<dd/mm/yyyy>
EMA/659352/2022

<name and address of the applicant/ marketing authorisation holder (MAH)>
<name of the product>

Addressed to:

EMA product and application business support PA-BUS

**Subject: Clinical study data proof-of-concept pilot participation letter**

Dear Sir/Madam,

By means of this participation letter, <name of applicant/ MAH> would like to formally confirm its intention to participate in the proof-of-concept (PoC) pilot on the submission and analysis of clinical study data from clinical studies in relation to their <initial marketing authorisation application ('iMAA')>/<post-authorisation application> submitted to the European Medicines Agency ('EMA') for <product><EMA procedure number> for <proposed indication>.

In addition to the main contact for this submission, the following person is nominated as Study Data Package Point of Contact for questions related to the study datasets and ancillary files: <name of the study data package expert> (<email address of the study data package expert>).

Yours sincerely,

<signature>

<name of applicant's or MAH's authorised representative>

<position>

**Official address** Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
**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 An agency of the European Uni

## 1. DEFINITIONS

1.1 'Applicant' means the party making an application to the EMA for approval to market a medicine within the European Union.
1.2 'AR' means assessment report.
1.3 'CHMP' means EMA's Committee for Medicinal Products for Human use.
1.4 'Data Protection Notice' means a document which informs data subjects about how their personal data is processed as part of a certain data processing activity, including the details and information about their data protection rights in accordance with Articles 15-16 of Regulation (EU) 2018/1725 (EUDPR) and Articles 14-15 or Regulation (EU) 2016/679 (GDPR).
1.5 'Records of Processing Activity' means a document containing general information on a certain data processing activity. This is a legal obligation under Article 31 of EUDPR and Article 30 of GDPR.
1.6 'Effective Date' means the date on which this participation letter is signed by the applicant's or MAH's authorised representative.
1.7 'EPAR' means European public assessment report.
1.8 'iMAA' means initial Marketing Authorisation Application.
1.9 'EU Legal Framework' means the EU Legal Framework for pharmaceuticals; Directive 2001/83/EC and Regulation (EC) No 726/2004.
1.10 'Marketing Authorisation Holder' or 'MAH' means the company or other legal entity that holds the authorisation to market a medicine in one, several or all European Union Member States.
1.11 'Participation Letter' means this letter.
1.12 'Personal Data' means any information relating to an identified or identifiable natural person ('data subject'); an identifiable natural person is one who can be identified, directly or indirectly, in particular by reference to an identifier such as a name, an identification number, location data, an online identifier or to one or more factors specific to the physical, physiological, genetic, mental, economic, cultural or social identity of that natural person.
1.13 'Union Data Protection Legislation'' means all applicable Union data protection legislation including Regulation (EU) 2016/679 ('General Data Protection Regulation' or 'GDPR') and applicable national data protection legislation of Member States, as well as Regulation (EU) 2018/1725 ('European Data Protection Regulation for European Union institutions, bodies offices and agencies' or 'EUDPR') as may be amended or replaced from time to time.
1.14 'NCA' means National Competent Authority of Union Member States.
1.15 'Clinical study data', also referred to as 'Standardised Study Data', mean individual patient data from clinical studies[1] in electronic structured format.

## 2. PURPOSE OF THIS PARTICIPATION LETTER

2.1 The purpose of this participation letter is to formally confirm the applicant's or MAH's intention to participate in the PoC Pilot on the submission and analysis of data from clinical studies[2] as part of a given iMAA or post-authorisation application submitted to EMA. By signing this participation letter, the applicant/MAH agrees to fulfil the obligations as set forth in this participation letter.

## 3. SCOPE OF THE POC PILOT

3.1 The CHMP's current clinical assessment of medicinal products for human use is mainly based on data from clinical summaries and information reported in clinical study reports. This information is provided in a format that does not directly allow disaggregation or any other form of further analysis, whereas EMA and NCAs may benefit from having access to clinical study data during the assessment of the medicinal product. Access to clinical study data can support both EMA and NCAs in understanding the submitted evidence and therefore inform the regulatory decisions on the benefit-risk balance of the product. More detailed information on the PoC pilot is included in the 'Information about the clinical study data proof-of-concept pilot for industry' (Appendix 1) and in the Questions and answers on the clinical study data proof-of-concept pilot for industry (link).

[1] Clinical studies include clinical trials as well as non-interventional studies in accordance with the definitions set out in Article 2 of Regulation (EU) No 536/2014.
[2] Formerly referred to as proof-of-concept pilot on the submission and analysis of raw data

3.2 The PoC pilot aims to investigate the benefits of visualising and analysing clinical study data to support the scientific assessment of medicinal products and to identify the associated operational, resource and technological needs. Participants in the PoC pilot will voluntarily submit clinical study data simultaneously with the standard information submitted in their iMAA or post marketing authorisation application. Participation in the PoC pilot will not delay the adoption of the scientific opinion by the CHMP.
3.3 The type of clinical study data analyses will include re-analyses, additional analyses and visualisations with the purpose of informing the assessment of the regulatory submission in which the data were included. The decision as to which analyses are performed will be driven by the CHMP and Rapporteur teams' needs, and will be individual to each submission. The EMA will share the results of any analyses conducted with the applicant/MAH so that the applicant/MAH can replicate the analyses. In addition, EMA, may share the clinical study data with NCAs for the purposes of peer-review and training and the applicant or MAH, in participating in the PoC pilot, consents to such disclosure accordingly.
3.4 Clinical study data submitted may also be used to explore the added value of pre-specified analyses, visualisations and characterisation of data packages in the form of user-friendly interactive dashboards or reports aiming to enhance understanding of the data underlying the clinical evidence supporting an application. This exploratory work includes part of an ongoing procurement procedure under one of EMA's framework contracts (EMA/2020/46/TDA: 575628-2021 - Result - TED). As a result, clinical study data may be shared with a third party for the purposes of such third party providing data analytical support ("third party disclosure") strictly limited to the aforementioned procurement. In participating in the PoC pilot, the applicant or MAH consents to EMA making such a third party disclosure. It is understood that where EMA contracts with such a third party, the third party is contractually obliged not to disclose to any other third party provided to it from EMA.

## 4. OBLIGATIONS OF THE APPLICANT/MAH

4.1 As part of the PoC pilot, the applicant or MAH is expected to participate to a 'data submission meeting' to introduce the data analysts to the key characteristics of the clinical study data files and accompanying documentation from their submission.
4.2 As part of the PoC pilot, the applicant or MAH commits to providing feedback on their participation in the PoC pilot upon request by EMA (e.g. on operational aspects of the PoC pilot).
4.3 It is the applicant's or MAH's responsibility to comply with Union data protection legislation and rely on the correct ground for lawfulness for the processing of personal data for the purpose of running the clinical studies and submitting clinical study data under the PoC pilot.

## 5. PERSONAL DATA PROCESSING IN THE POC PILOT

5.1 Union Data Protection Legislation apply to the processing of Personal Data with respect to the PoC Pilot. In this regard, EMA shall act in accordance with the EUDPR which is the Union regulation applicable to the processing of Personal Data by the Union institutions, bodies, offices and agencies; while NCAs shall act in accordance with the GDPR.
5.2 Further information on the processing of Personal Data in the PoC pilot is included in the Data Protection Notice (link) and the Records of Processing Activity (link) which are published on EMA's website.
5.3 Any questions and requests concerning the processing of personal data in the PoC pilot can be addressed to the Internal Controller within EMA (at datacontroller.analytics@ema.europa.eu) or to EMA's Data Protection Officer ('DPO'). The DPO can be contacted at dataprotection@ema.europa.eu or at the following address:

European Medicines Agency
PO Box 71010
1008 BA Amsterdam
The Netherlands

## 6. MISCELLANEOUS

6.1 This participation letter is governed by Dutch Law.
6.2 The applicant/MAH and EMA agree that in the event a dispute arises relating to the PoC pilot, all reasonable efforts to settle matters amicably will be used. If, despite such efforts, a dispute remains,

the parties irrevocably agree that the courts of Amsterdam, The Netherlands, shall have exclusive jurisdiction to settle any dispute arising out of or in connection with this letter (including a dispute regarding the existence, validity, or termination of this letter).

6.3 In case of any questions or complaints related to the PoC pilot, please contact rawdatapilot@ema.europa.eu.

**SIGNED BY**: <applicant's or MAH's authorised representative>

Date:_____
On behalf of <name of the applicant/ MAH>:

_____
Name:
Title:

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

**Appendix 1: Information about the clinical study data proof-of-concept pilot for industry**

14 October 2024
EMA/659352/2022

# Information about the clinical study data proof-of-concept pilot for industry

## Access to clinical study data for marketing authorisation and post-authorisation applications submitted to the EMA

The purpose of this document is to provide an overview about the proof-of-concept (PoC) pilot on the submission and analysis of data from clinical studies[3] as part of selected initial marketing authorisation applications (iMAAs) and post-authorisation applications submitted to the European Medicines Agency (EMA).

### *Definitions*

Clinical study data, also referred to as 'Standardised Study Data' mean individual patient data from clinical studies[4] in electronic structured format.

### *Background, expected benefits and objectives*

The EMA's Committee for Medicinal Products for Human use (CHMP) assesses initial marketing authorisation applications and post-authorisation applications on the basis of a comprehensive scientific evaluation of the quality, safety and efficacy of medicinal products. Currently the CHMP's clinical assessment is mainly based on data from clinical summaries and information reported in clinical study reports. This data is provided in a format that does not directly allow disaggregation or any other form of further analysis.

However, for certain regulatory procedures, regulators may benefit from having access to clinical study data during the assessment of the medicinal product. Access to clinical study data can assist regulators in understanding the submitted evidence and therefore inform the regulatory decisions on the benefit-risk balance of the product.

The EMA performed a retrospective review of previous assessment experiences with clinical study data, including the experiences of other international regulatory agencies for whom clinical study data analysis forms part of the assessment process. Based on this review, the following potential benefits of analysing and visualising data from clinical studies to support the regulatory assessment have been identified for selected key stakeholders:

[3] Formally referred to as proof-of-concept pilot on the submission and analysis of raw data
[4] Clinical studies include clinical trials as well as non-interventional studies in accordance with the definitions set out in Article 2 of Regulation (EU) No 536/2014.

- EU patients: Faster access to innovative, safe and effective medicines; Improved confidence in regulatory decision-making; Refined product labelling/targeting of subgroups within the recommended indications; Facilitation of cross-product analyses.
- Network/EU health agencies: Improved understanding of clinical study results to inform regulatory decision making; Reduced need to put questions of data interpretation to the applicant; Facilitation of cross-product analyses; Optimised use of inspections.
- Applicants/Marketing authorisation holders (MAHs): Workload reduction due to fewer complex questions; Shorter clock-stops; Earlier authorisation.

The PoC clinical study data pilot will investigate a subset of the potential benefits listed above in line with the defined scope. For example, cross-product analyses are not in scope of the pilot.

***Objectives***

The joint Big Data Task Force of EMA and the Heads of Medicines Agencies (HMA) proposed ten priority recommendations for the European Medicines Regulatory Network (EMRN) to realise the potential of Big Data. One of the priority actions recommends building EU Network capability to analyse Big Data via building computing capacity to receive, store, manage and analyse large data sets including patient level data (see HMA-EMA Joint Big Data Steering group Workplan 2023-2025 and the Committee for Medicinal Products for Human Use (CHMP) work plan 2025). The joint Big Data Task Force recommended conducting a PoC pilot to investigate the benefits of visualising and analysing clinical study data to support the scientific assessment of medicinal products and to identify the associated operational, resource and technological needs.

Learnings from the PoC pilot will be assessed by documenting practical learnings, e.g. on operational, resource and technological needs, and collecting feedback from all stakeholders involved, e.g. on the added value to the assessment process and operational aspects. This will include feedback from the Rapporteurs' assessment team, the Agency, and the applicant or MAH of the regulatory procedures concerned by the PoC pilot phase.

***Legal basis***

Clinical study data in electronic structured format is currently not systematically included as part of marketing authorisation and post-authorisation applications submitted to EMA. However, the Regulations which govern the work carried out by EMA allow for request of clinical study data during the assessment process.

In accordance with Article 7(c) of Regulation (EC) No 726/2004, the CHMP may request that the applicant supplements the particulars accompanying the application (e.g. clinical study data) within a specific time period in order to further qualify, as appropriate, the quality, safety and efficacy of a medicinal product. Article 16.3 of Regulation (EC) 1234/2008 provides a similar possibility for Type II variations applications. Under the terms of these Regulations, the applicant/MAH must answer such requests fully and promptly.

For the PoC pilot, applicants/MAHs with a centralised marketing authorisation/ post-authorisation application submitted to EMA that falls within the scope of the pilot will be invited to participate in the

pilot on a voluntary basis. The applicant/MAH will be asked to confirm their participation in the PoC pilot via a 'pilot participation letter'.

In processing the clinical study data, the Agency and National Competent Authorities (NCAs) in Union Member States will ensure personal data are protected in full compliance with the provisions of the Union Data Protection Regulation (EUDPR)[5] and the General Data Protection Regulation (GDPR)[6]. A Data Protection Impact Assessment for the clinical study data PoC pilot has been performed in 2022. The corresponding Data Protection Notice (link) and the Records of Processing Activity (link) are available on EMA's website.

***Timelines and scope***

The PoC pilot has been launched in September 2022, i.e. the date when clinical study data may be submitted for the first regulatory procedure included in the PoC pilot. The PoC pilot has initially been designed with an inclusion target of approximately ten procedures and an estimated duration of two to three years. Building on the insights the pilot has generated so far and captured in the pilot's interim report (link), the pilot is now extended until further notice. This will allow for inclusion of additional procedures, beyond the initially targeted number of ten applications. The extension aims to generate further learnings on the use of clinical study data in support of regulatory assessment, with a focus on addressing remaining knowledge gaps and further validation of the already identified benefits of clinical study data into regulatory decision-making.

Regulatory procedures meeting the following criteria will be eligible for the pilot:

- Type of regulatory procedures: Initial Marketing Authorisation Applications (iMAAs) and post-authorisation applications (e.g. variations or extension applications) submitted centrally to EMA are in scope for the upcoming PoC pilot with a primary focus on iMAAs. For variations, Type II variations with proposed change(s) to therapeutic indication(s) will be targeted.
- Type of data: Regulatory procedures that include data from clinical studies. The focus will be on analyses of clinical data to inform the benefit-risk assessment (clinical efficacy and modelling and simulation, including e.g. population pharmacokinetic/dynamic modelling, physiological based pharmacokinetic modelling). The pilot will also include analyses to inform the selection of sites for inspection of compliance with Good Clinical Practice.
- Clinical context: No restrictions are defined in relation to the disease area, the therapeutic indication, or the type and number of clinical studies presented in the application. However, the pilot intends to include a variety of regulatory procedures.

It is intended to select regulatory procedures at an early stage, preferably after the submission of the letter of intent and before submission of the application. The decision on whether a procedure may be included in the PoC pilot will be made by the CHMP Rapporteurs appointed to assess the specific marketing authorisation/variation application.

[5] Regulation (EU) 2018/1725 of the European Parliament and the Council of 23 October 2018 on the protection of natural persons with regard to the processing of personal data by the Union institutions, bodies, offices and agencies and on the free movement of such data, and repealing Regulation (EC) No 45/2001 and Decision No 1247/2002/EC.
[6] Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation).

Inclusion of a regulatory procedure in the PoC pilot will not delay the adoption of the scientific opinion by the CHMP. The Agency shall ensure that the opinion is adopted within the legal timeframes as laid out in Article 6 of Regulation (EC) No 726/2004 for iMAAs or in the Commission Regulation (EU) No 712/2012 for variations.

*Terms of participation*

For regulatory procedures which are selected for the PoC pilot the following considerations and requirements apply:

- Data standards: Data from clinical trials should comply with Clinical Data Interchange Standards Consortium (CDISC) Analysis Data Model (ADaM) and Study Data Tabulation Model (SDTM) study data standards. Furthermore, the Define-XML and optionally also the Analysis Results Metadata (ARM for Define-XML) should be submitted. Where a similar submission is planned/submitted to the FDA or PMDA, the same data standards may be followed. There are no specific requirements for non-interventional study data.
- Type of analyses: The decision about whether and which analyses should be performed to support the benefit-risk assessment (clinical efficacy and modelling and simulation, including e.g. population pharmacokinetic/dynamic modelling, physiological based pharmacokinetic modelling), will be taken by the CHMP Rapporteurs. Clinical study data analysis will be performed by either the CHMP Rapporteur teams at the NCAs of Member States, EMA staff or EMA contractors operating to the same standards of data security as EMA staff.
- Communication of results: Analysis results that are considered of relevance to the benefit-risk assessment, will be included in the assessment report and thus shared with the applicant together with the relevant information about the underlying analysis. Furthermore, applicants/MAHs might be asked to replicate the analysis results via the list of questions, list of outstanding issues or requests for supplementary information.

A Questions and Answers document for applicants/MAHs on the PoC pilot provides more details on the terms of participation (link).

***Ways for applicants or MAHs to become involved***

Applicants/MAHs can contact EMA via rawdatapilot@ema.europa.eu to express interest in participating in the PoC pilot or to ask further questions. Since the PoC pilot will include regulatory procedures providing the CHMP Rapporteurs' agreement, not all applicants/MAHs who express interest might be able to participate. If a specific procedure is deemed suitable for the PoC pilot by the CHMP Rapporteurs, applicants/MAHs may also be contacted directly by the EMA and asked whether the applicant/MAH would be willing to participate.

At the end of the PoC pilot the Agency will organise a workshop with external stakeholders to present and discuss the final learnings from the PoC pilot. A summary of the final outcomes of the PoC pilot will also be published respecting commercially confidential information.