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SCIENCE MEDICINES HEALTH

Submission Predictability

11th Industry Stakeholder Platform Meeting

24 November 2023

Francesca Day

Background

- At the 7th, 8th, 9th and 10th Industry Platform Meetings in 2021, 2022, and 2023, data was presented to highlight the very poor predictability of initial MAA submissions.
- In June 2022, it was agreed that a focus group would assembled 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.
- During 2023, the group has monitored all planned MAAs versus the actuals received

Planned monitoring

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- The focus group agreed to put in place close monitoring of all MAAs for 2023
- All Applicants that indicated an MAA submission date in 2023 were contacted in December 2022 to:
  - Confirm that they were still planning on a 2023 submission (with exact date)
  - Applicants with submission dates in H1 2023 but no letter of intent were asked to change their intended submission date
  - Inform applicants that their planned submission would be tracked
- The focus group planned to check every quarter the planned submissions against the received submissions
  - Applicants who failed to submit or changed their submission date would be asked to give a rationale
- The hope was that the active monitoring would in itself deter multiple changes, but that it would also serve as a data collection for the reasons for MAA delays.

2023 pipeline monitoring – Q1 to Q3 2023

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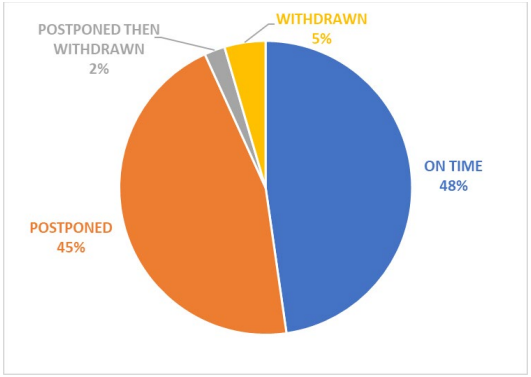
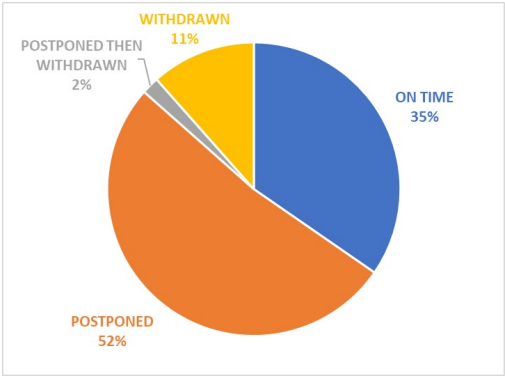
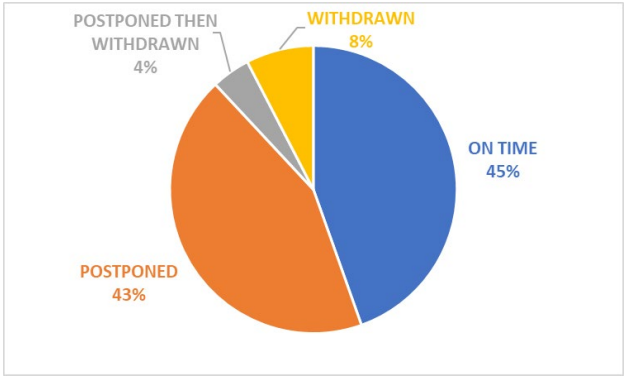
Q1



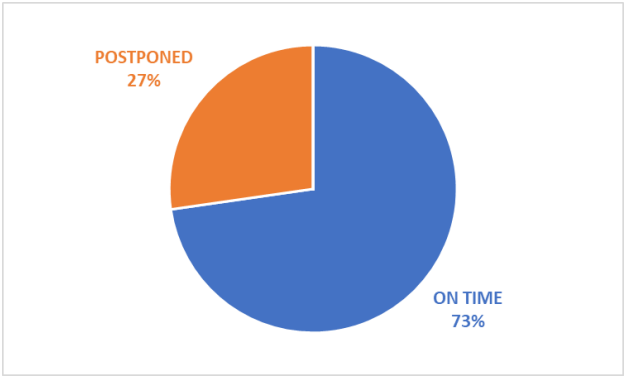
Q2



Q3

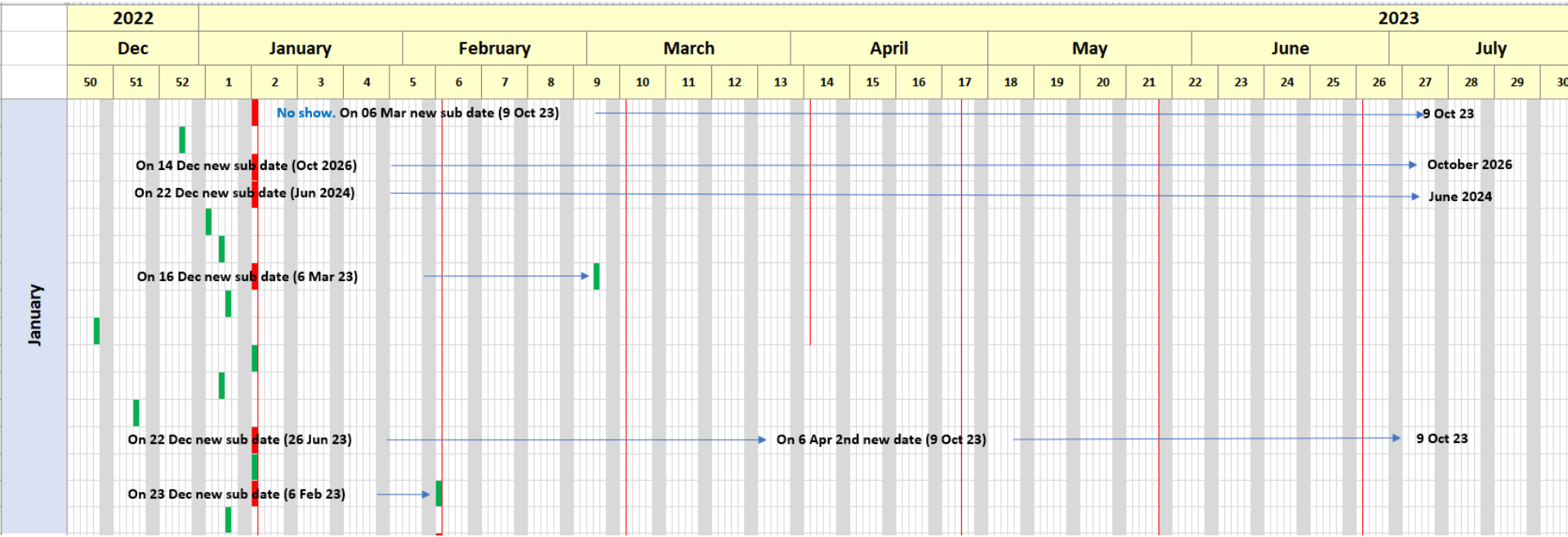


Q3*



* re-baselined in June

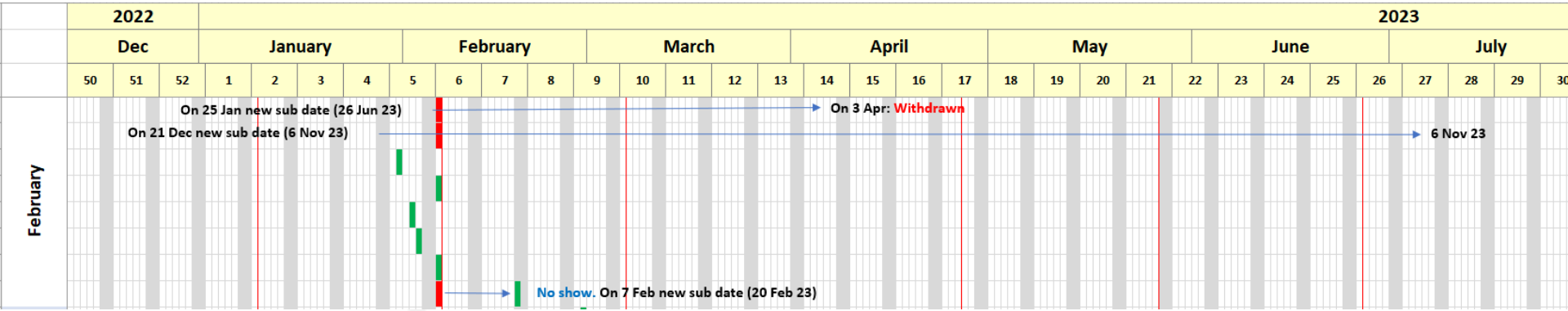
Sub deadline 09 Jan 2023



10/16 (62%) of expected MAAs* received

** All MAAs have LoI and were expected as of 1st Dec 2022*

Sub deadline 06 Feb 2023



5/8 (62%) of expected MAAs* received

** All MAAs have LoI and were expected as of 1st Dec 2022*

Sub deadline 06 Mar 2023

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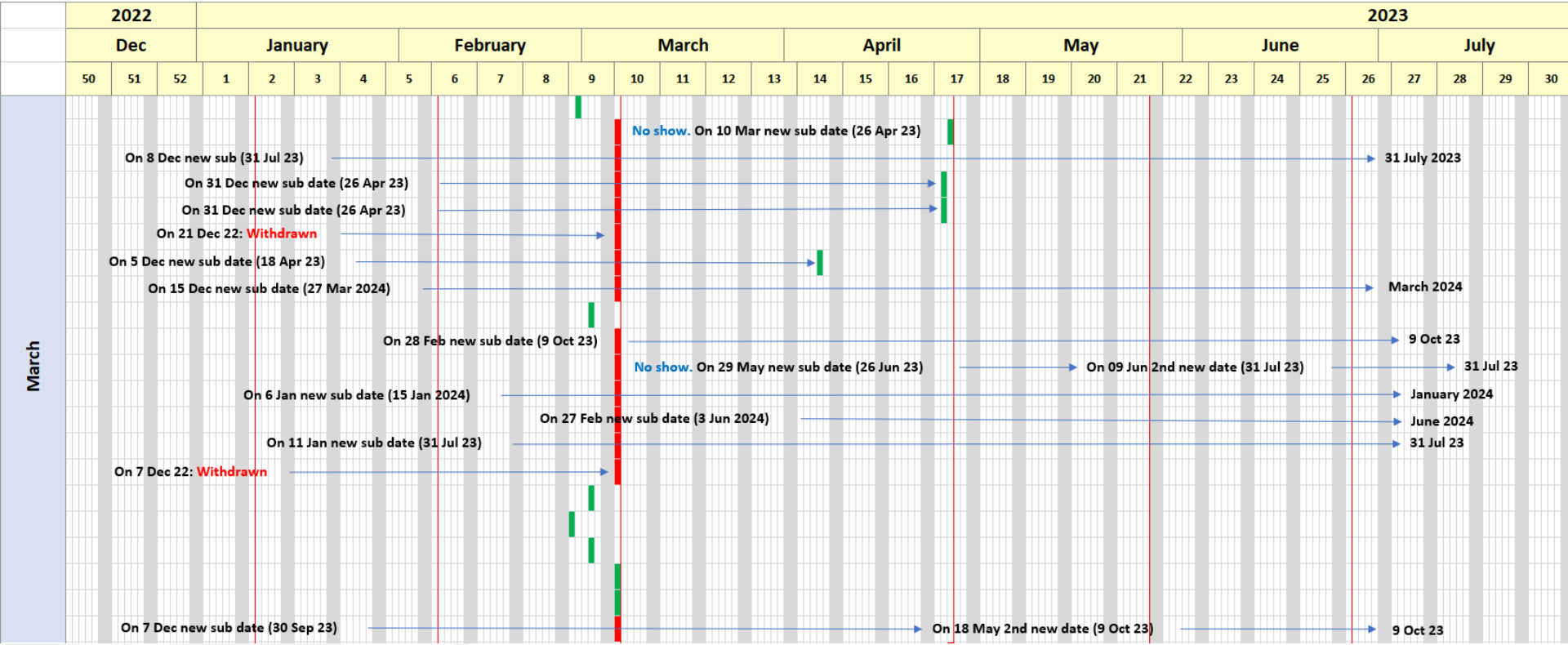

7/21 (33%) of expected MAAs* received

** All MAAs have LoI and were expected as of 1st Dec 2022*

Sub deadline 26 Apr 2023

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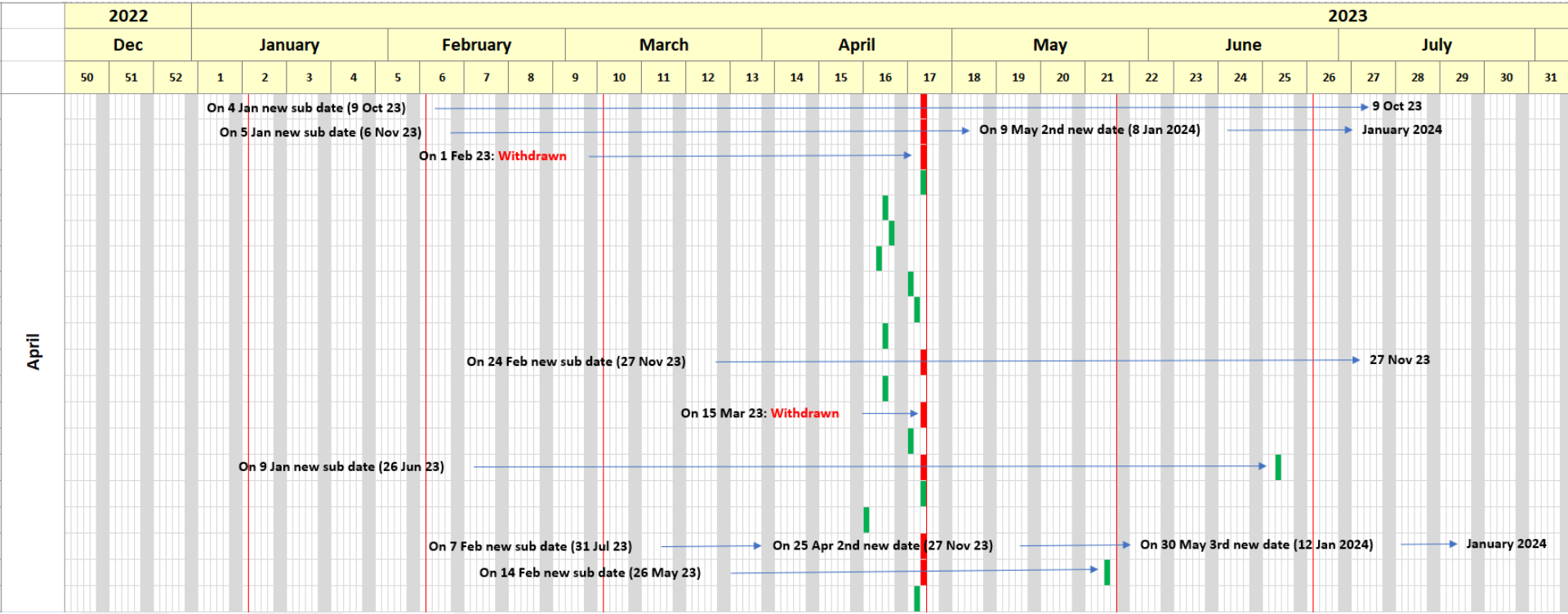
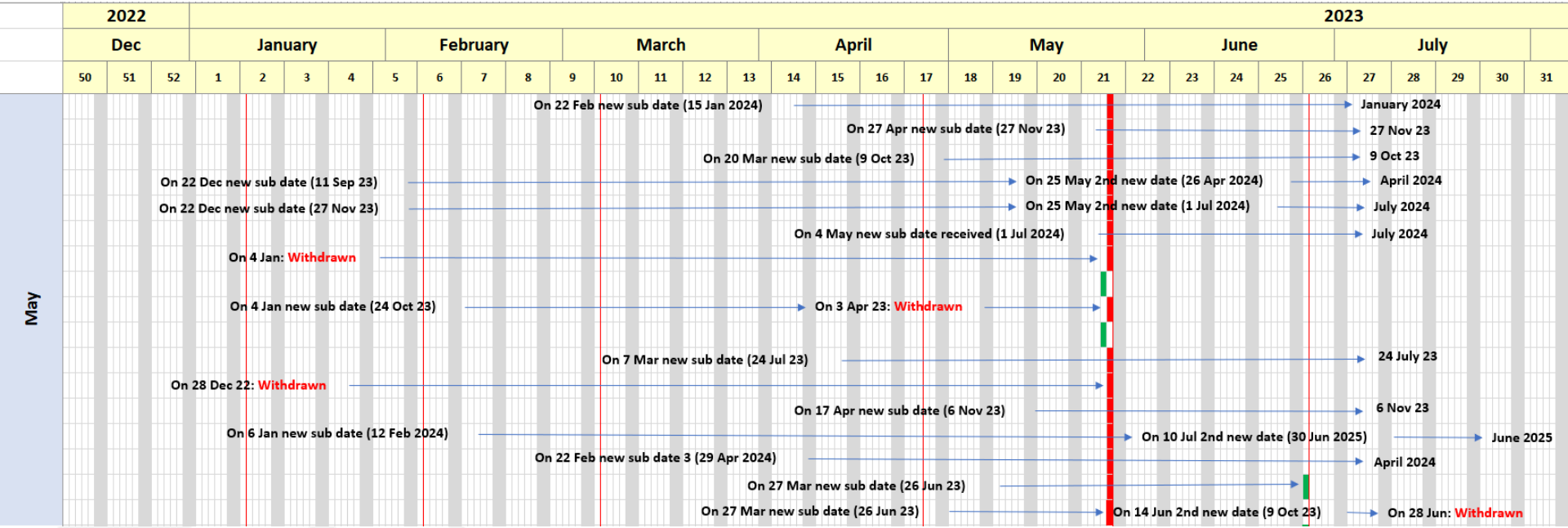


12/20 (60%) of expected MAAs* received

** All MAAs have LoI and were expected as of Dec 2022*

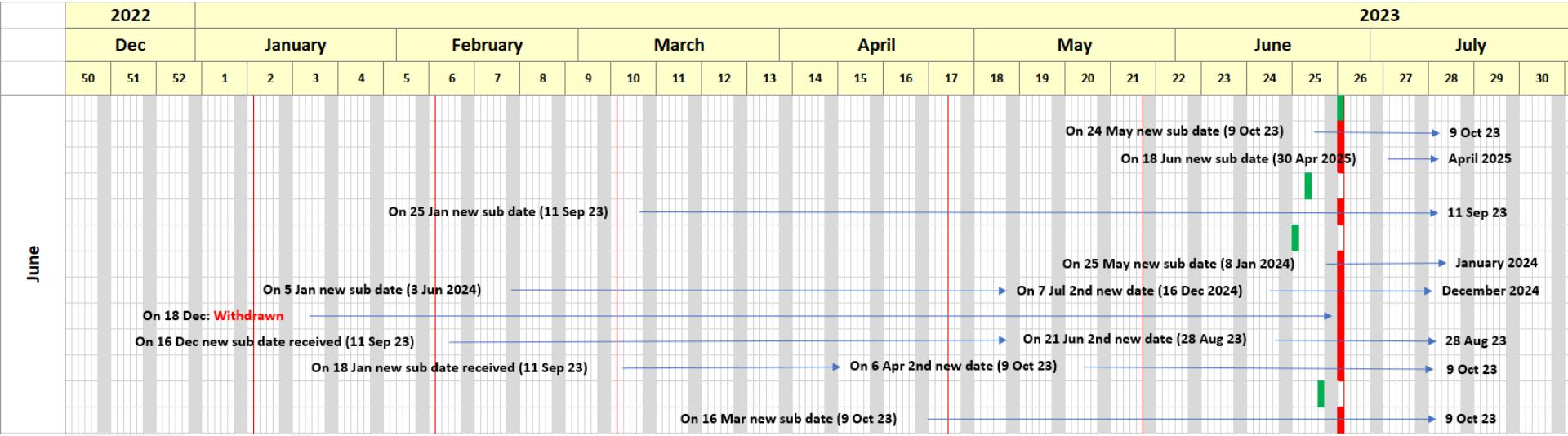
Sub deadline 26 May 2023



2/17 (12%) of expected MAAs* received

** All MAAs have LoI and were expected as of 1st Dec 2022*

Sub deadline 26 June 2023



4/13 (31%) of expected MAAs* received

** All MAAs have LoI and were expected as of 1st Dec 2022*

Sub deadline 31 July 2023

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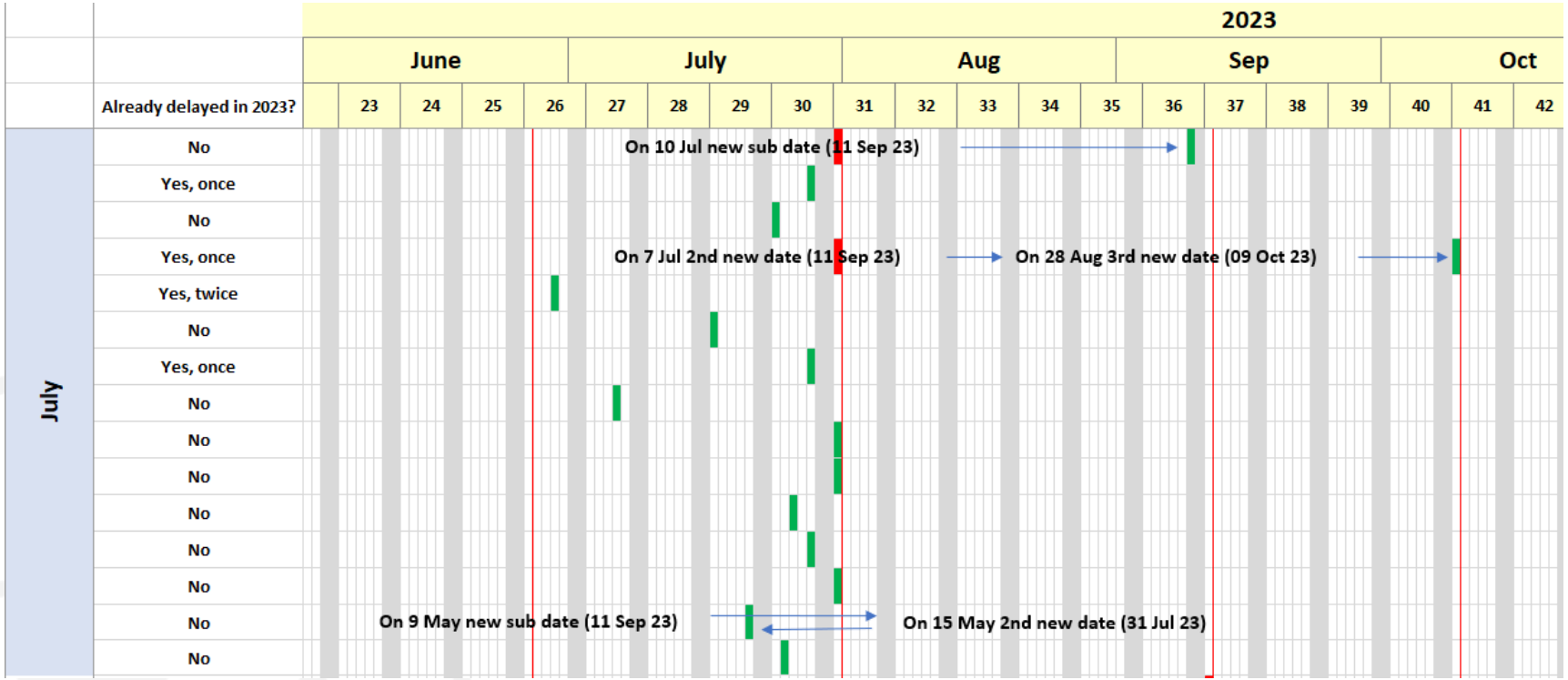
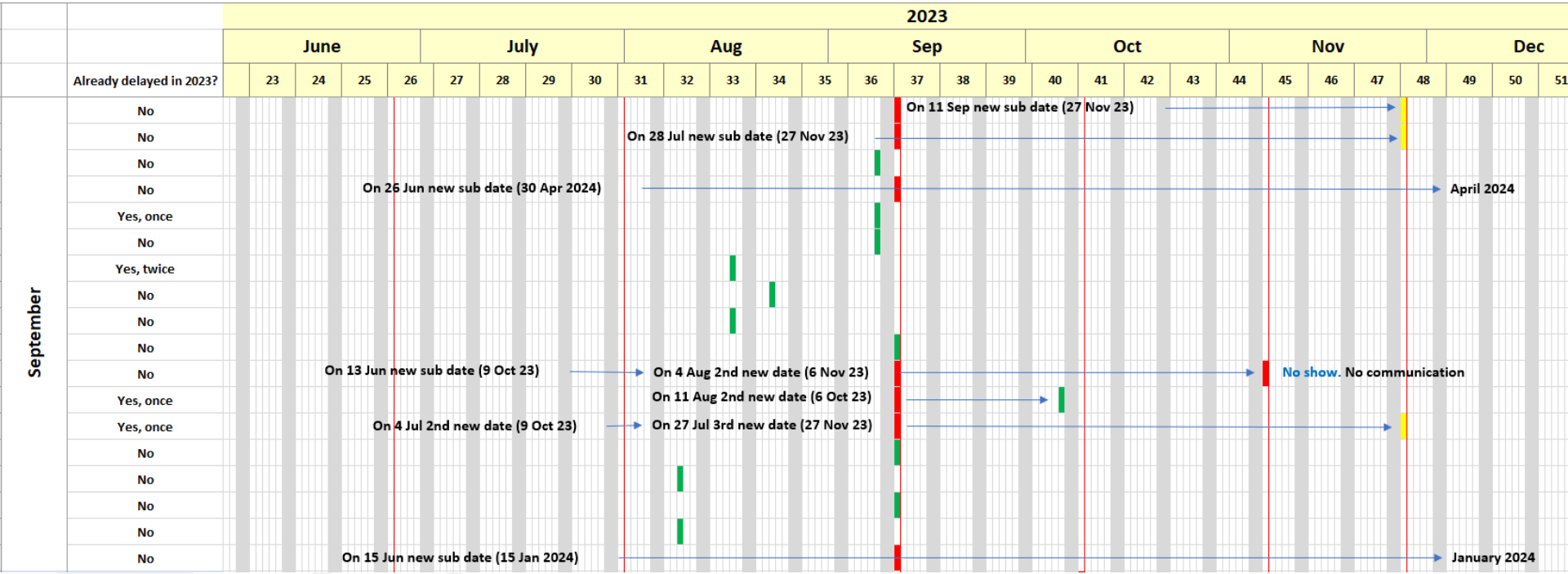


13/15 (87%) of expected MAAs* received

** All MAAs have LoI and were expected as of 30 Jun 2023*

Sub deadline 11 Sep 2023



11/18 (61%) of expected MAAs* received

** All MAAs have LoI and were expected as of 30 Jun 2023*

Sub deadline 09 Oct 2023

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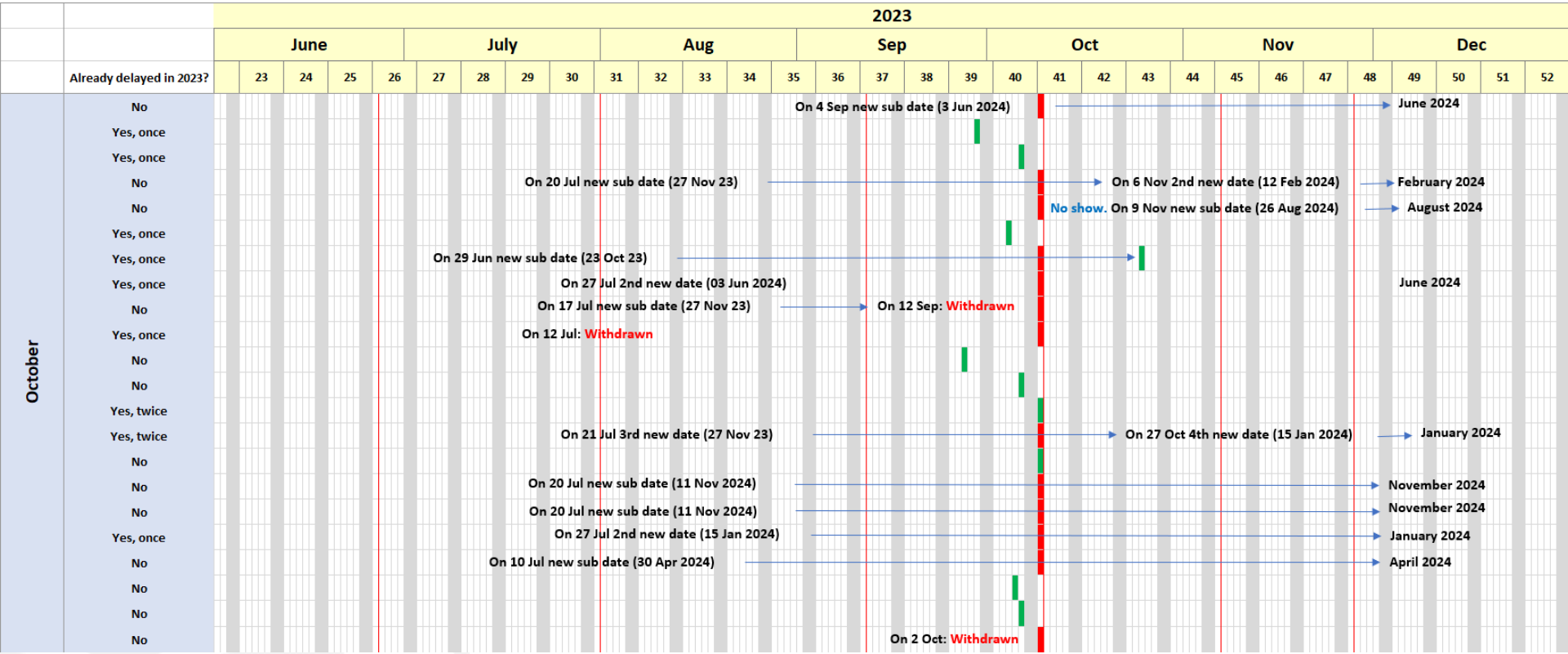
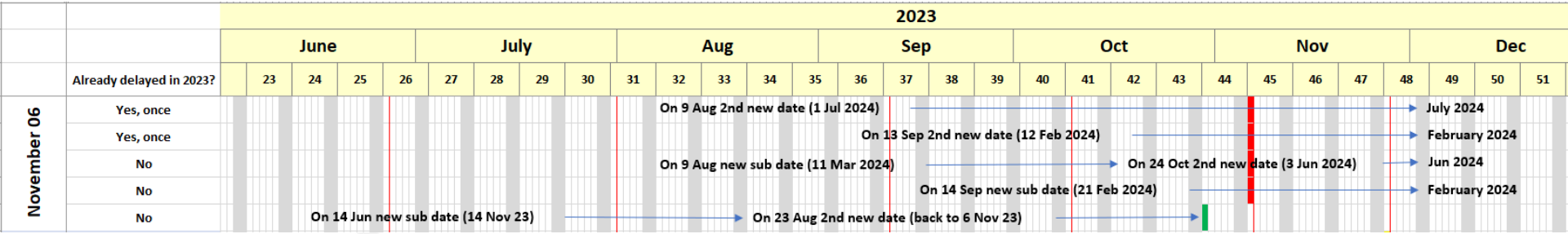


9/22 (41%) of expected MAAs* received

** All MAAs have LoI and were expected as of 30 Jun 2023*

Sub deadline 06 Nov 2023



1/5 (20%) of expected MAAs* received

** All MAAs have LoI and were expected as of 30 Jun 2023*

Sub deadline 27 Nov 2023

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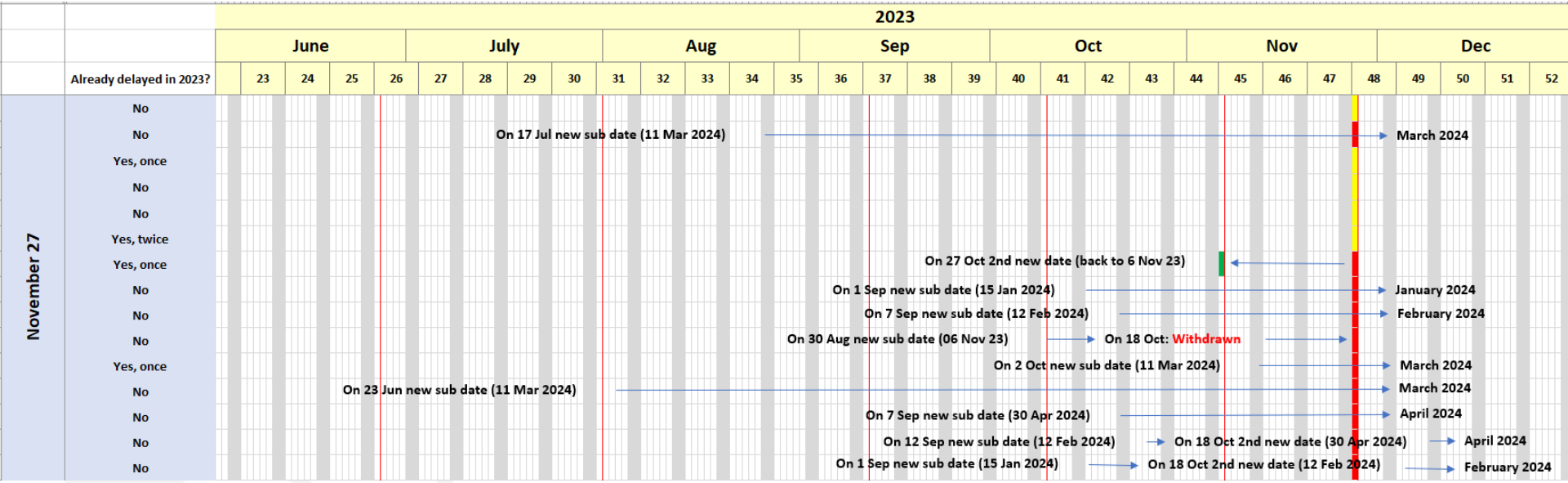

How many of the 15 expected MAAs* will we receive? 5 or less it seems.

** All MAAs have LoI and were expected as of 30 Jun 2023*

Conclusions

- Overall very disappointing that active monitoring seems not to have had any effect on submission predictability
- Next meeting of the Focus Group planned for early January 2024 to conclude the exercise
  - Will look at data more in detail
  - Will discuss more active measures, since passive ones not working

Next steps

Annex to the LoI

In the meantime, EMA will implement an annex to the LoI PDF form.

- Clearly expresses the LoI and Rapp appointment as "booking an appointment" with EMA and 3 NCAs (Rapp, Co-Rapp & PRAC Rapp) and therefore the importance of accurate information
- Will allow more context around the declared submission date
- Gives Member States more details on submissions, so they can make better informed bids

Annex to the LoI

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General guidance

Purpose

The purpose of this document is for the applicant to submit information related to their intended Marketing Authorisation Application (MAA) or EU-M4All[1] submission.

Reminder

By submitting the *Pre-submission Request Form – Centralised Procedure – Intent to submit a MAA* and this annex (also known collectively as "Letter of Intent") the Applicant is requesting EMA and the National Agencies to commit resources to the assessment of the dossier. As such, it is imperative that the indicated intended submission date is accurate.

Changes to the submission date may trigger a change of Rapporteurs if these have already been assigned. If the Applicant wishes to retain the Rapporteurs, the new submission date might need to be agreed with them. The Applicant will be asked to justify any changes to the intended submission date.

Guidance Text

Guidance on how to complete the sections below is provided in green text. Please remove this text before submitting this form. Click on Ctrl-Alt-Shift-S to view the "styles" window. Select "Guidance text" and click on the icon on the right, chose "Select all XXX instances", press the "Delete" key on the keyboard.

Annex to the LoI

EUROPEAN MEDICINES AGENCY

Background on Development Programme

Clinical studies

Please provide information on the clinical studies completed or ongoing which will be included in the dossier by completing the table below (in line with eCTD m5.2 tabular listing).

Table 1 – Ongoing and completed clinical studies

Study Identifier (link to study register)	Enrolment status (ongoing/completed) current number of subjects/ total number of subjects needed Last participant enrolment date (actual/estimated)	Study phase, design & Control type	Test product(s); Dosage regimen; Route of administration and duration of treatment/follow-up	Study population
<text>	<text>	<text>	<text>	<text>

Last LPLV and DBL dates

Please indicate the primary completion date (e.g., last-patient-last-visit) and the corresponding database lock date (actual or projected) for the last study data point to be included in the application. Please also indicate whether there is any other information (e.g., batch analysis data, GMP certificate, CE marking) or factors (e.g., difficulties in study conduct, lower than expected number of events, planned analyses etc.) which are on critical path or might affect the preparation of the dossier and therefore the submission date.

<Text>

Annex to the LoI

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Scientific advice

Please provide information on any relevant centralised scientific advice received by completing the table below.

Table 2 – Relevant centralised scientific advice

Date	Topic (quality/ nonclinical/ clinical)	Reference number
<text>	<text>	<text>

Quality dossier

Please indicate whether there has been a Quality-by-Design approach to the quality dossier. If so, please include details.

<Not applicable><Text>

Modelling and simulation

Please indicate whether the dossier includes extensive Pharmacokinetic modelling and/or simulations, in particular if these are relied upon for the main indication claims. If modelling and/or simulation are included, please include details.

<Not applicable><Text>

Medical device/companion diagnostic

Please indicate whether the product/indication is associated with the use of a medical device or companion diagnostic. If this is the case, please provide information on Notified Bodies opinions, where relevant.

<Not applicable><Text>

Complex clinical trial methodology

Please indicate whether your submission includes complex clinical trial methodologies, such as umbrella or basket trials, adaptive designs, multiple post-hoc analyses, use of external control, indirect comparisons, or real-world evidence, etc.

<Not applicable><Text>

Annex to the LoI

EUROPEAN MEDICINES AGENCY

Regulatory information

Please indicate whether you intend to apply for accelerated assessment, conditional MA, or MA under exceptional circumstances. For accelerated assessment, if applicable, please state the intended submission date of the request for accelerated assessment.

<Text>

Planned lifecycle of the product

Please indicate which line extensions, indication extensions and important variations (e.g., changes to manufacturing processes or sites) are planned following the potential approval of the MA, together with the expected submission date.

Table 2 – Planned lifecycle

Lifecycle type (Line Ext. or Ext. of Indication)	Brief description	Expected submission date (quarter and year)
<text>		

Clean-up of SIAMED

- EMA has >300 products with an intended submission date before December 2021 and where there has not been any communication with MAAs since that date.
- In approximately 20% of cases, Letter of Intent was submitted and Rapporteurs have been appointed.
- In Q1 24, EMA will start a clean-up exercise in our database.
  - EMA will send an email to the declared contact point requesting confirmation if there is still an intention to submit the MAA. If so to declare the new intended date.
  - MAAs should check if the contact points are still valid and if not to update them (see Q 2.7 of Pre submission guidance).
  - Products and appointed Rapporteurs where no reply is received will be removed from the Agency database.
- Industry associations will be informed on the launch of this clean up exercise through the Industry Stakeholders liaison.

Any questions?

Further information

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Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000

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