EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA and international cooperation

The EU medicines regulatory system and the European Medicines Agency: an introduction for international regulators and non-governmental organisations

London, 18-19 September 2017

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International Affairs, EMA

An agency of the European Union

Contents

Why International Regulatory Cooperation?

- Medicines manufacture and distribution are more and more globalised; manufacturing processes and supply chains, including generics, are increasingly complex

➢ Cooperation among regulators is essential to avoid duplication of work, release scarce resources for more critical areas and speed up patients access to new and/or affordable products

- New medicines are often complex products such as biotechnology, gene therapy or cell therapy products, or have sophisticated formulations involving e.g. micellar systems or nanoparticles

➢ Some regulators may lack the resources or specific competences to carry out assessments of these products before they are put on their markets

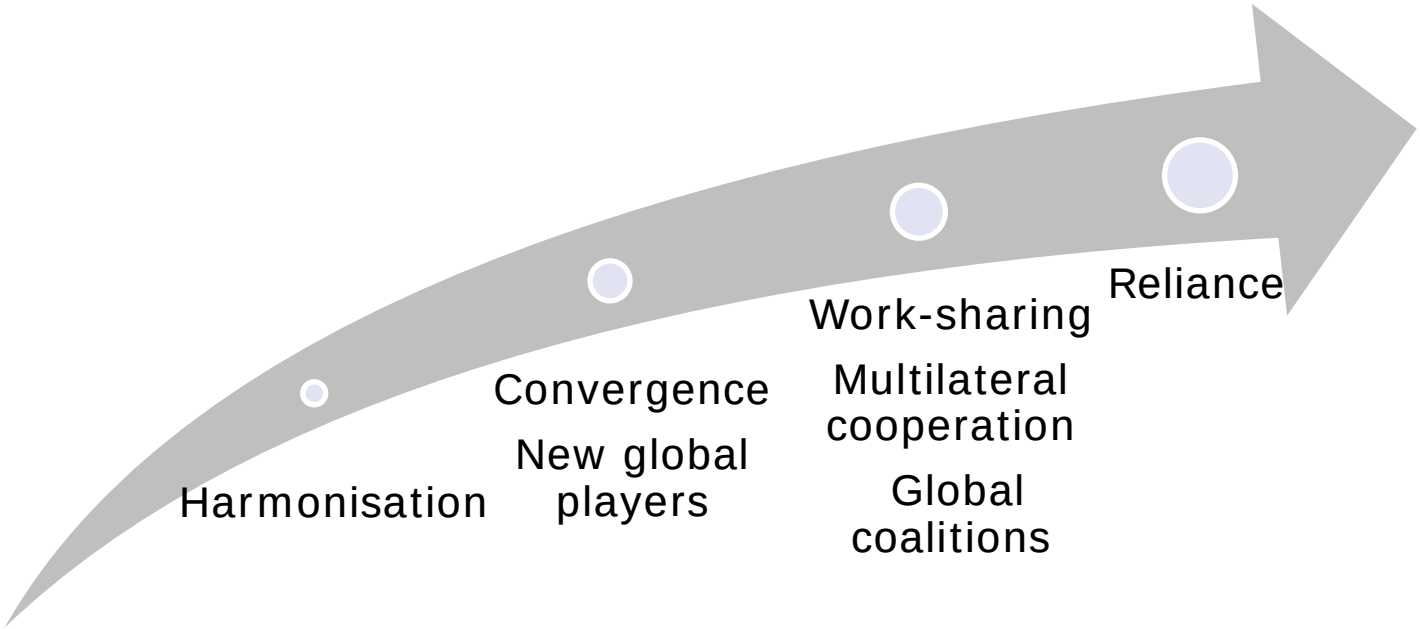
Network Strategy to 2020: Contributing to the Global Regulatory Environment

The EU strategy is built on 4 pillars, includes “Contributing to the global regulatory environment”

Enhancing international cooperation is part of our public health mission

http://www.ema.europa.eu/ema/index.jsp?curl=pages/about_us/general/general_content_000292.jsp&mid=WC0b01ac05800293a4

Changing Face of International Cooperation



International Cooperation at EMA

- Activities with FDA, PMDA, Health Canada, TGA, SwissMedic and WHO part of our daily work
- Almost every part of EMA involved in some way
- ~80% of all products going through EMA committees have some discussion at international level
- Growing interactions through multilateral ‘Clusters’
- 8-10 international calls per week
- Host 3-4 international visitors per month
- New countries and regions emerging as important players, especially China, India, Brazil, Africa

EMA and International Regulatory Cooperation

Bilateral

- Confidentiality arrangements
- Mutual recognition agreements (GMP)
- Other types agreements, e.g. specific mechanisms with China, India, Russia, Israel

Multilateral

- WHO engagement
- Strategic forums, e.g. ICMRA
- Work-sharing, e.g. IGDRP
- Convergence and harmonisation forums, e.g. ICH, IPRF, PIC/S
- Ad hoc, e.g. workshop with African regulators in Malta

http://www.ema.europa.eu/docs/en_GB/document_library/Leaflet/2016/10/WC500214180.pdf

Confidentiality agreement partners

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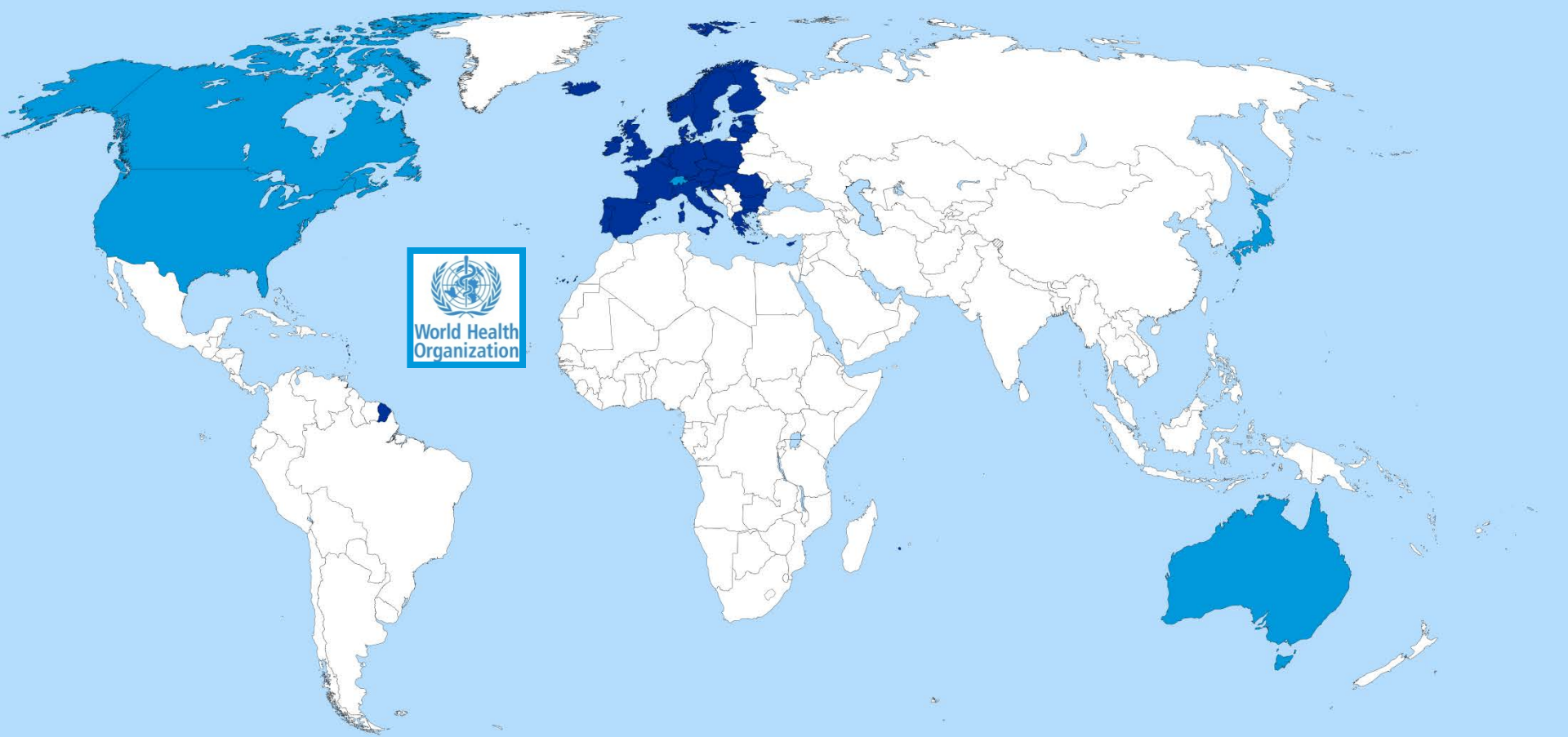

Mutual recognition agreement and ACAA* partners

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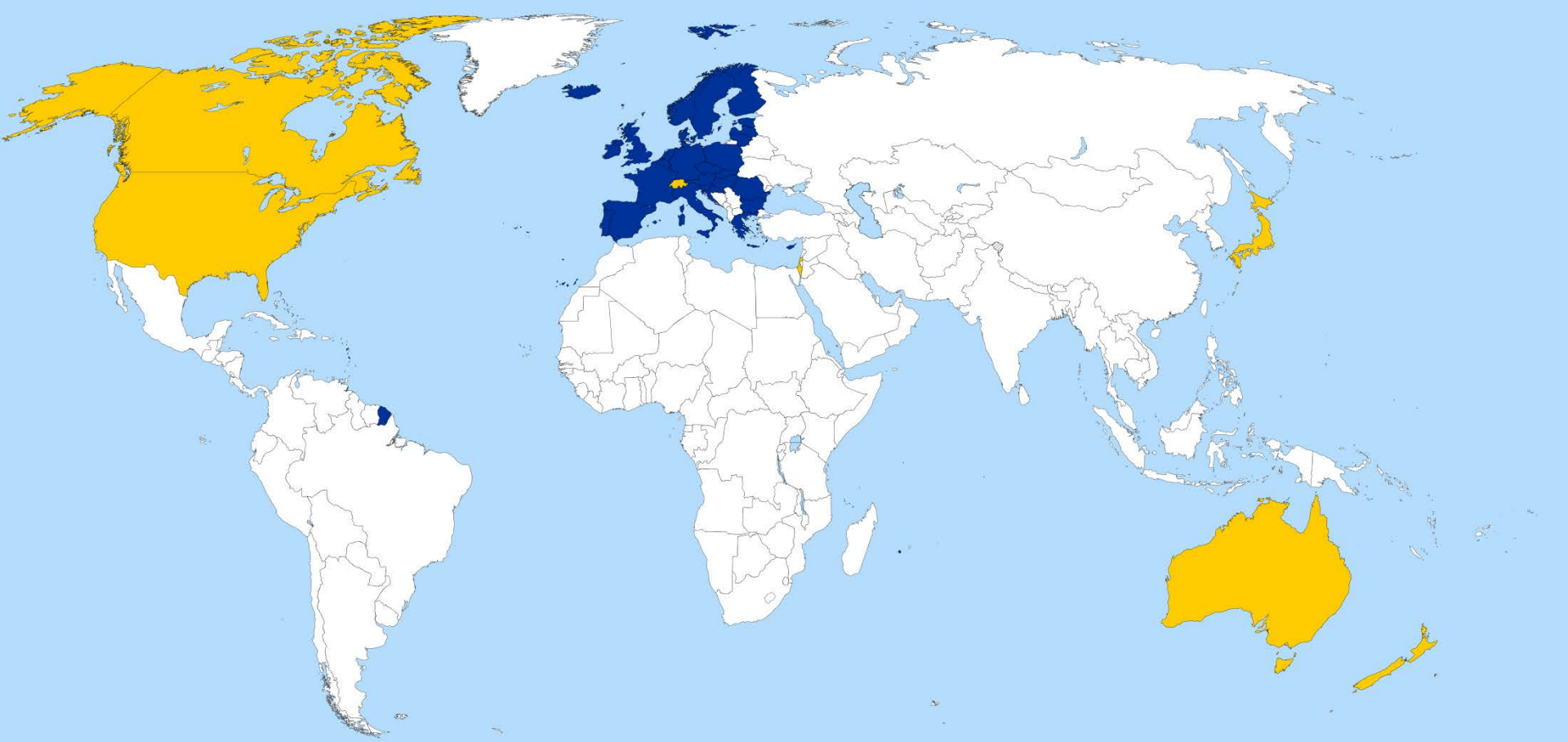
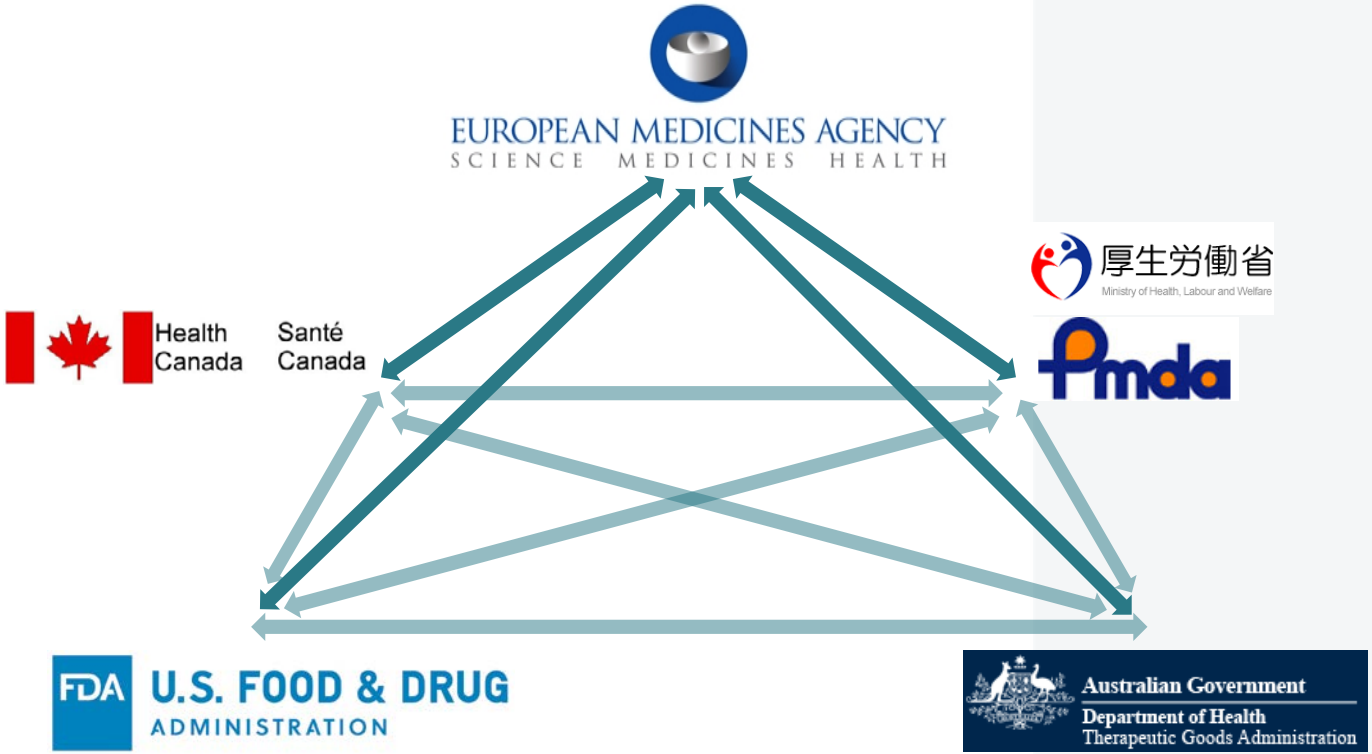


*ACAA: Agreement on Conformity Assessment and Acceptance of Industrial Products (Israel only)

Bilateral cooperation: confidentiality arrangements:



Additional CA's with EMA:

- *SwissMedic*
- *WHO*

EMA/FDA bilateral cooperation

Confidentiality arrangements

Protection of non-public information provided in confidence, allows for:

- Sharing of non-public, pre-decisional information and draft legislation and guidance
- Exchanges of staff (secondments, training)
- Experts' attendance and participation in scientific meetings

Scope:

Human and veterinary medicines under review by EMA (or other confidentiality partner agencies) and national products referred to the CHMP and PRAC

EMA fellowships to FDA

- Aim: advance scientific and regulatory understanding, usually a 2-week exchange
- 22 EMA fellowships at FDA in the last 4 years, with 5 more this year

This year:

GMP inspections

Extrapolation

Regulatory procedures

Combination products

ISO standardisation

Past years:

GMP inspections (x2)

Risk communication

Raw data analysis (x2)

Pharmacovigilance

Qualification of clinical outcome measures

ISO standardisation

Patient engagement

Veterinary medicines (x3)

Legal aspects

PhV inspections

Accelerated access to medicines

Rheumatology and gastroenterology

Quality of medicines

Transparency

Communications

Real world data and big data

Orphan medicines

Paediatric medicines

Clusters – operational mode of convening

- Core cadres of regulator experts/peers by topic area builds relationships
- Some include other regulatory partners – PMDA/MHLW (Japan), TGA (Australia), Health Canada, SwissMedic
- Regular meetings by telephone (1-2 hours)
- Facilitate timely information exchange
  - Increasingly focus on early development strategies or early safety signals
  - Share draft guidelines
- Follow-up meetings on specific topics in more depth
- Joint workshops or upcoming meetings of interest

Some current clusters:

Advanced Medical Products

Biosimilars

Blood Products

Oncology

Orphan Products

Paediatrics

Pharmacogenomics

Pharmacovigilance

Vaccines

Veterinary Medicines

New clusters:

Patient engagement

Rare diseases

Current activities: product development

- Orphan medicines
  - Single application form and annual report
- Paediatric medicines
  - Increasing number of common commentaries
- Parallel EMA-FDA scientific advice
- Parallel submissions for qualification of Biomarkers or Clinical Outcome Measures
  - Joint template agreed and published

In all cases goals are the same:

- ✓ *Support global development plans*
- ✓ *Scientific and public health convergence*
- ✓ *Reduce administrative burden*

Current activities: product evaluation and surveillance

Regular exchange (within clusters and separately)

- Share information on ongoing marketing authorisation applications
- Clusters with regular tele- or videoconferences, eg vaccines, blood products, biosimilars, oncology
- International pharmacovigilance teleconferences on current safety issues
- EMA shares pre-PRAC and pre-CHMP information via Early Notification System
- FDA gives advance notice on planned communications including Drug Safety Communications

✓ *Awareness of ongoing evaluations, opportunity for discussion, exchange of views*

✓ *Advance notice of important regulatory action*

✓ *Understanding in case of different outcomes*

Current activities: product evaluation and surveillance

Ad hoc exchange

- Ad-hoc product exchanges and teleconferences on specific review and safety issues
- Observers at PRAC and CHMP meetings, SAGs, ad hoc expert meetings / FDA Advisory Committee meetings

Current activities: international exchange on shortages

- Follows from EU initiative on minimising and preventing shortages relating to manufacturing and quality issues
- Raising awareness of existing shortages in different regions
  - Update on programs within regions to prevent shortages
  - Discuss reasons for shortages and ways to address them
- Rapid alert on identified shortages
- Quarterly teleconferences

Current activities: GMP inspection initiatives

- API inspection programme
  - Fosters greater international cooperation and information sharing to help to better distribute inspection capacity, allowing more sites to be monitored and reducing unnecessary duplication
  - Involves WHO, EDQM, several EU Member States, FDA, TGA, Health Canada and PMDA
- EU/US Mutual Recognition Agreement
  - Signed March 1st, 2017
  - Better use of inspection resources, avoiding duplication, increased inspection coverage
  - Signature of “Super CC” (confidentiality arrangement allowing FDA to share full inspection reports, including trade secret information with EU regulators) August 3rd, 2017

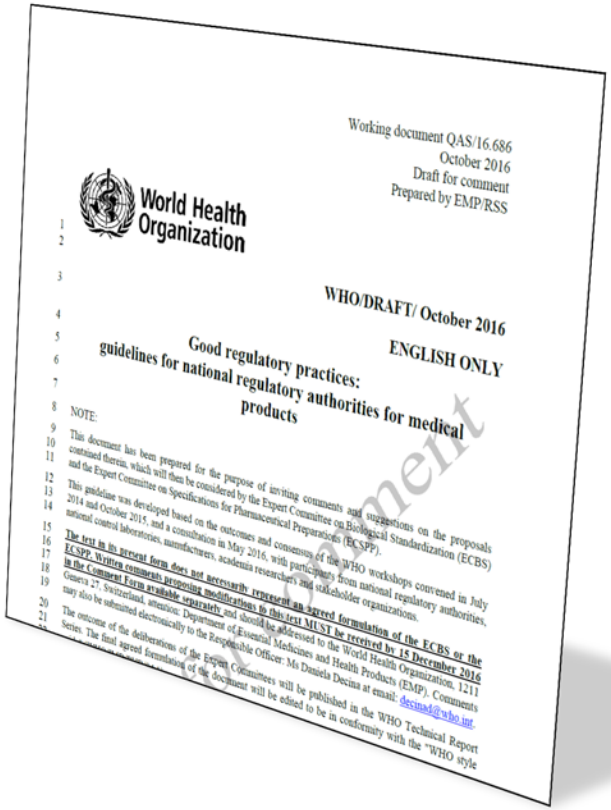
Current activities: GCP inspection initiatives

- GCP inspection initiative improved communications between agencies and strengthened trust in each other's efforts
  - Covers new chemical entities and biologics and FDA-EMA inspections
  - Conduct information exchanges on GCP-related information
  - Conduct collaborative GCP inspections and share information on GCP inspections and interpretation of GCP
  - Facilitates both agencies' inspection coverage and decision-making
- GCP bioequivalence inspection initiative involves inspections within national programmes (UK, IT, DE, FR, NL, ES)
  - Exchange of planned and conducted bioequivalence inspections
  - Possibility of joint (system related) or observed inspections
  - Aims to streamline inspection resources for bioequivalence studies

Promoting good reliance practices (GRP)

WHO GRP guideline offers helpful 2-step definition of reliance:

1) take into account (partly or fully) assessment done by others
2) retain responsibility for your own decisions



Working document QAS/16.686
October 2016
Draft for comment
Prepared by EMP/RSS

World Health Organization

WHO/DRAFT/ October 2016

ENGLISH ONLY

Good regulatory practices: guidelines for national regulatory authorities for medical products

NOTE:

This document has been prepared for the purpose of inviting comments and suggestions on the proposals contained therein, which will then be considered by the Expert Committee on Biological Standardization (ECBS) and the Expert Committee on Specifications for Pharmaceutical Preparations (ECSPP).

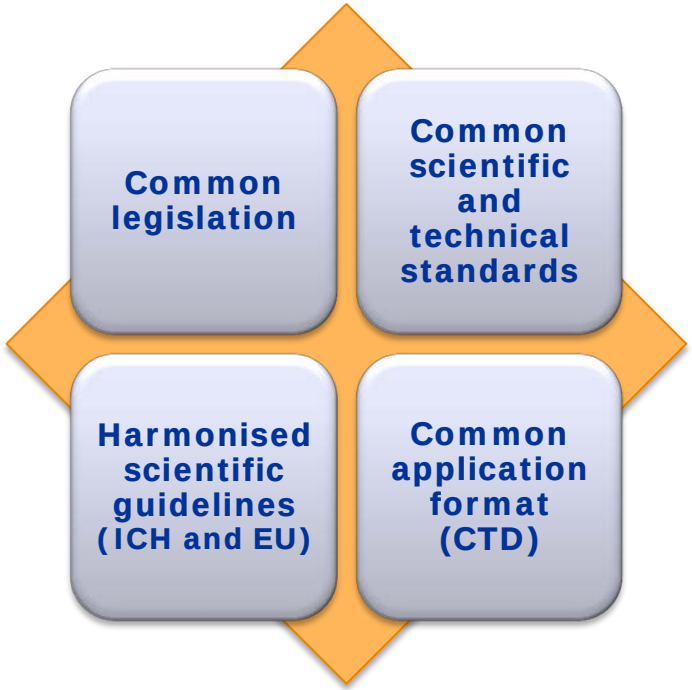
This guideline was developed based on the outcomes and consensus of the WHO workshops convened in July 2014 and October 2015, and a consultation in May 2016, with participants from national regulatory authorities, national control laboratories, manufacturers, academia researchers and stakeholder organizations.

The text in its present form does not necessarily represent an agreed formulation of the ECBS or the ECSPP. Written comments proposing modifications to this text MUST be received by 15 December 2016 in the Comment Form available separately and should be addressed to the World Health Organization, 1211 Geneva 27, Switzerland, attention: Department of Essential Medicines and Health Products (EMP). Comments may also be submitted electronically to the Responsible Officer: Ms Daniela Decina at email: decinad@who.int.

The outcome of the deliberations of the Expert Committees will be published in the WHO Technical Report Series. The final agreed formulation of the document will be edited to be in conformity with the "WHO style

Comment

EU reliance and work-sharing: building blocks



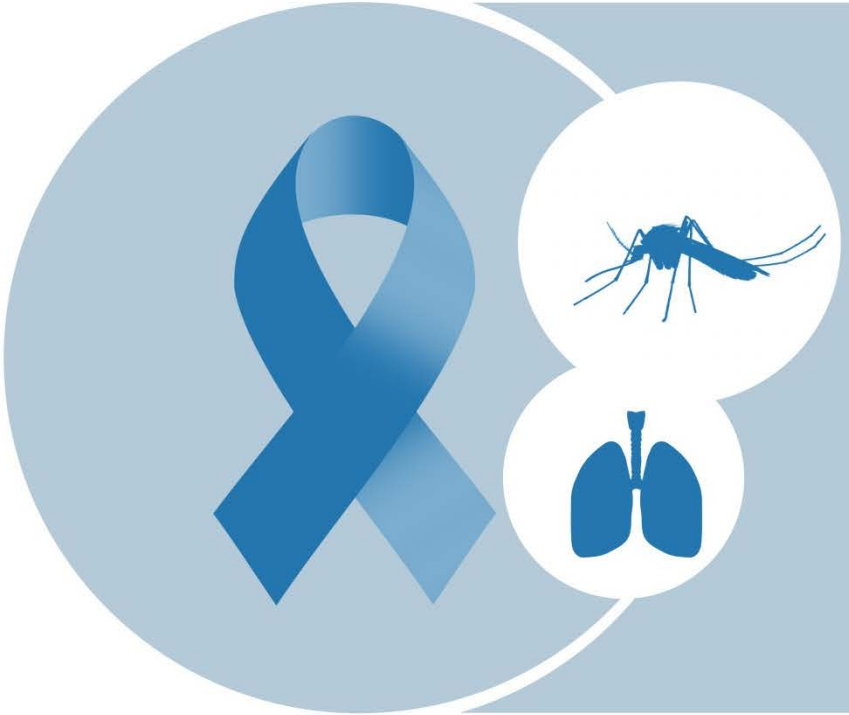
Complemented by common European approach to manufacturing and inspection

- EU GMP guide (same as PIC/S)
- Single format for manufacturing authorisations, GMP certificates

Reliance example 1: ‘Article 58’

- EMA assessment of quality, safety and efficacy of a medicine or vaccine intended for use only outside the EU
- Evaluation carried out with the WHO and relevant ‘target’ non-EU regulatory authorities
- Same standards and procedures as for medicines marketed in EU
- Benefit-risk assessment targeted at intended non-EU population and indication
- Licensing decision taken by non-EU regulators in countries where the medicine or vaccine will be used

Which medicines are eligible?



Vaccines or medicines used to prevent or treat public health priority diseases:

- Vaccines used in the WHO Expanded Programme on Immunization;
- Medicines for protection against diseases, such as HIV/AIDS, malaria and tuberculosis.

Reliance example 2:
WHO ‘SRA’ Collaborative Registration Pilot

Collaborative Registration aimed at facilitating and accelerating national registration of products assessed and pre-qualified by WHO

Extended to medicines authorised by Stringent Regulatory Authorities (SRA, as defined by WHO) and pilot with EMA launched end 2014

5 products in pilot (for AIDS, TB, malaria)

World Health Organization

Objective:

- Accelerate national approval process in countries where resources may be limited, based on the assessment work already carried out by the SRA
- Allows participating national authorities to retain their regulatory responsibilities and make own decisions

Reliance example 3:
International Generic Drugs Regulatory Programme

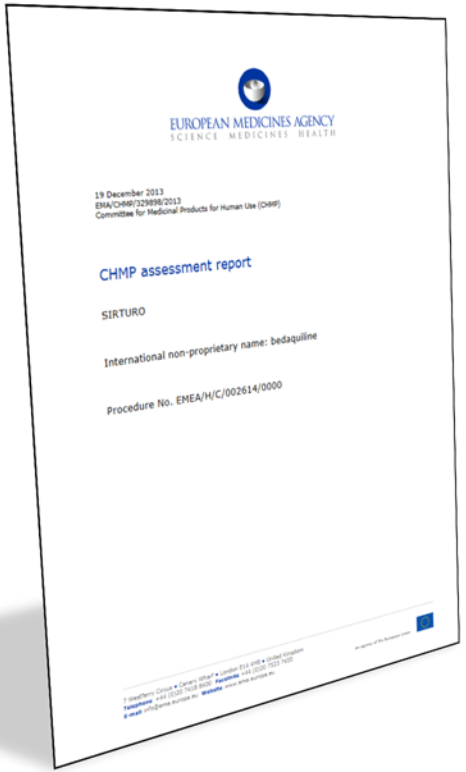
Pilot launched July 2014

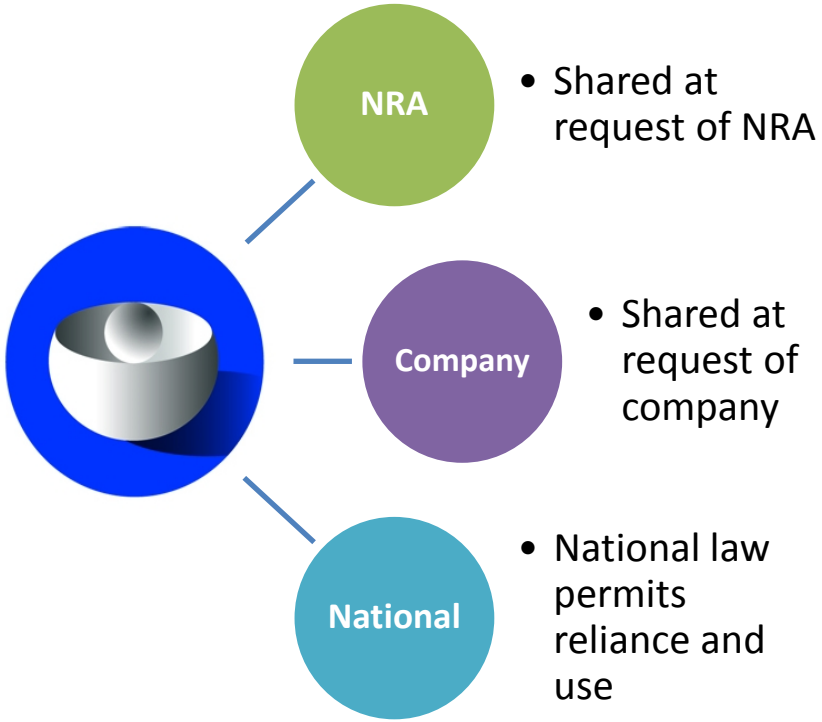
Uses EU decentralised procedure as model for sharing assessment reports during scientific assessment

Shared by the EU agencies in real time with the participating non-EU authorities:

- During decentralised procedures for generics participating in the pilot
- Upon request from the company applying for marketing authorisation
- Receiving authorities benefit from the information in the EU assessments but maintain their own regulatory responsibilities for decision-making

Sharing and using EMA assessment reports





Training opportunities

- Training is key part of the European system
- International partners regularly invited to workshops and training opportunities
  e.g. GMP, pharmacovigilance and GCP inspectors, PK/PD
- EU Network Training Centre
  launched 2015 *(access for non-EU regulators + WHO portal access planned for future)*
- Contributes to capacity building

Examples of EMA multilateral engagement

ICH/VICH

- Regulators and industry associations, global guideline harmonisation
- 💻 www.ich.org / 💻 www.vichsec.org

IPRF

- Regulators-only, identifies need for convergence/harmonisation by members
- 💻 www.i-p-r-f.org

ICMRA

- Regulators-only, global strategic leadership forum
- 💻 www.icmra.info

PIC/S

- Regulators-only, harmonised GMP standards and inspectorate quality systems
- 💻 www.icmra.info

Conclusions

It is no longer about whether regulators will cooperate with each other, it is about how best to do it

The EU system is an example of successful cooperation and reliance among regulators

International cooperation is part of EMA's and the European network's daily work

Striving for convergence is imperative

Early dialogue is encouraged

Any questions?

Further information

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