# Guideline for Management and Handling of Defective Medical products, 2019

**DRA-G-D3-DM-01**

Post-Marketing Control Division

Drug Regulatory Authority

Developed By:

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# DEFECTIVE PRODUCT GUIDELINE

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# DEFECTIVE PRODUCT GUIDELINE

## 1. Introduction

The Drug Regulatory Authority (DRA) is responsible for ensuring the quality, safety and efficacy of medical products in the country. In accordance with the rule 177 of the Bhutan Medicines Rules and Regulation 2012, this guideline for the management of defective and recalled medical products has been developed.

A quality defects in a medical product may be defined as an attribute of a medical product or component that may affect the quality, safety and efficacy of the product and which is not in line with the approved product authorization. Manufacturers, market authorization holders, healthcare professionals, wholesalers, retailers and patients/consumers can report product defects to the DRA. It is essential for timely management of product defects.

Accordingly, this guideline has been developed with the aim to guide the reporters on reporting product defects and as well assist the officials of the DRA in the management of defective medical products. This guideline describes in detail, the procedure for reporting and classification of product defects to effectively and promptly decide on the outcome of the defective medical products and recall of such products.

## 2. Scope

**2.1** This guideline is intended for:

i. Stakeholders;
   a) Marketing Authorization Holders (MAHs)
   b) Wholesalers and Retailers
   c) Manufacturers
   d) Healthcare professionals
   e) Patients/Consumers

ii. DRA

**2.2** This guideline covers the reporting of suspected defects involving following categories of medical products for both human and veterinary use:

i. Medical products registered and imported for supply in Bhutan;

ii. Medical products manufactured in the country;

iii. Medical products which are not registered in Bhutan but imported with authorization from DRA

**2.3** This guideline also covers the reporting of suspected defects of;

i. Medical devices

ii. TTI test kits

iii. Medical gases

iv. Health Supplements

## 3. Objectives

This guideline will:

i. Guide the stakeholders in reporting of suspected defective medical products to the DRA.

ii. Guide the DRA in assessing the suspected defective medical products reported to the DRA.

iii. Ensure that suspected defective medical products are assessed appropriately and in a required timeframe to withhold or recall the medical products.

## 4. Definitions

**4.1 Act** refers to the Medicines Act of the Kingdom of Bhutan 2003

**4.2 Authority** refers to the Drug Regulatory Authority

**4.3 Medical products** refers to medicinal products, Transfusion Transmitted Infection (TTI) test kits, medical devices used for both human and veterinary medicines

**4.4 Recall** refers to a permanent or temporary removal of medical products from the supply or use for reasons relating to deficiencies in the quality, safety and efficacy of the products.

**4.5 Regulatory action** refers to action taken by the DRA upon the recommendation by the recall committee.

**4.6 Stakeholders** refers to Marketing authorization holders (MAHs), Wholesalers and Retailers, Manufacturers, Healthcare professionals, Patients/Consumers

**4.7 Withdrawal** refers to the total withdrawal of a medical product from the market

## 5. Acronyms and abbreviations

**5.1 ADR;** Adverse Drug Reaction

**5.2 ATR;** Adverse Transfusion Reaction

**5.3 BMRR;** Bhutan Medicines Rules and Regulation

**5.4 CAPA;** Corrective And Preventive Action

**5.5 DRA;** Drug Regulatory Authority

**5.6 GMP;** Good Manufacturing Practice

**5.7 MAH;** Market Authorization Holder

**5.8 TTI;** Transfusion Transmitted Infection

**5.9 HS;** Health Supplements

## 6. Defective Medical Products

Defective medical product is a deficiency, which may produce an impact, whether directly or indirectly on the continuing quality, safety and efficacy of medical product and the health of the patient.

### 6.1 Classification of defective medical products

Suspected or confirmed product defect may be classified into three categories according to the risk posed to patient or animal health.

i. **Critical defects;** Critical defects are those defects, which have the capability to adversely affect the health of the patient.

Examples:

*a) Wrong product (label and contents are different products),*

*b) Correct product but wrong strength with serious medical consequences,*

*c) Microbiological contamination of a sterile product,*

*d) Chemical contamination with serious medical consequences,*

*e) Products of non-GMP compliant manufacturing firm,*

*f) Recurrent major medical product defects of same product with same batch.*

ii. **Major defects;** Major defects are those defects, which impair the therapeutic activity of the product. It may not be hazardous.

Examples:

*a) Mislabeling,*

*b) Missing or incorrect information (Leaflets/inserts),*

*c) Microbiological contamination of non-sterile product,*

*d) Chemical contamination/physical contamination with significant impurities*

*e) Non-compliance with pharmacopoeial specifications (assay, stability, fill/weight).*

iii. **Minor defects;** Minor defects are those defects, which have no important effect upon the therapeutic activity of the product, and do not otherwise produce a hazard.

Examples:

*a) Faulty packaging ex. wrong or missing batch number or expiry date,*

*b) Faulty closure*

### 6.2 Reporting of defective medical products to DRA

Following procedures are to be followed by stakeholders while reporting any suspected defective medical products to the DRA;

i. **What to report?**

a) The defective medical products may be suspected based on the organoleptic or physical verification of consignments and end-user's complaint.

b) The organoleptic or physical verification include visual check, friability or hardness check of the medical products. The defects can also be suspected based on the physical appearance such as:

- mislabeled drugs or in accurate or unreadable product labels/labeling
- sterile containers or vials that are leaking or capsule leakage
- abnormal smell, taste or tablet/capsule discolorations
- weight and sizes variations
- chipped, cracked, or broken and splitting tablets, or chipped syringes
- suspected product contamination
- vials with floating objects or foreign growths
- container closure defects and leaking vials

c) Any complaints from the use of Health Supplement can be reported to DRA using the annexure VI. However the defective products of health supplements can be reported by using the same form of medical product (Annexure I a)

ii. **How to report?**

a) The suspected defective medical products if observed or detected in the field should be reported to the Authority using the product defects complaint form attached as Annexure I or online reporting via DRA website. The verbal report will not be accepted.

b) The Reports should include minimum of following information.

- The brand name and the generic name
- The name of the manufacturer
- Batch number
- The strength and dosage form of the product
- Stock balance
- The expiry date
- Nature of the defects

- Storage temperature
- Reporters detail

c) Maintain the records of defective medical products reported to DRA

### 6.3 Action of DRA on the defective medical product reports

i. **Receipt of defective medical Product reports**

a) The Authority should acknowledge the reporter on the receipt of reports of suspected defective medical products and sample may be collected if required.

b) The Authority should maintain the record of the suspected defective medical products to establish the surveillance of other products.

ii. **Initial Assessment, Verification, and Spread of the Defective Products**

a) The DRA will assess and classify the defective medical products report using Annexure II to classify the defects. The initial assessment of the defective medical products is based on the organoleptic characteristics and visual examination of the defective medical products. While carrying out the assessment, the following considerations may be taken:

- Risk to the health of an individual (human or animal)
- Risk to the vulnerable patients as well as normal individuals
- Risks from the incorrect dosage (consider the therapeutic index),
- Long-term risk as well as immediate risk (e.g. if a completely dispensed container is faulty the impact on the individual will be cumulative, risk to persons administering a defective veterinary medical products, risk to the consumer of animal foodstuff in view of possible residues in the foodstuff): (detail out decision tree)

b) For critical defective medical products, alert the recall committee and recall the product based on the recall procedure of this guideline and other batches of the product should be monitored.

c) For major defective medical products, subject the product for Laboratory analysis and other batches of the same products should be reviewed to determine its distribution.

d) Direct communication with the reporter is important to obtain detailed information of the nature of defects.

e) Further communication with the individual who experienced the adverse reaction is also important to obtain the information of the nature of reaction.

f) Refer section 6.1 i. for frequently occurring major defective medical products for upgrading its classification into critical.

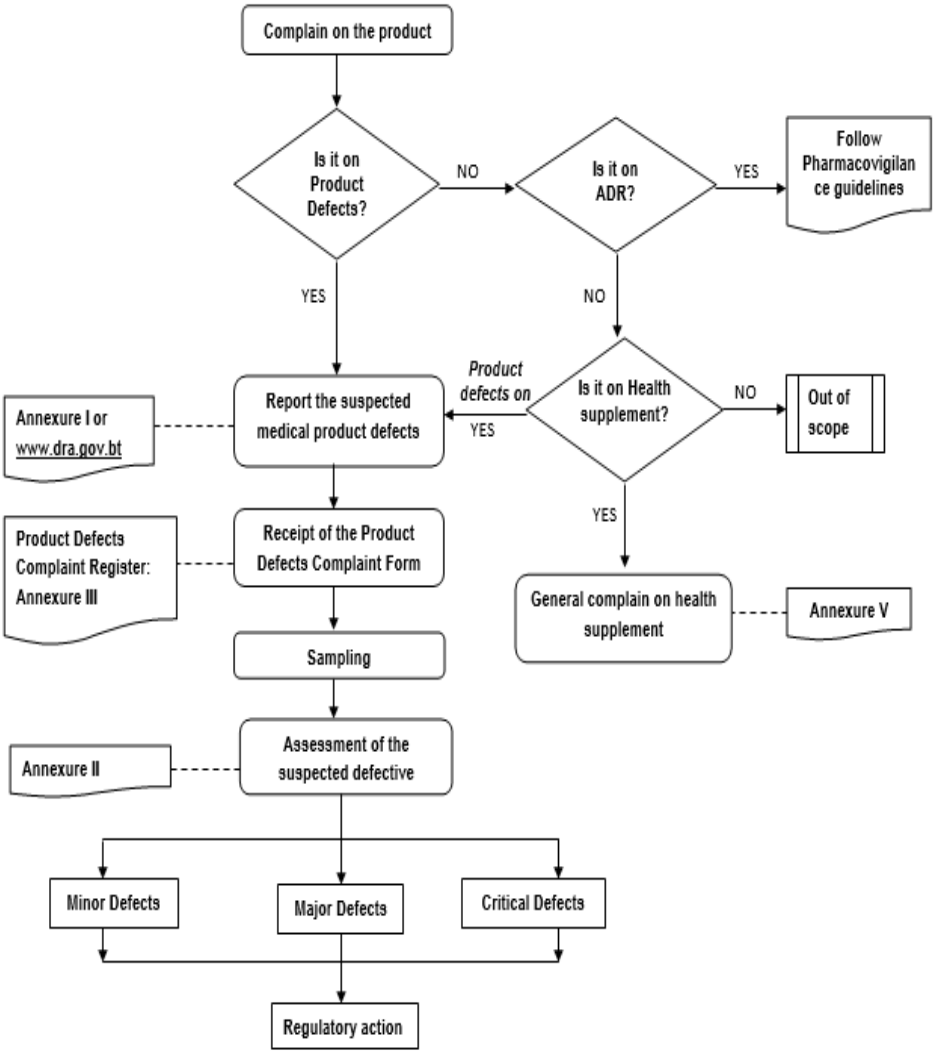
iii. **Secondary Assessment and Categorization of the Product Defects**

a) Based on the result of Laboratory Test Analysis, classify the product defects into critical/major/minor as per the definitions under this guideline.

b) The assistance from Government Analyst of National Drug Testing Laboratory may be sought for the interpretation of the Laboratory Test Analysis report.

c) For the products linked with the adverse drug events as reported by the National Pharmacovigilance Centre, the categorization of the product recall should be based on the Recall Committee formed under the section 7.1 of this procedure.

## 6.4 Process map flow of the defective medical product



## 7. Product Recall

The recall of defective medical products is based on the initial and secondary assessment of the medical product defect reports received by the DRA. The commencement of product recall is followed after alerting the Recall Committee about the defective medical products and convening the recall committee meeting. The Recall Committee decides the classification of recall, level of recall and recall timelines.

In the event of a recall, suppliers may be advised to plan for scenarios where there may be potential disruption of product supply.

### 7.1 Convene Recall Committee meeting.

Upon meeting two third of the recall committee members, the recall committee meeting is convened to categorize the class, level and timelines of recall.

Following are members of Product Recall Committee to decide on the recall of the products:

i. Drug Controller, DRA as Chairman

ii. Head of Pharmacy Department, Jigme Dorji Wangchuck National Referral Hospital (in case of Human Medicines)

iii. Principal Veterinary Officer/Chief Livestock Officer from Drug Technical Advisory Committee (in case Veterinary Medicines)

iv. Transfusion Specialist, JDWNRH (in case of TTI test kits)

v. Chief Regulatory Officer, Inspection Division, DRA

vi. Chief Regulatory Officer, Registration Division, DRA

vii. Chief Regulatory Officer, Post Marketing Control Division, DRA (as Member Secretary)

### 7.2 Classes of recall

Based on the degree of the defects of the medical product, the recall committee categorizes the recall into following:

i. **Class I Recall;** There is a reasonable probability that the use of or exposure to a medical product with **critical defects** may cause serious adverse health consequences or death.

ii. **Class II Recall;** The use of or exposure to medical products with **major defects,** which may cause temporary or medically reversible adverse health consequences.

iii. **Class III Recall;** A defective medical product, which is unlikely to cause any adverse health consequences but withdrawal may be required for other reasons such as non-compliance with the requirements of the Act or BMRR, faulty packaging and printings materials, Contamination (microbial spoilage, dirt or detritus, particulate matter), product specifications, labeling, inspection findings, etc.

For the minor defective medical product, Product Recall may be conducted based on the recommendations from the Recall Committee.

### 7.3 Levels of recall

Depending on the product's degree of hazard, channels by which the goods have been distributed and the extend/level to which distribution has taken place, following level of recall has been classified. One of these levels will be assigned during each product recall.

Expert opinion may be necessary to determine the significance of the hazard.

**i. Wholesale level:**

Usually initiated when the risk to patients or consumers is assessed to be low or where other measures can be taken to mitigate the risk to prevent disruption in supply of critical medical products (e.g. visual inspections or other interventions by healthcare professionals before supply to patients). The level of recall includes affected product or batch(es) from;

a) Wholesalers;

b) Government purchasing authorities etc.

The recalled product or batch(es) should be segregated in a secured area before the implementation of follow-up actions, e.g.

destruction of the products. All wholesale supply of the affected product or batch(es) should be suspended.

**ii. Retail level:**

Usually initiated when the risk to patients or consumers is assessed to be moderate to high but recall at consumer level is not deemed necessary (e.g. if the product is administered by healthcare professionals and not directly supplied to patients). The level of recall includes affected product or batch (es) from;

a) Retail pharmacists;

b) Medical, dental and other health care practitioners' establishments;

c) Other retail outlets;

d) Wholesale and hospital levels.

The recalled product or batch (es) should be segregated in a secured area before the implementation of follow-up actions, e.g. destruction of the products. All wholesale and retail supply of the affected product or batch (es) should be suspended.

**iii. Consumer level:**

Usually initiated when the risk to patients or consumers is assessed to be unacceptable, and where the product has been supplied to consumers. The level of recall includes affected product or batch (es) from;

a) Patients and other consumers; and

b) Wholesale, hospital and retail levels who had been supplied with the affected batch (es).

The recalled product or batch (es) should be segregated in a secured area before the implementation of follow-up actions, e.g. destruction of the products. All wholesale and retail supply of the affected product or batch (es) should be suspended.

### 7.4 Recall Timelines

Every supplier/company upon becoming aware of any defects in the medical products or upon the recall notification received from authority must ensure the recall of defective medical products within the following timelines:

i. **Class I recall;** recall within 24 hours up to a maximum of 72 hours

ii. **Class II recall;** recall within a maximum of 10 working days

iii. **Class III recall;** recall within a maximum of 30 working days

Every company who intends to recall defective medical products must notify DRA of, and the reasons for, the intended recall no later than 24 hours before the start of the intended recall.

### 7.5 Recall Procedure

Any batch of a product not meeting the defined quality standards has to be recalled from the market.

**i. Responsibilities of DRA**

a) **Recall Notification**: Based on the recommendations from the Recall Committee meeting, DRA shall notify the stakeholders in a following manner:

- Class I Recall; Notify the Market Authorization Holder within 24 hours from the date of confirmation by the Recall Committee for initiating the product recall of particular batch or all the batches of the product.
- Class II Recall; Notify the Market Authorization Holder within 2 working days from the date of confirmation by the Recall Committee for initiating the product recall of particular batch or all the batches of the product.
- Class III recall; Notify the Market Authorization Holder within 7 working days from the date of confirmation by the Recall Committee for initiating the product recall of particular batch or all the batches of the product.
- The authority should notify the Market Authorization Holder and the concern stockiest/in-charges to quarantine

the remaining stock during the investigation of the defective medical products.

b) **Inspection:** In order to ensure that the defective medical products are recalled as per the notification issued, the authority should conduct inspections.

c) **Press release:** For critical and non-critical medical defects and/or where the affected product is widely distributed, the authority may require the issuance of a press release to update the public on the recall in a timely manner

**ii. Responsibilities of the stakeholders**

a) **Initiation of recall;** Product recalls need to be initiated by the stakeholders upon the received of recall notification from the DRA. The product recalls should be conducted effectively by removing the affected product or batch(es) from the distribution chain within the timeline based on the class of recall. The stakeholders do not need to seek approval from DRA for initiating a product recall, but they must notify DRA of, and the reasons for, the intended recall no later than 24 hours before the start of the intended recall.

b) **Information to relevant agencies on the recall of medical product;** The responsible agencies should communicate the presence of defects and the recall actions taken, to the suppliers, customers/healthcare professionals and other relevant agencies through appropriate means to ensure effective and timely recall.

c) **Completion of recall**

The responsible agencies must inform DRA on the completion of a product recall by furnishing the Product Recall Completion Form (Annex IV). As a part of the recall completion report, responsible agency should update DRA on the follow-up actions that will be taken for the recalled products. Such actions include, but are not limited to:

- Destruction of the recalled products; the company should submit the certificate of destruction to DRA within 3 months from the completion of recall, unless otherwise justified.

- Re-introduction of the recalled products back into the market after appropriate CAPA has been implemented by the company; For this action, the company is required to seek and obtain prior approval from DRA, and if:
  - ✓ The products are in good condition;
  - ✓ It is known that the products have been transported, stored and handled under proper conditions;
  - ✓ The remaining shelf life period is acceptable;
  - ✓ The products have been examined and assessed by appropriate and qualified personnel, taking into account the nature of the product, any special storage conditions required, and the time that had elapsed since it was distributed.
- If any other actions are to be taken, specify them on the Product Recall Completion Form Reference:

***7.6*** *A Guide to Defective Medicinal Products, Medicines and Healthcare products Regulatory Authority, United Kingdom;*

***7.7*** *Guide to Reporting and Initial Investigation of Quality Defects in Medicinal Products for Human and Veterinary Use, Health Products Regulatory Authority, Ireland;*

***7.8*** *Reporting of therapeutic product defects and recall of therapeutic products, Health Science Authority, Singapore;*

***7.9*** *Uniform recall procedure for therapeutic goods, 2004 edition, Therapeutic Goods Administration, Australia;*

***7.10*** *Guidelines for Product Recall and Product Withdrawal, Pharmacy and Poisons Board, Republic of Kenya*

## Annexure I

### *a. Product defects complaint form for medicinal products*

| | **Product Defects Complaint Form** | | | |
|---|---|---|---|---|
| | **Document Number** | **Effective Date** | **Review Date** | **Version Number** |
| | DRA-F-D3-08-01 | 01-04-2018 | 01-07-2020 | 02 |

***Instructions:***

*i. This Form is used to report deficiencies/defects of medicines. Problems of this nature are usually found in a single batch(s) of a product.*

*ii. Do not report ADR on this form*

*iii. Use a separate form for each product reported*

*iv.* ***Return the completed form to Drug Regulatory Authority. (Fax no. 335803)***

| 1. Reporter (i.e Person reporting the Defects/Problem) | |
|---|---|
| Name: | |
| Occupation/Position: | |
| Institution/Organization: | |
| Address: | Telephone:<br>Facsimile: |
| 2. Complainant (i.e patient, customer, and client): **[IF ANY] or Leave it Blank** | |
| Name: | |
| Address: | Telephone:<br>Facsimile: |
| 3. Product Details | |

## DEFECTIVE PRODUCT GUIDELINE

| | |
|---|---|
| Name: | Brand name:<br>Generic name: |
| Composition(with strength): | |
| Batch no. | |
| Name & Address of the Manufacturer: | |
| Expiry Date: | |
| 4. Details of the Product Defects: *(If required, refer Quality Inspection Check Sheet for Pharmaceuticals Annex V, Guideline on Quality Inspection of Medical Supplies, Quality Assurance and Standardization Division, MoH)* | |
| Description of the Defects/Problem: | |
| 6. Details on Stock Balance and Storage: | |
| Do you have Stock Balance of the same batch product: | Please circle one: YES/NO<br>If Yes: How many? …… |
| Where was the product stored? | Please circle one:<br>Store Room/Dispensary?<br>If Others, give details: ..... |
| Storage Temperature (in degree Celsius) | (Please give the storage temperature as indicated on the thermometer at the time of reporting):……. |

| This Report was submitted by(Name): | Signature: | Date: |
|---|---|---|
| | | |

## DEFECTIVE PRODUCT GUIDELINE

**Leave this blank: For DRA's use only:**

1. Categorization of the type of Product Defects:

Critical ☐ Major ☐ Minor ☐ Not sure ☐

Alert Recall Committee YES ☐ NO ☐

| | | |
|---|---|---|
| **Reviewed by: (Post Marketing Control Division)** | **Signature:** | **Date of Review:** |

**Action taken:**

| **Prepared by** | **Reviewed by** | **Authorized by** |
|---|---|---|
| | | |

## Annexure I

### *b. Product defects complaint form for TTI test kits*

| | | | | |
|---|---|---|---|---|
| | **TTI test kits Defects Complaint Form** | | | |
| | **Document Number** | **Effective Date** | **Review Date** | **Version Number** |
| | DRA-F-D3-08-02 | 01-04-2018 | 01-07-2020 | 00 |

***Instructions:***

*i. This Form is used to report deficiencies/defects of TTI test kits. Problems of this nature are usually found in a single batch(s) of a product.*

*ii. Do not report Adverse Transfusion Reaction on this form*

*iii. Use a separate form for each product reported*

*iv.* ***Return the completed form to Drug Regulatory Authority. (Fax no. 335803)***

| 1. Reporter (i.e Person reporting the Defects/Problem) | |
|---|---|
| Name: | |
| Occupation/Position: | |
| Institution/Organization: | |
| Address: | Telephone:<br>Facsimile: |
| 2. Complainant (i.e patient, customer, and client): **[IF ANY] or Leave it Blank** | |
| Name: | |
| Address: | Telephone:<br>Facsimile: |

| 3. Product Details | |
|---|---|
| Name: | Brand name:<br>Generic name: |
| Product intended for: | |
| Batch no. | |
| Name & Address of the Manufacturer: | |
| Expiry Date: | |
| 4. Details of the Product Defects: | |
| Description of the Defects/Problem: | |
| 6. Details on Stock Balance and Storage: | |
| Do you have Stock Balance of the same batch product: | Please circle one: YES/NO<br>If Yes: How many? …… |
| Where was the product stored? | Please circle one:<br>Store Room/Dispensary?<br>If Others, give details: ..... |
| Storage Temperature (in degree Celsius) | (Please give the storage temperature as indicated on the thermometer at the time of reporting):……. |

| This Report was submitted by(Name): | Signature: | Date: |
|---|---|---|
| | | |

xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx

**Leave this blank: For DRA's use only:**

2. Categorization of the type of Product Defects:

Critical ☐ Major ☐ Minor ☐ Not sure ☐

Alert Recall Committee YES ☐ NO ☐

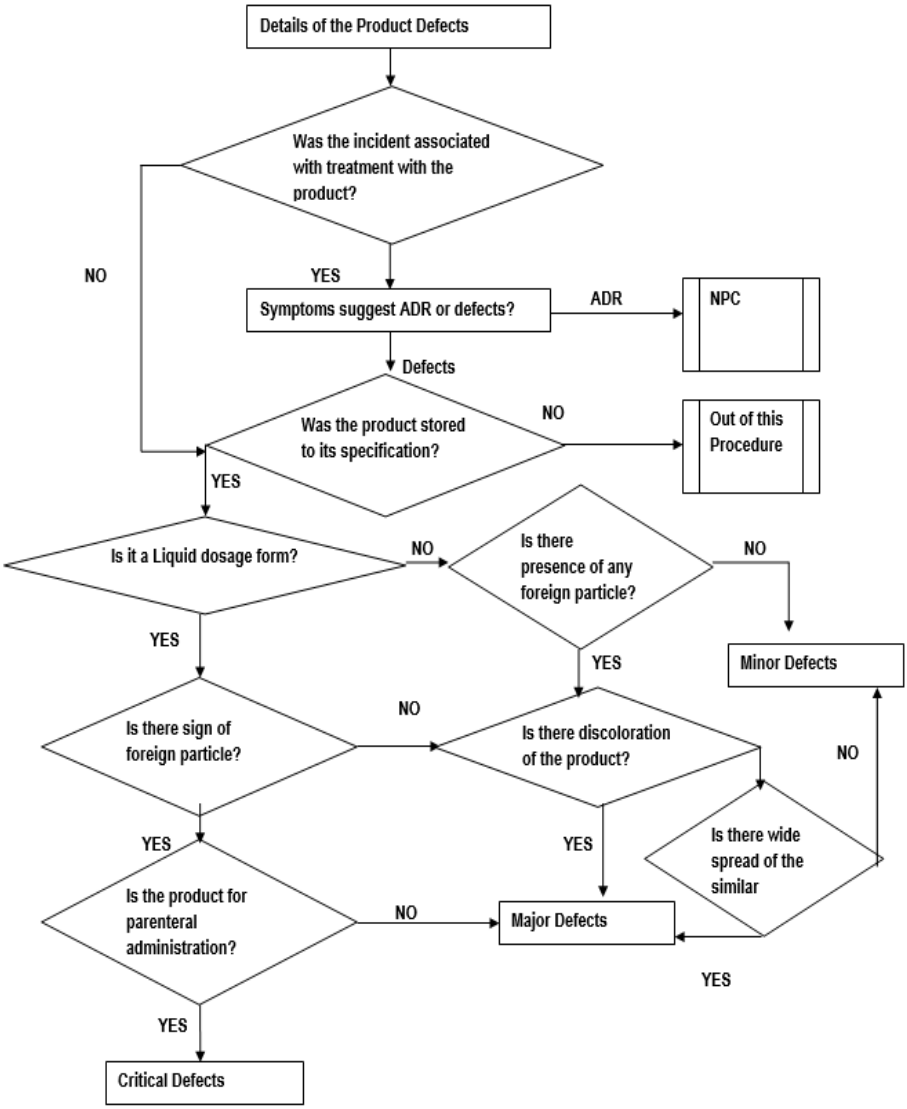
| | | |
|---|---|---|
| **Reviewed by: (Post Marketing Control Division)** | **Signature:** | **Date of Review:** |

**Action taken:**

| **Prepared by** | **Reviewed by** | **Authorized by** |
|---|---|---|
| | | |

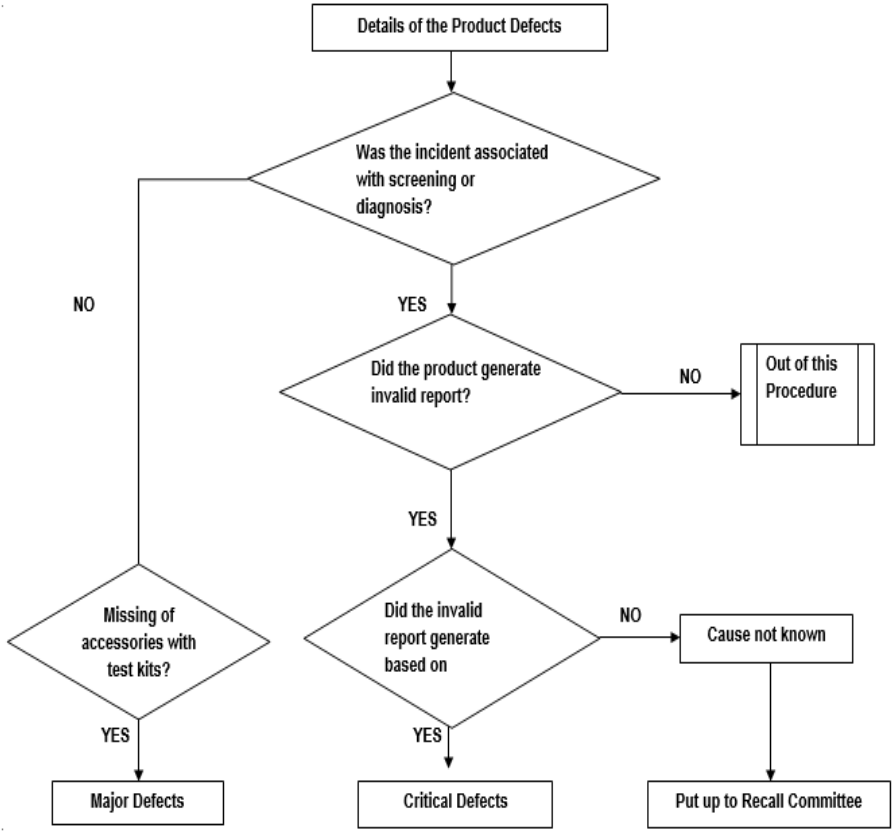
# Annexure II

## *a. Initial Defects Assessment Decision Tree for medicinal products*



## Annexure II

### *b. Initial Defects Assessment Decision Tree for medical products*



## Annexure III

***Product Defects Complain Register***

(Template Form)

| SI. No. | Product Details | Product Track number | Category of Defect | Immediate action taken | How it was resolved |
|---|---|---|---|---|---|
| | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |

## Annexure IV

***Product Recall Completion Form***

**Instructions:**
1. This form may take you 30 minutes to fill in.
2. You will need the following information to fill in the form:
   - Details of recall, including import and sales data, batches recalled, quantity recalled etc.

This form is to be submitted to the PMCD via email to **dra@dra.gov.bt**

**1 Details of company**

1.1 Name of company : _____
1.2 Address of company : _____
1.3 Name of reporting person : _____
1.4 Designation : _____
1.5 Office tel. : _____
1.6 Mobile tel. : _____
1.7 Fax : _____
1.8 Email : _____
1.9 Signature of reporting person: _____
1.10 Date : _____

**2 Details of recall**

2.1 Class of the recall : _____
2.2 Level of the recall : _____
2.3 Date of recall initiation : _____
2.4 Date of recall completion : _____

**3 Product details**

Additional products can be provided as an attachment.
3.1 Name of product : _____
3.2 Product license number or other reference number *(please indicate relevant reference number for unregistered therapeutic product)*:_____
3.3 Active ingredient(s): _____

3.4 Batch no: _____ Expiry date:_____
Batch no: _____ Expiry date:_____
Batch no: _____ Expiry date:_____
3.5 Quantity imported or manufactured in Bhutan:
_____
3.6 Quantity remaining in warehouse: _____
3.7 Quantity sold*: _____
3.8 Quantity recalled**: _____
*****Please attach sales record.
*Please provide names and addresses of purchasers and quantities recalled.

**4. Action(s) taken on affected stock(s)**

4.1 I confirm that the above recall has been completed on *(date)* _____and all recalled stocks have been planned for:

- Destruction,
- Re-introduction into the market upon approval by the Authority,
- Other actions upon approval by the Authority. Please specify the actions to be taken:

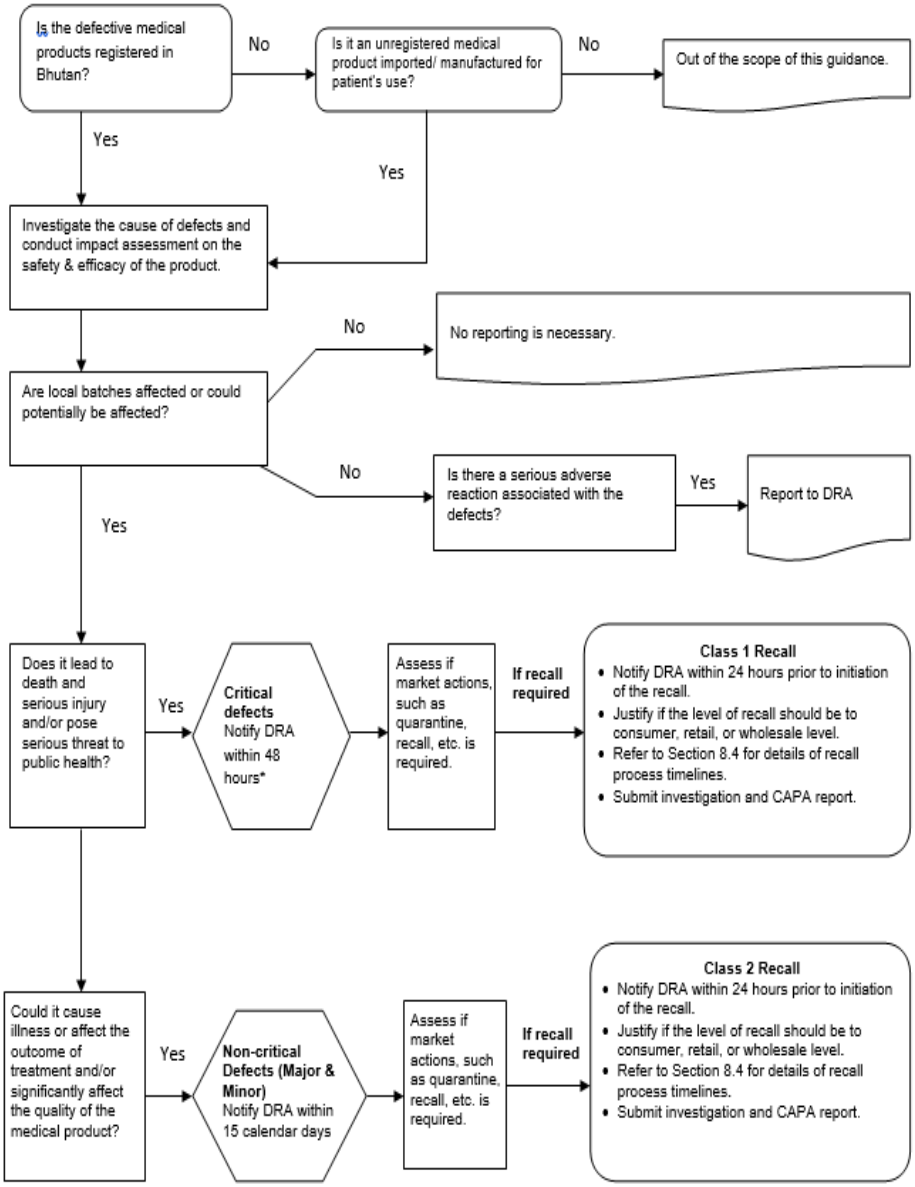
_____

_____

* Approval is not required. Documentary proof of action taken is required to be submitted once the recalled

# Annexure V

## *Flowchart on the summary of product defects and product recalls*



# Annexure VI

## *Health Supplement Incident Report Form*

| **1. Complainant Address** | | | |
|---|---|---|---|
| *Name;* | | | |
| *Address;* | | | |
| *Contact No;* | | | |
| *e-mail ID;* | | | |
| **2. Complainant** | **please tick (✓)the most appropriate** | **3. Complaint is about** | **please tick (✓)the most appropriate** |
| *Healthcare professional* | | *Product defects* | |
| *Competent person* | | *Adverse Reaction/event due to consumption of the product* | |
| *Patient/consumer* | | *Sale and distribution of product* | |
| *Other (Please specify)* | | *Other (please specify)* | |
| ***4. Details of the Health supplement;*** | | | |
| *Brand Name;* | | | |
| *Generic name;* | | | |
| *Batch number;* | | | |
| Name & Address of the Manufacturer: | | | |
| *Product used for;* | | | |
| ***5. Details of the complaint (please describe the complain)*** | | | |
| | | | |

***Signature;*** _____ ***Date;***

**Drug Regulatory Authority**

*Promoting availability of quality, safe and efficacious medicinal products for consumers*

Drug Regulatory Authority

Royal Government of Bhutan

P.O 1556

Phone: 337074.337075, Fax: 33580

Email: dra@gov.bt  Website: www.dra.gov.bt