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 of time from September 2013 to August 2015
1. INTRODUCTION

This report provides an overview of the audit activities conducted from September 2013 to August 2015 by the internal auditors of the Austrian Federal Office for Safety in Health Care / Austrian Medicines & Medical Devices Agency (BASG/AGES), coordinated by BASG/AGES quality management.

2. Developments in the pharmacovigilance system since the last report

Significant changes during the reporting period

Legislation and regulatory
No changes since the last report.

Standards and Procedures
Apart from regular updates of internal Quality documentation no changes since the last report.

Quality system for Pharmacovigilance Activities
No changes since the last report.
The methodology used by the agency to implement the new PV legislation into the existing QMS was highlighted by BEMA III assessors as a good practice. The assessors encouraged BASG/AGES to share the approach with the EU agencies, which was done via the HMA Pharmacovigilance Audit Facilitation Group (PAFG) and HMA Working Group of Quality Managers (WGQM).

Critical Pharmacovigilance Processes
No changes since the last report, but in the context of risk assessment for internal audits, the criticality of PV processes was reviewed, considering the PAFG/PRAC recommendation “Guidance on Network Risk Ratings of Pharmacovigilance Process Areas”, see 3.1.

Other changes
A new workflow and document management system was rolled out with July 1st 2013, supporting all marketing authorisation and life-cycle processes. The system is continuously extended and currently covers all MA-related PV processes, as RMP and PSUR assessment or safety-related variations.

In November 2013, the organisational structure was reorganised. Most support processes were centralised and are now in the responsibility of the mother organisation, AGES. PV-activities, which were formerly concentrated in one department, are now integrated into several other departments and cooperate as matrix.
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 risk assessment was performed by all managers of departments involved in PV activities and based on the previous audit strategy and the PAFG/PRAC recommendation “Guidance on Network Risk Ratings of Pharmacovigilance Process Areas”. For PV core processes there were only minor adjustments, but the audit strategy had to be extended to cover critical support and management processes of the PV system. The final audit strategy was prepared based on this risk assessment and was approved by Head of Agency on November 18th 2014.

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 Pharmacovigilance audits.

<table>
<thead>
<tr>
<th>Audit No</th>
<th>Audit title</th>
<th>Date of audit report</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>DCP as RMS (incl. RMP assessment) in new IT environment</td>
<td>10.12.2013</td>
</tr>
<tr>
<td>21</td>
<td>internal Audits</td>
<td>07.11.2013</td>
</tr>
<tr>
<td>26</td>
<td>ICSR and Signal Detection</td>
<td>24.03.2014</td>
</tr>
<tr>
<td>29</td>
<td>Quality System</td>
<td>29.01.2015</td>
</tr>
<tr>
<td>33</td>
<td>Implementation of CSP (safety-related variations of SmPC)</td>
<td>12.02.2015</td>
</tr>
</tbody>
</table>
3.2.3 DCP as RMS (incl. RMP assessment) in new IT environment

3.2.3.1 Objective and scope
Objective: Follow-up of implementation of new IT-System for marketing authorisation procedures and effectiveness of the process (for RMP assessment only: to check compliance with GVP module V)

Scope:
- Regulatory Affairs – National Procedures (reception of documents and technical validation)
- Quality Assessment of Medicinal Products
- Clinical Assessment (incl. interface to biostatistics assessors)
- Pharmacovigilance (RMP assessment)
- Invoicing department
- Regulatory Affairs – MR and DC Procedures (validation, internal and external regulatory communication, preparation of decision and PAR)

3.2.3.2 Audit body
Quality Management department & internal auditors

3.2.3.3 Opinion
Process: The auditors declared good traceability, though not all relevant steps are documented in the new IT system, but in personal mailboxes, desktops and server shares. The individual process steps are well managed, but there is no assigned responsibility for oversight of the overall process.
Rollout of new IT system: the auditors found the roll-out managed in the best possible way, though the implementation required substantial changes (especially in the reception unit). Migration of electronic data was partially incomplete, e.g. the status of procedures in clockstop had to be reassigned manually.
Ongoing use of new IT system: acceptance of the new tools was very divergent between departments. The auditors explained this by divergent level of process support: while in the regulatory departments all process steps were performed in the IT-system, the assessor still used excel spreadsheets to manage allocation of procedures to individual assessors, as the necessary functions were not supported by the new tool.

3.2.4 Internal Audits

3.2.4.1 Objective and scope
Objective: to check effectiveness of the audit system and compliance with GVP module IV
Scope: Quality Management department

3.2.4.2 Audit body
Internal auditor from mother organisation

3.2.4.3 Opinion
The internal audit process is well implemented, based on long standing accreditation (ISO 17025 and 17020) and certification (ISO 9001) of the organisation. Requirements from GVP modules I and IV were integrated into the process. The auditor identified some opportunities for improvement.
3.2.5 ICSR and Signal Detection

3.2.5.1 Objective and scope
Objective: To check effectiveness of the process after reorganisation and compliance with GVP modules VI + IX
Scope: Blood, Tissue & Vigilance department

3.2.5.2 Audit body
Quality Management department & internal auditors

3.2.5.3 Opinion
Both processes are designed and managed in line with GVP requirements. SOPs have to be updated to reflect the new organisational structure, including management of new agency-internal interfaces and changed contact points for the European network. Assessors of the ICSR group should have direct access to EPITT. The auditors suggested the implementation of an internal function for coordination of PV activities in order to prevent fragmentation. Major concerns were expressed regarding insufficient resources in the ICSR group, whose staff members are fully engaged in administration and have scarce time for assessment.

3.2.6 Quality System

3.2.6.1 Objective and scope
Objective: to check compliance of the quality system with GVP module I
Scope: Quality Management department

3.2.6.2 Audit body
Internal auditor from mother organisation

3.2.6.3 Opinion
Apart from minor observations GVP I requirements are fully implemented. The quality system is well maintained and traceable. Weaknesses include business continuity management.

3.2.7 Implementation of CSP

3.2.7.1 Objective and scope
Objective: to check compliance with GVP module I and effectiveness of the process (module XII not published yet)
Scope: Regulatory Affairs department

3.2.7.2 Audit body
Quality Management department & internal auditors

3.2.7.3 Opinion
Legal requirements are fulfilled, but the process is not sufficiently regulated by the quality system. The SOP for the process is outdated.
### 3.2.2.4 Audit outcomes and actions

Actions based on 3 audit outcomes which are reported and rated 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>25</td>
<td>KSTE-9QMHU2</td>
<td>insufficient human resources for fulfilment of legal obligations in the context of ICSR and signal management</td>
<td>major</td>
<td>recruitment of administrative staff</td>
<td>Dec 2014</td>
<td>complete</td>
<td>follow-up by line management and internal auditors (done)</td>
</tr>
<tr>
<td>25</td>
<td>KSTE-9RHFBT</td>
<td>no EPITT access for assessors performing ICSR and signal management</td>
<td>major</td>
<td>EPITT access implemented</td>
<td>Dec 2014</td>
<td>complete</td>
<td>follow-up by line management and internal auditors (done)</td>
</tr>
<tr>
<td>29</td>
<td>KSTE-9QLJUX</td>
<td>no structured business continuity plan in place</td>
<td>major</td>
<td>trigger of a BCP project at level of the mother organisation</td>
<td>planned for Dec 2015</td>
<td>open</td>
<td>follow-up by line management and internal auditors</td>
</tr>
</tbody>
</table>
4. FOLLOW-UP

4.1 SUMMARY OF ACTION PLANS FROM PRIOR BIENNIAL REPORTS

The following table provides an overview of earlier audit outcomes issued by the Quality management department and their implementation by the BASG/AGES at September 2015.

<table>
<thead>
<tr>
<th>For action from audit outcome graded as:</th>
<th>Total</th>
<th>Number implemented</th>
<th>Number not implemented</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Not started</td>
</tr>
<tr>
<td>Critical</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Major</td>
<td>3</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>3</td>
<td>3</td>
<td>0</td>
</tr>
</tbody>
</table>

4.2 OUTSTANDING ISSUES FROM PRIOR BIENNIAL REPORTS

Extension of the scope of the PV SOP on crisis management to the whole agency was planned after publication of GVP module XII, but done in Q1/2015 when it could be clarified that module XII will not affect the European Union regulatory network incident management plan. Follow-up is planned as internal audit in Q3/2015.

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.

[Signature]

Head of the National Competent Authority                      Date

85/08/2015