Item 10. Clear descriptions of outcome measures. If surrogate markers are being used when the drug is intended to decrease mortality, etc., they should be justified. Ensure that all intended measurements necessary. Ensure that no intended measurements are likely to be of more risk to participants, than they are likely to provide useful information.

Item 11. Indicate how known or likely adverse events will be dealt with. Clearly describe components requested in Section 3.

Item 12. Ensure that all components are adequately addressed. Answer the question, 'Is this the best statistical approach / method for the outcome measures / objectives?' Clearly indicate reasons for doing an interim analysis or for not doing one.

Item 13. Comment on the adequacy of each of the ethics components requested in terms of the proposed trial. Pay special attention to the Patient Information Leaflet and the Informed Consent process / form. Have they been properly modified for SA? Ensure that if any blood specimens are to be archived or kept for genetics research, that this is appropriately addressed in a separate consent form, and that it makes the various ethical aspects of this clear.

Item 14. Any other comments on the proposed trial – including the quality of the protocol, (e.g. well or poorly written / structured; or does it look like it was simply downloaded from a website?); the extent to which the four questions (which the reviewer must answer) can be satisfactorily answered; any other relevant information which the reviewer could take into account in making a recommendation to the CTC / MCC.

B. DECLARATION BY PRINCIPAL INVESTIGATORS

Name:

Title of Trial:

Protocol:

Site:

1. I have read and understood Item 1.5.5 on page 5 and Section 3 (pages 14 – 20) 'Responsibility of The Principal Investigator (PI) and Participating Investigators' of the *Clinical Trials Guidelines of the Department of Health:2000.*

2. I have notified the South African regulatory authority of any aspects of the above guidelines with which I do not / am unable to, comply. (If applicable, this may be attached to this declaration.)

3. I have thoroughly read, understood, and critically analysed (in terms of the South African context) the protocol and all applicable accompanying documentation, including the investigator's brochure, patient information leaflet(s) and informed consent form(s).

4. I will conduct the trial as specified in the protocol.

5. To the best of my knowledge, I have the potential at the site(s) I am responsible for, to recruit the required number of suitable participants within the stipulated time period.

6. I will not commence with the trial before written authorisations from the relevant ethics committee(s) as well as the South African Medicines Control Council (MCC) have been obtained.

7. I will obtain informed consent from all participants or if they are not legally competent, from their legal representatives.

8. I will ensure that every participant (or other involved persons, such as relatives), shall at all times be treated in a dignified manner and with respect.

9. Using the broad definition of conflict of interest below, I declare that I have no financial or personal relationship(s) which may inappropriately influence me in carrying out this clinical trial.

[*Conflict of interest exists when an investigator (or the investigator's institution), has financial or personal relationships with other persons or organizations that inappropriately influence (bias) his or her actions.*]*

*Modified from: Davidoff F, et al. Sponsorship, Authorship, and Accountability. (Editorial) JAMA Volume 286 number 10 (September 12, 2001)

10. I have* / have not (delete as applicable) previously been the principal investigator at a site which has been closed due to failure to comply with Good Clinical Practice. (*Attach details.)

11. I have* / have not (delete as applicable) previously been involved in a trial which has been closed as a result of unethical practices. (*Attach details)

12. I will submit all required reports within the stipulated time-frames.

Signature: Date:

Witness: Date:

C. PROVISIONAL DECLARATION BY CO- AND SUB-INVESTIGATORS AND OTHER STAFF INVOLVED IN A CLINICAL TRIAL

Name:

Title of Trial:

Protocol:

Principal Investigator's Name:

Site:

Designation:

13. I will carry out my role in the trial as specified in the protocol.

14. I will not commence with my role in the trial before written authorisations from the relevant ethics committee(s) as well as the South African Medicines Control Council (MCC) have been obtained.

15. If applicable to my role in the trial, I will ensure that informed consent has been obtained from all participants or if they are not legally competent, from their legal representatives.

16. I will ensure that every participant (or other involved persons, such as relatives), shall at all times be treated in a dignified manner and with respect.

17. Using the broad definition of conflict of interest below, I declare that I have no financial or personal relationship(s) which may inappropriately influence me in carrying out this clinical trial.

[*Conflict of interest exists when an investigator (or the investigator's institution), has financial or personal relationships with other persons or organizations that inappropriately influence (bias) his or her actions.*]*

*Modified from: Davidoff F, et al. Sponsorship, Authorship, and Accountability. (Editorial) JAMA Volume 286 number 10 (September 12, 2001)

18. I have not previously been involved in a trial which has been closed due to failure to comply with Good Clinical Practice.

19. I will submit all required reports within the stipulated time-frames.

Signature: Date:

Witness: Date:

D. DECLARATION BY REGIONAL MONITOR

Name:

Title of Trial:

Protocol:

Site:

20. I have read and understood Item 1.5.7 (p5) and Section 5.1 (p30-33) 'The Monitor' of the *Clinical Trials Guidelines of the Department of Health:2000.*

21. I have notified the South African regulatory authority of any aspects of the above guidelines with which I do not / am unable to, comply. (If applicable, this may be attached to this declaration.)

22. I will carry out my responsibilities as specified in the trial protocol and according to the *Clinical Trials Guidelines of the Department of Health:2000.*

23. Using the broad definition of conflict of interest below, I declare that I have no financial or personal relationship(s) which may inappropriately influence me in carrying out this clinical trial.

[*Conflict of interest exists when an investigator (or the investigator's institution), has financial or personal relationships with other persons or organizations that inappropriately influence (bias) his or her actions.*]*
*Modified from: Davidoff F, et al. Sponsorship, Authorship, and Accountability. (Editorial) JAMA Volume 286 number 10 (September 12, 2001)

24. I have* / have not (delete as applicable) previously been the monitor at a site which has been closed due to failure to comply with Good Clinical Practice. (*Attach details.)

25. I have* / have not (delete as applicable) previously been involved in a trial which has been closed as a result of unethical practices. (*Attach details)

26. I will submit all required reports within the stipulated time-frames.

Signature: Date:

Witness: Date

E. JOINT DECLARATION BY SPONSOR (OR REPRESENTATIVE) AND PRINCIPAL INVESTIGATOR (OR NATIONAL PRINCIPAL INVESTIGATOR) CONCERNING SUFFICIENT FUNDS TO COMPLETE STUDY*

Title:

Protocol:

I, <full name>, representing <sponsor or representative)

And

I, <full name>, Principal Investigator/National Principal Investigator

Hereby declare that sufficient funds have been made available to complete the above-identified study.

Signed Date

SPONSOR (or alternative)
Name
Address
Contact details

Signed Date

PRINCIPAL INVESTIGATOR (or National PI)
Name
Address
Contact details

*Section 4.13, page 26: Clinical Trials Guidelines 2000, Department of Health, South Africa.

F. STANDARDISED WORDING TO BE ADDED TO PATIENT INFORMATION LEAFLET. (PILS)

(Approved by Clinical Trials Committee on 15/07/2002)

If you have questions about this trial you should first discuss them with your doctor or the ethics committee (contact details as provided on this form). After you have consulted your doctor or the ethics committee and if they have not provided you with answers to your satisfaction, you should write to the South African Medicines Control Council (MCC) at:

The Registrar
SA Medicines Control Council
Department of Health
Private Bag X828
PRETORIA
0001

Fax: (012) 323-4474

e-mail: labusa@health.gov.za

G. MCC FORMAT FOR CVS OF INDIVIDUALS PARTICIPATING IN THE CONDUCT OF CLINICAL TRIALS IN SOUTH AFRICA.

Trial:

Protocol:

Designation: (e.g. National Principal Investigator, Investigator (Principal, Co- or sub-), Study Co-ordinator, Regional Monitor, Local Monitor, Contract Research Affiliate)

1. Personal Details
   Name:
   Work Address:
   Telephone Number:
   Fax Number:
   Cell-phone Number:
   e-mail address:

2. Academic and Professional Qualifications
3. Health Professions Council of South Africa (HPCSA) registration number if applicable (or other health professions body registration particulars if applicable – e.g. Nursing Council)
4. Current personal medical malpractice insurance details [medical and dental practitioners]
5. Relevant related work experience (brief) and current position
6. Participation in clinical trials research in the last three years (title, protocol number, designation) [If multiple trials, only list those with relevance to this application, or in the last year.]
7. Peer-reviewed publications in the past 3 years
8. Date of last GCP training (as a participant or presenter)
9. Any additional relevant information supporting abilities to participate in conducting this trial. [briefly]

Signature: Date:

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MEDICINES CONTROL COUNCIL

DEPARTMENT OF HEALTH
Republic of South Africa

MEDICINES CONTROL COUNCIL

SCREENING FORM FOR APPLICATION FOR REGISTRATION OF A MEDICINE

Where appropriate, abbreviations **Y, N, or N/A** must be used in filling out this form. The comment section may be used for any additional information or explanation.

Note: Applicants must ensure that the application is completed fully and accurately, presented in the prescribed format and that all required documentation is included. Each item must be referenced to the relevant page number of the application, where applicable

Applications that are incomplete or are non-compliant in any way will be returned as non-compliant.

Prospective Holder of the Certificate of Registration:			
Product Name:			
Date of Submission:			
	Y, N or N/A	**Page No.**	**MRA use**

• FRONT PAGE GENERAL INFORMATION:

1. Are full particulars of the prospective holder of the certificate of registration included on the application Front Page? (i.e., name, business and postal addresses, telephone, fax, e-mail, etc)			
2 Is the application signed by the Managing Director or authorised person?			
3. Is the letter of authorisation for communication on behalf of the prospective holder of the certificate of registration included in the application?			

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• PRODUCT INFORMATION/DOCUMENTATION

3. Please indicate the type of application using a check mark (✓) or a cross (×)

_____ Human Medicine
_____ Veterinary Medicine
_____ Biological Medicine

_____ AMRP
_____ New Chemical Entity
_____ New Indication
_____ New Dosage Form
_____ Multi-source (Generic) Medicine:
Immediate release
Controlled release
_____ Fast Track Application

• A. TECHNICAL INFORMATION: CLINICAL

4. New Chemical Entities and other applications with clinical data:

4.1 Is the product registered in any other country?			
4.2 Has proof of registration of the product in other countries been submitted in PART 1D?			
4.3 Has a copy (or copies) of the latest version of the approved package insert been included from regulatory authorities with which the product is registered in PART 1D?			
4.4 Was the product rejected for registration by any regulatory authority?			
4.5 If yes above, was rejection due to (i) safety (ii) efficacy (ii) safety and efficacy (iii) other reason (specify):.....			
4.6 Is the proposed package insert included in PART 1A?			
4.7 Has an electronic copy of the package insert also been submitted?			
4.8 Is information in the package insert cross-referenced to supporting evidence in PART 5 and/or the latest edition of the standard reference books?			
4.9 Is the package insert typed in double spacing?			
4.10 Does the package insert comply with Regulation 9 or 40?			
4.11 Is the proposed patient information leaflet (PIL) included in PART 1B?			
4.12 Has an electronic copy of the PIL also been submitted?			
4.13 Is information in the PIL cross-referenced to supporting evidence in PART 5 and/or the latest edition of the standard reference books?			
4.14 Is the PIL typed in double spacing?			
4.15 Does the PIL comply with Regulation 10?			
4.16 Have pre-clinical data been submitted in PART 4?			
4.17 Have clinical data been submitted in PART 5?			
4.18 Has residue depletion data and withdrawal time for veterinary medicines in food-producing animals been submitted in PART 5?			
4.19 Have the Clinical studies been indexed and numbered?			
4.20 Have all irrelevant raw data (individual patient data) been removed?			
4.21 Has either a Clinical Expert Report (CER) or an SBRA* report been			

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submitted?			
4.22 Are the tables and graphs in the CER cross-referenced to the documentation submitted?			
4.23 Have all the references referred to in the package insert been included?			
*Summary basis for registration application			
5 Generic Applications			
5.1 Have all the references referred to in the package insert been included?			
5.2 Is the proposed package insert included in Part 1A?			
5.3 Has the electronic copy of the package insert also been submitted?			
5.4 Is information in the package insert cross-referenced to the latest editions of the standard reference books and the latest version of the innovator package insert?			
5.5 Is the package insert typed in double spacing and in black print?			
5.6 Does the package insert comply with Regulation 9 or 40?			
• B. TECHNICAL INFORMATION: INSPECTORATE			
6. Does the label information comply with Regulation 8 or 48?			
7. Is a copy of the latest inspection report (not older than 2 years) from the Medicine Regulatory Authority of country of origin for the manufacturer of imported products available for inspection?			
8. Is a copy of the latest GMP certificate or copy of the appropriate manufacturing license, attached (not older than two years)?			
9. Date of submission and number of prospective holder of certificate of registration Site Master File:			
10. Provide license number and date of issue for holder of the certificate of registration:			
11. Is proof of registration of the Company as a pharmacy included (include copy of certificate)?			
12. Is proof of registration of the Responsible person as a pharmacist included (include copy of certificate)?			
10. Is the batch manufacturing record of the sample included in Part 2E?			
11. Is the CoA for the sample included?			
12. Is a permit to manufacture specified Schedule 5, Schedule 6 or Schedule 7 products included?			
13. Is Master documentation for PART 2E available for inspection?			

14. MANUFACTURING, TESTING AND PACKAGING FACILITIES

Please provide details by completing the following:

	License number and date of issue	Date of submission of SMF & number	Date of last inspection	Local or Foreign?	GMP Status	Is contract with HCR* in place?
Manufacturer 1 2.						
Packer 1 2						

MRF 2

Testing Lab 1 2						
*Holder of certificate of registration						
• C. TECHNICAL INFORMATION: PHARMACEUTICAL & ANALYTICAL						
16. General Administrative Information						
16.1 If Fast Tracking has been applied for, is a copy of the approval letter attached to the screening form?						
16.2. Has the application been submitted in the format prescribed by MRF 1?						
16.3 If the application is submitted in the EU format, has a separate document cross referencing the MRF 1 format to the EU format been submitted?						
17. Technical requirements						
17.1 Is a motivation for exemption included for PARTS not being addressed?						
17.2 Is the appearance of the sample comparable to the description given under identification in the package insert?						
17.3 Is a specimen of the label included in PART 1C?						
17.4 Has the solubility of the API(s) in water and in the solvent of choice been quantified in PART 2A?						
17.5 Has a recent (not older than 2 years) Certificate(s) of Analysis (CoA) for the API(s) been included in PART 2A?						
17.6 Has the method(s) of synthesis of the API(s) been submitted?						
17.7 Are stability data submitted in PART 2A for the API(s) in compliance with the guideline? Environmental test conditions (Temperature and humidity) ❖ Real time conditions ❖ Accelerated conditions Stability data submitted ❖ Real time data (months /years) ❖ Accelerated data (months) Stability Batches Number and types/sizes (production, pilot or experimental) of batches						
17.8 Where more than one manufacturer of the API is used, have comparative chemical and physical data in tabular format been submitted to demonstrate equivalence?						
17.9 Has the comparative chemical and physical data been generated from the same testing laboratory under the same conditions?						
17.10 Do all ingredients in the unit formula in PART 2B correspond with those in the batch formula in PART 2E?						
17.11 Have reasons been stated for overages in the quantity of the active pharmaceutical ingredient(s) (APIs) and /or other ingredients in PART 2B?						
17.12 Has the potency calculation been included for the API(s) in PART 2B?						
17.13 Has the composition and, where possible, quantities, of all auxiliary components (to facilitate manufacturing and processing of the final product), such as pH adjusters, etc. been stated separately?						

MRF 2

17.14 Have specifications and control procedures for all ingredients listed in PART 2B been submitted in PART 2C?			
17.15 Has the frequency of testing of water been stated in PART 2C?			
17.16 Have container specifications and control procedures been submitted in PART 2D?			
17.17 Are test results taken from the supplier's CoA clearly indicated?			
17.18 Is the batch manufacturing formulas and batch sizes included in PART 2E?			
17.19 Is a copy of the batch documentation for a real batch included in PART 2E?			
17.20 Is a comprehensive flow diagram or a description of the manufacturing process, detailing the various production stages, equipment types and sizes, sieve sizes, machine settings, duration of treatment, temperature, humidity, light, etc. included?			
17.21 Is documentation detailing the Packaging of product (procedures, packaging stages, equipment types, and conditions of temperature, humidity, light, etc.) included in PART 2E?			
17.22 Has a flow diagram for the Packaging procedures been included?			
17.23 Has a manufacturing validation protocol been included in PART 2E?			
17.24 Have specifications and control procedures for final product been submitted in PART 2F?			
17.25 Has assay method validation data been submitted in PART 2F?			
17.26 Are all the analytical and non-analytical release criteria and tests indicated in PART 2F?			
17.27 Are stability data submitted in PART 2G in compliance with the guideline? Environmental test conditions (Temperature and humidity) ❖ Real time conditions ❖ Accelerated conditions Stability data submitted ❖ Real time data (months /years) ❖ Accelerated data (months) Stability Batches ❖ Number and types/sizes (production, pilot or experimental) of batches			
17.28 Have details of the container, batch number, batch size, date of manufacture of the batch and storage conditions been reflected on the data sheet?			
17.29 Have all the stability specification parameters listed in PART 2F been included in the stability data presented in PART 2G?			
17.30 (a). Have stability data been derived with API sourced from the manufacturer identified in PART 2A?	a.		
(b). If not, have additional stability data derived from the source being applied for been submitted?	b.		
17.31 (a). Have stability data been derived from the product packed in packaging material detailed in PART 2D?	a.		
(b). If not, have additional stability data derived from the product packed in containers being applied for been submitted?	b.		

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17.32. Has validation data for the assay method (pharmacopoeial and or different to that in PART 2F) used in the stability testing been submitted			
17.33 Have complete pharmaceutical development data been submitted in PART 2H?			
17.34 Has an expert pharmaceutical report been submitted in PART 2H?			
17.35 Have details of expertise and the premises used in Part 2I been included?			
18. Generic Medicines: Proof of efficacy (PART 3)			
18.1 Is proof of safety and efficacy based on a bioequivalence study (*in vivo*) or are claims made on the basis of *in vitro* data only?			
18.2 Have all the components of the biostaudy been submitted including: a. Date and place of study: b. The Protocol c. Evidence of ethical approval d. Assay data validation plus representative chromatograms e. Investigator credentials f. Monitor's report g. Auditor's report?	a. b. c. d. e. f. g.	a. b. c. d. e. f. g.	a. b. c. d. e. f. g.
18.3 Was the biostudy performed using the innovator product currently registered and procured in South Africa?			
18.4 If not, (a) has comparative data to demonstrate equivalence of the reference product to the S.A. registered innovator product been submitted? (b) has the origin of the reference product and name of manufacturer together with the address of the manufacturing site been stated?.	a. b.		
18.5 If a biowaiver is requested, have motivation and justification with supporting data been included, i.e. comparative *in vitro* dissolution data comparing the test and reference products in three dissolution media, pH's 1.2, 4.5 and 6.8?			
18.6 If a biowaiver is requested for different strengths of the product, are the different strengths proportionally formulated?			
18.7 Have full details of each formulation strength been included with this application?			
18.8 Were the different strengths manufactured by the same manufacturer, at the same site, from API(s) sourced from the same manufacturer?			
18.9 Does your product meet the acceptance criteria for Cmax and AUC as prescribed in the Guidelines?			
18.10 Have appropriate quantitative methods been used to confirm *in vitro* similarity/differences and are the appropriate data included with this application? (i.e. similarity (f_2) and difference (f_1) factors)?			
18.11 Have full details of each formulation strength been included with this application?			

MEDICINES CONTROL COUNCIL

DEPARTMENT OF HEALTH
Republic of South Africa

MEDICINES CONTROL COUNCIL

GUIDELINES FOR THE DESTRUCTION OF SCHEDULE 5 MEDICINES AND SUBSTANCES

This document has been prepared to serve as a recommendation to applicants wishing to destroy any Schedule 5 medicines and/ or substances. It is not intended as an exclusive approach. Council reserves the right to request for any additional information to establish the safe destruction of any Schedule 5 medicine and / or substances.

REGISTRAR OF MEDICINES
MS. M.P. MATSOSO
DATE: 29/4/2003

Version 2003/1

INDEX

1 SCOPE OF THE GUIDELINES

These guidelines should be read in conjunction with the Medicines and Related Substances Control Act (Act 101 of 1965), and its supporting Regulations.

As these guidelines are constantly evolving due to harmonisation initiatives as well as due to new scientific developments, applicants are advised to always consult the latest information available. The Medicines Control Council endeavours to keep abreast of such developments and to keep its application requirements and evaluation procedures and policies in line with "best international practice".

The destruction of Schedule 5 medicines and substances may only take place in accordance with the Medicines and Related Substances Control Act (Act 101 of 1965)

2 DESTRUCTION AUTHORISED BY AN INSPECTOR

The destruction of Schedule 5 medicines and substances that have been entered into a register, may take place under the supervision of an inspector designated in terms of Section 40(1) of the Act, an officer of the SAPS or other person authorised in terms of the legislation to supervise this action.

2.1 All destruction must take place in accordance with local municipal regulations regarding the disposal of chemical or medicinal waste. The applicant (person requesting destruction) may be requested to prove that the method of destruction is in accordance with such regulations.

2.2 All medicines or substances must be destroyed in such a manner that does not allow recovery.

2.3 The inspector must, on behalf of the Medicines Regulatory Authority (MRA), provide a certificate of destruction and in the case of an officer of the SAPS, a case number must be provided which must be kept with the register for a period of 5 years.

2.4 All quantities destroyed must be indicated in the relevant register on the date of destruction and signed by the applicant, indicating the reference to the destruction certificate or case number.

3 PROCEDURE FOR WRITTEN AUTHORISATION OF DESTRUCTION FROM THE MEDICINES REGULATORY AUTHORITY:

The MRA may authorise the destruction of Schedule 5 medicines or substances in writing, without the presence of an inspector, if a pharmaceutical company or other institution in question, has sufficient personnel, procedures and capacity to follow the procedure described below.

4. APPLICATION FOR AUTHORISED DESTRUCTION

4.1 The Applicant must request permission for destruction of specific quantities of the medicines or substances in question in writing.

4.2 The request will indicate -

- the name of each medicine or substance to be destroyed,
- the exact quantities and batch numbers (if applicable) of the medicines or substances to be destroyed,
- the reason for the destruction and
- the names of the two pharmacists who will witness the destruction as required by the procedure. The MRA may consider a deviation from the requirement of two pharmacists in exceptional cases only. This will depend on the motivation supplied and on alternative arrangements to obtain sufficient control.

4.3 The MRA will authorise the destruction of the medicines or substances in question in writing, specifying the quantities indicated in the request, provided that the following procedure be followed:

5 GENERAL

5.1 Destruction may only take place after the written authorisation from the MRA has been received.

5.2 All destruction must take place in accordance with the local municipal regulations regarding the disposal of chemical or medicinal waste. The applicant may be requested to prove that the method of destruction is in accordance with such regulations.

5.3 All medicines and substances must be destroyed in such a manner that prevents their recovery.

5.4 The destruction must be properly documented:

- All quantities destroyed must be indicated in the relevant registers and signed by the witnesses required in the procedure. (See registers below)
- Destruction certificates (where applicable) and the letter of authorisation must be referenced in, or attached to the relevant Schedule 5 register and retained for the same period of time as the register itself. (5 years)

6. METHOD OF DESTRUCTION

6.1 Potent or large quantities of medicines and substances

6.1.1 Depending on the municipal regulations regarding the disposal of chemical or

medicinal waste, the applicant may choose an appropriate method of destruction such as incineration or destruction by a reliable contractor who specialises in waste disposal.

6.1.2 If a contractor is not used (eg. incineration), **two pharmacists** employed by the applicant must witness the **removal and destruction** of the correct quantities of the medicines or substances authorised for destruction, regardless of the where destruction will take place.

6.1.3 In the case of a contractor, where destruction does not take place at the premises of the applicant, and a certificate of destruction will beprovided, **two** pharmacists employed by the applicant must witness the **removal from the stock** of the correct quantities of the medicines or substances authorised for destruction and at least **one** of the **pharmacist** should accompany the goods to the place of **destruction**, to witness that these have actually been destroyed or disposed of in such a manner that precludes their recovery.

6.1.4 In the case of a contractor, a valid certificate of destruction must be obtained.

6.2 Small quantities

6.2.1 Small amounts of medicines or substances may be destroyed on the premises where these are kept. Appropriate methods must be used which are unlikely to cause any adverse health or environmental consequences, must be in accordance with local municipal regulatons and will not allow the drugs to be readily recovered. Two pharmacists employed by the company must witness the removal from stock and the destruction of the correct quantities of each medicine or substance.

7 SCHEDULE 5 REGISTER

7.1 The quantities of any medicines or substances destroyed must be entered into the register on the date of destruction.

7.2 The inscription in the register must be signed by the two pharmacists employed by the company, who witnessed their removal from stock destruction. The Managing Director must co-sign, unless the Managing Director was one of the pharmacists involved with the removal and destruction.

7.3 The letter of authorisation and the destruction certificate (if applicable) must be referenced in or attached to the schedule 5 register and retained for a period of 5 years.

8 LEGAL REPORTING REQUIREMENTS

8.1 If the amount of substance destroyed according to any method above, is more than :

- 1 milligram for potent narcotic drugs (fentanyl, sufentanil, alfentanil, etc.),
- more than 1 gram for all other narcotic drugs or
- more than 1 kilogram for any psychotropic substance,

the base amount of each substance destroyed must be indicated on the annual returns of specified Schedule 5 substances in terms of Regulation 29 of the Medicines and Related Substances Control Act (Act 101 of 1965), relating to the year in which the destruction took place.

MEDICINES CONTROL COUNCIL

DEPARTMENT OF HEALTH
Republic of South Africa

MEDICINES CONTROL COUNCIL

GUIDELINES FOR THE DESTRUCTION OF SCHEDULE 6 MEDICINES AND SUBSTANCES

This document has been prepared to serve as a recommendation to applicants wishing to destroy any Schedule 6 medicines and/ or substances. It is not intended as an exclusive approach. Council reserves the right to request for any additional information to establish the safe destruction of any Schedule 6 medicine and / or substances.

REGISTRAR OF MEDICINES
MS. M.P. MATSOSO
DATE: 29/4/2003

Version 2003/1

INDEX

1 SCOPE OF THE GUIDELINES

These guidelines should be read in conjunction with the Medicines and Related Substances Control Act (Act 101 of 1965), and its supporting Regulations.

As these guidelines are constantly evolving due to harmonisation initiatives as well as due to new scientific developments, applicants are advised to always consult the latest information available. The Medicines Control Council endeavours to keep abreast of such developments and to keep its application requirements and evaluation procedures and policies in line with "best international practice".

The destruction of Schedule 6 medicines and substances may only take place in accordance with the Medicines and Related Substances Control Act (Act 101 of 1965)

2 DESTRUCTION AUTHORISED BY AN INSPECTOR

The destruction of Schedule 6 medicines and substances that have been entered into a register, may take place under the supervision of an inspector designated in terms of Section 40(1) of the Act, an officer of the SAPS or other person authorised in terms of the legislation to supervise this action.

2.1 All destruction must take place in accordance with local municipal regulations regarding the disposal of chemical or medicinal waste. The applicant (person requesting destruction) may be requested to prove that the method of destruction is in accordance with such regulations.

2.2 All medicines or substances must be destroyed in such a manner that does not allow recovery.

2.3 The inspector must, on behalf of the Medicines Regulatory Authority (MRA), provide a certificate of destruction and in the case of an officer of the SAPS, a case number must be provided which must be kept with the register for a period of 5 years.

2.4 All quantities destroyed must be indicated in the relevant register on the date of destruction and signed by the applicant, indicating the reference to the destruction certificate or case number.

3 PROCEDURE FOR WRITTEN AUTHORISATION OF DESTRUCTION FROM THE MEDICINES REGULATORY AUTHORITY:

The MRA may authorise the destruction of Schedule 6medicines or substances in writing, without the presence of an inspector, if a pharmaceutical company or other institution in question, has sufficient personnel, procedures and capacity to follow the procedure described below.

4. APPLICATION FOR AUTHORISED DESTRUCTION

4.1 The Applicant must request permission for destruction of specific quantities of the medicines or substances in question in writing.

4.2 The request will indicate -

- the name of each medicine or substance to be destroyed,
- the exact quantities and batch numbers (if applicable) of the medicines or substances to be destroyed,
- the reason for the destruction and
- the names of the two pharmacists who will witness the destruction as required by the procedure. The MRA may consider a deviation from the requirement of two pharmacists in exceptional cases only. This will depend on the motivation supplied and on alternative arrangements to obtain sufficient control.

4.3 The MRA will authorise the destruction of the medicines or substances in question in writing, specifying the quantities indicated in the request, provided that the following procedure be followed:

5 GENERAL

5.1 Destruction may only take place after the written authorisation from the MRA has been received.

5.2 All destruction must take place in accordance with the local municipal regulations regarding the disposal of chemical or medicinal waste. The applicant may be requested to prove that the method of destruction is in accordance with such regulations.

5.3 All medicines and substances must be destroyed in such a manner that prevents their recovery.

5.4 The destruction must be properly documented:

- All quantities destroyed must be indicated in the relevant registers and signed by the witnesses required in the procedure. (See registers below)
- Destruction certificates (where applicable) and the letter of authorisation must be referenced in, or attached to the relevant Schedule6 register and retained for the same period of time as the register itself. (5 years)

6. METHOD OF DESTRUCTION

6.1 Potent or large quantities of medicines and substances

6.1.1 Depending on the municipal regulations regarding the disposal of chemical or

medicinal waste, the applicant may choose an appropriate method of destruction such as incineration or destruction by a reliable contractor who specialises in waste disposal.

6.1.2 If a contractor is not used (eg. incineration),**two pharmacists** employed by the applicant must witness the **removal and destruction** of the correct quantities of the medicines or substances authorised for destruction, regardless of the where destruction will take place.

6.1.3 In the case of a contractor, where destruction does not take place at the premises of the applicant, and a certificate of destruction will beprovided, **two** pharmacists employed by the applicant must witness the **removal from the stock** of the correct quantities of the medicines or substances authorised for destruction and at least **one** of the **pharmacist** should accompany the goods to the place of **destruction**, to witness that these have actually been destroyed or disposed of in such a manner that precludes their recovery.

6.1.4 In the case of a contractor, a valid certificate of destruction must be obtained.

6.2 Small quantities

6.2.1 Small amounts of medicines or substances may be destroyed on the premises where these are kept. Appropriate methods must be used which are unlikely to cause any adverse health or environmental consequences, must be in accordance with local municipal regulatons and will not allow the drugs to be readily recovered. Two pharmacists employed by the company must witness the removal from stock and the destruction of the correct quantities of each medicine or substance.

7 SCHEDULE 6 REGISTER

7.1 The quantities of any medicines or substances destroyed must be entered into the register on the date of destruction.

7.2 The inscription in the register must be signed by the two pharmacists employed by the company, who witnessed their removal from stock destruction. The Managing Director must co-sign, unless the Managing Director was one of the pharmacists involved with the removal and destruction.

7.3 The letter of authorisation and the destruction certificate (if applicable) must be referenced in or attached to the schedule 6 register and retained for a period of 5 years.

8 LEGAL REPORTING REQUIREMENTS

8.1 If the amount of substance destroyed according to any method above, is more than :

- 1 milligram for potent narcotic drugs (fentanyl, sufentanil, alfentanil, etc.),
- more than 1 gram for all other narcotic drugs or
- more than 1 kilogram for any psychotropic substance,

the base amount of each substance destroyed must be indicated on the annual returns of Schedule 6 substances in terms of Regulation 29 of the Medicines and Related Substances Control Act (Act 101 of 1965), relating to the year in which the destruction took place.

CTF 1

MEDICINES CONTROL COUNCIL

DEPARTMENT OF HEALTH
Republic of South Africa

MEDICINES CONTROL COUNCIL

APPLICATION TO CONDUCT CLINICAL TRIALS