EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Review of pre-submission interactions in the centralised procedure and best practices

3rd Industry stakeholder platform on the operation of the centralised procedure for human medicinal products

Presented by Michael Berntgen and Hector Boix Perales on 21 April 2016

An agency of the European Union

Why talk about Pre-submission meetings?

Pre-submission meetings address product-specific legal, regulatory and scientific issues and are intended

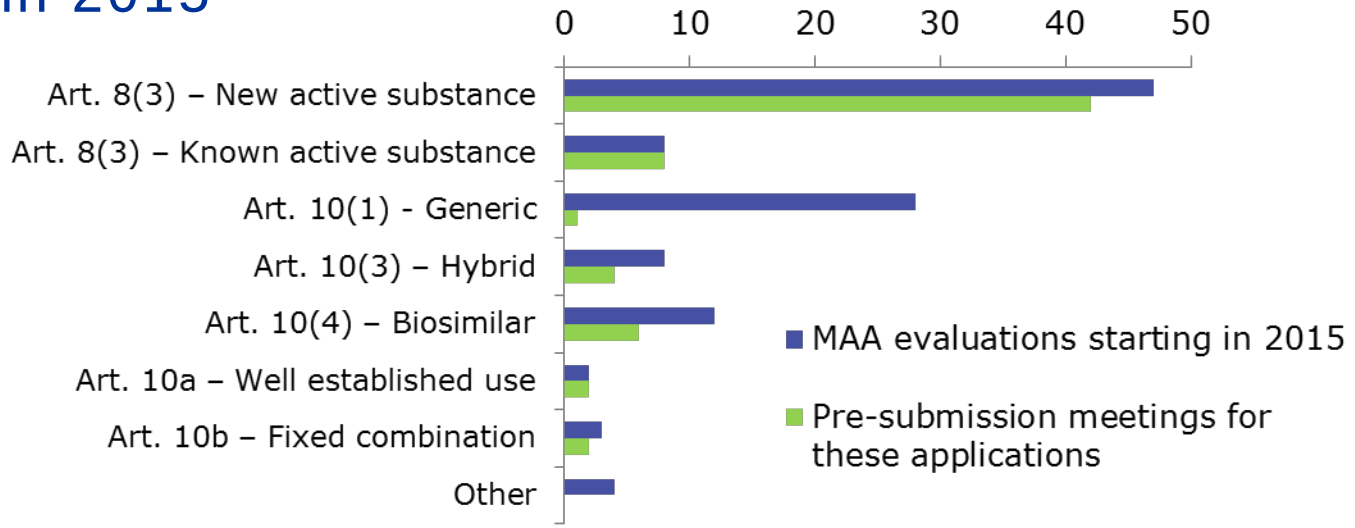
1. to facilitate the **validation** of the marketing authorisation application (MAA);
2. to support applicants in submitting applications for smooth **evaluation**.

Pre-submission dialogue is important for optimising the application dossier hence learning from experience should lead to continuous improvement of such dialogue.

Starting point: Review of experience with EMA pre-submission meetings

- Overall analysis for MAAs with evaluation start in 2015
- Detailed analysis of pre-submission meetings held in 4th quarter 2015.

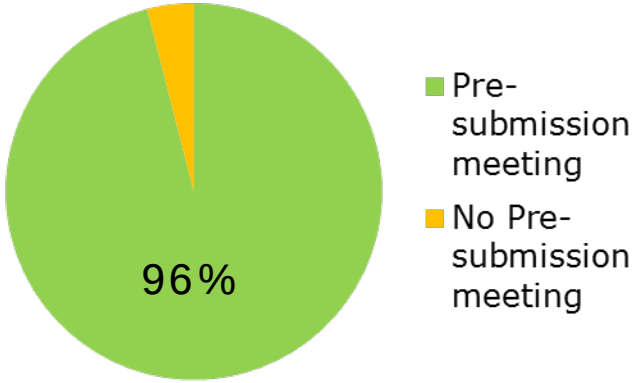
EMA pre-submission meetings for initial MAAs with evaluation start in 2015



In 2015, 58% of all applications for marketing authorisation had an EMA pre-submission meeting, and 91% of the applications were based on a "full dossier".

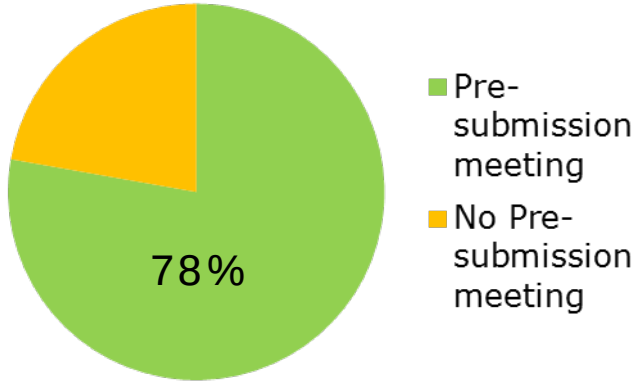
Specific aspects regarding type of product and applicant

Orphan medicinal product (N=25*)



* Of these 18 were Art. 8(3) – New active substance; 3 Art. 8(3) – Known active substance; 3 Art. 10(3) – Hybrid; 1 Art. 10a – Well established use

Small and medium sized company (N=18⁺)



⁺ Of these 12 were Art. 8(3) – New active substance; 1 Art. 8(3) – Known active substance; 1 Art. 10(3) – Generic; 2 Art. 10(3) – Hybrid; 2 Art. 10a – Well established use

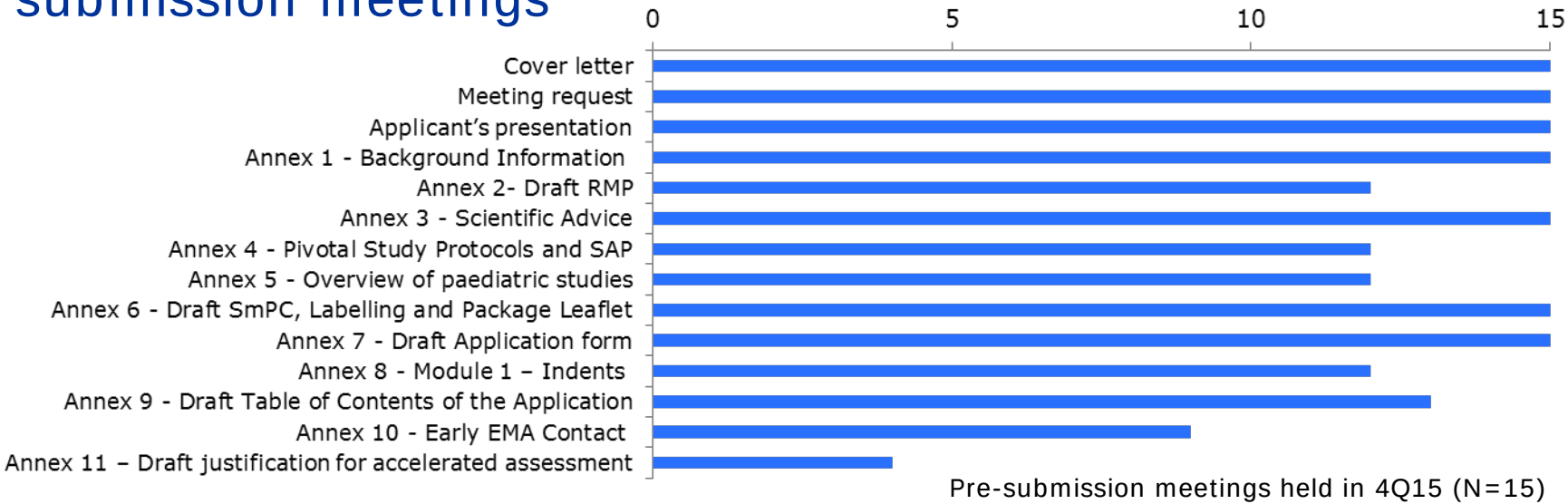
Note: MAA evaluations starting in 2015

Preparation by the EMA product team

Based on the briefing package and the presentation the team will review

- overall compliance of the intended submission package with applicable regulatory requirements,
- the draft justifications and whether additional information is needed,
- whether there are gaps that could be useful to discuss e.g. RMP-related topics
- the documentation against relevant scientific and regulatory guidelines (including relevant scientific advices considering the indication applied for and the RMP outline against similar products)
- the PI also considering other products in the same class (depending on maturity of the draft) and relevant guidance including core SmPC, as well as potential labelling, standards and mock-ups issues

Documentation provided by applicants in preparation of Pre-submission meetings

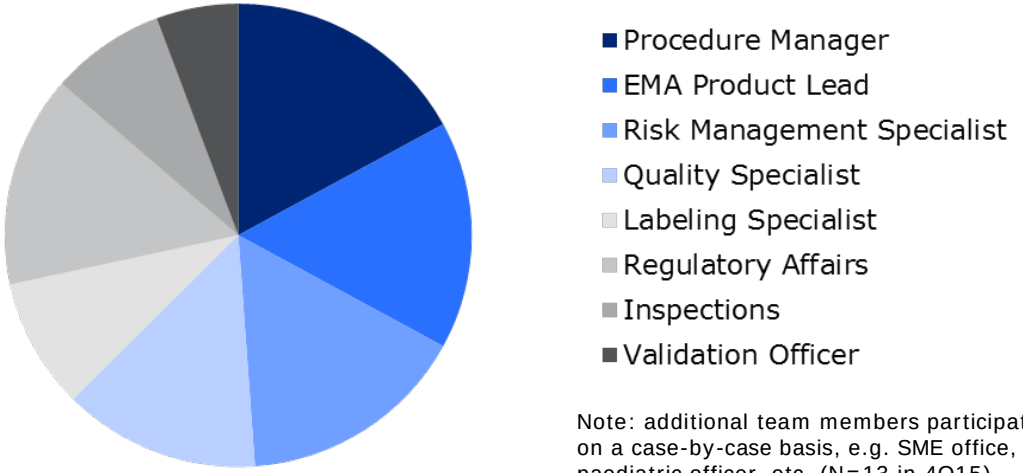


Pre-submission meetings held in 4Q15 (N=15)

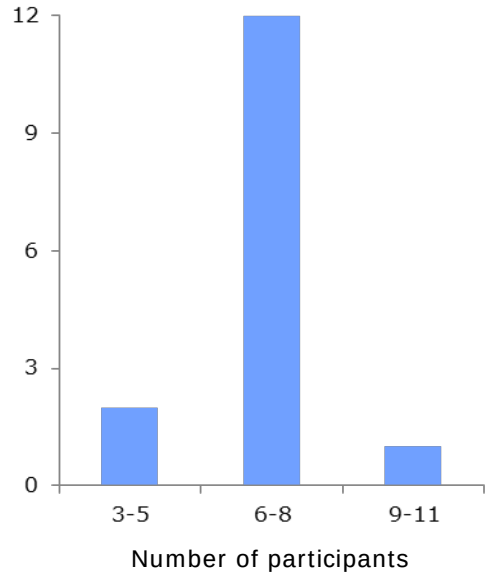
The required documentation is generally provided although some gaps are frequently identified (e.g. RMP-related documents) potentially leading to follow-up questions.

Attendance by members of the EMA Product Team

Distribution of roles from the EMA product team attending pre-submission meetings in 4Q15 (N=15):



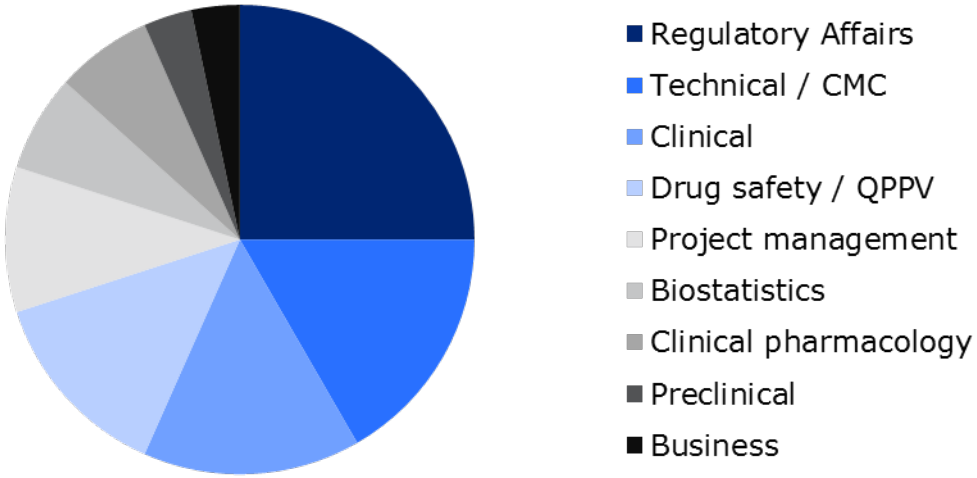
Note: additional team members participate on a case-by-case basis, e.g. SME office, paediatric officer, etc. (N=13 in 4Q15)

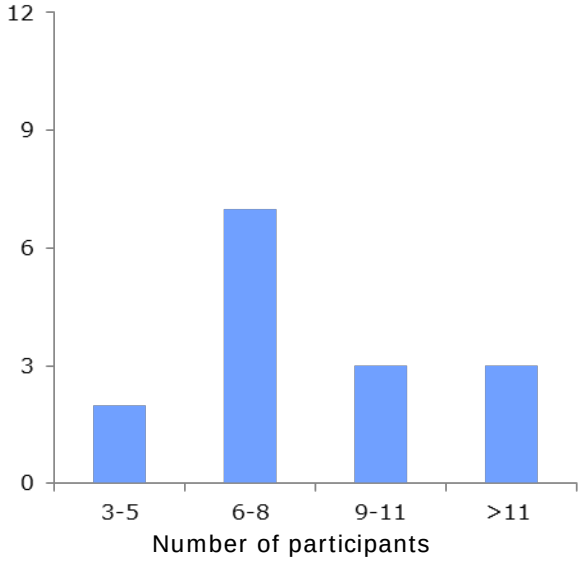


Pre-submission meetings held in 4Q15 (N=15)

Meeting participants from the applicant

Distribution of functions represented in applicants' attendees at pre-submission meetings in 4Q15 (N=15):

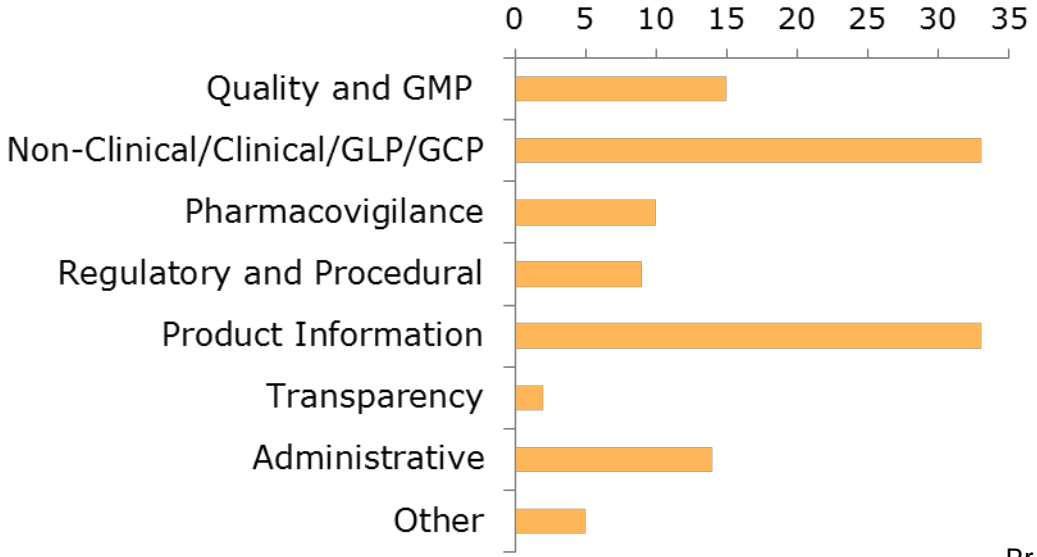




Pre-submission meetings held in 4Q15 (N=15)

Applicant's questions for discussion at the meeting

Number of questions



Most frequent topics

Quality development, GMP inspections

Clinical and paediatric development

Risk Management Plan

Legal basis, Legal status, Conditional MA, Accelerated assessment

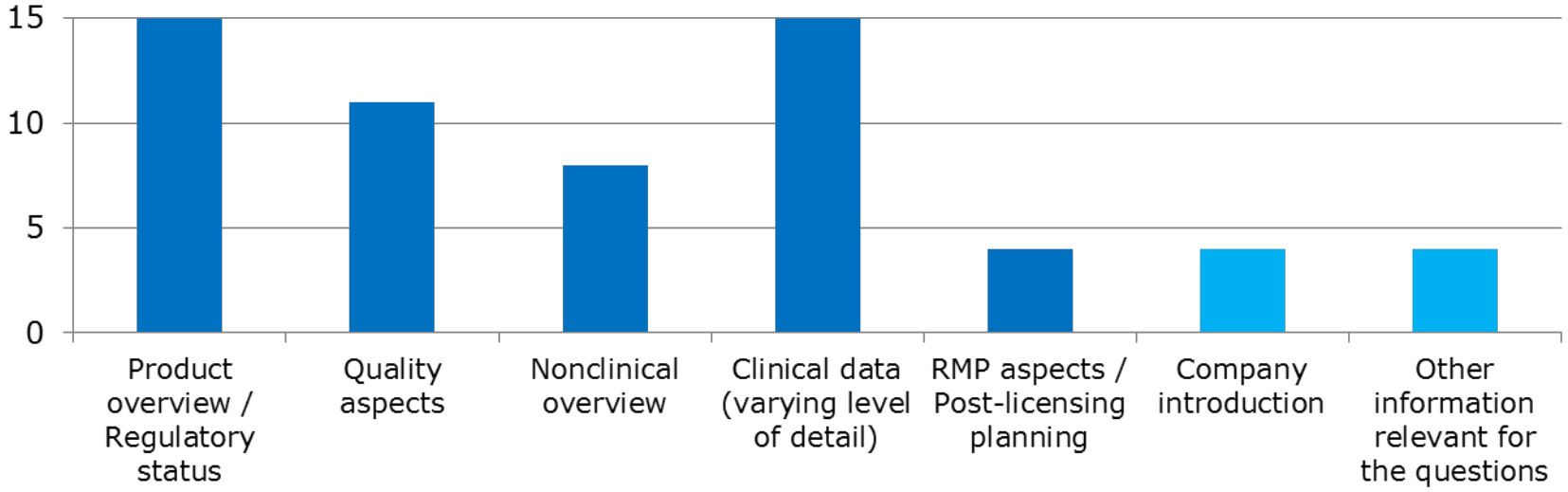
PL consultation, SPC guideline aspects

Publication of studies

Dossier format, fees

Pre-submission meetings held in 4Q15 (N=15)

Information provided in the applicant's presentation



Pre-submission meetings held in 4Q15 (N=15)

The presentations are heterogeneous with regard to extent and level of detail, particularly in the clinical area and the introduction of pivotal data for the application.

Some observations from reviewing applicant's presentations

From 15 presentations in 4Q15, all covered discussion items related to the technical completeness of the dossier in view of the validation whereas only one third posed more specific questions with relevance for preparation of the scientific evaluation.

Relevant information for the specific questions is generally provided. In 87% the questions were presented subsequent to an introductory presentation.

Variability in terms of introduction to the clinical data, from very high-level tabular listing of studies contained in the application to detailed review of study designs as well as efficacy and safety results. Total length usually 35-40 slides (maximum 80!).

Primary focus is on the review of pivotal data with other elements like prospective risk management planning or more specific labeling questions widely absent.

Highlights from this first review

EMA pre-submission meetings are held for almost all initial MAAs concerning a “full dossier”	With around 60 meetings requested per year they represent a significant investment by both applicants and regulators.
Whilst the objective is to prepare the submission and evaluation the focus by many applicants appear to be on the validation phase	There are opportunities for further improved engagement to add value to the dossier preparation for the evaluation.
Learnings from the pre-submission experience are crucial for improvement	The upcoming survey on initial marketing authorisation procedures will provide more data on experience.
Not covered by this review are pre-submission meetings with rapporteurs, timing of meetings ahead of submission as well as impact of the dialogue.	Additional reviews could be considered.

Thank you for your attention

Further information

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