27 June 2026

Study protocol: "Early stakeholder interaction and advice on RWD and RWE: a retrospective review"

Administrative details for the data analysis	
Title of topic	Early stakeholder interaction and advice on RWD and RWE: a retrospective review
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Background	
Title of topic	Early stakeholder interaction and advice on RWD and RWE: a retrospective review
Regulatory procedure	Not applicable
Background	Real-world data (RWD) and real-world evidence (RWE) are playing an increasingly important role in the evaluation of medicinal products within the European regulatory framework. As a result, questions regarding the generation and regulatory use of RWD/RWE are increasingly raised during early interactions between stakeholders and the European Medicines Agency (EMA), particularly through Scientific Advice (SA) and Protocol Assistance procedures. These interactions provide an opportunity for applicants to seek regulatory guidance on the use of RWD/RWE during medicine development and are documented in official EMA reports.
Aim	Analyse the nature of stakeholder requests related to real-world data (RWD) and real-world evidence (RWE), and the corresponding advice provided by EMA during Scientific Advice and Protocol Assistance procedures conducted between 2021 and 2025.

1. Rationale and background

The European Medicines Agency (EMA) supports innovation throughout the development of medicinal products, including the early stages before marketing authorisation. Real-world data (RWD) and real-world evidence (RWE) are increasingly discussed during these early interactions, particularly in areas where regulatory guidance is limited or evolving. Most formal discussions take place through Scientific Advice (SA) procedures, including Protocol Assistance for orphan medicines. The Scientific Advice Working Party (SAWP) provides official advice, which is documented in reports containing the questions submitted by applicants and the corresponding responses from EMA.

2. Research question and objectives

- **Objective 1:** Identify the EMA mechanisms and platforms through which stakeholders can seek advice on real-world data (RWD) and real-world evidence (RWE) during the pre-authorisation phase of medicinal product development.
  Research question 1: What mechanisms are available for stakeholders to obtain EMA advice on RWD/RWE during early medicinal product development?

- **Objective 2:** Characterise the nature and focus of RWD/RWE-related requests submitted during Scientific Advice (SA) procedures between 2021 and 2025.
  Research question 2: What were the main RWD/RWE-related topics discussed during Scientific Advice procedures from 2021 to 2025?

- **Objective 3:** Evaluate the advice and recommendations provided by EMA in response to RWD/RWE-related requests submitted through Scientific Advice processes.
  Research question 3: What types of advice and recommendations did EMA provide in response to RWD/RWE-related requests?

- **Objective 4:** Identify recurring challenges, evidence gaps, and areas for improvement in the provision of Scientific Advice on RWD/RWE topics.
  Research question 4: What challenges and gaps are most frequently identified in RWD/RWE-related Scientific Advice? What opportunities exist to strengthen regulatory support in this area?

3. Research methods

We will perform an analyses to characterise the use of RWE in Scientific Advices with the aim to (1) quantify the number of Scientific Advice addressing RWE conducted by the Agency between January 1, 2021, and December 31, 2025; (2) categorize the therapeutic areas covered by these procedures; (3) identify the main stakeholders requesting scientific advice from the Agency; (4) characterize the principal topics related to RWE discussed during early regulatory interactions; (5) examine the types of responses and proposals provided by the Agency in relation to the use of RWE; (6) identify potential gaps in current practices and explore opportunities for facilitating the use of RWE in early regulatory dialogue.

3.1. Data sources

The following items will summarize the main topics of the analyses:

Time frame: The analysis was limited to Scientific Advice and Protocol Assistance records available in official EMA repositories and completed between 1 January 2021 and 31 December 2025.

Language: Only documents written in English will be considered.

Procedures: Initial Scientific Advice (SA) and Initial Protocol Assistance (PA) procedures. Follow-up Scientific Advice, qualification procedures, ongoing applications, and withdrawn requests were excluded. Only completed stakeholder–EMA interactions were included in the analysis.

3.2. Search strategy

A two-step search strategy will be utilized. The **first step** will include an initial basic search using a combination of keywords with a tool called Scientific Explorer, a search engine used to aid European Medicines Regulatory Network's (EMRN) scientific staff to find information. Scientific Explorer has been initially developed to search information in the large dataset of scientific advice letters and enables searching key targeted information in document text in a standardised and validated key thanks to AI. An updated version of this tool has been released in 2026.

Scientific Explorer Terms	'Initial Scientific Advice - Human' **OR** 'Initial Protocol Assistance'	**AND**	Start date from '01/01/2021'	**AND**	Start date to '31/12/2025'	**AND**	'Completed'	**AND**	'Real world evidence'

Search string:

Adv.Search/Edit query: (Start date from '01/01/2021' AND Start date to '31/12/2025') [AND] (Application AI topics equals 'Real world evidence') [AND] (Procedure status equals 'Completed') [AND] (Process category equals 'Scientific advice') [AND] (Process type equals 'Initial Scientific Advice - Human' OR Process type equals 'Initial Protocol Assistance'

The **second step** will be realized performing a review of all internally available documents pertaining to the internal EMA RWE team records and IRIS to find out information about RWE contained in documents which belong to SA processes.

3.3. Source of evidence selection

Initial document screening

An initial screening will be conducted using the section entitled *"Summary of questions raised/issues discussed in the Scientific Advice"* from each Scientific Advice or Protocol Assistance record.

Full-text screening

Records identified as relevant during the initial screening will undergo full-text review. Any uncertainties or ambiguities classification will be resolved through discussion with a second investigator from the EMA RWE team.

3.6. Data extraction

Data will be extracted by a single researcher using a structured data extraction form.

3.7. Analysis of evidence

Data were analysed by a single researcher and revised through a consultation with a second investigator from the EMA RWE team.

3.8. Presentation of the results

The results will be presented as a descriptive narrative synthesis addressing the review objectives and research questions. Findings will be grouped into key categories and themes, followed by a discussion of the main results.

3.9. Plans for disseminating and communicating study results

A peer reviewed publication.

4. References

1. European Medicines Agency. **"Mandate, objectives and rules of procedure of the Scientific Advice Working Party (SAWP)"**. 2025.
2. European Medicines Agency.**"Annual Report"**. 2025.
3. Concato J, Corrigan-Curay J. **"Real-World Evidence - Where Are We Now?"**.N Engl J Med. 2022 May 5;386(18):1680-1682.
4. Flynn R, Plueschke K, Quinten C, et al. **"Marketing Authorization Applications Made to the European Medicines Agency in 2018-2019: What was the Contribution of Real-World Evidence?"**. Clin Pharmacol Ther. 2022 Jan;111(1):90-97.
5. Prilla S, Groeneveld S, et al. **"Real-World Evidence to Support EU Regulatory Decision Making-Results From a Pilot of Regulatory Use Cases"**. Clin Pharmacol Ther. 2024 Nov;116(5):1188-1197.