The CHMP Scientific Advice/Protocol Assistance

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NEW FRAMEWORK FOR SA & PA Scope

Article 57(1) (n) of Regulation (EC) No 726/2004:

- **"the Agency, acting particularly through its committees, shall undertake the following tasks: Advising undertakings on the conduct of the various tests and trials necessary to demonstrate the quality, safety and efficacy of medicinal products"**

Article 6 of Regulation (EC) No 141/2000

- **Protocol Assistance = Scientific Advice for companies developing Orphan Medicinal Products**

NEW FRAMEWORK FOR SA & PA
Legal basis

Regulation (EC) No 726/2004

- **Scientific Advice Working Party, standing Working Party**
- **Modernised framework allowing for advice to companies, in particular, small and medium sized enterprises**
- **More general and in-depth Scientific Advice**
- **Scientific Advice for the development of new therapies**
- **Involvement of, in particular, patients' organisations and health-care professionals' associations**

NEW FRAMEWORK FOR SA & PA Scope

In particular:

- **Products intended for the new mandatory centralised procedure**
- **Emerging therapies and New therapies**
- **Safety aspects**
- **Conditional marketing authorisation**
- **Exceptional Circumstances**
- **In the context of WHO opinion**
- **Significant clinical benefit for orphan drugs**

Quality requests

Quality: 20% of the requests

- **Comparability (38%)**
  - **Change in manufacturing**
  - **Biotechnology ‘similarity’**
  - **Change of formulation**
- **Stability (15%)**
- **TSE, viral safety (7%)**

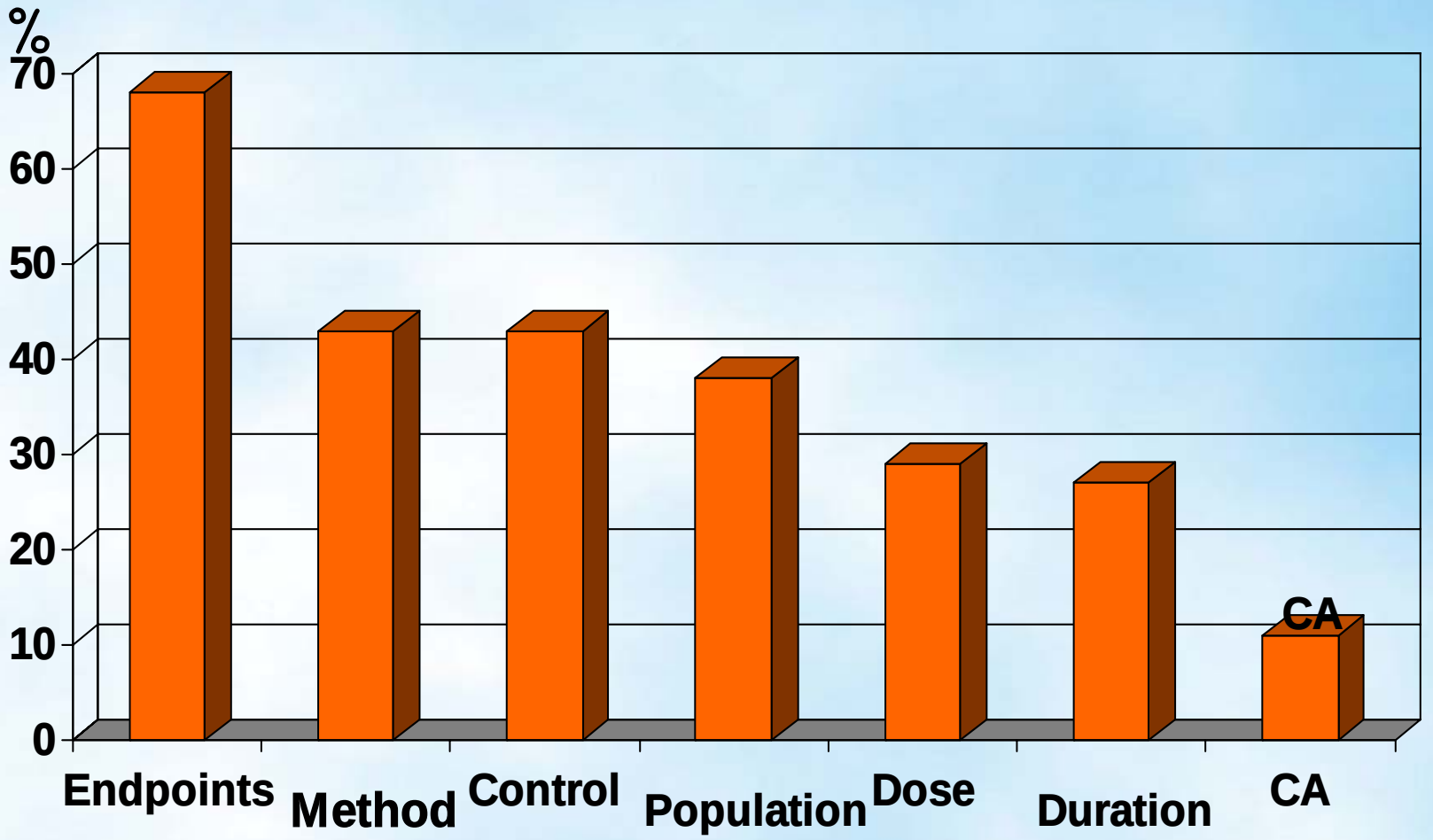
Preclinical requests

Preclinical: 30%

- **Carcinogenicity (waivers, timing, models) 38%**
- **Repro-toxicity (waivers/timing) 21%**
- **Bridging programme (e.g. new indication) 16%**
- **Studies in juvenile animals 3 %**

- **New hot issue: Pharmacological models for biological products**

Frequent clinical issues



Clinical efficacy

Endpoints

- **Primary (75% requests)**

- **Choice, acceptability, relevance**
- **Surrogate as opposed to hard clinical endpoints?**
- **Composite**

- **Secondary (30%)**

Clinical study methodology

- Non Inferiority – Superiority (28%)
- Analysis
- Blinding/Open trials
- Interim analysis / Phase II-III seamless designs: dose selection and confirmation, adjustment of sample size
- Number of studies for registration
- Conditional Approval
- Paediatric development

Scientific Advice
Impact on Marketing Authorisations

- **Begins to become visible ?**
  - **SA seems to correlate with positive outcome**

<u>but</u>

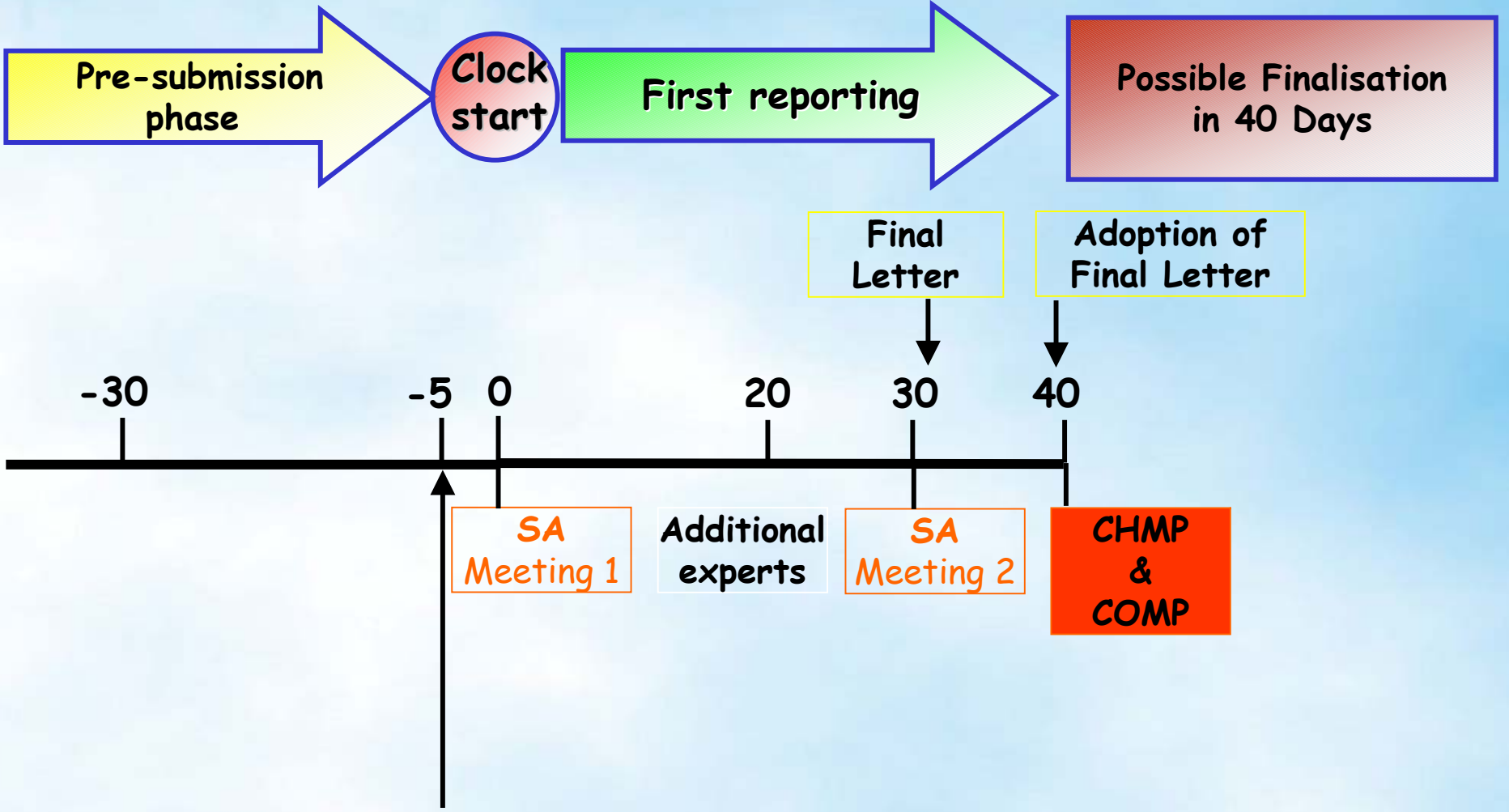
- **Scientific Advice is not a guarantee for positive outcome:**
  - **SA does not save weak data**
  - **SA does not have an impact if not followed**
  - **SA cannot have an impact if relevant issue was not part of the SA request**

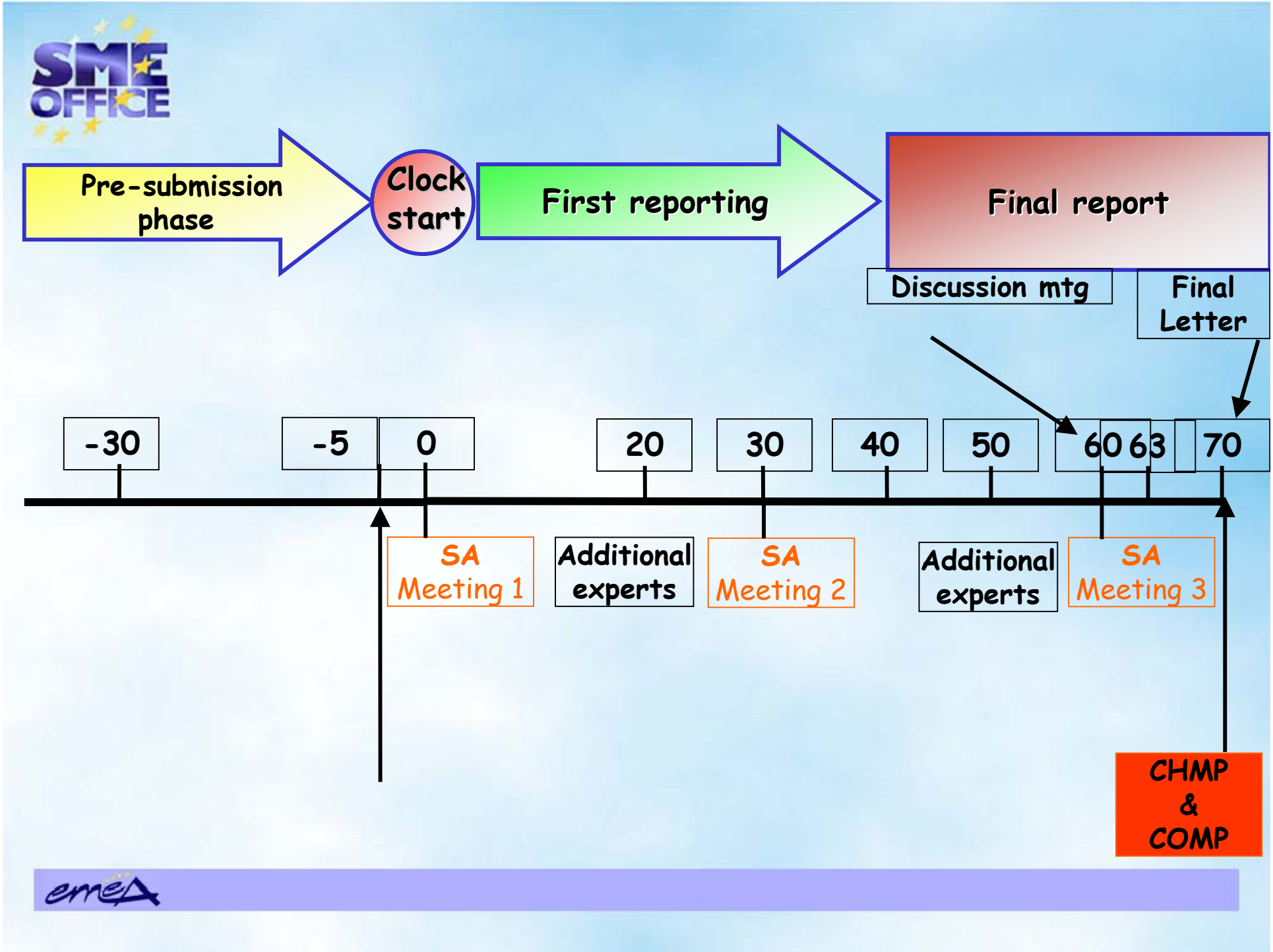
Procedure

A streamlined 70-day procedure (maximum) with possibility of finalisation in 40 days

Pre-submission meetings (still OPTIONAL)

- **with systematic involvement of co-ordinators and experts**
- **Receive early feedback on content**
- **Increase quality of request before start of procedure**


Pre-submission phase
Clock start
First reporting
Possible Finalisation in 40 Days
Final Letter
Adoption of Final Letter
-30
-5
0
20
30
40
SA Meeting 1
Additional experts
SA Meeting 2
CHMP & COMP


Pre-submission phase
Clock start
First reporting
Final report
Discussion mtg
Final Letter
-30
-5
0
20
30
40
50
60
63
70
SA Meeting 1
Additional experts
SA Meeting 2
Additional experts
SA Meeting 3
CHMP & COMP

Follow-up request

A new broader definition for follow-up advice:

- **Any subsequent request falling within the same therapeutic indication and area(s) as the initial request.**
- **Area = quality, or preclinical, or clinical including pharmacovigilance/risk management aspects…**

Follow-up request

Impact of the change:

More flexibility with reduced fee:

- **not restricted to the questions raised in the initial request. Initial request may be only on the dose-finding study, subsequent request on Phase III will attract only a reduced follow-up fee**

Opportunity for more interactions with SAWP

- **To ensure continuity for the CHMP support to the development of the medicinal product to reduce the uncertainty of the Marketing Authorisation outcome.**

Scientific Advice
Pre-Submission Meetings

- **Guidance on SA procedure & structure / content of SA request**

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EMEA SA Guidance Document
www.emea.europa.eu -
Regulatory Guidance - Application Guidance

Scientific Advice
Veterinary SA

http://www.emea.europa.eu/pdfs/vet/sciadvice/085402en.pdf

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