

**Report to the European Commission on
Pharmacovigilance audits carried out in the Irish
Medicines Board in Ireland
From 21 September 2012 to 20 September 2013**

1. INTRODUCTION

Article 101 (2) of the Directive 2001/83/EC states: "Member States shall, ...perform a regular audit of their Pharmacovigilance system and report the results to the Commission on 21 September 2013 at the latest and then every 2 years thereafter."

This report provides an overview of the audit activities conducted from 21 September 2012 to 20 September 2013 by the internal audit function of the Irish Medicines Board.

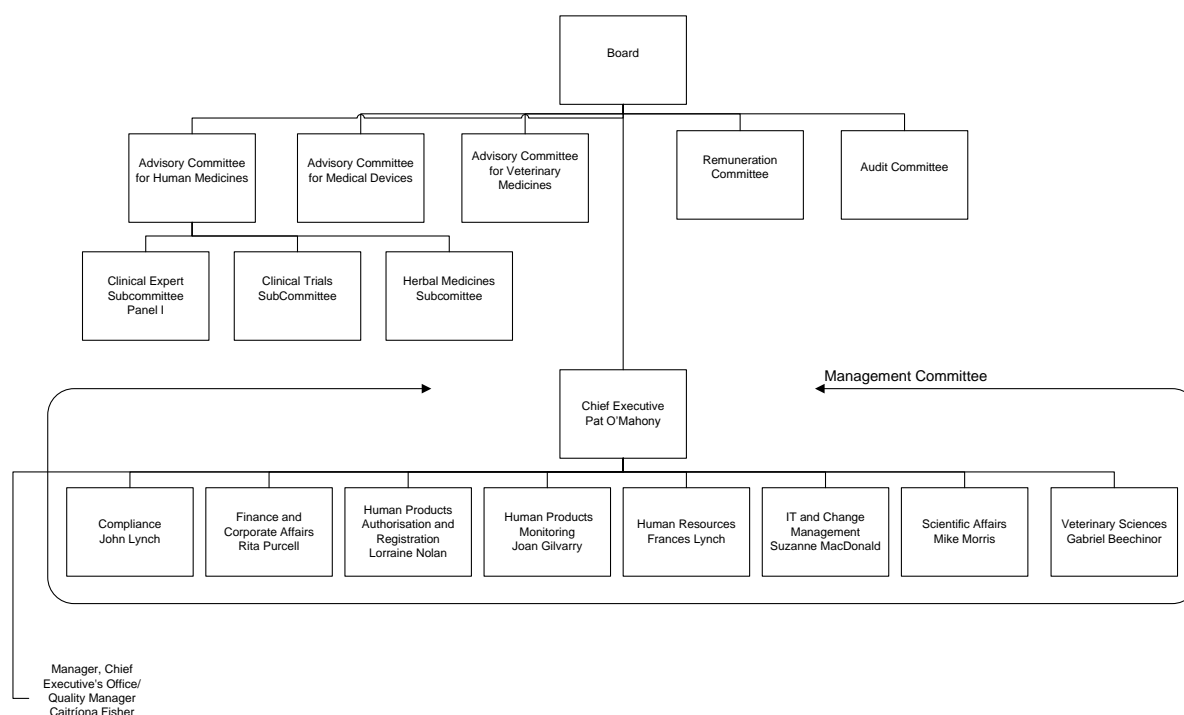
2. BRIEF DESCRIPTION OF THE PHARMACOVIGILANCE SYSTEM

2.1 Legislation

Directive 2011/83/EC, as amended in particular by Directive 2010/84/EC, has been transposed into Irish legislation by statutory instrument, Medicinal Products (Control of Placing on the Market)(Amendment) Regulations, 2012, S.I. No. 272/2012, on 25 July 2012.

2.2 Organisation structure, responsibilities and resources

The organisational structure of the agency is shown below.



The Human Products Monitoring department (see organogram above) is the main department responsible for the operation and management of the pharmacovigilance system. It is responsible for:

- Evaluation and follow up of nationally-occurring adverse reaction reports from consumers and healthcare professionals;
- Co-ordination of safety announcements, routine and ad-hoc exchange of pharmacovigilance-related information with relevant national bodies, the European Medicines Agency (EMA), WHO and national competent authorities in other Member States;
- Assessment of risk management plans, post authorisation safety studies, periodic safety update reports and safety referrals (under Articles 107i, 20, 31);

- Signal management (including data monitoring in EudraVigilance, signal validation/confirmation and evaluation of confirmed signals) and provision of advice on confirmation and quantification of risk and on regulatory options for managing risk;
- Providing pharmacovigilance advice and risk management input on safety variations and renewals where the agency is a lead Member State;
- Supporting the agency's contribution to the Pharmacovigilance Risk Assessment Committee (PRAC) and co-ordination nationally of PRAC-related activities;
- Monitoring regulatory action;
- Setting standards for procedures and methods to promote good vigilance practice;
- Contributing to education programmes for healthcare professionals, to develop their understanding of pharmacovigilance and to promote greater adverse reaction reporting;
- Providing educational material for patients on pharmacovigilance, their contribution to the system and to promote adverse reaction reporting.

There are a total of 30 staff in this department involved in pharmacovigilance activities. Technical staff are competent and experienced in a wide range of scientific, healthcare and life sciences disciplines and areas of medicine, at graduate and post-graduate level.

The Compliance department (see organogram above) is responsible for pharmacovigilance inspections. There is a total of 5 staff involved in these inspections. Staff are competent and experienced in scientific, healthcare and life sciences disciplines, at graduate and post-graduate level.

All staff are required to make a declaration of interests statement when they join and annually; the system for allocation of work ensures that staff are not assigned to work where there is any potential conflict.

2.3 Training

For new recruits, training is based on a lifecycle approach: induction training on the organisation and the role; department training on legal and regulatory matters, and practical training; and task-specific training plans depending on the nature and complexity of the work and the level of training needed.

For on-the-job training, technical staff are allocated cases of increasing complexity according to competence, experience and role. Expertise and awareness of safety-related issues are developed through discussions at team meetings. Cross-organisational training is provided on key topics. Staff take part in EMA-coordinated webinars and WHO web-learning programmes. Support is available for further education, depending on need, and budgetary and resource constraints. All staff engage in a performance development programme.

A variety of training methods are used, attendance is recorded and effectiveness monitored.

Annually, detailed training needs (technical and non-technical) are identified and a training plan is agreed for each department. A specific training related budget allocation is made to each department. The training plan is reviewed regularly, with the HR department, to ensure it is fulfilled.

2.4 Facilities and equipment

All staff in the Human Products Monitoring department involved in pharmacovigilance are located on one floor, while the inspectors are on another floor in a separate but linked building.

There is an MA application workflow system ('Nimbus') which allows access to applications details, templates, assessment reports and comments from other MSs, EMA or applicant, under a unique case number.

The ARISg adverse reaction management system has been customised for use as the agency national adverse reaction database. The workflow module facilitates the processing and submission of cases in line with legislative timelines. The database is fully searchable through use of a query module which incorporates standardised MedDRA queries.

There is a separate workflow system ('CWS') and database for sites that require authorisation/registration. It manages and acts as a directory for all site licensing and inspection activities including PV inspections.

2.5 Compliance management

Pharmacovigilance compliance management is managed by a dedicated team. ICSR/SUSAR data quality is monitored on an ongoing basis and reviewed monthly through QC procedures and corrective and preventative actions taken as needed. Compliance with reporting timelines is monitored through monthly key performance indicators.

2.6 Record management

Records relating to ICSRs and SUSARs are scanned as necessary and saved to the relevant case on the ARISg database.

Product-related files and correspondence are stored electronically to the relevant case in the Nimbus workflow system and managed through a standard e-submission system (Docubridge).

2.7 Documentation of the quality system

The agency documents its processes within a hierarchy of documents, according to an SOP. Documents are approved by the relevant directors or managers, according to the rules set out in the procedure. Approved documents are stored on an intranet which ensures that documents are legible and readily identifiable and that only the current approved version is accessible to staff at point of use. Obsolete documents are removed from the intranet and are thus not available for unintended use. External documents are controlled where appropriate and available on the intranet.

2.8 Business continuity arrangements

There is a cross-organisational crisis management plan in place. The top management team forms the crisis management team with input from additional experts, if required. The crisis operational team is made up of relevant staff in the relevant departments. Stakeholders' contact details and contact methods are available, including rapid alert contacts, healthcare professionals' contacts, and government and health service agencies contacts. Rules are included about escalation of 'incidents' to 'crises'.

A business continuity plan has been developed, originally for the flu pandemic; as part of this work, business processes were assessed for criticality and prioritised, and measures put in place to ensure continuity of service in critical areas should the plan be activated. Key personnel are identified in the plans for individual departments.

A disaster recovery plan is in place together with a specific IT disaster recovery plan.

The agency's contribution to the Rapid Alert and Non-Urgent Information system and to the Incident Review Network is co-ordinated and managed through the Human Products Monitoring department. This includes proactive identification of information to be exchanged through the EU network and consideration of reported incidents in terms of their public health impact and the likelihood of the identified concerns being addressed through routine measures. The agency provides 'out of hours' emergency numbers through telecommunication systems and staff who are issued with agency mobile phones/laptops also provide urgent responses to stakeholders.

2.9 Monitoring of performance and effectiveness

Quality objectives are set and monitored regularly.

A review of the system is part of management reviews, at both a strategic level and at the level of the quality system; actions arising from the reviews are logged and tracked.

The system is subject to regular audits by the agency's internal audit function. Audit reports are sent to the department's managers and the head of the department. Progress on CAPAs is reported to the management (executive) committee.

The processes are under continual review and improvement and quality documents revised as needed on an ongoing basis.

2.10 Delegation of tasks

There is no delegation of tasks.

3. INTERNAL AUDIT ACTIVITY FOR THE PERIOD UNDER REVIEW

3.1 RISK ASSESSMENT

A risk assessment exercise was conducted in order to determine the pharmacovigilance system audit priorities for the period under review. The final audit strategy was prepared based on this risk assessment and was approved by the head of the agency on 4 March 2013.

3.2 SUMMARY OF THE AUDITS FOR THE PERIOD UNDER REVIEW

3.2.1 AUDIT ASSIGNMENTS FOR THE PERIOD UNDER REVIEW

All audits listed were performed in line with the guidance provided in the GVP Module IV on pharmacovigilance audits.

Audit No	Audit title	Date of audit report
A2012-10	ICSRs	18 December 2012
A2013-07	PSURs where Ireland is the lead Member State	27 June 2013
A2013-08	Signal detection for products where Ireland is the lead Member State	19 August 2013

3.2.2 INDIVIDUAL CASE SAFETY REPORTS

3.2.2.1 Objective and scope

Objective: to review compliance against applicable legislation; to review conformance against quality system requirements; to assess the effectiveness of the process; and to identify opportunities for improvement.

Scope: the procedure on individual case safety reports from marketing authorisation holders for cases associated with a specific medicinal product.

3.2.2.2 Audit body

The agency's internal audit function

3.2.2.3 Opinion

The process of individual case safety reports was considered well-controlled with only minor non-conformances identified, all of which have since been addressed. A follow-up audit is not considered necessary at this time.

3.2.3 PERIODIC SAFETY UPDATE REPORTS WHERE IRELAND IS THE LEAD MEMBER STATE

3.2.3.1 Objective and scope

Objectives: to review compliance against applicable legislation and GVP guidelines; to review conformance against quality system requirements; to assess the effectiveness of the process; and to identify opportunities for improvement.

Scope: PSUR procedures where Ireland is the lead Member State.

3.2.3.2 Audit body

The agency's internal audit function.

3.2.3.3 Opinion

The auditors concluded that the PSUR processes are well controlled with only minor non-conformances identified, all of which are being actively addressed. For future pharmacovigilance audits, the following should be noted:

- Given that a revision to GVP Module VII on PSURs is underway, it will be essential that QMS documents are reviewed and kept up to date with EU guidelines as applicable.
- In the next audit of PSURs, it should be possible to review KPIs for the process.

3.2.4 SIGNAL DETECTION FOR PRODUCTS WHERE IRELAND IS THE LEAD MEMBER STATE

3.2.4.1 Objective and scope

Objectives: to review compliance against applicable legislation and GVP guidelines; to review conformance against quality system requirements; to assess the effectiveness of the process; and to identify opportunities for improvement.

Scope: signal detection for products where Ireland is lead Member State.

3.2.4.2 Audit body

The agency's internal audit function.

3.2.4.3 Opinion

The process is considered to be well controlled with only minor non-conformances identified all of which are being actively addressed. A follow-up audit is not considered necessary at this time.

3.2.5 Audit outcomes and actions

Actions based on 3 audit outcomes which are reported and rated in line with the weakness relative risk level as 'Critical' and as 'Major', in line with the guidance provided in the GVP Module IV Pharmacovigilance audits.

Audit No	Find No	Audit outcomes description	Grading	Action short description	Action end date	Comments on status of actions	Type of follow-up required
A2012-10	N/A						
A2013-07	N/A						
A2013-08	N/A						

4. FOLLOW-UP

4.1 SUMMARY OF ACTION PLANS FROM PRIOR BIENNIAL REPORTS

N/A

4.2 OUTSTANDING ISSUES FROM PRIOR BIENNIAL REPORTS

N/A

5. DECLARATION

The Irish Medicines Board confirms that this report contains a complete account of all pharmacovigilance system audit activity performed in the period under review to fulfil the obligations of this organisation under Directive 2001/83/EC.

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Head of the Approving Body

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Date