MEDICINES CONTROL COUNCIL

GENERAL INFORMATION

This guideline is intended to provide recommendations to applicants wishing to submit applications for the registration of medicines. It represents the Medicines Control Council's current thinking on the safety, quality and efficacy of medicines. It is not intended as an exclusive approach. Council reserves the right to request any additional information to establish the safety, quality and efficacy of a medicine in keeping with the knowledge current at the time of evaluation. Alternative approaches may be used but these should be scientifically and technically justified. The MCC is committed to ensure that all registered medicines will be of the required quality, safety and efficacy. It is important that applicants adhere to the administrative requirements to avoid delays in the processing and evaluation of applications.

Guidelines and application forms are available from the office of the Registrar of Medicines and the website.

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REGISTRAR OF MEDICINES
MS M HELA

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Not updated

GUIDELINES FOR THE REGISTRATION OF MEDICINES

GENERAL INFORMATION

NOTE: These guidelines outline the format and data requirements for preparation and submission of an application for registration of medicines, and should be read in conjunction with the Medicines and Related Substances Act, 1965 (Act 101 of 1965), and the Regulations to this Act.

1 INTRODUCTION

The registration of medicine in South Africa is governed by the provisions and requirements of the Medicines and Related Substances Control Act No. 101 of 1965, (hereafter 'the Act') and the Regulations and Guidelines published in terms thereof.

These Guidelines describe the information required for the registration of “medicines” and for an application to amend a registered medicine. The information submitted will be evaluated in terms of the provisions of the Act.

The aim of these Guidelines is to assist applicants in the preparation of documentation for the registration of medicines for human use. The types of medicine include a new medicine for a new chemical entity (NCE), a multisource (generic) product, a product line extension, and a biological medicine.

It is a legal requirement that data submitted for evaluation should substantiate all claims and should meet technical requirements of **quality**, **safety** and **efficacy** of the product for the purposes for which it is intended. The Guidelines are meant to guide the applicant in meeting the requirements of the Act. It is acknowledged, however, that in some instances scientific developments may dictate alternative approaches. When a deviation from a guideline is decided on, a detailed motivation giving the reason(s) for the deviation and justification for the alternative approach should be included in the expert report submitted with the application.

Whenever there is doubt, applicants are advised to consult the Medicines Control Council (MCC) for confirmation and/or clarification before completing and submitting the application form; refer to the website for contact details. Applicants should always refer to the **current** version of the relevant ***Guidelines for the Registration of Medicines*** and the Addenda thereto before completing the application form.

Guidelines are constantly evolving as a result of scientific developments and harmonisation of the requirements of regional and international regulatory authorities. The MCC (Council) endeavours to regularly update the guidelines to reflect current thinking and keep its technical requirements and evaluation policies in line with “best international medicines regulatory practice”.

2 GENERAL

2.1 SCOPE

Legislation requires that the Council shall register every medicine before it may be sold/marketed.

An application for the registration of a medicine should therefore be submitted for evaluation and approval.

These guidelines are relevant only to human medicines including biological and complementary medicines. Separate guidelines apply to the registration of medical devices.

2.2 APPLICANT/PROPOSED HOLDER OF THE CERTIFICATE OF REGISTRATION (PHCR)

2.2.1 Eligibility to apply for registration of a medicine is governed by Regulation 22 of the Act. An application may be made by any of the following:

a) a person, body corporate/juristic person, company, residing and doing business in South Africa;

b) a close corporation incorporated in South Africa; or

c) a company in South Africa with at least

- a responsible delegated person residing in South Africa and
- an authorised person residing in South Africa who must be a person with appropriate knowledge of all aspects of the medicine and who shall be responsible for communication with Council.

2.2.2 The application submitted should be signed by the pharmacist authorised to communicate with Council. This pharmacist should be in the full-time employ of the company and may be:

- the Responsible Pharmacist in terms of the Pharmacy Act, 1974 (Act 53 of 1974) as amended, or
- another registered pharmacist responsible for regulatory affairs and with appropriate knowledge of all aspects of the medicine.

This should be an original signature (scanned signature not acceptable).

The following should be included:

- proof of **current** registration (copy of certificate) of the pharmacist who signed the dossier, and
- proof of **current** registration of the Responsible Pharmacist in terms of Act 53;
- an individualised, person specific letter of authorisation for the signatory, issued by the person responsible for the overall management and control of the business (CEO). *(Note that such a letter is not required for the Responsible Pharmacist if the Responsible Pharmacist signs the application.)*

2.2.3 An Applicant/PHCR should submit a Site Master File (SMF) in accordance with the SMF guideline. For subsequent applications reference to the allocated SMF number will suffice.

2.3 CONFIDENTIALITY/SECRECY

The confidentiality of information submitted to the MCC is governed by Section 34 of the Act. The MCC, committee members or staff of the Medicines Regulatory Affairs (MRA), may NOT

- disclose to any person, any information acquired in the exercise of powers or performance of functions under the Act and relating to the business affairs of any person, except
  - for the purpose of exercising his/her powers, or for the performance of his/her functions under the Act, or
  - when required to do so by any competent court or under any law, or
  - with the written authority of the Director-General, or
- use such information for self-gain or for the benefit of his employer.

The MCC may insist on written confirmation of the identity and affiliation of an individual inquiring telephonically, or in person, about a medicine. No information shall be disclosed telephonically unless the Medicines Control Officer knows the enquirer is entitled to receive the information.

2.4 LANGUAGE

In terms of Regulation 22(4) of the Act, all applications and supporting data submitted to the MCC should be presented in English (British). Original documents not in English should be accompanied by an English translation.

2.5 WHERE TO SUBMIT APPLICATIONS

Applications should be posted to Private Bag X 828, Pretoria, 0001 or preferably be delivered by the applicant, rather than a courier, to Room NG090, Civitas Building, Andries Street, Pretoria, where they will be logged and acknowledged. All correspondence should be addressed to the Registrar of Medicines and should be clearly coded as indicated in section 13 of this guideline.

The MCC will not take responsibility for documents posted or delivered to any other place or in any other manner.

2.6 WHEN A PRODUCT SHOULD BE REGISTERED

A product is liable for registration with the Medicines Control Council if any of the following apply.

i) Any of the ingredients of a product is listed in one of the Schedules to the Act;

ii) The product is a medicine by virtue of the definition of a medicine in the Act.

The Act defines a medicine as:

> "any substance or mixture of substances used, or purported to be suitable for use, or manufactured or sold for use in;
>
> (a) the diagnosis, treatment, mitigation or prevention of disease, abnormal physical or mental state, or the symptoms thereof in man; or
>
> (b) restoring, correcting or modifying any somatic or psychic function in man;
>
> and includes any veterinary medicine."

iii) If the product falls under any of the pharmacological classifications as specified in Regulation 25 of the Act.

iv) The intended use of a product and the text/words used in promoting the product, even if no claims are reflected on the label, render the product registerable. A substance not ordinarily eaten or drunk by man cannot be considered a foodstuff just because no apparent medicinal claims are made for it.

The relevant provisions and guidelines shall apply to a medicine called up as a complementary medicine.

2.7 TYPES OF APPLICATIONS

Medicine applications for registration for humans are divided into the following types for the determination of fees and allocation to reviewers for evaluation:

2.7.1 New chemical entity applications that include **pre-clinical** and **clinical** information in support of the efficacy and safety of the formulation/dosage form, indication/s and dosage regimen.

2.7.2 Multisource/generic applications and innovator product line extension applications that include clinical information in support of efficacy and safety of the formulation/dosage form, or indication/s or dosage regimen.

2.7.3 Multisource/generic applications and innovator line extension applications that include comparative bio-availability/bioequivalence studies as proof of efficacy.

2.7.4 Multisource/generic applications and innovator line extension applications

- that include comparative dissolution studies as proof of efficacy
- that include any other comparative studies as proof of efficacy
- others, not mentioned above e.g. liquids/solutions.

2.7.5 Biological medicines: Biopharmaceuticals and Biosimilars

Biological medicine: A medicine where the active ingredient and/or key excipients have been derived from living organisms or tissues, or manufactured using a biological process. Biological medicines can be defined largely by reference to their method of manufacture (the biological process). These include *inter alia* medicines prepared from the following substrates:

2.7.5 Biological medicines: Biopharmaceuticals and Biosimilars - continued

(i) Microbial cultures (fermentation);

(ii) Plant or Animal Cell cultures (including those resulting from recombinant DNA or hybridoma techniques);

(iii) Extraction from biological tissues; and

(iv) Propagation of live agents in embryos or animals.

The living substrate may be genetically modified in a number of ways to provide the required active ingredient, including recombinant DNA technology or hybridoma techniques**.**

Biological Medicines include, but may not be limited to the following:

(i) Plasma-derived products, e.g. Clotting factors, Immunosera, etc;

(ii) Vaccines;

(iii) Biotechnology-derived medicinal products (rDNA products) e.g. rHu-antihemophilic factors, Hormones, Cytokines, Enzymes, Monoclonal antibodies, erythropoietins;

(iv) Human Gene therapy.

It has been the practice, in South Africa, that Council will decide that certain well-characterised low-molecular weight medicinal biological compounds, such as antibiotics, insulin etc be excluded from biological medicine status, and they are therefore not reviewed by the Biological Medicines Committee.

Biopharmaceutical: Patented biological medicine.

Biosimilar: A biological medicinal product referring to an existing biological medicinal product for which registration has been applied for.

2.8 EVALUATION PROCEDURES

Routine	
Expedited	refer point 6
AMRP	refer point 7

2.9 FEES

The following non-refundable fees are relevant:

2.9.1 A non-refundable screening fee payable with the screening submission.

2.9.2 An application fee payable with the full submission of the application for registration.

2.9.3 A registration fee, payable when the application complies with all the requirements for registration, and which is payable before a registration certificate is issued.

2.9.4 An annual retention fee to maintain registration.

2.9.5 A fee to cover any amendments to the dossier or certificate.

2.9.6 A fee to cover any inspection of any manufacturing site.

2.9.7 A fee to cover authorization of the use of an unregistered medicine.

2.9.8 The fees are published in the Government Gazette and are also available on the website.

2.9.9 Methods of payment: By cheque or electronic payment / direct transfer.

Also refer to the Bank Detail guideline for electronic payment / direct transfer.

2.9 Fees - continued

Cheques should be made out to "Medicines Control Council". Only bank guaranteed cheques will be accepted and are to be submitted in a separate envelope attached to a **copy** of the covering letter of the relevant submission(s).

Direct electronic payment should include a clear reference, e.g. the product application number or purpose of the payment. Proof of electronic payment / direct transfer must be submitted in a separate envelope attached to a **copy** of the covering letter of the relevant submission(s).

Refer to 4.7 below for payment submitted with new applications.

2.9.10 To ensure evaluation of the relevant submission(s) (2.9.3 to 2.9.7 above) a **copy** of proof of payment / cheque must also be attached to the *original* covering letter of the relevant submission.

2.10 SAME OR SEPARATE APPLICATIONS

For the purpose of registration the following products will be regarded as either being the same product or separate product applications:

TYPE OF APPLICATIONS	Application	
	Same	**Separate**
2.10.1 Each individual dosage form of a particular medicine		X
2.10.2 Variations of the active pharmaceutical ingredient (API) of a product		X
2.10.3 Tablets/Capsules/Suppositories/Lozenges		
a) Different pack-sizes of exactly the same strength and formulation.	X	
b) Different strengths and formulations.		X
c) Uncoated and coated tablets of the same strength and formulation.		X
2.10.4 Syrups/Liquids/Solutions (excluding parenterals)/Creams/Ointments		
a) Different container sizes of the same strength and formulation.	X	
b) The same container size of different strengths and formulations.		X
2.10.5 Ampoules and Vials and Large Volume Parenterals		
a) Ampoules or single dose vials containing identical solutions of the same strength but of different volumes (i.e. resulting in different total doses).		X
b) Ampoules containing solutions of different strengths.		X
c) Ampoules and single dose vials containing e.g. dry powder, crystals of different mass.		X
d) Ampoules and single dose vials containing the same respective masses of e.g. dry powder, crystals.	X	
e) Ampoules, single dose vials, as well as pre-filled disposable syringes and cartridges containing identical solutions of the same strength and same volume of liquid.	X	
f) Dental cartridges containing different volumes of fluids of the same strength (provided the dose remains constant).	X	
g) Ampoules containing “water for injection”, but of different volumes.	X	
h) Special ampoules of dry powder and “water for injections” contained in the same unit, but intended for mixing at the time of injection if water for injections is fully described in dossier.	X	
i) Ampoules containing identical solutions of different volumes used only as diluent in the reconstitution of a preparation for parenteral use.	X	

TYPE OF APPLICATIONS	Application	
	Same	**Separate**
j) Multidose vials containing different volumes of the same strength and formulation with the same dosage schedule.	X	
k) Multidose vials and a single dose ampoule or vial of the same formulation if the single-dose ampoule or vial corresponds to the dose indicated for the multidose vial.	X	
l) Multidose vials containing dry powder of different mass of the same formulation, and the same concentration when reconstituted.	X	
m) An ampoule of diluent packed together with any preparation including biological medicines if diluent is fully described in dossier.	X	
2.10.5 Ampoules and Vials and Large Volume Parenterals - continued	**Same**	**Separate**
n) Infusion solutions of the different volumes and of the same formulation which are packed in containers of exactly the same type of material depending on the relevant information submitted.	X	
o) Infusion solutions of the same formulation and of the same or different volume which are packed in containers made of different types of materials.	X	
p) A preparation, packed in plastic containers, intended to be marketed in glass containers containing the same volume and the same formulation.	X	
q) Products with the same strength and formulation but with different colours and/or flavours.		X
r) Applications containing the same API(s) applying for additional indications which render the product in a different scheduling status, or different pharmacological classification, or have any other restrictions imposed other than the original application.		X
s) Removal of antimicrobial preservative from single dose presentation of registered vaccine that included a preservative in the original approved formulation		X
2.10.6 Same formulation with different proprietary names whether of the same or different applicants		X

2.11 TRANSITIONAL CONVERSION TABLE

The Medicines Registration Form (MRF1) replaced the MBR1 form for the application for registration of a medicine prescribed by the Act. Biological medicines no longer have a separate form.

Circulars issued before and during the transformation process made reference to the Annexures of the previous MBR1 application forms. For ease of reference the following conversion table is included.

From 1 ~~July 2010~~ June 2011 submissions in ZA CTD (Common Technical Document for South Africa) format ~~will be accepted~~ are mandatory. Please refer to the Guidance for the Submission of the South African CTD/eCTD General & Module 1.

MBR1	Biol*	MRF1	SUBJECT
Annexures		**PART**	***** *biological*
Front page		1A	Administrative Data
1	15	1C	PI / PIL / Label
2	6	3B	Formulation / final filling lot formulation*
2	10	3B	Formulation diluent if applicable/ final filling lot reconstituting liquid/diluent*

MBR1	Biol*	MRF1	SUBJECT
Annexures		PART	* *biological*
3	-	3A	Active Pharmaceutical Ingredient (API)
-	4	3Aa)	Primary lot preparation and production and control tests*
-	2	3Ab)	Primary lot pharmaceutical ingredient specifications*
-	3	3Ac)	Primary lot pharmaceutical ingredient control procedures and laboratories*
4	-	3C	API and inactive pharmaceutical ingredient (IPI) specifications
5	5	3C	Pharm ingredient control procedures / primary lot control tests and laboratory*
6	3/5	3C	Pharmaceutical ingredient release laboratories
7	-	3F	Final product specifications and control
-	8	3F	Final filling lot and diluent analytical and other control tests*
8	9	3D	Containers and packaging materials / immediate container and laboratory*
9A	-	3F	Finished product (release criteria and laboratories)
9B	-	3D	Container and packaging material (release criteria and laboratories)
-	10	3F	Diluent / reconstituting fluid specifications, tests*
10	11	3G	Stability programme and data (also diluent if applicable)
11	7/10	3E	Manufacturing procedure / final filling lot and diluent production*
12	14	1D	Foreign registration
13	-	2	*In vivo* and/or *in vitro* equivalence studies as proof of efficacy
14	13	4	Pre-clinical studies / Clinical evidence of safety*
15	12	5	Clinical studies / Clinical evidence of efficacy*
16	-	3H	Pharmaceutical development
-	1	3I	Expertise and premises used for manufacturing of biological medicines*

2.12 CANCELLATION OR WITHDRAWAL OF APPLICATIONS

HCRs of medicines and applicants should, before applying to the Registrar, carefully consider any decision to cancel or withdraw, as the case may be, a registration or application for registration, as Council after consideration of all issues involved has resolved the following with immediate effect.

2.12.1 Any medicine

- of which the registration has been cancelled, or any "old medicine" of which the application for registration has been withdrawn by notice in the Government Gazette, and
- for which a written application or request to the Registrar of Medicines has been submitted by the holder of a certificate of registration or by the applicant,

will under no circumstances be re-instated.

2.12.2 Should the HCR or the applicant desire to re-register such medicine, a new application for registration of a medicine must be submitted in accordance with the requirements of the Act and the relevant Regulations.

2.12.3 An application for registration of a medicine may at whatever stage of processing be withdrawn by written application to the Registrar of Medicines. The withdrawal shall under no circumstances be reversed once such an application is approved and the approval confirmed in writing. A new application for registration must be submitted should the applicant wish to proceed with registration thereafter.

3 REQUIREMENTS OF AN APPLICATION

From 1 July 2010 submissions in ZA CTD (Common Technical Document for South Africa) format will be accepted. Please refer to the Guidance for the Submission of the South African CTD/eCTD General & Module 1.

3.1 PART 1 ADMINISTRATIVE INFORMATION

3.1.1 PART 1A Administrative Particulars

The details as per the application form should be completed.

a) applicant/prospective holder of the certificate of registration (refer to this guideline section 2.2).

b) "Business address" in relation to a business that is carried on in the Republic of South Africa, means the full physical address of the premises where such business is conducted.

c) Person authorised to communicate with Council. Refer to Regulation 22(2) of the Act.

d) Category. Refer to Regulation 25 of the Act.

e) "Proprietary name" means the name that is unique to a particular medicine and by which it is generally identified and which, in the case of a registered medicine, is the name approved in terms of Section 24 (8) of the Act in respect of such medicine. (Refer to section 8 of this guideline).

Medicines which are not identical in composition or strength are not regarded as the same medicine and should be submitted separately. (Refer to this guideline section 2.10).
However, different strengths of the same dosage form may be submitted individually in one dossier.

f) Pharmacological classification. Refer to Regulation 25 of the Act.

g) Dosage form: Select the most appropriate dosage form from this list, when completing the administrative data. This dosage form will also be reflected on the medicine registration certificate. Specify/qualify the type of tablet e.g. chew tablet, slow release tablet, uncoated, film-coated, sugar-coated, enteric-coated, dispersible tablet.

Blood bag	Gel	Pessary
Bone cement	Globule	Plaster
Beads	Granules	Pods
Caplets	Gum	Powder
Capsules (specify type, e.g. hard gelatine, soft gelatine, modified release)	Implant	Shampoo
	Infusion (parenteral)	Soap
	Inhaler	Solution
Cleansing bar	Injection	Sponge
Combination of dosage forms	Insert	Spray
Condom	Intra-uterine device	Stick
Cone	Jam	Suppository
Cord	Leaves	Suspension
Cream	Liquid	Swab
Cardioplegic solution	Lotion	Syrup
Chip (dental)	Lozenge	Tablet *(specify e.g. uncoated or film, sugar or enteric coated; chew, dispersible)*
Decoction	Lump	
Dialysate	Medical device	
Diluent for injection	Mouthwash	Tampon
Dental material	Nasal inhaler	Test kit
Dressing	Nasal spray	Tincture
Drops	Oil	Toothpaste
Elixir	Ointment	Towelette
Emulsion	Ovule	Transdermal therapeutic system
Enema	Paste	
Foam	Pellet	Vaginal ring
Gas		Wafer

3.1.1 PART 1A Administrative Particulars continued

h) 'Approved name' in relation to a medicine means the internationally recognised name of such medicine, or such other name as the Council may determine, not being a brand name or trade name registered in terms of the Trade Marks Act, 1963 (Act 62 of 1963). (Defined in Section 1 of the Act.)

i) The API and strength per dosage unit applies only in the case of a dosage form with a single API.

j) The descriptive name of biological medicine, e.g. viral vaccine, viral antiserum, bacterial vaccine, bacterial antiserum, allergen, immunoglobulin or blood product, as given in a recognised pharmacopoeia or where such name does not exist, a name determined by the Council.

k) The country of origin, i.e. the country where the original development was done. If development took place in more than one country all the countries should be specified.

l) The name and complete physical address including the country, of all the manufacturing and packer facilities/sites for the medicine should be given. The site performing each stage of manufacturing and packaging where these do not all occur at the same site, should be clearly indicated. The various stages of manufacturing and packing reflected should correspond with those submitted in PART 3E.

m) The name and complete physical address including the country, of the final product testing laboratory/ies (FPRC) and final product release responsibility (FPRR) should be given. If applicable the details of both the pre- and post- importation FPRC and FPRR should be given.

This information may be submitted on the next page as a separate appendix if necessary.

n) The following are required for all the manufacturing, packaging, FPRC and FPRR sites:

i) Site (Plant) Master File (SMF)

ii)
- Confirmation of a Technical agreement between the parties, and
- a schedule of the limits of responsibilities accepted by each of the parties as specified in a Technical agreement or addendum to the contract should be included

iii) From the country of manufacture, if not South Africa:

- A copy of manufacturing licence or a statement by the competent medicine regulatory authority that the manufacturing facility complies with GMP and
- A copy of the Certificate of GMP compliance in terms of the WHO Certification Scheme.
- Confirmation that the manufacturing site is inspected at regular intervals and a copy of the latest written inspection report (not older than 3 years), from a Medicine Regulatory Authority of the country of origin is available for inspection.
- A copy of the registration or marketing authorisation certificate.
- A Certificate of a Pharmaceutical Product in terms of the WHO certification scheme (Free Sales Certificate)

o) FPRR should be vested in a person who has appropriate knowledge of the relevant aspects of the medicine and who is either the holder of the certificate of registration or is in the employment of the holder of such a certificate.

p) For subsequent amendments to the dossier PART 1Ac) Amendment history, of the MRF1 should be completed in accordance with the Amendment guideline.

q) All subsequent responses to Committees' recommendations and Council resolutions must include a valid declaration that the response and information submitted is true, correct and relevant, i.e. PART 1A must be duly completed, dated and signed for each response.

3.1.2 PART 1B Table of Contents (TOC)

A comprehensive Table of Contents (TOC) of the dossier including the SUB-PARTs of the different PARTs should be included. The items listed in the TOC should include at least all the relevant aspects addressed in the registration guidelines and/or the narrative headings of the CTD where relevant.

Each heading and sub-heading of the MRF1 and/or sections of responses to recommendations should be identified by a page number or tab and should be tabbed accordingly. Should the heading not apply an explanation as to why the heading does not apply should be supplied on the relevant numbered page or cover page of the relevant tab.

3.1.3 PART 1C Labelling

Refer also to the guideline "Package insert amendments concerning urgent safety restrictions: Urgent safety restriction notice (USRN)"

a) PART 1Ca) Package inserts (Regulation 9 of the Act)

b) Headings and particulars in a package insert (Regulation 9 of the Act)

Refer to Package Inserts for Human Medicines Guideline.

c) PART 1Cb) Patient information leaflet (PIL) (Regulation 10 of the Act)

This guideline serves to help applicants with the correct way of presenting a patient information leaflet (PIL) for evaluation on application for registration of a medicine. Applicants are requested to follow the format stipulated in the guideline in conjunction with provisions set out under Regulation 10 of the Act

PILs should be typed in double-spaced text and should be in English (British) and at least one other official language.

The printing quality of the package insert should be clear to enable duplication, for inclusion into various documents, during the evaluation and registration process. The spelling and grammar in the package insert text should be checked thoroughly before submission of the application.

Reference to the package insert for each statement should be included in a broad margin left on the right hand side of each page of the patient information leaflet for this purpose. The exact page/s should be stated. No references should however be included in the finalised printed PIL.

An electronic copy (Word document) on diskette or CD of the package insert should be included.

Headings and particulars in a patient information leaflet (PIL)

In addition to the requirements of Regulation 10 the following should also be included under the relevant headings. Headings should be adapted to suit the specific dosage form, i.e. tablets are taken or given (e.g. to children), an injection administered, ointments applied, as the circumstance and the dosage form may require.

It should be ensured that the correct introductory statements to the PIL, which depend on the Scheduling Category of the product, are used.

The sub headings listed below are recommended:

Scheduling status

The scheduling status of the medicine as in the package insert.

Proprietary name and dosage form

Should be in accordance with PART 1 of the MRF1 as in the package insert.

What [Trade Name] Contains *Regulation 10 which refers to Regulation 9 (1)(c) of the Act.*

The composition of the medicine in accordance with the package insert.

c) Headings and particulars in a PIL – continued

What [Trade Name] is used for

The registered indications for use of the medicine, as accepted by Council, in the package insert.

Before taking [Trade Name]

The following information should be included:

- Contra-indications
- precautions
- warnings, e.g. warnings concerning sedative properties of the medicine; warnings concerning the risks involved with sudden withdrawal of the medicine, should be included
- interactions
- When umbrella/brand names are used, precautionary statements of the simultaneous usage of these products, so as to inform patients of their correct use, and potential safety concerns should be included. For example, if a range of products under the same umbrella name contains paracetamol, a product should not be used in conjunction with another product in the range that also contains paracetamol.

General statements to be included in this section: Regulation 10(1)(e)(v) of the Act.

"If you are taking medicines on a regular basis, concomitant use of the medicine may cause undesirable interactions. Please consult your doctor, pharmacist or other health care professional, for advice."

"If you are pregnant or breast feeding your baby while taking this medicine, please consult your doctor, pharmacist or other health care professional for advice*."*

(THESE STATEMENTS SHOULD BE BOXED AND BOLDFACED)

How to take [Trade Name]

The recommended dosage should be included here. (Any special information, which the patient may require for the proper and safe use of the medicine, should be provided).

Information on what to do in specific circumstances, for example, in the case of a missed dose, an unexpected reaction or in the case of an overdose, should be included.

"**Do not share medicines prescribed for you with others."** should be stated, as well as,

"In the event of overdosage, consult your doctor or pharmacist. If neither is available, rush the patient to the nearest hospital or poison control centre".

Possible Side effects

General statement to be included: Regulation 10(1)(g)

"Not all side-effects reported for this medicine are included in this leaflet. Should your general health worsen while taking this medicine, please consult your doctor, pharmacist or other health care professional for advice.

Storage and disposal information

Should contain information in accordance with MRF1 PART 3G on how to store the medicine properly, and how to dispose of unused medicine, such as by returning the medicines to the pharmacy.

The following statement should be stated:

"Keep all medicines out of the reach of children."

Presentation

In accordance with MRF1 PART 3D as in the package insert.

c) Headings and particulars in a PIL – continued

Identification of the medicine

In accordance with MRF1 PART 3F as in the package insert.

Registration number/reference number

As allocated by the Registrar in accordance with Section 15 of the Act and in the package insert.

The name and the business address of the holder of the certificate

In accordance with MRF1 PART 1A as in the package insert.

The date of publication of the patient information leaflet

Date of the council resolution as in the package insert.

Note: The responsibility for ensuring that the patient information leaflet is in line with the regulations, including assurance that the PIL corresponds with the information in the package insert, will essentially rest with the applicant.

d) PART 1Cc) Label (Regulation 8)

An example or a facsimile of the label should be included. Requirements, e.g. font size, as stipulated in the Regulation 8 of the Act, should be adhered to.

The following inclusions are permitted:

"For state use only – Not for sale" – for tender items

Note: Any deviation from the requirements described in these guidelines will require approval by Council in terms of Section 18(4) or Section 36 of the Act, prior to implementation.

Sugar quantity contained in medicines for oral or parenteral administration - Regulation (8)

3.1.4 PART 1D FOREIGN REGISTRATION

a) A list of countries, ~~including SADC countries~~ in which an application has been lodged, and the status thereof, should be furnished, detailing approvals, ~~Approvals (with indications),~~ deferrals, withdrawals and rejections~~, should be stated~~.

~~The Council aligns itself with~~ *moved, see below*

- ~~the following regulatory authorities: USA (FDA), UK (MHRA), Sweden (MPA,) Australia (TGA), Canada (Health Canada), European Union (EMA and Mutual Recognition procedure, excluding National procedure), Switzerland (Swissmedic) and Japan (MWH).~~
- ~~members of the PIC/S (Pharmaceutical Inspection Co-operation Scheme) for quality matters relating to GMP.~~

b) If the medicine has already been registered ~~in any of the countries mentioned above,~~ by any of the regulatory authorities with which Council aligns itself, include

- a copy of the ~~registration~~ certificate of registration ~~and the~~
- ~~approved package insert (data sheet), as well as~~ *moved*
- the conditions of registration, ~~should be provided.~~ and
- the approved package insert (data sheet/summary of product characteristics (SPC)) translated into English where relevant.
- ~~For rejections or withdrawals relating to safety matters the details for each case should be provided.~~ *Moved, reworded*
- ~~It should be stated whether data packages submitted in these countries, including the proposed indications, are essentially similar to those submitted to Council.~~

~~If not registered and/or applied for registration in the country of origin the reason should be given.~~ *moved*

c) The Council aligns itself with a regulatory authority which is

(1) ~~the following regulatory authorities~~ a member of the International Conference on Harmonization of Technical requirements for Registration of Pharmaceuticals for Human use (ICH) i.e.

USA (FDA), ~~UK (MHRA), Sweden (MPA,)~~ ~~Australia (TGA),~~ *moved* ~~Canada (Health Canada)~~ *moved*~~,~~ European Union (EMA and National Regulatory Authorities), ~~Mutual Recognition procedure, excluding National procedure),~~ ~~Switzerland (Swissmedic)~~ *moved* and Japan (MWH).

(2) an ICH observer, i.e. Switzerland (Swissmedic) and Canada (Health Canada) or

(3) a regulatory authority associated with an ICH regulatory authority member through a legally binding mutual recognition agreement i.e. Australia (TGA), Norway, Iceland and Liechtenstein.

(4) a member~~s~~ of the PIC/S (Pharmaceutical Inspection Co-operation Scheme) for quality matters relating to GMP.

d) Provide details of any negative decision by any regulatory authority reflected in PART 1D c).

e) If not registered and/or applied for registration in the country of origin the reason should be given.

3.2 PART 2 BASIS FOR REGISTRATION AND OVERVIEW OF APPLICATION

PART 2 addresses the basis for registration and makes provision for an overview of the application and consists of the following Sub-PARTs:

3.2.1 PART 2A Pharmaceutical and biological availability

Refer to the Pharmaceutical and Analytical guideline.

3.2.2 PART 2B Summary basis for registration application (SBRA)

If clinical/pre-clinical data are submitted without pre-clinical and clinical expert reports, a Summary Basis for Registration Application (SBRA), should be included in the application for registration to expedite the review process of the safety and efficacy of the medicine. (Refer to Clinical guideline)

3.2.3 PART 2C **Pharmaceutical Expert Report (PER)/**Quality Overall Summary (QOS)

Refer to Pharmaceutical and Analytical guideline

3.2.4 PART 2D Pre-clinical expert report

Refer to section 8 of this guideline

3.2.5 PART 2E Clinical expert report

Refer to section 8 of this guideline.

3.3 PART 3 PHARMACEUTICAL AND ANALYTICAL

Refer to the Pharmaceutical and Analytical guideline.

3.4 PART 4 PRE-CLINICAL STUDIES

Refer to the Clinical guideline.

Requests for exemption from the requirements of this PART should address the current formulation / product being applied for in addition to the API being well-known and documented.

3.5 PART 5 CLINICAL STUDIES

Refer to the Clinical guideline.

Requests for exemption from the requirements of this PART should address the current formulation / product being applied for in addition to the API being well-known and documented.

4 PREPARATION AND SUBMISSION OF AN APPLICATION

From 1 ~~July~~ June 201~~0~~1 submissions in ZA CTD (Common Technical Document for South Africa) format ~~will be accepted.~~ are mandatory (excluding veterinary medicines). Please refer to the Guidance for the Submission of the South African CTD/eCTD General & Module 1.

Note: The official headings, text and footer of the current version of the MRF1 may not be changed.

4.1 Applications for registration of a medicine should be submitted on the MEDICINE REGISTRATION FORM (MRF1) obtainable from the Registrar of Medicines or from the MCC website www.mccza.com

4.2 Each page of the application should

- be numbered and the printing should be in a font size with a legibility equivalent to at least Arial 10 point black on white and the copies including figures, tables, photo's should be clearly legible. Shading and/or coloured filling/background and/or print, e.g. in tables and headers, or across pages, is unacceptable and should be avoided.
- have a header reflecting the HCR, product name, dosage form and strength.

The pages should be numbered according to the MRF1, e.g. 3B.1 (referring to PART 3B, first page).

Double-sided copies are ~~allowed~~ required except for those of the package insert and patient information leaflet.

4.3 The application for registration of a dossier should have clearly labelled tabs to indicate each PART and sub-PART or appendices/documents/reports of the dossier. Responses to recommendations should comply with the format and requirements of the Amendments guideline. Each part / section of the response should be indicated by clearly labelled tabs.

4.4 Each PART or Sub-PART should contain a Table of Contents complying with 3.1.2 above.

4.5 The application for registration should be properly bound on the left side as this allows for easy update/addition of pages. The left margin of documents should be wide enough to allow for legibility after copying and binding.

Binding is left to the discretion of the applicant; however, the use of lever-arch files and ring binders is not accepted and the use of metal fasteners should be avoided regardless of the thickness of the document, as they injure and damage. The binding should enable the easy handling and evaluation of documents without it coming apart. The dossier should, therefore, be bound in units not exceeding 4 cm, including the binder, also depending on the binder used.

4.6 All documents and reports included in the registration dossier must comply with the requirements of the SA Guide to GMP Chapter 4 – Documentation, in particular also 4.2.6 and 4.2.7

4.7 Copies of both screening and final submission covering letters in addition to all screening outcome letters should be bound to the application dossier as indicated in the section 5 PRESENTATION OF SCREENING AND POST-SCREENING COPIES of this guideline.

4.8 Cheques or proof of payment should be submitted in a separate envelope attached to the original covering letter. No other documents should be attached.

4.9 The requirements with regard to metrication in accordance with the Trade Metrology Act should be applied in all documentation prepared locally, e.g. the package insert, patient information leaflet, label and completed section of all PARTs of the dossier.

4.10 The boxes in which documentation is submitted to the MCC should be clearly labelled. The following details should appear clearly **on each box**, preferably on the side:

a) Applicant name
b) Name of the product (at applicant's discretion) or the applicant's product identification code for each application (e.g. NCE-04NOV01)
c) The contents of the box, e.g. File numbers, PARTs, Sample, Covering letter, Cheque.
d) Number of boxes, e.g. 1 of 10
e) Type of application, e.g. routine, expedited review (fast track), or AMRP.
f) Colour stickers indicating screening (red) or post-screening (green).

4.10 In the case of expedited review (fast track), a copy of the approval letter should be attached in the front **of each volume**.

4.11 If the application is being submitted simultaneously with one or more additional applications for the identical product this should be stated and also confirmed that the submissions are identical except for the proprietary name. This information should also be included clearly in the covering letter of each product.

4.12 On receipt at the MCC, all applications for registration will be subject to pre-screening according to the checklist, attachment A, also completed by the applicant.

4.13 Upon successful pre-screening, the application will be logged onto the system and allocated a screening number. A letter acknowledging receipt of the application and receipt of the screening fee will be issued to the Applicant.

4.14 If the applicant does not comply with the pre-screening requirements the application will be returned to the Applicant as incomplete.

4.15 After successful pre-screening the application will be subjected to screening according to the screening form MRF2. The screening process endeavours to confirm that all the data required have been included and does not involve evaluation of either the data or any motivation for omission of data. Except for the Inspectorate requirements referred to, the MRF2 headings are in accordance with those of the MRF1 and the questions under each heading are in accordance with the relevant guidelines. Reference to the relevant guidelines should therefore be made if the meaning of any particular question is not clear. Motivation for the omission of data is required.

As from 1 July 2010 the pre-screening will become the first part of administrative screening and technical screening will be carried out by the evaluator before evaluation commences.

Omission of critical data or non-compliance with requirements may result in the application being recommended for rejection. For submissions in MRF1 format the applicant should still submit the completed MRF2 form.

4.16 The screening outcomes i.e. HOLD or RETURN AS INCOMPLETE will be communicated to the applicant together with reasons. Time frames for the applicant to submit outstanding information, or to collect the application, will also be communicated to the applicant. In the event of a dispute regarding outstanding information or time frames, the application will be tabled at the next Council meeting for a formal decision.

4.17 The ACCEPTED screening outcome, the required application fee, and the number of copies will be communicated to the applicant. At this point the application number will also be allocated. Applications for which an expedited review (fast-track) has been approved should be clearly marked. The allocated reference number and a copy of the approval letter should be included and also accompany any subsequent correspondence regarding an expedited review application.

4.18 The correct number of copies of application and additional documents required for the evaluation of the application, should be submitted in the format detailed in the section 5 PRESENTATION OF SCREENING AND POST-SCREENING COPIES of this guideline. **This date will be regarded as the date of application.**

5 PRESENTATION OF SCREENING AND POST-SCREENING COPIES

Certain PARTs of the application for registration should be duplicated and submitted as prescribed in the screening approval letter together with the application fee. Cheques or proof of payment should be submitted in a separate envelope attached to the original covering letter. No other documents should be attached.

No additional documentation, other than that which has been clearly stipulated below, may be bound in any of the sets identified below. Applicants who wish to submit applications in electronic format should make prior arrangements with the Registrar.

For submission in CTD / eCTD format, please refer to the Guidance for the Submission of the South African CTD / eCTD General & Module 1.

5.1 SCREENING SUBMISSION SET 1

As from 1 July 2010 the pre-screening check-list (Appendix A) and MRF2 (screening form) may be used by the applicant to ensure compliance with the Screening Template SA (intended for Official use only).

- Covering letter in the front of each volume
- Screening fee (please *do not include the application fee with the screening fee*)
- One complete application for registration dossier (MRF1) and the following:
  - Copy of the latest Inspection Report (not older than 3 years) from the Medicines Control Council and/or foreign regulatory body recognised by the Council for the manufacturer of imported medicinal products and medicines
  - GMP/WHO certificate
  - Certificate of analysis for the sample submitted
  - One sample of smallest pack size
  - Batch manufacturing documents for the sample should be submitted or available for inspection
  - Licence for Manufacturer, Packer, Laboratory
  - Proof of registration of the Company and the authorised person.

5.2 FULL SUBMISSION

Covering letter for final submission (this date becomes the date of application) and application fee, **all** screening outcome letters, plus the number of copies of the sets requested by MCC post screening (the amendments in response to the screening outcome must be included in the sets copied). Only the information indicated should be included in each set.

5.2.1 SET 2 (P + A)

- Covering letter in each volume
- Completed MRF2 (screening form)
- All screening outcome letters and amendments if relevant incorporated into the submission
- PARTs 1A to D, 2A (only if not a biostudy), 2C if applicable, 3A to I

5.2.2 SET 3 (NAMES and SCHEDULING)

- Covering letter in each volume
- PARTs 1A, C, and 3B

5.2.3 SET 4 (MEDICINE REGISTER)

- Covering letter in each volume
- PARTs 1A, C, 3B,
- PART 3E front page with manufacturing sites *only* if more than one site is involved where sites are linked to specific processes and 3Fb) if more than one site is involved and sites are linked to specific processes i.e. is more detailed than in PART 1Ab)

5.2.4 SET 5 (SCHEDULING NCE)

- Covering letter in each volume
- PARTs 1A, C, and 3B
- PARTs 2B, 2D and 2E

5.2.5 SET 6 (CLINICAL AMRP)

- Covering letter
- PARTs 1A to D, and 2B or 2D and 2E, as applicable

5.2.6 SET 7 (CLINICAL & BIOLOGICAL)

- Covering letter in each volume
- PARTs 1A to D, 2B, or 2D and 2E, 3B, 4 and 5.

5.2.7 SET 8 (BIOSTUDY or OTHER)

- Covering letter in each volume
- Completed MRF2 (screening form)
- All screening outcome letters and amendments if relevant incorporated into the submission
- PARTs 1A to D, 2A, 2C if applicable, 3A to I, 4 and 5.

5.2.8 Summary table of the sets generally required for applications

	Screening	*P+A*	*Names Scheduling Clinical generic*	*Register Medicine*	*Scheduling NCE*	*Clinical AMRP*	*Clinical*	*BA BE or Other*
SET	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**
New Chemical Entity medicines	1	3	~~5~~ 3	1	1	-	1	-
New Chemical Entity Biological medicines	1	~~5~~ 6	~~5~~ 3	1	1	-	3	-
Medicines with Pre-clinical & Clinical data	1	3	~~5~~ 3	1	-	-	1	-
Biological medicines with Pre-clinical & Clinical data	1	~~5~~ 6	~~5~~ 3	1	-	-	3	-
AMRP	1	3	~~5~~ 3	1	-	1	-	-
AMRP if NCE	1	3	~~5~~ 3	1	1	1	-	-
Medicines with dissolution or other data (including solutions and injections)	1	-	~~5~~ 3	1	-	-	-	3
Medicines with biostudy(ies)	1	2	~~5~~ 3	1	-	-	-	2

5.3 Acknowledgement of receipt

An acknowledgement letter will be sent to the applicant and evaluation of the application will proceed on receipt of the additional copies.

5.4 Communication

The applicant will not be permitted to communicate directly with the evaluator. All queries and concerns should be communicated through the secretariat.

The format of responses to Committees' recommendations and Council resolutions is addressed in the Amendments guideline.

6 EXPEDITED REVIEW PROCESS (FAST-TRACK)

The Medicines Control Council may, under certain circumstances, (as in most other national drug regulatory authorities) speed up the registration process for specific medicines that have important therapeutic benefit and which are required urgently to deal with key health problems. In such cases, an accelerated review system is applied. For further information refer to Regulation 5 of the Act.

The applicant should submit an expedited review request to the Minister of Health ~~and a copy thereof~~ for the attention of the Registrar of Medicines, before submitting the full application for screening. A copy of the approval letter must be submitted with the application. Products that will be considered for expedited review are:

- Medicines on the Essential Drugs List (EDL)
- New Chemical Entities that are considered essential for national health but do not appear on the Essential Drugs List.

6.1 MEDICINES ON THE EDL

A declaration from the applicant that such a medicine appears on the EDL is required.

6.2 NEW CHEMICAL ENTITIES

The following should be submitted with the application:

- A written notification from the Minister to the effect that the medicine is considered essential to national health;
- an expert report (which is not more than 2 (two) years old;
- a package insert (where the product has been approved) and
- a summary basis for the registration (SBRA) (refer to Clinical guideline for details of an SBRA).

The Registrar shall notify the applicant within 30 days of the date of receipt of the application whether or not the application is to be subjected to the expedited registration process as stipulated in Regulation 5 of the Act.

The Council may request any information with respect to an application under consideration and the information should be submitted by the applicant within a period indicated by Council, failing which the Council may reject an application.

The Council shall, within 9 months from the date of receipt of the application by the Registrar, make a decision with regard to the application and inform the applicant of such decision.

7 ABBREVIATED MEDICINE REVIEW PROCESS (AMRP)

The AMRP is a system initiated by Council to limit the evaluation time of pharmaceutical products that are registered in countries with which the Council aligns itself, if the evaluation report is readily available.

The abbreviated medicine review process is based mainly on the expert reports of the pharmaco-toxicological and clinical data. It should be noted that the AMRP is an abbreviated **evaluation** process and not an abbreviated **application**.

7.1 Only new chemical entities registered with one or more of the authorities with which the Council aligns itself will qualify for AMRP. (Refer to section 3.1.4 of this guideline).

7.2 The applicant should obtain the Expert Reviewers' reports on safety, quality and efficacy from the relevant medicines regulatory authority.

7.3 The certificate of approval of registration of the new chemical entity by one of the recognised registering authorities should be included. (Refer to section 3.1.4 of this guideline).

7.4 Written confirmation that the proposed package insert is based on the package insert and the complete dossier of the licensing country is required.

Apart from the approved package insert on which the submission is based, the package insert of the other countries where registration has been approved, should also be submitted.

7.5 Written confirmation that the data submitted to the MCC are identical to that submitted to the authority which has granted approval should be given. Raw data of experimental and clinical studies should be excluded. A letter authorising the MCC to contact the relevant MRA for an evaluator's report or assessor's report should be included.

7.6 Expert reports on chemical-pharmaceutical, pharmaco-toxicological and clinical documentation should be included.

7.7 Relevant correspondence between the applicant and the registering authority including the negative (e.g. queries, non-acceptance of certain claims/statements) as well as the positive correspondence should be included.

7.8 Written confirmation that the formulation applied for is identical to that approved by the registering authority should be given.

7.9 Applications for AMRP can only be accepted if the product has been approved by the said authorities within the last three years of the licence in the licensing country.

8 EXPERT REPORTS MRF1 PARTs 2C to E

8.1 *Expert report:* an objective and encompassing report on all the relevant aspects in the specific field of expertise of the reporter who is familiar/acquainted with the development of the product.

8.2 *Expert reviewer's report:* the report of the regulatory reviewer, after evaluation of the data submitted in support of approval for licensing.

8.3 All issues and properties of the product in the submission should be clearly identified and critically discussed in the Expert Reports in light of current scientific knowledge.

8.4 The Expert Report should address all the aspects in the package insert.

8.5 A list of the key references used in compiling the Expert Report should be attached.

8.6 The *curriculum vitae* of the expert should be included.

8.7 If the application for registration complies with the requirements for the AMRP system, it should be further determined whether the Expert Report reveals all the necessary information for Council to make a considered decision on registration. For this purpose an AMRP-SBRA should be drafted. An AMRP-SBRA should be based on the information in the Expert Reports only. Furthermore, written confirmation that the AMRP-SBRA was compiled from the Expert Report only, should accompany the AMRP-SBRA submission.

9 PROPRIETARY NAME POLICY [Section 15 (3) of the Act]

Refer to the current version of the guideline on Proprietary Names for Medicines

~~The term "PROPRIETARY NAME" is defined in the Regulations pertaining to the Act as follows:~~

> ~~"PROPRIETARY NAME, in relation to a medicine, veterinary or complementary medicine and medical device, means a name:~~
>
> ~~a) that is unique to a particular medicine, veterinary, or complementary medicine and medical device;~~
>
> ~~b) that is generally identifiable and approved in respect of that specific medicine, veterinary, or complementary medicine and medical device in terms of the Act. The Act states that a medicine, complementary medicine, veterinary medicine or device should be registered under such name as the Council may approve. "~~

~~In evaluating the safety of a medicinal product during the registration process, the Medicines Control Council is obliged to consider whether the proposed proprietary name of such a product could potentially pose public health and safety concerns or if it may be misleading. Mistaking one drug for another because of similar proprietary names can have serious consequences.~~

~~Since many medication errors are caused by look-alike and sound-alike medication names, it is evident that public health considerations should be paramount in determining whether a particular proprietary name may be used for a medicinal product.~~

~~In order to enable applicants to propose acceptable proprietary names for medicinal products, it is essential that:~~

~~a) consistent, non-arbitrary criteria are applied when reviewing the acceptability of proposed proprietary names;~~

~~b) a transparent procedure is in place for evaluating the acceptability of proposed names.~~

~~The MCC has adopted the WHO naming policy with adaptations.~~

~~9.1 SAFETY CONCERNS~~

~~In assessing the merits of a proposed proprietary name, the first and foremost issue considered is that of patient safety. Applicants are advised to consider the following guidelines bearing in mind the paramount criterion of "potential safety risk".~~

9 Proprietary Name Policy – Safety concerns - continued

9.1.1 The proposed proprietary name should not convey misleading therapeutic or pharmaceutical connotations.

An example may be the use of the name "SEDINAX" for a product intended to treat pain and fever containing only an analgesic or the name "PAINKID" for a product not indicated for paediatric use.

Similarly, the name "CARDIODORON" should only be used for medicinal products for the treatment of cardiovascular diseases.

9.1.2 A proprietary name may include a pharmacological/therapeutic connotation, provided that it is in line with the indications in the package insert. Each application, however, will be evaluated on merit.

9.1.3 It is important to bear in mind the claims made in the package insert in relation to the proposed name of the product, when considering the acceptability of names, hence the requirement of submission of package inserts in all instances.

9.1.4 The use of "umbrella/brand types" of names across products in associated therapeutic categories generally may not pose a problem. However, when such names are used for products in different commodity categories, the misrepresentation of non-medicines as medicines and vice versa would be considered unacceptable. It is the responsibility of applicants to include precautionary statements of usage of these brands, simultaneously, so as to inform patients of their correct use.

9.1.5 The proposed proprietary name should not be misleading with respect to the composition of the product.

9.1.6 The proposed proprietary name should not be liable to cause confusion in print, handwriting or speech with the proprietary name of another product.

9.1.7 For example, the names "AMYTAL" (barbiturate) and "AMITOL" (multivitamin) could have serious safety implications if a barbiturate is supplied to a patient instead of a vitamin.

9.1.8 When the name being applied for is identical/too similar to a name already approved for another product, applicants will be advised that the proposed name is too close to an existing name. Only if the existing product is registered will the name be disclosed. Disputes regarding similarity of names not identified by the Medicines Control Council at the time of registration/change are the responsibility of applicants, not the Medicines Control Council. If however, valid safety concerns are identified, the applicant will be advised accordingly.

9.1.9 Names which are identical to, or which are similar to, the names of products previously marketed will generally not be favourably considered regardless of whether such products are dormant or not.

9.1.10 If an objection is raised on the basis of similarity between the proposed proprietary name and an existing name, or name raising a risk of confusion in print, handwriting or speech, the objection will be evaluated taking into account other potentially distinguishing factors, such as:

- The pharmaceutical form
- The route of administration
- The indication and legal status/condition of supply

After assessing these factors as a whole, a decision on whether the proposed proprietary name poses a potential safety risk will be made.

9.2 INTERNATIONAL NON-PROPRIETARY NAMES' (INN) CONCERNS

The Medicines Control Council subscribes to the WHO guideline in respect of the protection of INN-stems and encourages the pharmaceutical industry to be continually aware of this issue (Document No. "WHO/EDM/QSM/99.6").

9.2.1 A proprietary name should not contain an INN-stem (as published by the WHO). The WHO stresses the importance of the need to protect INN-stems. Using a common stem indicates the relationship of pharmacologically related substances, which in turn forms part of the INN name. The orderly development of generic nomenclature could be hindered if these stems are not protected. The sentiments of the WHO in this regard are shared by the MCC, and are taken into consideration when considering proprietary names.

9.2.2 For example, "-ac" is an INN-stem for anti-inflammatory agents of the ibufenac group, and a proprietary name ending with "ac" would not be acceptable regardless of the API, which it contains. The reasons are protection of the stem and confusion, which could arise if the product does not contain an anti-inflammatory agent of the ibufenac group.

9.2.3 A proprietary name commencing with, or containing "ac" in another position within the name could, however, be considered.

9.2.4 The derivation of proprietary names from INN names, i.e. generic names is discouraged, as this practice could lead to confusion. For example, the choice of the name "METAPERAMIDE" for a product containing loperamide, could cause confusion if the product contains another loperamide type compound.

9.2.5 If a proprietary name is derived from a generic name, it should not be similar to the generic name, since it can lead to confusion. For example, the name "TRIMAZOLE" could be interpreted as being an antiprotozoal of the metronidazole group, an antifungal of the miconazole group or a brand of co-trimoxazole, even though the name does not contain an INN-stem for any of these groups.

9.2.6 In the case of single component generic medicines, applicants are encouraged to market their products under the complete generic name followed or preceded by their company name, acronym or other distinguishing feature.

9.2.7 Exceptions may be considered for the anti-retrovirals if these have been previously approved by a recognised Regulatory Authority and are accompanied by a motivation.

9.3 OTHER CONCERNS

9.3.1 The issue of whether a particular proprietary name may constitute an infringement of another entity's intellectual property rights cannot be one of the Medicines Control Council's concerns and is, therefore, not taken into account during consideration of the acceptability of a proposed proprietary name.

9.3.2. The proprietary name should preferably consist of only one word and should avoid qualification by letters or numbers. The use of short qualifications/abbreviations that do not carry an established and relevant meaning is unacceptable. Promotional qualifications/abbreviations/manufacturer's codes are also unacceptable. However, if other qualifications/abbreviations are to be included, appropriate justification should be provided (e.g. for insulin mixtures the proprietary name could be followed by a number or letter representing the fast-acting component of the mixture).

9.3.3. The use of descriptive abbreviations may also be acceptable if there is a need to distinguish different routes of administration for the same medicinal product, e.g. IV: intravenous, IM: intramuscular, SC: subcutaneous.

9.3.4 A proprietary name should not convey any promotional message with respect to the use of the product.

9.3.5 Use of capitals in proprietary names should reflect the proposed/approved trademark registration.

9.3.6 A different proprietary name is required for a medicinal product containing a pro-drug of another product containing the parent active substance. (An umbrella name is not acceptable).

9.3.7 In the case of a switch from "prescription" to "non-prescription" status for limited indications only, a new proprietary name should be chosen for the de-scheduled product.

9.3.8 Any phrase that implies superiority, including use of animal species associated with speed or strength, or implies superiority over other products, is not allowed.

9.3.9 The meaning of abbreviations, symbols, numerals and names, which are in a language other than English, should be explained in the covering letter accompanying an application. With regard to phrases which occur in the proprietary names of products, and which are not English, applicants are requested to submit to the Medicines Control Council, reputable interpretations / translations / explanations of the phrases in question, in relation to the claims made for the product; i.e. the intended use thereof.

~~*9 Proprietary Name Policy - continued*~~

~~9.3.10 Proprietary names will only be evaluated as part of a new application for registration or application for change. Requests for evaluation of acceptability of possible proprietary names prior to submitting a formal application will not be processed.~~

~~9.3.11 Proprietary names cannot be reserved for applications that have not yet been submitted.~~

~~9.3.12 Current policy will not be applicable to line extensions of older products unless a valid safety aspect has come to the fore, in which case, the applicant will be advised accordingly.~~

~~9.3.13 A list of names that are regarded as potentially misleading is available on request. Names, which may lead to self-diagnosis in conditions requiring professional diagnosis, or names implying efficacy that cannot be substantiated for the API(s), are included on this list.~~

~~9.3.14 As stated above, legislation determines that the name under which a medicine is registered shall be unique. The importance of this requirement cannot be over-emphasised, particularly when developing a range of products. Each strength and/or dosage form requires a unique name. Applicants should examine all available resources to establish that names are unique. Motivations should accompany applications where relevant, e.g. to justify the use of an identical or very similar name which appears in Martindale The Complete Drug Reference/other reference book for a product not containing the same ingredient(s) and which may be on the market elsewhere.~~

~~9.3.15 As with all registration matters, applicants always have the opportunity to submit comments in the event of a difference in opinion. Such comments will be forwarded to Council for consideration.~~

10 MANUFACTURING REQUIREMENTS

Only medicines manufactured, packed and quality controlled at sites compliant with the current principles of Good Manufacturing Practice (GMP) as prescribed by the Medicines Control Council will be considered for registration.

Council's general policy is that the standard to be used to assess compliance with current Good Manufacturing Practice (cGMP), is the South African Guide to Good Manufacturing Practice (SA guide to GMP) (latest edition) as minuted:

> "…that the Guide to Good Pharmaceutical Manufacturing Practice as amended, which was prepared jointly by the secretariat and the PMA, be considered as the standard determined by Council as referred to in the specific condition for registration of a medicine, namely, that the applicant shall ensure that the medicine is manufactured and controlled in accordance with Good Manufacturing Practice as determined by Council."

Under Section 22C of the Act, all South African manufacturers should be licensed (effective 2 May 2004).

The aim of these licensing requirements and standards is to protect public health by ensuring that medicines meet defined standards of quality and are manufactured in conditions that are clean and free of contaminants.

The Act requires that overseas manufacturers of medicine supplied to South Africa should comply with the same or equivalent manufacturing standards as expected of South African manufacturers.

Evidence in relation to compliance with Good Manufacturing Practices of the overseas manufacturer is required for applications for registration of imported medicines. When acceptable evidence of GMP compliance is not available, overseas manufacturers are inspected by the GMP Inspectorate before registration of the medicine is approved.

11 SAMPLES

All medicine applications for registration must include a sample of a unit pack, Section 15(1) of the Act.

12 STANDARDISED PACKAGE INSERT WARNINGS AND INFORMATION

In addition to the warnings required by Regulations 8, 9 and 10 of the Act, certain warnings and other information should be included in the package insert, unless the applicant can provide convincing evidence to the contrary. The wording need not be identical.

Please refer to the current version of "Package Inserts for Human Medicines: Standardised Texts" guideline.

13 CODING OF SUBMISSIONS

Coding of applications/submissions/correspondence facilitates distribution, processing and tracking. The coding of uncoded items occurs after receipt at Registry on the Ground floor, Room NG090, Civitas Building (see 2.5) where documents are logged into the internal mail/post system.

The following codes, placed on the **first page of each cover letter in bold lettering,** should be used for submissions to the MCC to reduce the possibility of misdirection.

Each code consists of three letters. The first letter represents the Section or Unit where the responsibility or function resides. The last two letters indicate the type of application or nature of the request. It should correspond with the specific request(s) stated in the covering letter.

When more than one code is applicable, each should be indicated, for example, VMC/VPC/VLC. A separate application should be submitted per Unit.

13.1 PRE-REGISTRATION (PHARMACEUTICAL AND ANALYTICAL)

The Pre-registration Unit is responsible for pre-registration applications and responses to resolutions and matters pertaining to a medicine during review for registration.

The following codes are recommended for applications and correspondence for the Pre-registration Unit:

CODE	SUBJECT	SUPPORTIVE DOCUMENTATION
PGC	Enquiries that are not technical or are not product-specific	Application letter and supporting information / motivation
PBE	Bioequivalence protocol	Cover letter, protocol, application form and any additional data
PBV	Bioequivalence protocol amendments (variations)	Cover letter, variations
PPI	Package insert: involving Composition, Identification, Presentation, and Storage conditions	Annexure 1 PART 1C / Module 1.3
PFA	Formulation change: Additions, deletions, reduction or increase in API or IPI, overages, potency calculations and other formulation changes.	Annexure 2 PARTs 3B and 3E / Modules 3.2.P.1 and 3.2.P.3.2
PPR	Responses to P&A Committee recommendations	Copy of recommendation, data, amendment schedule – see Amendments guideline
PRS	Source of API(s), Method of synthesis, Proof of equivalence (physical and chemical), Certificate of Analysis (CoA) for the API, Drug Master File.	Annexure 3 PART 3A / Modules, 3.2.R.3, 3.2.S
PRM	Specifications and control procedures for APIs and IPIs, release criteria and laboratories including frequency of testing	Annexures 4, 5 and 6 PART 3C / Modules 3.2.S.4 (FPP), 3.2.P.4
PFP	Specifications and control procedures for the final product	Annexure 7A and 7B PART 3F / Module 3.2.P.5

CODE	SUBJECT	SUPPORTIVE DOCUMENTATION
PVA	Manufacturing and analytical process validation protocol and report	Annexures 7B and 11 PARTs 3E and 3F / Modules 3.2.P.3 & 3.2.P.5
PCA	Specifications and control procedures for Containers.	Annexures 8A and 8B PART 3D / Module 3.2.P.7
PSE	Stability data, shelf-life confirmation and extension, Preservative efficacy and effect on ageing	Annexure 10 PART 3G / Module 3.2.P 8
PMP	Manufacturing and packaging process change and in-process control changes	Annexure 11, PART 3E / Module 1.5.2.3, 3.2.P.3, 3.2.P.2.3
PFR	Foreign registration, authorisation and package inserts (English translations)	Annexure 12 PART 1D / Module 1.10
PEF	Efficacy, Bioavailability, Bioequivalence, Proof of efficacy: acid neutralisation, inhibition zones, skin blanching, and membrane permeability.	Annexure 13 PART 2A / Modules 1.11, 2.5 and 2.7.1 (if applicable), 3.2.R.1, 5.3.1
PPD	Pharmaceutical development: batch numbers and sizes, source of product and of API, dates of manufacture.	Annexures 16 cross-referenced to Annexures 7, 10, 11 and 13 PART 3H xref to 2, 3E, 3F, + 3G Module 3.2.P.2

13.2 POST-REGISTRATION AMENDMENTS (PHARMACEUTICAL AND ANALYTICAL)

The Post-registration Unit is responsible for

a) changes of the manufacturer, packer and testing laboratories (FPRC and FPRR);

b) pharmaceutical changes or amendments to the registration dossier; and

The following codes are recommended for applications and correspondence for the Post-registration Unit: (Refer to the Amendments guideline for the required documentation)

CODE	SUBJECT
VGC	General correspondence involving enquiries on policy issues and changes that are not product-specific
VMC*	Change of manufacturer or site of manufacture, name and address change of manufacturer
VPC*	Change of packer, name and address change of packer
VLC*	Change of laboratory, name and address change of laboratory (FPRC or FPRR)
VPI	Package insert changes involving the Composition, Identification, Presentation and Storage conditions only.
VFA	Formulation change: Additions, deletions, quantity reduction or increase in API or IPI, overages, potency calculations and other formulation changes.
VRS	Change in source of API or method of synthesis
VRM	Specifications and control procedures for APIs and IPIs, release criteria and laboratories including frequency of testing
VFP	Specifications and control procedures for the final product
VVA	Manufacturing and analytical process validation protocol and report
VCA	Specifications and control procedures for Containers
VSE	Request for shelf-life, shelf-life confirmation; extension and reduction (including batch specific);; Preservative efficacy and effect on ageing
VMP	Manufacturing and packaging process changes and in-process control changes

CODE	SUBJECT
VFR	Foreign registration; notification of foreign submissions, approval or outcome
VEF	Proof of efficacy
VPD	Pharmaceutical development
VPU	Partial update for MBR1, MRF1 to ZA-CTD only
VUR	Full Update for registered medicines including those with a change in the proprietary name, manufacturer, packer and/or testing laboratories
VUO	Full Update for "Old Medicines" including those with a change in the proprietary name, manufacturer, packer and/or testing laboratories
VIA	Applications for exemption from post importation testing of medicines
VRR	Response to query or recommendation from the unit
VSB Urgent	Submission of data/information on request by the Unit with a specific deadline. These will be transferred to the Unit immediately after log-in for finalisation of applications. Failure to supply the required information within the specified period will result in relegation of the application to the end of the queue.

13.3 INSPECTORATE AND LAW ENFORCEMENT

The Inspectorate and Law Enforcement Unit is responsible for

a) inspection and evaluation of sites for the manufacturing, packing, and testing of medicines nationally and internationally, as well as inspection and evaluation of all storage and distribution sites for medicines;

b) investigation of complaints regarding registered and unregistered medicines;

c) monitoring compliance to the Act and prosecution in case of non-compliance;

d) monitoring the importation and exportation of medicines in consultation with customs authorities;

e) evaluation of proprietary names and changes thereto.

The following codes should be used for applications and correspondence for the Inspection and Law Enforcement Unit: (Any supporting documentation should be included with the cover letter.)

CODE	SUBJECT
BGC	General correspondence involving enquiries on policy and administrative issues
BAI	Advertising enquiries
BCA	Advertising complaints - legal
BCM	Complaints - manufacturing
BCQ	Complaints - quality
BEP	Export permits
BEQ	Exemption from any provision of Act 101 in terms of section 36
BFG	Site master file
BFP	Inspection follow-up
BFS	WHO free sale certificate / Certificate of Pharmaceutical Product
BII	Request for inspections
BIP	Import permit/MBR 20 Bill of Entry
BIR	Response to inspection reports

CODE	SUBJECT
BLA	Applications for licensing of manufacturer, wholesaler or distributor (Section 22C of the Act)
BLE	Law enforcement – complaints/theft of medicines
BLV	Application for amendment to a licence
BLM	Labelling matters
BNC	Application for proprietary name change
BOA	Request for once-off approval
BPP	Request for/inquiry on repackaging
BSR	Request for scheduling/Scheduled substances
BGMP	Request for GMP certificate

13.4 CLINICAL EVALUATION

The Clinical Evaluation Unit is responsible for

a) evaluation of clinical and pre-clinical data

b) evaluation of clinical aspects of the package insert and relevant changes to package insert;

The following codes should be used for applications and correspondence for the Clinical Evaluation Unit: (Any supporting documentation should be included with the cover letter.)

CODE	SUBJECT
CGC	General correspondence
CDR	Clinical data in support of registration
CDP	New indication/dosage schedule, other major changes for registered /old medicines
CPR	Package insert registration
CPA	Package insert amendments for clinical aspects of registered/ old medicines
CIS	PIL submissions for clinical aspects of registered / old medicines
CIA	PIL amendments for clinical aspects of registered / old medicines
CFT	Fast track requests
CSU	Periodic safety update reports
CUSRN	Urgent Safety Restriction Notice

13.5 CLINICAL TRIALS

The Clinical Trials Unit is responsible for the evaluation of

a) clinical trial applications and clinical trial amendments;

b) reports of adverse events arising from a clinical trial;

c) applications for named patient use of unregistered medicines;

d) applications for the use of unregistered medicines for clinical trial purposes.

The following codes should be used for applications and correspondence for the Clinical Trials Unit: (Any supporting documentation should be included with the cover letter.)

13.5 CLINICAL TRIALS continued

CODE	SUBJECT
TGC	General correspondence
TCA	Application to conduct a clinical trial
TCV	Amendment of an existing clinical trial
TCR	Response to CTC resolution
TAE	Report of adverse drug events arising from a clinical trial
TUM	Applications in terms of Section 21 of the Act (unregistered human medicines)

13.6 COMPLEMENTARY MEDICINES

The Complementary Medicines Unit is responsible for

a) evaluation and review of applications for the registration of Complementary Medicines;
b) receiving and collating initial and subsequent responses to the call-up notice as published in Government Gazette Number 23128 (22 February 2002);
c) evaluation and review of applications for the amendment of the register for Complementary Medicines;
d) issue of temporary permits for the manufacture, distribution and dispensing of Complementary Medicines.

N.B. Where applicable, the first code should be used for applications for registration of medicines. The second code should be used for amendments and other enquiries regarding registered medicines.

Supportive documentation for applications

Cover letter, Front Page & Annexures 1, 2 and 12 / Cover letter PARTs 1A, 1C 1D, 3B

CODE not registered	CODE registered	SUBJECT
MAR	MAX	Anthroposophical Medicines
MBR	MBX	Aromatherapeutic substances/ medicines
MCR	MCX	Ayurvedic Medicines
MDR	MDX	Chinese Traditional Medicines
MER	MEX	Energy substances
MFR	MFX	Homoeopathic Medicines
MGR	MGX	Nutritional substances with medicinal claims
MHR	MHX	Western Herbal Medicines
MIR	MIX	Unani-Tibb Medicines
MJR	MJX	Combination Homoeopathic/Flower Essence
MKR	MKX	Combination Complementary Medicines
MLR	MLX	Other Complementary Medicines
MGC		General correspondence not product-related

13.7 BIOLOGICALS

The Biologicals Sub-Unit is responsible for

a) biological pre-registration applications and responses to resolutions, and matters pertaining to biological medicines during review for registration
b) evaluation of technical changes to registered biological medicines and "old" biological medicines
c) evaluation of clinical aspects of the package insert and relevant changes to package insert for biological medicines
d) technical support to other units with respect to biological matters.

The following codes should be used for applications for the Biologicals Evaluation Sub-Unit:
(Any supporting documentation should be included with the cover letter.)

CODE	SUBJECT
QGC	General correspondence
QDR	Clinical data in support of registration
QDP	New indication/dosage schedule, and other major changes to the package insert of registered / old biological medicines (excluding the Composition, Presentation, Identification, and Storage Conditions)
QPI	Package insert for registration of biological medicines
QPA	Package insert amendments for clinical aspects of registered / old biological medicines
QSU	Periodic safety update reports for biological medicines
QSV	Annual strain update

Note: For biologicals:

- for any other activities not described above, the applications and/or queries should be directed to and properly coded for the relevant Units.
- relevant supportive documentation should be attached as per the Annexures described in the MBR1 form for biological medicines/ or as described in the MRF1 PARTs.

13.9 OPERATIONS AND ADMINISTRATION

The Operations and Administration Directorate is responsible for the following:

a) receiving and acknowledging applications for registration of medicines and for amendment of registration dossiers;
b) receiving correspondence dealing with administrative processes, registration and other application forms, and registration policy information documents and guidelines;
c) receiving fees payable to the Registrar;
d) applicant transfers and applicant name and address changes ;
e) proprietary name changes in consultation with the Names Committee;
f) cancellations of registered medicines and withdrawal of applications for the registration of medicines
g) co-ordination of Council and Committee reports on the evaluation of medicines;
h) preparation and distribution of Council and Committee documents;
i) handling personnel matters; and
j) processing of Council and Committee claims.

The following codes should be used for applications for the Operations and Administration Directorate:

CODE	SUBJECT
AGC	General correspondence: Routine enquiries, Registration policy and Registration queries
AFR	Screening, and Application for registration fees
AFJ	Retention fees
ARF	Registration fees
APF*	Payment of all other fees
ACC	Committee and Council claims
ACR	Evaluators and Chairperson reports
ACM	Council Documentation
ARR	Response to Council Resolution
AHR	Human Resources issues
AIM	Information Management matters
ANA	Submission of new applications and post-screening copies
VAC**	Applicant transfer, name and address change of the applicant
VAA**	Address only change for the HCR only
VNC**	Updates following a proprietary name change approval
VCR	Cancellation of registered medicine
VCO	Withdrawal of an application for registration of a medicine

** Refer to section 2.9*

**The applications are first evaluated by the Inspectorate – see code BNC
These submissions submitted in first time CTD format, will first be evaluated by the Post-registration unit.

14 UPDATE HISTORY

Date	Reason for update	Version & publication
May 2003	First publication released for implementation and comment	Version 1 May 2003
November 2003	Release for additional comment	Version 1, Nov 2003
November 2003	Deadline for comment	
December 2003	Date for finalisation/implementation	Version 1, Dec 2003
May 2006	General editing – page numbers in index, 2.5, 3.1.2, 3.1.3 a) b), 4.1, 4.4, 4.17, 8, 10, and amendment of sections 2.2.2, 2.9, 3.1.4, 4.2, 4.5, 4.6, 4.7, 4.14, 5, 5.2, 13.1, 13.2, 13,3, 13.4, 13.5, 13.6, 13.7, Attachment A	May06 v2, June 2006
12 July 2006	Date for implementation	
May 2007	Additions to 2.7.5, 2.10.5, 13.4; amendments to 4, 5.2, Attachment A	Version 3, May 2007
25 June 2007	Date for implementation	
March 2008	Amendment of sections 2.9, 2.10.5, 3.1.3 a), 4, 4.7, 4.10, 5.1, 5.2, 13.3, 13.4, Attachment A	Version 4 March 2008
1 May 2008	Date for implementation – except 3.1.3 a), b)	Version 4 April 2008
1 August 2008	Date for implementation of 3.1.3 a), b)	
August 2009, January 2010	1 Removal of section 12 "Standardised package insert warnings" and inclusion in new "Package Insert Standardised Texts" guideline 2 Removal of Attachment B re package insert information 3 Amendment to section 4.9	Version 5 January 2010
March 2010	Date for implementation	
June 2010	Inclusion of references to the ZA CTD – sections 2.11, 3, 4, 4.14, 5, 13.1	Version 6 June 2010
1 July 2010	Date for implementation	
	Amendment of section 2.5	
21 June 2010	Date for implementation	
	Amendment, for clarity, of sections 2.10.5 k), 3.1.2, 3.1.3 c), 3.1.4, 3.4, 3.5, 4.3, 4.5, new 4.6, 4.9 (original 4.8), 4.10 (original 4.9), 4.17, 5.2, 5.4, 13.3, 13.9 & new section 3.1.1 p)	
With immediate effect	Date for implementation	
March 2011	Amendment of name of "Post-registration Amendments", "Guidance for submission of SA CTD/eCTD Module 1" guidelines, and administrative amendments: Sections 2.5, 3, 3.1.1o), 4, 4.5, 5, 5.2.6, 5.2.8, 5.4, 13, 13.1, 13.2, Attachment A; new 4.11 and renumbered. Amendment of 2.2.2 for clarification & in line with CTD guideline. Clarification of 4.3 & 4.4 in accordance with Biostudies guideline 3.9 & 4.4 and insertion of 4.11 in accordance with P&A guideline 2.1.2.11. Deletion of "independent" in 6.2 & 8.1.	Version 7 March 2011

Date	Reason for update	Version & publication
	Insertion of "(including batch specific)" for shelf-life extension under working code VSE in accordance with Amendments guideline Type C Inspectorate category 19.	Version 7 March 2011
With immediate effect	Date for implementation	
June 2011	13.1 Correction	Version 7_1, June 2011
July 2012	Deletion of section 9 on Proprietary Names, Attachment A (pre-screening check-list) Amendment of 2.11, 3.1.4, 4, 4.2, 5.2.8, 6, 13.2, 13.9	Version 8, August 2012
With immediate effect	Date for implementation	

ATTACHMENT A

To be replaced with new screening template used in the EDMS from 1 July 2010

PRE-SCREENING CHECK LIST

PRODUCT NAME:
COMPANY:

COMPLIANCE WITH ADMINISTRATIVE CRITERIA	*	OFFICIAL USE	
		YES	NO
Box size (A4 box)			
Number of boxes			
Are the boxes clearly labelled on the side to specify the number and content of each box, e.g. set numbers, PARTs, sample, covering letter, cheque or proof of payment and product identification code? Does a colour sticker indicate the screening phase? (red = screening; green = post screening)			
Is the dossier correctly bound? (No lever arch files, metal file fasteners or ring binders, 4 cm thick including binder but not over-full for the binder used)			
Is each PART of the dossier properly marked with tabs according to the cover letter?			
Does each PART of the dossier have a Table of Contents?			
Is each page of the dossier numbered?			
Is a sample included in an envelope? (screening copy)			
Is the cheque or proof of payment for the screening fee or application fee, as applicable, submitted in a separate envelope, with the covering letter, but no other documents attached?			
Is the type of application indicated? (section 2.7.1 to 2.7.5 of General Information guideline) Is an approval letter regarding "fast track" status included if relevant?			
Is the completed screening form MRF2 included? (screening and post-screening copies)			

**** to be completed by the applicant***

Name and signature of applicant:	**Date:**

If there is a "NO" answer to any question above, immediately return the dossier to the applicant as incomplete						
Outcome:	Accept		Hold		Return as Incomplete	
Name and signature of MCC official:						
Date:						