16 September 2024
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Stakeholders & Communication Division

Early dialogue with healthcare professional organisations for marketing authorisation applications: 1-year report

1. Background/rationale

A pilot for early dialogue with patient organisations for orphan Marketing Authorisation Applications ran from January 2021 to May 2022. This pilot was supported by EMA's Committee for Medicinal Products for Human Use (CHMP) and aimed to capture patients' perspectives at the start of the evaluation of marketing authorisation applications, in order to provide insights to assessors to be considered early during the assessment process (as appropriate), to complement other engagement methodologies later in the process (e.g. scientific advisory groups and oral explanations), and to facilitate any further interactions as the procedures progress.

Patient perspectives requested include patients' experience, concerns and needs related to their condition, in particular: standard treatments and how acceptable they are; therapeutic/unmet medical needs; quality of life; what benefits would be hoped for in new medicines; and what level of side effects would be considered acceptable.

An outcome report on the pilot was published in July 2022. It concluded positively, with CHMP (Co) Rapporteurs recognising the usefulness and benefit of reaching out to patient organisations at the start of the assessment of (orphan) marketing authorisation applications. The added value was the assessment teams receiving direct insights from stakeholders which was a useful complement during the assessment of the marketing authorisation application dossier.

Based on this positive outcome, it was proposed to confirm the pilot methodology as a routine practice, and to extend it to non-orphan medicinal products as well as healthcare professional (HCP) organisations.

Early dialogue with HCP organisations started in May 2023. This report presents the outcome after twelve months of engagement, from May 2023 to April 2024, included.

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2. Early dialogue with HCP organisations – Purpose and methodology

2.1. Purpose

The purpose of consulting HCP organisations is the same as the purpose of consulting patient organisations as described in Section 1, i.e.: provide insights to assessors, complement other methodologies and facilitate further interactions.

Specifically, for HCP organisations, the purpose is to capture HCPs' insights on aspects of a condition and its currently available treatments at the early stage of the evaluation of marketing authorisation applications. HCPs are asked to share their experience of treating the condition, in particular: the standard of care or available treatments and to what extent they cover the intended indication; the treatment duration, and whether the duration needs to be optimised; any possible therapeutic/unmet medical needs; what benefits they would hope for in new medicines; and what level of side effects they would consider manageable for patients.

The early consultation does not aim to collect positions on the medicinal product under assessment from the consulted organisations.

Input is requested from organisations and not individual experts, and is therefore provided on behalf of organisations.

2.2. Published process

A process and frequently asked questions (FAQs) document was published in November 2023. It outlines the identification of procedures for consultation and general methodology (Section 2.1) as well as the purpose of early dialogue (Section 2.2).

To summarise, the medicinal products considered for patient and/or HCP consultation are new active substances only (i.e. no generic/biosimilar products) submitted for initial marketing authorisation application. Their selection for consultation is under the remit of the CHMP "core group" involved in patient and HCP engagement, composed of five CHMP members from different Member States. The Rapporteurs appointed for the application (hereafter referred to as "Rapporteurs") are systematically informed about the planned consultation and offered the opportunity to ask specific questions to organisations, in addition to the standard questions that are part of the template (see Annexes 1 and 2).

The input collected from organisations is shared with the Rapporteurs from the CHMP, other concerned committees such as the orphan committee (COMP) as well as with the applicants. Rapporteurs are also informed that the organisations can be contacted at any time for follow-up questions.

2.3. Identification of HCP organisations to contact

HCP organisations are identified by EMA's Public and Stakeholder Engagement Department based on the therapeutic indication of the medicinal product in question, as applied for by the applicant. The following organisations are contacted in order of priority:

- Eligible HCP organisations
- European Reference Networks, for rare diseases

- Non-eligible organisations, in specific cases where expertise is not otherwise available. In this case, EMA performs a brief assessment of the organisation's funding and transparency based on publicly available information to ensure independence.

Several organisations may be contacted for one application. This applies in particular when there are overlapping therapeutic areas concerned by the targeted indication.

2.4. Use of input

The use of input by the assessment team is measured by the inclusion of the input/ reference to the input in the Day 80 assessment report(s), and/or Day 120 List of Questions. These documents were reviewed for all medicinal products selected for consultation during this first year, and the outcome is presented in Section 3.3.

3. Outcome

3.1. Consultation phase

Between May 2023 and April 2024, consultation from HCP organisations was requested for 44 medicinal products. This translated into 77 requests sent to individual HCP organisations, one particular consultation leading on average to 1-3 requests depending on the number of organisations with relevant expertise (see also Section 2.3). One particular indication covering a range of infections to various organs led to 5 consultations.

Of note, no products were selected for consultation in April 2024; the month of April is therefore not shown in the figures below.

- **Responses received**

In total, 54 inputs were received from HCP organisations. The ratio of responses received *vs* requests sent to HCP organisations is presented in **Figure 1**:

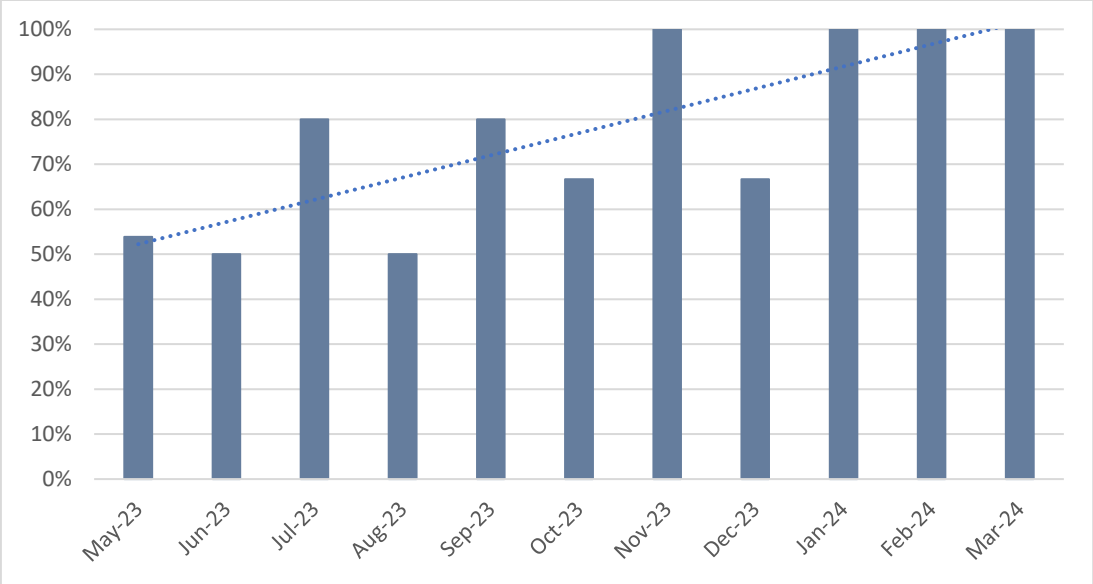


Figure 1: percentage of inputs received *vs* inputs requested from HCP organisations

- **Therapeutic areas**

The distribution of medicinal products (for which a consultation was requested) across therapeutic areas is shown in **Figure 2**. The distribution depends entirely on the applications received by EMA then selected by the CHMP core group, and is provided for indicative purposes only.

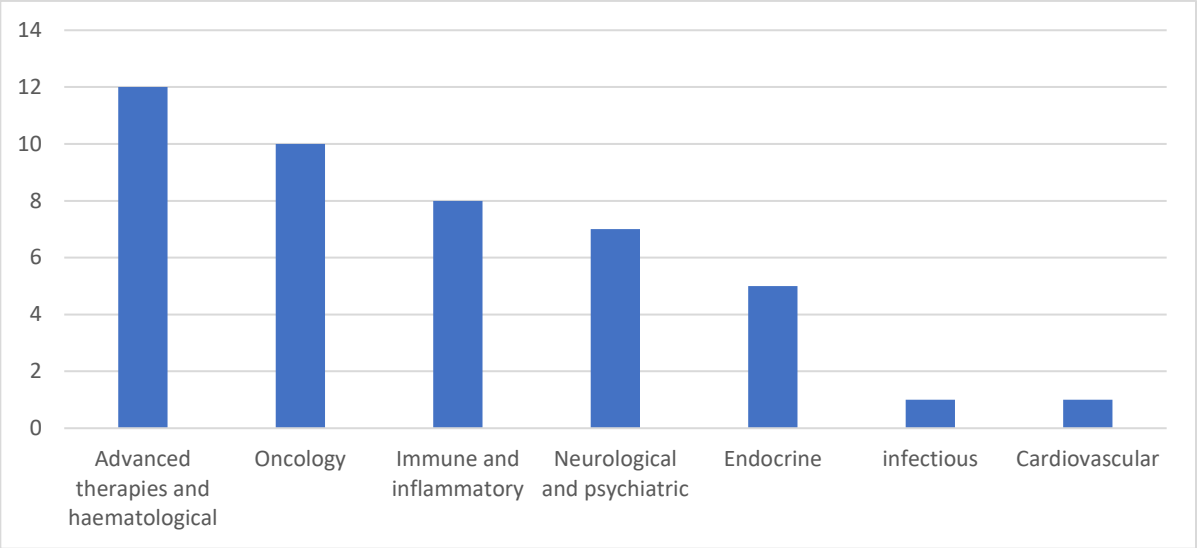


Figure 2: number of medicinal products for which a consultation from HCP organisations was requested, distributed per therapeutic area

- **European Reference Networks**

The number of European Reference Networks (ERNs) contacted every month is shown in **Figure 3**. This number depends entirely on the number of applications for orphan diseases received by EMA then selected by the CHMP core group, and is provided for indicative purposes only.

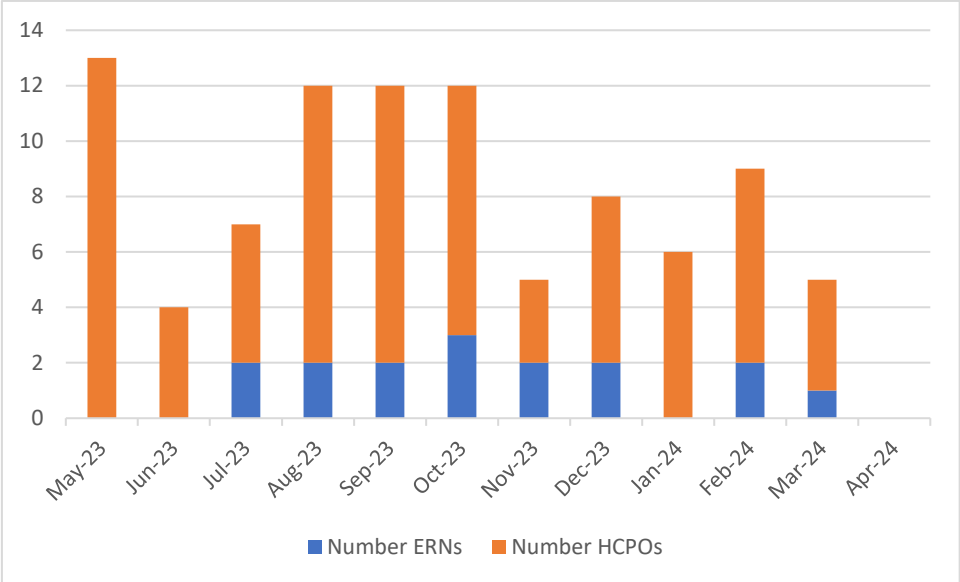


Figure 3: number of ERNs contacted in proportion of the number of HCP organisations contacted, per month

On average, one or two ERNs were contacted each month.

3.2. Content of input

There was a variability in the content of the input received from HCP organisations. Possible factors are discussed in Section 4.3.

Organisations are provided with the name of the active substance under evaluation for completeness and as this is publicly available information. This led some organisations to focus their input on the medicinal product itself rather than the indication. Mitigation factors are discussed in Section 4.3.

EMA's Public and Stakeholder Engagement department reviews all inputs received to remove personal information and identify whether there are any points that need clarification/ confirmation with the organisation before sharing the input further.

3.3. Use of input

Following sharing of input with Rapporteurs, the Day 80 Clinical and Overview assessment reports (ARs) as well as the Day 120 List of Questions (LoQ) for each product selected for consultation were reviewed to identify whether the input was reflected and in which section.

The ratio of products for which the input was reflected in one of the above documents at least is presented in **Figure 4**:

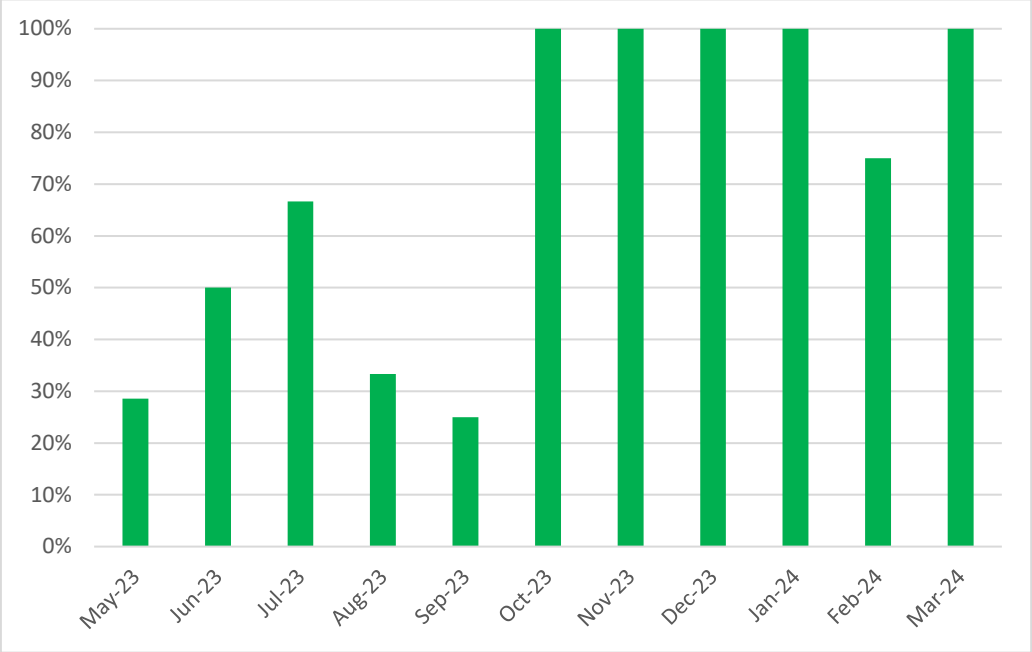


Figure 4: percentage of inputs reflected in Day 80 AR and/or Day 120 LoQ

4. Discussion

4.1. Changes applied to the input template

As more experience was gained with the methodology, the templates for collection of input from both patient and HCP organisations were revised to capture the latest lessons learned.

In March 2024, revised input templates were introduced. The main purpose of the changes made was to make it clearer that the input provided by the organisations would be shared with the pharmaceutical company, and that it may be shared further, in particular where the input is subject to disclosure in accordance with EMA's Policy on access to documents. An additional standard question on considerations for pregnant people/people of child-bearing potential was also added to the template.

The initial and revised templates are included in Annexes 1 and 2 of this report.

4.2. Consultation phase

The ratio of inputs received gradually increased with time, as can be seen with the trend line in **Figure 1** and the 100% ratio obtained on the last 3 months. This was the expectation, taking into account the time needed for organisations to become more familiar with the methodology and to put in place their own processes to collect input.

It remains challenging for some organisations to provide systematic input, with consideration to the volume of requests and short timelines. This applies in particular to organisations frequently contacted as they cover high frequency therapeutic areas (see **Figure 2**).

Of note, some organisations contacted sometimes indicated that the particular indication targeted was not in their remit, in which case they did not provide input. This also has an impact on the ratio figures presented in **Figure 1**, although minor.

4.3. Content of input

The variability in the input received mentioned in Section 3.2 is likely linked to factors such as availability of expertise, timelines for consultation (shortened for accelerated assessment procedures) and experience of the organisation with the early dialogue methodology. The completeness of the input received generally increased during the first year, as organisations became more familiar with the methodology and had the opportunity to put in place their own processes to collect input, as already indicated in Section 4.2, such as sharing the request with identified Key Opinion Leaders.

Organisations that provided input on the medicinal product rather than the indication were informed that the input would be shared with the applicant and asked whether they would like to make any modifications. Of note, Rapporteurs are systematically reminded that no judgement made by the organisations on the medicinal product should be reflected in the assessment. The input template (see Section 4.1) and template emails to organisations have been revised accordingly to clarify sharing rules. Further actions with regard to the published process and FAQs document and continuous dialogue with organisations are described in Section 5.

4.4. Use of input

Documentation of the input in at least one of the assessment documents, rather limited at the start of the process, reached 100% as of October 2023. With the exception of one procedure in February 2024, all products for which consultation was requested had the consultation referenced in at least one of the

assessment documents from October 2023 to April 2024. This also applies to the document of input from patient organisations.

In October 2023, the Day 80 Clinical assessment report was updated to include two new dedicated sections for Rapporteurs to document the HCP (and patient) input provided as part of the early dialogue methodology:

- Section 3.8, under 3. Clinical efficacy
- Section 3.10.3, under 3.10 Overall Rapporteur assessment of clinical efficacy.

This highlights the importance of dedicated sections in templates to support the assessment teams. Assessors are also becoming more familiar with the methodology and its added value, which translates into a better reflection in the assessment reports.

The Day 80 (D80) Overview and List of Questions assessment report template is being updated accordingly to ensure that the input will be captured throughout the evaluation and up to the European public assessment report (EPAR).

4.5. Update of existing guidance to applicants

A new question (5.1.13) was added to the EMA pre-authorisation guidance to increase awareness of the early dialogue methodology amongst applicants.

> **5.1.13 What is the CHMP early contact with patient and healthcare professional organisations? NEW Mar 2024**
>
> A methodology of engaging with patient organisations at the start of evaluation of new MAAs for orphan medicines by the CHMP was piloted in 2021-22 with a successful outcome.
>
> As part of the continued implementation of this methodology, it was agreed to expand the selection of medicines from orphan medicines to include also non-orphan ones and to reach out to healthcare professional organisations in addition to patient organisations.
>
> Input received from these organisations is shared with the Rapporteurs and with the Applicant for transparency.
>
> More details can be found in the process and FAQs.
>
> **References**
>
> - Pilot phase for CHMP early contact with patient / consumer organisations
> - Pilot on early dialogue with patient organisations for orphan marketing authorisation applications: Outcome Report
> - CHMP early contact with patient and healthcare professional organisations: process and FAQs

5. Conclusion and next steps

Based on the successful completion of one year of engagement with HCP organisations for early dialogue, the consultation will continue as a systematic methodology considered for all new

applications with new active substances. As mentioned, the CHMP core group (see Section 2.2) remains responsible for selecting the medicinal products for which a consultation is deemed relevant.

The following steps are proposed (the same steps apply for patient organisations):

- Present an outcome of the first year to the Healthcare Professionals Working Party members and consult organisations on the inclusion of their input in the EPAR – a discussion occurred at the Healthcare Professionals' Working Party meeting on 03 July 2024.
- Update the process and FAQs document to reflect the latest clarifications and changes.
- Include dedicated sections in the Day 80 Overview AR and EPAR to make the (public) reference to the input systematic, and discuss with CHMP members to harmonise how the input is referenced.
- On both sides (EMA and eligible organisations), continuously learn from each other, raise awareness and update each other on the methodology.
- Continue raising awareness about the methodology and its latest updates within EMA, the regulatory network, HCP organisations and ERNs.

ANNEX 1

Template input form to healthcare professional organisations

From May 2023 to February 2024

CHMP early contact with healthcare professionals

EMA engages with stakeholders and their representatives at multiple stages of its activities and the added value of including their perspectives in the evaluation of medicines has been well demonstrated. They are currently involved at various timepoints during the medicines' lifecycle, and we believe this can be further enhanced by establishing contact with relevant healthcare professional organisations at the start of the assessment of new medicines.

The CHMP provides recommendations on the approval and use of medicines in the European Union/ European Economic Area. Its key task is to assess all the scientific data when a company applies for a marketing authorisation. It decides whether a proposed medicine is made to the proper standards, works well and has benefits in treating the illness that outweigh the risks of side effects ('positive benefit-risk'). The CHMP then issues a positive or negative recommendation and the final decision is issued by the European Commission.

Reaching out to healthcare professionals when medicines are in active development will enable CHMP members to fully appreciate professionals' experience and concerns about the management of the diseases. This will help the CHMP understand aspects that are important for you, such as treatment options, treatment optimisation, unmet medical needs and what benefits they would hope for new treatments.

The CHMP has started its assessment of **active substance** intended for **indication** and is inviting **organisation** to share perspectives on behalf of healthcare professionals' organisations. See below for details.

We would appreciate your feedback by **Date**.

Your views will be shared with the CHMP (and any other relevant committee) and anonymously with the pharmaceutical company who has submitted the marketing authorisation application (personal names will be removed).

For any questions, please do not hesitate to contact the EMA Public and Stakeholders Engagement Department (replying to all on the email received).

HEALTHCARE PROFESSIONAL EXPERIENCE OF: **indication**
Please include below any aspects that are of particular importance to healthcare professionals, such as standard of care or available treatments and to what extent they cover the intended indication, the treatment duration and if in your view it needs to be optimised, therapeutic/unmet medical needs, what benefits you would hope for in new medicines as well as what level of side effects would consider manageable for patients. • Please also mention any aspects about the condition or its treatments that you feel are not well-understood or not sufficiently considered. • Please include anything else you feel is important for EMA to know. Please try to keep your main points to 1-2 pages, if necessary, include more details in an appendix. ☐ Tick here to confirm you give consent for EMA to share your views anonymously with third parties, as applicable.

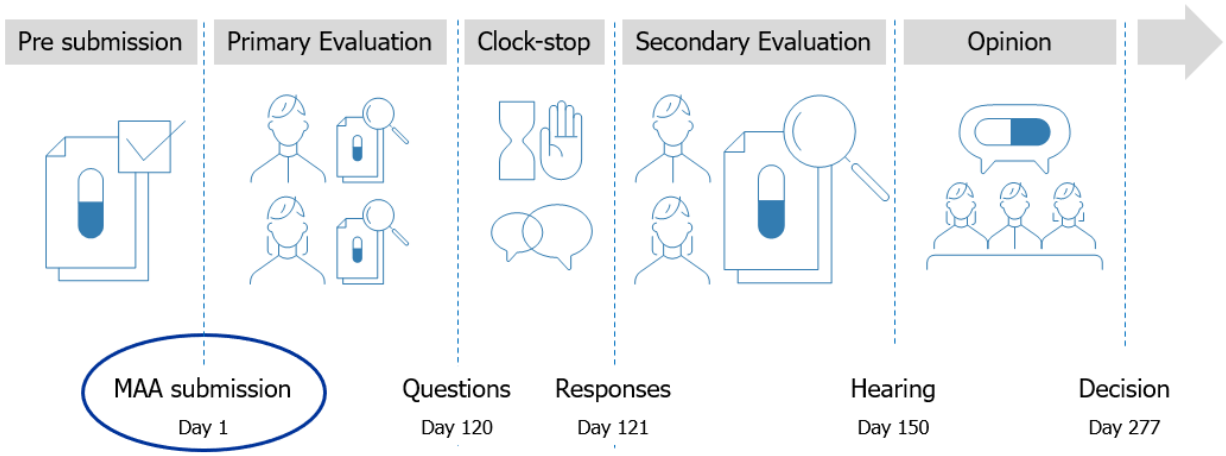
ANNEX 2

Template input form to healthcare professional organisations

From March to April 2024

CHMP early dialogue with healthcare professionals

EMA engages with stakeholders and their representatives at multiple stages of its activities and the added value of including their perspectives in the evaluation of medicines has been well demonstrated. Stakeholders are currently involved at various timepoints during the medicines' lifecycle, and we believe this can be further enhanced by engaging with relevant healthcare professional organisations at the start of the assessment of new medicines.



The CHMP provides recommendations on the approval and use of medicines in the European Union/ European Economic Area. Its key task is to assess all the scientific data when a company applies for a marketing authorisation. It evaluates whether a proposed medicine is made to the proper standards (quality), works well (efficacy) and has benefits in treating the illness that outweigh the risks of side effects (safety) ('positive benefit-risk'). The CHMP then issues a positive or negative recommendation and the final decision is issued by the European Commission.

Reaching out to healthcare professional organisations when medicines are in active development will enable CHMP members to fully appreciate their experience and concerns about the management of these conditions. This will help the CHMP understand aspects that are important for healthcare professionals, such as treatment options, treatment optimisation, unmet medical needs and what benefits they would hope for new treatments.

The CHMP has started its assessment of **active substance** intended for **indication** and is inviting **organisation** to share any relevant perspectives. See below for details.

We would appreciate your response by **Date**.

Your input and organisation name will be shared with the CHMP (and other relevant EMA committees, working parties and expert groups) and may be reflected in the assessment report that will be made public at the end of the procedure.

EMA will also share your input and organisation name with the pharmaceutical company that has submitted the marketing authorisation application.

Your input may be used for another application for the same condition, in which case, please note that it will also be shared with the pharmaceutical company submitting this new procedure.

Personal information, if included, will be removed before the feedback is shared.

Please also note that any document held by EMA may be subject to disclosure in accordance with Regulation (EC) No 1049/2001 of the European Parliament and of the Council of 30 May 2001 regarding public access to European Parliament, Council and Commission documents.[1]

By submitting your responses, you acknowledge and agree with the rules detailed above.

HEALTHCARE PROFESSIONAL EXPERIENCE OF:

indication

Please include below any aspects that are of particular importance to healthcare professionals, such as information on:

- the standard of care or available treatments and to what extent they cover the intended indication;
- the treatment duration; and, if in your view, the duration needs to be optimised;
- any possible therapeutic/unmet medical needs;
- what benefits you would hope for in new medicines; as well as what level of side-effects you would consider manageable for patients;
- considerations for pregnant people/people of child-bearing potential, where applicable.

Please also mention any aspects about the condition or its treatment that you feel are not well-understood or not sufficiently considered.

Please include anything else you feel is important for EMA to know. Please try to keep your main points to 1-2 pages; if necessary, include more details in an appendix.

[1] In this regard, please consult our webpage on Access to Documents for more information, available at https://www.ema.europa.eu/en/about-us/how-we-work/access-documents.

ANNEX 3

Figures

Table 1. One year of early dialogue with HCP organisations

Month/year of start of evaluation	Number of products selected for consultation	Number of HCP organisations contacted	Number of inputs received	Number of products for which the input was referenced in D80 AR and/or D120 LoQ
May 2023	7	13	7	2
June 2023	2	4	2	1
July 2023	3	5	4	2
August 2023	6	10	5	2
September 2023	4	10	8	1
October 2023	6	9	6	6
November 2023	2	3	3	2
December 2023	4	6	4	4
January 2024	3	5	5	3
February 2024	4	6	6	3
March 2024	3	4	4	3
April 2024*	0	0	N/A	N/A

**There is no start date in April for initial, full (non-accelerated) marketing authorisation applications. No products were selected by the core group for consultation.*