EMA/HMA catalogue of non-interventional studies (EU PAS Register) - new functionality

Industry Stakeholder Platform – Operation of EU Pharmacovigilance

22 November 2023

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The EU PAS Register

The EU PAS Register®, European Union Electronic Register of Post-Authorisation Studies, is a publicly available register of **non-interventional post-authorisation studies (PAS).**

The Register has a focus on observational research, and its purpose is to:

- Increase **transparency**
- Reduce **publication bias**
- Promote the **exchange of information** and **facilitate collaboration among stakeholders**, including academia, sponsors and regulatory bodies
- Ensure compliance with **EU pharmacovigilance legislation requirements**

The Scope of the EU PAS Register

THE SCOPE

EU pharmacovigilance legislation requires (EMA) to **make public the protocols and abstracts of results of non-interventional post-authorisation safety studies (PASS)** imposed as an obligation of marketing authorisation by a competent authority in accordance with **Article 10 or 10a of Regulation (EC) No 726/2004** or with Articles 21a or 22a of Directive 2001/83/EC.

Annex III of the Commission Implementing Regulation (EU) No 520/2012 further specifies that **the final report of imposed non-interventional PASS must provide the date of making it public (in EU PAS Register).**

PASS initiated, managed or financed voluntarily by a marketing authorisation holder and which are required in a Risk Management Plan (RMP) **should also be entered into the EU PAS Register to support the same level of transparency.**

Information on post-authorisation efficacy studies (PAES) that are outside the scope of the Clinical Trials Regulation **should also be entered in the EU PAS Register to support transparency on post-authorisation efficacy studies (PAES)**, whether they are initiated, managed or financed by a MAH voluntarily or pursuant to an obligation.

Background – need for change

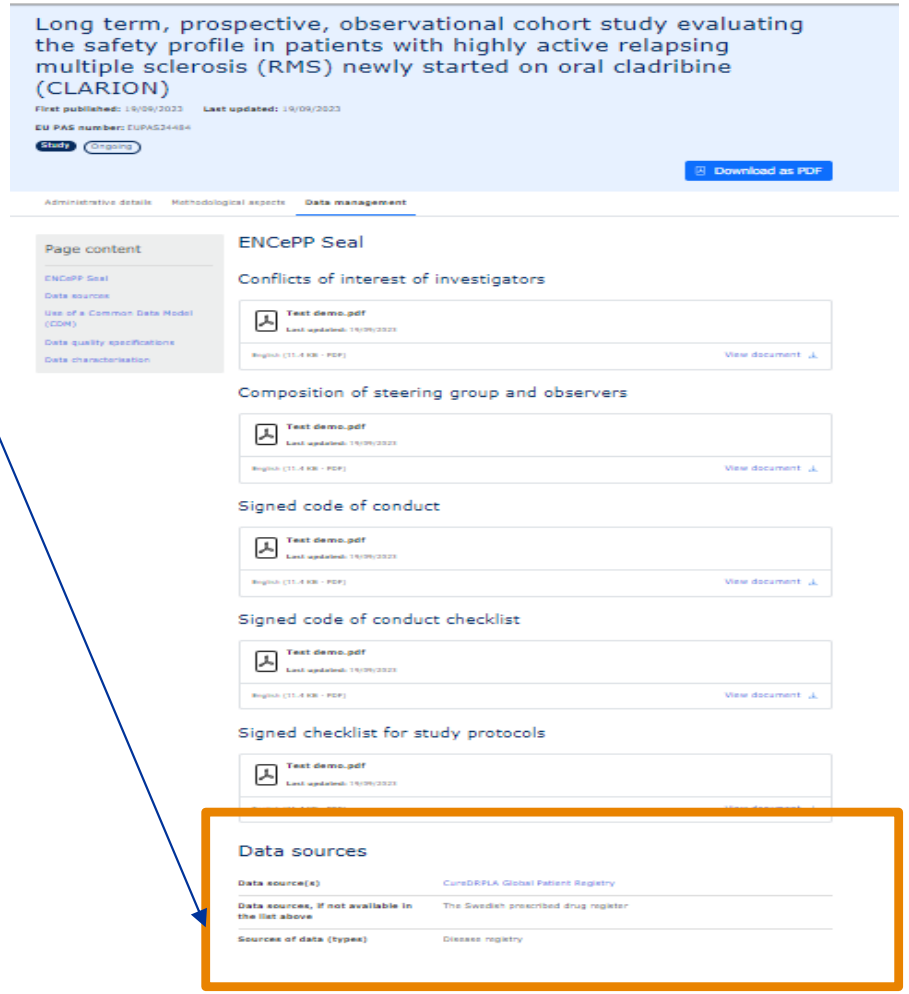
- ENCePP Resources Database and the EU PAS register® were initially set up in 2010 to promote exchange of information on observational research among stakeholders (including academia, sponsors and regulatory bodies)
- The current system was launched based on the relevant technical requirements identified at that time, however has limitations that do not allow to address current needs
- The new EU pharmacovigilance legislation that came into force in 2012 made it mandatory for MAHs to register PASS imposed as a legal obligation by regulators (RMP category 1 and category 2 studies) and for EMA to make public in a portal the protocol and an abstract of the study results of these studies
- Subsequently the EU Good pharmacovigilance practices Module VIII recommended to register all other PASS included in the RMP (RMP category 3 studies)
- Only a limited number of upgrades could be made since 2012

Key features – linked catalogues (1/5)

The **study catalogue and the data sources catalogue will be linked** with possibility to **view information about data sources used in the study and vice versa**

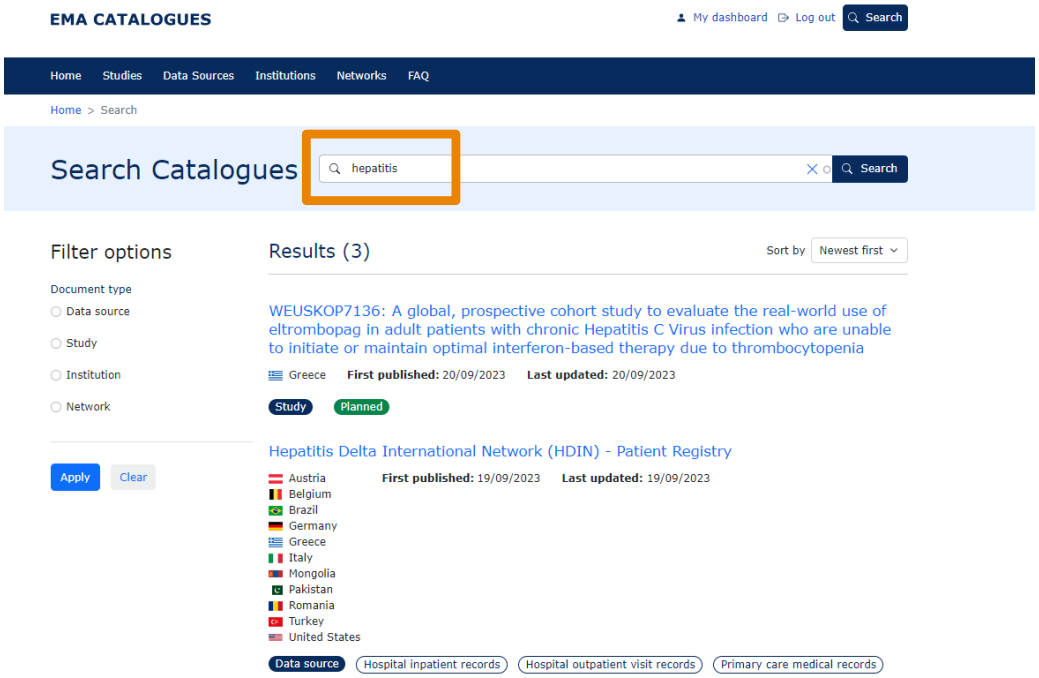
Support the **assessment of study protocols and study results** by providing quick access to information on the suitability of data source(s) proposed to be used in the study protocol or referred to in the study report

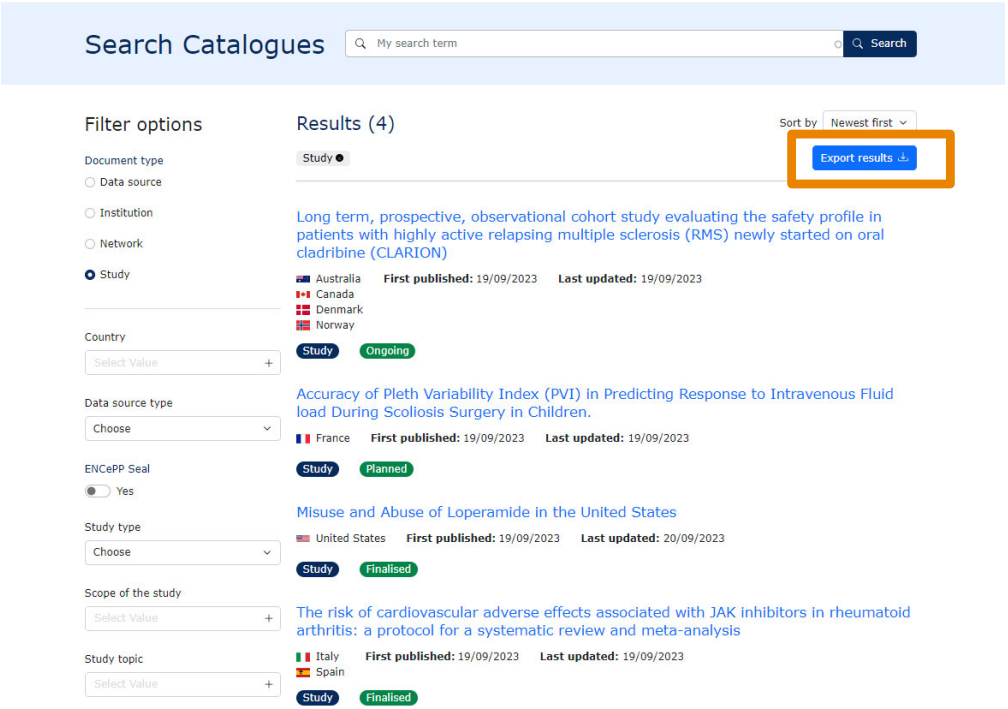
Draft **Good practice guide provides details and use cases on how the catalogue can be used** in this respect



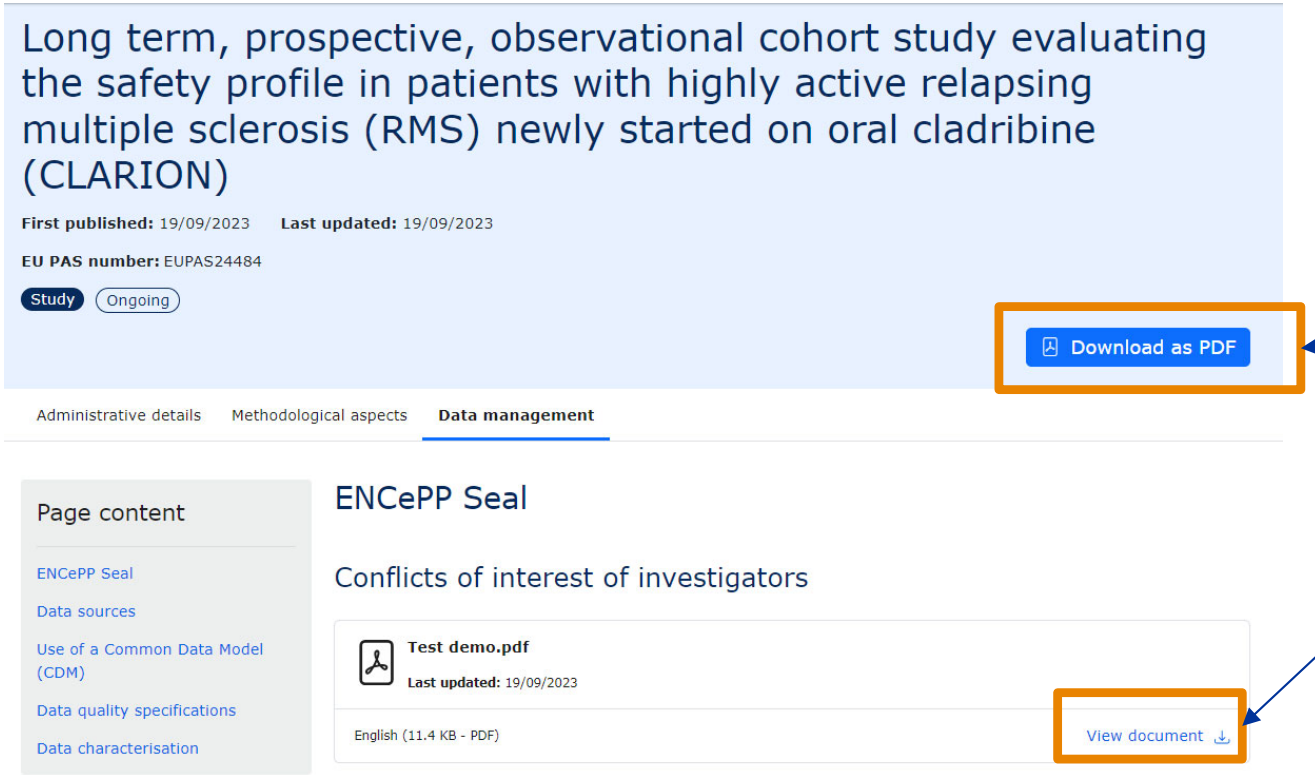
Key features – search (2/5)

- Possibility to **search** information: search for studies using various filters e.g. scope of study (e.g. safety, effectiveness), whether required by a regulator, RMP category, study status (planned, ongoing, finalized)
- Integrated search of studies and data sources
- Possibility to filter, sort and export search results in csv (including all fields of a study record)
- **Integration with EMA website content**: studies will be visible in the relevant **medicines overview page** in the EMA website (connection to summary of RMP, EPAR, PI) - this feature will be released after go-live in a second phase



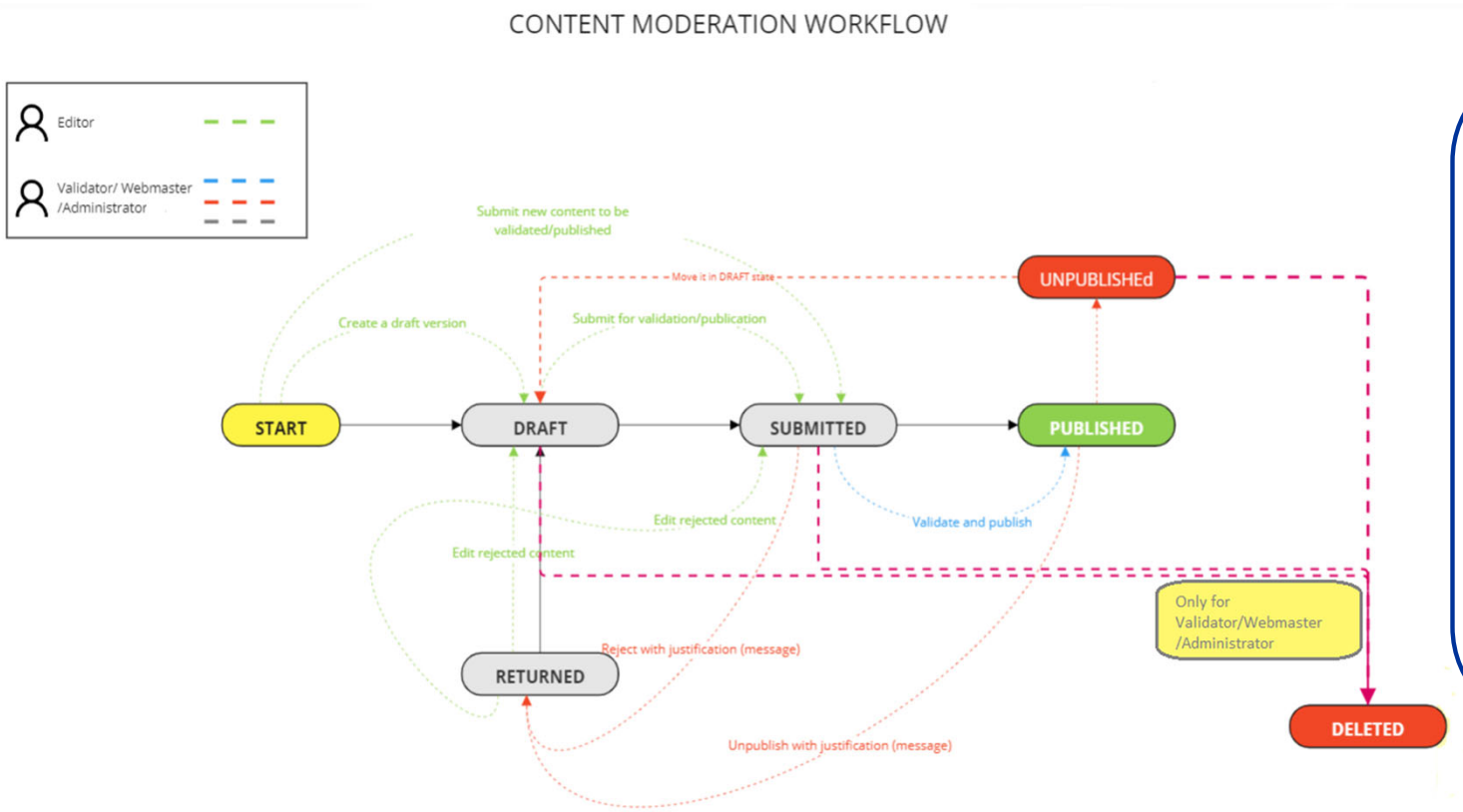


Key features – export (3/5)



Possibility to export information: **export of study records in PDF** form and **documents stored within a record e.g. study protocol**

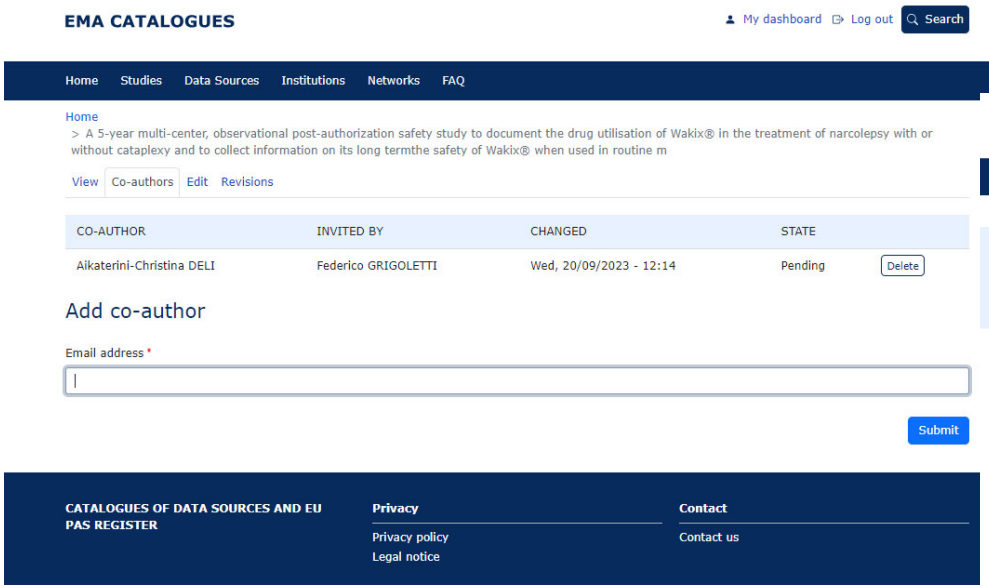
Key features – workflow (4/5)

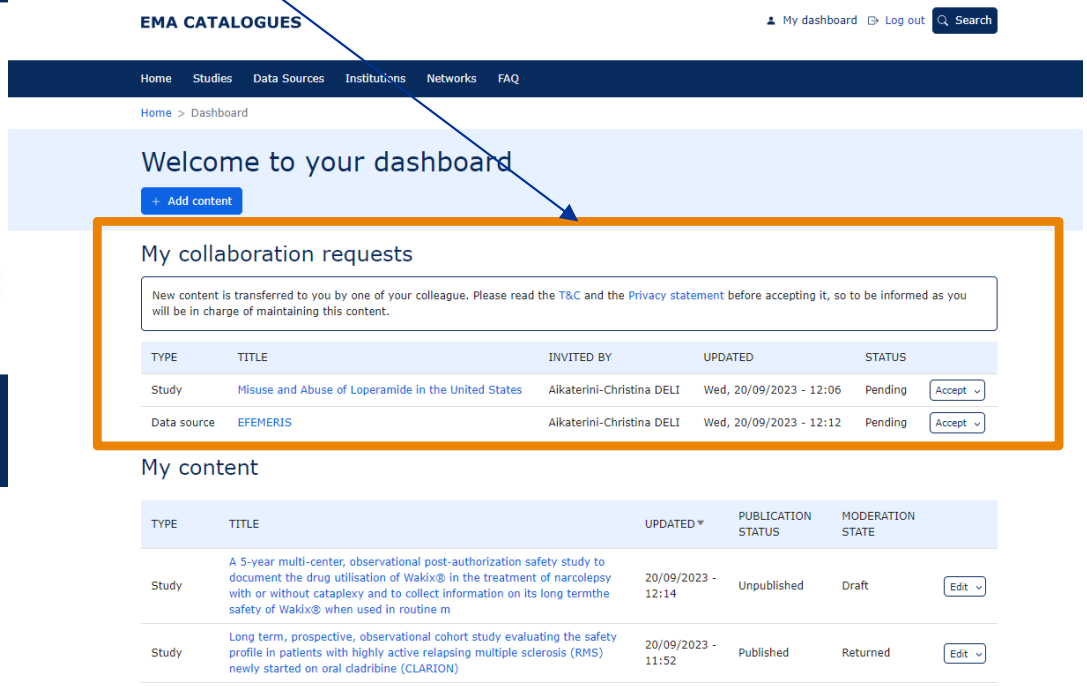


- User **registration and login:** EU login authentication service of the EC
- The approval/rejection of data will trigger **e-mail notifications to user submitting data** (i.e. the EMA administration functions)
- **Notifications will also prompt users** to update their records

Key features – collaboration (5/5)

Content owners will be able to **add collaborators**, who will be able to edit the records





Context – studies catalogue in the wider project scope

A **pilot study** (MINERVA) was conducted by a consortium including 16 organisations from 9 countries to propose an initial set of metadata elements to be collected

- The consortium conducted **interviews** and collected information from multiple key stakeholders (e.g.: FDA Sentinel, CNODES, EHDEN/OHDSI, AsPEN, Aetion, Fairplus) to build on an initial proposal of data elements to collect

A metadata **stakeholder workshop** was organised in April 2021 to further refine the proposal and collect further feedback

Two dedicated **surveys** were launched:

- (initial) open to ENCePP community
- (follow-up) Industry, ISPOR/ISPE, international regulators

Webinar involving TEHDAS, NCA representatives (via EUNDB, BDSG)

Finalised list published (EMA website)

A Partnership of the EU PE&PV Research Network, the SIGMA Consortium, and Collaborators

EUPAS 39322

Metadata list describing real world data

A list of metadata describing **real-world data sources** and **studies** is available below to help pharmaceutical companies and researchers to identify and use such data when investigating the use, safety and effectiveness of medicines.

List of metadata for Real World Data catalogues (PDF/299.03 KB)

First published: 10/06/2022
EMA/563896/2022

Real-world data are observational data stored in repositories such electronic health records and disease registries. Making use of these data sources can improve the evidence available to support **benefit-risk decisions** and facilitate getting better medicines to **patients**.

Study | Administrative Details

I. Study – Administrative details

1) *(EU PAS)* Study title and acronym: *<free text>* *(F1.2)*
2) *(EU PAS)* EU PAS register number: *<number>* (F2.2)
3) *(EU PAS)* Brief description of the study *<free text>* (F10)
4) *(EU PAS)* Study status <*select one:* planned | ongoing | finalised> (F11)
5) Institution conducting the study: *<free text|lookup of institutions>* *(F1.3)*

   Study institution contact name: *<free text>* *(F1.4)*
   Study institution contact email: *<free text>* *(F1.5)*
   Additional institutions: *<free text>* (F1.7)
   (EU PAS) Primary lead investigator name *<free text>* (F12)
   (EU PAS) Primary lead investigator contact email *<free text>* (F13)
   Primary lead investigator ORCID: *<number>* *(F1.6)*

6) *(EU PAS)* Study timelines: initial administrative steps, progress reports and final report

	Planned	Actual
Date when funding contract was signed	*<date>*(F19)	*<date>* (F19.1)
Start date of data collection	*<date>* (F20)	*<date>* (F20.1)
End date of data collection	*<date>* (F2.10)	*<date>* (F2.10.1)
Start date of data analysis	*<date>* (F21)	*<date>* (F21.1)
Date of interim report, if expected	*<date>* (F22)	*<date>* (F22.1)
Date of final study report	*<date>* (F23)	*<date>* (F23.1)

7) Network conducting the study (if applicable): *<free text|lookup of networks>* (F1.8)
8) *(EU PAS)* Country where the study is conducted *<select multiple:* ISO 3166-1 country codes>
9) Source of funding: *<select multiple*: EU institutional research programme | non-EU institutional research programme | EMA | national competent authority (NCAs) | other public funding (e.g.: hospital, university) | non for-profit organisation (e.g., charity) | pharmaceutical company and other private sector | no external funding| other> (F8.8)

   If 'other', further details on the scope of the study: *<free text>* (F8.8.1)

10) Protocol link: A link to the latest version of the protocol, if published *<weblink>* (F2.1)

    Protocol document *<uploaded document>* (F2.3)

11) *(EU PAS)* Study required by a regulator *<select one:* Yes | No | I don't know> (F14)
12) *(EU PAS)* Is the study required by a Risk Management Plan (RMP) *<select one*: Not applicable | EU RMP category 1 (imposed as condition of marketing authorisation | EU RMP category 2 (specific obligation of marketing authorisation | EU RMP category 3 (required) | Non-EU RMP only> (F14.1)
13) *(EU PAS)* Regulatory procedure number (RMP Category 1 and 2 studies only): *<free text>* (F14.2)
14) *(EU PAS)* Other study registration identification numbers and URLs as applicable: *<free text>*

Study | Data Management

VI. Study – Data management

43) *(EU PAS)* ENCePP seal *<Y/N> (F9)*

44) *(EU PAS)* ENCePP seal relevant documents:

- ☐ Conflicts of interest of investigators *<uploaded document> (F9.1)*
- ☐ Composition of steering group and observers *<uploaded document> (F9.2)*
- ☐ Signed code of conduct *<uploaded document> (F9.3)*
- ☐ Signed code of conduct checklist *<uploaded document> (F9.3.1)*
- ☐ Signed checklist for study protocols *<uploaded document> (F9.4)*

45) Number of data sources: *<number>* (F3.2)

46) Names of data sources: *<free text|lookup of data sources>* (F3.4)

47) Sources of data: <*select multiple*: clinical trial | non-interventional study | electronic healthcare records (EHR) | administrative data (e.g. claims) | drug utilisation data | drug dispensing/prescription data | disease registry | drug registry | population registry | pregnancy registry | spontaneous reporting system | laboratory data | -omics | social media | patient surveys | data from digital health wearables | expanded access program / compassionate use | published literature | other> (F8.7)

If 'other', further details on the sources of data: *<free text>* (F8.7.1)

48) CDM mapping: Were data sources in the study ETL-ed to a CDM? *<y/n>* (F4.1)

CDM name: *<free text>* (F4.2)

CDM mapping version: *<free text>* (F4.3)

49) The following data quality specifications apply for the study (tick as applicable):

- ☐ Data characterisation conducted (F5.1)

  If 'yes', Data characterisation moment: At what stages of the study were data characterisation steps or quality checks implemented? *< select multiple*: *after data extraction| after extract-transform-load to a common data model| after creation of study variables>* (F5.2)

  If 'yes', Data characterisation details: Provide a summary description of the data characterisation or quality check process *<free text| weblink>* (F5.7)

  If 'yes', Data characterisation results: Provide results of the data characterisation or quality checks, such as Sentinel Common Data Model level 1-4 checks. *<uploaded document| weblink>* (F5.8)
- ☐ Check conformance: Was a check of the conformance of data (i.e., data are in the correct format/syntax) completed? (F5.3)
- ☐ Check completeness (F5.4)
- ☐ Check stability: Was a check of the stability of data (e.g., codes) over time completed? (F5.5)
- ☐ Check logical consistency (F5.6)

50) Procedure of data extraction: Upload or provide a link (e.g., GitHub) to the procedures, such as codes or scripts, used to extract data from the data source instance used in the study *<uploaded document| weblink>* (F6.1)

51) Procedure of result generation: Upload or provide a link (e.g., Github) to the procedures, such as study scripts, used to generate the study results *<uploaded document| weblink>* (F6.2)

Study | Methodological Aspects

II. Study – methodological aspects

15) The study is concerning: <*select multiple*: human medicinal product | veterinary medicinal product | herbal medicinal product | medical device | disease/health condition | medical procedure | other> (F8.1)

If 'other', further details on the study topic: <*free text*> (F8.1.1)

16) Study type: <*select one:* clinical trial | non-interventional study | not applicable> (F8.2)

If 'Not applicable', further details on the study type: <*free text*> (F8.2.1)

If Study type = clinical trial

17) Clinical trial regulatory scope: <*select one:* pre-authorisation clinical trial | post-authorisation interventional clinical trial | post-authorization low-interventional clinical trial | clinical trial not subject to marketing authorization> (F8.2.2)

18) Phase of the clinical trial (where applicable): <*select one:* phase 1 | phase 2 | phase 3 | phase 4> (F8.4)

19) Clinical trial study design:

- Clinical trial randomisation: <*select one*: randomised clinical trial |non-randomised clinical trial> (F8.3)
- Clinical trial types : <*select multiple*: low-interventional clinical trial | single-arm trial | large simple trial | pragmatic clinical trial | cluster randomised trial > (F8.3.1)

If Study type = non-interventional study

20) Non-interventional study design: <*select one*: cohort| case-control| case-only| cross-sectional| ecological| cluster design| systematic review and meta-analysis| other> (F8.3.2)

If 'other' design of non-interventional study, further details: <*free text*> (F8.3.2.1)

21) Data collection methods: <*select one:* primary data collection| secondary data collection| combined primary and secondary data collection| no individual level data collected for the purpose of the study> (F8.5)

22) Scope of the study: <*select multiple*: effectiveness study (incl. comparative)| safety study (incl. comparative) | assessment of risk minimisation measure implementation or effectiveness | drug utilisation | healthcare resource utilization | disease epidemiology | patient reported outcomes | feasibility analysis | validation of study variables (exposure, outcome, covariate) | hypothesis generation (including signal detection) | method development or testing | scoping review (including literature review) | other > (F8.6)

If 'other', further details on the scope of the study: <*free text*> (F8.6.1)

23) *(EU PAS)* Study drug information - ATC <*ATC code*> (F15)

24) *(EU PAS)* Study drug information - INN <*INN list*> (F16)

25) *(EU PAS)* Study drug information - brand name <*free text*> (F17)

26) *(EU PAS)* Medical condition to be studied <*MedDRA list*> (F18)

27) *(EU PAS)* Additional medical condition(s) <*free text*> (F18.1)

28) *(EU PAS)* Population studied: A short description of the study population <*free text*> (F2.5)

29) *(EU PAS)* Population studied: Age groups: <*select multiple:* newborn infants (0 to 27 days) | infants and toddlers (28 days to 23 months) | children (2 to 11 years) | adolescents (12 to 17

30) *(EU PAS)* Special population of interest: <*select multiple*: immunocompromised | renal impaired | hepatic impaired | women of child-bearing age| pregnant women| lactating women| other > (F8.9)

If 'other', further details on the population of interest: <*free text*> (F8.9.1)

31) *(EU PAS)* Population: estimated number of subjects <*number*> (F2.5.2)

32) Setting: A short description of the study setting <*free text*> (F2.11)

33) Main study objective: A short description of the study objective <*free text*> (F8.10)

34) Interventions: A short description of the study interventions <*free text*> (F2.6)

35) Comparators: A short description of the study comparators <*free text*> (F2.7)

36) Outcomes: A short description of the study outcomes <*free text*> (F2.8)

37) Study design: A brief summary of the study design <*free text*> (F2.13)

38) Data analysis plan: A brief summary of the analysis method (e.g. risk estimation, measures of risk, internal/external validity) <*free text*> (F2.12)

39) Summary of results: A brief summary of the results of the study completion (from abstract) <*free text*> (F6.3)

Results tables <*uploaded document*> (F6.4)

40) Study publications: Peer-reviewed papers reporting the study <*AMA citation format*> (F7.1)

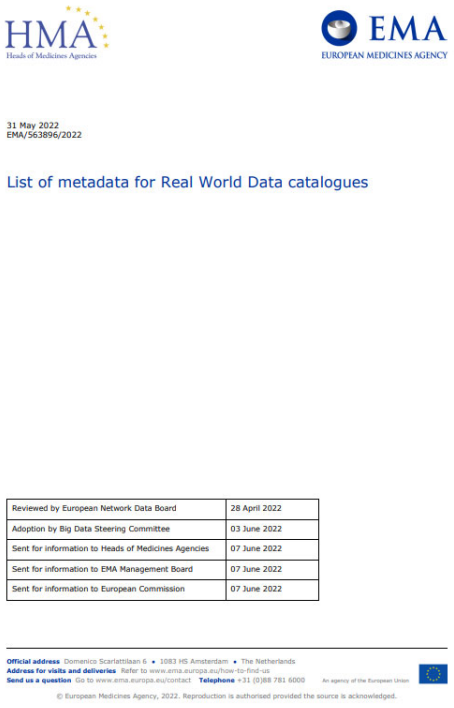
41) Study report: < *uploaded document|weblink*> (F7.2)

42) Study, other information: A list of URLs to other relevant resources describing the study <*weblink*> (F7.3)

Context – studies catalogue in the wider project scope

Type of data collected (additional to studies data)

Data Sources	Metadata containing the details of the data source (e.g. data source countries, data elements collected, etc.)
Studies	Metadata describing studies conducted using data sources described in the catalogue EU PAS Register
Institutions	Metadata describing any contributor to the catalogue, their role and expertise (institution country, etc.)
Networks	Metadata describing networks/consortia linking to institutions and studies in the catalogue (network name, website, etc.)



HMA Heads of Medicines Agencies

EMA EUROPEAN MEDICINES AGENCY

31 May 2022
EMA/563896/2022

List of metadata for Real World Data catalogues

Reviewed by European Network Data Board	28 April 2022
Adoption by Big Data Steering Committee	03 June 2022
Sent for information to Heads of Medicines Agencies	07 June 2022
Sent for information to EMA Management Board	07 June 2022
Sent for information to European Commission	07 June 2022

Summary – Upcoming Changes

The EU PAS will move from the current ENCePP website to EMA website

- The current ENCePP website will also be re-built
- Re-direct of weblinks will happen automatically
- Information on PASS studies to be integrated with other published product documentation

The information collected on studies is re-organised, expanded and linked with the information on data source
The current login will change to a two-factor authentication (this is for user submitting or managing data)

Existing studies data will be migrated to the new website

A downtime of 2-3 weeks will be needed for the switch between system

- Communication with exact dates will follow – likely early 2024

An EMA validation will occur in the backend before publication

All validated study information remains freely available to any website visitor