EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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

ASEAN Training Workshop on ICH Q5C
30-31 May 2011, Kuala Lumpur

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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
HARMONISATION
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

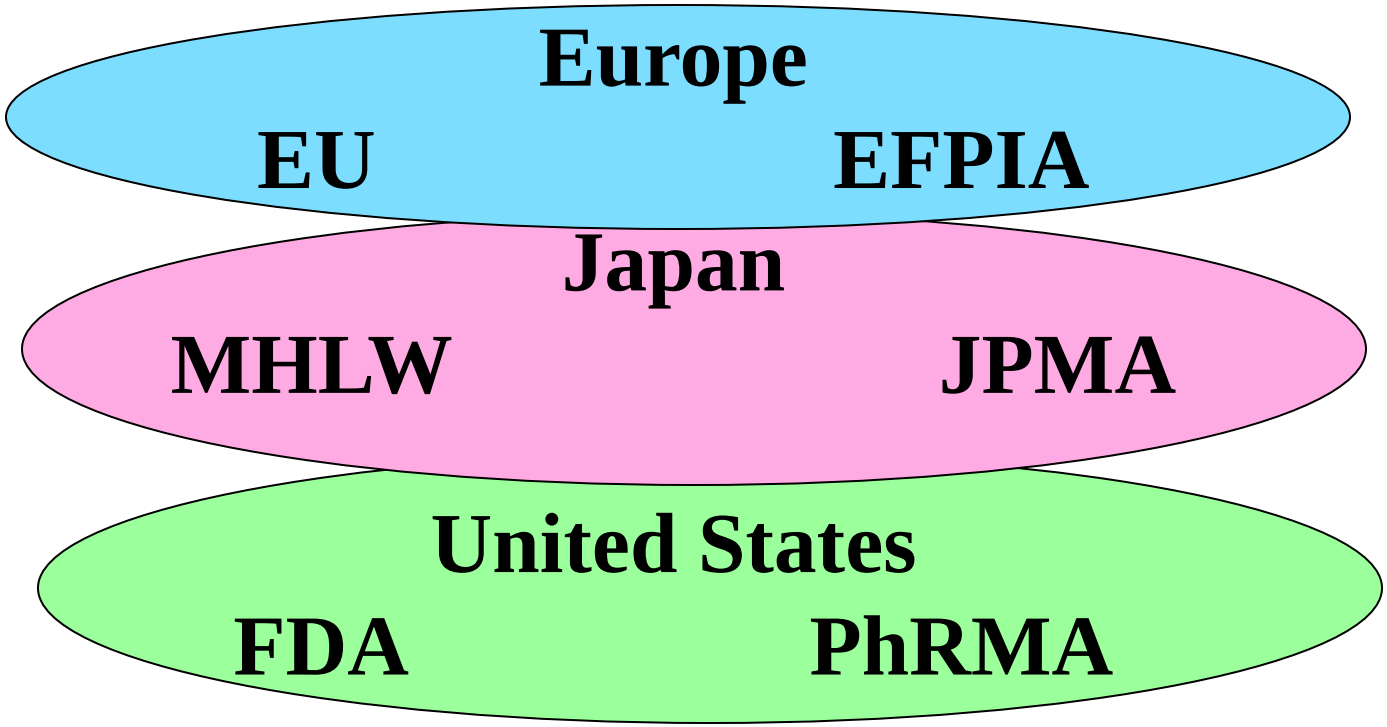
Objectives:

- 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

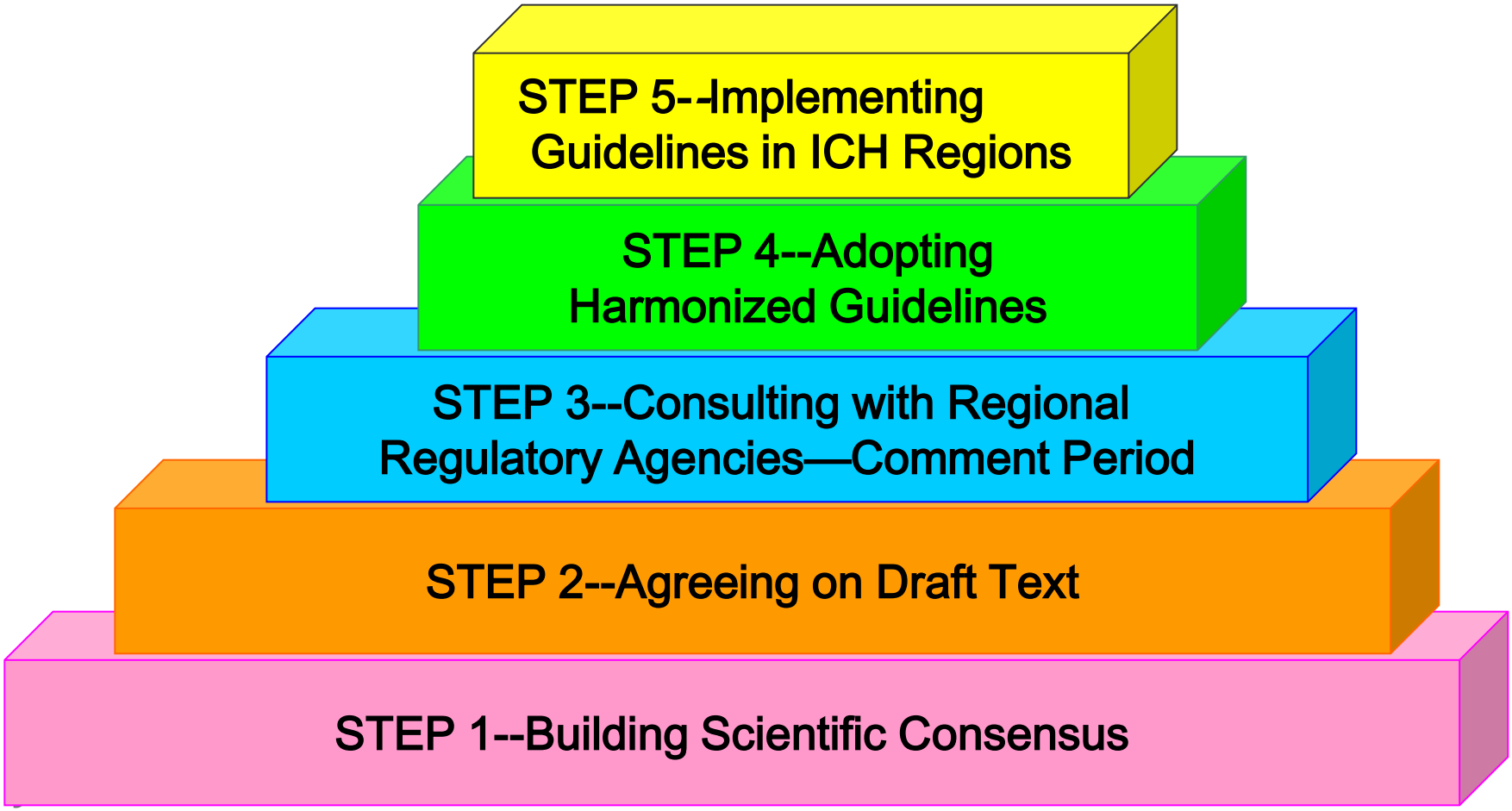
ICH Steering Committee Responsiblities

- 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



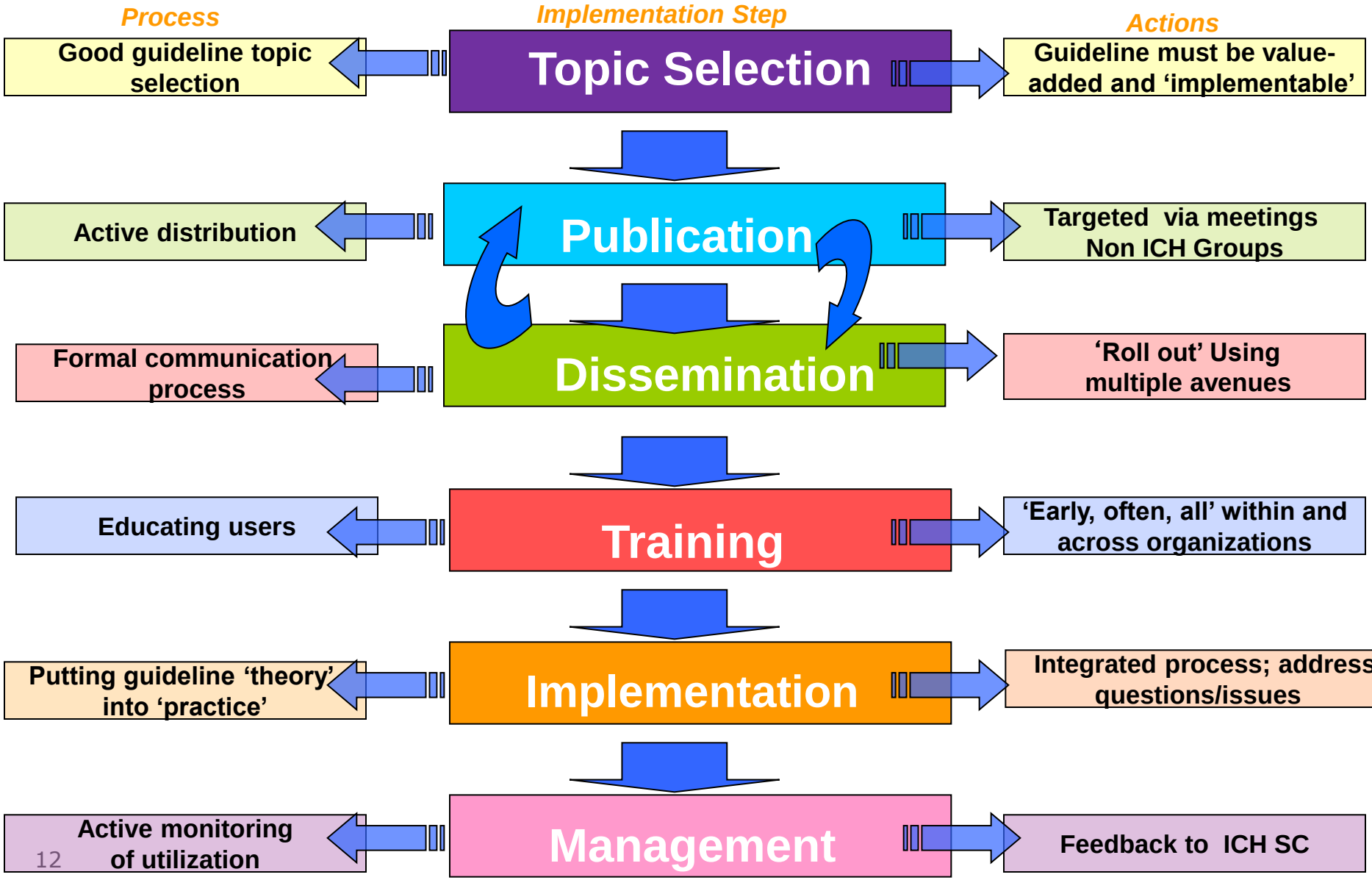
ICH Outcomes

- 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”

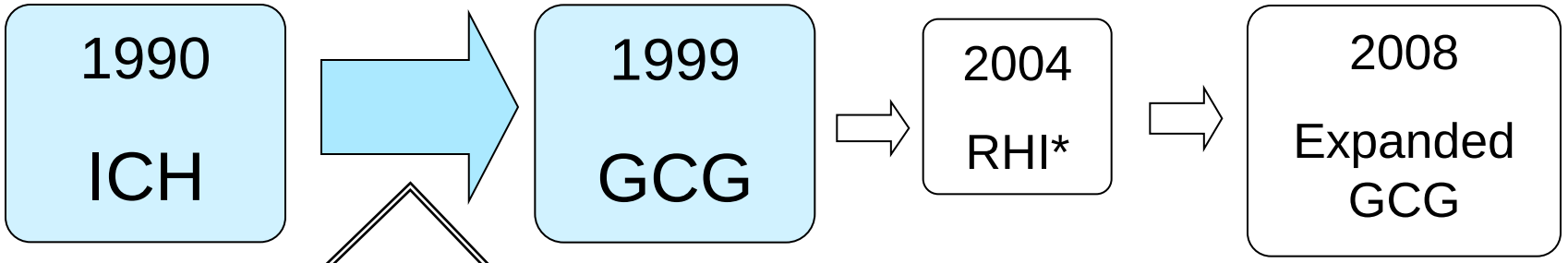
- ICH Steering Committee adopted a Procedures document that outlines and defines the variations of work “categories”
  - Defines roles and responsibilities
  - Updated every fall to reflect current harmonisation activities

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:

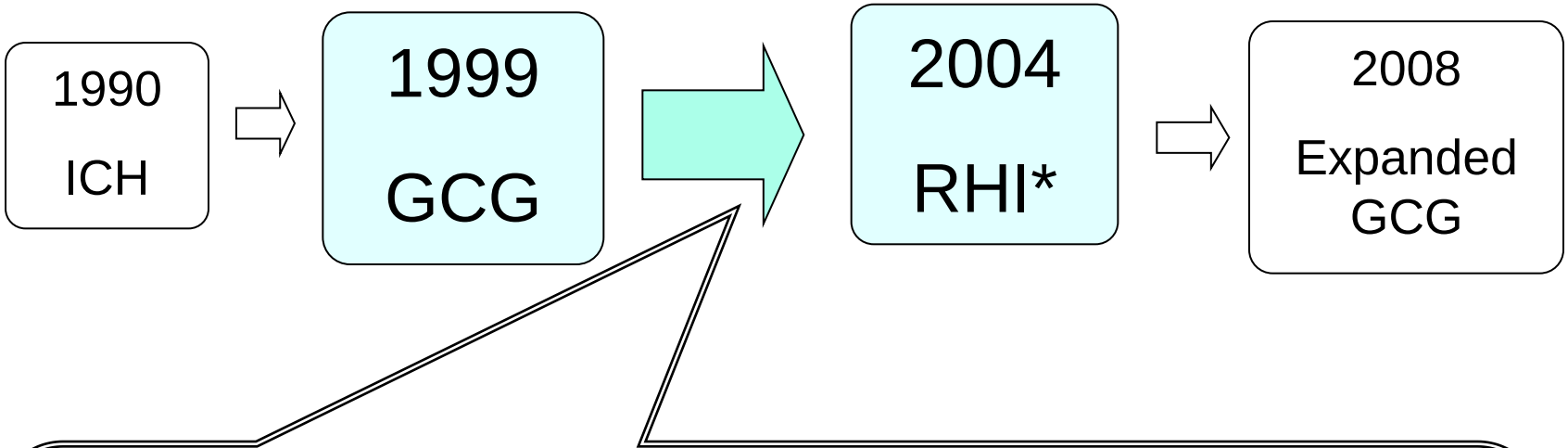
- Facilitate dissemination of information on ICH activities, guidelines and their use
- Promote a better understanding of ICH products

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:

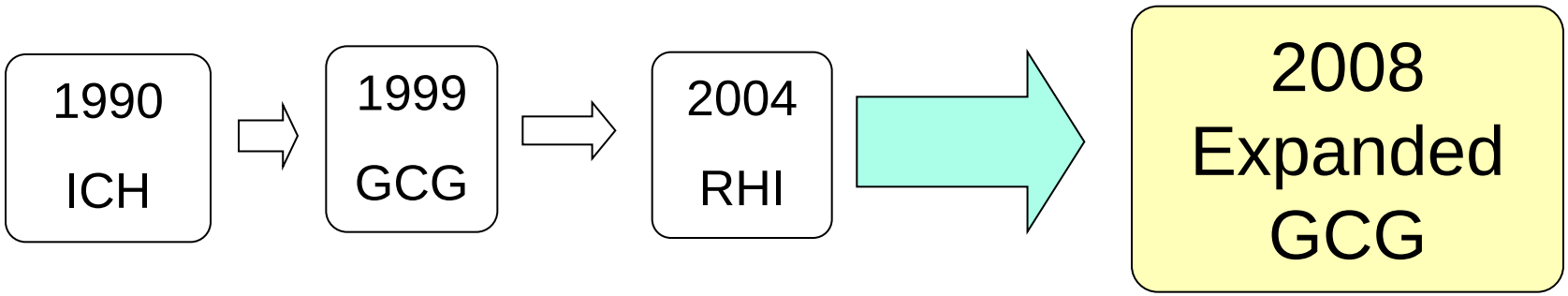
"To promote a mutual understanding of regional harmonisation initiatives in order to facilitate the harmonisation process related to ICH guidelines regionally and globally, and to facilitate the capacity of drug regulatory authorities and industry to utilise them"

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.

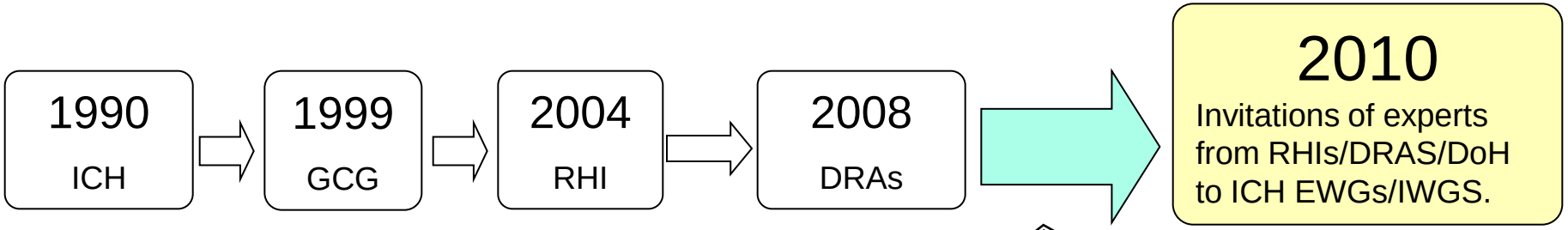
In Oct 2007, the ICH SC decided to invite a number of Drug Regulatory Authorities and Department of Health.

How the ICH Week looks

Saturday	Sunday	Monday	Tuesday	Wednesday	Thursday
ICH MedDRA Management Board		Regulators Forum	ICH Global Cooperation Group	ICH Steering Committee	
ICH Technical Working Groups					

Complementary

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

Human medicines committees

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

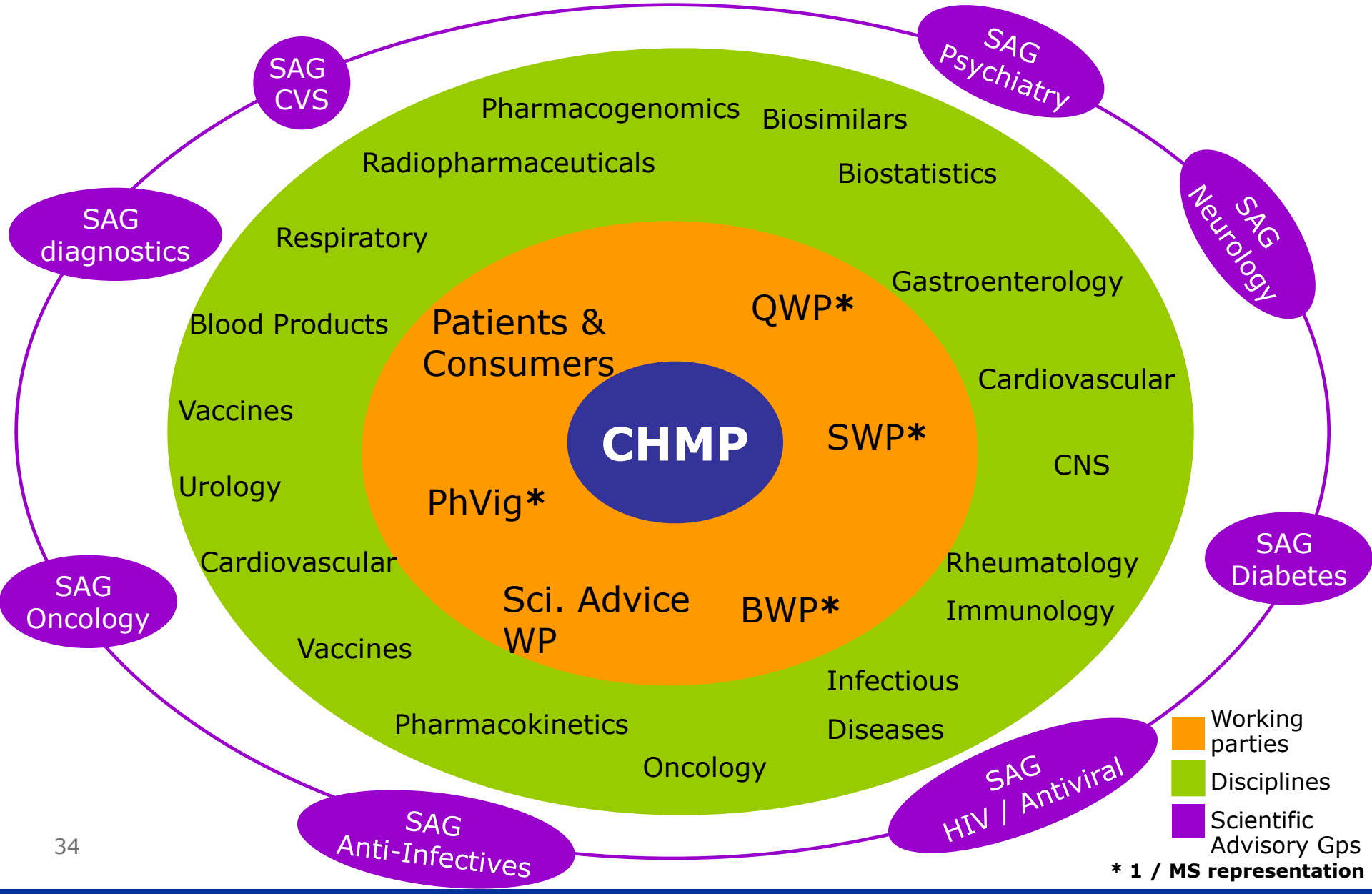
HMPC
(Committee for Herbal Medicinal Products)
Members: 1 per Member State + 1 alternate + max. 5 Co-Opted Members

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


SAG CVS
SAG Psychiatry
SAG diagnostics
SAG Neurology
SAG Oncology
SAG Diabetes
SAG Anti-Infectives
SAG HIV / Antiviral
Pharmacogenomics
Biosimilars
Radiopharmaceuticals
Biostatistics
Respiratory
Gastroenterology
Blood Products
Patients & Consumers
QWP*
Cardiovascular
Vaccines
CHMP
SWP*
CNS
Urology
PhVig*
Cardiovascular
Rheumatology
Sci. Advice WP
BWP*
Immunology
Vaccines
Infectious Diseases
Pharmacokinetics
Oncology
Working parties
Disciplines
Scientific Advisory Gps
* 1 / MS representation

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.

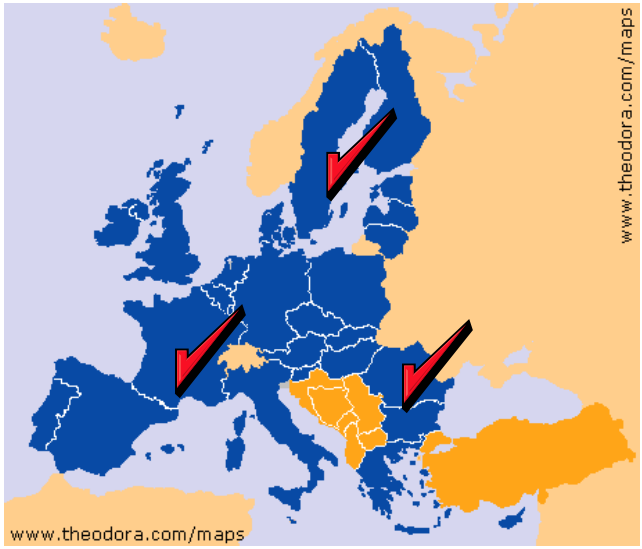
In particular, Member States shall be *free to choose* from the particulars shown in the marketing authorisation those *therapeutic indications* and *pack sizes* which will be covered by their social security bodies. "

The EU procedures of marketing authorisations

Centralised Procedure (via EMA)

Mutual Recognition procedure

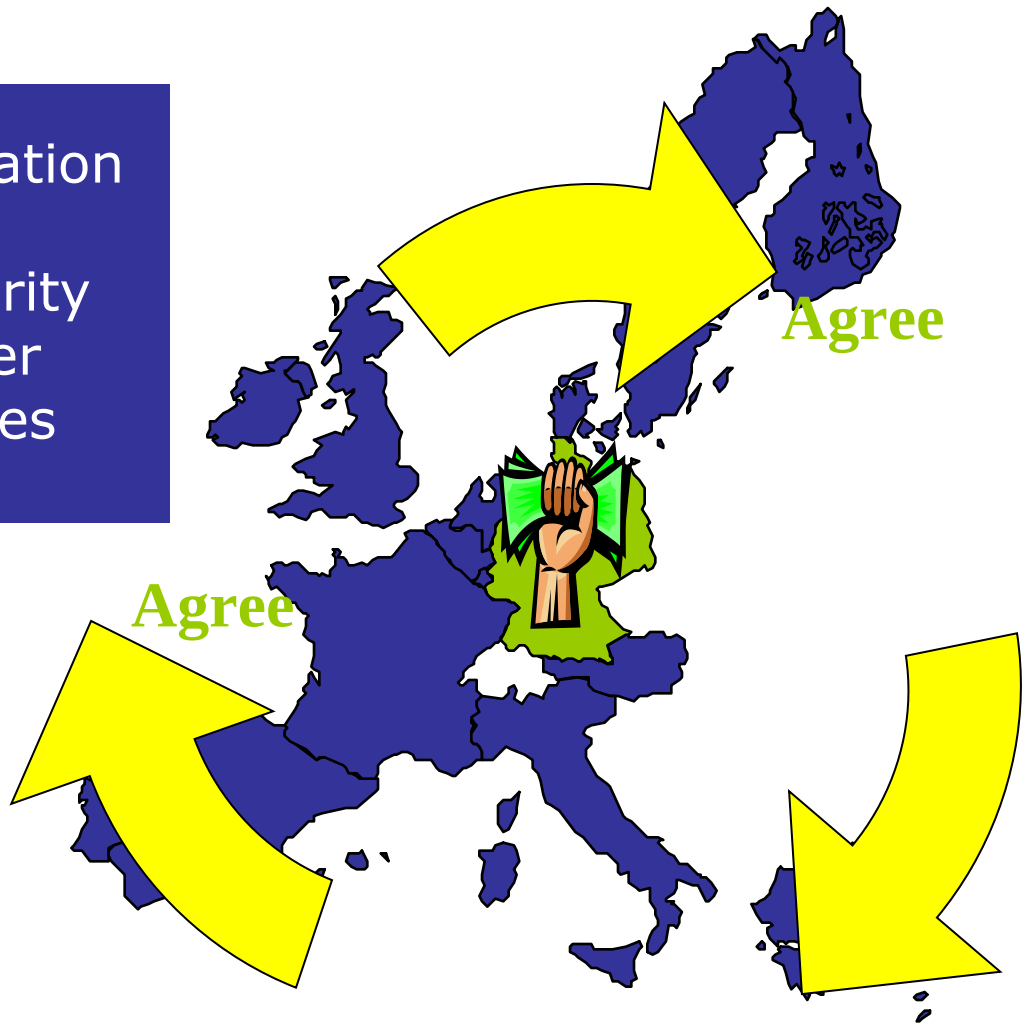
Decentralised Procedure



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

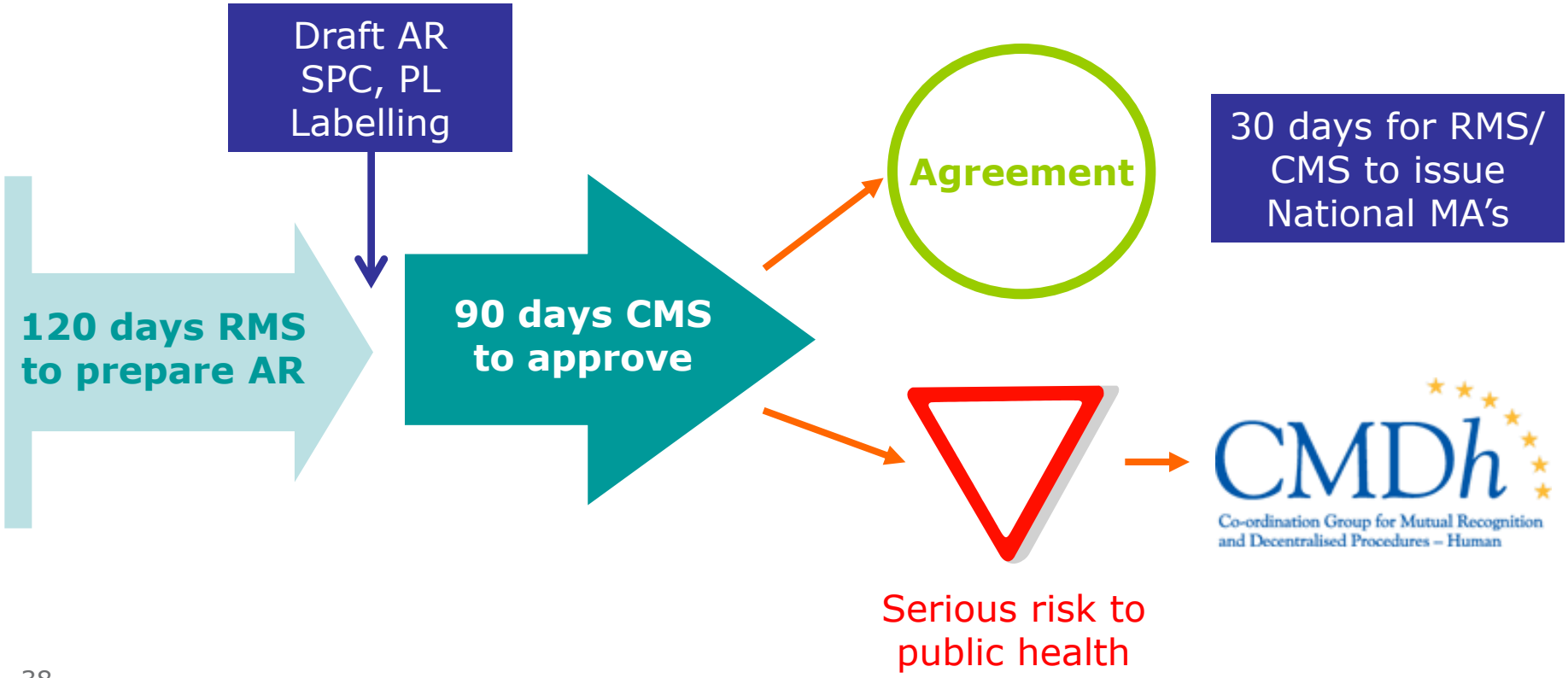
The mutual recognition procedure

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

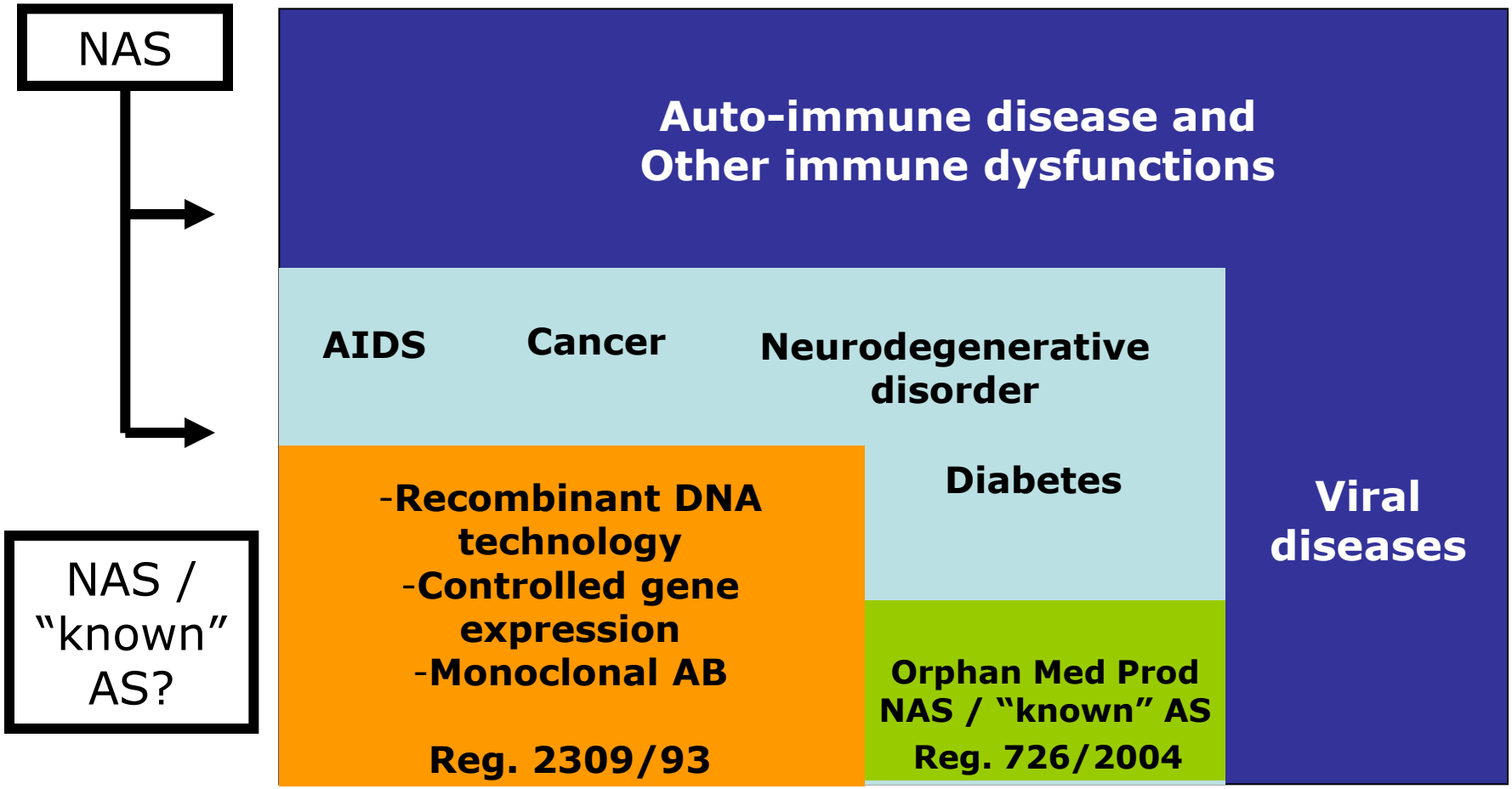
Centralised Procedure = "reserved" procedure

- 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

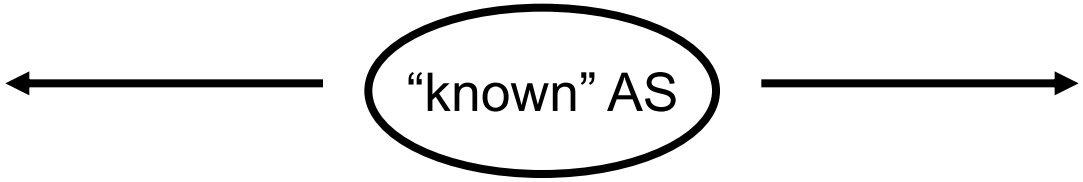
Art. 3(2)(b)

Significant Innovation

Therapeutic &/or Scientific &/or Technical

OR

Interest of Patients at Community Level

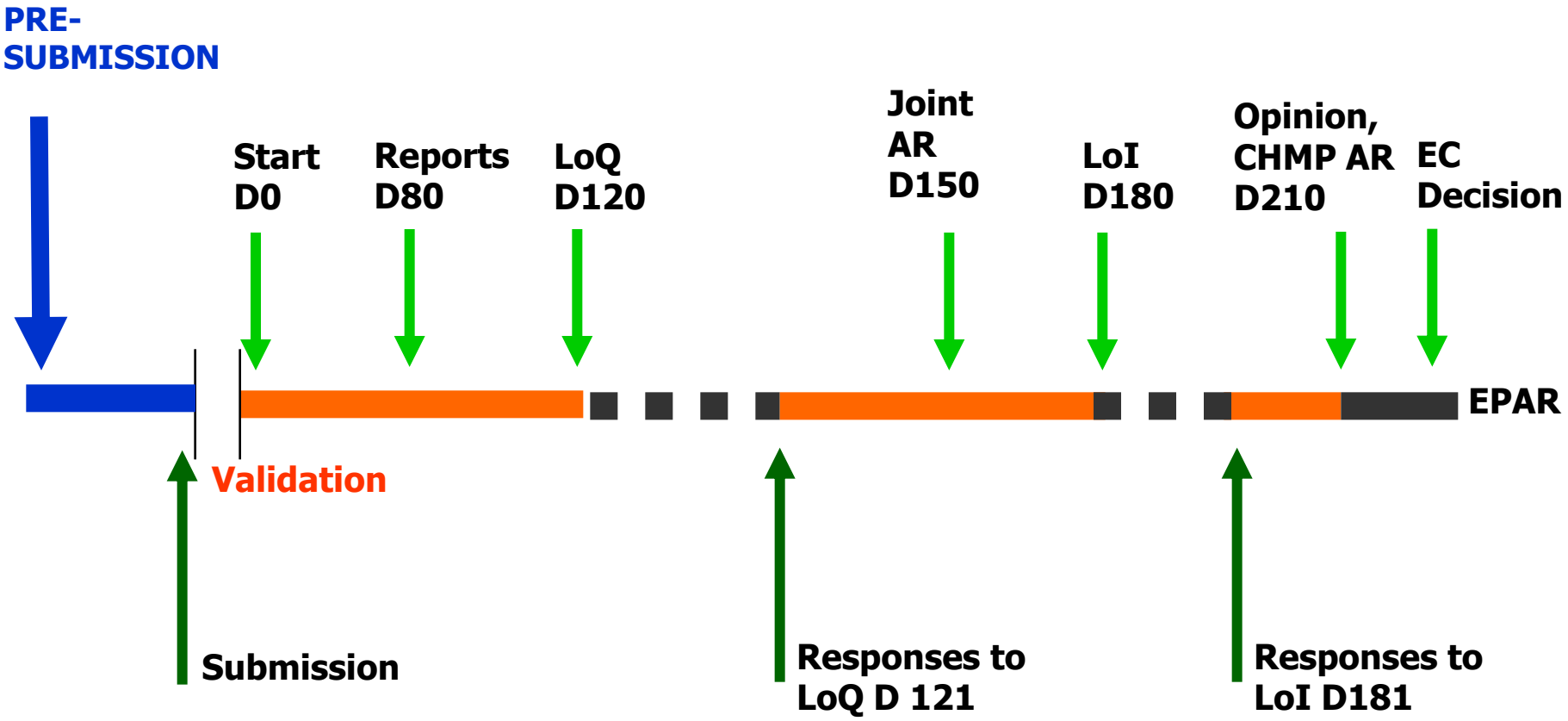


Structure of EU Marketing Authorization Applications (MAAs)

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

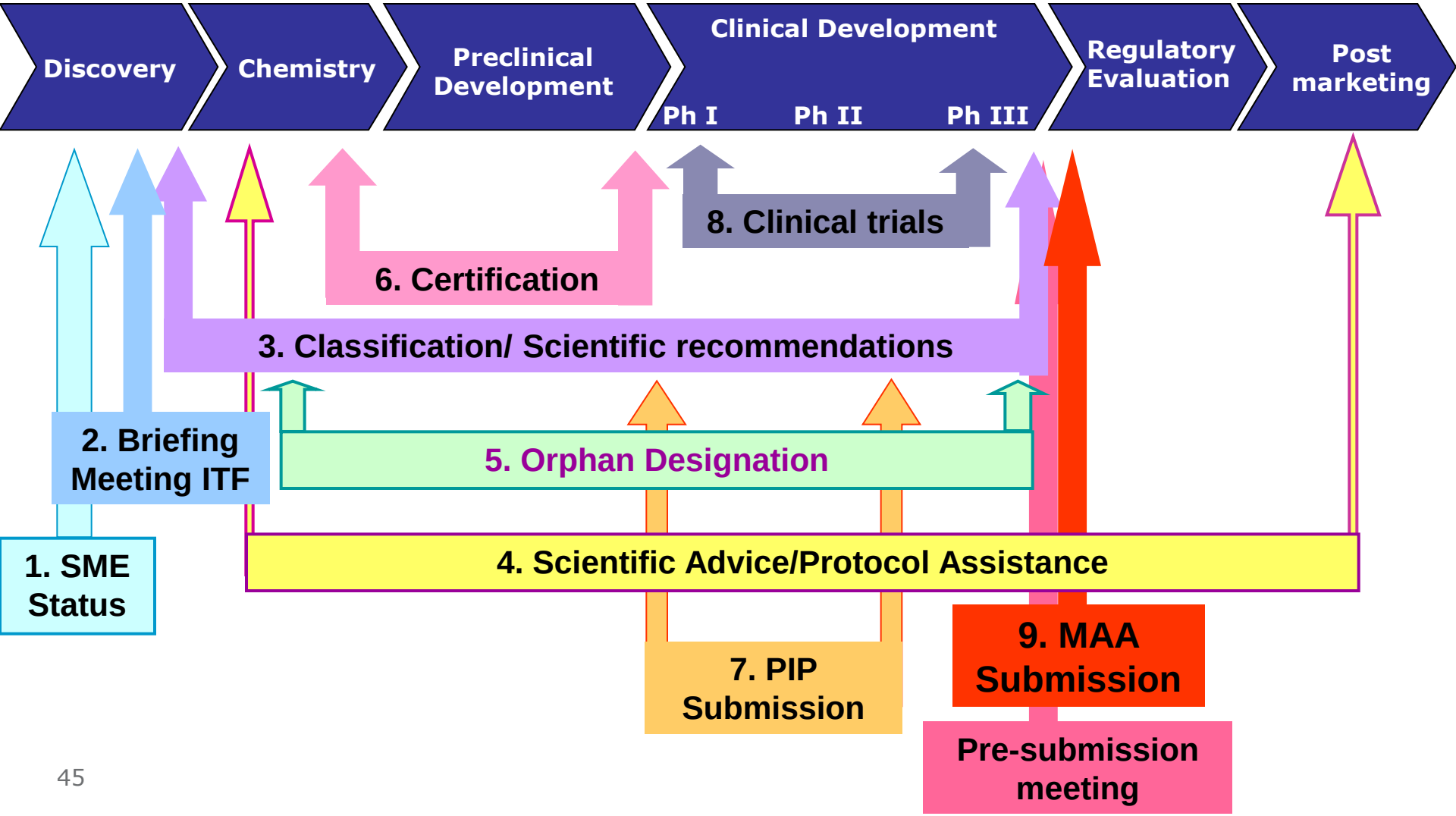


AR: Assessment Report, EPAR: European Public Assessment Report, LoQ: List of Questions, LoI: List of Outstanding Issues

Active time: evaluation

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

Regulatory processes throughout the EMA



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Thank you for your attention!

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