



MEDSAFE

NEW ZEALAND MEDICINES
AND MEDICAL DEVICES
SAFETY AUTHORITY

A BUSINESS UNIT OF
THE MINISTRY OF HEALTH

Guideline on the Regulation of Therapeutic Products in New Zealand

Part 11:

Clinical trials – regulatory approval and good clinical practice requirements

Section 1: Legislation

Section summary

This section identifies the legislation and guidelines to be read in conjunction with this part of the regulatory guidelines.

1.1 Legislation relating to clinical trials

The following legislation should be read in conjunction with this part of the guideline:

☞ [Medicines Act 1981](#)

Section 2	Interpretation - meaning of 'medical device'
Section 3	Meaning of 'medicine', 'new medicine', 'prescription medicine' and 'restricted medicine'
Section 4	Meaning of 'therapeutic purpose'
Section 17	Manufacturers, wholesalers, packers of medicines, and operators of pharmacies to be licensed
Section 18	Sale of medicines by retail
Section 20	Restrictions on sale or supply of new medicines
Section 30	Exemption for clinical trial
Section 47	Storage and delivery of medicines
Section 88	Refusal of licensing authority to grant licence
Part IV	Medical advertisements

☞ [Misuse of Drugs Act 1975](#)

Section 6	Dealing with controlled drugs (including import, supply, administration)
Schedules	Classes of Controlled Drugs

☞ [Misuse of Drugs Regulations 1977](#)

Regulation 31	Restrictions on supply on prescription
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☞ [Public Records Act 2005](#)

[Section 18](#) Disposal of public records and protected records

☞ [Privacy Act 1993](#)

☞ [New Zealand Public Health and Disability Act 2000](#)

☞ [Injury Prevention, Rehabilitation and Compensation Act 2001](#)

☞ [Hazardous Substances and New Organisms Act 1996](#)

☞ [Health and Disability Commissioner Act 1994](#)

☞ [Health Practitioners Competence Assurance Act 2003](#)

☞ [Health \(Retention of Health Information\) Regulations 1996](#)

☞ [Health Information Privacy Code 1994](#)

☞ [Injury Prevention, Rehabilitation and Compensation \(Code of ACC Claimants' Rights\) Notice 2002](#)

In addition to the legislation listed above, the following guidance documents should also be read in conjunction with this part of the guideline:

☞ [Note for Guidance on Good Clinical Practice \(CPMP/ICH/135/95\)](#)

☞ [Guideline on Strategies to Identify and Mitigate Risks for First-In-Human Clinical Trials with Investigational Medicinal Products \(EMA/CHMP/SWP/28367/07\)](#)

☞ [Researched Medicines Industry Guidelines on Clinical Trials Compensation for Injury Resulting from Participation in an Industry-sponsored Clinical Trial](#)

☞ [New Zealand Health and Disability Ethics Committee Ethical Review Process](#)

☞ [National Ethics Advisory Committee Ethical Guidelines for Intervention Studies](#)

☞ [Clinical Safety Data Management: Definitions and Standards for Expedited Reporting \(ICH Harmonised Tripartite Guideline E2A\)](#)

☞ [Health Research Council Guidelines on Ethics in Health Research](#)

Section 2: Overview of Regulation of Clinical Trials in New Zealand

Section summary

Under Section 30 of the Medicines Act 1981, approval from the Director-General of Health is required before a clinical trial using a new medicine may commence in New Zealand. The approval process for clinical trials is administered by Medsafe.

The New Zealand Health and Disability Ethics Committee administers the ethics approval system, which applies to all clinical trials conducted in New Zealand.

Approvals under other legislation may be required for clinical trials using certain types of medicines.

All clinical trials in New Zealand are expected to be conducted in accordance with internationally accepted Good Clinical Practice standards.

2.1 Requirement for approval under Section 30 of the Medicines Act 1981

[Section 30 of the Medicines Act 1981](#) requires that an approval from the Director-General of Health (given on the recommendation of the Health Research Council) is obtained before a clinical trial involving the use of a new medicine commences in New Zealand.

The application and approval process for clinical trials under Section 30 of the Act is administered by Medsafe – the medicines and medical devices regulatory authority for New Zealand. A committee of the [Health Research Council of New Zealand](#) considers applications and makes recommendations on whether trials should be approved. Approvals are issued by Medsafe under a delegation from the Director-General of Health.

The application and approval procedure administered by Medsafe is described in Section 3 of this guideline. Approval of a clinical trial by a Health and Disability Ethics Committee is a separate process that is not administered by Medsafe. Further detail is provided in Section 2.6 of this guideline.

Medsafe also administers a self-certification scheme for clinical trial sites that have patients in residence, and maintains a list of sites for which it has received evidence of compliance with Good Clinical Practice requirements. See Section 4 of this guideline for further details.

2.2 Good Clinical Practice requirements

From 1 January 2011, all clinical trials in New Zealand are expected to be conducted in accordance with the internationally accepted standards set out in the [Note for Guidance on Good Clinical Practice \(CPMP/ICH/135/95\)](#) issued by the [European Medicines Agency \(EMA\)](#).

Where there is a conflict between the CPMP guideline and specific requirements relating to clinical trials that are set out in Section 30 of the Medicines Act 1981, modified CPMP requirements apply in New Zealand. These modifications are described in Section 5 of this guideline.

2.3 What is a clinical trial?

The term 'clinical trial' is not defined in the Medicines Act. While there is no single internationally accepted definition, for the purpose of regulating clinical trials conducted in New Zealand, the definition in the *Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95)* applies. This defines a clinical trial as:

Any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of an investigational product(s), and/or to identify any adverse reactions to an investigational product(s), and/or to study absorption, distribution, metabolism, and excretion of an investigational product(s) with the object of ascertaining its safety and/or efficacy.

2.4 Determining whether a clinical trial requires approval under the Medicines Act

[Section 30 of the Medicines Act 1981](#) provides an exemption from the requirement for Ministerial consent to distribute a new medicine if the medicine is to be distributed solely for the purpose of using it in a clinical trial that has been approved by the

Director-General of Health. Hence the approval of the Director-General of Health, given under Section 30 of the Medicines Act 1981, is required before any clinical trial using a new medicine may commence in New Zealand.

A *new medicine* is a medicine for which Ministerial consent for distribution in New Zealand has not been granted or has lapsed because the medicine has been generally unavailable in New Zealand for five or more years. The terms *medicine* and *new medicine* are defined in [Section 3 of the Medicines Act 1981](#).

The following points will assist applicants in determining whether a clinical trial involves use of a new medicine and therefore requires approval under Section 30 of the Medicines Act 1981.

- ☞ The term 'new medicine' applies to medicines (as defined in the Medicines Act) for which Ministerial consent for distribution in New Zealand has not been granted. These 'unapproved medicines' include new chemical or biological entities and new dosage forms and strengths of approved medicines.
- ☞ Approval under Section 30 is not required for a clinical trial that uses only medicines for which Ministerial consent for distribution in New Zealand has been granted (i.e. approved medicines). This applies even if the trial is investigating a new indication. However, the medicine used in the trial must be the actual medicine for which consent for distribution in New Zealand has been granted.
- ☞ Placebos used in clinical trials are not considered to be new medicines.
- ☞ In some circumstances, a substance that is commonly used as an ingredient in a food, dietary supplement or cosmetic is used in a clinical trial. That substance, when administered to human beings for a therapeutic purpose as part of a clinical trial, is considered to be a *new medicine* and approval for the trial under Section 30 of the Medicines Act 1981 is required.
- ☞ Medical devices are specifically excluded from the definition of the term *medicine*. Clinical trials of medical devices do not require approval under New Zealand legislation, but Medsafe would like to be informed by email of any such trials (via devices@moh.govt.nz). It should be noted, however, that [Health and Disability Ethics Committee](#) approval should be obtained for clinical trials of medical devices.
- ☞ Clinical trials using products that are new medicines under New Zealand legislation do require approval under Section 30 even if those products are not considered medicines in other jurisdictions. For example, a clinical trial using an injectable facial filler would require approval under Section 30, even though such products are considered medical devices in other jurisdictions. Any queries regarding the categorisation of a product to be used in a clinical

trial should be directed to Medsafe and will be considered on a case-by-case basis.

- ☞ A study using a xenotransplantation procedure is not a clinical trial that is regulated under Section 30 of the Medicines Act 1981. Xenotransplantation is regulated as a *specified biotechnical procedure* requiring the approval of the Minister of Health. See [Medicines Act Part 7A](#) for details. A trial involving xenotransplantation is expected to be carried out in accordance with Good Clinical Practice standards (see Section 5 of this guideline for further details).
- ☞ If an approved medicine is repacked for use in a clinical trial, this does not make it a new medicine or cause the trial to require approval under Section 30.

The requirement for a clinical trial involving a new medicine to be approved under Section 30 of the Medicines Act 1981 applies to all types of clinical trials, including pharmacokinetic, bioequivalence and *first in human* studies.

Approval must be obtained for each study using a *new medicine*. Any subsequent amendment of a trial protocol must also be approved. If there is to be an open extension phase of a clinical trial, the protocol for the open extension phase should ideally be submitted as part of the original clinical trial application. A subsequent application may be made for approval of an open extension phase provided it can be shown that extension of the study will yield scientifically valid results. Extension trials using safety endpoints are considered to be scientifically valid.

2.5 Other legislative requirements relating to clinical trials

For a clinical trial involving a [new organism](#), compliance with the requirements of the [Hazardous Substances and New Organisms Act 1996](#) (HSNO Act) is required. Applicants should be aware that the timeline for obtaining approval under HSNO legislation is likely to be significantly longer than the timeline for obtaining approval under the Medicines Act. For further information, contact the [Environmental Risk Management Authority](#).

The following table indicates the legislative requirements for clinical trials conducted in New Zealand using different sorts of investigational products.

Type of investigational product used in	Type of approval required
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the trial	Medicines Act 1981 Section 30	HSNO Act 1996
New (unapproved) medicine containing a new chemical entity	√	x
New (unapproved) medicine containing a new organism	√	√
New (unapproved) dose form or strength of an approved medicine	√	x
New (unapproved) generic medicine not containing a new chemical entity	√	x
Approved medicine used to investigate a new indication or new dosage regime	x	x
Medical device (as defined in New Zealand legislation), containing a hazardous substance or new organism	x	√
Medical device (as defined in New Zealand legislation), not containing a hazardous substance or new organism	x	x

For a trial involving the use of a [Controlled Drug](#), it will also be necessary to comply with the requirements of the [Misuse of Drugs Act 1975](#) and associated regulations, which set out licensing requirements for importation, possession and supply of controlled drugs, as well as storage and prescribing requirements.

2.6 New Zealand Health and Disability Ethics Committee approval

Requirements relating to New Zealand Health and Disability Ethics Committee approval of clinical trials are provided on the [New Zealand Health and Disability Ethics Committee](#) website. These requirements relate to all clinical trials, regardless of whether they are trials that require approval under Section 30 of the Medicines Act.

Ethics committee approval is a separate process from approval under Section 30 of the Medicines Act and is not administered by Medsafe.

The New Zealand Health and Disability Ethics Committee's primary role is to safeguard the rights, health and wellbeing of consumers and research participants by providing independent ethical review of proposed research.

As part of the ethical review process, the ethics committee will determine whether:

- The study complies with the requirements of the Privacy Act 1993 and the Code of Health and Disability Services Consumer Rights
- Trial participants are eligible for no-fault compensation under the Injury Prevention, Rehabilitation and Compensation (code of ACC Claimants Rights) Notice 2002 or, if they are not eligible, whether adequate compensation is provided for.

The New Zealand's Health and Disability Services Commissioners Code of Rights requires that patients have access to services such as [Advocacy Services](#) when they are enrolled in a clinical study. It is desirable but not essential to appoint a patient advocate to a study. If no advocacy service is appointed the sponsor must tell patients how and where they can obtain such services if they require them.

For all trials, the application for Ethics Committee approval may be made at any time before, during or after consideration of the application for approval under Section 30.

Further information on the ethics committee system for the assessment of clinical trials in New Zealand can be found on the [New Zealand Health and Disability Ethics Committee](#) website.

Section 3: Application for Approval of a Clinical Trial under Section 30 of the Medicines Act

Section summary

This section describes the application and approval procedure administered by Medsafe for the approval of clinical trials under Section 30 of the Medicines Act 1981.

3.1 Role of Medsafe in the clinical trial approval procedure

Medsafe administers the application and approval process for clinical trials under a delegation from the Director-General of Health. Medsafe receives and processes applications, liaises with the relevant Health Research Council committee (see Section 3.2) and the applicant, and issues approval letters. All communication regarding an application for approval of a clinical trial must be addressed to the Clinical Trial Co-ordinator at Medsafe.

3.2 Role of the Health Research Council in the clinical trial approval procedure

[Section 30 of the Medicines Act](#) authorises the Director-General of Health to approve a clinical trial on the recommendation of the [Health Research Council of New Zealand](#) (HRC).

The HRC maintains two standing committees to consider clinical trial applications and make recommendations to the Director-General. The Standing Committee on Therapeutic Trials ([SCOTT](#)) considers applications for pharmaceutical-type medicines, and the Gene Technology Advisory Committee ([GTAC](#)) considers applications for trials involving gene and other biotechnology therapies.

The Terms of Reference for these committees are published on the Health Research Council website. The sponsor of a clinical trial should read these documents before

submitting an application as they provide guidance on the committee processes and the data requirements for applications to be considered by each committee.

3.3 Submitting an application for approval of a clinical trial under Section 30 of the Medicines Act

An application for approval of a clinical trial under [Section 30 of the Medicines Act](#) is made by the person responsible for the trial in New Zealand. This person is referred to in the Medicines Act as ‘the applicant’.

The applicant must be the person in New Zealand who takes legal responsibility for the conduct of the trial in New Zealand. For more information on the responsibilities of the applicant, see Section 4.3.

At present, an application may be made by completing an online application or a paper-based application. In the future Medsafe will be moving to a fully electronic system and will only be accepting applications made using the online system.

Medsafe operates an abbreviated approval process for eligible clinical trial applications. For more information about this process, see Section 3.6.

3.3.2 Making an online application

An online application is made using the Online Forms available at <https://www.ethicsform.org/nz/SignIn.aspx>

The applicant must complete the form, attach the supporting documentation and covering letter, and submit the application electronically. No paper copies should be sent to Medsafe.

3.3.1 Making a paper-based application

To make a paper-based application, the applicant must complete and sign an **Application for approval of a clinical trial under Section 30 of the Medicines Act 1981** form (see [Form 11.1 in Schedule A](#) of the *Guideline on the Regulation of Therapeutic Products in New Zealand*).

When making an application for approval of a clinical trial using a gene or other biotechnology medicine, only Part A of the application form needs to be completed. When making an application for approval of a clinical trial using any other medicine (including applications made under the abbreviated approval process), Parts A, B and C of the application need to be completed.

The completed application form, covering letter and one copy of the supporting documentation should be submitted to Medsafe at the following address:

Postal address:	Courier Address:
Manager Medsafe PO Box 5013 WELLINGTON 6145 Attention: Clinical Trials Co-ordinator	Manager Medsafe 20 Aitken Street WELLINGTON 6011 Attention: Clinical Trial Co-ordinator

To avoid delaying consideration of applications by the relevant Health Research Council committee, applicants are asked to send further copies of the application form and supporting documentation directly to the relevant committee as set out below.

If the application is to be considered by the SCOTT committee of the Health Research Council, the applicant should send 4 copies of the completed application form and supporting documentation to SCOTT at the following address:

Postal Address:	Courier Address:
SCOTT Secretary c/- The Pegasus Centre P O Box 2856 CHRISTCHURCH 8140	SCOTT Secretary C/- The Pegasus Centre 31 Tuam Street CHRISTCHURCH 8011

Note: If the application is eligible for the abbreviated clinical trial approval process (see section 3.6) please **do not** send any copies of the application to SCOTT.

If the application is to be considered by the GTAC committee of the Health Research Council, the applicant should send 10 copies of the application form and supporting documentation to GTAC at the following address:

Postal Address:	Courier Address:
GTAC Secretary PO Box 5541 Wellesley St AUCKLAND 1141	GTAC Secretary Level 3 110 Stanley Street AUCKLAND 1010

3.4 Administrative processing of clinical trial applications

Medsafe will undertake administrative processing of the application (including sending it to the relevant Health Research Council committee) and send an acknowledgement letter and invoice to the applicant within 7 days of receiving an application.

The fee for an application for approval of a clinical trial under [Section 30 of the Medicines Act 1981](#) is set out in [regulation 61 of the Medicines Regulations 1984](#). The Director-General of Health may, under regulation 61A, grant a waiver of the fee in certain circumstances (e.g. for a clinical trial conducted for the public good or specific types of bioequivalence studies utilising new generic medicines). See the [Medsafe Fee Schedule](#) for current fee details. A request for a fee waiver should be included with the application.

Payment of the invoice should be made within 7 days and is required to validate the application. A clinical trial approval will not be issued until payment has been received. Applicants must ensure that all subsequent communication regarding the application is sent through Medsafe.

3.5 Consideration of applications for approval of clinical trials under Section 30 of the Medicines Act

Applications are considered by the relevant committee of the Health Research Council (SCOTT or GTAC). Following its consideration of an application, the committee conveys its recommendation to Medsafe. The committee may:

- ☞ Recommend that the clinical trial is approved
- ☞ Recommend that the clinical trial is approved subject to certain conditions
- ☞ Request more information in relation to the application
- ☞ Recommend that the clinical trial is not approved

Within 45 calendar days of receiving the application, Medsafe will notify the applicant of the outcome of the Director-General's consideration, and will then liaise with the applicant regarding any proposed conditions of approval (such as amendment to the trial protocol) or requests for further information. All correspondence relating to the application must be addressed to Medsafe.

If, following resolution of any issues relating to the application, the decision is to approve the trial, Medsafe will issue an approval letter. If there is a decision to decline an application, the reasons for this decision will be provided to the applicant. The applicant then has 28 days in which to lodge an appeal with the Medicines Review Committee. The appeal provisions are set out in [Section 88 of the Medicines Act 1981](#).

3.6 Abbreviated clinical trial approval process

Medsafe operates an abbreviated approval process for eligible clinical trial applications.

To be eligible for the abbreviated approval process the application must be for a clinical trial that meets the following criteria:

- ☞ The clinical trial is a bioequivalence study that utilises an investigational product that contains the same active pharmaceutical ingredient included in a medicine that is approved for distribution in New Zealand; and
- ☞ The proposed route of administration for the investigational product is the same as that for the approved medicine; and
- ☞ The proposed dosage for the investigational product is within the recommended dosage range for the approved medicine.

Please note that this abbreviated approval process does not apply to bio-similar products.

To make an application under the abbreviated approval process, the applicant must complete the application process described in section 3.4.

A reduced fee will be applied to eligible applications. See the [Medsafe Fee Schedule](#) for current fee details.

Approvals for eligible clinical trials will be issued by Medsafe within five working days.

Section 4: Certification of Clinical Trial Sites

Section summary

Medsafe administers a *Clinical Trial Site Self-Certification* scheme covering sites which have study participants in residence while the clinical trial medicines are administered. The self-certification is site-specific and provides a description of the site's facilities and procedures for dealing with any emergencies and a list of key personnel. It is completed by the person responsible for the site and should be updated whenever there is a change to key personnel or critical procedures at the site.

4.1 Sites requiring certification under the scheme

[Section 30 of the Medicines Act 1981](#) sets out the information that must be provided in an application for approval of a clinical trial. Section 30(3)(g) specifies that the application must include information about the site(s) at which the trial is to be conducted and the facilities available at those sites. This information is to be taken into consideration in deciding whether to grant approval for the trial.

If a site has study participants in residence while clinical trial medicines are administered, information about the facilities and procedures in place to deal with emergencies is required to be provided. In order to facilitate the collection and processing of this information for both the regulator and for applicants, Medsafe administers a *Clinical Trial Site Self-Certification* scheme.

The scheme does not cover sites where participants attend clinics as outpatients and no trial medicine is administered on site. For such sites, the name and location of each site and the name(s) of the investigator(s) will be provided by the applicant when applying for approval of the trial.

4.2 Operation of the site certification scheme

Under this scheme, the person responsible for clinical trials at the site (i.e. the lead investigator at that site) completes a **Clinical trial site self-certification** form (see [Form 11.2 in Schedule A](#) of the *Guideline on the Regulation of Therapeutic Products in New*

Zealand), providing a description of the site's facilities and procedures and a list of key personnel. The certification can be made at any time and does not need to coincide with submission of an application for approval of a particular clinical trial.

On receipt of a completed **Clinical trial site self-certification** form, Medsafe will process the certification and place the name and address of the site and the name of the lead investigator on a list of *Certified Clinical Trial Sites* published on the Medsafe website (www.medsafe.govt.nz).

Site certification must be completed for each location (e.g. private premises, or a unit within an institution such as a hospital) at which clinical trial medicines are administered to trial participants. There may be more than one clinical trial site within an institution.

Re-certification of a clinical trial site is required whenever there is any change to key personnel or critical procedures at the site.

4.3 Applicant responsibilities relating to certification of clinical trial sites

When submitting an application for approval of a clinical trial, the applicant is required to specify, for each proposed site at which trial medicines will be administered, whether certification has been completed and whether the information provided in the certification is still current. It is the responsibility of the applicant to liaise with the lead investigator at each site regarding site certification status.

If certification for a site is current, no further action is required. If there is no certification for a site, or if the existing certification is out of date, it is the responsibility of the applicant to obtain a completed **Clinical trial site self-certification** form from the lead investigator at the site and submit it to Medsafe with the application for approval of the clinical trial. Medsafe will process the site certification in the normal way. An approval will not be granted for a clinical trial until certification has been completed for all sites for which it is required.

Section 5: Good Clinical Practice Requirements

Section summary

This section establishes the requirement for clinical trials to be conducted in accordance with the CPMP Note for Guidance on Good Clinical Practice and explains the modifications to the CPMP guideline that are needed to achieve alignment with New Zealand regulatory requirements.

From 1 January 2011 all clinical trials conducted in New Zealand are expected to be conducted in accordance with the *Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95)*. This applies whether or not approval under the Medicines Act is required for the trial.

In some cases, requirements set out in CPMP/ICH/135/95 do not cover, or are in conflict with, particular provisions in the Medicines Act 1981 or in other relevant New Zealand legislation (e.g. legislation relating to reporting requirements or the retention of records). For this reason, some of the requirements specified in CPMP/ICH/135/95 must be modified in order to achieve compliance with New Zealand law.

Modifications are required in respect of:

- ☞ the definitions and obligations of particular persons (see Section 5.1);
- ☞ the manufacture, labelling and dispensing of investigational products (see Section 5.2);
- ☞ the retention of records (see Section 5.3);
- ☞ adverse event reporting (see Section 5.4); and
- ☞ clinical trial reporting requirements (see Section 5.5).

5.1 Responsibilities of the applicant, sponsor, investigator and monitor

Sections 1, 4 and 5 of the CPMP guideline set out the obligations of the applicant, sponsor, investigator and monitor in clinical trials. In contrast, the Medicines Act uses the terms applicant and investigator, but does not refer to a sponsor or monitor. The responsibilities of those involved in conducting clinical trials in New Zealand are outlined below.

5.1.1 Applicant and New Zealand sponsor

The CPMP guideline defines *sponsor* as an individual, company, institution or organisation which takes responsibility for the initiation, management and/or financing of a clinical trial.

The Medicines Act does not use the term *sponsor* but refers to an *applicant*. The applicant is the person who imports or manufacturers or commissions the manufacture of a new medicine for use in a clinical trial. The responsibilities of the *applicant* under New Zealand legislation are defined in [Section 30 of the Medicines Act 1981](#) and parallel those of the *sponsor* in the CPMP guidelines (with the exception of reference to financing the trial).

In New Zealand, the term *applicant* is used when referring to the person who makes the application for approval of the trial.

Once the trial is approved, the applicant becomes the *New Zealand sponsor*, assuming responsibility (including legal liability) for the trial in New Zealand. The *New Zealand sponsor*, who must be a person in New Zealand, is responsible for:

- the preservation of records
- reporting adverse events (see below)
- notifying any changes in protocol to the Director-General of Health (through Medsafe)
- informing the Director-General of Health of the identifying name or mark by which the trial medicine may be recognised before the trial medicine is distributed if it is not a medicine for which consent for distribution in New Zealand has been granted (see Medicines Act 1981 Section 30(7)(a)).

While the supporting documentation required to be submitted with an application may be prepared by the overseas sponsor of the trial, it is the person responsible for the trial in

New Zealand who must make the application to the Director-General for approval of the trial.

Similarly, it is the New Zealand sponsor who is responsible for ensuring that the trial is conducted in accordance with both New Zealand law and Good Research Practice standards.

In the case of a multi-centre trial that is being conducted and administered by a research body outside New Zealand, it is common for the principal investigator in New Zealand to undertake the role of applicant (and subsequently New Zealand sponsor).

5.1.2 Investigators

The *principal investigator* is the person with overall responsibility for the conduct of the clinical trial in New Zealand. There is only one principal investigator for a trial, regardless of the number of trial sites involved.

The principal investigator must be resident in New Zealand, have competence and experience in a relevant field of study, and hold appropriate qualifications that are recognised within New Zealand. Where the principal investigator is not medically qualified, the trial protocol must identify the clinician responsible for medical supervision of the trial and oversight of the medical care of the participants in the trial.

A *lead investigator* is the person responsible for the conduct of a trial at a particular trial site. For a multi-centre trial, there will be a lead investigator for each trial site. Where a trial is conducted by a team of investigators at a particular site, the lead investigator is the responsible leader of the team. The principal investigator for the trial may also be the lead investigator at a particular trial site.

An *investigator* is an individual who is designated to conduct clinical trial procedures at a particular trial site. All investigators must have New Zealand-recognised qualifications and experience appropriate to their particular role in the conduct of the trial.

5.1.3 Monitor

The *monitor* (or clinical research associate) is an individual appointed by the sponsor and responsible for carrying out monitoring activities in accordance with the sponsor's requirements to ensure that the trial is conducted and documented properly. The monitor should be independent of the clinical trial site, be qualified by scientific and/or clinical knowledge and have appropriate training and experience.

5.2 Investigational products

The CPMP GCP guideline discusses investigational products in points 4.6, 5.12, 5.13 and 5.14. It requires investigational products, including active comparators and placebos, to be manufactured in accordance with applicable GMP.

In New Zealand, investigational products are required to be manufactured in accordance with the New Zealand Code of Good Manufacturing Practice for Manufacture and Distribution of Therapeutic Goods found at:

<http://www.medsafe.govt.nz/regulatory/Guideline/NZRGMPart1.asp>

Annex 13 of the Code provides additional guidelines for investigational medicinal products. The Medicines Act also places a number of conditions on the distribution of a medicine under Section 30 of the Act.

Section 30(7)(b) requires that every label on every package of a medicine used in a clinical trial must have the words *“To be used by qualified investigators only”*. It is Medsafe’s practice to accept these words or words of similar meaning.

Section 30(7)(c) requires that every person to whom the trial medicine is distributed must be approved to conduct the trial (i.e. be an approved investigator), and the medicine must be used solely by that person or under his/her direction for the purposes of the trial.

Supplying clinical trial medicines to trial participants is not considered to be *prescribing* or *dispensing* and the requirements set out in Part 7 of the Medicines Regulations 1984 do not apply. However, where clinical trial medicines are required to be repacked ready for supply to trial participants, this must be undertaken by a person who is the holder of a packing licence or is otherwise authorised to pack medicines (see [Section 17 of the Medicines Act 1981](#)).

Clinical trial medicines may be supplied to trial participants by an investigator, pharmacist, nurse or other suitably qualified member of the clinical trial team. The arrangements for supply to patients should be specified in the clinical trial protocol at the time the application for approval of the trial is made. The investigator may subsequently submit a protocol amendment delegating responsibility for supply to another suitably qualified person.

The quantity of trial medicine to be supplied to trial participants at one time should be specified in the trial protocol. Where a clinical trial uses a product containing a substance listed in a [schedule to the Misuse of Drugs Act 1975](#), the supply restrictions relevant to that class of controlled drug will apply. The restrictions are set out in the following table:

Controlled Drug class	Period of supply
Class A	1 month
Class B	1 month
Class C	3 months

The investigational product(s) should be stored as specified by the sponsor (see 5.13.2 and 5.14.3 of the CPMP/ICH/135/95 guideline) and in accordance with [Section 47 of the Medicines Act 1981](#) (Storage and delivery of medicines), and [Part 5 \(regulations 26-37\) of the Medicines Regulations 1984](#).

5.3 Preservation of records

The preservation of records is detailed in sections 4.9.4, 4.9.5 and 5.15 of the CPMP GCP guideline. In New Zealand the following points must also be taken into consideration:

- ☞ The New Zealand applicant/sponsor is responsible for ensuring that a complete set of study records and data relating to New Zealand trial participants is retained.
- ☞ The trial records may be held by the principal investigator or transferred to another responsible person. The applicant/sponsor must hold information on the location of the records, the name of the person responsible for their retention, and the means by which prompt access can be assured.
- ☞ For international multi-centre trials the records for New Zealand patients may be stored overseas providing they are maintained in an accessible form until they are disposed of in accordance with New Zealand law.
- ☞ The timeframes for retention of records will depend on the nature and duration of the trial. The New Zealand applicant/sponsor must ensure compliance with New Zealand privacy legislation and the Health (Retention of Health Information) Regulations 1996. In no case should the period of retention be less than 10 years from the date the study ends.
- ☞ If records relating to a clinical trial are part of a patient's hospital record, adequate steps must be taken to ensure that the patient's hospital records are retained for 10 years after the end date of the study, since the normal time to destruction interval in hospitals and institutions may be less than this.

- ☞ Records of trials conducted at District Health Board sites must be retained until approval of the Chief Archivist is sought for their disposal ([Section 18 of the Public Records Act 2005](#)). Further information on the disposal process can be found on the Archives New Zealand website: <http://www.archives.govt.nz/advice/appraisal-and-disposal-information>. Records of trials not conducted at District Health Board sites must be retained for at least 10 years.
- ☞ Records, which may be in hard-copy or electronic form, must remain readily accessible for the duration of the required retention period. Advice on standards for electronic records is available at: <http://continuum.archives.govt.nz/files/file/standards/s5/index.html>

5.4 Reporting adverse events

The reporting requirements for adverse events are detailed in section 4.11 and 5.17 of the CPMP GCP Guideline. The reporting requirements in New Zealand differ from those set out in the CPMP GCP Guideline in that only expedited reports of serious adverse events occurring in New Zealand trial participants must be sent to Medsafe.

In line with the CPMP guideline, the investigator should report adverse events (as detailed in the protocol) to the New Zealand sponsor.

5.4.1 Notifying overseas actions relating to an investigational product

Medsafe must be informed within 7 calendar days of any of the following actions occurring in relation to an investigational product being used in a clinical trial in New Zealand:

- ☞ withdrawal from continued development
- ☞ withdrawal from the market in another jurisdiction, for any reason
- ☞ termination of an overseas study using the investigational product due to serious or unexpected adverse events. The reasons for halting the study and the arrangements for halting the New Zealand arm of the study are required to be included in the report.

5.4.2 Expedited reporting of suspected unexpected serious adverse reactions (SUSARs) occurring in New Zealand trial participants

The New Zealand sponsor is required to report all fatal or life-threatening suspected unexpected serious adverse reactions (SUSARs, as defined in [ICH GCP/ICH E2A](#)) occurring in New Zealand trial participants where the treatment is known.

Reports must be sent to Medsafe (see Section 5.6 for addresses) or using the online system at <https://nz.ethicsdatabase.org> within 7 days of the sponsor receiving an investigator's report of a SUSAR.

Adverse reactions occurring in a clinical trial participants are considered to be unexpected if they are not outlined in the protocol and investigator's brochure, and are not defined study end-points (e.g. death or hospitalisation).

5.4.3 Reporting other adverse events

The New Zealand sponsor is required to hold reports of all (worldwide) SUSARs. These reports should not be routinely sent to Medsafe, but must be held in an accessible form and made available to Medsafe on request.

The reporting requirements of the Health and Disability Ethics Committees are outlined in their [guidelines](#).

All adverse reactions to approved medicines used in clinical trials should be reported to the [Centre for Adverse Reactions Monitoring](#) (CARM).

5.5 Study reporting requirements

The New Zealand sponsor is required, under [Section 30\(7\)\(d\)\(ii\) of the Medicines Act 1981](#), to submit routine progress reports to Medsafe at 6 monthly intervals throughout the duration of the trial.

To submit a routine progress report the New Zealand sponsor must submit a signed copy of the completed **Clinical trial six monthly report** form to Medsafe (see [Form 11.3 in Schedule A](#) of the *Guideline on the Regulation of Therapeutic Products in New Zealand*) or using the online system at <https://nz.ethicsdatabase.org>.

The first report should be sent to Medsafe not more than 6 months after the date of approval of the trial, whether or not recruitment of New Zealand trial participants has commenced.

Section 30(7)(d)(iii) requires that, on termination of the trial, a final report should be sent to Medsafe (see Section 5.6 for addresses). The report should include a copy of the results of the trial and all the adverse events recorded during the trial, together with an evaluation and discussion.

The reporting requirements of the Health and Disability Ethics Committees are outlined in their [guidelines](#).

5.6 Addresses for sending adverse reaction reports and study reports to Medsafe

Postal address:	Courier Address:
Manager Clinical Risk Medsafe PO Box 5013 Wellington 6145 Attention: Clinical Trial Co-ordinator	Manager Clinical Risk Medsafe 20 Aitken Street WELLINGTON 6011 Attention: Clinical Trial Co-ordinator
Fax Number: 64 4 819 6806	E-mail: info@medsafe.govt.nz