GUIDELINES FOR RECALL/ WITHDRAWAL OF MEDICINES

This document has been prepared to serve as a recommendation to applicants regarding the recalls of medicines, and the SAHPRA's current thinking on the safety, quality and efficacy of medicines. SAHPRA reserves the right to request for any additional information to establish the safety, quality and efficacy of a medicine and may make amendments in keeping with the knowledge which is current at the time of consideration of data which has been submitted regarding any recalls. The Authority is committed to ensure that all medicines that are registered are of the required quality, safety and efficacy. It is important for applicants to adhere to these requirements.

Version 1 – Implementation	May 2003
Version 2 – Inclusion of name and source of API	March 2007
Version 3 – Dec 2008 update to include the Rapid Alert Notification to PIC/S and a SAHPRA website notice (8), finalization of the recall within 30 days (9), update of the contact details (11), editing of Annex 1 and Annex 2 to remove section on "official use", and general editing of the document.	December 2008
Version 3 Implementation	31 March 2009
Version 4 Implementation	April 2020

CEO OF SAHPRA: DR BOITUMELO SEMETE-MAKOKOTLELA

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1 INTRODUCTION

The guidelines for recall/withdrawal of medicines is the result of an agreement between the holder of the certificate of registration/parallel importer of the medicine and the South African Health Product Regulatory Authority (SAHPRA). Its purpose is to define the action to be taken by the Cluster: Regulatory Compliance Unit: Directorate: Inspectorate and Regulatory Compliance and the holder of the certificate of registration /parallel importer of the medicine, when medicines for reasons relating to their safety, quality and efficacy are to be removed from the market.

The Chief Executive Officer, the Senior Manager and Manager: Inspectorate and Regulatory Compliance and the Medicines Control Officer(s) are responsible for recall/ withdrawal, and will monitor closely the effectiveness of the holder of the registration certificate/parallel importer's recall actions and provide a scientific, technical and operational advice.

Each holder of a certificate of registration certificate (HCR)/parallel importer should advise the Medicines Regulatory Compliance of the names, after hours and telephone numbers of two persons who have authority to discuss and, if necessary, implement a recall.

These guidelines serve to remind the holder of a certificate of registration/parallel importer that SAHPRA expects them to take full responsibility for medicines recalls, including follow-up checks to ensure that the recalls are successful and that corrective actions are taken.

Most recalls are conducted on voluntary basis. The Authority can recall medicines when registration thereof has been cancelled, or when medicines are sold illegally in South Africa or when the medicines are no longer of quality, safe and efficacious. If the recalling performance is deemed inadequate the Authority is prepared to take appropriate actions to remove the product from sale or use.

2 DEFINITIONS

Recall - means the removal of specific batch/batches of a medicinal product from the market for reasons relating to deficiencies in the quality, safety or efficacy.

Withdrawal - means the total withdrawal of a medicinal product from the market

Medicine - means any substance or mixture of substances used or purporting to be suitable for use or manufactured or sold for use in-

(a) the diagnosis, treatment, mitigation, modification 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 or organic function in man, and includes any veterinary medicine.

Parallel importation - means the importation into the Republic of a medicine protected under patent and/or registered in the Republic that has been put onto the market outside the Republic by or with the consent of such patent holder.

Parallel importer - means a person who parallel imports a medicine into the Republic on authority of a permit issued in terms of regulation 7(3) of the Medicines and Related Substances Control Act, 101 of 1965.

Holder of a certificate of registration - means a person in whose name a registration certificate has been granted and who is responsible for all aspects of the medicine, including quality and safety and compliance with conditions of registration.

Quarantined Stock (in the context of a recall) - means the stock of product that has been put on hold for destruction or rework. The stock has been released for sale and has not yet been despatched or has not left the direct control of the holder of a certificate of registration/ parallel importer. (Refer regulation 43(1) of the Medicines and Related Substances Act, Act 101 of 1965).

3 PROVISIONS OF THE ACT

3.1 Section 19 (1) of the Medicines and Related Substances Act, Act 101 of 1965 - *No person shall sell any medicine unless it complies with the prescribed requirements. Any person who contravenes provision of this sub-section shall be guilty of an offence.*

3.2 Regulation 43(1) of the Medicines and Related Substances Control Act, Act 101 of 1965 - *Every medicine shall comply with the standards and specifications which were furnished to SAHPRA on the form prescribed by regulation 22 and which have been accepted by SAHPRA with regard to such medicine.*

4 NOTIFICATION/INITIATION OF THE RECALL

The recall of a medicine can be initiated as a result of reports referred to the holder of a certificate of registration/parallel importer or Regulatory Compliance from various sources, e.g. manufacturers, wholesalers, retail and hospital pharmacists, doctors. A report may relate to *inter alia* an adverse drug reaction to a particular batch(es), product quality deficiency, technical complaints experienced with regard to the printed packaging material, contamination, mislabelling, counterfeit including adulterated medicines etc.

When initiating a recall, the holder of a certificate of registration should take the following aspects into consideration: the extent of public warnings and the successfulness of the recall.

It is imperative that before or upon initiating a recall, the applicant immediately on becoming aware of a problem, notifies the CEO of SAHPRA or in his/her absence his/her designate of the potential recall.

Therefore it is advisable that no recall, regardless of the level, should be undertaken without consultation with the SAHPRA and without agreement on the recall strategy. However, in case of a potential significant health hazard to patients, during the weekend/public holidays the HCR/ parallel importer may within 24 hours disseminate information on the recall. This includes precautionary measures to quarantine stock pending the initiation of the recall.

5 INFORMATION REQUIRED FOR THE ASSESSMENT OF A RECALL

Each recall is a unique exercise. However, in tailoring an appropriate recall strategy, there are a number of factors common to all recalls that need to be considered. Certain information is essential to permit the assessment of the validity of the report of the problem or recall, the potential danger to consumers and the action appropriate to the situation. The HCR/ parallel importer should gather all relevant information on the recall, which includes the product, its distribution, and action proposed. The HCR/ parallel importer should make available to the Authority all the relevant information regarding the recall on the report form provided as **Annex1**. The information required may be included in **Annex 1** but not limited to it only.

6 CLASSIFICATION OF RECALLS

Recalls are classified into both the **class** according to the level of health hazard involved (risk to the patient) and **type** which denotes the depth or extent to which the product should be recalled from the distribution chain, e.g. Class I, Type C recall, etc.

Class I
Class I is for defective/dangerous/potentially life-threatening medicines that predictably or probably could result into serious health risk/adverse events or even death.

Class II
Class II is for medicines that possibly could cause temporary or medically reversible adverse health problem or mistreatment.

Class III
Class III is for medicines that are defective and are unlikely to cause any adverse health reaction or which do not comply with the requirements of Act 101 of 1965 in terms of the requirements of printed packaging material, product specification, labelling, etc.

Type A

A type A recall is designed to reach all suppliers of medicines (all distribution points) i.e. wholesalers throughout the country, directors of hospital services (private as well as state hospitals), retail outlets, doctors, nurses, pharmacists, authorised prescribers and dispensers and individual customers or patients through media release (radio, television, regional and national press). **Action: Recall letter to all distribution points plus media release**.

Type B

A type B recall is designed to reach wholesalers throughout the country, directors of hospital services (private as well as state hospitals), retail outlets, doctors, nurses, pharmacists, authorised prescribers and dispensers. **Action: Recall letter to all distribution points.**

Type C
A type C recall is designed to reach wholesale level and other distribution points (e.g. pharmacies, doctors, hospitals) this can be achieved by means of a representatives calling on wholesalers and/or retail outlets.

If it is known where the product in question had been distributed to, specific telephone calls or recalls letters to arrange for the return of the product could be made.

Action: Specific telephone calls, recall letters to/representatives calling at distribution points if known where the medicines have been distributed.

NOTE: Decisions on the Class and Type of a recall to be initiated are a matter of the Authority in consultation with a holder of the registration certificate and shall be based on the evidence and/or expert opinion of the SAHPRA and HCR.

7 RECALL LETTER CONTENTS

Recall letters should include factual statements of the reasons for the recall of the product, together with special details that will allow the product to be easily identified.
The text of the recall letter is to be sent to the office of the Inspectorate and Regulatory Compliance for approval before being despatched. The letter, which must be sent by post and facilitated e-mail or facsimile, should be dispatched within 24 hours of receiving approval from the Inspectorate and Regulatory Compliance directorate. A signed copy of the approved recall letter (or facsimile) to customers is to be sent to the office of the Inspectorate and Regulatory Compliance. In case of an international distribution of the recalled product the applicant should immediately inform the responsible applicant / distributor and or endeavour to make information available to the regulatory authority in that country.

Recall communication from the holder of the registration certificate to the distribution chain should be written in accordance with the following directive:

1. Shall be on the company's letterhead and signed by the Responsible Pharmacist or authorised person.
2. The heading should indicate that it is an **"Urgent Medicine Recall".**
3. The heading should also indicate the classification and type of the recall.
4. Name of product, dosage form, strength, registration number, pack size, batch number(s), expiry date and any other relevant information necessary to allow absolute identification.
5. Nature of the defect (be brief and to the point).
6. Urgency of the action.
7. Reason for the action (reason for recall).

7 ***Recall Letter Contents - continued***

8. Indication of a health risk (this should also state exactly what the product may do if taken, i.e. sideeffects).
9. Provide specific information on what should be done in respect of the recalled medicine. Method of recovery or product correction, which will be used.
10. Where necessary a follow-up communication shall be sent to those who failed to respond to the initial recall communication.
11. Contact telephone number and facsimile return numbers (preferably toll free)
12. A request to retain the letter in a prominent position for one month in case stock is in transit (*where applicable*).
13. Where recalled stock has been distributed to a limited number of hospitals and the recall letter is not to be sent to all hospitals in the province, the letter should include the following:

    "*If any of the recalled stock could have been transferred from your hospital to another, please let that hospital know or alternatively inform our company so that we can make contact with the hospital supplied from your hospital*".

NB: The recall communication shall not contain any material that can be viewed as promotional in nature.

The letter and the envelope shall indicate in bold red type "MEDICINE RECALL" and be marked "URGENT".

8 MEDIA RELEASE

In the case of a recall where a media release is indicated, the holder of a certificate of registration and the Authority make the text of the media release jointly. Expert advice may also be required.
In the case of a Class I or customer level recalls, where it is necessary to issue a media statement, the text of the media release is developed by the holder of the registration certificate, in consultation with the Authority. The Authority may request expect advice before approving any media release statements.

The media release should contain sufficient and relevant detail to uniquely define the product, together with a clear outline of the problem (without causing unnecessary alarm) and must state the appropriate response by the consumer/client.

A 24-hour access telephone number of the holder of the registration certificate should be given for further information. The media release will be issued by the holder of the registration certificate.
In the event that the holder of the registration certificate refuses to do a media release the Authority will do the release.

Choice of the daily media – this should be done in consultation with the Authority and consideration should be given to the need to inform all ethnic groups in their language.

Recommended text to appear on the media release:

1. Shall be on the company's letterhead and signed by the Responsible Pharmacist or authorised person.
2. The heading should indicate that it is an **"Urgent Medicine Recall".**
3. The heading should also indicate the Classification and Type of the recall.
4. Name of product, dosage form, strength, registration number, pack size, batch number(s), expiry date and any other relevant information necessary to allow absolute identification.
5. Nature of the defect (be brief and to the point).
6. Urgency of the action.
7. Reason for the action (reason for recall).
8. Indication of a health risk (this should also state exactly what the product may do if taken, i.e. side effects).
9. Provide specific information on what should be done in respect of the recalled medicine. Method of recovery or product correction, which will be used.
10. Contact telephone number and facsimile return numbers (preferably toll free)
11. A request to retain the media release in a prominent position for one month in case stock is in transit (*where applicable*).

8 Media Release - continued

N.B The CEO / designate shall publish the recall details in the form of a notice on the sahpra website and, where applicable, inform the Pharmaceutical Inspection Co-operation Scheme (PIC/S) of the recall as per the PIC/S (PI 010-2) procedure for handling rapid alerts and recalls from quality defects.

9 POST RECALL PROCEDURES

The HCR/ parallel importer has a legal responsibility for implementing the recall action, and for ensuring compliance with the recall procedure. At two weeks after the implementation of the recall (or at other **agreed times**) the HCR/ parallel importer is to provide the SAHPRA with an interim report on the effectiveness of the recall and within 30 days of the recall having been instituted the SAHPRA shall be furnished with a final recall report (as per **Annex 2).**

These reports may include but not limited to the following:

- Details on the investigation into the cause of the defect.
- The corrective actions proposed/implemented and the dates of implementation to prevent a recurrence of the problem.
- The extent of distribution of the relevant batch in South Africa as well as to the international market.
- The success of the recall i.e. quantity of stock returned, corrected, outstanding, etc.
- Confirmation, where applicable, (e.g. hospitals, pharmacists, doctors, customers, other international regulatory authorities / holder of distribution authorization in the foreign country) that the recall letter was received.
- The method of destruction or disposal of the recalled goods.

These reports establish the effectiveness of the recall and form the basis of the report to the SAHPRA. Unless satisfactory reports are received, further recall action may have to be considered.

NOTE: An additional interim report may be requested even before the 30 days have elapsed.

FOLLOW - UP ACTION

- The follow- up action consists of an evaluation on the effectiveness of the recall and an investigation of the reason for the recall and corrective actions taken to prevent a recurrence of the problem.
- The Medicines Control Officer shall evaluate the reports received from the recalling site and an assessment made of the effectiveness of the recall action
- On completion of a recall or during the process of a recall, the recalling site is requested to provide details of the corrective actions and time lines proposed to prevent a recurrence of the problem which gave rise to the recall.
- Where the nature of the problem and appropriate corrective actions are not apparent, investigation and in some cases Good Manufacturing Practice audits may be necessary.
- Apparent follow-up actions will be taken by the SAHPRA or Inspectorate and Regulatory Compliance directorate of SAHPRA. This might include a review of the medicine dossier by the SAHPRA and any appropriate action instituted by the SAHPRA based on the outcome of the review of the applicable dossier.
- Once the recall has been handled satisfactory, the SAHPRA will determine closure of the recall.

10 REFERENCES

1. Circular 9/98 of the Medicines Control Council/ (Now called SAHPRA).
2. Uniform Recall Procedure for the Therapeutic Goods.
3. PIC/S Procedure for Handling Rapid Alerts and Recalls arising from quality defects, Procedure.

11 CONTACT DETAILS

1. Ms Andrea Keyter
Acting Director: Inspectorate and Regulatory Compliance Directorate
Tel: 012 842 7585
Email: Andrea.keyter@sahpra.org.za

2. Ms Daphney Fafudi
Acting Deputy Director: Regulatory Compliance
Tel: 012 842 7579
Mokgadi.fafudi@sahpra.org.za

3. Mr Mlungisi Wondo
Medicines Control Officer
Tel: 012 842 7579
Mlungisi.wondo@sahpra.org.za

4. Ms Portia Nkambule
Chief Regulatory Officer
Salaminah.mashishi@sahpra.org.za

5. Dr Boitumelo Semete-Makokotlela
Chief Executive Officer: SAHPRA
Ditshego.molefe@sahpra.org.za

12 UPDATE HISTORY

Date	Reason for update	Version
April 2020	New	2020/2
September 2004	Formatted and edited; correction of Class III	1.1
March 2007	Inclusion of API and the source (manufacturer) thereof as recommended by PIC/S assessment team. Replacement of the definition of "stock recovery" with "quarantined stock". Inclusion of requirement that the letter and envelope shall be written in bold red type "MEDICINE RECALL" and be marked "URGENT". Inclusion of submission of the final report within 90 days of medicine recall.	2
September 2008	Inclusion of inspections and website notice. Finalization of recall within 30 days. Inclusion of Rapid Alert Notice to PIC/S as per the PIC/S requirement (PI 010-2). Updated contact details.	3
April 2020	Name of Organisation and its personnel	

13 ANNEX 1 – Recall Information (INITIAL REPORT to SAHPRA)

Recall information	Information by the HCR/Parallel importer
Origin of report	

1. Name of person/organisation reporting the problem	
2. Company	
3. Physical address	
4. Telephone number	
5. Facsimile number	
6. E-mail address	
7. Date of report	
8. Name of recipient at the MRA/SAHPRA	
Product (medicine) details	
1. Name of product affected	
2. Name of Active Pharmaceutical Ingredient (API)	
3. Source (Manufacturer) of the API	
4. SAHPRA allocated registration number	
5. Dosage form	
6. Strength of the product	
7. Pack size/type	
8. Batch number and expiry date	
9. Manufacturer/holder of the certificate of registration, address and contact details	
10. Date manufactured	
11. Date released	
12. Total quantity prior to distribution	
13. Quantity released for distribution prior to the recall	
14. Date of distribution	
15. Local distribution (include distribution list)	
16. international distribution (give full details and quantity)	
Nature of defect	

1. Source of complaint (e.g. patient/ hospital/pharmacy/manufacturer, etc)	
2. Details of complaint	
3. Number of complaints received	
4. Initial date complaint was received	

Recall information	**Information by the HCR/Parallel importer**
5. Name and address of any Medicines Regulatory Authorities notified	
6. Action taken so far (if any) / Proposed action and its urgency	
7. Type of hazard/health risk and assessment of risk to the user (including clinical safety reports)	
8. Proposed recall classification and type	
9. Other relevant information	

N.B: The above information could be provided verbally but should be confirmed in writing within **two working days**

14 ANNEX 2- Post recall information /FINAL REPORT to SAHPRA

Post recall information	**Information by the HCR / Parallel importer**
1. Name of product	
2. Name of Active Pharmaceutical Ingredient(s) (APIs)	
3. Source (Manufacturer) of the APIs	
4. SAHPRA allocated registration number	
5. Dosage form	
6. Strength of product	
7. Pack size/type	
8. Batch number and expiry date	
9. Nature of defect	
10. Action taken (taking into account the area of distribution of recalled medicine), if exported confirmation from the Regulatory Authority and the holder of the distribution authorization in the foreign country	
11. Urgency of the action taken	
12. Reason for the action	
13. Indication of the health risk and the reported clinical problems	
14. Steps taken to prevent re-occurrence of the problem	
15. Fate of the recalled product (including the decision taken)	
16. The result of the recall-quantity of stock returned, corrected, outstanding, etc	
17. Confirmation that customers have received the recall letter (include mailing list)	
18. Copies of all recall correspondence including previous correspondences to SAHPRA regarding this recall.	