South African Health Products
Regulatory Authority
Building A
Loftus Park
Arcadia
Pretoria

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GUIDELINES FOR MEDICINE RECALL/ WITHDRAWAL AND RAPID ALERTS

This document has been prepared to serve as a recommendation to applicants regarding the recalls and withdrawal of medicines, and the South African Health Products Regulatory Authority 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. SAHPRA 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.

Document History

Version	Date	Reason for amendment
Version 2	February 2022	Update to new template
Version 3	June 2022	• Update to new template • Aligning regulations from previous legislation • Added more information on handling rapid alerts • Change document number from 5.07 to SAHPGL-INSP-RC-05

BOITUMELO SEMETE-MAKOKOTLELA

CHIEF EXECUTIVE OFFICER

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List of abbreviations and definitions

Table 1: List of Abbreviations

SAHPRA	South African Health Products Regulatory Authority
SOP	Standard Operating Procedure
PIC/S	Pharmaceutical Inspection Corporation Scheme
HCR	Holders of certificate of registration
MCO	Medicine Control Officer
API	Active Pharmaceutical Ingredient

Table 2: List of 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 5(1) of the Medicines and Related Substances Control Act, 101 of 1965.

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 Products Regulatory Authority in South Africa. Its purpose is to define the action to be taken by the Inspectorate and Regulatory Compliance Unit 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 CEO of SAHPRA, the senior manager Inspectorate and Regulatory Compliance, the manager: Regulatory Compliance Unit and the Medicines Control Officers (MCOs) 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 SAHPRA 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. SAHPRA 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 SAHPRA is prepared to take appropriate actions to remove the product from sale or use.

2. Purpose

This document has been prepared to serve as a recommendation to applicants regarding the recalls and withdrawal of medicines, and the South African Health Products Regulatory Authority 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. SAHPRA 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.

3. Background

Medicines may be recalled for an assortment of reasons including safety, mislabeling, contamination, and deviations in strength or potency. Recalls may be conducted as a voluntary action by the manufacturer or supplier.

4. Scope

These guidelines are applicable to all quality defective product reports and to all reported incidents of safety and efficacy received for all drugs including vaccines & biological. These guidelines are expected to be followed by licensees (manufacturers, importers, wholesalers, distributors, retailers) and the recall could be voluntary or statutory. The procedure may also be used by SAHPRA when urgent action is required to protect public or animal health. These guidelines would help in adopting a stepwise procedure to be followed in recall strategy and also help in recall evaluation at every level and achieve compliance within the time frame.

5. PROVISION OF THE ACT

a) 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.

b) 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 the Authority on the form prescribed by regulation 22 and which have been accepted by the Authority with regard to such medicine

c) Regulation 43(4) (i) of the Medicines and Related Substances Control Act, Act 101 of 1965 - (i) in the event of a recall of a medicine, comply with the terms of the recall of the medicine.

6. Notification/Initiation of the Recall

The purpose of a recall notification is to convey:

- That the product in question is subject to a recall.
- That further distribution or use of any remaining product should cease immediately.
- Instructions regarding what to do with the product.

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 SAHPRA 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, mislabeling, 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 Authority 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 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.

The withdrawal/recall of a particular batch/es of a product from the market may be prompted by the following but are not limited to:

- Serious reports of adverse drug reactions not included in the package insert
- Unexpected frequency of adverse reaction stated in the package insert
- Incorrect formulation of a product
- Incorrect labeling of a product
- Unfavorable result of ongoing stability studies

7. 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 SAHPRA 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.

8. 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

Defects are dangerous or potentially life threatening medicinal products that predictably or probably could result into serious health risk/adverse events or even death. A Rapid Alert notification must be sent to all contacts of the rapid alert notification list, irrespective of whether or not the batch was exported to the country.

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.

Examples:

- Wrong product (label and contents are different products)
- Correct product but wrong strength, with serious medical consequences
- Microbial contamination of sterile injectable or ophthalmic product
- Chemical contamination with serious medical consequences
- Mix-up of some products (rogues) with more than one container involved
- Wrong active ingredient in a multi-component product, with serious medical consequences.

Class II

Defects could cause illness or mistreatment, but are not Class I. A rapid alert notification should be sent to all contacts of the rapid alert notification list as it might be difficult to know where a batch has been distributed. If the product distribution is known, the notification should be only sent to the contacts concerned.

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

Examples:

- Mislabelling, e.g. wrong or missing text or figures
- Missing or incorrect information (leaflets or inserts)
- Microbial contamination of non-injectable, non-ophthalmic sterile product with medical consequences

- Chemical/physical contamination (significant impurities, cross-contamination, particulates)
- Mix up of products in containers (rogues)
- Non-compliance with specification (e.g. assay, stability, fill/weight)
- Insecure closure with serious medical consequences (e.g. cytotoxics, child-resistant containers, potent products).

Class III

Defects may not pose a significant hazard to health. This 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:

Example:

- Faulty packaging, e.g. wrong or missing batch number or expiry date
- Requirements of printed packaging material, product specification, labelling, etc.
- Faulty closure
- Contamination, e.g. microbial spoilage, dirt or detritus, particulate matter

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, authorized 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, authorized 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 SAHPRA in consultation with a holder of the registration certificate and shall be based on the evidence and/or expert opinion of SAHPRA and HCR.

9. Recall Notification

- The applicant/distributor communicates and engages with the Authority (SAHPRA). This involves information gathering and/or intent from Applicant to recall or withdraw affected batches of stock in the market.
- Based on information received from the Applicant (see Form No. GLF-RC-INSP-05A [Annexure 1]), the risk, the Type and Class of recall is determined by SAHPRA.
- The recall communication should not contain irrelevant information, promotional materials, or any other statement that may detract from the message. Where necessary, follow-up communication should be sent by the Applicant to those who fail to respond to the initial recall communication.
- A recall communication can be accomplished by e-mail, telephone, social media, electronic and print media, or special delivery letters conspicuously marked, preferably in bold red, depending on the classification (The letter by the applicant to the customers or distribution chain should also be marked; "URGENT MEDICINE RECALL" for Class I and Class II recalls see Annex 2).
- N.B: The recall information could be provided verbally but should be confirmed in writing within two working days
- SAHPRA will decide whether a public recall announcement is mandatory and who should issue such warning to the Public (through public media).
- The purpose of a public warning is to alert the public that a product being recalled presents a serious health hazard.
- The recall strategy will specify the type of public warning, for example: General public warning through the general news media, either national or local as appropriate, or public warning through specialized news media, e.g., professional journals or publications, trade or ethnic press, or to specific segments of the population such as physicians, hospitals, etc.

10. 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 SAHPRA Inspectorate Regulatory Compliance for approval before being dispatched to customers. The letter, which must be sent by e-mail, should be dispatched within 24 hours of receiving approval from the Inspectorate and Regulatory Compliance Unit. A digitally signed copy of the approved recall letter (or facsimile) to customers is to be sent to Regulatory Compliance Unit via email. In case of an international distribution of the recalled product the applicant should immediately inform the responsible applicant / distributor and or endeavor to make information available to the regulatory authority in that country.

Recall Letter from the holder of the registration certificate to the distribution chain should be written in accordance with the following directive (see Form No. GLF-RC-INSP-05B [Annexure 2]):

i. Shall be on the company's letterhead and signed by the Responsible Pharmacist or authorized person.

ii. The heading should indicate that it is an "Urgent Medicine Recall".

iii. The heading should also indicate the classification and type of the recall.

iv. 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.

v. Nature of the defect (be brief and to the point).

vi. Urgency of the action.

vii. Reason for the action (reason for recall).

viii. Indication of a health risk (this should also state exactly what the product may do if taken, i.e. side- effects).

ix. Provide specific information on what should be done in respect of the recalled medicine. Method of recovery or product correction, which will be used.

x. Where necessary a follow-up communication shall be sent to those who failed to respond to the initial recall communication.

xi. Contact telephone number and facsimile return numbers (preferably toll free)

xii. A request to retain the letter in a prominent position for one month in case stock is in transit (where applicable).

xiii. 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:

xiv. "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".

xv. 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"

11. Media Release

In the case of a recall where a media release is indicated, the holder of a certificate of registration and SAHPRA 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 SAHPRA. SAHPRA may request expert 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 SAHPRA will do the release via the Communication Unit.

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

Recommended text to appear on the media release:

i. Shall be on the company's letterhead and signed by the Responsible Pharmacist or authorized person.

ii. The heading should indicate that it is an "Urgent Medicine Recall".

iii. The heading should also indicate the Classification and Type of the recall.

iv. 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.

v. Nature of the defect (be brief and to the point).

vi. Urgency of the action.

vii. Reason for the action (reason for recall).

viii. Indication of a health risk (this should also state exactly what the product may do if taken, i.e. side- effects).

ix. Provide specific information on what should be done in respect of the recalled medicine. Method of recovery or product correction, which will be used.

x. Contact telephone number and facsimile return numbers (preferably toll free)

xi. A request to retain the media release in a prominent position for one month in case stock is in transit (where applicable).

12. 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 (post recall) report (as per Form No. GLF-RC-INSP-05C [Annexure 3]).

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 satisfactorily 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 unit on behalf of the SAHPRA as directed by the Authority. 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, and the recall certificate post destruction or disposal of the recalled goods, then SAHPRA will determine consider closure of the recall.

13. Rapid Alerts

Rapid Alerts are as a result of triggers that compel SAHPRA to initiate recalls. However, not all quality defects result in recall of medicinal products. The Rapid Alert System may be used for notification to authorities concerned about the quality of products or an embargo on the distribution of products following suspension or withdrawal of a manufacturing / wholesale authorisation. It can also be initiated by an Authority, ie SAHPRA, as a result of a track of market quality or a safety event or by detecting a fraudulent drug.
SAHPRA may publish the recall details in the form of a notice on the SAHPRA website and, where applicable, inform the stakeholders of the recall.

14. Contact Details

Email for recalls: Recalls@sahpra.org.za

Ms Daphney Fafudi

Manager: Regulatory Compliance Unit

Email: Mokgadi.fafudi@sahpra.org.za

Mr Deon Poovan

Senior Manager: Inspectorate and Regulatory Compliance Directorate

Email: deon.poovan@sahpra.org.za

The Office of Ms Portia Nkambule

Chief Regulatory Officer

Email:Salaminah.mashishi@sahpra.org.za

The Office of Dr Boitumelo Semete-Makokotlela

Chief Executive Officer: SAHPRA

Email:Ditshego.molefe@sahpra.org.za

15. References

15.1.Related Procedures

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

15.2.Related Templates

- GLF-INSP-RC-05A *(Latest version)* – Recall Notification
- GLF-INSP-RC-05B *(Latest version)* – Recall Letter to Customers

16. Validity

This guideline is valid for a period of 5 years from the effective date of revision and replaces [Guideline for Recalls/ Withdrawal of Medicine, Document No. 5.07]. It will be reviewed on this timeframe or as and when required.

17. Annexure

18.1 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	
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	

18.2 ANNEX 2 - Recall Letter to customers

Company B Letter Head

URGENT MEDICINE RECALL – CLASS? – TYPE?

Dear Customer,

We hereby inform you that we are recalling the following batches of Product A

Product A	Batch / Lot number(s)	Expiry Date	Manufacturing date	Pack Size	First release date for sale	Quantity initially released	Recall Classification (As confirmed by SAHPRA)
							Class ? Type ?

This recall is initiated because……(give reasons)

We request that you refrain from selling any of the affected batch(s) of Product A and return them to your supplying warehouse or distributor with immediate effect. Company B will collect all your stock which will be replaced …….

For further product information, please call Company B on….phone contact number

We thank you in advance for your co-operation and apologise for any inconvenience caused.

Yours faithfully,

……

18.3 ANNEX 3 - 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 –ie destruction) NB: A destruction certificate must be supplied to SAHPRA in order to close the recall)	
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.	