Making Medicines Affordable

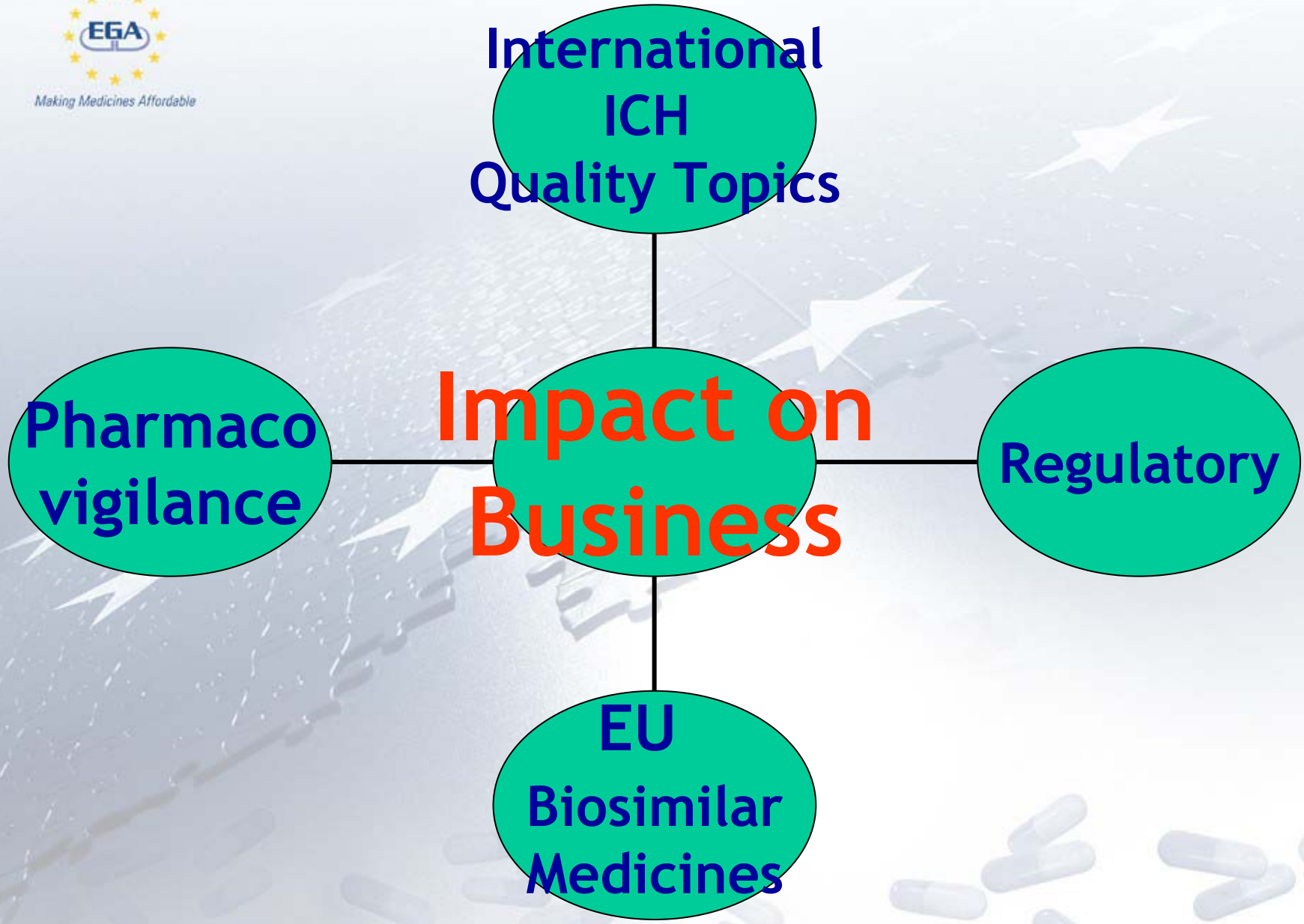
EUROPEAN GENERIC MEDICINES ASSOCIATION

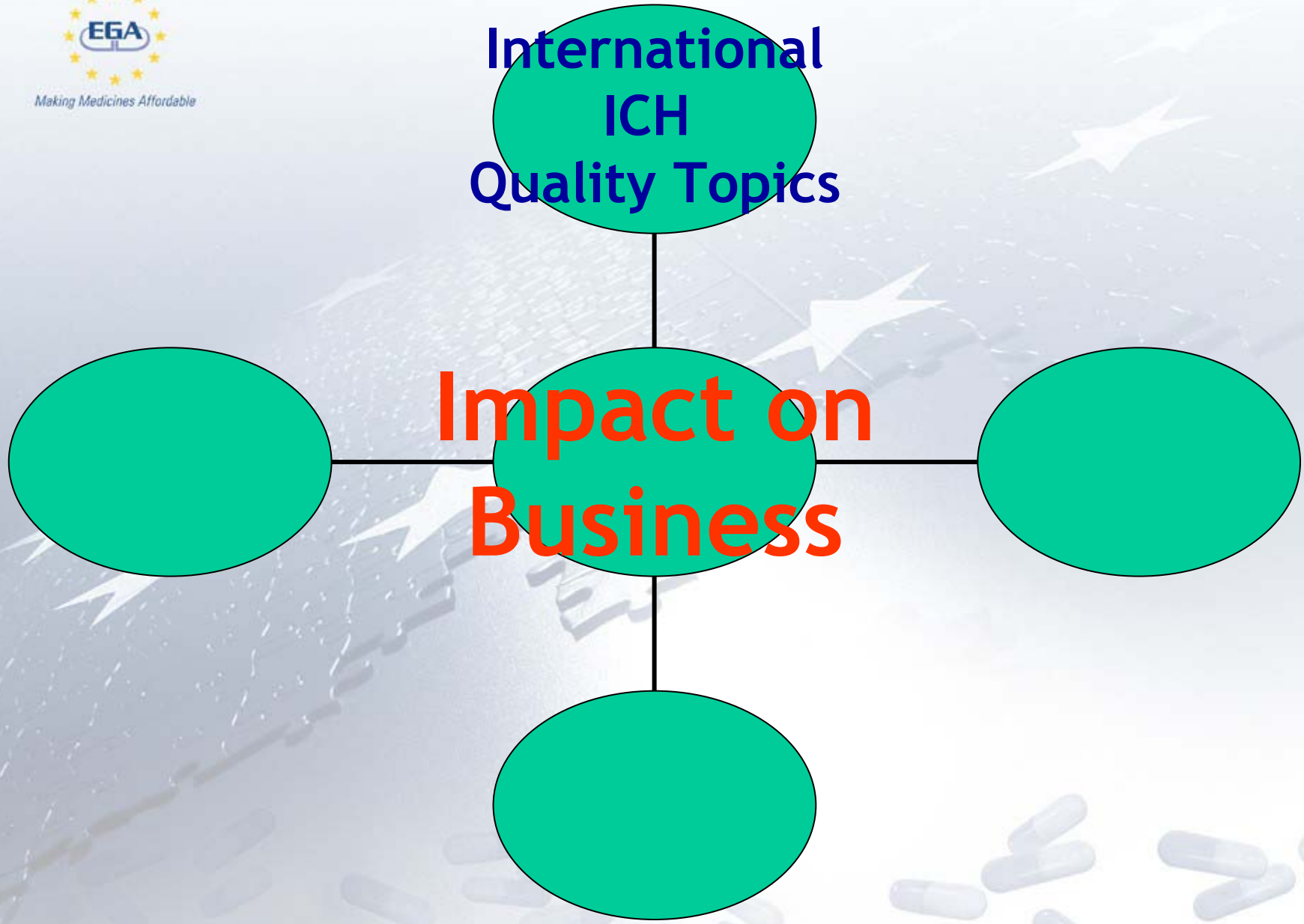
Making Medicines Affordable

Key Regulatory Developments at International and European Level and their Impact on Business Development of Generic Companies

13th EGA Annual Conference
Istanbul, 14th-16th June 2007

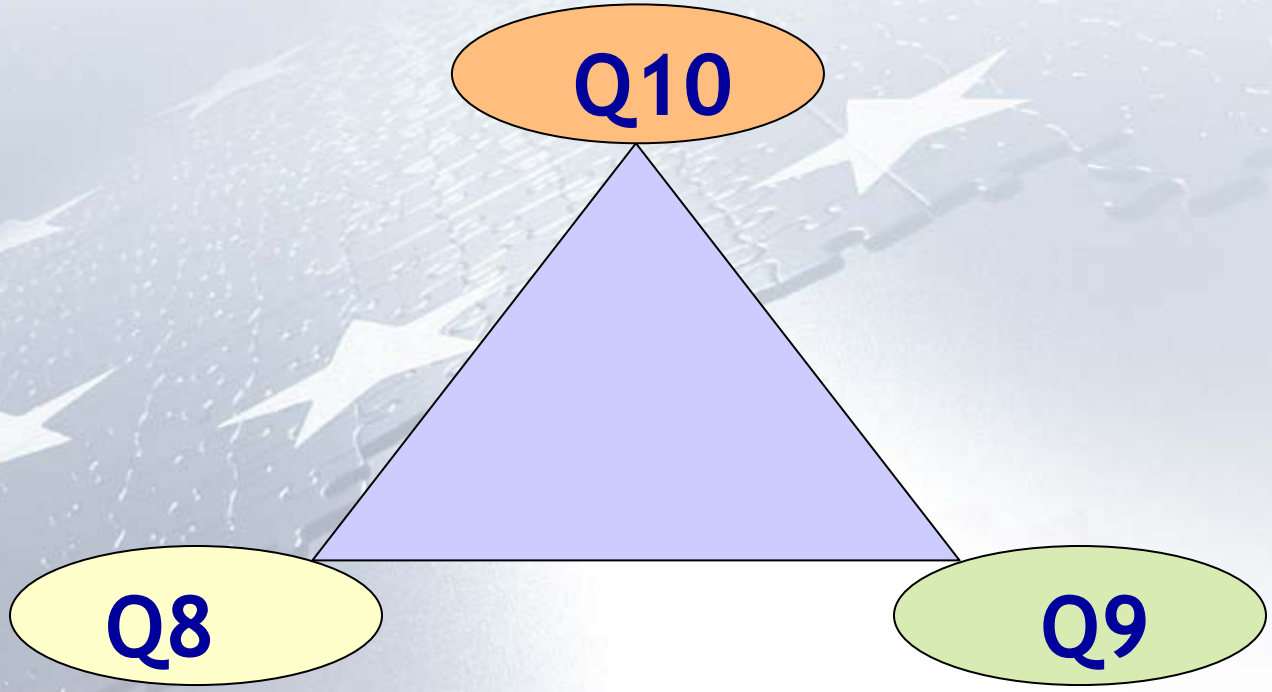
Suzette Kox
EGA Senior Director Scientific & Regulatory Affairs


International
ICH
Quality Topics
Pharmaco vigilance
Impact on Business
Regulatory
EU
Biosimilar
Medicines


International
ICH
Quality Topics
Impact on
Business

Foundation for a Modern Risk-Based Approach to Pharmaceutical Quality and Manufacturing

Pharmaceutical Quality System (PQS)



Pharmaceutical Development

Quality Risk Management

Complimentary Guidelines

- **Q10 (ICH step 3) complements adopted guidelines**
  - Q 8 'Pharmaceutical Development'
    - which describes what should be submitted to a regulatory authority +
  - Q9 'Quality Risk Management'
    - which provides principles and examples of quality risk management that can be applied to all aspects of development and manufacture of a medicinal product, including aspects of inspection

Pharmaceutical Quality Systems (PQS)

- i.e. system to direct and control a pharmaceutical company with regard to quality

- ICH Q10 augments GMPs by describing specific quality system elements and management responsibilities

29.5.07 http://www.emea.europa.eu/whatsnewp.htm

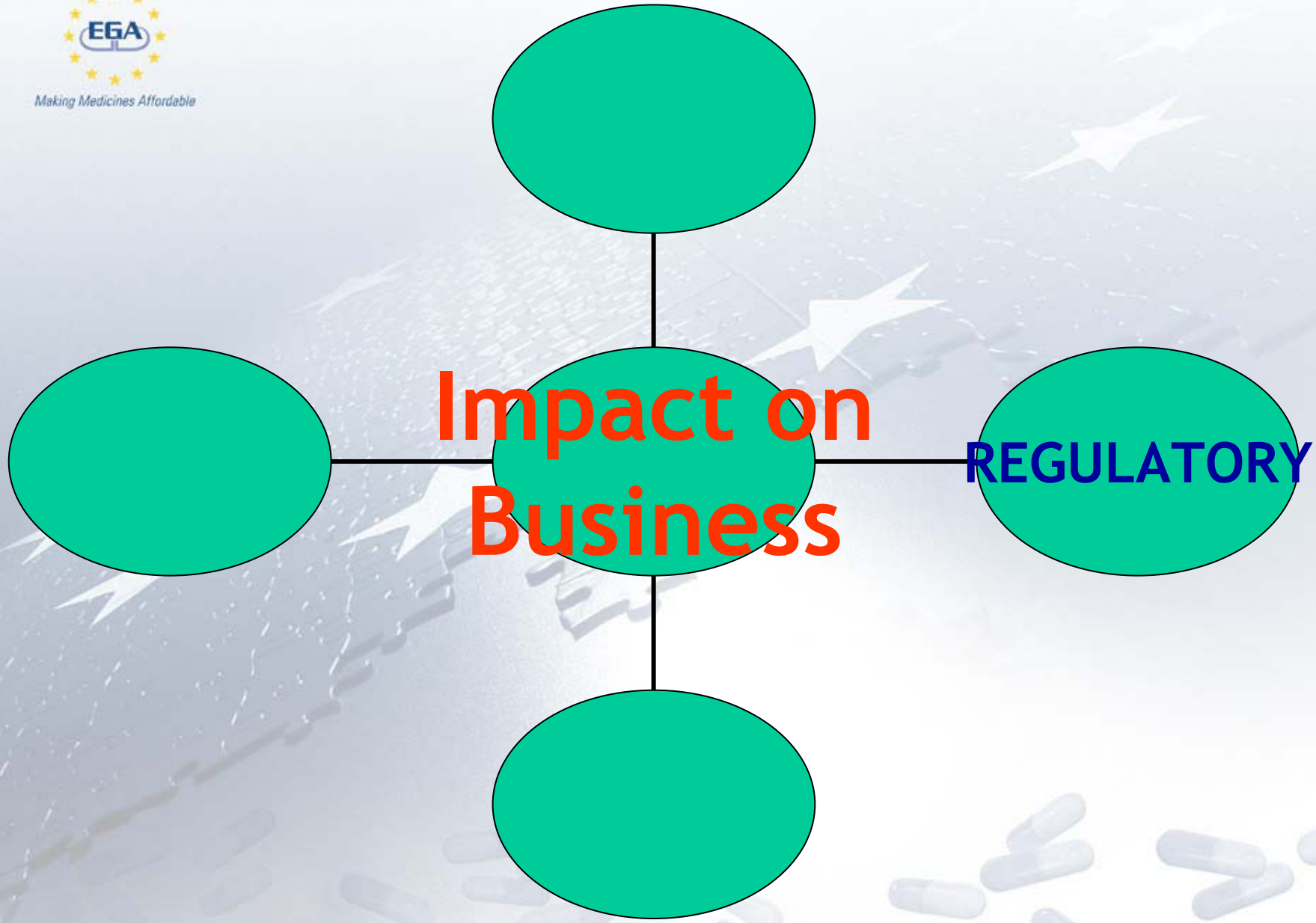
Management Responsibilities

ICH Step 3 Document

- **Senior management should**
  - commit to an effective PQS
  - establish a quality policy describing overall intentions and directions
  - ensure quality planning
  - determine and provide adequate and appropriate resources
  - ensure appropriate communication processes
  - be responsible for management review and for oversight and review of outsourced activities

EU-US Workshop on Administrative Simplification

- **EU / Industry round table** (8.6.07)
- **EU/US workshop in Brussels** (28.11.07)
- **Opportunities**
  - Parallel scientific advice for Biosimilars
  - One Clinical phase III for US/EU provided phase I studies with EU + US reference products reveal same results
  - One BE study for generics for US + EU
  - MRA of inspections of FP and API manufacturers


Impact on Business
REGULATORY

GMP Directive on Excipients Coming

- **GMP for certain excipients required by new Pharma Law**
- **Consultation ongoing on possible impacts of different policy options via online questionnaires**
  - questionnaires for excipient manufacturers and excipient users
  - Deadline for response: 30 July 2007
  - Small and medium size enterprises specifically encouraged to contribute

http://ec.europa.eu/enterprise/pharmaceuticals/pharmacos/new.htm(22.3.07)

API GMP but NOT GMP Certificate Required under EU Law

- **EudraGMP Launched**
  - 7000 GMP inspection certificates expected to be included /year
- **Inspection questionnaire sent to EU inspectors**
- **Sabine Atzor/EC at 2nd EFCG Conference**
  - GMP certificate is NOT foreseen in legislation and guidelines agreed by Member States

27.5. 07: http://www.emea.europa.eu/Inspections/WhatsNew.html

Generic Medicines
More Indications Possible

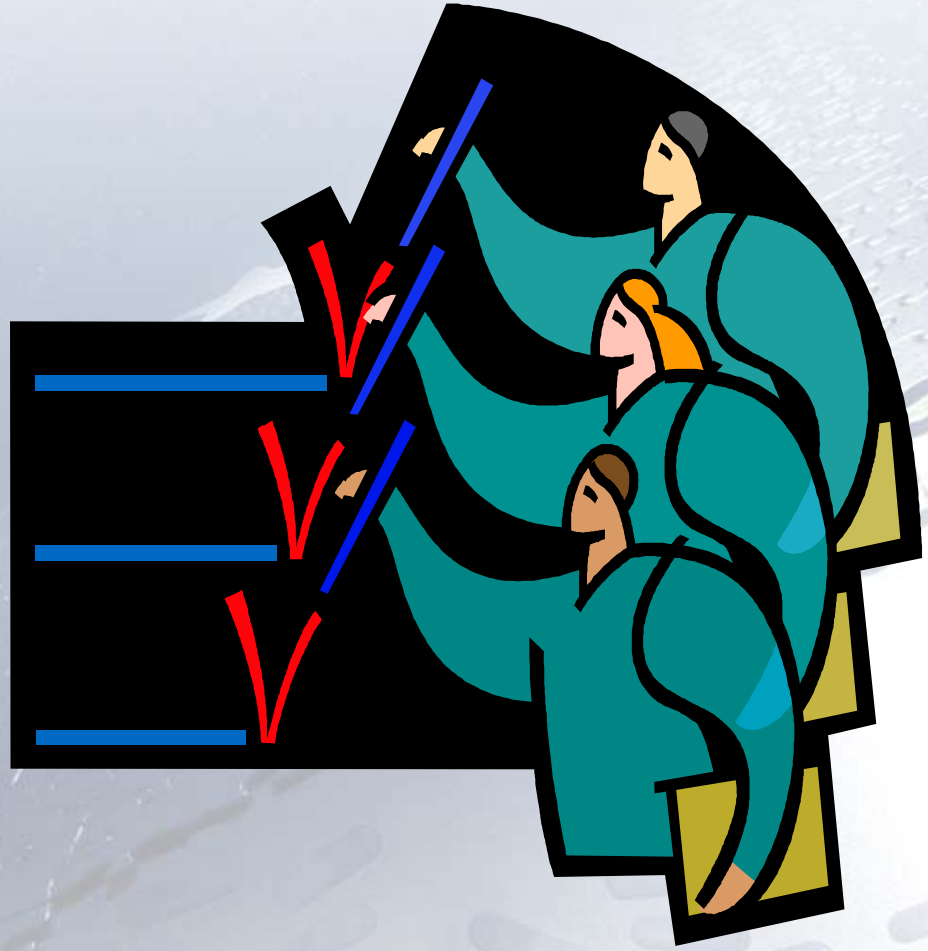
- Agreement reached regarding processing of generic applications with more or fewer indications than Reference Product

- Deviation in indications should no longer be an obstacle

Co-ordination Group for Mutual Recognition and Decentralised Procedures - Human

- http://www.hma.eu/uploads/media/generic_indications.pdf

SmPC Harmonisation Process Goes On



- CMD(h) criteria, mandate and first list published
- CMD(h)'s work on 2nd list ongoing
- EGA proposals submitted

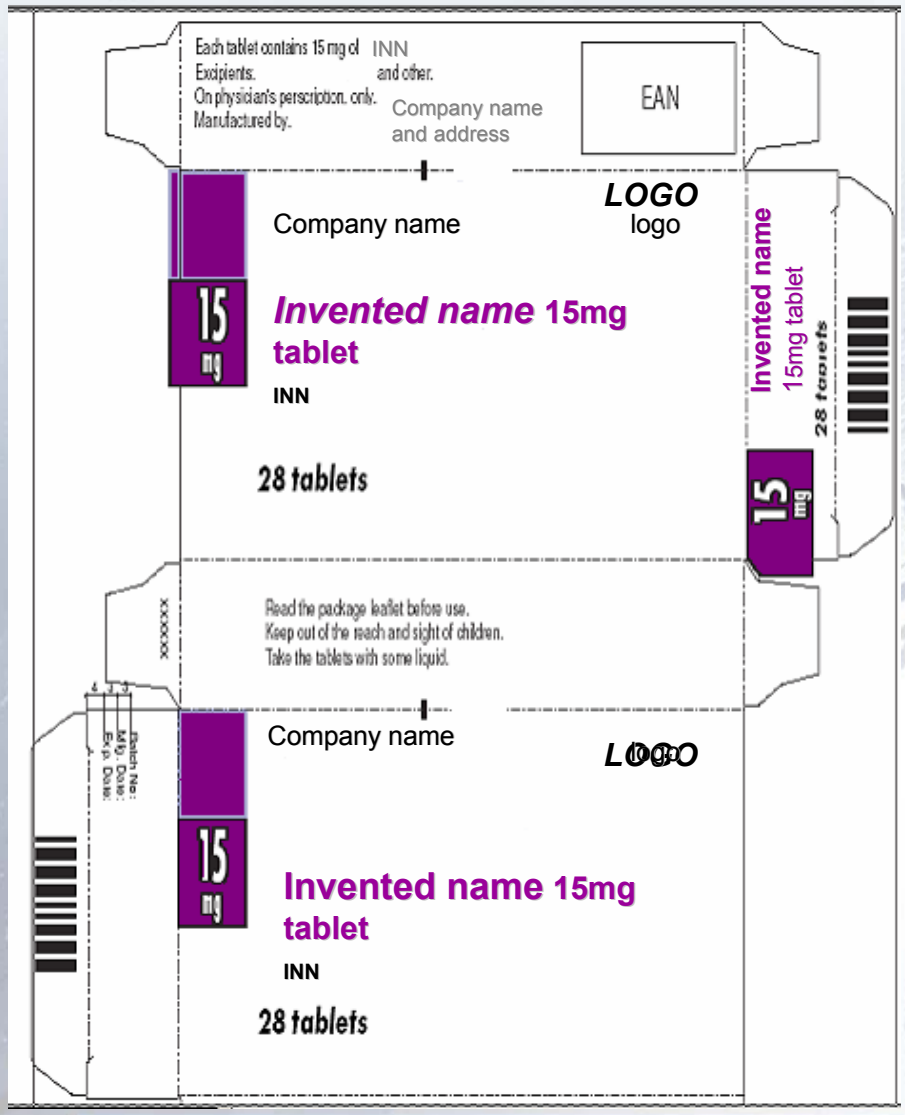
http://www.hma.eu/86.html

Single Naming for Generic Medicines

- **If RP is a Community Product, whatever the registration procedure used**
  - single name required for generic medicines
    - Invented name or
    - INN + MAH/Trademark
- **EC reminder to Pharmaceutical Committee**
  - *'National rules on naming of medicinal products should not run counter to the provision provided by the pharmaceutical acquis for a generic product authorised via the centralised procedure to have a single name, chosen by the applicant in accordance with Art. 1(20) of Directive 2001/83/EC'*

29.5. 07:
http://ec.europa.eu/enterprise/pharmaceuticals/pharmacos/new.htm

For Generics of CP Products
- Single name & Pack design flexibility -



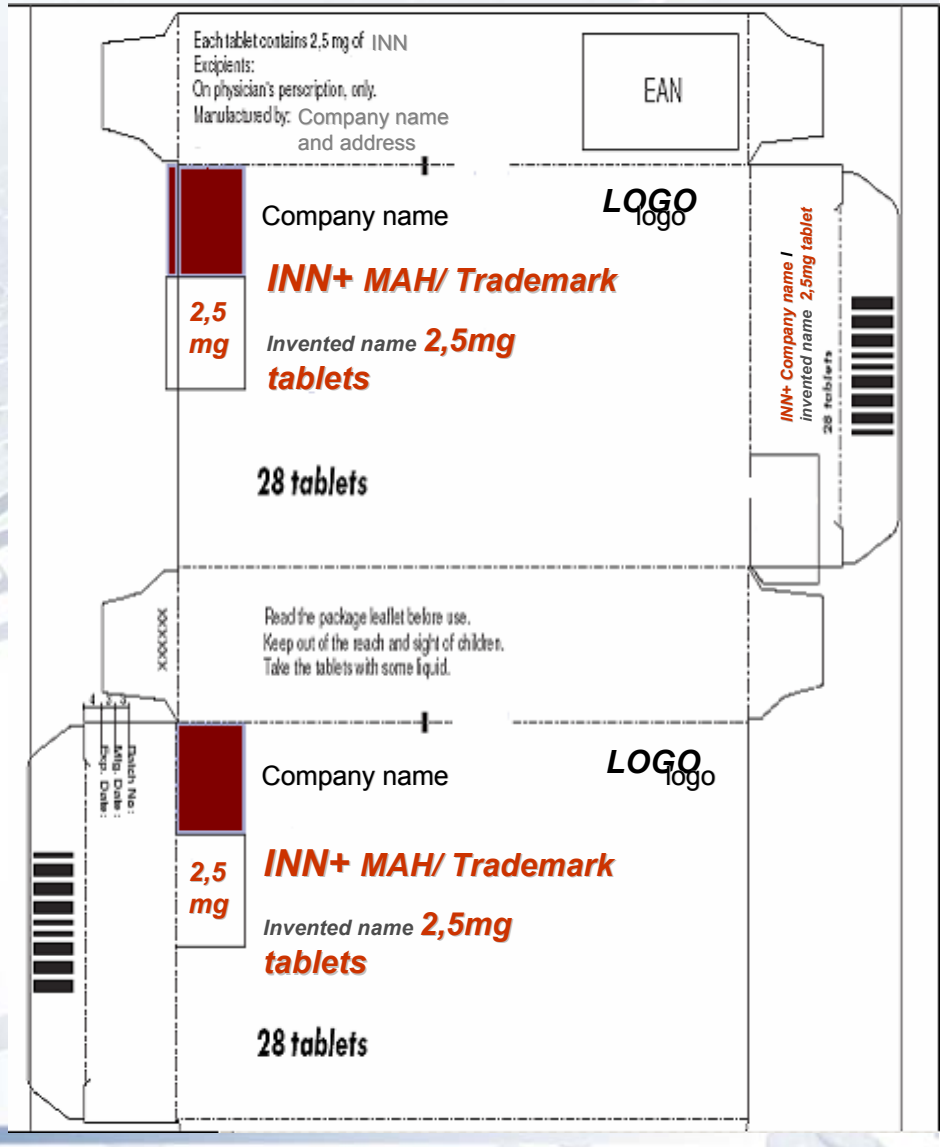
Countries Needing Invented Name to Market

- Invented name, strength, pharm. form
- **INN**
- MAH + address

For Generics of CP Products- Single name & Pack design flexibility -

Countries Needing INN + MAH or Trade mark to Market

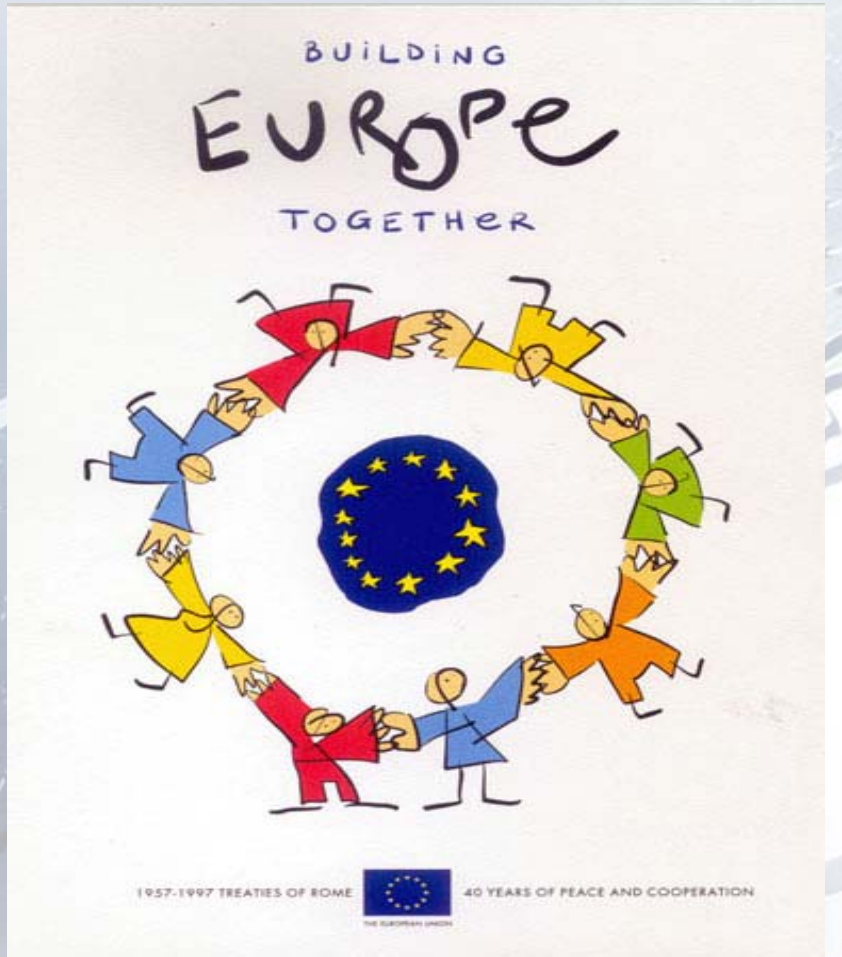
- **INN MAH or Trade mark**
- **Invented name, strength, pharmaceutical form**
- **MAH + address**



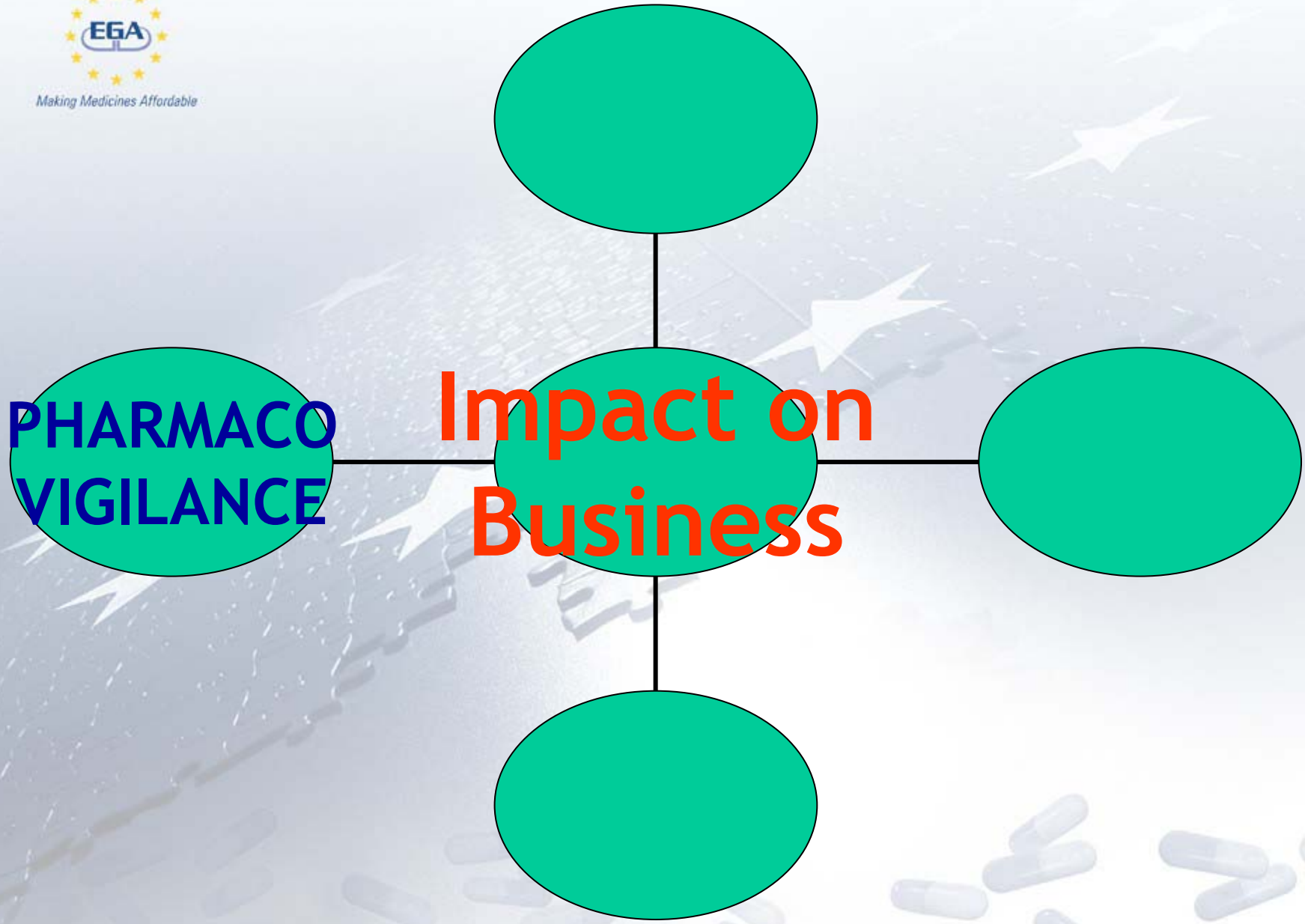
Usage Patents in Centralised Procedure

- **In MRP and DCP the right approach**
  - Allows patented information to be omitted from the product information for distribution at national level
- **Similar solution must be found for CP**
- **Tripartite meeting EC/EMEA/EGA imminent**

Bulgaria & Romania



- 2 additional markets part of the EEA registration systems covering now 30 Member States


PHARMACO VIGILANCE
Impact on Business

EU Harmonised Birthdates + Related Data Lock Points for All Substances

- Registered after 76: list published
- Before 76: ongoing

—>PSUR synchronisation + assessment

—>PSUR worksharing

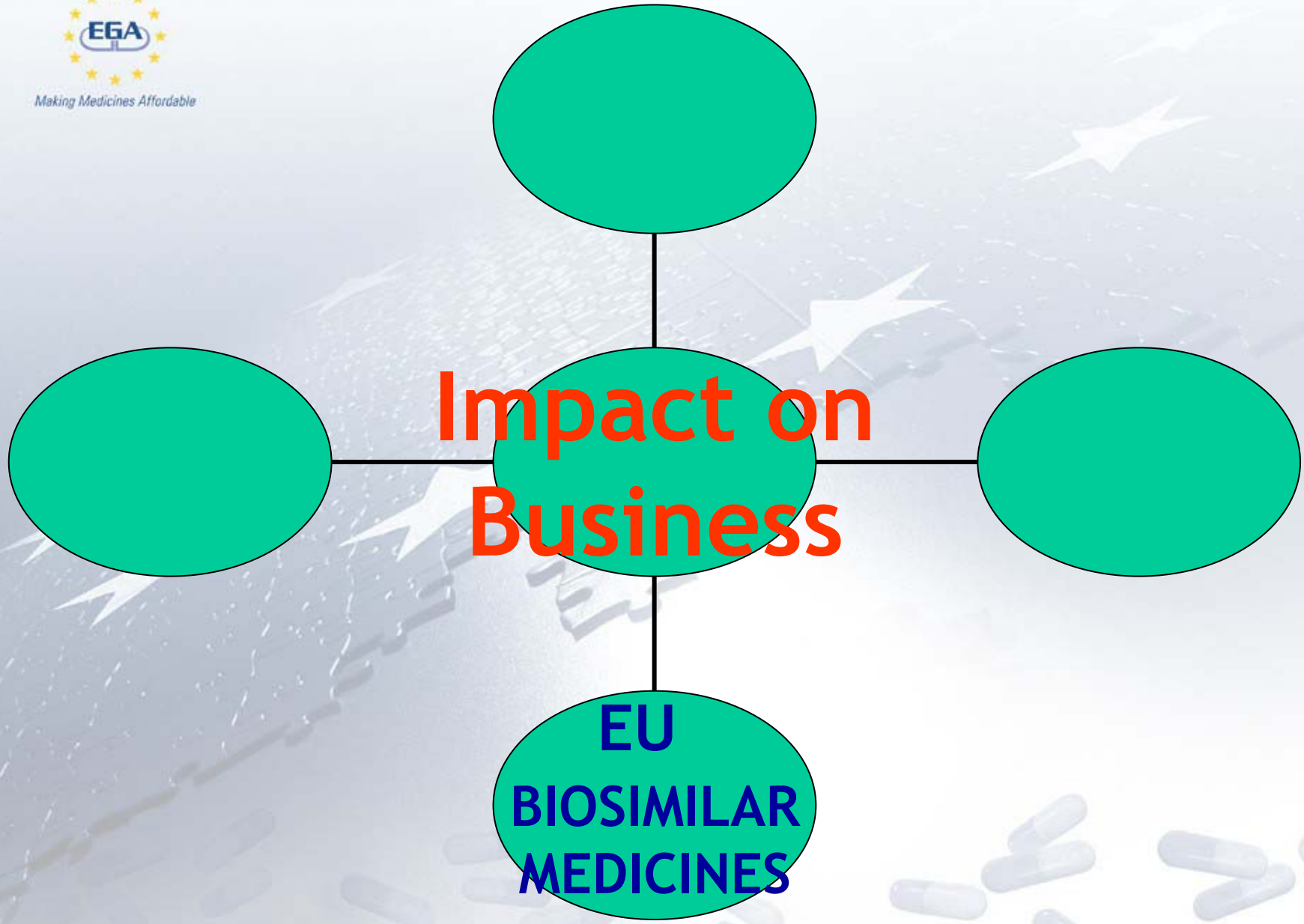
—>Increase of safety + reduction of workload

http://www.hma.eu/80.html

New PhV Legislation Announced by Com. Verheugen

- **Aim**
  - Strengthening the system
  - Rationalisation
  - Reduction of administrative burden
  - Harmonisation
- **Impact assessment during 2007**
- **Legal proposal in 2008**

10.4.07 (volume 9a)
26.2.07: EC announcement
http://ec.europa.eu/enterprise/pharmaceuticals/pharmacos/new.htm


Impact on Business
EU BIOSIMILAR MEDICINES

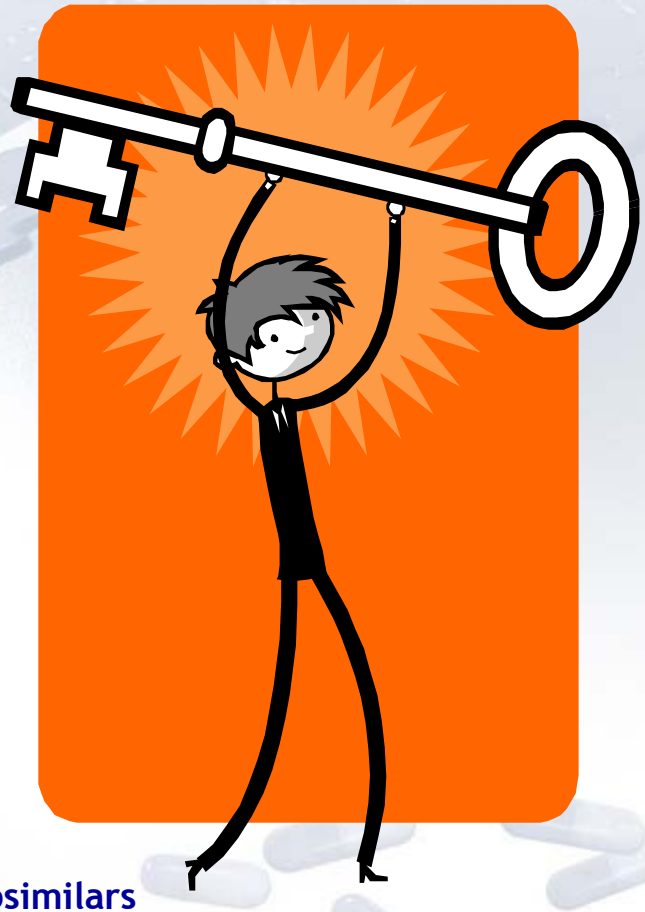
WHO Informal Consultation on INN Policy for Biosimilar Medicines
4-5 Sep.2006

- *'It was concluded that biosimilar products do not require special considerations in terms of nomenclature'*
- *'However, the importance of regulatory issues was emphasized'*

Dr Jeewon Joung, WHO at 5th EGA Symposium on BSM May 2007

EU Key to INN Issue for Biosimilar Medicines (BSM)

- **EGA's claims finally heard:**
  - only scientific considerations should be taken into account
  - **INN decision for BSM is a <u>regulatory and not a WHO</u> decision**



http://www.egagenerics.com/pol-positions.htm#biosimilars

Reminders

- Naming, labelling, pharmacovigilance, traceability, interchangeability, substitution are not based on INN alone and are not criteria for INN allocation
- Variability is inherent to all biologicals e.g. manufacturing processes, batch-to-batch
- Due to improvements in analytical technology, BSMs are better studied and characterized than reference products characterized 10 or more years ago

public statement by regulators

EU Perspective on INN Naming for Biologics

- Biologicals range in complexity and variability exists within a given product
- INNs perform limited range of functions for complex biological substances
- Difficult to define 'differences' in a complex pattern
- If molecular 'differences' are described for each substance, INN system becomes a pseudo-proprietary naming system

JH. Trouvin, Chair of Biologics WP, INN Ad Hoc Meeting on Biologicals, WHO 23 April 2007

EU Reflections for Considerations at WHO Level

- INNs should have "high level" utility – identification
  - Up to Regulatory Authorities to assess Benefit / Risk
  - INN for proteins (glycosylated in the native form) should be based on AA sequence
  - Modifications of the native state (e.g. deglycosylation, pegylation etc.) could be generally indicated in the INN, abandoning the Greek letter system

- Further discussions necessary (193 WHO Member States)

Making Medicines Affordable

World Health Organization

- WHO requested to develop global regulatory consensus and guidance for 'Biosimilars'/'FOP'*
- WHO, worldwide Regulators, EGA, IFPMA mtg.
- Working group to be set up

- Outcomes to be presented to WHO Expert Committee on Biological Standardization 10/2007
- **Impact on global approach to biopharmaceutical developement and approval (long term)**

* 12th ICDRA recommendation in Workshop H, "Global challenges for regulation for vaccine and other biologicals"


Thank You for
Your Attention

Acronyms

- ICH:International Conference on Harmonisation of technical requirements for registration of pharmaceuticals
- MRP: Mutual Recognition Procedure
- DCP: Decentralised Procedure
- CP: Centralised Procedure
- RP: Reference Product
- GMP: Good Manufacturing Practices
- SmPC: Summary of Product Characteristics
- PSUR: Periodic Safety Update Reports
- PhV: Pharmacovigilance
- MRA: Mutual Recognition Agreement
- FOPs: Follow On Proteins (US terminology)
- INN: International Non Proprietary Name
- AA: Amino Acid
- ICDRA: International Conference of Drug Regulatory Agencies