Post-market surveillance for IVDs

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WORKSHOP WITH NEGLECTED TROPICAL DISEASES (NTD) DIAGNOSTICS MANUFACTURERS

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Post-market surveillance by manufacturers

- Post-market surveillance is the process conducted by the manufacturer to collect and analyze experiences with a product on the market.
- Manufacturers should have a PMS plan to:
  - consider all **user feedback** (complaints, technical support callouts, maintenance, etc.)
  - review **scientific literature** and other information sources
  - review **production** records,
  - conduct **post-market performance follow-up**.

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Incident reporting 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
- **Implements** corrective/preventive actions
  - to eliminate the cause of detected nonconformity or undesirable situation or identify opportunities for improvement before a problem is identified

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 occurred	ASAP but no later than 10 calendar days
Death, serious deterioration in state of health might have occurred	ASAP but no later than 30 calendar days

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Example: human African trypanosomiasis (HAT) RDT

- Suspect substandard HAT RDT
  - False positive results
  - Patients retested with another brand of RDT and found negative
- Action by authorities:
  - Facility manager notifies the manufacturer
  - Microscopy or presumptive treatment used instead
  - Specific lot number was quarantined nationwide

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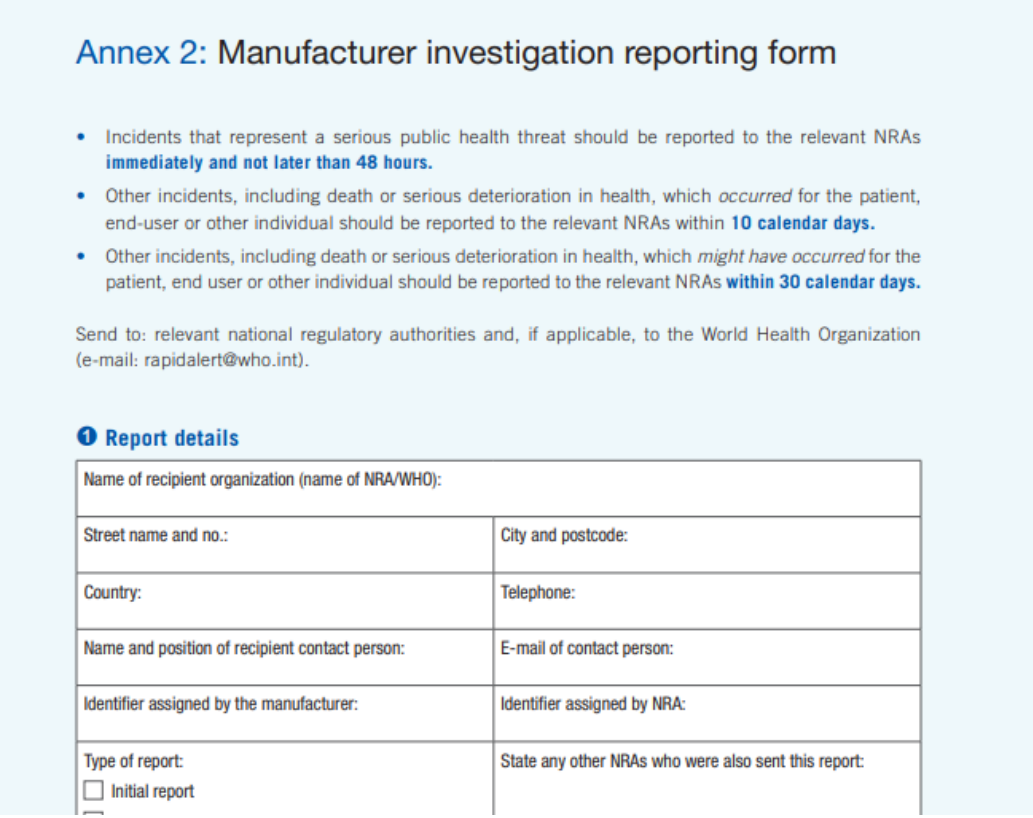
Manufacturer investigation report



Annex 2: Manufacturer investigation reporting form

- Incidents that represent a serious public health threat should be reported to the relevant NRAs **immediately and not later than 48 hours.**
- Other incidents, including death or serious deterioration in health, which *occurred* for the patient, end-user or other individual should be reported to the relevant NRAs within **10 calendar days.**
- Other incidents, including death or serious deterioration in health, which *might have occurred* for the patient, end user or other individual should be reported to the relevant NRAs **within 30 calendar days.**

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

❶ Report details

Name of recipient organization (name of NRA/WHO):	
Street name and no.:	City and postcode:
Country:	Telephone:
Name and position of recipient contact person:	E-mail of contact person:
Identifier assigned by the manufacturer:	Identifier assigned by NRA:
Type of report: ☐ Initial report	State any other NRAs who were also sent this report:

Templates can be found for

- User feedback form
- Manufacturer investigation form
- Field safety corrective action report

Guidance for post-market surveillance and market surveillance of medical devices, including in vitro diagnostics

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Manufacturer investigation report

- Manufacturer conducts investigation
  - Sends investigation report to NRA (and to WHO if PQ or EUL)
- Root cause analysis
  - Test retained samples of affected lot – **compiled with specifications yes/no**
  - Review complaint record for affected lot – **other complaints yes/no**
  - Review all complaints for the product – **other complaints yes/no**
  - Review batch manufacturing records for affected lot – **any deviations or nonconformances**

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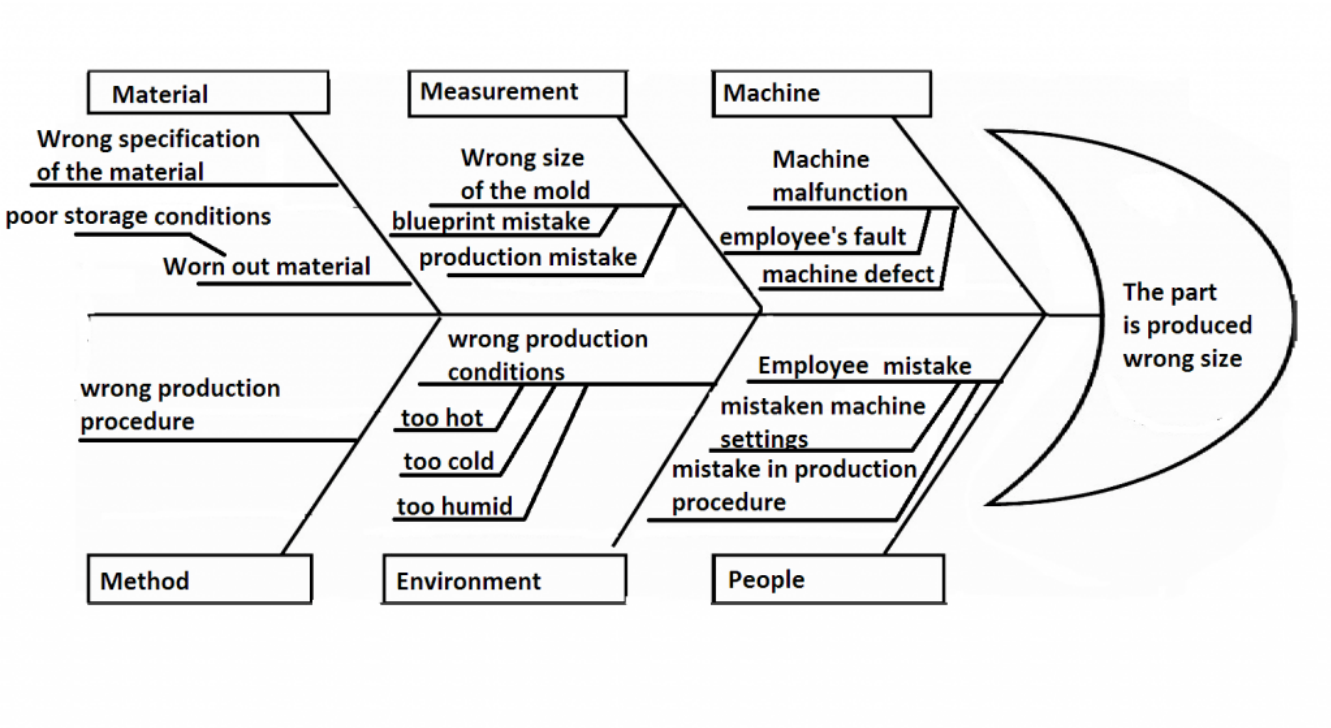
Root cause analysis

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



Investigation report

Testing retained samples of affected lots

- What specimens were used?
  - Final QC lot release panel, or
  - Specific investigation panel,
  - Capillary or venous whole blood
- What was the acceptance criteria?
  - Same final QC lot release
  - Or against IFU claims
- Any physical inspection of components
  - Specimen transfer devices
  - Buffer vials

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Closing out an incident

- Observations can’t be replicated by the manufacturer
  - Manufacturing defect could be ruled out
  - Then what is probable root cause?
- Role of reliance
  - If another regulator reviewed the same investigation report
  - Sharing field safety notices
- Risk assessment (severity vs occurrence)
  - Not all sites affected , restricted to one lot?
  - Best case scenario
    - Over treatment – give empirical treatment, give treatment to false positives
  - Worst case scenarios
    - Under treatment – if no testing then no treatment (risk of death
    - Testing services for malaria were interrupted

- 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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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 and adverse events)
  - **Market surveillance** activities for regulators
- Reflects 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

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Thank you

For more information, please contact:
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