

EDQM Conference

Quality of Medicines in a Globalised World: Dreams and Reality

14-15 October 2010
Prague, Czech Republic



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Plenary Session

-  Dr Patrick Deboyser
-  Dr Kristin Raudsepp
-  Mr Jean-Marc Spieser



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EDQM Conference
« Quality of Medicines in a Globalised World : Dreams and Reality »
Prague – 14-15 October 2010

«The European Commission perspective »

Patrick Deboyser
Advisor to the Director General
DG Health & Consumers
EUROPEAN COMMISSION



Outline of speech:

- State of play on quality of medicines
- The Proposal on falsified medicines
- Vision for the future



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Health & Consumers

State of play on quality of medicines (1)

- EU legislation:
 - Directive 2001/83/EC (Community Code for Human Medicines)
 - Directive 2001/82/EC (Community Code for Veterinary Medicines)
 - Guide on good manufacturing practices
- EMA Working Groups
- EDQM: OMCL network, Pharmacopoeia
- Interested parties meetings
- H(v)MA Working groups
- Joint audit programme (MS)
- Databases



Directorate-General for
Health & Consumers

State of play on quality of medicines (2)

- International Conference on Harmonisation (ICH) – full set of quality guidelines, e.g.:
 - Q9 : Quality Risk Management
 - Q10: Pharmaceutical Quality System
- Mutual recognition agreement (MRA) providing for mutual recognition of GMP inspection results (no more re-testing of batches) with:
 - New Zealand
 - Australia
 - Canada
 - Switzerland
 - Japan



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State of play on quality of medicines (3)

- PIC/s : collaboration on GMP, training
- WHO: follow-up of the quality group
- Commission/EMA/FDA collaboration on inspection
- Confidentiality agreement (US, Japan)
- Bilateral discussions (India, China, Russia,...)



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The Proposal on falsified medicines

- Legislative proposal amending Directive 2001/83/EC as regards the prevention of the entry into the legal supply chain of medicinal products which are **falsified** in relation to their identity, history or source - COM(2008)668 of 10 December 2008
- Types of measures:
 - (1) Safety features
 - (2) Clear responsibility for all actors in the supply chain
 - (3) Active substances (API)
- Progress so far



The Proposal on falsified medicines

Types of measures: (1) Safety features

- Obligatory (and harmonised) safety features allowing identification and authenticity checks, and tracing of each pack
 - Scope: **prescription medicines** and risk-based
 - Characteristics set out in implementing measures
 - Specific rules for the removal or cover-up of the feature
- Obligation on manufacturers to **report** any suspicion of falsification



The Proposal on falsified medicines

Types of measures: (2) Clear responsibility for all actors

- Update of obligations for **wholesale distributors**
- Definition & obligations for **traders** (negotiating the sale and purchase of medicines)
- Provisions for **introduction** of medicines (not placed on EU market)
- Obligations for exporting wholesale distributors
- Good distribution practices certificates - GDP database by EMA
- Obligation on distributors to **report** any suspicion of falsification



The Proposal on falsified medicines

Types of measures: (3) Active ingredients (API)

- Clarification: direct obligations for manufacturers of APIs
- **Notification** of manufacturers and importers of APIs established in the EU
- Specific provisions for **import of APIs**:
 - Third country listed by Commission (Commission Decision) or
 - 'Written confirmation' by the competent authority of the third country
- Mandatory **audits** of manufacturers and importers



The Proposal on falsified medicines

Progress so far:

- New Health Commissioner J. Dalli supported falsified medicines as a priority for swift negotiation in Parliamentary hearing
- Council and European Parliament are discussing intensively the legal proposal, and notably:
 - Definition of falsified medicines
 - Safety features (time frame for implementation, for prescription and non-prescription based on risk, use for other purposes)
 - Notification of API manufacturers and importers
 - Internet sales
 - Sanctions



Vision for the future:

- Increase public health protection through high quality medicines, notably by fighting falsified medicines
- Call for efficient use of inspection and testing resources: making MRA fully operational for the new Member States
- Pursue fruitful collaboration with EDQM, WHO, PIC/S, ICH and call for efficient and enhanced worksharing

**DG Health & Consumers DG
EUROPEAN COMMISSION**



Thank you!

Current and new issues concerning global markets and the quality of medicines – agency view

Dr Kristin Raudsepp
Director General
Estonian State Agency of Medicines
Heads of Medicines Agencies (HMA)

The presentation

- Well-known and new issues about the quality of medicines
- Challenges and opportunities of the globalisation
- What are the agencies doing

Background information on HMA network



European Economic Area (EEA)

European Union
+ Iceland, Liechtenstein and Norway

www.hma.eu

•since 1996

•aim - to protect and promote public and animal health in Europe

The Heads of Medicines Agencies is a network of the Heads of 44 national competent Authorities from the 27 EU member states and the 3 countries from the EEA
Estonia 1,3 million

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Network

- Each MS separately
- HMA together
- Each MS through EMA Management board and scientific committees

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Globalisation doesn't mean quick harmonization

- Globalization in an economic context refers to the reduction and removal of barriers between national borders in order to facilitate the flow of goods, capital, services and labor. It also means transnational circulation of ideas.
- Considerable barriers remain
- In the world of medicinal products we must acknowledge the global nature of the pharmaceutical industry and its overall complexity and prepare ourselves to be ready for that and never forget the importance of international cooperation.

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Globalisation vs national interests of the agency

- Global priorities are sometimes contradictory to national priorities (different resources, differences in economies, culture, politics)
- A lot has been done to harmonise public standards between Member States for the protection of public health
- Total harmonisation will not be possible

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Important ongoing projects

- The Council of Europe – Medicrime convention
- ICH VICH
- EDQM - Certification of Suitability to the monographs of EP (CEP)
- EDQM Eur Pharmacopoeia, Pharmacopoeia Discussion Group (PDG)
- EDQM – coordination European network of OMCLs + information exchange of counterfeit medicines + MRP/DCP Product Market surveillance programme
- EDQM – preparing the resolution to harmonise quality and safety norms for pharmacy prepared medicines
- Official Control Authority Batch Release (OCABR) of blood and plasma derivatives, human vaccines and veterinary immunobiologicals
- European Commission intensified global cooperation on different levels
- WHO pre-qualification programme
- PICs quality defects
- Co-operation agreements EDQM, EMA, FDA
- EMA Quality WP
- National MAs – Baltic or other regional cooperation activities
- HMA Product testing WG

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Quality – do we all understand it similarly?

- Quality of the medicinal product is a very important parameter, effectiveness and safety of the product are based on it on a large scale
- What is the pharmaceutical preparation of high-quality - the common understanding may vary
- Inequality in availability/affordability often takes to different meaning/understanding of products' quality

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Well-known and new issues about the quality of medicines

- We would like to know that all operators involved in the pharmaceutical supply chain comply and supervise compliance with EU standards (incl. GMP principles), regardless of the country of origin
- Advanced therapies – are the requirements for their quality absolutely clear?
 - new medical products based on genes, cells and tissues
 - '-Omics' and Personalised Medicine
 - Nanomedicines

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Trends about the quality

- The HMA noted the large impact of globalised trade on the supply of pharmaceuticals over the past 20 years.
- The great majority of Active Pharmaceutical Ingredients (APIs) are sourced from outside Europe or North America. Finished products, especially generics, are also very likely to come into the EEA from countries with rapidly expanding pharmaceutical manufacture, such as India.
- raising concerns over the quality assurance of medicines and Active Pharmaceutical Ingredients (APIs) sourced from third countries
- Information exchange is essential (EudraGMP, etc)

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Challenges and opportunities of the globalisation

- Error or mistake or defect spreads very quickly over the world
- Quickly spreading infectious diseases
- Quickly spreading counterfeited products
- Patients get information worldwide (often also medicines). The different handling of the problem needs very good argumentation and communication from agency
- Guidelines available, but may be interpreted differently (even Eur Pharmacopoeia)
- Mutual trust
- Easily vulnerable markets of medicinal products – based mainly on import or few manufacturer

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Challenges and opportunitiescont'd

- Applicability and surveillance of the local law may be questionable, difficult and resource-demanding if the company and its responsible persons are in another side of the world and in different legal room
- Increased need for cooperation and information exchange between assessors, inspectors, OMCLs makes lots of the personell of the agency lots of time travelling around
- To face the challenges of globalization no regulator should forget the complexity of the supply chain and the multiplicity of outsourced activities and must handle it in an efficient way
- "Stronger" regulates the "weaker" from strength position – often no ideal cooperation
- Differences in classification: medicines in one country – food additive in another – non-harmonised, often based on court-cases
- Adequate level of pooling of data and knowledge/expertise across the world – is it possible

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Supporting systems

- E-systems
 - helpful, but often unreasonably overpriced development and maintenance
 - Not “talking” to each other
 - Development and requirements not harmonised
 - Information in them secure?

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Challenges on the level of agency

- Long term strategy – what will be the responsibility of national agency and what will be centralised in Europe, or in world
- To provide continuous professional development for staff
- Resource planning
 - You don't need so many specialists, but you may need the whole dept of international relations to manage all the information moving around
 - You must give and you will get

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Raising concerns over counterfeits

- The growth of international trade through more complex supply routes has created opportunities for organised crime to move into counterfeit ('falsified') medicines, where potential profits are large and criminal penalties generally low.
- This is a problem which regulatory authorities around the world share; there is much to be gained by international co-operation. (EDQM database)

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Targets of HMA

- Effective communication
- Harmonised decisions
- Harmonised training, continuous professional development for staff of regulatory agencies
- Promote harmonised interpretation of guidelines
- Support work sharing and mutual trust
- Ensure the prudent use of resources
- Improve the quality of the work
- Foster science-based, pragmatic and consistent assessment, inspection and laboratory control practices and decision making

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HMA strategy

- Developing the Heads of Medicines Agencies Strategy for the European Medicines Regulatory Network
- 2005 the first HMA Strategy paper was adopted, Revision in 2007
- In July 2009, HMA endorsed a proposal to draft a five-year strategy 2011-2015 for the European Medicines Regulatory Network
- In July 2010 it was published for comments to all stakeholders (40 answers got)
- In October adoption planned by HMA
- Action plan

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Heads of Medicines Agencies Strategy 2011-2015

- The aim of the new strategy is to identify key challenges which face the network over the next five years and how the network can best respond to these challenges for the benefit of the European population.

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Taking into account

- European Medicines Agency's (EMA) developing Roadmap to 2015
- the recently published Ernst & Young report, for the European Commission, of the EMA and the system for marketing authorisation of medicines in the EU
- A Changing Environment - significant political, economic, social and legislative developments, such as the global economic downturn and the recent H1N1 pandemic
- rapid technological change, scientific innovation and other factors which impact on human and animal health

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Challenges influencing the HMA

but outside the possibility to change by NCA

- **Legal** (pharmapackage, clinical trials, etc)
- **Scientific: horizon scanning and pipeline work** (advanced therapies, device/medicine combinations, HTA)
- **Social and political** (demographic, increased patient expectations to healthcare, Lisbon Treaty)
- **Trade and industry** (globalisation, industrial consolidations, concerns over rising costs of innovation)

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European Risk Management Strategy

- 2002 developed together with EMA covering all medicinal products for human use

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Mutual recognition of control results

PRINCIPLES FOR MUTUAL RECOGNITION OF CONTROL RESULTS

Endorsed by HMA on 28 October 2009

-is recognised as one of the key components of a collaborative approach to the sampling and analysis of medicinal products between Medicines Agencies.
- Sharing of workloads and acceptance of results is necessary for the success of this collaboration. It must be possible for Competent Authorities to take appropriate regulatory action on the basis of reports they receive without further confirmatory testing otherwise the concept of work sharing and collaboration fails.
- Equally it should be recognised that there are circumstances when re-testing is needed and they should be identified to avoid confusion.

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Key themes the HMA believe making a real difference over the next five years

- **Safeguarding public and animal health**, particularly through:
 - strengthening surveillance of the benefits and risks of medicines in the European population,
 - good communication,
 - strengthened monitoring of the quality of medicines;
- **Supporting innovation**, particularly through:
 - efficient and proportionate regulation of clinical trials e.g. by using Voluntary Harmonisation Procedure (VHP); and
 - the provision of excellent scientific and regulatory advice.
- **Further improving the operational efficiency of medicines authorisation by the Decentralised and Mutual Recognition Procedures (DCP/MRP)**, particularly through:
 - risk-based regulation
 - harmonisation of assessment
 - work-sharing
 - training
 - best use of IT.

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How the Network can “make a difference” in the next five years

- **A. Public and Animal Health**
- Regulatory contributions to public health and animal health and welfare
- Pharmacovigilance – human
- Pharmacovigilance – veterinary
- Inspections and quality issues
- Additional areas of competence, including devices for human therapy
- Availability of pharmaceuticals

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- **B. Regulation**
- Risk-based management of resources, reducing administrative burden and improving regulatory efficiency
- Human Clinical Trials – consistency of implementation / harmonisation
- Regulation of Veterinary Medicines

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- **C. Communications**
- Interactions with industry /stakeholders, and website presence
- Developing opportunities for dialogue with stakeholders
- Developing the HMA web presence

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- **D. Strengthening the Network**
- Resources
- Making MRP and DCP work better
- Information Technology
- Training

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Agency needs more resources, networks need more cooperation and coordination

- Today's pharmaceutical supply chain includes a big number of pharmaceutical operators and this needs a large number of supervision activities.
- Increasing demand for inspections worldwide
- Increasing demand for maximising the efficiency of existing resources through cooperation, worksharing and limitation of duplication of the work by regulatory agencies from various regions, especially when common (e.g. ICH) standards are agreed.

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Conclusions

- European agencies have analysed very carefully the challenges of the globalisation
- Agencies put a big effort improving the cooperation and networking and finding best strategies for the future development and consequently saving of resources and costs and reduction of duplication of work.
- Agencies work to improve the quality and consistency of the work of the European Regulatory Network
- Urge everyone to engage in the future collaboration - pooling of knowledge/expertise across the world

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Current & New Issues Concerning Global Markets And The Quality of Medicines – The EDQM Perspective -

Prague, 14 October 2010

Dr Susanne Keitel,

European Directorate for the Quality of Medicines &
HealthCare, Council of Europe



Globalisation & Quality of Medicines

- Old or New story?
 - The role of the Pharmacopoeia
- Possible Impact on EDQM activities?
 - Pharmacopoeia
 - Certification procedure
 - OMCL Network
 - The fight against counterfeit medicines
- Conclusion



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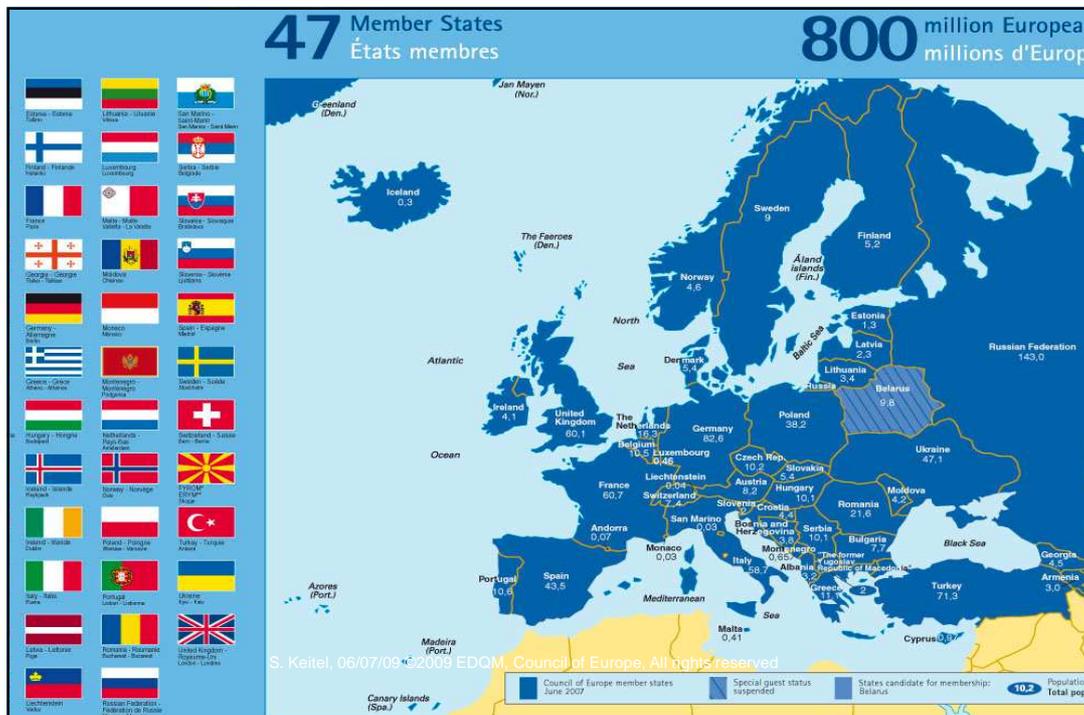
The Council of Europe



- Founded on **5 May 1949** by 10 countries
- An international organization in Strasbourg which comprises **47 countries** of Europe.
- The primary aim of the **Council of Europe** is to create a common democratic and legal area throughout the whole of the continent, ensuring respect for its fundamental values: **human rights, democracy** and **the rule of law**.
- Mr Thorbjorn Jagland, Secretary General of the Council of Europe since 1 October 2009 (Norwegian)



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Globalisation - Old or New Story?

The role of the Pharmacopoeia

- Historically collections of medical recipes to ensure accurate dispensation of medicines by pharmacists.
- Today, major role in the regulatory process and the control of active pharmaceutical ingredients (APIs), excipients and drug products used by industrial manufacturers, official medicines' control laboratories, regulatory authorities.



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Old or New Story?

The role of the Pharmacopoeia (cnt'ed):

- provides public standards, specifications, and test methods likely to be used by independent analysts for quality control.
- plays an important role in the fight against falsified and counterfeited medicines, a growing threat to public health.



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Evolving with a Changing World

Globalisation encompasses the exchange of goods and services over broad distances

- Necessitates increased standardisation to ensure consistent product quality, regardless of source
- Need to reflect different sources of medicinal substances in pharmacopoeial test methods, especially in view of the shift of API production from Europe and the US to India and China.



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Evolving with a Changing World

- Pharmacopoeial monographs to cover products on the market to avoid unnecessary restriction of choice of substance supply and limitation of access to affordable, quality medicines.
- Test methods must be sufficient and robust, based on technologies that are state-of-the-art and available globally at reasonable costs.



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Pharmacopoeias: Growing Need for Global Harmonisation

- First major shift in the 60's: the “Europeanisation”
 - Convention on the Elaboration of a European Monograph facilitated free movement of medicines throughout Member States and ensured access to medicines for European citizens.
- Today, this convention has 37 signatory parties from Europe as well as 23 observers from all over the world, including the United States and China.



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Pharmacopoeias: Growing Need for Global Harmonisation

- The 90's creation of the Pharmacopoeial Discussion Group (PDG) by Europe, Japan, and the US—all representatives of the ICH—represented a step towards pharmacopoeial harmonisation at a broader level.
- More than 40 excipient monographs and 27 general methods have been harmonised among the three pharmacopoeias.
- **However, much remains to be done in this area!**



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The Role of the EDQM



EDQM is a leading organisation that protects public health by

- enabling development,
- supporting implementation, and
- monitoring application

of quality standards for safe medicines and their safe use.

Our standards are recognised as a scientific benchmark world-wide. The European pharmacopoeia is legally binding in European member states.

Similarly, EDQM develops guidance and standards in the area of blood transfusion, organ transplantations and consumer health issues.



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Challenges for the Pharmacopoeia

New topics:

- need to follow developments in medical practice, e.g. development of quality standards not only for classical European homeopathy, but also for other traditional medicines.
- Need to consider new technologies, e.g. shift from chemically defined to biotechnologically derived substances in the production of medicines.



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Challenges for the Pharmacopoeia

New approaches:

- Changes in the pharmaceutical industry, e.g. quality risk management, and quality systems (ICH Q8, Q9, Q10).
- A pharmacopoeia defines legally binding quality standards that will be used in cases of dispute

BUT

- A pharmacopoeia must allow for sufficient flexibility to encourage innovation, e.g. Process Analytical Technology (PAT) in the production and control of API and finished products.

Need for a tiered system, considering the different needs of the global pharmaceutical industry and small- and medium-sized enterprises, while ensuring protection of public health.



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Challenges for the Pharmacopoeia

Counterfeited medicines:

- A pharmacopoeia will never be able to control all possible potential adulterations and resulting impurities, but must be vigilant and capable of adjusting its standards to market developments and quickly revising its monographs when the need arises.
- However, contributions vital to overall success of multidisciplinary, multi-sectorial and international cooperation in fighting counterfeited medicines!

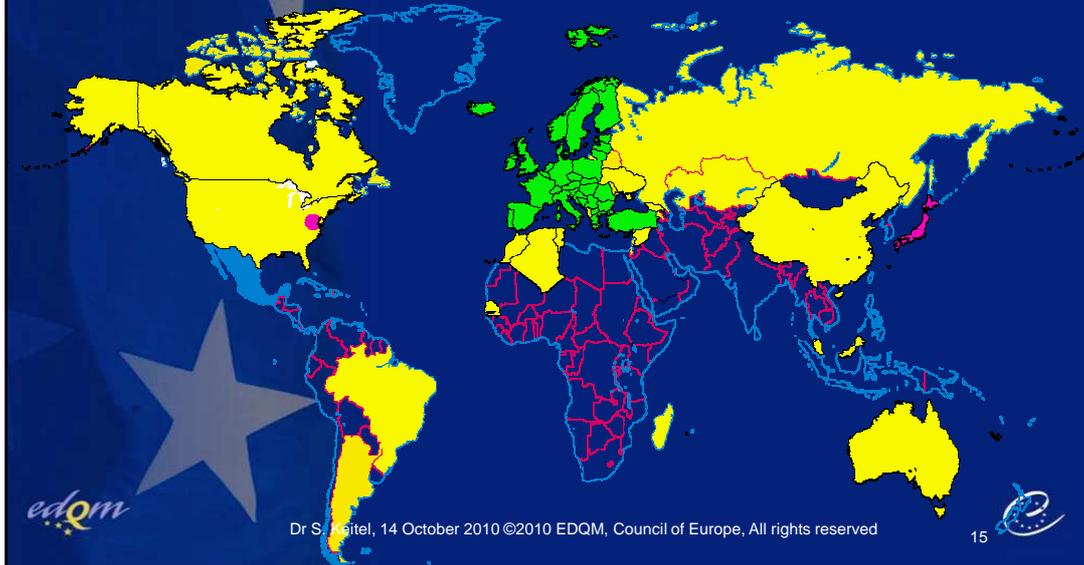


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A Need to Strengthen Collaboration Worldwide



Possible Impact for the EDQM?



Further development of the Certification of Suitability Procedure? Increased International Collaboration?

- European pharmaceutical legislation requires applicant to demonstrate suitability of pharmacopoeial monograph to control the quality of active substances used
- EDQM's certification scheme acknowledged by EU regulators as the "preferred way" for existing substances
- Recognised throughout Europe and in many other countries (e.g. Canada)
- Includes risk-based GMP inspections for API

Possible Impact for the EDQM?



Further development of the Official Medicines Control Laboratories (OMCL) Network? Additional collaboration possible?

- Created on 26 May 1994.
- OMCLs support regulatory authorities in controlling the quality of medicinal products for human and veterinary use available on the market.
- EDQM in charge of the co-ordination of network activities and responsible for smooth organisation of work.
- Restricted EU/EEA and general network, including observers.



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Possible Impact for the EDQM?

• Further strengthening contributions to the fight against counterfeit medicines?

- providing public health authorities with model approaches and strategies on risk communication;
- promoting a network of (Single) Points of Contact (SPOCs);
- sharing model approaches with other international institutions and organizations.
- Developing specific training sessions (multisectorial) to develop common approaches, communication between police, customs and health authorities in this field.
- The Council of Europe's MEDICRIME Convention.



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Conclusion

- Globalisation poses significant challenges for the pharmacopoeia and other EDQM activities in protecting public health
- No stakeholder can master these challenges alone, but let us overcome them together in a strengthened collaboration!



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Thanks a lot for your attention!



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