Report to the European Commission on Pharmacovigilance audits carried out in BASG/AGES (Austrian Federal Office for Safety in Health Care / Austrian Medicines and Medical Devices Agency), Austria

Period: April 2012 to 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 Q2 2012 to September 1st, 2013 by the internal auditors of the Austrian Medicines & Medical Devices Agency (BASG/AGES), coordinated by BASG/AGES quality management. The beginning of this period was chosen because the audit strategy was revised in the beginning of 2012 according to the then current draft of GVP module IV, so the programme for the audit year 2012 (from Q2 2012 to Q1 2013) was already in line with the upcoming requirement.

2. BRIEF DESCRIPTION OF THE PHARMA COVIGILANCE SYSTEM

Legislation

Pharmacovigilance activities are regulated in Austria nationally by the Medicinal Products Act, which was updated in 2013 in order to transpose the European PhV requirements into national legislation.

Organisation structure, responsibilities and resources

The Austrian Medicines & Medical Devices Agency is a business division of the Agency for Health and Food Safety (AGES), which is owned by the Republic of Austria. The Medicines & Medical Devices Agency has currently a staff of 322 FTE. All pharmacovigilance tasks are performed by the PhV department by a staff of 24 FTE (with the exception of PhV inspections, which are performed by the inspections department).

The agency is mostly funded by fees, supplemented by direct governmental funding.
Training

20 out of 27 PhV staff holds an academic degree. All staff receives introductory and ongoing training; requirements are regulated by SOPs. During annual appraisal interviews, individual training plans for ongoing training are defined.

Facilities and equipment

In the agency moved to a completely renovated building in early 2012.

A new ICSR database (VigilanceONE), supporting signal detection and exchange with EudraVigilance, was established in late 2010. A web portal for electronic reporting (including consumer reporting) was added in December 2012. For marketing authorisation processes (including assessment of RMPs, renewal PSURs and tracking of safety related changes of SmPCs), a fully electronic workflow system was established in July 2013.

Compliance management

Procedures and processes are defined for all critical steps, including quality control of submission and assessment of pharmacovigilance data. Independence of the organisation is legally ensured. All staff is requested to submit and regularly update declarations of potential conflicts of interest, which are evaluated by the direct supervisor. A code of conduct is in place and published on the website of the agency.

Record management

Recording and retention times are regulated for data and documents in paper and electronic format. Retention times were updated in 2012 to be conform to the new requirements (Commission Implementing Regulation (EU) No 520/2012 and GVP I). Access to the building, server rooms and archives is restricted and monitored. Traceability is monitored by internal audits.

Documentation of the quality system

The quality system of the agency was developed by extending the system in place for the OMCL, where it was established in 2000. Pharmacovigilance activities are covered by the quality system and regular internal audits since 2006. All pharmacovigilance core processes are regulated by SOPs and are performed by the agency. The quality system, including the pharmacovigilance system, is subject to regular external assessment (ISO 9001 certification of the complete agency and additionally accreditation of OMCL [ISO 17025] and inspectorate [ISO 17020]).

Business continuity arrangements

Business continuity arrangements are in place, including
- protection of individual health of staff (occupational health provisions, first aid and fire protection regulations)
- deputy regulations and cross training
- backup information channels (including remote access by notebook and mobile phone for staff with key functions)
- backup and restore exercises for electronic data

Monitoring of performance and effectiveness

Performance is monitored by input/output, processing time (for all processes) and throughput time (for selected processes). For ICSR reporting, compliance with reporting targets is closely monitored.
Formal monitoring of effectiveness was introduced in 2012, including tracking of safety related changes of SmPC, monitoring of trends in ISCR and marketing data, as well as media surveillance. The system in place was selected as “best practice” by BEMA III assessors in March 2013.

Delegation of tasks

There is no delegation or outsourcing of PhV processes.

3. INTERNAL AUDIT ACTIVITY FOR THE PERIOD UNDER REVIEW

3.1 RISK ASSESSMENT

An internal audit system was established in 2000 and was extended to PhV activities in 2006. The general strategy for internal audits requests process audits of selected individual business cases with focus on traceability and compliance to internal and external requirements. At least one internal process audit is performed per department (several departments may be involved in one audit) and at least once per year an audit with a complete system checklist (ISO 9001, 17020 and/or 17025) is performed. Preparation of the audit programme was risk-based, but the risk assessment was not formalised until 2012.

A risk assessment exercise was conducted in early 2012, based on an advanced draft of GVP module IV, in order to determine the pharmacovigilance system audit priorities for the period under review. The resulting audit strategy, was approved by the head of agency on May 4th 2012. It assigns basic risk levels to all PhV core processes and defines minimum audit frequencies for these risk levels. Changes may upgrade the risk rating.

For several PhV core processes that were rated as high risk, the audits that were due 2012 according to the audit strategy were postponed to 2013, as it was expected that changes by the new PhV legislation and GVP requirements would lead to significant changes of the human PhV processes. A veterinary PhV process was audited instead, to ensure appropriate audit coverage of the PhV department. With fulfilment of the 2013 audit programme, all PhV processes will have been audited in the frequency foreseen by the audit strategy.

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 GVP Module IV Pharmacovigilance audits.

<table>
<thead>
<tr>
<th>Audit No</th>
<th>Audit title</th>
<th>Date of audit report</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/2012</td>
<td>Crisis management</td>
<td>July 17th 2012</td>
</tr>
<tr>
<td>4/2012</td>
<td>PhV inspections</td>
<td>Oct 18th 2012</td>
</tr>
<tr>
<td>13/2012</td>
<td>SUSARs and DSURs</td>
<td>May 16th 2013</td>
</tr>
<tr>
<td>15</td>
<td>DHPC</td>
<td>June 20th 2013</td>
</tr>
</tbody>
</table>

3.2.2 CRISIS MANAGEMENT

3.2.2.1 Objective and scope
Objective:
To check effectiveness of agency-wide internal communication in a crisis situation.

Scope:
- pharmacovigilance department: signal detection, trigger for crisis management, EU/EEA communication (NUI, PHVWP and IRN)
- inspections department, quality defect and GMP units: assessment, batch recall, triggered GMP inspection
- OMCL: quality defect analysis, quality assessment
- marketing authorisation department and CHMP member: quality assessment, trigger of Art. 36 referral
- head of agency & communications: crisis coordination & public communication

3.2.2.2 Audit body
Quality management department & internal auditors

3.2.2.3 Opinion
All necessary steps to manage the crisis were performed and communicated timely and effectively. However, this was partially the result of effective improvisation rather than efficient internal communication structures. Crisis management is regulated only for the PhV department, an agency-wide SOP is not in place.

3.2.3 PHV INSPECTIONS

3.2.3.1 Objective and scope

Objective:
To check compliance with new requirements from ISO 17020:2012 and GVP module III (June 19th 2012 draft for public consultation) and effectiveness of the process.

Scope:
- inspections department, clinical trials unit

3.2.3.2 Audit body
Quality management department & internal auditors

3.2.3.3 Opinion
The process is appropriately documented and traceable. Requirements for internal and international coordination of risk based inspection planning need updates in line with GVP III. Documentation of inspection planning should be improved.

3.2.4 NATIONAL RENEWAL VET. (INCL. PSUR ASSESSMENT)

3.2.4.1 Objective and scope

Objective:
To check compliance with ISO 9001 and effectiveness of interfaces.

Scope:
- marketing authorisation department, veterinary unit (regulatory, clinical assessment)
- pharmacovigilance department, veterinary unit (PSUR assessment)
3.2.4.2 Audit body
Quality management department & internal auditors

3.2.4.3 Opinion
The PhV SOP for vet. PSUR assessment emphasises the process for periodic rather than renewal PSURs. Interaction with MA department during renewal procedures is not formalised, but works well due to close personal communication between assessors. As due to restricted resources PSUR assessment reports are only drafted in case of questions or objections, traceability is not ensured.

3.2.5 SUSARS AND DSURS

3.2.5.1 Objective and scope

Objective:
To check compliance with ISO 9001 and effectiveness of the processes after change in responsibility (from clinical trials to PhV department).

Scope:
- pharmacovigilance department, ICSR and PSUR units

3.2.5.2 Audit body
Quality management department & internal auditors

3.2.5.3 Opinion
The administrative processes are effective, but human resources are lacking for DSUR assessment. The interaction between PhV and clinical trials unit should be improved and formalised.

3.2.6 DHPC (DIRECT HEALTHCARE PROFESSIONAL COMMUNICATION)

3.2.6.1 Objective and scope

Objective:
To check compliance with GVP modules I and XV and effectiveness of the process.

Scope:
- pharmacovigilance department, safety communications unit

3.2.6.2 Audit body
Quality management department & internal auditors

3.2.6.3 Opinion
The relevant SOP is rather general and should be detailed in the critical steps. GVP XV requirements are mostly in place, but a systematic check of implementation was not performed. A planned review of safety information published on the website of the agency should be implemented. System requirements from GVP I are in place, but need updating in respect to retention times of records.
3.2.2.4 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.

<table>
<thead>
<tr>
<th>Audit No</th>
<th>Find No</th>
<th>Audit outcomes description</th>
<th>Grading</th>
<th>Action short description</th>
<th>Action end date</th>
<th>Comments on status of actions</th>
<th>Type of follow-up required</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/2012</td>
<td>1750</td>
<td>The final report of a triggered inspection was not forwarded back to the MA department that requested the inspection</td>
<td>Major</td>
<td>Training</td>
<td>August 2012</td>
<td>complete</td>
<td>check by line management, internal audit (done)</td>
</tr>
<tr>
<td>1/2012</td>
<td>1751</td>
<td>Effective, but inefficient agency-wide coordination of crisis management</td>
<td>Major</td>
<td>Regulation by agency-wide SOP</td>
<td>pending</td>
<td>implementation postponed until publication of GVP module XII</td>
<td>check by line management, internal audit</td>
</tr>
<tr>
<td>13/2012</td>
<td>1871</td>
<td>A risk based approach for assessment of DSURs should be introduced to mitigate the lack of human resources</td>
<td>Major</td>
<td>Introduction of a risk based approach for assessment of DSURs</td>
<td>pending</td>
<td>pilot phase ongoing</td>
<td>check by line management, internal audit</td>
</tr>
</tbody>
</table>
4. FOLLOW-UP

Section does not apply for the first report.

5. DECLARATION

The Austrian Federal Office for Safety in Health Care 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.

Marcus Müllner

20.8.13

Sept. 20th, 2013