EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

9th Industry Stakeholder Platform Meeting

Topic 4: Network sustainability and update on CHMP AR revamp project

24 November 2022

Fran Day - EMA

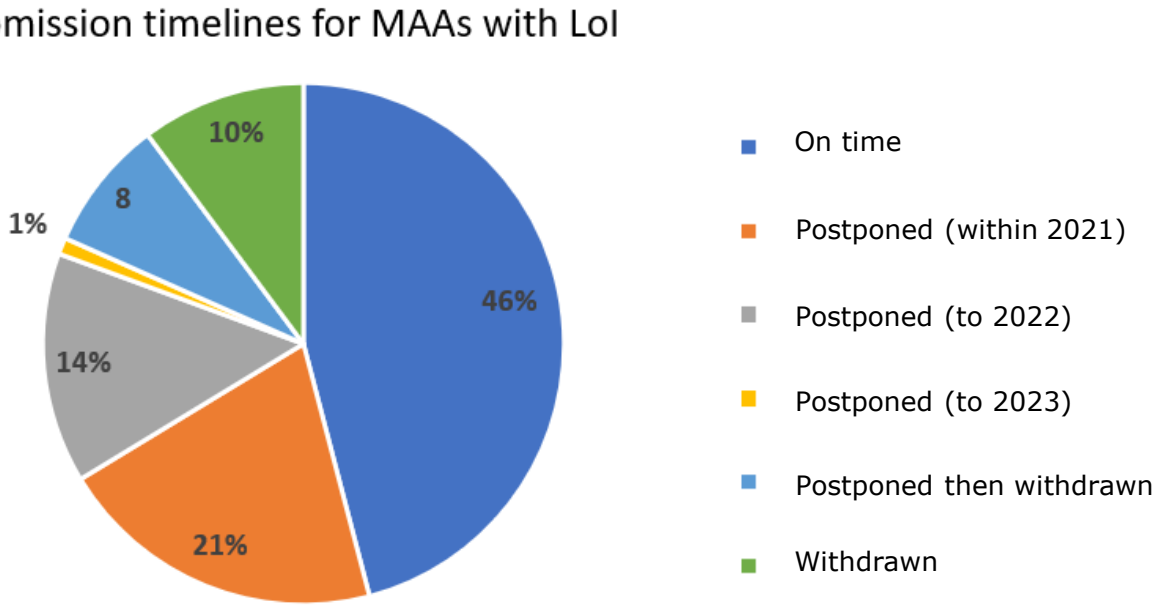
Submission predictability

Background

- At the 7th and 8th Industry Platform Meetings in December 2021 and June 2022, data was presented to highlight the very poor predictability of initial MAA submissions.
- In June 2022, it was agreed that a focus group would be put together to try and perform a root case analysis of the reasons for delay and to propose solutions.
- The kick-off of the focus group occurred on 22 November 2022.

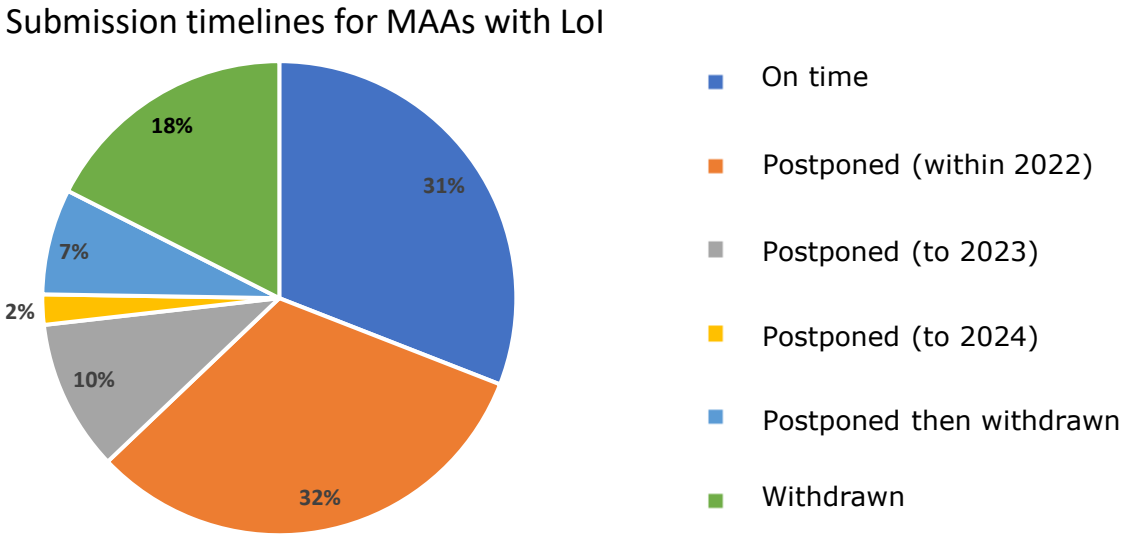
The problem

These data show the actual submissions of initial MAAs in 2021 versus what was projected in Dec 2020. All the submissions had a Letter of Intent.



The problem persist

These data show the actual submissions of initial MAAs in 2022* versus what was projected in Dec 2021. All the submissions had a Letter of Intent.



* Data cover period Jan-Oct 2022

Previous initiatives tackling the problem

- Work of the HMA Taskforce in 2017
- EMA analysis presented at the 7th and 8th Industry Stakeholder Platform
- Network Capacity Project

Planned monitoring

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- All Applicants that have indicated an MAA submission date in 2023 will be contacted in December 2022 to:
  - Confirm that they are still planning on a 2023 submission (with exact date)
  - Applicants with submission dates in H1 2023 but no letter of intent will be asked to change their intended submission date
  - Inform applicants that their planned submission will be tracked
- Every quarter the planned submissions will be checked against the received submissions
  - Applicants who fail to submit or change their submission date will be asked to give a rationale
- The hope is that the active monitoring will in itself deter multiple changes, but it will also serve as a data collection for the reasons for MAA delays.

CHMP AR Revamp Project

Project objectives

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CHMP
Workplan 2022

Activity areas

Improve/optimise the initial evaluations assessment report with the aim to simplify, avoid replication of work and meet/consider stakeholders' expectations. Examine the best use of available resources at CHMP and EMA to achieve this goal.

Key objectives

- Review ways to improve the efficiency, robustness, consistency and soundness of outputs throughout the initial MAA evaluation process.

Activities in 2022

CHMP activities to achieve the objectives set for this area:

- Optimise the related assessment report templates (e.g. benefit-risk section, efficacy section of overview template) to avoid duplication of information while facilitating inclusion of all relevant information (e.g. explanation of the therapeutic indication, efficacy and safety in subgroups and outcomes of SAG meetings and oral explanations).

CHMP topic leaders: Johann Lodewijk Hillege

Other contributors:

Member/alternate	Name	MS
Member	Kristina Dunder	SE
Member	Jayne Crowe	IE

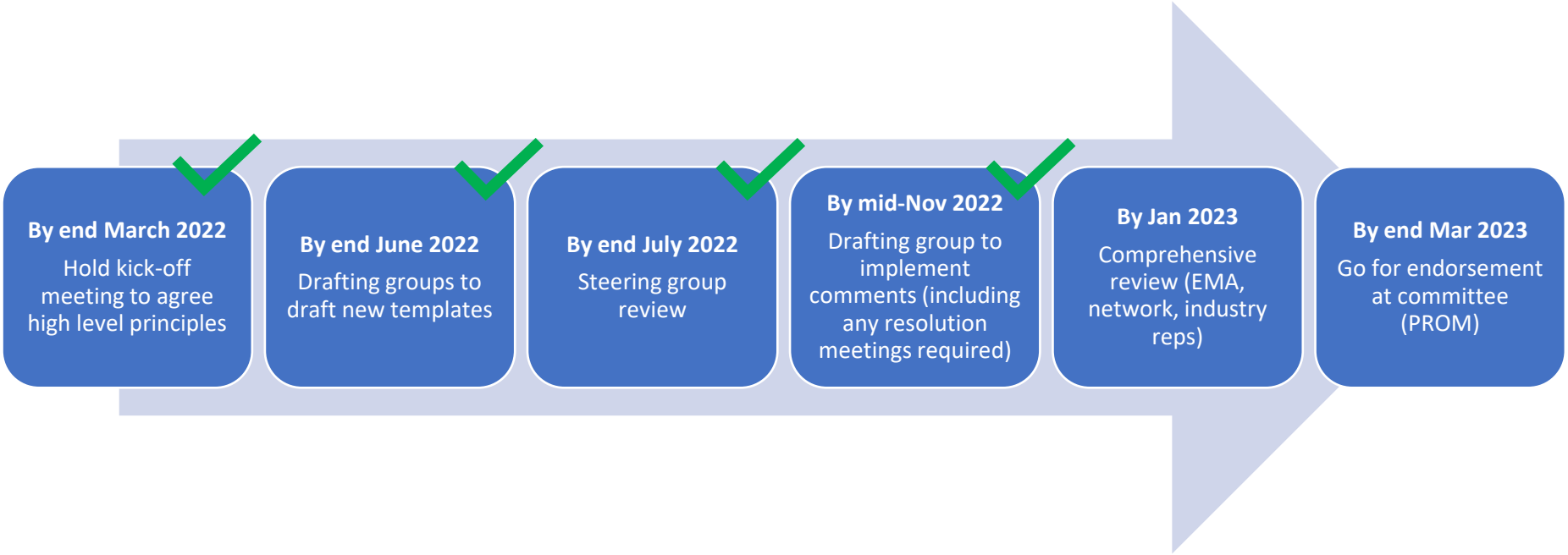
Key drivers

Maximise efficiency

No loss of transparency (EPAR)

Ensure legal and regulatory compliance

Timelines



The project is broadly on track to deliver by end Q1 2023

Decisions taken

The current Overview template will be retired and the CHMP AR template will serve as the overview template as well.

- The CHMP AR template already includes all sections currently in the Overview
- Having 2 separate templates that are so similar is not efficient

Agreed to have the possibility that Applicants pre-fill the factual sections of the D80 q/n/c ARs, leaving comment boxes for assessors.

- Meeting held with Industry reps was positive (agreed to a pilot)
- Also met with ONC FDA division – they already have this approach (Assessment Aid)

Decisions taken

Agreed that D80 q/n/c ARs should be aligned with eCTD (ICH M4)

The aim is to remove redundancy, avoid repetition, streamline the CHMP AR & final EPAR (less than 100 pages?)

Agreed to remove most of the administrative information (legal basis, etc) from the D80 q/n/c ARs and include it only (in minimal form) in the CHMP AR template

Agreed to simplify the green guidance text in the templates

Decisions taken

Agreed that the new templates will include technical restrictions so that authors will not be able to change or delete headings or mess up formatting

Agreed to move the CHMP AR to a collaborative platform – e.g. SharePoint – and use that for CHMP AR co-authoring

Agreed to adopt response templates so that applicants submit their responses in a format that can be easily used by the assessors directly, with no copy/paste. Request the submission of WORD as well as PDF.

Screen-shots – D80

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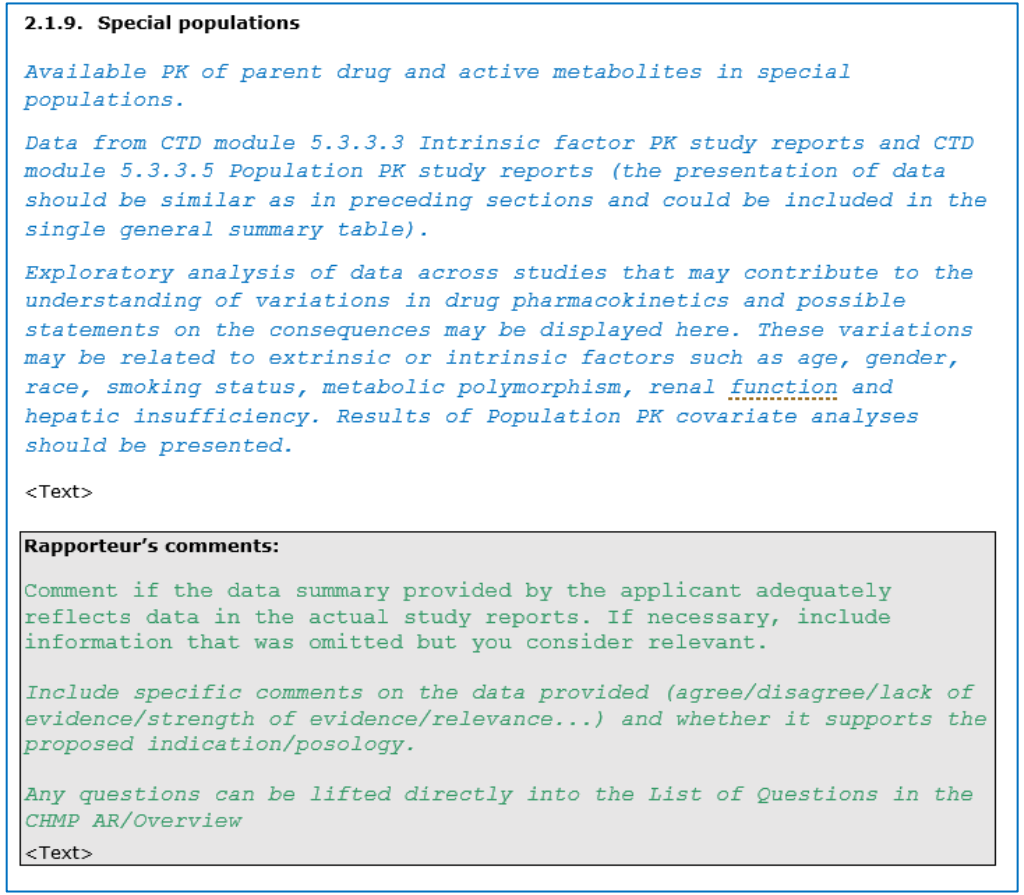
In the pilot, the applicants will be asked to complete the factual parts of the template (blue guidance text is for them). Outside of the pilot, assessors will continue to complete them.

Assessors will be able to comment on the company's position in comment boxes



2.1.9. Special populations

Available PK of parent drug and active metabolites in special populations.

Data from CTD module 5.3.3.3 Intrinsic factor PK study reports and CTD module 5.3.3.5 Population PK study reports (the presentation of data should be similar as in preceding sections and could be included in the single general summary table).

Exploratory analysis of data across studies that may contribute to the understanding of variations in drug pharmacokinetics and possible statements on the consequences may be displayed here. These variations may be related to extrinsic or intrinsic factors such as age, gender, race, smoking status, metabolic polymorphism, renal function and hepatic insufficiency. Results of Population PK covariate analyses should be presented.

<Text>

Rapporteur's comments:

Comment if the data summary provided by the applicant adequately reflects data in the actual study reports. If necessary, include information that was omitted but you consider relevant.

Include specific comments on the data provided (agree/disagree/lack of evidence/strength of evidence/relevance...) and whether it supports the proposed indication/posology.

Any questions can be lifted directly into the List of Questions in the CHMP AR/Overview

<Text>

Screen-shots – CHMP AR/Overview

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Administrative information

Will be automatically retrieved by SIAMED and/or completed by EMA staff.

[this part relates to the outcome of the procedure and should be checked before the opinion to ensure that it is correct in SIAMED]

Name of the medicinal product:	*Use of capital in the invented name as per the approved trademark registration*
Applicant:	
Active substance(s):	
<International non-proprietary name(s)><common name(s)>:	*Common name needed, instead of INN, for vaccines and some ATMPs*
Pharmaco-therapeutic group (ATC code(s)):	*If the group and the code are not yet assigned, indicate: not yet assigned*
Pharmaceutical form(s)[1]:	
Strength(s)[1]:	
Route(s) of administration[1]:	
Type of Marketing Authorisation Applicantion:	*Eg full, conditional, exceptional circumstances*
Legal Basis:	*Eg 8(3), 10(a) etc.*
New Active Substance:	<Applied for><Granted><Not granted><Not applied for>
Orphan Designation:	<Yes><No>
Orphan Similarity Report Appended:	<Yes><Not applicable>

Admin info has been extensively streamlined, in the D80 reports as well as the CHMP AR.

Screen-shots – CHMP AR/Overview

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2.5.3.2. Main study(ies) (phase III = therapeutic confirmatory trials)

*Section (including sub-sections) to be completed by **Rapporteur**. Co-Rapporteur only to add if in disagreement or major omission.*

The following tables summarise the efficacy results from the main studies supporting the present application. These summaries should be read in conjunction with the discussion on clinical efficacy as well as the <benefit risk assessment><biosimilarity assessment> (see later sections). [Repeat the table for each pivotal study]

2.5.3.2.1. < Study #1 identifier>

Title: <title> *{as indicated on the study report}*		
Study identifier	<code> *{list all codes starting with the protocol number followed by – as available - EudraCT number, ISRCT number, other codes that allow cross-referencing to publications}*	
Design	<free text> *{describe key elements of the design (cross-over, parallel, factorial, dose-escalation, fixed-dose response) including randomization, blinding, allocation concealment, mono-/multi-centre, etc.}*	
	Duration of main phase:	<time>
	Duration of Run-in phase:	<time> <not applicable>

Factual sections will be filled by the Rapporteur. Co-Rapp may add if there are errors or omissions

2.5.5. Conclusions on the clinical efficacy

***Rapporteur** and **Co-Rapporteur** to independently add their positions by D80. These will be merged by D120.*

A brief statement about the conclusions that can be drawn from the clinical efficacy documentation should be provided here (this may be the same as the clinical efficacy information in the SPC, pharmacodynamics from section 5.1.).

For biosimilars, conclude if the submitted efficacy data support biosimilarity.

***Rapporteur's position:** [Title to be deleted and sections merged when preparing the D120 JAR]*

<Text>

***Co-Rapporteur's position:** [Title to be deleted and sections merged when preparing the D120 JAR]*

<Text>

Conclusion/discussion sections will have space for both Rapp and Co-Rapp who will co-author independently

Screen-shots – Response template

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Responses to Questions adopted by CHMP at <D120><D180><Dxxx>

The questions from Rapporteur and Co-Rapporteur should be copy/pasted directly into this template document, without any amendments.

The applicant is expected to respond to the questions directly in this document and submit both PDF and MS Word versions at the time of response.

All sections (i.e. question, applicant's response and assessment of the applicant's response) should be replicated as many times as needed and questions placed under each relevant topic (i.e. DP, DS; pharmacology, PK, toxicology; clinical pharmacology, efficacy, safety, PhV; etc). ASMF related questions are answered separately.

The applicant may choose whether one joint response document or several separate response documents are prepared. In the case of multiple response documents, an informative title should be added on the front page.

The questions should follow the same order and numbering as included in the list adopted by CHMP. Questions must not be combined.

Applicants will be asked to submit responses using the template (also providing a WORD version)

1.1.1 Drug substance

Question <number>

Copy/paste the questions (D90, D120, D180, etc) verbatim, retaining the original numbering. After each question, copy/paste the title for applicant's response as well as the box for (Co)-Rapp assessment.

<Question text>

Applicant's response:

The applicant adds their complete responses concerning each question. It is not acceptable to just refer to annexes. However, annexes may be used and referred to if large data packages, new data, space consuming tables or pictures need to be included to support the responses. Annexes referred to should be easily identified in the response.

<Response text>

Rapporteur's assessment of applicant's response:

<Text>

Co-Rapporteur's assessment of applicant's response:

<Text>

Rapporteurs will have comment boxes where they can make their assessment of the applicant's response

Next steps

Step	Date
Teams to come back with Draft concept	By mid-May
Authoring of Draft 1	By 30 Jun 22
Steering Group review	By ~~29 July 22~~ 31 Aug 22
PROM consultation	~~September~~ 31 October 2022 PROM
Authoring of Draft 2	By ~~28 Oct 22~~ 18 Nov 22
Steering Group review	By ~~30 Nov 22~~ 06 Jan 23
Comment resolution meeting	w/b ~~19 Dec 22~~ 16 Jan 23
Final Draft	By 31 Jan 23
Final Draft endorsement by Steering Group	By 28 Feb 23
PROM Endorsement	March 2022 PROM

The first review (D80 ARs, + B/R section) is complete. Drafting groups are have updated the templates based on comments.

The second review (updated D80 ARs + CHMP AR & response template) begun on 19 November and included industry representatives.

Other ongoing activities

Other activities

There are a number of ongoing and planned activities aimed to try and address the current network capacity issues. A few examples below.

- A focus group looking at defining what is critical and what is "nice-to-have" in terms of assessment and questions is planned to kick-off before the end of the year.
- Agreed to request the submission of WORD documents (for M2, SmPC, RMP, responses, etc...). Guidance is being updated and it should be the new normal by the end of the year.
- Activities are starting, looking at the EU training network, the possibility of new, centralised, training for assessors.
- An internal review of the MNAT administrative processes is ongoing (with a view to simplifying).