Report to the European Commission on Pharmacovigilance audit carried out in the Agency for Medicinal Products and Medical Devices (HALMED), Croatia, 01/07/2013 to 16/09/2013

1. INTRODUCTION

The report is prepared in the context of the obligation under Article 101 (2) of the Directive 2001/83/EC that 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".

Since the Republic of Croatia has joined the European Union on 01/07/2013, this report provides an overview of the audit activities conducted from 01/07/2013 to 16/09/2013 by the Agency for Medicinal Products and Medical Devices (hereinafter referred as "HALMED"), Croatia, based on the internal audit planned for this specific situation: the Agency for Medicinal Products and Medical Devices becoming the competent authority of the new EU member state that has to fulfil the Union legal requirements in the field of pharmacovigilance. For this purpose the action plan was prepared that included adoption of all requirements set in Good pharmacovigilance practices within HALMED's units responsible for pharmacovigilance activities. The realisation of achieved goals has been examined during the above mentioned audit whose details are given in the report below.

2. BRIEF DESCRIPTION OF THE PHARMACOVIGILANCE SYSTEM

HALMED reports about developments in its pharmacovigilance (PHV) system:

- **Legislation**
  The new Medicinal Products Act published in the Croatian Official Gazette 76/13, as well as the new Ordinance on Pharmacovigilance published in the Croatian Official Gazette 83/13 came into force on 01/07/2013 transposing all requirements of the *acquis communautaire* into the legislation of the Republic of Croatia in the field of medicines regarding pharmacovigilance.

- **Organisation structure, responsibilities and resources**
  Two HALMED units are dedicated to performe of pharmacovigilance activities, the Department for Pharmacovigilance and Rational Pharmacotherapy (established in 2005), as well as the Department for Licencing, GMP and GVP Inspection (established in 2013 according to the new Medicinal Products Act). Both units have well defined duties and responsibilities. The resources in the Department for Pharmacovigilance and Rational Pharmacotherapy are adequate. The recruiting of PHV inspectors is in the process and is planned to be finished by the end of October 2013.

- **Training**
  The policy and the procedure for identifying training needs of personnel, including new members of staff being supervised by appointed mentors, has been defined. The annual training programme is relevant to the present and anticipated tasks of the units included in PHV activities. The training plan for new staff is carefully adjusted to specific needs. The system of annual evaluation of the training actions' effectiveness has been established.

- **Facilities and equipment**
  All facilities and equipment needed for PHV activities fit for purpose.

- **Compliance management**
  HALMED has established suitable quality system procedures and processes for the purpose of compliance management that ensure:
  - the evaluation of the quality and completeness of PHV data submitted;
  - the assessment of PHV data and its processing in accordance with the legal timelines;
  - the independence in the performance of PHV activities;
  - the effective communication with patients, healthcare professionals, marketing authorisation holders and the general public; as well as
  - conducting of inspections.

  PHV activities are performed in line with the corresponding procedures.

- **Record management**
  According to the record management system that has been put in place, HALMED records all PHV information and ensures that it is handled and stored to allow accurate reporting, interpretation and verification of that information. The system includes the management of the PHV data quality, timely access to all records; effective internal and external communication; and the adequate retention of records during the applicable retention period. The policy and procedure for personal data protection has been established giving guarantee that all PHV activities have been performed in conformity with legal provisions, ensuring data security and confidentiality.

- **Documentation of the quality system**
  All adopted elements, requirements and provisions of the HALMED PHV quality system are documented in a systematic and orderly manner in the quality manual, quality policies and plans, as well as corresponding standard operating procedures that are managed in accordance to Good documentation practices.

- **Business continuity arrangements**
  There is a new procedure for Business continuity in place integrating already established IT business continuity arrangements like back-up of data. The new business continuity plan will be finished by the end of 2013.

- **Monitoring of performance and effectiveness**
  The Quality Manual defines the processes to monitor the performance and effectiveness of the HALMED pharmacovigilance system and its quality system that include periodic reviews of the systems by responsible management, including annual Management review; risk-based internal audits or external audits; compliance monitoring; and evaluating the effectiveness of actions taken with medicinal products for the purpose of minimising risks and supporting their safe and effective use in patients.
  Additionally, HALMED has developed the procedure and corresponding PHV inspection programme for monitoring the compliance of marketing authorisation holders with legally required pharmacovigilance tasks and responsibilities.

- **Delegation of tasks**

  Not applicable

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 quality manager of HALMED on 30/07/2013.

3.2 SUMMARY OF THE AUDITS FOR THE PERIOD UNDER REVIEW

3.2.1 AUDIT ASSIGNMENTS FOR THE PERIOD UNDER REVIEW

The audit listed below was performed in line with the guidance provided in the GVP Module IV – Pharmacovigilance audits.

Audit No	Audit title	Date of audit report
13-13	Extraordinary internal audit 13-13	12/09/2013

3.2.2 Extraordinary internal audit 13-13

3.2.2.1 Objective and scope
The objective of the audit was to determine the compliance of HALMED pharmacovigilance system with the Guideline on good pharmacovigilance practices.
The scope of the audit included compliance with:

- Module I
- Module II
- Module III
- Module IV
- Module V
- Module VI
- Module VII
- Module VIII
- Module IX
- Module X
- Module XV

of the Guideline on good pharmacovigilance practices.

3.2.2.2 Audit body
Office for quality management of HALMED

3.2.2.3 Opinion
In my professional judgment as quality manager, sufficient and appropriate audit procedure has been conducted and evidence gathered to support the accuracy of the conclusions reached and contained in this report. The conclusions were based on a comparison of the situations as they existed at the time of audit against the audit criteria defined in Quality manual and corresponding standard operating procedures.
The internal auditing team concluded that a few specific nonconformities were noted (see 3.2.2.4); generally, however, all pharmacovigilance processes evaluated are adequate,

appropriate, and effective to provide reasonable assurance that potential risks are being properly managed and objectives are met.
The overall opinion on the HALMED Pharmacovigilance quality system is satisfactory and can assure the high quality of pharmacovigilance activities.

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.

Audit No	Find No	Audit outcomes description	Grading	Action short description	Action end date	Comments on status of actions	Type of follow-up required
13-13	1	Although there is an established practice, based on corresponding IT SOP related to business continuity management in IT Department of HALMED, there is no comprehensive business continuity management plan in accordance with SOP "Business continuity management" for other relevant activities in HALMED.	major	To make comprehensive business continuity management plan for all relevant activities in HALMED	31/12/2013	-	-
	2	There is no SOP that defines the content for the submission of quarterly progress reports for the Directorate and Management Board of HALMED and lists all relevant areas within the pharmacovigilance system as well as performance indicators for their monitoring. However, reports are submitted regularly having relevant areas and corresponding performance	major	To write SOP	31/12/2013	-	-

		indicators.					
	3	HALMED website in English has not been completely updated and is not in line with the Croatian original.	major	To prepare an action plan for an update of the HALMED website in English	31/12/2013	-	-
	4	Evaluation of effectiveness of risk minimization measures is not fully implemented.	major	It is necessary to provide additional data sources for a more complete assessment of the effectiveness of measures for risk minimization that would include the access to e-Health Insurance chart.	01/06/2014	-	-

4. FOLLOW-UP

4.1 SUMMARY OF ACTION PLANS FROM PRIOR BIENNIAL REPORTS

Not applicable

4.2 OUTSTANDING ISSUES FROM PRIOR BIENNIAL REPORTS

Not applicable

5. DECLARATION

The Agency for Medicinal Products and Medical Devices (HALMED) confirms that this report contains a complete account of all pharmacovigilance system audit activities performed in the period under review to fulfil the obligations of this organisation under Directive 2001/83/EC /Regulation (EC) No. 726/2004.

Viola Macolić Šarinić, MD, PhD, Clinical pharmacologist and toxicologist

Viola M. Šarinić

..... **16/09/2013**

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Head of the Agency for Medicinal Products and Medical Devices **Date**