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SCIENCE MEDICINES HEALTH

Main lessons learnt so far on the qualification of registries

Registries' perspectives

Jan Hillert, Big MS Data Network, Karolinska Institutet & University Hospital, Sweden

Lutz Nährlich, European Cystic Fibrosis Society Patient Registry, University Giessen, Germany

Joint HMA/EMA multi-stakeholder workshop on Patient Registries
12 & 13 February 2024

Overview of Registries / Data sources

Name	Qualification output	Disease(s)	Launch date	Geographical coverage	Number of patients	Purpose for qualification
European Cystic Fibrosis	Opinion (2018)	Cystic fibrosis	2008	Europe	54 043 (2021)	PAES, PASS
EBMT	Opinion (2019)	Blood-related disorders	1974	Worldwide (centres in each continent)	+700 000 (2023)	Drug utilisation, PAES, PASS
International Niemann-Pick Disease Registry	Advice (2021)	Niemann-Pick disease	2013	Europe, North America, South America	500+ (2024)	PAES, PASS, Natural history data
Big MS Data Network	Advice (2022)	Multiple sclerosis	2014	Europe + Worldwide	+250 000	PASS
Enroll-HD	Opinion (2022)	Huntington's disease	2012	Europe, North America, Australasia, Latin America	21 561 (2024)	PAES, PASS
TREAT-NMD	Advice (2022)	Neuromuscular diseases	2007	Worldwide (centres in each continent)	65 750	PAES, Natural history data, Clinical trial control arm data, outcome measures validation
World Federation of Haemophilia Gene Therapy Registry	Advice (2023)	Haemophilia	2023	Worldwide	N/A	PAES, PASS
HARMONY BD platform	Advice (2023)	Blood cancers	2017	Worldwide (centres in each continent)	165 892 (2023)	External control arms, PAES, PASS, surrogate endpoints validation, natural history data

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Reasons to apply for qualification of the registries

To enable active participation in future regulatory mandated PASS and PAES

To concentrate all efforts on 1 patient registry with a broad access, use scenarios and non-profit based governance strategy instead numerous registries

To seek regulatory advice on work required by our registry to support use cases

To provide a level of assurance in the use of registry data for regulatory purposes

To build trust in the quality of the registry data among our stakeholders

To streamline the registry's internal processes to a higher standard of quality

Challenges encountered

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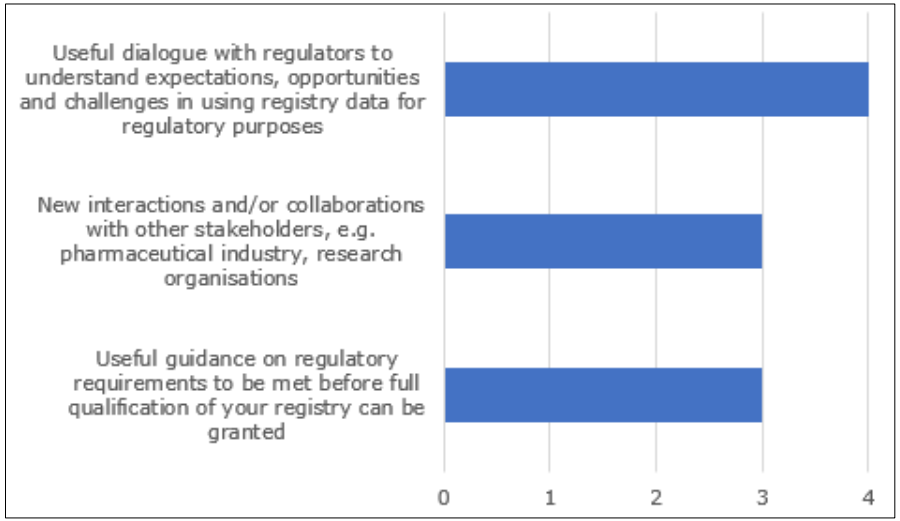
Application preparation	During qualification	After opinion/advice
4 out of 6 registries	**5 out of 6 registries**	**3 out of 6 registries**
Limited experience in undertaking such a regulatory activity	Significant number of documents required after the initial submission package, leading to challenges on resources to generate the documents	Application not successful in obtaining a qualification opinion; reversion to a Letter of Support and roadmap for resubmission instead
	Cumbersome, time-consuming administrative process to submit/update information through the systems	
Difficulty in understanding what was required for the submission, including format/level of details and process	The requirement of a letter of intent was unclear	Lack of triangle discussions limit the possibility to prepare the registry for upcoming demands and to get a feedback from the EMA on the performance of registries
	Some unexpected requirements, e.g., need to write minutes of meetings	
Different "languages" and cultures (EMA, scientist, MAH)	Very short timelines for a multinational non-profit organization not familiar with the application process. More time is needed for internal discussions and preparations	Multiplication of items to report on based on the number of registries involved
	Not prepared to report on data quality mechanisms, policies and efforts already in place, e.g., on technical platforms sometimes provided by external suppliers	

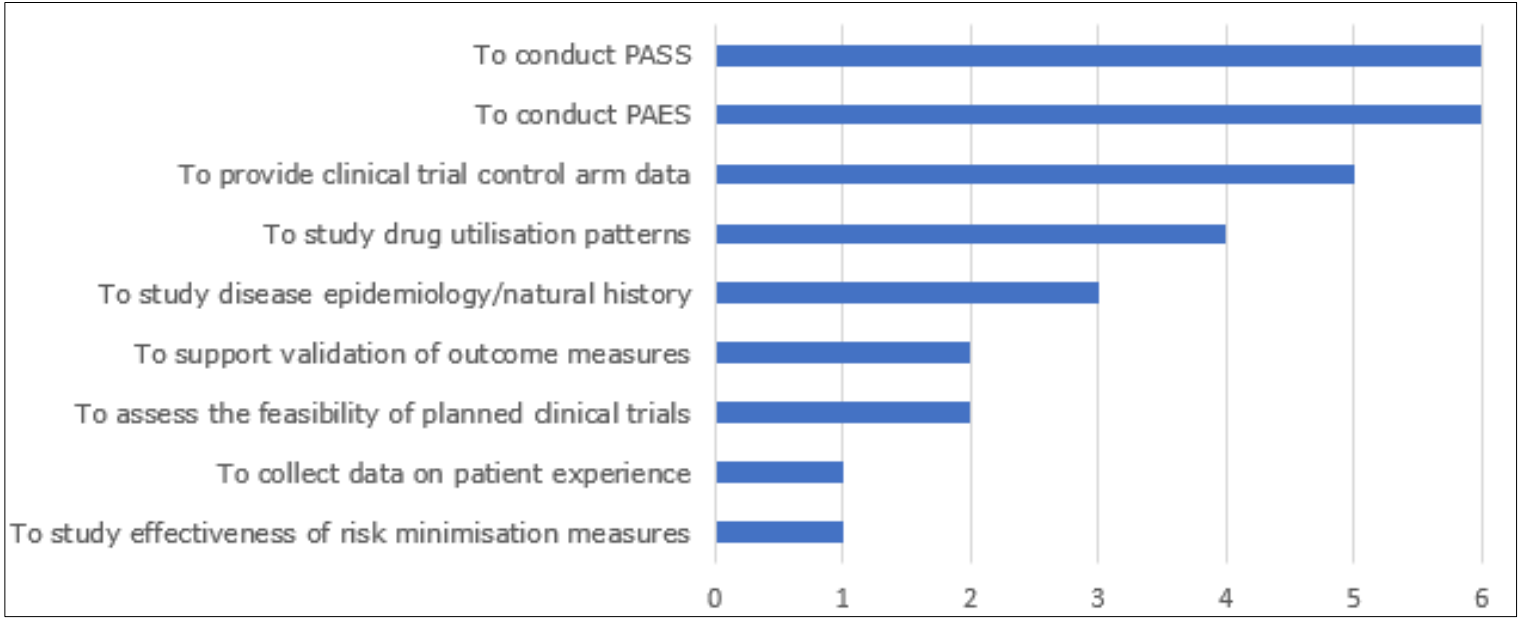
Opportunities



In addition…

- Letter of Support useful in interactions with pharmaceutical companies
- Kicked-off conversations to defend the quality of the data with stakeholders
- Financial support for data collection and data quality efforts
- Focus on data quality, standardized internal procedures, translation into a common data model, processes documentation

Contexts of use of registry data relevant for qualification



Suggestions for improvement

Pre-qualification

During qualification

Post-qualification

Suggestions for improvement

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Pre-qualification

- Guidance more specific to the qualification of registries, e.g., on who should apply and when, how, on the outcome of the process → 5/6
- Dedicated template/check list to help structuring applications in line with regulators' expectations → 5/6
- Additional mechanisms to support registries not familiar with the regulatory context and process, e.g., webinar with step-by-step instructions and a mock submission to be used as training material; scoping meeting with registries planning to seek qualification → 3/6
- Peer network of organisations with experience in qualification and willing to help applicants could be beneficial → 1/6

Suggestions for improvement

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During qualification

- Clearer procedure timelines → 4/6
- Timelines too short (1/6) or too long (1/6)
- More regular communication to applicants on the status of the procedure → 5/6
- Need for active involvement of other stakeholders (e.g. Other regulators than SAWP / PRAC, Industry, patients, experts in the field) → 2/6
- Grant qualification to registries with the potential to be useful, regardless of whether they have started collecting data to increase credibility and encourage sites to participate in the registry → 1/6

Suggestions for improvement

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Post-qualification

- A re-evaluation of the elements qualified should be performed on a regular basis to ensure the standards are maintained over time → 3/6
- Regular interactions between contact points of key stakeholders (to be defined) should be established to ensure continuous dialogue → 2/6

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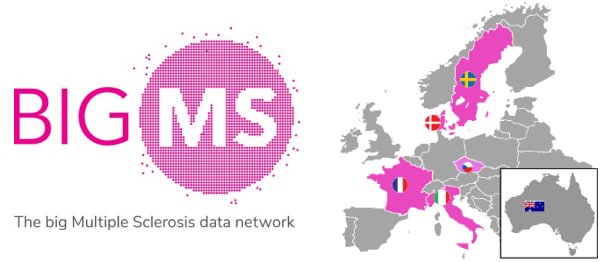
BigMS Data Network:

- Sought Qualification Opinion for PASS
- Received Advice and Letter of Support

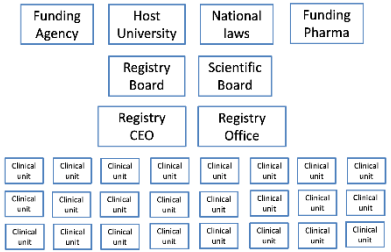
- Principal shortcomings:
  - ”Extent of safety data collected”
  - ”Central quality control”

- Challenges:
  - Converge complex organizations
  - Align and harmonize complex information
  - Demonstrate equal capability of catching adverse events

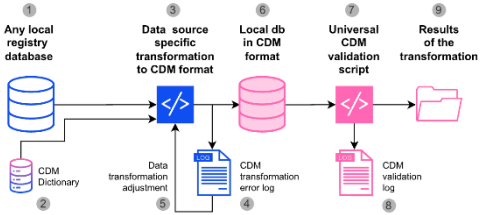


Registry	Estab-lished	Number of centres	Estimated number of patients	Number of publications
Danish MS Registry	1956	30	30,000	179
Swedish MS Registry	2000	64	20,000	280
OFSEP (France)	1980		67,000	155
Italian MS Database Network	2001	26	65,000	45
Czech Republic	2013	15	17,500	20
MSBase	2001	210	75,000	120
Total	**2014**	**355**	**275,000**	**< 620**

Eco system of an MS registry



Common Data Model



Request Tool update

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European Cystic Fibrosis Society Patient Registry

PROCESS: Multi-stakeholder workshop -> Qualification process

- Granularity of dataset (annual dataset / disease-specific medication / complications)
- Governance incl. informed consent form and aggregated data

LIABILITY: Internal/External incl. data quality / standards / timeliness / communication

- Commitment to work on EMA's requirements
- Balance between core activities and PMV studies

IMPACT:

- Drug utilisation of an Orphan drug in 40 countries (EUPAS43022) (2020-2024)
- PAES for an Orphan drug and a specific age group including 11 countries (2020-2024)

KEYS TO SUCCESS: Harmonisation, Sustainability, Transparency, Independency