

A PROPOSAL FOR A
TRANS TASMAN AGENCY
TO REGULATE
THERAPEUTIC PRODUCTS

DISCUSSION PAPER

JUNE 2002

FOREWORD

This discussion paper has been prepared to seek comment from stakeholders in Australia and New Zealand on a proposal for a trans-Tasman joint agency for the regulation of therapeutic products.

The proposal for a joint agency has been developed against the background of the Trans Tasman Mutual Recognition Arrangement and initiatives to harmonise the regulation of therapeutic products between Australia and New Zealand.

Australian and New Zealand Governments have agreed in principle to progress the proposal to bring the two regulatory arrangements for therapeutic products closer together, thereby removing unnecessary barriers to trade for Australian and New Zealand therapeutic products industries.

We will continue to work with stakeholders in further refining the proposal over the coming months. Subject to a final decision from both Governments to proceed with the establishment of a joint agency, draft legislation will be developed and further input from stakeholders will be sought as this process continues.

We encourage you to give full consideration to the proposals in this paper and to provide comment that will inform the development of new regulatory arrangements that will work well for consumers, industry sectors, health professionals and Governments in both countries.

Graham Peachey
Director
Trans Tasman Group
Therapeutic Goods Administration
June 2002

Susan Martindale
Project Leader
JTA Project Team
Medsafe
June 2002

SUBMISSIONS ON THIS DOCUMENT

This discussion paper has been published to allow further opportunity for informed public comment on the proposals developed by the project team. Your submissions on the proposals in this paper are invited and will help shape the proposed joint agency for the regulation of therapeutic products in Australia and New Zealand.

This document is available on the following websites:

www.jtaproject.com
www.health.gov.au/tga
www.medsafe.govt.nz
www.moh.govt.nz

Further copies can also be obtained on request from the project team at the addresses given below.

HOW TO MAKE A SUBMISSION

Submissions should be made to one of the addresses given below by

Friday 2 August 2002

Where possible, your submission should contain relevant evidence to support your views.

Submissions will be available to the public. Any information that you do not wish to be made public should be sent separately and clearly marked CONFIDENTIAL.

Addresses for submissions or for further information:

The Director
Trans-Tasman Group
Therapeutic Goods Administration
PO Box 100
Woden ACT 2606
AUSTRALIA

OR

Team Leader
JTA Project Team
Medsafe
PO Box 5013
Wellington
NEW ZEALAND

Trans.Tasman@health.gov.au

susan_martindale@moh.govt.nz

Fax: +61 2 6232 8196

Fax: +64 4 496 2229

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EXECUTIVE SUMMARY

This discussion paper contains proposals for

- the establishment of a joint Australia/New Zealand agency for the regulation of therapeutic products; and
- the regulatory scheme that would be administered by such an agency.

During 2000, the Australian and New Zealand Governments gave in-principle agreement to the establishment of a joint agency for the regulation of therapeutic products (which include prescription and over-the-counter medicines, medical devices, complementary medicines and many dietary supplements) as a means of implementing the Trans Tasman Mutual Recognition Arrangement (TTMRA). This is subject to Australia and New Zealand being able to reach agreement on the establishment, governance, reporting requirements and accountability arrangements for the agency, and the regulatory framework to be administered by the agency. It is also dependent on the outcome of an analysis of the costs and benefits of the proposed scheme.

It is expected that a final decision on whether to proceed with the establishment of a joint agency will be made by each Government in the second half of 2002. If a joint agency is to be established, work will proceed on developing new legislation to be introduced to Parliaments in 2003. The earliest date for commencement of operation of a joint agency is expected to be mid to late 2004.

WHAT WILL THE AGENCY'S ROLE BE?

The proposed Australian/New Zealand agency for the regulation of therapeutic products (the Agency) would be responsible for ensuring the quality, safety, efficacy and timely availability of therapeutic products manufactured or supplied in Australia and/or New Zealand or exported from the Australia/New Zealand market.

HOW WILL THE AGENCY BE DESIGNED?

The Agency would be overseen by a Ministerial Council of two Ministers - the Australian and New Zealand Ministers of Health. The Ministerial Council would appoint the Board and would be responsible to the two Parliaments for the operation of the Agency.

The Agency would have a Board of five members, responsible to the Ministerial Council for the Agency's strategic direction and financial management. The Board would not make decisions in relation to technical matters, or individual therapeutic product licensing applications.

The Managing Director would be a member of the Board, the chief executive of the Agency responsible to the Board for financial and administrative matters, and the "statutory decision-maker" responsible for making decisions in relation to therapeutic products.

The Agency would be accountable to the Governments and stakeholders in both countries for its performance.

The Agency would have offices in both Australia and New Zealand. It is proposed that the Agency's internal organisation would be based broadly on a scheme of regulation by type of product.

HOW WILL THE AGENCY BE ESTABLISHED?

Three basic approaches to establishing the Agency have been identified. Each would involve Australia and New Zealand entering into a treaty in relation to the institutional and regulatory framework for the joint agency, and each country legislating to give effect to aspects of these arrangements. In particular, under any of these approaches both countries would enact legislation that would recognise the Agency as the therapeutic products regulator for that country, and would give effect to the regulatory decisions of the Agency.

The difference between the three approaches lies in the extent to which issues relating to the establishment and legal personality of the Agency are addressed in the treaty or in national legislation. Final decisions on establishment options will be made following the conclusion of negotiations between the two Governments.

Under the proposed approach, the standards and requirements that would apply to therapeutic products would be prescribed by a treaty and by new legislation in Australia and New Zealand. This new framework would replace the existing *Australian Therapeutic Goods Act 1989*, and Regulations and Orders, and the existing *New Zealand Medicines Act 1981* and Regulations.

The Treaty described above would set out broad enduring principles and goals for the scheme.

An Act in each country would contain the broad regulatory matters and obligations that must be contained in primary legislation, such as making it an offence to supply therapeutic products that have not been licensed by the Agency or which do not comply with requirements and standards prescribed in the Rules and Orders.

A single set of Rules made by the proposed Ministerial Council, which would be analogous to regulations in the current systems, would contain much of the detail of the regulatory requirements. For example, the Rules would set out the mandatory requirements for obtaining a licence to supply a therapeutic product.

Orders would be made by the Agency's Managing Director in relation to more technical issues, such as manufacturing standards and labelling requirements.

It is proposed that the Ministerial Council and the Agency's Managing Director would be given the power to make delegated legislation in the form of Rules and Orders. This delegated legislation would have direct effect in both countries, without needing to be incorporated into domestic legislation.

HOW WILL THE REGULATORY SCHEME WORK?

The Agency would regulate products used for a therapeutic purpose. Therapeutic products would include:

- prescription and over-the-counter (OTC) medicines;
- medical devices; and
- products currently regulated in Australia as complementary medicines; and
- products marketed as dietary supplements in New Zealand (other than food-type dietary supplements), including herbal and homoeopathic medicines.

The regulatory activities of the Agency would include pre-market assessment or evaluation, product licensing, post-market surveillance, licensing of manufacturers, setting of standards and communicating decisions and information.

Whilst the regulatory scheme is designed to deliver common regulatory outcomes in the two countries, it is recognised that the scheme would need to enable either country to 'opt out' of a common regulatory decision in extraordinary circumstances (eg. to accommodate differing public health policy imperatives).

The Agency would regulate therapeutic products using a risk management approach, in which the degree of regulatory control would be proportional to the risk associated with use of the product.

Prescription and OTC medicines, complementary medicines and dietary supplements (other than food-type dietary supplements)¹ would be classified according to risk into one of three classes based on ingredients, intended purpose and type of product. Class I would comprise low-risk products (eg. most complementary healthcare products and sunscreens). Class II (medium risk) would include most over-the-counter medicines. Class III products would include prescription medicines and other specified products (eg. vaccines, biotechnology products, radiopharmaceuticals, injectable dosage forms and products intended to carry indications for serious diseases). The Agency's internal organisation would be based on a scheme of regulation by type of product. In such a scheme there would be separate regulatory units within the Agency for regulation of prescription, OTC and complementary healthcare products.

Medical devices would also be classified according to risk into one of six classes, using the manufacturer's intended purpose and a set of risk-based classification rules, consistent with the framework recommended by the Global Harmonisation Task Force (GHTF).

It is proposed that the Agency would operate a cost recovery scheme in which cost recovery arrangements would be consistent with government policy and relate to the range of regulatory activities including pre-market evaluation or assessment of products and/or substances, post-market surveillance, standard setting, and the auditing and licensing of manufacturers.

¹ For convenience complementary medicines and dietary supplements (other than food-type dietary supplements) are referred to in the discussion paper as 'complementary healthcare products', further discussion of the terminology to be used to describe this type of product is provided in Part F of the paper.

The Agency would consult with industry representatives to ensure that fees and charges accurately reflected the cost of regulating a particular industry sector or a product group and were borne equitably within and across the relevant sector or product groups.

Activities that the Agency may perform under contract (eg. chemical hazard and risk assessments for Australia or pharmacy audits for New Zealand) would be outside the scope of the joint scheme and would be funded separately from payments under those contracts.

Product licensing

It is proposed that authorisation to import, export or supply therapeutic products would be granted by a product licence issued by the Agency, unless the product was specifically exempted from the requirement for a product licence. The product licence (PL) holder or their authorised agent would be the sponsor of the product.

Each PL would carry a unique number and, generally, a separate PL would be issued for each new product, although it would be possible to 'group' more than one product in the same PL in certain circumstances. The Agency would maintain a register of licensed products.

The product licence document would provide a summary of the particulars of the product and set out or refer to the conditions under which the product could be supplied.

In order to obtain a product licence, the sponsor would be required to submit an application to the Agency. The application processes, data requirements and evaluation/assessment processes would be different for different types of products and different risk classifications. Class I products would be granted a product licence on the basis of self-certification by the sponsor, using an electronic application lodgement and assessment system.

The Agency would set timeframes for evaluating and processing applications. Appropriate mechanisms would be put in place to allow accelerated evaluation to occur in defined circumstances. An orphan medicines programme would facilitate the availability of medicines for use in rare diseases.

Expert advisory committees

Expert advisory committees would be established to provide the Managing Director of the Agency with scientific and regulatory advice. Members would be selected from relevant experts in both countries. Committees would be established to provide advice on matters such as standards for therapeutic products, matters relating to the evaluation and licensing of products (with a separate committee for each broad category of product), adverse reactions and scheduling.

Licensing of manufacturers

Manufacturers of medicines and complementary healthcare products would be required to comply with specified manufacturing principles. The Agency would audit manufacturers

for compliance with the code and would issue manufacturing licences. Evidence of compliance with manufacturing principles would also be required for any overseas site manufacturing a medicine or complementary healthcare product.

Post-market surveillance

The Agency would use a systematic, risk-based approach to post-market surveillance of therapeutic products. Post-market surveillance activities would include: random and targeted testing of products; adverse reaction monitoring; medical device incident monitoring; product problem reporting and recalls; auditing of manufacturing facilities; audits of applications (eg. those relying on sponsor self-certification or self-assessment); and monitoring of products in the market place to ensure they are being marketed in compliance with the terms and conditions of the product licence.

Clinical trials and access to unlicensed therapeutic products

Use of therapeutic products in clinical trials would be regulated under a joint clinical trial scheme. All clinical trials, including those using licensed products, would require the approval of the relevant institutional ethics committee(s) and would have to be notified to the Agency. Clinical trials would also require scientific approval. Comment is sought on different options for obtaining scientific approval of clinical trials.

A number of mechanisms would be put in place to allow patients access to unlicensed therapeutic products in defined circumstances.

Therapeutic products for export

Therapeutic products that are not the subject of a product licence but are to be exported from Australia or New Zealand to a third country would require an export only licence, and the Agency would provide appropriate export certification to meet international requirements. Comment is sought on specific options for administering the export licensing scheme.

Advertising

Under a joint agency, advertisements for therapeutic products directed exclusively to healthcare professionals would be governed by industry codes of practice, which would be consistent with an Australia/New Zealand therapeutic products advertising code.

The regulatory scheme that would apply to direct-to-consumer advertising is currently under review as part of the joint agency project. It is anticipated that the regulatory arrangements for direct-to-consumer advertising of therapeutic products would be co-regulatory and simplified wherever possible. That approach would be based on:

- a single Australia/New Zealand advertising code and advertising oversight body;
- a single pre-clearance system for advertisements;
- single administrative and complaints arrangements; and
- joint (Australia/New Zealand) industry codes of practice.

Scheduling of medicines

The proposals set out in the paper advance the recommendations of the Galbally Review² in Australia relating to scheduling.

It is proposed that under a joint agency, there would be a single scheme for the scheduling of medicines and substances in medicines. The initial scheduling decision would be made as part of the evaluation and approval process for the substance or medicine.

An expert advisory committee on medicine scheduling would advise the Managing Director on scheduling matters; would consider proposals to change the scheduling classification of a medicine; and would be able to review scheduling decisions made by the Managing Director.

HOW WILL PRESCRIPTION MEDICINES BE REGULATED?

Under a joint agency, the application and evaluation processes and the data requirements for prescription medicines would be similar to those currently applied in both countries, and would be consistent with international best practice. It is proposed that the legislation would set timeframes for processing applications, with cost penalties for the Agency if the timeframes were not met.

Strict criteria would be set down by the Agency in relation to requirements for demonstrating bioequivalence for generic medicines.

HOW WILL OTC MEDICINES BE REGULATED?

Under a joint agency, the application and evaluation processes and the data requirements for OTC medicines would be similar to those currently applied in both countries, and would be consistent with international best practice. It is proposed that the Agency would set timeframes for processing applications.

HOW WILL COMPLEMENTARY HEALTHCARE PRODUCTS BE REGULATED?

There is no universally accepted collective term or definition for the groups of products often referred to as complementary healthcare products, complementary medicines or natural health products. These products fall under the broad definition of "medicine" because of the way in which they act. However, some stakeholders do not agree with the use of the term "medicine". Comment is sought on appropriate terminology and definitions to be used in the legislation.

In Australia, complementary healthcare products are regulated as complementary medicines under therapeutic goods legislation. In New Zealand, they are generally marketed as dietary supplements and controlled under food legislation.

² A Review of Drugs, Poisons and Controlled Substances Legislation.

It is proposed that a joint agency would regulate complementary healthcare products as therapeutic products, using a risk-based approach. Most complementary healthcare products (around 95%) would be low-risk (Class I), and therefore could be licensed quickly on the basis of sponsor self-certification using an electronic system.

Safety of ingredients used in low-risk complementary healthcare products would be controlled by the Agency maintaining a list of permitted ingredients that had been assessed as being safe for use in Class I products. Any products falling into Class II (medium risk) or Class III (high risk) would be evaluated by the Agency for safety, quality and effectiveness before a product licence was granted.

HOW WILL MEDICAL DEVICES BE REGULATED?

Consistent with the endorsed recommendations of the GHTF, all medical devices would have to meet a set of essential principles relating to their design, manufacture and clinical performance before a product licence could be granted. The level of regulation would be proportional to the degree of risk involved in the use of the device.

For the lowest risk devices, a product licence would be granted on the basis of sponsor self-certification. For the higher risk classes, the Agency would be able to take account of documentation from overseas bodies in which it had confidence. Where adequate evidence was not available, or where the device presented specific types of risks (eg. contained material of human or animal origin), the Agency would undertake evaluation of the medical device before granting a product licence.

Mechanisms would be developed to allow access to unlicensed medical devices in appropriate circumstances. A medical device exported from Australia or New Zealand to a third country would require an export only licence.

HOW WILL COMPLIANCE BE MONITORED AND ENFORCED?

The Agency would have responsibility for monitoring compliance with the regulatory system it administered, and would have the power to request information, to request samples for testing, and to search premises and seize goods. The Agency would also have the power to impose sanctions (eg. cancel a product licence or recall a product) and prosecute offences.

HOW WILL REGULATORY DECISIONS BE REVIEWED?

It is proposed that the Agency's regulatory decisions would be open to challenge in two ways:

- through a two-stage merits review process, consisting of a right to ask the Agency to carry out a review of one of its decisions, with a further right to ask for a review of a decision to be carried out by a merits review panel external to the Agency; and
- through judicial review proceedings brought in the courts of either country.

WHAT WILL THE TRANSITIONAL ARRANGEMENTS BE?

Following the passage of legislation implementing a new joint regulatory scheme for therapeutic products and commencement of operation of the Agency, there would need to be a period of transition to the new system. At commencement of operation of the Agency, therapeutic products legally on the market in Australia could continue to be supplied in Australia and therapeutic products legally on the market in New Zealand could continue to be supplied in New Zealand.

For certain types of products (eg. medical devices and complementary healthcare products in New Zealand) the initial permission to supply would lapse at the end of a defined transition period. Because these products had not previously been subject to pre-market regulation, continued supply would be subject to the sponsor applying for and being issued with a product licence based on evaluation or assessment in accordance with the requirements of the Agency.

Considerable further work and consultation will need to occur over the next few months as the details of appropriate mechanisms and durations for transition are developed. The following principles have been developed to guide this work.

The transition arrangements would:

- provide adequate assurance about the safety, quality and efficacy of products on the product licence register, without requiring extensive re-evaluation of data, which cannot be justified on public health and safety grounds;
- ensure that manufacturers and sponsors of therapeutic products in both countries are treated in a fair and equitable way, taking into account relevant past regulatory practices;
- impose the lowest possible compliance costs consistent with adequately protecting public health and safety;
- permit sponsors already in the market in either country to continue to market in that country during the transition period without having to apply for a dual-country licence; and
- facilitate early reduction of existing trade barriers.

Australian and New Zealand officials will present recommendations on the proposed joint regulatory scheme to their respective Governments later this year after considering stakeholder comments on the proposals in this paper.

INTRODUCTION

There is a general expectation in the Australian and New Zealand communities that therapeutic products will be safe, effective and of good quality and that governments will set standards and regulations to reflect these expectations. At the same time, those manufacturing and marketing therapeutic products expect that regulations, including standards, will be appropriate, commensurate with the assessed risk of their products and consistent with international practice. Governments have traditionally responded to community expectations by establishing well-designed regulatory systems that aim to protect public health and safety whilst imposing minimal compliance costs.

1. INTERNATIONAL TRENDS IN THE REGULATION OF THERAPEUTIC PRODUCTS

In most developed countries regulatory arrangements for therapeutic products are predicated on the principle that the cost of product failure is likely to be far greater than the collective cost to industry, government and consumers of building and maintaining regulatory systems and rebuilding confidence when failures occur.

Internationally there is a well-established trend towards harmonisation of the way in which therapeutic products are regulated. This trend has occurred because therapeutic products are continually evolving and becoming more complex, which in turn makes it more expensive for companies to test and validate products to meet the requirements of different regulatory agencies. There is extensive international trade in therapeutic products, and governments have recognised the benefits of harmonising regulation.

Regulators around the world have joined in a number of initiatives such as the International Conference on Harmonisation (in relation to medicines) and the Global Harmonisation Task Force (in relation to medical devices). Worldwide there is a movement towards countries entering into Mutual Recognition Agreements with other regulators in whom they have confidence. Under these agreements, countries recognise each other's expertise. It is against this backdrop that work has been undertaken on the regulation of therapeutic products in the context of the Trans-Tasman Mutual Recognition Arrangement.

2. THE TRANS-TASMAN MUTUAL RECOGNITION ARRANGEMENT AND THE JOINT THERAPEUTIC PRODUCTS AGENCY PROPOSAL

The Trans Tasman Mutual Recognition Arrangement (TTMRA) was agreed to by the Commonwealth, the States and Territories, and New Zealand, in 1998. Its objective is, *inter alia*, to allow goods produced in Australia to be traded without regulatory impediment in New Zealand, and vice versa. At present, therapeutic goods is one of six areas in which mutual recognition under the TTMRA has not yet been achieved. Therapeutic goods currently have a Special Exemption from the mutual recognition requirements of the TTMRA.

Australian and New Zealand officials have been directed to undertake a cooperation programme designed to identify responses to the TTMRA in the area of therapeutic goods (prescription medicines, over the counter medicines, complementary medicines and many

dietary supplements, and medical devices). These options include permanent exemption from the TTMRA, mutual recognition, or harmonisation of requirements between the two countries. In accordance with the terms of the TTMRA, officials have been required to report on progress to their respective Governments in annual Co-operation Reports.

The 2001 Co-operation Report prepared by the Therapeutic Goods Administration (TGA) and Medsafe recommended that the therapeutic goods Special Exemption be extended to 30 April 2003, to facilitate the resolution of outstanding issues currently impeding mutual recognition. The Commonwealth gazetted the Trans Tasman Mutual Recognition Arrangement regulations in April 2002, formalising this extension.

Investigation of the joint agency option has been a priority project on the co-operation programme over the last two to three years. Officials have been required to report progress to their respective Governments at regular intervals and are obliged to resolve the exemption consistent with the overall intent of the TTMRA, whilst ensuring public health and safety.

During 2000, the Australian and New Zealand Governments gave in-principle agreement to the establishment of a joint agency for the regulation of therapeutic products. This in-principle agreement is subject to Australia and New Zealand being able to reach agreement on the establishment, governance, reporting requirements and accountability arrangements for the agency, and the regulatory framework to be administered by the agency. It is also dependent on the outcome of an analysis of the costs and benefits of the proposed scheme.

It is expected that a final decision on whether to proceed with the establishment of a joint agency will be made by each Government in the second half of 2002. If a joint agency is to be established, work will proceed on developing new legislation to be introduced to Parliaments in 2003. The earliest date for commencement of a joint scheme is expected to be mid to late 2004.

3. DEVELOPMENT OF THE JOINT AGENCY PROPOSAL

Establishment of a joint agency would have the effect of bringing the pre-market assessment of therapeutic products, post market monitoring, enforcement and recalls for Australia and New Zealand under a common regulatory framework for each type of product. There would exist one regulator, common regulatory outcomes (except in extraordinary circumstances) and opportunities for a single market in therapeutic products.

It is anticipated that a joint regulatory scheme would facilitate trans-Tasman trade, reduce compliance costs and combine the field of regulatory experts of both countries to sustain regulatory capability in the medium to longer-term while protecting public health and safety.

Australian and New Zealand officials on the trans-Tasman joint agency project team have developed proposals for implementing a joint agency for the regulation of therapeutic products. These proposals have been developed following broad consultation with a

range of stakeholder groups, including industry and consumer representatives and professional associations over an 18-month period and are presented in this discussion paper. The publication of this discussion paper is a further step in the consultation process and will be followed by meetings with major interest groups to refine the proposals and to develop the operational detail.

The proposed regulatory framework is designed to:

- be responsive to the public health needs of each country;
- deliver common regulatory outcomes;
- enable New Zealand and Australian participation;
- be accountable through Ministers to the national Parliaments and national Governments of Australia and New Zealand;
- provide a transparent and informed decision-making process; and
- ensure national sovereignty is preserved.

In developing the regulatory framework, the project team has considered the strengths and weaknesses of the current regulatory schemes in both countries, and taken account of international trends in the regulation of therapeutic products. The resulting set of proposals contains many elements from the current New Zealand and Australian regulatory systems, together with some new elements that are not currently used, but which are consistent with global recommendations on best regulatory practice.

4. REGULATION OF THERAPEUTIC PRODUCTS IN AUSTRALIA AND NEW ZEALAND

4.1 Australia

In Australia, the *Therapeutic Goods Act 1989* and its associated regulations cover medicines (prescription, OTC and complementary medicines), medical devices and a small number of other therapeutic products (e.g. tampons and hospital-grade and household disinfectants). The TGA administers the legislation and regulates the supply of therapeutic products through:

- pre-market controls;
- licensing of manufacturers; and
- post-market surveillance, (including compliance testing, adverse reactions and device incident monitoring, enforcement activities and product problem reporting and recalls).

If the joint agency proposal were not implemented, Australia would continue to regulate prescription, OTC and complementary medicines as at present. The Australian Parliament has recently passed the amendment Bill to the Therapeutic Goods Act, which will enable the implementation of a new medical device regulatory framework based on the Global Harmonisation Task Force approach. This new regulatory framework for medical devices is to be implemented in October 2002.

4.2 New Zealand

The regulatory framework for therapeutic products in New Zealand is based on the *Medicines Act 1981* (which deals with medicines and medical devices), the *Dietary Supplement Regulations 1985* under the *Food Act 1981* (which deal with dietary supplements), and the *Misuse of Drugs Act 1975* (which deals with Controlled Drugs). The current legislation does not adequately regulate complementary medicines/healthcare products or medical devices.

In New Zealand, Medsafe undertakes substantially the same regulatory functions for prescription and OTC medicines as the TGA undertakes in Australia. In addition, Medsafe undertakes some activities performed by the Australian States and Territories. For example, Medsafe is responsible for monitoring aberrant prescribers, auditing and licensing medicine wholesalers and for quality audits of pharmacies.

Australia and New Zealand use a very similar framework for the regulation of prescription and OTC medicines, which is consistent with global harmonisation initiatives. Current differences in the approach taken are mostly at the operational level.

New Zealand has for some time recognised the need to develop new legislation to regulate medical devices and complementary medicines/healthcare products. Development of proposals for what became known as the planned "Healthcare and Therapeutic Products" bill began in the early 1990s. However, despite extensive development work and consultation on an appropriate legislative framework for therapeutic products in New Zealand, legislation was neither drafted nor introduced into Parliament. With the subsequent change of Government, and the Government's decision to investigate the possibility of entering into a joint arrangement with Australia for the regulation of therapeutic products, the proposals for new "Healthcare and Therapeutic Products" legislation were not progressed and no longer have any standing. It should be recognised, however, that the regulatory framework proposed for the bill was very similar to that now being proposed for regulation of therapeutic products by a joint agency.

In the event that the joint agency does not go ahead, New Zealand would still require new legislation to adequately regulate the full range of therapeutic products. Prescription and OTC medicines would continue to be regulated along the same lines as at present, consistent with the recommendations of the International Conference on Harmonisation and the World Health Organisation (WHO). Medical device regulation, consistent with the approach recommended by the Global Harmonisation Task Force, would be developed and could be expected to be similar to that proposed for the joint agency. It is envisaged that complementary medicines/healthcare products would be regulated as therapeutic products, using a risk management approach and applying the same range of regulatory mechanisms as those proposed for the joint agency and currently used in Australia and proposed for Canada.

A particular issue for New Zealand is the shortage of local technical expertise. Consideration would need to be given to the best way of overcoming the difficulties created by a global shortage of technical expertise, particularly in regulating increasingly complex products.

5. IMPLEMENTATION PROCESS AND TIMELINE

After considering stakeholder comments on the proposals in this paper, later this year officials from each country will present recommendations to their respective Governments on establishing the proposed agency and the proposed joint regulatory scheme. If both Governments agree to establish a joint agency, the following indicative implementation activities would occur:

Late 2002	Report-back to Australian and New Zealand Governments for policy approval to proceed.
Late 2002	Implementation process commences.
	Drafting instructions issued for: <ul style="list-style-type: none"> - Parliamentary Bills (for a new Act in each country) - subordinate legislation (for a single set of Rules that will apply in both countries).
Late 2002 - 2004	Development, in consultation with stakeholders, of treaty, legislative and administrative arrangements that establish: <ul style="list-style-type: none"> - the regulatory scheme - the Agency, including structure, governance, accountability, accommodation, human resources, corporate services etc.
2003	Conclusion and signing of Treaty. Passage of Treaty through respective parliamentary procedures (including, in Australia, the Joint Standing Committee on Treaties)
2003	Passage of legislation establishing the Agency and the regulatory scheme through respective Parliaments, including Select Committee processes and the opportunities for public scrutiny of the Bills.
2004	Legislation and Treaty enter into force at same time.
Mid 2004	Agency commences operation.

PART A: DESIGN AND ROLE OF THE AGENCY

1. ROLE OF THE AGENCY

The Agency would be responsible for ensuring the quality, safety, efficacy and timely availability of therapeutic products manufactured or supplied in Australia and/or New Zealand or exported from the Australia/New Zealand market.

2. NAME OF THE AGENCY

The name of the Agency has yet to be decided.

Question 1:

Do you have any suggestions for a suitable name for the Agency?

3. GOVERNANCE AND ACCOUNTABILITY

3.1 Key Issues in Designing the Agency

The structure of the Agency is important because it allocates decision-making responsibility and establishes the governance and accountability arrangements for the Agency.

The proposed structure and governance arrangements for the Agency have been developed in order to ensure that the Agency will perform its role effectively and efficiently, and will be accountable to Governments and stakeholders in both countries for its performance of its responsibilities. The Governments have agreed as a basic principle that the Agency should be no less accountable to Ministers, Parliament and other stakeholders than comparable public sector organisations in either New Zealand or Australia.

3.2 The Governance Framework

The key elements of the Agency's proposed governance framework would be:

The Ministerial Council

The Agency would be overseen by a Ministerial Council of two Ministers - the New Zealand and Australian Federal Ministers of Health. The Ministerial Council would appoint the Board and would be responsible to the two Parliaments for the operation of the Agency.

The Board

The Agency would have a board of five members, responsible to the Ministerial Council for the Agency's strategic direction and financial management. The Board would not make decisions in relation to technical matters, or individual therapeutic product marketing applications.

The Managing Director

The Managing Director would be a member of the Board, the chief executive of the Agency responsible to the Board for finance and administration matters, and the "statutory decision-maker" responsible for making decisions in relation to therapeutic products.

3.3 Ministerial Council

The Agency would be overseen by a Ministerial Council (described under Section 3.2). The composition of the Ministerial Council and its role would be set out in a treaty between the two countries.

The role of the Ministers on the Council would be to represent the interests of the two countries in relation to the Agency's:

- strategic direction;
- capability (ability to function effectively);
- integrity (e.g. ensuring the Agency adopts and exhibits values and behaviours appropriate to a public body); and
- financial performance.

This oversight role would ensure the Agency is responsive to Ministers and Parliaments in both countries. The Ministers would be responsible to their respective Parliaments for the operation of the Agency.

The Ministerial Council would appoint the members of the Board, including the Managing Director.

The Council would also make delegated legislation (Ministerial Council Rules). These Rules would include:

- details of the governance arrangements that apply to the Agency, (e.g. the processes to be followed by the Agency's Board);
- requirements relevant to the regulation of therapeutic products (e.g. the requirements that must be met to before you can sell a product); and
- fees and charges.

3.4 Board

The Board would be responsible to the Ministerial Council for the Agency's strategic direction and financial performance.

The Board would have five members:

- the Chair;
- the Managing Director of the Agency (and statutory decision-maker);
- a person with broad experience in the Australian public health sector;
- a person with broad experience in the New Zealand public health sector; and
- a person with broad commercial experience.

Board members would be appointed on merit (because of their skills and experience) and would be required to act in the interests of the Agency, rather than as representatives of particular countries or stakeholder groups.

It is proposed that appointments to the Board would be made by the Ministerial Council on the following basis:

- The Managing Director and the Chair would be appointed with the agreement of both Ministers. It is essential that both Governments have confidence in these key board members.
- In the first instance, consensus would be sought on the remaining three Board member appointments.
- Failing consensus on the remaining three members, the Australian health sector person and the person with commercial experience would be selected by the Australian Minister, and the New Zealand health sector person would be selected by the New Zealand Minister of Health.
- A majority of the Board members would be Australian citizens or residents.³
- All instruments of appointment would be signed by the Australian Minister.

3.5 Managing Director

The Agency would have a Managing Director appointed by the Ministerial Council who would:

- be a member of the Board;
- be the chief executive of the Agency;
- be the "statutory decision-maker" in relation to therapeutic product approvals; and
- make technical orders, such as labelling requirements.

The Managing Director would be accountable to the Board for financial and administrative matters and would provide regular reports to the Board on relevant issues, including:

- key events and significant activities over the period, especially unforeseen issues and action being taken;
- analysis of the business environment in which the Agency operates, and covering action to address risk and vary strategy;
- significant changes, including restructuring and changes in key personnel or infrastructure of the Agency;
- a review of the Agency's key financial targets such as operating results against budget; and
- a review of output performance against measures of cost, quantity, quality and timeliness.

³ This includes NZ citizens resident in Australia.

The staff of the Agency would be accountable to the Managing Director.

The Managing Director of the Agency would be responsible for regulatory decisions in much the same way as the Secretary of the Department of Health and Ageing (under current Commonwealth therapeutic goods legislation in Australia) and the Minister of Health in New Zealand are each currently responsible for regulatory decision-making. The Managing Director would be accountable for regulatory decisions through a merits review process (see Part I; Section 2) and through judicial review (see Part I; Section 3).

Expert advisory committees would provide advice to the Managing Director in connection with regulatory decisions – see Part C; Section 2.4 for more detail.

3.6 Stakeholder Input

A range of stakeholders has interests in the operation and outcomes of the Agency, including other government agencies and departments, State and Territory governments in Australia, consumers, industry groups and professional groups. The Agency would have in place mechanisms for ensuring appropriate stakeholder consultation and input to its operation. For example, it is proposed that meetings between the Agency and key stakeholders be held twice a year, with minutes of proceedings being available to the Board and to the Ministerial Council. It is also envisaged that there would be bilateral discussions on particular topics (e.g. sector-specific matters) as required.

The function of stakeholder liaison meetings would be to advise the Agency's Managing Director on issues affecting the constituencies of the stakeholders (e.g. the impact of a particular regulatory requirement on industry compliance costs or on consumer choice). Such meetings would advise on the regulatory scheme in general, rather than on particular regulatory decisions.

3.7 Financial and Administrative Accountability

The Agency would be subject to essentially the same accountability arrangements as an Australian Commonwealth authority or New Zealand Crown entity, including:

- a requirement to provide plans/statements of intent to both Governments, which would be tabled in the Parliaments;
- a requirement to submit annual reports to the Ministerial Council, including audited financial statements (these reports would be tabled by Ministers in their respective Parliaments); and
- a joint audit carried out by the New Zealand and Australian Auditors-General.

There will be no unnecessary duplication of reporting requirements. For example there will be only one annual report, one set of financial statements and one audit process.

3.8 Accountability under Other Legislation

The Agency would be subject to the laws of both countries in relation to access to information (the Freedom of Information Act in Australia and the Official Information Act in New Zealand), and review of administrative decisions by the Ombudsman.

3.9 Accountability to Parliaments

The Agency would be accountable to the Australian and New Zealand Parliaments in essentially the same way as Commonwealth authorities in Australia and Crown entities in New Zealand. They will be accountable:

- via the Ministers on the Ministerial Council; and
- directly to Parliamentary committees.

Question 2:

The governance and accountability arrangements described above have been developed by officials and have the in-principle agreement of both Governments.

Are there any aspects of the governance and accountability arrangements that you feel could be improved? If so, what alternative(s) would you recommend, and why?

4. INTERNAL ORGANISATION OF THE AGENCY

The Agency would have offices in both New Zealand and Australia. There may be a mix of employment arrangements within the Agency. Individual staff in the Agency would be employed on terms and conditions no less favourable than those that currently apply. It is proposed, for example, that existing staff from the TGA would continue to be employed under the Australian Public Service Act conditions.

It is proposed that the Agency's internal organisation would be based broadly on a scheme of regulation by type of product. In such a scheme there would be separate regulatory units within the Agency, each of which would be responsible for overseeing all aspects of the regulation of a category of products. For example, there may be separate regulatory units for:

- prescription medicines;
- OTC medicines;
- medical devices; and
- products currently regulated as complementary medicines in Australia and as dietary supplements in New Zealand (other than food-type dietary supplements, see Part F; Section 6.2).

Additionally, there would be other units in the Agency structure with responsibility for undertaking corporate activities and those regulatory activities that apply to more than one type of product (such as problem reporting and recalls, surveillance, licensing and auditing of manufacturers, export certification and laboratory testing facilities). There would also be

other units to administer the activities that may be undertaken by the Agency but which are outside the scope of the joint therapeutic products regulatory scheme (e.g. chemical hazard assessment in Australia and pharmacy audits in New Zealand). Operationally, the regulatory units could set up agreements with the other units for the provision of services.

The detailed internal organisation of the Agency will be developed further during implementation planning⁴. The Managing Director and the Board will have ongoing responsibility for these matters once the Agency is established.

Question 3:

What are the key issues that should influence the internal organisation of the Agency?

⁴ The period from the time both governments approve the joint agency proposal to the commencement of operation of the Agency, during which time legislation will be drafted and detailed technical requirements settled.

PART B: ESTABLISHING THE AGENCY AND THE REGULATORY SCHEME

1. ESTABLISHING THE AGENCY

Three basic approaches to establishing the Agency have been identified. Each would involve Australia and New Zealand entering into a treaty in relation to the institutional and regulatory framework for the joint agency, and each country legislating to give effect to aspects of these arrangements. In particular, under any of these approaches both countries would enact legislation that would recognise the Agency as the therapeutic products regulator for that country, and would give effect to the regulatory decisions of the Agency.

The difference between the approaches lies in the extent to which issues relating to the establishment and legal personality of the Agency are addressed in the treaty or in national legislation. For ease of reference these approaches are described as the "national legislation approach", the "treaty approach" and the "blended approach".

1.1 The National Legislation Approach

Under the national legislation approach, the Agency would be established under either Australian or New Zealand legislation. A treaty would set out the agreed governance and operational arrangements for the Agency, and would require one country to enact legislation to give effect to this arrangement. The legislating country would then enact detailed legislation giving effect to the agreed governance and operational arrangements. Changes to those arrangements would be effected by changing that country's legislation.

This approach is asymmetrical, and would be likely to give rise to concerns in the non-legislating country. If the Agency were established under Australian legislation, for example, this would not deliver an equivalent degree of voice to New Zealand stakeholders or accountability to the New Zealand Parliament, at least without a number of safeguards designed to ensure effective New Zealand voice and accountability. However there would then be a risk that these safeguards would impede timely changes to the regulatory scheme, and could make the Agency less responsive to all stakeholders.

1.2 The Treaty Approach

Under the treaty approach, the Agency would be established under the Treaty, rather than requiring the Agency to be established under the law of one of the countries. In other words, the Treaty would not only set out the agreed governance and operational arrangements for the Agency, but would go on to establish the Agency and provide for it to be a legal person. Legislation in each country would recognise the legal personality of the Agency created by the treaty.

Some concerns have been identified in relation to this approach. In particular, there is a concern that the Agency would be an international organisation, with international legal personality. This may have unintended consequences.

1.3 A Blended Approach

Under the blended approach:

- a treaty would establish the Ministerial Council, and the Board of the Agency. The membership of the Board would be specified in the Treaty. The functions of the Board would be specified in the treaty and in Ministerial Council Rules;
- the Board would not be given legal personality by the treaty;
- the Board would be given legal personality by the conferral of corporate status on the Board under an Australian Act. That body corporate would be the Agency. The Australian Act would provide for the Agency to have the functions specified in the Treaty and Rules and the capacity to perform those functions; and
- the Treaty would require the Australian Government:
 - to introduce legislation along these lines, and
 - not to introduce any amendment to these provisions without consent of the New Zealand Government.

This approach addresses the key issues identified in relation to establishment mechanisms. In particular, it is intended to ensure that:

- key aspects of governance would be determined in (or under) the Treaty, by agreement between the two participating Governments;
- the Agency would be a single legal entity;
- the Agency would not be an international organisation; and
- voice and accountability concerns of both countries would be addressed because the Board would be established by the Treaty, and its composition and operation would be governed by the Treaty and Ministerial Rules, and not by domestic legislation in either country.

No significant difficulties have been identified in relation to this option.

Final decisions on establishment options will be made following the conclusion of negotiations between the two Governments.

Question 4:

Do you have any concerns in relation to the blended approach described above?

If so, how might these concerns be addressed?

2. REGULATORY FRAMEWORK

2.1 The Regulatory Framework for Therapeutic Products - Overview

The standards and requirements that would apply to therapeutic products would be prescribed by the Treaty and by new legislation in Australia and New Zealand. This new framework would replace the existing Australian Therapeutic Goods Act, Regulations and Orders and the existing New Zealand Medicines Act and Regulations.

The Treaty described above would set out broad enduring principles and goals for the joint regulatory scheme.

An Act in each country would contain the broad regulatory matters and obligations that must be contained in primary legislation, such as making it an offence to supply therapeutic products that have not been licensed by the Agency or which do not comply with requirements and standards prescribed in the Rules and Orders.

A single set of Rules made by the proposed Ministerial Council, which would be analogous to regulations in the current systems, would contain much of the detail of the regulatory requirements. For example, the Rules would set out the mandatory requirements for obtaining a licence to market a product.

Orders would be made by the Agency's Managing Director in relation to more technical issues, such as manufacturing standards and labelling requirements.

An indicative outline of the regulatory content of the Treaty, Acts, Rules and Orders, is provided in Appendix 2.

2.2 Delegated Legislation Made by the Ministerial Council and the Agency

One of the key features of the proposed new legislative framework is the proposal that the Ministerial Council and the Agency's Managing Director will be given the power to make delegated legislation in the form of Rules and Orders, as described above. This delegated legislation would have direct effect in both countries, without needing to be incorporated in domestic legislation.

In New Zealand and Australia the Executive Government and statutory office holders already have these powers. In both countries these powers are subject to a number of controls, including publication requirements, Parliamentary scrutiny and judicial review. These controls would need to be adapted to apply to Rules and Orders made under the joint scheme, including:

- requiring consultation with stakeholders as part of the process of making delegated legislation;
- requiring that the instruments be publicly available free of charge (it is proposed to publish the instruments on the internet);
- making the instruments subject to the *New Zealand Regulations (Disallowance) Act 1989*, and the disallowance regime provided for under the *Australian Acts Interpretation Act 1901*. A Rule or Order disallowed in either country would be ineffective in both. In relation to certain Rules that address matters that would generally be included in primary legislation in Australia or New Zealand, but which are contained in Rules to ensure uniformity (e.g. the power to cancel or suspend a product licence), it might be appropriate to consider additional safeguards; and
- providing that the instruments are subject to judicial review in the same circumstances and on essentially the same grounds as other delegated legislation, before the courts of either country. A Rule or Order set aside in either country would be ineffective in both.

PART C: REGULATORY SCHEME FOR THERAPEUTIC PRODUCTS

1. OVERVIEW

1.1 Scope of the Regulatory Scheme

The Agency would regulate products represented to be for, or likely to be taken to be for, a therapeutic purpose. These products are referred to in this discussion paper as 'therapeutic products'.

Therapeutic products would include prescription and OTC medicines, medical devices and products currently regulated in Australia as complementary medicines. They would also include products regulated in New Zealand as herbal medicines, homoeopathic medicines and dietary supplements (other than food-type dietary supplements).

Therapeutic product - a product that is represented in any way to be, or that is likely to be taken to be, for therapeutic use; or
an ingredient or component in the manufacture of therapeutic products; or
a container or part of a container for therapeutic products.

Therapeutic use - use in, or in connection with:

- preventing, diagnosing, curing or alleviating a disease, ailment, defect or injury in humans; or
- influencing, inhibiting or modifying a physiological process in humans; or
- testing the susceptibility of humans to a disease or ailment; or
- influencing, controlling or preventing conception in humans; or
- testing for pregnancy in humans; or
- the replacement or modification of parts of the anatomy in humans.

Some products would be excluded from regulation by the Agency, such as foods (including food-type dietary supplements), cosmetic-like products (e.g. hair dyes, denture adhesives and some sunscreens) and personal aids such as incontinence pads, because they would not meet the definition of 'therapeutic product'.

The Managing Director would be able to declare a product to be, or not to be, a therapeutic product, a medicine or a medical device, consistent with the legislative definitions for these types of products. This power would be of particular use in dealing with products at the interfaces between therapeutic products and foods, cosmetics and personal aids. Safeguards would be put in place to ensure that the Managing Director could not use this power to extend the definition of 'therapeutic product' beyond that intended by the legislation and without appropriate parliamentary scrutiny.

1.2 Terminology

The term 'therapeutic product' is used in this paper to describe collectively the products falling within the scope of the joint regulatory scheme. A review of international approaches shows that a range of terms is used to describe collectively medicines (including many complementary medicines) and medical devices. Such terms include 'medical products'⁵, 'health products'^{6,7}, and 'therapeutic products'^{8,9}. There is no standard internationally agreed term. The term 'therapeutic good' is currently used in the Australian legislation to describe prescription, OTC and complementary medicines and medical devices but this term is not well understood by the general public. There is no similar collective term in New Zealand legislation.

Of the three collective terms used in other countries to describe the group of products to be regulated by the Agency, 'health product', 'therapeutic product' and 'medical product', the term 'health product' is considered to be too general and may apply to products such as those for personal hygiene. It is therefore proposed that either 'therapeutic product' or 'medical product' be the term used in the legislation to describe collectively the products to be regulated by the joint scheme.

Question 5:

Please indicate your preferred collective term to describe the products to be regulated by the Agency.

Give reasons to support your proposal.

1.3 Types of Therapeutic Products

Internationally, therapeutic products are generally categorised broadly as medicines and medical devices depending on the means by which they achieve their action. Additionally, some types of products may meet the definition of therapeutic product but may not be medicines or medical devices.

1.3.1 Medicines

Under a joint regulatory scheme, medicine would be defined as:

Medicine - a therapeutic product that is represented to achieve, or is likely to achieve, its principal intended action by pharmacological, chemical, immunological or metabolic means in or on the human body.

⁵ The Swedish Medical Products Agency (Läkemedelsverket) regulates medicines (including natural remedies and homeopathic products), medical devices and cosmetics

⁶ The French Agency for Health Safety of Health Products (L'Agence française de sécurité sanitaire des produits de santé) regulates medicines, medical devices and cosmetics

⁷ The Health Products and Food Branch of Health Canada regulates therapeutic products, food, natural health products, biologics and genetic therapies

⁸ Swissmedic, the Swiss Agency for Therapeutic Products regulates medicines (including complementary and herbal medicines) and medical devices

⁹ The Therapeutic Products Directorate within Health Canada's Health Products and Food Branch regulates drugs and medical devices

This definition is consistent with international approaches.

The types of products currently regulated as 'medicines' in both Australia and New Zealand would continue to be regulated as medicines under a joint agency. These would include:

- prescription medicines;
- medical gases;
- vaccines;
- allergens;
- biotechnology medicines;
- plasma products, including immunoglobulins;
- radiocontrast agents;
- dialysis solutions; and
- over-the-counter (OTC) medicines.

Additionally, radiopharmaceuticals, many sunscreens, products currently regulated in Australia as complementary medicines and products regulated in New Zealand as herbal medicines, homoeopathic medicines and dietary supplements (other than food-type dietary supplements) would also meet the proposed definition of 'medicine'. All of these product types are regulated in Australia as therapeutic products. However, most are not currently regulated as therapeutic products in New Zealand. Therefore, the proposals in this paper would extend the scope of therapeutic products legislation in New Zealand. See Parts D and E for further information.

There is no internationally accepted collective term to describe the group of products currently regulated in Australia as complementary medicines and products regulated in New Zealand as herbal medicines, homoeopathic medicines and dietary supplements (other than food-type dietary supplements). For convenience, these products are referred to collectively in this discussion paper as 'complementary healthcare products'. The use of this term in the discussion paper does not necessarily mean that it would be used in the legislation to be administered by a joint agency. The regulation of complementary healthcare products, including a discussion on appropriate terminology, is covered in more detail in Part F.

For the purposes of discussion in this paper, all products meeting the proposed definition of 'medicine' are referred to collectively as 'medicines'.

1.3.2 Medical devices

Under a joint regulatory scheme medical device would be defined as:

<p><i>Medical device</i></p> <p>(a) any instrument, apparatus, appliance, material or other article (whether used alone or in combination, and including the software necessary for its proper application) intended, by the person under whose name it is or is to be supplied, to be used for human beings for the purpose of one or more of the following:</p> <ul style="list-style-type: none">• diagnosis, prevention, monitoring, treatment or alleviation of disease;• diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap;• investigation, replacement or modification of the anatomy or of a physiological process;• control of conception; <p>and does not achieve its principle intended action in or on the human body by pharmacological, immunological or metabolic means, but may be assisted in its function by such means; or</p> <p>(b) an accessory to such an instrument, apparatus, appliance, material or other article.</p>

This definition is consistent with international approaches.

1.3.3 Other therapeutic products

The joint regulatory scheme would also make provision for the regulation of therapeutic products that do not meet the definitions of medicine or medical device. Such products would include tampons and hospital-grade and household disinfectants. Additionally, the scheme would cater for new types of products developed using emerging technologies and which are not medicines or medical devices. Further information is provided in Part G; Section 3.

Question 6:

Do you agree with the overall scope of the regulatory framework set out above?

If not, in what respects should it be modified, and why?

1.4 Principles of the Regulatory Scheme

Governments have agreed that the regulatory scheme should be designed to:

- be responsive to public health needs of each country;
- deliver common regulatory outcomes;
- enable New Zealand and Australian participation;
- be accountable through Ministers to both Parliaments and both Governments;
- provide a transparent and informed decision-making process; and
- ensure national sovereignty is preserved.

The proposed regulatory scheme outlined in this paper has been developed having regard to the above principles and the need to ensure that regulatory controls will:

- enhance public health and safety;
- facilitate access to appropriate, safe and effective therapeutic products;
- manage access to needed but unapproved therapeutic products;
- utilise international regulatory best practices;
- make decisions in an acceptable timeframe; and
- provide useful and appropriate information to consumers.

The proposed regulatory framework for the Agency has also been developed having regard to the Council of Australian Governments' *Principles and Guidelines for National Standard Setting and Regulatory Action by Ministerial Councils and Standard-Setting Bodies* and the New Zealand Code of Good Regulatory Practice *Principles of Efficiency, Effectiveness, Transparency, Clarity and Equity*.

Whilst the regulatory scheme is designed to deliver common regulatory outcomes in the two countries, it is recognised that the scheme would need to enable either country to 'opt out' of a common regulatory decision. The opt-out could only be invoked in extraordinary circumstances (e.g. to accommodate differing public health policy or public health imperatives).

The opt-out may be:

- general or substance/product-specific; and
- invoked at any time in the life-cycle of a product.

Where one country invoked the opt-out from a regulatory decision to approve a product, this would generally be reflected in the product licence for that product, such that the licence would be limited to one jurisdiction only. An example might be Australia invoking the opt-out in relation to abortifacients. In this circumstance, abortifacients approved by the Agency would receive a New Zealand-only product licence.

Where a country invoked the opt-out in relation to a scheduling decision (see Part D; Section 4), this would result in different access controls applying in each country to products in that class.

Question 7:

Are there other principles you think should be applied when developing further detail on the regulatory framework for therapeutic products?

Question 8:

Under what circumstances do you think it should be possible to invoke the opt-out mechanism?

1.5 Risk-based Approach to Regulation

There are potential risks associated with the use of any therapeutic product. The objective of regulation is to protect public health by managing these risks without imposing excessive compliance costs on industry or unduly restricting consumer choice. The Agency would provide structures and mechanisms to regulate therapeutic products using a risk management approach.

As described in Section 1.3, therapeutic products would be categorised broadly, on the basis of the means by which they achieve their action, as medicines or medical devices. Within each category, products would be regulated according to the level of the assessed risk.

Medicines would be classified according to risk into one of three classes based on ingredients, intended purpose and type of product (for example injectable solution, oral tablet or topical cream):

Class I	Low-risk (e.g. most sunscreens, most complementary healthcare products)
Class II	Medium-risk (e.g. most OTC medicines, some complementary healthcare products)
Class III	High-risk (e.g. prescription medicines, vaccines, biotechnology medicines, radiopharmaceuticals, injectable medicine dosage forms, medicines for use in serious diseases, which may include some complementary healthcare products)

Operationally, the regulation of medicines would be handled by appropriately skilled and qualified staff working in three separate units within the Agency. (See Part A; Section 4). The three units would regulate:

- prescription and other specified Class III medicines (see examples above);
- OTC medicines; and
- complementary healthcare products.

Further detail on the risk-based approach to the regulation of prescription and OTC medicines is presented in Part E of this discussion paper. The risk-based approach to the regulation of complementary healthcare products is covered in Part F.

Consistent with the framework recommended by the Global Harmonisation Task Force, *medical devices* would be categorised into one of six medical device classes using the manufacturer's intended purpose, and a set of risk-based classification rules:

Class I	Low-risk (e.g. walking aids, non-sterile examination gloves, scalpels, manual drills and saws, dental curing lights)
Class IIa	Low to medium-risk (e.g. dental drills, anaesthetic breathing circuits, single-use catheters, X-ray film)
Class IIb	Medium–high-risk (e.g. insulin pens, baby incubators, stents, haemodialysers, external pacemakers, orthopaedic implants, external defibrillators, radioactive therapy sources)
Class III	High-risk (e.g. heart valves, absorbable sutures, vascular prosthesis, vascular stents, heparin coated catheters, IUDs, condoms with spermicides).
AIMD generators,	Active Implantable Medical Devices (e.g. implantable pulse implantable electrodes and implantable drug infusion devices). AIMDs are treated as Class III devices
IVD	<i>In Vitro</i> Diagnostic Devices such as serology and nucleic acid amplification tests used to detect HIV, hepatitis A/B/C etc, rubella

Further detail on the risk-based approach to the regulation of medical devices is presented in Part G of this discussion paper.

Question 9:

Do you agree that the Agency should adopt a risk-based approach to the regulation of therapeutic products? If not, what alternative approach would you suggest?

Why would this alternative approach be more effective in achieving the overall objective of protecting public health and safety?

1.6 Regulatory Activities

The regulatory activities that would be undertaken by the Agency are described in the following table:

Table 1: Activities to be undertaken by the Agency

Technical evaluation	<ul style="list-style-type: none"> • evaluating and assessing products for safety, quality and efficacy • evaluating substances for inclusion in the lists of substances permitted in Class I medicines (see Part E; Section 2.2 and Part F; Section 8.2) • collecting and evaluating data on problem reports and adverse reactions to therapeutic products and ensuring appropriate follow-up actions (see Part D; Section 8 and Part G; Section 2.9)
Regulatory action substances	<ul style="list-style-type: none"> • determining level of access to medicines ("scheduling") (see Part D; Section 4) • regulating access to unlicensed products (see Part D; Section 9 and Part G; Section 2.15) • exempting and excluding therapeutic products and/or persons from certain requirements (see Part C; Section 2.2.8) • recalling and issuing warning statements for therapeutic products (see Part D; Section 8.3 and Appendix 5) • imposing conditions on the supply of therapeutic products through the inclusion of conditions on the product licence or export only authorisation (see Part C; Section 2.2.1 and Part D; Section 10) • enforcing compliance through administrative and criminal sanctions for breach of regulatory requirements in legislation, product licences, export only licences, manufacturing licences, etc. (see Appendix 5)
Expert advice	<ul style="list-style-type: none"> • providing secretariat and technical support to expert advisory committees • receiving and actioning advice from expert advisory committees

Decision making	<ul style="list-style-type: none"> • granting, refusing, varying, suspending and revoking product licences for one or both jurisdictions and licences for export only products • granting, refusing, varying, suspending and revoking licences to manufacture therapeutic products in Australia or New Zealand. (see Part C; Section 2.2) • declaring that a product or type of product is or is not a therapeutic product, or a medicine or a medical device (see Part C; Section 1.1) • maintaining a database, or Register, of therapeutic products that are authorised for marketing in one or both jurisdictions or are authorised for export only (i.e. export from the Australia/New Zealand market) (see Part C; Section 2.3)
Post-Market Surveillance	<ul style="list-style-type: none"> • implementing appropriate post-market surveillance programmes for different types of products (see Part D; Section 8 and Part G; Section 2.9)
Communicating decisions	<ul style="list-style-type: none"> • publishing information and guides • publishing regulatory decisions by providing access to a database, or Register, of therapeutic products that are authorised for marketing in one or both jurisdictions or are authorised for export only (i.e. export from the Australia/New Zealand market)
Setting standards	<ul style="list-style-type: none"> • setting and monitoring standards for therapeutic products, processes and premises, including requirements for manufacturing, product information, labelling, etc (see Part C; Section 2.7) • setting and monitoring standards for advertising of therapeutic products (see Part J)
Approving activities	<ul style="list-style-type: none"> • auditing and licensing manufacturers (see Part D; Section 7)

Certain regulatory activities currently carried out by the TGA, Medsafe and/or Australian States and Territories would not be covered by the therapeutic products regulatory scheme or included in the legislation administered by the Agency. However, the Agency may provide services in relation to these activities on behalf of the responsible Australian and/or New Zealand agencies. Further information is provided in Appendix 4.

New Zealand officials will be consulting separately on those aspects of medicines regulation that will remain a New Zealand only responsibility. These generally relate to controls on prescribing and dispensing and the wholesale and retail supply of products within New Zealand. A separate consultation process in New Zealand will seek comment on any aspects of these controls that need updating for inclusion in new legislation.

1.7 Protection and Release of Information

Both Australia and New Zealand have legislative schemes that guarantee the right to access information held by a public sector agency - the *Official Information Act 1982* in New Zealand and the *Freedom of Information Act 1982* in Australia.

The purpose of both Acts is to provide for openness in government to facilitate accountability and participation in government decision-making processes by those outside of government.

In accordance with the principle of "no lesser accountability", it is proposed that, as a starting point, the Agency would be subject to both Acts. Interested parties would then have the right to request information from the Agency on the same basis as would apply if the Agency were a public sector agency operating only in Australia or New Zealand. More detailed work will be carried out to ensure that, in practice, the Agency is able to provide a consistent approach to information access.

The right to access information is currently subject to a number of limitations. The *Official Information Act 1982* and the *Freedom of Information Act 1982* allow certain classes of information (e.g. personal information) to be withheld in specified circumstances.

In addition, both Australia and New Zealand have obligations under the GATT TRIPS agreement that require both countries to protect certain confidential information provided in support of an application for consent to distribute a medicine containing a new active substance.

The provisions are designed to protect data from "unfair commercial use" or disclosure. Australia and New Zealand have adopted similar policies to protect this information and, in practical terms, this means that information is protected for a period of five years from the date of product approval.

Question 10:

Are there any other categories of information that would be held by the proposed joint agency and which should be subject to controls on its release, either permanently or for a defined time period?

Please identify any such categories and explain why you take this view. Please provide relevant material and comment to justify your view bearing in mind the recognised public interest in maintaining open government.

1.8 Other Requirements

Therapeutic products might also need to meet requirements set by other regulatory agencies in Australia or New Zealand. For example, legislation relating to bio-security, endangered species, and customs controls may be relevant to the use in products of materials of biological origin or materials from native, rare or endangered species. The Agency would not be responsible for the administration of this additional legislation. These matters are beyond the scope of this paper.

1.9 Fees and Charges

1.9.1 Cost recovery principles

Currently, in both Australia and New Zealand, cost recovery schemes operate for the funding of regulatory activities relating to therapeutic products.

The Agency's costs would relate to the full range of activities that fall within the scope of the Agency's enabling legislation and that are required for it to perform its role in the protection of public health and safety. These activities would include pre-market evaluation or assessment of products and/or substances; post-market monitoring and compliance; standard setting as appropriate; and the auditing and licensing of manufacturers.

It is proposed that, under a joint agency, a cost recovery scheme would be based on the following principles:

- cost recovery arrangements would be consistent with the objectives of the Agency and relate to the activities of regulation;
- the operating cost of the Agency would be fully funded by fees and charges recovered from industry;
- the costs to be recovered from industry would reflect the appropriate amount of regulatory activity needed to evaluate and manage the risks of different products;

- the level of fees and charges would be set to recover the full cost of the Agency's operations as efficiently and equitably as possible, and not be used for revenue raising purposes. Generally, the administrative costs of regulation would be recovered;
- cross subsidisation of regulatory activities within the Agency would be avoided;
- cost recovery arrangements would be subject to the Agency's accountability and reporting requirements;
- industry would be consulted on the development and implementation of the Agency's cost recovery arrangements;
- an ongoing and transparent process for reviewing the Agency's fees and charges would be developed in consultation with industry;
- an effective and efficient financial management system would be established to minimise handling costs for the fee payer and overheads for the Agency; and
- legal authority would be provided in the legislation for all fees and charges collected by the Agency.

The final principles of cost recovery would be subject to the Australian Government's final response to the Productivity Commission's report on *Cost Recovery by Government Agencies* and similar views of the New Zealand Government.

Activities that the Agency may perform under contract (for example, chemical hazard and risk assessments for Australia or pharmacy audits for New Zealand) are outside the scope of the joint scheme and would be funded separately from payments under those contracts.

1.9.2 Application of the principles

To achieve full cost recovery, a range of fees and charges would apply. For example, fees could apply to the licensing of products and the licensing of manufacturers. There could be one-off fees for evaluation of a product licence application or audit of a manufacturing facility and annual fees for maintaining a product licence or a manufacturing licence.

From time to time a schedule of fees and charges would be published. The schedule of fees and charges would be publicly available and would be published on the Agency web site.

The Agency would consult with industry representatives about the structure of the proposed schedule to ensure that the fees and charges accurately reflected the cost of regulating a particular industry sector or a product group and were borne equitably within and across the relevant sector or product groups.

Following consultation, the proposed schedule of fees and charges would be referred to the Board for consideration. The Board would then make its recommendation to the Ministerial Council in the form of a proposed Rule.

It is proposed that, as a guide for planning purposes, the new Agency would agree with industry representatives on a transparent and publicly available index for applying "inflation adjustments" to fees and charges. The index adjustment adopted could not be applied

without consultation, but its use would ensure that the Agency has adequate funds to meet general price increases without adversely impacting on service levels.

Question 11:

Are there any other principles you think should be applied to the setting of fees?

Give reasons for your proposals.

2. REGULATORY MECHANISMS

2.1 Introduction

Throughout the life of a therapeutic product, various regulatory mechanisms come into play. The tools applied to manage the risk associated with the product will depend on the stage in the life cycle and the type of product. The major regulatory tools and the points at which they impact on a product are shown in Figure 1.

2.2 Authorisation to Supply Therapeutic Products in Australia and/or New Zealand

2.2.1 Product licences

It is proposed that a therapeutic product could only be:

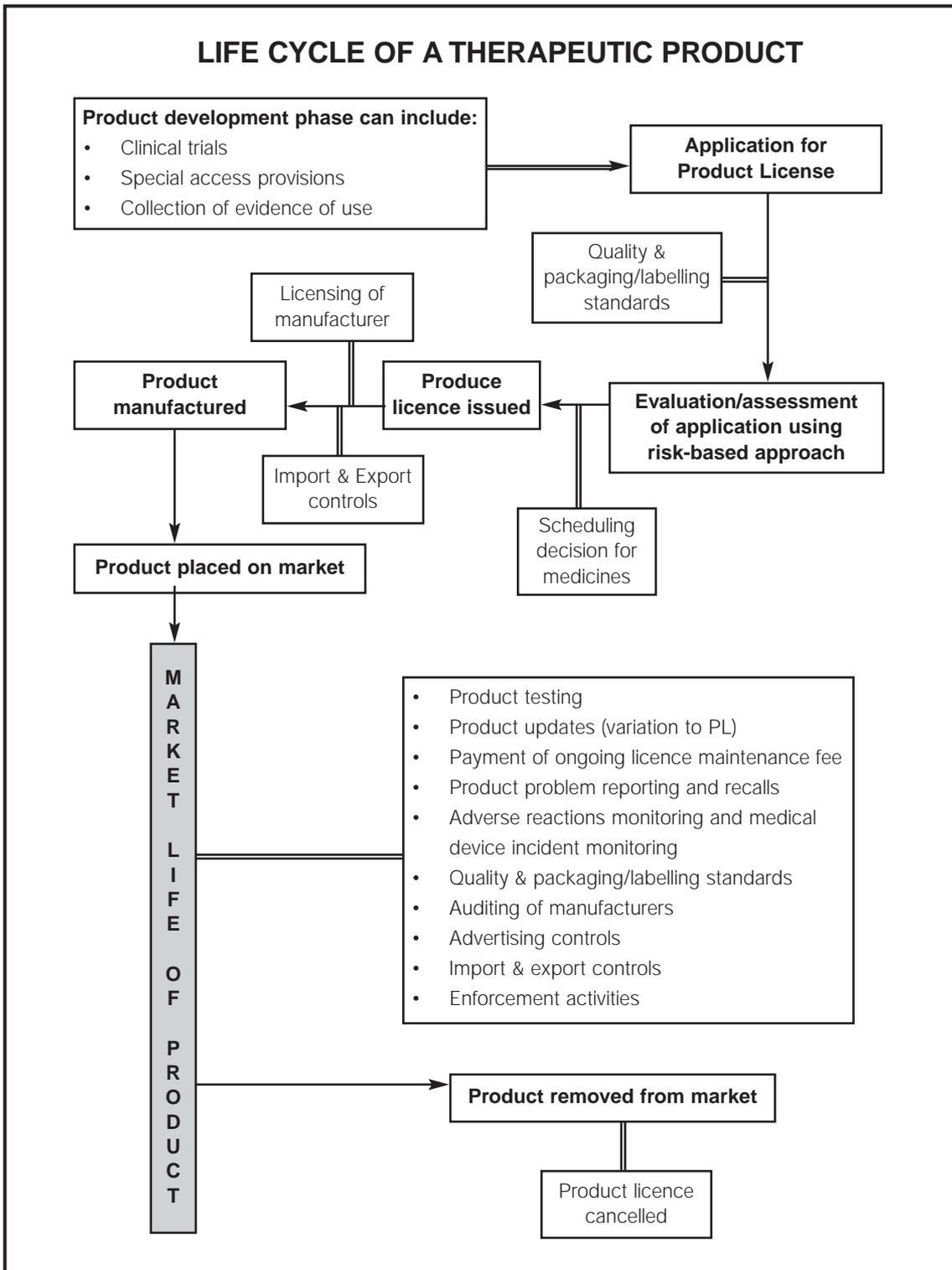
- imported into Australia or New Zealand; or
- exported to a third country from Australia or New Zealand; or
- supplied in Australia or New Zealand

by, or with the approval of, the holder of a product licence (PL) issued by the Agency, unless the product was specifically exempted from this requirement.

Product licence – an authorisation (issued under the legislation administered by the joint agency) for the sponsor to supply the therapeutic product/s that is/are the subject of the licence. Supply of the product/s would also be subject to other relevant legislation in the two jurisdictions (e.g. intellectual property law).

The obligation to hold a PL would be contained in the Acts. The means by which a sponsor would obtain a PL and the requirements to be met would be set out in the Rules and technical orders. The circumstances under which a product would be exempt from the requirement for a PL would be set out in the Rules.

Figure 1: Life Cycle of a Therapeutic Product



The PL holder or their authorised agent would be the sponsor of the product.

Sponsor – an individual or a company in Australia or New Zealand with the legal responsibility for the product in the jurisdiction(s) for which the product licence is valid.

Each PL would carry a unique number and, generally, a separate PL would be issued for each new product. The circumstances that would make a therapeutic product a new product would be set out in the Rules and would depend on the type of product (medical device or medicine), the risk classification of the product and the nature of the difference or change. In certain circumstances, it would be possible to 'group' more than one product in the same PL (see Section 2.2.2 below).

The product licence document would provide a summary of the particulars of the product and set out or refer to the conditions under which the product could be supplied.

In the case of a Class I medicine, it is proposed that the PL would include the following:

- PL number, which becomes the unique identifier for the product;
- date the PL was issued;
- name of the sponsor;
- product name;
- export name(s) of the product (if different from the product name);
- dosage form;
- route of administration;
- names and quantities of the active ingredients;
- names of excipients;
- indications the product is intended to carry;
- directions for use¹⁰
- container type & size &/or closure type¹⁰
- export versions of indications, directions for use and substitution of excipients;
- quantities of excipients that are restricted by quantity or concentration¹⁰
- name(s) and address(es) of the manufacturer(s) of the product;
- jurisdiction in which the product is authorised for supply (New Zealand or Australia or both); and
- conditions subject to which the PL is granted, including required warnings.

In the case of a Class II or Class III medicine, it is proposed that the PL would include the following:

- PL number, which becomes the unique identifier for the product;
- date the PL was issued;
- name of the sponsor;
- product name;
- export name(s) of the product (if different from the product name);
- dosage form;
- names and quantities of the active ingredients;
- names and quantities of excipients;
- approved indications for the product;
- directions for use;

- container and closure type;
- export versions of indications, directions for use, container type and substitution of excipients;
- name(s) and address(es) of the manufacturer(s) of the product;
- jurisdiction in which the product is authorised for supply (New Zealand or Australia or both); and
- conditions subject to which the PL is granted.

In the case of a medical device, the PL would contain information about the medical device including:

- PL number (unique entry number from the Register);
- date PL was issued;
- name and address of the sponsor;
- Global Medical Device Nomenclature System (GMDNS) code of the device product;
- jurisdiction in which the product is authorised for supply (New Zealand or Australia or both);
- conditions associated with the supply of that device product; and
- class of the device product.

For information on the GMDNS, see Part G; Section 2.5.

2.2.2 Separate and distinct products

In certain circumstances a therapeutic product would be considered to be separate and distinct from other therapeutic products for the purposes of the regulatory scheme. The circumstances that would make a therapeutic product a 'new therapeutic product' may depend on the type of product (medical device or medicine) and/or the risk classification of the product. These circumstances would be set out in the Rules.

Generally, a new therapeutic product would need a separate product licence. However, in particular circumstances, it would be possible to 'group' more than one product on the same product licence. For example, two medicines with the same sponsor and differing only in relation to indications for use, could be 'grouped' on the same product licence and have the same product licence number. Another example could be two or more medical gases with the same sponsor and comprising the same chemical elements or chemical compounds and differing only in the proportions of each element or compound in the mixture.

The authority to group products in one PL would be contained in the Rules. The circumstances in which products could be grouped would be set out in Orders. The detail of the Orders would be developed during implementation planning.

Medical devices

The criteria for determining if a medical device would be separate and distinct from other medical devices, and require a separate line entry in the Register, are set out below by device class.

A Class I device would be a separate and distinct medical device if it had a different:

- manufacturer, or
- sponsor; or
- GMDNS code (at the template name level).

A Class IIa, IIb, or I (sterile or measuring function) device would be separate and distinct medical device if it had a different:

- manufacturer; or
- sponsor; or
- medical device classification; or
- GMDNS code (at the generic device group level).

A Class III or AIMD device would be a separate and distinct medical device if it had a different:

- manufacturer; or
- sponsor; or
- medical device classification; or
- GMDNS code (at the generic device group level); or
- unique product identifier (e.g. product or model number).

Medicines

The criteria for determining if a medicine would be separate and distinct from other medicines, and require a separate line entry in the Register, are set out below by medicine class.

A Class I medicine would be a separate and distinct product if it had a different:

- product name; or
- dosage form; or
- active ingredients; or
- quantities of active ingredients; or
- indications; or
- excipients¹¹;
- or, for a Class I medicine containing any excipient that was a restricted ingredient, if it had a different:
 - quantity or concentration of an excipient that is restricted by quantity or concentration; or
 - directions for use where the medicine contains excipients that are restricted by quantity or concentration and the restriction relates to single or daily dosage limits.

¹¹ Some excipient changes, as specified on the PL, would be permitted in certain circumstances. For example, an excipient such as a compression aid or lubricant may be declared on the PL, but only be included in some batches. The circumstances in which such changes could occur would be set out in Orders.

A Class II or III medicine would be a separate and distinct product if it had a different:

- product name; or
- indications; or
- directions for use; or
- dosage form; or
- type of container; or
- formulation or composition.

2.2.3 Obtaining a product licence

In order to obtain a product licence, the sponsor would be required to submit an application to the Agency. The proposed application processes are described in Parts E, F and G of this discussion paper.

The application processes, data requirements and evaluation/assessment processes would be different for different types of products and different risk classifications.

The legislation and guidelines would set out the requirements for the format and data requirements of submissions to support product licence applications. For example, the Act would create the obligation to submit an application in the required format, the Rules would spell out the format and technical orders and guidelines might expand on technical detail.

2.2.4 Validity of a product licence

Once issued, a PL would generally remain valid provided annual fees are paid, unless suspended or cancelled by the Agency or cancelled at the request of the sponsor.

It is proposed that, in exceptional circumstances and in consultation with the sponsor, the Agency could issue a provisional PL for a time-limited period subject to conditions and further assessment of the product at the end of the authorisation period. This would be similar to the provisional consent mechanism currently used in New Zealand. For example, a provisional licence might be issued for a new HIV treatment on the basis of interim data from an ongoing clinical programme and where the interim data indicated that the product was likely to be of significant clinical benefit.

2.2.5 Jurisdiction of a product licence

Applicants would be able to apply for a product licence for both Australia and New Zealand (an Australia/New Zealand PL) or a licence for only one country (an Australian PL or a New Zealand PL). For each product type and risk classification, the same pre-market assessment process would apply regardless of where the product was to be marketed.

In exceptional circumstances, one Government may choose not to have a particular type of product authorised for supply in that country. In such a case, a sponsor would not be able to obtain a dual-country product licence. Refer to Section 1.4 of Part C for further information.

2.2.6 Conditions of a product licence

A PL would be granted subject to standard conditions, which would relate to (but not be limited to) such matters as:

- the duty of the sponsor to report certain matters to the Agency;
- the duty of the sponsor to retain samples and maintain information about the product and to make these available to the Agency on request;
- the responsibilities of the sponsor in relation to advertising; and
- the duty of the sponsor to update product particulars when specified changes are made to the product.

The standard conditions may be different for different types of products and risk classifications.

The PL could not be used to impose any conditions relating to the price of the product.

In addition to the standard conditions, the PL would set out any special conditions applying to the marketing of a particular product. For example, a special condition might be imposed on a product requiring the inclusion of a warning statement on the label of the product.

The obligation to comply with conditions would be contained in the Acts. The means for complying with conditions would be set out in the Rules. The standard conditions for different types of products would be set out in Orders.

PL details for medical devices are dealt with further in Part G; Section 2.5

2.2.7 Suspension or cancellation of a product licence

The Agency would be able to suspend or cancel a PL in the event that the sponsor failed to comply with their obligations or the Agency received new information on the safety, quality or efficacy of a product that made such an action necessary. Appropriate safeguards would be put in place to ensure that sponsors were informed and given adequate opportunity to respond to concerns and to seek a review of a decision to suspend or cancel a PL.

In certain serious circumstances, the Agency would have the power to cancel a PL with immediate effect. In other circumstances, the Agency would be obliged to advise the sponsor of an intention to cancel a PL and give the sponsor the opportunity to respond to the proposal. The sponsor could continue to supply the product until such time as the Agency made a decision to cancel the PL for the product.

In some circumstances, the Agency would be able to suspend a PL. For example, where the Agency was concerned that there was a risk of death, serious illness or serious injury from continued supply of the product. Suspension would stop further supply of the product pending provision of additional information by the sponsor to enable the Agency to determine whether or not the PL should be cancelled. The period of suspension could be up to six months and could be extended for a further period of up to six months, after

which time, if the sponsor had not been able to justify continuation of the PL, it would be cancelled.

The Agency could also cancel a PL at the request of the sponsor.

The power to suspend or cancel a PL would be contained in the Acts. The circumstances in which a PL may be suspended or cancelled would be contained in the Rules.

Suspension and cancellation of a product licence for a medical device is dealt with further in Part G, Section 2.14.

2.2.8 Exemption from requirement for a product licence

Certain products would be exempt from the requirement to hold a PL. The products, or types of products, that would be exempt would be set out in the Rules. The Rules would also set out any conditions applying to the supply of exempt products.

It is proposed that products, or types of products, exempt from the requirement for a PL would include (but not be limited to) the following:

- Products imported under personal importation provisions;
- Starting materials;
- Clinical trial products;
- Unlicensed products for use in individual patients under special arrangements (e.g. Special Access Scheme or authorised prescriber arrangements);
- Medicines compounded extemporaneously by a health practitioner (such as a pharmacist, herbalist, traditional Chinese medicine practitioner, traditional Maori healer etc.) to meet the needs of an individual patient; and
- Custom made medical devices.

Generally, conditions would apply to the circumstances in which a therapeutic product was exempt from the requirement for a PL.

Question 12:

Do you support the concept of product licensing for therapeutic products?

Question 13:

What requirements should be imposed on licence holders through the "standard conditions" on a product licence?

Question 14:

Are the criteria for determining what is a separate and distinct product reasonable? If not, what criteria should be used and why would these criteria be more appropriate?

2.2.9 Parallel importation

Parallel importation is the importation of therapeutic products acquired legally from the holder of the intellectual property rights in the exporting country, and imported into the importing country without the consent of the holder of the relevant intellectual property rights in that country. This can occur even if the global company owns the intellectual property rights in both countries.

In both Australia and New Zealand, a range of regulatory mechanisms currently operate to place controls on sponsors and manufacturers of therapeutic products and on pharmacists, to ensure that the quality, safety and efficacy of medicines are maintained throughout the distribution chain and that therapeutic products can be traced or recalled in the event of a problem. The effect of these mechanisms is to protect public health and to ensure effective monitoring and compliance with product safety standards. These mechanisms also have the effect of limiting parallel importation of therapeutic products.

It is not intended that the establishment of a joint scheme for the regulation of therapeutic products in Australia and New Zealand would alter existing arrangements in either country in relation to parallel importation. The proposed product licensing scheme would have the same effect as the current regulatory mechanisms in protecting public health and safety. As described in Part C; Section 2.2.1, under the proposed licensing scheme, a therapeutic product could only be imported into Australia or New Zealand, exported from Australia or New Zealand to a third country, or supplied in Australia or New Zealand by or with the approval of the holder of a product licence for the relevant country, unless specifically exempted from this requirement. This would ensure traceability of the product and that the supplied product was equivalent to the product that had been licensed. This would also have the effect of maintaining the *status quo* in relation to parallel importation.

2.3 Register of Therapeutic Products

The Agency would maintain a register of licensed products. This would facilitate post market monitoring of licensed products and enable the regulator to react quickly in the event of a safety alert.

The Register would contain particulars for:

- therapeutic products with current PLs; and
- therapeutic products for which the PL had been suspended or cancelled.

The information maintained in the Register would differ depending on the type of product and the risk classification of the product. The Register would be divided into parts to accommodate these differences.

The requirement for the Agency to maintain a Register would be established in the Acts. The Rules would provide for the creation of new parts to the Register as necessary to accommodate new types of products in the future.

Question 15:

Certain information held in the Register of Therapeutic Products would be available to the public.

What information should be publicly available?

What additional information should be available to sponsors?

2.4 Expert Advisory Committees

Both Australia and New Zealand have expert advisory committees as part of their regulatory systems for therapeutic products. The existing committees provide the regulatory authorities in both countries with independent, expert advice of a high standard. It is proposed that expert advisory committees would form a key part of a joint regulatory scheme.

Expert advisory committees would be established to provide the Managing Director of the Agency with scientific and regulatory advice. The general principles applying to expert advisory committees would be:

- Each committee would be established in the Rules.
- The composition, functions and mode of operation of each committee would be set out in the Rules.
- Committee members would be selected from relevant experts in Australia and New Zealand and the overall balance of each committee would reflect contemporary practice (including medical practice) in both countries.
- Membership of each committee would be determined on the basis of requisite expertise (not jurisdiction). Members would not be appointed to represent particular jurisdictions or interests, unless justified by the committee's terms of reference.
- Members of committees would be appointed by the Ministerial Council, with appointment decisions based on recommendations from the Managing Director.
- Appointment of members would be subject to confidentiality and conflict of interest requirements.
- Each committee could appoint sub-committees.
- The role of each committee would be advisory. Regulatory decisions would be the responsibility of the Managing Director or his/her delegate. Committees might be asked to advise on changes to regulatory requirements.

It should be noted that subsidisation of medicines would not be within the scope of the joint regulatory scheme. Therefore, bodies such as the Pharmaceutical Benefits Advisory Committee in Australia and PHARMAC in New Zealand would not be part of the regulatory scheme and are not included in this discussion.

The range of expertise and experience on expert advisory committees includes but is not necessarily limited to:

- general medical practice;
- specialist medical practice of a kind relevant to the committee's functions;
- pharmaceutical chemistry;
- pharmacology;
- toxicology;
- microbiology;
- medicine scheduling;
- consumer interest;
- complementary medicine practice;
- community pharmacy;
- manufacture of therapeutic products; and
- government regulation.

It is proposed that the committees established in the initial set of Rules and operational from the time the Agency commences business would include, but not necessarily be limited to the following.

2.4.1 Advisory committee on standards for therapeutic products

An advisory committee on standards of therapeutic products would advise the Managing Director on matters concerning standards for therapeutic products, labelling and packaging of therapeutic products and manufacturing principles for therapeutic products. This committee would also draw on expertise from the other advisory committees.

2.4.2 Advisory committee for medical devices

An advisory committee for medical devices would advise the Managing Director on matters concerning the quality, safety and performance of medical devices.

2.4.3 Advisory committee for prescription and specified Class III medicines

An advisory committee for prescription and specified Class III medicines would advise the Managing Director on matters concerning the quality, safety, efficacy and availability of prescription and other Class III medicines and other therapeutic products referred to the Committee. Such matters would include:

- pre-market evaluation of new products and changes to products;
- scheduling;
- standards; and
- specific labelling and other information requirements.

2.4.4 Advisory committee for OTC medicines

An advisory committee for OTC medicines would advise the Managing Director on matters concerning the quality, safety, efficacy and availability of OTC medicines and other therapeutic products referred to the Committee. Such matters would include:

- pre-market evaluation of new products and changes to products;
- evaluation of new substances;
- scheduling;
- standards; and
- specific labelling and other information requirements.

2.4.5 Advisory committee for complementary healthcare products

An advisory committee for complementary healthcare products would advise the Managing Director on matters concerning the quality, safety, efficacy and availability of complementary healthcare products and other therapeutic products referred to the Committee. Such matters would include:

- pre-market evaluation of new products and changes to products;
- evaluation of new substances;
- scheduling;
- standards; and
- specific labelling and other information requirements.

2.4.6 Advisory committee on adverse reactions to medicines

Under a joint regulatory scheme, an advisory committee would advise the Managing Director on matters concerning adverse reactions to medicines and the risk-benefit profiles of marketed medicines. Currently there are differences between Australia and New Zealand in arrangements for adverse reaction monitoring. It is envisaged that, in the lead up to implementation of joint arrangements for adverse reaction monitoring, committees in the two countries would provide advice on these matters, facilitating a smooth transition to a single advisory committee.

2.4.7 Advisory committee on medicine scheduling

An advisory committee on medicines scheduling would:

- advise the Managing Director on matters concerning medicine scheduling;
- consider proposals to change the scheduling classification of a medicine, with input from other relevant expert advisory committees; and
- review scheduling decisions.

See Part D; Section 4 for further information on proposed scheduling arrangements under a joint agency.

Question 16:

Do you think the range of expert advisory committees described above is appropriate?

If not, what other expert advisory committees should there be, and what would be the functions of these committees?

2.5 Power to Request Information

The Agency would be able to request information in relation to any PL application or any application to vary the terms or conditions of a PL. The Agency would also be able to request information in relation to any therapeutic product authorised for marketing in Australia or New Zealand or both countries, authorised for export only or exempt from the requirement for a product licence.

The power to request information would be contained in the Acts. The Rules would set out the circumstances under which the Agency may request information and the type of information the Agency may request. Offence provisions relating to requests for information would be contained in the Acts. Administrative penalties that would apply if the sponsor refused or failed to comply with a request would be set out in the Rules.

2.6 Powers to Request and to Obtain Samples

The Agency would have powers to request and to obtain samples of therapeutic products. These powers would be contained in the Acts. The circumstances in which samples could be requested or obtained and the procedures to be followed would be set out in the Rules.

2.7 Standards for Therapeutic Products

The Agency would set and monitor standards for medicines and other specified therapeutic products. These would include standards for the quality of products, ingredients in products, containers, closures and packaging (for example, child resistant closures and packaging), presentation, and labels on products. The standards would be contained in Orders to be developed during implementation planning.

Therapeutic products would be required to conform to standards unless specifically exempted in the legislation or with the written consent of the Managing Director. The obligation to comply with standards would be contained in the Acts. The circumstances in which a product should comply with a standard would be contained in the Rules. It would be an offence not to comply with a standard.

Standards for medical devices are dealt with at Part G; Section 2.8.

2.8 Review of Regulatory Decisions

Certain regulatory decisions would be subject to review (this is often referred to as an "appeal". For further detail, see Part I).

PART D :

REGULATION OF MEDICINES

As discussed in Part C; Section 1.3.1, it is proposed to define 'medicine' as:

a therapeutic product that is represented to achieve, or is likely to achieve, its principal intended action by pharmacological, chemical, immunological or metabolic means in or on the human body.

If this definition is applied, the broad term "medicine" would include:

- prescription medicines and OTC medicines, including:
- medical gases;
- vaccines;
- allergens;
- biotechnology medicines;
- plasma products, including immunoglobulins;
- radiopharmaceuticals;
- radiocontrast agents;
- dialysis solutions;
- most sunscreens; and
- complementary healthcare products.

Some stakeholders do not agree that complementary healthcare products should be defined as "medicines". For the purposes of this part of the discussion paper, the above definition of "medicine" has been applied in order to explain elements of the regulatory scheme that apply to all products with the mode of action covered by the definition. Part E describes in more detail some elements of the regulatory scheme applying to prescription and OTC medicines. Part F describes elements of the scheme applying to complementary healthcare products, including a further discussion on terminology and definitions.

1. RISK-BASED APPROACH TO REGULATION

1.1 Introduction

As discussed in Part C; Section 1.5, there are potential risks associated with the use of any therapeutic product.

The risk associated with a medicine is determined by a number of factors, including:

- The hazard ¹² of the substances contained in the medicine;
- The risk associated with the quality in manufacture of the dosage form of the medicine (e.g. injections and eye drops are required to be sterile, whereas tablets are not);

¹² Hazard is the capacity of the substance to produce an adverse health effect

- The quality of the medicine (e.g. poor quality medicines may be a safety concern if they are contaminated or adulterated with unsafe ingredients or contain unsafe degradation products or impurities; or they are ineffective due to stability problems or because they do not contain the labelled active ingredients);
- The purpose for which the medicine is intended to be used (e.g. serious disease or non-serious self-limiting condition); and
- The circumstances under which the medicine is to be used or sold (e.g. under supervision of an appropriately qualified healthcare professional or self-selection from a supermarket shelf).

Currently in Australia and New Zealand, both the TGA and Medsafe use risk-based approaches to the regulation of prescription and OTC medicines. The following proposals have been developed using the existing systems as a base and building on them.

1.2 Risk Classification

In the proposed regulatory scheme for medicines under a joint agency, medicines would be classified into three broad classes according to risk: Class I, Class II and Class III. The risk classification can be summarised in the Table 2.

Table 2: Risk classification for medicines

Intrinsic risk of the active ingredients in the medicine	Indication	
	Serious disease ¹³	Non-serious disease
Low intrinsic risk	Class III	Class I
Medium intrinsic risk	Class III	Class IIa ¹⁴ Class IIb
High intrinsic risk	Class III	Class III

The risk associated with a medicine may be managed in various ways:

- a requirement to comply with specified minimum standards or requirements, e.g. standards for good manufacturing practices to minimise the risk of quality problems;
- standard requirements for labels to ensure that errors in selecting and/or using medicines are minimised;
- pre-market evaluation or assessment to ensure that quality standards are met, the risk-benefit profile is acceptable and the medicine is efficacious for the proposed indication(s);

¹³ "Serious disease" refers to diseases, conditions, ailments or defects that cannot generally be diagnosed or treated without consulting a suitably qualified healthcare professional. Examples include cardiovascular disease, asthma and cancer.

¹⁴ It is proposed that Class II medicines be sub-classified as IIa and IIb depending on the requirement for professional supervision at point of sale. Class IIa medicines would be those medicines currently scheduled as 'pharmacist only' medicines.

- provision of adequate information to the consumer to facilitate appropriate use of the medicine;
- access controls (through medicine scheduling) to ensure that 'higher risk' medicines are used or sold under appropriate professional supervision;
- controls on medicine packaging designed to minimise the potential for harm (e.g. requirements for child resistant closures, controls over pack size);
- controls over advertising to ensure that advertisements are not false or misleading and are consistent with the terms of the medicine's product licence; and
- post-market monitoring systems to ensure that the marketed medicine continues to be of acceptable quality, safety and effectiveness and is being supplied in line with its product licence.

Tables 3, 4 and 5 summarise the types of medicine in each proposed class and the mechanisms that may be used to manage any risks associated with medicines in each class.

Table 3: Class I Medicines

Medicines in the class	Mechanisms for managing the risk
<p>Medicines that:</p> <ul style="list-style-type: none"> • Contain only low risk substances <p>AND</p> <ul style="list-style-type: none"> • Are not required to be sterile <p>AND</p> <ul style="list-style-type: none"> • Are intended to carry medium or general level indications for health maintenance, health enhancement or non-serious diseases, conditions, ailments or defects <p>OR</p> <ul style="list-style-type: none"> • Specified homoeopathic medicines 	<p>Minimal regulation at market entry: Licensing based on self-certification by the sponsor that the medicine complies with specified requirements</p> <ul style="list-style-type: none"> • Validation of key requirements by the Agency • Positive list of 'low risk' substances maintained in legislation <p>Requirement for evaluation and approval of new substances for 'Class I status'</p> <p>Compliance with specified standards, including specified principles of good manufacturing practice and product label requirements</p> <p>Controls over types of indications permitted for Class I medicines</p> <p>Desk-based post-market review (random and targeted) to check compliance of sponsor certifications</p> <p>Adverse reaction monitoring programme</p> <p>Random and targeted post-market laboratory testing</p> <p>Controls over advertising</p> <p>Surveillance activities</p>

Table 4 : Class II Medicines

Medicines in the class	Mechanisms for managing the risk
<p>Medicines that:</p> <p>Contain 'medium risk' substances</p> <ul style="list-style-type: none"> • substances that are scheduled as 'pharmacist only' or 'pharmacy' medicines or meet the requirements for scheduling as such • unscheduled 'new' substances that have not been approved for use in Class I medicines and do not meet the requirements for scheduling as prescription only medicines <p>AND</p> <p>Are intended to carry indications for health maintenance, health enhancement or indications for non-serious diseases, conditions, ailments or defects</p>	<p>Pre-market evaluation of an appropriate data set to determine quality, safety and efficacy of the medicine and acceptable risk benefit profile</p> <p>Scheduling as a pharmacist only medicine or pharmacy medicine (may not apply in all cases)</p> <p>Compliance with specified standards, including specified principles of good manufacturing practice and product label requirements</p> <p>Requirement for an approved product information (PI) document (for Class IIa medicines)</p> <p>Requirement for consumer medicines information consistent with the PI (for Class IIa medicines)</p> <p>Adverse reaction monitoring programme</p> <p>Random and targeted post-market laboratory testing</p> <p>Assessment of periodic safety update reports (new active substances only)</p> <p>Controls over advertising</p> <p>Controls over conditions of sale ¹⁵</p> <p>Surveillance activities</p>

Table 5 : Class III Medicines

Medicines in the class	Mechanisms for managing the risk
<p>Medicines that:</p> <p>Contain 'high risk' substances</p> <ul style="list-style-type: none"> • substances scheduled as 'prescription only' or meeting the requirements for scheduling as 'prescription only' <p>OR</p> <p>Are intended for the <i>in vivo</i> diagnosis of a disease, disorder or condition</p> <p>OR</p> <p>Are intended to carry indications in relation to a serious disease, condition, ailment or defect</p> <p>OR</p> <p>Are specified product types</p> <ul style="list-style-type: none"> • medical gas • vaccine • allergen¹⁶ • biotechnology medicine • immunoglobulin • radiocontrast agent¹⁷ • radiopharmaceutical • dialysis solution • special dosage form such as transdermal system and osmotic pump • injectable medicine dosage form • plasma product¹⁸ • medical device dependent upon the release of a substance for some or all of its action 	<p>Pre-market evaluation of an appropriate data set to determine quality, safety and efficacy of the medicine and acceptable risk-benefit profile</p> <p>Scheduling as a prescription only medicine (may not apply in all cases)</p> <p>Compliance with specified standards, including specified principles of good manufacturing practice and product label requirements</p> <p>Requirements for an approved product information (PI) document and consumer medicines information consistent with the PI</p> <p>Adverse reaction monitoring programme</p> <p>Laboratory testing</p> <ul style="list-style-type: none"> • Pre-market testing for specified product types • Random and targeted post-market testing <p>Assessment of periodic safety update reports (may not apply in all cases)</p> <p>Controls over advertising</p> <p>Controls over prescribing and dispensing¹⁹</p> <p>Market surveillance</p>

¹⁶ except an allergen for skin patch testing on unbroken skin

¹⁷ except barium sulphate preparation for radiological use

¹⁸ unless coated on a medical device

¹⁹ outside the scope of the joint agency legislation

Question 17:

Do you agree with the risk-based approach to the regulation of medicines described in this section of the paper?

If not, what alternative approaches would you like to see applied? Please indicate why you consider the alternative approach would be more appropriate.

2. PRODUCT LICENSING FOR MEDICINES

Under the proposed product licensing scheme described in Part C; Section 2.2 of this discussion paper, a sponsor would generally need to obtain a product licence for a new medicine before it could be supplied in the Australia/New Zealand market.

As described in Section 1 above, the Agency would regulate medicines according to the risk classification (Class I, II or III medicine). The factors used to determine the risk classification of a medicine would also determine:

- a) the product licensing process to be followed for the medicine;
- b) which unit in the Agency would carry out the pre-market evaluation or assessment of and issue the product licence for the medicine; and
- c) the extent of pre-market evaluation or assessment required for the medicine.

Class I medicines would be issued a product licence on the basis of sponsor self-certification and validation by the Agency of key requirements. Class II and III medicines would be required to undergo a pre-market evaluation of quality, safety and efficacy before they could be issued a product licence.

The sponsor of a new medicine would need to decide on the medicine risk classification in order to determine the data requirements for a product licence application. The sponsor would base their decision on the legislation and the guidelines issued by the Agency and could seek advice from the Agency in situations where the decision was not clear.

In general, product licence applications for medicines scheduled as prescription only and certain Class III medicines specified in legislation would be submitted to the unit responsible for the evaluation of prescription medicines and evaluated by that unit. However, a sponsor could submit a justification for evaluation of the new medicine by another regulatory unit where appropriate. Criteria on which such a justification could be based would be developed by the Agency and could include factors such as:

- whether the medicine, on balance, is likely to meet the criteria for non-prescription medicines (i.e. not a prescription-only medicine);
- whether the medicine meets the definition of a complementary healthcare product;

- the dosage form, strength, route of administration and/or proposed pack size of the new medicine;
- the nature of the condition to be treated by the medicine;
- whether the medicine is available without prescription in other countries with comparable regulatory systems to Australia/New Zealand;
- whether the product contains a substance that has a closely related chemical structure and similar therapeutic action to other substances that are in a less restrictive schedule.

Product licence applications for non-prescription medicines (other than medicines meeting the definition of 'complementary healthcare product') would be submitted to the unit responsible for evaluation or assessment of OTC medicines. For Class III medicines the unit could seek advice from or refer aspects of an application to the prescription medicines unit should specialist expertise be required, for example, where the medicine was intended to carry indications for serious diseases and specialist clinical expertise was required.

Product licence applications for medicines containing new active substances (other than medicines meeting the definition of 'complementary healthcare product') would generally be submitted to the prescription medicines unit for evaluation or assessment unless the sponsor was able to justify evaluation of the application by the OTC medicines unit. The sponsor could apply to the OTC medicines unit for evaluation of the new substance for use in Class I medicines if they had evidence to support classification of the substance as 'low risk'.

As a general rule, product licence applications for medicines meeting the definition of 'complementary healthcare product' would be submitted to the unit responsible for the assessment and evaluation of complementary healthcare products. For Class III complementary healthcare products, the unit could seek advice from or refer aspects of an application to the prescription medicines unit should specialist expertise be required. Such situations might include applications for medicines intended to carry indications for serious diseases (where expert clinical advice was required) and applications for novel dosage forms (where particular expertise in pharmaceutical chemistry was required).

Product licence applications for medicines containing new active substances and meeting the definition of 'complementary healthcare product' would be submitted to the unit responsible for evaluation and assessment of complementary healthcare products. The sponsor could apply for evaluation of the new substance for use in Class I medicines if they had evidence to support classification of the substance as 'low risk'.

A summary of the proposed product licensing processes to apply to different types of medicines is shown in Table 6.

Table 6: Product Licensing Processes for Prescription and OTC Medicines

Type of medicine	Currently regulated as therapeutic product by		Proposed product licensing process under joint agency			
	Australia	New Zealand	Sponsor self-certification	Pre-market evaluation & approval		Exempt ²⁰
			Class I	Class II	Class III	
Medicines containing substances scheduled prescription only or meeting the requirements for scheduling as such	✓	✓			✓	
Complementary healthcare products containing substances scheduled prescription only or meeting the requirements for scheduling as such	✓	✓			✓	
Medicines intended to carry indications for serious diseases	✓	✓			✓	
Complementary healthcare products intended to carry indications for serious diseases	✓	✓ ²¹			✓	
Medical gases	✓	✓			✓	
Vaccines	✓	✓			✓	
Allergens (except allergens for skin patch testing on unbroken skin)	✓	✓			✓	
Biotechnology medicines	✓	✓			✓	
Immunoglobulins	✓	✓			✓	
Radio contrast agents (except barium sulphate preparation for radiological use)	✓	✓			✓	

²⁰ Conditions may apply

²¹ In New Zealand, therapeutic claims are not permitted on products supplied as dietary supplements. Making a therapeutic claim for a dietary supplement would put the sponsor in breach of the Medicines Act. Under a joint agency, these types of products would be considered to be therapeutic products and would be regulated as complementary healthcare products.

Type of medicine	Currently regulated as therapeutic product by		Proposed product licensing process under joint agency			
	Australia	New Zealand	Sponsor self-certification	Pre-market evaluation & approval		Exempt ²⁰
			Class I	Class II	Class III	
Radiopharmaceuticals	✓	✗			✓	
Irrigation solutions	✓	✓			✓	
Special dosage forms such as transdermal systems or osmotic pumps	✓	✓			✓	
Injectable medicine dosage forms	✓	✓			✓	
Plasma products, unless coated onto devices	✓	✓			✓	
Orphan products	✓				✓	
OTC medicines intended to carry general or medium level indications or indications for non-serious diseases (other than Class I medicines or exempt medicines)	✓	✓		✓		
Antiseptics	✓	✓		✓		
Sunscreen preparations other than Class I or exempt	✓	✗		✓		
Complementary healthcare products containing substances other than Class I substances or prescription only substances and intended to carry indications for non-serious diseases	✓	✓		✓		
Complementary healthcare products intended to carry high level indications for non-serious diseases	✓	✓		✓		

Type of medicine	Currently regulated as therapeutic product by		Proposed product licensing process under joint agency			
	Australia	New Zealand	Sponsor self-certification	Pre-market evaluation & approval		Exempt ²⁰
			Class I	Class II	Class III	
OTC medicines containing specified substances ²² in any combination if: <ul style="list-style-type: none"> • non required to be sterile; and • having only general or medium level indications 	✓	✗/✓	✓			
Uncompounded, scheduled BP substances	✓	✓ (exempt)	✓			
Sunscreens for dermal application: <ul style="list-style-type: none"> • SPF4+ if tested and labelled according to standard AS/NZS 2604; or • SPF4 or less if containing human or animal tissue 	✓	✗	✓			
Medicated throat lozenges: <ul style="list-style-type: none"> • containing only volatile oils and their constituents, with or without vitamin C; and • having only general or medium level indications 	✓	✓	✓			
Medicated space sprays (only volatile oils)	✓	✓	✓			

Type of medicine	Currently regulated as therapeutic product by		Proposed product licensing process under joint agency			
	Australia	New Zealand	Sponsor self-certification	Pre-market evaluation & approval		Exempt ²⁰
			Class I	Class II	Class III	
Complementary healthcare products containing specified substances ²² in any combination if: <ul style="list-style-type: none"> • not required to be sterile; and • having only general or medium level indications 	✓	✗/✓	✓			
Homoeopathic preparations	✓	✓ (exempt)	✓ ²³			
Antiperspirants if Al, Zn, Zr salts	✓	✗				✓
Unmedicated anti-acne cleansers having only cleansing action or purpose	✓	✗				✓
Anti-dandruff products (once determined to be unscheduled)	✓	✓				✓
Medicated insect repellents (once determined to be unscheduled)	✓	✗				✓
Sunscreens below SPF 4 if tested and labelled according to standard AS/NZS 2604: 1997 and not containing any human or certain animal origin	✓	✗				✓
Allergen patch tests	✓	✓				✓
Radiopharmaceutical 'cold kits' made in hospitals	✓	✗				✓

²³ Under current Australian legislation, some homoeopathic preparations are exempt from registration or listing in the ARTG. As part of implementation of a joint agency consideration will be given to which, if any, homoeopathic preparations should be exempt from product licensing under the joint scheme.

Type of medicine	Currently regulated as therapeutic product by		Proposed product licensing process under joint agency			
	Australia	New Zealand	Sponsor self-certification	Pre-market evaluation & approval		Exempt ²⁰
			Class I	Class II	Class III	
Personal-use imports	✓	✓				✓
Imports held in bond for export, or awaiting certain permit or approvals, or for clinical trials	✓	✓				✓
Imports for specified visiting groups	✓	✓				✓
Non-commercial exports, unless for clinical trials or prohibited	✓	✓				✓
Goods made specially by a licensee for a hospital or institution where there are no similar licensed goods available, or made specially for a patient	✓	✓				✓
Samples not for use in humans	✓	✗				✓
Extemporaneously compounded medicines	✓	✓				✓
Medicines used solely for experimental purposes in humans	✓	✓				✓

3. STANDARD TERMINOLOGY FOR MEDICINES

The Agency would require the use of standard terminology to ensure accuracy and consistency in records in the Register, particulars on the product licence, and information about therapeutic products. The use of standard terminology would assist healthcare professionals and consumers in recognising and comparing products. It would also assist in the retrieval of information from the Register and in electronic provision and validation of information provided to the Agency. Wherever possible the Agency would use internationally accepted terminology.

3.1 Substance Names

Standardised and accurate naming of ingredients assists with the clear identification and safe use of therapeutic products. Use of standardised terminology for naming ingredients allows the similarities and differences between product formulations to be readily identified, enabling consumers and healthcare professionals to make informed choices about the products they use. Allowing different names to be used to describe the same ingredient can lead to confusion. Consumers may unwittingly select two or more products containing the same ingredient referred to by different names, with the possibility of over-dosing on that ingredient.

Standardisation of naming is not a simple process. Many ingredients have common names that are readily recognised by consumers but are quite different from the pharmacopoeial, scientific or internationally approved name. For example, while the common name "St John's Wort" would be recognised by many consumers, the botanical name, *Hypericum perforatum* may not be. Further complications arise when different names are used in different reference texts and nomenclature systems. For example, the internationally recognised name for what we know as "lignocaine" is "lidocaine". Such differences are not easily resolved, and moving to a single, internationally recognised naming system takes time and effort. However, the potential longer-term benefits to public health and safety and international harmonisation make the effort worthwhile.

It is proposed that standard terminology for ingredient names would be required in the following circumstances:

- In applications to the Agency;
- On product labels;²⁴
- In product formulation records in the Register; and
- In product information and consumer medicine information.

It is proposed that, under a joint scheme, the naming of ingredients would generally be based on the World Health Organisation's International Non-proprietary Name (INN) system²⁵. The INN system came into operation in 1953 and the list of INNs now includes accepted names for over 7,000 substances, and is growing steadily.

The naming process involves close collaboration between the World Health Organisation (WHO) and national nomenclature committees around the world to identify a single, internationally acceptable name for each active substance used in pharmaceutical medicines. Following receipt of a proposal for naming a new substance, the WHO committee reviews the name and seeks input from member countries to ensure there is no conflict with registered trademarks. Once cleared, this name becomes the recommended International Non-proprietary Name or rINN for the substance.

National nomenclature committees around the world have traditionally published their own lists of names, such as British Approved Names (BAN) and United States Adopted Names (USAN). However, more and more countries are now adopting the INN name as the list expands and gains recognition.

²⁴ The sponsor could also include a common name or synonym on the product label, in addition to the approved name.

²⁵ More information on the INN system can be found on the WHO web site at

<http://www.who.int/medicines/organization/qsm/activities/qualityassurance/inn/innguide.shtml>

Australia has for many years operated a national naming system in which each substance has an approved name that is required to be used in an application and on product labels. For chemical substances, the approved name is known as the Australian Approved Name (AAN). These names come from a variety of sources – some are INNs, some are British or US names, and some have come from other pharmacopoeias or reference texts. The naming Committee in 1998 made a decision to adopt INNs, where possible. Work is underway to change approved names to INN, where approved names were adopted prior to 1998. For biological substances, an Australian Biological Name (ABN) is approved. A scheme is also in place to ensure systematic naming of herbal substances in therapeutic products. New Zealand does not have a national naming system, but has for some years encouraged the use of INNs where they exist, while allowing the use of acceptable synonyms on labels.

Ingredients used in therapeutic products fall broadly into three categories: chemical substances, biological substances and herbal substances. INNs are predominantly chemical active substance names and the INN system does not generally apply to herbal substance names or to biological substance names. The Agency would adopt appropriate naming conventions for biological and herbal substances.

Issues relating to the naming of different types of substances are outlined below. More detailed work will be required to establish the naming rules and develop an implementation plan for moving to standardised naming of ingredients.

Chemical substance names

It is proposed that the INN would be the preferred name for a chemical substance in therapeutic products. INNs are not available for all chemical substances used in therapeutic products. Furthermore, in certain circumstances the Agency may choose not to adopt a particular INN because the substance in question already has a long history of use under a well-established name and to change that name may be confusing to consumers and healthcare professionals.

Where there is no INN for the substance, the proposed INN (pINN) would be used if available. If there were no recommended (rINN) or proposed INN (pINN), then the name of the substance would be chosen from another source of reference, according to a hierarchy to be developed by the Agency. Other sources of reference for chemical substance names could include the BAN, the USAN, Pharmacopoeias and the Merck Index, etc.

Herbal substances

It is proposed that the Agency would adopt a system of standard terminology for herbal substances based on that currently in use in Australia. In this system, herbal substances are named by identifying the herb species, the plant part(s) and the preparation. Common names could be used on labels, in conjunction with the approved name, if the sponsor wished to do so.

Substances of biological origin

Where there is no INN, if the ingredient is obtained directly from an animal then the common animal name, animal part and animal preparation is used, e.g. Bovine cartilage powder. Scientific names could be used on the labels in conjunction with the required common name. A virus or metabolic component name is obtained from the pharmacopoeias or other references. The name for pro-biotic ingredients is usually obtained from the International Journal of Systematic Bacteriology or International Journal of Food Microbiology or Bergey's Manual of Systematic Bacteriology.

The naming of genetically modified ingredients is evolving as new ingredients are produced. Currently, there are two methods of determining an approved name if an ingredient is genetically modified. One naming method is by using an approved biological product descriptor with the name. For example, if a product contains Somatropin from *E. coli* genetically modified by recombinant DNA technology it would be recorded as Somatropin rbe. The other method is by adopting an ingredient name that defines that ingredient as a genetically modified ingredient. For example, Drotrecogin alfa (inactivated), which is recombinant human factor XIVA. The reference for these names is the BAN, the Pharmacopoeias or less frequently the INN. It should be noted that existing approved names for genetically modified ingredients may change as the problems and processes for naming them are understood.

3.2 Homoeopathic Preparations

There is no international nomenclature system for homoeopathic medicines. The naming of homoeopathic substances is based on the monograph names specified in the homoeopathic pharmacopoeia. These monograph names are in the various *Materia Medica* that are used by practitioners and consumers to identify the medicines and their symptom pictures. These *Materia Medica* also have cross-referencing indexes to search for a substance by its common, pharmaceutical and Latin names.

The main homoeopathic pharmacopoeia used are:

- HPUS: Homoeopathic Pharmacopoeia of the United States
- GHP: German Homoeopathic Pharmacopoeia
- HAB: Homoeopathisches Arzneibuch, Amtliche Ausgabe
- PhF: Pharmacopoe Francaise (Official French Pharmacopoeia) ²⁶
- BHP: British Homoeopathic Pharmacopoeia
- APC: Anthroposophic Pharmaceutical Codex

In many cases the names are the same in each homoeopathic pharmacopoeia, but there are also many that differ. The naming system used to provide the botanical identification of the substances also varies. Examples include the Linnaean system and the Millar system. These naming systems identify the species used, but that name is not necessarily used as the monograph name for the actual homoeopathic medicine.

The common chemical name for minerals is generally not used in homoeopathy. The name used is often a Latin version of the scientific name, but can also be the name of the "natural" substance from which the medicine has been made.

²⁶ For homoeopathic products only

Nomenclature for homoeopathic preparations is complex, and further work on this issue will need to be undertaken in consultation with homoeopathic product manufacturers and nomenclature experts.

3.3 Other Standard Terms

The Agency would also require the use of standard terminology in applications, on product labels and in information to consumers and prescribers for the following:

- container types;
- closures;
- dosage forms;
- routes of administration; and
- units and expressions of proportion.

Standard terminology would ensure accuracy and consistency of information in applications and in the Register and would assist in electronic submission of applications and the retrieval of information from the Register.

4. SCHEDULING OF MEDICINES

4.1 Current Arrangements

Scheduling is a mechanism used to set access restrictions on medicines when there is a risk to public health and safety. Australia and New Zealand have common restriction categories of:

- Prescription medicines that are only available on prescription from a registered medical practitioner (or other authorised prescriber in New Zealand);
- Pharmacist medicines that must be sold by a pharmacist;
- Pharmacy medicines that must be sold in a pharmacy; and
- Unscheduled or General Sale medicines that do not warrant scheduling and may therefore be sold from any retail outlet.

Between State and Territory jurisdictions in Australia, there are minor differences in the detail of implementation of scheduling decisions.

The scheduling mechanism reflects the need for a healthcare professional to be involved in the supply of certain medicines in order to facilitate safe use. The scheduling levels for substances that are in medicines are set by considering a number of criteria such as the toxicity of the substance, its proposed use, the potential for community harm, and the ability of the consumer to self-diagnose the condition.

Australia and New Zealand currently operate separate mechanisms for scheduling medicines, drawing on advice from their respective scheduling committees.

In Australia, the National Drugs and Poisons Schedule Committee (NDPSC) is constituted under the Therapeutic Goods Act and makes recommendations on the scheduling of medicines and poisons that are given legal effect through legislation at State and Territory

level. A scheduling decision must receive support from a majority of jurisdictions (including New Zealand). The Commonwealth and the New Zealand NDPSC members each have a vote. A recent review (the Galbally review) has recommended separating the scheduling of medicines from poisons.

In New Zealand, the Medicines Classification Committee (MCC) is a Ministerial advisory committee; in practice its recommendations are accepted or rejected by the Minister's delegate and given legal effect through an amendment to the Regulations under the Medicines Act.

Work on the harmonisation of medicine scheduling between Australia and New Zealand has been underway for some time. This work is being undertaken by the Trans-Tasman Scheduling Sub-committee of the NDPSC. To facilitate harmonisation of scheduling the Therapeutic Goods Act was amended to add a New Zealand member to the NDPSC. Since 2000, an NDPSC member has also, from time to time, attended MCC as an observer.

4.2 Proposed Arrangements under a Joint Agency

It is proposed that under a joint agency, there would be a single scheme for the scheduling of medicines and substances in medicines.

Under this proposal, the initial scheduling decision would be made as part of the evaluation and approval process for the substance or medicine, as proposed under the Australian Review of Drugs, Poisons and Controlled Substances Legislation ("Galbally Review").

Before making a scheduling decision, the Agency's decision-maker would be able to seek advice from the expert advisory committees that assess the safety of new prescription or OTC medicines or complementary healthcare product active ingredients or products. These committees would be joint Australia/New Zealand committees whose members are selected on the basis of their technical expertise (see Part C; Section 2.4 for further information on the expert advisory committees).

An advisory committee on medicine scheduling would be established in the legislation. The members of the committee would have relevant expertise, including expertise in the product areas, consumer affairs, pharmacy practice, medical practice and medicine scheduling, and some members would be drawn from governments.

The committee would:

- provide advice to the Managing Director in relation to scheduling matters;
- consider proposals to change the scheduling classification of a medicine, with input from relevant expert advisory committees; and
- be able to review scheduling decisions made by the Managing Director.

Persons not happy with a scheduling decision could, after internal review, seek recourse to an external merits review body (see Part I for further information on review of decisions).

Recommendations would be given legal effect in New Zealand by Orders issued by the Agency under the new joint agency legislation. In Australia, scheduling decisions would be published in the Standard for the Uniform Scheduling of Drugs and Poisons and State and Territory legislation would give effect to the decision. If, as recommended by the Galbally Review, Australian States and Territories implement complementary therapeutic goods legislation, it might be sufficient for State and Territory legislation to simply apply the joint agency Orders on packaging, labelling and advertising that give effect to the scheduling recommendation.

This proposal advances the recommendations of the Galbally Review in Australia relating to scheduling. The Report of this Review is due to be considered by the Council of Australian Governments in mid-2002, together with a Response to the Review.

5. INFORMATION ABOUT MEDICINES

5.1 Labelling Requirements

Product labels are important for consumers. They enable consumers to identify products and provide consumers with sufficient information to choose appropriately (for self-medication products) and to use the products safely and effectively, throughout the lifetime of the product – at purchase, during use and storage, and at disposal.

It is proposed that the Agency would set standards for the labelling of products. The obligation to comply with a range of standards, including the labelling standard, would be contained in the Acts. The labelling standard would be set out in the technical Orders, and developed during implementation planning. The standard would take into account stakeholder comments and the outcome of a recent review of labelling undertaken in Australia.

The term 'label' covers the label attached to the container (eg. bottle, tube or blister pack), the primary pack (e.g. carton) and any printed information supplied with the container or primary pack (e.g. package insert).

Sponsors of Class II and III medicines would be required to provide labels (draft or actual) in their applications to license new products or to vary the licensed product particulars where the variation affected the label. Class I products would be required to comply with labelling requirements. Sponsors of Class I products would be required to certify compliance with labelling requirements when making a product licence application, and to submit labels (draft or actual) on request by the Agency.

It is proposed that labels would be required to include some or all of the following:

- the product name;
- the name(s) of all active ingredients in the product;
- the quantity and proportion of all active ingredients in the product;
- any excipient (as defined in the technical orders);
- the name of the dosage form;

- the quantity of the product;
- warning statements, where these apply;
- the batch number of the product;
- the expiry date of the product;
- the storage conditions applicable to the product;
- directions for use of the product;
- the name and address of the sponsor or supplier of the product;
- a statement of the purpose or purposes for which it is intended that the product be used;
- the product licence number.

Individual evaluation or assessment areas within the Agency would be responsible for different categories of products, and recommendations on the labelling of individual products would be made as part of the licensing process. These evaluation/assessment areas would be able to seek advice from expert advisory committees (see Part C; Section 2.4).

Consistent with current approaches in both countries, it is proposed that a label would fall within the definition of an advertisement and would therefore be required to comply with relevant advertising requirements.

5.2 Information for Prescribers

In Australia, the term "product information" refers to a document that is approved by the TGA and contains information about a medicine, which is primarily for the use of healthcare professionals. In New Zealand, this document is referred to as a "Data Sheet". Both countries currently require all prescription medicines to have an approved product information document. This document is evaluated and approved as part of the pre-market approval process.

It is proposed that, under the joint agency, the requirement for product information documents for certain types of medicines will continue.

For many products, the same product information document, formatted to meet current TGA requirements, is used in both countries. Amendments are made where necessary to reflect the approval details (such as different dosages or indications) in either country. It is proposed that the Agency would adopt this format, thereby minimising the changes required for existing products.

It is proposed that all licensed Class III and Class IIa medicines (i.e. prescription and pharmacist medicines) would be required to have an approved product information document. This document is designed to present a scientific, objective account of the medicine's usefulness and limitations, for the benefit of healthcare practitioners recommending or prescribing the product. It is to be devoid of promotional material.

All product licence applications for Class III and Class IIa medicines would need to include, for approval, a draft product information document. The content of product information documents would be required to be supported by data available to the Agency for evaluation.

Changes to the product information document would require submission of a product licence variation. It is proposed that minor administrative changes to the document (e.g. change to sponsor contact details) would be self-assessable.

The requirement for certain products to have an approved product information document would be established in the Rules. Detail of the format and content of the product information document would be set out in the Orders.

5.3 Information for Consumers

The purpose of the consumer medicine information (CMI) document is to provide consumers with easily understood information to help them use medicines safely and effectively. In some instances, the CMI supplements and supports the counselling activities of healthcare practitioners. In other cases, in the absence of professional intervention, it is the only source of information available to the patient.

Currently in Australia, a CMI is required for all prescription and pharmacist medicines. In New Zealand, provision of CMI is voluntary, but is available for a wide range of prescription and pharmacist medicines. Current requirements for format and content of CMI in both countries are closely aligned.

It is proposed that under a joint agency, CMI would be required for all prescription medicines and pharmacist medicines. Additionally, consideration will be given to requiring CMI for all medicines, in recognition of the fact that consumers of non-prescription medicines have an equal or greater need for information about their medicines in the absence of advice from a healthcare professional. The Agency would work with stakeholders to further develop strategies for introducing CMI for all medicines.

The CMI would be required to be based on the product information document approved by the Agency. A mechanism would need to be developed to facilitate production on CMI for those medicines for which there is no approved product information document. The CMI would not be permitted to contain promotional material.

The CMI requirements would be established in the Rules. Detail on the format and content of the CMI document would be set out in the Orders.

Question 18:

Do you agree with the proposal to extend the requirement for CMI to all medicines?

What do you see as the advantages and the disadvantages of such a proposal?

Question 19:

A limitation of CMI is that it often is not readily available to consumers. How could this limitation be addressed under a joint agency?

Question 20:

Should it be a requirement that CMI be provided as part of the packaging and labelling of a medicine? Should there be any obligation at all on the sponsor to assist consumers in obtaining CMI? Are there other approaches that should be considered?

6. REGULATION OF INGREDIENTS AND INTERMEDIATE PRODUCTS

6.1 Excipients

New excipient ingredients would generally require prior approval by the Agency before they could be used in therapeutic products. In the case of Class II and III medicines, data on a new excipient ingredient would be required in the product licence application and the acceptability of the new excipient would be considered in the context of the finished product.

In the case of Class I medicines, the list of ingredients permitted in Class I medicines would include a section for excipient ingredients. A sponsor wishing to use a new excipient in Class I medicines would be required to submit an application for evaluation of that excipient for suitability to be used in Class I medicines (see Part E Section 2.2 and Part F Section 8.2 for further details). The extent of information that would be required in an application might vary depending on factors such as the history of use of that excipient in foods, or in other therapeutic products.

6.2 Drug Master Files

Active ingredients are commonly manufactured by a company other than the manufacturer of the finished product. In such cases, the manufacture, quality control and stability of the active ingredient are usually described in a 'Drug Master File' (DMF), submitted to a regulatory authority by the manufacturer of the active ingredient. Both Australia and New Zealand currently have provision for the submission and evaluation of DMFs, and it is proposed that these provisions would continue under a joint agency.

During the evaluation process, the Agency would require access to information about active ingredients in Class II and Class III medicines. Where the sponsor of the finished

product could not supply this information in the product licence application, they may refer to a DMF previously submitted by the manufacturer of the active ingredient. In order to refer to the DMF in a product licence application, a sponsor would require the written permission of the active ingredient manufacturer.

Finished product sponsors would be responsible for the quality of their products and the raw materials used to manufacture them. Therefore, the sponsor of the finished dose form would be required to provide written assurance to the Agency that there is a formal agreement between themselves and the active ingredient manufacturer. This written agreement should ensure that information would be communicated to the sponsor, and to the Agency, before any significant changes were made to the method of manufacture or specifications of the active ingredient. DMFs would need to be updated periodically to reflect any changes in the specifications of the active ingredient.

The DMF could, if required, be presented by the active ingredient manufacturer in two sections, with the first (open) section containing information accessible to the finished dose form manufacturer/sponsor and the second (closed) section containing information not accessible to the finished dose form manufacturer/sponsor.

A DMF would not be required for any active substance that is controlled according to a relevant monograph in a pharmacopoeia approved by the Agency and that is manufactured by a method liable to leave only impurities mentioned in the pharmacopoeial monograph.

6.3 Proprietary Ingredients and Proprietary Intermediate Products

A proprietary ingredient is generally a formulated ingredient, obtained from another manufacturer, for which the details are not known to the sponsor. Colours, flavours, fragrances and printing inks are often sourced as proprietary ingredients.

A proprietary intermediate product is a partially formulated therapeutic product such as an ointment or cream base, a preservative pre-mix or an active pre-mix, obtained from another manufacturer, for which the details are not known to the sponsor.

It would be the responsibility of the sponsor to ensure the quality and safety of any therapeutic product containing a proprietary ingredient or proprietary intermediate product and to ensure that those therapeutic products complied with all relevant regulatory requirements.

To assist sponsors, the Agency would put in place arrangements for the appropriate management of proprietary ingredients and proprietary intermediate products used in therapeutic products. These arrangements would include a process for suppliers of proprietary ingredients to lodge formulation details with the Agency and to vary the details. The application format, application form and data requirements would be set out in legislation and/or guidelines. Details of the application process will be developed during implementation planning.

Sponsors of finished products would be able to cross-reference proprietary ingredient and proprietary intermediate product details in their product licence applications.

7. LICENSING OF MANUFACTURERS

7.1 Manufacturing Principles

The manufacturing and quality control of medicines for supply in, or export from, Australia/New Zealand would be required to be of an acceptable standard.

The criteria used to assess standards of manufacture of medicines would be set out in manufacturing principles, i.e. standards, established in the Rules and set out in technical orders. The manufacturing principles could include codes of Good Manufacturing Practice.

The term Good Manufacturing Practice (GMP) is used internationally to describe a set of principles and procedures which, when followed by manufacturers of therapeutic products, help ensure that the products manufactured will have the required quality. A basic tenet of GMP is that quality cannot be tested into a batch of product but must be built into each batch of product during all stages of the manufacturing process.

Australia and New Zealand signed a Mutual Recognition Agreement on GMP in 1996 that allows both countries to recognise each other's GMP inspections.

New Zealand has adopted the Pharmaceutical Inspection Co-operation Scheme (PIC/S) GMP Guide. Australia is expected to adopt the PIC/S GMP Guide as a Manufacturing Principle in July 2002. A decision on which guidelines the Agency would adopt would be made as part of implementation planning.

Compliance with a specified GMP requirement is used by most countries as the basis for licensing manufacturers of medicinal products. Compliance is established through inspections of manufacturers carried out by trained auditors employed by the regulatory agency.

The Agency would determine the manufacturing principles to be applied and would audit and licence manufacturers. The Agency would be able to seek the advice of an expert advisory committee before determining the manufacturing principles. The Agency would be able to develop interpretative guidelines for manufacturing principles for medicines of different types and different risk classifications. For example, it is anticipated that there would be interpretative guidelines for the application of GMP to the manufacture of sunscreens and certain types of complementary healthcare products.

7.2 Australian and New Zealand Manufacturers

Anyone intending to manufacture medicines in Australia or New Zealand for supply in, or export from, Australia/New Zealand would be required to hold a manufacturing licence issued by the Agency. The obligation to hold a manufacturing licence would be contained in the Acts.

A licence to manufacture would be specific to the manufacturer for specific steps in the manufacture of specific types of medicines at specific manufacturing premises.

Some medicines and some persons could be exempted from the requirement for a manufacturing licence.

A manufacturer would be able to apply for a licence to manufacture medicines in Australia/New Zealand:

- The application format, application form and data requirements would be defined in the legislation.
- The Agency would assess the application.
- The Agency could request further information in relation to the application and/or may inspect the manufacturing premises to which the application relates.
- The Agency would make a decision on the application.
- Possible outcomes of the process would be:
 - manufacturing licence granted;
 - manufacturing licence granted with conditions. Appeal rights would apply to conditions; and
 - manufacturing licence refused. Appeal rights would apply.

The Agency would be able to suspend or cancel a manufacturing licence. The circumstances under which this may occur would be defined in the Rules.

7.3 Overseas Manufacturers

For a medicine manufactured wholly or partially overseas, the sponsor would be required to provide evidence that the medicine was manufactured to a standard of GMP equivalent to that expected of Australian and New Zealand manufacturers of the same type of products before they could obtain a product licence.

Consistent with current practice in both Australia and New Zealand, acceptable evidence would take the form of either:

- documentation that demonstrates that the overseas manufacturer(s) could produce the medicine to the standard required by the appropriate code of GMP (the nature of the documentation would be defined in the legislation and/or guidelines) ²⁷; or
- an audit by the Agency at the place of manufacture.

Evidence of compliance with the appropriate code of GMP would be required for each overseas site at which the medicine is manufactured.

7.4 International Agreements

The Agency would be able to share information in relation to manufacturers, manufacturing facilities and manufacturing standards under international agreements made between Australia and New Zealand and other countries or regions. For current MRAs, MOUs and memberships of organisations such as PIC/s, the relevant MRA/MOU partners and

²⁷ For further information, refer to New Zealand Regulatory Guidelines for Medicines, Volume 1 or the TGA Guidelines on Standard of Overseas Manufacturers.

organisations would need to be advised of the proposed new Agency since there is an obligation to advise them of any significant changes. The MRA/MOU partner or organisation such as PIC/S may decide to assess the competence of the new GMP arrangements within the new Agency.

8. POST- MARKET SURVEILLANCE OF MEDICINES

8.1 Introduction

The regulation of medicines involves a balance between pre-market assessment activities and post-market monitoring and surveillance. The objective of the pre-market assessment of medicines is to ensure that when available for supply, the products are safe for the intended use(s), of appropriate quality, efficacious and truthfully and adequately labelled for the intended population(s) and use(s). However, it is not possible to assure the complete safety of a product before it comes into widespread use. The development of an effective programme for post-market identification of unsafe or potentially unsafe products is therefore an essential element in minimising the risk associated with their use.

The essential elements of an appropriately targeted, transparent, and rigorous post-market monitoring system for medicines include:

- Development of a systematic risk-based approach to monitoring and surveillance including:
 - random and targeted laboratory testing
 - auditing of manufacturing facilities
 - adverse reactions monitoring
- Targeted and random audits (full and partial) of Class I products and audits of self-assessable changes made to Class II and Class III products.
- Market surveillance to ensure that products available for consumers are authorised for supply in the relevant market and that product particulars conform to those on the product licence and in the Register; and
- Appropriate penalties for breaches of legislation to minimise the potential for misleading conduct in the market place.

8.2 Adverse Reactions Monitoring

Comprehensive adverse reaction monitoring ("pharmacovigilance") programmes would be included to monitor the safety of marketed prescription medicines, OTC medicines and complementary healthcare products available in Australia and/or New Zealand. The programmes would operate in Australia and New Zealand under the directorship of the Agency, and would provide for:

- the submission of reports of suspected adverse reactions to medicines and vaccines and problems with products, in either electronic or written form to Australia or New Zealand. The submission of these reports would be mandatory for sponsors and voluntary for healthcare professionals and consumers;
- guidance for the reporting of these reactions, including the types of reports that must or may be submitted;

- electronic database/s, with capacity to store and process information from either country or from both countries;
- systems for the review of reports in both countries;
- systems for communicating, within the Agency, information on actual or potential problems with therapeutic products, and for developing policy on pharmacovigilance matters;
- systems for the dissemination of information to healthcare professionals and consumers on problems with therapeutic products;
- country-specific licences and recalls in appropriate circumstances; and
- encouragement and, on occasion, funding of supplementary monitoring programmes and research into specific problems.

The requirement for sponsors to forward information about adverse reactions to medicines would be set out in the Act. The type of information and method of reporting would be set out in the Rules.

The pharmacovigilance programmes would operate under the guidance of an advisory committee, which would:

- provide advice to the Agency on the safety of therapeutic products and on general policy matters relating to pharmacovigilance;
- review some reports of problems with therapeutic products received by the Agency; and
- make recommendations to the Agency on steps that may be taken to follow-up safety-related concerns for therapeutic products.

The role, functions and constitution of the advisory committee would be set out in the legislation. The advisory committee would be independent and operate under its own terms of reference. The membership of the committee would include experts in the evaluation of product safety and at least one member with expertise in each of the relevant product areas (prescription medicines, OTC medicines and complementary healthcare products).

8.3 Problem Reporting and Recalls

Medsafe and the TGA currently share information and co-operate closely in the investigation of problems and recall of therapeutic products. Codes of practice for handling recalls are already closely aligned, and it is anticipated that the ability to deal efficiently with problems in both countries will be even further enhanced in a joint agency.

The Agency would have systems, procedures and strategies in place for the reporting of problems with therapeutic products, for the removal of therapeutic products from supply or use, and for corrective action when problems occur.

The problems covered could include:

- a defect or deficiency thought to have arisen during manufacture, storage or handling;

- a deficiency in the efficacy, safety or quality of a product, including situations where a therapeutic product is found not to be in compliance with statutory or agreed standards; and
- situations where product tampering is suspected.

The systems for reporting problems with therapeutic products could include:

- guidance and forms for sponsors, suppliers, prescribers, consumers and other stakeholders for the reporting of problems with therapeutic products, including information on the types of problems that may be reported;
- persons nominated by and located in each state, territory or region in Australia and New Zealand, to whom information on problems with therapeutic products can be conveyed, and who would collate this information (recall officers); and
- persons located in the Agency offices in Australia and New Zealand, who have overall responsibility for coordinating and assessing information on problems with therapeutic products and for instigating further action if required (recall coordinators).

Depending on the nature of the problem and on the country in which the problem originated, therapeutic products for which a problem has been established could be:

- recalled for permanent removal from the market; or
- recalled temporarily so that some corrective action may be undertaken before supply re-commences.

Recalls would be classified by the Agency, in consultation with the sponsor where appropriate, according to the European classification system, as follows:

- Class I recalls occur when products are potentially life-threatening or could cause a serious risk to health;
- Class II recalls occur when product defects could cause illness or mistreatment, but are not Class I; or
- Class III recalls occur when product defects may not pose a significant hazard to health, but withdrawal may be initiated for other reasons.

The above classifications take into account situations where the sponsor has not complied with conditions of registration or licensing for therapeutic products; and/or where a product has been removed or withdrawn from the Register. The level of recall could be decided by the Agency in consultation with the sponsor, and could range from the wholesale level to the consumer level, depending on the classification of the recall.

Recalls would be expected to be conducted by the sponsor on a voluntary basis, but would also be enforceable by parts of the legislation for therapeutic products, including those parts relating to manufacturing of therapeutic products, compliance with conditions of licensing, standards and product tampering. Parts of the legislation relating to consumer protection and trade matters in general could also determine whether or not a recall should be conducted (e.g. compliance with the *Trade Practices Act 1974* currently underpins some of the recall requirements in Australia). There would also be provision for the Agency to instigate a mandatory recall procedure in cases where the sponsor is unwilling or unable to conduct the recall voluntarily.

The recovery of products subject to a recall would be the responsibility of the sponsor, with assistance and guidance on the appropriate strategy provided by the Agency. The Agency would oversight the conduct of the recall and monitor its progress and effectiveness, and could request follow-up action, including asking the sponsor to take remedial action to prevent recurrence of the situation.

Details of the roles, functions and responsibilities of the recall officers, the recall coordinators, the Agency and the sponsor, in reporting problems with therapeutic products and in initiating and conducting recalls, would be described in publicly available guidelines.

8.4 Laboratory Testing

The Agency would be responsible for appropriate laboratory testing programmes for medicines, medical devices and other therapeutic products to assist with:

- the pre-market assessment of certain products and types of products;
- the investigation of adverse reaction reports and complaints from consumers and healthcare professionals in relation to therapeutic products; and
- post-market monitoring of therapeutic products for compliance with relevant standards and other requirements in relation to quality, safety and efficacy.

The Agency would have in place systems to ensure the integrity of its testing programmes and processes for legally obtaining samples.

8.5 Post-market Monitoring of Class I Medicines

The proposed regulatory scheme as presented in this discussion paper allows for early market access for Class I medicines. For these products, the onus would be on the sponsor to provide relevant data in a prescribed format and to certify that the product complies with relevant requirements. Facilitating early market access in this way means that there is an increased need to develop a comprehensive risk-based system for post-market monitoring.

It is proposed that systems would be put in place for the Agency to conduct random and targeted post-market reviews of Class I medicines licensed under the sponsor self-certification scheme:

- to enhance consumer confidence in the efficacy, safety and quality of Class I medicines; and
- to ensure a high level of industry compliance with regulatory standards and guidelines for Class I medicines.

The Agency would be able to request and review information such as:

- product labels and packaging;
- promotional and advertising material;
- specifications and analytical certificates for the product;
- bibliography of sources of evidence to support indications; and

- evidence to support the safety and efficacy of the product (in certain circumstances).

The Agency would be able to take action if, as a result of a post-market review of a Class I medicine, it determined that any of the sponsor's certifications were incorrect and/or there were concerns about the quality, safety or efficacy of the product.

9. ACCESS TO UNLICENSED PRODUCTS

9.1 Medicines Used in a Clinical Trial

9.1.1 Current arrangements

Currently, before a clinical trial can proceed in either Australia or New Zealand, both ethical and scientific approval for the trial is required. The main difference between the two countries is in the way that these approvals are obtained.

In Australia, there are two possible routes for obtaining approval to perform a clinical trial. Firstly, there is the clinical trial notification (CTN) route, in which a human research ethics committee associated with the institution in which the trial is to be conducted can give both ethical and scientific approval for the trial. Following approval by the institutional ethics committee, the conduct of the trial is simply notified to the TGA. Secondly, there is the clinical trial exemption (CTX) route in which the sponsor first submits an application to conduct the trial to the TGA for evaluation and comment. The primary responsibility of the TGA is to review the safety of the product and the institutional ethics committee is responsible for considering the scientific and ethical issues of the proposed clinical trial protocol.

In New Zealand, a centralised government scientific expert committee (the SCOTT committee) gives scientific approval and an ethics committee associated with the institution in which the trial is to be conducted gives ethical approval.

Although the mechanisms for approval are different in each country, the outcomes are the same.

Institutional ethics committees in Australia do have scientific representation, but there may be occasions when a committee feels it lacks expertise in a specific field, particularly when the proposal is to trial a novel or emerging therapy. In these cases the committee has the right to request that the proposal to be considered by others with more experience in that area. Under the present Australian scheme these types of proposal, where the institutional ethics committee believes it does not have sufficient scientific expertise, are often submitted to the TGA as a CTX application. The institutional ethics committee may also seek advice independently, or request an independent review of the sponsor.

9.1.2 Proposed arrangements under a joint scheme

Under a joint Agency, it is proposed that a clinical trial scheme would be developed that would draw on the best features of the current Australian and New Zealand schemes.

Under the joint Agency scheme, it would be necessary for a sponsor to obtain both scientific and ethical approval of a clinical trial.

In the majority of cases an appropriately constituted institutional ethics committee in either Australia or New Zealand would be able to provide both scientific and ethical approval of a trial with subsequent notification to the Agency (similar to the current Australian CTN scheme).

In some cases sponsors may need to seek approval from two separate committees; an expert scientific committee and an institutional ethics committee. In other cases sponsors may wish to submit an application to conduct the trial to the Agency for evaluation and comment, similar to the current Australian CTX scheme.

The factors that might influence the choice of route would include the nature of the product and the type of clinical trial. For example, a Phase III trial of a new indication for an existing medicine might be appropriate for approval by an institutional ethics committee alone, whereas a trial involving a gene therapy product might require separate approval from an expert scientific committee.

To facilitate this joint scheme, it is proposed that expert scientific committees, similar to the SCOTT committee in New Zealand, could be set up in Australia. These committees would consider and advise on the scientific content of clinical trial proposals where the institutional ethics committee did not believe it had the appropriate expertise to do so. Currently, in Australia, this type of committee would be established under the auspices of the Australian Health Ethics Committee (AHEC) a principal committee of the National Health and Medical Research Council (NHMRC). In this regard, it should be noted that the Australian NHMRC would usually seek funding reimbursement from the relevant stakeholder.

An alternative proposal would be that the Agency could set up a joint Australia/New Zealand expert scientific committee to oversee the scientific content and approval of clinical trial applications under circumstances where institutional ethics committees were unable to do so.

The establishment of expert scientific committees would satisfy the desire of certain institutional ethics committees to have access to more specialised scientific knowledge and would provide a more uniform approach to clinical trial approval in both Australia and New Zealand, however, there would be obvious cost implications in setting up such a scheme.

Possible advantages of more unified schemes would be potential increases in industry investment in clinical trials in Australia and New Zealand and an increased access for patients to new experimental therapies.

Medicines used in clinical trials would be exempt from the requirement for product licensing, provided the trial was approved by an institutional ethics committee and, where appropriate, by an expert scientific committee.

All clinical trials, irrespective of the approval process, would be required to be notified to the Agency. The Agency would maintain a database of all clinical trials involving therapeutic products conducted in Australia or New Zealand.

The requirement for a clinical trial to be approved and notified to the Agency would be set out in the legislation.

Question 21:

Should the mechanisms for clinical trial approval be unified in Australia and New Zealand?

If so, should there be separate centralised expert scientific approval committees in each country or should there be a joint Australia/New Zealand expert scientific committee?

9.2 Unlicensed Medicines Supplied to Individuals

Currently in Australia, a medical practitioner may prescribe any unlicensed medicine to a patient with a life-threatening disease or condition (i.e. a "Category A patient"). The medical practitioner is required to inform the TGA of the use of the medicine, but approval from the TGA is not required. However, unlicensed medicines can only be prescribed to patients with non life-threatening diseases following approval by the TGA through a special access scheme (SAS). In addition, the TGA is able to grant certain medical practitioners authority to prescribe a specified unlicensed medicine or class of unlicensed medicines to specified recipients or classes of recipients suffering from serious (but not necessarily life-threatening) medical conditions. In this situation, the medical practitioner becomes an "Authorised Prescriber" and may prescribe unlicensed medicines within the terms of the authority, without the requirement for further approval from the TGA.

The Australian scheme is designed to limit the use of unlicensed and therefore unevaluated products to only those situations where they are genuinely needed. The Australian scheme also gives oversight to practitioner behaviour and prevents abuse of a system designed to allow patients access to unlicensed medicines. This protects patients from the risks associated with the use of products for which there may not be adequate assurance of quality, safety and efficacy.

In New Zealand, medical practitioners can access unlicensed medicines from local manufacturers and distributors without any requirement to obtain approval from Medsafe. In this situation, the supplier of the product is required to keep a record of the supply and to forward this information to Medsafe. A medical practitioner can also manufacture or import an unlicensed medicine without seeking approval or reporting the use of the medicine to Medsafe. The risk with the current New Zealand system is that pharmaceutical manufacturers may be able to supply unsafe, unlicensed medicines to patients via medical practitioners without any regulation.

It is proposed that access to unlicensed medicines would be maintained under a joint Agency. However, further work is required to develop the mechanisms for allowing access to unlicensed medicines and for limiting their use to those situations where they are genuinely needed.

Question 22:

What mechanisms should a joint agency put in place to provide an appropriate degree of assurance:

- of patient protection;
- of informed consent; and
- that sponsors do not use the scheme for supply of unlicensed medicines as a means of de facto marketing?

9.3 Personal Importation

It is proposed that under a joint Agency, an individual would be able to import an unlicensed medicine into Australia or New Zealand where:

- the medicine is for use by either the importer or a member of the importer's immediate family; and
- the medicine does not contain a substance which is a prohibited import under the Australian Customs legislation or is restricted under New Zealand Misuse of Drugs legislation; and
- the product is not an injection containing material of human or animal origin (except insulin); and
- the quantity imported does not exceed three months' supply per importation and the total quantity imported per year does not exceed 15 months' supply at the manufacturer's recommended maximum dosage.

In the case of a prescription medicine, the medicine could only be imported if the importer had a prescription issued by an appropriately registered medical practitioner (i.e. a prescription written by an Australian-registered medical practitioner in the case of a medicine imported into Australia, and by a New Zealand-registered medical practitioner in the case of a medicine imported into New Zealand).

In both countries, other controls apply to certain therapeutic products such as drugs of dependence, antibiotics and other substances that may be dangerous if used therapeutically or contain substances restricted under other legislation. Importation of these products could require written permission from the Agency or from another appropriate authority.

10. MEDICINES FOR EXPORT

10.1 Regulation of Export Medicines

Under a joint agency, export medicines for commercial supply would fall into two categories:

- those intended for supply in Australia and/or New Zealand as well as for export; and
- those intended solely for export to a country outside the Australia/New Zealand market ('export only' medicines).

Products falling into the first category could be exported with the endorsement of having been licensed for supply in the Australia/New Zealand market and therefore considered suitable for supply to Australian and New Zealand consumers. This is important to exporters for two reasons; the high international standing the joint agency is likely to have as a regulator of therapeutic products and the emphasis in the WHO certification scheme on the domestic status of exported therapeutic products.

Products falling into the second category would be exported without this endorsement. There is a range of opinion about the level of regulation that should be applied to medicines intended only for export. Some suggest that medicines should not be allowed to be exported unless they are licensed for the domestic market. At the other end of the spectrum are those who suggest that the role of the Agency should be limited to regulation of products for the domestic market and that the Agency should leave regulation of export only medicines entirely to the importing country. In the latter case, the importing country may request a WHO Certificate of Pharmaceutical Product from the exporting country to assist in its consideration of the product.

A requirement that all export medicines be licensed for domestic supply before they may be exported would limit export opportunities for Australian and New Zealand industry. An approach where export only medicines were not regulated at all would mean that Australia and New Zealand were not complying with their international public health obligations (see below). It would also make it more likely that the Australia/New Zealand market could become a source of sub-standard medicines, adversely affecting its reputation as an exporter of safe, high quality medicines.

International obligations

International arrangements are in place, which have the objective of preventing the manufacture and sale of sub-standard and counterfeit medicines around the world.

Australia and New Zealand are participants in the WHO Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce ('the Scheme'). A Member State intending to use the Scheme to support the export of pharmaceutical products should first satisfy itself that it possesses:

- an effective national licensing system, not only for pharmaceutical products, but also for the responsible manufacturers and distributors;

- GMP requirements, consistent with those recommended by WHO, to which all manufacturers of finished pharmaceutical products are required to conform;
- effective controls to monitor the quality of pharmaceutical products registered or manufactured within its country, including access to an independent quality control laboratory;
- a national pharmaceuticals inspectorate, operating as an arm of the national drug regulatory authority, and having the technical competence, experience and resources to assess whether GMP and other controls are being effectively implemented, and the legal power to conduct appropriate investigations to ensure that manufacturers conform to these requirements by, for example, examining premises and records and taking samples; and
- administrative capacity to issue the required certificates, to institute inquiries in the case of complaint, and to notify expeditiously both WHO and the competent authority in any Member State known to have imported a specific product that is subsequently associated with a potentially serious quality defect or other hazard.

Maintenance of standards

A regulatory system that requires export medicines to meet appropriate standards of quality and safety would enable Australia and New Zealand to meet their international obligations and has the potential to facilitate exports by enhancing the reputation of medicines exported from the Australia/New Zealand market. In general, medicines for export would be expected to meet similar standards to those applying to medicines intended for the Australia/New Zealand market. However, in limited circumstances, appropriate standards may be developed specifically for medicines intended for export. An example might be product labelling where a standard might be developed, which specified the minimum information to appear on the label of a medicine for export. This information would not necessarily be the same as that required on the label of a medicine intended for supply in the Australia/New Zealand market.

The following proposals for the regulation of medicines for export aim to support Australia's and New Zealand's international public health obligations and maintain appropriate standards for Australian and New Zealand products whilst being consistent with regulatory best practice principles.

10.1.1 Export of medicines licensed for supply in the Australia/ New Zealand market

If a medicine were already the subject of a product licence for supply in Australia and/or New Zealand, the sponsor would be able to export that medicine without further regulation, provided that:

- the medicine to be exported was identical to that authorised in Australia and/or New Zealand (within the definition of 'separate and distinct product' – see under Part C; Section 2.2.2);

- any different export name(s) were included in the Register entry for the medicine and on the PL; and
- the medicine was authorised in the jurisdiction from which it is to be exported i.e. New Zealand, Australia or both.

10.1.2 Export only medicines

Sponsors of medicines intended solely for export outside the Australia/New Zealand market would be required to obtain an export only medicine licence²⁸. The licensing system would provide the following benefits:

- it would provide a mechanism to ensure that export only medicines meet appropriate quality and safety standards, consistent with international public health obligations;
- the Agency would have in its records the particulars required to provide export certifications on export only medicines; and
- in the event of a safety concern related to a particular substance, manufacturer or sponsor, the Agency would be able readily and rapidly to identify all medicines at risk, whether supplied in the Australia/New Zealand market or exported from it and take appropriate action.

Two approaches to export only licences are under consideration and comment is invited on the merits of each approach.

Option 1

Under this option, the export only medicine licence would relate to a specific sponsor and would list all the export only medicines the sponsor was permitted to export.

To obtain a licence, the sponsor would be required to submit an application containing specified information about each export only medicine and certifying that each medicine complied with specified quality and safety criteria. It would be a requirement that each medicine was manufactured in accordance with the principles of GMP.

In certain circumstances, there would be a requirement for the sponsor to obtain a clearance from the Agency for an export only medicine. These circumstances would be based on safety considerations, e.g. new substances (not in any medicine in the Register) and substances of human/animal origin, and would be set out in Orders.

The sponsor could apply to list additional export only medicines on the licence or to vary the particulars of an existing export only medicine.

Option 2

The export only licence would be product-specific. The sponsor would be required to obtain a separate licence for each export only medicine. This type of licence would be more akin to the product licence for supply in the Australia/New Zealand market.

²⁸ The export only process would not apply to medicines exported from Australia to New Zealand or vice versa. These medicines would require a PL for supply in the Australia / New Zealand market.

The application process and requirements would be similar to those described under option 1.

The main difference between the two options would be in the fee structure. This is because, under option 1 the sponsor would have a single export only medicine licence to maintain, whereas under option 2 the sponsor would need to apply for and maintain separate licences for each export medicine. This could translate to more flexible fee arrangements under option 1, particularly in relation to the way fees were structured for the initial licence and subsequent additional export only medicines added to that licence.

Question 23:

Which option for export only licensing do you prefer and why?

10.1.3 Separate and distinct products

The following framework sets out the circumstances in which:

- a medicine for export would be different from a medicine licensed for supply in the Australia/New Zealand market; and
- an export only medicine would be different from another export only medicine

Class I medicines for export would be taken to be separate and distinct from other Class I medicines licensed for supply in Australia or licensed for export only, if they had:

- Different active ingredients; or
- Different quantities of active ingredients; or
- Different excipients; or
- Different dosage form; or
- Different indications or claims which would make them Class II or Class III medicines; or
- For medicines that contain any excipient that is a restricted ingredient:
 - Different quantity or concentration of an excipient that is restricted by quantity or concentration; or
 - Different directions for use where the medicine contains excipients that are restricted by quantity or concentration and the restriction relates to daily dosage limits.

Class II and Class III medicines for export would be taken to be separate and distinct from other Class II and Class III medicines licensed for supply in Australia or licensed for export only, if they had:

- Different active ingredients; or
- Different quantities of active ingredients; or
- Different excipients; or
- Different quantities of excipients ²⁹; or
- Different dosage form.

²⁹ Within limits specified in technical orders, which could describe the batch to batch quantity variation permissible for some types of excipients (eg pH adjusting ingredients, granulating fluid etc)

Direct substitution of certain ingredients (e.g. proprietary ingredients, empty capsule shells) might be "groupable" so that, while multiple "export alternatives" to the product licensed domestically would be possible, they would each be entered in the Register. This would allow for the automatic selection of formulation details for inclusion in an export certificate and would also assist the Agency in any follow-up action in the event of a safety concern. In this case the export certificate would still indicate that the product was licensed for supply to the Australian and/or New Zealand market, with Agency comment such as:

"This product has been reformulated for export in that the flavouring [name of excipient for export] has been substituted for the flavouring [name of Aust/NZ approved excipient]".

Other differences that are relevant to the safety or quality of a product (but which do not create a separate and distinct product) may also exist between a product licensed for domestic supply and the product for export. A separate mechanism would be in place for the sponsor to notify the Agency of the details of the "export version" (e.g. different product name, directions for use, absence of warning statements, indications or container type ³⁰). These differences would be recorded in the Register and an appropriate comment included on an export certificate (where such a certificate is requested). For example, if the product to be exported had different directions for use, the Agency comment on a Certificate of Pharmaceutical Product would indicate that:

"The directions for use of the product for export have been modified to meet the requirements of the importing countries."

Question 24:

Are the criteria for determining what is a separate and distinct product reasonable? If not, what criteria should be used and why would these criteria be more appropriate?

10.2 Export Certification

A sponsor would be able to apply to the Agency for an export certificate to be issued for a medicine licensed for supply in Australia/New Zealand or for export only (e.g. WHO Certificate of Pharmaceutical Product).

The application format, application form and data requirements would be set out in guidelines.

The Agency could define timeframes for the processing of an application.

The export certificate could include details about the product licence arrangements in Australia/New Zealand.

³⁰ For Class II or III medicines

10.3 Export of Medicines for Donations or for Humanitarian Purposes

Medicines would be exempt from requirements for licensing and inclusion in the Register if they are intended as donations or humanitarian aid provided they meet the following criteria:

- they have been obtained legally;
- they are not for commercial supply;
- they do not contain substances the export of which is prohibited in Australia or New Zealand; and
- they are not intended for use in clinical trials in humans.

PART E :

REGULATION OF PRESCRIPTION AND OTC MEDICINES

1. INTRODUCTION

This part of the discussion paper deals with specific aspects of the regulation of prescription and OTC medicines, in particular the regulation of market entry and should be read in conjunction with Part D. In this part of the paper, prescription and OTC medicines include:

- *in vivo* diagnostic agents;
- medical gases;
- vaccines;
- allergens;
- biotechnology medicines;
- plasma products, including immunoglobulins;
- radiocontrast agents;
- radiopharmaceuticals;
- dialysis solutions; and
- most sunscreens.

These are essentially therapeutic products meeting the proposed definition of medicine (i.e. a therapeutic product that is represented to achieve, or is likely to achieve, its principal intended action by pharmacological, chemical, immunological or metabolic means in or on the human body), other than complementary healthcare products.

With the exception of sunscreens and radiopharmaceuticals, prescription and OTC medicines are regulated in both New Zealand and Australia under therapeutic products legislation. In New Zealand, Medsafe undertakes substantially the same regulatory functions for prescription and OTC medicines as the TGA undertakes in Australia. Australia and New Zealand use a very similar framework for the regulation of prescription and OTC medicines, which is consistent with global harmonisation initiatives. Current differences in the approach taken are mostly at the operational level.

2. OTC MEDICINES

OTC medicines would fall into all three broad risk classifications as follows:

- Class I OTC medicines (for example, most sunscreens and medicated throat lozenges);
- Class II OTC medicines (most OTC medicines including non-prescription analgesics, most topical antifungals, most cough and cold remedies, hayfever treatments containing antihistamines, and antiseptics); and
- Class III OTC medicines (those medicines intended to carry indications for serious diseases, conditions, ailments or defects but supplied without a prescription, such as a glyceryl trinitrate spray for angina).

2.1 Class I OTC Medicines

A sponsor would be able to apply for a product licence to supply a Class I OTC medicine in Australia and/or New Zealand, i.e. a single-country licence or a dual-country licence.

Class I OTC medicines would generally be granted a product licence on the basis of sponsor self-certification and validation by the Agency of key requirements. Variations to low-risk OTC medicines would follow a similar process.

The processing of product licence applications for Class I OTC medicines would be managed by the unit in the Agency responsible for OTC medicines. As part of its post-market monitoring activity, the Agency may undertake random or targeted audits of Class I OTC medicines to check that the certifications made by the sponsor were correct.

Class I OTC medicines would be permitted to contain only substances specified in a list of permitted substances. This list would be set out in Orders. The circumstances in which a medicine would be a Class I medicine would be set out in the Rules, together with the matters to be certified by the sponsor.

A sponsor would apply for a product licence for a Class I OTC medicine using an electronic application lodgement and validation system. Using such a system, a product licence could be issued very rapidly following submission of a valid application (within 24-48 hours), the turn-around time limited only by the time required to process the fee payment. For further details on product licensing, see Part C, Section 2.2.

Conditions could be imposed on the licence and failure to comply with these conditions could result in cancellation of the product licence.

Most sunscreens would be regulated as Class I OTC medicines. Further information about the regulation of sunscreens is provided in Part E; Section 2.4.

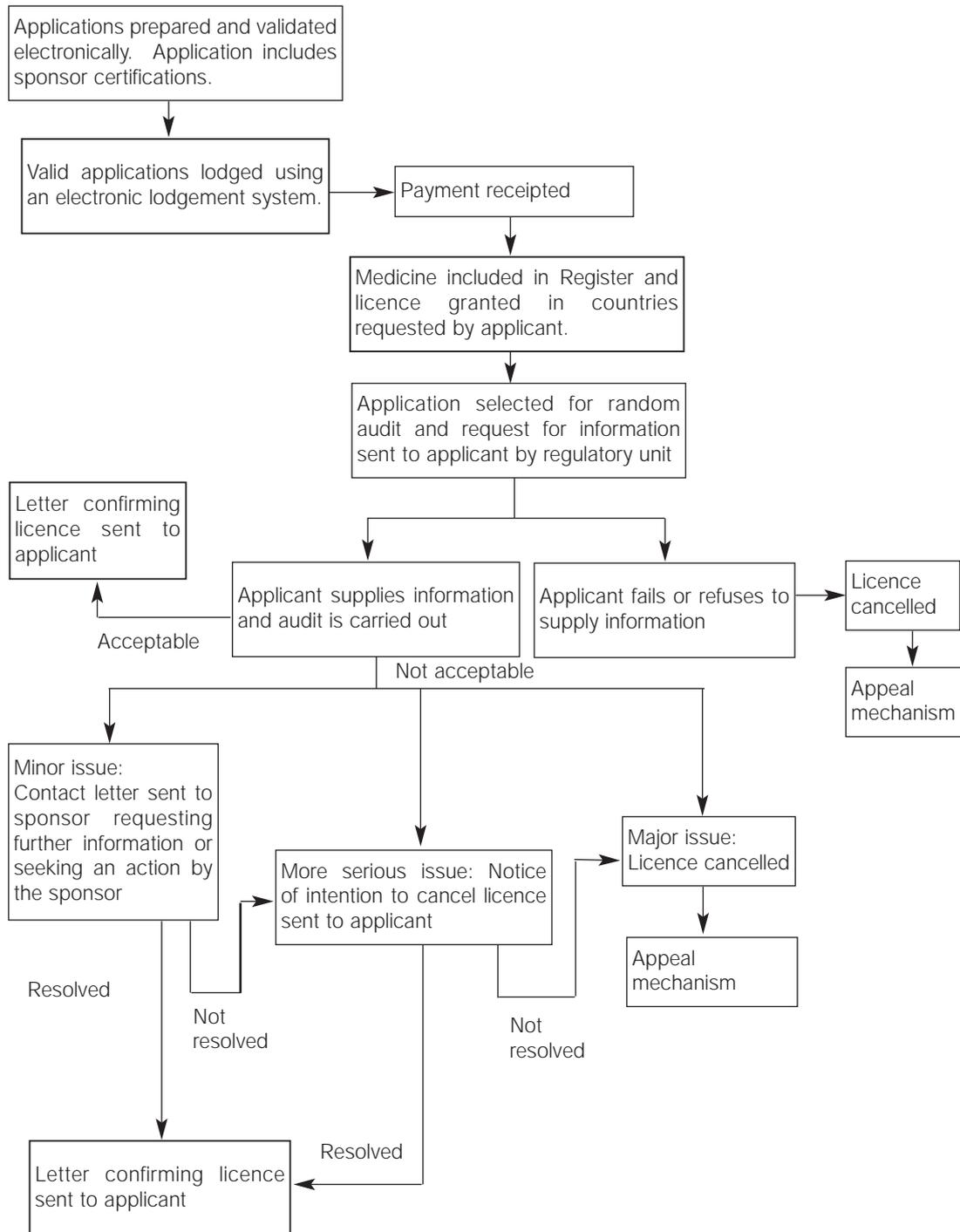
2.2 Class I OTC Medicine Substances

A sponsor would be able to apply for approval of a substance for use in Class I OTC medicines. The application format, application form and data requirements would be set out in the legislation and/or guidelines.

The Agency could undertake a preliminary screening of the application prior to accepting it for evaluation, and may seek the advice of an expert advisory committee or other relevant experts before making a decision. The Agency would define timeframes for the processing of an application. As part of the evaluation process, the Agency would consider the appropriate scheduling of the substance.

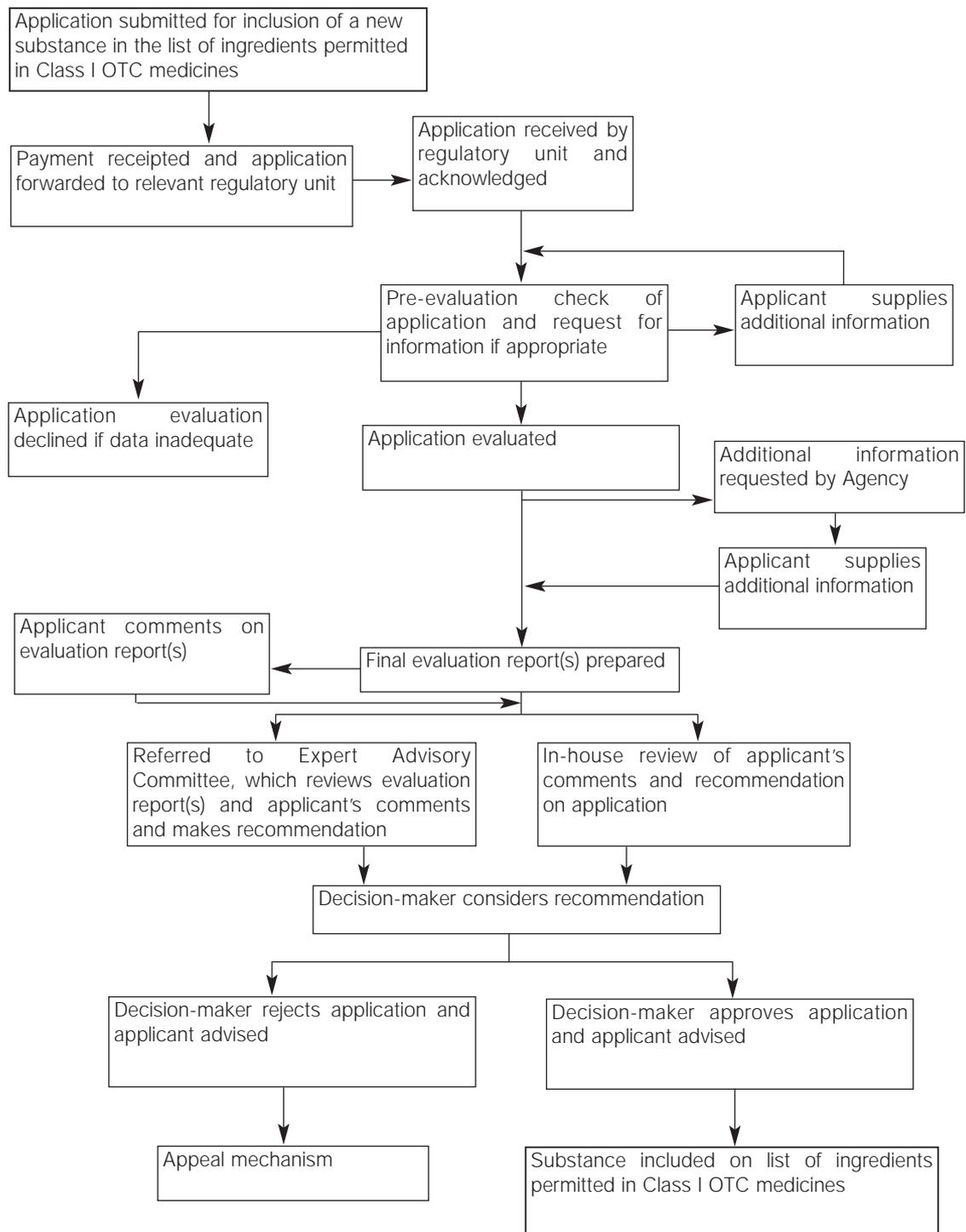
If the decision were to approve the substance, it would be included in the list of substances permitted in Class I medicines. This list would be published in a technical order. If the application were rejected, appeal provisions would apply (see Part I for further information about review of decisions).

Figure 2: Indicative Process for Licensing of New Class I OTC Medicine ³¹



³¹ This diagram is indicative only and shows the likely major activities in the licensing process

Figure 3: Indicative Process for Inclusion of a New Substance in the List of Permitted Ingredients in Class I OTC Medicines³²



³² This diagram is indicative only and shows the likely major activities in the evaluation process

2.3 Class II and III OTC Medicines

The evaluation of product licence applications for Class II and III OTC medicines would be managed by the unit in the Agency responsible for OTC medicines.

2.3.1 Product licence applications

A sponsor would be able to apply for a product licence to supply a Class II or Class III OTC medicine in Australia and/or New Zealand, i.e. a single-country licence or a dual-country licence.

Class II and III OTC medicines would require pre-market evaluation and an approval process before they could be granted a product licence.

The application format, application form, data requirements (including the nature of the evidence required to be held or submitted), and fees for a product licence application would be defined in legislation and/or guidelines.

Legislation would outline the circumstances when separate applications would be needed for the same medicine in a different form or for a different use. The Agency may undertake preliminary screening of applications prior to accepting them for evaluation.

2.3.2 Data requirements and evaluation process

The data requirements and pre-market evaluation processes applying to Class II and III OTC medicines would differ depending on the level of risk associated with different types of medicines within those broad classifications. For example, the data requirements, and therefore the extent of evaluation, are likely to be more substantial for a medicine containing a new chemical entity or a novel fixed combination product than would apply in the case of a generic version of an existing medicine containing well-known ingredients.

The documentation to support a licensing application would be required to be in English and compiled in accordance with the guidelines applying at the time. The application format and data content of the dossier would be in accordance with best international regulatory practice, consistent with the current approach in both countries. The requirements would be specified in Agency-specific and/or international guidelines. The Agency could adopt international guidelines with amendments and commentary. Adoption of new guidelines impacting upon the regulatory process would only occur after consultation with industry and consumer representatives.

During the evaluation of applications, the Agency would be able to seek advice from an expert advisory committee or other experts before making a decision on the application.

As part of the evaluation process, the Agency would consider the appropriate scheduling of the medicine and any new substances contained therein.

A decision may be made to approve the application in full (or in part), in which case a product licence would be issued for the jurisdiction(s) requested by the applicant. If the application (or any part of the application) were rejected, appeal provisions would apply (see Part I for further information about review of decisions).

Conditions could be imposed on the licence and failure to comply with these conditions could result in cancellation of the product licence.

2.3.3 Variations to licensed products

A sponsor would be able to apply to vary the details in relation to a licensed Class II or III OTC medicine. The legislation would set out the circumstances in which a change to a medicine was a variation rather than the creation of a new medicine.

There would be different types of variation applications depending on the nature of the change:

- major variation requiring evaluation and approval;
- minor variation requiring evaluation and approval; and
- possible arrangements for self-assessable changes requiring notification to the Agency and an assurance by the sponsor that they hold appropriate evidence to support the changes.

The different types of variation would be set out in the legislation and different fees would apply to different types of variation.

The application format, application form, data requirements (including the nature of the evidence required to be held or submitted), and fees would be defined in legislation and/or guidelines.

The Agency may undertake a preliminary screening of applications for major variations.

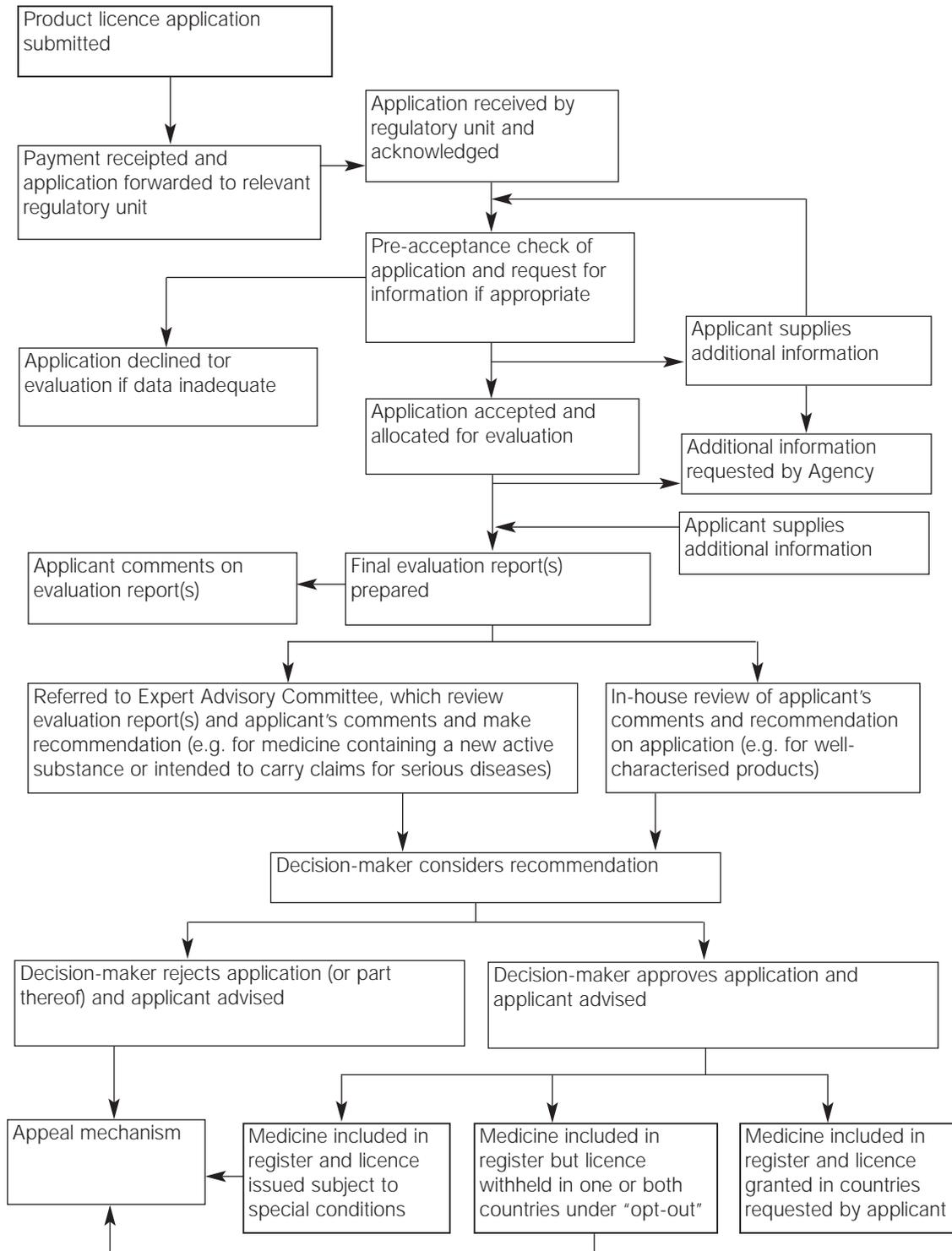
The Agency would evaluate major and minor variations and may seek advice from an expert advisory committee and/or other experts before making a decision on the variation application.

If the decision were to approve a major or minor variation in full (or in part), the entry in the Register would be amended and an updated product licence could be issued. If a variation application (or any part of the application) were rejected, appeal provisions would apply (see Part I for further information about review of decisions).

For self-assessable changes, the entry in the Register would be amended and an updated product licence could be issued.

The Agency would define timeframes for processing applications for product licence variations.

Figure 4: Indicative Process for Licensing of a New Class II or III OTC Medicine ³³



³³ This diagram is indicative only and shows the likely major activities in the licensing process

2.4 Sunscreens

Currently, sunscreens are not regulated as therapeutic products in New Zealand. However, in Australia, they are regulated as therapeutic products, except when specifically excluded from the definition of a therapeutic good under the Therapeutic Goods Act. It is proposed that, under a joint regulatory scheme, sunscreens would be regulated as therapeutic products and that the regulatory arrangements for sunscreens would be broadly similar to those currently operating in Australia.

In Australia, sunscreens are regulated as 'therapeutic goods' under the Therapeutic Goods Act except in the following circumstances:

- if the primary purpose is not sunscreensing (or another therapeutic use) and the label does not claim a sun protection factor (SPF); or
- if the product is a secondary sunscreen which is tinted, unmedicated and for application to the lips (i.e. lipstick with sunscreen) or tinted facial makeup, but not a moisturiser.

In these circumstances, the sunscreen is excluded from the regulatory scheme. It is proposed that the same criteria would be used to determine which sunscreens were excluded from a joint regulatory scheme.

Most sunscreens in Australia are required to be 'listed' in the Australian Register of Therapeutic Goods (ARTG). Sunscreens fall into this category where:

- the SPF is equal to or greater than 4;
- the performance statements and markings on the label comply with Standard AS/NZS 2604 1998;
- the product does not contain ingredients of human origin or certain ingredients of animal origin; and
- the product is intended to carry only permitted indications.³⁴

These products are required to have a licensed manufacturer and must comply with all other aspects of the legislation (e.g. labelling requirements). Under a joint scheme, it is proposed that sunscreens in this category would be regulated as Class I OTC medicines. This category would contain the majority of sunscreens regulated under a joint scheme.

Some sunscreens in Australia are exempt from inclusion in the ARTG and the requirement to have a licensed manufacturer. These products are still considered to be therapeutic products and must comply with other requirements under the Therapeutic Goods Act (e.g. labelling requirements). Sunscreens fall into this exempt category where:

- the SPF is less than 4;
- the performance statements and markings on the label comply with Standard AS/NZS 2604 1998; and
- the product does not contain ingredients of human origin or certain ingredients of animal origin.

It is proposed that, under a joint scheme, sunscreens in this category would be exempt from the requirement for a product licence and the requirement to have a licensed manufacturer.

³⁴ Currently in Australia, these products could not carry a claim for treatment of a condition that is a "prohibited" or "restricted" representation as described in the *Therapeutic Goods Advertising Code*.

In Australia, any sunscreen that does not otherwise fall into the 'excluded', 'listed' or 'exempt' categories described above is required to be 'registered' in the ARTG. It is proposed that, under a joint scheme, sunscreens in this category would require licensing as Class II or Class III medicines. It is not anticipated that many products would fall into this category.

Question 25:

Do you agree with the proposed criteria for categorising sunscreens?

If not, what alternative approaches would you propose, and why?

3. PRESCRIPTION MEDICINES AND OTHER SPECIFIED CLASS III MEDICINES

The evaluation of product licence applications for prescription and other specified Class III medicines would be managed by the unit in the Agency responsible for prescription medicines.

Specified Class III medicines would include:

- medical gases;
- vaccines;
- most allergens;
- biotechnology medicines;
- plasma products, including immunoglobulins;
- most radiocontrast agents;
- radiopharmaceuticals;
- dialysis solutions;
- special dosage forms such as transdermal systems and osmotic pumps;
- injectable medicine dosage forms; and
- medical devices dependent upon the release of a substance for some or all of their action.

3.1 Product Licence Applications

A sponsor would be able to apply for a product licence to supply a prescription or other Class III medicine in Australia and/or New Zealand, i.e. a single-country licence or a dual-country licence.

Prescription and other specified Class III medicines would require pre-market evaluation and an approval process before they could be granted a product licence.

Legislation would outline the circumstances when separate applications would be needed for the same medicine in a different form or for a different use. The Agency would undertake preliminary screening of applications prior to accepting them for evaluation.

3.2 Data Requirements and Evaluation Processes

The data requirements and application and evaluation processes would be similar to those currently used in Australia and New Zealand.

The data requirements and pre-market evaluation processes applying to prescription and other specified Class III medicines would differ depending on the level of risk associated with different types of medicines within that broad classification. For example, the data requirements, and therefore the extent of evaluation, are likely to be more substantial for a medicine containing a new chemical entity than would apply in the case of a generic version of an existing medicine containing well-known ingredients.

The documentation to support a licensing application would be required to be in English and compiled in accordance with the requirements applying at the time. It is anticipated that the full provisions of the Common Technical Document (CTD)³⁵, which outlines the presentation of the application dossier, would apply under a joint agency. The data content of the dossier would be in accordance with best international regulatory practice, as specified in relevant international guidelines. The Agency would adopt international guidelines, or where necessary, develop Agency specific guidelines. The Agency would also be able to adopt international (e.g. CPMP/ICH) guidelines with amendments and commentary. The adoption of guidelines impacting upon the regulatory process would only occur after consultation with industry and consumer representatives.

Details of the administrative requirements (Module 1 of the CTD) for an application to the Agency would be developed during implementation planning. Requirements would be expected to include:

- Covering letter;
- Completed Application Form;
- Overseas Regulatory Status;
- Proposed Product Information and Consumer Medicine Information;
- Proposed labelling and packaging;
- Specific requirements for different types of applications;
 - information for bibliographical applications
 - information for abridged 'generic' applications; and
- GMP certifications

Environmental risk assessment for products containing, or consisting of genetically modified organisms (GMOs), and for non-GMO-containing medicinal products may be required. It is possible that the requirements for environmental risk assessment would be different in Australia and New Zealand. It is likely that antibiotic resistance data would be required.

During evaluation of applications, the Agency would be able to seek advice from an expert advisory committee or other experts before making a decision on the application.

As part of the evaluation process, the Agency would consider the appropriate scheduling of the medicine and any new substances contained therein.

A decision may be made to approve the application in full (or in part), in which case a product licence would be issued for the jurisdiction(s) requested by the applicant. If the application (or any part of the application) were rejected, appeal provisions would apply (see Part I for further information about review of decisions).

Conditions could be imposed on the licence and failure to comply with these conditions could result in cancellation of the product licence or other sanctions.

3.3 Evaluation Timeframes

In common with some other major agencies (e.g. FDA and EMEA), Australia has agreed timeframes for the evaluation of prescription medicines. Currently in Australia these timeframes are statutory and there is a financial penalty on the TGA if these timeframes are not met. The TGA also has target timeframes agreed with industry, which are shorter than the statutory timeframes. In New Zealand Medsafe has target timeframes for the evaluation of prescription medicines.

Statutory timeframes help to ensure timely access to important new medicines. However, when a statutory timeframe with penalties is in place, an agency must maintain sufficient resources to ensure that those timeframes can be met even during periods when the workload is at its highest. Skilful use of contract resources can assist in this regard.

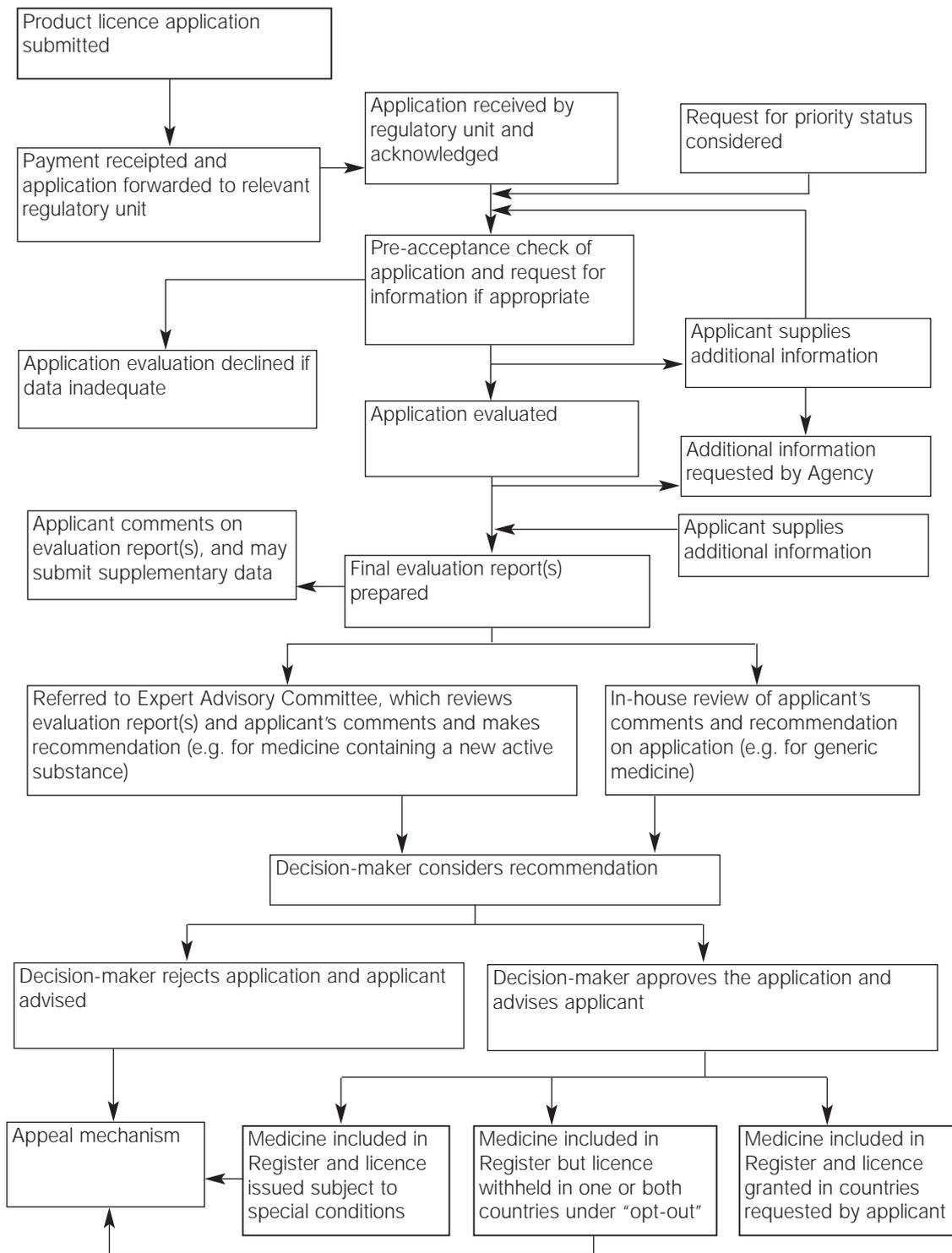
It is proposed that evaluation timeframes for prescription medicines and other specified Class III medicines would be imposed by legislation, and it is envisaged that this legislation would support cost penalties for the Agency if timeframes were not met by the Agency. Legislation would also allow the Agency to request additional information from the sponsor during the evaluation of the application.

Question 26:

Recognising that imposing statutory timeframes on the evaluation process has the potential to result in increased fees, do you think there should be statutory timeframes?

If so, should there be a penalty on the Agency for not meeting the timeframe?

Figure 5: Indicative Process for Licensing of a New Prescription Medicine ³⁶



³⁶ This diagram is indicative only and shows the likely major activities in the licensing process

3.4 Accelerated (or Priority) Evaluation

The Agency would aim to deal with all product licence applications in a timely manner. However, there may be circumstances where an accelerated evaluation process may be in the interest of public health. Such circumstances could include:

- a new medicine intended for the treatment or diagnosis of a serious, life-threatening or severely debilitating disease or condition;
- a medicine offering significant economic benefits over and above current therapy;
- supply of medicines in emergency situations (e.g. bio-terrorism); and
- more rapid availability of important new medicines for payment of a higher fee.

It is proposed that the Agency would have the facility to offer accelerated evaluation of new prescription and other specified Class III medicines. There would need to be mechanisms in place to ensure that target timelines for the evaluation of other medicines were not compromised by any accelerated (or priority) evaluation system.

For an application to receive priority status the sponsor would be required to make a commitment to give priority to answering questions posed by the Agency. Failure of the sponsor to respond adequately to questions within agreed timeframes would result in loss of priority status. The Agency would have target timeframes for processing applications with priority status.

There would be no expectation that orphan medicine applications would gain automatic priority. If the sponsor of an orphan medicine could demonstrate significant clinical need, then priority status could be granted on the basis of clinical need consistent with the granting of priority status to non-orphan medicines. For further detail on orphan medicines, see Part E; Section 4.

It has been proposed that the Agency could offer an accelerated (priority) evaluation service to sponsors wishing to pay an additional fee and that this may provide a benefit by making new medicines available more quickly. Any such scheme would need to be consistent with international trade obligations and public health policy in each country.

Inevitably, when some applications have a priority based on the ability of the sponsor to pay, other applications, some of which may be for important and potentially life saving medicines, may be disadvantaged in terms of speed of processing. This would be an important ethical consideration in determining the details of any accelerated (or priority) evaluation system under a joint agency.

The additional fee for an accelerated evaluation service would need to be set at such a level to enable the Agency to have sufficient resources to meet the accelerated timeframes without compromising the timeliness of evaluation of other medicines. If this did not happen the reputation of the Agency would be compromised.

Question 27:

Do you agree that the Agency should have an accelerated (or priority) evaluation system for prescription and other specified Class III medicines?

If so, what criteria should be used to determine when priority status should apply to an application? Please give reasons to support your view.

3.5 Product Licence Variations

A sponsor would be able to apply to vary the details in relation to a prescription or other specified Class III medicine. The legislation would set out the circumstances in which a change to a medicine was a variation or resulted in a new medicine (separate and distinct product).

There would be different types of variation applications depending on the nature of the change:

- major variation requiring evaluation and approval;
- minor variation requiring evaluation and approval; and
- possible arrangements for self-assessable changes requiring notification to the Agency, and an assurance by the sponsor that it holds appropriate evidence.

The different types of variation and the fees applicable to different types of variation would be set out in the legislation.

The application format, application form, data requirements (including the nature of the evidence required to be held or submitted) would be consistent with the requirements of the CTD and defined in legislation and/or guidelines.

The Agency could undertake a preliminary screening of applications for major variations.

The Agency would evaluate major and minor variations and may seek advice from an expert advisory committee and/or other experts before making a decision on the variation application.

If the decision were to approve a major or minor variation in full (or in part), the entry in the Register would be amended and an updated product licence could be issued. If a variation application (or any part of the application) were rejected, appeal provisions would apply (see Part I for further information about review of decisions).

For self-assessable changes, the entry in the Register would be amended and an updated product licence could be issued.

The Agency would define timeframes for processing applications for product licence variations.

3.6 Generic Prescription Medicines

Under a joint agency, applications to license a new generic medicine in Australia and New Zealand would in general need to be accompanied by bioavailability data demonstrating bioequivalence with an Australian and a New Zealand innovator product. The Agency would need, in most cases, to hold safety and efficacy data for these innovator products.

In certain circumstances (e.g. a wide therapeutic index, and ideal physical, chemical, pharmacological and pharmacokinetic properties) it may be possible to justify use of an overseas innovator product in bioequivalence studies. Such justification could be based on the results of chemical and physical analyses that demonstrate an acceptably high level of similarity between the Australian and/or New Zealand innovator product(s) and the overseas innovator product used in the bioequivalence study.

Strict criteria would be set down by the Agency for demonstrating that innovator products are sufficiently similar to obviate the need for additional bioequivalence studies.

In cases where the innovator product was only licensed in Australia and not in New Zealand or vice versa, the generic medicine could only obtain a licence for the country in which the innovator product was licensed.

Question 28:

Do you consider the Agency should adopt the approach described above in determining bioequivalence of generic medicines?

If not, what alternative approach should be used?

4. ORPHAN MEDICINES

Orphan medicines are medicines used to treat, prevent or diagnose rare diseases. The rarity of the disease means that under normal circumstances the products are not commercially viable and companies often do not develop and market such products because the financial return is small compared with the costs of development and marketing. The lack of an appropriate product may deprive patients with rare diseases of diagnosis and treatment. These patients have a right to receive treatment with products of the same quality, efficacy and safety as those used to treat patients with common illnesses.

It is proposed that the Agency would have an orphan therapeutic products scheme based broadly on the Orphan Drugs Program currently operating in Australia, which is in turn based on the US Food and Drug Administration model. New Zealand does not currently have a formal policy for orphan products.

The scheme would encourage sponsors to market orphan products by reducing costs and by providing other incentives. The first step for a sponsor would be to apply to the Agency for orphan product designation. If orphan designation were given, the sponsor could then submit a product licence application. The data requirements for an application for approval of an orphan product would be the same as those applying to non-orphan products.

In order to qualify for orphan designation, a product would be required to be for use in the treatment or diagnosis of a disease affecting only a small number of individuals. The prevalence figures applied under the current US and European orphan schemes are 75 and 50 affected individuals per 100,000 of population, respectively. In order to obtain orphan designation in Australia currently, a prevalence figure of less than 11 affected individuals per 100,000 of population is normally required.

Incentives for sponsors to obtain product licences for orphan products under a joint Agency could include:

- waiving of application and evaluation fees;
- reduction in annual licence fees; and
- offering a period of market exclusivity to orphan products.

With regard to the period of market exclusivity, the current US programme grants an exclusivity period for orphan products of up to seven years. Under the current European programme the exclusivity period is up to ten years.

The Australian Orphan Drugs Program is currently under review. Any changes that arise from this review would be considered for adoption by the Agency.

Question 29:

How should an orphan products programme work under a joint agency?

Question 30:

What cut-off should apply to the number of affected individuals before orphan designation could be obtained?

Question 31:

Should a period of market exclusivity be offered to orphan products? If so, how should this be achieved?

PART F: REGULATION OF COMPLEMENTARY HEALTHCARE PRODUCTS

1. INTRODUCTION

There is no internationally accepted collective term to describe the group of products currently regulated in Australia as complementary medicines and products regulated in New Zealand as herbal medicines, homoeopathic medicines and dietary supplements (other than food-type dietary supplements). For the purpose of this discussion paper, for convenience, these products are referred to collectively as 'complementary healthcare products'. The use of this term in the discussion paper does not necessarily mean that it would be adopted for use in the legislation to be administered by a joint agency (see discussion in Section 3, below).

Complementary healthcare products include herbal medicines, vitamin and mineral supplements, other nutritional supplements, traditional medicines such as Ayurvedic medicines and Traditional Chinese Medicines (TCM), homoeopathic medicines, and aromatherapy oils.

These types of products meet the definition of 'medicine' proposed for the joint agency, i.e. a therapeutic product that is represented to achieve, or is likely to achieve, its principal intended action by pharmacological, chemical, immunological or metabolic means in or on the human body. Therefore, under a joint agency, many of the regulatory mechanisms and processes that would apply to other medicines, would also apply to complementary healthcare products. This part of the discussion paper deals with specific aspects of the regulation of complementary healthcare products, in particular the regulation of market entry and should be read in conjunction with Part D.

Whereas the current regulatory schemes for prescription and OTC medicines in New Zealand and Australia are very similar, there are marked differences in the way complementary healthcare products are regulated in the two countries. In Australia, these types of products are regulated as medicines under the Therapeutic Goods Act. They are referred to collectively in the legislation as 'complementary medicines'. In New Zealand, many complementary healthcare products are sold under the Dietary Supplements Regulations (under the Food Act). Under the proposals in this discussion paper, many products sold as dietary supplements in New Zealand would be classified as therapeutic products and regulated as such under the legislation to be administered by the joint agency.

2. OBJECTIVES OF REGULATION

Complementary healthcare products cover a wide spectrum from vitamins used to supplement the intake when the diet is inadequate, to herbal preparations, which may be used to treat a wide range of diseases. A significant proportion of the population use these products and see their use as a means of taking responsibility for their own health.

Consumers have an expectation that the complementary healthcare products they purchase will be safe and of good quality. They have a right to expect that the product they purchase will meet certain standards, such as:

- containing the stated amounts of the named active ingredients, as shown on the label;
- not containing other unnamed and potentially harmful active ingredients;
- being manufactured under appropriate conditions, with adequate controls on the quality of the ingredients and the final product;
- being free from harmful levels of contaminants;
- being labelled with sufficient information to enable them to make an informed decision about using the product; and
- carrying information about the benefits of the product that are truthful, based on sound evidence and not exaggerated.

Consumers may be put at risk if any of these expectations are not met. The level of risk will vary and will depend on a number of factors. Regulation of complementary healthcare products should apply a system of controls that aims to manage the risks associated with the safety and quality of products and the claims made about those products. The regulatory framework should be designed to manage the risks in a way that is efficient and cost-effective, does not impose inappropriate compliance costs on the industry, and does not unnecessarily restrict the range of products consumers are able to access.

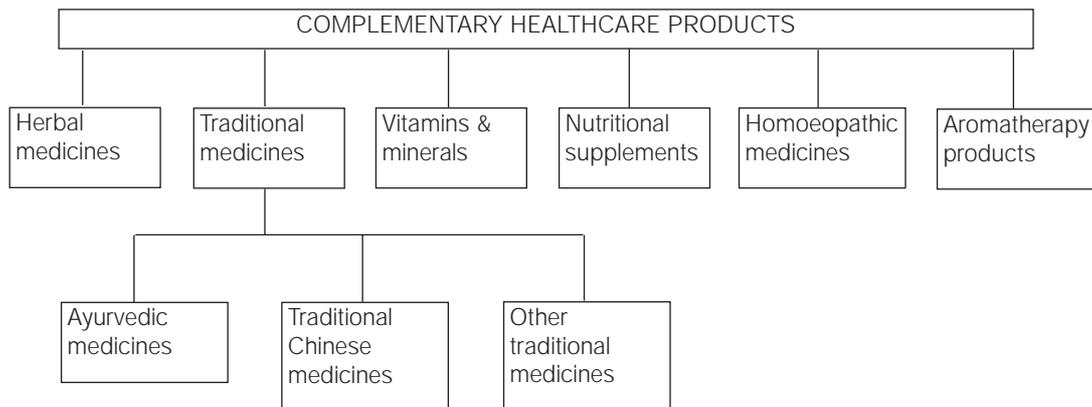
These are the principles being applied in developing the framework for regulating complementary healthcare products under the proposed joint agency.

3. TERMINOLOGY

The products referred to in this paper as 'complementary healthcare products' constitute a range of different types of products as shown in Figure 6.

It will be necessary to use a term in the legislation of the joint agency that describes collectively this group of therapeutic products. It is important to note that the term used in legislation would not preclude sponsors using any other term to describe their products in the market place provided that term is truthful and not misleading.

Figure 6: Types of complementary healthcare products



A number of collective terms have been proposed to the project team, including:

Natural health product

This term has been proposed because it is the term that is to be used in the proposed new Canadian regulatory scheme for these types of products. It is also argued that these types of products contain substances that are either derived from nature or are 'nature-identical' (i.e. a synthetic duplicate of the naturally occurring substance). Clearly, however, whilst some of these products contain active ingredients derived from nature, others contain synthetically produced active ingredients and many of the excipient ingredients are synthetically produced also. It could therefore be argued that the term 'natural health product' is misleading.

Complementary healthcare product

This term has been proposed as a means of differentiating these types of products from other medicines based on the proposition that these products are intended to promote "wellness" and the maintenance or enhancement of good health (i.e. avoiding disease) rather than the management of disease. Whilst this is true for some types of products in this category, other products are clearly intended for use in the management of disease. Furthermore, some prescription medicines, such as vaccines and anti-malarials, are for the purpose of maintaining good health by preventing disease. Thus there is no clear distinction between complementary healthcare products and other medicines on the basis of purpose of use.

Complementary medicine

This term has been proposed because these products meet the proposed definition of 'medicine'. Many products already sit comfortably within the 'medicine' category (e.g. Traditional Chinese Medicines, Ayurvedic medicines, homoeopathic medicines, herbal medicines) and are clearly intended for use in the management of disease. Some would argue that products such as vitamins and minerals should not be classed as medicines because they are intended only to supplement the normal dietary intake of nutrients. However, it should be noted that many vitamins and minerals are intended (and promoted) for use in the management of disease (e.g. calcium in treatment and prevention of osteoporosis).

Question 32:

What do you consider to be the appropriate collective term for these products in the legislation and why?

4. DEFINITIONS

It will be necessary to develop a definition for the group of products being referred to in this paper as "complementary healthcare products", for inclusion in the legislation to be administered by the joint agency.

As with terminology, there is no single, internationally accepted definition for this group of products, but there are a number of proposed or existing definitions that may be useful in developing a suitable definition to be used by the Agency.

As a starting point, three different definitions are provided below.

Question 33:

What are the strengths and weaknesses of these definitions?

Question 34:

How do you think this group of products should be defined in the legislation to be administered by the Agency?

Please provide justification for your proposed definition.

4.1 Health Canada – Proposed Definition for “Natural Health Product”

Health Canada's proposed Natural Health Products Regulations define a *natural health product* as:

- a substance or combination of substances in which all the medicinal ingredients are substances set out in Schedule 1; or
- a homoeopathic preparation; or
- a traditional medicine

that is manufactured, sold or represented for use in:

- a) the diagnosis, treatment, mitigation or prevention of a disease, disorder or abnormal physical state or its symptoms in humans;
- b) restoring or correcting organic functions in humans; or
- c) maintaining or promoting health or otherwise modifying organic functions in humans.

However, a natural health product does not include a substance set out in Schedule 2 or any combination of substances that includes a substance set out in Schedule 2.

Schedule 1 includes:

1. a plant or plant material, an alga, a fungus or a non-human animal material;
2. an extract or isolate of a substance described in (1), the primary molecular structure of which is identical to that which it had prior to its extraction or isolation;
3. specified vitamins, their salts or derivatives;
4. an amino acid or any of its salts;
5. an essential fatty acid;
6. a synthetic duplicate of a substance described in any of items 2 to 5;
7. a mineral; or
8. a probiotic.

Schedule 2 includes:

- a) antibiotics; and
- b) substances intended to be administered by injection.

4.2 Australian TGA - Definition of “Complementary Medicine”

The Australian *Therapeutic Goods Act 1989* defines a complementary medicine as a therapeutic good consisting wholly or principally of one or more designated active ingredients, each of which has a clearly established identity and:

- a) a traditional use; or
- b) any other use prescribed in the Regulations.

A designated active ingredient includes:

- an amino acid
- charcoal
- a choline salt
- an essential oil

- plant or herbal material (or a synthetically produced substitute for material of that kind), including plant fibres, enzymes, algae, fungi, cellulose and derivatives of cellulose and chlorophyll
- a homoeopathic preparation
- a microorganism, whole or extracted, except a vaccine
- a mineral including a mineral salt and a naturally occurring mineral
- a mucopolysaccharide
- non-human animal material (or a synthetically produced substitute for material of that kind) including dried material, bone and cartilage, fats and oils and other extracts or concentrates
- a lipid, including an essential fatty acid or phospholipid
- a substance produced by or obtained from bees, including royal jelly, bee pollen and propolis
- a sugar, polysaccharide or carbohydrate
- a vitamin or provitamin

Traditional use means use of the designated active ingredient that:

- a) is well documented, or otherwise established, according to the accumulated experience of many traditional healthcare practitioners over an extended period of time; and
- b) accords with well-established procedures of preparation, application and dosage.

4.3 Definition for “Complementary Healthcare Product” Proposed by an Industry Stakeholder Group

A complementary healthcare product is a substance or mixture of substances that:

1. Either:
 - (a) originates from a plant, animal or mineral source, including nature identical; and/or
 - (b) is found in the metabolic pathway; and/or
 - (c) is an isolate obtained from plant, animal, mineral or microorganism in such a manner that the primary molecular structure is unaltered from the original material;
 and:
2. which may be, but is not limited to being, classified as a herbal, homoeopathic, traditional or nutritional; and
3. for which there is an indication for health and well-being or for the treatment, modification, alleviation or prevention of disease, abnormal physical or mental health or the symptoms thereof;
4. or any other substance as agreed by the Managing Director of the Agency.

5. INTERNATIONAL TRENDS IN THE REGULATION OF COMPLEMENTARY HEALTHCARE PRODUCTS

While there is no formal international agreement on what constitutes best practice in the regulation of complementary healthcare products, there are some clear trends emerging in the way these products are regulated across a number of jurisdictions. Common elements in the regulatory frameworks include:

- pre-market assessment of the safety of ingredients;
- a requirement for products to be manufactured in licensed premises;
- appropriate levels of evidence required to support indications;
- standards for labelling and product information; and
- post-market activities including product testing and adverse reaction monitoring.

The table presented in Appendix 3 provides a brief summary of the regulation of complementary medicines and dietary supplements in a number of countries.

6. HOW ARE THESE PRODUCTS CURRENTLY REGULATED IN AUSTRALIA AND NEW ZEALAND?

6.1 Australia

Complementary medicines (including herbal medicines, vitamin and mineral supplements, nutritional supplements, traditional medicines such as Traditional Chinese Medicines, homoeopathic medicines, and aromatherapy oils) are regulated as therapeutic products under the *Therapeutic Goods Act 1989*. The legislation is administered by the TGA, a part of the Commonwealth Department of Health and Ageing. Within the TGA, the Office of Complementary Medicines (OCM) is responsible for regulating complementary medicines.

The objective of the legislation is to ensure the quality, safety, efficacy and timely availability of therapeutic products supplied in or exported from Australia. There are three key processes in the regulatory scheme:

- Licensing of manufacturers
- Pre-market assessment of products
- Post-market monitoring

Licensing of manufacturers

- Manufacturers must be licensed and their processes and facilities must comply with the principles of GMP.
- Regular inspection and audit of manufacturing facilities ensures ongoing compliance with GMP.
- Arrangements are in place to allow for certification of the standard of overseas manufacturing facilities based, wherever possible, on documentary evidence of compliance with GMP principles.

Pre-market assessment of products

- Therapeutic products may not be supplied in Australia unless they are included in the ARTG, or are specifically exempt from this requirement.
- The TGA adopts a risk-based approach to the regulation of therapeutic products.
- Higher risk products, such as prescription medicines, are individually evaluated for quality, safety and efficacy before they may be released on to the market. These products are included on the ARTG as 'Registered' products.
- Low risk products, such as most complementary medicines, are not individually evaluated before they are released on to the market. They may be marketed following self-certification by the sponsor and validation of key requirements by the TGA. These products are included on the ARTG as 'Listed' products. Low risk (Listed) medicines may contain only specified low risk ingredients and are permitted to make only general or medium level claims (health maintenance and health enhancement claims and certain claims for non-serious self-limiting conditions).

Post-market monitoring

The post-market monitoring system includes market surveillance, laboratory testing, adverse reaction monitoring and desk-based reviews of individual products or types of products.

The Australian regulatory system aims to ensure public health and safety and enhance consumer confidence in complementary medicines without unnecessary regulatory impost on the industry. This is achieved through an appropriately balanced risk management framework involving Listed (low risk), Registered (higher risk) and Exempt (special cases) complementary medicines.

Listed complementary medicines

Low risk complementary medicines are included in the ARTG via a simple, low cost and very quick process known as Listing. These Listed medicines are considered low risk because they contain only substances that are considered to be low risk, they are manufactured in accordance with the principles of GMP and they carry indications for health maintenance and health enhancement or certain indications for non-serious self-limiting conditions. The majority of complementary medicines are Listed (or low risk) medicines.

- Ingredients that are approved for inclusion in Listed medicines have been evaluated by the OCM for safety and quality when used in the community and have been reviewed by an expert advisory committee, the Complementary Medicines Evaluation Committee (CMEC).
- Listed medicines are not evaluated for efficacy prior to market entry and are restricted to certain types of therapeutic claims such as 'maintaining good health' or 'may assist with symptomatic relief of [a non-serious disease]'. The claims that may be made for a Listed medicine are described in the Levels of Evidence Guidelines ³⁷.

Sponsors are required to hold appropriate evidence to support claims and this may be evaluated by the TGA should a concern arise.

Registered complementary medicines

- Complementary medicines that contain higher risk ingredients or ingredients that have not been approved for inclusion in a Listed medicine or for which higher level therapeutic claims are intended, are required to be Registered to ensure that the product is safe for the intended use.
- Registered complementary medicines are evaluated by the OCM for safety, quality and efficacy and are reviewed by CMEC.
- Registered complementary medicines for which serious disease claims are made (i.e. indications similar to those for prescription medicines) are evaluated by the OCM and reviewed by the CMEC in consultation with the prescription medicines expert committee, the Australian Drug Evaluation Committee.

Exempt complementary medicines

- Certain types of complementary medicines are exempt from Listing or Registration. These include:
 - Starting materials (i.e. the ingredients used to make the finished medicine)
 - Raw herbs
 - Personal use imports (conditions apply)
 - Medicines used solely for experimental purposes in humans (conditions apply)
 - Medicines dispensed or extemporaneously compounded for a particular person for therapeutic application to that person (this allows complementary healthcare practitioners, such as herbalists and homoeopaths, to prepare medicines for individual patients)

6.2 New Zealand

Under current legislation in New Zealand, complementary healthcare products fall into one of two categories – dietary supplements or medicines.

Products that are dietary supplements are regulated under the Dietary Supplements Regulations. These regulations are made under the Food Act. There is no requirement for pre-market approval for dietary supplements. However, there are restrictions on the allowable daily intake for certain substances and therapeutic claims are not permitted for dietary supplements. There is no legal requirement for products to be manufactured to GMP standards, although some manufacturers choose to seek Government certification that they meet GMP requirements in order to facilitate export of products.

Under current legislation, if a therapeutic claim is made for a complementary healthcare product, the product is then a medicine and is regulated under the *Medicines Act 1981*. Pre-market approval must be obtained for medicines and this approval is only given after full assessment of the safety, quality and efficacy of the product. The medicines legislation is not designed to deal with complementary healthcare products. However, difficulties relate to the requirement to provide scientific data, usually in the form of clinical trial results, as evidence that the product is effective for its intended purpose. Evidence for the

effectiveness of complementary healthcare products is usually based on a long history of use and it would be costly and impractical to undertake the studies required to meet the data requirements for approval as a medicine.

Since it is illegal to make therapeutic claims for dietary supplements, compliance with the current legislation deprives consumers of the information they require to make an informed decision to purchase the product and to use it safely. New Zealand therefore requires new legislation that recognises the place of complementary healthcare products within the overall therapeutic products range, and regulates those products in a way that meets the needs of consumers, industry and the Government.

Identifying this need for new legislation has occurred independently of the proposal for a joint agency with Australia. Now, as part of the joint agency project, New Zealand and Australia are working to identify the best way of jointly regulating complementary healthcare products. If the joint agency proposal does not proceed, New Zealand will need to independently develop new legislation in this area.

Products regulated under the New Zealand Dietary Supplements Regulations fall into two broad types; food-type dietary supplements such as flavoured beverages with added herbals and other substances, and therapeutic-type supplements presented in pharmaceutical dose forms. The existence of this hybrid category of products means there is no clear dividing line in New Zealand between the food and medicine regulatory frameworks. This is not the case in Australia where products must either comply with the *Australia New Zealand Food Standards Code* or with the Therapeutic Goods Act. It is desirable to have a harmonised food/therapeutic products boundary to ensure that all foods meet applicable food standards and all therapeutic products are regulated appropriately.

Implementing the proposed regulatory system described in this paper coupled with the repeal of the Dietary Supplements Regulations would align the regulatory arrangements for food and therapeutic products in Australia and New Zealand. By then, products sold as food-type dietary supplements would be required to comply with joint Australia-New Zealand food regulation under the *Agreement between the Government of New Zealand and the Government of Australia Establishing a System for the Development of Joint Food Standards*.

ANZFA and the New Zealand Ministry of Health will shortly publish discussion papers outlining proposals in relation to a regulatory framework for food-type dietary supplements. The Ministry of Health document will describe proposals to remove foods sold as dietary supplements from the scope of the Dietary Supplements Regulations ahead of their repeal. The ANZFA document will focus on the food regulatory measures that could be applied to such products.

7. THE RISK MANAGEMENT APPROACH TO REGULATING COMPLEMENTARY HEALTHCARE PRODUCTS

Complementary healthcare products would be regulated by a separate unit within the Agency using a risk based approach.

7.1 Types of Risk and Risk-management Options

Risks associated with the ingredients used in the product

An ingredient in the product may present a risk related to its toxicity. Many, but not all, of the substances used in complementary healthcare products have a low intrinsic risk.

Complementary healthcare products generally contain active ingredients that are found in nature or are identical to substances found in nature. However, this does not necessarily mean they are safe. When a substance is extracted from a plant or other natural source and supplied in isolation in a concentrated form, it may produce toxic effects that would not be seen if the same substance was ingested in small quantities, in combination with all the other substances in the natural source or plant that may moderate its effects. It is well recognised that in herbal medicine, isolating and concentrating a particular constituent of a plant can produce a substance more hazardous than the herb from which it was extracted. Safety of ingredients is, therefore, an important issue for complementary healthcare products.

This risk can be managed by placing controls on the range of ingredients that can be used in those complementary healthcare products that are classed as "low risk". These products are not required to undergo an evaluation by the regulator before they can be placed on the market.

This can be achieved by having a list of "low risk" substances (sometimes referred to as a "positive list" or "white list"). Substances are placed on the list following a safety evaluation carried out by the regulator. Products containing substances not included on this list can still be marketed, but the application submitted by the sponsor would be required to contain more information and would be evaluated for quality, safety and efficacy before being approved for supply.

Restriction on the range of ingredients used in products can also be achieved by maintaining a list of prohibited ingredients. The regulator would add substances to this list following the emergence of concerns about their safety. This is commonly referred to as a "black list".

The advantages of having a "positive list" or "white list" of ingredients are that:

- The list is transparent. Product sponsors can immediately ascertain whether their product contains any ingredients that are not on the list and therefore have not been evaluated as "low risk".
- The public is protected from exposure to substances that have not been evaluated for safety. Where a "black list"³⁸ is used, generally a substance is not listed until after a safety issue has been identified.

Risks associated with product quality

A poor quality product may contain substances it should not contain and that could be harmful or not effective for the proposed indications. The harmful substance may have entered the product accidentally during manufacture because the manufacturing process

³⁸ A "black list" is a list of substances not permitted in "low risk" products.

was not adequately controlled or because contaminated or poor quality starting materials were used. Alternatively, substances that are not named on the label may have been deliberately added to the product during manufacture to enhance its effectiveness.

This risk can be managed by requiring manufacturers of complementary healthcare products to be licensed. In order to obtain a licence, the manufacturer must be able to show that they comply with the Code of Good Manufacturing Practice – a set of principles relating to quality in manufacture. The same principles apply to all types of medicines, but the way in which compliance with the code can be achieved may vary according to the sorts of products being manufactured.

Risks associated with inadequate consumer access to information

The consumer may not have access to appropriate information about how to use the product safely. Many consumers self-select complementary healthcare products from supermarket or health food store shelves. There may be a risk to the patient if they have a medical condition that makes the product unsuitable for them, or if the product contains a substance that can interact with other medications they are taking. Without adequate information, consumers can unwittingly put themselves at risk of potentially serious adverse reactions or interactions.

This risk can be managed by having standards for labelling and product information, requiring that consumers are provided with adequate information about how to use the product, and with the warnings and precautions necessary to enable them to use the product appropriately.

Risks associated with the claims made about a product

Consumers make the decision to use a complementary healthcare product in the expectation that it will produce a particular benefit – either in preventing illness or treating an existing disease. If the product does not achieve the anticipated benefit, the consumer may be put at risk. This risk could be serious if they are taking the product in the expectation that it will treat or control a serious or life-threatening disease such as asthma, diabetes or cancer.

The risk associated with the claims for a particular product is therefore greater when that product is promoted for the treatment of a serious condition. The less effective the product is in treating the condition, the greater the risk of harm to the consumer. For this reason, it is considered unsafe to allow indications or claims relating to the treatment of serious diseases to be made unless those claims have been evaluated and found to be appropriate.

This risk can be managed by:

- prohibiting claims on all complementary healthcare products. This is considered inappropriate for two reasons. Firstly, it does not meet the needs of the sponsor to be able to promote a product for its intended purpose. Secondly, it does not meet the needs of the consumer to be provided with adequate and appropriate information about the product; or

- placing controls on the sorts of claims that can be made for products and the level of evidence that is required to substantiate those claims. Indications and claims can generally be categorised as general level (e.g. nutritional support, or relief of symptoms not related to a specific disease), medium level (e.g. reducing the risk of developing a disease or relieving symptoms of a disease) or high level (e.g. treating or preventing a disease). The higher the level of indications and claims made for the product, the greater the level of regulatory scrutiny applied.

7.2 Risk Categories for Complementary Healthcare Products

Applying a risk management approach to the regulation of therapeutic products requires that the level of regulation is consistent with the level of risk associated with the product. For the purposes of determining the appropriate level of regulation to be applied, complementary healthcare products can be divided into risk categories. The risk category for a product is determined by two factors - the hazard associated with its ingredients and the types of indications made for the product (see Section 7.1).

Most complementary healthcare products contain low risk ingredients, and provided they do not carry high level claims or claims related to serious diseases, would be regulated as low risk products. It is estimated that around 95% of complementary healthcare products would fall into this category. The regulation applied to low-risk complementary healthcare products at market entry would be light, enabling rapid access to the market whilst providing consumers with assurance about the safety and quality of products.

For the small number of products that contain high-risk ingredients or carry high level indications or indications related to serious diseases, increased scrutiny would be required to check the quality and safety of the product and the validity of the claims. These products would be considered medium or high-risk products and would be regulated accordingly.

Consistent with the risk-based approach to the regulation of medicines described in Part D, complementary healthcare products would be classified into three classes depending on the assessed risk.

Class I products would be those containing only substances from the list of permitted substances for use in Class I products, and intended to carry medium or general level indications. Most complementary healthcare products would fall into the Class I category.

Class II products would include those containing a scheduled (pharmacy or pharmacist only) medicine or meeting the requirements for scheduling as such, but not intended to carry indications for serious diseases, conditions, ailments or defects. They would also include those complementary healthcare products containing unscheduled ingredients not permitted to be used in Class I products.

Class III products would include those containing substances scheduled as prescription only medicines, or meeting the requirements for scheduling as prescription only medicines. They would also include those complementary healthcare products intended to carry indications for serious diseases, conditions, ailments or defects.

The allocation of products to risk categories is summarised in Table 7.

Table 7: Risk categories for complementary healthcare products

Intrinsic risk of the active ingredients in the product	Indication	
	Serious disease ³⁹	Non-serious disease
Low intrinsic risk	Class III	Class I
Medium intrinsic risk	Class III	Class II
High intrinsic risk	Class III	Class III

7.3 Maintaining a Register of Complementary Healthcare Products

For a risk management approach to work, the regulator must maintain a database of information about products on the market. This database enables the regulator to react quickly in the event of a safety alert relating to a particular ingredient or type of product. For example, if there is a local or international alert about the safety of a substance that is used as an active ingredient or an excipient in complementary healthcare products, it is essential that the regulator is in a position to react quickly by contacting sponsors marketing products containing that substance. Product may need to be recalled, or warnings added to labels in response to an alert and any delay in responding may place consumers, and ultimately sponsors, at increased risk.

The database would need to contain, as a minimum, the following information about each product on the market:

- name and contact details of sponsor;
- name of the product;
- description of the dose form;
- active ingredients and strengths;
- list of excipients;
- site(s) of manufacture; and
- indications for which the product is licensed.

This information can be captured electronically from the application when an electronic lodgement system is used.

8. PRODUCT LICENSING FOR COMPLEMENTARY HEALTHCARE PRODUCTS

Under the proposed product licensing scheme described in Part C; Section 2.2 of this discussion paper, a sponsor would generally need to obtain a product licence for a new complementary healthcare product before it could be supplied in the Australia/New Zealand market.

³⁹ "Serious disease" refers to diseases, conditions, ailments or defects that cannot generally be diagnosed or treated without consulting a suitably qualified healthcare professional. Examples include cardiovascular disease, asthma and cancer.

The Agency would regulate complementary healthcare products according to the risk classification described above (see also Part D for further information about the risk-based approach to the regulation of medicines). The factors used to determine the risk classification of a complementary healthcare product would also determine:

- the product licensing process to be followed for the product; and
- the extent of pre-market evaluation or assessment required for the product.

8.1 Class I Complementary Healthcare Products

A sponsor wishing to market a Class I complementary healthcare product in Australia and/or New Zealand would be required to obtain a product licence. In order to obtain a product licence, the sponsor would prepare and submit an electronic lodgement providing details about the product and the claims being made, and confirming that it is manufactured in licensed premises. This information would be assessed electronically and, provided the application was complete and in the correct format, a product licence would be issued. It is expected that this process would be completed within 24 to 48 hours.

Details of the information to be electronically submitted by the sponsor would be set out in legislation and would be expected to include the following:

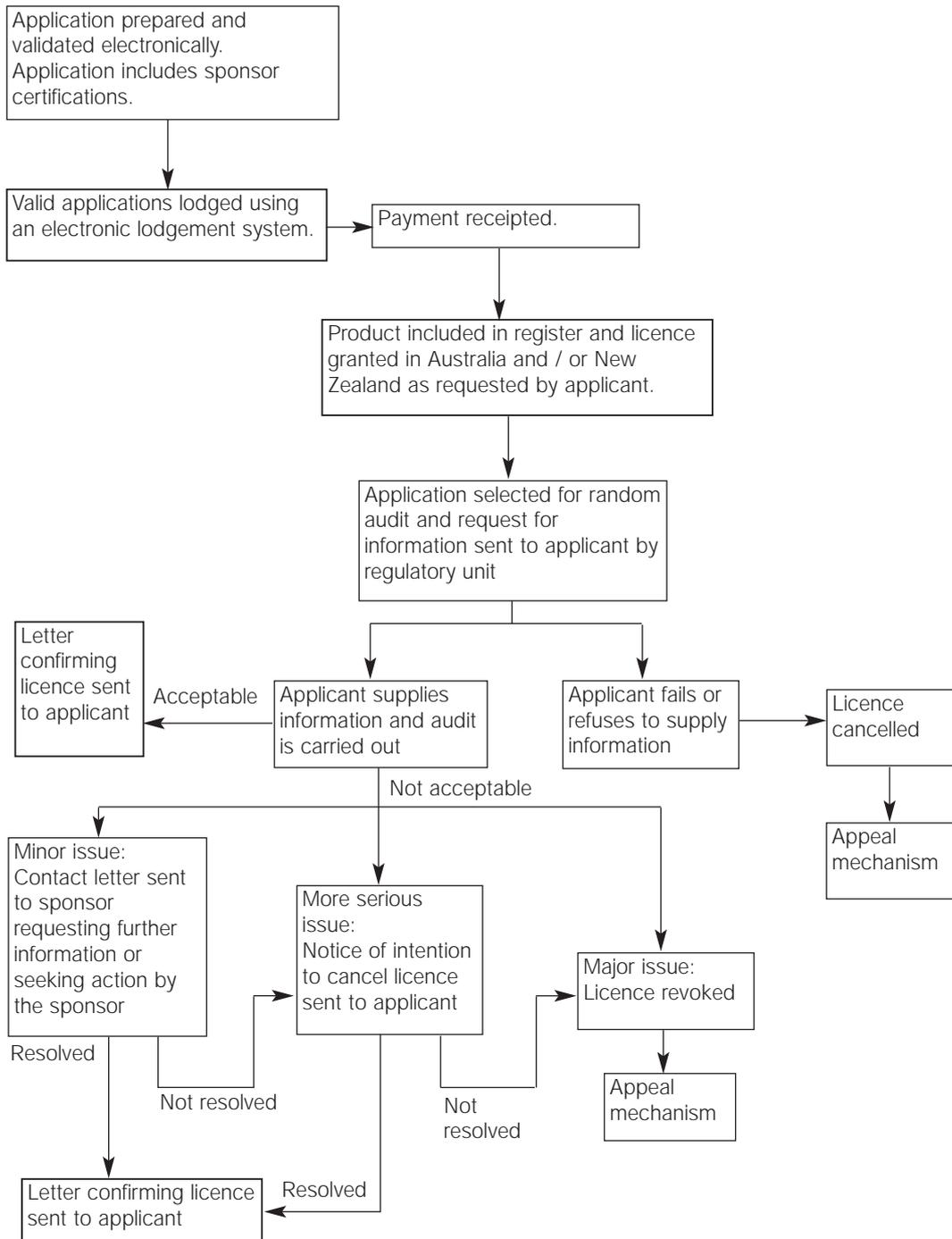
- name of the sponsor;
- product name;
- export name(s) of the product (if different from the product name);
- dosage form;
- route of administration;
- manufacturer/s of the product;
- names and quantities of the active ingredients;
- names of excipients;
- indications for the product;
- directions for use (in certain circumstances);
- container type & size &/or closure type (in certain circumstances);
- quantities of excipients that are restricted by quantity or concentration (in certain circumstances); and
- conditions subject to which the licence was granted, including required warnings.

The legislation would also specify what constitutes a separate product for the purposes of product licensing. There would be provision for grouping products under a single product licence in certain circumstances. For further detail on what constitutes a separate product for the purposes of product licensing, see Part C, Section 2.2.2.

The product details would be recorded in the Register of therapeutic products and would be reflected on the product licence issued to the sponsor.

An indicative application and licensing process for a Class I complementary healthcare product is summarised in Figure 7.

Figure 7: Indicative Process for Licensing of a New Class I Complementary Healthcare Product ⁴⁰



⁴⁰ This diagram is indicative only and shows the likely major activities in the licensing process

8.2 Class I Complementary Healthcare Product Substances

The Agency would maintain a "white list" of substances that had been evaluated for safety and determined to be suitable for use in Class I complementary healthcare products. It is expected that the initial list would comprise those substances already approved for use in "listed" medicines in Australia, as well as those substances used in dietary supplements marketed in New Zealand that had been assessed as meeting the safety criteria for inclusion in the list.

Only products containing ingredients from this list would be able to go through the electronic application and assessment process for Class I products described in Section 8.1. Applications for products containing other ingredients would be evaluated by the Agency as Class II or Class III complementary healthcare products.

A sponsor wishing to market a product containing a new ingredient would be able to apply to have the ingredient added to the list.

An application for the evaluation of a new substance for use in Class I complementary healthcare products would need to include information on:

- characterisation of the substance;
- history and mode and patterns of previous human use;
- reports of adverse reactions;
- biological activity;
- toxicology testing; and
- clinical trials to identify risks.

This information would usually be from published sources, but may also come from studies commissioned by the sponsor.

The application requirements and application format would be set out in legislation and/or guidelines. The Agency would evaluate the application and may seek the advice of an expert advisory committee and/or other experts before making a decision. If an application were to be rejected, appeal provisions would apply.

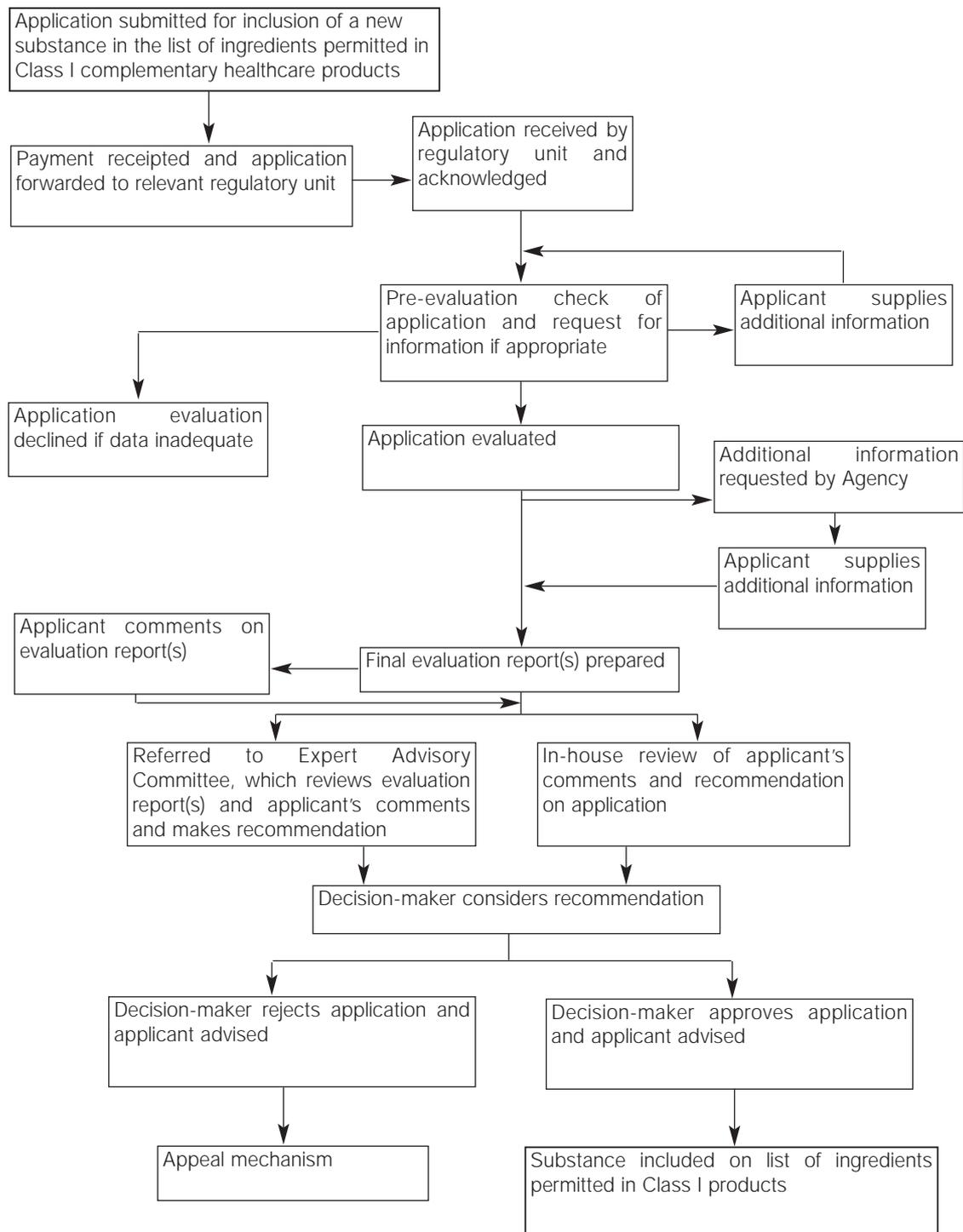
The Agency would set target timeframes for processing applications. Once the substance had been included in the permitted ingredients list, the sponsor could proceed with a product licence application for the product containing that ingredient as a Class I complementary healthcare product.

The first sponsor wishing to use a new ingredient would prepare the application and pay the relevant fee. Once the substance had been added to the list, other sponsors would be free to use it as an ingredient in Class I products. This may act as a disincentive to sponsors to apply for addition of new substances to the list. It has been suggested that consideration be given to developing a mechanism for cost sharing by which subsequent sponsors wishing to use the ingredient would pay a proportion of the substance evaluation fee, with this amount being credited to the original applicant.

Question 35:

What mechanism(s) would you propose to enable sharing of the costs of evaluation of new substances? Give details.

Figure 8 : Indicative Process for Inclusion of a New Substance in the List of Permitted Ingredients in Class I Complementary Healthcare Products ⁴¹



⁴¹ This diagram is indicative only and shows the likely major activities in the evaluation process

8.3 Class II and III Complementary Healthcare Products

These products would undergo a pre-market assessment and approval process before they could be granted a product licence. The data requirements for applications and the evaluation processes undertaken would reflect the different levels of risk associated with the products.

The legislation would specify what constitutes a separate and distinct product for the purposes of product licensing. The application format and data requirements would be set out in legislation and/or guidelines. The Agency would define timeframes for processing applications and may undertake a preliminary screening of an application prior to accepting it for evaluation.

The Agency would be able to seek advice from an expert advisory committee and/or other experts before making a decision on an application. If an application were to be rejected in part or in full, appeal provisions would apply.

As part of the evaluation process, the Agency would consider the appropriate scheduling of the medicine and any new substances contained therein.

An indicative application and licensing process for Class II and III complementary healthcare products is summarised in Figure 9.

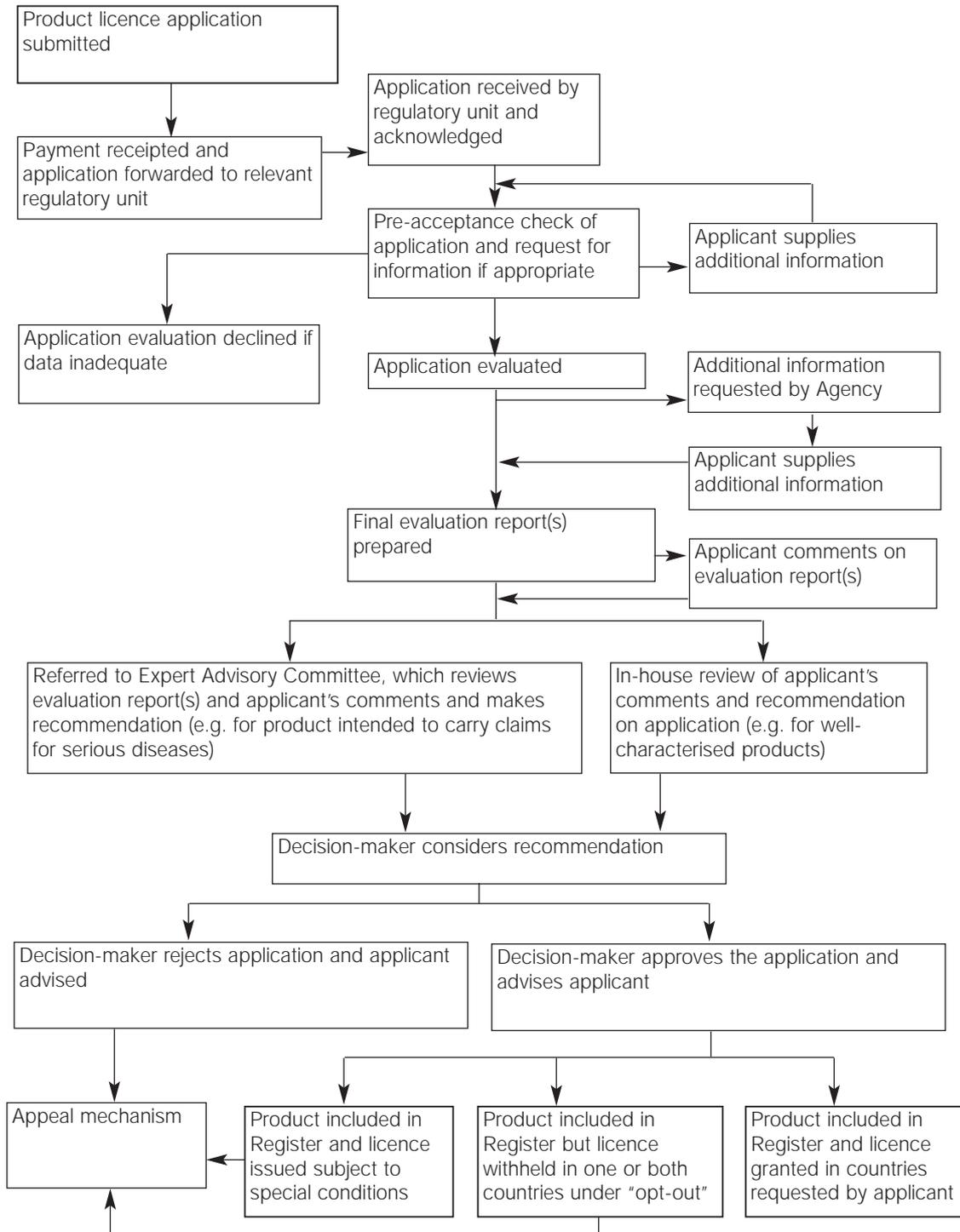
8.4 Indications for Complementary Healthcare Products

The levels and kinds of evidence that would need to be available to support indications for complementary healthcare products would be set out in legislation and/or guidelines. Indications (and any advertising claims) would be required to be truthful and not mislead the consumer or lead to unsafe or inappropriate use of the product.

For Class I products, it would be the responsibility of the sponsor to ensure that they held adequate evidence to support the indications at the time of product licence application. Indications could be based on scientific evidence or on evidence of traditional use. The higher the level of the indication, the greater the level of supporting evidence required. However, high level indications including indications for serious diseases would not be permitted for Class I products. The Agency may audit sponsors in order to determine that they do indeed hold adequate evidence to support the indications.

For Class II and III products, evidence to support the indications would be required to be submitted to the Agency as part of the application package.

Figure 9 : Indicative Process for Licensing of a New Class II or Class III Complementary Healthcare Product ⁴²



9. POST-MARKET SURVEILLANCE

Post-market monitoring is a key element of therapeutic product regulation. Products are sampled and submitted to random testing to ensure that they meet appropriate standards. Targeted testing is also carried out where a problem with a particular product or type of product is identified.

Information about adverse reactions, interactions and other product problems is gathered in order to ensure that consumers are being provided with adequate information about products. For example, if an interaction between a complementary healthcare product and another therapeutic product is identified, it is important that consumers and healthcare practitioners are made aware of the interaction and how to deal with it. The outcome of this sort of monitoring may range from a requirement for a warning to be added to a label, to the requirement for a product to be removed from the market in extreme circumstances.

The proposed regulatory scheme as presented in this discussion paper allows for early market access for Class I complementary healthcare products. For these products, which represent around 95% of all complementary healthcare products, the onus would be on the sponsor to provide relevant data in a prescribed format and to certify that the product complies with relevant requirements. Facilitating early market access in this way means that there is an increased need to develop a comprehensive risk-based system for post-market monitoring and surveillance.

It is proposed that systems would be put in place for the Agency to conduct random and targeted post-market reviews of Class I complementary healthcare products licensed under the sponsor self-certification scheme:

- to enhance consumer confidence in the efficacy, safety and quality of Class I complementary healthcare products; and
- to ensure a high level of industry compliance with regulatory standards and guidelines for Class I complementary healthcare products.

The Agency would be able to request and review information such as:

- product labels and packaging;
- promotional and advertising material;
- specifications and analytical certificates for the product;
- bibliography of sources of evidence to support indications; and
- evidence to support the safety and efficacy of the product (in certain circumstances).

The Agency would be able to take action if, as a result of a post-market review of a Class I complementary healthcare product, it determined that any of the sponsor's certifications were incorrect and/or there were concerns about the quality, safety or efficacy of the product.

Further information on post-market monitoring and surveillance systems is provided in Part D; Section 8.

10. ADVERTISING

Controls on advertising are designed to ensure that information in advertisements is truthful and is consistent with the product details and conditions on the product licence. For further detail on proposals for the regulation of advertising, see Part J.

11. OTHER REGULATORY ACTIVITIES

There is a range of other regulatory activities that the Agency would perform in relation to complementary healthcare products and that would be broadly similar to those applying to other medicines. These other activities are described in detail in Part D of this paper and include:

- scheduling (see Part D; Section 4);
- licensing of manufacturers (see Part D; Section 7);
- access to unlicensed products (see Part D; Section 9);
- provision of information to consumers and to prescribers, including product labelling (see Part D; Section 5);
- standardised terminology (see Part D; Section 3);
- regulation of export medicines (see Part D; Section 10); and
- regulation of ingredients and intermediate products(see Part D; Section 6).

PART G: REGULATION OF MEDICAL DEVICES

1. BACKGROUND

1.1 Regulation of Medical Devices in Australia

Australia has a well-established regulatory system for medical devices and is in the process of adopting a new system, which is in line with international best practice and is based on the principles endorsed by the Global Harmonisation Task Force (GHTF). The Bill to amend the Therapeutic Goods Act 1989 to allow the implementation of the new system was passed by the Australian Parliament in March 2002. It is planned to implement the new regulatory system on 1 October 2002.

1.2 Regulation of Medical Devices in New Zealand

Currently New Zealand has minimal medical device regulation and is considering a change to its medical device regulations with a view to achieving some consistency with the GHTF approach before the commencement of the proposed joint agency.

Regulation of medical devices in New Zealand is out of step with the rest of the developed world because there is no requirement for products to meet minimum standards of safety, quality and performance. Because there is no register of products on the market and no complete record of contact details for suppliers, the ability to trace and recall defective product quickly and effectively is limited.

It is difficult to quantify the level of risk without adequate information about the products in the marketplace and an assessment of the risks associated with particular medical devices. However, it is clear that inadequate regulation leaves New Zealand open to becoming a dumping ground for substandard product that cannot be marketed in other countries that apply international best practice standards to the regulation of medical devices. This exposes users of medical devices to an unacceptable level of risk, and exposes the health sector to the costs of remedial action when defective products fail and users are harmed.

While this review of medical device regulation in New Zealand is being carried out in the context of a proposed joint agency with Australia, the regulatory framework for medical devices will need to be updated regardless of whether the joint agency goes ahead. Any new regulatory framework introduced would be based on the GHTF recommendations, and could be expected to contain the same elements as the framework being proposed for the joint agency.

1.3 Global Harmonisation Task Force

The GHTF was conceived in 1992 in an effort to respond to the growing need for international harmonisation in the regulation of medical devices. The purpose of the GHTF is to encourage convergence in regulatory practices relating to medical devices.

The five member countries of the GHTF are Australia, the United States of America, Canada, the European Union and Japan and all are committed to adopting the GHTF approach into their regulatory systems.

The GHTF provides a forum in which official representatives of national regulatory bodies, working with medical device manufacturers and other organisations possessing relevant expertise, can develop principles for harmonising global approaches to regulating the safety, clinical performance and quality of medical devices in ways that protect public health, promote technological innovation and facilitate international trade.

The recommendations of the GHTF set out requirements for the safety, quality and performance of medical devices. These include:

- the classification of a medical device according to the level of risk associated with its use;
- a set of comprehensive essential principles for the design, manufacture and clinical performance of medical devices;
- conformity assessment procedures;
- the use of international standards as the preferred means of demonstrating conformance;
- adverse incident and post market surveillance requirements; and
- auditing practices.

2. REGULATORY SCHEME FOR MEDICAL DEVICES

2.1 General

It is proposed that a regulatory framework for medical devices representing international best practice, based on the principles endorsed by the GHTF, should be used by the Agency.

Under the proposed scheme, a therapeutic product could only be imported into Australia or New Zealand, exported to a third country from Australia or New Zealand or supplied in Australia or New Zealand by or with the approval of the holder of a product licence for the relevant country, unless specifically exempted from this requirement.

The proposed regulatory framework uses a risk-based approach to ensure that the level of regulation is proportional to the degree of risk involved in the use of the medical device. Under this system the sponsor would need to demonstrate to the Agency that the medical device they wish to supply in the Australia/New Zealand market complies with the Essential Principles for safety and performance. To do this, a sponsor would need to have an agreement with the manufacturer of the device, providing access to the evidence of conformity with the Essential Principles and the documentation establishing the quality and

performance characteristics of the device. Alternatively, a manufacturer may provide the information directly to the regulator on behalf of one or more nominated sponsors.

The system is based on:

- a set of risk based rules by which medical devices would be classified into six categories;
- a set of Essential Principles for the safety and performance of all medical devices;
- a number of conformity assessment procedures used to ensure medical devices conform with the Essential Principles;
- a requirement for manufacturers of medical devices, other than the lowest risk category, (Class I-non-sterile and non-measuring) to manufacture the devices according to a quality management standard;
- the presumption that a medical device conforms with the Essential Principles if compliance with nominated harmonised standards can be demonstrated;
- post-market monitoring by both the manufacturer/sponsor and the Agency; and
- requirements for advertising.

2.2 Definition of a Medical Device

For the purposes of this paper, a medical device is defined (as in the new Australian legislation) as:

Any instrument, apparatus, appliance, material or other article (whether used alone or in combination, and including the software necessary for its proper application) intended, by the person under whose name it is or is to be supplied, to be used for human beings for the purpose of one or more of the following:

- diagnosis, prevention, monitoring, treatment or alleviation of disease;
- diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap;
- investigation, replacement or modification of the anatomy or of a physiological process;
- control of conception;

and that

does not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means, but may be assisted in its function by such means;

or

an accessory to such an instrument, apparatus, appliance, material or other article.

2.3 Risk-based Classification System

Medical devices would be classified by the manufacturer according to the intended purpose of the medical device and the degree of risk involved to the patient and the user. The device classifications would be determined using a set of rules which take into

account the level of invasiveness in the human body, duration and location of use and whether the device is powered or not.

Classifying medical devices in this way allows the level of regulation to be proportional to the level of risk posed by using the device.

There would be six classes of medical device. Examples of the types of device included in each class are listed below.

Class I low risk

e.g. ostomy pouches, cervical collars, compression hosiery, beds, wheelchairs, walking aids, spectacles, stethoscopes, external electrodes, gels, software for image processing, tubing for gravity drips, cotton wool, gauze dressings, dental impression materials, examination gloves, prostatic balloon dilatation catheters, scalpels, manual drills and saws, thermographic imagers, dental curing lights, removable dentures.

Class IIa low-medium risk

e.g. anaesthetic breathing circuits, devices for storage or transport of organs for transplantation, devices for long-term storage of corneas, sperm, embryos etc, hydrogel dressings, tracheal tubes, vaginal pessaries, fixed dental prostheses, suction catheters, single-use catheters, infusion cannulae, bridges, crowns, dental filling materials, dental drills, hearing aids, magnetic resonance equipment, gamma cameras, and X-ray films.

Class IIb medium-high risk

e.g. haemodialysers, cell separators, insulin pens, brachytherapy devices, surgical adhesives, stents, infusion ports, orthopaedic implants, peripheral vascular grafts, penile implants, non-absorbable sutures, lung ventilators, baby incubators, blood warmers, external pacemakers, external defibrillators, surgical lasers, lithotripters, linear accelerators, radioactive therapy sources, diagnostic X-ray sources, intensive care monitoring systems, apnea monitors, ventilators, anaesthetic machines, blood pumps for heart-lung machines, condoms, contraceptive diaphragms, contact lens care products, blood bags implantable intra-ocular lenses, viscoelastic products (synthetic) for eye surgery, sterilants and instrument grade disinfectants.

Class III high risk

e.g. absorbable sutures, temporary pacing leads, neurological catheters, cortical electrodes, vascular prostheses, vascular stents, heparin coated catheters, condoms with spermicides, heart valves, intra-uterine contraceptive devices, breast implants (other than saline or water filled), devices of animal origin.

AIMD high risk

e.g. implantable cardiac pacing systems, implantable pulse generators, implantable electrodes and implantable drug infusion devices (AIMDs are treated as Class III devices).

IVD *In vitro* diagnostic devices

e.g. tests to detect HIV antigens, Hep B surface antigen, rubella anti-bodies, or a cholesterol serum test.

From the Australian experience it is anticipated that approximately 50 percent of medical devices to be regulated will be classified as low to medium risk.

2.4 Essential Principles

All medical devices must conform to the specified criteria for safety and performance set out in the "Essential Principles". The Essential Principles define the results to be achieved, or the hazards to be dealt with, but do not specify how these are to be achieved. This provides flexibility for manufacturers and sponsors, and caters for technological advancement.

A manufacturer must be able to demonstrate that their medical device complies with the Essential Principles. Evidence of compliance would be provided to the Agency either by the manufacturer directly, or by the device sponsor in Australia/New Zealand.

There are two types of Essential Principles - General Principles, which always apply to all devices, and Particular Principles, which only apply to some devices. Both the General Principles and the relevant Particular Principles have to be met in order to meet the Essential Principles.

There are six General Principles that must be met for all medical devices:

- the use of the medical device must not compromise health and safety;
- the design and construction of the medical device must conform with safety principles;
- a medical device must be suitable for the manufacturer's intended purpose;
- a medical device must be designed and manufactured in a way that ensures it is safe to use over the intended life of the device;
- a medical device must not be adversely affected by transport or storage; and
- the benefits of the medical device must outweigh any undesirable side-effects for the performances intended.

The Particular Principles are more specific and relate to design and construction. Further information is available at <http://www.ghtf.org/sg1/inventorysg1/sg1-n20r5.doc>.

Labelling requirements are also set out in the Essential Principles.

2.5 Product Licence

As described in Part C; Section 2, a sponsor would require a product licence issued by the Agency, before they could legally supply the medical device in the Australia/New Zealand market.

A product licence would be issued for a medical device if the sponsor could demonstrate that the product complied with the Essential Principles and that the appropriate conformity assessment procedures had been applied by the manufacturer.

To retain the product licence once it had been issued, the sponsor would have to actively monitor the performance of the medical device in the market place.

The product licence would contain information about the medical device including the:

- product licence number;
- name and address of the sponsor;
- Global Medical Device Nomenclature System (GMDNS) ⁴³ code of the device product;
- date the product licence was granted;
- country for supply (Australia or New Zealand, or both);
- conditions associated with the supply of that device product; and
- class of the device product.

As described in Section 2.1, to obtain a product licence the sponsor would have to firstly ensure that the device conformed with the essential principles, then provide documentary evidence to the Agency in support of the product licence application demonstrating that the device conformed with the essential principles. In most cases this would involve forming a relationship with the manufacturer to ensure that evidence of conformity assessment, and information relating to design, safety and performance of the device, were available when required either to the sponsor or to the Agency. A signed declaration of conformity (with the essential principles) by the sponsor must accompany every application for a product licence.

The broad steps involved for a sponsor in obtaining a product licence are set out below by device class.

Class I (Non-sterile, non-measuring)

- ensure device is correctly classified taking into account the manufacturers intended purpose
- ensure device conforms with essential principles either by obtaining a conformity assessment certificate or other evidence of conformity from the manufacturer acceptable to the Agency
- sign declaration of conformity (self declaration)
- determine GMDNS code for the device
- send completed application for product licence (either by electronic lodgement or paper)
- receive product licence (device legally able to be marketed in jurisdiction marked on product licence)

⁴³ The Global Medical Device Nomenclature System (GMDNS) is an international standard prepared by European Committee for Standardisation (CEN) and published by the International Standards Organisation (ISO). The GMDNS specifies the requirements and guidance for the construction of a nomenclature system for medical devices in order to facilitate co-operation and exchange of regulatory data on an international level between interested parties such as regulatory authorities, manufacturers, suppliers, health care providers and end users. The GMDNS provides rules and guidelines for nomenclature design which will ensure that nomenclatures built upon this standard will be simple to use, rational, applicable by all grades of professions of users and suitable for both computerised and printed matter.

Class III, AIMD, IIa, IIb or Class I (sterile or measuring)

- ensure device is correctly classified taking into account the manufacturers intended purpose
- ensure device conforms with essential principles either by obtaining a conformity assessment certificate or other evidence of conformity from the manufacturer acceptable to the Agency; OR arrange for the device to be assessed for conformance with the essential principles by the Agency or by another regulatory body acceptable to the Agency (note: if the device was made in either Australia or New Zealand, the conformity assessment would have to be conducted by the Agency).
- sign declaration of conformity
- determine GMDNS code for the device
- send completed application for product licence (either by electronic lodgement or paper)
- receive product licence if application approved (device legally able to be marketed in jurisdiction marked on product licence)

The broad steps involved in applying for a product licence are set out in Figure 12.

2.6 Conformity Assessment Procedures

A manufacturer would be required to follow an appropriate conformity assessment procedure to demonstrate that their device complied with the Essential Principles.

The level of conformity assessment required for a medical device would be commensurate with the level and nature of risk posed by the medical device to the patient or user. This would range from manufacturer self-assessment for the lowest risk (Class I) medical devices through to a full quality systems audit and product design examination for conformity with the Essential Principles for the highest risk (Class III and AIMD) devices.

All manufacturers would have to meet quality systems standards and (with the exception of those manufacturing the lowest risk devices) be audited and have their systems certified.

The conformity assessment procedures available to the different device classes are shown at Table 8.

The legislation would specify the documentation required to be held by the manufacturer and made available as evidence of conformity with the Essential Principles. In certain circumstances, the Agency would have to issue a conformity assessment certificate, while in other cases the Agency would carry out an application audit of certificates and technical documentation from overseas. The level of assessment performed by the joint agency would depend on the class of the device. Consideration would also be given to whether the medical device was CE marked or not. The levels of assessment to be performed by the joint agency are set out in Table 8 (Conformity Assessment Matrix).

Under the provisions of the Mutual Recognition Agreements which both Australia and New Zealand respectively have with Europe (EC-MRA) or the European Federation of Free Trade

(EFTA-MRA), medical device products can be assessed by a designated European Notified Body to the regulatory requirements (Essential Principles) of the importing country (Australia or New Zealand). Therefore, with the exception of specified high-risk devices (which are excluded from the MRA), medical device products that have been assessed against the Essential Principles under the provisions of the EC-MRA will not be required to undergo conformity assessment certification or an application audit by the joint agency.

The level of confidence ascribed by the joint agency to various regulatory systems or paths that may be used by overseas medical device manufacturers is set out in descending order in Figure 10: "Evaluation to the Essential Principles". Details of acceptable evidence of conformity assessment compliance, and relative indicative timeframes for obtaining a product licence using the different evidence of conformity assessment compliance, are also set out in Figure 10.

2.7 Sponsor's Declaration

A company or person who supplies a medical device into the joint Australia-New Zealand market, or either the Australian or the New Zealand market would be known as a "sponsor".

Sponsors would be required to declare that all requirements have been met, and that they hold, or have access to, sufficient information to demonstrate compliance of the medical device with the Essential Requirements. Sponsors would be required to have a direct link with the manufacturer of the devices they market. This link would be demonstrated by having a written agreement with the manufacturer to ensure that the Essential Principles have been met and an appropriate conformity assessment procedure has been followed.

Table 8: Conformity Assessment Matrix

PRODUCT ORIGIN	CLASS	AGENCY CONFORMITY⁴⁴ ASSESSMENT CERTIFICATION	APPLICATION AUDIT⁴⁵
Manufactured in Australia or New Zealand	I (non-sterile or non-measuring function)	N	N
	I (measuring) I (sterile)	Y	N
	IIa IIb III AIMD		
EC - MRA	I (non-sterile or non-measuring function)	N	N
	I (measuring) I (sterile)	N	N
	IIa IIb III AIMD	N N	N N
EFTA - MRA	Specified High Risk Devices ⁴⁶	Either Y (must)	or Y (must)
Product manufactured overseas and CE marked	I (non-sterile or non-measuring function)	N	N
	I (measuring) I (sterile)	N	Y (may)
	IIa IIb	N	Y (may)
	III AIMD	N	Y (must)
Manufactured overseas and not CE marked	Specified High Risk Devices ⁴⁷	Either Y (must)	or Y (must)
Manufactured overseas and not CE marked	I (non-sterile or non-measuring function)	N	N
	I (measuring) I (sterile)	Y	N
	IIa IIb III AIMD		

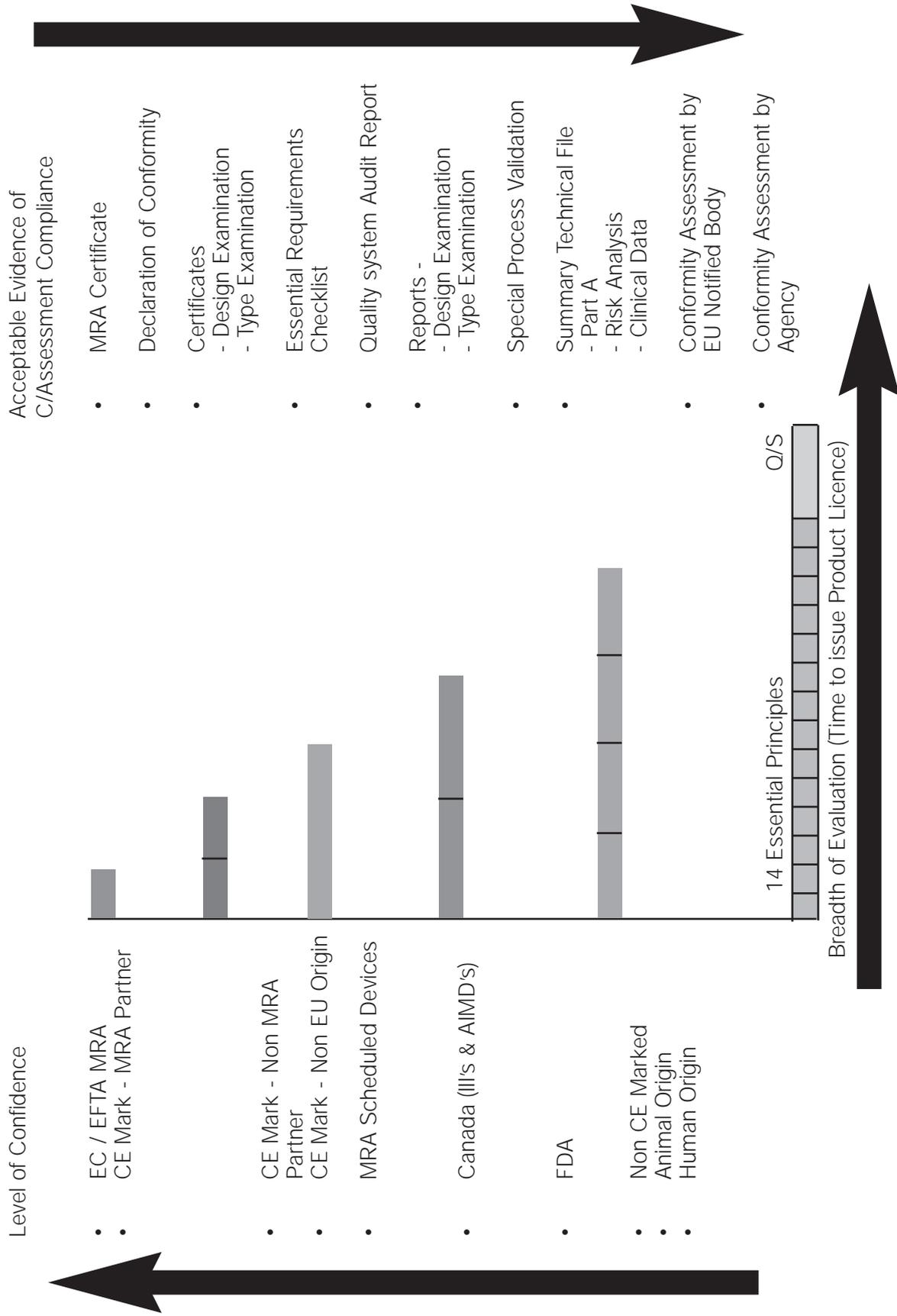
⁴⁴ Conformity assessment certification by the Agency involves the full conformity assessment for the device.

⁴⁵ An application audit would involve the Agency checking if the application is in the approved form or if matters certified in the Sponsor's Declaration are correct, and could include a review of overseas certification for quality management systems or product certification, a review of quality management systems audit reports or product evaluation reports undertaken by overseas regulatory authorities, or full or partial on-site audits.

⁴⁶ Specified high-risk devices - For example devices of animal origin rendered non-viable & those of bacterial and or recombinant origin for use in or on the human body.

⁴⁷ Specified high-risk devices - For example non-saline breast implants

Figure 10: Evaluation to the Essential Principles



2.8 Standards

2.8.1 Medical device standards

Standards (medical device and conformity assessment) would be specified by the Agency and would include most European "Harmonised" standards (EN Standards) and may include International Standards Organisation (ISO) standards and other international standards. The standards would be specifically chosen as they demonstrate compliance with one or more of the Essential Principles.

The safety and performance requirements for medical devices would be set out in the Essential Principles. Medical device standards would be specified by the Agency, and would be a means by which, or a tool that may be used by a manufacturer, to demonstrate compliance of a medical device with the relevant Essential Principles. However, compliance with the specified medical device standards would not be mandatory, and other ways, including other relevant standards, may be used to demonstrate compliance with Essential Principles. Medical device standards would be the preferred mechanism for demonstrating compliance with the Essential Principles as compliance with the relevant specified medical device standard would be presumptive evidence of compliance with the Essential Principles relevant to that standard.

It may be necessary to use a number of appropriate medical device standards to demonstrate compliance with all the Essential Principles because one standard will typically not be written to address all of the relevant Essential Principles in relation to a particular medical device.

To claim compliance with a standard the device must fall within the scope of the Standard and the requirements of the Standard must be explicitly applied. Compliance cannot be claimed if relevant aspects of the standard have been ignored, or methods or requirements modified.

2.8.2 Conformity assessment standards

Conformity assessment standards would apply to conformity assessment procedures and would relate to the obligations on the device manufacturer including establishing an appropriate quality management system, including where appropriate, implementation of certain production processes (e.g. sterilisation). This is because the aim of the quality system is to ensure the particular product is manufactured consistently.

2.9 Post-market Monitoring

Post-market monitoring of medical devices would include the following elements:

2.9.1 Adverse event reporting

There would be a requirement for manufacturers and sponsors to report adverse events involving their medical devices to the Agency within specified timeframes that would depend on the seriousness of the incident. Adverse event reports would be investigated

initially by the manufacturer or sponsor, and could be investigated by the Agency if appropriate. Where the results of the investigation warranted it, the sponsor or manufacturer would be required to issue a safety alert, or in more serious cases, a recall notice. Health care professionals and consumers would also be able to voluntarily report adverse events to the Agency.

2.9.2 Market surveillance

The product licence holder would be required to actively monitor the performance of the medical device in the market place.

2.9.3 Agency post-market surveillance

The Agency would undertake post-market surveillance activities such as:

- targeted laboratory testing of medical devices for compliance with the Essential Principles;
- random product sampling and testing;
- audits of product licence applications and documents supplied in support of the application, such as conformity assessment certificates; and
- inspection of sponsor distribution records.

2.10 Conformity Assessment Certificates

A conformity assessment certificate for a medical device may be issued by the Agency, or through an appropriate overseas regulatory authority participating in a Mutual Recognition Agreement, and would signify one or more of the following:

- the relevant conformity assessment procedure had been applied to the device;
- the device complied with the Essential Principles; and
- other certification requirements of the conformity assessment procedures had been met.

A conformity assessment certificate would be required before a valid application for a product licence could be made.

2.11 Suspension and Revocation of Conformity Assessment Certificates

The Agency could suspend or revoke a manufacturer's conformity assessment certificate (issued by the Agency) if the ongoing requirements for a quality management system, compliance with the Essential Principles or other certification requirements for conformity assessment procedures were not met. The maximum period of suspension would be six months (with provision for a six month extension) during which the product licence would also be suspended.

2.12 Register

All medical devices for which a product licence had been granted would be included in a register of therapeutic products, to be maintained by the Agency.

2.13 Product Licence Conditions

Two types of conditions associated with the supply of a medical device product would be applied to the product licence issued by the Agency.

2.13.1 Standard conditions

A number of standard conditions would apply to all product licences. These would include conditions relating to:

- the requirement for the sponsor or manufacturer to hold, or have access to, information about the medical device including that relating to:
 - the application of conformity assessment procedures; and
 - compliance with the Essential Principles, and other requirements;
- the inspection of premises where the kind of device mentioned in the Product Licence is dealt with;
- the inspection of related documents, and
- the provision of samples of the device.

2.13.2 Special conditions

Various other conditions relating to the manufacture, supply, disposal or destruction, intended purpose, records (including distribution records), and matters dealing with the Essential Principles for the kind of device mentioned in the Product Licence may be imposed on a licence.

2.14 Suspension and Cancellation of a Product Licence

Breaching the Product Licence conditions may lead to the suspension or cancellation of the Product Licence.

2.14.1 Suspension

The Product Licence for a medical device could be suspended if there is a potential risk of death, serious illness or serious injury from the use of the device. The period of suspension could be up to six months and could be extended for a further period of up to six months.

2.14.2 Cancellation

The Product Licence for a medical device could be cancelled if:

- there is an imminent risk of death, serious illness or serious injury from the use of the device;
- a conformity assessment certificate for that device is revoked;
- the product licence is suspended and the period of the suspension expires before the suspension is revoked; or
- there are serious breaches relating to advertising for the device.

Figure 11: Assessment procedures for medical devices

Assessment Procedures

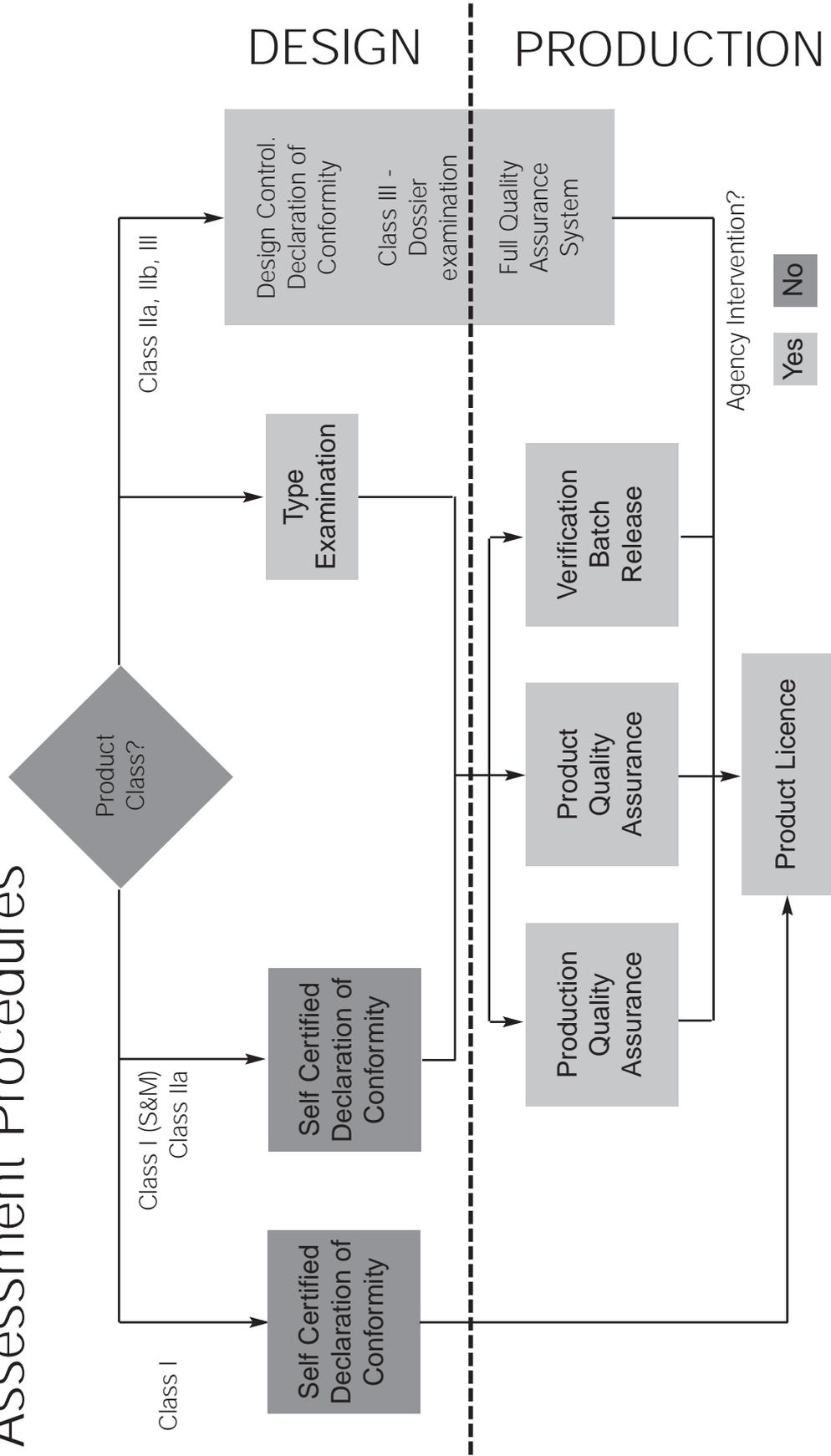
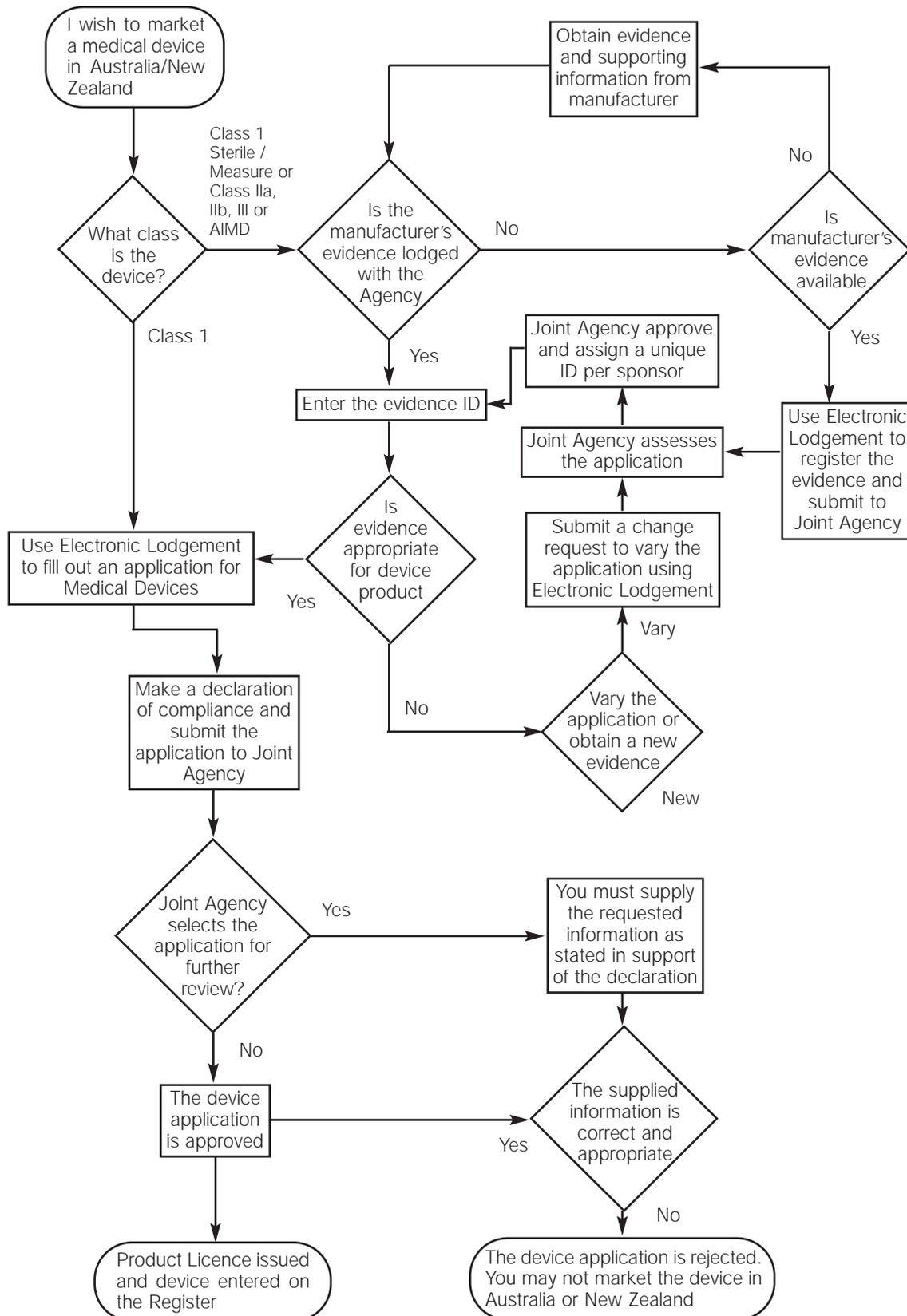


Figure 12: Indicative process for obtaining a product licence for a medical device



2.15 Exemption from Licensing and Access to Unlicensed Medical Devices

There would be three circumstances under which a medical device would be exempt from the requirement for product licensing.

2.15.1 Custom-made devices

Most custom-made devices would not require a product licence and would be readily accessible to the public through a variety of outlets. A custom-made device is a medical device that has been manufactured specifically in accordance with the written prescription of a duly qualified medical practitioner or other professional which gives, under their responsibility, specific design characteristics; and is intended for the sole use of a particular patient.

2.15.2 Medical devices used in a clinical trial

It is proposed that under a joint agency access could be gained to unlicensed medical devices through their use in clinical trials.

Currently, before a clinical trial can proceed in Australia, both ethical and scientific approval for the trial is required. There are two possible routes for obtaining approval to perform a clinical trial. Firstly, there is the clinical trial notification (CTN) route, in which a human research ethics committee associated with the institution in which the trial is to be conducted can give both ethical and scientific approval for the trial. Following approval by the institutional ethics committee, the conduct of the trial is simply notified to the TGA. Secondly, there is the clinical trial exemption (CTX) route in which extensive evaluation by the regulator prior to commencement of the trial is required.

In New Zealand, medical devices are currently not licensed or approved for use and therefore no centralised procedure exists for the approval of clinical trials of medical devices except that institutional ethics committee approval is required for a clinical trial involving new technology.

Under the joint agency scheme, it would be necessary for a sponsor to obtain both scientific and ethical approval before a clinical trial of a medical device could be performed in either Australia or New Zealand.

Sponsors would be able to submit an application to conduct the trial to the Agency for evaluation and comment, similar to the current Australian CTX scheme. Ethics approval would be required from the institutional ethics committee where the trial was to be performed.

However, in the majority of cases an appropriately constituted institutional ethics committee in either Australia or New Zealand would be able to provide both scientific and ethical approval of a trial with subsequent notification to the Agency (similar to the current Australian CTN scheme).

There may be occasions when an institutional ethics committee felt it lacked expertise in a specific field, particularly when the proposal is to trial a novel device. In these cases the committee has the right to request that the proposal to be considered by others with more experience in that area. Under the present Australian scheme these types of proposal, where the institutional ethics committee believes it does not have sufficient scientific expertise, are often submitted to the TGA as a CTX application.

To facilitate a joint scheme, it is proposed that expert scientific committees could be set up in Australia and New Zealand. These committees would consider and advise on the scientific content of clinical trial proposals where the institutional ethics committee did not believe it had the appropriate expertise to do so. Currently, in Australia, this type of committee would be established under the auspices of the Australian Health Ethics Committee (AHEC) a principal committee of the National Health and Medical Research Council (NHMRC). In this regard, it should be noted that the Australian NHMRC would usually seek funding reimbursement from the relevant stakeholder.

An alternative proposal would be that the Agency could set up a joint Australia/New Zealand expert scientific committee to oversee the scientific content and approval of clinical trial applications under circumstances where institutional ethics committees were unable to do so.

The establishment of expert scientific committees would satisfy the desire of certain institutional ethics committees to have access to more specialised scientific knowledge and would provide a uniform approach to clinical trial approval in both Australia and New Zealand, however, there would be obvious cost implications in setting up such a scheme.

Possible advantages of more unified schemes would be potential increases in industry investment in clinical trials in Australia and New Zealand and an increased access for patients to new experimental therapies.

Medical devices used in clinical trials would be exempt from the requirement for product licensing, provided the trial was approved by an institutional ethics committee and, where appropriate, by an expert scientific committee.

All clinical trials, irrespective of the approval process, would be required to be notified to the Agency. The Agency would maintain a database of all clinical trials involving medical devices conducted in Australia or New Zealand.

The requirement for a clinical trial to be approved and notified to the Agency would be set out in the legislation.

Question 36:

Should the mechanisms for approval of clinical trials of devices be unified in Australia and New Zealand?

Should there be separate centralised expert scientific approval committees? If so, should there be committees in each country or should there be a joint Australia/New Zealand expert scientific committee?

2.15.3 Medical devices supplied to individuals

In Australia there are three Special Access Schemes (SAS) by which individuals can gain access to unapproved medical devices through a medical practitioner. The schemes are designed to limit the use of unlicensed and therefore unevaluated medical device products to only those situations where they are genuinely needed. They also enable oversight of practitioner behaviour and prevent abuse of a system designed to allow patients access to unlicensed devices. This protects patients from the risks associated with the use of products for which there may not be adequate assurance of quality, safety and efficacy.

It is proposed that access to unlicensed devices would be maintained under a joint Agency. However, further work is required to develop the mechanisms for allowing access to unlicensed devices and for limiting their use to those situations where they are genuinely needed.

It is proposed that three mechanisms broadly based on the current Australian schemes would enable individuals to gain access to unlicensed medical devices under the Agency.

Authorised prescribers

The Agency would be able to grant certain medical practitioners authority to prescribe a specified unlicensed device or class of unlicensed devices to specified recipients or classes of recipients suffering from serious (but not necessarily life-threatening) medical conditions. In this situation, the medical practitioner would become an "Authorised Prescriber" and could prescribe unlicensed devices within the terms of the authority, without the requirement for further approval from the Agency.

Individual patient use

An individual patient use scheme (IPU) would provide consumers, with access to unapproved medical devices for their personal use, through an authorised prescriber, where:

- the consumer has a demonstrated clinical need for the device;
- the consumer is likely to benefit from the use of the "experimental" device; and
- no other device currently on the market is suitable.

Authorised user access

An authorised user access scheme (AUA) would allow authorised medical practitioners to use an unapproved medical device on a specified patient group for specified indications. This would enable, for example, a medical practitioner to use an unapproved medical device, for a defined period of time, on a group of patients suffering from a serious illness. This situation may arise where the medical device is highly specialised and has a limited

market, or where there is an urgent need for access to such a device while it is undergoing evaluation prior to approval. An authorised practitioner would need to be:

- a specialist medical practitioner in hospital practice;
- endorsed by either the ethics committee of the hospital in which the practitioner practices for the particular use, or by the relevant specialist College or Society; and
- authorised by the Agency through an office in the country where the practitioner is working.

Question 37:

What mechanisms should a joint agency put in place to provide an appropriate degree of assurance:

- of patient protection;
- of informed consent; and
- that sponsors do not use the scheme for supply of unlicensed medical devices as a means of de facto marketing.

2.15.4 Personal importation

It is proposed that under a joint Agency, an unlicensed medical device could be imported into Australia or New Zealand when:

- the medical device is for use by either the importer or a member of the importer's immediate family; and
- the medical device does not contain a substance which is a prohibited import under the Australian Customs legislation or is restricted under New Zealand Misuse of Drugs legislation; and
- the medical device does not contain a product that is an injection containing material of human or animal origin (except insulin); and
- the quantity imported does not exceed three months' supply per importation and the total quantity imported per year does not exceed 15 months' supply.

2.16 Offences Relating to Medical Devices

Offences relating to medical devices would be set out in the legislation. Types of activities that would be offences include:

- non-compliance with the Essential Principles;
- failure to apply conformity assessment procedures (manufacturers and sponsors);
- the importing, exporting, supply or manufacture of unlicensed medical devices; false or misleading representations about licensed medical devices; breaches of product licence conditions or conditions relating to a conformity assessment certificate; and
- failure to report, within the specified timeframe, an adverse event involving a licensed medical device.

2.17 *In Vitro* Diagnostic Devices

In vitro diagnostic devices (IVDs) would be regulated as medical devices under the proposed joint agency scheme. They would be regulated under a risk-based classification system and would need to meet Essential Principles for safety and performance. Manufacturers would be required to meet quality management standards, and undertake conformity assessment procedures demonstrating conformance with essential principles, comply with standards. Sponsors would be required to report adverse events within specified timeframes. Those IVDs used for blood typing and for screening and/or diagnosis of infection with blood borne pathogens would be regarded as high-risk devices.

2.18 Medical Devices for Export

Medical devices intended for export to countries outside the single Australia/New Zealand market would be required to be licensed by the Agency.

Medical devices for export would fall into two categories:

- those intended for supply in Australia and/or New Zealand as well as for export; and
- those intended solely for export to a country outside the single Australia/New Zealand market ('export only' medical devices).

A medical device intended solely for export from Australia or New Zealand to a third country would require licensing as an 'export only' medical device before it could be exported from either Australia or New Zealand. The export only process would not apply to medical devices exported from Australia to New Zealand or vice versa. These would require a product licence for supply in Australia and/or New Zealand.

Medical devices manufactured in Australia or New Zealand for 'export only' would be required to meet the same regulatory requirements as Class I devices, including the requirement for a signed declaration of conformance with the Essential Principles.

3. OTHER ISSUES

3.1 Other Therapeutic Products

There are a small number of therapeutic products that are not medicines and do not fit the definition of a medical device, such as hospital and household grade disinfectants and menstrual tampons.

Internationally the way in which these products are regulated varies. For example, Europe classifies menstrual tampons as personal hygiene products; the US, Canada and Europe regulate hospital and household disinfectants through environmental agencies.

It is proposed that menstrual tampons would be regulated outside the joint scheme. In Australia they would be regulated as they are currently, by the Agency under a contract.

It is also proposed that sterilant and instrument grade disinfectants would be regulated by the Agency for both countries. In contrast, it is proposed that the regulation of hospital, household and commercial grade disinfectants would be outside the joint scheme. In Australia they would be regulated by the Agency under a contract, but in New Zealand they would continue to be regulated by the Environmental Risk Management Authority (ERMA) under the Hazardous Substances and New Organisms legislation.

3.2 Medical Device-Medicine Combination Products

Products comprising a medical device in combination with a medicine that assists the medical device to achieve its intended purpose would require a product licence. To obtain a licence, it would be necessary to demonstrate that the medical device conforms to the Essential Principles and that the "secondary" medicine component meets the applicable regulatory requirements for medicines.

3.3 Products of Human Origin and Animal Origin

Devices containing products of human origin and/or animal origin (where that product has not been rendered non-viable) would be assessed within the Agency. These products do not fall under the scope of new medical device regulation currently being developed internationally, and are generally regulated at the national level due to inherent risks of disease transmission. The Agency would treat these products as high-risk and would apply a level of regulation commensurate with that risk, and in particular address the issues of Transmissible Spongiform Encephalopathies (TSE).

3.4 Expert Advisory Committee

An expert advisory committee on medical devices would be established. The role of the Committee would be to provide expert scientific, clinical and consumer advice on medical devices to the Agency. The functions and constitution of the committee would be set out in the Rules (see Part C; Section 2.4).

3.5 Standard Terminology for Medical Devices

Standardised terminology (Global Medical Device Nomenclature System codes) for medical devices would be used in the Register, although non-standardised names could be used in the market place. However, standardised terminology for the medicine component of medical device / medicine products would be required.

PART H: SURVEILLANCE AND ENFORCEMENT

1. INTRODUCTION

The joint agency would have responsibility for monitoring compliance with the new regulatory system it would administer.

The purpose of the joint agency's monitoring function would be to prevent the import, export, manufacture, supply, distribution or promotion of therapeutic products which were:

- unsafe;
- of unacceptable quality; or
- marketed or advertised in association with untrue claims, especially claims about the product's safety or efficacy.

2. MONITORING POWERS

It is proposed to provide the Agency with the powers it would need to carry out its monitoring function including the power to:

- request information;
- require persons to answer questions;
- request samples of goods to test their compliance with required standards; and
- search premises and seize goods and other items.

The types of powers proposed are the same as currently available to the TGA and Medsafe under the Therapeutic Goods Act and Medicines Act respectively.

3. ENCOURAGING COMPLIANCE

The Agency would undertake activities which would be designed to encourage compliance with the new regulatory system including:

- educating industry about regulatory requirements;
- encouraging self regulation by the industry; and
- cooperating with industry to ensure regulatory compliance in areas such as advertising practices.

4. ENSURING COMPLIANCE AND PUNISHING NON COMPLIANCE

To deal with non-compliance, the Agency would require powers to require compliance and to punish those who have not complied.

Accordingly, it is proposed that the Agency would have the power to impose administrative sanctions as well as have the power to take prosecutions through the New Zealand and Australian courts to impose criminal sanctions.

5. ADMINISTRATIVE SANCTIONS

Examples of the types of administrative sanctions proposed are the power to:

- cancel a licence to sell a product;
- recall products;
- require corrective advertising;
- publish a warning about the goods (for example in cases where the goods pose a health risk); and
- negotiate or apply to the courts for an enforceable undertaking modelled on the power currently available to the Australian competition law regulator, such as undertakings by industry to implement compliance programmes.

6. PROSECUTING OFFENCES

6.1 Prosecutions

Agency staff would also take prosecutions through the New Zealand and Australian courts to punish non compliance with the new framework.

In New Zealand, the Agency's staff would investigate alleged unlawful activities involving therapeutic products and initiate prosecutions in the New Zealand criminal courts where appropriate. In Australia offences would be investigated by Agency staff and prosecuted in the State criminal courts by the Commonwealth Director of Public Prosecutions, just as they are now.

6.2 Offences

The starting point for the types of offences that would be included in the new framework has been to consider the current offences in the Medicines Act and Therapeutic Goods Act respectively. The next step will be to consider the changes that would be required to give effect to the new requirements, which would be introduced as part of the regulatory framework described in this paper. A preliminary list of proposed offences is set out in Appendix 5.

There are also a number of specific issues about offences, which are under consideration and are outlined below.

Strict liability offences

Some offences are called strict liability offences. A strict liability offence is an offence where the prosecution must prove the defendant committed an unlawful act or failed to perform an obligation, but need not prove that the defendant intended to commit the offence. Strict liability offences are often created by regulatory statutes, to ensure that there are appropriate incentives to comply with the regulatory regime.

Further work will be carried out on what offences should be strict liability offences under the new framework. Possible examples include:

- importing restricted products without written approval;
- importing or supplying products that do not conform to the standard for those products;
- manufacturing a product without a licence;
- exporting a product that does not conform to required standards; and
- importing, exporting, manufacturing, or supplying products without a licence.

Offences committed in both countries

Both Australian and New Zealand Courts would have jurisdiction to hear cases where an offence (such as supplying unlicensed products) is alleged to have been committed in both countries.

However, a person would only be charged under the Act of one country. The prosecuting authorities would agree on the most appropriate country in which to bring the prosecution. Courts would also be able to decline to hear a prosecution if they consider it would more appropriately be dealt with in the other country.

In practice it is likely that prosecutions will usually be brought in the country in which the defendant is resident or, if the defendant is a company, in the country under whose laws the company has been incorporated. But where an offence occurs in the other country it would be open to the prosecutors to proceed in the courts of that country.

Safeguards would be adopted to ensure that this flexibility did not result in unfairness to a defendant:

- a defendant would also be able to request that prosecuting authorities agree to a change of jurisdiction; and
- a defendant would be able to go to court to seek an order that the matter go before a particular Court.

Extended jurisdiction

Because offences could be prosecuted in either country, the legislation of both countries would need to provide that the offences in that legislation also apply to conduct that occurred in the other country.

Service and execution of court documents

Currently TGA and Medsafe have cooperative arrangements in place to provide evidence required for the prosecution of offences in the other country.

However, under the new arrangements the usual court rules and procedures of a court hearing a 'dual offence' would not be enough. They would need to be augmented by provisions compelling the attendance of defendants and witnesses at court, and the taking of evidence from across the Tasman (including documents) in order to prosecute the offence.

Existing schemes for dealing with trans-Tasman evidential issues under the *Evidence Amendment Act 1994* and the *Evidence and Procedure (New Zealand) Act 1994* would assist with taking evidence in one country for the purpose of proceedings in the other. These statutes provide for approval from the High Court in New Zealand or the Federal Court or a State or Territory Supreme Court in Australia before a subpoena can be served in the other country, even if the proceedings are in a lower court. Further consideration will be given to whether this requirement is appropriate in the context of a joint regulatory regime. New provisions would also be required to enable the enforcement of fines and mandatory orders (e.g. to cease marketing a product) made in one country in the other country.

7. CRIMINAL SANCTIONS - PENALTIES

Criminal sanctions would be available where there is serious failure to comply with regulatory requirements.

It is proposed that a court would be able to impose a range of penalties depending upon the severity of the offence and the culpability of the person prosecuted.

It is also proposed that companies that commit offences should face a higher fine than individuals, while individual offenders and directors of companies would also be liable for imprisonment in the case of serious offences as well as or instead of a fine.

Levels of penalties

The appropriate level of penalties that should apply to an offence under the new framework are under review as part of this project. The review will be guided by the existing criminal law policies of each country and will involve consultation with government agencies responsible for overseeing criminal law policy.

This process will include an assessment of whether the levels of current penalties for offences in the Medicines Act and the Therapeutic Goods Act are appropriate for transfer to the new system. Given that a number of the penalties in question have not been updated for some time (especially in the case of the Medicines Act) it is likely that these penalties will increase.

8. SPECIFIC ISSUES

As well as comment on the general issues discussed above comments are also sought on two specific enforcement problems, namely product tampering and counterfeiting.

8.1 Product Tampering

Product tampering presents serious safety risks to public safety. While it is not possible to make products "tamper-proof" (and to claim to be able to do so would be misleading), tamper-evident packaging can be used to provide consumers with a warning that tampering may have occurred. Tamper-evident packaging systems provide an indicator or entry-barrier that, if breached or missing, can reasonably be expected to warn consumers that the package has been tampered with.

Packaging guidelines

In 2000, Australia published *Guidelines for the Tamper-Evident Packaging of Medicines, Complementary Healthcare Products and Medical Devices*. The guidelines can be viewed in full at: www.health.gov.au:80/tga/docs/pdf/tepguide.pdf

These guidelines were developed collaboratively between industry associations, the TGA, State and Territory Health Departments and consumer groups. They also draw on international experience and recent developments in regulation in the United Kingdom, United States of America and Canada. The guidelines are designed to protect the interests of the community, individual companies and the industry as a whole.

Application of the guideline is currently voluntary and monitored by industry associations.

However, it is intended that the requirement for tamper-evident packaging on therapeutic products will become mandatory in Australia in 2004. There is currently being considered by the Industry Government Crisis Management Committee.

While many products on the market in New Zealand are already supplied in tamper-evident packaging, there would be costs associated with the Agency adopting mandatory requirements for tamper-evident packaging.

Product tampering offences

In 2000 Australia introduced mandatory requirements for sponsors to notify the TGA of actual or potential tampering incidents and to take remedial action. Significant penalties for non-compliance were introduced at the same time. It is proposed that similar provisions should apply under the joint scheme.

Question 38:

Should tamper-evident packaging be mandatory for products licensed by the Agency for sale in Australia and/or New Zealand?

If so, what sort of time period would industry need to introduce tamper evident packaging?

Question 39:

If tamper-evident packaging was not mandatory, how could the public be adequately protected from the risks associated with undetected tampering?

8.2 Counterfeit Products

Counterfeit products are those that are presented as, or made to resemble, licensed products. Because they pose significant public health risks as they are generally of poor quality and often ineffective, the World Health Organisation has asked member states to take steps to eliminate trade in counterfeit medicines.

Under the proposed legislation it would be a criminal offence to import, export, manufacture or supply a counterfeit therapeutic product.

PART I: REVIEW OF REGULATORY DECISIONS

1. INTRODUCTION

This part of the paper discusses how the Agency will be accountable for its regulatory decisions.

The proposal is that the Agency's regulatory decisions will be open to challenge in two ways:

- through a two stage merits review process, consisting of a right to ask the Agency to carry out a review of one of its decisions, with a further right to ask for a review of a decision to be carried out by a merits review panel external to the joint agency; and
- through judicial review proceedings brought in the courts of either country.

Decisions made by the Agency on some issues, such as release of information, could be reviewed under the normal procedures that apply under the relevant national statute. So in Australia a decision not to release information under the Freedom of Information Act would be reviewed by the Administrative Appeals Tribunal (AAT), and in New Zealand a decision not to release information under the Official Information Act would be reviewed by the Ombudsman. (The merits review process described below would only apply to regulatory decisions in relation to therapeutic products).

2. MERITS REVIEW

Merits review is a process where a reviewer steps into the shoes of the decision maker and examines whether the appropriate decision was made.

Both New Zealand and Australia have merits review processes. In Australia the AAT provides independent review of a wide range of administrative decisions made by the Australian Commonwealth government and some non-government bodies. In New Zealand a number of statutes provide for merits review of decisions under that statute, by specific bodies established for that purpose.

It is proposed that a two stage merits review process apply to the joint agency. The first stage will involve an internal review carried out by the Agency itself. If a person is dissatisfied with the outcome of that review, then the second stage is that they will be entitled to have the matter referred to an independent external review panel.

The internal review proposed will be based on the existing practices of Medsafe and the TGA. Informal consultations between industry and officials will continue. If formal internal review is sought, the Managing Director would appoint a person with relevant expertise and experience to review the decision. That person will review the material provided to the

initial decision maker and the reasons for the initial decision; and will then provide fresh advice to the Managing Director on the issue. The Managing Director will consider the review report and decide the issue.

Designing the external review involves more novel issues. Existing mechanisms for external merits review will need to be redesigned to ensure they are appropriate in circumstances where applications may be made in either Australia or New Zealand, and the panel would be making binding decisions for both countries.

2.1 Trans-Tasman External Merits Review Possibilities

There are three possible approaches to external merits review for the Agency. Each would require Australia and New Zealand to legislate.

It is proposed that the choice of which approach to take be made according to the need:

- to give effect to the principle of "no lesser accountability" to Australian and New Zealand stakeholders;
- to ensure that a review panel has access to the scientific and medical expertise it will require to undertake its functions;
- to ensure that the panel is competent to make judgments as to the impact of wider questions of public interest on the particular matter before it; and
- to ensure that its decisions are consistent and robust.

The public interest aspect arises as the regulator must consider the interests of the public to whom the product will be marketed, not just those of the applicant seeking marketing approval. There is often a benefit in balancing the needs of a variety of patients when considering granting approval.

Based on past applications for review, between two and seven applications for external review are likely each year.

Approach 1 – A specialist trans-Tasman panel

This option would involve establishing a permanent specialist trans-Tasman panel to review the Agency's decisions. Like other specialist review bodies in each country it could have full and part time members to conduct the review and would be supported by administrative staff.

Approach 2 – A trans-Tasman Division of the AAT

This approach would involve establishing a trans Tasman division of the current AAT (or its suggested successor the Administrative Review Tribunal).

This approach would enable the review panel to share the infrastructure and resources of the wider AAT while building expertise in reviewing therapeutic products decisions.

Part time appointees could reflect the range of specific scientific and medical expertise required to make regulatory decisions in a complex environment. But it would be difficult for that wide range to be represented when a tribunal of only three members reviews a decision. The adversarial approach that has developed with AAT matters is also of

concern to some. A collegiate or inquisitorial process better addresses the public interest aspect referred to above.

Under approaches 1 and 2 the volume of cases (based on current numbers of applications for review in New Zealand and Australia) is unlikely to justify a separate body or a new division of an existing one.

Approach 3 - Individually constituted review panels

Under this option the Australian and New Zealand Ministers who are responsible for the Agency (the Ministerial Council), perhaps in consultation with each country's Attorney-General, could appoint an independent expert review panel on a case by case basis to consider applications for review.

Each panel would consist of individuals with the relevant medical and technical expertise to allow them to consider the particular case to be reviewed, as well as individuals with expertise on procedural and legal issues. Panel members would be appointed on the basis of their expertise, and not as national representatives: it is expected that they would be drawn from Australia, New Zealand and overseas.

An inquisitorial approach of a review panel, assisted by the collegiate approach of bodies such as ADEC that draw together the views of a variety of experts, make it more likely that the public interest needs are adequately addressed.

2.2 Standing to Seek Merits Review

At present a person or organisation whose interests are affected by a decision may ask the AAT to review that decision.

In Australia, the Federal Court has ruled that because of the objects of the Therapeutic Goods Act, one company does not have standing to seek the review of a decision concerning a competitor's product.

In New Zealand, there are similar restrictions on standing in some New Zealand statutes such as the Resource Management Act.

It is proposed that only the party directly affected by a decision of the Agency would have the standing to apply for both internal and external merits review.

2.3 Costs

At present parties who seek merits review of regulatory and administrative decisions in New Zealand or Australia generally pay their own costs. It is proposed to apply the same approach to the Agency's merits review system.

2.4 Questions of Law and Appeals on Points of Law

During external merits review questions of law arise from time to time. At present the review body can ask the court to determine a question of law to assist it with its review. In

addition, a person who considers that the merits review body has made an error of law has the right to appeal to the court on questions of law only.

Consistent with the approach suggested below for judicial review, the Australian Federal Court and the New Zealand High Court should both be able to review questions of law that arise in the context of external merits reviews. It is suggested that where the review is being conducted in Australia, applications to determine questions of law and appeals would be made to the Federal Courts. Where an external merits review is being conducted in New Zealand, such applications and appeals would be heard by the High Court. In each case, the usual rights of appeal would be available in each country. A similar approach should apply to appeals on points of law that arise during a review.

3. JUDICIAL REVIEW

3.1 The Agency's Decision Making

Most of the Agency's decisions about the regulation of therapeutic goods will be made by the Managing Director of the Agency (or the Managing Director's delegate) in accordance with Ministerial Council Rules.

Australian and New Zealand legislation will be drafted to ensure that these and any other decisions made under the new system will be reviewable under the existing judicial review processes of either country, in the same way as if they had been made by a domestic regulatory body under domestic law.

Adaptation of existing judicial review processes

It is proposed to enable decisions made by the Agency to be reviewed under the usual Australian and New Zealand judicial review processes, subject to a number of changes made to accommodate the proposed new single regulatory system.

The key components of the proposed system are:

- the Federal Court of Australia and the High Court of New Zealand will each have jurisdiction to review any decision made by the Agency;
- an aggrieved person will be able to choose to seek review in the Court of either country;
- only one court will review any given case. It will not be possible to apply to one court to review a matter (for example the High Court in New Zealand) and subsequently start fresh proceedings about the same matter in the other court (for example the Federal Court of Australia);
- where an aggrieved person has sought review in either the Federal Court of Australia or the High Court of New Zealand, that Court will be able to stay proceedings and let the other Court hear the case, on application by other parties or otherwise, if it considers that the other Court is the more appropriate forum (focusing on the centre of gravity of the review proceedings);

- the right to apply for review will be limited to those who are directly adversely affected by the decision. Most of the time this will limit the right to apply for review to the party in respect of whom an adverse decision is made, for example a sponsor who has had their application for a product licence declined. Competitors will not be able to use the process to delay approval of a licence;
- evidence will be able to be given on either side of the Tasman using video links and the like;
- decisions of one court will be effective in both countries. If for example the Federal Court of Australia sets aside a decision of the Authority, that decision will be treated as set aside in both Australia and New Zealand; and
- to achieve consistency, each Court will be consulted about establishing formal and informal methods of conferring and noting the other's decisions.

3.2 Grounds for Review

It is proposed to apply the current grounds for judicial review in New Zealand and Australia to the decisions of the joint agency. The current remedies available in New Zealand and Australia on review will also apply.

The current grounds for review under the Australian Administrative Decisions (Judicial Review) Act (the AD(JR) Act) (which are essentially the same as the grounds for review at common law) are as follows:

- breach of the rules of natural justice
- non-observance of procedures required by law to be observed
- no jurisdiction to make the decision
- the relevant Act did not authorise the making of the decision
- improper exercise of the power, namely exercising a power:
 - for a purpose other than a purpose for which it is conferred
 - that is so unreasonable that no reasonable person could have so exercised the power
 - in such a way that the result is uncertain
- exercising a discretionary power
 - in bad faith
 - at the direction or behest of another person
 - in accordance with a rule or policy without regard to the merits of the particular case
 - or any other abuse of the power.
- error of law
 - fraud
 - no evidence or other material to justify the making of the decision
 - the decision was otherwise contrary to law.
- taking an irrelevant consideration into account
- failing to take a relevant consideration into account

The Federal Court will be able to provide persons aggrieved by decisions made under the new system with the usual remedies that are available under the AD(JR) Act remedies:

- setting aside a decision
- referring the matter back to the original decision maker for further consideration
- declaring the rights of the parties
- directing the parties to do, or to refrain from doing, any act in order to do justice between the parties.

In New Zealand judicial review will be able to be sought in the High Court, with the usual rights of appeal to the Court of Appeal, on the established common law grounds. There are no material differences between the grounds for review under New Zealand common law, and the grounds available at common law or under the AD(JR) Act in Australia as described above. Similar review remedies will also be available in New Zealand, at common law and under the *Judicature Amendment Act 1972*.

Question 40:

Is the proposed two-stage merits review process appropriate?
How could it be improved?

Question 41:

Which option is most appropriate for the external merits review body?
Why?

Question 42:

Are the proposed arrangements for juridical review of the Agency's decisions appropriate? How could they be improved?

PART J:

ADVERTISING

Regulation of advertising ensures socially responsible advertising and marketing of therapeutic products in a way that promotes the appropriate and safe use of these products.

1. ADVERTISEMENTS FOR HEALTHCARE PROFESSIONALS

Under a joint agency, advertisements for therapeutic products directed exclusively to healthcare professionals would be governed by industry codes of practice, which would be consistent with an Australia/New Zealand therapeutic products advertising code.

2. DIRECT-TO-CONSUMER ADVERTISING

The regulatory scheme that would apply to direct-to-consumer advertising is currently under review as part of the joint agency project. An independent reviewer has been engaged to consult individually and widely with industry, consumer representatives and healthcare professionals in both countries. The reviewer has the assistance of a broadly based expert group made up of Australian and New Zealand industry and consumer representatives. A smaller working group with stakeholders from both countries and chaired by an advertising academic will help guide the review.

For this reason the indicative outline below is not detailed and does not assume to anticipate options that the review might propose.

It is anticipated that the regulatory arrangements for direct-to-consumer advertising of therapeutic products would be co-regulatory and simplified wherever possible. That approach would be based on:

- a single Australia/New Zealand advertising code and advertising oversight body;
- a single pre-clearance system for advertisements;
- a single administrative and complaints arrangement; and
- joint (Australia/New Zealand) industry codes of practice.

Under a co-regulatory approach:

- industry, consumers and governments would be involved in setting the advertising code;
- industry bodies would exercise a delegation to approve advertisements;
- a complaints body comprising industry and consumer representatives:
 - considers complaints about advertisements
 - could impose administrative sanctions
 - recommends regulatory action to the Agency

- industry bodies would:
 - apply industry codes of conduct to advertisements and other promotional material that do not require approval (eg advertising to health care professionals, letterbox drops, brochures, point-of-sale material, fliers, catalogues, etc.)
 - consider complaints about that material
 - impose industry sanctions for non-compliance with the advertising code.
- the Agency would be able to deal with advertising breaches by:
 - taking administrative action, such as cancelling a product licence
 - commencing, or referring matters for, criminal prosecution.

All advertisements directed to consumers in all media, including those for products exempt from holding a product licence, would have to comply with the advertising code.

The Rules would set out:

- the circumstances in which advertising is permitted, including permitting advertising to health care professionals
- the formal process for approving advertisements;
- the circumstances in which approval could be withdrawn or made conditional;
- which bodies could be given the authority to approve advertisements; and
- an advertising complaints handling mechanism.

The scheme would need to accommodate national differences, notably the current capacity to advertise prescription medicines in New Zealand, but not in Australia. That could be achieved under the Rules.

Sanctions for not complying with the advertising requirements are likely to include:

- appropriate fines under offence provisions in the Acts in each country;
- corrective advertising; and
- suspension or cancellation of a product licence.

PART K: TRANSITIONAL ARRANGEMENTS

1. PRINCIPLES APPLYING TO TRANSITIONAL ARRANGEMENTS

Following the passage of legislation implementing a new joint regulatory scheme for therapeutic products and commencement of operation of the Agency, there would need to be a period of transition to the new system. Considerable further work and consultation will need to occur over the next few months as the detail of appropriate mechanisms and durations for transition are developed. The following principles have been developed to guide this work.

The transition arrangements would:

- provide adequate assurance about the safety, quality and efficacy of products on the product licence register, without requiring extensive re-evaluation of data, which cannot be justified on public health and safety grounds;
- ensure that manufacturers and sponsors of therapeutic products in both countries are treated in a fair and equitable way, taking into account relevant past regulatory practices;
- impose the lowest possible compliance costs consistent with adequately protecting public health and safety;
- permit sponsors already in the market in either country to continue to market in that country during the transition period without having to apply for a dual-country licence; and
- facilitate early reduction of existing trade barriers.

Some of the issues that have been identified, and preliminary proposals for the transition process, are presented below.

2. PRODUCT LICENSING

It is proposed that the new legislation under which the Agency operates would introduce a product licensing regime for therapeutic products (see Part C; Section 2.2 for details of the product licensing regime).

3. PRODUCTS ON THE AUSTRALIAN OR NEW ZEALAND MARKETS AT COMMENCEMENT OF OPERATION OF THE AGENCY

At start-up of the new legislation and commencement of operation of the Agency ('commencement') it would be necessary to have a mechanism in place to enable existing products already on the market in either country to remain on the market in that country until a product licence has been issued by the joint agency. The following proposals are presented schematically in Figure 13.

3.1 Medicines

A medicine that is registered or listed on the Australian Register of Therapeutic Goods (under the *Therapeutic Goods Act 1989*) or that is distributed in New Zealand with the consent of the Minister (under the *Medicines Act 1981*) would be issued with a product licence valid for the country in which it has regulatory permission for supply at the time of commencement. Products falling into this category would include most prescription and OTC medicines and products regulated in Australia as complementary medicines.

A medicine that is legally being supplied in New Zealand at commencement but which is not required under the Medicines Act to have consent for distribution, would be issued with an interim product licence for New Zealand, which would be valid for a limited period. This period would be known as the 'transition period'. The duration of the transition period is still to be determined. At the end of the transition period, the licence would lapse unless the sponsor had applied for and obtained a product licence based on evaluation or assessment in accordance with the requirements of the Agency (a 'joint agency product licence'). Products falling into this category would include many dietary supplements, sunscreens and radiopharmaceuticals.

Under the legislation to be administered by the joint agency, it is possible that some medicines currently exempted from listing or registration in Australia would become liable for product licensing under a joint agency. If this were to occur, such products would be issued with an interim product licence for Australia, which would be valid for the duration of the transition period. If the sponsor wished to continue supplying the product after the period they would need to apply for and obtain a joint agency product licence.

3.2 Medical Devices

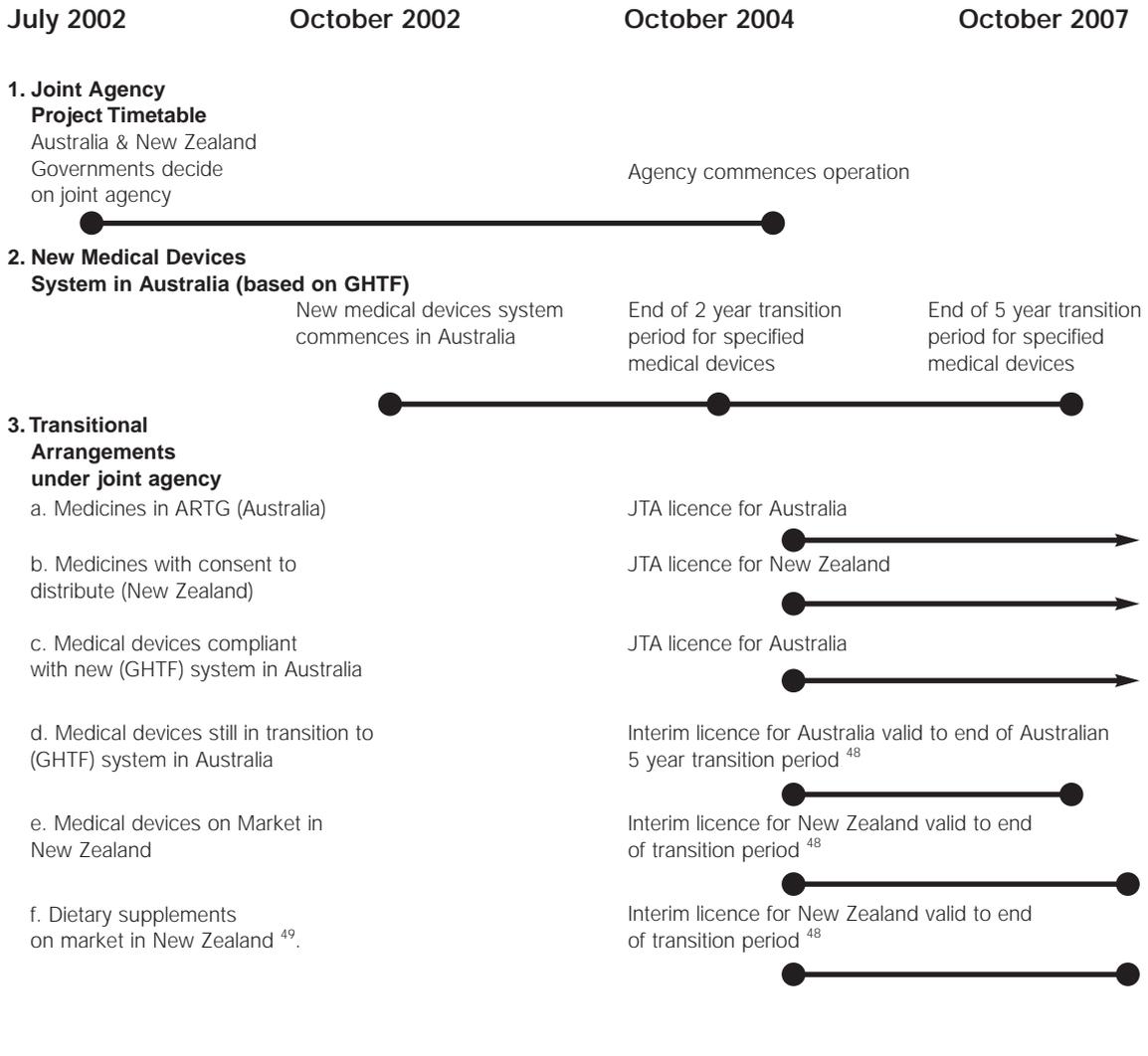
In Australia, most medical devices are required to be listed or registered in the ARTG (under the Therapeutic Goods Act). Under the current legislation, some devices are excluded from the regulatory scheme. The Australian Parliament has recently passed legislation amending the Therapeutic Goods Act. The new legislation is expected to take effect by September 2002 and will introduce a new regulatory system for medical devices in Australia, consistent with the recommendations of the GHTF.

Under the new Australian system, some devices that are currently not regulated will become subject to the new scheme. These products will be allowed a 2-year transition period in which to become compliant with the regulatory requirements and included in the ARTG. Devices that are subject to the current regulatory system will generally have a 5-year transition period in which to become compliant with the new (GHTF) scheme.

It is proposed that the joint agency would adopt a regulatory scheme for medical devices, which is based on the GHTF recommendations. It follows that the joint agency scheme is likely to be very similar to the new Australian system. Therefore, it is proposed that medical devices legally supplied in Australia at the time of commencement continue to be subject to the transitional arrangements put in place by the amended Australian legislation.

A medical device that is legally being supplied in New Zealand at commencement would be issued with an interim product licence for New Zealand, which would be valid for a 'transition period'. The duration of this transition period is still to be determined. At the end of the transition period, the licence would lapse unless the sponsor had applied for and obtained a joint agency product licence based on evaluation or assessment in accordance with the requirements of the Agency.

Figure 13 : Summary of Proposed Transitional Arrangements for Existing Products



⁴⁸ Product licence would lapse at the end of the transition period. The duration of the transition period is yet to be determined. Sponsors wishing to continue marketing one of these products would need apply for and obtain a JTA licence in accordance with the Agency's requirements.

⁴⁹ Dietary supplements other than 'food-type dietary supplements'

4. PROCESS FOR OBTAINING A PRODUCT LICENCE

For products that had not previously been subjected to a pre-market assessment or evaluation process by the TGA or Medafe (such as medical devices and dietary supplements marketed in New Zealand) the sponsor would be required to make an application in accordance with the requirements of the joint agency, just as if they were applying for a product licence for a new product.

The transition periods to be allowed for these types of products to become compliant with the new scheme are still to be determined. The transition periods would be determined taking into account both the public health and safety objective of the Agency and the resource implications for both sponsors and the Agency. They may differ depending on the product type and risk classification.

For products already approved by the TGA or Medsafe, a simple administrative process could be used to issue a single-country licence for the existing market at commencement. The procedure and requirements to be met by sponsors wishing to obtain dual-country licences for these types of products are still to be developed.

It is anticipated that there would be many instances where the products marketed in Australia and New Zealand will be essentially the same, but with differences in some of the approved details, such as indications, manufacturing sites or shelf lives. Differences in comparator products used in bioequivalence studies for generic medicines are also likely to be an issue.

It would be up to sponsors to decide whether they wished to rationalise these differences and market a single product in both countries, although there would be obvious advantages in doing so. Some work would be required on the part of sponsors and the Agency in moving to dual-country licensing for existing Australian-approved and New Zealand-approved products. Further work is required to identify appropriate mechanisms to facilitate moving to a dual-country licence where it is the sponsor's wish to do so.

5. LICENSING OF MANUFACTURERS

For those manufacturers holding an Australian or New Zealand manufacturing licence at commencement, there would be a smooth transition to the new system, because Australia and New Zealand have a Mutual Recognition Agreement covering GMP for medicines. It is anticipated that a joint agency licence would be issued on the next occasion of payment of the licence fee.

A transition period would be required to allow manufacturers not currently required to be licensed to carry out any required upgrading of their manufacturing sites and procedures to meet the requirements of the Code of Good Manufacturing Practice. The length of the transition period is still to be determined, however, it is anticipated that this process could take three to five years.

During the transition period, sponsors would only be able to obtain a single-country product licence for the existing market for any product not made in licensed premises. At the end of the transition period it would become illegal to market such a product.

6. LIST OF PERMITTED INGREDIENTS FOR USE IN CLASS I MEDICINES AND COMPLEMENTARY HEALTHCARE PRODUCTS

A number of ingredients used in dietary supplements marketed in New Zealand are not currently included in the Australian list of permitted ingredients for use in Class I medicines. It is proposed that, as part of the implementation planning phase, there be a process by which the list of substances permitted for inclusion in Class I medicines could be expanded prior to start-up of new legislation. This would enable many dietary supplements currently on the New Zealand market to be categorised as Class I medicines after the substance has been assessed for quality and safety. A safety assessment would be required to be done before a new substance could be added to the list. This work would need to be done by people with appropriate expertise and could be funded as part of the Government-funded set-up costs of the Agency. Work has already commenced to identify substances that would need to be considered for inclusion on the list.

7. LABELLING AND PRODUCT INFORMATION

It is anticipated that a period of up to five years would be required to complete the move to common labelling standards for therapeutic products. Some form of labelling exemption may be required for certain products during the transition period.

8. CLINICAL TRIALS

The legislation would need to include a provision that allows clinical trials in progress at commencement to continue. Clinical trials commencing after the start-up date would be required to follow the joint agency clinical trial process (see Part D; Section 9.1).

9. PRODUCTS UNDER EVALUATION BY TGA OR MEDSAFE AT COMMENCEMENT

It is proposed that, as a general rule, therapeutic products under evaluation by the TGA or Medsafe at commencement would be transferred to the joint agency and be considered as applications to the joint agency. Further detail on this proposal needs to be developed.

APPENDIX 1: GLOSSARY

1. LIST OF ACRONYMS

AAN	Australian Approved Name
AGRD	Australian Guidelines for the Registration of Drugs
AIMD	Active Implantable medical device
APIS	Active Pharmaceutical Ingredients
ARTG	Australian Register of Therapeutic Goods
BAN	British Approved Name
CEO	Chief Executive Officer
CMEC	Complementary Medicines Evaluation Committee
CMI	Consumer Medicine Information
COAG	Council of Australian Governments
CPMP	Committee on Proprietary Medicinal Products
CTD	Common Technical Document
CTX	Clinical Trial Exemption
DMF	Drug Master File
ERMA	Environmental Risk Management Authority
FDA	Food and Drug Administration (USA)
GATT	General Agreement on Tariffs and Trade
GHTF	Global Harmonisation Task Force
GMO	Genetically Modified Organism
GMP	Good Manufacturing Practice
GMDNS	Global Medical Devices Nomenclature System

HIV	Human Immunodeficiency Virus
HREC	Human Research Ethics Committee
ICH	International Conference on Harmonisation
INN	International Non-proprietary Name
IPD	Individual Patient Data
ISO	International Standards Organisation
IUD	Inter-uterine Device
IVD	<i>In vitro</i> diagnostic device
JTA	Joint trans-Tasman Therapeutic Products Agency
MC	Ministerial Council
MD	Managing Director
MCC	Medicines Classification Committee
MRA	Mutual Recognition Agreement
NDPSC	National Drugs and Poisons Scheduling Committee
NHMRC	National Health and Medical Research Council
NZ	New Zealand
OTC	Over-the-counter
PI	Product information
PIC	Pharmaceutical Inspections Convention
PIC/S	Pharmaceutical Inspection Cooperation Scheme
PL	Product licence
SAS	Special Access Scheme
SPF	Sun Protection Factor
TGA	Therapeutic Goods Administration

TRIPS	Trade-Related aspects of Intellectual Property Rights, including trade in counterfeit goods
TSE	Transmissible Spongiform Encephalopathies
TTMRA	Trans Tasman Mutual Recognition Arrangement
TTTIDC	Trans-Tasman Therapeutics Inter-Departmental Committee
US	United States of America
USAN	United States Adopted Name
WHO	World Health Organisation

2. GLOSSARY OF TERMS

This glossary of terms used in the discussion paper is intended to assist the reader and is not intended to give legal definitions. Definitions in the glossary are generally based on terminology currently used by the TGA or Medsafe, or have been developed during work on the joint agency project.

Aberrant prescribers are prescribers (including doctors, midwives, dentists) in New Zealand who improperly prescribe, administer or supply prescription medicines.

Active implantable medical device means:

(a) an active medical device designed for implantation, totally or partially, into the human body:

- surgically; or
- by other medical intervention, into a natural orifice; and

(b) includes an accessory designed for use with the device.

Active ingredient means a therapeutically active substance included in a medicine.

Advertisement includes any statement, pictorial representation or design, however made, that is intended, whether directly or indirectly, to promote the use or supply of the products.

Australian Approved Names List means the document entitled 'Australian Approved Names for Therapeutic Substances', as in force from time to time, published by the TGA.

Australian Register of Therapeutic Goods is a register created under Section 17 of the Therapeutic Goods Act for the purpose of compiling information in relation to, and providing for evaluation of, therapeutic products for use in humans.

Batch means a quantity of a product that is:

- (a) uniform in composition, method of manufacture and probability of chemical or microbial contamination; and
- (b) made in one cycle of manufacture and, in the case of a product that is sterilised or freeze dried in one cycle.

Batch number means a number, or a combination of numerals, symbols or letters, which is given by a manufacturer to a batch of products, to uniquely identify that batch and from which it is possible to trace that batch through all stages of manufacture and distribution.

CE mark is a mark of conformity used by the European Union that indicates the product meets the European regulatory requirements for that product. For a medical device, it signifies the device complies with the Essential Principles for the European system of regulation of medical devices.

Common Technical Document – the harmonised application format developed by the International Conference on Harmonisation for applications for approval of medicines.

Complementary healthcare practitioner means persons who are registered or are recognised as homoeopathic practitioners, chiropractors, naturopaths, nutritionists, practitioners of traditional Chinese medicine, podiatrists or osteopaths.

Conformity assessment certificate means an attestation of conformity (within the meaning of the EC Mutual Recognition Agreement or the EFTA Mutual Recognition Agreement) issued by an approved conformity assessment body.

Container means the vessel, bottle, tube, ampoule, syringe, vial, sachet, strip pack, blister pack, wrapper, cover or other similar article that immediately covers the products, but does not include an article intended for ingestion (e.g. a capsule shell).

Counterfeit - therapeutic products are considered counterfeit if the label or presentation of the product, any document or record relating to the product or its manufacture, or any advertisement for the product contains a false representation of:

- (a) the identity or name of the product;
- (b) the formulation, composition or design specification of the product or of any ingredient or component of them;
- (c) the presence or absence of any ingredient or component of the product;
- (d) the strength or size of the products (other than the size of any pack in which the products are contained);
- (e) the strength or size of any ingredient or component of the product; or
- (f) the sponsor, source, manufacturer or place of manufacture of the product.

Directions for use includes information on:

- (a) appropriate doses of the products; and
- (b) the method of administration or use of the products; and
- (c) the frequency and duration of treatment for each indication of the products; and
- (d) the use of the products by persons of particular ages or by persons having particular medical conditions.

Disallowance – Parliament allows other bodies to make delegated legislation (e.g. the Agency's Rules and Orders), but usually requires the provisions to be tabled in Parliament, and may disallow provisions it considers inappropriate.

EC Mutual Recognition Agreement means the Agreement on Mutual Recognition in relation to Conformity Assessment, Certificates and Markings between Australia and the European Community, as in force from time to time.

EFTA Mutual Recognition Agreement means the Agreement on Mutual Recognition in relation to Conformity Assessment, Certificates and Markings between Australia and the European Free Trade Association, as in force from time to time.

Excipient means an ingredient of a medicine other than an active ingredient.

Extemporaneously compounded medicines are medicines prepared from starting materials by a health practitioner or pharmacist to meet the needs of a particular patient, usually because the medicines are not commercially available.

Global Harmonisation Task Force is a voluntary group of representatives from national regulatory bodies and medical device manufacturers. It provides a forum in which these representatives can harmonise global approaches to regulating the safety, clinical performance and quality of medical devices in ways that protect public health, promote technological innovation and facilitate international trade.

Governance covers the processes by which organisations are directed, controlled and held to account.

Harmonisation means to bring into alignment the technical guidelines and requirements for product regulation of two countries, motivated by the principles of the Trans Tasman Mutual Recognition Arrangement.

Hazard is the capacity of the substance to produce an adverse health effect.

Implementation planning stage describes the period from the time both governments approve the joint agency proposal to the commencement of operation of the Agency, during which time legislation will be drafted and detailed technical requirements settled.

Indications means the specific therapeutic use(s) of the product.

Intellectual property is a legal term referring to ownership of ideas and applications, including trademarks, patents and copyrights.

International Conference on Harmonisation (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use. The ICH brings together the regulatory authorities of Europe, Japan and the United States and experts from the pharmaceutical industry in the three regions to discuss scientific and technical aspects of product registration. The ICH makes recommendations on ways to achieve greater harmonisation of technical guidelines and requirements for product registration in order to reduce the need to duplicate the testing carried out during the research and development of new medicines.

Label means a display of printed information:

- (a) on or attached to the products; or
- (b) on or attached to a container or primary pack in which the product is supplied; or
- (c) supplied with such a container or pack.

Manufacture means:

- (a) to produce therapeutic products; or
- (b) to engage in any part of the process of producing therapeutic products or of bringing a product to its final state, including engaging in the processing, assembling, packaging, labelling, storage, sterilising, testing or releasing for supply of the product or of any component or ingredient of the product as part of that process.

Manufacturing licence is written authority to manufacture therapeutic products for use in humans on particular premises.

Manufacturing principles means the written principles to be observed in the manufacture of therapeutic products or use of therapeutic products in humans.

Medical device means:

- (a) any instrument, apparatus, appliance, material or other article (whether used alone or in combination, and including the software necessary for its proper application) intended, by the person under whose name it is or is to be supplied, to be used for human beings for the purpose of one or more of the following:
- diagnosis, prevention, monitoring, treatment or alleviation of disease;
 - diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap;
 - investigation, replacement or modification of the anatomy or of a physiological process;
 - control of conception;
- and does not achieve its principle intended action in or on the human body by pharmacological, immunological or metabolic means, but may be assisted in its function by such means;
- (b) or an accessory to such an instrument, apparatus, appliance, material or other article.

Medicine – a therapeutic product that is represented to achieve, or is likely to achieve, its principal intended action by pharmacological, chemical, immunological or metabolic means in or on the human body.

Mutual recognition is a term that applies to an agreement reached between two countries to recognise each country's regulatory assessment and approval of therapeutic products.

Nomenclature is a system of names or naming in relation to therapeutic products.

Pharmacopoeia - a reference text that specifies tests and standards for ingredients and finished dosage forms. Commonly used pharmacopoeias include the British Pharmacopoeia (BP), the European Pharmacopoeia (EP) and the United States Pharmacopoeia (USP).

Poison means an ingredient, compound, material or preparation which, or the use of which, may cause death, illness or injury and includes any ingredient, compound, material or preparation referred to in a schedule to the current (Australian) Poisons Standard.

Presentation, in relation to therapeutic products, means the way in which the product is presented for supply, and includes matters relating to the name of the product, the labelling and packaging of the product and any advertising or other informational material associated with the product.

Primary pack, in relation to therapeutic products, means the complete pack in which the product, or the products and its container, is to be supplied to consumers.

Product licence – an authorisation (issued under the legislation administered by the Agency) for the sponsor to supply the therapeutic product/s that is/are the subject of the licence in Australia and/or New Zealand. Supply of the product/s would also be subject to other relevant legislation in the two jurisdictions (e.g. intellectual property and customs law).

Quality, in relation to therapeutic products, includes the composition, strength, potency, stability, sterility, purity, bioburden, design, construction, and performance characteristics of the product.

Scheduling, means determining the level of access to a medicine substance or product (i.e. prescription, pharmacist only, pharmacy or unscheduled medicine).

Sponsor – is an individual or a company in Australia or New Zealand with the legal responsibility for a therapeutic product in the Australia/New Zealand market.

Standard, in relation to the regulation of therapeutic products, describes:

- (a) a measure which serves as the basis to which sponsors should conform; or
- (b) the degree of excellence expected of a Joint Agency by its stakeholders.

Supply includes:

- (a) supply by way of sale, exchange, gift, lease, loan, hire or hire-purchase; and
- (b) supply, whether free of charge or otherwise, by way of sample or advertisement; and
- (c) supply, whether free of charge or otherwise, in the course of testing the safety or efficacy of therapeutic products in persons or animals; and
- (d) supply by way of administration to, or application in the treatment of, a person or animal.

Tamper – therapeutic products are tampered with if:

- (a) they are interfered with in a way that affects, or could affect, the quality, safety or efficacy of the product; and
- (b) the interference has the potential to cause, or is done for the purpose of causing, injury or harm to any person.

Therapeutic product:

- a product that is represented in any way to be, or that is likely to be taken to be for therapeutic use; or
- an ingredient or component in the manufacture of therapeutic products; or
- a container or part of a container for therapeutic products.

Therapeutic use means use in or in connection with:

- preventing, diagnosing, curing or alleviating a disease, ailment, defect or injury in humans; or
- influencing, inhibiting, or modifying a physiological process in humans; or
- testing the susceptibility of humans to a disease or ailment; or
- influencing, controlling or preventing conception in humans; or
- testing for pregnancy in humans; or
- the replacement or modification of parts of the anatomy in humans.

Treaty is a written international agreement between countries that usually imposes obligations on those countries. Those obligations can be implemented and imposed on the country's citizens through domestic legislation

APPENDIX 2: INDICATIVE LEGISLATIVE OUTLINE

1. THE TREATY

1.1 Preamble

1.2 Definitions

1.3 Objectives

- a) To safeguard the public health and safety of Australians and New Zealanders by establishing and maintaining a regulatory regime that will ensure the quality, safety, efficacy and timely availability of therapeutic products in both countries.
- b) Common standards for products, manufacturing, packaging, labelling.
- c) A single approval regime for therapeutic products with respect to the manufacture, supply, import, export and recommendations on the appropriate scheduling of products.
- d) Establishment of an Agency to perform the regulatory responsibilities under this regime for both countries, which is accountable to Government and other stakeholders of both countries.
- e) The regulatory regime is to be consistent with fundamental principles of regulation: COAG, NZ Code of Good Regulatory Practice.

1.4 The Agency's Regulatory Functions

- a) Regulation of therapeutic products – Governments agree to legislate to ensure that the decisions of the Managing Director (MD) will be effective according to their tenor on both sides of the Tasman (including decisions as modified or set aside following merits review or judicial review), subject only to differences in product licences and the opt-out regime and appropriate transition arrangements for existing approvals.
- b) Product licence regime – licences may distinguish between countries based on:
 - (i) scope of licence requested (sponsor may seek approval for only one country);
 - (ii) differing social/public health and safety/economic/market structure factors, which affect scheduling outcomes;
 - (iii) general opt-outs applicable to a class of product, which alter the approval or scheduling outcome for one country (eg abortifacients in Australia, nicotine patches in NZ);
 - (iv) requirements of Ministerial Council (MC) Rules.

- c) Opt-out – exceptional circumstances in which a Government can opt out, and process for seeking consensus on issues where there is an opt-out in effect:
 - (i) may be general or substance/product-specific;
 - (ii) may be pre-approval or post-approval;
 - (iii) product licences subject to opt-out decisions, and new licences issued must be consistent with them.
- d) Enforcing compliance – Governments to cooperate to enable the Agency to enforce consistent compliance with regulatory regime in both countries.

1.5 Legislation in Relation to Regulatory and Compliance Issues

Governments agree to legislate to:

- (i) give effect to regulatory regime;
- (ii) ensure effective enforcement and judicial cooperation in both countries, including investigating compliance, providing for summoning of defendants, witnesses and documents, giving of evidence and enforcement of sanctions.

1.6 Establishment and Functions of the Agency

- a) The Board will be incorporated by Australian law as a body corporate (the Agency) to perform specified therapeutic products regulatory functions for both Australia and New Zealand.
- b) The Agency will have the following functions and powers:
 - (i) Specified therapeutic products regulatory and enforcement functions in Australia and New Zealand;
 - (ii) Additional functions specified in MC Rules;
 - (iii) Powers of natural person, and regulatory powers conferred by legislation in Australia or New Zealand;
 - (iv) Powers exercisable only for purpose of performing functions.
- c) The Agency cannot enter into international agreements except with the prior approval of the Australian and New Zealand governments.

1.7 Governance of the Agency

- a) Governance structure
 - (i) Ministerial Council (MC) established consisting of Aus (federal) and NZ Ministers of Health.
 - (ii) Board established. Members appointed by MC (rules made by the MC would set out appointment processes for Board members (including for acting appointments) qualifications, terms of office, terms of disqualification for Board).
 - (iii) Managing Director, appointed by MC.

- b) MC's role
 - (i) Oversight of the Agency.
 - (ii) MC responsible for oversight of Board and accountable to Governments and legislatures for Agency performance.
 - (iii) MC agrees on appointment and removal of Board members and MD.
 - (iv) MC makes MC rules to give effect to Treaty's objectives in relation to: institutional issues, including functions, composition and appointment of the Board;
the regulatory framework, including the approval process.
MC Rules may be made subject to the same controls as domestic regulations, eg. disallowance. MC Rules not effective if disallowed in either country.
 - (v) Decision-making by MC (consensus, except for default rules with respect to appointment and removal of specified Board members prescribed by MC Rules).
 - (vi) Power to establish Expert Advisory Committees on terms set out in MC Rules.
- c) Board's role
 - (i) Responsible to MC for finance and administration of the Agency.
 - (ii) No role in regulatory decision-making – monitoring finance administration and strategic role only.
 - (iii) Board decision-making processes and procedures prescribed by MC Rules.
- d) Membership of Board
 - (i) Chair, MD and three others (a person with broad Australian health regulatory experience, person with broad New Zealand health regulatory experience, and person with broad commercial experience).
 - (ii) The Board is to consist of persons appointed to Board positions as well as persons acting in those positions.
 - (iii) Chair and MD require MC consensus. MC endeavours to agree on appointment of other members. Failing agreement, Aus Min selects Aus health and business persons. NZ Minister selects NZ health person. Three Board members to be Australian citizens or residents. All instruments of appointment to be signed by the Australian Minister on behalf of the MC.
 - (iv) Terms, qualifications etc to be in MC Rules.
- e) MD's role
 - (i) MD will be CEO of the Agency and responsible to the Board for finance and administration.
 - (ii) MD exercises regulatory powers (including making technical Orders) in accordance with MC Rules - not accountable to Board for exercise of regulatory powers, accountable for this through merits review and judicial review.
- f) Good governance principles

Basic principles including applicable Commonwealth Authorities and Companies Act and NZ Crown Entities principles.

1.8 Employment Regime for Agency Staff

Basic principles: look to applicable Australian/NZ public sector employment regimes.

1.9 Accountability of the Agency

Accountability:

- a)
 - (i) normal accountability arrangements in each country including planning and reporting should apply so far as practicable;
 - (ii) accountability arrangements should not be less than those which apply to Commonwealth Authorities in Australia or Crown Entities in NZ;
 - (iii) avoid unnecessary duplication eg one annual report, one audit.
- b) Annual reports to MC, including audited financial statements prepared in accordance with the MC Rules.
- c) Auditors-General are joint auditors: required to cooperate in conduct of audit ⁵⁰.
- d) Each country may apply its laws in relation to Ombudsmen, Freedom of Information/Official Information, privacy, human rights/anti-discrimination.
- e) Parliamentary accountability - general principle is that it is accountable as if a normal Commonwealth authority/ crown entity.

1.10 Review of MD'S Regulatory Decisions

- a) Merits review
Each Government to legislate for:
 - (i) internal merits review in accordance with MC Rules to be followed, if necessary by
 - (ii) external merits review of decisions before a merits review panel. Members of the panel will be appointed by MC. Issues of law may be referred/appealed to Federal Court in Australia or High Court in NZ. Basic principles on place of hearing for merits review and questions of law – depends on "centre of gravity" of the hearing.
- b) MD's decisions subject to judicial review on normal principles in either country. Any decision reviewable before either court – first seised hears the case, unless it considers that it is more appropriate in the interests of justice and of the parties for it to be heard in the other country, in which case it will stay its proceedings while that review proceeds. MD's decision as upheld/varied/set aside applies in both countries.
- c) Governments agree to legislate to facilitate the conduct of proceedings in merit reviews and judicial reviews, including service of proceedings, summoning witnesses and documents, giving of evidence and recognition of outcomes.

1.11 Funding

Basic funding principles for the Agency.

⁵⁰ This would not preclude the Auditors-General agreeing on the manner of auditing e.g. by contracting an accounting firm.

1.12 Withdrawal from Joint Arrangement

- a) Either country may withdraw from joint arrangement on [X years] notice.
- b) On withdrawal:
 - (i) The Agency becomes an Australian agency governed solely by the legislation of the Australian government;
 - (ii) The NZ government is entitled to use intellectual property, data, access to staff (for a defined period) to enable new arrangements to be put in place for NZ;
 - (iii) Governments will negotiate in good faith on financial implications (with arbitration as fall-back).

1.13 Regulatory Changes by One Country

Governments to consult before changing laws on regulatory and compliance issues. Notice of change must be given to the other Government [6 months, or less with consent].

1.14 Transitional Provisions

1.15 Relationship to Other International Obligations, TTMRA etc.

The regulatory regime must be consistent with current and future international obligations.

Relationship to TTMRA.

1.16 Provision for Consultations on Request of Either Party

1.17 Dispute Resolution Procedures

1.18 Provision for Review of Treaty

1.19 Amendment of Treaty

1.20 Participation of Third Parties

1.21 Entry into Force

2. THE ACT

1. Objects (quality, safety and efficacy etc) and other formalities (application, definitions etc)
2. High-level elements of the regulatory regime for therapeutic products including:
 - pre-market requirements
 - products to comply with standards set out in Orders
 - products to be licensed before being imported, exported or supplied
 - exemptions as set out in Orders
 - products to go through the pre-market assessment process that is appropriate for those products, as set out in detail in the MC Rules
 - sponsors to hold evidence supporting indications when therapeutic products are licensed
 - manufacturers to hold a licence, details in MC Rules
 - new medical device regime as is proposed currently for Australia.
 - post-market
 - sponsors to maintain and supply records
 - comply with advertising requirements set out in or given force by MC Rules and Orders
 - investigation etc powers eg to call for samples, enter and take samples/documants, test, recall, and vary, suspend, cancel entry/licence
3. Offences for not complying with above
4. Framework for review of decisions
5. The Agency recognised.
6. The Agency's organisational accountability, what is adopted or not adopted from current legislative requirements
7. The Agency's staffing arrangements (but not conditions)
8. Fees and charges framework
9. Power to make Rules/Regulations
10. Other necessary matters

3. RULES MADE BY THE MINISTERIAL COUNCIL

1. Details of the pre-market processes including application, procedures, and where appropriate, processing time frames applicable to:
 - prescription medicines
 - over the counter medicines
 - complementary healthcare products
 - medical devices
2. Expert advisory committees, including: membership, terms of reference, processes, conflicts of interest, payments
3. GMP requirements
4. Product licences: processes, procedures and conditions
5. Exemptions
6. Access scheme for unapproved products
7. Scheduling

8. Orphan drugs requirements
9. Advertising requirements
10. Record keeping requirements for sponsors
11. Import and export requirements
12. Enforcement powers details e.g. sampling, testing.
13. Review and complaint processes
14. Fees and charges
15. Institutional issues: governance, accountability
 - Board member qualifications, terms, nomination/appointment process, removal process
 - details of performance and financial reports to be prepared, when and how
 - accounting and audit requirements

4. ORDERS MADE BY THE MANAGING DIRECTOR

These would include:

1. Product quality and safety standards
2. List of products excluded from regulation
3. List of products exempt from specified requirements
4. Approved terminology
5. Good Manufacturing Practice details
6. Labelling requirements
7. Advertising details
8. Product specific requirements e.g. tampons, AIDS test kits
9. List of substances permitted to be used in Class I medicines.

APPENDIX 3: INTERNATIONAL APPROACHES TO REGULATION OF COMPLEMENTARY MEDICINES AND DIETARY SUPPLEMENTS

	UK ⁵¹	EU ⁵²	Canada ⁵³	Australia	USA
Regulator	Medicines Control Agency (MCA)	European Medicines Evaluation Agency (EMA) and national authorities	Health Protection Branch of Health Canada	Therapeutic Goods Administration	Food Section of Food & Drug Administration (FDA)
Legislative environment	Vitamins, minerals and amino acids regulated as foods (dietary supplements). Herbs and homeopathics regulated as medicines.	Regulated as medicines. Proposal that low risk traditional herbal medicines have a simplified procedure.	Regulated as Natural Health Products (NHPs) (separate legislation)	Regulated as Complementary Medicines (as a subgroup of medicines under Therapeutic Goods Act)	Regulated as Dietary Supplements under the Dietary Supplement Health and Education Act (DSHEA)
Risk based regulatory framework	No, but proposals are developing along these lines		Yes	Yes	Yes
Claims	Claims prohibited for dietary supplements and homeopathics. Claims for other products must be substantiated as for medicines	Bibliographic evidence for 'well established' medicines. Evidence required for 'traditional use' medicines	3 levels of claims: • Structure function • Risk reduction • Therapeutic or treatment claim. The stronger the claim, the better the evidence must be.	Claims but must be backed up by scientific evidence or evidence of traditional use. The stronger the claim, the better the evidence must be.	3 levels of claims: • Structure function • Health • Nutrient content As per the DSHEA
Good Manufacturing Practice (GMP)	GMP required as for medicines	GMP required as for medicines	GMP required as for medicines but interpretation guidelines to be developed	GMP required as for medicines	No GMP required (but Rule being developed)
Safety assessment of substances and products	Advisory Boards incl. Committee on Safety of Medicines, Ethics Forum	Proposed Committee for Herbal Medicinal Products (to liaise closely with Committee for Proprietary Medicinal Products)	Advisory Panel on NHPs	Complementary Medicines Evaluation Committee (CMEC)	No pre-market assessment. Safety concerns dealt with by FDA.
Permitted list of ingredients ("white list")	Proposal for a "white list" is being developed for traditional herbal medicines		Yes	Yes	No
Labelling	Specific labelling requirements for licensed products	Specific labelling requirements (Germany requires full labels + warnings)	Specific labelling requirements	Specific labelling requirements	Specific labelling requirements (as per the DSHEA)
Post-market monitoring	Licensed products included with medicines in post-market monitoring system	Included with medicines in post-market monitoring system	New system being developed based on product margin of safety.	Included with medicines in post-market monitoring system	Requirement to report adverse reactions to FDA, but no systematic testing programme

⁵¹ The UK adopts many of the practices of the EU

⁵² As at February 2002, there is a proposal (2002/0008 (COD)) Directive of the European Parliament and of the Council amending the Directive 2001/83/EC as regards traditional herbal medicinal products.

⁵³ The Regulations for the Canadian regulatory framework for Natural Health Products is currently in a consultative phase.

APPENDIX 4: ROLE OF THE AGENCY IN ACTIVITIES OUTSIDE THE SCOPE OF THE REGULATORY SCHEME

Certain regulatory activities currently carried out by the TGA, Medsafe and/or Australian States and Territories would not be covered by the joint scheme or included in the legislation administered by the Agency. However, the Agency may provide services in relation to these activities on behalf of the responsible Australian and/or New Zealand agencies.

Table 9 summarises the current arrangements in place in Australia and New Zealand for handling these activities and the proposed arrangements under a joint agency.

The proposed future arrangements under a joint agency take into account the existing legislative and administrative arrangements in Australia and New Zealand and the requirements for, availability of and location of relevant scientific and technical expertise to undertake these activities. The consolidation of activities requiring similar scientific and technical expertise under the umbrella of the joint agency should help ensure critical mass in some specialities and greater flexibility in use of resources. It should also ensure that staff development and training is cost effective and that career streams are established and maintained.

Table 9 : Arrangements for Handling Activities Outside the Scope of the Joint Agency Legislation

Activity	Activities currently undertaken by		Activities currently undertaken by	
	Australia	New Zealand	Australia	New Zealand
Regulation of agricultural and veterinary chemicals	National Registration Authority ⁵⁴ ; and TGA	Ministry of Agriculture and Forestry	NRA; and Joint Agency under agreement with NRA ⁵⁵	Ministry of Agriculture and Forestry
Chemical hazard and risk assessment for public health	TGA on behalf of other agencies	ERMA	Joint Agency under agreements with relevant agencies	ERMA
Chemicals – scheduling or access restrictions	States and Territories	ERMA	States and Territories	ERMA
Regulation of industrial chemicals	National Industrial Chemicals Notification & Assessment Scheme, within the TGA	ERMA	Joint agency under agreement with Department of Health and Ageing	ERMA
Evaluation, licensing and compliance monitoring of gene technology	Gene Technology Regulator ⁵⁶ ; and Prescribed agencies, including the TGA	ERMA ⁵⁷	Gene Technology Regulator; and Joint agency under agreement with the Gene Technology Regulator	ERMA ⁵⁸

⁵⁴ The National Registration Authority for Agricultural and Veterinary Chemicals (NRA) is the regulator and the TGA carries out toxicological assessments for and provides advice to the NRA.

⁵⁵ The joint agency would carry out toxicological assessments for and provide advice to the NRA

⁵⁶ The Gene Technology Regulator is a Statutory Office Holder who administers the gene technology legislation and makes decisions under the legislation. The office of the Gene Technology Regulator is established within the TGA to provide administrative support to the Regulator. Under the Gene Technology Act and its regulations, the TGA is one of a number of prescribed organisations with which the Gene Technology Regulator is required to consult.

⁵⁷ Other than medicines

⁵⁸ Other than medicines

Table 9 : Arrangements for Handling Activities Outside the Scope of the Joint Agency Legislation (continued)

Activity	Activities currently undertaken by		Activities currently undertaken by	
	Australia	New Zealand	Australia	New Zealand
Licensing of wholesalers and sellers	States and Territories	Medsafe (for licensing of medicine wholesalers and retailers)	States and Territories	Joint agency under agreement with the Ministry of Health
Regulation of professional practice	States and Territories; and Professional associations	Professional associations; and Medsafe ⁵⁹	States and Territories; and Professional associations	Professional associations; and Ministry of Health ⁶⁰
Implementation of controls and procedures required as the competent national reporting authorities under the international drug control treaties	TGA on behalf of Department of Health and Ageing ⁶¹	Medsafe and Ministry of Health	Joint agency under agreement with Department of Health and Ageing	Joint agency under agreement with Ministry of Health

⁵⁹ For matters such as prescription requirements, record-keeping, custody and storage of medicines, auditing pharmacies and monitoring of aberrant prescribing and abuse of prescription and OTC medicines.

⁶⁰ For matters such as prescription requirements, record-keeping, custody and storage of medicines, auditing pharmacies and monitoring of aberrant prescribing and abuse of prescription and OTC medicines.

⁶¹ TGA, as a division of the Department of Health and Ageing, undertakes these activities.

Table 9 : Arrangements for Handling Activities Outside the Scope of the Joint Agency Legislation (continued)

Activity	Activities currently undertaken by		Activities currently undertaken by	
	Australia	New Zealand	Australia	New Zealand
Issuing import and export permits for substances controlled under Australian customs legislation (but not subject to international control) or New Zealand Misuse of Drugs legislation	TGA on behalf of Department of Health and Ageing ⁶²	Medsafe	Joint agency under agreement with Department of Health and Ageing	Joint agency under agreement with Ministry of Health
Issuing licences to possess, cultivate, or deal in controlled substances	States and Territories	Medsafe	States and Territories	Joint agency under agreement with Ministry of Health

⁶² TGA, as a division of the Department of Health and Ageing, undertakes these activities.

APPENDIX 5: SANCTIONS AND OFFENCES

1. PROPOSED ADMINISTRATIVE SANCTIONS

1.1 Recalls

The Agency should have the powers under the Act to recall:

- products that are not approved by the Agency;
- batches of products that do not conform to standards; or
- products that are the target of actual or potential tampering.

Currently, Medsafe and the TGA also have a role in ‘voluntary’ recalls where the agency expresses concern about a product and the sponsor chooses to recall the product. This is the more common approach to recalls and was used in the Australian paracetamol recalls.

Consideration should be given to making the recall decision one that is not subject to merits review. Currently a request for a review does not stop a recall, but the review serves no purpose unless accompanied by an application to a court to stay the recall.

Another alternative to a recall by the Agency is for it to publish a public warning where a product presents a danger to the public. Both agencies have this power now. Medsafe in particular has found it to be very effective.

1.2 Cancelling a Product Licence

It is proposed to authorise the Agency to cancel a product licence:

- immediately, for reasons including:
 - imminent risk of death, serious illness or serious injury
 - the sponsor's request
 - the product contains prohibited imports
 - certifications given when the product licence was issued are incorrect
 - non-compliance with a direction from the advertising complaints body
- after giving notice and considering the sponsor's submissions for:
 - unacceptable quality, safety or efficacy
 - the product has become a separate and distinct product
 - certain other certifications given when the product licence was issued are incorrect
 - failure to comply with a product licence condition
 - failure to notify adverse reactions
 - failure to comply with an applicable standard
 - failure to comply with advertising requirements
 - failure to pay annual charges

It is also proposed to authorise the Agency to suspend a product licence.

There is currently no provision in Australia for suspending the listing or registration of goods but it is proposed that there will be. A licence could be suspended for the same grounds as cancellation. Suspension would be appropriate for less serious transgressions.

Consideration should be given to adopting a similar approach to suspension as is proposed for devices in amendments that were before the last Australian Parliament. To ensure that suspension is not viewed as the easier option when cancellation is really warranted, it is proposed to allow for a device to be suspended for up to 6 months to allow a sponsor to remedy a problem. A suspension would be renewable for only one more period. If the problem still persists after 12 months, cancellation must be then considered.

1.3 Cancelling a Manufacturing Licence

It is proposed that the agency may cancel or suspend on notice on:

- conviction for an offence
- breach of a licence condition
- failure to observe manufacturing principles (GMP)
- ceasing to manufacture the products specified in the licence
- failure to pay annual charges

2. PROPOSED CRIMINAL OFFENCES

It will be an offence:

- to import, supply or export products that do not conform to standards
- to breach a condition of exemption from complying with standards
- to import, export, manufacture or supply of products that do not hold a current product licence and are not on the Register and are not exempt from holding a product licence;
- not to comply with other regulatory requirements such as observing a condition of a product licence and reporting adverse reactions
- to carry out a step in the manufacture of non-exempt therapeutic products without a licence
- to breach a condition of a manufacturing licence
- to import, export, manufacture or supply counterfeit therapeutic products
- to label a container or package that contains therapeutic products with a number that is not the correct product licence number
- to make a false statement in a product licence application
- not to notify the Agency if the person becomes aware of certain information relating to a product (eg that the product may be harmful)
- not to comply with a request for information in a notice from the Agency that relates to an application that has been withdrawn or that has lapsed, if the information requested is certain information eg whether the product is harmful
- to make a statement in an application for a search warrant something that the person knows is false or misleading.