European Commission

Pharmaceutical Committee

Update on the European Commission expert group on Safe and Timely Access to Medicines for Patients (STAMP)

28 April 2016

Health and Food Safety

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STAMP discussions

- **Three meetings** in 2015
- Experiences from national schemes for early patient access to innovative medicines
- Optimisation of existing regulatory tools for early access
  - → **Conditional marketing authorisations (CMA)**
  - → **Accelerated assessment procedure and PRIME**
  - → **EMA's adaptive pathways pilot project**

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STAMP discussions

- **10 March 2016 meeting**
- Updates on early access initiatives – adaptive pathways and PRIority Medicines (PRIME)
- New topics
  - → **repurposing of established medicines**
  - → **real world evidence**
  - → **compassionate use**
  - → **personalised medicine**

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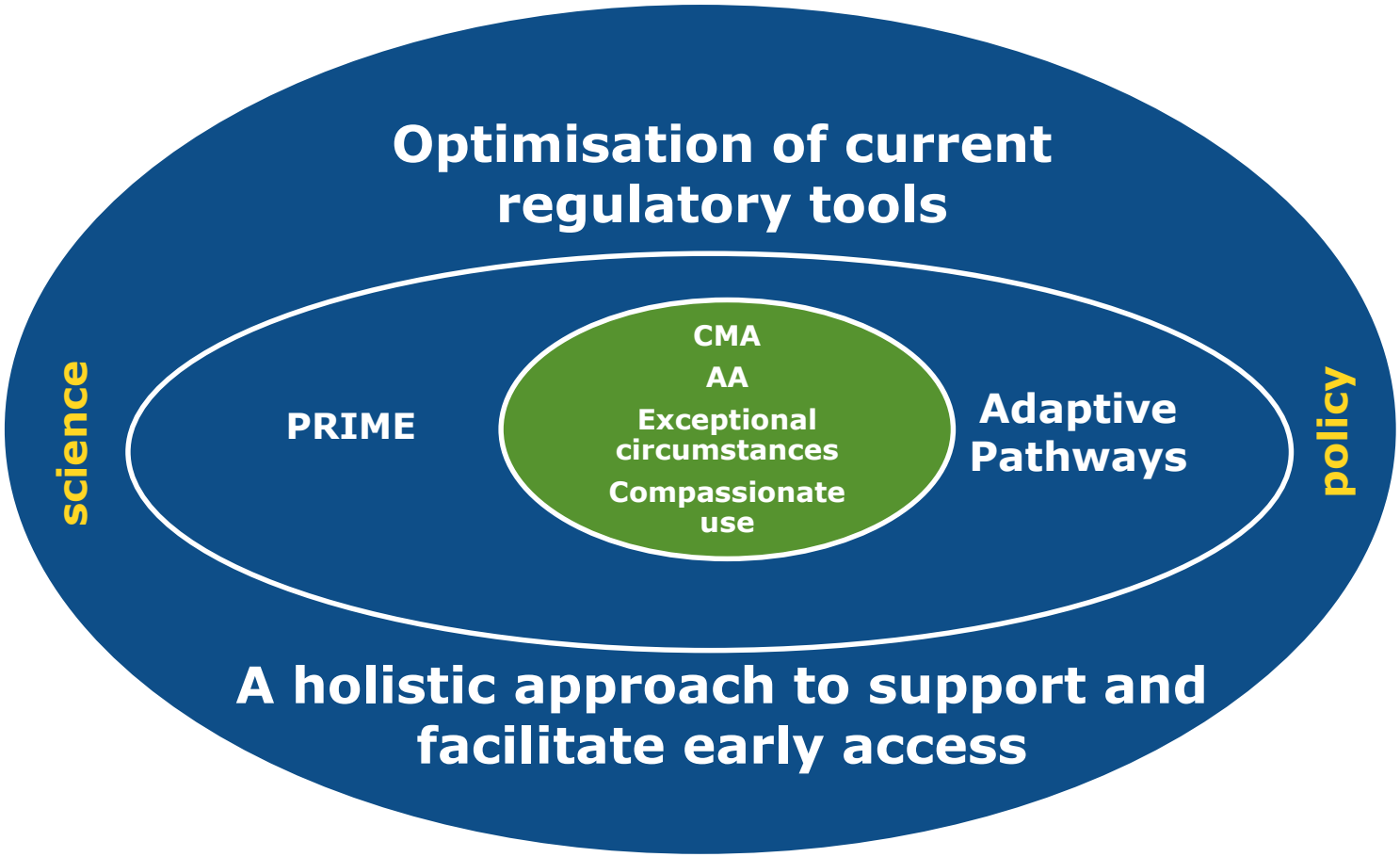
Bigger picture



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PRIME – Priority Medicines

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Problem statement

- Drug development is scientific and regulatory challenging
- Opportunity for better use of the existing regulatory tools, especially for promising new medicines with high public health potential
- Importance of early dialogue with regulators and scientific advice
- Complementarity with initiatives in place at National level
- Difficulty in obtaining capital investments for academic sponsors and SMEs
- EU Medicines Agencies Network Strategy to 2020 "to ensure timely access to new beneficial and safe medicines for patients"

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PRIME - discussion at STAMP

- **Eligibility criteria:** Criteria of major public health interest and in particular therapeutic innovation for selection of 'PRIME' products

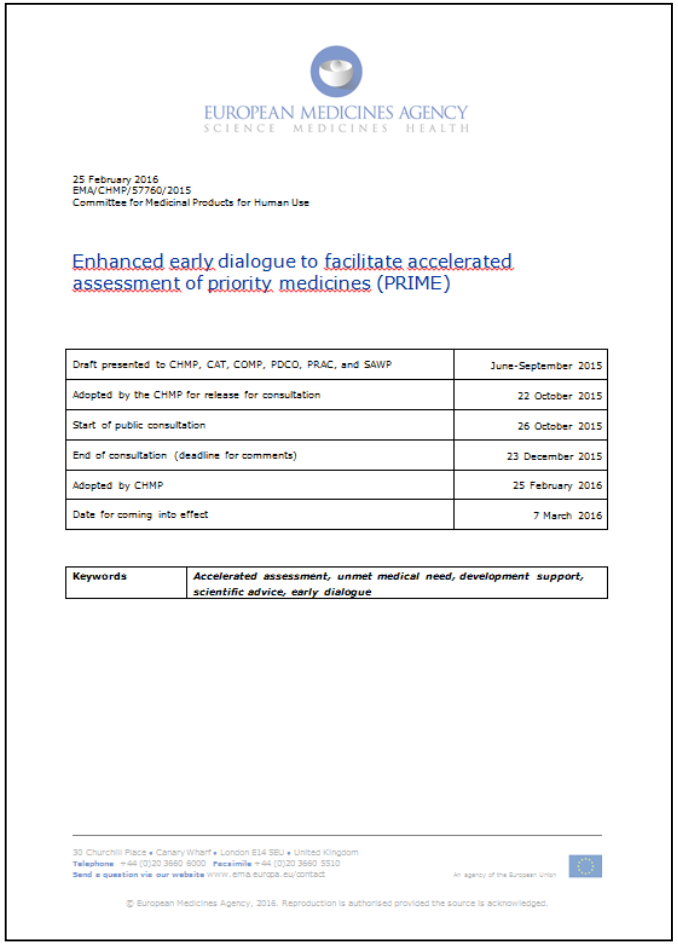
- ✓ *Need for clear eligibility criteria for selection and if necessary withdrawal of medicinal products from the scheme*

- ✓ *For real innovative products for unmet medical needs with high public health impact (major therapeutic advantage over existing therapies).*

PRIME

After discussions at all STAMP 2015 meetings

- Draft reflection paper adopted by CHMP
- Public consultation
- Review of comments and revision of the document
- Finalisation and adoption of the document
- Scheme launched on 7 March



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SCIENCE MEDICINES HEALTH

25 February 2016
EMA/CHMP/57760/2015
Committee for Medicinal Products for Human Use

Enhanced early dialogue to facilitate accelerated assessment of priority medicines (PRIME)

Draft presented to CHMP, CAT, COMP, PDCO, PRAC, and SAWP	June-September 2015
Adopted by the CHMP for release for consultation	22 October 2015
Start of public consultation	26 October 2015
End of consultation (deadline for comments)	23 December 2015
Adopted by CHMP	25 February 2016
Date for coming into effect	7 March 2016

Keywords	*Accelerated assessment, unmet medical need, development support, scientific advice, early dialogue*

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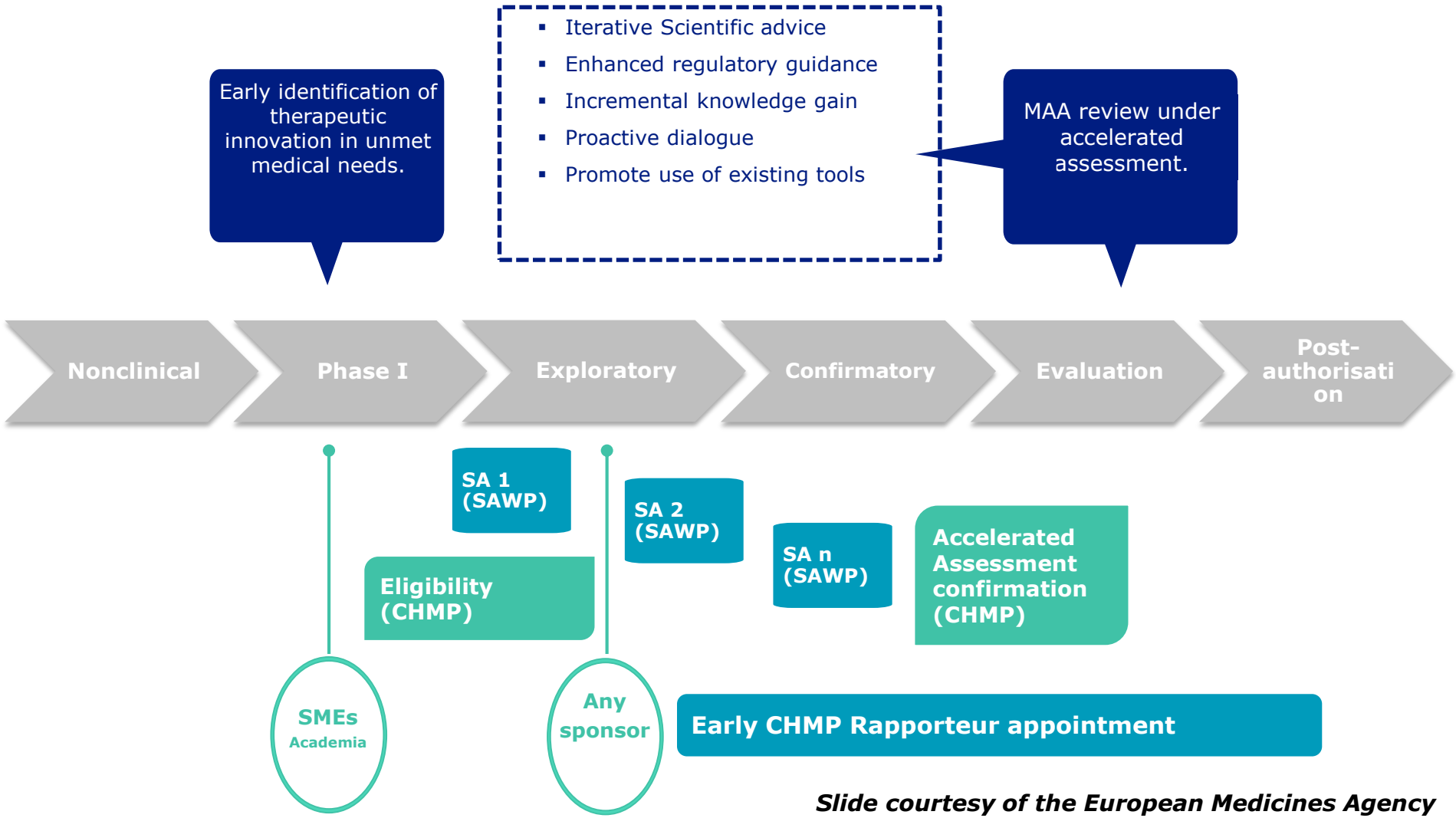
Overview of PRIME scheme



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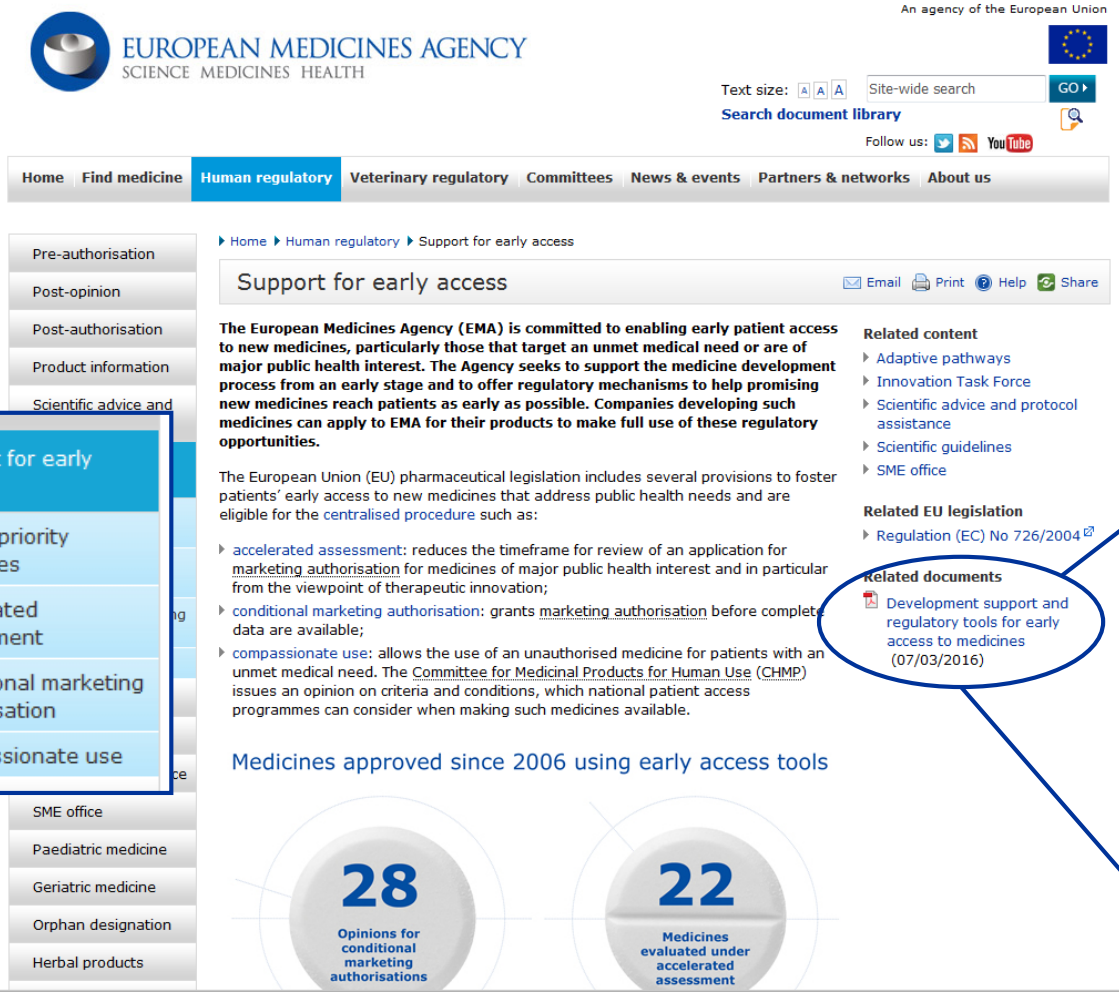
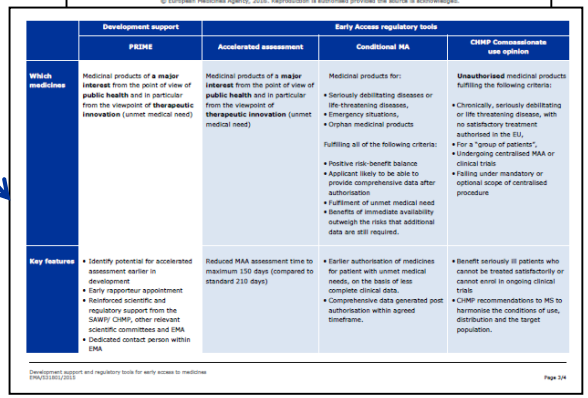
Launch of PRIME and updated guidelines





http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000856.jsp&mid=WC0b01ac058096f643

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Conditional Marketing Authorisation

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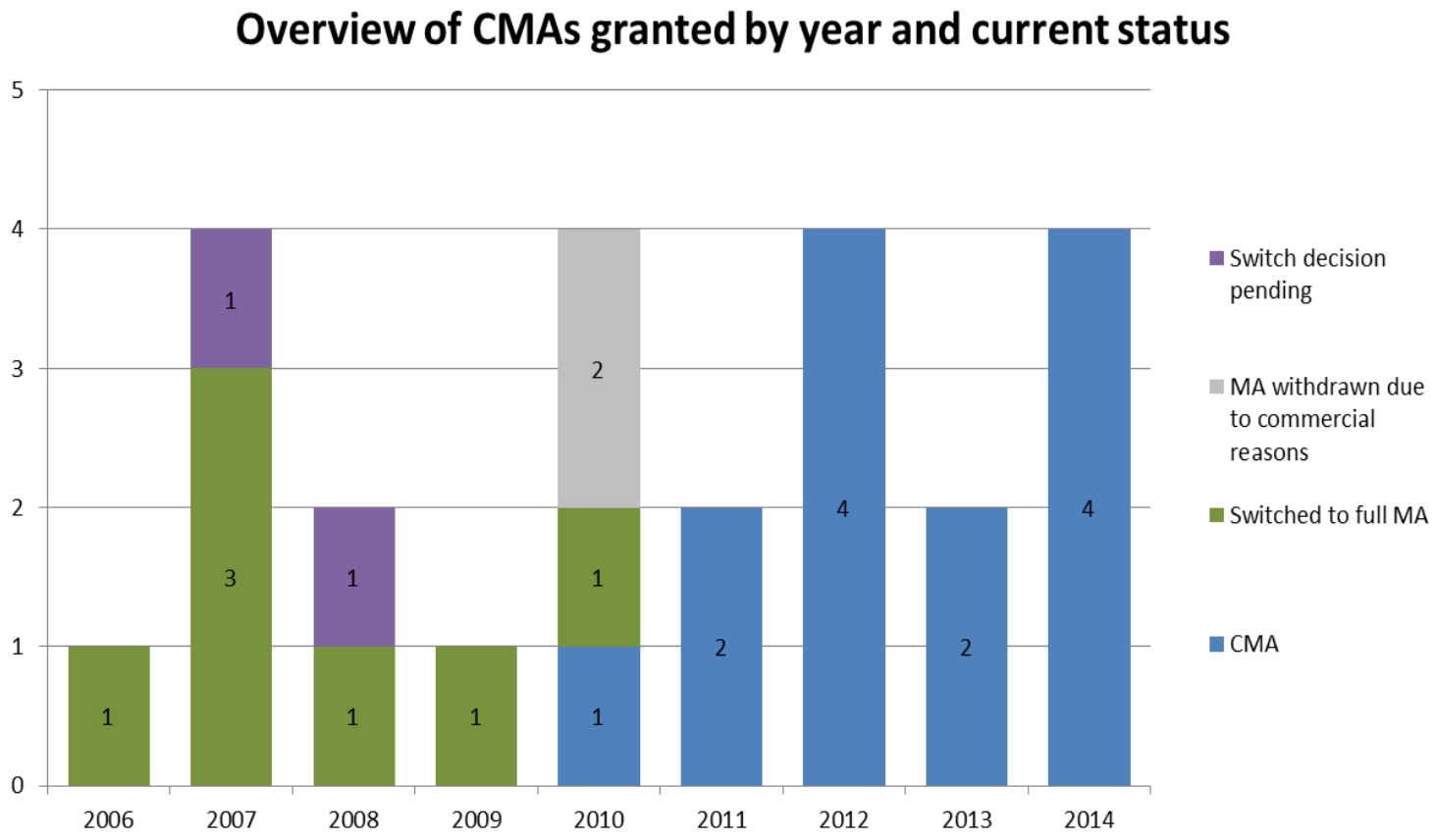
Conditional Marketing Authorisations (CMAs)

To 2014 - total 24 CMAs granted, 2 withdrawn for commercial reasons



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Conditional Marketing Authorisation (CMA)

❖ Reflection:

Can the use of CMA within the current legal framework **be optimised** by:

- ✓ clarifying and rationalising further the application of the legal requirements and procedural aspects of CMA
- ✓ improving the confidence in and perception of CMA by all stakeholders?

❖ Process:

- **CHMP:**

✓ Reflections on Conditional MA

✓ Revision of CHMP Guideline – public consultation ended 30 September

✓ CMA guideline adopted

- **STAMP:**

✓ Discussion of regulatory and legal aspects related to the criteria and application of CMA within the legal framework

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Conditional marketing authorisation Discussion at STAMP

- **Scope** limited to seriously debilitating/life-threatening diseases
- **Criteria** "unmet medical need"; "major therapeutic advantage". Consider role of improved patient care (major therapeutic advantage)

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Conditional marketing authorisation Discussion at STAMP

- **Change negative perception:**

✓ Prospectively planned CMA vs reactive CMA ('rescue solution')

✓ early dialogue including with HTA bodies

✓ Reassurance for post-authorisation phase:

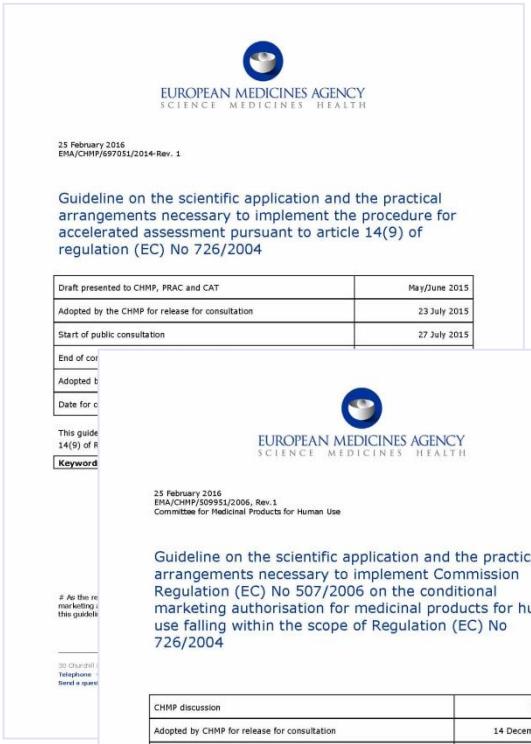
- **Feasibility of Specific Obligations (SOs) at the time of imposition**
- **Regulatory actions** to be taken in case of delays/negative outcome of SOs
- **Streamlining annual renewals** with Periodic safety update reports (PSUR) assessments, rather than requiring (re) submission of PSUR data

Update of CHMP Guidelines on accelerated assessment and conditional MA

- Reflections on the experience
- Drafting of guideline update
- Consultation with other committees
- Public consultation
- Review of comments and revision of the guideline
- Favourable opinion of the European Commission*
- Finalisation and adoption of the guideline February 2016

* for CMA guideline only

Update provided to STAMP



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SCIENCE MEDICINES HEALTH

25 February 2016
EMA/CHMP/697051/2014-Rev. 1

Guideline on the scientific application and the practical arrangements necessary to implement the procedure for accelerated assessment pursuant to article 14(9) of regulation (EC) No 726/2004

Draft presented to CHMP, PRAC and CAT	May/June 2015
Adopted by the CHMP for release for consultation	23 July 2015
Start of public consultation	27 July 2015

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SCIENCE MEDICINES HEALTH

25 February 2016
EMA/CHMP/509951/2006, Rev.1
Committee for Medicinal Products for Human Use

Guideline on the scientific application and the practical arrangements necessary to implement Commission Regulation (EC) No 507/2006 on the conditional marketing authorisation for medicinal products for human use falling within the scope of Regulation (EC) No 726/2004

CHMP discussion	July 2006
Adopted by CHMP for release for consultation	14 December 2006
End of consultation (deadline for comments)	31 March 2007
Drafting of revision 1 of the guideline	January – May 2015
Consultation with PRAC, CAT, COMP, PDCO	June 2015
Adopted by CHMP for release for public consultation	23 July 2015
Start of public consultation	27 July 2015
End of consultation (deadline for comments)	30 September 2015
Receipt of a favourable opinion of the European Commission	22 February 2016
Final guideline adopted by the CHMP	25 February 2016
Date for coming into effect	1 June 2016

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Key changes to CHMP Guideline on CMA

- Encouragement of early dialogue and **prospective planning**
- '**Positive benefit-risk balance**' vs. comprehensive dossier
- Scope of CMA to cover serious debilitation and life-threatening effects also in the **long-term**
- Exceptionally, **improvements in patient care** as a possible major therapeutic advantage
- Guidance on situations when a **second product** can still address the same unmet medical need
- Confirmation of **significant benefit for orphan medicinal products**
- Clarifications on some further aspects (e.g. compatibility with **accelerated assessment**)

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Legal aspects on CMA

- amendment of an existing marketing authorisation to include a new 'conditional' indication
- reinforce actions in case of non-compliance with specific obligations
- reinforce the prospective planning of CMA application
- CMA for orphan medicinal products

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EMA's pilot project on Adaptive Pathways

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ADAPTIVE PATHWAYS

EMA Pilot

- Launched in March 2014
- Relevant for medicines with the potential to treat serious conditions where there is an unmet medical need.
- Cooperation between a wide range of stakeholders

How AP fits within the current EU regulatory framework?

- **Scientific issues-EMA pilot project**
- **Legal-policy issues-28 MSs at Pharmaceutical Cttee**

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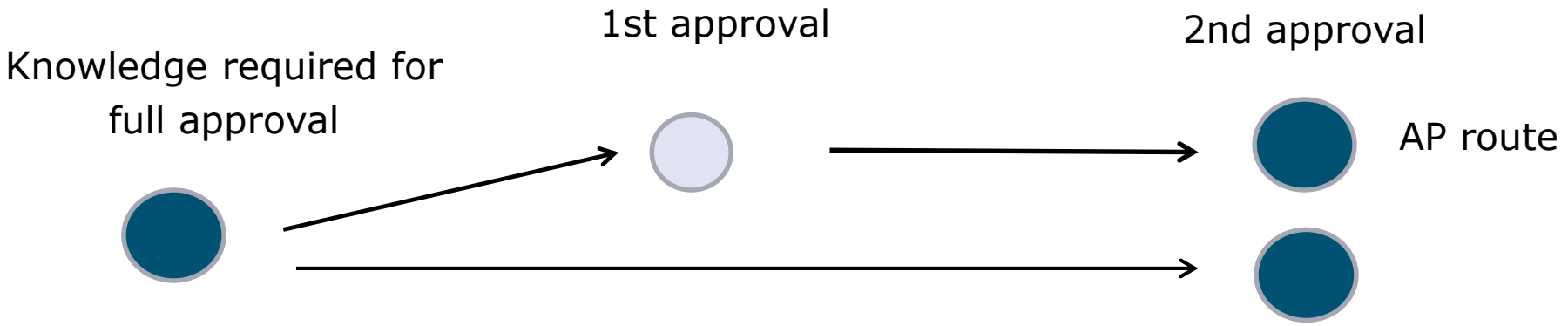
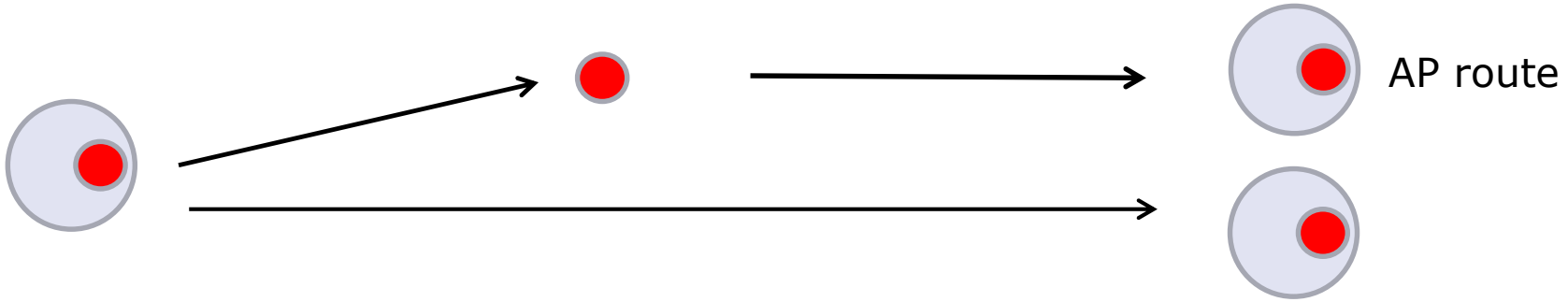
The Adaptive Pathways concept

1) Conditional approval scenario



2) Expansion of indication scenario



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Adaptive pathways Discussion at STAMP

Some of the **issues under discussion**:

- ✓ Involvement of other stakeholders, particularly HTA bodies
- ✓ How to deal with real world data and registries in the process
- ✓ How to govern the 'adaptive period' dealing with patients, healthcare professionals, HTAs and payers
- ✓ How to facilitate harmonisation/interchange between data sources
- ✓ Tools to control prescription
- ✓ A questionnaire was circulated to the members of the STAMP

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NL Presidency expert meeting:

- positive interaction between different experts
- demand for better involvement of whole “chain” from beginning
- upstream: already quite a lot of exchange of information between MA and HTA (more effective?)
- downstream: complex as different health systems
- opportunities: common problems, alignment of patient

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EMA questionnaire on adaptive pathways

- other stakeholders need to be involved, for planning and implementation
- product prioritisation - Who should select the products?
- meaning of “need” (clinical, public health, cost reduction?)
- entry and exit schemes
- joint guideline development
- prescription controls
- feasibility of post-authorisation data acquisition
- making the most use of available data, access to other stakeholders

STAMP 4th meeting 10 March 2016

- Repurposing of established medicines/active substances
- Real world evidence (RWE) data collection
- Compassionate use
- Personalised medicines

Discussion on Repurposing

- Barriers to repurposing
- Potential incentives
- Off label use
- Collection of information from Member States
- Regulatory options

Discussion on Real World Evidence

- Examples of collection of real world data presented
- Access to and use of data
- Link to adaptive pathways pilot

Discussion on Compassionate Use

- Presentations by EMA and industry
- Requests for CHMP opinion on conditions of use of a medicine in compassionate use
    - **Exploration of why not widely used**
- Member States requirements

Discussion on Personalised medicine

- 7 December 2015 Council Conclusions
- Presentation of ongoing and future research activities
- Views sought on potential impact on design of clinical trials, authorisation and post authorisation stages
- *In vitro* diagnostics considered an important issue

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Thank you for your attention

More information:

http://ec.europa.eu/health/documents/pharmaceutical-committee/stamp/index_en.htm

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