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ORIGINAL REPORT

# Registries in European post-marketing surveillance: a retrospective analysis of centrally approved products, 2005–2013

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## ABSTRACT

**Purpose** Regulatory agencies and other stakeholders increasingly rely on data collected through registries to support their decision-making. Data from registries are a cornerstone of post-marketing surveillance for monitoring the use of medicines in clinical practice. This study was aimed at gaining further insight into the European Medicines Agency's (EMA) requests for new registries and registry studies using existing registries and to review the experience gained in their conduct.

**Methods** European Public Assessment Reports were consulted to identify products for which a request for a registry was made as a condition of the marketing authorisation. All centrally authorised products that received a positive opinion of the EMA Committee for Medicinal Products for Human Use between 1 January 2005 and 31 December 2013 were included. Data regarding registry design and experiences were collected from EMA electronic record keeping systems.

**Results** Of 392 products that received a positive Committee for Medicinal Products for Human Use opinion during 2005–2013, 31 registries were requested for 30 products in total. Sixty-five percent were product registries whereas 35% were disease registries and 71% of the registries had a primary safety objective. Most commonly reported issues with registries were delayed time to start and low patient accrual rates.

**Conclusions** The delays found in getting new registries up and running support the need to improve the timeliness of data collection in the post-marketing setting. Methodological challenges met in conducting this study highlighted the need for a clarification of definitions and epidemiological concepts around patient registries. The results will inform the EMA Patient Registry initiative to support use of existing patient registries for the post-authorisation benefit–risk monitoring of medicinal products. © 2017 Commonwealth of Australia. Pharmacoepidemiology & Drug Safety © 2017 John Wiley & Sons, Ltd.

KEY WORDS—registries; post-marketing surveillance; observational research; regulatory science; European Medicines Agency

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## INTRODUCTION

The clinical evidence in support of a marketing authorisation for a new medicinal product largely originates from randomised controlled trials. A marketing authorisation for the European Union (EU) as a whole (i.e. a central authorisation) will only be granted if the benefit–risk profile of a medicinal product is deemed positive by the Committee for Medicinal Products for Human Use (CHMP). At the time of authorisation, marketing authorisation holders may be requested to collect additional data about their product post-authorisation in case of well-reasoned scientific uncertainties regarding aspects of the benefits and/or risks of the product.[1] The new pharmacovigilance legislation, Regulation (EU) No. 1235/2010 [2] and Directive 2010/84/EU,[3] applicable in the EU since July 2012, included a strengthened legal basis for regulatory authorities to request post-authorisation safety and efficacy studies as a legal obligation. It defined a post-authorisation safety study as "any study relating to an authorised medicinal product conducted with the aim of identifying, characterising or quantifying a safety hazard, confirming the safety profile of the medicinal product, or of measuring the effectiveness of risk management measures." Whilst a patient registry

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can be requested by a EU regulatory authority through this legal framework, the widely accepted definition of a patient registry is that of an organised system that uses observational study methods to collect uniform data to evaluate specified outcomes for a population that is defined by a particular disease, condition, or exposure and that is followed over time.[4,5] A patient registry is therefore viewed as a data collection structure or a data source within which studies can be performed rather than a study aimed at answering a specific research question.[6,7] It may provide data on patients and on disease and treatment outcomes, including data on patient-reported outcomes, clinical conditions, drug utilisation patterns, safety, and effectiveness, as well as on their determinants. Many patient registries exist in Europe. A recent review identified 1028 registries in 33 countries, the majority of them (64%) being disease or condition based.[4] In Sweden alone, 103 healthcare quality registries focusing on specific disorders have been initiated, mostly by physicians and recorded data on aspects of disease management, self-reported quality of life, lifestyle, and general health status, providing an important source for research.[8] Based on the observation that the design of requested post-authorisation studies by the CHMP has often used a new or existing registry,[1] the European Medicines Agency (EMA) launched in 2014 an initiative on patient registries in order to explore ways to optimise use of the existing patient registries for regulatory decision-making and facilitate the establishment of high-quality new registries if none provide adequate source of post-authorisation data for this purpose.[9] The present study was started as part of this initiative to provide information on how often and for what type of products registries have been requested at initial marketing authorisation of new centrally approved products.

## METHODS

### *Identification of newly authorised centrally approved products*

All medicinal products that received a positive CHMP opinion through the centralised authorisation system (which implies unique application and unique assessment valid to all EU countries) between 1 January 2005 and 31 December 2013 were identified. All full applications relating to new active substances, known active substances, well-established use products, biosimilars, and fixed combination products for which a full dossier was submitted and assessed were included in the study. All generic and hybrid applications (i.e. applications that do not contain a full dossier but rely on a reference medicinal product) and duplicate applications (i.e. multiple applications with different brand names but for the same active ingredient) were excluded because they are not imposed different post-authorisation commitments than those requested to the original medicinal product. For all products in the study, we identified via individual European Public Assessment Reports (www.ema.europa.eu) whether a legally binding requirement for a registry was included as a condition of the marketing authorisation.

Data collected for all products in the study included the European Birth Date (date of marketing authorisation in the EU), the International Birth Date (date of first marketing authorisation worldwide), whether the granting of the marketing authorisation was conditional (i.e. authorisation granted while the collection of comprehensive data is ongoing in order to address unmet medical needs, such data being still generated post authorisation in agreed timelines) or was granted under exceptional circumstances (i.e. authorisation granted when comprehensive data on efficacy and safety cannot be obtained, but it is still appropriate to grant the authorisation due to exceptional circumstances), whether the product had an orphan indication at the time of the initial marketing authorisation, and whether the marketing authorisation had been withdrawn or was still active at the end of data collection (June 2015).

### *Identification of registries*

European Public Assessment Reports were manually reviewed to assess whether or not a registry was requested as a legal obligation. First we identified all requirements that might have been fulfilled using a registry as the term 'registry' was not always specified. Subsequently, the relevant submitted study protocols were reviewed to confirm whether or not the requested study indeed concerned a registry. All post-authorisation studies that had the following characteristics were included: non-interventional, no inclusion criteria other than the use of the product (in case of a product registry) or a diagnosed condition (in case of a disease registry) and that followed the included patients long term—i.e. until the registry was terminated, until death, or until the patient was lost to follow-up. We excluded non-interventional post-authorisation studies with a short-term objective (2 years or less), after which data collection was stopped—unless such studies were specifically called a registry in the study protocol—as such short-term studies were considered designed to answer a specific research question and not to provide a data collection system on disease or treatment outcomes.



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### *Data collection method*

Procedures for centrally approved products are coordinated by EMA. All procedural documents are filed electronically (European Public Assessment Reports, study protocols, Periodic Safety Update Reports, and assessment reports), and these records were used to collect relevant data. For all products for which a registry—as previously defined—was requested, we first identified the protocol of the registry submitted by the marketing authorisation holder and extracted the following information from the approved protocol: name of the registry; planned duration; planned number of patients to be included; whether the design concerned a product or disease registry; whether a new registry was initiated or whether the registry was already existing; primary objective and secondary objectives; whether a quality of life and/or resource use questionnaire was included; what interval was specified for periodic follow-up data collection; and the minimum period of follow-up per patient that was required to fulfil regulatory obligations.

For all products with a requested registry, we extracted information from Periodic Safety Update Reports, annual re-assessment reports (if applicable), risk management plans and assessment reports (if applicable), and progress reports and assessment reports from EMA record management systems. As these documents are not publicly available, we present only aggregated results based on this information. From these documents, we identified whether any issues were flagged in the assessment such as delayed start, problems with inclusion of sufficient numbers of patients, or low data quality. In addition, we collected information on protocol amendments if they were made, as well as explanations provided by either the marketing authorisation holder or the assessor for any issue reported. For all registries, the following data were extracted from the most recent study report: the number of enrolled patients, the number of active sites, and the number of countries where the registry was active. Data collection ended in June 2015.

### *Data analysis*

All data were extracted by one researcher (JB). A second researcher was consulted (KB) whenever there was doubt on whether or not a study should be included as a registry. We calculated the accrual of patients to registries by dividing the planned number of patients by the expected duration of the registry. We then compared the planned accrual rate with the actual accrual rate calculated as the number of patients included at the most recent study report divided by the time between the enrolment of the first patient and the most recent study report. Statistical analyses were performed with SAS for Windows. All data regarding product or registry characteristics that were extracted from non-publicly available documents are only presented in aggregated form. All product-level data as they are presented in this paper are publicly available information.

## RESULTS

### *Newly authorised centrally approved products*

We identified 392 products that received a positive CHMP opinion between 1 January 2005 and 31 December 2013. After excluding generic/hybrid and duplicate applications, 335 products were included (Figure 1). Seventy products had an orphan indication at initial marketing authorisation (21%), 17 received a conditional marketing authorisation (5%), and 21 were approved under exceptional circumstances (6%). By June 2015, 19 (6%) products had been withdrawn from the market. We identified 54 products to which a registry may have been requested as a legal obligation. After consulting the study protocols, there were 30 products for which we confirmed that a registry was used to fulfil the condition of the marketing authorisation. As there was one product that had a request for two different registries (one paediatric and one adult registry), 31 requested registries were identified in total (Table 1).

### *Registries*

Of the products for which registries were requested, 67% (20 products) had an orphan indication at initial marketing authorisation, 6% (2 products) concerned conditional approvals, and 47% (14 products) were approved under exceptional circumstances (Figure 1). By the end of data collection (June 2015), six products (20%) were no longer marketed. One product was withdrawn for safety reasons, one product was withdrawn for commercial reasons, and four products received a marketing authorisation but were never launched. Products for which registries were requested are listed in Table 1.

### *Registry design*

Eleven registries (35.5%) were designed as a disease registry and 20 registries (65%) as a product registry (Table 2). New registries were created for six disease (54.5%) and 18 product registries (90%). For one product, a combination of a new registry and an amendment to an existing registry was used. The primary objective of the registries was safety ($n$ = 22, 71%), effectiveness/efficacy ($n$ = 3, 10%), safety in pregnancy ($n$ = 3, 10%), and disease epidemiology



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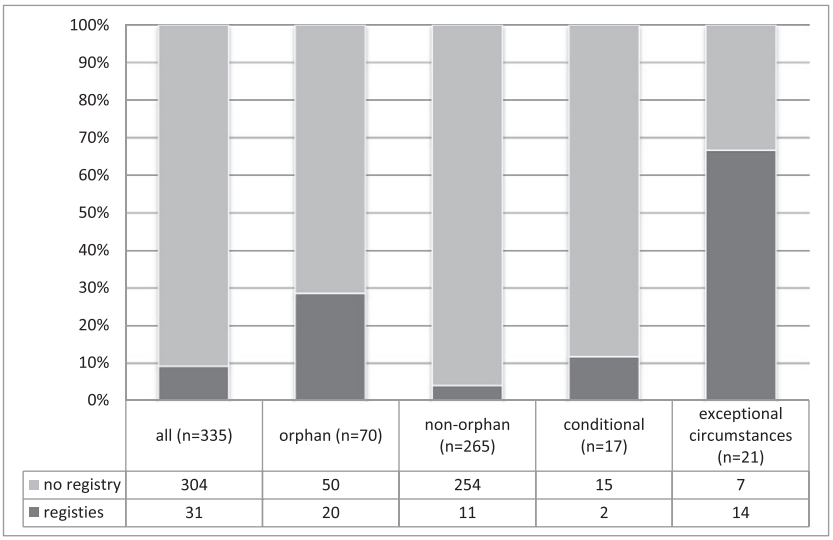


Figure 1. Proportion of products with a registry by marketing authorisation

($n$ = 3, 10%). Twenty-nine registries (93.5%) had safety objectives either as primary or secondary objectives, whereas 12 registries (38.7%) had effectiveness/efficacy as one of its objectives.

*Registry experiences*

Seven registries were never started, due to either the product not being launched in Europe or due to slow uptake or limited use of the product in EU countries (Table 2). For two registries, patient recruitment had not yet started by June 2015, and 15 registries were still enrolling patients at the time of the most recent study report. Although 11 of 24 active registries were planned to finish by the beginning of 2015, only two were completed at the time of data collection for this study. Twenty-five protocols specified the planned number of patients to be enrolled in the registry with minimum and maximum numbers of patients of 50 and 3000 patients (mean: 552; median: 300). There was no restriction on the number of patients to be included in five registries, and a detailed protocol could not be retrieved for one registry. We examined how many registries enrolled the first patient within one year and within two years of the European Birth Date. Ten of 24 registries (42%) started patient accrual more than one year after the European Birth Date (Table 2). For the majority of registries for which both the planned and actual number of patients included was available (14 registries in total), the accrual rate of planned versus actual patients was lower than expected (Figure 2). In addition, the accrual rate was less than half the planned rate for six out of 14 registries. No specific problem for setting up the registry was reported for nine registries (37.5%). Problems most frequently reported were low accrual rate ($n$ = 13, 54.2%), a delay in the start of the registry ($n$ = 9, 37.5%), and amendment of the registry protocol ($n$ = 9, 37.5%). Other reported issues were low data quality or missing data, low use of the product, and reduced enrolment due to other issues ($n$ = 3, 12.5% for each) (Table 3).

For 14 registries, we could identify the individual countries where the registry had enrolled patients. Nineteen EU countries were reported, France being the most frequent (12 (86%) registries), followed by Italy and Germany (both 10 (71%) registries) (Figure 3). Data collection relevant to HTA included quality of life (6), resource use (1), both (2), and a variable not specified (1).

## DISCUSSION

Patient registries already exist in Europe for many diseases,[4] and they are increasingly important to support the life-cycle evaluation of the benefit–risk of authorised medicines by regulators. In the field of rheumatoid arthritis, for example, patient registries provided data for recent publications on topics as diverse as prescription patterns, [10] disease outcomes, [11] effectiveness [12] and safety [13] of biologicals, health-related quality of life, [14] and socio-economic impacts of the disease.[15] We found in this study that, at initial marketing authorisation, a registry was imposed as a legal obligation to 9% of all centrally authorised



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Table 1. All products with identified registry required as a legal obligation

| Year | INN | Product name | Marketing status | MedDRA system organ class | Orphan | Cond appr | Exc cir |
|---|---|---|---|---|---|---|---|
| 2005 | Galsulfase | Naglazyme | Active | Metabolism and nutrition disorders | Yes | No | Yes |
| 2006 | Recombinant antithrombin alfa | Atryn | Active | Vascular disorders | No | No | Yes |
| 2006 | Deferasirox | Exjade | Active | Blood and lymphatic system disorder | Yes | No | No |
| 2006 | Deferasirox | Exjade | Active | Blood and lymphatic system disorder | Yes | No | No |
| 2006 | Dlofarabine | Evoltra | Active | Neoplasms | Yes | No | Yes |
| 2006 | Sitaxentan sodium | Thelin | Withdrawn | Respiratory, thoracic and mediastinal disorders | No | No | No |
| 2006 | Idursulfase | Elaprase | Active | Metabolism and nutrition disorders | Yes | No | Yes |
| 2006 | Rufinamide | Inovelon | Active | Nervous system disorders | Yes | No | No |
| 2007 | Raltegravir | Isentress | Active | Infections and infestations | No | No | No |
| 2007 | Lenalidomide | Revlimid | Active | Neoplasms | Yes | No | No |
| 2007 | Mecasermin | Increlex | Active | Musculoskeletal and connective tissue disorders | Yes | No | Yes |
| 2008 | Eptotermin alfa | Opgenra | Active | Musculoskeletal and connective tissue disorders | No | No | No |
| 2009 | Tocofersolan | Vedrop | Active | Metabolism and nutrition disorders | No | No | Yes |
| 2009 | Diaminopyridine | Firdapse | Active | Nervous system disorders | Yes | No | Yes |
| 2009 | Rilonacept | Rilonacept Regeneron | Withdrawn | Immunomodulating agents | Yes | No | Yes |
| 2009 | Canakinumab | Ilaris | Active | Musculoskeletal and connective tissue disorders | Yes | No | Yes |
| 2010 | Pandemic influenza vaccine (h1n1) (split virion, inactivated, adjuvanted) | Humenza | Withdrawn | Vaccine | No | Yes | No |
| 2010 | Pandemic influenza vaccine (h5n1) (split virion, inactivated, adjuvanted) | Pumarix | Withdrawn | Vaccine | No | No | Yes |
| 2010 | Pirfenidone | Esbriet | Active | Respiratory, thoracic and mediastinal disorders | Yes | No | No |
| 2011 | C1 inhibitor, human | Cinryze | Active | Skin and subcutaneous tissue disorders | No | No | No |
| 2011 | Telavancin | Vibativ | Active | Infections and infestations | No | No | No |
| 2011 | Tafamidis | Vyndaqel | Active | Nervous system disorders | Yes | No | Yes |
| 2012 | Pegloticase | Krystexxa | Active | Musculoskeletal and connective tissue disorders | No | No | No |
| 2012 | Brentuximab Vedotin | Adcetris | Active | Musculoskeletal and connective tissue disorders | Yes | Yes | No |
| 2012 | Ivacaftor | Kalydeco | Active | Respiratory, thoracic and mediastinal disorders | Yes | No | No |
| 2012 | Teduglutide | Revestive | Active | Gastrointestinal disorders | Yes | No | No |
| 2013 | Lomitapide | Lojuxta | Active | Metabolism and nutrition disorders | No | No | Yes |
| 2013 | Cholic acid | Kolbam | Withdrawn | Metabolism and nutrition disorders | Yes | No | Yes |
| 2013 | Pomalidomide | Imnovid | Active | Neoplasms | Yes | No | No |
| 2013 | Defibrotide | Defitelio | Active | Gastrointestinal disorders | Yes | No | Yes |
| 2013 | Autologous peripheral blood mononuclear cells activated with pap-gmcsf (sipuleucelt) | Provenge | Withdrawn | Neoplasms | Yes | No | No |

INN: international nonproprietary name. Cond appr: conditional approval. Exc cir: exceptional circumstances.

products in Europe between 2005 and 2013 and to 66.6% of products authorised under exceptional circumstances. However, 65% of all registries were set up as product registries, whereas 35% were designed as disease registries, in this case based on the specific requirement to use an existing disease registry or to collect data on non-users of the product (e.g. effectiveness objective or to compare the incidence of serious adverse events in users of other, similar treatments). Because multiple product registries may lead to inefficiency and duplication of efforts, the EMA initiative on patient registries seeks to increase the use of existing registries and facilitate the collaboration between registry coordinators, such as physicians' associations, patients' associations, academic institutions or national agencies responsible for overseeing healthcare services, and potential users of registry data, such as medicine regulators and pharmaceutical companies.[9]

A lag time between the date of marketing authorisation and inclusion of the first patient in the registry was relatively common in the registries surveyed, and, in turn, delays in completion of patient inclusion and collection of sufficient follow-up data were frequently



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Table 2. Characteristics of registries

| Type of registry ($N = 31$) | *n* | % | | |
|---|---|---|---|---|
| Disease | 11 | 35% | Existing | 4 |
| | | | New | 6 |
| | | | Combination | 1 |
| Product | 20 | 65% | Existing | 2 |
| | | | New | 18 |
| Objectives ($N = 31$) | *n* | % | | |
| *Primary* | | | *Secondary* | |
| Safety | 22 | 71% | Effectiveness/efficacy | 8 |
| | | | Pregnancy safety | 1 |
| | | | Disease epidemiology | 2 |
| | | | Drug utilisation | 2 |
| | | | Effectiveness of risk reduction | 1 |
| Pregnancy safety | 3 | 10% | | |
| Effectiveness/efficacy | 3 | 10% | Safety | 2 |
| Disease epidemiology | 3 | 10% | Effectiveness/efficacy | 1 |
| | | | Safety | 2 |
| Status of registries ($N = 31$) | *n* | % | Note | |
| Abandoned without any accrual | 7 | 23% | | |
| Accrual not started by June 2015 | 2 | 6% | MAs from 2011 and 2013 | |
| Ongoing accrual | 15 | 48% | | |
| Follow-up only | 4 | 13% | | |
| Closed | 2 | 6% | One discontinued accrual at 24% | |
| Missing information | 1 | 3% | | |
| Planned finalisation ($N = 31$) | *n* | % | Actual | |
| Not stated | 8 | 26% | | |
| Open ended | 4 | 13% | | |
| Beyond 2015 | 8 | 26% | | |
| By 2015 | 11 | 35% | Achieved with full accrual | 1 |
| | | | Discontinued with partial accrual | 1 |
| | | | Delayed | 9 |
| Date of first patient accrual ($N = 24$) | *n* | % | Note | |
| Within one year of EBD | 14 | 58% | | |
| One to two years from EBD | 7 | 29% | Includes one not yet started | |
| More than two years from EBD | 3 | 13% | Includes one not yet started | |

EBD: European Birth Date.

reported. This may be explained at least partly by delays in the launch of products in all EU countries immediately after a central marketing authorisation (which would result in an apparent slow uptake in this study given that enrolment was assessed from launch date rather than from European Birth Date) but also by a low motivation of healthcare professionals and/or hospitals/sites to participate in the registry.[16] It is also possible that expectations with regard to patient inclusion were too optimistic, as it is difficult to anticipate all factors that may affect the feasibility of patient inclusion at the time of authorisation such as administrative workload, informed consent, and difficulty of collecting outcomes data in practice. Reliance on the willingness of centres to participate in the registry may impact on the extent to which the registry patients recruited into the registry accurately reflect the entire population of treated patients, which is a common challenge for registries.[17] Selection bias caused by differences between patients included in a registry versus eligible patients that were not included could be considerable.[5,18] It is therefore critical that such differences can be measured and taken into account when analysing data. Regulators therefore prefer existing patient registries to specific product registries because they allow comparisons between patients with different treatments based on similar sets of data most often collected for another purpose and on similar data collection methods that facilitate risk stratification and confounder adjustment. Addressing these concerns will be critical if registries are increasingly used to collect effectiveness data in the context of early patient access to innovative treatments.[19] As the registries in this study were predominantly aimed at collecting safety data, the experience with requesting registries with primary effectiveness objectives is relatively limited.

We found considerable variation in methods for registry design and conduct based on the protocols that we assessed. For example, a variety of different methods were used to calculate the number of patients to be included in a particular registry, including estimates based on the number of patients in Europe or estimates based on detecting outcomes with a certain incidence. Furthermore, recruiting large numbers of patients is difficult for patients with rare diseases. Sharing of experience, data elements, methods, and best practice between registries established for same diseases would be useful and is supported by resources allowing to identify active registries, including the Registry of Registries (RoR) in Europe (http://www.patientregistries.eu/ror), the Registry of Patient Registries (RoPR) in the United States (https://patientregistry.ahrq.gov/), or the EU post-authorisation study register (EU PAS Register) (http://www.encepp.eu/encepp_studies/indexRegister.shtml).

Our study has a number of limitations. Importantly, there is a very thin demarcation line between a registry and a study. For example, although the AHRQ Users' Guide on registries defines a patient registry as "an organized system that uses observational study methods



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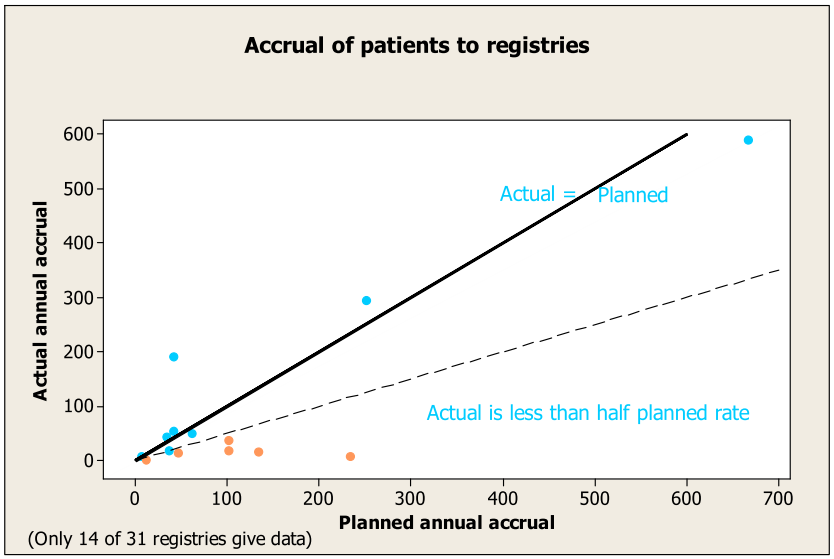


Figure 2. Difference between planned number of patients and actual number of patients included. Abscises represent the numbers of patients accrued in registries. The full line indicates the situation where actual and planned numbers are equal. The dotted line indicates the situation where the actual rate is equal to half of the planned rate. Blue dots are above this line; orange dots are below it. [Colour figure can be viewed at wileyonlinelibrary.com]

Table 3. Problems reported with registries

| Problem | *N* | % |
|---|---|---|
| No problems reported | 9 | 37.5 |
| Delayed start | 9 | 37.5 |
| Low accrual rate | 13 | 54.2 |
| Protocol amendment required | 9 | 37.5 |
| Low data quality or missing data | 3 | 12.5 |
| Low use of product | 3 | 12.5 |
| Enrolment reduced due to other issues | 3 | 12.5 |

Percentages are based on a total of 24 registries that initiated patient inclusion.

to collect uniform data (…)",[5] it also describes the models of case series, cohort, case–control, and case-cohort as study designs applicable to registry data. When collecting data for this article, we found that the terms registry and study are sometimes used interchangeably in regulatory requests to companies for post-authorisation data, a confusion that may be augmented by classifying a registry as a post-authorisation safety study. Based on our view that the duration of a registry is normally open-ended and that of a study is dictated by the collection of data needed for the primary objective, we chose arbitrarily a minimum duration of 2 years for a study to be included in our sample of registries (based on the evaluation of its design), unless the term "registry" was specifically mentioned in the request. Had another criterion been chosen, different results may have been found. A clarification of definitions and epidemiological concepts around patient registries is probably needed to improve consistency of future research. In addition, this study only included registries imposed as a legal obligation. It did not include all registries that might be set up by companies to monitor their products, as not all registries are established following a legal obligation, and many disease registries are currently active in Europe that might have considerable experience with collecting and assessing effectiveness data.[4] All registries were followed up until June 2015, which means that they did not have the same duration of follow-up. This may limit the interpretation of data on accrual rates if accrual is not constant over time, as a catch-up of the patient population may have occurred after June 2015. We did not explore factors that accounted for successful patient accrual versus low accrual rates, and this is an area for future research. Although several data checks were performed to cross-reference findings, all data were extracted manually by a single researcher which could have resulted in some errors. Notwithstanding, this study is the first to report a systematic overview of registry characteristics based on a substantial number of protocols. In addition, we accessed non-published documents that allowed us to report detailed findings.

This study was performed in the context of EMA initiative on patient registries to gain insight into the experience to date. The delays we found in getting new registries up and running may support increased use of existing patient registries to improve the



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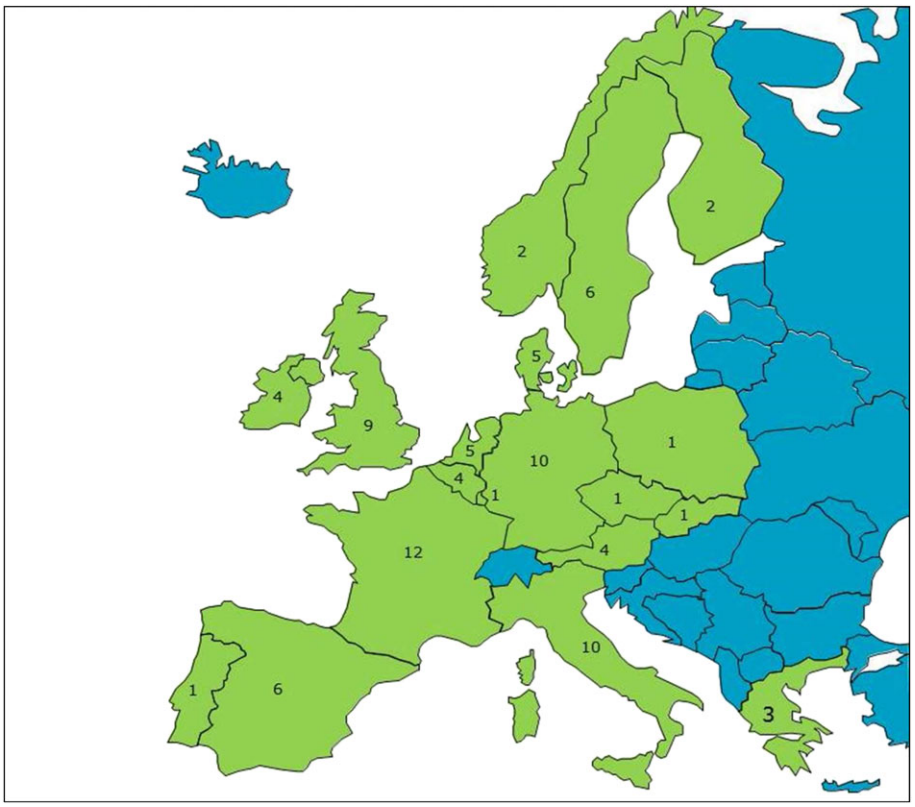


Figure 3. Countries where registries requested as legal obligations on a marketing authorisation are active. This figure is based on 14 different registries that provided information on all individual countries where the registry was active. The number in each country indicates how many of the 14 registries were active in that particular country. [Colour figure can be viewed at wileyonlinelibrary.com]

timeliness of data collection in the post-marketing setting, but this result will need to be carefully assessed. The results will underpin ways to improve the conduct of patient registries in Europe to monitor the benefit–risk of medicinal products.

## DISCLAIMER

The views expressed in this article are those of the authors and may not be understood or quoted as being made on behalf of or reflecting the position of the European Medicines Agency or one of its committees or working parties. The manuscript has been subject to the European Medicines Agency's peer-review process, which checks for compliance with confidentiality rules in force at the Agency.

## CONFLICT OF INTEREST

This initiative received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors. All authors report no conflict of interest.

The results reported in this paper have been presented previously in a poster presentation at ICPE 2015 (Boston, USA).

KEY POINTS

- Review of all newly centrally authorised products shows that registries are frequently requested to marketing authorisation holders as key monitoring tools with data collected most commonly for safety but also for effectiveness and disease epidemiology; the majority of registries are requested for orphan medicinal products and products authorised under exceptional circumstances;
- Despite the very large number of disease registries existing in Europe, the majority of requested registries are established as new product registries;
- Time to start of data collection and rate of recruitment are challenges for requested registries;
- Clarification of definitions and epidemiological concepts around patients registries, and the demarcation between registries and studies, is needed to improve consistency of future research.



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## ETHICS STATEMENT

The authors state that no ethical approval was needed.

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