EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA survey on post-authorisation procedures

2nd Industry Stakeholder Platform Meeting / Operation of the centralised procedure
9 November 2015

Presented by:

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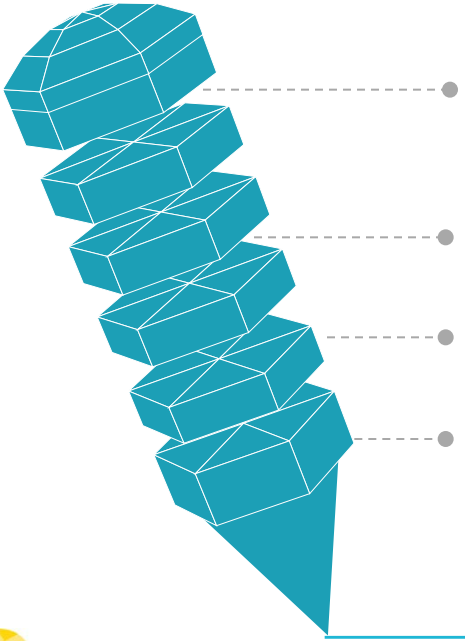
Agenda

1. Introduction
2. Summary of feedback of Industry Respondents
3. Summary of feedback of EMA Respondents
4. Overall conclusions

EMA survey on post-authorisation procedures

INTRODUCTION

Objectives



Monitor practical implementation of post-authorisation procedures, from both industry and EMA perspectives, and enhance mutual understanding of issues arising;

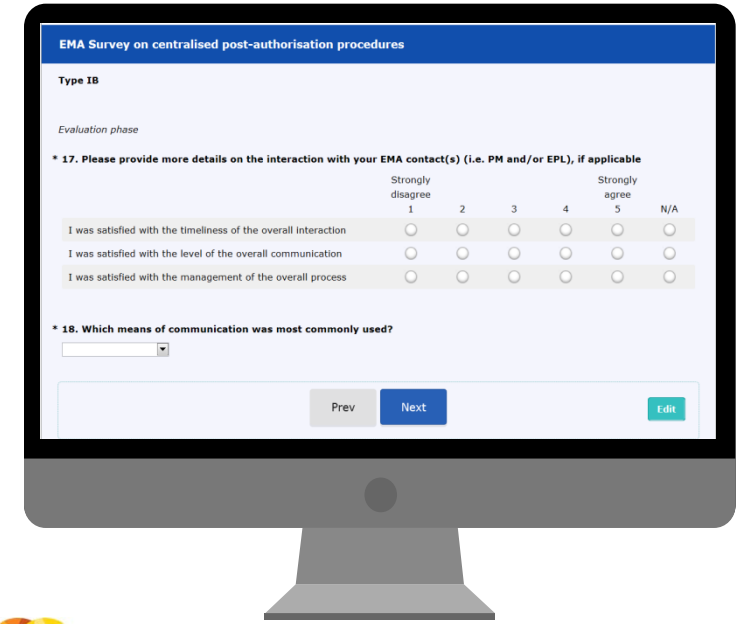
Elicit direct feedback from MAHs on certain post-marketing authorisation procedures (Type IB/II/PSURs);

Enable continuous improvement of processes and guidance related to centralised procedures;

Further increase transparency in interactions between EMA and industry stakeholders.

What do we aim to achieve?

Scope & methodology



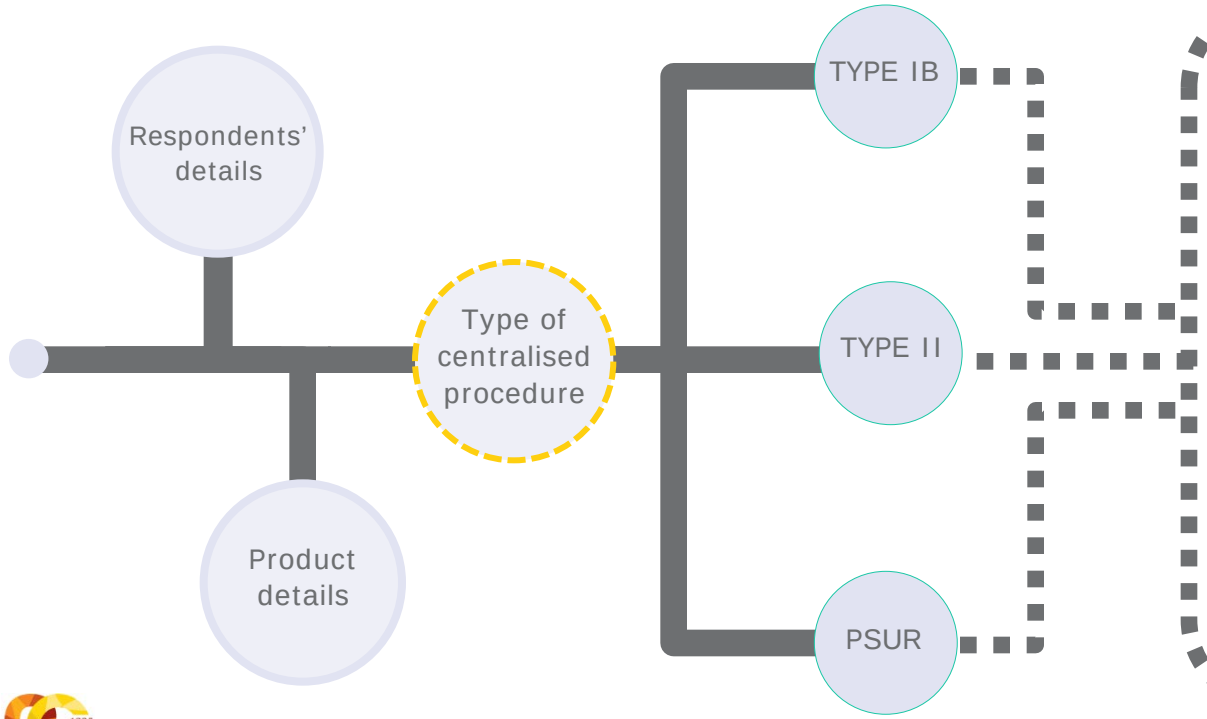
Scope: *Centralised (human) Post-authorisation procedures: Type IB/ Type II/ PSURs (CAPs only)*

Period: *1 April – 30 Sept 2015*

Methodology:

- *Web based survey*
- *~25 questions (per procedure type);*
- *Response formats:*
  - *Dichotomous Scale (Yes/ No),*
  - *5-point Rating Scale (Strongly disagree – Strongly agree: 1– 5),*
  - *Multiple choice and multiple response,*
  - *Free text;*
- *Questions mutually agreed with EFPIA WG and shared with other Industry Organisations.*

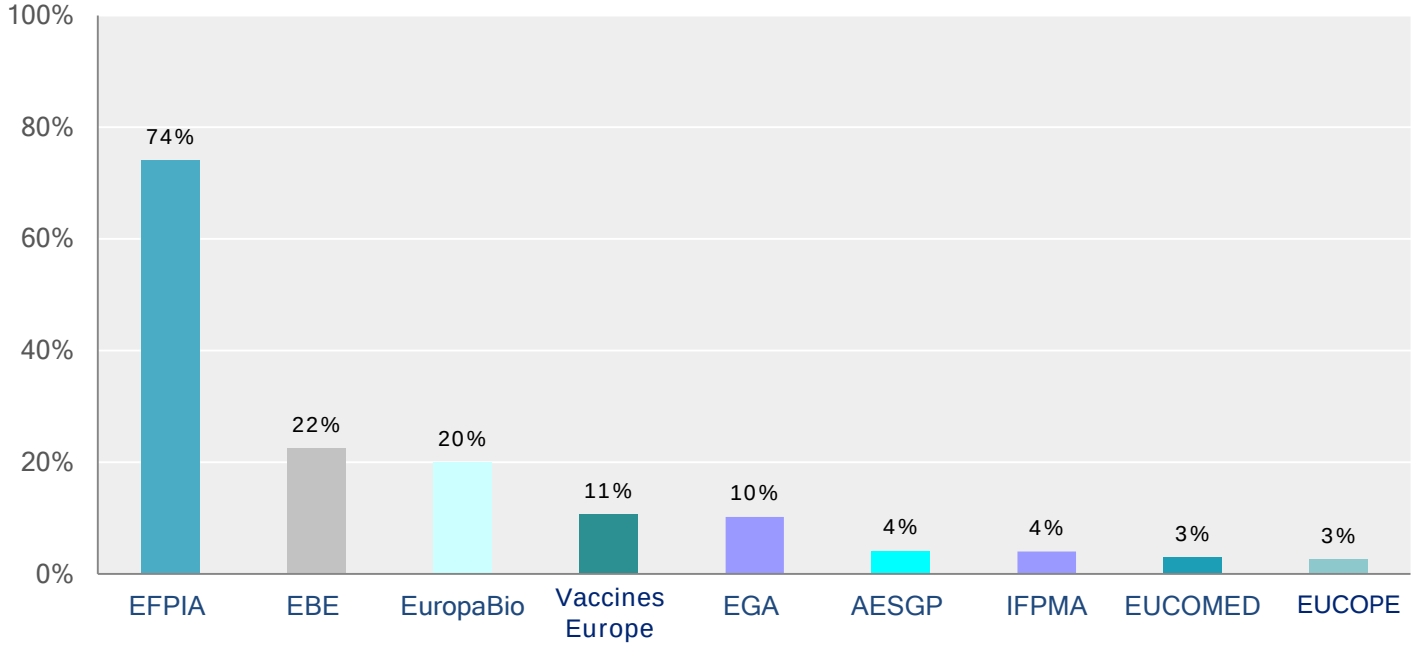
Survey structure



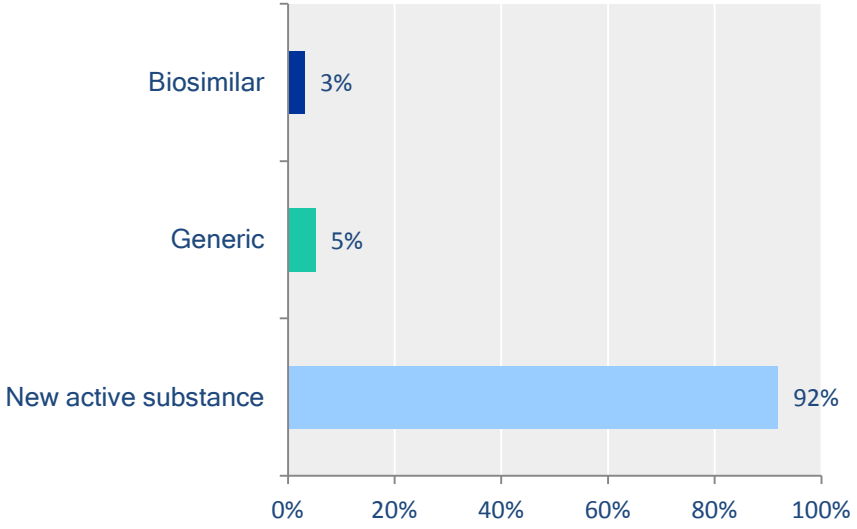
Pre-submission, Validation, Evaluation Phase:

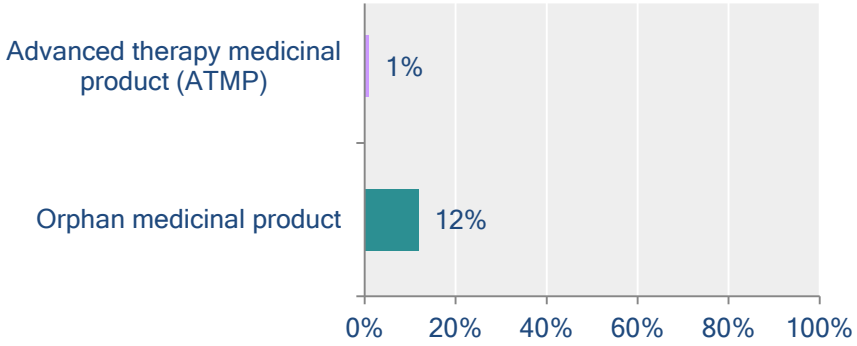
- ***Qualitative aspects:*** *EMA Guidance /Committee Reports/Request for Supplementary Info/ Recommendations etc…*
- ***General aspects:*** *Communication/ Interaction with product team (satisfaction/timeliness/ communication channels)*

MAHs Industry organisation – affiliation profile of respondents



Product types





Response rate – EMA & Industry

Overall response rate:

- *EMA: N= 270*
- *INDUSTRY: N= 196*

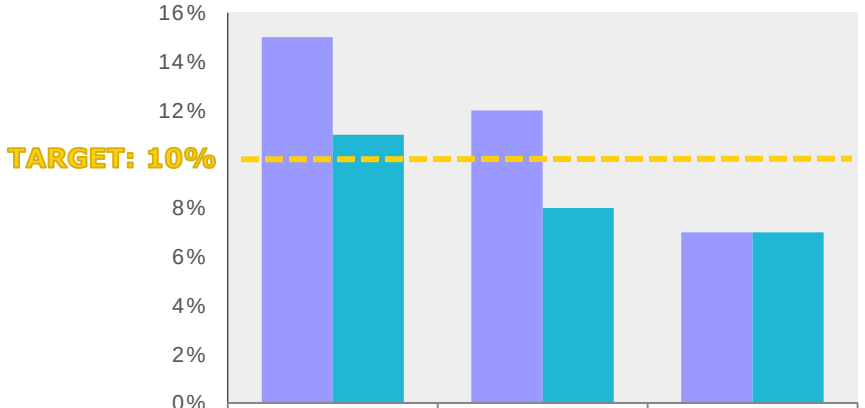
Objectives:

- *To sample at least **10%** of total annual volume for each procedures.*

Result:

- *EMA: Target met for TYPE IBs and TYPE IIs*
- *INDUSTRY: Target met for TYPE IBs*

***Note:** Differences in underlying data set between EMA and Industry respondents.*



	TYPE IB	TYPE II	PSURS
EMA Estimated annual volume	15%	12%	7%
INDUSTRY Estimated annual volume	11%	8%	7%

EMA survey on post-authorisation procedures

FEEDBACK OF INDUSTRY RESPONDENTS

Outcome of the survey on post authorisation procedures

Summary of feedback from all Industry Respondents

2nd Industry stakeholder platform - operation of the centralised procedure, 9 Nov 2015

Judith Creba and Craig Johnson

Agenda

Presubmission

- EMA guidance
- Query service
- Validation

Evaluation

- Communication
- Assessment Reports
- Timelines
- Product Information & Notification/opinion

Overall conclusions & areas for further exploration

EMA post-authorisation guidance (Q&A)

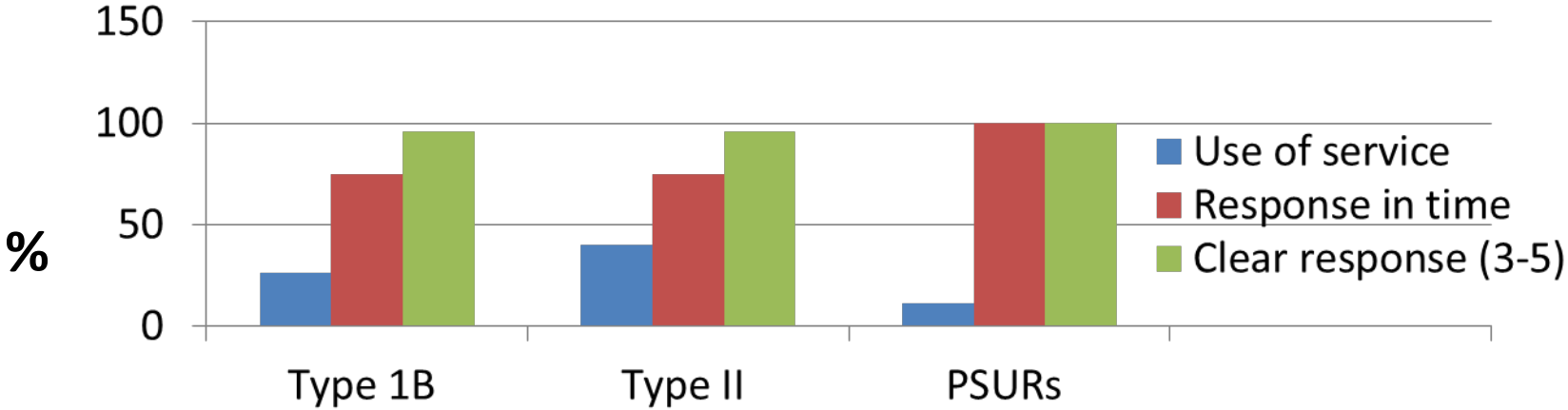
- Majority of respondents (65-90%) used the guidance, but some did not
  - Type 1A /1B application form (n=95) - 35% did not use
  - Type IB Q&A (n=95) – 20% did not use
  - Type II (n=63), PSUR (n=35) Q&A – 9-10% did not use

- Guidance for the procedures covered in the survey is generally clear and addresses the needs of applicants

> 90% score 3-5

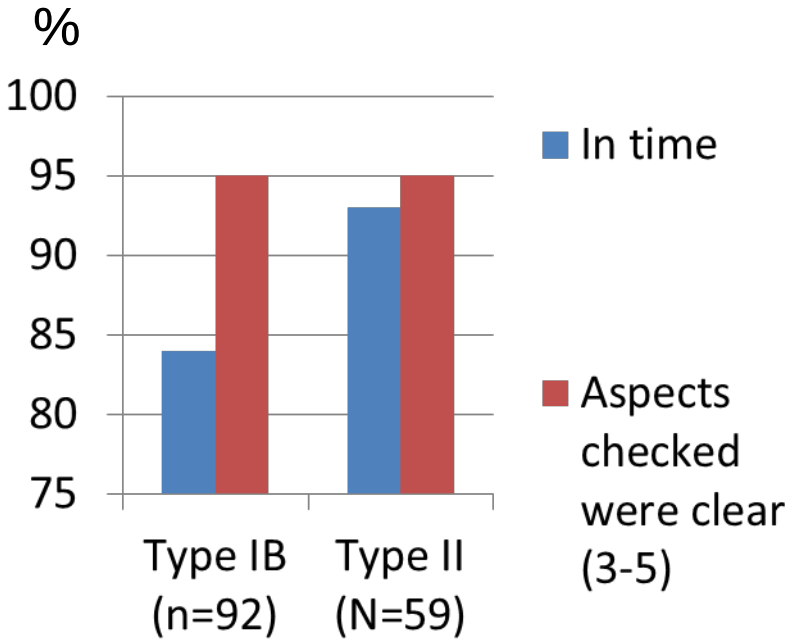
- Free text indicates additional clarity could be given in some areas e.g.
  - **Type IB**: Timelines, eApplication form , location of information, product information/ linguistic review, availability of Assessment Reports
  - **Type II** : Definitions/categorisation e.g. New indications, RMP amendments, PASS studies, PAMs, number of variations to be filed for same change
  - **PSUR** : Post procedural handling e.g. when revision of annexes involved, implementation of SMPC change after PRAC recommendation

Presubmission Query Service



- Presubmission query service is not used by the majority of applicants
- When used, responses are clear, and generally timely (75%)
- Applicants knew which mailbox to use for their query for type IB (92%) and type II (96%), less so for PSURs (50%) but very small n of 4
- Feedback indicates further dialogue required to resolve queries in specific procedures quickly to avoid susequent delays in validation

Validation



Validation generally timely, but some delays:

- Type Ib (16%) and Type II (7%)

Reasons for delay (free text)

- Not always given to applicants
- Applicants need to prompt Agency as no feedback within timeline
- Complex/grouped variations
- RSI received later or second request for additional information

- Aspects (admin and dossier content) checked during validation are clear (95%) but sponsors are not always notified of validation
- Some general comments mention lack of consistency at validation and that some questions are unnecessary (information already in application)

Evaluation phase - Communication

- High level of company satisfaction with interactions with EMA

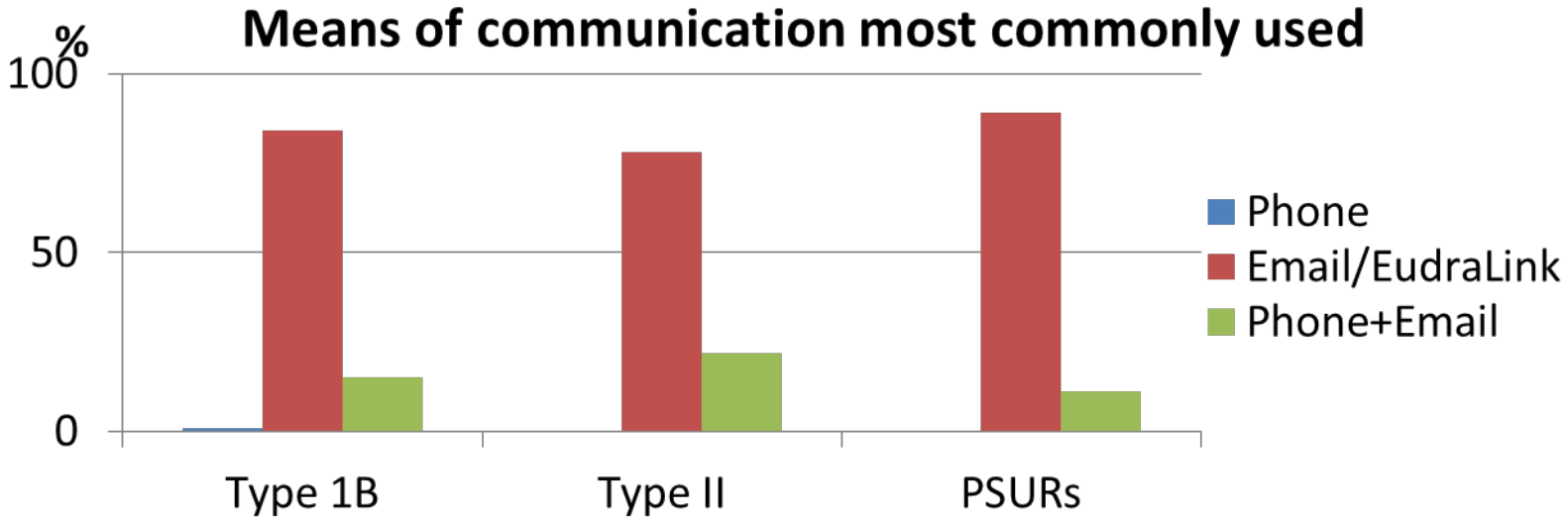
>90% score 3-5

  - Similar pattern across procedures for interaction timeliness, communication level and process management
    - For lower scores (1-2), not possible to assess with more granularity (e.g. whether PM, EPL and/or Rapporteurs)
    - 1 (of 29) PSUR respondent “strongly disagreed”
- High level of clarity on contact points
  - Slightly less so for PSURs than for T.II variations

12% unclear

3% unclear

Evaluation phase - Communication



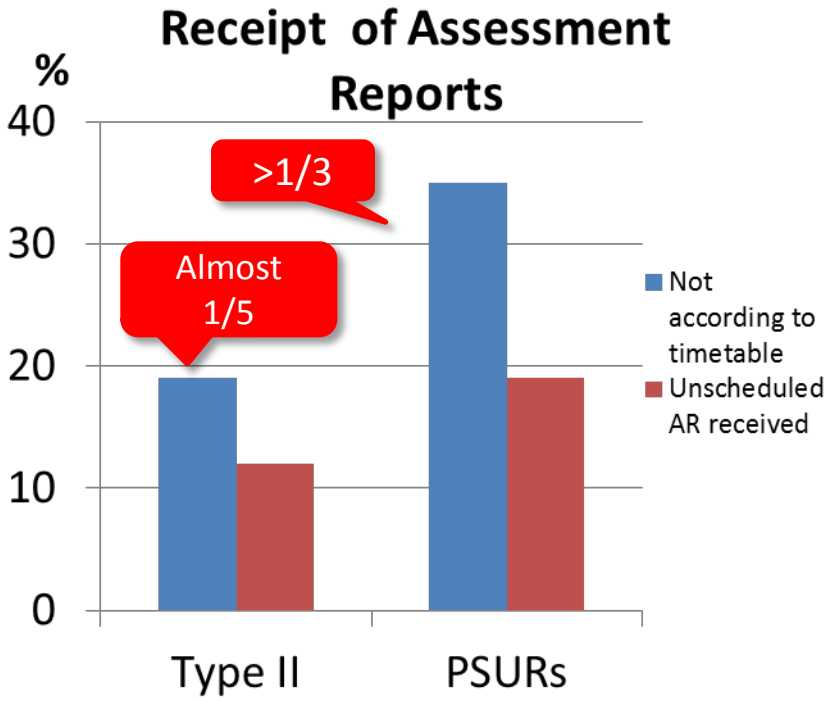
- Email/EudraLink most commonly used
- No issues identified from free-text comments

Evaluation phase – Assessment Report

- Quality of Assessment Reports generally rated highly
- High proportion of respondents agreed that:
  - Structure is clear and easy to follow ~90% score 4-5
  - Conclusions/RSI/regulatory actions are justified in report >80% score 4-5 (>90% for variations)
  - PSUR ARs generally clear on issues needing immediate response ~80% score 4-5
  - Higher % of negative responses for PSURs than variations
    - 1 “strongly disagreed”
    - But fewer responses overall

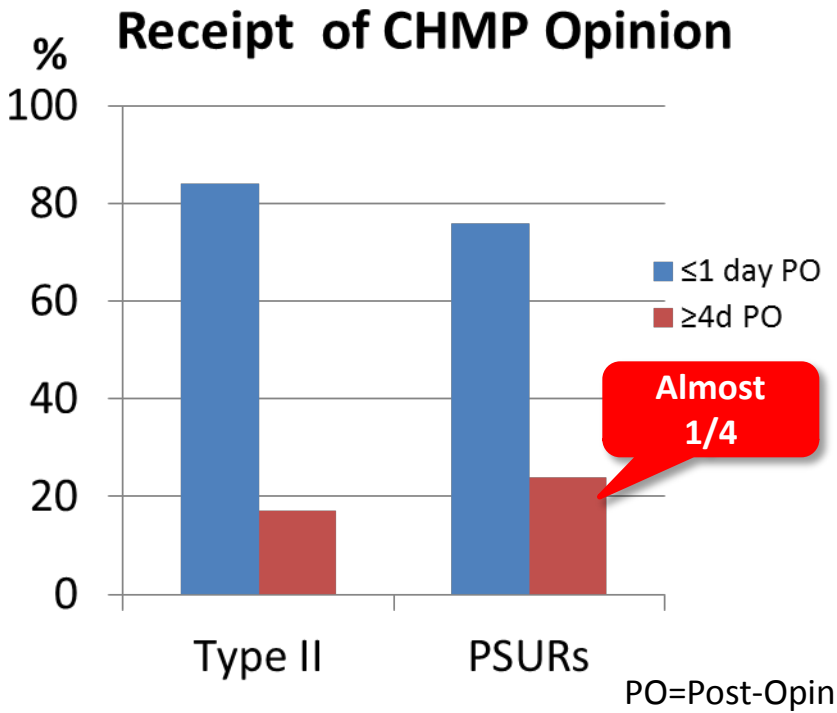
Evaluation phase - Timelines

- High level of clarity on relevant timelines
  - Less so for PSURs (15% unclear) than for T.II variations (2% unclear)
- AR often received late
  - No or poor communication/explanation of delay in most cases
- Unscheduled ARs occasionally received
  - Generally updates, e.g. following MAH response
  - Did not appear to impact procedures



Evaluation phase – Product Information & Notification/Opinion

- Where applicable, comments on PI sometimes not sent early enough to facilitate discussion
  - More often for T.II (22%) than PSUR (14%)
- Type IB notifications usually in <30d (11% (n=10) later)
  - 1 later than 30d was workshare – reasons for others not clear
- Most T.II and PSUR Opinions received in ≤1d
  - <u>But</u> significant proportion ≥4d after Opinion



PO=Post-Opinion

Overall conclusions

- Much feedback on Type IB and II variations and PSURs positive
- Some signs of more need for improvement with PSUR procedure than variations? (caveat: relatively small “n”)
  - Less clarity on contact points and timelines
  - Some lack of clarity in AR on issues needing immediate response
  - Late AR and Opinions

Possible areas for improvement to explore

- Specific suggestions for guidance documents
- Presubmission query service
  - Timeliness of responses
- Validation
  - Communication (completion/delays)
  - Consistency/ content
- Communication of AR delays
- Timely availability of PI comments to facilitate discussion
- Late receipt of Opinions for Type II variations and PSURs

EMA survey on post-authorisation procedures

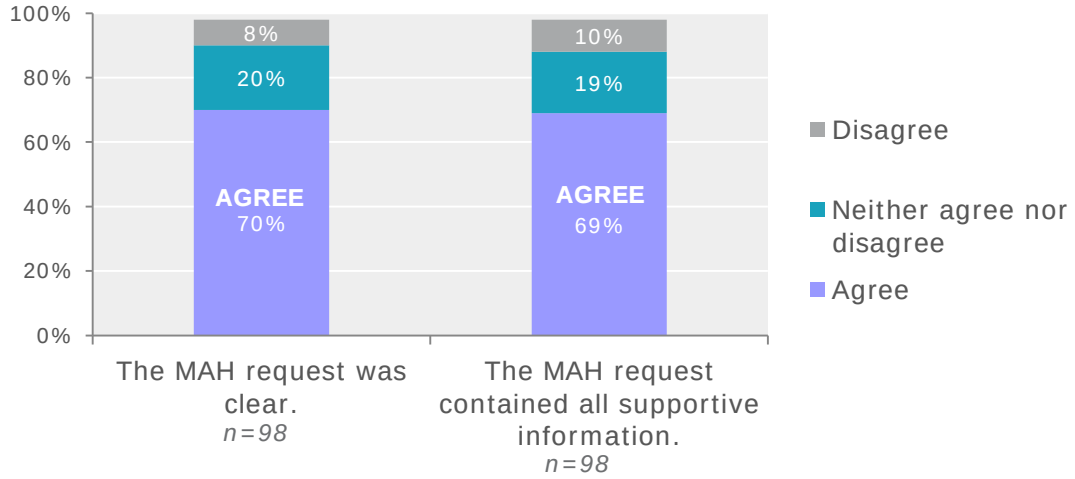
FEEDBACK OF EMA RESPONDENTS

Pre-submission phase

Pre-submission phase

PQS queries

- *The majority of MAHs (80%, n= 98) are already aware of the of Post-Authorisation Guidance (Q&A) available on the EMA website but seek confirmation of their interpretation (according to provided comments).*
- *The majority of MAH requests were clear and contained all supportive information.*



SAMPLE COMMENTS

"The company interpretation of Variations regulation was not totally correct. Hopefully helped."

"Applicant wanted confirmation on their interpretation."

"The PAG could clarify that for ATMPs CAT involvement is always required therefore weekly Type II timetables is N/A."

"The need for a linguistic review was unclear for the MAH."

PQS queries – internal data

(Source: Internal data based on queries received between April 2014-Aug 2015)

- *The type of queries received differs among the procedures:*

	TYPE IB	TYPE II	PSURs
Classification	**59%**	30%	-
Grouping	19%	19%	-
Submission content	18%	**39%**	**56%**
Work-sharing	2%	3%	-
Timetable & receipt of submission	2%	9%	17%
EURD list	-	-	25%
PSUR follow-up	-	-	2%

- *The areas for update/development of new guidance identified in the survey should be complemented by an in-depth analysis of pre-submission query service.*

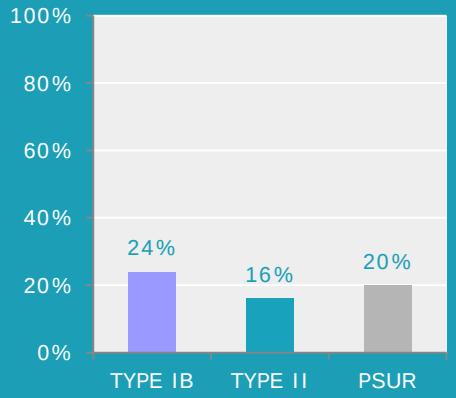
Validation phase

Validation phase

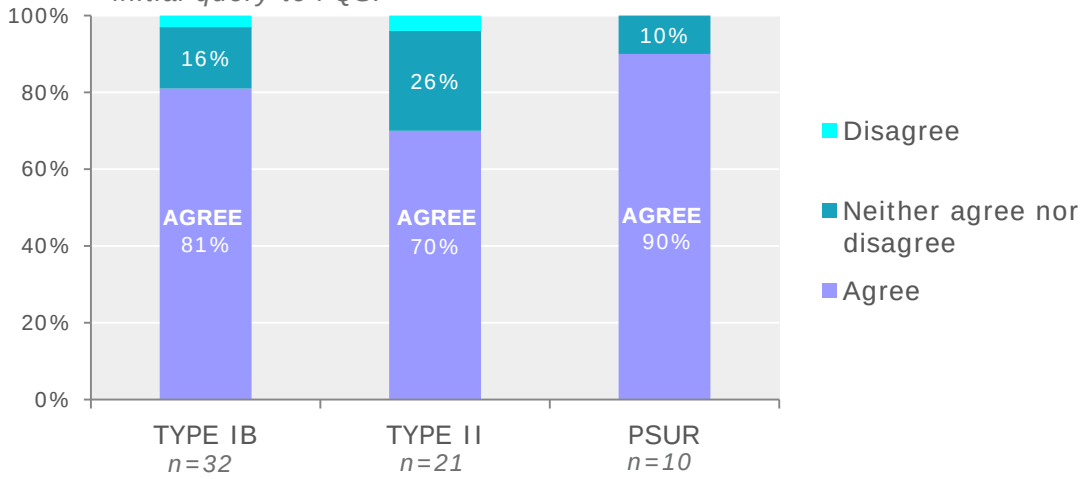
Receipt of application

- *PQS consultation according to procedures type.*
- *Majority of MAHs (87%) followed pre-submission advice.*

Advice sought in at least 24% of Type IBs, 16% of Type IIs and 20% of PSURs submitted.



The data submitted in the procedure was fully in line with the information provided in the initial query to PQS.



Validation phase
TYPE IB and TYPE II

- 84% of the TYPE IB procedures were validated (or RSI issued) within 7 days of submission.
- 100% of TYPE II procedures were validated within deadlines.

- *Validation rated satisfactory overall.*
- *Most common problems:*

TYPE IB (n=132)	TYPE II (n=97)	
23%	8%	Deficiencies in the application form
21%	12%	Incomplete documentation
13%	4%	Incorrect classification of changes
6%	5%	Precise scope not clear or incomplete

- *A request for supplementary information during validation was issued in 44% of Type IB* and 48% of Type II procedures.***

(*) Type IBs received Jan-Aug 2015; (**) Type IIs received Sep-Oct 2015

Receipt of application

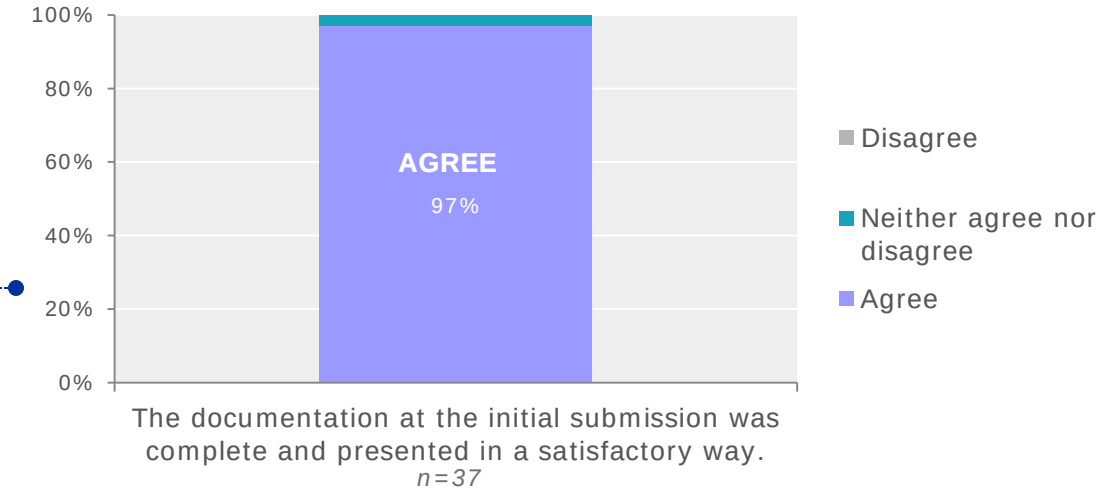
PSURs

SAMPLE COMMENTS

"The MAH has included a full study report as an Appendix. This should have been submitted separately following the appropriate regulatory procedure if needed, as the PSUR should include integrated summaries."

"PSUSA number as per EURD list wasn't included in the cover letter."

- *High level of satisfaction in the quality of submissions of PSURs.*



- *84% of all MAHs submitted a correct cover letter template.*

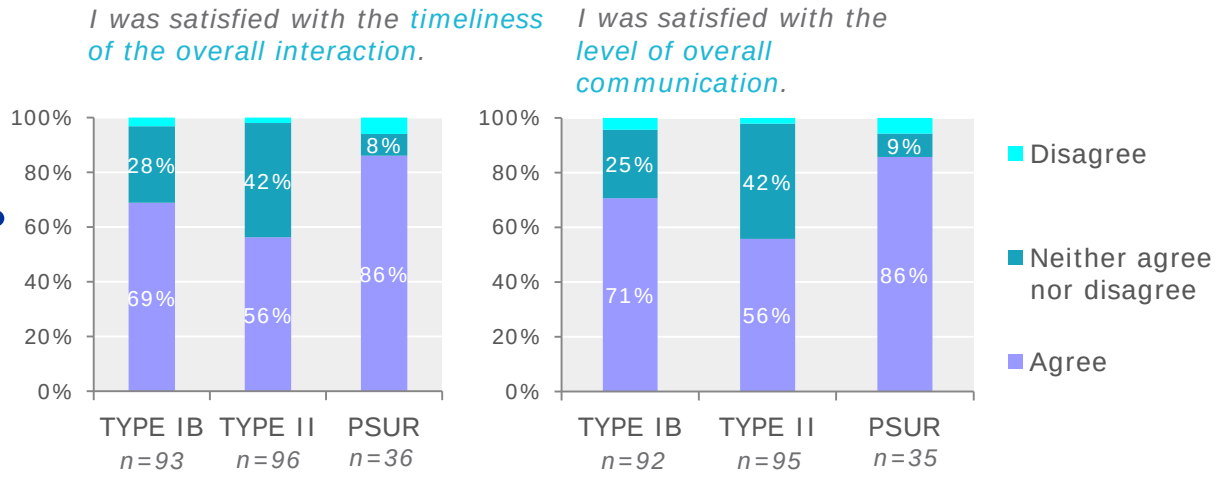
Evaluation phase

Evaluation phase
Communication

Means of communication (across all procedure types):

- Email / Eudralink: **84%**
- Both phone & email: **15%**
- Phone : **1%**

- *Overall satisfaction in the timeliness and the level of communication with MAH across the three procedures.*



- *Variability of Communication with MAHs depending on type of procedure: 38% of Type IBs, 86% of Type IIs, 75% of PSURs procedures.*

Evaluation phase

Assessment report circulation

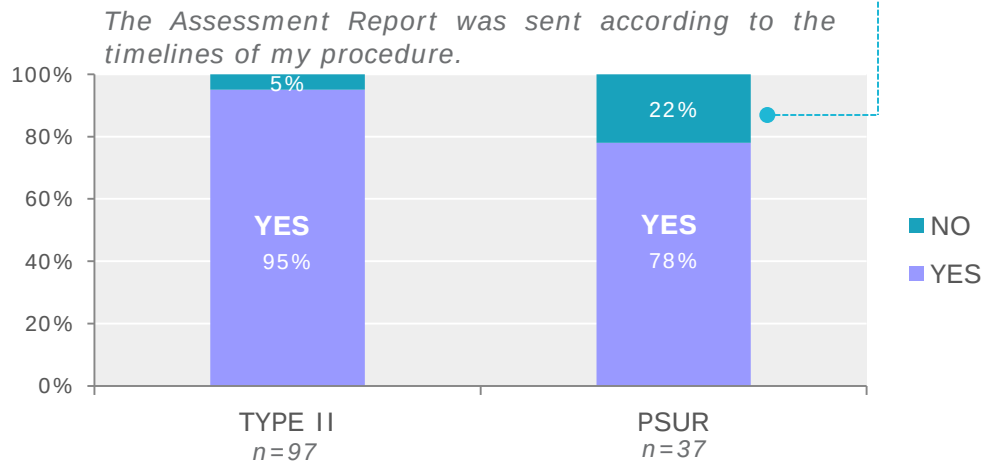
SAMPLE COMMENTS

"Delay in circulation of Preliminary Rapp AR (2 days) and updated AR (1 day)."

"Delayed responses from MAH."

"Rapporteur circulated only PRAC AR (...) the CHMP AR received on CHMP week."

- *Circulation of Assessment Reports according to timelines in majority of cases. Delays in PSUR Assessment Report circulation identified (small sample size acknowledged).*



- *Reported delays due to late circulation of Assessment Report from Rapporteur as well as longer internal EMA confidentiality checks.*

SAMPLE COMMENTS

"Last minute comments from a MS were received (a LEG was recommended) (..) and the PSUSA was marked for discussion on Monday PRAC (..)."

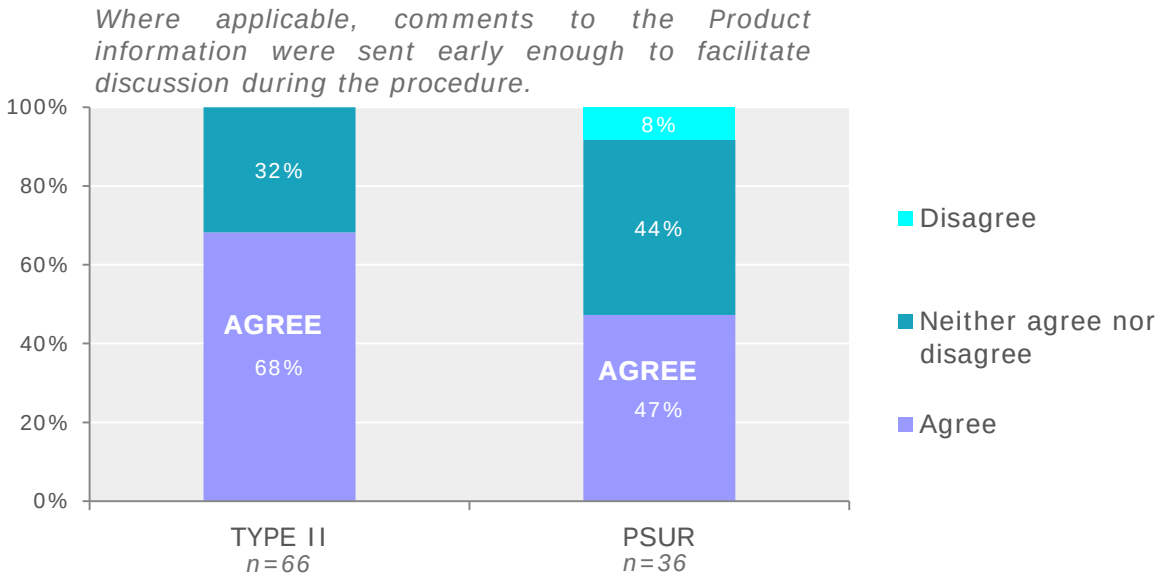
"The MAH was not reachable (…) and did not provide the PI on time as requested."

"The MAH added comments to the PI between PRAC recommendations and CHMP opinion without informing the PM. This lead to very late discussions with CHMP Rapp and PRAC Rapp to agree on changes and last minute amendments to CHMP opinion."

Evaluation phase

Regulators comments circulation

- *Overall satisfaction with the timeliness of the circulation of the comments on the Product information.*



Evaluation phase

Timeliness / finalisation

- *The opinion of Type IIs and Recommendation/opinion of PSURs were issued within legal deadline in 100% of procedures.*

- *97% of Type IB notifications were issued in less that 30 days. Delays reported mainly due to pending clarifications from MAH or updates of documentation at finalisation.*

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OVERALL CONCLUSIONS

General conclusions

Overall positive feedback across 3 procedures:

- *Content, clarity of EMA pre-submission guidance;*
- *Clarity and completeness of Pre-submission queries (PQS), when used/needed;*
- *Overall quality of submission by applicants;*
- *Timeliness, level of communication and management of procedure management at EMA and from Industry;*
- *Validation and evaluation timelines;*
- *Clarity and new structure of single assessment reports.*

General conclusions

Potential areas for further improvement:

- *Post-authorisation guidance – Specific suggestions for update and/further development of guidance in certain areas;*
- *Pre-submission query service (PQS) - Review timeliness of response;*
- *Validation – Consistency and communication of outcome;*
- *Assessment Reports/ product information comments / final opinions - Circulation timelines and communication of delays where they arise.*

Thank you for your attention

European Medicines Agency

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