

Guide to Quality Defect Investigation Reports



1 SCOPE

This guide addresses the format and content required of quality defect investigation reports for the following categories of medicinal products:

- Medicinal products which are the subject of a marketing authorisation (MA) or registration;
- Medicinal products manufactured in Ireland and which are distributed in Ireland or elsewhere;
- Medicinal products distributed inside and outside the EU by Irish wholesalers and exporters;
- Promotional samples of medicinal products issued to healthcare professionals;
- Exempt medicinal products for human use which are supplied to the order of a registered doctor or a registered dentist for use by his/her individual patients under his/her direct personal responsibility, or in the case of unauthorised veterinary medicinal products, medicinal products supplied in accordance with the cascade system;
- Investigational medicinal products manufactured and distributed for the purposes of performing clinical trials.

This guide does not cover products regulated under the biocidal products directive or medicated feeding stuffs directive.

2 INTRODUCTION

Quality defect investigation reports are required by the Health Products Regulatory Authority (HPRA) during the investigation of quality defects.

A quality defect in a medicinal product may be defined as an attribute of a medicinal product or component which may affect the quality, safety and / or efficacy of the product, and / or which is not in line with the approved marketing authorisation for the product.

Reports of suspected quality defects may be received by the HPRA from a number of sources. Once confirmed, quality defects are classified according to their potential threat to patient or animal well-being and public health in general.

All reports of suspected quality defects received by the HPRA, and suspected quality defects identified by HPRA staff, are investigated by the Market Compliance Section of the HPRA. In addition, the marketing authorisation holder (MAH), manufacturer and/or wholesaler is/are

required to initiate an investigation to establish the extent and root cause(s) of the quality defect, and to propose corrective actions to prevent a recurrence.

3 CLASSIFICATION OF QUALITY DEFECTS

Critical quality defects

These are quality defects which are potentially life threatening or could cause serious risk to health. Examples are:

- Wrong product (label and contents are different products).
- Correct product but wrong strength, with serious medical consequences.
- Microbial, physical or chemical contamination, with serious medical consequences.
- Mix up of products ('rogues') within a pack, for example, two different blister strips within one outer carton, or, two different tablets within the one blister strip.
- Wrong active ingredient in a multi-component product with serious medical consequences.
- Serious adverse reactions which are batch or product related (most likely to be first notified to the Human Product Safety Monitoring department in an urgent safety report).

Major quality defects

These are quality defects which could cause illness or mistreatment but not to a life threatening extent. Examples are:

- Mislabelling - wrong or missing text or figures.
- Missing or incorrect information - leaflets or inserts.
- Microbial, physical or chemical contamination, with medical consequences.
- Mix up of products ('rogues'), for example, a case of product A contains one or more packs of product B.
- Non-compliance with specification (e.g. assay, stability, fill/weight).
- Insecure closure with serious medical consequences (e.g. cytotoxics, child-resistant containers, potent product).

Minor quality defects

These are quality defects which are not likely to pose a significant hazard to health. Examples are:

- Faulty packaging, for example, wrong or missing batch number or expiry date.
- Faulty closure.
- Microbial, physical or chemical contamination which is unlikely to have medical consequences.

4 GENERAL REQUIREMENTS FOR INVESTIGATION REPORTS

On completion of the company investigation to establish the root cause(s) of the quality defect, a detailed investigation report should be submitted to the Market Compliance Section for review. This report should describe the steps taken to investigate and to correct the source of the quality defect.

The expected timeframe for HPRA receipt of the investigation report is normally **four weeks** from the date of request by the Market Compliance Section. If the investigation report cannot be submitted within the requested timeframe, a modified timeframe may be agreed.

The overall responsibility for preparing the investigation report and for forwarding the report to the Market Compliance Section normally rests with the MAH (if applicable), though this action may be delegated to the manufacturer by the MAH holder.

In cases where the source of the defect is identified at a wholesaling facility, the HPRA may request the investigation report directly from the wholesaler.

Where a quality defect occurs with a medicinal product which is manufactured in Ireland but which does not hold a marketing authorisation (MA) in Ireland (i.e. where the product is manufactured for export), the HPRA will request the investigation report directly from the manufacturer.

For a quality defect relating to an exempt medicinal product, the company which submitted the notification of placement of product on the Irish market is responsible for submitting the investigation report.

If the quality defect results in a recall action, the company will be required to submit a recall report. In such cases a quality defect investigation report will not be required, as the relevant information will be detailed in the recall report.

5 REQUIRED FORMAT AND CONTENT OF INVESTIGATION REPORTS

The quality defect investigation report should typically contain two sections, titled:

- **Executive Summary**
- **Details of Investigation**

These are detailed below;

- 1 The '**Executive Summary**' should provide a high level overview of the quality defect issue and be approximately half a page in length. Important actions such as the issuance of Caution-In-Use Notifications should be outlined in brief.
- 2 The section titled '**Details of Investigation**' should include:
 - Exact product name
 - Active substance name(s)
 - Product strength(s)
 - Pharmaceutical form (e.g. tablets, solution for injection, powder for solution for infusion, etc.)
 - Description of the packaged product (e.g. tablets in a polyethylene tub, blisters in a carton, etc.)
 - Pack size (e.g. 28s)
 - Batch number(s) affected and expiry date information for such batch(es)
 - Marketing Authorisation (PA/VPA/EU) number(s), Parallel Import (PPA) number(s), or Product Registration number(s), if applicable
 - Name and address of the manufacturer of the finished product which performed QP-release to the marketplace
 - Name and address of Irish manufacturer(s) involved in any stages of the manufacturing process (if applicable)
 - Name and address of the primary wholesaler in Ireland (if any)
 - Territory of product distribution (i.e. country names where the affected batch(es) was/were distributed)

- Total quantity of packs manufactured for the affected batch(es)
- Total quantity of units from the affected batch(es) distributed on the Irish marketplace
- Date the quality defect issue was first discovered by the MAH or manufacturer
- Date the quality defect issue was reported to the HPRA
- Description of investigation carried out (this should be comprehensive)
- Cause(s) of the quality defect
- Extent of the quality defect (e.g. number of packs affected per batch)
- Specific corrective action(s) arising from the investigation, and a timeline for the completion of each corrective action identified
- Planned completion date(s) for outstanding corrective action(s).

6 FURTHER INFORMATION

For further information, contact:

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