EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Recent update of the guidance for Parallel EMA/FDA scientific advice

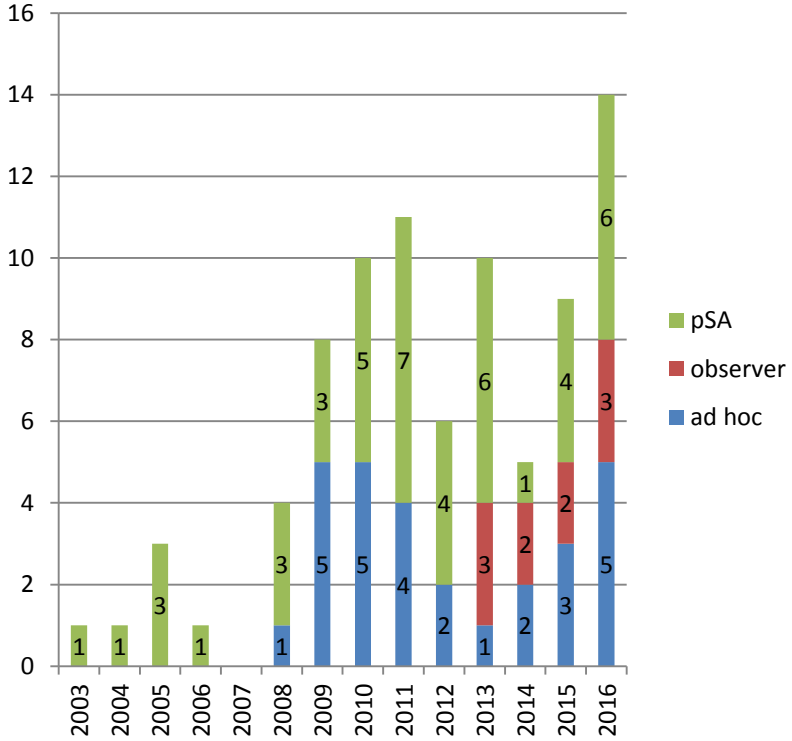
Industry stakeholder platform on research and development support, 15.11.2017

Presented by Thorsten Vetter

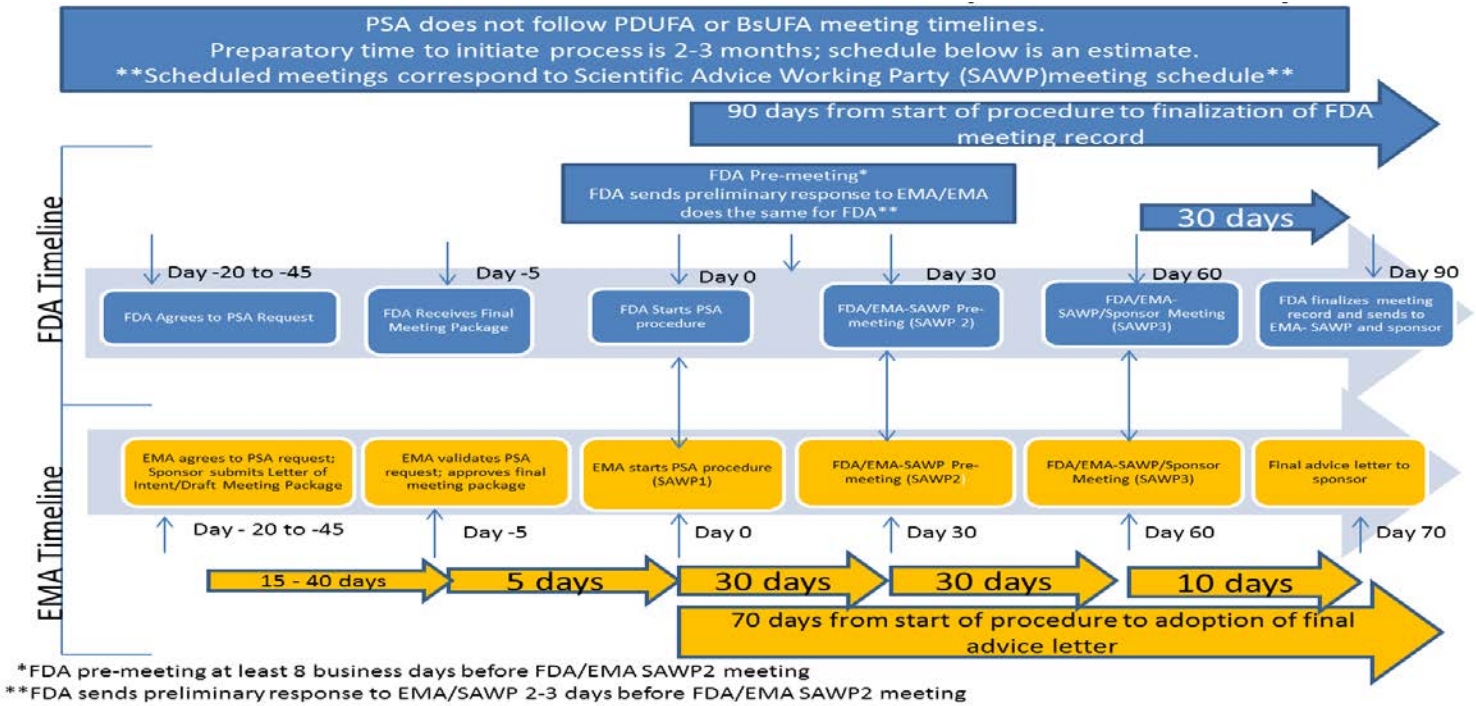
Experience with parallel FDA interactions

- Limited uptake of parallel interactions by applicants
- Reasons include lack of awareness of PSA tools, perceived process challenges, preference to discuss with Agencies separately, and the level of convergence

These considerations triggered a review of the **General Principles** for PSA which have been published in April 2017



Parallel Scientific Advice (FDA-EMA)



PSA updated General Principles (1/3)

- The goal of the PSA program is to provide a mechanism for EMA assessors and FDA reviewers to ***concurrently exchange with sponsors their views on scientific issues*** during the development phase of new medicinal products
- ***Increase dialogue*** between the two agencies and sponsors from the beginning of the lifecycle of a new product, provide a ***deeper understanding of the bases of regulatory decisions***, ***optimize product development***, and ***avoid unnecessary testing replication*** or ***unnecessary diverse testing methodologies***.
- ***Voluntary*** and usually occur at the request of the sponsor

PSA updated General Principles (2/3)

- Focus on ***sharing information and perspectives***. Achieving ***harmonization and increased convergence is a potential beneficial outcome*** of the PSA process
- **Candidates**: ***important medicinal products***, [..] for indications ***lacking development guidelines***, or if guidelines do exist, those for which EMA's and FDA's ***guidelines differ*** significantly. In addition ***biosimilars***, products with significant ***clinical safety, animal toxicology, or unique manufacturing concerns***. Previous PSAs have involved medicinal products for ***oncology, anti-infectives, rare diseases, the paediatric population, and cardiovascular disease, as well as post-licensure commitment clinical trials***.

PSA updated General Principles (3/3)

- A PSA request does not guarantee the PSA procedure will be granted
- After a PSA procedure, ***each agency will retain its individual regulatory decision-making authority regarding drug development issues and marketing applications***.
- The advice of each agency may still differ after the joint discussion
- However, ***both agencies will strive to provide PSA responses that are convergent***.

New element: Consultative Advice

- Alternatively both agencies can engage in a "***consultative advice***". In this case, a limited number of experts from either side will be invited to participate in the discussions of the other agency.
- Allows sponsors to request scientific advice from one regulatory agency and **concurrently notify the other regulatory agency** of the request. At the invitation of the first agency, the **second will participate in the sponsor meetings or teleconferences as able**. Unlike the parallel scientific advice process, the **second** agency will be expected to **only engage on top level issues**. The review and sponsor meeting will follow the timelines of the regulatory agency from whom the sponsor initially seeks scientific advice. **Only the initially contacted regulatory agency will provide written scientific advice**

Examples for parallel EMA/FDA scientific advice

Type of engagement	Product	Topic	Outcome
Participation as observers	DILI Qualification Advice SAFE-T / IMI	Proposal for a panel of markers to improve DILI monitoring in clinical trials	FDA observed F2F meeting and pursued independent Qualification procedure, FDA and EMA issued Letters of Support
Formal parallel SA/QA	Licensed medicinal product	Agreement on design of PAES (post-authorisation efficacy study)	Tripartite meeting and discussions between agencies allowed to harmonise the PAES design
Formal parallel SA/QA	Investigational product	Genetic GI disease / paediatric development	Very helpful discussion on programme design, use of natural history data to identify suitable efficacy endpoints, historic controls, FU planned on final Ph2/3 design

Take home messages

- Parallel interactions are very helpful tools and uptake should be encouraged
- Important to chose right tool for purpose
- Particular benefit foreseen in the context of PRIME/Breakthrough Designation
- Update of General Principles provides clear framework and indicates feasibility without significant increase in procedural burden

Revised general principles:
http://www.ema.europa.eu/ema/pages/includes/document/open_document.jsp?webContentId=WC500014868

Any questions?

Further information

Scientificadvice@ema.europa.eu

European Medicines Agency
30 Churchill Place • Canary Wharf • London E14 5EU • United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

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PSA Timeline Chart

Day	FDA	EMA
Anytime	Sponsor submits informal request for Parallel Scientific Advice to FDA and EMA	
Day -20 to -45	FDA agrees to informal PSA request; Sponsor submits formal PSA request to FDA.	EMA agrees to informal PSA request; Sponsor submits letter of intent (formal PSA request) and draft package
Day 0 to -24		EMA reviews draft package; appoints coordinator
Day -5	FDA receives final meeting package	EMA validates PSA request; approves final meeting package
Day 0	FDA PSA process starts	EMA PSA process starts (SAWP1)
Day 15-20	FDA pre-meeting	
Day 25-28	FDA sends preliminary responses to EMA	EMA sends preliminary responses to FDA
Day 30	Joint FDA/EMA meeting (SAWP2)**	Joint FDA/EMA meeting (SAWP2)
Day 60	Sponsor/FDA/EMA meeting (SAWP3)	Sponsor/FDA/EMA meeting (SAWP3)
Day 70 to 90	FDA issues final meeting record (day 90 for FDA)	EMA issues final advice letter (day 70 for EMA)

*PSA does not follow PDUFA or BSuFA meeting timelines. Preparatory time to initiate process is 2-3 months; schedule above is an estimate. Scheduled meetings correspond to Scientific Advice Working Party (SAWP) meeting schedule.
**Best Practice: FDA and EMA develop a list of common issues/answers to questions. Both agencies send to sponsor preliminary common issues (EMA)/answers to questions (FDA). Sponsor sends in a revised proposal and meeting package prior to SAWP3.