Marketing Authorisation Application Survey results

Survey to Industry, Rapporteurs and EMA

Platform meeting with pharmaceutical industry - 3rd July 2017

Industry speakers: Fiona Reekie

EMA speakers: Marie-Helene Pinheiro, Thomas Castelnovo, Gaelle Andriantafika and Mia Van Petegem

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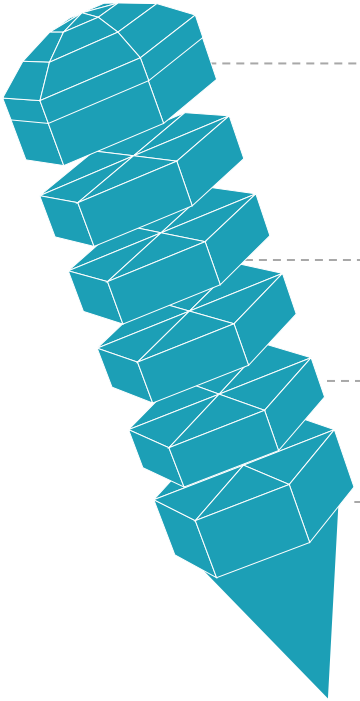
Survey Objectives



*Understanding the **performance of the initial Marketing Authorisation application procedure***

***Direct feedback** from **Applicants/CHMP Rapporteurs/EMA** on the process*

*Enable **continuous improvement of MAAs submissions, processes and guidance** related to centralised procedures*

*Further **increase transparency in interactions** between **EMA** and its **network and industry stakeholders**.*

Scope, methodology, timing (1/3)

Scope

Initial Marketing Authorisation Application:
Procedural & content questions covering

- **Pre-submission to validation phase**
  - *PAG*
  - *PSM*
  - *AA*
  - *Validation*
  - *Interactions*
- **Primary evaluation phase: Day 1 to 121**
  - *Dossier*
  - *Labelling*
  - *Adherence SA*
  - *clarification meetings*
  - *Interactions*
- **Opinion finalisation phase: Day 121 to 210**
  - *Responses*
  - *Clarification meeting*
  - *SAG*
  - *OE*
  - *Interactions*

Methodology

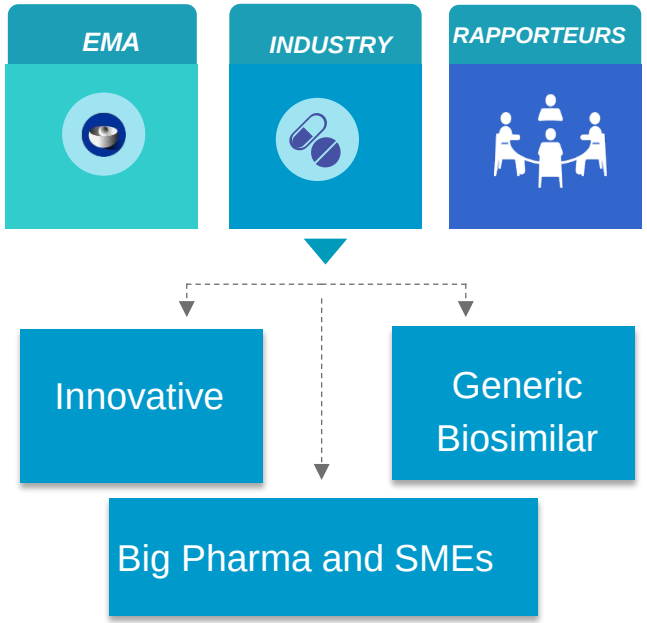
- **Web based survey**, *coordinated by EMA*
- **Survey Drafting Group**
  - *CHMP representatives consulted*
  - *EFPIA Working Group and Industry Stakeholder Associations consulted*
- **Survey Analysis Group**
  - *EMA & Industry Stakeholder Associations Working Group*
- **Survey combined the following response formats:**
  - *Dichotomous scale (Yes/No)*
  - *5-point rating scale (1 Strongly disagree; 2 disagree; 3 Neither agree nor disagree, 4 Agree; 5 Strongly agree*
    For the analysis : 1&2 rating=disagree; 4&5=agree; 3=neither/nor
  - *Multiple choices and multiple responses*
  - *Free text*

Period

- *6 Month period covered*
- *September 2016 –February 2017*

Survey methodology (2/3)

Stakeholders surveyed



Target

50% any ongoing MAA (40 to 50 MAA) reaching either Validation, D121 or Opinion stage

Validation

- Industry
- EMA

Late in clock-stop or after LoQ responses

- (Co-)Rapporteurs
- Industry
- EMA

Opinion

- (Co-)Rapporteurs
- Industry
- EMA

MAA Survey – Sample analysed and completion rate (3/3)

Target: *capture 50% of any ongoing MAA (~ 50 MAAs) reaching either Validation, D121 or Opinion*

- ***Validation:*** **65 MAAs**

EMA survey completed	Applicants survey completed
100%	97%

- ***Day 1-121:*** **45 MAAs**

  49 MAAs for Rapp.

EMA survey completed	Applicants survey completed	Rapp/Co-Rapp survey completed
100%	87%	76%/79%

- ***Day 121-Opinion:*** **48** MAAs

EMA survey completed	Applicants survey completed	Rapp/Co-Rapp survey completed
100%	92%	88%/90%

Results: *Excellent completion rate overall for the 3 phases across participants*

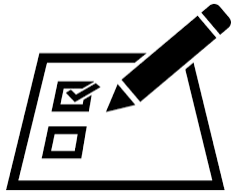
Disclaimer: *Number of procedures, products, meetings etc. presented by stakeholders may vary due to the differences of response rates.*

Stakeholders surveyed

Pre-submission meeting -validation phase

This is a joint industry presentation on behalf of the trade associations shown

PSM to Validation survey to Industry: Results



- Topics covered through 27 questions:
  1. Applications details
  2. Procedural advice Q&A guidance
  3. Pre-submission meeting
  4. Accelerated assessment
  5. Validation – Impact on procedure
  6. Overall feedback on the interaction with EMA during pre-submission phase

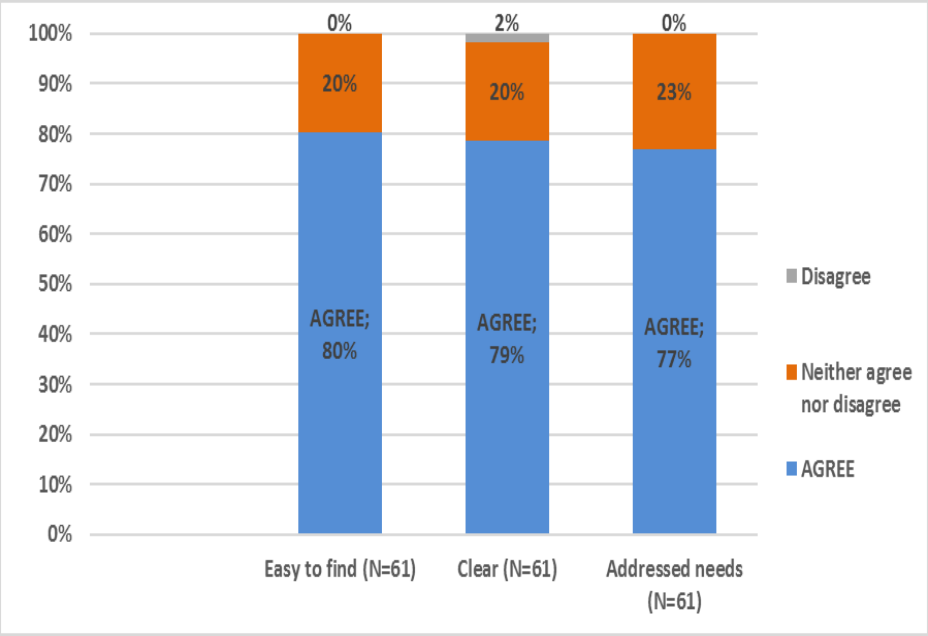
- ✓ 63 MAA captured
- ✓ Industry completion rate: 97%

2. Pre-submission guidance

EMA Q&A guidance is a valuable aid to submission preparation

- 97% of applicants consulted the procedural advice Q&A
- 80% easily found the information*
- 79% found the information clear*
- For 77% information addressed the needs*

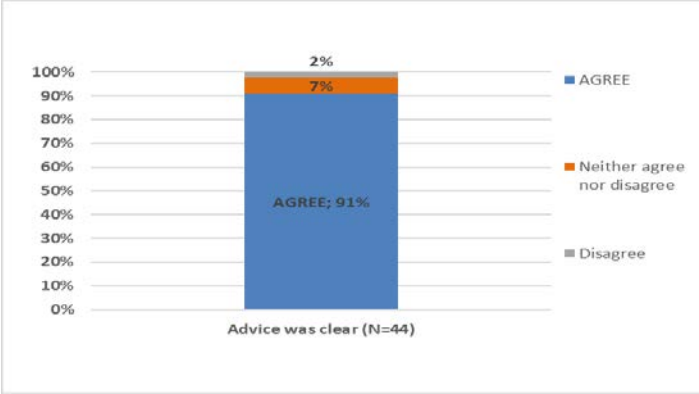
* Excludes 2 applicants who did not provide ratings



3. Pre-submission Meeting *(1/3)*

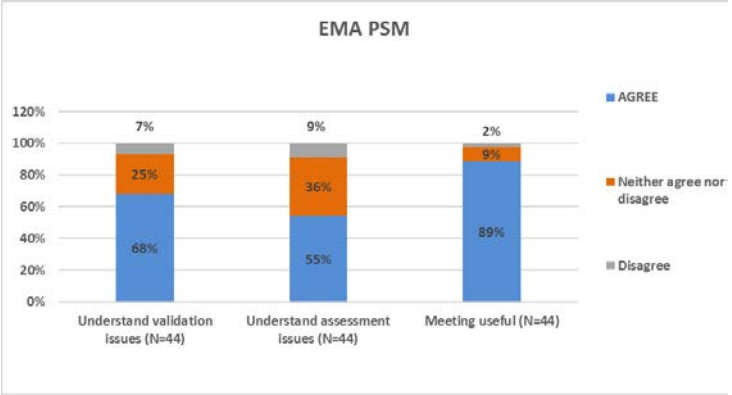
- 70% of applicants had a pre-submission meeting
  - Vast majority of respondents (90%, 4+5) considered the advice on their questions was clear
- 68% of applicants had separate pre-submission meeting with (co-) rapporteur
  - 100% with rapporteur
  - 86% with co-rapporteur
  - 23% with PRAC rapporteur
  - 7% had other contact
- 33% of applicants had further advice from EMA (not SA)

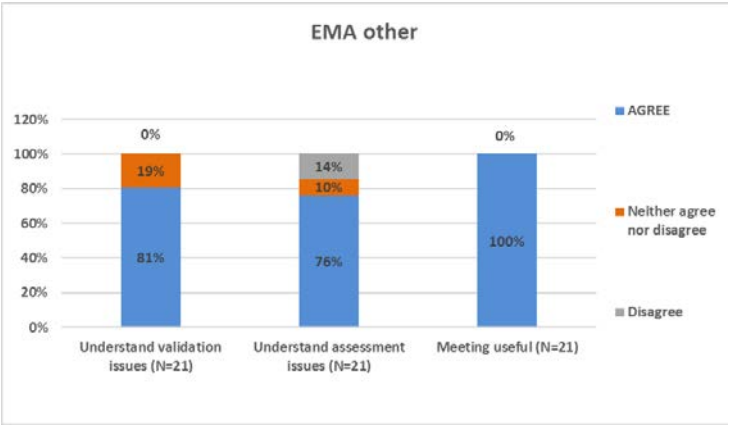
* In 1 procedure there was no co-rapporteur



3. Pre-submission Meeting *(2/3)*

- EMA pre-submission advice is highly appreciated and considered useful
- Most frequently mentioned additional aspects to be covered are:
  - Sharing of recent EMA experience on common validation issues
  - Discussion of the eAF submitted by the applicant





3. Pre-submission Meeting *(3/3)* - Feedback from (Co-)Rapporteur

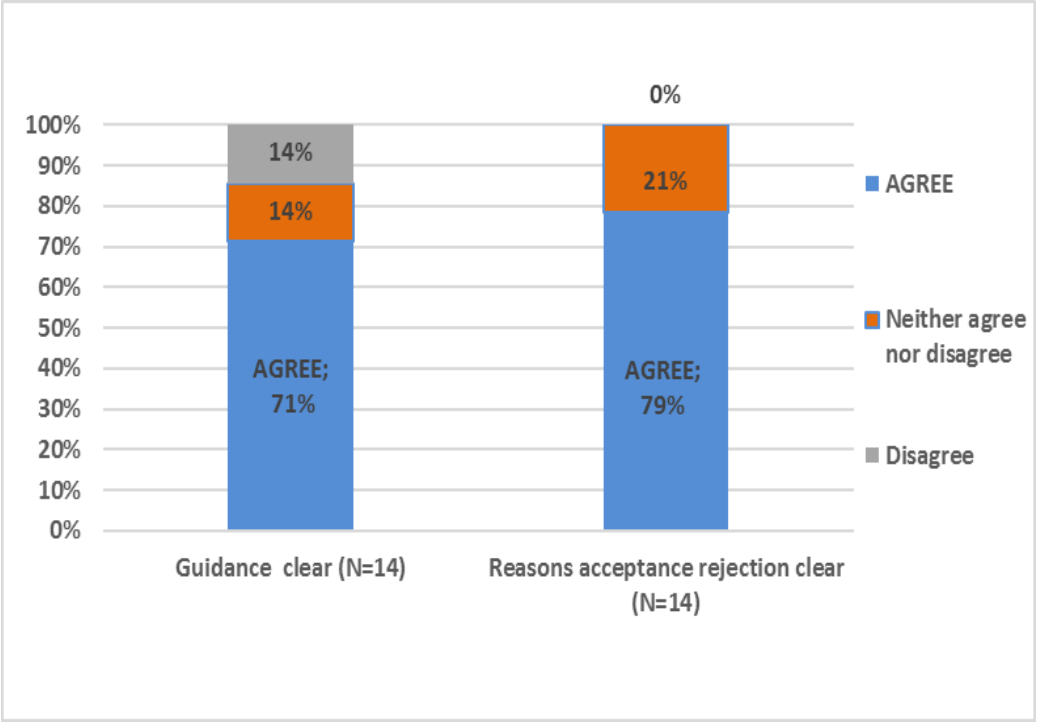
Most valuable aspects of pre-submission meetings with members of the assessment team include:

- Possibility to introduce product, development strategy and dossier
- Face to face interaction with assessors appreciated
- Interaction with assessment team allows to:
  - Exchange points of focus during dossier review and potential issues
  - Address specific questions on clinical package, address potential gaps in submission package and already discuss intent to provide updated information at day 121
  - Get better knowledge of (co-)rapporteur expectations

4. Accelerated Assessment

From 14/63 (22%) requesting accelerated assessment:

- The majority found that guidance and reasons for acceptance/rejection were clear
- However, 14% (n=2) did not agree that guidance was clear:
  - *'Clearer guidance on user testing requirements under accelerated assessment procedure.'*
  - *'We found the template for the accelerated assessment request difficult to complete.'*



5. Validation *(1/2)* - Submission timing and gateway

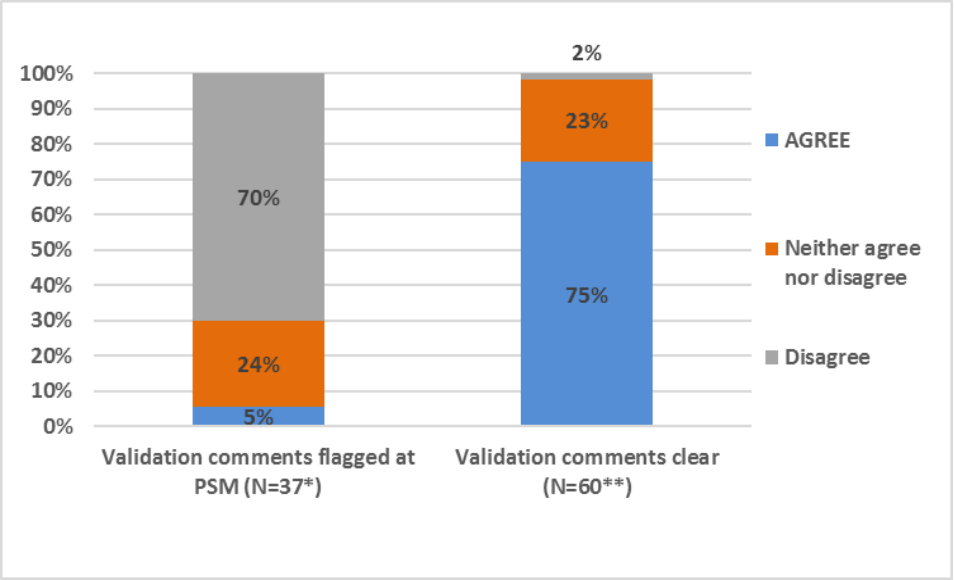
- 37 applicants (59%) submitted the application on the date indicated with the letter of intent.
- 17 of the 26 who did not submit on the predicted date (65%) informed EMA and rapporteurs about the potential delay.
- The gateway is working well in the majority of cases with 83% of responders reporting no difficulties that delayed submission, however, this leaves 17% reporting delays due to the gateway

5. Validation *(2/2)* - Dossier content

The majority of validation comments (89%) were related to amendments needed for documents.

Missing documents were at the basis of 48% of validation comments.

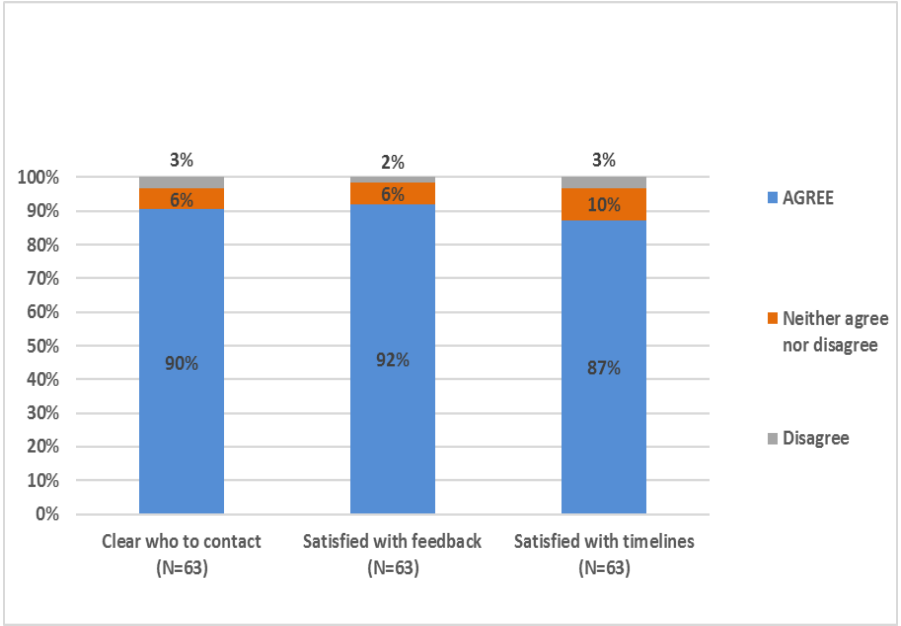
- These deficiencies were not necessarily flagged at the pre-submission meeting.
- In only 5% of the applications, did they delay the procedure start
- Questions regarding validation were dealt with satisfactorily in 96% of 53 cases where question was deemed applicable.



6. Interaction with EMA contacts

The guidance on who to contact at EMA is generally clear (90% agree)

- Most applicants are satisfied with the quality (92%) and timeliness (87%) of the interaction
- In a minority of cases, experience is less satisfactory (2% and 3% give a score of 2 to quality and timeliness respectively)



Industry conclusions pre-submission - validation phase

- Overall, responses indicate that the pre-submission to validation phase does not cause major difficulties
- Pre-submission Q&A's received good ratings but written comments indicate that improvement is possible in terms of clarity, access to the right information and level of detail.
- The opportunity to meet with EMA, (co-)rapporteur or other members of the assessment team is frequently used and highly valued
- 40% of Marketing Applications were not made on the date given in the Letter of Intent and the EMA was not consistently informed of changes in date
- Although the pre-submission meeting generally is highly graded, it does not pick up all validation issues which included missing documents in almost half of submissions
- The Submission gateway is working well in the majority of cases but 17% encountered issues

Overall recommendations - PSM to validation

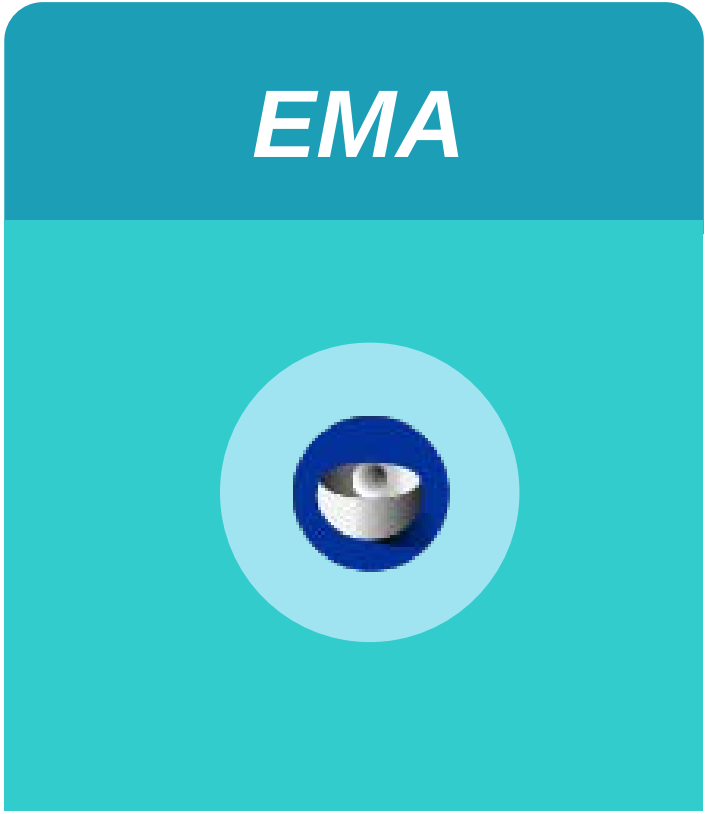
- PSMs beneficial
- Validation issues – too frequent and creating administrative burden for both Industry and EMA

Possible solutions

- Attendance by the EMA validation team at the PSM or better communication to validation team; some agreements that are made at the pre-submission are raised during validation
- A more direct focus on validation and more structured discussion of the draft application form is proposed as a fixed item on the pre-submission meeting agenda
- Better awareness of the pre-authorisation Q&A (4.3) which lists the most common validation issues
- Applicants to request clarifications prior submission

Stakeholders surveyed

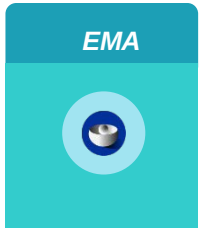
Pre-submission meeting -validation phase



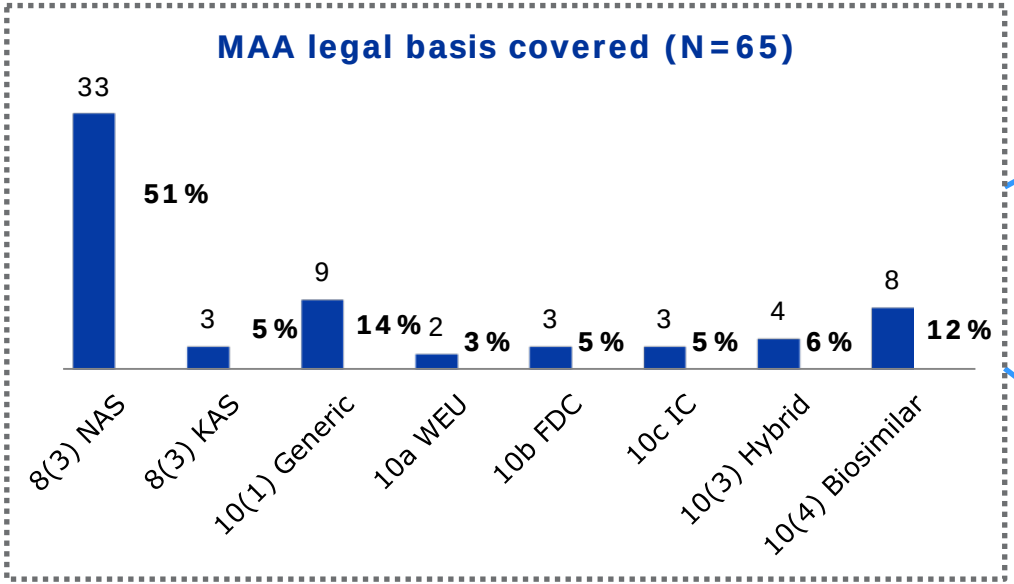
Pre-submission to validation survey to EMA - Results

- Topics covered through 24 questions:
  1. Applications details
  2. Validation – Impact on procedure
  3. Pre-Authorisation guidance
  4. Pre-submission meeting
  5. Accelerated assessment
  6. Overall feedback on the interaction with applicants during pre-submission phase

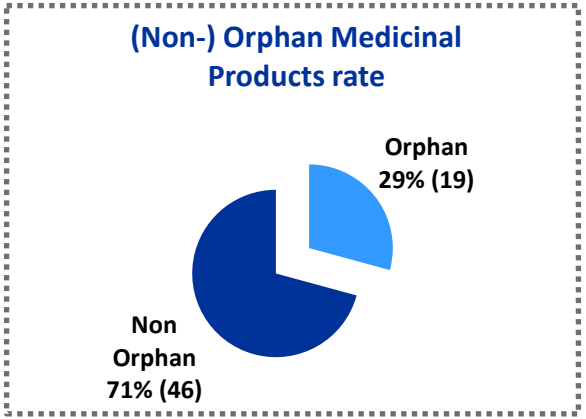
- ✓ 65 MAA captured
- ✓ EMA completion rate: 100%

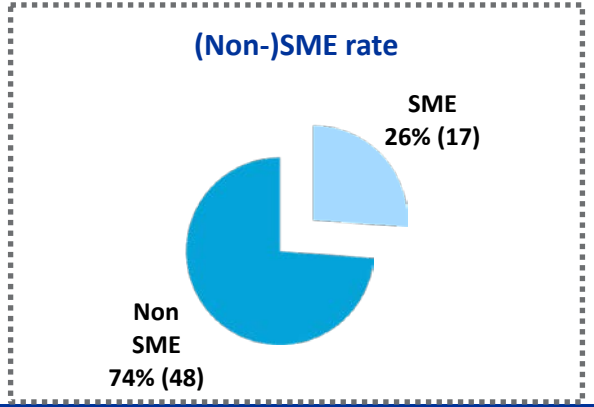


1. Applications details (1/2)



New Active substance: NAS, Known Active substance: KAS, Well-Established Used: WEU, Fixed Dose Combination: FDC, Informed Consent: IC,





1. Applications details (2/2)

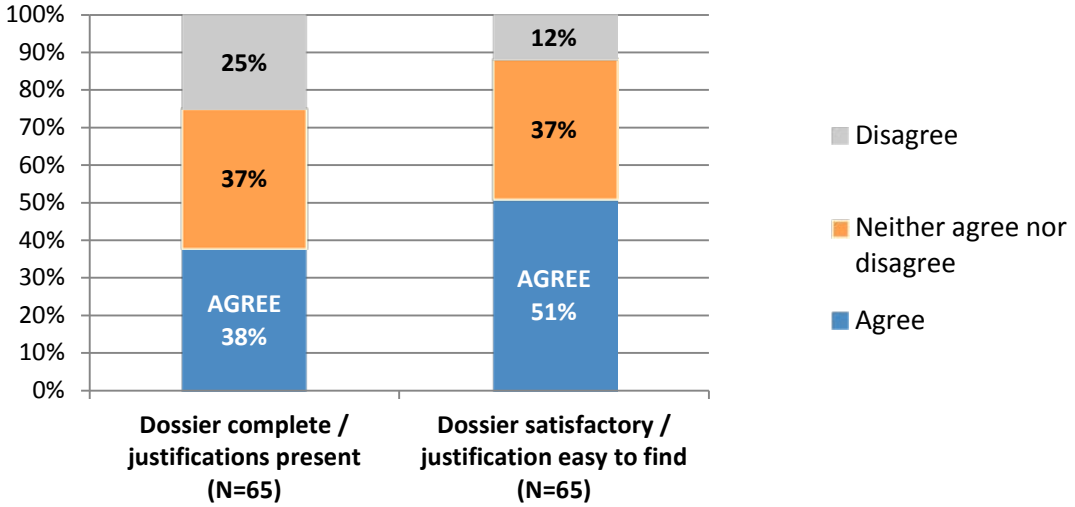
- Orphan products & SME applicants: in line with EMA records of previous years

	2015 (full year)	2016 (full year)	Survey (6 months)
Orphan	23	19	19
SME	14	31	17

- Sample surveyed captured significant numbers of orphan and SME
- Majority of NAS legal bases (51%), followed by Generics (14%) and Biosimilars (12%) in line with current trends
- Overall, sample captured can be considered representative

2. Validation: impact on the procedure (1/3)

- A short majority agreed that the dossier was complete & presented in a satisfactory way; non negligible proportion of “neither agree or disagree” rating



2. Validation: impact on the procedure (2/3)

- **Validation comment in almost all cases (97%)** – **Only 2 applications with no question.**
  - Vast majority of applicants respond accordingly to the agreed timelines (94%)
  - In half of the applications (44%) the responses were incomplete and required a follow up
- **Issues most commonly seen are purely administrative & non blocking issues**
  - **Quality + GMP aspects (92%):** most frequent issues relate to inconsistencies of the Application Form (90%) with qualitative and quantitative composition of the medicinal product (62%)
  - **(Non) clinical/GLP/GCP issues (83%):** more than half of the issues relates to GLP/GCP information, as much as observed for issues related to Module 5
  - **Product Information (30%)**:**95% relate to inconsistencies with the application form** (ATC, strength, pharmaceutical form, route of administration, container, pack size, product name)
- **Validations issues almost systematically on the application form**
  - Most queries related to quality & GMP matter (81%)
  - Applicant's contact person & details & (75%)
  - Nonclinical/clinical and GCP/GLP aspects (65%)

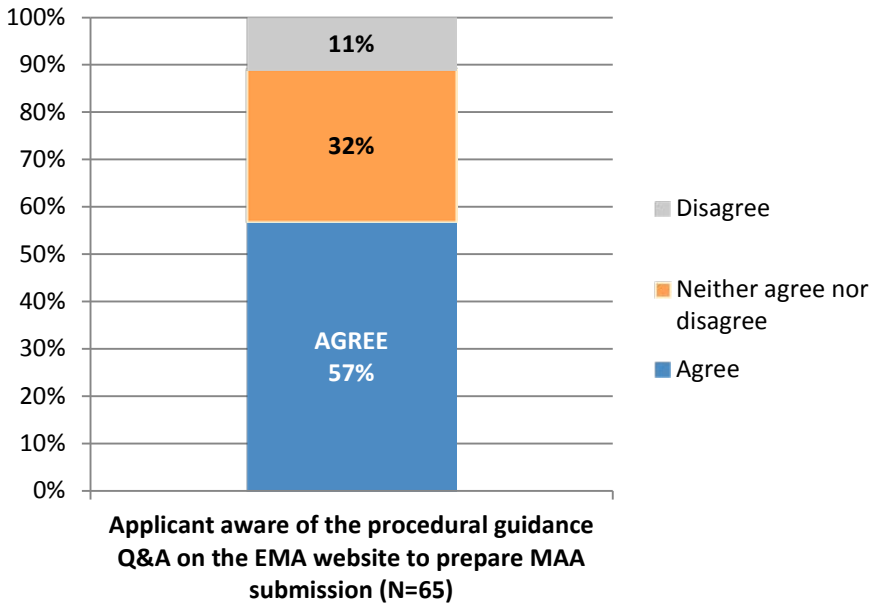
2. Validation: impact on the procedure (3/3)

- **EMA should investigate opportunities to increase awareness on**:
  - ✓ the validation process
  - ✓ the most common issues encountered at validation (published on EMA website)
  - ✓ the procedural pre-submission guidance

- **Applicant should also increase awareness on the EMA requirements; particular focus could be on reducing discrepancies in the application form and the dossier submitted**

- **Applicants are encouraged to request clarifications prior submission**

3. Pre-authorisation Guidance



- **Short majority (57%) agreed that applicants were aware of the procedural guidance (Q&A on EMA website)**
- **Non negligible proportion of "neither agree nor disagree" rating**
- **Analysis per legal basis and SME vs non SME did not show a clear pattern**

➢ **Combined with the almost 100% validation questions rate, these results indicate the need for EMA to increase general awareness and ease access to the procedural presubmission guidance**

4. Pre-submission Meeting (1/4)

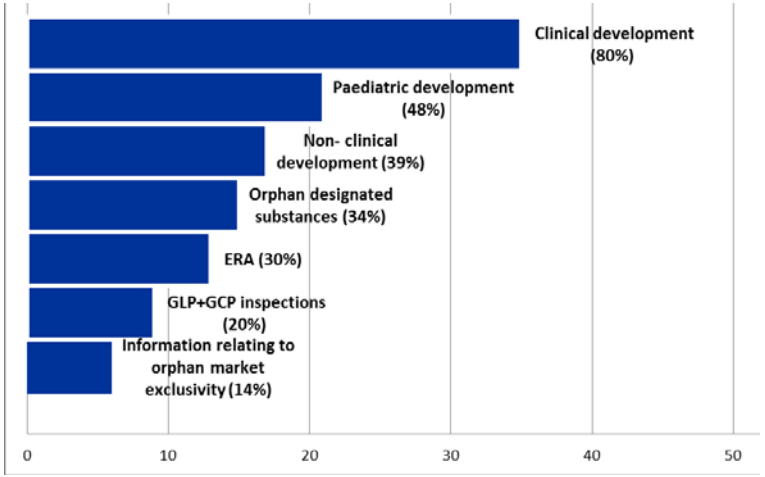
- Pre-submission dialogue in almost 85% applications surveyed
  - **Pre-submission meeting** in almost **75%** (48/65) of the submitted dossier
  - Almost **10%** of interactions through **written/verbal advices (when no meeting took place)**
  - Approximately 15% of applications with **no interaction** prior submission with EMA (mainly Generics and informed consent)
- A follow-up advice necessary in more than 50% of the PSM
- Most of SME (14/17) and orphan applications (17/19) had a PSM
- PSM with EMA was requested for all biosimilar applications

4. Pre-submission Meeting – Topics (2/4)

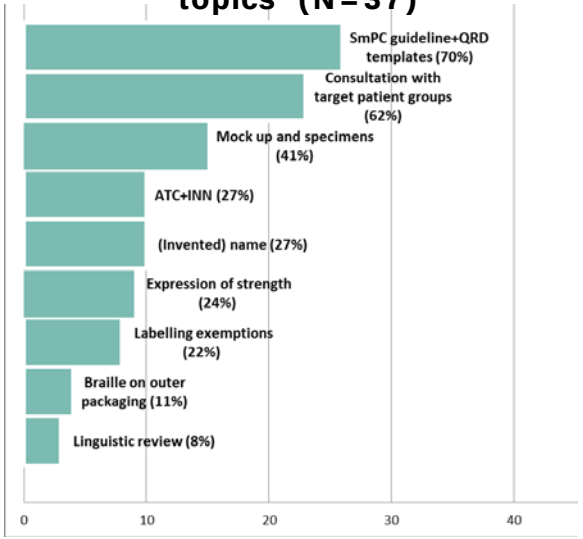
More than 92% of the PSM topics with EMA relates to (Non)Clinical + Clinical, GLP/GCP information followed by the PI aspects:

- (Non)Clinical+GLP/GCP:92%
- Product Information: 77%
- Regulatory/Procedural:75%
- Quality+GMP: 67%
- Administrative: 65%
- Pharmacovigilance: 52%
- Transparency:23%
- Other: 19%

(Non) Clinical + Clinical, GLP/GCP topics (N=44)



Product Information topics (N=37)



- **Various topics are discussed but mainly related to the development programme and the SmPC for the PI**

4. Pre-submission Meeting – Usefulness (3/4)

SAMPLE COMMENTS

Most valuable aspects gathered:

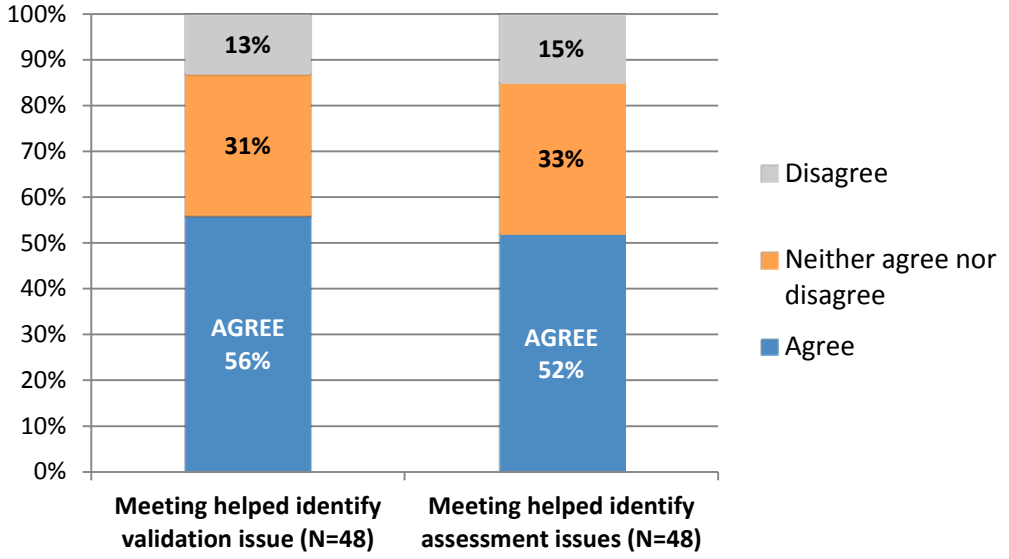
Advice provided on regulatory requirements e.g. legal basis and its requirements, orphan similarity/maintenance, accelerated assessment, GMP, RMP.

Face to face meeting with the applicant

Clarification on the procedure

Presentation of the product and the development programme

- Short majority agreed that the meeting helped identified validation issue & assessment issue; non negligible proportion of "neither agree or disagree" & "Disagree" rating



4. Pre-submission Meeting (4/4)

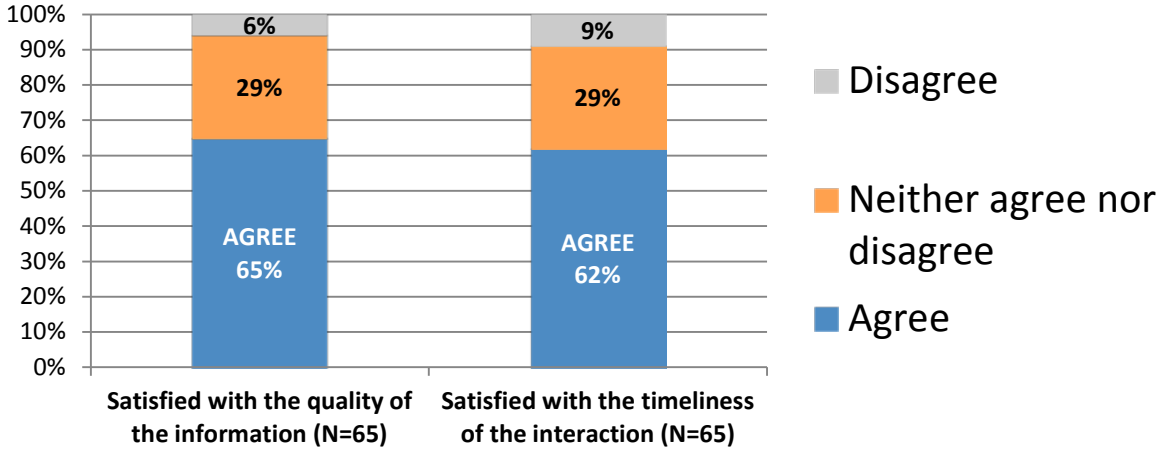
- **Overall, there is a very high level of interaction with EMA prior to submission, mostly via pre-submission meetings**
- **Meetings helped identified validation issues as no blocking validation questions raised; however ~100% non-blocking validation issues**
- **Investigate opportunities to make better use of pre-submission meeting to further anticipate and identify the non-blocking validation issues (right forum?)**

5. Accelerated Assessment

- Over 65 applications, 22% [14] requested an accelerated assessment
- All justifications for requesting AA were in line with available template, 13 were discussed at PSM meeting and were timely received
- **Very good level of awareness from applicants on the AA process & early dialogue occurred**

6. Satisfaction on interaction with applicants

- EMA satisfied with the quality of the information & timeliness of interactions during the pre-submission phase



- **Overall EMA feedback positive**
- **Overall interaction during pre-submission activities could be improved**

Stakeholders surveyed

Primary evaluation phase:

DAY 1-121

This is a joint industry presentation on behalf of the trade associations shown

Day 1 to 121 survey to Industry - Results

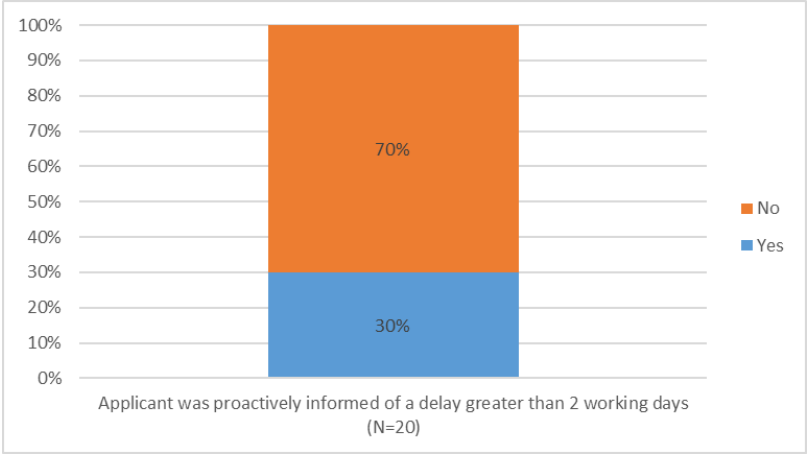
- Topics covered through 13 questions:
  1. Applications details
  2. Assessment reports in primary phase
  3. Labelling review in primary phase
  4. Clarification meeting
  5. Overall feedback on the interaction with EMA during the primary assessment phase

- ✓ 39 MAA captured
- ✓ Industry completion rate: 87%

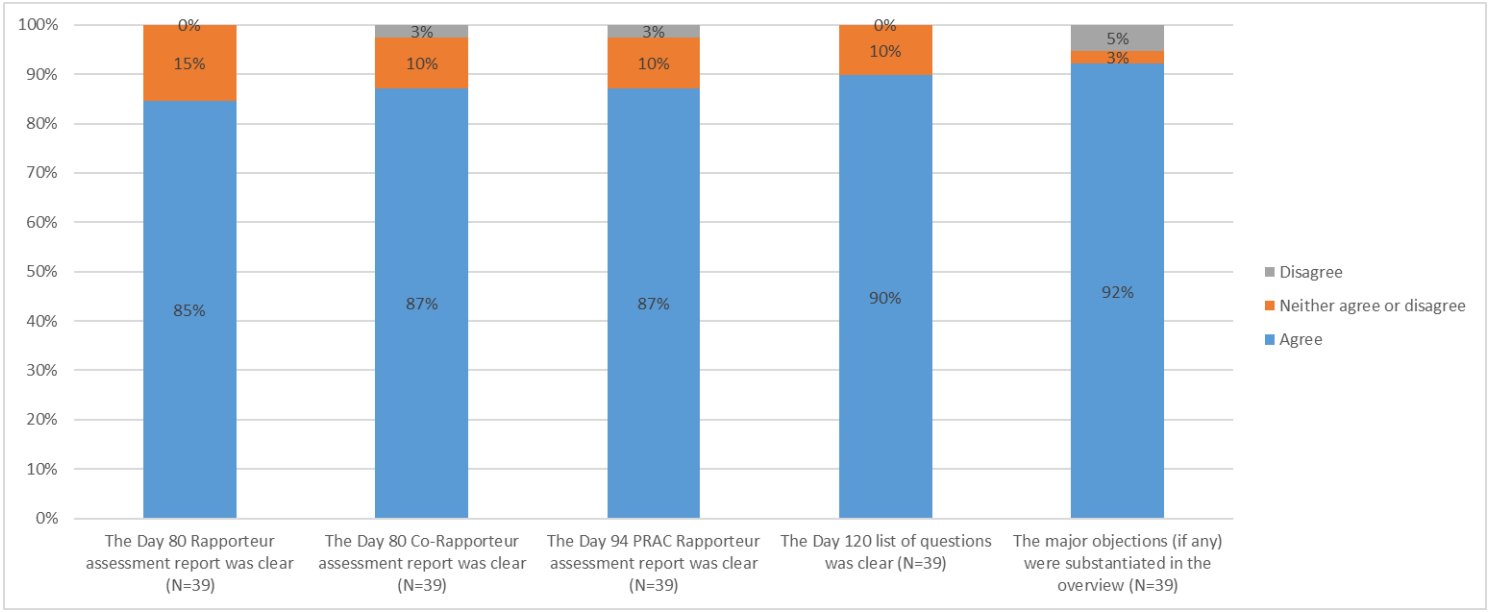
2. Assessment phase: AR circulation timeliness

Majority of Assessment Reports received within 2 days of the due date

- 54% of Day 80 Rapp Assessment Reports
- 67% of Day 80 CoRapp Assessment Reports
- 79% of Day 94 PRAC Rapp Assessment Reports
- 30% of respondents were proactively informed of a delay

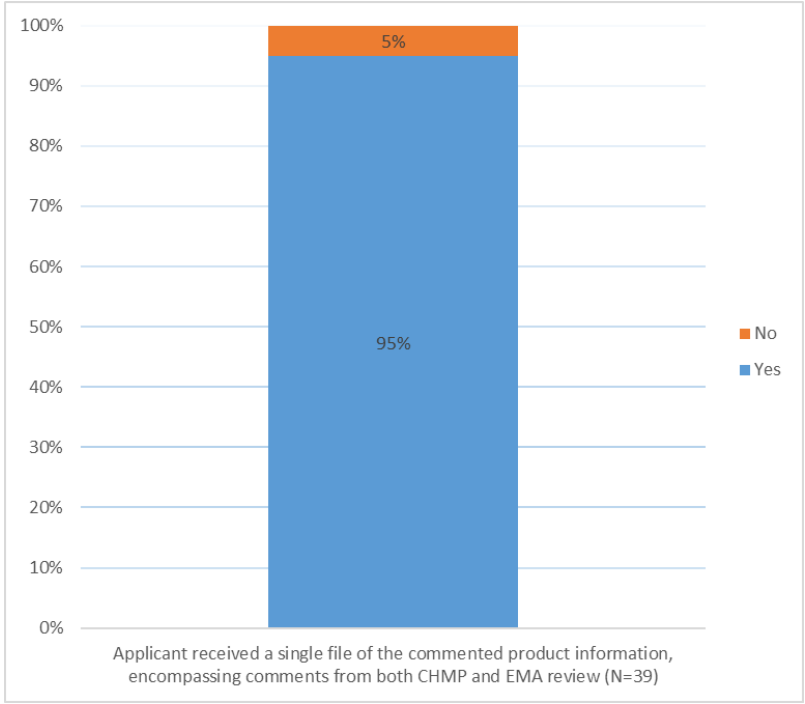


2. Assessment phase: AR Clarity



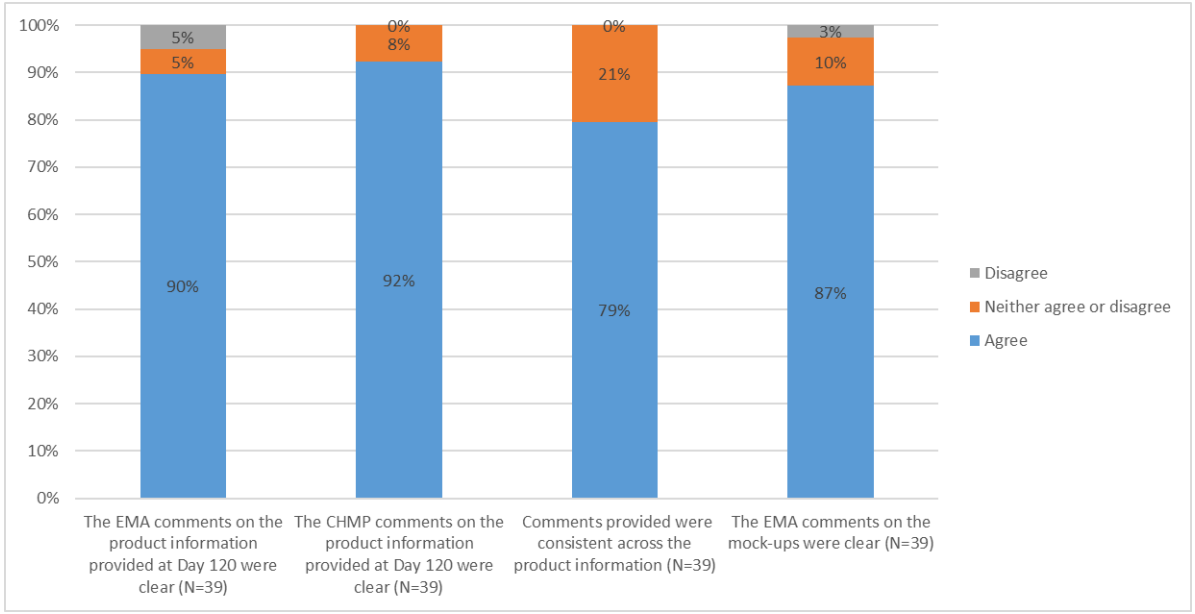
Clarity of assessment reports was reported as a positive in the majority of cases

2. Assessment phase: product information circulation



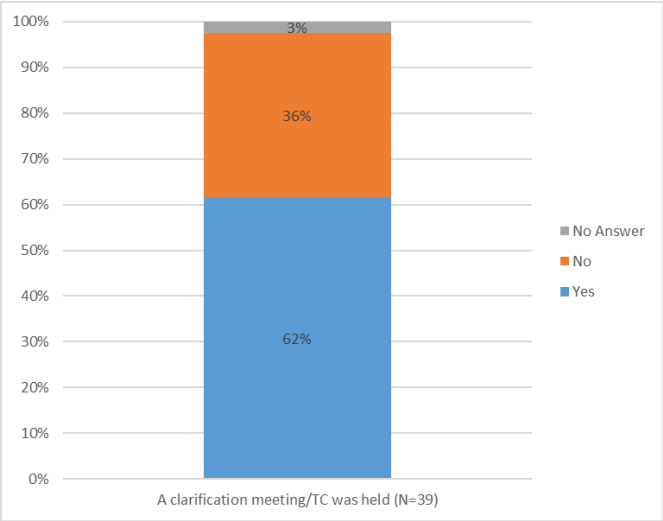
The majority of respondents received a single file encompassing comments from both the CHMP and EMA

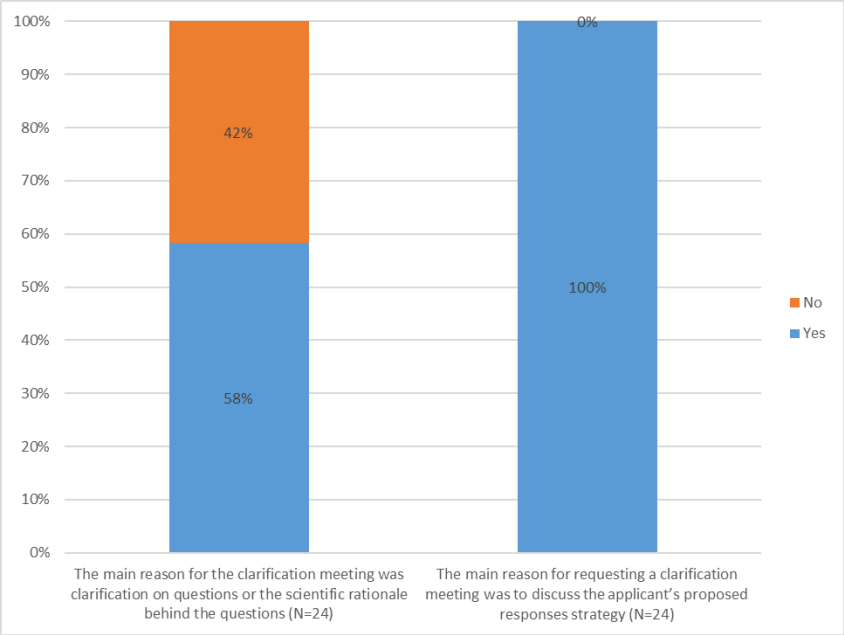
3. Assessment phase: product information clarity



The clarity of comments on Product Information was considered positive by the majority of respondents

4. Clarification meetings *(1/2)*

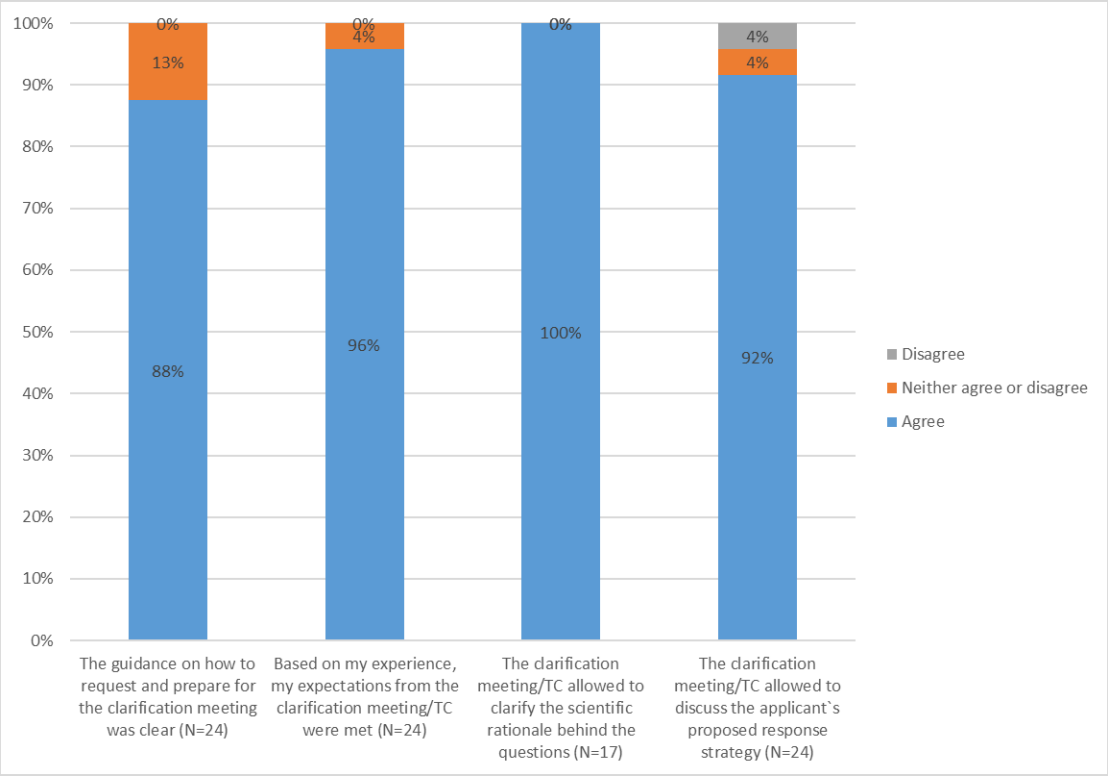




Clarification meetings more common for NCE MAAs

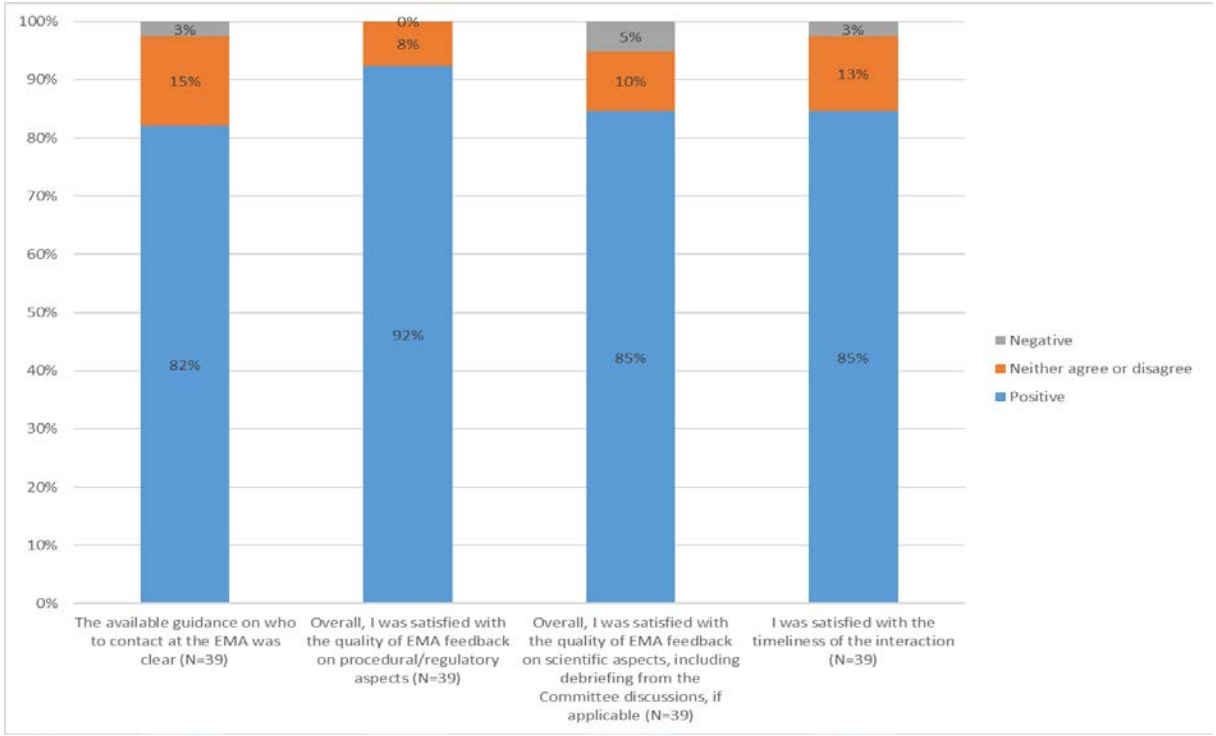
4. Clarification meetings *(2/2)*

Clarification meetings are well regarded



4. Interaction during primary phase

Contact with the EMA was generally positive



Conclusion

- Overall, responses indicate that Day 0 to Day 120 of the Centralised Procedure is well run
- Although assessment reports are usually provided in accordance with the timetable, delays are not uncommon and are not always proactively communicated to the Applicant
- The Assessment reports, questions and major objections are of high quality (clarity, consistency etc) as are the comments on the Prescribing information and mock ups
- The clarification meetings are particularly valued for their usefulness, especially for discussing the Applicant’s response strategy
- Interactions with EMA are very positive

Overall recommendations

Investigation into the delay of the (Co-)Rapp Assessment Reports may be warranted

- Is sufficient time included for EMA legal review or is this a resource issue for the Rapporteurs?
- Should this be reflected in the published procedure timetables?
- Consistency of communication from EMA to Applicant regarding delays would be appreciated

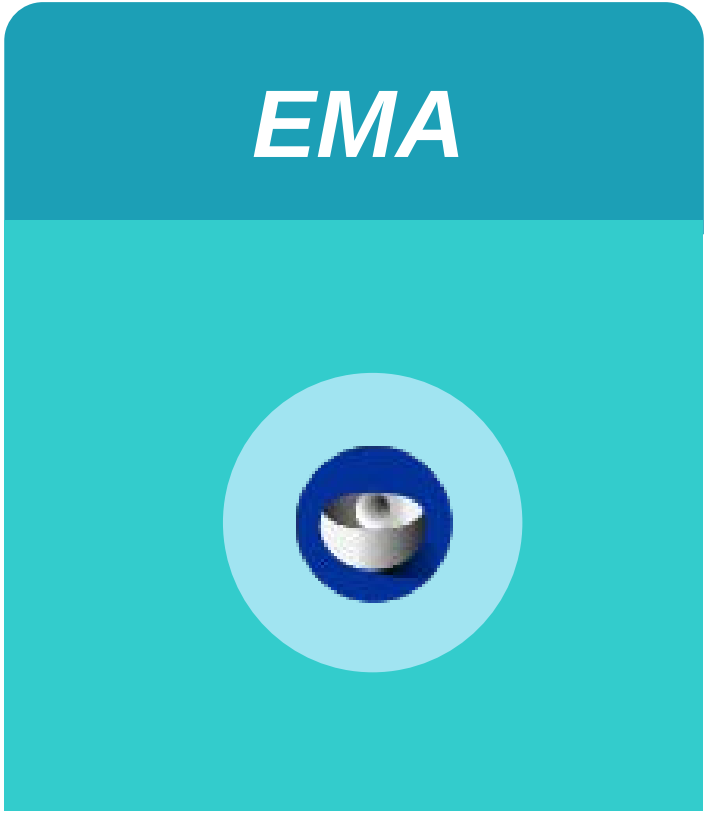
EMA Contact Points

- Although 82% of responders thought the guidance clear on who to contact at the EMA, the comments referred to some uncertainty regarding contacting EPL/EPM

Stakeholders surveyed

Primary evaluation phase:

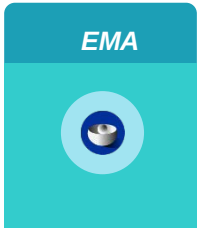
DAY 1-121



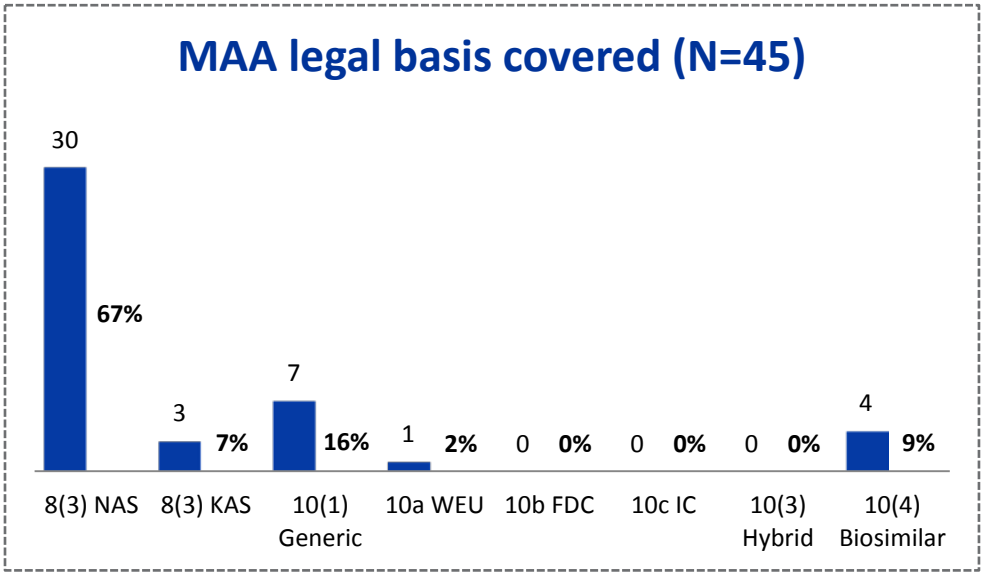
Day 1 to 121 survey to EMA - Results

- Topics covered through 13 questions:
  1. Applications details
  2. Labelling review in the primary assessment phase
  3. Clarification meeting
  4. Overall feedback on the interaction with applicants during the primary assessment phase

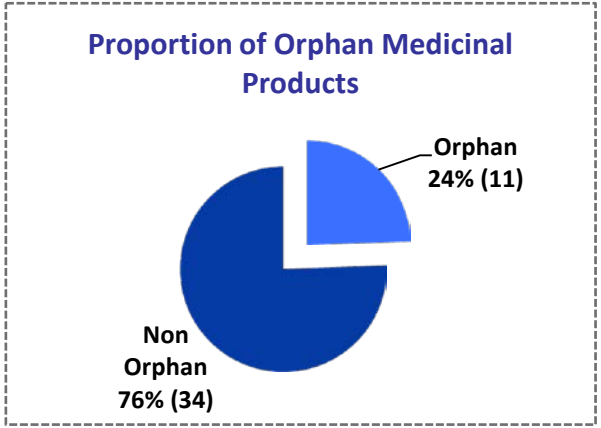
- ✓ 45 MAA captured
- ✓ EMA completion rate: 100%

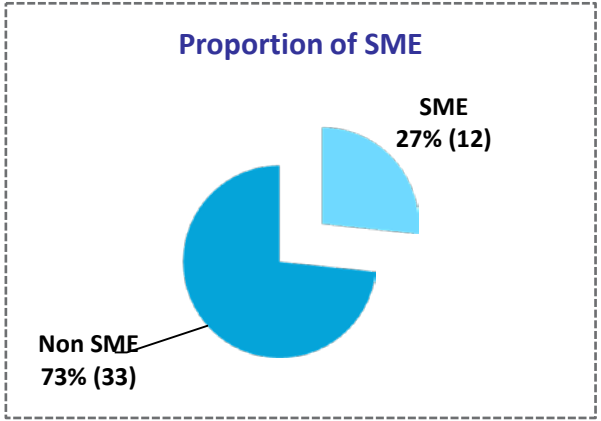


1. Application details

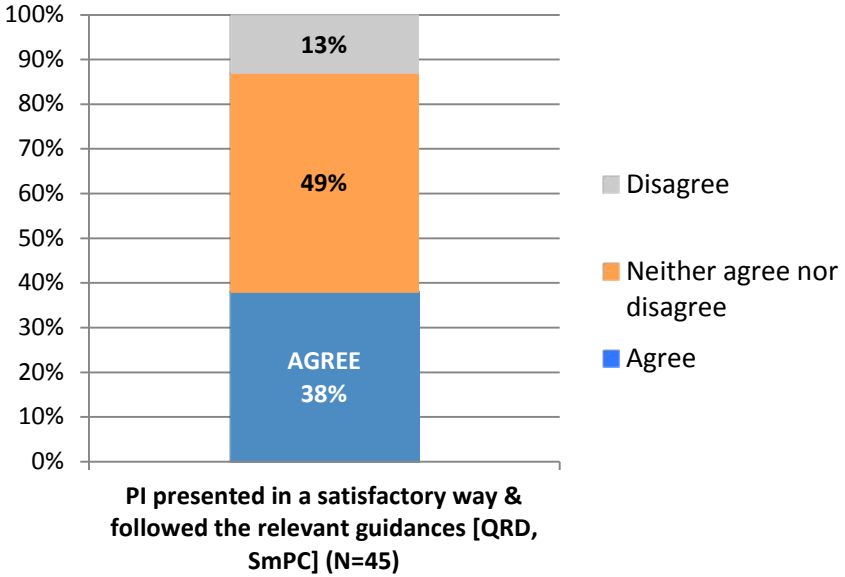


New Active substance: NAS, Known Active substance: KAS, Well-Established Used: WEU, Fixed Dose Combination: FDC, Informed Consent: IC,





2. Labelling review



- EMA mainly neither agrees nor disagrees (rated 3)
  - Most relevant comments: “almost empty SmPC”; principle of SmPC guideline not always correctly implemented; poor compliance with the QRD template & SmPC guideline”

- **Adherence to guidance & template could be improved**
- **EMA should investigate opportunities to increase awareness on existing guidances**

3. Clarification meetings

(across 45 applications)

SAMPLE COMMENTS

"Written clarification substituted meeting in 2 occasions;

Very positive feedback on the usefulness of the meeting;

Meeting clearly needed & much facilitated the understanding of major issues."

- ❖ Meeting in 62% [28] of applications (<2/3 applications)
  - Applicants clearly specified scope & topics to be discussed – 93%
  - Briefing document a week before the meeting – 79%
- ❖ Most of the meeting happened for NAS (85%); and/or orphan product (82%) and/or SME applicants (83%)
- ❖ EMA considered that the meeting facilitated the progress of the procedure in almost ¾ of the meetings

➢ **Majority of applicants displayed very good adherence to the guidance with the requirements (clarity of scope & topics and briefing documents provided timely)**

4. Satisfaction on interaction with applicants

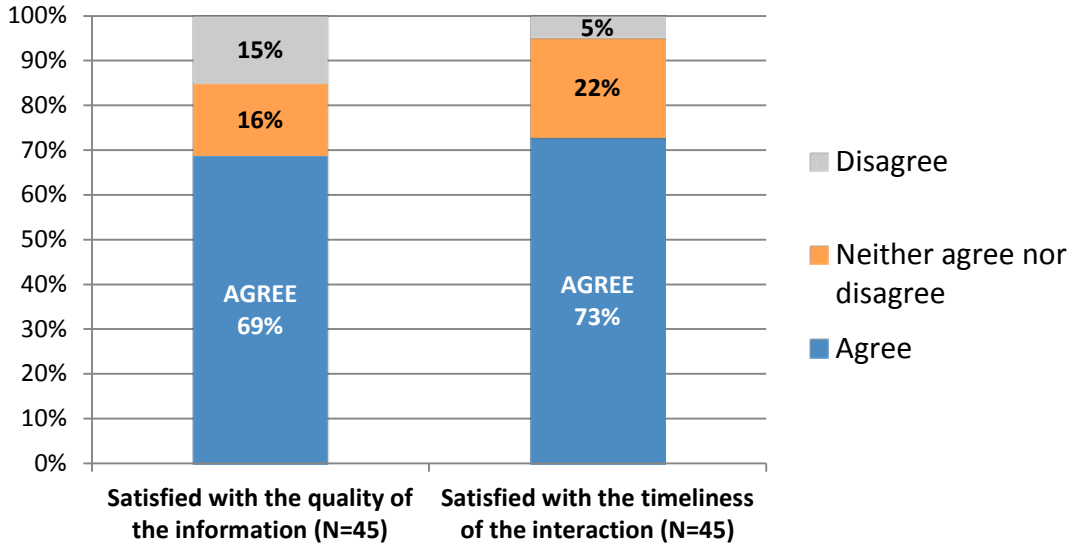
SAMPLE COMMENTS

"Applicant communicated well, in a timely and pro-active manner;

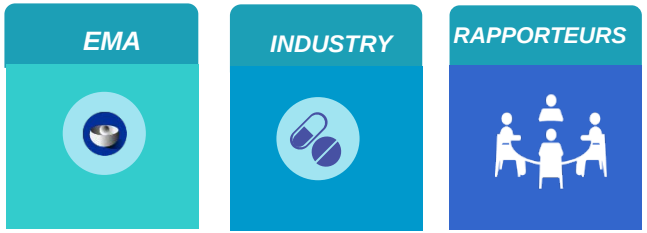
No problems identified with the interaction with the applicant at all."

➢ **Overall EMA feedback positive**

- EMA satisfied with the quality of the information (69%) & timeliness of interactions (73%) during the 1st phase of assessment



Stakeholders surveyed



Primary evaluation phase:

DAY 1-121

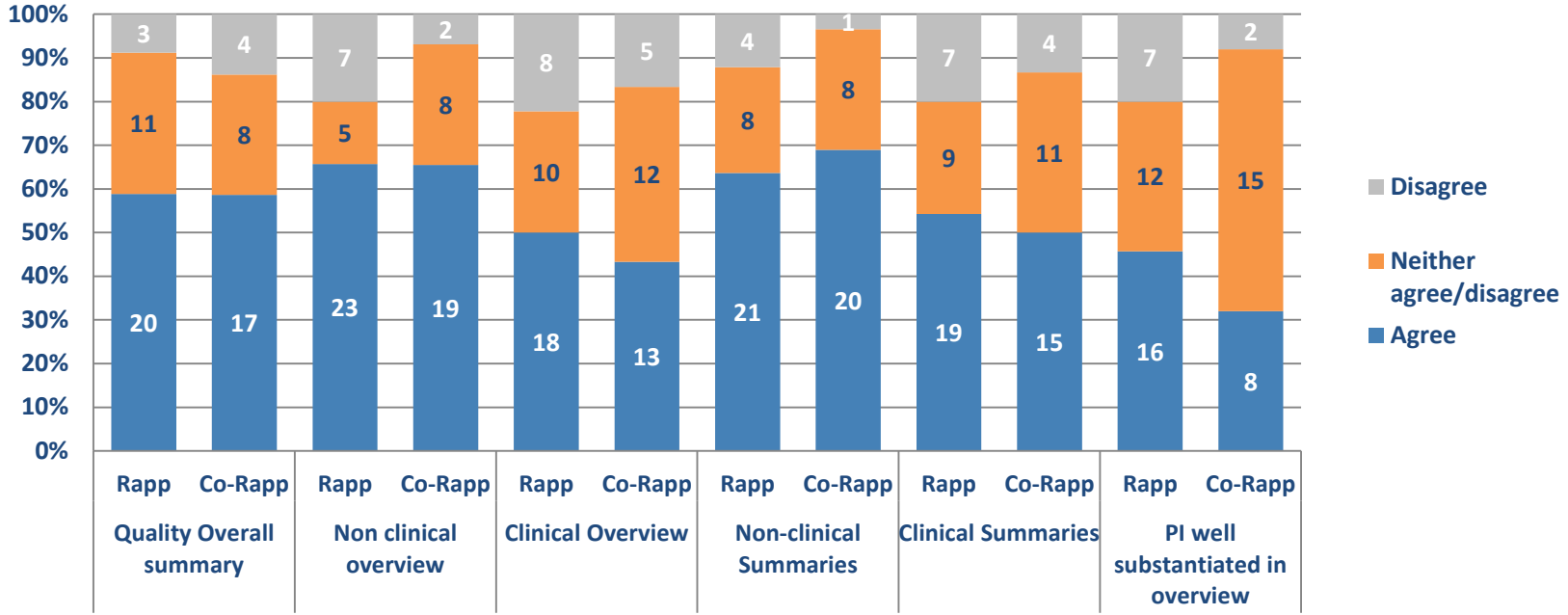
Day 1 to 121 survey to Rapporteurs- Results

- Topics covered through 11 questions:
  1. Applications details
  2. Satisfaction with relevant parts of the dossier (Quality, Non-clinical, Clinical, Product Information, RMP)
  3. Adherence to scientific advice
  4. Labelling review in primary phase
  5. Clarification meeting
  6. Overall feedback on the interaction with applicants during the primary assessment phase

- ✓ 49 MAA captured
- ✓ Completion rate: 76/79% (Rapporteur/Co-Rapporteur)

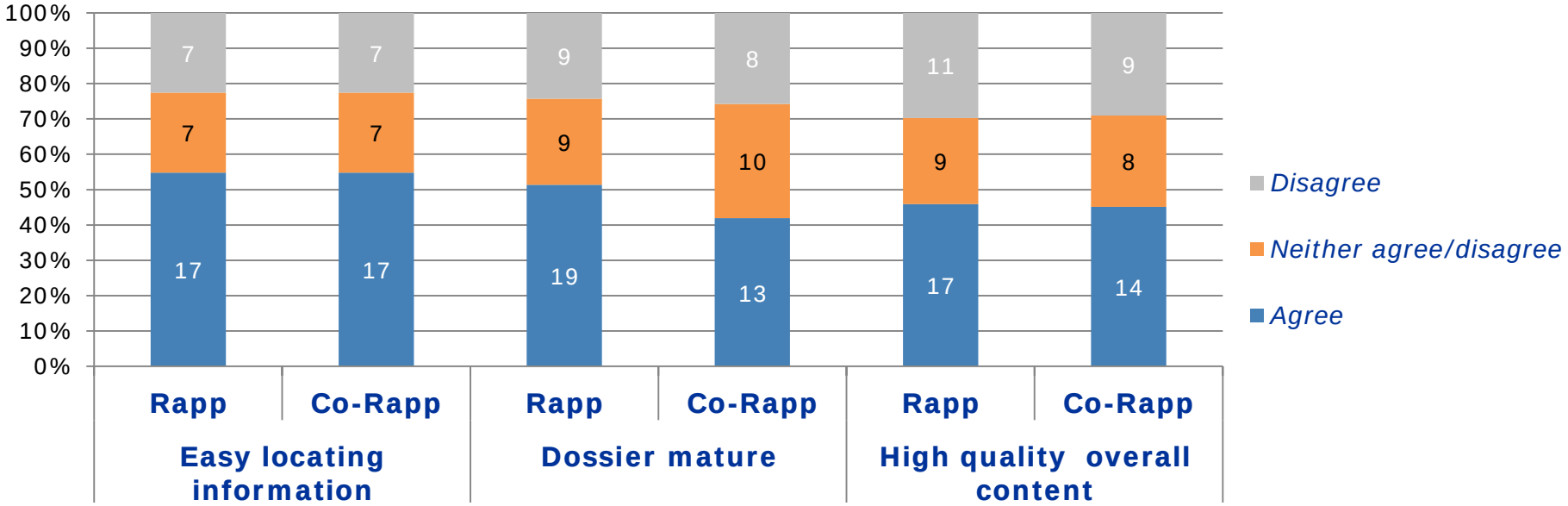
2 & 4. Dossier content satisfaction level

- Positive ratings varied from 32% to 65% of responses (lowest: Clinical Overview and PI well substantiated in overview)
- Large proportion “undecided/3” ratings



2. Dossier overall content quality

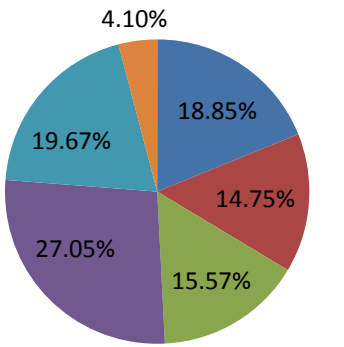
Average level of satisfaction of initial MAAs content [45-55%]



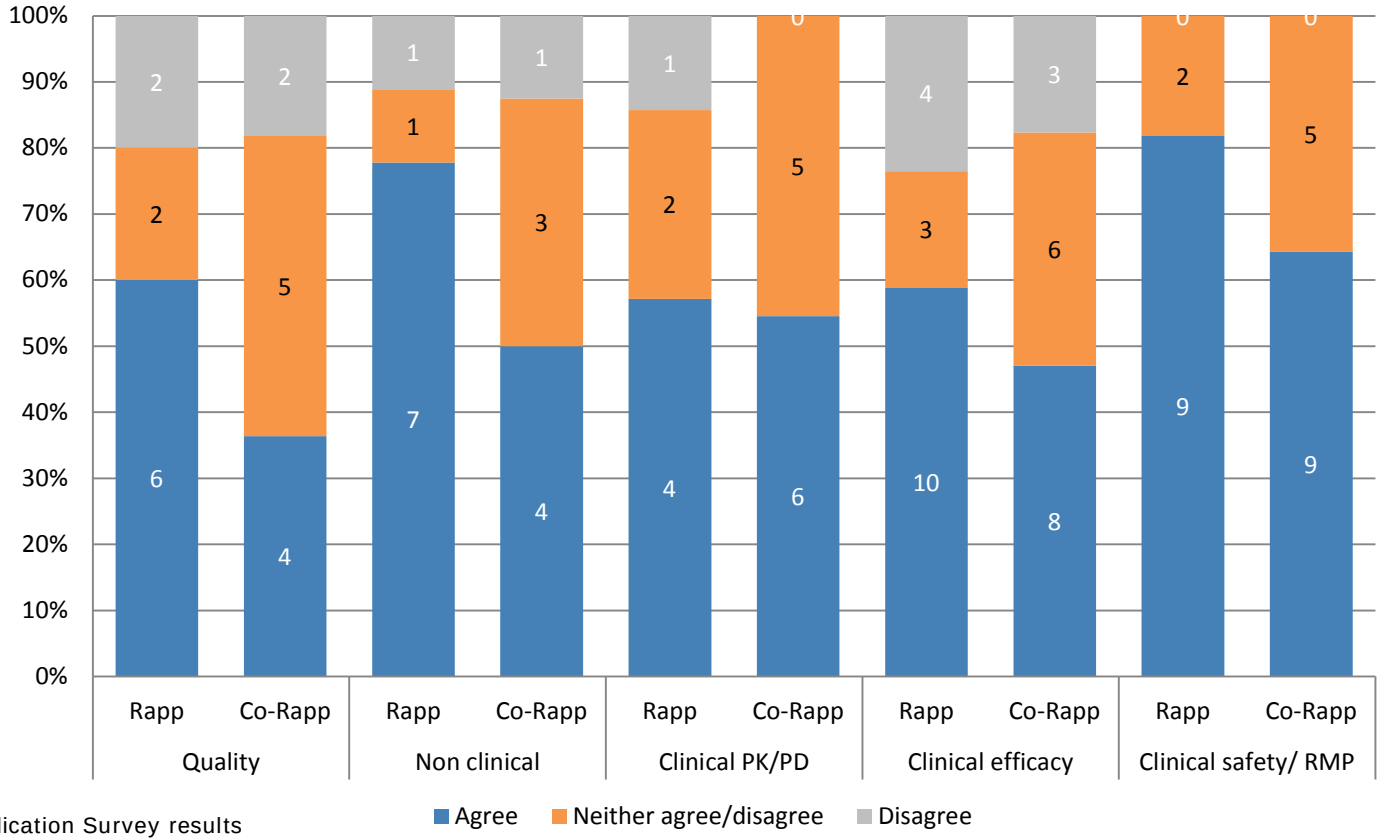
Considerations:

- in 20-25% responses rapporteurs considered dossier not mature enough and information not easy to find.
- In 30% responses rapporteurs were not satisfied with the quality of the overall content.

3. Adherence & scope of scientific advice



- Quality
- Non clinical
- Clinical PK/PD
- Clinical Efficacy
- Clinical Safety/RMP
- Other



3. Adherence to scientific advice: scope details

Adherence to Scientific Advice in the majority of the cases

Examples of non-adherence :

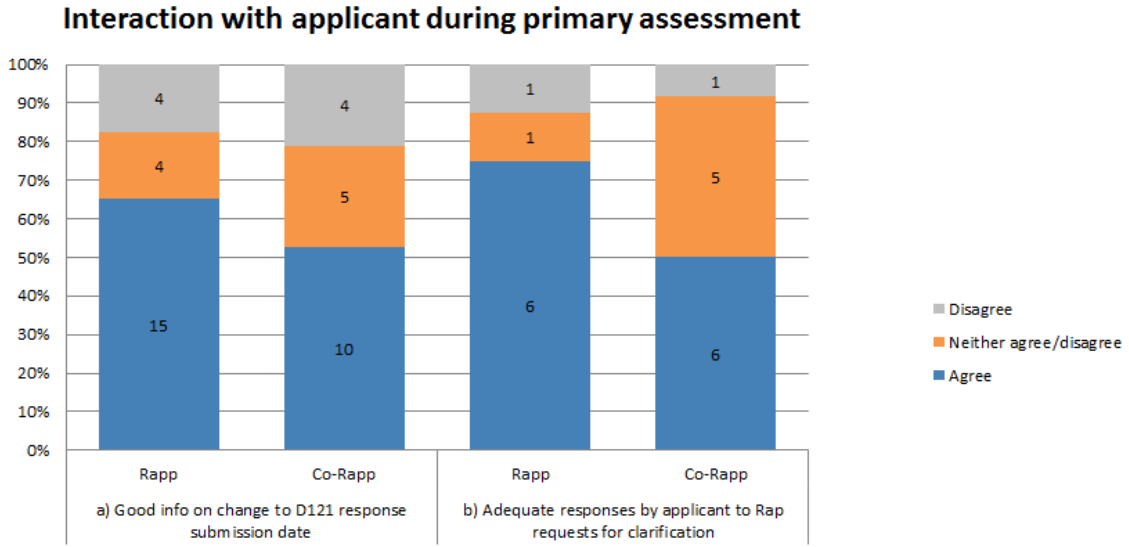
- Quality : Process validation package; definition of starting materials; amount of stability data
- Clinical : disease model; choice of comparator; choice of endpoint

→ If deviating justification to be presented in Overview

6. Interaction with applicants

- Overall ± 60% satisfaction with **information on response date change** and **response to ad-hoc clarification requests**

Overall feedback Day 1-121



Conclusions and recommendations

- Responses indicate moderate level of satisfaction with the content of the initial dossier (40-50% positive ratings on overall content, 30% negative)
  - Improvements could be made in the presentation of the application, e.g. clinical overview including substantiating the information proposed for the PI.
  - Applicants are encouraged to ensure all relevant data can be easily located and include clear references to the location of relevant data/information in CTD (hyperlinks).
  - The need for mature dossiers was highlighted.

- Most applications considered adherent to Scientific Advice
  - In the event of deviation(s), a clear and sound justification is recommended in the MAA; this is likely to facilitate the proceeding of the assessment

- Feedback on interaction with applicants generally positive
  - Applicants should provide accurate estimates of the planned submission dates – be as realistic as possible. This is important for the work schedules of the assessment teams.
  - In case of changes to submission deadlines, EMA and Rapporteur teams should be informed asap.

Stakeholders surveyed

Opinion finalisation phase:

Day 121-210

This is a joint industry presentation on behalf of the trade associations shown

Day 121 to CHMP Opinion survey to Industry: Results

- Topics covered through 25 questions:

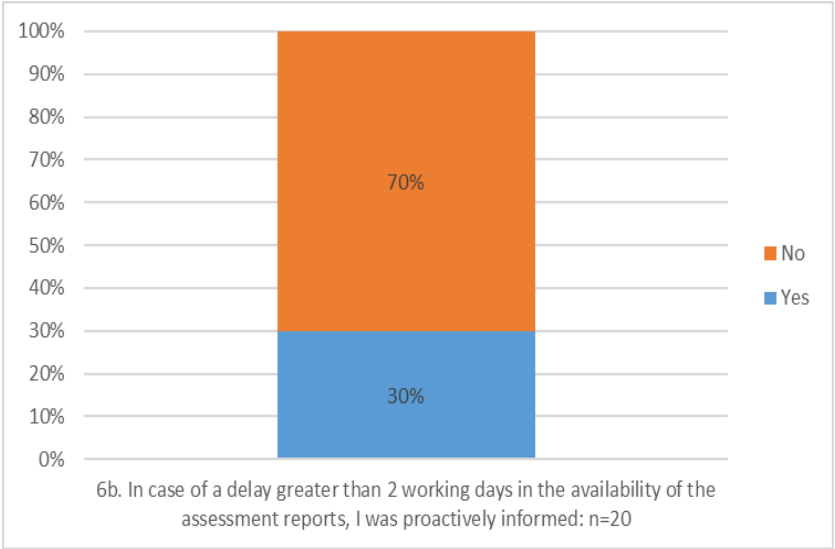
1. Applications details
2. Assessment reports in final assessment phase
3. Clarification meeting
4. SAGs/Ad-hoc experts groups
5. Oral explanation at committee plenaries
6. Finalisation of commitments and opinion documents
7. Overall feedback on interactions with applicants during the final assessment phase

- ✓ 44/48 MAA captured
- ✓ Industry completion rate: 92%

2. Assessment phase: AR circulation timeliness

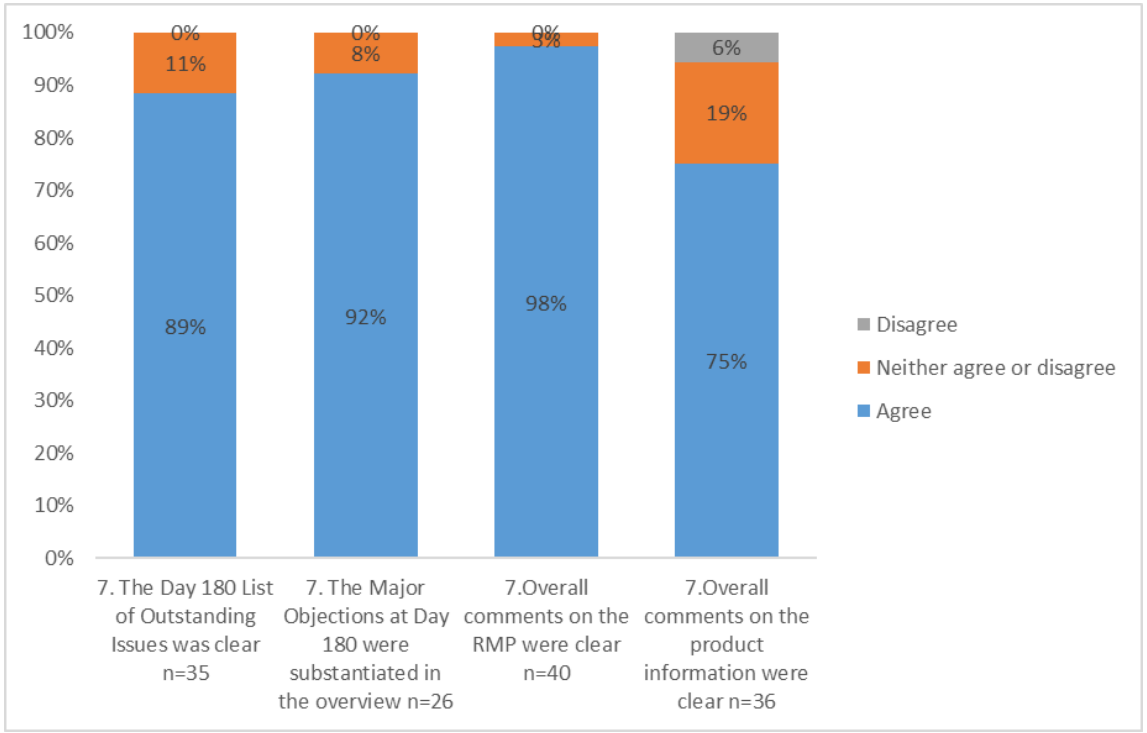
Majority of Assessment Reports received within 2 days of the due date

- 51% of Day 150 Rapp Assessment Reports (n=37)
- 68% of Day 194 Rapp Assessment Reports (n=31)
- 30% of respondents were proactively informed of a delay



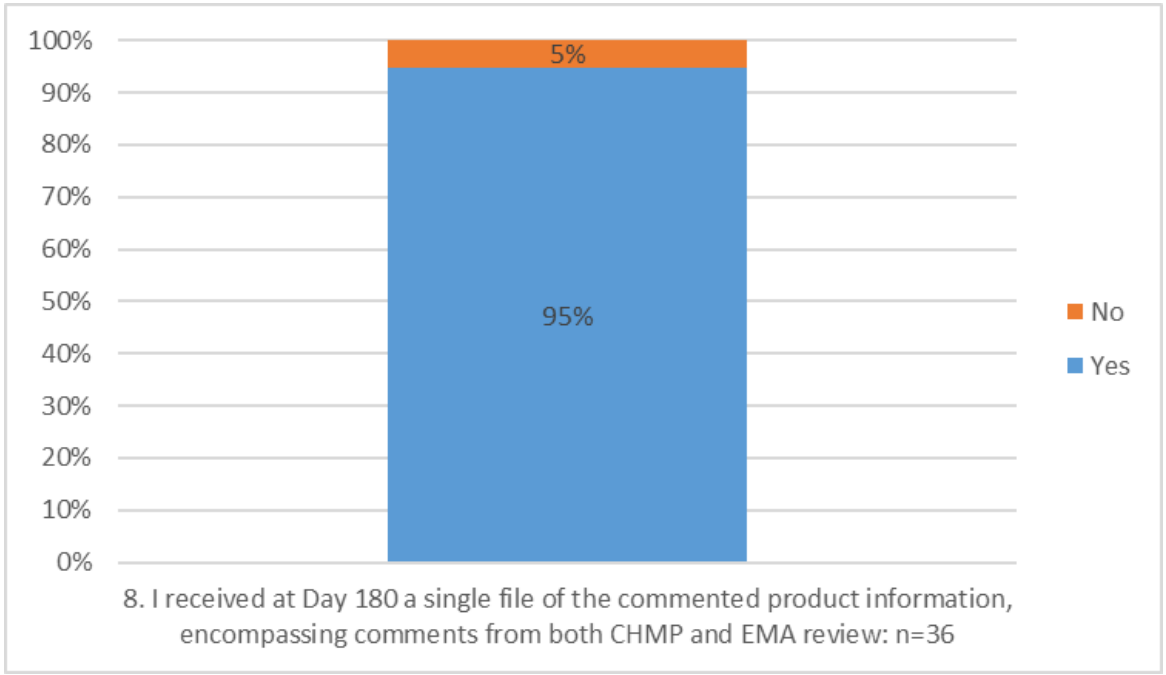
2. Assessment phase: LoQ clarity

Comments and questions were clear and substantiated in assessment reports



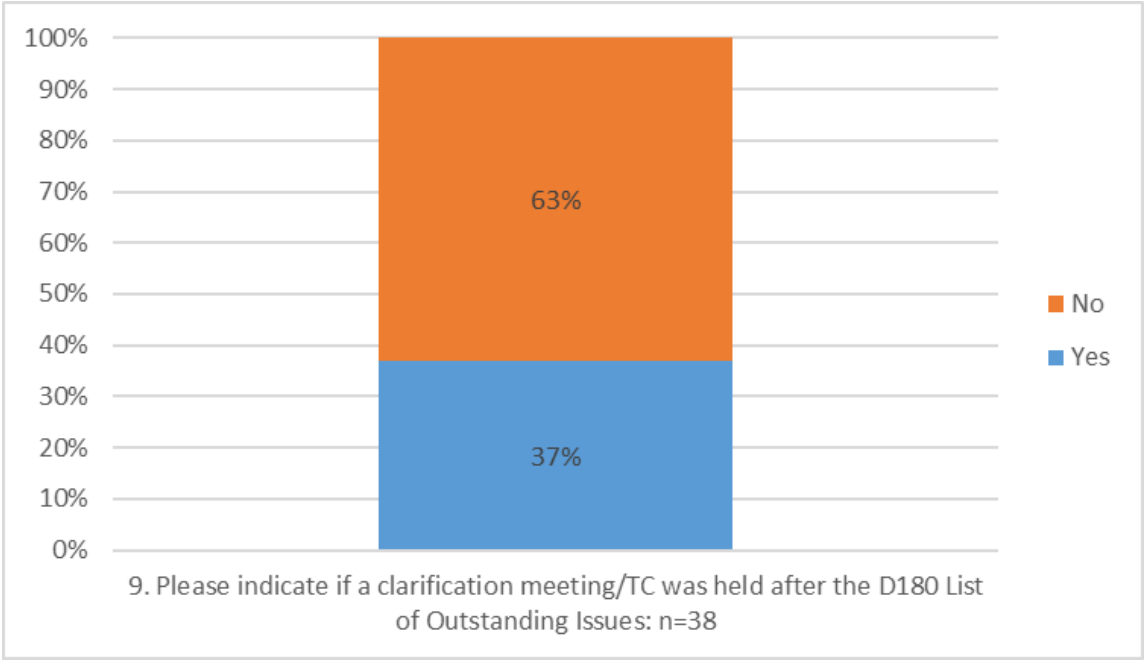
2. Assessment phase: 180 AR circulation timeliness

In most cases, a single consolidated assessment report was received at D180



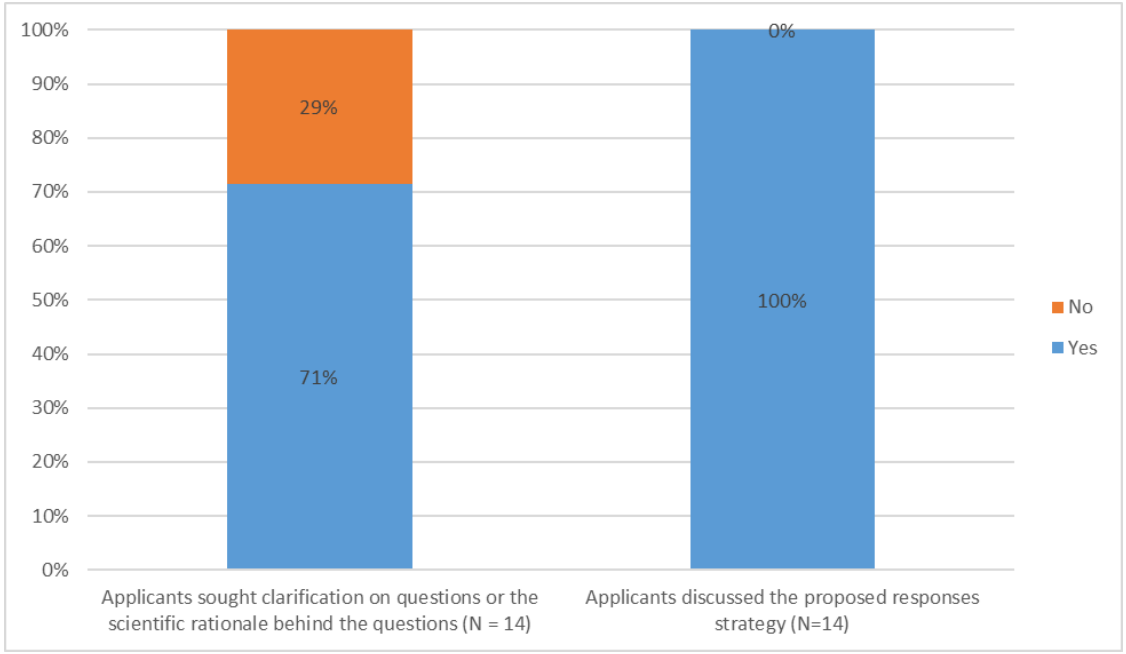
3. Clarification meetings *(1/3)*

Clarification meetings were held for:
9 'Other' licences
5 NCEs
2 Biosimilars



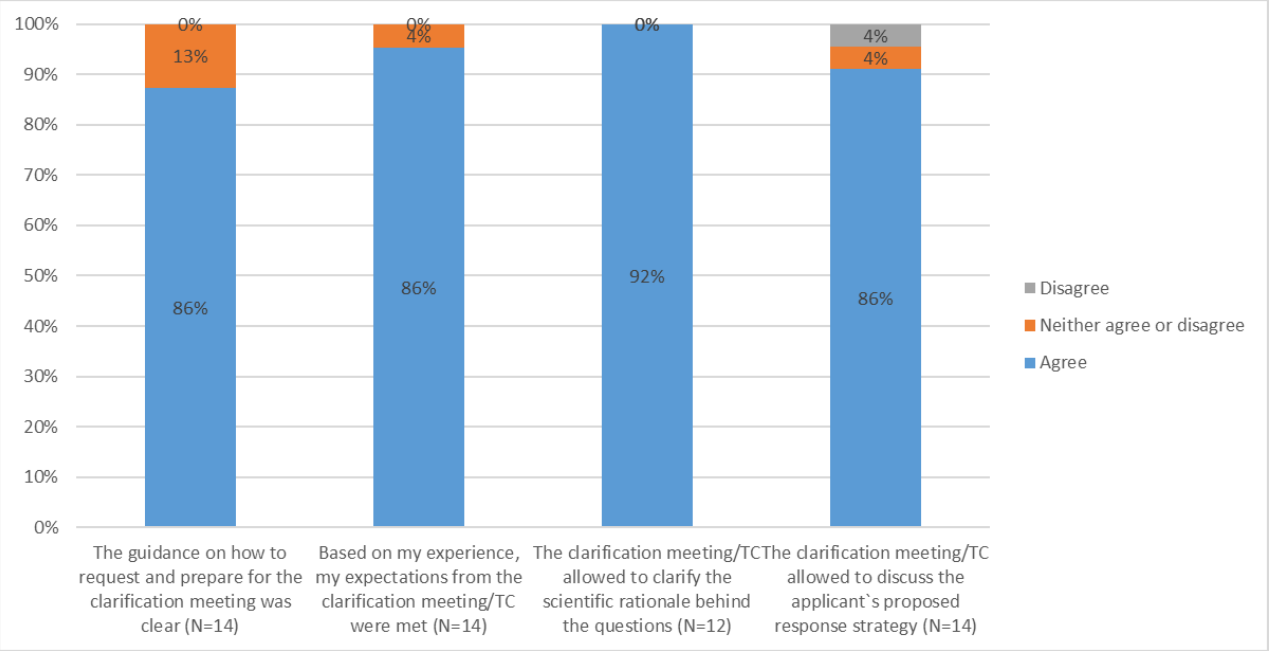
3. Clarification meetings usefulness *(2/3)*

Clarification meetings are particularly useful for discussing response strategy



3. Clarification meetings usefulness *(3/3)*

Clarification meetings are well regarded

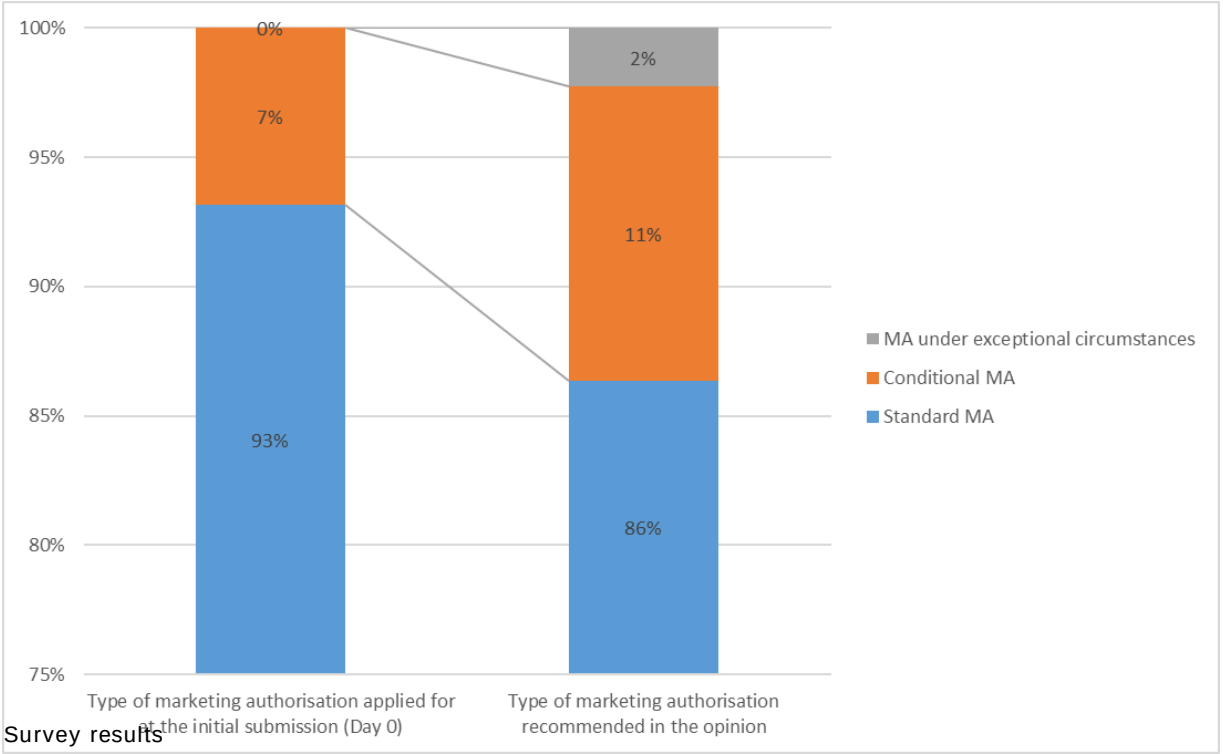


4 & 5. SAGs and oral explanation

Only 2 SAGs and 3 Oral explanations were held - too few for any conclusions

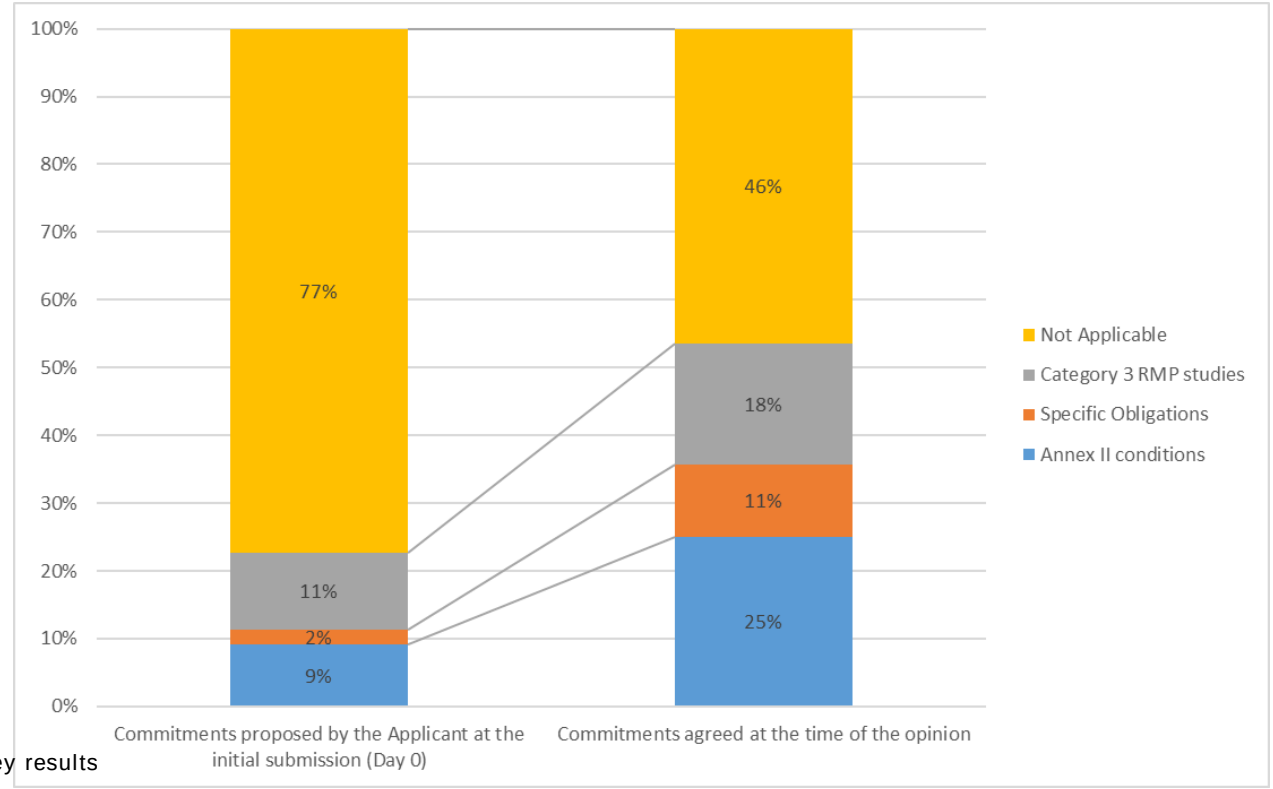
6. Opinion category switch

Changes in type of MA can occur during assessment



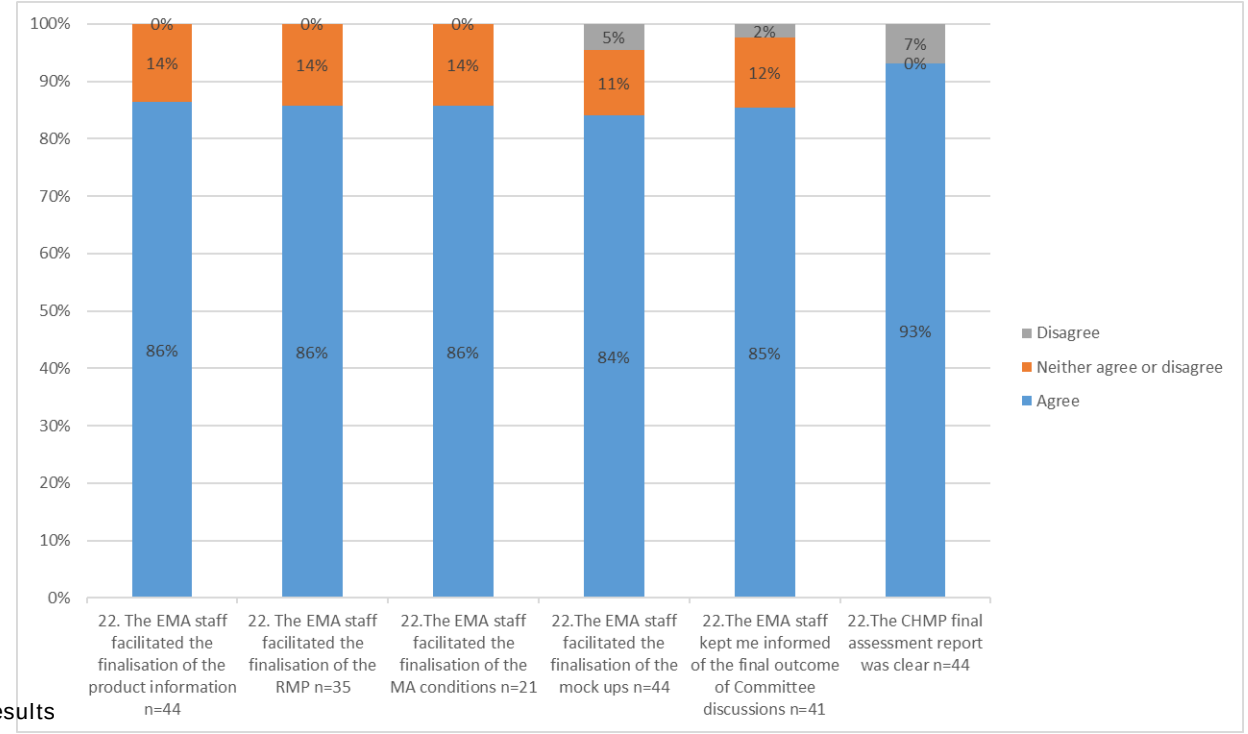
6. Opinion category

More conditions on the licences are imposed during assessment than are foreseen by the Applicant



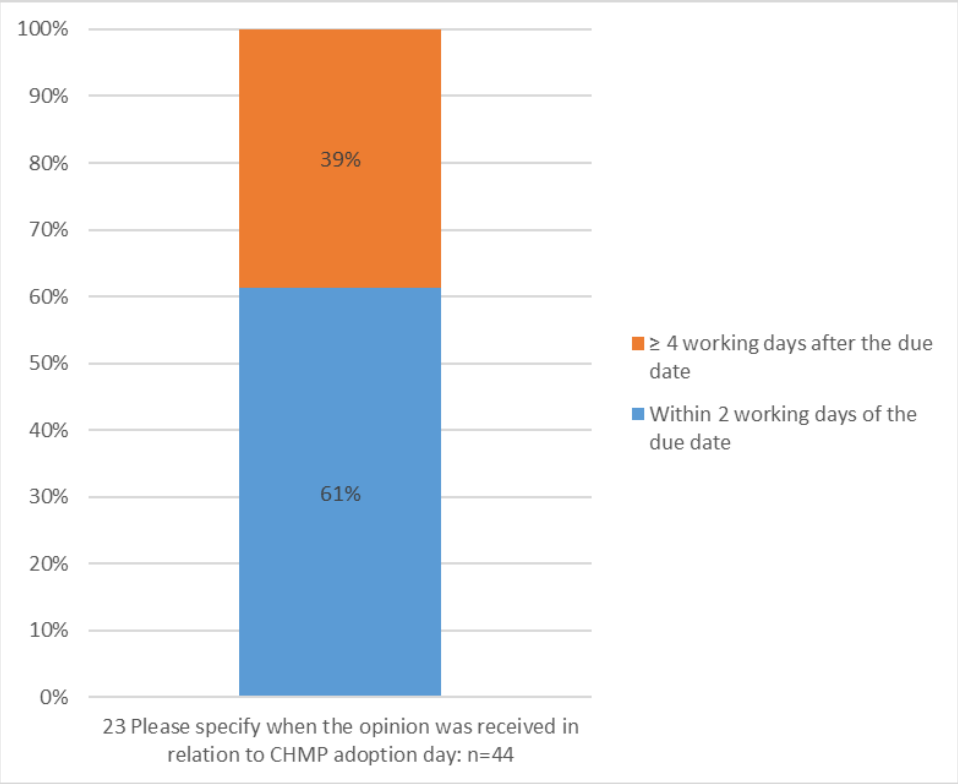
6. Interaction level of satisfaction

There are high levels of satisfaction with EMA interaction during finalisation stages to CHMP Opinion



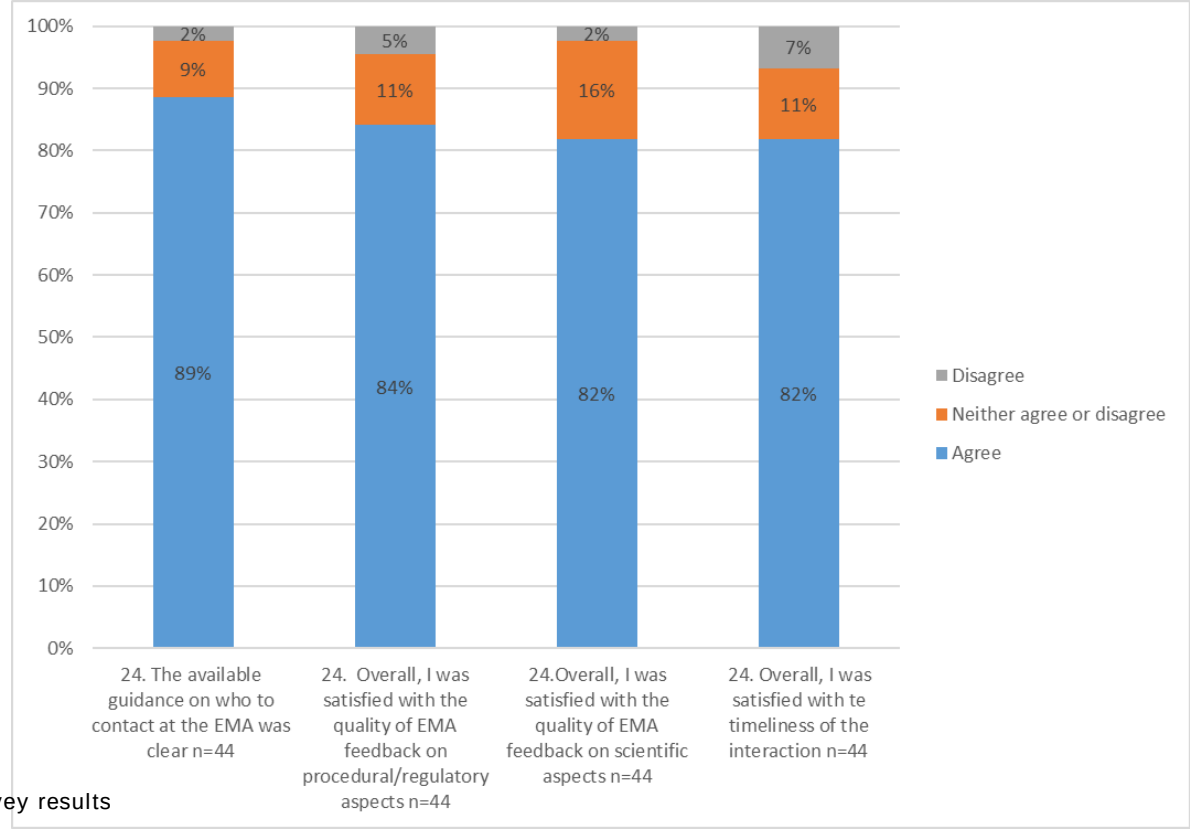
6. Opinion receipt timeliness

CHMP Opinion was not received within 2 working days in a number of cases



7. Interaction with EMA

Contact with the EMA was generally positive



Conclusion (1/2)

- Overall, responses indicate that Day 121 to Day 210 of the Centralised Procedure is well run.
- Delays in assessment reports are similar to those seen earlier in the procedure and again, are not always proactively communicated to the Applicant
- The Assessment reports, questions and major objections are of high quality (clarity, consistency etc)
- As for D0 – D120, the clarification meetings are particularly valued for their usefulness, especially for discussing the Applicant's response strategy, too few SAGs and Oral Explanations were held to draw any conclusions

Conclusion (2/2)

- Standard licences were granted in the majority of cases, however, a few applications for standard licences were granted Conditional approval/approval under Exceptional Circumstances
- More conditions (ANX, Specific Obligations, RMP studies) were imposed during assessment than had been proposed in initial applications
- Interactions with EMA and their facilitation of documents for opinion are very positive
- However, the actual opinion was quite often received at least 4 days post CHMP meeting leading to concerns regarding the timelines for providing translated annexes and there was a lack of awareness regarding timing/content of the EMA CHMP meeting Press Release

Overall recommendations

Again, investigation into delay of Assessment Reports may be warranted

- Is sufficient time included for EMA legal review or is this a resource issue for the Rapps?
- Should this be reflected in the published procedure timetables?
- Consistency of communication from EMA to Applicant regarding delays would be appreciated

There was a lack of awareness of the possibility of further rounds of D180 questions

- Perhaps a Q and A in Pre-authorisation guidance, including the timetables for assessment, would be helpful

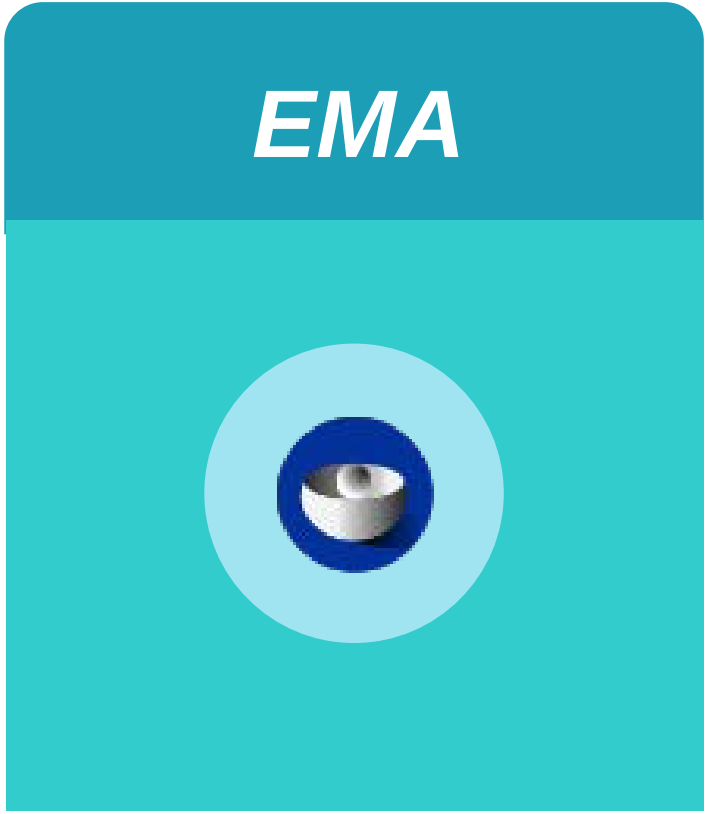
The timing of receipt of CHMP Opinion was not consistent and there was a lack of awareness of the timing/content of the Press release from the CHMP meeting

- Perhaps a Q and A in Pre-authorisation guidance would be helpful

Stakeholders surveyed

OPINION FINALISATION PHASE:

DAY 121-210

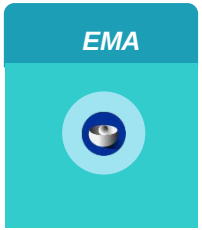


Day 121 to 210 survey to EMA - Results

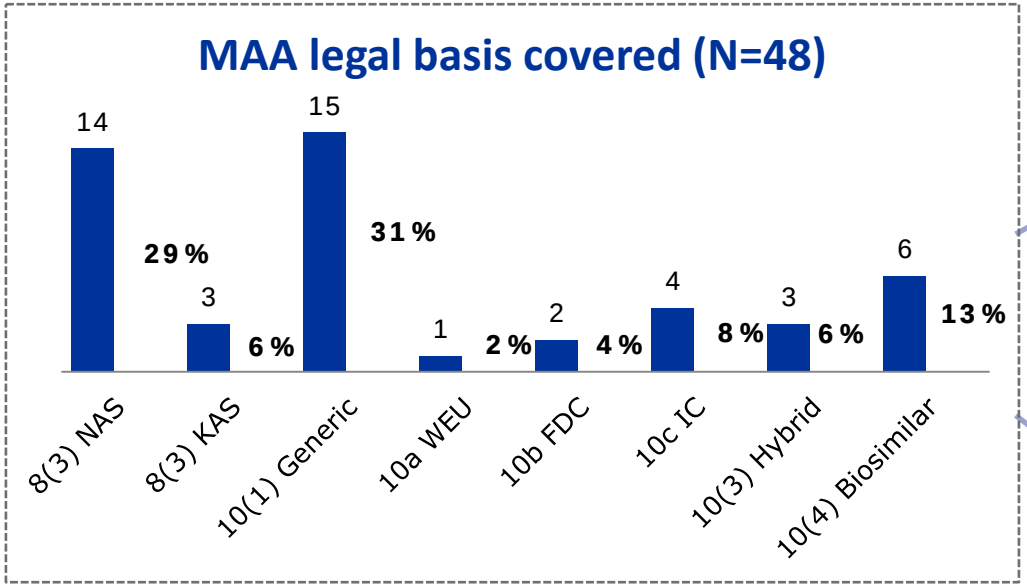
- Topics covered through 25 questions:

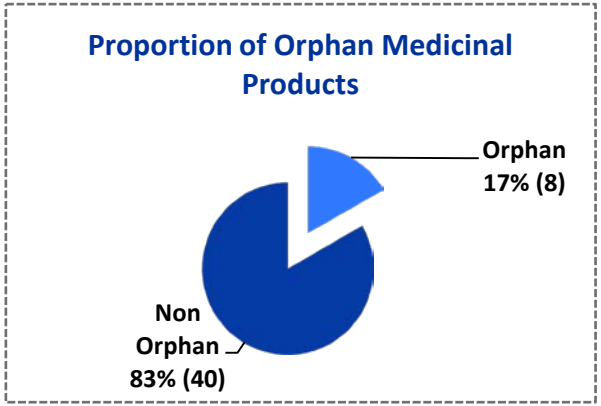
1. Applications details
2. Clarification meeting
3. SAGs/Ad-hoc experts groups
4. Oral explanation at committee plenaries
5. Finalisation of commitments and opinion documents
6. Overall feedback on interactions with applicants during the final assessment phase

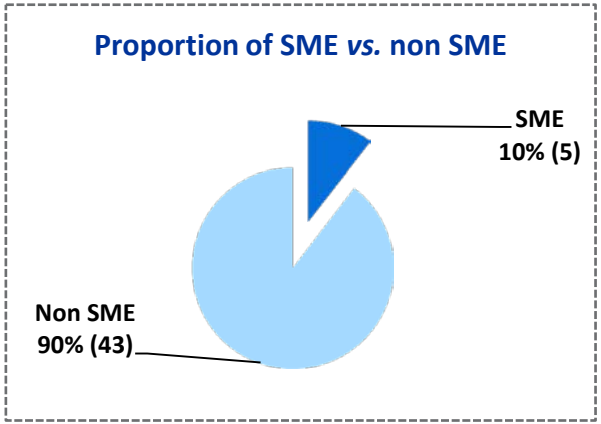
- ✓ 48 MAA captured
- ✓ EMA completion rate: 100%



1. Application details (1/2)







New Active substance: NAS, Known Active substance: KAS, Well-Established Used: WEU, Fixed Dose Combination: FDC, Informed Consent: IC,

1. Application details (2/2)

- Orphan products & SME applicants: in line with EMA records of previous years

	2015 (full year)	2016 (full year)	Survey (6 months)
Orphan	18 (8 in 1st 6 months)	16 (8 in 1st 6 months)	8
SME	9	5	5

- High proportion of generic and informed consent (IC) applications: almost 40% of the opinions
- May explain certain results of this survey phase: low number of clarification meetings, SAGs/Ad-hoc expert groups and oral explanations.

2. Clarification meetings

(across 48 applications)

❖ Meeting in 42% [20] of applications (<50% applications)

- Applicants clearly specified scope & topics to be discussed – 100%
- Briefing document a week before the meeting – 80%

❖ Approximately 50% of the meeting happened for NAS; almost all orphan had a clarification meeting; 2 SME had a meeting

❖ EMA considered that the meeting facilitated the progress of the procedure in almost all meetings – 85%

➢ **Majority of applicants displayed excellent adherence to the guidance ⟺ very good level of awareness**

➢ **High proportion of generics and informed consent may explain the low number of meetings**

SAMPLE COMMENTS

"Meeting was crucial;

Meeting particularly useful as allowed applicant to define their strategy and led to the cancellation of the Oral Explanation;

Meeting needed to clarify complex issues and explore options for a conditional approval."

3. SAGs or Ad Hoc expert group meetings

- Only 2 meetings captured in the survey
- Briefing documents & applicant presentations considered informative and clear for one meeting, no opinion for the 2nd meeting
- In both cases: debriefing meeting occurred as per EMA process & EMA strongly agreed that the discussion contributed to reaching the final outcome

- Results showed that Applicants, Rapporteurs and EMA showed excellent process compliance
- **No conclusion can be drawn from the only 2 cases**

4. Oral explanation

- Only 3 OEs captured in the survey; OE scopes: Quality / Efficacy / Bioequivalence
- Objections subject to the OE raised from D180 in 2 cases, from D120 for the quality objection.
- Applicants submitted presentations in a timely fashion in all cases. A debriefing meeting after the OE occurred systematically as per EMA process; with systematic attendance from the Rapporteurs, EPL and PM. Other specialists (Regulatory, Quality, RMS) attended on an ad-hoc basis.

- Results showed that Applicants, Rapporteurs and EMA showed excellent process compliance
- **No conclusion can be drawn from the only 3 cases**

5. Finalisation of commitments and opinion documents (1/2)

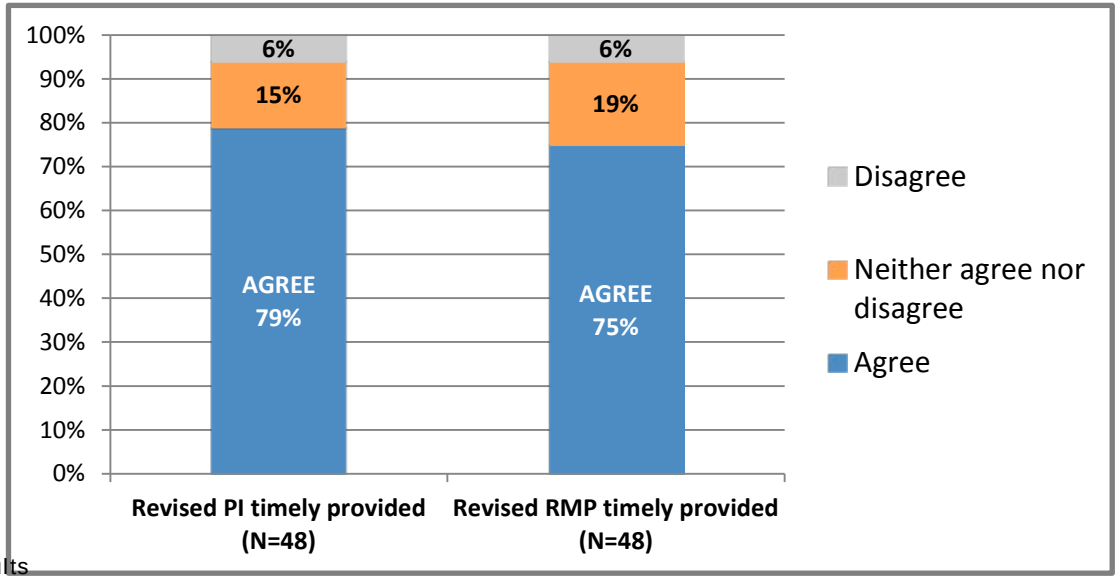
SAMPLE COMMENTS

"Exchange of information and documents with applicant and rapporteurs as well as finalisation was very smooth and efficient;

Company was quick to implement requested changes in RMP and PI, prior to opinion;

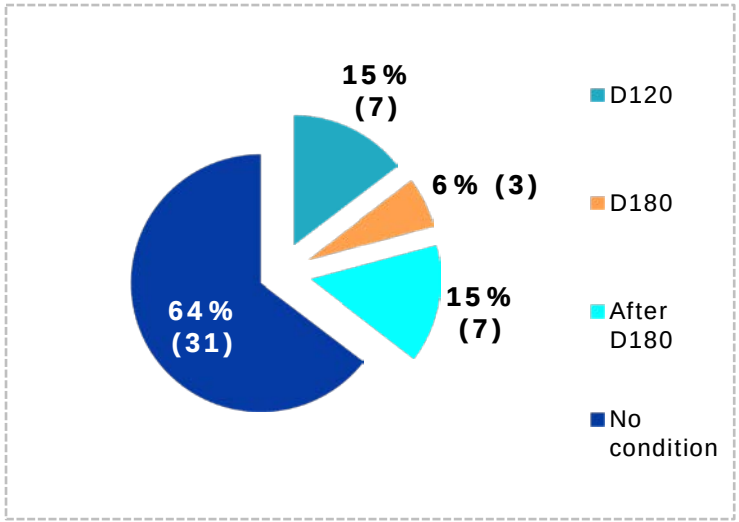
The revised RMP came late which resulted in a delay in sending out final documents."

- **Significant majority of applicants provided the requested PI (79%) and RMP (75%) revisions for opinions finalisation in a timely manner**



5. Finalisation of commitments and opinion documents (2/2)

❖ Timing for Annex II conditions



- ❖ Annex II condition in 35% (n=17) of the opinion
- ❖ Almost 60% conditions were raised from D180 only i.e. last stages of the evaluation

➢ **EMA could investigate with Committees opportunities to prompt earlier potential need for conditions to the marketing authorisation**

6. Satisfaction on interaction with applicants

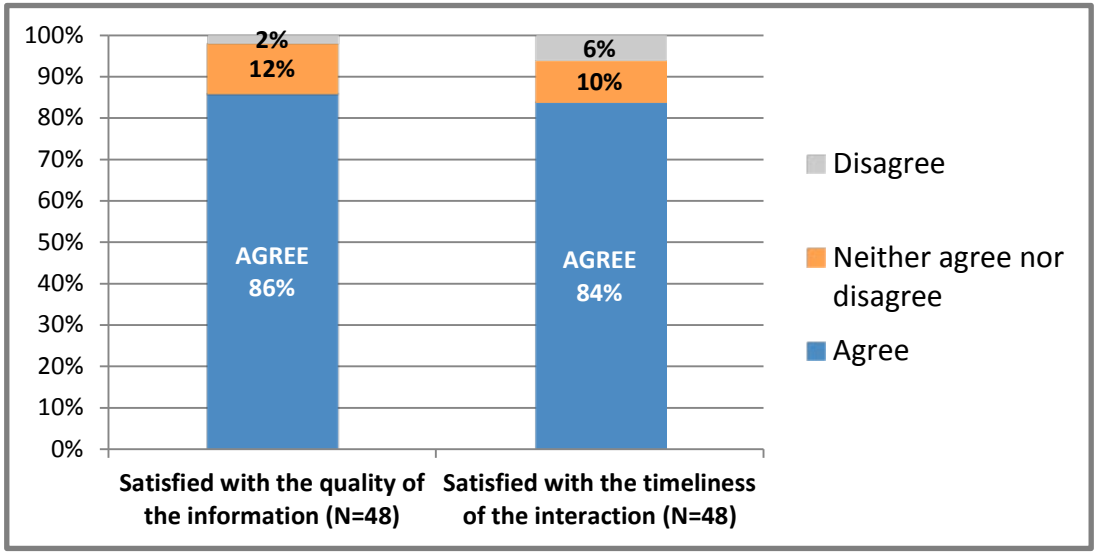
SAMPLE COMMENTS

"Applicant was professional & pro-active;

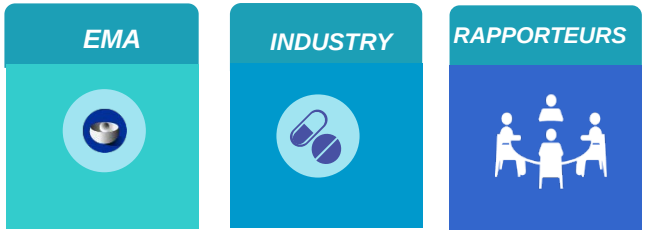
Company was fully aware of EMA processes & procedures, timelines and interactions with committees;

Interaction with company was very good and with quick responses, information submitted was clear and well organised."

- **Overall EMA feedback very positive (multiple positive comments)**
  - EMA highly satisfied with the quality of the information (86%) & timeliness of interactions with applicants (84%) during the last phase of assessment



Stakeholders surveyed



Opinion finalisation phase: Day 121-210

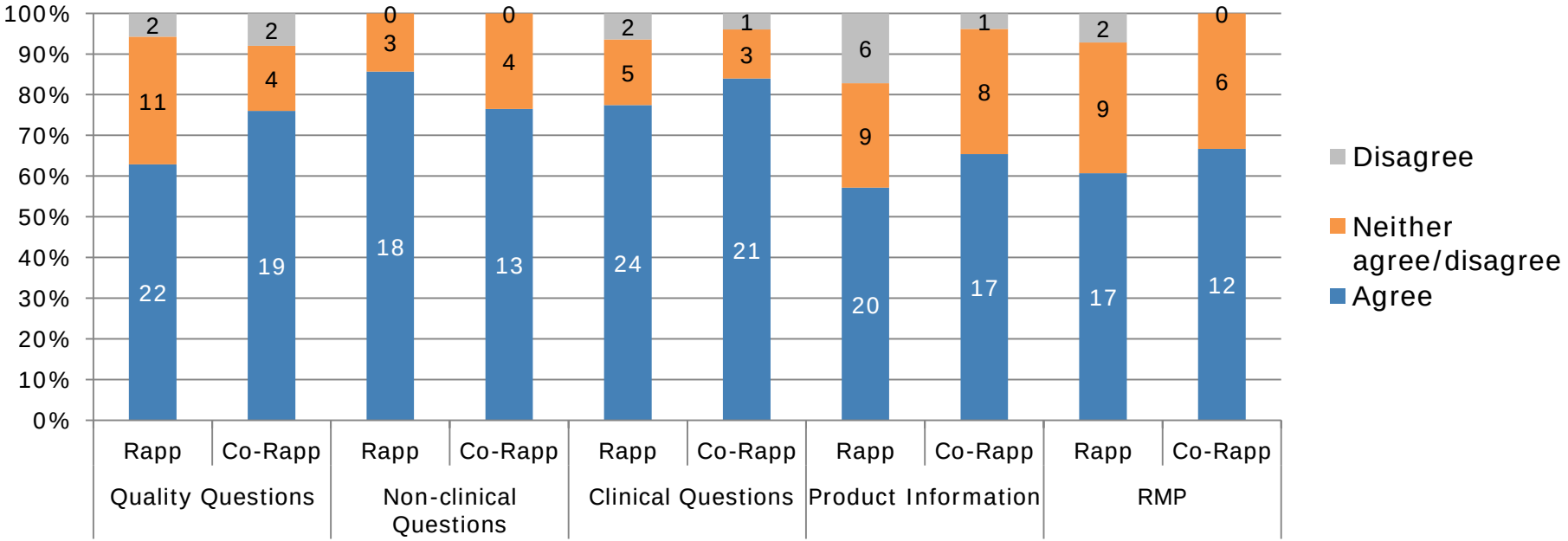
Day 121 to Opinion survey to Rapporteurs- Results

- Topics covered through 11 questions:
  1. Applications details
  2. Satisfaction with responses (Quality, Non-clinical, Clinical, Product Information, RMP)
  3. Clarification meeting
  4. Scientific Advisory Group/Ad-hoc Expert Group
  5. Oral explanation
  6. Overall feedback on the interaction with applicants during the final assessment phase

- ✓ 48 MAA captured
- ✓ Completion rate: 88/90% (Rapporteur/Co-Rapporteur)

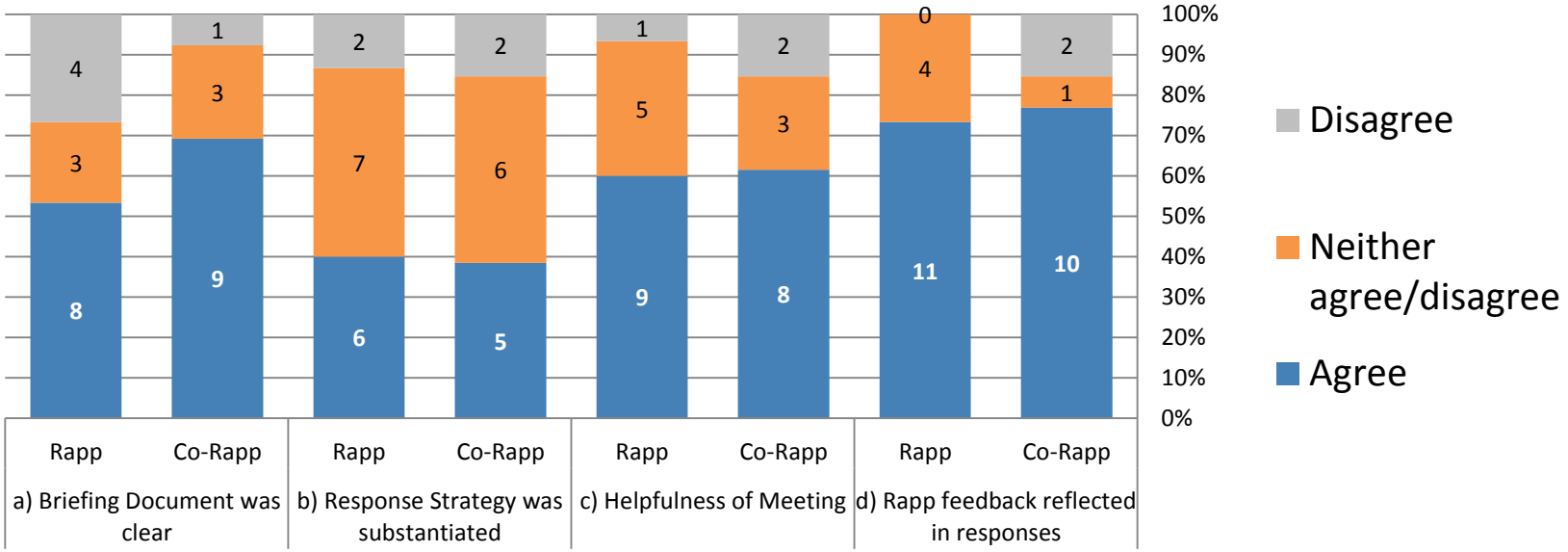
2. Applicant's responses to LoQ/LoOI - satisfaction level

- Positive ratings in 60-80% suggest high level of satisfaction with the responses to LOQ/LoOIs.
- PI & RMP responses scored slightly lower compared to other areas.



3. Clarification Meetings

- Overall, 28/70 responses confirmed that a clarification meeting was held during the second phase of the assessment.
- 60% agree meeting is helpful.
- Only ± 40% considered response strategy was well substantiated in the briefing documents

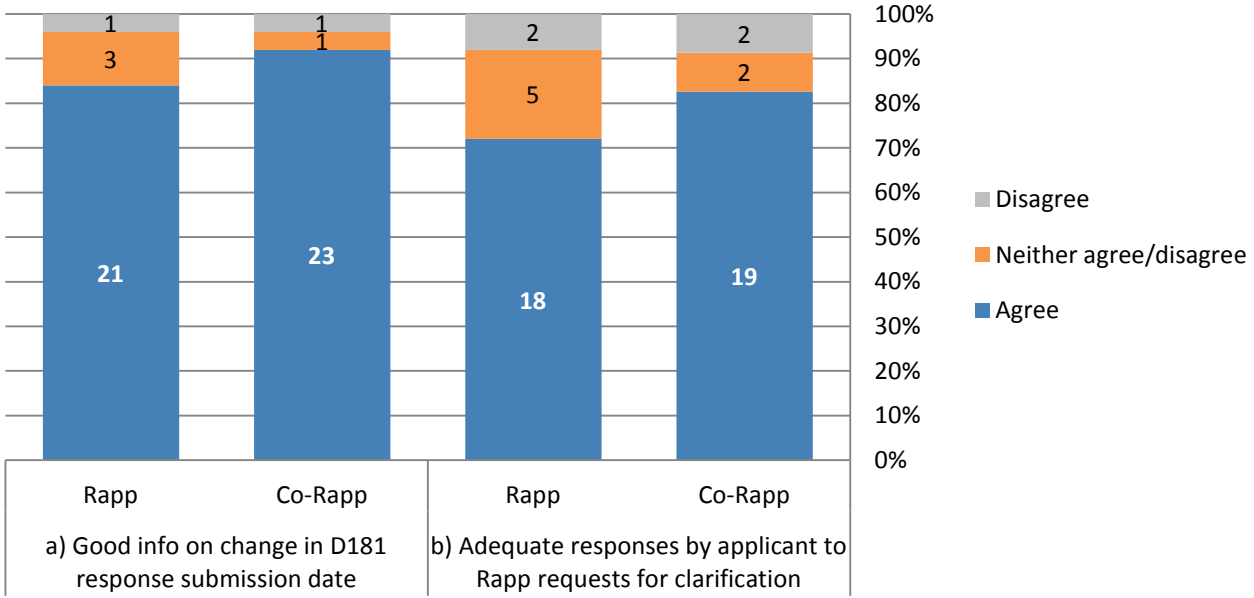


4 & 5. SAGs and oral explanation

- Only 2 SAGs and 3 Oral Explanations covered by the survey.
- Generally positive ratings for SAGs:
  - Informative briefing documents and presentation by applicant.
  - Expert discussion helpful to reach final outcome.
- Mixed feedback on helpfulness of Oral Explanations.
- Overall, numbers too low to draw firm conclusion.

6. Overall feedback on interaction with applicant

- Very positive, higher satisfaction level compared to primary assessment phase



Conclusions and recommendations

- Better level of satisfaction with responses to LOQ & LoOIs (approx. 70% positive ratings)
  - PI & RMP responses scored slightly lower compared to other areas, but still good ratings → carefully consider all CHMP comments on the PI/RMP - when deviating from CHMP requests, clearly explain reasons why.
  - Same recommendations as at D1-121 regarding need for information to be easy to locate and maturity of the dossier/responses.
  - Late submission of large datasets are problematic and should be avoided.

Conclusions and recommendations

- Clarification meetings generally considered helpful.
  - However, some negative ratings.
  - The need for a clarification TC/meeting should be carefully considered.
    - The main purpose of the meeting is to make sure that the issues with the application are well understood and to facilitate the preparation of responses.
    - No pre-assessment/endorsement of responses.
  - If Applicants wish to have a clarification TC/meeting, a clear outline of the response strategy should be presented to make the most of the meeting.

- Feedback on interaction with applicant at Opinion stage very positive.
  - Same recommendations as for Day 1-121.

General conclusions

Stakeholders surveyed

General conclusions

EMA & (Co-)Rapporteurs' positive feedback across the 3 phases of the procedure

- ✓ *Overall very good level of satisfaction across the 3 phases (increase from validation to opinion)*
- ✓ *High level of interaction during pre-submission phase (PSM)*
- ✓ *Good quality of information and timeliness of the interaction (especially at opinion phase)*
- ✓ *Very good level of awareness of applicants on guidance for clarifications meeting and accelerated assessment*
- ✓ *Clarification meeting generally considered helpful*
- ✓ *Most applications considered adherent to scientific advices*

General conclusions

Areas identified for optimisation

- *EMA*
  - ✓ Increase awareness on validation process (most common issues encountered)
    - Will help identification of non blocking validation issue prior submission
  - ✓ Increase awareness on SmPC guidance & QRD template and pre-authorisation guidance.
  - ✓ Assessment Reports/ final opinion - Circulation timelines and communication of delays
  - ✓ Optimise timing for Annex II condition request
  - ✓ Clarify role EPL vs PM

General conclusions

Areas identified for optimisation

- *Industry*
  - ✓ *Accuracy of MAA submission date – communications of delays to EMA & Rapporteurs*
  - ✓ *Validation: increase awareness on guidance & consistency between application form, PI and dossier*
  - ✓ *Improve the presentation of the application (data easily located, hyperlinks etc.)*
  - ✓ *Adherence to PI guidelines (SmPC & QRD) & better substantiate the proposed PI in the clinical overview and address CHMP comments*
  - ✓ *Need for mature dossier & responses – late submission of large datasets should be avoided*

Acknowledgement

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