Industry Training Workshop

Product Defect Reporting and Recall Procedures

29 October 2024, 2 – 4.30pm (Singapore Time)

Defective Medicine Management Unit
Vigilance and Compliance Branch
Health Products Regulation Group
Health Sciences Authority, Singapore

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Caveat

This presentation is intended to provide general guidance. Every effort has been made to ensure that the information is up to date and factual, we do not, however, warrant its completeness. Please note that product defect issues are complex, and it is not possible to a comprehensive solution to all potential scenarios. For specific concerns or questions, we recommend that companies consult with HSA directly.

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Outline of Industry Training Workshop

1. Product Defect Reporting
   a) Overview of legislative requirements
   b) Responsibility of company
   c) Sources of defect
   d) Top issues reported to HSA
   e) Product defect reporting form
   f) Timelines for reporting product defect
   g) Reportable and non-reportable defects
   h) Questions relating to product defects
   i) Investigation report & health hazard assessment
   j) Corrective action and preventive actions
   k) Common misconceptions

2. Product Recall Procedure
   a) Overview of regulatory framework
   b) Class and level of recall
   c) Recall timelines
   d) Key considerations when to initiate recall
   e) Product recall completion form
   f) Recall reconciliation
   g) Effectiveness of recall
   h) Questions and common misconceptions
   i) Case scenario

3. Communications Strategies
   a) Dear Purchaser Letter vs Dear Healthcare Professional Letter
   b) Example of a Dear Purchaser Letter
   c) Deficiencies in communication letters

4. Tools developed for product defect and recall procedures
5. Knowledge baseline quiz post to the training workshop
6. Q & A

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Industry Engagement

Nov 2016
Release of HSA guidance on product defect and recall of therapeutic medicines

Jan 2019
Online Product Defect Reporting and Product Recall Completion Forms (FormSG)

May 2019
Risk Classification Tool &
E-video on product defect and recall reporting

Graduate Certificate for Health Products Regulation by Duke-NUS CoRE

Jul 2024
Survey with companies

Oct 2024
Industry Training Workshop on Therapeutic Product Defects and Product Recall

Jun – Jul 2018
Survey and phone interviews with industry on format of reporting forms

Aug 2018
Talk on "Reporting of Therapeutic Product Defects and Recall" at 4th WHO-UMC-HSA Inter-Regional Pharmacovigilance Training Workshop in Singapore

Mar 2020
Nitrosamine briefing to Industry

Jul 2019
Feedback session with Industry

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Agenda

1. **Product Defect Reporting**
2. Product Recall
3. Communication Strategies
4. FAQ

1. Overview of legal requirements
2. Responsibility of company
3. Sources of defect
4. Top nature of issues reported to HSA
5. Product defect reporting form
6. Timelines for reporting product defect
7. Reportable and non-reportable defects
8. Questions relating to product defects
9. Investigation report & health hazard assessment
10. Corrective action and preventive actions
11. Common misconceptions

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Legal Requirements & Responsibilities of Company (Product Defect Reporting)

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Defective Product

A health product has a **defect** if —

a) it has or has possibly been adulterated or tampered with;

b) it is or is possibly a counterfeit or an unwholesome health product;

c) it is or is possibly of inadequate quality or unsafe or inefficacious for its intended purpose; or

d) it fails or could possibly fail to satisfy such other standards or requirements as may be prescribed.

Source: Health Products Act Section 42(6)

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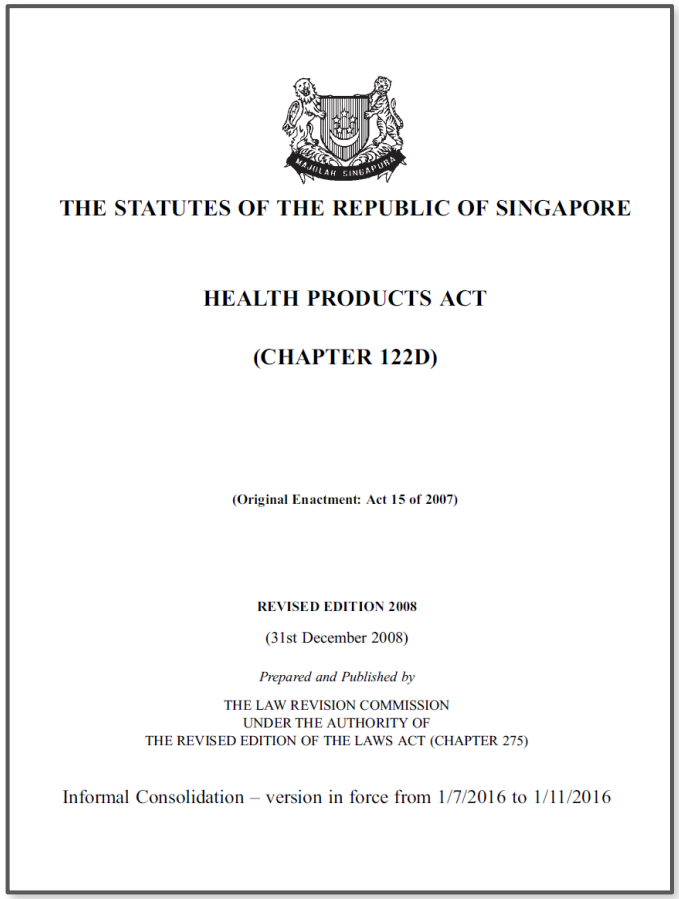
Legal Requirements



THE STATUTES OF THE REPUBLIC OF SINGAPORE

HEALTH PRODUCTS ACT

(CHAPTER 122D)

(Original Enactment: Act 15 of 2007)

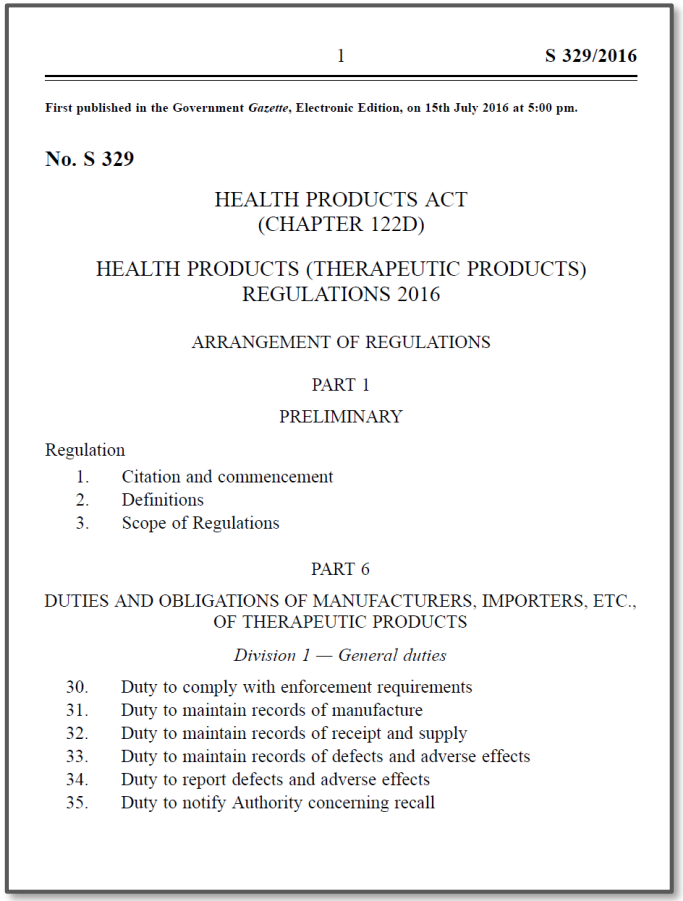
REVISED EDITION 2008

(31st December 2008)

Prepared and Published by

THE LAW REVISION COMMISSION
UNDER THE AUTHORITY OF
THE REVISED EDITION OF THE LAWS ACT (CHAPTER 275)

Informal Consolidation – version in force from 1/7/2016 to 1/11/2016



1 S 329/2016

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No. S 329

HEALTH PRODUCTS ACT
(CHAPTER 122D)

HEALTH PRODUCTS (THERAPEUTIC PRODUCTS) REGULATIONS 2016

ARRANGEMENT OF REGULATIONS

PART 1

PRELIMINARY

Regulation

1. Citation and commencement
2. Definitions
3. Scope of Regulations

PART 6

DUTIES AND OBLIGATIONS OF MANUFACTURERS, IMPORTERS, ETC., OF THERAPEUTIC PRODUCTS

Division 1 — General duties

30. Duty to comply with enforcement requirements
31. Duty to maintain records of manufacture
32. Duty to maintain records of receipt and supply
33. Duty to maintain records of defects and adverse effects
34. Duty to report defects and adverse effects
35. Duty to notify Authority concerning recall

1. Health Products Act
2. Health Products (Therapeutic Products) Regulation
3. Health Products (Cell, tissue and gene therapy products) Regulations

Refer to Health Products Act 2007, Section 42: "Reporting of defects and adverse effects to Authority" -- Where the **manufacturer, importer, supplier or registrant of a health product** becomes aware of any defect in the health product, it is the duty of such person to inform the Authority within the prescribed time of the defect or adverse effect.

(Supplier: Sell, display, transfer possession, supply, possess)

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Responsibility of Company

Regulation 34(1) of the Health Products (Therapeutic Products) Regulations

Every manufacturer, importer, supplier or registrant of a therapeutic product must, upon **becoming aware of any defect** in the therapeutic product, report the defect to the Authority —

a) if the defect represents a **serious threat** to persons or public health, **within 48 hours**; or
b) in all other cases, **within 15 days,**

after the manufacturer, importer, supplier or registrant, as the case may be, first receives notice of the defect

A person who fails to comply shall be guilty of an offence and shall be liable on conviction to a fine not exceeding $20,000 or to imprisonment for a term not exceeding 12 months or to both.

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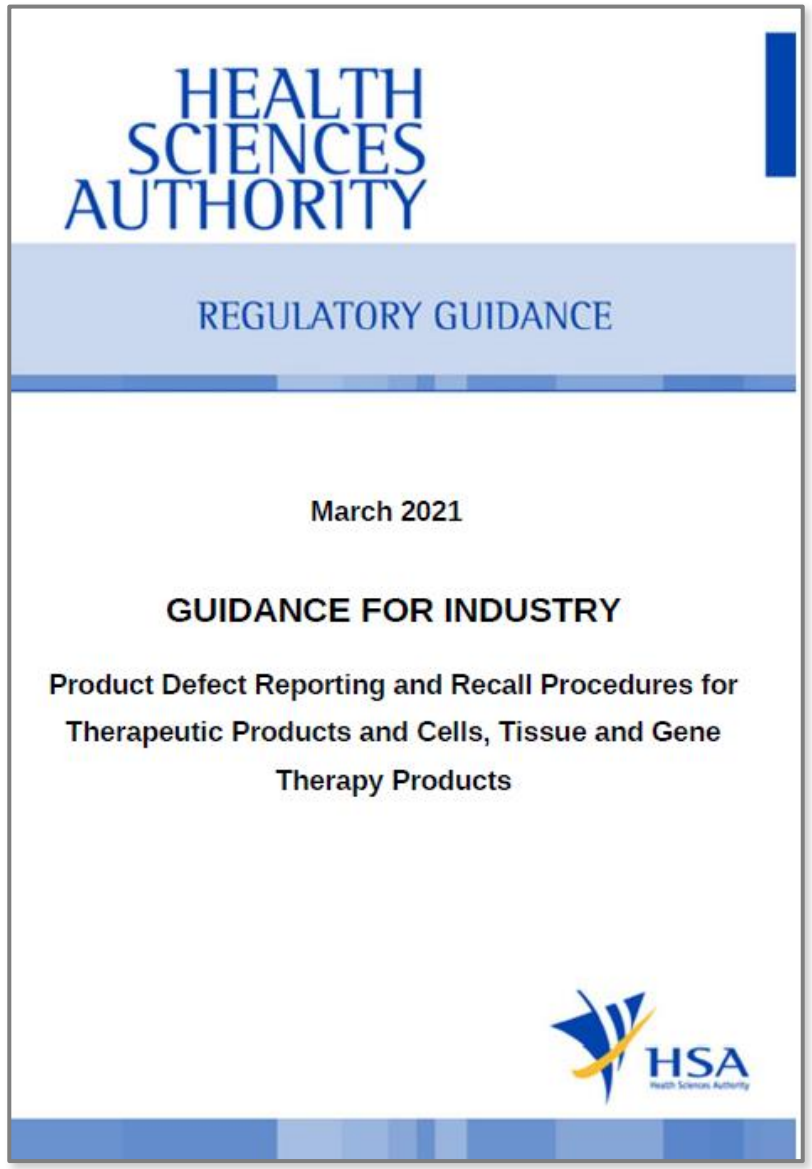
HSA Guidance for Industry



Applicable to product types:

1. Therapeutic products
2. Unregistered products for patients' use in Singapore - Special Access Route (SAR)
3. Registered products imported on consignment basis or via special consignment
4. Cells, tissue and gene therapy products
5. Products manufactured in Singapore for distribution outside of Singapore; and
6. Products used in clinical trials in Singapore

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Responsibility of Company

- Ensure therapeutic products, Cell, Tissue, and Gene Therapy Products (CTGTPs) meet the required standards of safety, efficacy and quality for patient use

- Have adequate systems and appropriate procedures in place to investigate, review, report product defects and if necessary, recall defective product from market

- Prevent further exposure to defective products

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HSA Guidance notes on Good Distribution Practice

Documentation and Product Complaints

5.2 Written procedures should be available to describe the different operations which may affect the quality of the products or of the distribution activities: personnel training, receipt and checking of incoming products, storage, deliveries, cleaning and maintenance of premises, pest control, monitoring and recording of the storage conditions, security of stocks on site, withdrawal of saleable stock, returned products, complaints, recalls, self-inspection, audit and assessment of contract acceptor, etc. The associated records of actions taken or conclusions reached should be maintained.

6.2 The procedure for handling product complaints shall ensure that the complaints received are investigated and followed through, and that corrective actions are taken to prevent recurring problems. All original details of the product complaint, investigations and subsequent corrective and preventive actions taken, including product recall should be documented in the product complaint record.

6.4 If a product defect is discovered or suspected in a batch, consideration should be given to determine whether other batches are also affected.

6.5 Product complaint records should be retained and periodically reviewed to evaluate trends, product related frequencies, and severity with a view to taking additional, and if appropriate, immediate corrective action.

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Product Defect Reporting

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HSA's Sources of Product Defects

Source of information about product defects and recalls

- Environmental scanning of selected regulatory agencies' webpages
- Company product defect reports
- Information sharing by overseas drug regulators and international working groups
- Media and Others

	2021	2022	2023	2024
Company	66.30%	47.11%	41.59%	40.53%
Environmental scanning	18.78%	26.67%	25.66%	29.47%
International work grp	13.81%	24.00%	26.55%	25.26%
Media	0.55%		3.98%	2.11%
Others	0.55%	2.22%	2.21%	2.63%

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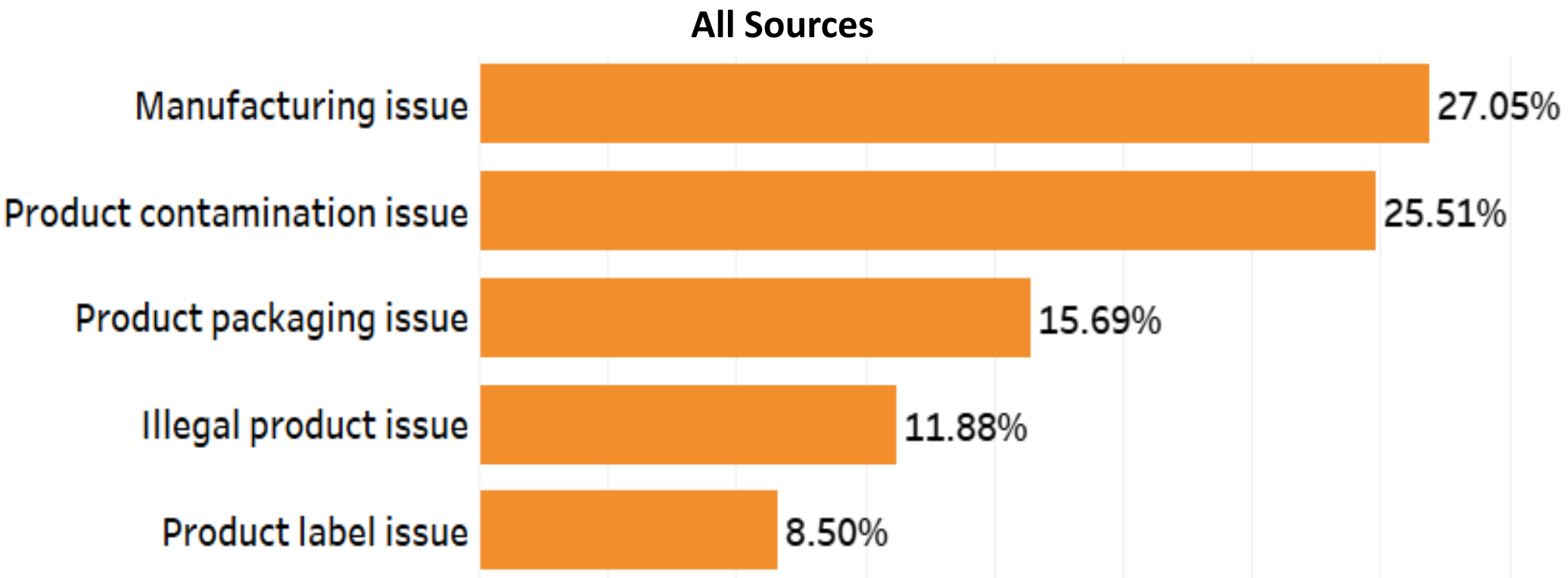
Top Defect Issues Reported to / Picked up by HSA (2011 – 2024)



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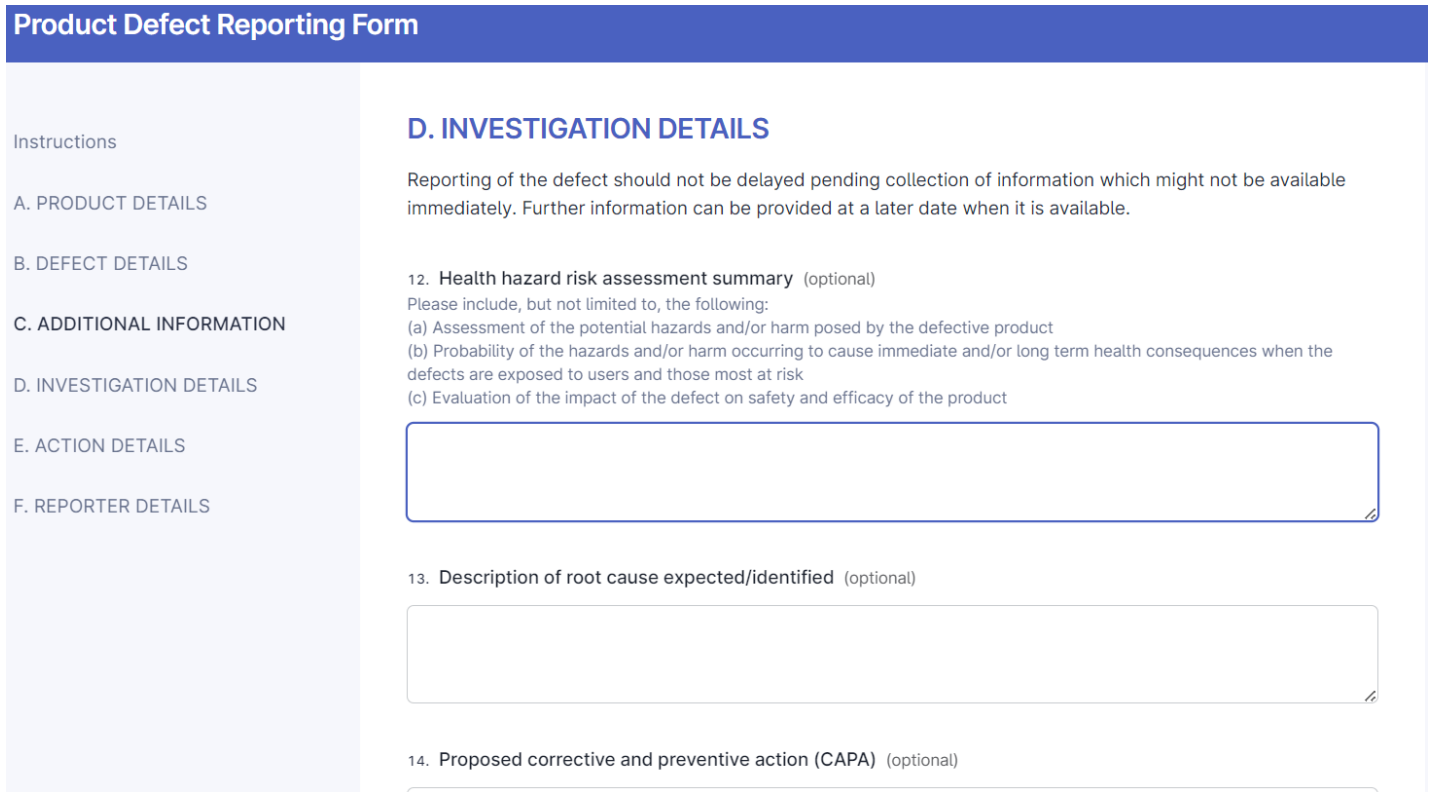
Details include in Product Defect Reporting Form:

- Product Name
- Manufacturer details
- Nature of the defect
- When was the defect discovered
- Date local company became aware of the defect
- Investigation information (summary or report if available)
- Proposed actions to be taken
- Is the product on tender supply

https://go.gov.sg/product-defect-reporting-form



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Timelines for Reporting Product Defects to HSA

The timeline starts when the manufacturer, importer, supplier or registrant **becoming aware of defect**.

Critical defect

- Can pose serious threat to the intended users or public health
- Can lead to death or serious injury e.g. result in hospitalisation

To consider particularly the impact of the defect on medicines that can cause serious harm to patients when the quality/safety/efficacy is impacted (e.g. injectables, life-saving medicines, chronic medicines, medicines for vulnerable populations such as children, elderly, or immunocompromised individuals)

→ Report within 48 hours

Non-critical defect

May cause illness or affect outcome of a person's medical treatment and/or affect quality of product

→ Report within 15 calendar days

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Reportable and non-reportable defects

Considerations

Examples

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Need for Product Defect Reporting

- Defects can affect the safety, quality and/or efficacy of the products.

- It is therefore important for such issues to be reported to HSA to **ensure that appropriate actions are taken to mitigate risks** to patients and consumers, and that corrective and prevention actions are taken to prevent recurrence of the issue.

As such, **all defects that can potentially affect** the safety, quality and/or efficacy of a product supplied or to be supplied in Singapore **are reportable** to HSA.

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Points to Consider on Defects Reportable to HSA

1. Defect likely to affect quality, safety and/or efficacy of the product:

- Manufacturing deviations or non-compliances to Good Manufacturing Practices (GMP)
- Out-of-specification issues
- Product mix-ups, product contamination issues
- Product packaging or labelling issues

2. The above includes situations where the affected batches have not been imported or supplied in Singapore but where the root cause can affect subsequent batches (e.g. systemic manufacturing issue).

3. Past case(s) of similar nature; cluster of incidences; not isolated event

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Examples of Critical Defect (Pose Serious Threat to Patients)

Manufacturing issue	Product formulation issue	• Active ingredient absent • Wrong active ingredient used
Product mix up	Product mix up	• Different strengths in same container e.g. 10mg and 20mg • Blisters with different strengths or ingredients packed in same box • Active and inactive pills incorrectly filled in a contraceptive pill pack • Wrong product filled
Product contamination physical	Contamination with glass and/or metal particle	• Visible foreign particles i.e. metal or glass
Product contamination with body fluid	Contamination with body fluid	• Contamination with blood, blood derivatives, saliva, sweat, tears
Product contamination microbial	Contamination with microbes	• Contamination with bacteria, virus, fungi (e.g. mould, yeast) – e.g. in sterile products

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Examples of Non-critical Defects

Manufacturing issue	Out of specification or out of trend test result	• Out of specification (OOS) and out of trend (OOT) test result in non-sterile products; can be results from drug product stability testing, deviations to drug product release specification, deviations to drug product shelf-life specification, deviations to drug substance specification
	Manufacturing non-compliance	• Good Manufacturing Practice (GMP) non-compliance • Revoked or suspended GMP Certificate
Product packaging issue	Primary packaging issue	• Missing product seal • Faulty child-resistant cap
	Secondary packaging issue	• Inner foil pouch damaged • In cases where the issue concerns labelling, it shall be classified as 'Product outer label issue' instead of 'Product secondary packaging issue'
Product label issue	Inner label issue	• Label missing on bottle • Text missing on label
	Outer label issue	• Misprinted outer carton label

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Examples of Non-critical Defects

Product physical issue	Product deposit	• Product crystals, precipitate, or sedimentation present
	Product physical issue	• Abnormal shape / size / colour / taste/ smell • Abnormal consistency / viscosity / texture • Capsule has extra shell
	Product adhesion issue	• Issues with adhesiveness of transdermal patch

It should be noted that the above are listed as possible examples of non-critical defects. Companies should assess each individual product defect to determine if it is a critical or non-critical defect as the potential impact of the defect on patients would depend on the specific case (e.g. indication of use, patient population, potential safety issue, etc).

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Non-reportable Defects

Certain **non-critical defects** are considered non-reportable e.g.:

User-related issues

- Defects arising **from improper handling, storage, or administration** by the users, rather than the product itself

Cosmetic issues

- **Cosmetic differences** that do not affect the intrinsic quality, efficacy or safety of the medicine

Isolated Incidents

- **Single occurrences** that are not part of a recurring pattern or cluster of similar defects
- Affected batch is not distributed but product is marketed locally

Non-supply (not yet marketed)

- Product is not supplied, and the defect is **not due to systemic manufacturing** issue

Company will need to

1. Assess if other or future batches will be affected
2. Report to HSA if the root cause **is due to manufacturing deviation and / or require variation submission to rectify defect**
3. Maintain a record of complaints related to these non-reportable defects
4. All investigation records to be made available upon HSA's request

If in doubt, please discuss with HSA.

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Examples of Non-reportable Defects

Defect issues
Minor cosmetic damage to outer packaging, blister damaged / tablets crushed probably during shipment, is a supply chain issue and affected products are not distributed
A batch with an **outdated logo** on the outer packaging, though the product inside is unaffected
Slightly **misaligned label** on the bottles, making it aesthetically unappealing but readable
Smaller font size than usual on the bottle label, making it slightly harder to read but the information is still legible
A batch with **smudged ink** on the blister pack, making the lot number slightly hard to read.*
The registered product is not distributed and the affected manufacturer is not registered in Singapore.
A slightly **different shade of colour** than previous batches, due to a minor variation in the colorant used during manufacturing
A batch is labeled with a **shorter shelf life** (1 year instead of the intended 2 years) due to a printing error. However, the actual shelf life remains 2 year
Patient returned an effervescent product (expired) and appeared bloated within the intact blister.
Isolated incidents of chipped tablets that was not due to manufacturing issue

* To review the need to use better ink

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Question 1

Do I need to report to HSA when the product is not yet on the market or imported?

Scenario: A pharmaceutical company manufactures a vaccine that has been distributed to several countries. During routine post-marketing surveillance, it was discovered that several batches of the vaccine contained **glass particles** due to an **issue in the manufacturing process**.

Mr Reg was informed by his company headquarters. The **same vaccine and affected manufacturer are registered in Singapore** but the product has not yet been marketed or distributed to healthcare providers. Does he need to report to HSA?

Answer: Yes

Rationale: The glass particles can pose a **serious health risk** as they can cause inflammation, infection, or serious injury if injected. This defect is a **systemic issue** resulting from manufacturing deviations or non-compliance to good manufacturing practice (GMP) at a manufacturing plant (which may be located in Singapore or overseas). This must be reported to HSA regardless of whether the affected batches are imported into Singapore or not. This is to **ensure that a proper investigation has been conducted and the manufacturing issue adequately addressed** (including submission of variation application) to ensure that the issue will not affect **subsequent batches imported to Singapore**.

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Question 2

Is lack of efficacy considered a product defect issue?

Scenario: A pharmaceutical company manufactures a **blood pressure medication** that is widely used to manage hypertension. Several patients reported that their blood pressure remained uncontrolled despite taking the prescribed doses. Further investigation revealed that several batches of the product contain only **80% of the active ingredient**, lower than the approved specification of 90% - 110%, due to a **manufacturing error**. The defective medication batches were also shipped to Singapore and have already been distributed to pharmacies.

Answer: Yes

Rationale: Lack of efficacy due to product quality issues is considered a product defect.

Uncontrolled hypertension due to **reduced potency** can lead to heart attacks, strokes, or other **severe complications**. For situations where lack of efficacy is reported (e.g. by healthcare professional or patient) but there is no visual defect or out-of-specification, it may be considered as an adverse event report instead.

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Question 3

Is missing QR code on product label reportable?

Scenario: A pharmaceutical company manufactures prescription medications with a **QR code** printed on the packaging. The QR code links to the **approved e-labelling** of the product (i.e. **package insert and/or patient information leaflet**). During routine quality checks, the company discovers that a batch of medication with missing QR codes on the packaging has been shipped and distributed. The packs of the product do not contain the physical copy of the package insert / patient information leaflet.

Answer: Yes

Rationale: Without the QR code, healthcare providers and patients are unable to access **critical information** about the product. This could impact the safe and effective use of the medication, potentially leading to medication errors or delayed identification of safety concerns.

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Question 4

Do I need to report out-of-specification relating to tablet hardness and thickness? Manufacturer justified that the quality and efficacy of the tablets are not impacted.

Answer: Yes

Rationale: Out-of-specification (OOS) results relating to tablet hardness and thickness should still be reported, even if the manufacturer has justified that quality and efficacy are not impacted. Regulatory authorities would require notification of **deviations from registered specifications**, as they could have potential implications to the product's stability, handling, or use by patients.

While the justification provided by the manufacturer may mitigate concerns, it is important to document and report the OOS findings to ensure full transparency and compliance with regulatory requirements. Reporting also allows for further assessment by the authorities to determine if additional actions are necessary.

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Question 5

Is isolated case reportable?

Scenario: A pharmaceutical company manufactures epinephrine auto-injectors (pens) used to treat severe allergic reactions (anaphylaxis). A patient experienced a severe allergic reaction and attempts to use their epinephrine pen. However, the **pen failed to activate**, and the medication was not delivered. The healthcare provider reported the malfunction to the company, but after reviewing the case, the company concluded that it was likely **an isolated incident** due to **improper handling or storage** by the patient. As a result, the company did not report the defect to regulatory authorities.

Subsequently, **several similar reports** of epinephrine pens failing to activate emerge from different users. At this point, the company realized that the problem was **not isolated and was due to a manufacturing defect** in several batches of the pens, which caused the activation mechanism to malfunction. It was initially overlooked due to the assumption that it was a handling error.

Answer: Isolated case due to patient mishandling is non-reportable. However, isolated incident due to manufacturing defect is reportable. As part of the product quality review in PIC/S GMP requirements, company needs to review complaints to decide if they need to improve their product even if it does not need to be reported as a product defect. E.g. they may need to improve on the design of the pen to make it more user friendly if the number of complaints due to improper handling by user is consistently high.

Note: Concept is applicable to "**Faulty calibrated droppers or pump**" (failure to deliver the correct dose) to check if it is a manufacturing issue.

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Question 6

Do I need to report cracked vials due to transportation mishandling?

Scenario: A pharmaceutical company manufactures an antibiotic injection used to treat bacterial infections, such as sepsis. This product is packaged in glass vials. Hospital reported **cracked vials or leaks** to the company. The company initially concluded that the cracks occurred during **transport** due to **rough handling or improper packaging** by the shipping company. They considered it was an isolated issue and instructed the shipping provider to be more careful with future deliveries.

Subsequently more reports of cracked vials come in from different regions. **Upon further investigation**, it was discovered that the cracking was due to a **manufacturing issue**. During the sterilisation process, the glass vials were exposed to excessive heat, making the glass more brittle and prone to cracking.

Answer: The above is reportable as it is due to a manufacturing issue. Cracked vials can pose serious health risk. **Sterility** of injection cannot be guaranteed and contaminated vials can cause patients to develop severe infections. Leaking vials can result in **dosing errors**, patients may not receive the full therapeutic dose of the antibiotic, which can lead to treatment failure and worsening of their condition.

Rationale: Defect due to **transportation mishandling is non-reportable**. However, do not assume that the problem was related to transportation issues. Failing to investigate thoroughly can delay the recall of a seriously defective product thus putting patients at risk. Company should **monitor and trend the number of complaints**. If it remains high, there is a need to improve the secondary packaging of the product e.g. thicker shipper boxes even if it is not a manufacturing issue.

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Question 7

Do I need to report chipped tablets?

Scenario: Company received reports of **chipped tablets from hospitals**. The tablet is used to prevent blood clots in patients at high risk of stroke. Company advised pharmacies to inspect the tablets for chips and report any issues, but no immediate recall was issued. After **further investigation**, it was found that the issue was due to a manufacturing defect affecting the tablet coating and compression process, causing the tablets to be more fragile and prone to chipping.

Answer: The above is reportable as it is due to a **manufacturing defect issue**. Chipped tablets make it difficult to ensure consistent dosing. Broken tablets disintegrate quickly and may affect the bioavailability and therapeutic efficacy of the active ingredient. Patients could receive underdosed amounts leading to risk of formation of blood clots.

Comments: Review all complaints and continued monitoring of similar defect / complaint for distributed batches that **were manufactured during the period of manufacturing defect**. However, when chipped tablets are discovered within acceptable quality limit (AQL) before release into the market, there is no need to report as product defect.

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Investigation reports, health hazard assessment, corrective & preventive actions

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A) Defect details and initial evaluation

1. **Detailed description of defect**: Include size, composition, and test reports.
2. **Sample evaluation**: Review the defective product (include photos if available).
3. **Cause and timing**: Explain how and when the defect occurred and was discovered.

B) Batch and distribution analysis

1. **Distribution records**: Provide local distribution details of affected batches. Indicate if it is under ALPS tender contract.
2. **Batch review**: Review whether other batches and products could be affected. Explain why the defect impacts only selected batches. Test retention samples if needed.

C) Historical and regulatory context

1. **Complaint review**: Review records for previous complaints and deviations.
2. **Regulatory actions**: List any actions taken by authorities or the company (e.g., recalls).

D) Root cause and risk analysis

1. **Root cause**: Identify the root cause(s) of the defect.
2. **Impact on patients**: Evaluate how the defect will affect patients' current treatment and health, especially in vulnerable groups like children, the elderly, and immunocompromised individuals.

E) Market and corrective actions

1. **Market actions**: Determine appropriate market actions for affected batches, e.g., quarantine or recalls. Consider product use and assess potential supply impact.
2. **Corrective and Preventive Actions (CAPA):** Describe steps taken to prevent the recurrence of similar defects.

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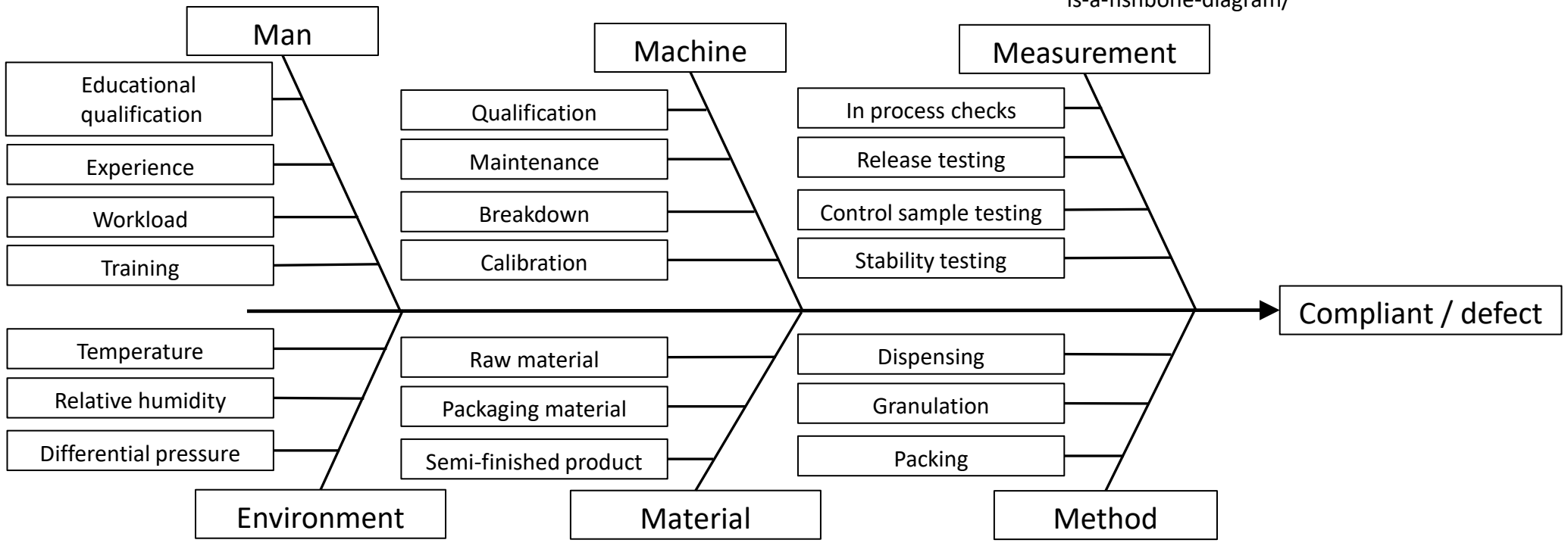
Examples of Tools Used in Investigation

5 M's analysis to identify root causes

1. Manpower
2. Machine (equipment, technology)
3. Material (includes raw material)
4. Method (process)
5. Measurement / medium (inspection, environment)

Fishbone (Ishikawa) diagram

Ref: https://pharmaceuticalupdates.com/2021/05/31/what-is-a-fishbone-diagram/



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Health Hazard Assessment

A systematic evaluation of the potential health risks associated with a defect in a pharmaceutical product

Assess the severity, likelihood, and consequences of a defect's impact on patient safety, thereby guiding appropriate regulatory and corrective actions

A) Hazard identification

1. Determine defect
2. Understand how defect could potentially harm patients

B) Risk analysis

1. Assess the likelihood it will go wrong or probability of defect occurring
2. Evaluate the potential for both short- and long-term health impacts, considering factors like toxicity, route of administration, dosage, and duration of use

D) Assessment of scientific and technical evidence

1. Conduct a thorough review of all available evidence, including laboratory test results, toxicology reports, and stability studies.
2. Historical data and expert opinions can further inform the assessment, as well as input from stakeholders or regulatory bodies

C) Impacts on patients

1. Analyze how the defect may affect patient treatment and overall health outcomes.
2. Consider special risk factors for populations such as children, the elderly, pregnant women, or immunocompromised individuals.

Ref: ICH guideline Q9 on quality risk management

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Considerations Behind Requested Documents / Information

		Risk Considerations		Extend of Impact Considerations	
No	**Documents / Info**	Clinical / Toxicology Risk	Immediate and long-term CAPAs with timelines	Impact to other batches and products	Supply issue
1	Investigation report (root cause & main investigation steps)		✓	✓	✓
2	Batch distribution data		✓	✓	✓
3	Health hazard assessment	✓	✓	✓	✓
4	Overseas regulatory action		✓	✓	✓

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Recommended Timelines for Submission of Document

Document	Timelines
Preliminary investigation & assessment (e.g. affected batches, root cause etc)	**Within 5 working days** from date of initial awareness of the defect (for critical defects) Within 15 calendar days from date of initial awareness of the defect (for non-critical defects)
Health hazard assessment (to determine the potential health risks associated with product defect)	**Within 15 calendar days** from date of report to HSA
Investigation report including CAPA	**Within 30 calendar days** from date of report to HSA An interim report at 30 days may be provided if closure is not possible

A thorough investigation should be completed in a timely manner within 30 days. However, some investigation may be more complicated and could exceed the time frame for submission of information. Requests for extension should be made based on the complexity of the investigation.

For critical defects that pose a serious threat to the intended users or public health, information must be submitted to HSA as soon as possible.

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Submission of Document

Additional documents that may be submitted to support assessment of defect

- Certificate of Analysis
- Stability studies of the affected / potentially affected batch(es)
- GMP certificate
- Inspection findings report
- Re-inspection report
- Letter of Undertaking

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Risk Mitigating Solutions

Reduce or Remove Risk

1. Product quarantine (retail vs wholesale)
2. Suspension of sales and supply
3. Product recall
4. Cease importation
5. Suspension of registration

Prevent Recurrence -CAPA

1. Manufacturing process change
2. Formulation change
3. In-process control change

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Question 8

CAPA: Revising product specifications for stability-related impurities

Scenario: A pharmaceutical company reported **degradant impurity** at 36-month stability study (1.1% vs Spec of NMT 1.0%). The degradant impurity exhibits a low acute toxicity potential and is devoid of mutagenic potential (AMES test). Instead of reducing the shelf life from 36 months to 24 months, the company proposes to increase the specifications of degradant impurity and the total impurities at release to remain unchanged.

Comments: A product defect report must be submitted. Widening of impurities specification should not be first approach.

Company should perform and investigatiion, determine **root cause** of the out-of-specification, especially if the impurity level has always been well within specification since registration; do a **trending** for historic stability data to determine if there is a shift in trends. Discuss the findings with HSA.

Changes can only be implemented after the MIV application has been approved.

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Question 9/10

Do I need to submit CAPA effectiveness report?

- CAPA effectiveness report is used to demonstrate that the actions taken to correct a product defect or non-compliance issue have been successful in preventing recurrence and ensuring product safety, quality, and efficacy. This may be requested when the CAPA is not finalised or disputable.

Can I request to bring in unaffected batches meant for another country via special consignment route as part of Corrective and Preventive Actions (CAPA)?

- Special consignment can be considered to mitigate out-of-stock situations. However, except for the artwork, the product from the **unaffected source** should have the same specifications as those locally. Refer to guidance on HSA website: hsa.gov.sg/therapeutic-products/register/special-access-routes/special-consignment-by-a-product-registrant

- If company needs to bring in the batch affected by the defect, please do not submit for special consignment approval. The request for the release of affected batch should be made as part of the defect reporting process.

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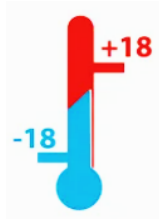
Question 11



Should company report a temperature excursion if it occurs frequently and what are the actions to be taken?

Scenario: A pharmaceutical company manufactures insulin, a critical medication for managing blood sugar levels in patients with diabetes. Insulin must be stored between 2°C and 8°C to maintain its efficacy. During distribution, it was discovered that several shipments of insulin vials were exposed to temperatures of up to 10°C for a day due to a **failure in transport refrigerator system**.

Answer:

- Company to assess whether the temperature excursion is within company SOP (to be supported by forced degradation data that temperature excursion is within acceptable limits and will not affect product quality). If it is outside of allowable excursion limit per SOP, **the batch should be rejected and cannot be released**. This **does not need to be reported**
- If affected batches of defective insulin have already been distributed → **Recall** is to be considered. Patients and healthcare providers are to be notified to stop using the product and switch to unaffected batches. Please report to HSA
- If it is marginally outside of the established excursion limit, the batch is **not yet released** and there is a **shortage** if the batch is not released, to discuss with HSA
- Company needs to conduct investigation to determine how the temperature excursion occurred and to ensure proper cold chain management of future shipments.

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Question 12

How should defective radiopharmaceuticals be handled?

Scenario: A pharmaceutical company recalls an **out of specification** radiopharmaceutical that has not been supplied to patient. The product was kept at the healthcare institution's waste decay room. How should the defective product be handled?

Comments: Radioactive pharmaceuticals require additional measures to ensure they are safely handled. The product should be disposed appropriately. HSA will consider providing the exception of allowing the product to be stored safely within the healthcare institution's premises for a brief stipulated period, but the regulatory requirements of its disposal must be adhered to.

i) The radiopharmaceutical must be disposed with the proof of the disposal to be submitted within 3 months (as with all recalled products); or

ii) Evidence showing that the radiopharmaceutical was shipped back to the manufacturer.

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Recap –
Common Misconceptions

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Common Misconceptions

1. **Product defect reporting is required only when the affected batch is supplied in Singapore.**

   If it is a systemic issue, it will indicate a wider problem within the manufacturing process that could affect future batches. Reporting ensures HSA is aware of potential risks and appropriate actions are taken. This is a proactive approach to public health, safeguarding against future risks and preventing batches with similar issues from reaching the market

2. **I am a distributor. Hence, I am not responsible for reporting product defect.**

   As a distributor, you are part of the supply chain and have a responsibility to ensure that unsafe or defective products do not reach the public. Distributors are also legally obligated to report product defects. You can report the defect to the product registrant who will then follow-up on the defect reporting to HSA e.g. investigation, CAPA etc.

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Common Misconceptions

3. **I can submit a post-approval variation application instead of a product defect report**

   No. Deviations from specifications are product defects. Regulations mandate that any product defect that may impact safety, efficacy, or quality must be reported when it is identified. A variation application alone does not fulfill this legal obligation.

   Variation applications are meant for prospective changes for future batches not imported into Singapore.

4. **I do not need to submit the investigation report for unregistered products imported for patients' use via the Special Access Route (SAR)**

   For unregistered products, HSA will still require an investigation report if there is a concern about product quality, safety, or efficacy. For the next SAR application, HSA will require the company to confirm that the issue has been addressed.

   It is still necessary and possible to request and obtain an investigation report from the manufacturer or supplier, especially if the defect affects the quality or safety of the product.

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Agenda

1. Product Defect Reporting
2. **Product Recall**
3. Communication Strategies
4. FAQ

1. Overview of legislative requirements
2. Class and level of recall
3. Recall timelines
4. Key considerations when to initiate recall
5. Product recall completion form
6. Recall reconciliation
7. Effectiveness of recall
8. Case scenario

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Legal Requirements & Responsibilities of Company (Product Recall)

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Product Recall

MIMS Multidisciplinary

Home | News | Diseases | Conferences | Special Reports | Multimedia

Medical News | Supplement | Case Studies | CME | Clinical Review | Practice Insights | Drug Updates

HSA recalls 8 brands of ranitidine products islandwide

Pearl Toh

26 Sep 2019

The Singapore Health Sciences Authority (HSA) has recalled eight brands of ranitidine products containing trace amounts of the nitrosamine impurity NDMA*, which is a potential human carcinogen.

Home

mypaper TUESDAY SEPTEMBER 20, 2011 A4

Drug with 'foreign particles' suspended

THE Health Sciences Authority (HSA) has suspended the licence for Zerin, a drug containing paracetamol and which is used to relieve fever and pain.

Small foreign particles had been found in some tablets from different batches, the HSA said yesterday after investigating four reports of product defects regarding Zerin tablets since last month.

Laboratory tests showed that the foreign particles are inert, non-toxic substances and pose minimal risk to consumers.

The tests also showed that the paracetamol content in the tablets complies with registered specifications.

Although the health risks to consumers are low, all sales and distribution of Zerin tablets have been discontinued at public health-care institutions, private medical clinics and pharmacies.

"Consumers who have already taken the affected product should not be unduly alarmed as the product defect has been assessed to pose minimal risk to health," HSA said.

Zerin tablets are manufactured by Bangladeshi company Jayson Pharmaceuticals and distributed here by Ziwell Medical.

The product was approved for use by the authorities in November 1996 but, at the time, only small quantities were sold here.

From November 2005, HSA observed larger quantities of Zerin being sold here.

HSA said it is working with Ziwell Medical and Jayson Pharmaceuticals to ascertain the cause of the product defects.

It added that it has worked with the drug companies and health-care providers here to ensure that there are sufficient supplies of other brands of paracetamol to meet demand.

As an added precaution, HSA has suspended the local licences of all products manufactured by Jayson Pharmaceuticals.

The other product by the company that is available here is Histacin – an antihistamine, which is a type of drug used to control symptoms of allergies.

HSA advises consumers who have stocks of Zerin tablets to stop consuming the product.

myp@sph.com.sg

STOPPED: Despite the drug's suspension, the HSA says that the health risks to consumers of Zerin are low. (PHOTO: HSA)

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Product Recall

- A process of removing or correcting products that are deemed **unsafe or defective**.
- Initiated to protect consumers from harm.
- Companies should consider and initiate a **product recall** to remove defective batches from the market where necessary and feasible.
- HSA can request companies to conduct a recall to mitigate potential risk to consumers. An official letter to direct the recall can be issued by HSA.

  [Under Section 42(2)(c), HSA can require the manufacturer, importer, supplier or registrant of the health product to recall the health product and take such measures as the Authority may specify to secure the immediate stoppage of the manufacture, import, supply, use or administration (as the case may be) of the health product.]

Note: Exchange initiated for business reasons rather than due to a product defect is not classified as a recall.

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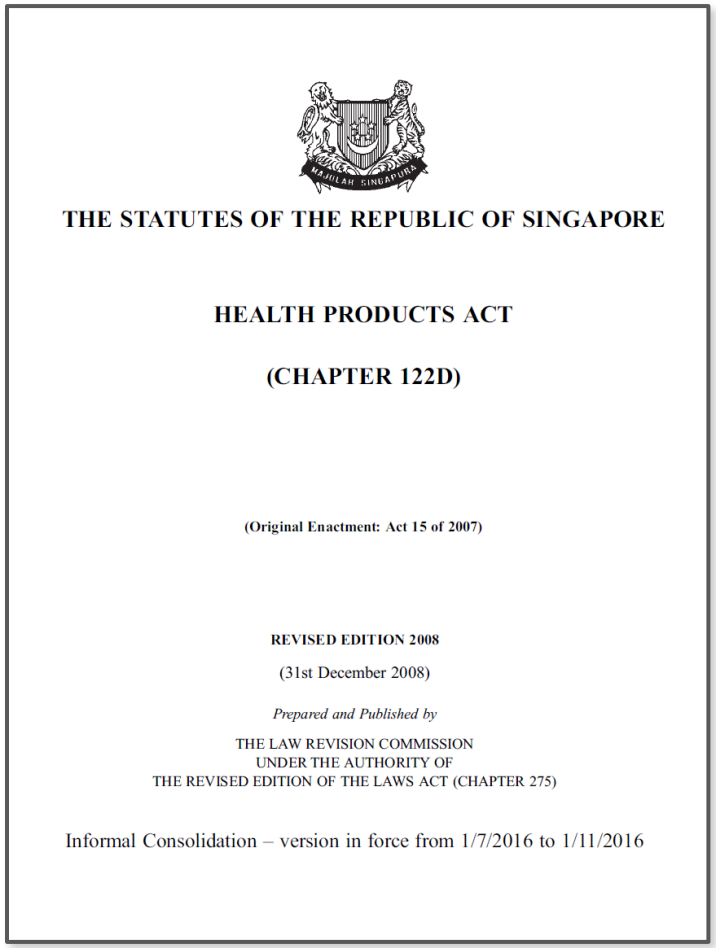
Legal Requirements To Notify HSA



THE STATUTES OF THE REPUBLIC OF SINGAPORE

HEALTH PRODUCTS ACT

(CHAPTER 122D)

(Original Enactment: Act 15 of 2007)

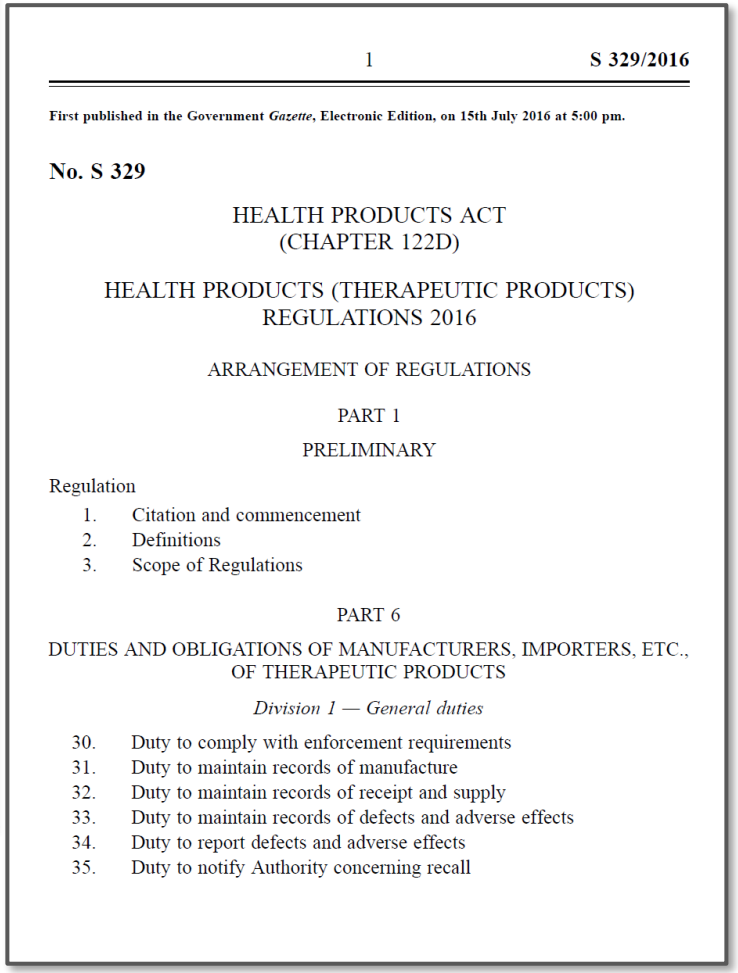
REVISED EDITION 2008

(31st December 2008)

Prepared and Published by

THE LAW REVISION COMMISSION
UNDER THE AUTHORITY OF
THE REVISED EDITION OF THE LAWS ACT (CHAPTER 275)

Informal Consolidation – version in force from 1/7/2016 to 1/11/2016



1 S 329/2016

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No. S 329

HEALTH PRODUCTS ACT
(CHAPTER 122D)

HEALTH PRODUCTS (THERAPEUTIC PRODUCTS) REGULATIONS 2016

ARRANGEMENT OF REGULATIONS

PART 1

PRELIMINARY

Regulation

1. Citation and commencement
2. Definitions
3. Scope of Regulations

PART 6

DUTIES AND OBLIGATIONS OF MANUFACTURERS, IMPORTERS, ETC., OF THERAPEUTIC PRODUCTS

Division 1 — General duties

30. Duty to comply with enforcement requirements
31. Duty to maintain records of manufacture
32. Duty to maintain records of receipt and supply
33. Duty to maintain records of defects and adverse effects
34. Duty to report defects and adverse effects
35. Duty to notify Authority concerning recall

Refer to Health Products (Therapeutic Products) Regulations

Section 35: "For the purposes of section 44(1) of the Act, every manufacturer, importer, supplier or registrant of a therapeutic product who intends to recall a therapeutic product must immediately, but in any case **no later than 24 hours before the start of the intended recall**, **notify the Authority** of, and the reasons for, the intended recall.

A person who fails to comply shall be guilty of an offence and shall be liable on conviction to a fine not exceeding $20,000 or to imprisonment for a term not exceeding 12 months or to both.

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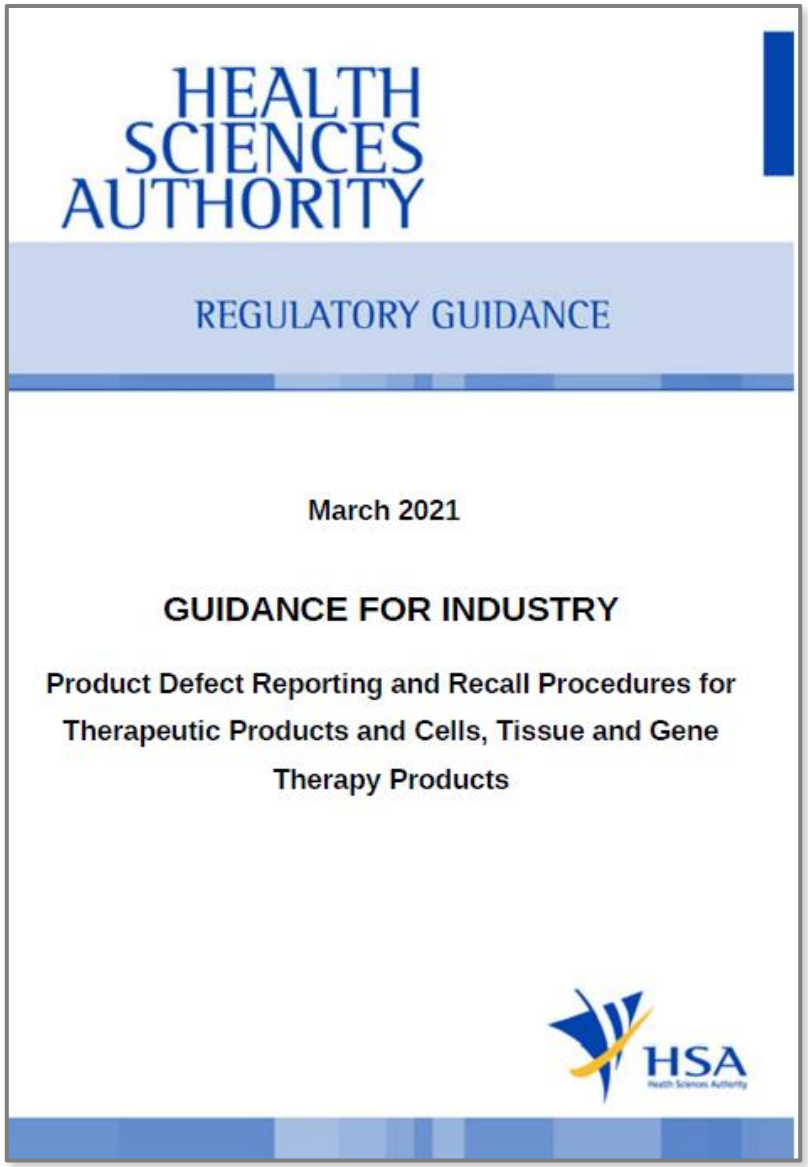
Guidance for Industry



- Product recalls may be initiated by the company.
- Company does not need to seek approval from HSA for initiating a product recall BUT must notify HSA **no later than 24 hours before the start of the intended recall**
- If necessary, HSA may **escalate** the class and/or level of product recall.
- Ensure that your recall procedures are **effective**.
- Maintain an **accurate list of all supplied customers** so that they can be notified expeditiously in the event of a recall. A written communication is recommended so that customers will have record of the recall and instructions.
- **Evidence of receipt or acknowledgment** of the **recall notice** by customers.
- Keep HSA informed of the **progress of the recall**.

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Product Recall

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Product Recall

- 2 dimensions to a recall
  - Class: speed of the recall
  - Level: depth of the recall

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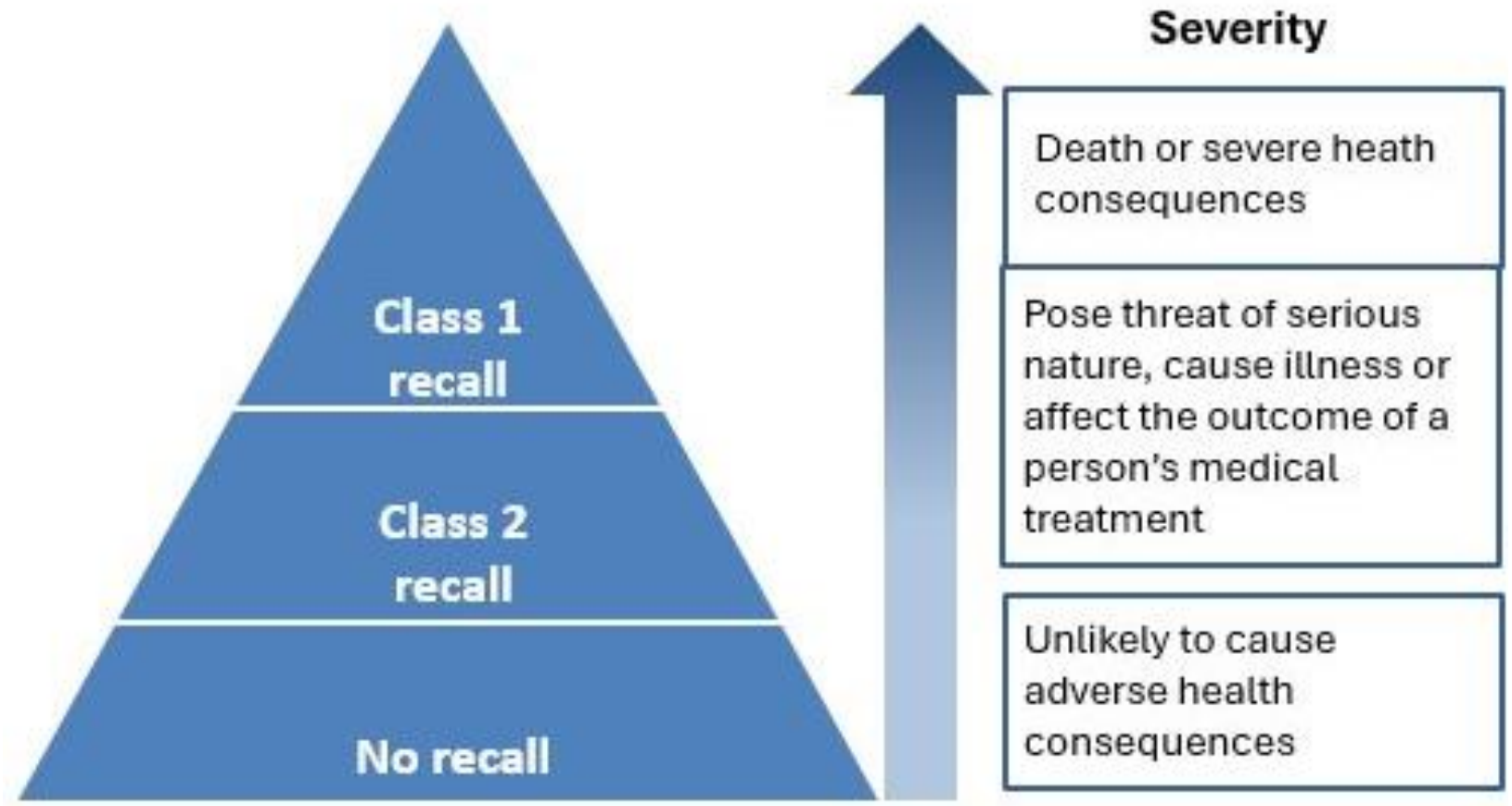
Class of Recall

Determine Severity to patient



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Recall Timelines

Class 1 Recalls

0	• Notify HSA of Recall
1 day	• **Conduct Class 1 Recall**
1 day	• Issue Dear Purchaser Letter
1 wk	• Recall all affected stocks
90 days	• Dispose recalled stocks

Class 2 Recalls

0	• Notify HSA of Recall
1 day	• **Conduct Class 2 Recall**
3 days	• Issue Dear Purchaser Letter
3 wks	• Recall all affected stocks
90 days	• Dispose recalled stocks

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Level of Recall

Supplier (raw materials)

Manufacturer

Importer / Wholesaler / Distributor

Retailer

Patient

Consumer level recall

Retail level recall

Wholesale level recall

Depends on:

- **Extent of distribution**
- **Potential hazard** of the affected product; risk to patients

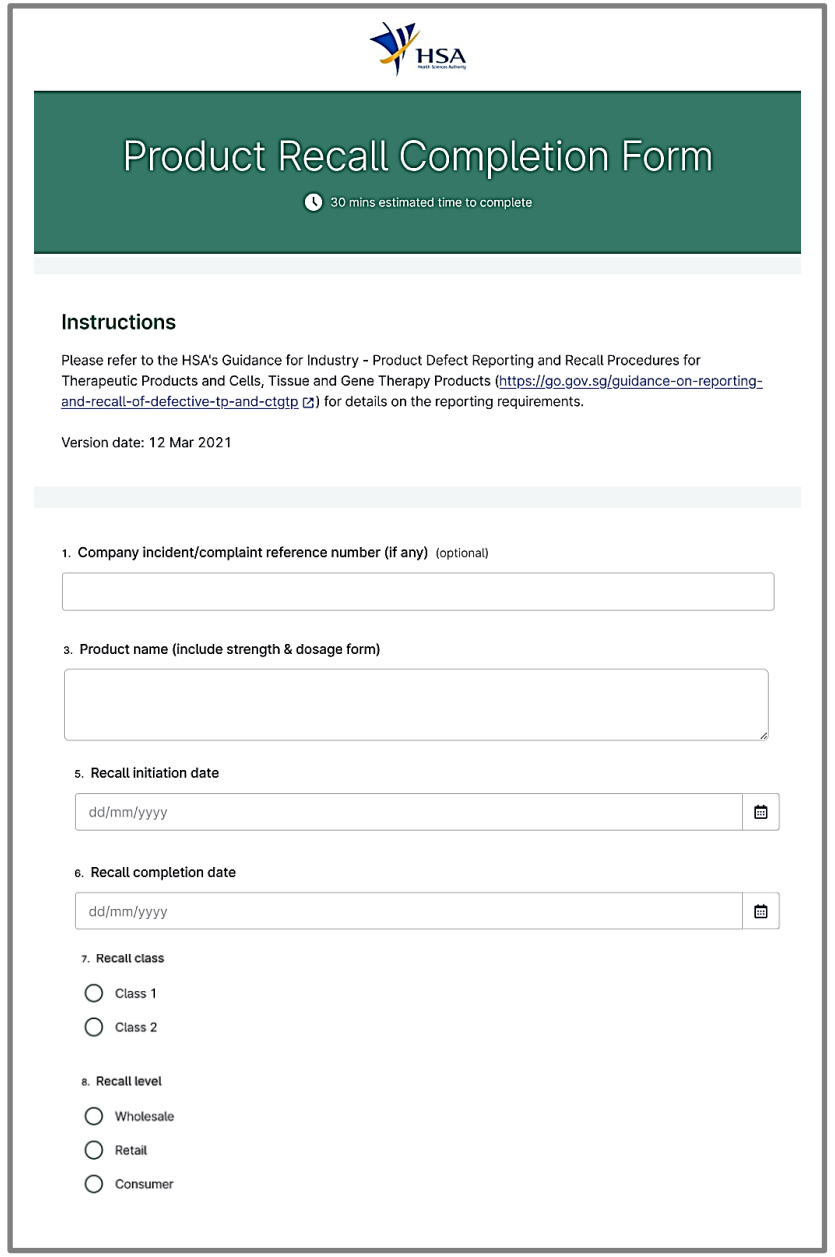
If the recall only extends to the wholesale level, the company needs to explain the rationale for not recalling at retail / consumer level.

Product Recall Completion Form

Furnish the Product Recall Completion Form upon completion of the product recall, together with a report of reconciliation of quantities of each affected batch (i.e. sold and returned quantities)

Update HSA of the follow-up actions for the recalled products (e.g. submit certificate of destruction to HSA **within 3 months** from completion of recall)

https://go.gov.sg/product-recall-completion-form



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Reconciliation and Effectiveness of Recall

Recall reconciliation

1. Product distributed to each customer (who, amount, date, batch no.)
2. Product returned by each customer (who, amount, date, batch no.)
3. Product not recovered (amount, explanation of any discrepancies e.g. sold, consumed or lost)
4. Product still in inventory (amount, batch no.)
5. Quantity recalled matched quality returned, held in quarantine or destroyed

Effectiveness check of recall

1. Verify notification to confirm all affected parties are notified about the recall
2. Evidence of receipt of recall notice by recipients (e.g. acknowledgment of communication)
3. Measure the response rate
4. Track and document the amount of recalled product returned, recovered, or destroyed, as well as for those non-recovered product
5. Conduct on-site checks (warehouse, retailers) to confirm that no affected products are still being sold
6. Implement corrective actions (e.g. product disposal, refunds)

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Questions (Recall)

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Question 13

Hospitals and clinics would pre-pack the medicines into smaller pack or syrup bottles. My products could be in a bottle of 500's, 10x10 strips of tablets or 1L of syrup. In the event of recall, can I not take back the loose tablets or syrup?

Answer: No

In the event of a recall, all affected products including loose tablets or repackaged syrups must be returned, regardless of their original packaging. This is to ensure patient safety and prevent the use of potentially defective medicines which must be properly disposed of.

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Question 14

Who is responsible for recalling the products from vending machines?

Answer: Products supplied via vending machines should be treated in the same manner as products supplied via other supply mechanisms.

If a recall is necessary to remove the product from supply to patients/consumers, suppliers have **the ultimate responsibility** to promptly recall the defective medicine in a timely manner. They should work with all the relevant stakeholders involved in the distribution chain (including wholesalers and retailers) to ensure an effective recall and tracking of all distributed products. The expectations should be clarified with the parties who are responsible for the supply of the products in the vending machines to ensure that products supplied in the vending machines are retrieved and recalled as per the required recall timelines.

Product registrants should convey this to your purchasers who have supplied the products via vending machines.

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Question 15

Is there requirement for the recall simulation to be conducted if actual recall does not happen within 12 months?

Answer: A licensed importer or wholesaler is expected to maintain a GDP-compliant quality system that ensures that the effectiveness of the arrangements for product recall is evaluated.

Typically within a year, a company will perform some assessments, e.g. a regular interval recall simulation, if there is no actual product recall. Though HSA does not prescribe the frequency of the evaluation, company should use a risk-based approach to have an adequate frequency of the product recall exercise.

If we had a near miss incident this year (traceability completed, stocks have been quarantined at market warehouse level while waiting for the product incident review meeting), can we consider this to be a recall simulation?

Answer: A licensed importer or wholesaler is expected to maintain a GDP-compliant quality system, and the company should have an established procedure on product recall. The company should ensure that the SOP guides the company on how actual product recalls and the activities/assessments that should be performed to ensure that the effectiveness of the arrangements for product recall is evaluated.

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Common Misconceptions

1. **1-to-1 exchange with purchasers due to a product defect is not considered recall.**

   Any form of taking back the product that has been identified as having *a defect / deviation from registered specification* is considered a recall.

2. **My recall is expected to exceed the stipulated timeline, but I don't think I need to send a request to HSA to ask for an extension.**

   Class 1 – To complete recall within 1 week, Class 2 – Within 3 weeks.
   Company should notify HSA promptly of the reason(s) for delay and propose reasonable timeline for completion.

3. **Company can wait to destroy their recall products.**

   Company should plan for destruction of recalled products by a licensed waste disposal company. The certificate of destruction should be submitted within 3 months from recall completion. This document is an important part of the recall process to ensure that defective products are safely and appropriately disposed of. Timely submission ensures transparency, accountability, and that the defected products are no longer a risk to public health. If there are delays, the company should inform the regulatory authority with a valid justification and propose a reasonable timeline for completion.

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Case Studies

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Case 1: Microbial contamination in stability samples

Pharma Sing Pte Ltd is the product registrant for ABC 5% injection. Pharma Global Inc is their global counterpart. This **injection** is a generic drug and a prescription only medicine. It is indicated for use in children, adults and elderly for the treatment of disease X. The shelf life of the product is **36 mths**.

In **May 2024, HSA was first alerted** to the recall of one batch of ABC Injection in Country A. There was **microbial contamination** detected in the stability samples. The issue was discovered due to **changes in appearance of the solution** which did not conform to the specifications.

When HSA contacted Pharma Sing on **28 May 2024**, **company initially not aware of the issue. Company initially proposed not submiting product defect reporting form** as the batch recalled in Country A **was not imported into Singapore**.

The OOS was confirmed by Pharma Global Inc. **on 28 Feb 2024**, but **local registrant was not informed by their global team**.

Subsequent investigations identified more batches impacted because there could be lapses in the aseptic manufacturing process. The local batches are from the same manufacturing site of the recalled batch.

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Case 1: Microbial contamination in stability samples

Pharma Sing Pte Ltd then **submitted a product defect report (PDR) on the 10 Jun 2024.** Based on the investigation report attached, 5 batches are implicated. A medical risk assessment was provided which indicated that there was a risk of patients developing systemic infection that might lead to **critical and life-threatening infections and even death**.

critical defect to be reported 48hrs upon aware

Batch	Mfg Date	Expiry	Distribution Details
BN001	Feb 2023	Jan 2026	Last distributed in Apr 2024
BN002	Mar 2023	Feb 2026	Last distributed in May 2024
BN003	Apr 2023	Mar 2026	Last distributed in May 2024
BN004	Apr 2023	Mar 2026	100 vials remaining in the warehouse
BN005	May 2023	Apr 2026	Not yet distributed

In the PDR, Pharma Sing proposed a Class 2 wholesale level recall with the issuance of a Dear Purchaser Letter (DPL).

HSA requested the company to conduct a Class 1 retail level recall due to the serious health risk from the defect. HSA informed that a Class 1 retail recall would need to be completed within 1 week.

Microbial contamination of injectables can pose serious risk to patients thus it warrants a Class 1 recall

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Case 1: Microbial contamination in stability samples

The recall was initiated on 11 June 2024 and a copy of the Dear Purchaser Letter was provided to HSA and distributed to all their purchasers.

On 18 June 2024, the recall completion form was not submitted to HAS. They informed HSA of their inability to complete the recall within 1 week due to logistical constraints, but only after HSA proactively reached out for an update. Pharma Sing then requested for an extension of 1 week to complete the recall.

After the recall Pharma Sing engaged Super Waste Pte ltd to destroy the recalled product and the certificate of destruction was provided to HSA.

Learning point: the decision to submit product defect should be based on root cause. Even if OOS batch is not imported into SG, **if the root cause is a systemic issue**, product defect should still be submitted. When the whole manufacturing plant is affected, even if the affected product is not registered in Singapore, all other sterile registered product in Singapore will be affected and a product defect reporting form needs to be submitted.

Pharma Sing **should inform HSA** if unable to complete the recall within the required timelines and **to request for extension** of timelines.

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Case 2: Company's request to widen registered specification of assay value of the active ingredient due to OOS detected in stability study

Ceutical Pte Ltd is the product registrant for ABC 5mg Tablet. Ceutical submitted MIV-1 to widen the registered specification of assay value from 95.0% – 105.0% to 90.0% – 110.0% for stability testing.

Current specification	Proposed MIV changes
95.0 – 105.0%	Widen to 90.0% – 110.0%

In the MIV application, it was noted that the reason of MIV submission was due to out-of-specification for assay value (93.9% – 94.5%) for 3 batches. The shelf life of the product is 36 mths.

Reportable defect

Stability test result of batch A, B, C at 18mth
93.9 – 94.5% (OOS)

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Case 2: Company's request to widen registered specification of assay value of the active ingredient due to OOS detected in stability study

Based on the Ceutical's medical risk assessment, the assay value of 93.9% – 94.5% does not pose a risk to patients and has no impact on safety and efficacy of the product. Hence, did not submit product defect report.

Additionally, countries A and B had already approved the widening of the specifications (90.0% – 110.0%).

Ceutical's MIV application was not approved by HSA. Even if the OOS is marginal and not affect the safety and efficacy, it does not justify the widening of assay specification.

Past stability data showed assay results were well within 95.0% at 36 months. As such , **thoroughly investigate the root cause must be performed** before widening specifications.

Ceutical should submit a product defect form & indicate that a variation application will follow.

Do not conceal out-of-specification issues by submitting a variation application without a product defect report.

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Agenda

1. Product Defect Reporting
2. Product Recall
3. **Communication Strategies**
4. FAQ

- Dear Purchaser Letter vs Dear Healthcare Professional Letter
- Example of a Dear Purchaser Letter
- Deficiencies in communication letters

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DPL vs DHCPL

	Dear Purchaser Letter (DPL)	Dear Healthcare Professional Letter (DHCPL)
Purpose	To provide **logistic** instructions	To advise on the clinical implications
Target audience	Purchasers, nurses, clinic assistants or the licence holders of the place of practice i.e. doctors	Healthcare professionals
Content	Give clear **instructions on what to do** with the product, such as: • Notify on product quarantine • Notify on product recall • Notify on product shortage • Acknowledgment receipt/Recall form	Provide advisory on patient management, such as: • Update on labelling changes • Update on safety information • Notify on product withdrawal • Notify on product recall (Descriptive; elaborating on scientific evidence, adverse drug reactions)
Review by HSA	Generally, no need to be vetted or approved by HSA except cases specifically requested by HSA	Yes
Publish on HSA Website	No	Yes (Abstract)

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Elements of Dear Purchaser Letter on Recall

<Company logo>
<Date of letter>

To: <Audience>

Urgent: Product Recall Notice of <Product>

We are writing to inform that <Company> is initiating a <Class 2 retail level> recall of <product> (SIN no). This recall is due to <defect issues> identified in certain batches. Following a health hazard assessment, it is determined that <describe risk to patients>. This recall is a precautionary measure. So far, we have not received any reports of adverse effects related to the affected batches.

Include these details:
- List of affected batches
- How did the defect occur
- Frequency of defect
- New batches to be available by <estimated date>

Please check your inventory and quarantine any affected stock to prevent further distribution or use, while waiting for the product to be collected by <Company>. Please complete the acknowledgment form included with this letter, indicating the amount of affected stock on hand.
Return the form to <Company> and await further instructions for product collection. If you have any questions regarding this matter, please contact <company details>.

<Provide image of affected product if any>

- Date
- Audience
- Subject
- Background
- Defect issue and potential risk
- Affected product/batch
- Instructions for quarantine, recall, refund
- Contact details

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Examples of deficiencies in communication letters

Content and clarity

1. Title of letter unclear
2. Did not specify the issue or purpose of communication.
3. Did not indicate the reason for recall i.e. defect issue.
4. No mention of how the defect was discovered.
5. No mention of the assessed or potential risk.

Specific instructions and required actions

1. Did not indicate the deadline when the retailers need to return the affected product.
2. The recall should include both unopened and opened packs.

Distribution and contact information

1. Did not state the affected batches distributed.
2. Did not provide company contact details e.g. email or telephone no.

Acknowledgement

1. Did not include the recall acknowledge form in the letter.

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Tools Developed for Product Defect and Recall Procedures

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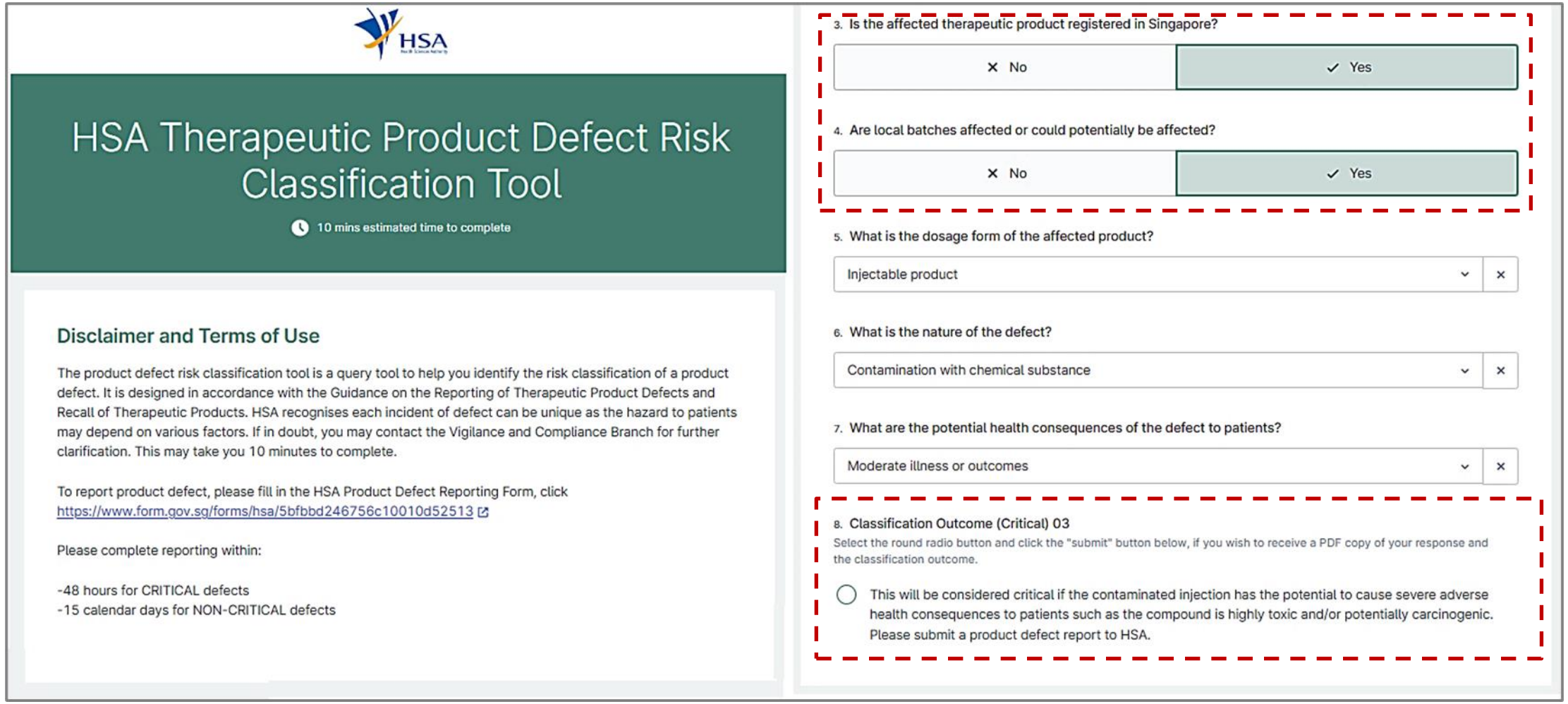
HSA Therapeutic Product Defect Risk Classification Tool

https://go.gov.sg/tp-defect-risk-classification-tool



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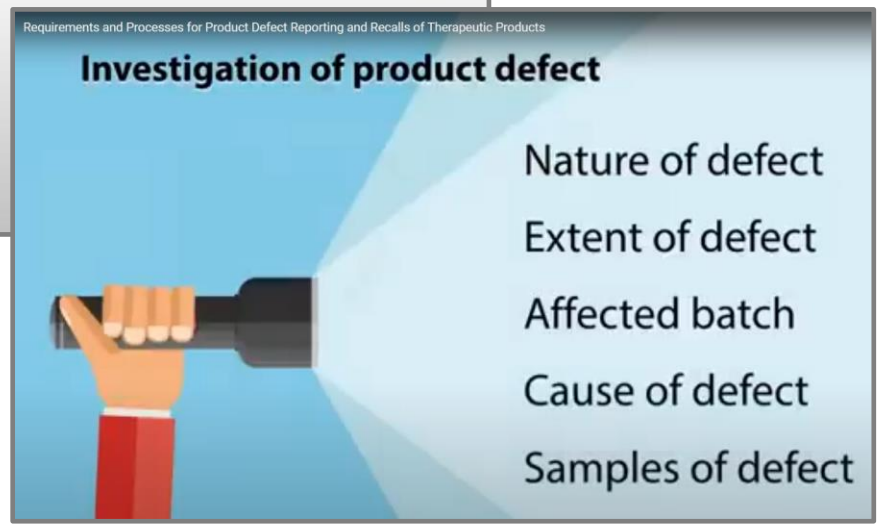
E-Video on product defect and recall reporting



HSA has created a video to explain/educate on the process and need for product defect and recall reporting

https://www.youtube.com/watch?v=3OrHKggrjm4

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Agenda

1. Product Defect Reporting
2. Product Recall
3. Communication Strategies
4. **FAQ**

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Questions

1. **Can there be a system for companies to track and store historical records of product defects and recalls?**

   Currently, HSA is providing the online FormSG reporting forms to submit defects and recall completion. Companies can save the submitted pdf forms for tracking of reports. Legally, companies are supposed to maintain records of the defects. It is also their responsibility to track and keep records as part of GDP and GMP.

2. **Is using non-registered testing methods reportable?**

   Non-registered testing methods can be considered a reportable defect, especially if it affects the safety, quality, or efficacy of the product. It is advisable to report such deviations to HSA, explaining the reason for the use of non-registered methods and the potential impact on the product.

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Question

3. May I know how we should handle distributed products meant for another country?

Scenario: A pharmaceutical company distributed a batch of a drug product in Singapore and realized the packaging was intended for another market (Country A). This issue arose due to a mix-up of the products intended for shipment to Singapore and Country A. The outer packaging and package inserts for Singapore and Country A are not the same but the information are generally aligned and does not affect the clinical use of the product.

Answer: While there is no safety or quality issue with the product, incorrect packaging may pose a potential risk of confusion among patients and healthcare professionals. As such this is deemed a reportable defect.

Comments: This packaging differed from the registered specification for the Singapore market, thus violating local regulatory requirements.

Note: *Special Consignment route (i.e. to bring in a registered product from unregistered site) is not applicable since the batch has already been imported into Singapore. It is a non-compliance issue rather than a product defect. Product recall may be required*.

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