Report to the European Commission/Management Board[1] on Pharmacovigilance audits carried out in the Agency for Medicinal Products and Medical Devices (HALMED), Croatia
[period of time from 16/09/2013 to 21/09/2015]

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".

This report provides an overview of the audit activities from 16/09/2013 to 21/09/2015 conducted by the Agency for Medicinal Products and Medical Devices (hereinafter referred as "HALMED"), Croatia, based on the internal audit which are planned to fulfil the Union legal requirements in the field of pharmacovigilance.
For this purpose HALMED has planned to perform 3 internal audits to check the compatibility of all requirements set in Good pharmacovigilance practices guidelines within HALMED's units responsible for pharmacovigilance activities.

The realisation of achieved goals has been examined during the internal audit whose details are given in the report below.

2. BRIEF DESCRIPTION OF THE PHARMACOVIGILANCE SYSTEM

Since the last report the only change that was implemented is in a connection with:
- Quality system for Pharmacovigilance Activities
Full implementation of requirements as set in Module XVI.

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 27/01/2014.

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.

Audit No	Audit title	Date of audit report
6-14	Internal audit 6-14	10/07/2014
4-15	Internal audit 4-15	30/3/2015
12-15	Internal audit 12-15	18/09/2015

3.2.2 Internal audit 6-14

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 II
- Module III
- Module V
- Module VI
- Module VII
- Module X

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 the 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).
Evaluated pharmacovigilance processes are adequate, appropriate, and effective to provide reasonable assurance that potential risks for public health are being properly managed and objectives are met.

3.2.3 Internal audit 4-15

3.2.3.1 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 VI
- Module VIII
- Module IX
- Module XV

of the Guideline on good pharmacovigilance practices.

3.2.3.2 Audit body
Office for quality management of HALMED

3.2.3.3 Opinion
In my professional judgment as the 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).

Evaluated pharmacovigilance processes are adequate, appropriate, and effective to provide reasonable assurance that potential risks for public health are being properly managed and objectives are met.

3.2.3 Internal audit 12-15

3.2.3.1 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 IV
- Module V
- Module VII
- Module X
- Module XVI

of the Guideline on good pharmacovigilance practices.

3.2.3.2 Audit body

Office for quality management of HALMED

3.2.3.3 Opinion

In my professional judgment as the 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)
Evaluated pharmacovigilance processes are in line with new edition of PV guidelines, adequate, appropriate, and effective to provide reasonable assurance that potential risks for public health are being properly managed and objectives are met.

The overall opinion for reported period on the HALMED Pharmacovigilance quality system is that system is satisfactory and can assure the high quality of pharmacovigilance activities.
According to BEMA III requirements, and BEMA assessment performed, HALMED has the best practice in field of Pharmacovigilance audit.

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.

Audit No	Find No	Audit outcomes description	Grading	Action short description	Action end date	Comments on status of actions	Type of follow-up required
6-14	1	RMP Abstracts are not available on HALMED website.	Major	HALMED should develop a strategy for putting summaries of RMP's on the web. It is necessary to establish an action plan that will lay down the necessary steps to fulfil the legal requirement	30/06/2015	CAPA implemented	next internal audit
4-15	1	All process steps of the exchange of information on the signals are not recorded and adequately monitored.	Major	Develop a tracker of all activities carried out by e-RMR (date of receipt of e-RMR, responsible assessor, date of inspection, etc.). Recorded training related to signal handling.	30/06/2015	CAPA implemented	next internal audit
	2	Evaluation of effectiveness of risk minimization measures is not being fully implemented.	Major	It is necessary to provide additional data sources for a more complete assessment of effectiveness of measures for risk minimization that would include the access to e-Health Insurance chart..	30/06/2016	In progress	CAPA and next internal audit
12-15	1	A list of additional monitoring of drugs published on HALMED website is not up to date.	Major	After the entry into force of the revised SOP (at least once a month) regularly update the list of	31/12/2015	In progress	CAPA and next internal audit

Audit No	Find No	Audit outcomes description	Grading	Action short description	Action end date	Comments on status of actions	Type of follow-up required
				additional monitoring of medicines published on the website HALMED			

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* HALMED and their implementation by the HALMED at 25/09/2015.

For action from audit outcome graded as:	Total	Number implemented	Number not implemented	
			Not started	In progress
Critical	0	0	0	0
Major	4	3	0	1
Total	4	3	0	1

4.2 OUTSTANDING ISSUES FROM PRIOR BIENNIAL REPORTS

Evaluation of effectiveness of risk minimization measures is not fully implemented.
It is necessary to provide additional data sources for more complete assessment of the effectiveness of measures for risk minimization that would include the access to e-Health Insurance chart.
HALMED conducted series of interviews with representatives of responsible governmental institutions and still needs additional time to solve this issue connected also with IT tool that must be implemented at national level.

5. DECLARATION

The Agency for Medicinal Products and Medical Devices (HALMED) 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 /Regulation (EC) No.726/2004[2].

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Head of the Agency for Medicinal Products and Medical Devices

Date 21/09/2015

2 Delete as necessary – National Competent Authorities are required to 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. (Directive 2001/83/EC Art.101(2), The European Medicines Agency is required regular independent audits of its pharmacovigilance tasks and report the results to its Management Board on a 2-yearly basis. (Regulation (EC) No.726/2004 Art 28f)