HMA
Heads of Medicines Agencies

EMA
EUROPEAN MEDICINES AGENCY

Real-world evidence framework to support EU regulatory decision-making

4th report on the experience gained with regulator-led studies from February 2025 to February 2026

An agency of the European Union

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Executive Summary

This fourth annual report outlines the progress in integrating real-world evidence (RWE) into regulatory decision-making, aligned with the European Medicines Regulatory Network (EMRN) strategy to 2028 and in anticipation of the provisions from the new pharmaceutical legislation. It comprises two RWE generation pathways coordinated by the European Medicines Agency (EMA): DARWIN EU®, and studies commissioned via framework contracts.

Covering the period from 8 February 2025 to 7 February 2026, 108 research topics were assessed, with 48 new topics identified. The vast majority (88%) were addressed through DARWIN EU®, highlighting the increased capability and capacity of this pathway. Feasibility assessments showed a high success rate, with 77% of assessed topics deemed feasible, resulting in 43 completed and 45 ongoing studies by February 2026 – a 49% increase compared with the previous year.

Research focused primarily on drug utilisation, disease epidemiology, medicines safety and studies addressing the design and feasibility of planned studies, a category which increased considerably in the period.

Nervous system disorders, oncology, immunology, anti-infectives, and cardiovascular diseases remained the most frequently addressed therapeutic areas.

Research topics were identified across a diverse range of regulatory and public health decision-makers: EMA scientific committees and working parties, EMA internal functions, European Centre for Disease Prevention and Control (ECDC), HTA bodies/payers and the European Commission (EC).

DARWIN EU® demonstrated both maturity and increased capacity. The number of complex studies nearly doubled, two very complex studies were initiated for the first time (in pregnancy and oncology), and the median number of data partners per study increased from three to six. Studies conducted by consortia under the EMA framework contracts, most of them complex, continue to add value, particularly for very complex topics, special populations and rare diseases.

The median study duration of 4.8 months remained compatible with most regulatory timelines, enabling timely integration of RWE into regulatory processes. Such rapid results are a key benefit from the regulator-led approach being advanced by the EMRN.

Operationally, significant progress was made in expanding and consolidating the network. DARWIN EU® grew to 40 data partners across 18 European countries, covering over 250 million European patients. Improvements were implemented in feasibility assessment, data quality, analytical pipelines, reporting, transparency, and governance.

During the period, a survey to investigate the value of the evidence generated was conducted among study requesters and 30% of respondents reported direct use of RWE in formal regulatory decisions, while others highlighted its value for preparedness, methodological learning, and future decision-making.

Overall, the report confirms that regulator-led RWE generation through DARWIN EU® is increasingly impactful, scalable, and strategically aligned with EU regulatory priorities, while continued efforts are needed to enhance data harmonisation, quality, and interpretability to maximise its potential.

List of abbreviations

Acronyms/term	Description
ADHD	Attention-deficit hyperactivity disorder
ATC	Anatomical Therapeutic Chemical classification
AWaRe	Access, Watch, Reserve
CAT	Committee for Advanced Therapies
CDM	Common data model
CHMP	Committee for Medicinal Products for Human Use
CMDh	Coordination Group for Mutual Recognition and Decentralised Procedures - Human
COMP	Committee for Orphan Medicinal Products
DARWIN EU	Data Analysis and Real-World Interrogation Network EU
ECDC	European Centre for Disease Prevention and Control
EHDS	European Health Data Space
EMA	European Medicines Agency
EMRN	European Medicines Regulatory Network
FWC	Framework contract
HMPC	Committee on Herbal Medicinal Products
HTA	Health technology assessment
MAA	Marketing authorisation application
MSSG	Medicines Shortages Steering Group
NSCLC	Non-small cell lung cancer
OD	Orphan Designation
OMOP	Observational Medical Outcomes Partnership
OTS	Off-the-shelf
PAH	Pulmonary Arterial Hypertension
PDCO	Paediatric Committee
PIP	Paediatric Investigation Plan
PRAC	Pharmacovigilance Risk Assessment Committee
PSUSA	Periodic safety update single assessment
RWD	Real-world data
RWE	Real-world evidence
SAWP	Scientific Advice Working Party
SPOC	Medicine Shortages Single Point of Contact Working Party
US	United States of America
VMP	Vaccine Monitoring Platform
WHO	World Health Organisation

Highlights

Demand for EMA-led RWE remains strong but more focused

- **108 research topics** assessed and **88 studies** completed or ongoing (an increase of 49% versus previous reporting period). These were conducted via the two RWE generation pathways available: DARWIN EU® and the framework contracts for scientific studies
- A shift toward **feasibility-driven, higher-value questions** has led to fewer new topics being initiated
- **Close to 80% feasibility rate**, indicating better alignment between regulatory questions and available data

DARWIN EU is maturing rapidly in scale, scope, and research question complexity

- The network has grown to reach **40 data partners across 18 European countries**, covering **over 250 million patients**, with additional inclusion of US data
- **More complex analyses are being executed**, with:
    - Nearly **doubling of the number of complex studies** compared to last period.
    - Launch of the **first two "very complex" studies** (in pregnancy/mother-child and oncology)
    - **Median number of data partners participating per study doubled** (from 3 to 6)

The value of RWE extends beyond "yes/no" decisions — it builds regulatory knowledge, preparedness, and confidence

- **30% of studies directly supported a formal regulatory decision** in an active procedure
- In addition, **44% improved clinical or methodological understanding** and **15% supported preparedness** (shortages, public health, antimicrobial resistance, future procedures)
- Timing constraints and data granularity remain the main barriers to even higher procedural impact

Operational efficiency has improved and speed is maintained

- Median DARWIN EU study duration: **~5 months**, compatible with many (but not all) regulatory timelines
- **Blanket/umbrella protocol approvals** at 8 data partners significantly reduce study duration
- Further speed improvements are anticipated to be limited; focus is now on an ever greater, quality of outputs, including clarity of reports, and improved **data quality** with increased breadth of mapping and harmonisation

1. Introduction

Well-informed decisions on medicines - spanning development, authorisation, reimbursement, use, and monitoring - depend on excellence in clinical evidence (Clinical Evidence 2030). Europe's shifting policy environment, marked by the EHDS and pharmaceutical legislation reform, is opening new opportunities for excellence in evidence generation through greater access to healthcare data, more innovative study designs, advanced analytics, and more patient-centred approaches to medicines development. Notably, the pharmaceutical legislation reform supports the use of real-world evidence (RWE) to complement clinical trial data in regulatory decision-making[1]. It also emphasises that the Agency should be able to use such data, through current frameworks that are in place, including the Data Analysis and Real-World Interrogation Network (DARWIN EU) and the European Health Data Space interoperable infrastructure. These provisions in the new Pharma Regulation result from inter-institutional negotiations and are still pending formal adoption later this year.

Covering the period from 8 February 2025 to 7 February 2026, this report on the experience gained in RWE generation marks the fourth year of DARWIN EU and the second operational year following its establishment phase in 2022-2024 (see the Report on regulatory-led studies using real-world data section). As with previous reports, the focus is on RWE generation via mostly two pathways established by the European Medicines Agency (EMA): DARWIN EU® and studies commissioned via the framework contracts for scientific studies. The report also covers the value of EMA-generated RWE for regulatory decisions, progress made on operational aspects since the last report, as well as methodological advice provided on the use of real-world data (RWD) within regulatory submissions. Research topics originated from evidence gaps identified during scientific assessment of EMA committees and divisions or EMA's collaborative work with other EU network stakeholders (e.g., Health Technology Assessment (HTA) bodies, European Centre for Disease Prevention and Control (ECDC)). The report does not cover RWE generated at the national competent authority level or by other EU agencies without EMA involvement or those submitted by industry.

This report highlights how EMA-led RWE generation aligns with the focus areas of the European Medicines Regulatory Network (EMRN) strategy to 2028, by focusing on generating strong scientific evidence, which is incorporated into decision making processes or can inform, for instance, strategies for prevention of medicine shortages or antimicrobial resistance.

[1] Recital (60) and Article 169 of the Regulation laying down Union procedures for the authorisation and supervision of medicinal products for human use and establishing Rules governing the European Medicines Agency, as agreed in interinstitutional negotiations on 11 December 2025

2. Real-world evidence generated for the European Medicines Regulatory Network and other stakeholders

2.1. Research topics assessed

A total of 108 research topics were assessed, out of which 48 (44%) were identified in the reporting period from 8 February 2025 to 7 February 2026, (i.e., 'new research' topics), and 60 (56%) were identified before 8 February 2025 and carried over (i.e., 'carried over' topics). The vast majority of the research topics (88%, 92) were addressed via the DARWIN EU pathway, while 15 were addressed via EMA's framework contract for scientific studies ('Quality, safety and efficacy studies of medicines') and only one was conducted in-house, a pathway which is being phased out.(Figure 1)

There were 43 studies completed (41 via DARWIN EU and two via framework contract) and 45 ongoing studies (32 via DARWIN EU and 13 via FWC) by 7 February 2026. In addition, some research topics assessed were not initiated (6) at requester recommendation, despite being feasible.

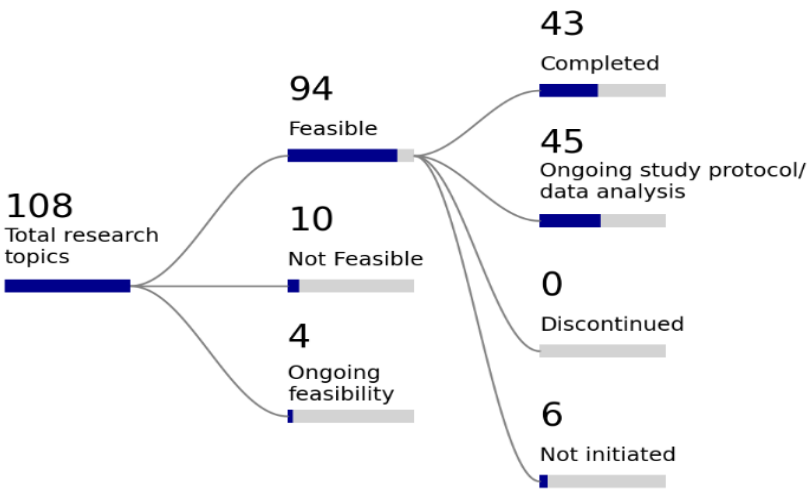


Figure 1. Research topics identified or addressed during the reporting period

This flowchart includes research topics identified during the reporting period (8 February 2025 to 7 February 2026) or addressed during the reporting period but identified before 8 February 2025. 'Not initiated' are studies that were feasible, however after additional discussions with the requester were not considered needed at the moment.

Considering only the new research topics assessed during the reporting period (N=48), which were all handled via DARWIN pathway, 41 were feasible, leading to a feasibility percentage similar to that reported in 2025 (77% vs 76%, respectively).

Most of the new research topics requested during the reporting period were requested by PRAC (N=12, 25%) and EMA internal teams (N=11, 23%), followed by CHMP (N=6, 12%) and SAWP (N=4, 8%) (Figure 2). No new requests were received during the reporting period from PDCO, ECDC and CAT.

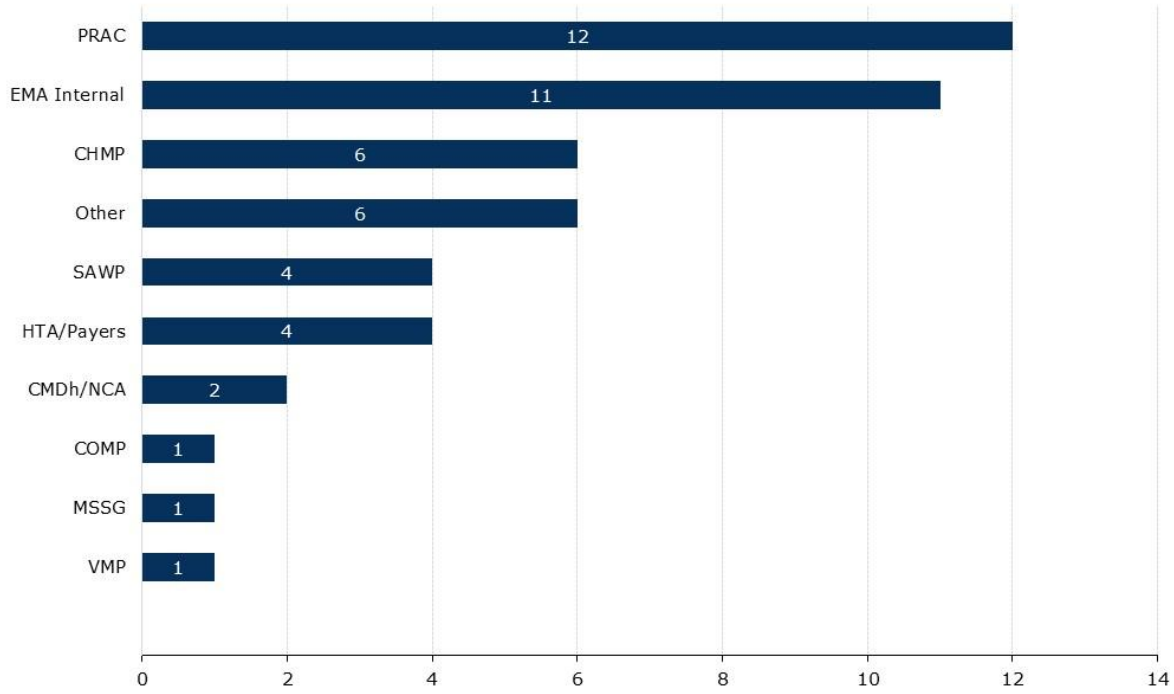


Figure 2. New research topics by requester (n=48)

All assessed research topics (108) focused on 12 therapeutic areas. The most common were nervous system treatments (23, 21%), antineoplastic and immunomodulating agents (16, 15%), anti-infectives (14, 13%) and cardiovascular system (14, 13%) (Figure 3). As in the previous report they remain the most frequent therapeutic areas for which RWE generation is requested. However, research on the anti-infectives declined from position 1 to 4, while studies on the nervous system increased from position 3 to 1.

Referring to the most recent research topics requested in the period (N=48), these were, in decreasing order of frequency: nervous system, cardiovascular system and antineoplastic and immunomodulating agents.

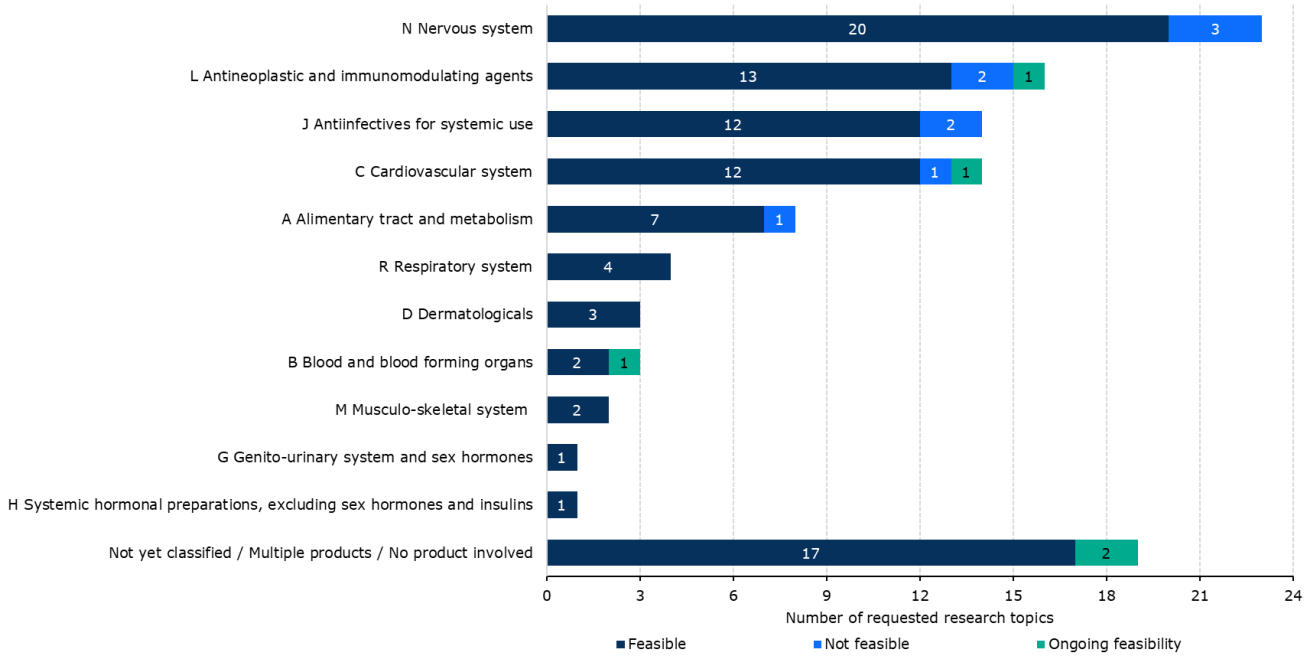


Figure 3. Feasibility of research topics by Anatomical Therapeutic Chemical (ATC) classification (n=108)

The ATC main group was assigned to each research topic based on the medicinal product under evaluation which triggered the research topic, or the substance studied in the study if there is no procedure applicable. 'Not yet classified/Multiple products/No product involved' category includes research topics for which the medicine has not yet been classified in the ATC system, the research topics which comprises several medicinal products or research topics which do not include medicinal products (e.g., disease epidemiology studies).

Regarding regulatory procedures that triggered studies, which was the case for 17 of the new research topics, 6 were related to safety signal evaluation followed by procedures to inform upcoming MAAs and PSUSA (5 each) (**Figure 4**).

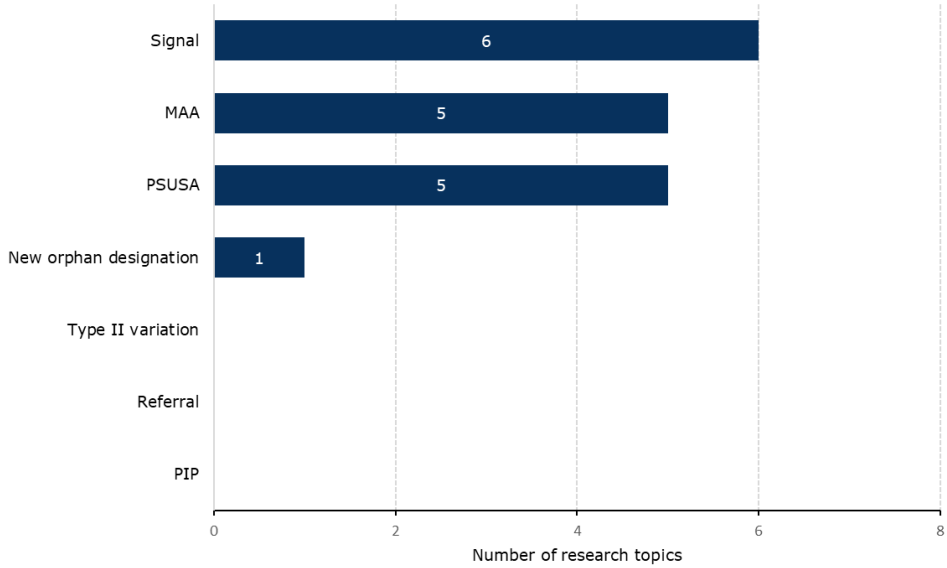


Figure 4. New research topics identified during the reporting period, by type of regulatory procedure
MAA = Marketing authorisation application; PSUSA= Periodic safety update single assessment

2.2. Completed and ongoing studies

A total of 88 studies were conducted during the reporting period (43 completed and 45 ongoing), representing a 49% increase from the previous reporting period.

Of the 88 studies (addressing a total of 101 use case types), most aimed at generating evidence in relation to drug utilisation (N=34, 34%), followed by disease epidemiology (N=18, 18%), design and feasibility of planned studies (N=17, 17%) and medicines safety (N=16, 16%) (Figure 6). In comparison to the previous reporting period, the proportion of studies addressing the design and feasibility of planned studies increased considerably (from 4% to 17%).

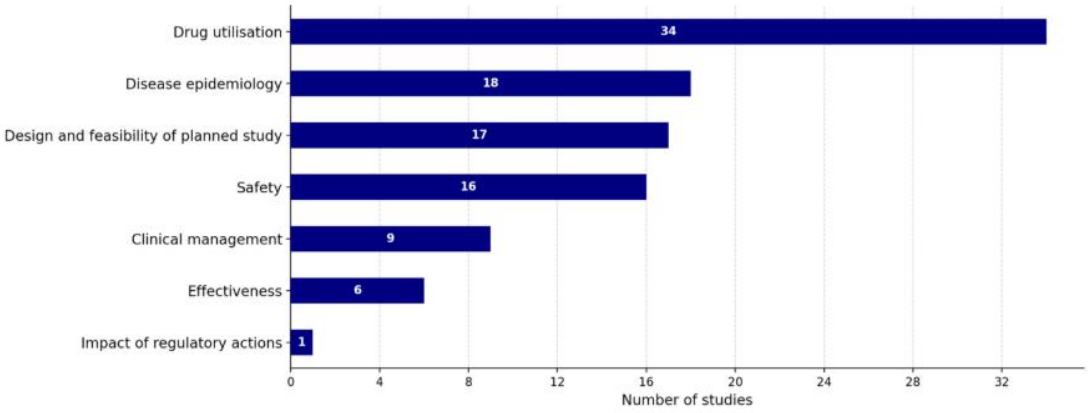


Figure 5. Number of conducted studies by use case type during the reporting period

Depending on the scope, a research topic may be assigned to one or more categories (e.g., a study aiming to describe incidence of a disease and prevalence of related prescribed treatments could represent both categories: disease epidemiology and drug utilisation). Therefore, the values presented in the bars sum up more than 88.

The median study duration within DARWIN EU was 4.8 months (IQR: 4–6 months) from protocol approval to study results. An off-the-shelf (OTS) study had a median duration of 4.6 months while a complex study a median of 5.5 months. The current operational pace allows DARWIN EU to be effectively incorporated into the timelines of most regulatory procedures, although exceptions remain. While efforts to enhance efficiency are ongoing, substantial additional gains in speed, while maintaining quality of studies and its deliverables, are becoming increasingly challenging to achieve.

Regarding studies conducted via DARWIN EU, the number of complex studies almost doubled in the period (from 18 to 35), including for the first time the conduct of two very complex studies (as per DARWIN EU classification), initiated in pregnancy and oncology areas. The median number of data partners used per study also doubled from three in the previous reporting period to six during this reporting period. These indicators reflect the increased maturity of the network that can now tackle more complex questions.

All 15 FWC studies were considered complex and focused mostly on assessing fitness for use of RWD for specialised disease areas (Chimeric Antigen Receptor T-cell therapy, Duchenne Muscular Dystrophy) or exploring methodological topics such as target trial emulation (TTE) and estimand frameworks.

The first two very complex studies started in the period are described below:

Enabling pregnancy and mother-child research in DARWIN EU® - PeriNet

This study aims at assessing and improving the readiness of the DARWIN EU® Data network to support research involving maternal and child health, through the following five specific objectives: (1) to identify data partners in the DARWIN EU® Data Network with available data on pregnancy, pregnancy

start and end dates, pregnancy outcomes, and mother and child linkage; (2) to optimise and validate OMOP pregnancy algorithms for DARWIN EU® data partners with pregnancy-related data; (3) to establish a convention for the mapping of pregnancy-related data and parent-child linkage data to the OMOP Common Data Model (CDM), exploring the use of the Perinatal Extension Table (PET); (4) to characterise pregnancies and mother-child linkage over time for DARWIN EU® data partners with pregnancy-related data; (5) to create a database with aggregate counts related to pregnancy and mother-child linkage to better support feasibility assessment in this population. The project utilises data from 17 data sources across 12 European countries.

Optimising Oncology - Enhanced Preparedness of the DARWIN EU® Network - OncoNET

The DARWIN-OncoNet project aims to strengthen the DARWIN EU® Network's ability to generate high-quality RWE for regulatory questions in oncology. The initiative focuses on improving oncology-related data quality, especially for treatment, grade and stage variables, oncology specific outcomes, and enhancing analytical pipelines such as treatment patterns, to enable future studies in the field of oncology. It will also create a database with aggregate counts related to oncology to better support feasibility assessment in this population. The project focuses on 10 different cancers and utilises data from 17 data sources across 14 European countries.

2.3. Studies by requester

As in the previous reporting period, there was a broad range of requesters for studies (Figure 6).

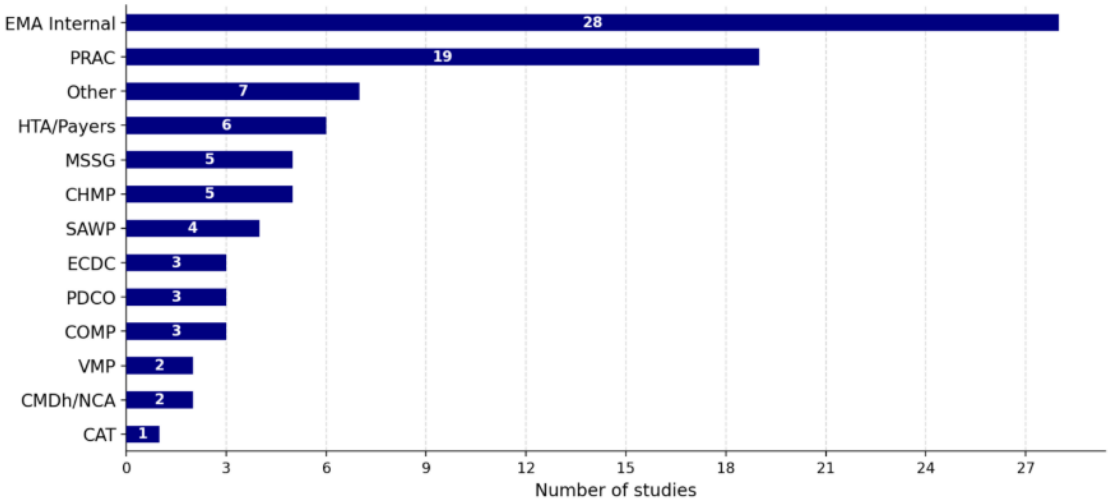


Figure 6. Number of ongoing or completed studies (n=88) during the reporting period by requester

EMA Committees

PRAC: During the reporting period, **nineteen** studies were conducted (either still ongoing or completed by the end of the reporting period) to support PRAC assessments, of which four were related to safety signal procedures, nine conducted in the context of PSUSAs, one evaluating the impact of risk minimisation measures, two drug utilisation studies (paracetamol and opioids) and the remaining five contributing to preparedness in the areas of pregnancy, feasibility of future safety studies and pharmacogenomics.

The process for identifying evidence gaps for which RWE generation would be needed continued as agreed last year for both signal and PSUSA procedures. The decision of study's initiation is made during

the PRAC plenary, results are then published once the final version of the report is approved by the committee, and the concerned company(ies) is informed about the study, including results.

CHMP and SAWP: Within the context of **CHMP** activities, five studies were ongoing or completed. Two were linked to initial MAAs and aimed to generate evidence directly in the procedure while three were preparatory studies in the areas of Duchenne Muscular Dystrophy and Alzheimer's disease. More specifically, the study on Alzheimer's disease provided contextual information on the incidence and prevalence of this disease in the general adult population in six European countries, as well as demographic and clinical characteristics of individuals diagnosed with this disease. The study on Duchenne Muscular Dystrophy is a complex framework contract study aimed to evaluate the fitness for use of registries in this disease area and assess their data quality.

In addition, four studies were ongoing in the context of **SAWP**, regarding Angiotensin II receptor blockers (ARBs) prescribing in children and acute myeloid leukaemia natural history and treatment patterns.

PDCO: In collaboration with PDCO, three studies were completed and one ongoing. The completed studies referred to the use of antiretroviral therapies in paediatric patients and characterisation of individuals diagnosed with paediatric pulmonary arterial hypertension. The ongoing study is a neonatal study, the first one ever conducted via DARWIN EU, studying seizures and treatments thereof in neonates.

COMP: Two studies were completed and one ongoing in the period: description of tetanus immunoglobulin use and tetanus-prone wounds in Europe, treatments in women diagnosed with ovarian cancer, and one methodological study on methods to estimate prevalence of selected cancers.

Other stakeholders

HTA bodies/Payers: In collaboration with HTA bodies and payer organisations, one complex study estimating the overall survival in patients with advanced or metastatic non-small cell lung cancer (NSCLC) treated with selected immunotherapies as first line of treatment was completed (see Section 3.3). The other ongoing studies addressed the following topics: characterisation of patients with multiple myeloma, including treatments and survival, and capacity and capability of the DARWIN EU network to capture appropriately information on obesity.

MSSG: Five studies (out of which four completed) were performed during the reporting period to support the MSSG and the SPOC Working Party in monitoring the demand and stock levels of critical human medicines. These requests examined trends in the use of ADHD medications, salbutamol inhalation products and their alternatives, essential medicines in intensive care units and medicines likely to be used during public health emergencies. These efforts aim to monitor availability and effective management of critical medications in different healthcare settings and can be regularly rerun to continuously inform the team on utilisation trends and upcoming shortages in Europe.

VMP: Two studies were conducted to inform vaccine safety and effectiveness topics identified in the VMP Research Agenda. The studies investigated: brand-specific influenza vaccine effectiveness in the Nordic countries (framework contract study) and vaccine coverage and incidence of influenza-related outcomes to inform preparedness for annual seasonal influenza vaccine effectiveness studies.

ECDC: In collaboration with ECDC, three drug utilisation studies on antibiotics part of the WHO Watch/Access and reserve use categories were conducted (see section 3.3).

European Commission: In collaboration with the European Commission, a study on prescription of antipsychotic drugs in children in Europe was conducted.

Patient organisations: In collaboration with Cystic Fibrosis Europe, a pan-European patient organisation that represents people with cystic fibrosis and their families across Europe, a drug utilisation study and a study to characterise patients diagnosed with cystic fibrosis in Europe were completed. The two studies aimed to generate evidence on the clinical characteristics and monitoring of patients with a cystic fibrosis diagnosis in routine clinical care.

3. Usefulness and impact of RWE

3.1. Survey on perceived value of RWE by the requesters

To understand the value of the evidence generated, the study requesters were asked about the impact of the DARWIN EU study results, whether they were helpful for decision making. The response rate was 67.5% (27 out of 40 surveys sent, only for DARWIN EU completed studies).

Approx. 30% of the responders indicated that the study results were used to support a formal regulatory decision. Although direct immediate regulatory impact in ongoing procedures is important and the easiest to measure, the value of RWE goes beyond immediate impact, being also used to prepare for future procedures, to monitor shortages, to enhance collaboration with other stakeholders, or for methodological improvements, as highlighted by 59% of the respondents.

Even with a very ambitious study duration offered by DARWIN EU, the regulators require the results to be delivered in weeks, which is incompatible with the current model in which approval from institutional scientific boards is needed before obtaining and analysing data, and in fact, with any model that requires a protocol based access to the data. Further work is necessary to guarantee delivery within timelines and maximise impact.

A second reason identified in some cases, is the lack of adequate data, specifically data which is granular enough to answer the question precisely, and this can be partially addressed by increasing data quality, extending mapping to the CDM and onboarding of dedicated, more specialised data sources such as disease registries.

Table 1. The regulatory impact of DARWIN EU studies (N=27 responses)

Impact category	(%)
Translated into regulatory decisions[1]	30%
Preparedness for shortages, public health emergencies or other domains	15%
Helped to improve clinical or methodological knowledge	44%
Unknown	11%

1 - For example: supporting labelling changes (or no need for change), scientific advice, signal procedures, feasibility of future imposed studies requested by committees

3.2. Areas of improvement

When asked for areas of improvement for RWE generation, a strong and recurring theme concerned heterogeneity of results which was seen as a barrier for comparability and interpretability of results. There was a clear call for improved data harmonisation, including more consistent coding, shared definitions, and aligned analytical approaches across countries in order to reduce methodological heterogeneity. In addition, there is some inherent clinical heterogeneity arising from different populations, and healthcare systems which should not be corrected but rather considered in interpretation.

Respondents working in complex and rare disease areas (e.g., cystic fibrosis) emphasised the gap between routine healthcare data and disease-specific registries, noting challenges related to missing information which made drawing conclusions difficult.

Some respondents called for study objectives to be more closely matched with regulatory needs, while others requested more clear outputs or clearer methodological explanations. An improved discussion and interpretation section was requested.

Other respondents noted that early feasibility studies should be more informative and clarify population size, exposure patterns, and outcome frequencies before committing to more resource-intensive investigations. Of note, enhanced feasibility studies started to be implemented towards the end of the reporting period.

3.3. Illustrative use cases

DARWIN EU® - Overall survival in patients with locally advanced or metastatic non-small cell lung cancer treated with selected immunotherapies as first line of treatment

This DARWIN EU® study aimed to understand NSCLC treatment outcomes in a real-world setting and provides insights into the (comparative) effectiveness of first-line treatments of advanced or metastatic NSCLC with selected immunotherapies (alone or in combination with chemotherapy) versus chemotherapies alone.

This was the first study to compare effectiveness in oncology performed via DARWIN EU®. The study was performed at the request of HTA bodies and Payers.

Patients treated with selected immunotherapies were matched 1:1 to patients treated with chemotherapies based on propensity scores using age, sex, index year, tumour stage, and WHO performance status. The results of the study indicated an overall survival benefit associated with the use of pembrolizumab (which was the most frequently used immunotherapy) over chemotherapies when used as first-line treatment in patients diagnosed with locally advanced or metastatic NSCLC. The survival benefit found for pembrolizumab in this observational study (based on RWD) is in line with results from pivotal clinical trials (KEYNOTE-024, KEYNOTE-189, KEYNOTE-042) as well as with a nationwide observational study conducted in Norway (Hektoen et al., 2025). The results for other immunotherapies (nivolumab and the combination nivolumab+ipilimumab) suggest also improved survival compared to chemotherapies, but the results should be interpreted with caution due to the limited size of these two treatment cohorts; the use of other immunotherapies could not be studies due to paucity of data.

DARWIN EU® - Clozapine and the risk of agranulocytosis - updated risk-minimisation measures

This study investigated the incidence and timing of agranulocytosis and neutropenia in new users of clozapine, a medication used for treatment-resistant schizophrenia and Parkinson's disease associated psychosis. Despite its effectiveness, clozapine is thought to be underused due to the risk of severe blood-related side effects and the burden of long-term monitoring to prevent the side-effects.

The study included over 40,000 patients from five European databases and aimed to provide RWE on how often and especially when these side effects occur after the start of clozapine treatment. The incidence of agranulocytosis and neutropenia was very low across all data sources, with most events occurring within the first two months of treatment. The risk remained minimal throughout the follow-up period, and there were no significant differences by age or sex. The median time to event varied by country however, overall, the probability of not developing these conditions remained high.

PRAC used the results, alongside other evidence in its assessment, to update its recommendations for clozapine monitoring, including less frequent blood count monitoring and focusing solely on the absolute neutrophil count (ANC), which were shown by the current evidence to be more specific and the most relevant marker for the risk of neutropenia.

DARWIN EU® - Incidence, period prevalence, and characterisation of individuals with paediatric pulmonary arterial hypertension

The study was initiated as part of the paediatric investigation plan (PIP) for an endothelin receptor antagonist used for the treatment of pulmonary arterial hypertension (PAH). Its scope was subsequently broadened to address a wider question about paediatric PAH that could support future regulatory decisions. The objectives were to estimate the incidence and prevalence of PAH in children and to characterize paediatric patients at the time of first PAH diagnosis in terms of demographics, underlying aetiology, comorbidities, treatment patterns (including endothelin receptor antagonists and phosphodiesterase-5 inhibitors as mono- or combination therapy), and to calculate the occurrence of clinical outcomes such as hospitalisation and mortality over a five-year follow-up. The study received positive feedback from PDCO, since it filled an existing knowledge gap in the area and helped to address some of the issues raised by the applicant.

DARWIN EU® - Drug Utilisation Study of Antibiotics of the WHO AWaRe classification of antibiotics for evaluation and monitoring of use

The WHO 2023 AWaRe classification (who.int) categorizes 258 antibiotics into three groups of 'Access', 'Watch', and 'Reserve' based on their role in the treatment and impact on antimicrobial resistance. This study has been conducted in conjunction with the European Centre for Disease Prevention and Control (ECDC), building on the knowledge of a previous study conducted in 2022/2023 (DARWIN EU® P1-C1-003 study), which focused only on the 'Watch' category, and expanding its initial scope to the other categories (Access and Reserve) when repeating the 'Watch' category with more recent data and more data sources.

Results were presented per Access, Watch and Reserve lists, reporting most prescribed classes and individual substances, including seasonal trends with duration of use and indication. In Access category, across all data sources, penicillins (led by amoxicillin–clavulanic acid) were the most frequently prescribed antibiotics. In Watch category, the most prescribed classes were macrolides, fluoroquinolones, 2nd- and 3rd-generation cephalosporins. Reserve category antibiotic use was generally low but varied widely across data sources, with the highest usage observed for oxazolidinones, lipopeptides and polymyxins. Reserve antibiotics, including linezolid and daptomycin, showed increasing but still limited use, reflecting their restricted role in managing resistant infections.

Overall, these findings may support optimising antibiotic use across Europe and through harmonised stewardship strategies, and the detailed outputs for individual antibiotics provide additional insights that can inform policy and antimicrobial resistance activities.

DARWIN EU® - Trends in utilisation of Attention-Deficit Hyperactivity Disorder (ADHD) medications

Attention-Deficit/Hyperactivity Disorder (ADHD) is a chronic neurodevelopmental disorder affecting both children and adults. In recent years, demand for ADHD medicines has increased markedly in Europe, accompanied by reports of constrained supply, regulatory approvals, and market changes. A first study was completed during the previous reporting period, and then repeated with additional data partners and more recent data during this reporting period, aiming to characterise trends in ADHD medication use in Europe from 2010 to 2024.

The repeated study was conducted using six data sources from five European countries (Denmark, Germany, Norway, Spain and Sweden) and included individuals aged ≥3 years using any approved ADHD

medication. A total of 973,816 individuals initiated at least one ADHD medication during the study period, with prevalence and incidence that increased across all data sources during the period, with greater use in Scandinavian countries than in Spain and Germany. Methylphenidate was the most frequently used medication throughout. Atomoxetine was the second most common in earlier years but was gradually overtaken by lisdexamfetamine between 2015 and 2019. Guanfacine use, indicated only for children, also increased steadily in later years.

Stratified analyses showed higher use among boys than girls in all paediatric age groups, although the gap narrowed among older adolescents after 2020 due to a steeper rise girls. Among adults, use increased in both sexes, with a more pronounced rise among females since 2020, leading to higher prevalence and incidence among females in Denmark, Germany, Norway, and Sweden by the end of the study period. Initiators the Scandinavian data sources were older on average than those in Spain and Germany, and males predominated overall (54%-68%).

ADHD medication use increased consistently across five European countries from 2010 to 2024. These trends align with previous evidence and may reflect greater awareness, improved diagnosis, and evolving clinical guidelines. Continued monitoring is needed to support optimal ADHD management across Europe.

DARWIN EU® - Prescription trends of ketamine and esketamine

Ketamine and esketamine are authorised for use in anaesthesia and for sedation in medical procedures, as well as for managing treatment-resistant depression. The non-medical use of ketamine has become a growing concern within the European Union, prompting law enforcement actions to monitor its illicit trafficking and misuse. To better understand the scope of this issue, a DARWIN EU study has been conducted to examine legitimate prescription trends for ketamine and esketamine in collaboration with European Union Drug Agency (EUDA).

The results showed distinct patterns of ketamine and esketamine prescriptions across different healthcare settings. Ketamine prescriptions were consistently infrequent in primary care settings, with little variation over time. In contrast, hospital-based data sources showed a gradual increase in ketamine prescribing in the later years of the study. Esketamine prescriptions remained rare across all data sources (with highest use in Finland). Overall, ketamine and esketamine utilisation at the population level in Europe remained limited over the past decade, with slightly increasing trends for ketamine observed in hospital settings since 2021.

These findings provide important baseline information for ongoing monitoring of ketamine and esketamine utilisation in clinical practice, and supported the EUDA in contextualising these results within its monitoring of non-medical use.

4. Methodological support on relevance of RWD sources and study designs for regulatory purposes

EMA can provide methodological input on the relevance of RWD sources, study designs, and analytical approaches to address specific research questions for regulatory purposes. This support is delivered through established regulatory pathways, including early interactions and advice mechanisms, as well as regulatory evaluations conducted by EMA committees.

In this context, the EMA RWE team is involved in the review of requests related to the use of RWD for regulatory purposes raised by marketing authorisation applicants or holders, as well as by non-for-profit organisations.

The aims of this activity are to:

- *Support regulatory feedback to applicants in the frame of early interactions and advice mechanisms*, such as Innovation Task Force (ITF), portfolio and technology meetings (PTM), qualification of novel methodologies (QoNM), PRIME, scientific advice (SA) and other non-binding exchanges including interaction with patient registries. This input supports the preparation of evidence packages by improving their quality, completeness, and relevance in view of future submission within regulatory procedures, such as e.g., a marketing authorization application or post approval commitment
- *Support regulatory evaluation by the EU Regulatory Network* through active participation in peer-review activities. Members of EMA working parties and committees, as well as assessors from national competent authorities, can seek methodological input across all stages of product development and evaluation, procedures and therapeutic areas.

The scope of the support offered include the exploration of existing RWD sources and their fitness-for-purpose in a specific context, comparison against data sources known to EMA, discussion on the feasibility of applicant-proposed study designs, or exchanging views on protocols or reports of a study using RWD.

Between February 2025 and January 2026, the team was involved in 52 requests that included at least one question related to RWD. Of these, 49 were raised during early interactions and advice mechanisms, including 32 scientific advice procedures, representing an increase compared to the previous year, and 3 related to regulatory evaluations. Examples of these requests included cases where historical data was used as benchmark for clinical trials endpoints, or where patient registry data were used as comparator in an externally controlled clinical study. Portfolio and technology meetings, aimed at discussing and anticipating future scientific and regulatory needs, addressed recurring topics such as the use of RWD to inform benefit-risk of medicines, innovative study designs and methodologies including pragmatic trials and target trial emulation. Figure 8 shows the number of methodological support requests by ATC classification and pathway.

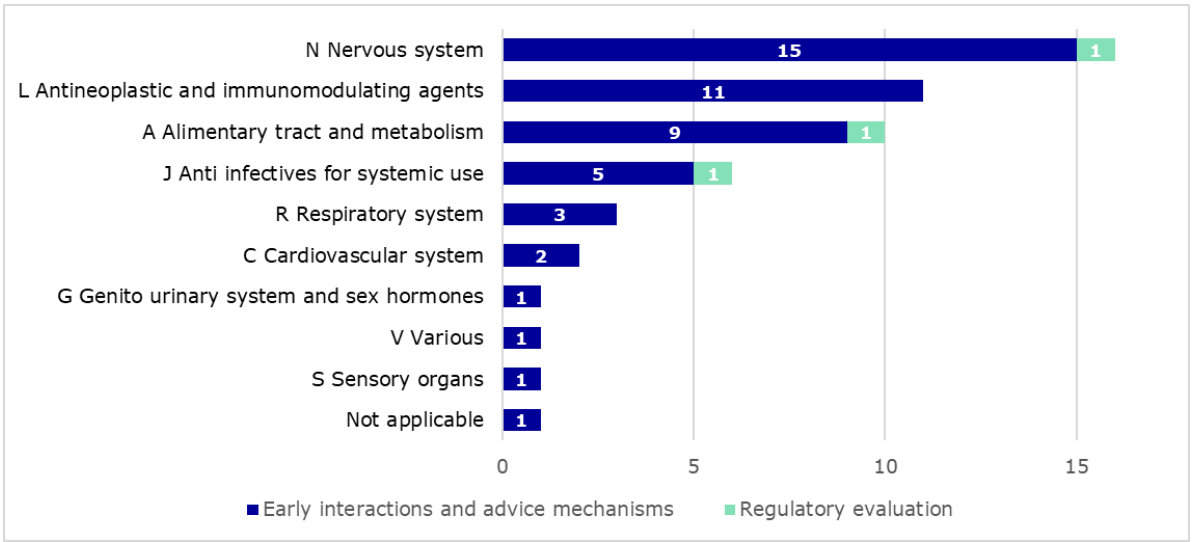


Figure 7. Number of requests for methodological advice by Anatomical Therapeutic Chemical (ATC) classification and pathway (n=52)

5. Progress made on operational aspects

This section reports on the progress made so far in the implementation of the recommendations made by the advisory board and other stakeholders since the last report in five key areas, as listed below.

The activities which became routine are only briefly listed, while the focus is on achievements in the reporting period and newly started activities to address these recommendations.

Access to data sources
Wider access to more diverse and complementary data sources.

- **Widened access to additional data partners** to complement the existing network, with **a larger range of diverse and complementary data,** including **additional European countries** to increase geographical representativeness. During this reporting period, the DARWIN EU® network expanded from 30 to 40 data partners, across **18 European countries,** covering over **250 million patients** in Europe (Figure 8). In line with the recommendation from the Advisory Board, the fourth and last wave of data partners focused on covering areas of special interest such as paediatric population and cancer registries. Two new European countries (Poland and Lithuania) were added to the network as well as three US data sources (adding close to 230 million patients from the US).

  The list of new data partners can be found here.

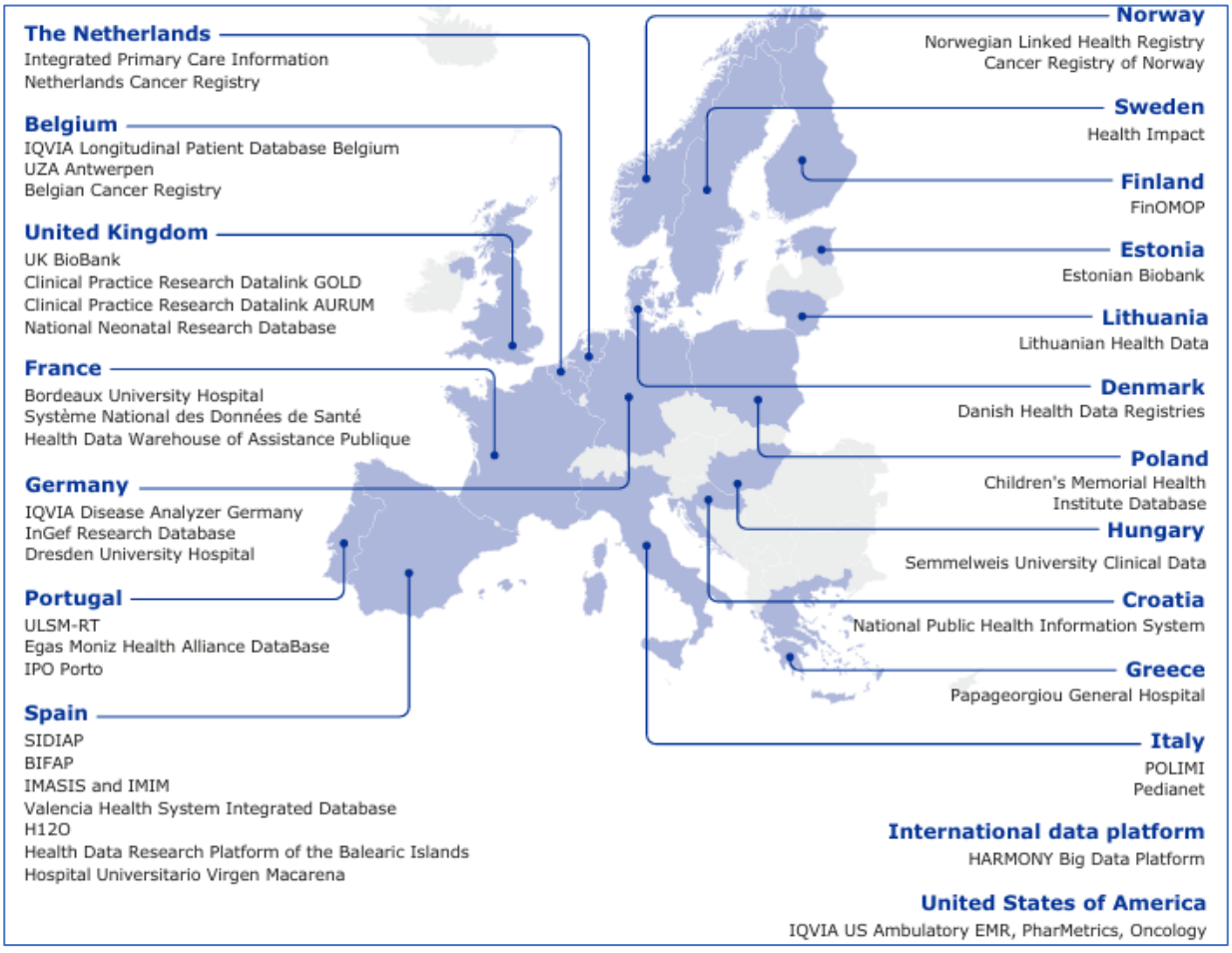
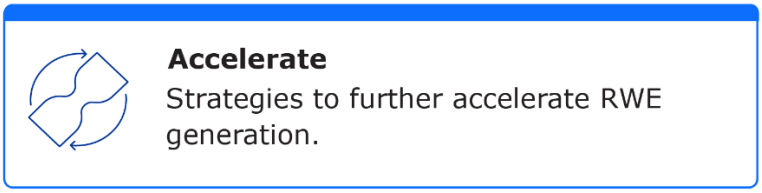


Figure 8. DARWIN EU Network as of February 2026

This network composition refers to the reporting period. Any post reporting updates are published in the Factsheet: DARWIN EU - Making health data count at: Data Analysis and Real World Interrogation Network (DARWIN EU) | European Medicines Agency (EMA)

Enhancing access to and use of more diverse data sources will be further facilitated via Lot 5 – Pharmacoepidemiological research of the new EMA FWCs, which covers the period 2026-2030. With capacity for both secondary use of data and primary data collection, 10 research organisations and academic institutions will provide access to multiple data sources, complementary to DARWIN EU's data partners. This pathway also has capability to address research questions that may not be feasible via DARWIN EU, for example when very specialised data or expertise is needed, such as on studies on rare diseases. More information on the technical specifications of the new contracts and the description of services that can be delivered by Lot 5 is available on the EU Funding & Tenders Portal.



All previously described strategies to accelerate study conduct such as phenotype standardisation, obtaining blanket protocols for faster approvals, improvement of processes and templates are continuing and considered routine activities.

As of now, eight data partners have blanket or umbrella approval for study protocols, allowing faster study start-up and reduced administrative burden, by avoiding submitting a full, new approval application each time the data partner is selected for a specific study. This significantly shortens timelines from study conception to execution — critical in fast-moving or time-sensitive research — and improves efficiency. Overall, for the network, the protocol approval by the local Institutional Review Boards ranges from 14 to 78 days (approximately 2.5 months), with a median of 23 days.

While additional efforts to enhance efficiency are ongoing, substantial additional gains in speed are becoming increasingly challenging to achieve. Future development efforts will therefore prioritise the consolidation of both data quality and the quality of study deliverables, especially of study reports.

- **Revise periodically and improve the standard analytical pipelines:** In 2025, three new additions or updates to the analytical pipelines were made: treatment patterns updated module, the meta-analysis module, and the incidence/prevalence rates with external denominator.
- **Streamline, harmonise and improve processes and templates:** New protocol and report templates were developed and applied during the study period to improve quality and readability of deliverables. Redundancies have been also reduced to limit risks of errors, discrepancies and protocol/report writing and review time. Additional efforts will be undertaken to streamline and substantially shorten the report template, to be possibly used for "simple" OTS studies.
- **Improve feasibility process:** The feasibility process was revised and now includes a fitness-for-use assessment, that considers, beyond presence of key variables and their counts, also their reliability, the relevance of the setting covered and representativeness and coverage of the data source. The development of feasibility process is still ongoing.
- **Increase transparency on data source description and justification for data source selection for RWD studies**: Standardised text related to each data partner was developed to address content and key information for each data source, but also data reliability as verified at onboarding and at each new CDM update release A section on justification for data source selection (the relevance component of the Data Quality Framework) is now a standard part of protocols and reports, and together with standardised database descriptions aims to increase transparency on feasibility and fit-for-use processes and help interpretation of results.

- **Improve data quality, increase breadth of mapping and harmonisation:** Data partners undergo a comprehensive quality check at onboarding and at each new CDM update, which occurs on average every 6 months. In addition, a tracker of quality issues is maintained, and each issue is addressed as soon as possible as well as their impact on study results documented. The Data Quality Framework for EU medicines regulation: applications to Real-World Data was published in March 2026 and the DARWIN EU Coordination Centre is currently adhering to its recommendations.

Regulatory context
Anticipate RWE needs of decision makers by identifying research questions earlier.

All previously reported strategies to anticipate RWE needs such as review of portfolio of upcoming initial marketing authorisation applications, screening of PSUSAs and signal assessment procedures and involvement of the EMA RWE team in EMA Portfolio and Technology meetings are now part of standard practice. As well as the screening of research needs outlined in the VMP research agenda and/or triggered by research needs outlined in the VMP research agenda and/or triggered by EMA's Emergency Task Force (ETF) and the EMA's Public Health Threats team.

Capacity and capability
Develop educational and knowledge management sharing tools.

Development of educational material and tools specifically designed for regulatory decision makers such as Pharmacoepidemiology and RWE curriculum (with release of the last two modules end of 2025) continued alongside Real-World Academy events (4 events in 2025 addressing the following topics: 1) RWE use cases in collaboration with CHMP, 2) RWE in pregnancy, 3) Target trial emulation framework, and 4) Feasibility assessment).

In addition, multi-stakeholder workshops related to RWD and RWE were organised during this reporting period, such as on **Patient Registries for Alzheimer's disease** (in December 2025) to enable the generation of meaningful safety and efficacy/effectiveness data using existing patient registries.

Collaboration and Communication
Close collaboration with decision makers and other stakeholders.

- **Interactions with the Committees, SAWP and CMDh** members, circulation of a quarterly **RWE newsflash** to the regulatory network, publication of study protocols and reports in the Catalogue of RWD studies are now routine activities. These will be supported shortly by the addition of links to the study analysis code packages; and visual abstracts, for even more transparency.

- **Inteaction with data partners**: In March 2025, EMA held its first meeting with the DARWIN EU data partners to show how DARWIN EU studies are integrated into the regulatory work, followed by a face-to-face event in autumn discussing achievements and challenges. We aim for this to be a regular opportunity to enhance collaboration.
- **Industry involvement:** Regular dialogue with industry representatives started in 2024 and continued in 2025 in the form of quarterly meetings in which industry and EMA representatives brainstorm about DARWIN EU and RWE developments in general. Industry is also involved in reviewing selected study protocols, for example for complex studies where their product is concerned.

Annex 1 List of EMA-led RWD studies initiated in the period

Topic	Pathway	Study Requester	Study Status	Procedure	HMA/EMA Catalogue identifier
Descriptive study of tetanus immunoglobulin use and tetanus-prone wounds in Europe	DARWIN EU	COMP	Completed	New OD	EUPAS1000000685
Treatment patterns in postmenopausal women in European countries: A real-world observational study	DARWIN EU	EMA internal	Ongoing - Results	N/A	EUPAS1000000821
RR2 Drug utilisation study of prescription opioids	DARWIN EU	PRAC	Completed	PSUSA	EUPAS1000000615
Capturing obesity in DARWIN EU	DARWIN EU	HTA/Payers	Ongoing - Results	N/A	EUPAS1000000820
Antipsychotic prescribing in children in Europe: a descriptive analysis of trends and patient characteristics	DARWIN EU	Other	Completed	Not linked to an ongoing procedure	EUPAS1000000592
Trends in utilisation of Attention-Deficit Hyperactivity Disorder (ADHD) medications	DARWIN EU	CMDh/NCA	Completed	Other	EUPAS1000000678
RR Childhood hypertension and sartans prescribing in children	DARWIN EU	SAWP	Completed	Not linked to an ongoing procedure	EUPAS1000000714
Assessment of immunoglobulin use in clinical practice	DARWIN EU	Other	Ongoing - Results	Not linked to an ongoing procedure	EUPAS1000000823
Drug Utilisation Study of terbinafine-containing products	DARWIN EU	PRAC	Completed	PSUSA	EUPAS1000000790
DARWIN EU® - Enhanced Preparedness of the DARWIN EU Network for regulatory questions in oncology – DARWIN OncoNet	DARWIN EU	EMA internal	Ongoing - Protocol	Not linked to an ongoing procedure	EUPAS1000000824
Characterisation of aliskiren users	DARWIN EU	PRAC	Completed	PSUSA	EUPAS1000000768
Alzheimer's disease: Incidence, prevalence, and individual's characteristics	DARWIN EU	CHMP	Completed	Not linked to an ongoing procedure	EUPAS1000000826

Topic	Pathway	Study Requester	Study Status	Procedure	HMA/EMA Catalogue identifier
Encephalitis risk in pediatric varicella vaccine recipients	DARWIN EU	PRAC	Completed	Signal	EUPAS1000000813
RR Childhood hypertension and sartans prescribing in children	DARWIN EU	SAWP	Completed	Not linked to an ongoing procedure	EUPAS1000000714
Characterisation of individuals with cystic fibrosis in Europe	DARWIN EU	Other	Completed	Not linked to an ongoing procedure	EUPAS1000000710
Time to onset of thromboembolic events in patients with selected types of cancer	DARWIN EU	EMA internal	Ongoing - Results	Not linked to an ongoing procedure	EUPAS1000000814
Drug utilisation study in individuals with cystic fibrosis in Europe	DARWIN EU	Other	Completed	Not linked to an ongoing procedure	EUPAS1000000708
Characterisation of individuals with cystic fibrosis in Europe	DARWIN EU	Other	Completed	Not linked to an ongoing procedure	EUPAS1000000709
Capturing obesity, obesity-related variables, and changes in weight over time across the DARWIN EU® network (4 studies)	DARWIN EU	HTA/Payers	Ongoing - Results	N/A	EUPAS1000000820
Characterization of data capture related to suicidality in DARWIN EU network	DARWIN EU	EMA internal	Ongoing - Results	Not linked to an ongoing procedure	EUPAS1000000825
Characteristics of individuals with acute graft vs. host disease with intestinal involvement	DARWIN EU	CHMP	Ongoing - Results	MAA	EUPAS1000000878
Potential association between beta blockers and breast cancer	DARWIN EU	PRAC	Ongoing - Protocol	Signal	To be published
Treatment characterisation and post-diagnosis outcomes in individuals with Alzheimer's disease	DARWIN EU	CHMP	Ongoing - Results	Not linked to an ongoing procedure	EUPAS1000000827
Background incidence rates of selected vaccine adverse events of special interest (AESIs) in European data sources	DARWIN EU	Other	Ongoing - Results	Not linked to an ongoing procedure	To be published

Topic	Pathway	Study Requester	Study Status	Procedure	HMA/EMA Catalogue identifier
Estimating the incidence of myocarditis among young males across Europe	DARWIN EU	EMA internal	EMA internal	Ongoing - Protocol	To be published
Population demographics and disease frequency across the DARWIN EU® network (3 studies)	DARWIN EU	EMA internal	Ongoing - Protocol	Not linked to an ongoing procedure	To be published
Assessing the potential association between venlafaxine and incident heart failure in adult patients with depression or anxiety disorder	DARWIN EU	PRAC	Ongoing - Results	Ongoing - Results	To be published
Drug utilisation study of intramuscular depot olanzapine	DARWIN EU	MSSG	Ongoing - Protocol	Other	EUPAS1000000980
Characterization of data capture related to suicidality in DARWIN EU network (2 studies)	DARWIN EU	EMA internal	Ongoing - Results	Not linked to an ongoing procedure	EUPAS1000000825
Multiple myeloma: patient characterisation, treatments, and survival in the period 2012–2024	DARWIN EU	HTA/Payers	Ongoing - Results	Other	EUPAS1000000757
Neonatal seizures: Incidence, prevalence, patient characterisation, and treatments in European countries	DARWIN EU	PDCO	Ongoing - Results	PIP	EUPAS1000000822
Assessing feasibility of investigating acute myeloid leukaemia: incidence, patient characteristics, treatments, and survival in the period 2015–2024 (2 studies)	DARWIN EU	SAWP	Ongoing - Results	Other	EUPAS1000000773
Description and assessment of fitness-for-purpose of real-world data (RWD) sources on Duchenne Muscular Dystrophy for regulatory decision-making	Funded (FWC)	CHMP	Ongoing - Protocol	Not linked to an ongoing procedure	EUPAS1000000748
Characterisation of systemic treatments for the management of ovarian cancer	DARWIN EU	COMP	Ongoing - Results	N/A	EUPAS1000000815
TARGET-EU: Effectiveness of BNT162b2 mRNA COVID-19 vaccine in healthy individuals or	Funded (FWC)	EMA internal	Ongoing - Results	Not linked to an	To be published

Topic	Pathway	Study Requester	Study Status	Procedure	HMA/EMA Catalogue identifier
with stable pre-existing medical conditions against SARS-CoV-2 infection				ongoing procedure	
TARGET-EU: Nivolumab plus ipilimumab with chemotherapy versus pembrolizumab with chemotherapy in patients with non-oncogenic metastatic non-small-cell lung cancer with <1% PD-L1 tumour expression	Funded (FWC)	EMA internal	Ongoing - Results	Not linked to an ongoing procedure	To be published
TARGET-EU: Dapagliflozin and major adverse cardiovascular events in type 2 diabetes	Funded (FWC)	EMA internal	Ongoing - Results	Not linked to an ongoing procedure	To be published
TARGET-EU: Rivaroxaban and risk of major gastrointestinal bleeding in elderly patients with non-valvular atrial fibrillation	Funded (FWC)	EMA internal	Ongoing - Results	Not linked to an ongoing procedure	To be published
TARGET-EU: Comparison of single-device vilanterol/fluticasone furoate with other single-device inhaled corticosteroid and long-acting beta agonist combinations in the risk of pneumonia in adolescents with asthma	Funded (FWC)	EMA internal	Ongoing - Results	Not linked to an ongoing procedure	To be published
TARGET-EU: The risk of angiooedema and other safety events in heart failure patients treated with sacubitril/valsartan compared to angiotensin-converting enzyme inhibitors	Funded (FWC)	EMA internal	Ongoing - Results	Not linked to an ongoing procedure	To be published
TARGET-EU: Risk of adverse birth and neurodevelopmental outcomes in children born alive to fathers exposed to valproate versus levetiracetam for generalised epilepsy	Funded (FWC)	EMA internal	Ongoing - Results	Not linked to an ongoing procedure	To be published
TARGET-EU: Tolvaptan and risk associated to hepatotoxicity in	Funded (FWC)	EMA internal	Ongoing - Results	Not linked to an	To be published

Topic	Pathway	Study Requester	Study Status	Procedure	HMA/EMA Catalogue identifier
autosomal dominant polycystic kidney disease				ongoing procedure	
TARGET-EU: Clinical benefit of bevacizumab in metastatic colorectal cancer	Funded (FWC)	EMA internal	Ongoing - Results	Not linked to an ongoing procedure	To be published
Coverage of meningococcal vaccines by the target population in Europe	DARWIN EU	PRAC	Completed	PSUSA	EUPAS1000000675
Characterisation of acute renal outcomes and diabetic complications among patients with concomitant use of metformin and iodinated contrast agents	DARWIN EU	PRAC	Completed	PSUSA	EUPAS1000000662
Incidence, period prevalence, and characterisation of individuals with paediatric pulmonary arterial hypertension	DARWIN EU	PDCO	Completed	Not linked to an ongoing procedure	EUPAS1000000716
Feasibility of studies on early (pre-symptomatic) stages of type 1 diabetes in DARWIN EU network	DARWIN EU	EMA internal	Completed	MAA	EUPAS1000000756
Proof-of-concept: Preparedness for annual seasonal influenza vaccine effectiveness studies - Vaccine coverage and incidence of influenza-related outcomes	DARWIN EU	VMP	Completed	Other	EUPAS1000000803
Clozapine and the incidence of agranulocytosis over time	DARWIN EU	PRAC	Completed	Signal	EUPAS1000000549
Prevalence of selected cancers	DARWIN EU	COMP	Completed	Other	EUPAS1000000715
Paracetamol prescribing and paracetamol overdose in Europe: a descriptive analysis of trends and patient characteristics	DARWIN EU	COMP	Completed	N/A	EUPAS1000000584

Annex 2 List of EMA-led RWD studies finalised in the period

Topic	Pathway	Study Requester	Procedure	HMA/EMA Catalogue identifier
Descriptive study of tetanus immunoglobulin use and tetanus-prone wounds in Europe	DARWIN EU	COMP	New OD	EUPAS1000000685
RR2 Drug utilisation study of prescription opioids	DARWIN EU	PRAC	PSUSA	EUPAS1000000615
Antipsychotic prescribing in children in Europe: a descriptive analysis of trends and patient characteristics	DARWIN EU	Other	Not linked to an ongoing procedure	EUPAS1000000592
Trends in utilisation of Attention-Deficit Hyperactivity Disorder (ADHD) Medications	DARWIN EU	CMDh/NCA	Other	EUPAS1000000678
RR Childhood hypertension and sartans prescribing in children	DARWIN EU	SAWP	Not linked to an ongoing procedure	EUPAS1000000714
Drug Utilisation Study of terbinafine-containing products	DARWIN EU	PRAC	PSUSA	EUPAS1000000790
Characterisation of aliskiren users	DARWIN EU	PRAC	PSUSA	EUPAS1000000768
Alzheimer's Disease: Incidence, Prevalence, and Individual's Characteristics	DARWIN EU	CHMP	Not linked to an ongoing procedure	EUPAS1000000826
Encephalitis Risk in Pediatric Varicella Vaccine Recipients	DARWIN EU	PRAC	Signal	EUPAS1000000813
RR Childhood hypertension and sartans prescribing in children	DARWIN EU	SAWP	Not linked to an ongoing procedure	EUPAS1000000714
Characterisation of individuals with cystic fibrosis in Europe (including 2 studies)	DARWIN EU	Other	Not linked to an ongoing procedure	EUPAS1000000709 EUPAS1000000710
Drug utilisation study in individuals with cystic fibrosis in Europe	DARWIN EU	Other	Not linked to an ongoing procedure	EUPAS1000000708
ADEPT: The utilisation of antiseizure medications in pregnant women, other women of childbearing potential, and men: a multi-database study from 7 European countries	Funded (FWC)	PRAC	Other	EUPAS1000000212
Overall survival in patients with advanced or metastatic non-small cell lung (NSCLC) cancer treated with selected immunotherapies as first line of treatment	DARWIN EU	HTA/Payers	Other	EUPAS1000000112
Drug Utilisation Study on Antibiotics in the 'Watch' category of the WHO	DARWIN EU	ECDC	N/A	EUPAS1000000665

Topic	Pathway	Study Requester	Procedure	HMA/EMA Catalogue identifier
AWaRe classification of antibiotics for evaluation and monitoring of use				
Incidence rates of venous thromboembolic events in patients with selected cancers	DARWIN EU	EMA internal	Signal	EUPAS1000000440
Characterising the use of JAK inhibitors in Europe: a Drug Utilisation Study	DARWIN EU	PRAC	Not linked to an ongoing procedure	EUPAS1000000424
Trends in utilisation of Attention-Deficit Hyperactivity Disorder (ADHD) Medications	DARWIN EU	MSSG	Other	EUPAS1000000219
Association between genetic polymorphisms of interest and risk of myopathy among statin users	DARWIN EU	PRAC	N/A	EUPAS1000000369
Association of venous thromboembolism with non-steroidal anti-inflammatory drug use in women 15-49 years using hormonal contraceptives	DARWIN EU	PRAC	PSUSA	EUPAS1000000443
Characterisation of exposure to acitretin and purpura and related conditions	DARWIN EU	PRAC	PSUSA	EUPAS1000000429
Impact of risk minimisation measures related to the risk of meningioma in women using nomegestrol and chlormadinone	DARWIN EU	PRAC	N/A	EUPAS1000000455
Brand-specific influenza vaccine effectiveness in the Nordic countries	Funded (FWC)	VMP	N/A	EUPAS1000000481
Drug Utilization of salbutamol products for inhalation and therapeutic alternative inhalation products	DARWIN EU	MSSG	N/A	EUPAS1000000403
Prescription trends of ketamine and esketamine	DARWIN EU	Other	N/A	EUPAS1000000436
Prevalence of hypertrophic cardiomyopathy (HCM) and obstructive hypertrophic cardiomyopathy (oHCM) in six European countries	DARWIN EU	CHMP	MAA	EUPAS1000000430
Use of antiretroviral therapies in paediatric patients	DARWIN EU	PDCO	PIP	EUPAS1000000545
Drug utilisation and patient characterisation of statin usage	In-house	EMA internal	N/A	EUPAS1000000764
Monitoring prescription of essential medicines administered in ICU	DARWIN EU	MSSG	N/A	EUPAS1000000534

Topic	Pathway	Study Requester	Procedure	HMA/EMA Catalogue identifier
Eye disorders in women with breast cancer treated with anastrozole, letrozole or tamoxifen	DARWIN EU	CMDh/NCA	PSUSA	EUPAS1000000599
Monitoring prescription of medicines for public health emergencies at risk of shortages	DARWIN EU	MSSG	N/A	EUPAS1000000473
Coverage of meningococcal vaccines by the target population in Europe	DARWIN EU	PRAC	PSUSA	EUPAS1000000675
Characterisation of acute renal outcomes and diabetic complications among patients with concomitant use of metformin and iodinated contrast agents	DARWIN EU	PRAC	PSUSA	EUPAS1000000662
Incidence, period prevalence, and characterisation of individuals with paediatric pulmonary arterial hypertension	DARWIN EU	PDCO	Not linked to an ongoing procedure	EUPAS1000000716
RR1 Drug Utilisation Study of prescription opioids	DARWIN EU	PRAC	PSUSA	EUPAS1000000479
Feasibility of studies on early (pre-symptomatic) stages of type 1 diabetes in DARWIN EU network	DARWIN EU	EMA internal	MAA	EUPAS1000000756
Proof-of-concept: Preparedness for annual seasonal influenza vaccine effectiveness studies - Vaccine coverage and incidence of influenza-related outcomes	DARWIN EU	VMP	Other	EUPAS1000000803
Clozapine and the incidence of agranulocytosis over time	DARWIN EU	PRAC	Signal	EUPAS1000000549
Prevalence of selected cancers	DARWIN EU	COMP	Other	EUPAS1000000715
Paracetamol prescribing and paracetamol overdose in Europe: a descriptive analysis of trends and patient characteristics	DARWIN EU	PRAC	N/A	EUPAS1000000584
DUS of Antibiotics of the WHO Access classification of antibiotics for evaluation and monitoring of use	DARWIN EU	ECDC	Not linked to an ongoing procedure	EUPAS1000000663
DUS of Antibiotics of the WHO Reserve classification of antibiotics for evaluation and monitoring of use	DARWIN EU	ECDC	Not linked to an ongoing procedure	EUPAS1000000664

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Real-world evidence framework to support EU regulatory decision-making: 4th report on the experience gained with regulator-led studies from February 2025 to February 2026
EMA/66577/2026