licence holder is able to show that he/she has taken steps to remove the grounds for suspending the licence.

In addition to these provisions, it will be possible for the Authority to add an immediate condition to a product licence, prior to any suspension, which would require the licence holder to undertake certain actions such as labelling changes or distributing correspondence to healthcare professionals notifying them of potential problems with the product.

## **PART L: MANUFACTURE OF HCTS**

### **A. Manufacturing Licences**

Australian and New Zealand manufacturers of Class, 2, 3 and 4 HCTs will be required to hold a manufacturing licence issued by the Authority, unless exempted from this requirement.

The Authority will assess a manufacturer for compliance with the required Manufacturing Principles. The Manufacturing Principles to be observed in the manufacture of HCTs will relate to:

- the standards to be maintained in the manufacture;
- the premises and the equipment to be used;
- procedures for quality assurance and quality control to be employed;
- the qualifications and experience required of people employed in its manufacture;
- the manufacturing practices to be employed in its manufacture; and
- other manufacturing matters relevant to the quality, safety and efficacy of the HCT.

### **B. Obtaining a Manufacturing Licence**

The process for obtaining a manufacturing licence for HCTs will be the same as the process for assessment of any other manufacturer of a therapeutic product (as will the processes for renewal and variation of a manufacturing licence)

### **C. Conditions on a Manufacturing Licence**

It is proposed that there will be statutory conditions and conditions that the Authority may impose on a case by case basis.

For example, as per medicines/medical devices, the Authority may obtain information from the applicant, may require the applicant to allow an authorised person to inspect the premises, equipment, processes and facilities etc that will be used to manufacture HCTs.

### **D. Suspension or Revocation of Manufacturing Licence**

As for all other manufacturing licences, the Authority will have the power to revoke a manufacturing licence or suspend a licence for a period of time.

## **PART M: ADVERTISING AND CONSUMER INFORMATION**

It is proposed that advertising in respect of HCTs must be consistent with the Australia and New Zealand Therapeutic Products Advertising Code (Advertising Code) and the Advertising Rule, and in New Zealand with the prohibitions on advertising of HCTs included in Section 92F of the *Health Act 1956*, which set out minimum requirements for advertising but leaves decisions on the type of advertising that is permitted in each country to be determined by local legislation.

Where advertising of HCTs is permitted it is proposed that it must only represent the HCT as effective for indications specified in the licence.

In line with the proposals in the draft Medicines Rule, the Authority will also be able to impose requirements with respect to the information to be provided in product information documents and consumer information documents for certain HCTs.

## **PART N: ADVERSE EVENT REPORTING**

It is intended that reportable events or reactions for HCTs will be those 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 to provide assistance to stakeholders regarding reporting procedures and responsibilities in relation to the different classes of HCTs.

It is important to note that an HCT may give rise to an adverse result that is not unexpected across a patient population (for example, function inadequately in a given patient). It is not intended that anticipated events of this type would be reported to the Authority (just as they are not for other therapeutic goods).

The intention is that unintended and unanticipated serious events be reported (for example, transmission of an infectious or malignant disease where there was no intention that such a disease be transmitted or engraftment issues due to culture or storage failure). In such circumstances it is important that relevant information be communicated to the Authority so that the Authority can work to identify where system failures occurred and to minimise the risk of such failures being repeated.

It is proposed that the Authority will require each licence holder to have an appropriate system of product vigilance in place to assure licence holder responsibility and liability for its products on the market and to ensure that appropriate action can be taken when necessary.

The Authority may ensure that the licence holder is compliant with their product vigilance obligations by means of inspection and would have the authority to take action against the licence holder should it fail to meet its obligations.

Principles similar to those proposed for medicines, blood and medical devices as described in the Consultation Paper on Product Vigilance in the ANZTPA will be developed for HCTs. A copy of this Consultation paper is available on the ANZTPA website (<http://www.anztpa.org/consult/consdocs2.htm>).

Included as part of a Product Vigilance System, all product licence holders would be obligated to:

- Maintain records of all reported suspected adverse reactions/events associated with the use of their product occurring in Australia or New Zealand.
  - Such reports include those obtained from spontaneous reporting by healthcare practitioners and consumers, published reports, and postmarket study reports. Licence holders will have obligation to follow-up all complaints, reports of problems, incidents, or suspected adverse reactions or events associated with the use of their products to obtain comprehensive information, if available.

- Promptly inform the Authority of all serious suspected adverse reaction/event reports occurring in Australia or New Zealand within the timeframe specified by the Authority.
  - For HCTs, this would be no later than 15 calendar days of initial receipt or discovery.
- Indicate what action the licence holder proposes in relation to the conditions of the product licence (including, when available, the approved Product Information and the Consumer Medicine Information), in situations where adverse reaction or adverse event reports impact on the safety profile of a product.
- Inform the Authority that another regulator has indicated intention to act (or has acted) to withdraw or suspend a therapeutic product that the licence holder holds a product licence for in Australia or New Zealand. This must be communicated to the Authority within 72 hours of the licence holder becoming aware of the action.
- Ensure all information that the Authority has defined as relevant to the risk-benefit balance of a therapeutic product is reported to the Agency fully and promptly - this includes advising of safety-related regulatory action carried out in Europe, the United States, or Canada.
- Respond fully to requests from the Authority for additional information necessary for evaluation of the benefits and risks of a therapeutic product, including but not limited to the provision of information about the volume of sales of the therapeutic product concerned.
- Where Product Information and Consumer Medicine Information is required, licence holders must ensure the currency of these documents is maintained with regard to safety information.

## **PART O: EXEMPTIONS AND EXCEPTIONS**

It is proposed that the exemptions and exceptions for HCTs include, but not be limited to, the following.

### **A. Single surgical procedures**

It is proposed that the Authority will exempt from regulation single medical procedures, irrespective of their nature. For example, it is proposed that the following medical 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.

### **B. Exceptional release/acceptance**

The Authority will develop Standards for the management of the exceptional release of an HCT when the supply of Class 1 or 2 cells or tissues is not compliant with the Standards, in the absence of any alternative product.

The Standard would be based on existing transplantation protocols and as part of the Standard the Authority will require that certain documentation be maintained by the accepting Agency including, for example:

- a record of the exceptional release including:
  - the nature and gravity of the risk;
  - the medical emergency necessitating the release;
  - the test not completed or the conditions not met and the reasons that justify the exceptional release;
  - the date and time of the authorisation; and
  - the signature of the requestor(s) of the exceptional release.
- a record for informing the recipient and/or next of kin regarding the need for exceptional release including the extenuating circumstances and the risks of proceeding versus not proceeding with the HCT transplant. The process of informing the recipient or next of kin shall be documented in the recipient's records.

### **C. 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.

### **D. Clinical trials**

It is proposed that clinical trials utilising HCTs be regulated in a manner consistent with clinical trials for other types of products. For further information regarding the proposed approach please refer to the Clinical Trials Consultation Paper on the ANZTPA website at <http://www.anztpa.org/consult/clintrials.htm>

### **E. Import of HCTs for personal use**

Currently, in Australia, individuals may import medicines and other therapeutic goods without the goods being entered on the ARTG, subject to certain requirements being met, including requirements under the Customs Prohibited Import Regulations. However, the Personal Importation Scheme does not allow the import of injections that contain substances of human origin unless they are approved under the Special Access Scheme.

The legislation is not currently well adapted for dealing with HCTs particularly where the HCTs are not in the form of a traditional injectable medicine but are instead proposed to be used for direct implantation. It is therefore proposed that appropriate amendment be made to clarify the regulatory requirements in relation to the personal importation of HCTs.

### **F. Custom made HCTs (no exemption)**

It is intended that custom made HCTs developed by medical practitioners will not be exempt under the new arrangements.

Currently in Australia, extemporaneously dispensed medicines (except for gene therapies) are exempt from the requirements for pre-market approval and in some cases the people who developed such custom made products are also exempt from the requirements for licensing of manufacturers (such as medical practitioners).

It is proposed that under the new trans-tasman arrangements, there will be no exemptions for custom made products, and for the people who produce such custom made products. This ensures that all HCTs are subject to consistent requirements regardless of the organisation or individual applying the therapy. One exception will be products made and used within a single surgical procedure.

This is an equitable approach to regulation and provides a level of certainty for the industry and for consumers in relation to the safety and quality of HCTs.

## **PART P: FEES AND CHARGES**

Article 15 of the Treaty provides that fees and charges may be collected by the Authority in connection with the performance of its functions and that these fees and charges will be prescribed in Rules.

The fees and charges will be designed to recover the full costs of the Authority's activities in an efficient and equitable manner and will comply with such other principles or requirements as may be prescribed in the Rules.

The Ministerial Council will seek recommendations from the Board in respect of fees and charges and ensure appropriate stakeholder consultation.

The Authority may engage in activities that fall outside the scope of the joint regulatory scheme. For activities that the Authority performs that do not fall within the joint regulatory scheme, either Australia or New Zealand may agree to provide funding to the Authority in connection with such activities, or the Authority may be empowered to collect fees or charges in respect of such activities.

Further details regarding fees and charges will be incorporated into a fees and charges Draft Rule including fees and charges for Biologicals.

## **PART Q: TRANSITION PROVISIONS**

The overarching principles to apply to the transitional arrangements are outlined in Article 21 of the Treaty, that is,

*“On and after the commencement date, the manufacture, supply, import, export or promotion of a therapeutic product that was lawful in the territory of one Party immediately before the commencement date continues to be lawful in the territory of that Party for a specified period by virtue of the deemed grant of a transitional approval under the Scheme on the terms and conditions (if any) that applied in respect of the manufacture, supply, import, export or promotion of that therapeutic product before the commencement date.”*

### **A. Current Approvals**

#### **i) Product Approvals**

The Treaty obligations on both countries mean that at the commencement of the joint scheme, all products that could be lawfully supplied in Australia or New Zealand can continue to be supplied in the country in which they were being supplied lawfully, for the duration of the specified transition period of three years from the commencement date of the joint scheme.

All products currently included on the ARTG defined as HCTs approved for supply in Australia, and legally manufactured in Australia will be granted transitional approval in the form of an Interim Product Licence that permits the continued supply of the product in Australia only. The Interim Product Licence will impose the same conditions as those that applied to the inclusion of that product on the ARTG.

Any HCT product supplied in New Zealand that has been granted either Ministerial consent or provisional consent under the New Zealand Medicines Act will be granted transitional approval in the form of an Interim Product Licence that permits the continued supply of the product in New Zealand only. The Interim Product Licence will impose the same conditions as those that applied in the granting of Ministerial consent or provisional consent under the New Zealand Medicines Act.

It will be illegal to supply a therapeutic product in Australia and/or New Zealand after commencement of the joint regulatory scheme if the product is not the subject of either an Interim or an ANZTPA Product Licence.

During the transition period, all products including those on the interim New Zealand registers will need to apply for (and be granted) a full Authority product licence issued by the Authority or, at the end of the transition period, the transitional approval will lapse.

Products that are available in both Australia and New Zealand prior to commencement of the joint scheme will not be entitled to a full Authority

product licence enabling supply in both countries until the sponsor of the product has demonstrated that the product complies with all requirements under the joint scheme.

A result of this arrangement is that where a product is legally available in both Australia and New Zealand prior to commencement of the joint scheme, it will be granted two transitional approvals (one for Australia and one for New Zealand) until such time as a full Authority product licence has been applied for, and granted.

It will be possible for the Authority to impose additional or different conditions on a transitional approval in accordance with the Rules. Every transitional approval will lapse at the end of the transition period. Therefore, prior to the end of the transition period, all products will need to demonstrate that they meet the standards of the Authority in order to obtain a full Authority product licence enabling supply in both countries.

At the end of the transition period, any product that has not gained a full Authority product licence from the Authority will no longer be able to be supplied. This condition will be imposed in order to ensure sponsors apply for a full Authority licence thus ensuring that all approved products meet the Authority standards.

### **Preparation for transition**

As most Class 2 products are collected, manufactured and utilised locally in each country, preparing the product for transition to an ANZTPA Product Licence will focus on product safety and quality, and compliance with GMP issues.

Some Class 3 and 4 HCT products have been regulated through GMP licensing requirements. For these products, prior to the end of the transition period sponsors must submit a product dossier containing the required information.

Where Class 3 and 4 products are approved and marketed in both countries there may be differences in the product details for those registrations. In preparation for transition to the joint scheme, sponsors of Class 3 and 4 HCTs in particular should review their current product ranges and marketing authorisations to take advantage of the “single market” opportunities provided by the joint regulatory scheme. Sponsors might find it useful to refer to the information in the document titled *Plain English Guide to the Draft Medicines Rule, Draft Medical Devices Rule, and Key Components of the Draft Administration and Interpretation Rules*, which was released in May 2006 and is available on the ANZTPA website ([www.anztpa.org](http://www.anztpa.org)).

Class 1 HCTS transition times are still being determined.

Having demonstrated compliance with Authority standards, a full Authority Product Licence will be issued enabling supply in both Australia and New Zealand.

## **ii) Manufacturing Approvals**

On the date of commencement of the joint scheme, lawful manufacture of therapeutic products in Australia and New Zealand will continue to be lawful by the deemed grant of a transitional approval to the lawful manufacturer of these products.

In other words, any manufacturer of therapeutic products authorised under the Therapeutic Goods Act or the Medicines Act in either Australia or New Zealand will be granted a transitional approval that applies on the terms under which the existing approval was issued. This transitional approval will be valid for a period of two years.

During the period of the transitional approval, the holder of the transitional approval will have to apply to the Authority for a full Authority manufacturing licence. This licence application will be assessed against requirements under the joint scheme and will be issued under the terms and conditions of all full Authority manufacturing licences issued by the Authority.

## **iii) Other Activities and Exemptions**

Apart from existing product and manufacturing approvals, there may be other regulatory actions that will already have been commenced at the time the joint scheme comes into existence such as suspensions of manufacturing licences, pending cancellations, prosecutions, recalls, monitoring action and audits, and property that has been seized under search powers. In order to accommodate the finalisation of these activities, the regulatory action will be finalised under the legislation existing when the activity was commenced.

All post-market surveillance activities, appeals and reviews that were commenced under the Therapeutic Goods Act or the Medicines Act but not completed by the commencement date of the joint scheme, will be completed under the legislation under which the activity was commenced.

Upon commencement of the joint scheme, products, persons or activities that were exempt from regulatory requirements under the Therapeutic Goods Act and Medicines Act will continue to be exempt from regulatory requirements for the duration of the transition period or for the period stated in the exemption (whichever is the shorter).

At the end of the transition period the exemption will only remain in place if the Authority legislation or Rules continues to specifically exempt these products, persons or activities. If, at the end of the transition period, the Authority legislation or Rules no longer exempts these products, persons or activities, then the exemption will cease and compliance with the relevant requirements under the joint scheme will need to be demonstrated.

It is anticipated that clinical trials that are ongoing at commencement of the joint scheme will be allowed to be finalised under the same conditions of

exemption that were applied under the Therapeutic Goods Act and Medicines Act. Clinical trials commencing after commencement of the joint scheme will have to comply with relevant requirements under the joint scheme.

## **B. Applications In Progress**

The transitional system set up in each country will deal with applications for product approvals received by the TGA under the Therapeutic Goods Act and Medsafe under the Medicines Act prior to commencement of the joint scheme but not finalised by the commencement date of the joint scheme.

The transitional systems will ensure that applications for product approvals are determined on the same basis as applied to the application before the commencement date of the joint scheme and will provide for the grant of transitional approvals. These transitional approvals will be valid only for the duration of the transition period and only in the country where the original application was received.

Applicants whose applications for product approval were lodged under the Therapeutic Goods Act or the Medicines Act but which are not, or are unlikely to be, finalised by the commencement of the joint scheme, may elect to have their applications determined by the Authority under the joint scheme rather than under the legislation under which they were submitted. In order to do this, the applicant will need to withdraw the original application and resubmit the appropriate application to the Authority. Every applicant to whom this situation applies must elect within three months of the commencement of the joint scheme to either have their application completed in accordance with the legislation under which the application was made (and any applicable Rules and Orders) or withdraw their application and make a new application for a full Authority product licence in accordance with the requirements of the Authority.

If an application is withdrawn under this provision, a full refund of the original application fee will be made to the sponsor and the sponsor will then have to pay the full Authority evaluation fee. Any statutory timeframes applying to evaluations will restart on the day the new application was made to the Authority.

## **C. Products not currently regulated by the TGA**

HCTs that are not regulated prior to the commencement of ANZTPA that are supplied in a lawful way may still be supplied after the commencement of the joint agency but will be required to have transitional approval for the duration of the transition period.

The Rule will set out the length of the transition period and the timeframes for lodgement of applications prior to the end of the transition period.

## **D. The Transition Period**

### **i) Existing Products**

All therapeutic products that are entered on the ARTG in Australia or have Ministerial Consent in New Zealand will receive transitional approvals that are valid for a period of three years from the commencement date of the joint scheme.

It may be possible to grant extensions of time in which to obtain a full Authority product licence under certain circumstances. Following the transition period, extensions to transitional approvals will only be granted to products that can demonstrate an ongoing program designed to demonstrate conformance to the Authority standards. However, holders of transitional approvals will be encouraged to gain full Authority product licences during the transition period by incurring increased fees for applications received during any period of extension.

As a general principle, an Interim Product Licence (for either country) would become an ANZTPA Product Licence without further evaluation where compliance with the ANZTPA requirements can be demonstrated. There will be no fees payable in transferring to an ANZTPA Product Licence where evaluation or assessment is not required. Where compliance with ANZTPA requirements cannot be demonstrated and an additional evaluation or assessment is required the requisite fees will be payable. As the standards documents are currently different in Australia and New Zealand, the TGA and Medsafe are conducting a 'gap analysis' in relation to the requirements for the ANZTPA TSF. The outcome of this analysis will be a single standard to apply in both countries. For Class 2, it is envisaged that the difference would predominantly relate to labelling issues.

In exceptional circumstances (i.e. a clearly demonstrated clinical need) certain products that are unable to demonstrate compliance with Authority standards may be issued a conditional product licence enabling continued supply in the country in which they were legally supplied prior to commencement of the joint scheme.

### **ii) Existing Manufacturing Licences**

Licensed manufacturers in Australia and New Zealand will be able to continue to manufacture under the terms of their existing licence for a period of no more than two years following commencement of the joint scheme. During this two-year transition period, manufacturers will need to submit an application to the Authority for a full Authority manufacturing licence. Given that current Australian and New Zealand processes for the granting of manufacturing licences are well aligned, gaining a full Authority manufacturing licence should not be significantly more onerous for manufacturers than maintaining their current national licences.