



## Reinforcing patient safety in Europe

14-15 June 2011  
Zagreb, Croatia



27 May 2011  
EMA/404541/2011  
Administration

# Reinforcing patient safety in Europe

## Conference programme

14-15 June 2011  
Zagreb, Croatia



7 Westferry Circus • Canary Wharf • London E14 4HB • United Kingdom

**Telephone** +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8416

**E-mail** [info@ema.europa.eu](mailto:info@ema.europa.eu) **Website** [www.ema.europa.eu](http://www.ema.europa.eu)

An agency of the European Union



Cover photograph is © Zagreb Tourist Board.

# Programme overview

---

## Day 1 Tuesday, 14 June 2011

---

08.00	Registration
09.30	Welcome coffee
10.00	Welcome address*
11.10	Session 1: Accession preparation I
12.45	Lunch break
14.00	Session 2: Accession preparation II
15.00	Session 3: Non-clinical assessment requirements
16.00	Coffee break
16.30	Session 4: Legislation
21.00	Welcome drink and conference dinner

## Day 2 Wednesday, 15 June 2011

---

09.00	Session 5: Benefit risk and risk minimisation
10.00	Session 6: Product information
10.45	Coffee break
11.15	Session 6: Product information (cont'd)
11.45	Session 7: Pharmacovigilance
12.45	Lunch break
14.00	Session 8: Crisis management case studies
15.30	Closure

### \* Interpretation

The language of the conference is English.

Simultaneous interpretation in English and Croatian will be for the welcome address only.



# Introduction

---

## Scope of the IPA project

---

The Instrument for Pre-accession Assistance (IPA) programme was launched by the European Commission in 2009 to support the participation of the following beneficiaries in the activities of the European Union (EU) agencies, such as the European Medicines Agency: Albania, Bosnia and Herzegovina, Croatia, the former Yugoslav Republic of Macedonia, Kosovo (under UNSC Resolution 1244/99), Montenegro, Serbia, Turkey, and (since 2010) Iceland.

In the context of medicinal products, the IPA programme is designed to establish between the Agency and the beneficiaries an open dialogue and working mechanisms that facilitate the harmonisation of technical standards, the adoption of legislative requirements, and the smooth integration of the beneficiaries' representatives into the work of the Agency.

In the EU legislative framework for medicines, there are a large number of directives and regulations relating to the issuing of marketing authorisations and to the economic regulation of the pharmaceutical market that need to be applied and implemented effectively. The body of knowledge relating to this implementation is constantly evolving as the EU scientific committees and their working parties develop guidelines and gain experience in new therapies and new technologies. Without any involvement in these procedures, it is extremely difficult to acquire the necessary knowledge to be able to participate in the EU regulatory system for medicines.

### Target groups

The target groups are the national competent authorities dealing with the regulation of medicines for human and veterinary use in the beneficiaries, their information officers, legal officers, scientists and stakeholders.

### Aims of the programme

The main aim of the IPA programme is to build contacts and relationships between the Agency and the beneficiaries' national competent authorities responsible for medicines, in preparation for their future collaboration in the EU regulatory network. This should enable the Agency, the existing Member States and the beneficiaries to work as equal, mutually respected partners from the day of accession.

To achieve this aim, the programme offers assistance to the national competent authorities of the beneficiaries in aligning their standards and practices with those established in the EU.

A specific activity of the programme is to contribute to the creation of communication and information exchange systems that will enable the effective participation of the beneficiaries in the networks of the EU regulatory system for medicines.

## Supporter of the conference

---

The conference is supported by the European Commission, as part of the preparation for the enlargement process, under the auspices of the President of the Republic of Croatia and of the Croatian Ministry of Health and Social Welfare.



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

## Welcome to all participants

---

Dear colleagues,

On behalf of the European Medicines Agency, I am pleased to welcome you to this regulatory conference in Zagreb, Croatia.

The conference will provide key information about legislative, procedural and scientific aspects of medicines regulation in the EU such as the *acquis communautaire*, with a view to informing the full cross-section of stakeholders in Croatia.

This conference also represents the continuity of a fruitful collaboration between HALMED and the EMA. The previous conferences held in Split and Rijeka were the first stones that set down the foundation for a successful partnership which have served to strengthen and promote a deeper understanding and awareness of the legislation and regulatory procedures which uphold the European regulatory system.

I am confident that this conference will reinforce the cooperation between Croatia and the European regulatory network in order to support your efforts towards EU membership.

**Andreas Pott**

Acting Executive Director  
Head of Administration  
European Medicines Agency



Agency for Medicinal Products  
and Medical Devices of Croatia

## Welcome to all participants

---

Dear colleagues,

Welcome to Zagreb, Croatia's capital city, and to yet another regulatory conference co-organised by the European Medicines Agency (EMA) and the Croatian Agency for Medicinal Products and Medical Devices (HALMED).

Considering that the patient is in the centre of our activities, it comes as no surprise that this year's conference is dedicated to improving patient safety in Europe. This conference is also a continuation of the previous conferences, held in Split and Istanbul in 2007, in Rijeka in 2008 and in Belgrade in 2010, for candidate countries and potential candidate countries for accession to the European Union.

For many years, we have been actively preparing for functioning within the integrated European area. Today, when we stand at the doorstep of entry into the EU, we can be truly satisfied with all that we have achieved in the area of medicines regulation in Croatia. The preceding period has been a very successful one and, in the context of Croatia's accession to the EU, a great deal of the work has been completed.

However, there are regulatory issues that we would like to discuss with you, and which will be covered in this two-day conference. We are often faced with regulatory issues that have a direct impact on patient safety, and for this reason, it is good that we now have the opportunity to work together towards resolving them.

It is our pleasure to work towards expanding and integration of the European regulatory network, for the benefit of all European citizens. We hope that this conference will allow us all to better fulfil our roles in this area, which is of vital importance for patient health.

I wish you all a warm welcome.

A handwritten signature in blue ink that reads "Siniša Tomić".

**Siniša Tomić**

Head of the Agency for Medicinal Products and Medical Devices of Croatia

# Programme details

---

Tuesday, 14 June 2011

## 8.00 Registration

---

Ground floor for badge collection.  
Coffee and croissants will be served before the conference begins in room Maskimir.

## 9.30 Welcome coffee

---

## 10.00 Welcome address

---

### **Andreas Pott (conference chair)**

European Medicines Agency

### **Siniša Tomić (conference co-chair)**

Agency for Medicinal Products and Medical Devices of Croatia, Croatia

**Additional speakers to be confirmed**

## 11.10 Session 1: Accession preparation I

---

11.15

### *Legal framework*

#### **Vincenzo Salvatore (chair)**

European Medicines Agency

The presentation will focus on the legal implication of accession, with particular regard to the implementation of EU pharmaceutical legislation in the new Member State. Compliance with existing regulations and directives, alignment with the *acquis communautaire*, transitional period and upgrading of existing marketing authorisations will be specifically covered. The respective role and responsibilities assigned to the European Medicines Agency and to national competent authorities in the European medicines regulatory network will also be addressed, taking namely into account the new challenges posed by the new EU pharmaceutical package on pharmacovigilance, fight against counterfeit medicines and information to patients.

11.35

### *Situation in Croatia*

#### **Siniša Tomić**

Agency for Medicinal Products and Medical Devices of Croatia, Croatia

Regulatory framework for medicinal products in Croatia is well aligned with the EU legislation and HALMED expects upon accession to join the integrated EU regulatory framework without major difficulties. Since its establishment in 2003, HALMED has been continuously undertaking all necessary measures to be well prepared for the accession. However, there are still a few challenges to overcome before the accession, such as dossier upgrading, improving quality and consistency of published product information, enhancement of our eCTD-related workflows and balancing stipulations of the current Croatian legislation with the requirements of the new EU regulation on variations.

Presently, the main task of HALMED is to maintain the current operational regulatory framework in the pre-accession period and yet to be ready to fully implement EU legislation from day one of the accession.



**11.55** *Perspectives from a new Member State*

**Romaldas Maciulatis**

State Medicines Control Agency, Lithuania

This presentation will provide a short description of the Lithuanian regulatory system and the historical perspectives, including phasing-in to the EU regulatory system and evolution during the critical first years. The experience gained during the transitional period and as a consequence the obstacles faced will be shared, particularly the unexpected ones. As the lessons learned, the attempts to solve the issues and solutions will be discussed. Case reports of typical failures and difficulties when acting in the new and constantly changing EU regulatory framework will be provided. In particular, the interaction between national and EU obligations and worksharing experience will be discussed.

**12.15** *Phasing-in (product specific)*

**Anthony Humphreys**

European Medicines Agency

The pharmaceutical acquis extends automatically upon the date of formal accession of a new Member State. This has immediate consequences with respect to the national market for pharmaceuticals. This presentation seeks to highlight these consequences for the Member State concerned, and the expected impact on the continued regulatory supervision and authorisation of supply for various categories of medicinal products to the market.

*Q&A*

**12.45** **Lunch**

---

Lunch will be served at the restaurant and in the room Miskimir.

**14.00** **Session 2: Accession preparation II**

---

**Anthony Humphreys (chair)**

European Medicines Agency

**14.05** *Preparing for dossiers evaluation*

**Peter Bachmann**

Federal Institute for Drugs and Medical Devices, Germany

**14.25** *Adapting to Community procedures*

**Truus Janse de Hoog**

Medicines Evaluation Board, The Netherlands

In this presentation, the Community procedures Art. 30 and 31 of Directive 2001/83/EC will be discussed. The main principles of these procedures will be explained, as will the different steps in the procedures and the lifecycle management of products after implementation of the Commission decision.

The CMDh has an important role in selecting candidates for harmonisation of SmPCs and PLs via the Art. 30 referral. The SmPCs and PLs that are harmonised via this route are the standard for the SmPC and PL of generic products. It is important to take this information into account with the update of national dossiers. The products fall under the scope of the mutual-recognition procedure after full harmonisation of the SmPC. After accession, the repeat-use procedure can be used to bring the nationally approved products into the mutual-recognition procedure, so that the harmonisation of the dossier is maintained during the lifecycle of these products.

*Q&A*

## 15.00 **Session 3: Non-clinical assessment requirements**

---

### 15.05 *Non-clinical assessment requirements: perspectives from regulators*

#### **Maria Nieto-Gutierrez (chair)**

European Medicines Agency

During the non-clinical development of a medicinal product, the goal is to determine whether the product is safe for use in humans and the compound exhibits pharmacological activity that justifies the regulatory approval. The non-clinical safety requirements cover the areas of pharmacology, pharmacokinetics and toxicology carried out in animals or in vitro. Non-clinical guidelines facilitate harmonisation of the non-clinical studies in Europe and at the international level. At the European level, the Safety Working Party (SWP) provides recommendations to the Committee for Medicinal Products for Human Use (CHMP) on all matters relating directly or indirectly to non-clinical aspects of safety.

### 15.25 *Non-clinical assessment requirements: perspectives from a Member State*

**Speaker to be confirmed**

*Q&A*

## 16.00 **Coffee break**

---

## 16.30 **Session 4: Legislation**

---

### 16.40 *Variations Regulation: the framework after the revision*

#### **Vincenzo Salvatore (chair)**

European Medicines Agency

The presentation will focus on the current legal framework for the examination of variations to the terms of the marketing authorisation for medicinal products, as laid down in Commission Regulation (EC) No 1234/2008. It will address the background of the revision of the variations framework and provide an insight into the legislative history of the Regulation. Moreover, it will explain the classification of variations in type-1A, type-1B and type-2 variations, as well as the procedures to be followed according to the respective classifications. Additionally, the classification of unforeseen variations will be explained.

### 17.00 *Variation Regulation: quality*

#### **Keith Pugh**

Medicines and Healthcare products Regulatory Agency, United Kingdom

*Q&A*

### 17.30 *Generics in the centralised procedure: current issues*

#### **George Wade (co-chair)**

European Medicines Agency

Since the beginning, the CP has been regarded as a restricted procedure for mainly innovative products, but recent changes in the legislation have also opened the door to non-innovative products. Centralised submission of generic versions of centrally authorised reference products is an option for applicants who may also, if they wish, go into the national procedures like the DCP, depending on what sort of market they want. Initially, the advantages of a pan-European authorisation were apparent mainly to the larger generic companies, but more recently there is interest from smaller companies. The EMA has been meeting with the EGA on a number of issues of common concern, e.g. flexibility for applicants and consistency in assessment, and overall, the handling of generic versions of centrally authorised reference products continues to be a significant part of the EMA's core business.

## 17.50 *Interchangeability of generics*

### **Truus Janse de Hoog**

Medicines Evaluation Board, The Netherlands

Two medicinal products are considered to be interchangeable if they contain the same active substance, the same pharmaceutical form and strength, and bioequivalence has been proven in accordance with the bioequivalence guideline. This principle has been applied for many years for immediate-release formulations of generic products. It has been the basis for generic substitution in many countries.

Now, the pharmaceutical landscape has changed considerably, with the availability of biosimilar products, complex formulations such as liposomal packaging of molecules, and generics from locally acting products such as inhalers.

The bioequivalence guideline does not cover aspects related to generic substitution, as this is subject to national legislation. What is the role of national competent authorities with regard to substitution; should potential problems with interchangeability be taken into account during the assessment? How should the health professionals be informed about interchangeability of products?

## 18.10 *Non-prescription switching*

### **Anthony Humphreys**

European Medicines Agency

Changing the classification for the supply of a medicinal product from prescription to non-prescription, or 'switching', can also be done by simultaneous switch at European level, rather than market to market. The presentation highlights the possible entry points to centralised switching, and illustrates the particularities and benefits of the centralised switch at the same time as reporting on the experience accrued so far by the EMA in this field.

### *Q&A*

## 18.40 *Electronic submission in the EU: tools*

### **Karin Grondahl**

Medical Products Agency, Sweden

Electronic submission is now the main format for marketing authorisation applications in the EU. The preferred format to be used is the eCTD, but also the NeeS format is normally accepted. There are specifications and guidance documents to be followed by applicants to facilitate the handling of electronic documents in assessment and archiving. There are also review tools available to make use of the special features of the eCTD format to further improve the use.

To be able check the adherence to the specifications and guidelines, there are special validation criteria published both for eCTD and NeeS, and there are different vendor's tools to use for technical validation of the electronic submissions. The criteria have recently been updated and the new versions will come into force on 1 September 2011. Hopefully, the new criteria will lead to a more harmonised way of technical validation by the different tools and by the different NCAs.

### *Q&A*

## 21.00 **Welcome drink and conference dinner**

---

Please join us at the **Okrugljak restaurant**

Mlinovi 28, 10000 Zagreb

Phone: (+385) 1 4674 112

<http://www.okrugljak.hr/home.aspx>

Bus transfer is organised from and to the Westin Hotel (meeting-point in the lobby).

Outbound: 20.30

Inbound: 22.30, 23.00

# Programme details

---

Wednesday, 15 June 2011

## **9.00**      **Session 5: Benefit-risk and risk minimisation**

---

### **9.05**      *Assessment and communication*

#### **Eric Abadie (chair)**

Agence Française de Sécurité Sanitaire des Produits de Santé

The assessment of the benefits and risks in the context of a new drug application is a central element of the scientific evaluation of a marketing authorisation application and related variations.

The assessment must reach, as objectively as possible, a sufficient level of confidence that a set level of quality, efficacy and safety of the new medicinal product has been demonstrated. This requires evaluation of all relevant data, as well as the use of judgement and arguments. Article 26 of Directive 2001/83 as amended states that the marketing authorisation shall be refused "if the benefit-risk balance is not considered to be favourable or if therapeutic efficacy is insufficiently substantiated". The CHMP is endowed with the task of assessing the benefit-risk balance of new medicinal products. Questions have been raised regarding a) the optimal methodology to establish the benefit-risk balance of new medicinal products, and b) the transparency of the methods used by the CHMP to reach conclusions on benefit-risk. This presentation will try to answer these questions and will address the way the CHMP communicates to its stakeholders and to the public.

### **9.25**      *Risk minimisation*

#### **Maarten Lagendijk**

Medicines Evaluation Board, The Netherlands

The risk management plan (RMP) has been mandatory since the end of 2005. Since then, the RMP should be part of the marketing authorisation application (MAA). However, the competent authorities can also request an RMP for products already authorised before 2005, based on safety issues identified during its lifecycle. The RMP is meant to be a tool for identifying the gaps in the knowledge of the product, and for proposing actions to fill in those gaps.

The RMP contains two parts. The first part concerns the identification of the safety specifications for the product and the pharmacovigilance plan to obtain more information on the possible risks. The second part concerns the need for risk minimisation activities. If additional risk minimisation is needed, a risk minimisation plan should also be submitted in this second part of the RMP.

Routine risk minimisation is achieved through the summary of product characteristics (SmPC) and the patient information leaflet (PIL). However, for some risks those routine activities may not be sufficient, and additional risk minimisation is necessary.

The presentation will focus on risk minimisation and the different activities that can be considered additional risk minimisation. It will also focus on the challenges concerning risk minimisation that still remain, such as evaluation of the effectiveness of the additional activities.

#### **Q&A**

## 10.00 **Session 6: Product information**

---

### 10.05 *Product information management*

#### **Alexios Skarlatos (chair)**

European Medicines Agency

An overview will be given of the procedures governing the handling of product information within the centralised procedure, covering, in particular, new chemical entities, generics and biosimilars, as well as certain types of referrals. The roles and responsibilities of the main actors (EMA, national competent authorities, industry, and patients' organisations) in the field of product information will also be presented. Finally, issues related to the review of labelling/packaging components, as well the review of invented names, will also be addressed.

## 10.45 **Coffee break**

---

### 11.15 *Readability testing*

#### **Kim Sherwood**

Medical Products Agency, Sweden

User test has been a regulatory requirement in producing package leaflets/patient information since 2005. A user test itself does not ensure understandable patient information, but is a tool in the development of clear patient information. The aim in performing a user test is to ensure that 'patients' can find, understand and act upon information. The result of a user test should be used to amend the patient information. In this presentation we will discuss what a user test is, how it should be assessed and lessons learned since 2005.

*Q&A*

## 11.45 **Session 7: Pharmacovigilance**

---

This session will introduce the new EU pharmacovigilance legislation, which will apply from July 2012, and provide attendees with an overview from the EMA's perspective and from a Member State's perspective. The session will identify the key changes for industry and national competent authorities, and look at the implementing measures needed in the areas of ADR reporting, PSURs, additional monitoring and transparency in the run-up to the introduction of the new system. The EMA perspective will concentrate on the roles and responsibilities of the new PRAC committee, as well as the intensive work undertaken by Member States and the EMA to prepare for the new legislation.

### 11.50 *Summary of the new pharmacovigilance legislation*

#### **Henry Fitt (chair)**

European Medicines Agency

### 12.20 *New pharmacovigilance legislation: perspective from a Member State*

#### **Mick Foy**

Medicines and Healthcare products Regulatory Agency, United Kingdom

*Q&A*

## 13.00 **Lunch**

---

**14.00**

## **Session 8: Crisis management case studies**

---

### **Anthony Humphreys (chair)**

European Medicines Agency

**14.05**

### ***Crisis management case studies: introduction***

#### **Michael Forstner**

F. Hoffmann-La Roche Ltd

Crisis is a process of transformation where the old system can no longer be maintained. In this presentation, we are going to look at the development from an issue to a crisis, how intervention at different steps could be more or less effective in preventing a crisis from getting out of control, and how to plan for a crisis by setting up and testing crisis response plans and crisis teams. Finally, examples of successful and unsuccessful crisis management will be discussed, as will lessons learnt.

**14.25**

### ***Crisis management case studies: communication***

#### **Anthony Humphreys**

European Medicines Agency

The public perception and acceptance of risk associated with the use of medicinal products is a moving target in the context of wide access to diverse sources of information updated in real time. This represents a challenge to the regulatory network that is charged with fulfilling a primary duty of care to the patients using such medicinal products. This presentation seeks to provide an insight into how the network has dealt with this challenge, through reviewing experience gained with individual product case studies.

#### ***Q&A***

**14.55**

### ***Safety aspects of vaccines: evaluation and pharmacovigilance***

#### **Phil Bryan**

Medicines and Healthcare products Regulatory Agency, United Kingdom

Safety evaluation of vaccines carries specific challenges which do not necessarily apply to pharmacovigilance of other pharmaceutical products. These include use in healthy individuals, mass population exposure, a dynamic balance of risks and benefits, and inherent biological variability. A fall in confidence in vaccine safety can have a wide-ranging impact.

These challenges necessitate careful risk management in advance of major new immunisation programmes and tailored pharmacovigilance strategies. This session will outline the key aspects of signal detection, risk evaluation, communication and risk minimisation to ensure robust risk management for new vaccines.

#### ***Q&A***

**15.30**

## **Closure of the conference**

---

### **Sylvie Bénéfice**

European Medicines Agency

### **Siniša Tomić**

Agency for Medicinal Products and Medical Devices of Croatia, Croatia

# Notes

---

## Conference secretariat

---

European Medicines Agency  
7 Westferry Circus, Canary Wharf  
London E14 4HB, United Kingdom

**Telephone** +44 (0)20 7418 8400

**Facsimile** +44 (0)20 7418 8501

**Secretariat** [jpa.conferences@ema.europa.eu](mailto:jpa.conferences@ema.europa.eu)

**External participants** [extpax@ema.europa.eu](mailto:extpax@ema.europa.eu)

**Website** [www.ema.europa.eu](http://www.ema.europa.eu)

## Conference venue

---

The Westin Hotel  
Izidora Kršjnjavoga 1, Zagreb 10000, Croatia

**Telephone** +385 1 489 2000

**Website** [www.westinzagreb.com](http://www.westinzagreb.com)