Post-market and market surveillance of medical devices including IVDs

Manufacturers obligations

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Monitoring quality, safety, and performance of medical devices

After a product is placed on the market, its risk/benefit profile can be impacted by:

- Inherent product variability
- Factors affecting the medical device's use
- Environment
- Different user interaction
- Unforeseen medical device failure; or
- Misuse.

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WHO normative guidance

- Covers all medical devices, including IVDs, without prejudice to national legislation
- Describes
  - **Post-market surveillance** activities for manufacturers
  - **Feedback** procedure for users (rather than just complaints)
  - **Market surveillance** activities for regulators
- Reflects new international standards/guidance
  - ISO/TR 20416:2020 Medical devices — Post-market surveillance for manufacturers
  - IMDRF/AE WG/N43 Terminologies for Categorized Adverse Event Reporting (AER): terms, terminology and codes

https://www.who.int/health-topics/substandard-and-falsified-medical-products#tab=tab_1

Link to WHO guidance here

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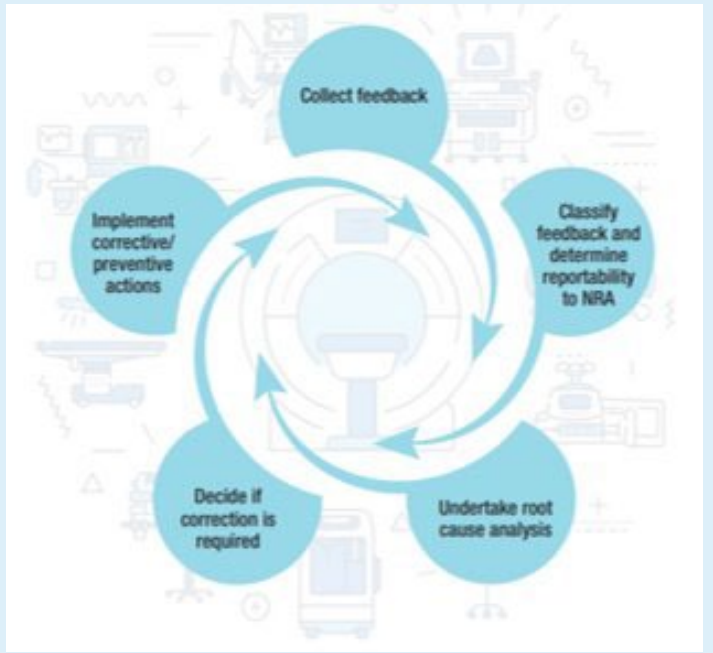
Post-market surveillance by manufacturers

- **Collects** user feedback
- **Classifies** feedback and determines **reportability to regulator**
  - Uses IMDRF N43 terminology
- **Undertakes** root cause analysis
- **Decides** if correction (repair, modification, adjustment, relabeling, destruction or inspection of a product without its physical removal to some other location) is required (informs users by field safety notice)
- **Implements** corrective/preventive actions (to eliminate the cause of detected nonconformity or undesirable situation or identify opportunities for improvement before a problem is identified), if required



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Collecting user feedback

Users should provide the following information:

- Contact details for reporter
- Email/phone number
- Product details
- **Lot number/serial number**
- Event details
- How many devices and how many patients were involved
- Description of **event (what went wrong)** and **health impact** (death, serious deterioration in health, misdiagnosis etc.)

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WHO reviews – classification of feedback

Annex	Useful terms as examples
Annex A (Medical Device Problem)	**A090803** (false negative) **A090804** (false positive) **A090805** (non reproducible results)
Annex G (Medical Device Component)	**G01006** (test strip) **G0200803** (user interface) **G02011** (device reader)
Annex E (Health Effects - Clinical Signs and Symptoms or Conditions)	**E2301** (alteration in body temperature) **E0403** (immunodeficiency) **E1102** (hepatitis)
Annex F (Health Effects - Health Impact)	**F13** (misdiagnosis/misclassification) **F04** (delay to diagnosis) **F05** (delay to treatment/therapy)

- IMDRF N43 terminology
  - Annex A - Medical Device Problem
  - Annex G - Medical Device Component
  - Annex E - Health Effects - Clinical Signs and Symptoms or Conditions
  - Annex F - Health Effects - Health Impact

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Role of manufacturer – determining reportability

What to report	Time to report to NRA
Serious public health threat*	Immediately but no later than 48 hours
Death, serious deterioration in state of health of patient, user or other person occurred	ASAP but no later than 10 calendar days
Death, serious deterioration in state of health of patient, user or other person might have occurred	ASAP but no later than 30 calendar days

*Any event type or device deficiency which could result in imminent risk of death, serious deterioration in the state of health, serious injury, or serious illness of more than one patient, user or other person that requires prompt remedial action.

- **Who** to report to
  - All relevant NRAs
  - WHO (if WHO recommended product)
- **How** to report
  - Use relevant NRA report form
  - Default, WHO report form
- **When** to report
  - Follow national timelines
  - Default, WHO timelines

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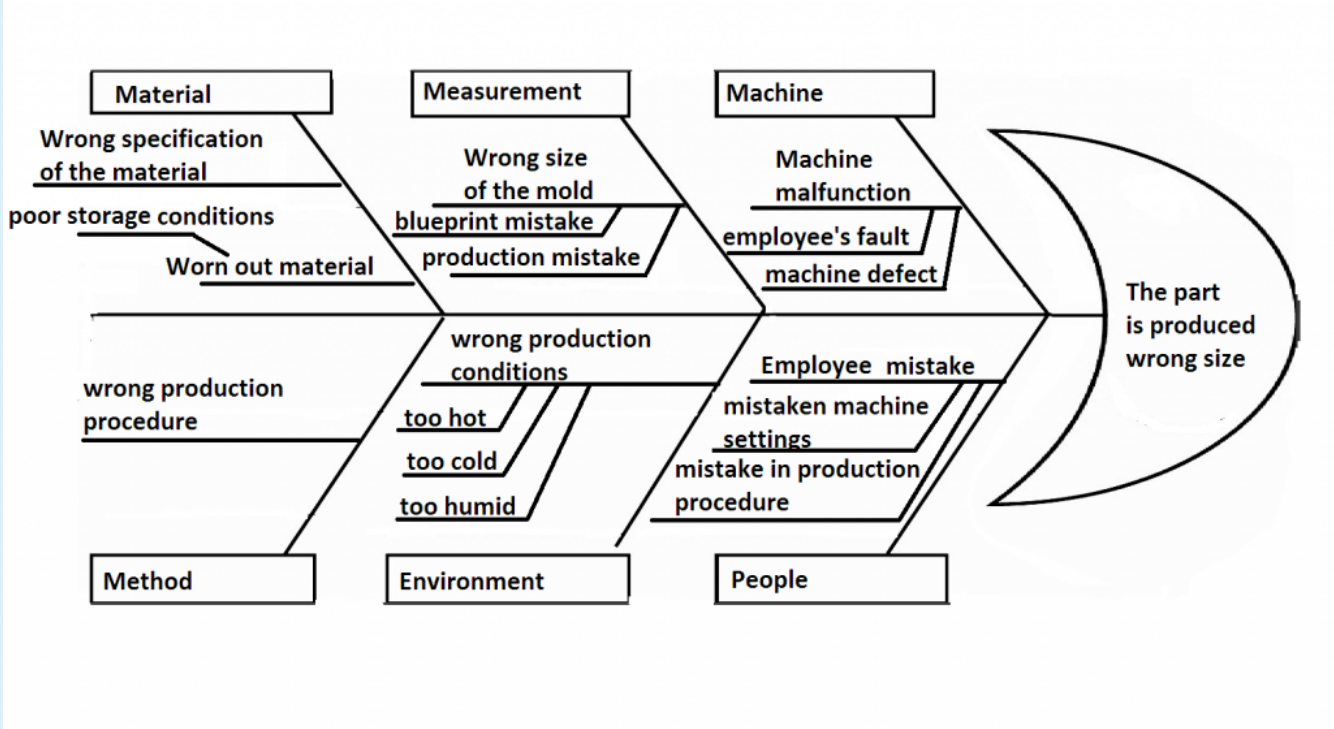
WHO reviews root cause analysis

- Manufacturer investigation should contain:
  - Root cause cause analysis (how/why did this happen)
  - Analysis regarding related areas (is this same issue impacting/occurring elsewhere)
  - Scale and scope of issue
- Manufacturer should use documented procedures, and tools



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WHO reviews – classification of investigation

Annex	Useful terms as examples
Annex B (Cause Investigation - Type of Investigation)	**B02** (Testing of Device from Same Lot/Batch Retained by Manufacturer) **B14** (Analysis of Production Records)
Annex C (Cause Investigation - Investigation Findings)	**C1403** (Change in Target Marker/Variant/ Mutant) **C1304** (Incorrect Interpretation of Results/Data) **C060201** (Improper Composition/ Concentration) **C0501** (Inadequate Labelling and/or Instructions for Use)
Annex D (Cause Investigation – Investigation Conclusion)	**D13** (Falsified Device) **D1101** (Failure To Follow Instructions) **D0302** (Quality Control Deficiency)

- IMDRF N43 terminology
  - Annex B - Cause Investigation - Type of Investigation
  - Annex C - Cause Investigation - Investigation Findings
  - Annex D - Cause Investigation – Investigation Conclusion

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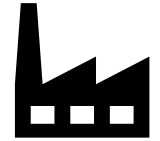
Role of other economic operators

- Other economic operators means authorized representatives, distributors, importers
- Supplier agreements between manufacturers and their respective EOs are necessary:
  - EOs may receive feedback from users, but EOs must forward immediately to the manufacturer for investigation.
  - EOs may translate feedback
  - EOs may conduct part of investigation, at the request of the manufacturer.
  - Depending on the jurisdiction, EOs may report incidents to NRAs on behalf of manufacturers.



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Role of manufacturer – implementing FSCA

- FSCA may include:
  - return of a type of device to the manufacturer or its representative (i.e. recall)
  - device modification*
  - device exchange
  - device destruction (i.e., recall)
  - advice given by the manufacturer regarding the use of the device

*Device modifications include:

- retrofitting in accordance with the manufacturer's modification or design change
- permanent or temporary changes to the labelling or IFU
- software upgrades including those carried out by remote access
- modification to the clinical management of patients to address the risk of death or serious injury or death specifically to the characteristics of the device.

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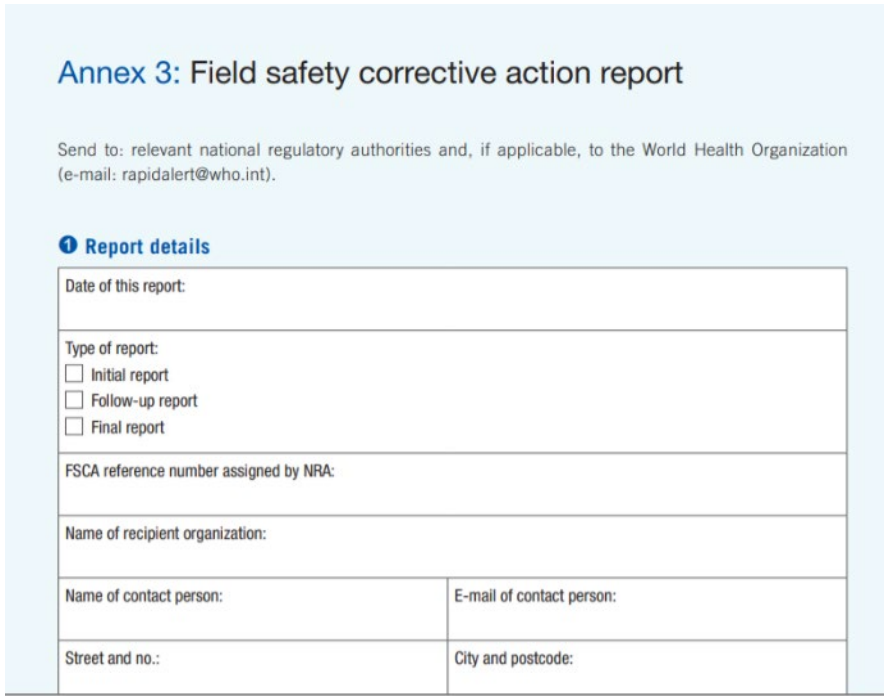
WHO reviews - field safety notices and FSCA reports

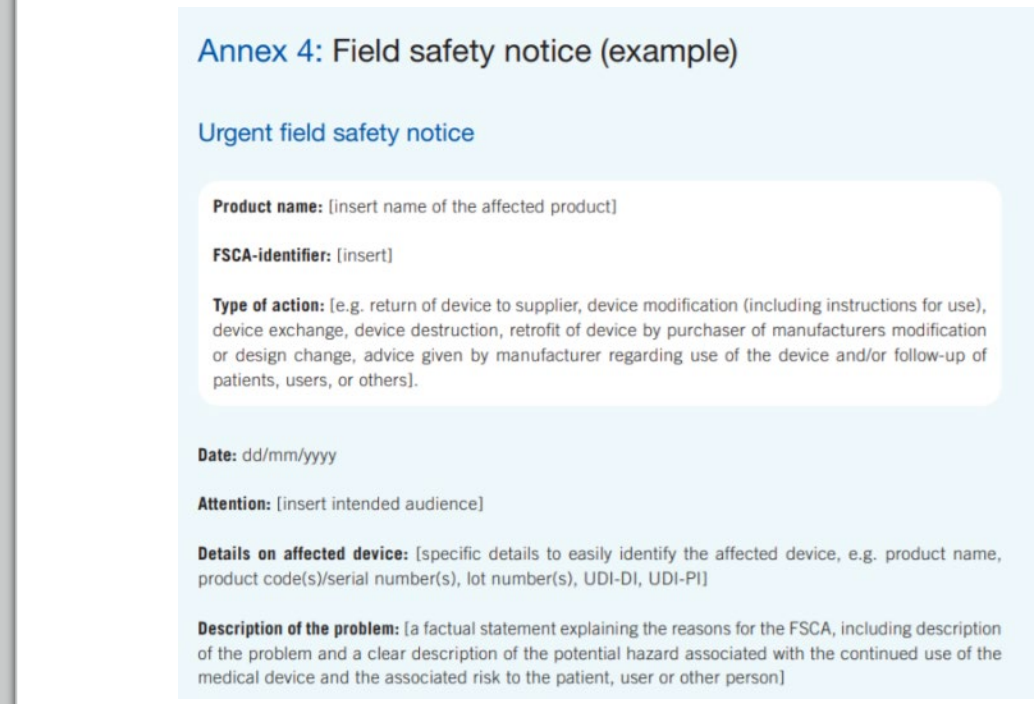


Annex 3: Field safety corrective action report

Send to: relevant national regulatory authorities and, if applicable, to the World Health Organization (e-mail: rapidalert@who.int).

❶ Report details

Date of this report:	
Type of report: ☐ Initial report ☐ Follow-up report ☐ Final report	
FSCA reference number assigned by NRA:	
Name of recipient organization:	
Name of contact person:	E-mail of contact person:
Street and no.:	City and postcode:



Annex 4: Field safety notice (example)

Urgent field safety notice

Product name: [insert name of the affected product]

FSCA-identifier: [insert]

Type of action: [e.g. return of device to supplier, device modification (including instructions for use), device exchange, device destruction, retrofit of device by purchaser of manufacturers modification or design change, advice given by manufacturer regarding use of the device and/or follow-up of patients, users, or others].

Date: dd/mm/yyyy

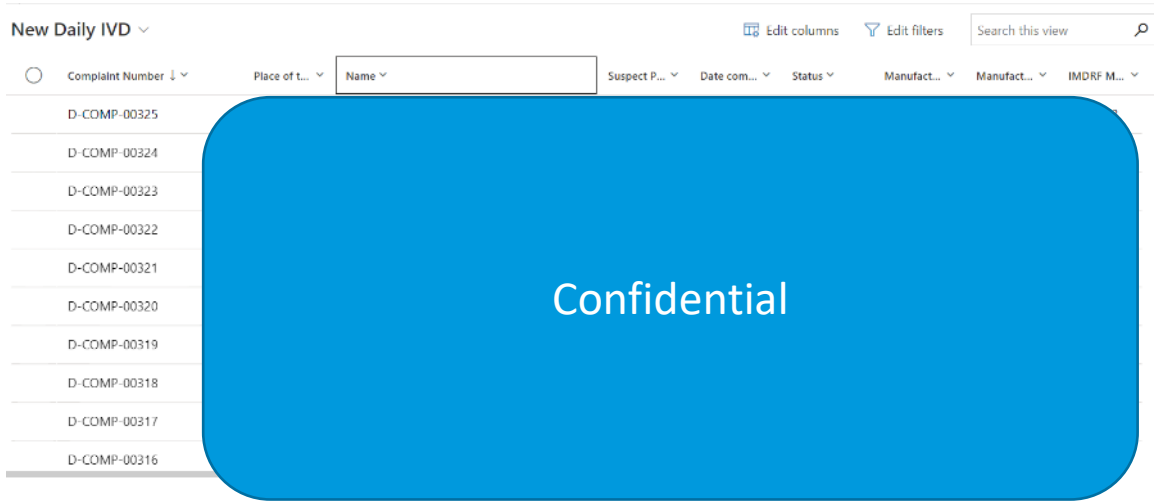
Attention: [insert intended audience]

Details on affected device: [specific details to easily identify the affected device, e.g. product name, product code(s)/serial number(s), lot number(s), UDI-DI, UDI-PI]

Description of the problem: [a factual statement explaining the reasons for the FSCA, including description of the problem and a clear description of the potential hazard associated with the continued use of the medical device and the associated risk to the patient, user or other person]

Global Surveillance and Monitoring System for substandard/falsified medical products

- GSMS is mandated by Member States, all substandard/falsified medicines, vaccines, IVDs entered



[Information about WHO Member State mechanismon substandard/falsifiedmedical products]

2021-2022, 194 incidents reported to WHO

- Substandard (99.2%), falsified (0.8%)
- 70.9% reported by manufacturer
- HIV (28.2%), SARS-CoV-2 (28.2%), malaria (4.3%)
  - 419M mRDTs vs. 190 M HIV RDTs sold in 2020
- 35.8% (EURO), 25.2% (PAHO), 15.4% (WPRO)
- Root cause not determined (65.6%)
- FSCAs implemented (28.7%)

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Thank you

For more information, please contact:
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