

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

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-  Ms Suzette Kox
-  Dr Barbara Steinhoff
-  Dr Jochen Wieda
-  Dr Matthew Moran
-  Mrs Beam Suffolk
-  Dr Ilka Von Hoegen



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Impact of Globalisation: Matching Dreams with Reality

Industry Perspective

Georges France

Pfizer VP Global Quality Strategy
EFPIA TDOC
ICH Q-IWG EFPIA Topic leader

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DISCLAIMER

*I attend this conference representing
EFPIA. The views expressed here are
the current views of EFPIA, but shall in
no way be binding for EFPIA."*

efpia Globalisation : Industry Perspective

European Federation of Pharmaceutical Industries and Associations

- Proposed agenda
 - Opportunities provided by the New Quality Paradigm
 - Challenges of globalisation
 - The problem of counterfeiting of medicines
 - EDQM with European Pharmacopoeia : a key role in the changes

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efpia Industry Perspective: The Ideal

European Federation of Pharmaceutical Industries and Associations

Blue sky Approach



EFPIA Values

- Access
- Innovation
- Mobilization
- Security

- **New Quality Paradigm**
 - **Science and risk based approaches**
 - Facilitate innovation and continuous improvement
 - Along the product life cycle
 - Enhance Quality by Design
 - **Facilitate rapid access to high quality medicine**
 - Improve process robustness
 - Enabling product life-cycle strategy

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efpia The Challenges of the Globalisation

European Federation of Pharmaceutical
Industries and Associations

- Globalisation

- New actors
 - Regulators
 - Suppliers
- Security of the supply chain
 - Counterfeiting
 - Substandard
- Value and reality of reaching **Global** standards
 - Harmonisation process (ICH), Mutual Acceptance
- More specifically : Multi-variate versus Univariate
 - QbD is moving industry towards a multi-variate world
 - Current focus pharmacopoeial monographs is on univariate testing model



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efpia The Challenges of the Globalisation

European Federation of Pharmaceutical
Industries and Associations

- Globalisation

Role of Growing production sources

- China
- India
- Korea
- Brazil
- Mexico
- Russia



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In the global pharmaceutical world

- Risk Management Approach
 - Inspections
- Harmonisation in
 - Regulatory review & submission
 - Inspections
- Enabling product life- cycle strategy
- Opportunity to use a more science and risk-based approach



Is it dream or reality ?

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The problem of counterfeiting and substandard medicines

- EDQM is in a position to:
 - Significantly contribute to the establishment of compliance with global quality standards
 - Play a role in the fight against falsified and counterfeited products that are increasingly circulating on the global market

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Where EDQM could impact the changes :

- **Challenges Around Globalisation**
 - Global, Harmonised Pharmacopoeias
 - A Single Standard
 - Our excipients are sourced globally
 - Our patients are global
 - Patients do not benefit from multiple standards across the world
 - Global approach to reference standards
 - Global Inspections
 - Global approach to Supply Chain Integrity and Security

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Where EDQM could impact the changes :

- **Adoption of the new Quality Paradigm by pharmacopoeias**
 - Quality Risk Management
 - Science and risk based approaches and decision making
 - Facilitate and enhancing innovative technologies which support process understanding and control
 - Enabling product life cycle strategy



Protection of Public Health

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efpia  Pharmacopoeial Harmonisation
European Federation of Pharmaceutical
Industries and Associations

- Welcome EDQM's commitment to promote global quality and safety by involving all stakeholders and fostering cooperation on initiatives of critical importance
 - Continued **leadership and stewardship** of EDQM in PDG Harmonisation Process
- Driving for full harmonisation of General Chapters and Excipients (minimally)
 - Strengthening of dialogue and collaboration with interested parties on issues of critical importance for the protection of public health

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efpia  Pharmacopoeial Harmonisation
European Federation of Pharmaceutical
Industries and Associations

- Welcome EDQM's dialogue and collaboration with key regions around the world to facilitate capacity building and cooperation

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- **EFPIA Survey on foreign inspection**

- Industry experienced an increase in the level of inspections, especially when several regulatory authorities inspect one manufacturing site
- Suggest focus is on appropriate coverage of the global supply chain to decrease the risk that higher risk sites may not be adequately inspected
- Opportunities by using **risk based approach** to inspection scheduling and further cooperation between global agencies exist

- **Using QRM approach EDQM & OMCLs have a key role to play in the area of foreign inspections**

- More sharing of information
- Greater collaborations to prevent redundancy and inspection fatigue
- Greater coverage of vulnerable areas

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- **CEPs, OMCLs, General Notices Monographs and Chapters**

- Explore opportunities to support the new Quality paradigm
- Ensure General Chapters and monographs do not inhibit adoption of innovative approaches to pharmaceutical development & manufacturing

- **Scientific dialogue**

- Enhance opportunities for EDQM through provision of technical advice to support the QbD approach some companies are taking in applications

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efpia Conclusions

European Federation of Pharmaceutical
Industries and Associations

- EDQM leadership to promote the adoption and implementation of appropriate global quality standards for medicinal products for patients across the world
- Encourage EDQM continued leadership on pharmacopoeial harmonisation
- Look for new areas to continue supporting Quality by Design approach from new quality paradigm
- EFPIA welcomes the opportunity to continue contributing to the work of EDQM to brainstorm new solutions and to convert vision into reality

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efpia Acknowledgments

European Federation of Pharmaceutical
Industries and Associations

- Mike James (GSK)
- Janeen Skutnik (Pfizer, PDG, IPEC)
- Graham Cook (Pfizer; British Pharmacopoeia Commission)

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EDQM International Conference

**Quality of Medicines in a
Globalised World:
Dreams and Reality
EGA's Perspective**

Prague, 14 October 2010

SUZETTE KOX
SR. DIRECTOR SCIENTIFIC AFFAIRS, EGA

The image contains the EGA logo and tagline at the top. Below them, the text 'EDQM International Conference' is written in a bold, blue, sans-serif font. This is followed by the main title 'Quality of Medicines in a Globalised World: Dreams and Reality EGA's Perspective' in a larger, bold, blue, sans-serif font. The date 'Prague, 14 October 2010' is written in a blue, sans-serif font. At the bottom, the name 'SUZETTE KOX' is written in a bold, blue, sans-serif font, with 'SR. DIRECTOR SCIENTIFIC AFFAIRS, EGA' written below it in a smaller, blue, sans-serif font. The background features a faint, stylized map of Europe and several white pills.

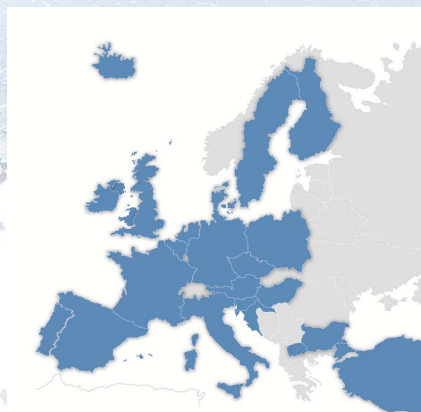
Contents



- Snapshot: EGA & Generic Medicines
- Scope: Quality in Legal Supply Chain
- EGA Recommendations for Today and Tomorrow
- Dreams: Medium and Long Term

Snapshot: EGA & Generic Medicines

- Official representative body of the European generic and biosimilar pharmaceutical industry
- Generic medicines account for nearly 50% of packs dispensed in the EU and 18% of pharmaceutical expenditure



SCOPE: Quality of Medicines in Legal Supply Chain



Legal Supply Chain

Illegal Sources & Chains
(incl. internet)

“50% of medicines purchased over the internet from sites that conceal their physical address are counterfeit”

(source: WHO)

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Ensuring Patient Safety by Ensuring High Quality Medicines

- High quality ingredients
- High quality manufacturing processes
- High quality controls and testing
- Continuous monitoring, risk-assessment and risk-management

Quality is never an accident

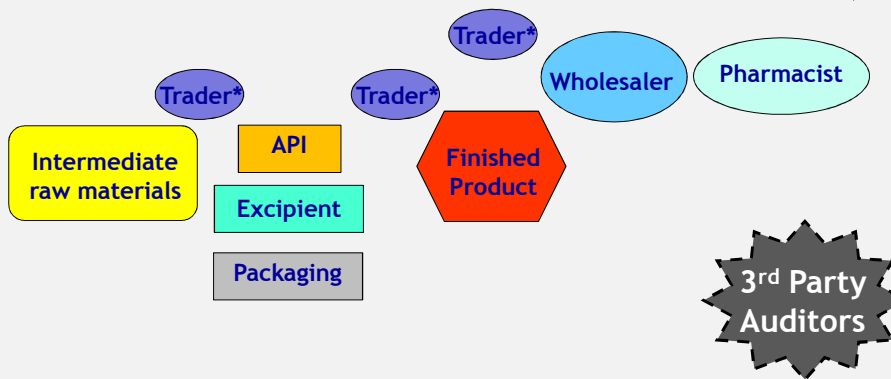




Making Medicines Affordable

Maintenance of Continuous Supply Chain Integrity

Complex Pharmaceutical Supply Chain



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Trader: also includes brokers, agents, business-to-business platforms*



Making Medicines Affordable

Today: Greater & Better Supervision by Industry

- Regular supervision by audits
 - Risk-based sampling process
- Business with **Certified Partners ONLY**
 - Beyond technical agreements
 - Relationship with API manufacturers is an essential part of maintaining integrity
 - Uninterrupted and timely exchange of information
 - Continuous Quality Assurance





Today: Increased GMP Inspections by Authorities



- **Efficient Quality Assurance Assessment (snapshot)**
 - Particularly when unannounced
 - Risk-based approach to prioritisation
 - Means of enforcement: RA sanctions
- **Harmonisation of communication: Rapid Alert / Serious GMP non-compliance / CEP suspension / CEP withdrawals**

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Tomorrow: European Commission New Directive on Falsified Medicines (GMP)

- **Reinforcing mandatory audits by qualified auditors for GMP compliance**
- **Expanding the use of the EU wide database on GMP (API and FP manufacturers)**
- **Promoting EU and international collaboration**

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Tomorrow: EC New Directive on Falsified Medicines (GDP)

- Establishing an EU wide database of wholesalers (GDP)
- Issuing GDP certificates after each inspection
- Strengthening & harmonising provisions on inspections (e.g. wholesalers, brokers and traders of APIs)

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Medium Term: Enhanced Scrutiny Through International Cooperation

- Streamline inspections at a global level for **GREATER & BETTER** supervision
- Build on existing international cooperation schemes
 - e.g. Include APIs and non-local inspections in existing MRAs
 - e.g. Leverage on PIC/S experience to assess 'equivalence of standards'



International Cooperation ctd.

- Support increased development of bi-lateral agreements to facilitate exchange of information, training, common understanding and confidence building
 - e.g. Key API exporting countries



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Long Term: Dreams at EU Level



- Creation of a truly centralised and well resourced EU inspectorate for optimal coordination
 - Within the EU and internationally
 - Using EudraGMP as
 - Central repository
 - GMP certificates, Manufacturing Authorisations, GMP non-compliance, incl. in 3rd countries*
 - Planning and alert tool
 - Accessible by Member States, Mutual Recognition Partners, EDQM and other worldwide regulatory agencies and UN institutions

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Long Term: Dreams at Global Level



■ Work towards

- Truly global harmonised standards for pharmaceutical products and APIs, including Pharmacopoeias
- A long term global inspection framework
- A Harmonised International Regulatory System
 - Mutual recognition of approvals and inspections

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*Thanks to EDQM for setting
the scene and paving the road
in that direction*

Thank you for your attention

Acknowledgment: Julie Maréchal/EGA

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**EDQM Conference
"Quality of Medicines
in a Globalised World:
Dreams and Reality"**

**Recommendations from Industry:
AESGP**

**Prague, 14 - 16 October 2010
Dr. Barbara Steinhoff, BAH (Bonn)**



**Association of the European Self-Medication Industry
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AESGP: Who are we?

- AESGP represents the manufacturers of non-prescription medicines in Europe
- Founded in 1964
- Our offices are located in Brussels
- Membership in WSMI



AESGP Mission

- To create a favourable climate for the growth of the self-care market
- To ensure that consumers receive quality medicines by respecting state-of-the-art standards in pharmaceutical manufacturing



General Recommendations

AESGP support all initiatives improving the pharmaceutical quality of medicines

- EMA hearings (e.g. QWP)
- EDQM projects (surveys and meetings)
- WHO activities on quality control
- ICH initiatives, e.g. PDG as "pro-active" harmonisation



General Recommendations

The OTC industry

- appreciates bilateral discussions with the EDQM on a regular basis
- welcomes early involvement of industry in revisions of monographs
- takes part in surveys on the utilisation of Ph.Eur. methods e.g. alternative methods for microbiological testing



General Recommendations

The OTC industry

- appreciates introductory notes to Pharmeuropa draft monographs explaining changes
- wishes to have pragmatic approaches in case Ph.Eur. monographs are applied to established products (e.g.: FAQs explaining the new chapters on microbiological quality, 2.6.12, 2.6.13, 5.1.4)



General Recommendations

The OTC industry

- proposes to take established good methods from other pharmacopoeias also from outside of Europe into consideration (e.g. assay of ginseng in the USP) ("do not invent the wheel twice")
- would like to know whether producers of reagents and reference substances have submitted their pre-registration and/or registration documents according to REACH in order to ensure further availability



Herbal Medicinal Products

EDQM/HMPC

- Close co-operation between Ph.Eur. expert groups (e.g. 13A, 13B) and HMPC:
 - classification of extracts depending on the presence of constituents with known therapeutic activity
 - information on the analytical methods used → dosage recommendation



Herbal Medicinal Products

Analytical methods (I)

- New methods e.g. HPLC normally have a higher selectivity and specificity
- Lower assay values as compared to established methods e.g. photometry
- Gap between standardisation and published dosage recommendations



Herbal Medicinal Products

Analytical methods (II)

- Option to determination of a conversion factor in order to establish a correlation where possible
- Industry is willing to collect and submit data
- Appropriate transition period necessary (e.g. horse-chestnut and horse-chestnut dry extract, standardised, Pharmeuropa 20.3, July 2008)
- Next: anthraquinone-containing herbal drugs



Herbal Medicinal Products

Heavy Metals

- Limits Cd, Pb, Hg set for herbal drugs (Ph.Eur. general monograph) based on data from industrial practice *)
- Proposed for extracts (general monograph)
- Higher Limits in individual monographs (e.g. Cd in Tormentil, Willow bark, Fumitory)
- Should be defended within worldwide development of guidelines (ICH)

* Pharmeuropa Scientific Notes 2009-1:37-49



Herbal Medicinal Products

Water for preparation of extracts

- Monograph urgently needed
- Proposal submitted by industry July 2001
- Pharmeuropa 21.2 (April 2009)
- Health authorities ask for (narrow) specifications in case potable water is used for extraction (under defined conditions permitted by NfG CPMP/QWP/158/01)



Herbal Medicinal Products

Monographs on herbal drugs used in TCM

- Access of TCM products to market possible if in accordance with CD 2004/24/EC
- Defined and controlled quality important
- But: focus primarily on plants which have commercial relevance in the existing European market



Homoeopathic Medicinal Products

General

- AESGP welcomes Ph. Eur. initiatives on homoeopathic medicinal products
- Important for mutual recognition
- Harmonisation, but national traditions and existing products must be respected
- Monographs and manufacturing methods



Homoeopathic Medicinal Products

Monographs

- Needed to ensure access to the market in all Member States (CD 2001/83/EC)
- Monographs on starting materials (plant, animal, mineral origin) for use in homoeopathic and anthroposophic medicine
- Defined and controlled quality important



Homoeopathic Medicinal Products

Manufacturing methods

- Publication of manufacturing methods: "Methods of preparation of homoeopathic stocks and potentisation" (no. 2371; 01/2011)
- Important: no exclusion of "other methods"
- CD 2004/27/EC expressively recognises methods described in national pharmacopoeias



Homoeopathic Medicinal Products

Microbiology

- Chapter 5.1.4 "special Ph.Eur. provisions for oral dosage forms containing raw material of natural (animal, vegetal or mineral) origin"
- Homoeopathic medicinal products not covered by chapter 5.1.8
- Maintain the acceptance criteria of chapter 5.1.4 for homoeopathic medicinal products

AESGP 



EDQM Conference “Quality of Medicines in a Globalized World: Dreams and Reality”

Dr. Jochen Wieda
IFAH-Europe Council Chair

Prague, 14 Oct 2010



Regulatory environment in animal health

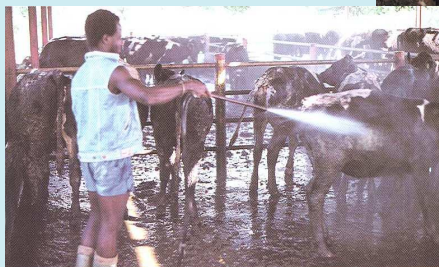
- Environment highly regulated
- Consolidation of industry ongoing
- Time to market becoming more and more important
- Increasing regulatory requirements and higher level of detail in applications demanded (especially for CMC); to be taken into account for keeping regulatory compliance (less room for flexibility on post-approval change control)
- Limiting factor for innovation

Reasons for such an environment

- Automatic transposition of human medicinal product requirements to veterinary medicinal products (VMPs) without impact assessment
- Application of VICH guidelines to all products, whereas their scope was originally limited to new VMPs.
- ⇒ Expenditure and regulatory effort constantly increase in order to keep well established VMPs on the market.

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Example: Request for purified water (instead of tap water) for an ectoparasiticide (pour-on)



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Differences between human and veterinary medicinal products



- Produced in smaller batch sizes
- Smaller and much more diverse market
- Smaller margins
- Mid-sized companies
- Need for affordable medicines for food-producing animals
- Resource constraints (maintenance vs. innovation)

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Recommendations from IFAH-Europe



Need for more pragmatic regulatory requirements on existing products, where:

- proven quality standards already apply
- the pharmacovigilance report of a product shows no significant adverse drug reactions
- a well established product shows a good history of safe use

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Global concept

Industry

- Increase work efficiency and use synergies between regional registration efforts
 - Minimize administrative hurdles and facilitate time to market process
 - Harmonization of technical data requirements:
 - rationalize the development of new products
 - potentially reduce R&D costs
 - facilitate the evaluation by regulatory authorities (shared resources)
- ⇒ Improve availability of new and innovative medicines

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Global concept – Points to be considered

- **Industry**
Global organization requires clear definition of roles and responsibilities
- **Authorities**
National variability in regulatory requirements should be limited to existing products
- **International organizations**
Harmonization of requirements leading to most stringent common level must be avoided

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