07 April 2026

H2-25 MAAs pipeline monitoring exercise

ANALYSIS OF THE MARKETING AUTHORIZATION APPLICATIONS BEHAVIOUR

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1. Introduction

Unreliable long-term planning for initial marketing authorization applications (MAAs) for centralised procedures has been a recurrent problem for the network for many years, but it has become unsustainable with resources stressed to the limit by the COVID-19 pandemic. In June 2022 (link) it was decided to create a focus group to perform a root cause analysis of the reasons for such delays and to propose solutions to improve the trend. The *Focus group on submission predictability*, formed by regulators and industry representatives[1], started its work in November 2022. A close monitoring of the MAAs pipeline was performed during the year 2023, and in July 2024 a final report containing the analyses and recommendations for improvement was published (link). To assess the effectiveness of the adopted measures, a further close monitoring of the MAAs pipeline was performed during the second half of the year 2025.

2. The work of the focus group

Similarly to the 2023 monitoring exercise, in the second monitoring carried out in the second half of 2025, all applicants that had indicated an MAA submission date between June 2025 and December of the same year (H_2-25) in their letters of intent (LoI) were contacted in advance to make them aware of both this proactive monitoring and to request the confirmation of their submission planning. In early June 2025, a baseline with all expected submissions was created. Monthly submissions received during H_2-25 were compared with the projections in the baseline. The focus group met regularly to analyse the results of the H_2-25 monitoring.

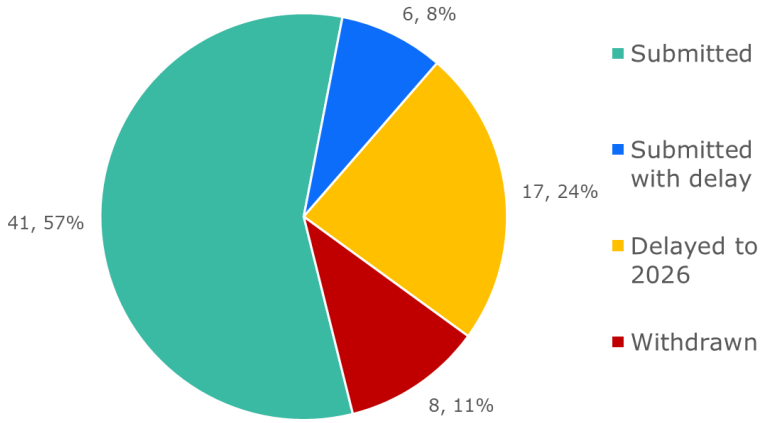
2.1. The monitoring

The focus of the analysis was the comparison of the actual MAAs received with the baseline of MAAs with a LoI at the beginning of June 2025.

The outcome of the monitoring is summarised below.

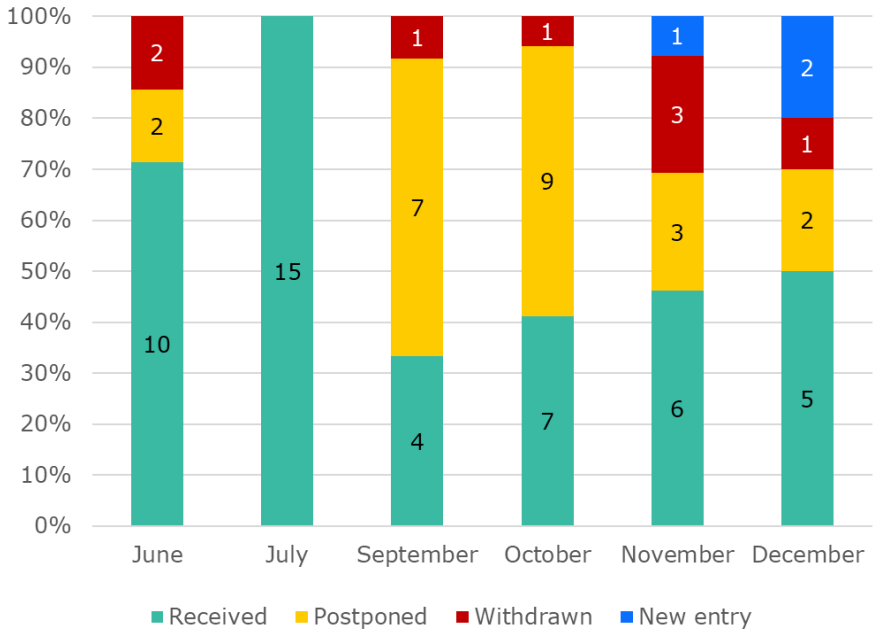
[1] The focus group is formed by representatives of EMA, CMDh, CHMP, PRAC, CAT, EFPIA, EUCOPE, EuropaBio, Europharm, Vaccines Europe, and Medicines for Europe

Fig. 1 H_2-25 MAAs submission trend compared with the forecast issued in June 2025.



The percentage of MAAs submitted on time was 57% with 8% of the applications submitted within the year but with a delay vis-à-vis the date indicated in the LoI. This represents an improvement from the behaviour observed during the 2023 monitoring where the MAAs submitted on time for the same period were 48% with 13% of applications submitted within the year but with a delay. The percentage of MAAs withdrawn or postponed to the following year is comparable to what observed in 2023.

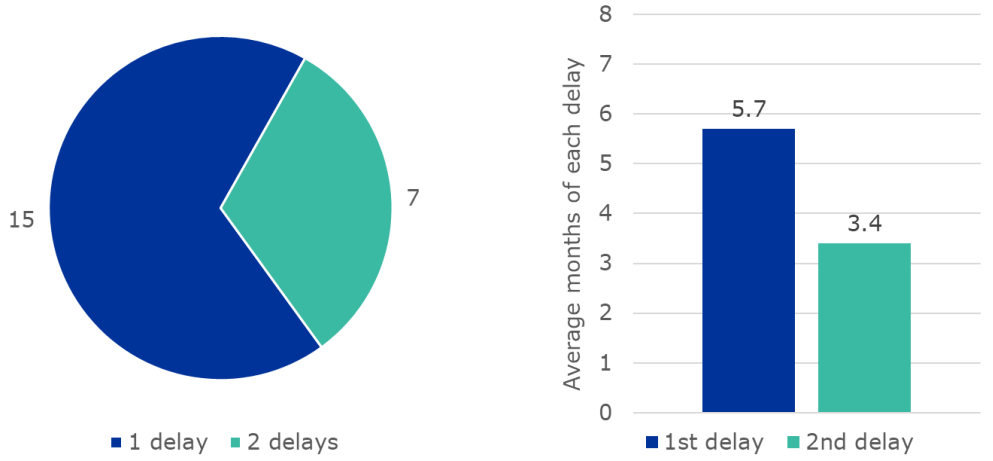
Fig. 2 Monthly monitoring of the MAAs pipeline behaviour during the second half of 2025 (baselined to Jun-25).



MAAs are submitted following predefined timetables. We have monitored these monthly submissions. Figure 2 shows the trend in the monthly submissions compared to the projections available in June 2025 for MAAs with a LoI. The new entry category represents the MAAs not included in the June forecast but nonetheless submitted, and it comprises mainly of generics or biosimilars applications, where applicants are unfortunately in the habit of not submitting the LoI 6 to 7 months ahead of the

planned submission, as this should be[2]. After the first two quite promising months, the reliability of the submissions drastically decreased, surprisingly reaching its lowest in September i.e., just three months from the information collected by the Agency to prepare the June forecast.

Fig. 3 Monitoring of the delays experienced during H_2-25 MAAs (baselined to Jun-25).



To measure the extent of the delays and hence the workplan disruption of the regulatory network, we have captured the number of delays, the extent of the delays, and as well the advanced notice the applicants give to the regulators.

Figure 3 quantifies the delays observed within the MAAs pipeline during the period under review. The panel on the left depicts the number of delays while the panel on the right shows the average extent of the delay. The majority of the applications had only one delay but the extent of the delay is similar for the average delay.

More striking behaviour was highlighted by the analysis of the advance notice the applicants give to regulators i.e., the heads-up of the upcoming change in their planned MAA submission date.

[2] Letter of Intent (LOI) should be provided about 6 to 7 months before the planned Marketing Authorisation Application (MAA) submission Pre-authorisation guidance | European Medicines Agency (EMA)

Fig. 4 Monitoring of the advance notice received before a delay in the MAAs submission.

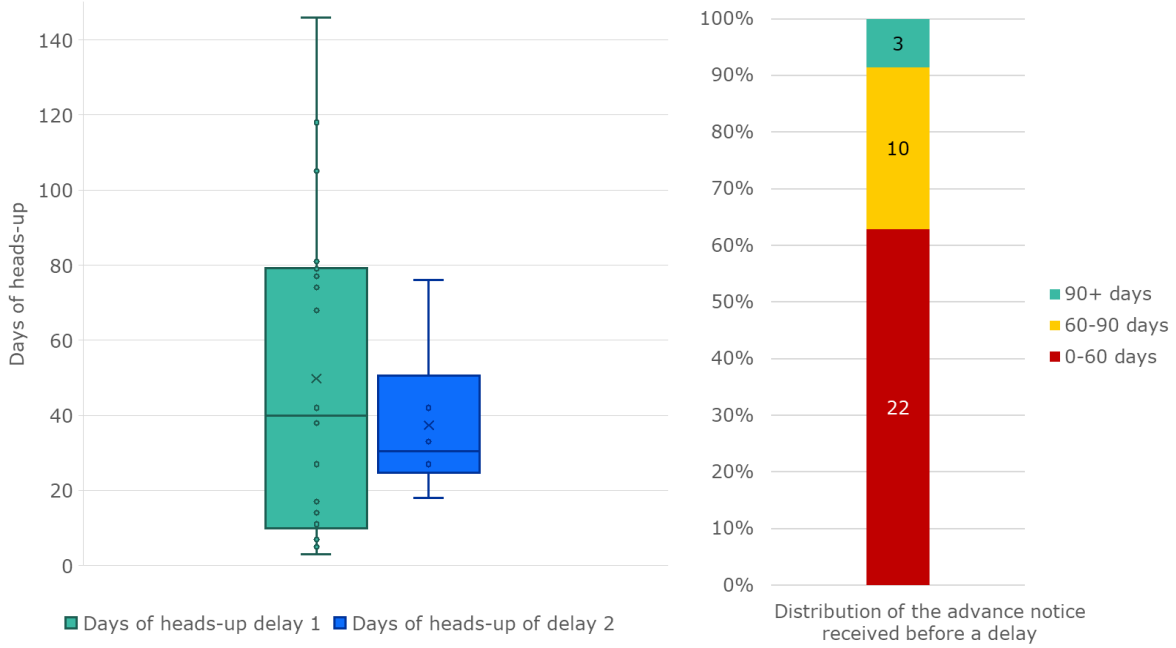
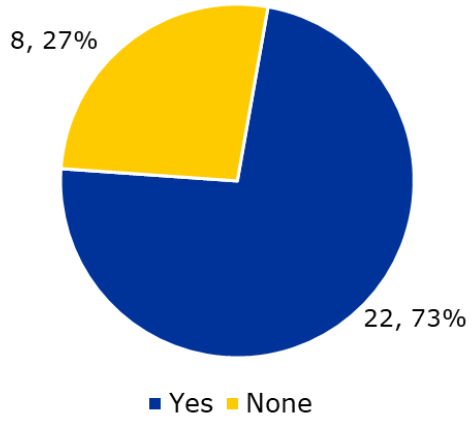


Figure 4 shows how variable this advanced notice is. At the panel on the left, looking at the MAAs delaying once, the advanced notice ranged from three to 146 days, with an average of 51 days. When analysing the second delay, we oberved similar behaviour with the minimum set at 18 days, the maximum at 76 days, and an average of 37 days. The panel on the right highlights that in over 60% of cases, the advance notice was given less than 60 days before the delay, while only three cases provided a more acceptable notice period of over 90 days. Therefore, the applicants do not give sufficient advance warning to the regulators to adjust their workplans and thereby causing major disruption in the workload allocation of the assessors.

To help plan the regulatory network's workload, the Agency sends automatic emails to prospective applicants three months before the planned submission date, requesting confirmation and, if changes occur, a justification. This information is essential to identify measures that could improve submission predictability.

Most of the applicants do respond to the request to confirm their submission date (>90%). However, of those initiating a change only 73% of the applicants provided a justification for this (Fig. 5). It should be noted that, while this is an improvement compared to the previous monitoring exercise, we do receive justifications that are not informative on the real reasons for the change in date. This is not ideal as it doesn't give sufficient input to EMA to identify possible solutions to rectify the trends impacting submission dates.

Fig. 5 Percentage of responders to the EMA request for justification of the change in submission plan.



We have classified the justifications received into four main categories and sub-clusters:

Justification cluster	Justification sub-cluster
Clinical / Scientific evidence	Study blind / Endpoint outcomes; Clinical Data availability
Chemistry, Manufacturing, and Controls (CMC)	Manufacturing and supply issues; CMC Data insufficient; GMP / QP audit timing
Regulatory / Procedural	Delays internal to applicant; Alignment with FDA; Accelerated assessment request; Address Rapporteur Feedback; Alignment FDA/EMA; Procedural delays in Rapp appointment
Strategic / Commercial / Organizational	Internal delays due to resource constraints; Business prioritization; Change of strategy - national submission instead of CP; Commercial Partnership discussions

The majority of the justifications provided fell within the *Regulatory / Procedural* cluster. While some delays may reflect the challenge of aligning health authority submissions (e.g., FDA/EMA alignment) or health authority guidance received close to submission date i.e., addressing Rapporteur feedback a number of companies listed internal delays or resource constraints, these may be primarily attributable to insufficient preparedness and inadequate planning on the part of the applicants.

2.2. Conclusions and next steps

With the second monitoring exercise in H_2-25, we have observed a slight improvement in the predictability of MAAs submissions versus 2023 and registered an increased communication engagement by the applicants. The outcome of the analysis is therefore confirming that the various initiatives that the Agency and the Focus Group have undertaken to draw attention to the problem (e.g., increased communication, workshops, etc) are slowly reversing the trend observed in the past years. Nonetheless, there is still quite some room for improvement in the communication between applicants and regulators as shown by the very short advanced notice provided by the applicants and the high percentage of applicants omitting to justify the change in their submission plans.

As the current pharmaceutical legislation limits the enforcement of stricter measures, continued emphasis will be given to the communication activities that draw attention to the problem, the consequences to the network, and stimulate applicants to improve communication with regulators on their submission planning.

The regulators will continue their monitoring activity and predictability assessment.

However, a further systematic monitoring to assess the effectiveness of the adopted measures is not envisaged. Instead, the Agency will focus on potential new approaches that could be implemented to improve submission predictability as part of the work towards the implementation of the New Pharmaceutical Legislation.