FAQ: OUT-OF-SPECIFICATION (OOS) REPORT BY THE PRH

1. What is an Out-of-Specification (OOS)? Under what circumstances must OOS results be reported to NPRA?

An Out-of-Specification (OOS) result/incident refers to any analytical test outcome that falls outside the predetermined acceptance criteria or specifications established for a pharmaceutical product or its components as registered with the National Pharmaceutical Regulatory Agency (NPRA) as well as any non-compliance to the labelling (& Package insert) requirements. The result may indicate a potential compromise in product quality, safety, or efficacy. OOS result/incident must be reported to NPRA whenever they arise during the product lifecycle and could potentially impact product quality or public health. This includes OOS findings that may lead to product recalls or further investigation due to GMP non-compliance.

2. What is the process after reporting an OOS result/incident?

The PRH is required to undertake a thorough investigation including root cause analysis and corrective and preventive actions (CAPA). A complete investigation report, health hazard assessment, and CAPA plan must be submitted to NPRA within the specified timelines.

3. What are the timelines for reporting OOS result/incident?

For critical defects— those posing a significant threat to public health / may lead to death of, or serious injury to, any person—notification to NPRA must be made within 48 hours.

For non-critical defects— defect that do not meet the criteria of ‘’critical defect’’ but may cause illness or affect the outcome of a person’s medical treatment and/or affect the quality of a product, reporting should occur within 15 calendar days.

4. What regulatory measures may NPRA implement upon receipt of an OOS report?

Based on the risk assessment, NPRA may enforce one or more of the following actions:

- Initiation of product recall or market suspension
- Issuance of Dear Healthcare Professional Communications (DHPC) or public advisories
- Cancellation or suspension of product registration
- Implementation of other appropriate risk mitigation measures

5. Where to submit OOS reports and related documentation?

All reports and supporting documents should be directed to the following contact points: Surveillance and Complaints Section Centre of Compliance and Quality Control National Pharmaceutical Regulatory Agency (NPRA)

E-mail for OOS reports: oos_sva@npra.gov.my

6. What actions should be taken if new impurities such as nitrosamine or newly found contaminants above the specification limits are detected in a finished product?

- Immediately notify NPRA with detailed information including test results, preliminary root cause analysis, and risk mitigation plans.
- Conduct a thorough investigation to identify the root cause of contamination.
- Implement corrective and preventive actions (CAPA) to control and eliminate the source of nitrosamines.
- Assess the safety impact of the impurity on patients, considering carcinogenic or mutagenic potential, especially for nitrosamines.
- Consider the need for market actions such as product recalls or batch quarantines if the impurity poses significant risk.
- Update risk assessments and product labelling as per requirement, following the guidelines or based on recommendations from NPRA; for example, update the product specifications to include impurities limit if advised by NRPA.

FAQ: PIC/S RAPID ALERT AND ASEAN POST-MARKETING ALERT SYSTEM (PMAS)

1. What is a PIC/S Rapid Alert?

PIC/S Rapid Alerts are urgent notifications exchanged among Participating Authorities of the Pharmaceutical Inspection Co-operation Scheme (PIC/S) regarding significant public health risks related to pharmaceutical products, including quality defects, falsification/adulteration, or safety issues that require immediate regulatory action.

2. What is the ASEAN Post-Marketing Alert System (PMAS)?

The ASEAN Post-Marketing Alert System (PMAS) is a regional information-sharing mechanism established by ASEAN Member States to facilitate timely exchange of alerts related to health products after they have been marketed. It covers pharmaceuticals, medical devices, cosmetics, traditional medicines, and health supplements. The system enables regulatory authorities across ASEAN to share information on product recalls, safety concerns, quality defects, adulteration, falsification, and other significant regulatory actions to protect public health.

3. What types of events trigger PIC/S Rapid Alerts and ASEAN PMAS alerts?

- Events leading or highly likely to lead to serious public health threats such as death, serious injury, or potential for such outcomes if the event recurs.
- Quality defects, adulteration, falsification, safety concerns, unregistered/unlicensed products, or other regulatory non-compliance issues.
- Field safety corrective actions or import restrictions due to safety concerns.
- Non-Compliance with Good Manufacturing Practice (GMP)

4. What actions can be taken following a Rapid Alert or PMAS alert?

- Recall, suspension, or withdrawal of products from the market.
- Cancellation or suspension of product registration.
- Labelling changes or public announcements/bans.
- Import restrictions or other regulatory controls.

5. What are the responsibilities of regulatory authorities and industry?

Regulatory authorities must monitor post-market data, investigate reported issues, issue alerts promptly, and coordinate with other ASEAN Mutual Recognition Arrangement (MRA) or PIC/S members.

Industry stakeholders (manufacturers, importers, distributors) must cooperate with investigations, implement corrective actions, and report adverse events or complaints as required.

6. How are Rapid Alerts issued and managed?

Competent authorities issue Rapid Alerts through a formal network, providing detailed information including product identification, defect description, and recommended actions. Alerts are classified by severity and must be transmitted promptly. Follow-up communications may be issued as needed.