



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

ICH and EU regulatory framework and the role of the European Medicines Agency (EMA)

GCC Workshop on Similar Biological Medicinal Products (Biosimilars)

19-20 April 2011, Riyadh





Outline

- **Overview ICH and the Global Cooperation Group**
- European Medicines Agency (EMA)
- European Regulation of Medicinal Products
- Procedural Aspects (Centralised Procedure)



Agenda: International Conference on Harmonisation (ICH)

- To provide a brief overview of ICH
- Explain the role of the Steering Committee
 - Responsibilities
 - Membership
 - Function
- Report on the mandate of the Global Cooperation Group
 - Shift from information-sharing to training
 - Membership (RHIs*, DRAs*)

*RHI: Regional Harmonisation Initiatives

*DRA: Drug Regulatory Authority



ICH

INTERNATIONAL CONFERENCE ON
HARMONIS/ZATION
of
Technical Requirements
for the Registration of
Pharmaceuticals for Human Use

<http://www.ich.org>

Hosted by ICH Secretariat
IFPMA, Geneva, Switzerland



ICH Background

Unique harmonisation project involving the regulators and research-based industries of US, EU and Japan

→ started in 1990

- WHO, Canada, and EFTA* are observers

Objectives:

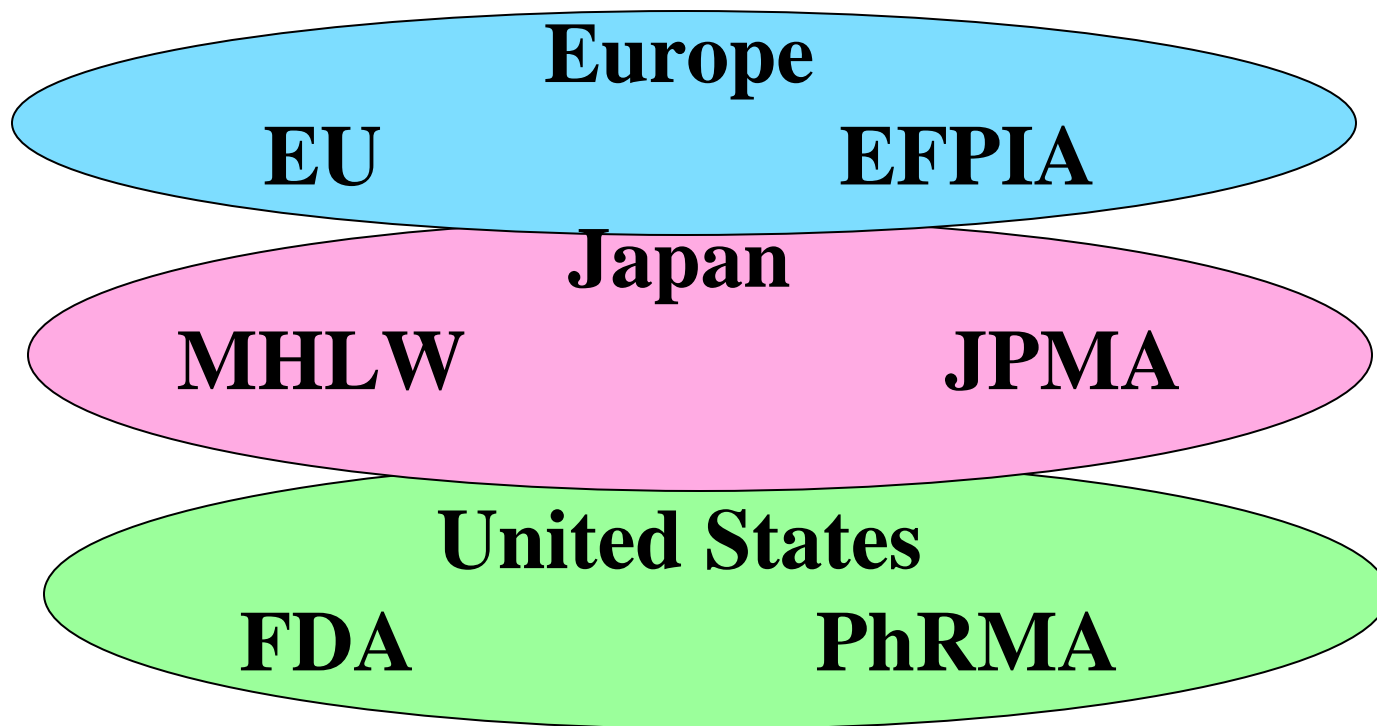
- to improve efficiency of new drug development and registration process
- To promote public health, prevent duplication of clinical trials in humans and minimise the use of animal testing without compromising safety and effectiveness

Accomplished through the development and implementation of harmonised guidelines and standards

* European Free Trade Association (EFTA) is an intergovernmental organisation set up for the promotion of free trade and economic integration to the benefit of its four Member States: [Iceland](#), [Liechtenstein](#), [Norway](#) and [Switzerland](#).



ICH Membership



Observers: WHO, Canada, EFTA



ICH Steering Committee Responsibilities

- The body that governs ICH
- Determines ICH policies and procedures
- Decides on the adoption of ICH projects
 - Selects topics for harmonisation
 - Endorses the creation of Expert Working Groups
- Monitors and facilitates the progress of Expert Working Groups
- Signs off ICH documents



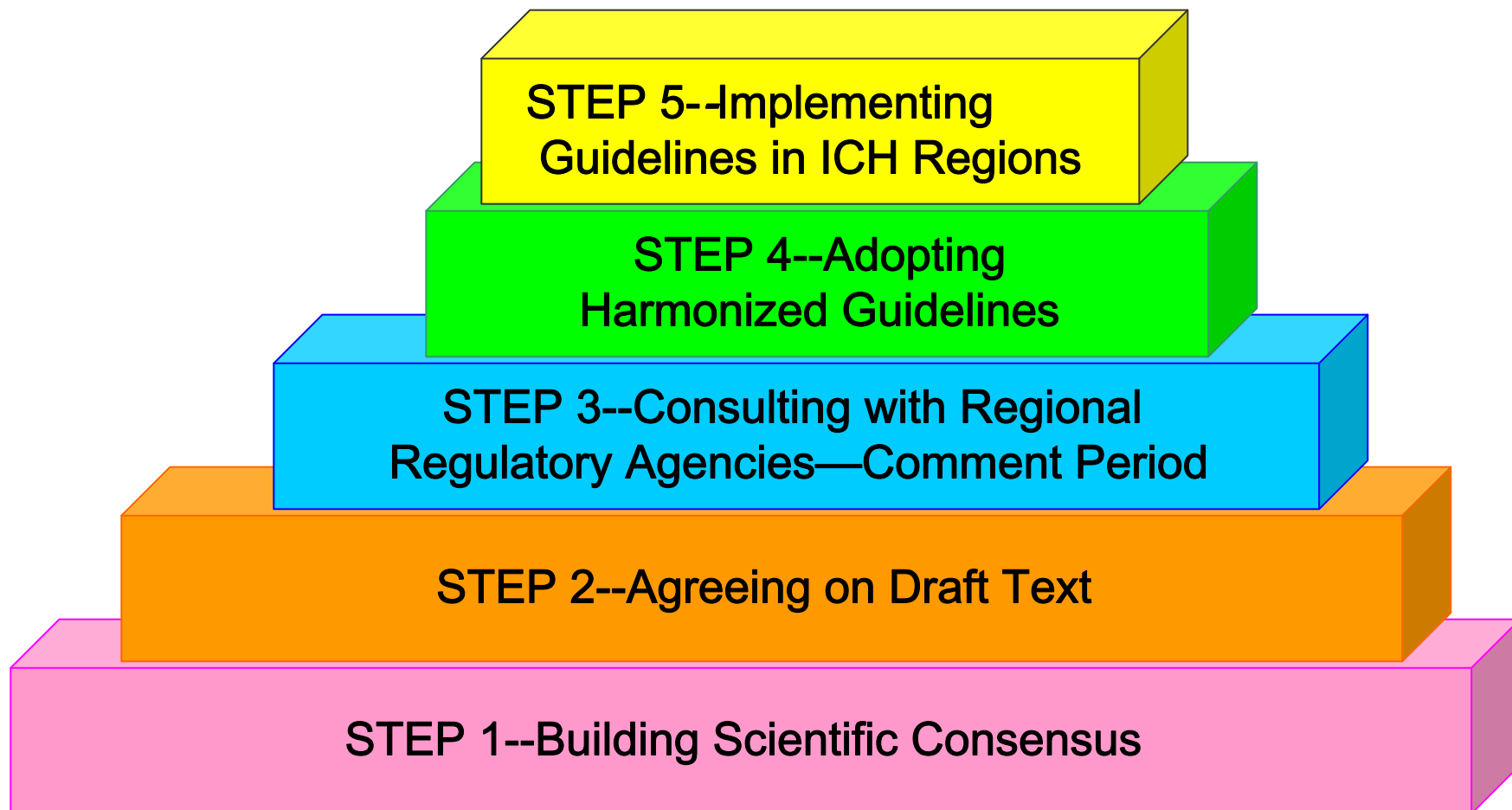
ICH Structure





Steps of ICH Harmonization

After adoption of a topic by the Steering Committee





ICH Outcomes

- Over 50 guidelines on technical requirements on: Quality, Safety and Efficacy
 - **Efficacy** - 14 topics/17 guidelines
 - **Safety** - 8 topics/16 guidelines
 - **Quality** - 9 topics/23 guidelines
- Electronic Standards for the Transfer of Regulatory Information
- Common Technical Document (CTD & eCTD)
- Maintenance of ICH Controlled Terminology Lists
- Medical dictionary for adverse event reporting and coding of clinical trial data (MedDRA)
- Scope of ICH products now extends over the product life cycle and beyond new drugs (**OTC and Generics**)

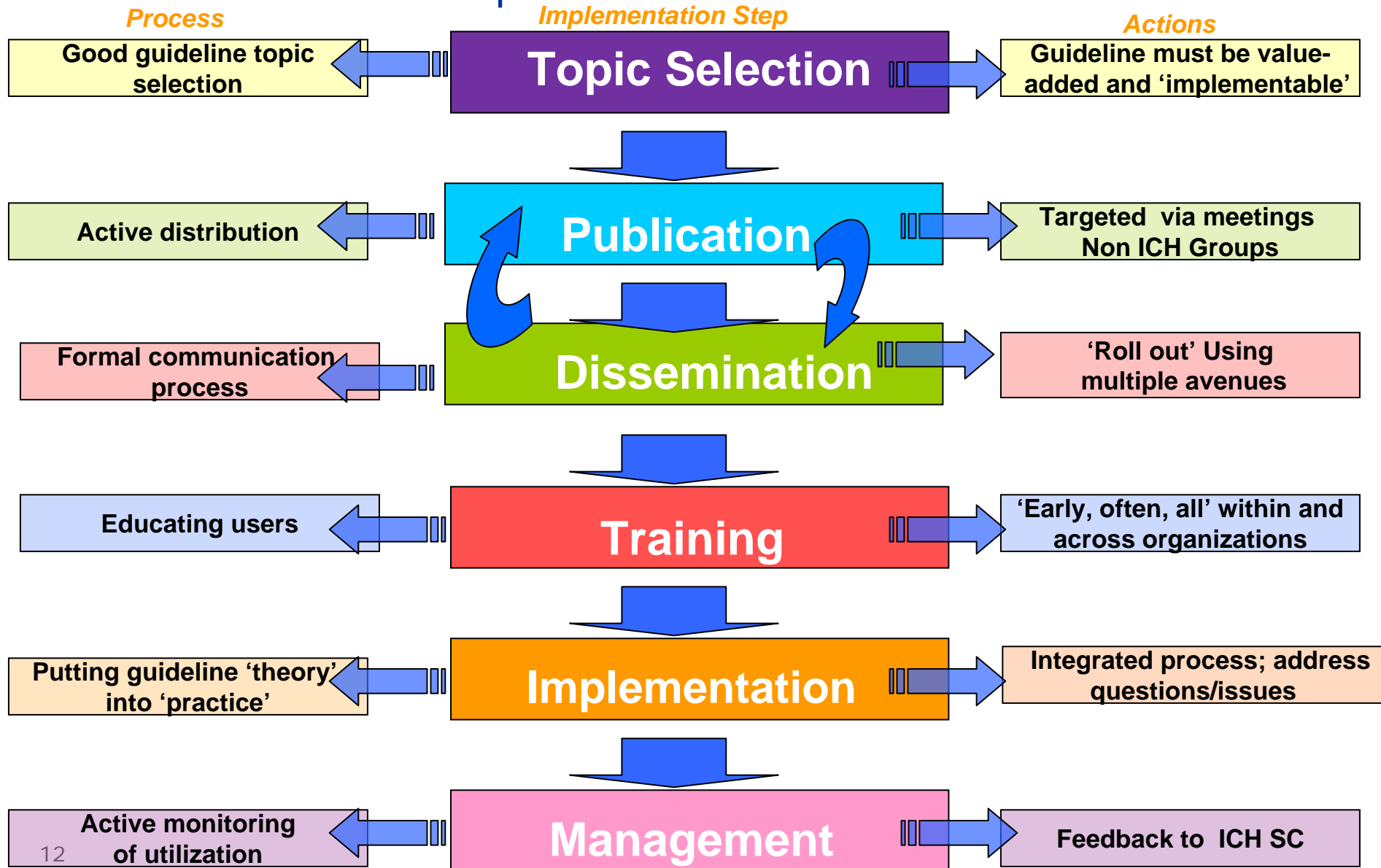


ICH: Keys to success

- Effective management and administration
 - Through ICH Secretariat and Steering Committee
- Joint participation of regulators and industry
- Science based and consensus driven
- Frequent, concurrent meetings of SC and Working Groups that are outcomes based
- Commitment of all parties to implement harmonized guidelines
- Well-defined process and procedures



ICH Implementation Process Flow





Operating Procedures

- The work product of ICH has grown more complex over time - not simply “new topics”
- ICH Steering Committee adopted a Procedures document that outlines and defines the variations of work “categories”
 - Defines roles and responsibilities
 - Updated every fall to reflect current harmonisation activities



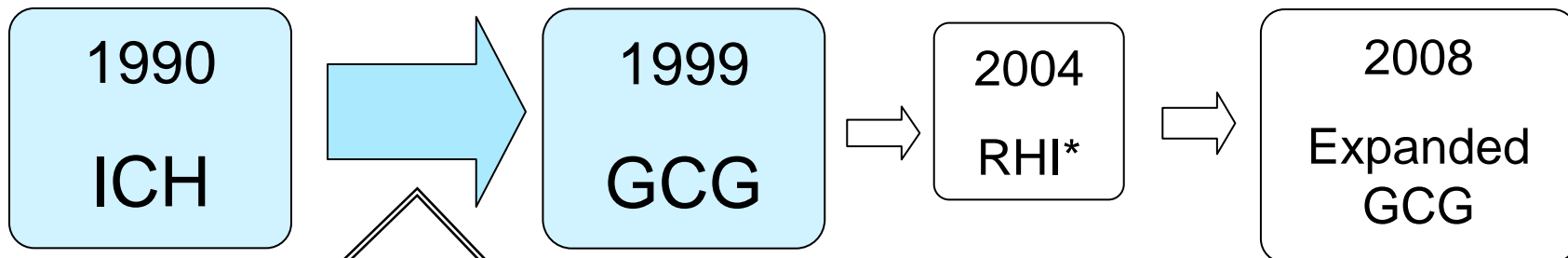
Categories: ICH Harmonisation Activities

- New guideline topics under development
- Existing topics under revision
- Existing topics under maintenance
- Existing topics needing clarification for implementation (Questions and Answers)



ICH GCG: History

Interest beyond the 3 regions



Initially focused on development of guidelines and standards for use in the ICH “regions”

Growing interest in ICH products beyond ICH countries

*RHI: Regional Harmonisation Initiatives



ICH Global Cooperation Group (GCG)

Created in 1999 as a sub-committee of ICH SC to:

- Facilitate dissemination of information on ICH activities, guidelines and their use
- Promote a better understanding of ICH products

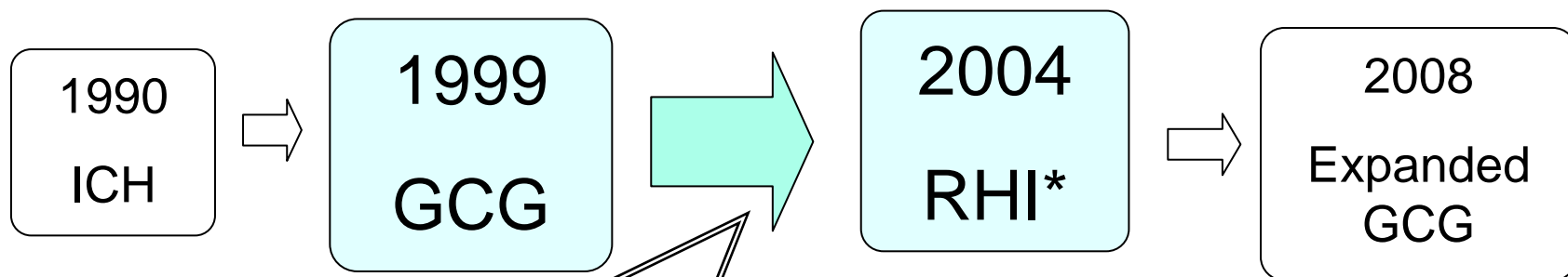
By:

- Information-sharing through literature and presentations by GCG members at international meetings

Same membership as ICH



..... Not enough



More proactive approach was needed to respond effectively to growing interest in ICH guidelines.

Decided to invite representatives from non-ICH regions to be part of GCG.

*RHI: Regional Harmonisation Initiatives



ICH6, Osaka, November 2003: An Important Milestone

Endorsement by ICH SC of new Mandate & Terms of Reference that call for:

- The ongoing participation of Regional Harmonisation Initiatives
- More proactive approach
- Greater transparency



Regional Harmonisation Initiatives now part of GCG

APEC

- Asia-Pacific Economic Cooperation (21 member economies)

ASEAN

- Association of the Southeast Asian Nations (10 economies)

GCC

- **Gulf Cooperation Council (6 Gulf states)**

PANDRH

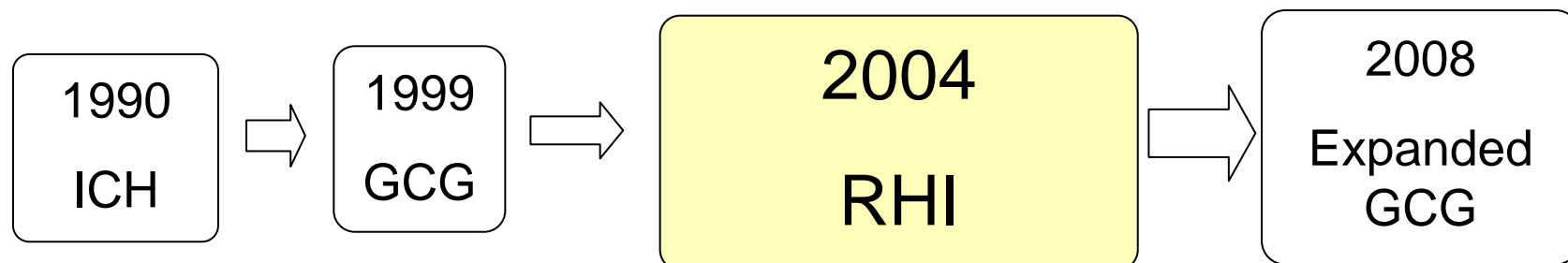
- Pan American Network for Drug Regulatory Harmonisation

SADC

- Southern African Development Community (15 countries)



Adopted new GCG mission statement



May 2005, Brussels:

*“To promote a **mutual understanding** of regional harmonisation initiatives in order to facilitate the harmonisation process related to ICH guidelines regionally and globally, and to facilitate the capacity of drug regulatory authorities and industry to utilise them”*



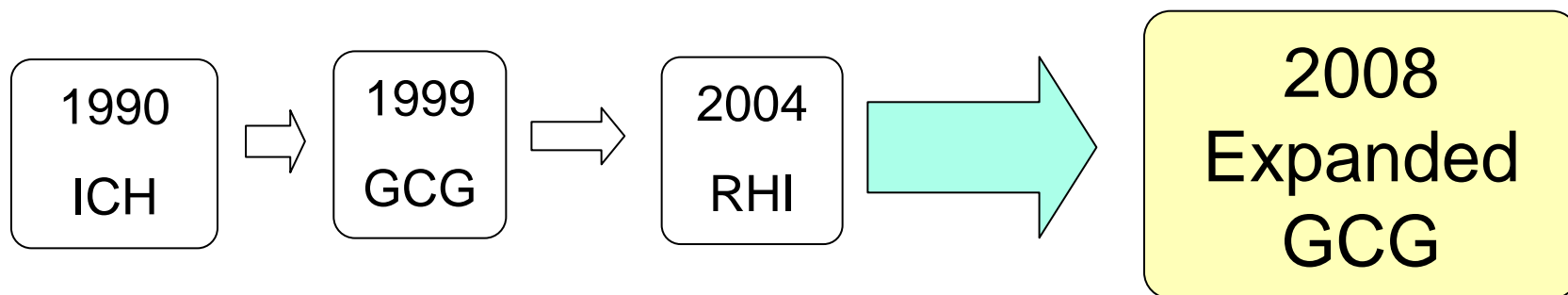
Training: A Key Focus

Framework and mechanisms established:

- Strategy document lays out principles for effective, strategic use of training resources
- Clearing house of training events created to identify opportunities
- Procedures and templates under development to improve efficiency and effectiveness of process – including 2 year planning cycle
- Public access: all training materials to be posted on the ICH website



Expanded GCG

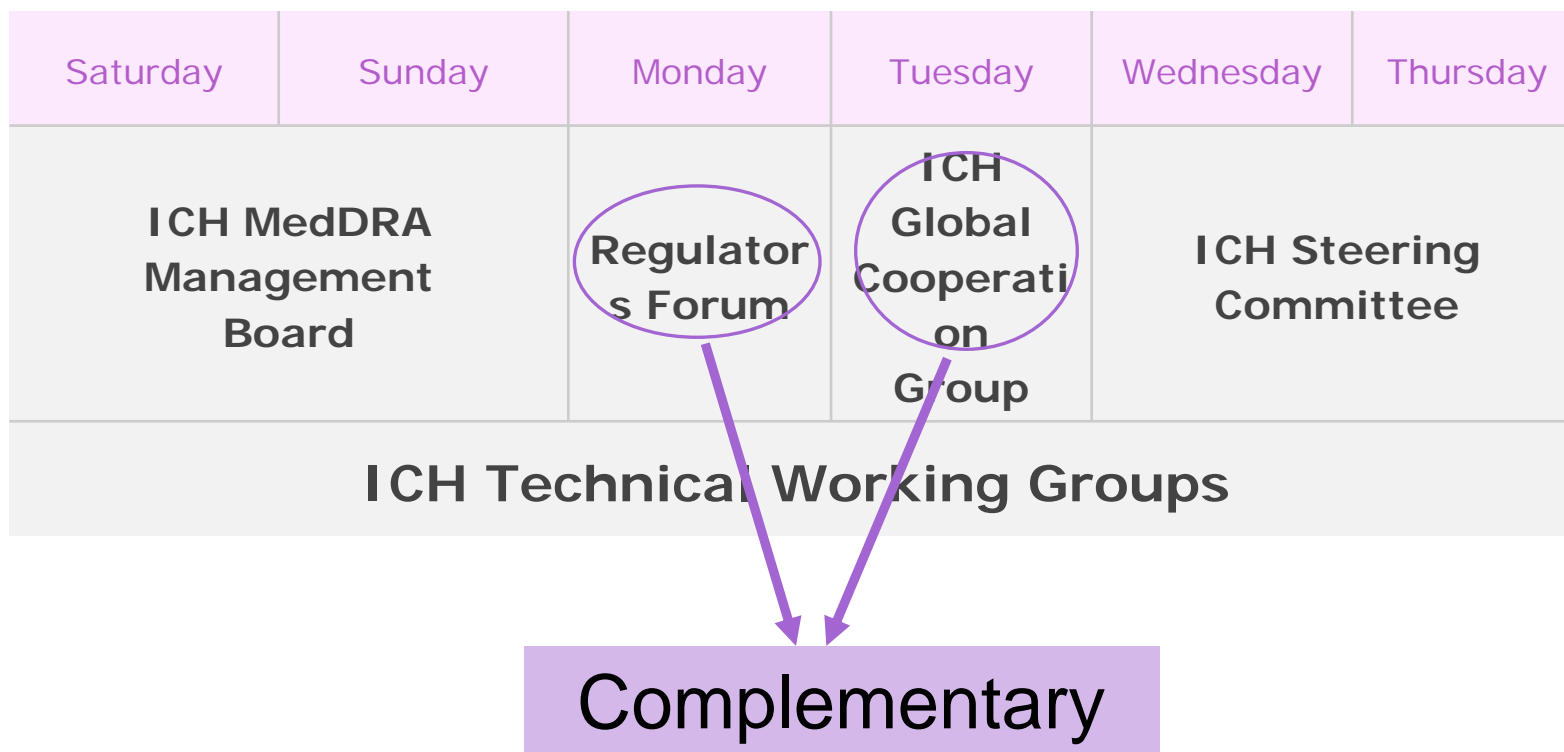


ICH has recognised the need for changes to mirror global face of drug development.

In Oct 2007, the ICH SC decided to **invite a number of Drug Regulatory Authorities and Department of Health.**

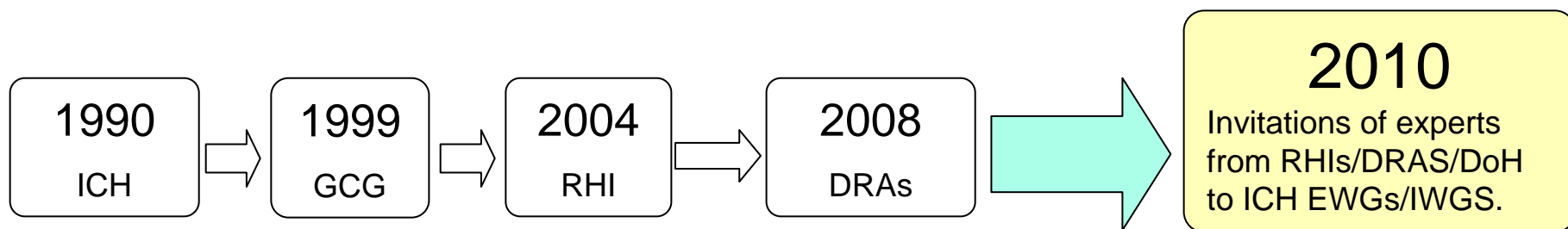


How the ICH Week looks





Opening of ICH Technical Working Groups to Experts from RHIs and DRAs/DoH



ICH has recognised the need for a new level of involvement of the GCG to provide direct technical contributions to the work of ICH, a more global perspective, and to advance implementation of ICH guidelines. In November 2010, the ICH SC decided to invite RHIs and DRAs to nominate technical experts as active members of ICH Expert Working groups.



Beyond ICH: Regulatory Forum

- Regulators only
- ICH + China, India, Brazil, Russia, Taiwan, Singapore, Australia



ICH: Keys to Success

- Well-defined process
- Effective management and administration
- Limited number of players with common focus
- Comparable regulatory, technical and financial capacity
- Commitment of all parties



EMA Efforts towards Harmonisation and Transparency

- Participation in SC and expert groups
- Public comments are collected and shared with ICH colleagues thereby providing a conduit for non-ICH organizations' input into the ICH Process
- Recent EMA-CHMP proposals adopted by the ICH SC: revision of the guidelines for
 - Genotoxicity,
 - Carcinogenicity
 - Preclinical Requirements for Clinical Trials
- Recent EMA CHMP proposals just adopted by the ICH SC: Addendum to the guideline for Non-clinical testing of biotech products and Q&A on the geriatrics guideline.
- GCG: EMA opened certain CHMP working party meetings to GCG as training, sends experts to regional workshops



Conclusion on ICH

- Considerable progress to date in promoting a better knowledge of ICH guidelines and the challenges faced by other regions in their use
- GCG efforts have evolved from information sharing to active dialogue to results-oriented actions
- Important new developments should further accelerate progress
- Learning from each other, in a climate of trust and cooperation, can greatly increase the strength of all harmonisation efforts
- Moving towards more efficient regulatory systems and increased availability of safe, effective and quality pharmaceuticals on a global level



Outline

- Overview of ICH and the Global Cooperation Group
- **European Medicines Agency (EMA)**
- European Regulation of Medicinal Products
- Procedural Aspects (Centralised Procedure)



Introduction

- The European Medicines Agency (EMA) is a decentralised body of the EU.
- The mission of the Agency is to foster scientific excellence in the evaluation and supervision of medicines, for the benefit of public and animal health serving over 500 million users of medicinal products
- Responsible for centralised procedure and co-ordination of EU network + plays a role in stimulating innovation and research in the pharmaceutical sector.





A networking Agency

- Member States have pooled their sovereignty for authorisation of medicines
- EMA is designed to coordinate the existing scientific resources of Member States
- EMA is not an FDA for Europe
- All parties linked by an IT network (EudraNet)





An interface of co-operation and co-ordination of Member States' activities

- Centralised procedure, eligible human and veterinary products
 - Single marketing authorisation application valid throughout EU
- Six scientific Committees
- EU Network for scientific advice & expertise constitutes of
 - 27 EU Member states
 - > 40 national competent authorities
 - 4,500 European experts
- Coordination of activities: Pharmacovigilance (new lex 2012), Inspection
- Referral or arbitration procedures for medicines approved via non-centralised authorisation procedures




PATIENTS

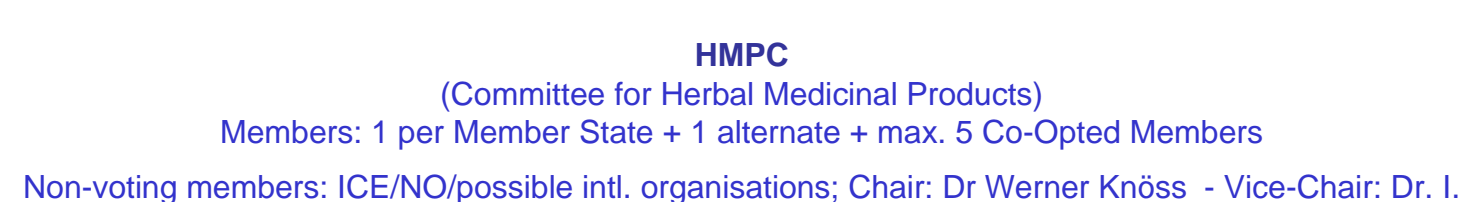
HCP




CHMP
 (Committee for Human Medicinal Products)
 Members: 1 per Member State + 1 alternate + 5 co-opted Members
 Non voting members: ICE/NO; Chair : Dr. E. Abadie – Vice Chair: Dr. T. Salmonson



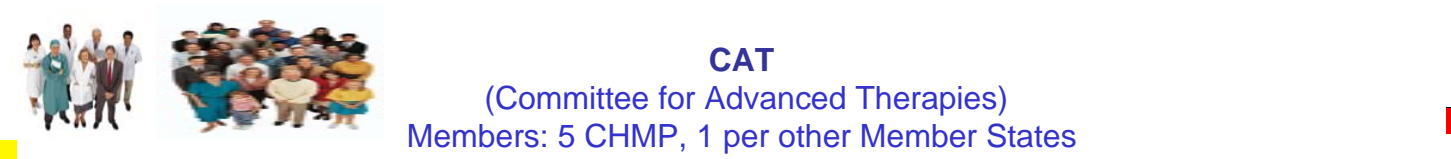
COMP
 (Committee for Orphan Medicinal Products)
 Members: 1 per Member State +3 additional Members + **3 Patient Organisations**
 Non voting Members: ICE/NO; Chair : Dr. K. Westermark – Vice Chair: Mrs. B. Byskov Holm



HMPC
 (Committee for Herbal Medicinal Products)
 Members: 1 per Member State + 1 alternate + max. 5 Co-Opted Members
 Non-voting members: ICE/NO/possible intl. organisations; Chair: Dr Werner Knöss - Vice-Chair: Dr. I. Chinou



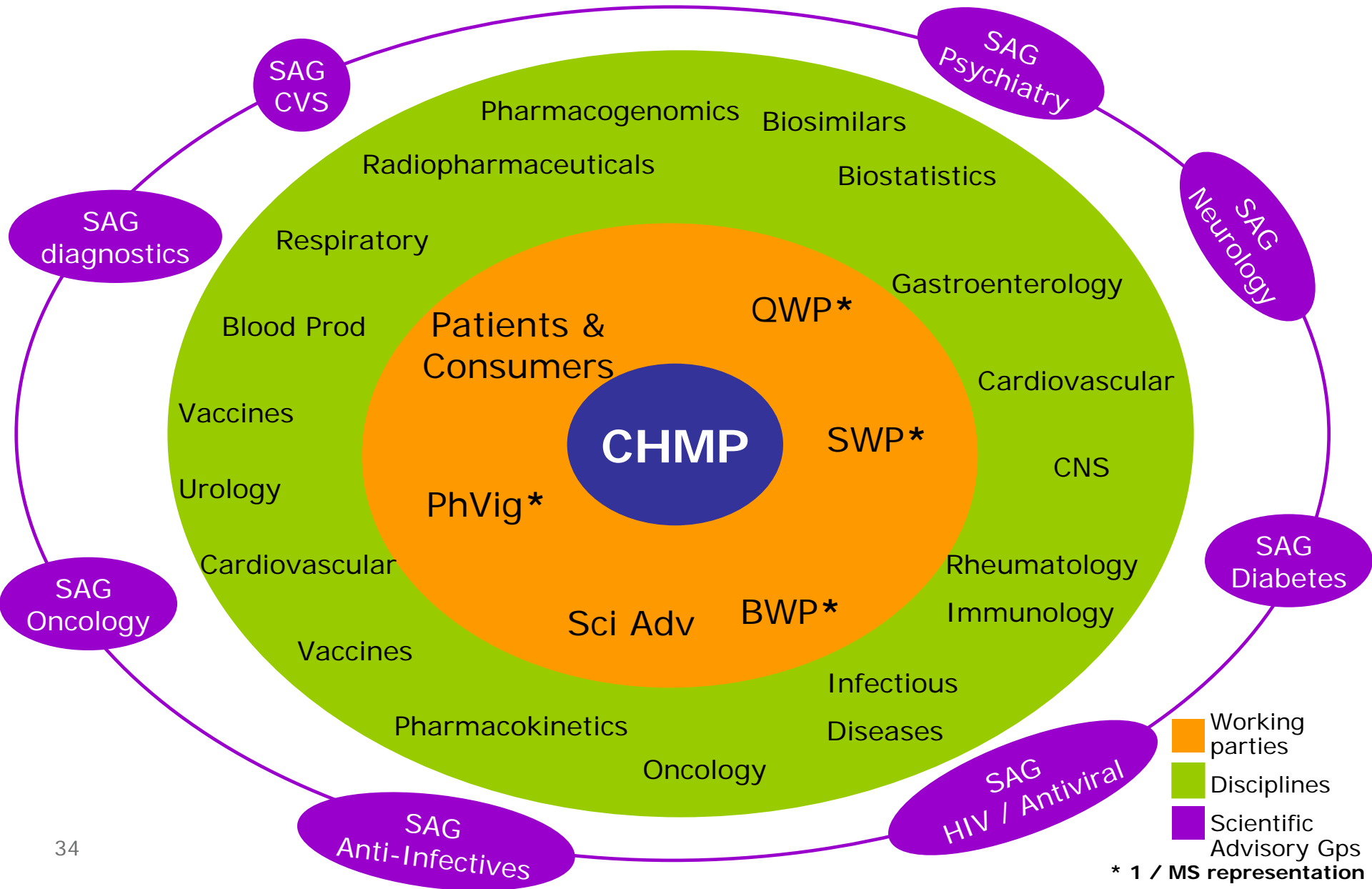
PDCO
 (Paediatric Committee)
 Members: 5 CHMP, 1 per other Member States
3 HCP, 3 Patient Organisations + 1 Alternate per member Non voting members: ICE/NO; Chair: Dr. D. Brasseur - Vice-Chair: Dr. G. Pons



CAT
 (Committee for Advanced Therapies)
 Members: 5 CHMP, 1 per other Member States
2 HCP + 2 alternates appointed by EC, **2 Patient Organisations + 2 alternates** appointed by EC
 Non voting members: ICE/NO; Chair: Dr. C. Schneider - Vice-Chair: Dr. P-A. Salmikangas



MB/QRD/PCWP
Future PRAC





The EMA is **not** responsible for:

- Evaluation of all medicines in the EU
- Controlling, advertising of medicines
- Research/development of medicines
- Price and reimbursement
- Clinical trial approval
- Medical devices
- EU healthcare policies

Activities, e.g. pricing, reimbursement, are under the responsibility of each MS in the EU

Article 1

“The provisions of EU Regulation shall not affect the powers of Member States’ authorities as regards setting the prices of medicinal products or their inclusion in the scope of the national health system or social security schemes on the basis of health, economic and social conditions.

In particular, Member States shall be free to choose from the particulars shown in the marketing authorisation those therapeutic indications and pack sizes which will be covered by their social security bodies. ”

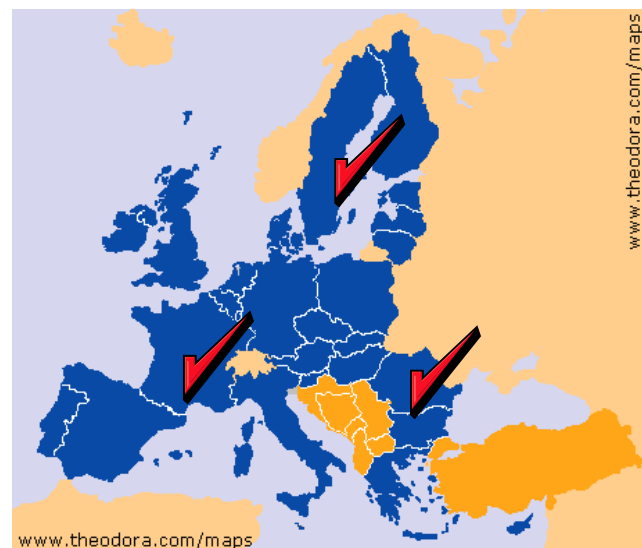


The EU procedures of marketing authorisations

**Centralised Procedure
(via EMA)**

**Mutual Recognition
procedure**

**Decentralised
Procedure**

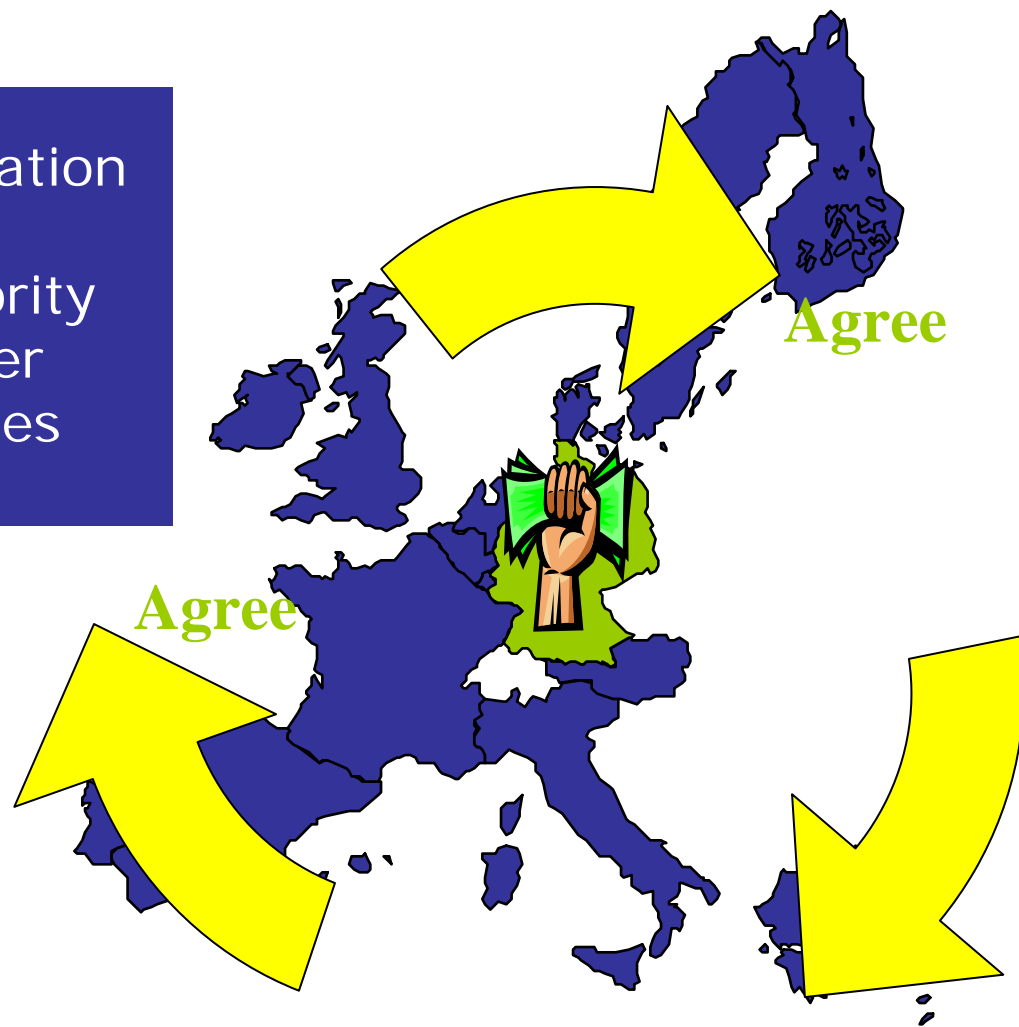


Better Resource Utilisation
Harmonised Scientific Opinions
Harmonised Information to Doctors / Patients



The mutual recognition procedure

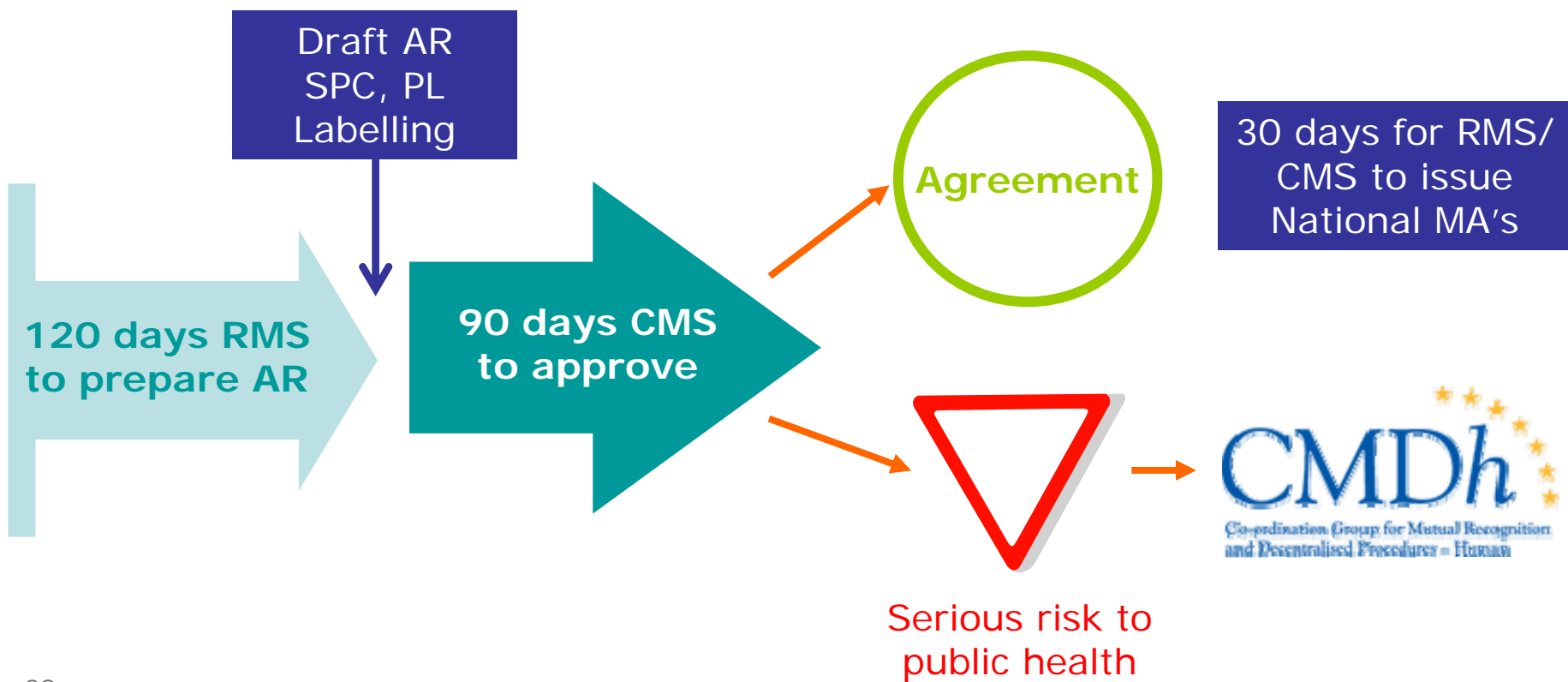
One initial National Authorisation issued by:
- 1 National Regulatory Authority
- recognised by up to 29 other National Regulatory Authorities





The decentralised procedure evaluation

Collaborative Evaluation MS level without any pre-existing National MA

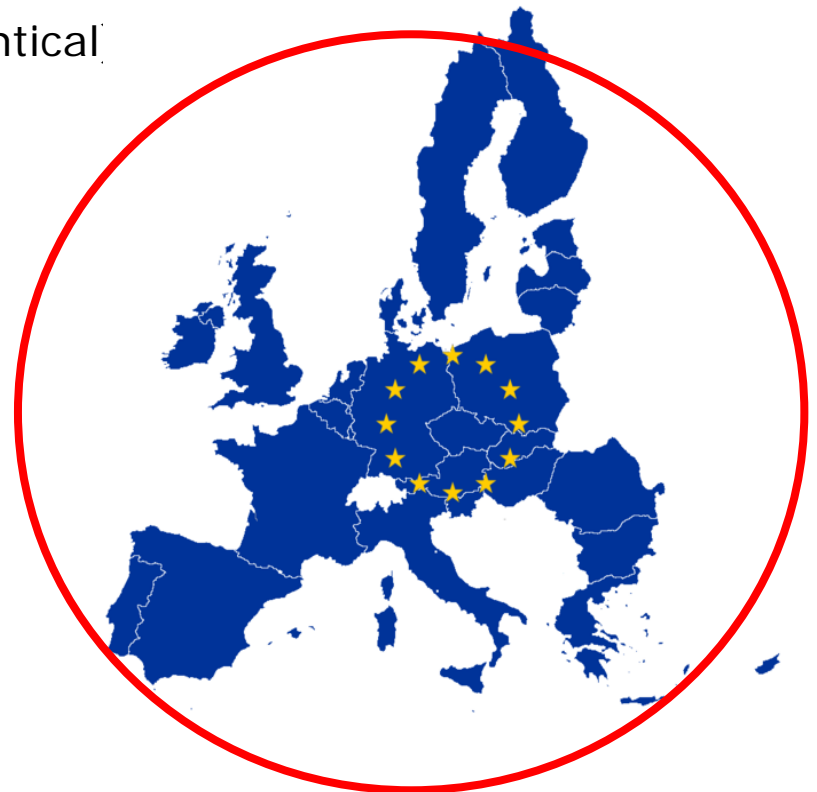




The centralised procedure

Regulatory review Process

- **1 Marketing Authorisation** valid EU
- **1 Invented name** (Tradename)
- **1 Common Labelling** (22 languages identical)
 - Summary of Product Characteristics (SPC)
 - User Package Leaflet & Package Labelling
- **Maximum time limit**
 - **210 days** Evaluation → Opinion





The centralised procedure

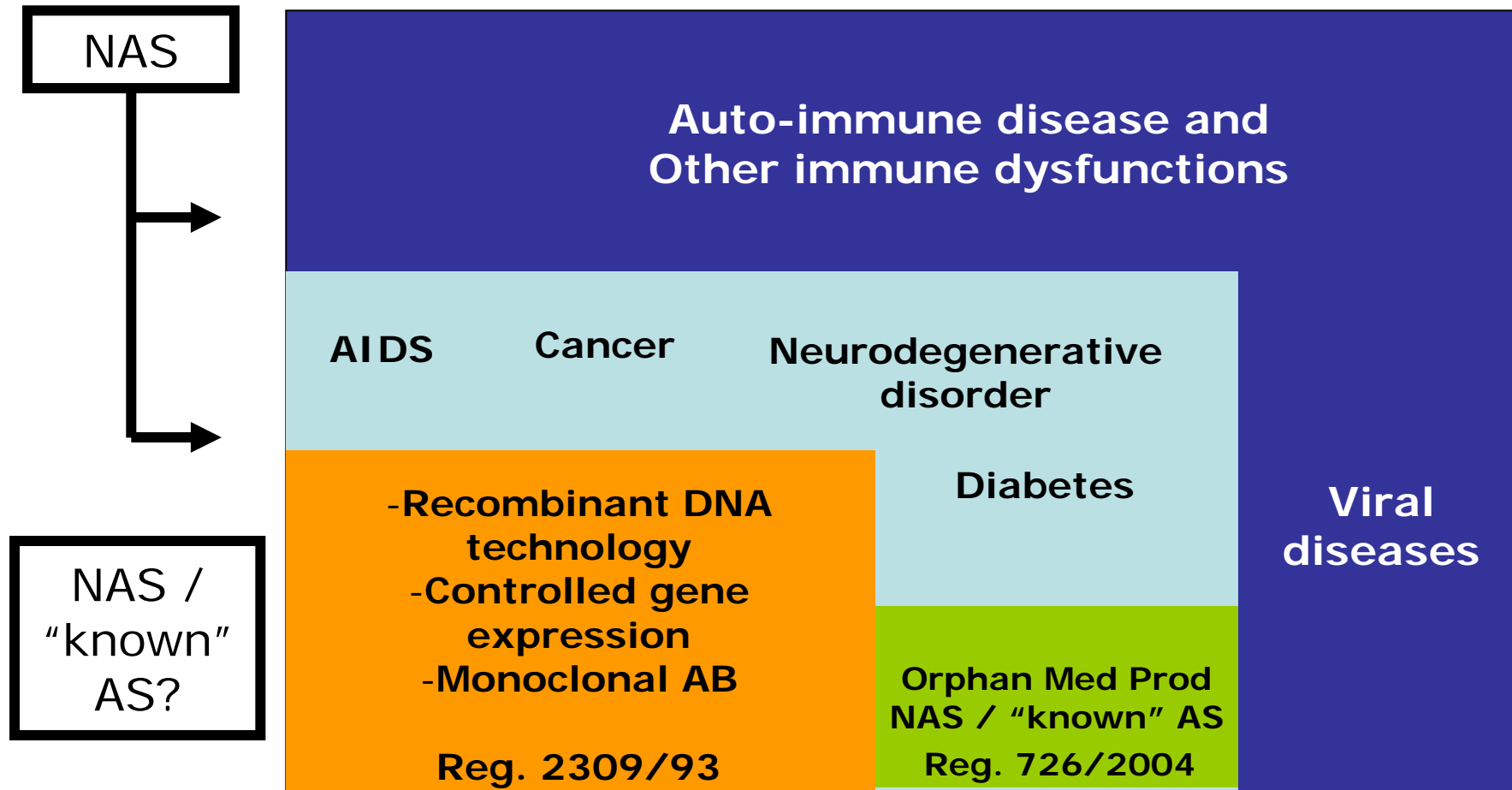
Centralised Procedure = “reserved” procedure

- Not open to all products: dedicated to **innovative** products
 - Some legally obliged to use CP
 - Not for ‘old’ substances in established indications
- Example: aspirin for headache
 - May be open to ‘old’ substances in a new delivery system, or in a new indication e.g. aspirin for Alzheimer's disease

Products eligible are **defined in the legislation**
Annex to Regulation (EC) 726/2004



Access to Medicines: Mandatory Scope





Access to Medicines: Optional Scope

Art. 3(2) of Regulation (EC) No 726/2004

Art. 3(2)(a)

New Active Substances

Art. 3(2)(b)

Significant Innovation

Therapeutic
&/or
Scientific
&/or
Technical

OR

Interest of Patients at
Community
Level

← "known" AS →



Structure of EU Marketing Authorization Applications (MAAs)

The Common Technical Document (CTD)

MODULE 1

Administrative and regional information, "Risk Management", "Risk Reduction" and Pharmacovigilance Plans

MODULE 2

Overviews and summaries of Modules 3 to 5

MODULE 3

Quality (manufacturing process, control methods, analytical tests)

MODULE 4

Pre- clinical investigations (animal models)

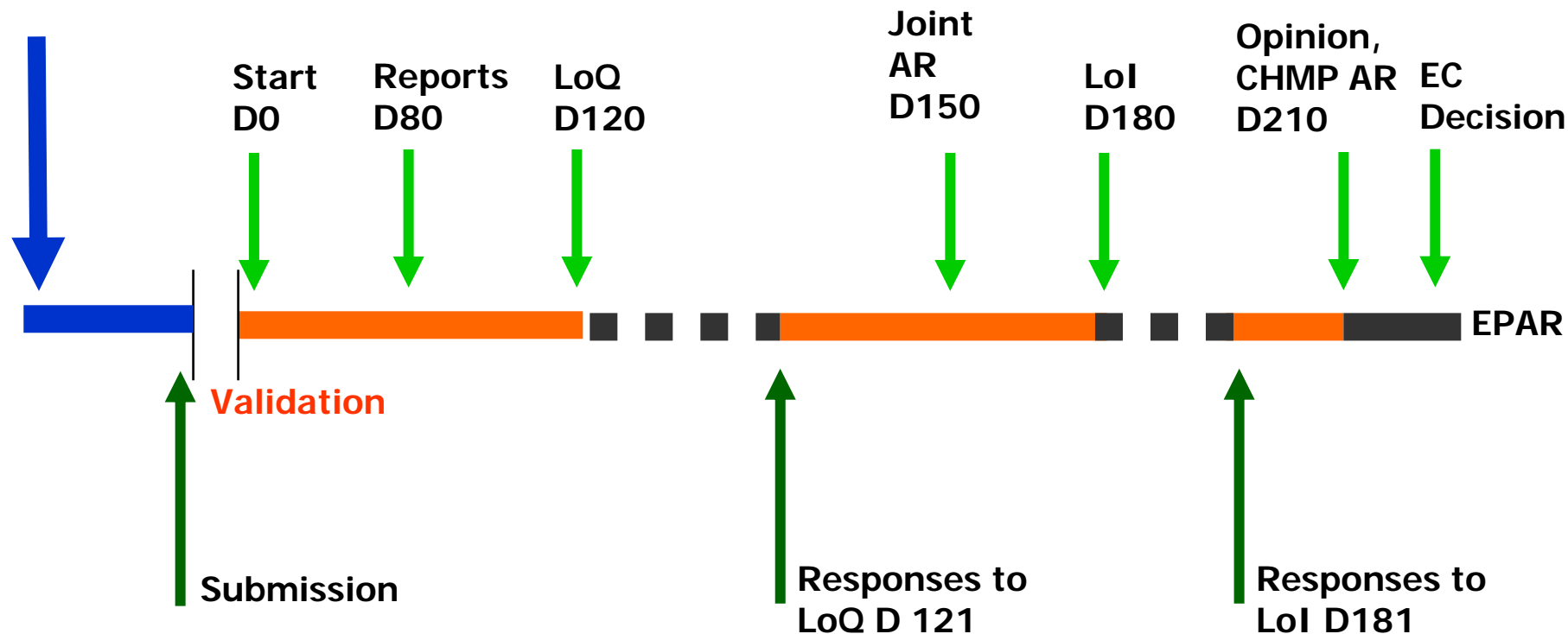
MODULE 5

Clinical investigation (Phases I to III)



Centralised Procedure Assessment Procedure

PRE-SUBMISSION



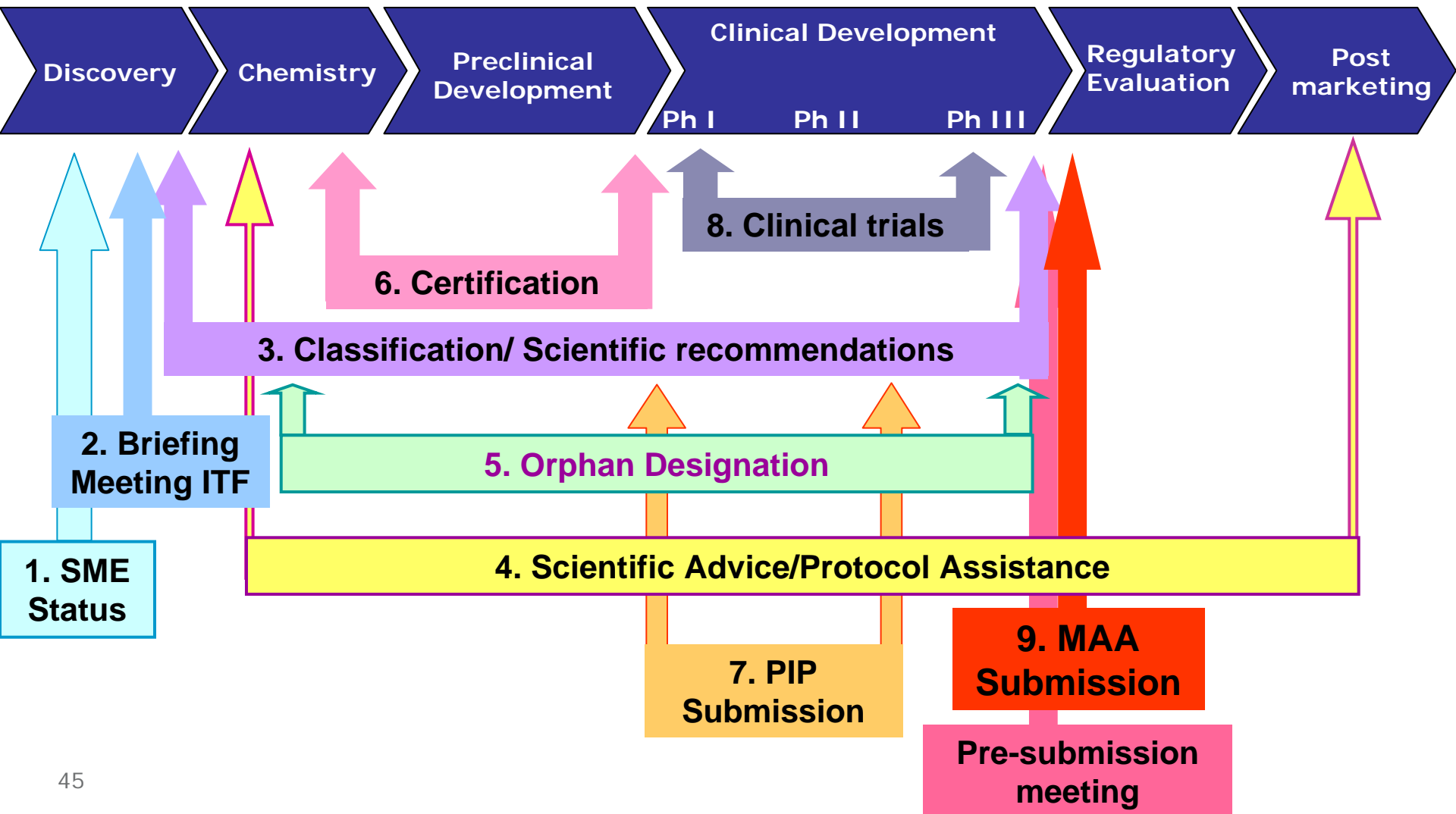
AR: Assessment Report, EPAR: European Public Assessment Report, LoQ: List of Questions, LoI: List of Outstanding Issues

 Active time: evaluation

 Clock Stop: i.e. time for the applicant to prepare responses



Regulatory processes throughout the EMA





EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Thank you for your attention!

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