MEDSAFE
New Zealand Medicines and Medical Devices Safety Authority

Guideline on the Regulation of Therapeutic Products in New Zealand

Clinical trials – regulatory approval and good clinical practice requirements

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Contents

Definitions

Adverse reaction/Adverse drug reaction (ADR)	In the pre-approval clinical experience with a new medicine or its new usages, particularly as the therapeutic dose(s) may not be established: All noxious and unintended responses to a medicinal (investigational) product related to any dose should be considered adverse drug reactions. This refers to situations where a causal relationship between a medicinal (investigational) product and an adverse event is at least a reasonable possibility, ie, the relationship cannot be ruled out.
Adverse event (AE)	Any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. An adverse event (AE) can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not it is related to the medicinal (investigational) product.
Applicant	The entity who imports or manufactures or commissions the manufacture of a medicine for use in a clinical trial and applies for approval of a clinical trial under section 30 of the Medicines Act. See also **sponsor**.
Approved medicine	A medicine which has been granted consent under section 20 or section 23 (provisional consent) of the Medicines Act to be sold, supplied, distributed or advertised in New Zealand (sometimes referred to as having **marketing authorisation** or **consent to distribute**).
Approved conditions (of an approved medicine)	Approved conditions of a medicine are the particulars generally outlined in the sponsor's data sheet and displayed in the Medsafe product application search. These include but are not limited to indications, contraindications, dose, strength, administration and manufacturing.
Bioequivalence trial	A trial with the primary objective of showing that the response to two or more treatments differs by an amount which is clinically unimportant. This is usually demonstrated by showing that the true treatment difference is likely to lie between a lower and an upper equivalence margin of clinically acceptable differences.
Biosimilar medicine (biosimilar)	A new biological medicine that is similar to another biological medicine already approved in New Zealand. The active substance of a biosimilar is similar, but not identical, to that of the biological reference.
Blinding/Masking	A procedure in which one or more parties to the trial are kept unaware of the treatment assignment(s). Single-blinding usually refers to the subject(s) being unaware, and double-blinding usually refers to the subject(s), investigator(s), monitor, and, in some cases, data analyst(s) being unaware of the treatment assignment(s).
Certificate of analysis	A certificate issued by the manufacturer of a medicine that provides a summary of testing results on samples of products or materials together with the evaluation for compliance to a stated specification.

Clinical drug development	Clinical drug development, defined as studying a drug in humans, is conducted in a sequence that builds on knowledge accumulated from non-clinical and previous clinical studies. Although clinical drug development is often described as consisting of four temporal phases (phases 1–4), it is important to appreciate that the phase concept is a description and not a requirement, and that the phases of drug development may overlap or be combined.
Clinical Trial Site	The location(s) where trial-related activities are actually conducted (eg, clinical trial units, hospitals).
Clinical Trial/Study Report	A written description of a trial/study of any therapeutic, prophylactic, or diagnostic agent conducted in human subjects, in which the clinical and statistical description, presentations, and analyses are fully integrated into a single report.
Consumer	Consumer is defined as a person who is not a healthcare professional such as a patient, lawyer, friend, or relative of a patient.
Contract	A written, dated, and signed agreement between two or more involved parties that sets out any arrangements on delegation and distribution of tasks and obligations and, if appropriate, on financial matters. The protocol may serve as the basis of a contract.
Contract Research Organisation (CRO)	A person or an organisation (commercial, academic, or other) contracted by the sponsor to perform one or more of a sponsor's trial-related duties and functions.
Coordinating Investigator	An investigator assigned the responsibility for the coordination of investigators at different centres participating in a multicentre trial.
Critical incident	A life-threatening or disabling event arising from the study medicine.
First in Human (FIH) Trial	A FIH trial evaluates an investigational product in humans for the first time, to study the human pharmacology, tolerability and safety of the investigational product and to compare how effects seen in non-clinical studies translate into humans.
Good Clinical Practice (GCP)	A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects are protected.
Good Manufacturing Practice (GMP)	The standards manufacturers of medicines are required to meet to ensure their products are consistently safe, effective and of acceptable quality.
Gene Technology Advisory Committee (GTAC)	A Committee of the HRC that undertakes scientific assessment of clinical trials that involve the introduction of nucleic acids, genetically manipulated micro-organisms, or viruses or cells into human subjects. It also makes recommendations to the Director-General of Health on whether or not trials should be approved.
Individual Case Safety Report (ICSR)	The complete information provided by a reporter at a certain point in time to describe an event or incident of interest. The report can include information about a case involving one subject or a group of subjects.
Institution (medical)	Any public or private entity or agency or medical or dental facility where clinical trials are conducted.

Interim Clinical Trial/Study Report	A report of intermediate results and their evaluation based on analyses performed during the course of a trial.
Investigational medicine/ Investigational (medicinal) product (IMP)	A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial, including an approved medicine when used or assembled (formulated or packaged) in a way different from the approved form, when otherwise used outside of its approved conditions (eg, an unapproved indication), or when used to gain further information about an approved use.
Investigator	A person responsible for the conduct of the clinical trial at a trial site. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the **principal investigator**.
Investigator's Brochure	A compilation of the clinical and non-clinical data on the investigational product(s) which is relevant to the study of the investigational product(s) in human subjects
Clinical trial monitor (or clinical research associate)	The clinical trial monitor (or clinical research associate) oversees the progress of a clinical trial, and of ensures that it is conducted, recorded, and reported in accordance with the protocol, Standard Operating Procedures (SOPs), Good Clinical Practice (GCP), and the applicable regulatory requirements.
Multicentre trial	A clinical trial conducted according to a single protocol but at more than one site, and therefore, carried out by more than one investigator.
New medicine	A medicine for which: • consent for distribution in New Zealand (marketing authorisation) has not previously been granted (unapproved medicines); • approval has been previously granted but the medicine has undergone substantial change(s) which requires referral under section 24(5) of the Act; • approval has been previously granted but has since lapsed (approval lapsed).
Non-clinical study	Biomedical studies not performed on human subjects.
Participant/trial participant	An individual who participates in a clinical trial, either as a recipient of the investigational product(s) or as a control. A participant may also be referred to as a **subject**.
Patient perspective	Patient perspective information describes the attitudes and preferences of patients with respect to the therapeutic context, benefits, and risks. Such information may be obtained directly from patients or indirectly from other stakeholders (eg, parents and caregivers) using qualitative, quantitative, or descriptive methods.
Product Specification File	A reference file containing, or referring to files containing, all the information necessary to draft the detailed written instructions on processing, packaging, quality control testing, batch release and shipping of an investigational medicinal product.
Standing Committee on Therapeutic Trials (SCOTT)	A Committee of the HRC that undertakes scientific assessment of clinical trials and makes recommendations to the Director-General of Health on whether or not trials should be approved.

Serious adverse event (SAE)/Serious adverse drug reaction (sADR)	In accordance with the ICH E2A guideline, a serious adverse event or reaction is any untoward medical occurrence that at any dose: • results in death • is life-threatening (see NOTE below) • requires inpatient hospitalisation or results in prolongation of existing hospitalisation • results in persistent or significant disability/incapacity • is a congenital anomaly/birth defect, • is a medically important event or reaction. (NOTE: The term "life-threatening" in the definition of "serious" refers to an event/reaction in which the patient was at risk of death at the time of the event/reaction; it does not refer to an event/reaction which hypothetically might have caused death if it were more severe.)
Signal	A report or reports of an event with an unknown causal relationship to treatment that is recognised as worthy of further exploration and continued surveillance.
Significant Safety Issue (SSI)	A safety issue that could adversely affect the safety of participants or materially impact on the continued ethical acceptability or conduct of the trial.
Sponsor	An individual, company, institution, or organisation which takes responsibility for the initiation, management, and/or financing of a clinical trial.
Sub-investigator	Any individual member of the clinical trial team designated and supervised by the investigator at a trial site to perform critical trial-related procedures and/or to make important trial-related decisions (eg, associates, residents, research fellows).
Suspected Unexpected Serious Adverse Reaction (SUSAR)	A serious adverse reaction, the nature or severity of which is unexpected in that it is not consistent with the applicable product information (e.g., Investigator's Brochure for an investigational medicinal product).
Urgent Safety Measure (USM)	A measure required to be taken in order to eliminate an immediate hazard to a participant's health or safety.

1 Legislation

Section summary

This section identifies the legislation and other guidelines to be read in conjunction with this guideline (Clinical trials – regulatory approval and good clinical practice requirements).

1.1 Legislation relating to clinical trials

Table 1 provides the legislation that should be read in conjunction with this part of the guideline.

Table 1: Legislation relating to clinical trials

Legislation	Relevant section(s)
Medicines Act 1981 "Medicines Act"; "the Act"	Section 3A 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 4 Medical advertisements
Medicines Regulations 1984 "Medicines Regulations"; "the Regulations"	Regulation 39 Conditions under which authorised prescribers and veterinarians may prescribe medicines Part 5 Manufacture, packing, storage and handling
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
Misuse of Drugs (Medicinal Cannabis) Regulations 2019	Regulation 25 Research activity
Public Records Act 2005	Section 18 Disposal of public records and protected records
Privacy Act 2020	
New Zealand Public Health and Disability Act 2000	
Accident 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 2020	
Injury Prevention, Rehabilitation and Compensation (Code of ACC Claimants' Rights) Notice 2002	
Radiation Safety Act 2016	

1.2 Additional guidance material relating to clinical trials

In addition to the legislation listed in Table 1 above, the guidance documents in Table 2 may also be helpful.

Table 2: Additional guidance materials relating to clinical trials

Author/Organisation	Guidance documents
Council for International Organizations of Medical Sciences (CIOMS)	• Patient involvement in the development, regulation and safe use of medicines (2022) • International guidelines on good governance practice for research institutions (2023)
Ethics Review Manager (Ethics RM)	• Ethics RM User Manual • Ethics RM account login page
European Medicines Agency (EMA)	• ICH E6 (R2) Good clinical practice – Scientific guideline (EMA/CHMP/ICH/135/1995) • Strategies to identify and mitigate risks for first in-human and early clinical trials with investigational medicinal products – Scientific guideline (EMEA/CHMP/SWP/28367/07 Rev. 1) • Requirements to the chemical and pharmaceutical quality documentation concerning investigational medicinal products in clinical trials – Scientific guideline (EMA/CHMP/QWP/545525/2017 Rev. 2) • ICH E2A Clinical safety data management: definitions and standards for expedited reporting – Scientific guideline (CPMP/ICH/377/95) • ICH E2F Development safety update report – Scientific guideline (EMA/CHMP/ICH/309348/2008)
Health and Disability Ethics Committees (HDECs)	• Standard Operating Procedures for HDECs • Guidance on protocol deviation submissions
Health Research Council of New Zealand (HRC)	• Guidelines for Researchers on Health Research involving Māori • Pacific Health Research Guidelines • HRC Research Ethics Guidelines
International Atomic Energy Agency (IAEA)	• Good Practice Guideline
International Conference on Harmonisation (ICH)	• Integrated Addendum to ICH E6(R1): Guideline for good clinical practice E6(R2) • Clinical Safety Data Management: Definitions and Standards for Expedited Reporting E2A
Medicines and Healthcare products Regulatory Agency (MHRA)/Health Canada	• Guideline on how to increase transparency when presenting safety information in the Development Safety Update Report (DSUR): region-specific requirements for Canada and the United Kingdom
Medicines New Zealand	• Medicines New Zealand Guidelines on Clinical Trials Compensation for Injury Resulting from Participation in an Industry-Sponsored Clinical Trial

Ministry of Health	• National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition) • Code of Practice for Nuclear Medicine
National Ethics Advisory Committee (NEAC)	• National Ethical Standards for Health and Disability Research and Quality Improvement

2 Overview of Regulation of Clinical Trials in New Zealand

Section summary

Under section 30 of the Medicines Act, approval from the Director-General of Health is required for clinical trials using medicines that do not otherwise have approval to be distributed in New Zealand.

Medsafe administers the approval process for clinical trials.

The Health and Disability Ethics Committees administer 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 of a clinical trial under Section 30 of the Medicines Act 1981

Section 30 of the Medicines Act allows the Director-General of Health to approve clinical trials involving medicines that do not otherwise have approval to be distributed in New Zealand. The Director-General's approval allows for the medicine to be supplied for the sole purpose of being used in a clinical trial. This approval is required for all types of clinical trials of medicines, including pharmacokinetic, bioequivalence and first-in-human studies. A clinical trial must not commence before the Director-General of Health has given approval for the trial.

The application and approval process for clinical trials is administered by Medsafe, the New Zealand Medicines and Medical Devices Safety Authority. See section 3 of this guideline for the full application and approval procedure, with a summary in Table 3 below.

Table 3: Summary of the application and approval process for clinical trials

1. An application is made online via Ethics RM.
2. A committee of the Health Research Council (HRC) considers the application.
3. The HRC makes a recommendation to the Director-General on the clinical trial application.
4. The applicant is issued with an: approval, provisional approval, request for further information or a decline letter by Medsafe based on the HRC recommendation. Medsafe acts under authority delegated from the Director-General of Health.

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

Ethics approval of a clinical trial by a Health and Disability Ethics Committee is also required. It is a separate process that is not administered by Medsafe. See section 2.6 of this guideline for more information.

2.2 Good Clinical Practice requirements

All clinical trials are expected to be conducted in accordance with the internationally accepted standards, Integrated Addendum to ICH E6(R1): Guideline for good clinical practice E6(R2) (ICH E6(R2)). Medsafe recommends that trials are conducted in accordance with the interpretation set out in the CHMP guidance document, ICH E6 (R2) Good clinical practice – Scientific guideline (EMA/CHMP/ICH/135/1995) published by the European Medicines Agency (EMA) (the CHMP GCP guideline).

Where there is a conflict between the CHMP GCP guideline and specific requirements relating to clinical trials that are set out in section 30 of the Medicines Act, the Act takes precedence and modified CHMP requirements (in particular, the reporting requirements) apply in New Zealand. These modifications are described in section 5 and section 6 of this guideline.

2.3 What is a clinical trial?

The term 'clinical trial' is not defined in the Medicines Act. For the purposes of this guideline, the CHMP GCP guideline definition is used:

> 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.

In addition to the above definition, the following criteria also apply:

- the assignment of each participant to a particular therapeutic strategy is decided in advance and does not fall within normal clinical practice
- the decision to administer or use the product is taken together with the decision to include the participant in the trial
- diagnostic or monitoring procedures additional to those used in normal clinical practice are applied to the participant.

In this guideline, the terms 'clinical trial' and 'clinical study' are used interchangeably, as are the terms 'investigational medicine' and 'investigational (medicinal) product' (IMP).

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

The following points will help applicants determine whether a clinical trial requires approval under section 30 of the Medicines Act. Table 4 describes situations where approval is not required, and Table 5 where approval is required.

Table 4 Clinical trials that do not require approval under section 30 of the Medicines Act[a]

A clinical trial involving only **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 formulation for which consent for distribution in New Zealand has been granted.
Placebos are not considered medicines. Therefore, a clinical trial involving only approved medicines and placebos does not require approval.
A **"laboratory observational" or other observational type extension** to a clinical trial, where no medicines are given to the participants, does not require approval.
Medical devices are specifically excluded from the definition of the term *medicine*. There is no provision under the current legislation (the Medicines Act) to require approval of clinical trials involving medical devices. Applicants can ask Medsafe to determine the categorisation of the product if they are unsure whether the product is a medical device or a medicine. For more information on clinical trials involving medical devices see section 7 of this guideline.
Radiopharmaceuticals are not medicines under section 30 of the Medicines Act. Refer to the Radiation Safety Act 2016 and the Ministry of Health's Code of Practice for Nuclear Medicine. General guidance is also available. This includes recommendations in the International Atomic Energy Agency's Good Practice document.
Xenotransplantation is regulated as a *specified biotechnical procedure* requiring the approval of the Minister of Health. See Medicines Act 1981 Part 7A for details. Any 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).

[a] If a trial listed in this table also meets any of the criteria in Table 5, approval under section 30 is required.

Table 5: Clinical trials that require approval under section 30 of the Medicines Act

Any clinical trial involving: • **New medicines**, which includes **unapproved medicines** and medicines for which **approval has lapsed**. See the Product/Application Search on Medsafe's website for the approval status of medicines. • **New dose forms or dose strengths or different formulations** of an approved medicine. These are also considered new (ie, unapproved) medicines. Note if a **rescue medicine** is specified in the clinical trial protocol it is also considered a trial medicine and the same criteria for approval apply.
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 is required.
Clinical trials involving products that are not medicines in other jurisdictions but are considered to be new **medicines under New Zealand legislation** require approval before they can proceed. More information on the categorisation of a product can be found on the Medsafe website: Categorisation of Products.
Any subsequent **amendment to the protocol of an approved trial** must also be approved by the Director-General of Health. See section 6.4.1 of this guideline for more information.
An **extension to a clinical trial, where an investigational medicine is involved**, requires approval. This includes trials only investigating safety endpoints. 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. However, a subsequent application for approval may be made provided it can be shown that extension of the study will yield scientifically valid results.

2.5 Other legislative requirements relating to clinical trials

A clinical trial involving medicines containing human tissues or cells (eg, stem cells, blood products) may also have to comply with the Human Tissue Act 2008.

A clinical trial involving a new organism or genetically modified organism requires compliance with the Hazardous Substances and New Organisms Act 1996. Applicants should contact the Environmental Protection Authority about their obligations. Email: info@epa.govt.nz.

A clinical trial involving the use of a controlled drug requires compliance with the Misuse of Drugs Act 1975 and associated regulations. These set out licensing requirements for importation, possession and supply of controlled drugs, as well as storage, prescribing requirements, and requirements for additional approvals (eg, Ministerial approval). For further information, contact Medicines Control by email at: medicinescontrol@health.govt.nz. Additional requirements for medicinal cannabis products are outlined in section 2.5.1 below.

Clinical trials should also comply with the requirements of the Privacy Act 2020.

2.5.1 Additional approval/licensing requirements

Depending on the proposed activities to be conducted and the medicines involved as part of the clinical trial, additional licensing and/or issuing of an approval may be required under the Misuse of Drugs Act 1975 and Medicines Act 1981, before the clinical trial can take place.

For example, clinical trial sites or entities contracted on behalf of the clinical trial may require licensing and/or issuing of an approval to pack, import or manufacture medicines required for the specific clinical trial. For further information, contact Medicines Control by email at: medicinescontrol@health.govt.nz.

For clinical trials involving medicinal cannabis products, a medicinal cannabis licence with a research activity is required in addition to any other licensing requirements. Approval of the clinical trial must be obtained before making an application for a Medicinal Cannabis licence. For further information, refer to Part 4 of the Guideline on the Regulation of Medicinal Cannabis in New Zealand: Guidance for Applicants for a Medicinal Cannabis Licence or contact the Medicinal Cannabis Agency by email at: medicinalcannabis@health.govt.nz.

Note the timeline for obtaining approval for a relevant licence may differ significantly from Medsafe's timeline for approval of the clinical trial.

2.6 Health and Disability Ethics Committees approval

All clinical trials must comply with the Health and Disability Ethics Committees' (HDEC) requirements, regardless of whether they are trials that require approval under section 30 of the Medicines Act.

Ethics Committees approval is a separate process from clinical trial approval under section 30 of the Medicines Act and is not administered by Medsafe.

For all trials, the application for Ethics Committees approval may be made at any time before, during or after consideration of the application for clinical trial approval under section 30. Ethics approval is required before a trial can begin.

For particulars about Ethics Committees approval, applicants should contact the Health and Disability Ethics Committees at: hdecs@health.govt.nz

2.7 Advocacy Services

The Health and Disability Commissioner (Code of Health and Disability Services Consumers' Rights) Regulations 1996 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.

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 an authority delegated 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 outcome letters.

In general, all communication regarding clinical trial applications should be sent using the Ethics Review Manager (Ethics RM) system. However, for general enquiries, you can also send an email to: askmedsafe@health.govt.nz with 'ATTN Clinical Trial Coordinator' in the subject line.

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. The Gene Technology Advisory Committee (GTAC) considers applications for trials involving gene and other biotechnology therapies.

3.3 Submitting an application for approval of a clinical trial

An application for approval of a clinical trial is made by the entity who takes legal responsibility for the trial in New Zealand. For the purposes of this guideline and in line with the Act, the entity is referred to as 'the applicant'. For more information on the responsibilities of the applicant, see section 4.3, section 5.2.1 and section 6 of this guideline.

Applications for approval of clinical trials must be made using the online system, as outlined in section 3.3.1 below. Paper-based/emailed applications will not be accepted.

3.3.1 Making an online application for a clinical trial

An online application for clinical trial approval is made using the NZ Ethics RM system (Ethics RM).

The applicant must first create an account to get access to Ethics RM. Instructions for creating an account and how to prepare and submit applications electronically are on this website (see the Help section). In Ethics RM, one applicant owns the project, but they can assign project access to others.

The applicant should use the 'SCOTT / GTAC Application' Online Form in Ethics RM. Applicants should note that an application to the Health and Disability Ethics Committees for ethics approval should be made on the separate 'HDEC Application' Online Form in Ethics RM.

Delivery site addresses for the trial medicines should be clearly stated on the application form. These delivery site addresses will be included on the approval letter issued by Medsafe if the trial is approved. Applicants should be aware that Customs will not clear delivery of any investigational medicine to unapproved sites or investigators if these are not on the approval letter.

3.4 Administrative processing of clinical trial applications

On receipt of the online application, Medsafe will send an acknowledgement letter and an invoice to the applicant within 7 days.

Payment of the invoice should be made within 7 days. A decision will not be issued until payment has been received.

3.5 Clinical trial application fee and fee waiver

The application fee for approval of a clinical trial under section 30 is set out in regulation 61 of the Medicines Regulations 1984. See the Medsafe Fee Schedule for current fee details. The basic administration fee for the application is non-negotiable and non-refundable. However, the Director-General of Health may, under regulation 61A, waive or refund, in whole or part, the fee in certain circumstances. Applications for fee waiver will only be considered when they are submitted with the initial application. Applications will be considered on a case-by-case basis.

The criteria for fee waivers are outlined in section 3.5.1 of this guideline.

3.5.1 Criteria for fee waiver

A waiver, in whole or part, may be considered for clinical trials meeting all of the criteria shown in Table 6. Applications for fee waivers are made by letter to Medsafe through the Ethics RM submission at the time of application. Applications should outline how the trial meets the criteria.

Table 6: Criteria for fee waiver

The trial is being conducted in the interests of public health in New Zealand, for example: • the trial aims to meet an unmet clinical need (eg, there is currently no treatment available for a condition) • the trial aims to address equity issues • the trial is expected to result in a change to clinical practice
The trial is a non-commercial trial (ie, not funded or sponsored by the pharmaceutical industry)
The trial is being conducted only in Australasia

Trials being run by the pharmaceutical industry are not eligible for a fee waiver, however bioequivalence trials are eligible for an abbreviated approval process with a reduced fee (see section 3.7 of this guideline).

3.6 Consideration of applications for approval of clinical trials

Applications are considered by the relevant standing committee of the Health Research Council (SCOTT or GTAC). The HRC undertakes scientific assessments of clinical trial applications.

The Terms of Reference for these standing committees are published on the HRC website. The applicant should read these documents before submitting an application, as they provide information on how applications are assessed. Additional guidance for First in Human (FIH) and early phase clinicals trials is outlined in <add link to 'Considerations for FIH and early phase clinical trials'>.

Following its consideration of an application by the relevant standing committee, the HRC conveys its recommendation to Medsafe. The standing 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 delegate's consideration of the HRC's recommendation, through Ethics RM. Medsafe will liaise with the applicant regarding any proposed conditions of approval (such as amendment to the trial protocol) or requests for further information.

Following the resolution of any issues relating to the application, if the Director-General's delegate's decision is to approve the trial, Medsafe will issue an approval letter. If the decision is 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.

3.7 Abbreviated clinical trial approval process for bioequivalence studies

Medsafe operates an abbreviated approval process for eligible clinical trial applications for bioequivalence studies. This abbreviated approval process **does not apply to biosimilar products**. To be eligible, the criteria in Table 7 must be met.

Table 7: Criteria for abbreviated approval process for clinical trials

The clinical trial is a bioequivalence study that uses an investigational product that contains the same active pharmaceutical ingredient included in a medicine that is approved in New Zealand (approved medicine); **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.

A reduced fee applies to clinical trial applications meeting these criteria, and an outcome will be issued within five working days. See the Medsafe Fee Schedule for current fee details.

4 Notification of Clinical Trial Sites

Section summary

Medsafe administers a *Clinical Trial Site Notification* scheme covering sites which have study participants in residence while the clinical trial medicines are administered. The notification is site-specific and confirms the site's procedures for dealing with any emergencies arising from a clinical trial. It is completed by the person responsible for the site and should be updated whenever the information in the original notification form is changed.

4.1 Notification of Clinical Trial sites

Section 30(3)(g) of the Medicines Act specifies that the clinical trial 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 taken into consideration in deciding whether to grant approval for the trial.

If study participants are staying overnight or longer for monitoring purposes as a result of receiving a study medicine, information about the facilities and procedures in place to deal with possible emergencies (Critical Incidents) arising from the study medicines must be in place. A Critical Incident is described as a life-threatening or disabling event arising from the study medicine.

Medsafe administers a voluntary *Clinical Trial Site Notification* scheme to facilitate the collection and processing of this information for both the regulator and for applicants (see section 4.2 and section 4.3 below).

4.2 Operation of the Clinical Trial Site Notification scheme

Under the Clinical Trial Site Notification scheme, the person responsible for the site (where study participants stay overnight) completes a Clinical Trial Site Notification form and notifies Medsafe that the site has adequate emergency procedures in place. In most instances, the person responsible for the site will be a site staff member who has responsibility for managing the site, its staff and its procedures (eg, the site manager).

The notification 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 notification, Medsafe will add the site to the Notified Clinical Trial Sites webpage.

If there is a change to any of the information in the original notification form Medsafe should be re-notified of the clinical trial site.

4.3 Applicant responsibilities relating to trials being conducted at notifiable clinical trial sites

Applicants requesting approval of a clinical trial where subjects are kept overnight for monitoring purposes as a result of receiving the study medicine should check that Medsafe has been notified of the proposed clinical trial site. This can be done by checking Medsafe's Notified Clinical Trial Sites webpage. If Medsafe has not been notified of the site, the applicant should contact the person

responsible for the site (eg, the site manager) to submit a notification.

Medsafe recommends that applicants should not commence a clinical trial that requires trial subjects to stay at a site overnight (or longer) unless Medsafe has been notified of the site.

5 Good Clinical Practice Requirements

Section summary

This section establishes the requirement for clinical trials to be conducted in accordance with the CHMP GCP guideline and explains the modifications that are needed to achieve alignment with New Zealand regulatory requirements.

5.1 Compliance with Good Clinical Practice

All clinical trials are expected to be conducted in accordance with ICH E6(R2) as interpreted in the CHMP GCP guideline, even those that do not require approval from Medsafe.

In some cases, requirements set out in the CHMP GCP guideline conflict with or do not cover provisions in the Medicines Act 1981 or in other relevant New Zealand legislation (eg, legislation relating to reporting requirements or the retention of records). For this reason, some of the requirements specified in the CHMP GCP guideline must be modified to achieve compliance with New Zealand law.

Modifications are required in respect of:

- the definitions and obligations of particular persons (see section 5.2)
- the manufacture, labelling and dispensing of investigational products (see section 5.3)
- the retention of records (see section 6)
- adverse event reporting (see section 6.2 and section 6.3)
- notification of actions/issues relating to an investigational medicine (see section 6.4)
- clinical trial reporting requirements (see section 6.5).

Clinical trials should be designed with the best interests of patients in mind and should include the patient perspective (ie, a patient-centric design). It is desirable to involve patients in the design of the clinical trial. See the CIOMS report on Patient involvement in the development, regulation and safe use of medicines.

5.2 Responsibilities of the applicant, sponsor, investigator and monitor

Sections 1, 4 and 5 of the CHMP GCP 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.

5.2.1 Applicant and New Zealand sponsor

The CHMP GCP 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*. According to the Act, the application for approval of a clinical trial must be made by the person who imports or manufactures or commissions the manufacture of a medicine in New Zealand for use in a clinical trial (the *applicant*).

For the purposes of this guideline, once the trial is approved, the applicant is considered to be the *sponsor*, assuming responsibility for the trial in New Zealand.

The responsibilities of the applicant/sponsor under New Zealand legislation are defined in section 30 of the Act and parallel those of the sponsor in the CHMP GCP guideline (except for the reference to financing the trial).

The sponsor, who must be a person in New Zealand, is responsible for:

- the preservation of records (see section 6.1 of this guideline)
- reporting adverse events (see section 6.2 of this guideline)
- notifying significant actions/issues relating to clinical trial (see section 6.3 of this guideline)
- notifying and seeking approval for any changes in the clinical trial protocol to the Director-General of Health (see section 6.4.1 of this guideline)
- providing clinical trial progress reports (see section 6.4.2 of this guideline)
- 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 (section 30(7)(a) of the Act)
- ensuring that the trial is conducted in accordance with both New Zealand law and Good Clinical Practice standards (see section 5.1 of this guideline).

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 (the applicant) who must make the application to the Director-General for approval of the trial.

In the case of a multicentre trial that is being conducted and administered by a research body outside New Zealand, it is common for the investigator or coordinating investigator in New Zealand (or a local person or company, such as a clinical research organisation acting in that capacity) to undertake the role of applicant (and subsequently, the sponsor).

5.2.2 Investigators

The *coordinating investigator* is the person with overall responsibility for the conduct of the clinical trial in New Zealand. There is only one coordinating investigator for a trial, regardless of the number of trial sites involved. If there is only one trial site, then the investigator at that site will be the responsible person for the conduct of the trial in New Zealand.

The coordinating investigator should 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 (coordinating) 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.

An *investigator* is the person responsible for the conduct of a trial at a particular trial site. For a multicentre trial, there will be an investigator for each trial site. Where a trial is conducted by a team

of investigators at a particular site, the principal investigator is the responsible leader of the team.

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

5.2.3 Monitor

The *clinical trial monitor* (or clinical research associate) is an individual appointed by the sponsor and is responsible for carrying out monitoring activities to ensure that the trial is conducted, recorded, and reported in accordance with the protocol, Standard Operating Procedures (SOPs), Good Clinical Practice (GCP), and the applicable regulatory requirements.

The monitor should be independent of the clinical trial site, be qualified by scientific and/or clinical knowledge and have appropriate training and experience.

5.3 Quality of Investigational products

The CHMP GCP guideline provides guidance on the quality requirements for investigational products which should be followed. Investigational products, including active comparators and placebos, are expected to be manufactured in accordance with applicable Good Manufacturing Practice (GMP).

Section 30 of the Medicines Act also places conditions on the labelling, distribution and supply of an investigational medicine.

5.3.1 Manufacture of investigational medicines

In New Zealand, investigational products are expected to be manufactured in accordance with the New Zealand Code of Good Manufacturing Practice for Manufacture and Distribution of Therapeutic Goods (the Code; see Part 1: Manufacture of Pharmaceutical Products). Annex 13 of the Code provides additional guidance specific to investigational medicinal products.

Where the investigational medicine is manufactured in New Zealand, the manufacturer should hold a Product Specification File that describes the specifications of the investigational medicine manufactured for the clinical trial and an outline of the manufacturing process which includes processing, packaging, quality control testing, batch release and shipping of an investigational medicine. The manufacturer must issue a Certificate of Analysis for the medicine to the sponsor of the trial.

The Product Specification File must be consistent with specifications in the clinical trial documents (eg, specifications of the investigational product in the Investigator's Brochure, trial protocol, etc.).

Information on the quality of the investigation medicine should be included in the clinical trial application.

The sponsor of the trial should verify that each batch of the investigational medicine meets the approved specifications and is suitable for use before it is released for use in the trial.

Manufacturers and packers of investigational products must hold appropriate licences for these activities (section 17 of the Medicines Act).

5.3.2 Labelling of investigational medicines

Section 30(7)(b) of the Act 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***".

The investigational product should be labelled according to Annex 13 of the Code (Annex 13). This includes (but is not limited to) information detailed in Table 8. See Annex 13 for the full requirements.

Table 8: Information that should be included on labels

The name, address and telephone number of the sponsor, contract research organisation or investigator (the main contact for information on the investigational product, clinical trial and emergency unblinding). New Zealand contact details must be used, so that in the event of an emergency, the person(s) responsible for the trial in New Zealand can be easily contacted. Note: The address and telephone number of the main contact do not need to appear on the label if the participant has been given a leaflet or card with these details which they have been instructed to keep in their possession at all times. Participants may also be provided with an internet link to the trial information and main contact details to keep on their mobile phone or electronic device.
Pharmaceutical dosage form, route of administration (may be excluded for oral solid dose forms), quantity of dosage units and in the case of open label trials, the name/identifier and strength/potency.
Batch and/or code number to identify the contents and packaging operation trial participant identification number.
A trial reference code allowing identification of the trial, site, investigator and sponsor if not given elsewhere.

5.3.3 Distribution and supply of investigational medicines

Section 30(7)(c) of the Medicines Act requires that every person to whom the investigational medicine is distributed must be approved to conduct the trial (ie, be an approved investigator), and the medicine must be used solely by that person or under their direction for the purposes of the trial.

Procedures addressing the use of the investigational medicine should be documented in the in the clinical trial protocol (or other relevant documents) and submitted in the clinical trial application. For example, the arrangements for receipt, handling, storage, dispensing, supply, administration, and disposal of the investigational medicine. These activities may be carried out by the approved investigator or other suitably trained and qualified staff under their direction. Any delegation of trial activities by the approved investigator should be recorded on a delegation log.

The quantity of trial medicine to be supplied to trial participants at one time should be specified. Where a clinical trial uses an investigational medicine 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 maximum period of supply is 1 month.

The investigational medicines should be stored as specified by the sponsor and handled in accordance with section 47 of the Medicines Act (Storage and delivery of medicines), and Part 5 (regulations 26-37) of the Medicines Regulations 1984.

Where investigational 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, as specified in section 17 of the Medicines Act.

5.3.4 Cold chain requirements for particular investigational medicines

Some investigational medicines may require cold storage. Cold storage requirements for a particular investigational medicine must be strictly adhered to in order to ensure that the quality of the product is not compromised in the lead-up to, and during the clinical trial.

Clinical trial investigators using vaccines that require cold storage should follow the recommendations in the National Standards for Vaccine Storage and Transportation 2017, and where relevant the 2021 Addendum.

6 Records and Reporting

Section summary

This section describes the records and reporting requirements for clinical trials.

6.1 Preservation of records

The applicant/sponsor is responsible for ensuring that a complete set of study records and data relating to New Zealand trial participants is retained.

Preservation of clinical trial records must comply with New Zealand privacy legislation (Privacy Act 2020) and the Health (Retention of Health Information) Regulations 1996. The following points should be considered:

- Trial records may be held by the coordinating 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 all trials, the records may be stored overseas provided they are stored in accordance with New Zealand privacy legislation and Health (Retention of Health Information) regulations and 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. Records must be kept for a minimum of 10 years from date the study ends.

Refer to Archives New Zealand for general advice on standards for electronic storage, retention and disposal of public records.

6.2 Reporting adverse events/individual case safety reports

The sponsor is responsible for reporting adverse events associated with investigational medicines being used in clinical trials to Medsafe. The requirements for reporting are outlined in section 6.2.1 to 6.2.3 below. For further guidance on reporting requirements for adverse events refer to <add link to 'Clinical Trial Safety Monitoring and Reporting for Investigational Products'>.

6.2.1 Expedited reporting of suspected unexpected serious adverse reactions

Serious adverse reactions occurring in 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 endpoints.

Expedited reporting of fatal or life-threatening suspected unexpected serious adverse reactions (SUSARs) is required for some clinical trials. The requirements for reporting ICSRs of SUSARs

depends on whether or not there is a pharmacovigilance system in place for the trial.

If there is no pharmacovigilance system in place for the trial:

- The sponsor is required to report ICSRs of fatal or life-threatening SUSARs occurring in New Zealand trial participants where the treatment is known (ies, unblinded). These reports should be submitted **within 15 days** of the sponsor becoming aware of the event.
- All other ICSRs of SUSARs that are not fatal or life-threatening do not need to be routinely reported but must be held in an accessible form and made available to Medsafe on request.

If there is a pharmacovigilance system in place for the trial:

- Expedited reporting of ICSRs of SUSARs occurring in New Zealand trial participants is not required.
- ICSRs of all SUSARs must be held by the sponsor in an accessible form and made available to Medsafe on request.

Details of the pharmacovigilance system should be included in the clinical trial application. Refer to the EMA ICH E2E Pharmacovigilance planning scientific guideline for more information on pharmacovigilance systems.

6.2.2 Reporting other adverse events

The sponsor is expected to hold reports of all New Zealand AEs. These reports should not be routinely reported to Medsafe but must be held in an accessible form and made available to Medsafe on request.

6.2.3 How to submit individual case safety reports

Reportable ICSRs can be submitted to Medsafe via:

- the CIOMS form through Ethics RM, or
- the CARM reporting webform.

If the webform is used, include the protocol number in the 'additional information' field on the last page of the form.

6.3 Notifying Medsafe of significant actions/issues

Medsafe must be informed through Ethics RM **within 15 calendar days** of the sponsor becoming aware of any of the following actions/issues:

- withdrawal of the investigational medicine from continued development, for any reason
- withdrawal of the investigational medicine from the market in another jurisdiction, for any reason
- serious breaches occurring in a clinical trial that are likely to significantly affect the reliability and robustness of the data or the rights, safety, or wellbeing of participants (eg, serious breaches of the trial protocol or GCP requirements, critical or major adverse audit findings, fraudulent activity, or other serious misconduct)
- significant safety issues (SSIs).

If urgent safety measures (USMs) are required to be taken in order to eliminate an immediate hazard to a participant's health or safety, these may be instigated before Medsafe is notified. However they must be reported to Medsafe through Ethics RM **as soon as possible**, but no later than **seven calendar days** after taking such measures.

For further guidance on reporting requirements for SSIs/USMs refer to <add link to 'Clinical Trial Safety Monitoring and Reporting for Investigational Products'>.

6.4 Study reporting requirements

6.4.1 Amendments to the trial

Once a clinical trial has been approved, any changes to the trial protocol must be submitted to Medsafe through Ethics RM for approval. This includes changes to trial sites and/or investigators and other protocol amendments. Changes must be approved before they can be implemented.

Changes to other essential trial documents such as the Investigator's Brochure (see the CHMP GCP guideline for other examples) do not require prior approval. These changes should be notified through Ethics RM, together with the submission of the changed documents. However, they do not need to be approved prior to implementation.

If responsibility for the supply of investigational products is changed to another suitably qualified person already named in the protocol as a key person, this should be recorded in the delegation of authority (DOA) log, but a protocol amendment is not required.

It is the applicant/sponsor's responsibility to keep the Medsafe clinical trial approval letter details up to date by submitting any changes to sites and investigators. Applicants are reminded that Customs may not release investigational medicines to unapproved sites or to investigators if they are not specified on the approval letter.

Note, applications for approval of a new study phase (eg, from Phase 1 to 2) that was not specified in the original clinical trial application must be submitted as a new clinical trial application, not as an amendment. If you are unsure if a new clinical trial application or an amendment is required, send an email to: askmedsafe@health.govt.nz.

6.4.2 Study progress reports

Section 30(7)(d)(ii) of the Act requires the sponsor to submit routine progress reports to Medsafe every 6 months. Reports should be submitted through Ethics RM.

If the trial has not commenced within two years of the approval, the application will be revoked. The sponsor will need to re-apply for the trial.

The first progress report should be sent no more than 6 months after the date of approval of the trial, whether or not recruitment of New Zealand trial participants has commenced. Subsequent reports must be submitted at 6-monthly intervals throughout the duration of the trial in New Zealand.

A detailed safety report should be submitted annually with one of the 6-monthly progress reports. The Development Safety Update Report (DSUR) may serve as the safety report. For more information on periodic safety reporting see <add link to 'Clinical Trial Safety Monitoring and Reporting for Investigational Products'>.

Medsafe should be informed when the New Zealand trial, or the New Zealand arm of a multinational trial, is completed. There is no need to continue submitting 6-monthly progress reports or DSURs once the NZ arm has been completed, even if the trial continues elsewhere.

6.4.3 Final report

Section 30(7)(d)(iii) requires a copy of the results of the trial to be sent to Medsafe on completion of the clinical trial.

Prior to the End of Trial report being available, Medsafe should be sent a 'Notification of Conclusion of the Study' using the Post-Approval Form (PAF) in Ethics RM. This allows Medsafe to be informed that the study has ended in New Zealand but may be ongoing globally.

At the global End of Trial, a copy of the results of the trial (eg, a synopsis of the final report) should be sent to Medsafe when available, using the Post-Approval Form in Ethics RM. The full report should not be routinely sent to Medsafe but must be held in an accessible form and made available to Medsafe on request.

Medsafe recommends that the outcome of the study be reported to the trial participants.

6.5 Health and Disability Ethics Committees reporting requirements

The reporting requirements for HDECs are outlined in the Standard Operating Procedures for HDECs, Guidance on protocol deviation submissions and National Ethical Standards for Health and Disability Research and Quality Improvement.

The <add link to 'Clinical Trial Safety Monitoring and Reporting for Investigational Products'> document also summarises the HDEC monitoring and reporting requirements.

For further information on HDEC reporting requirements, applicants should contact HDEC directly.

7 Clinical Trials Involving Medical Devices

There is no provision under the current medicines legislation (the Medicines Act) to require approval of clinical trials involving medical devices. However, Medsafe would like to be informed by email of any clinical trials of medical devices via devices@health.govt.nz. This is so that Medsafe has some knowledge of these trials should any issues later arise. Notifying a trial to Medsafe does not constitute an approval or endorsement of the trial.

All clinical trials must comply with the Health and Disability Ethics Committees' (HDEC) requirements, regardless of whether they are trials that require approval under section 30 of the Medicines Act.

Clinical trials involving medical devices are expected to be conducted in accordance with international best practice.

For information on safety monitoring and reporting requirements for clinical trials involving devices see <add link to 'Clinical Trial Safety Monitoring and Reporting for Investigational Products'>.

Appendix 1: Essential documents to be submitted with a Clinical Trial application and to support changes proposed to be made to the trial

A1.1 Documents that must be included with the initial application

- Signed and dated CV for coordinating investigator
- Signed and dated CVs for other investigators and sub-investigators
- GMP certification for manufacturer
- GMP certification for packer
- Signed Investigator consent form
- Investigator's Brochure
- Signed Protocol
- Signed Agreement between Involved Parties
- Sample labels

Applicants may submit any other documents that they consider are pertinent to the trial such as quality documentation for investigational products and the pharmacovigilance system.

A1.2 Minimum list of documents that should be submitted after approval

- Adverse Event Reports (see section 6.2 and section 6.3 of this guideline)
- Signed and dated CVs for new investigators
- Signed Investigator consent form / Signed protocol for new investigators
- Protocol Amendments including Note to Files and Protocol Clarification Letters
- Protocol deviations where they result in the suspension of a trial
- Six monthly progress reports
- Updated GMP certification for manufacturer
- Updated GMP certification for packer
- Updated Investigator's Brochure
- Updated labels

Applicants may submit any other documents that they consider are pertinent to the trial.

A1.3 Minimum list of documents that should be submitted after the trial has completed in New Zealand

- Notification of Conclusion of the Study (when trial sites in New Zealand have been closed out and the trial is completed in New Zealand)
- A copy of the results of the trial when this is available (eg, a synopsis of the final clinical study report)

Applicants may submit any other documents that they consider are pertinent to the trial.