Submission date: 28 June 2019

Submission of comments on 'Discussion Paper: Use of patient disease registries for regulatory purposes – methodological and operational considerations' (EMA/763513/2018)

Comments from:

Name of organisation or individual
EFA – European Federation of Allergy and Airways Diseases Patients' Associations Submitted by EFA Policy Officer Panagiotis Chaslaridis (Panagiotis.chaslaridis@efanet.org) in coordination with EFA Working Group on Food Allergy, EFA Working Group on Allergy & Asthma, EFA Working Group on Atopic Eczema, EFA Working Group on Patient Education, and EFA Working Group on COPD. www.efanet.org

Please note that comments will be sent to the **ICH M10 EWG** for consideration in the context of Step 3 of the ICH process.

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1. General comments

Stakeholder number *(To be completed by the Agency)*	General comment (if any)
	EFA welcomes EMA's discussion on the use of patient disease registries because of its important link with Real World Data collection and the most universal scope on disease prevalence, development and patient behaviour. Moreover, EFA is glad to see that EMA acknowledges the key role that Real World Evidence can play in decision-making, and therefore the need to highlight some important principles and good practices drawn from the highly diverse landscape of registries across the EU.

2. Specific comments on text

Line no.	Stakeholder no.	Comment and rationale; proposed changes
pp. 6-7 (Executive Summary)		Comment: EFA would like to stress the urgent need for stronger links between existing patient registries within the same disease. As patients, we strive for a **one-disease registry in Europe**. Allergy and asthma constitute examples of umbrella diseases involving conditions that present great variations in terms of severity, symptoms, time elements, care pathways, etc and therefore common terminologies and common core data elements are necessary to improve understanding and ensure comparability, transferability and exploitability of data. Besides, especially in the case of chronic diseases, it is important for national patient registries to ensure **alignment and interoperability** among Member States, as well as with other EU tools such as the Electronic Health Records, which can maximise the credibility of extracted data, while supporting continued and improved care for patients. Proposed change (if any): (complete text) *Core data elements: a list of core data elements to be collected in all patients is proposed. They should be harmonised or mapped across registries for a same disease to support regulatory evaluations and facilitate implementation of a common data quality system, data exchange, common data analysis and interpretation of results from different registries.* ***One-disease registries should further include specific elements such as severity, symptoms, time elements, care pathways, to ensure registries truly inform regulation and research about specific needs.***
Lines 20-22, p.13 (nature)		Comment: It would be very encouraging if EMA gives a signal that **patient organisations are a highly relevant third party** to control and maintain patient registries - a practice that is not yet well expanded. Proposed change (if any): (complete) *'A registry study is an investigation set up to answer a research question that uses data collected in the registry, and which may be initiated, managed or financed by a pharmaceutical company, a regulatory authority**, a patient association** or another organisation'.*
Lines 32-37, p.13		Comment: In order not to duplicate data collection through several sources, registries should serve to oversee medical treatment but also additional therapies such as rehabilitation or smoking-cessation programmes. In addition, EFA would like

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(data collection)		to see a strong statement on the future link between digital health tools and patient registries, as they are a clear source of data and inspiration for preventative public health, i.e. linking respiratory disease prevalence with air quality monitoring. Proposed change (if any): (complete) *4) Data collection: depending on the purpose of the registry, different types of data can be collected, such as data on demographic characteristics,* ***diagnostic tests****, treatments* ***and therapies****, diseases,* ***events such as hospitalisations, self-management tools including digital health,*** *patient-related outcomes, or comorbidities. In a study, data collection or extraction is restricted to the data necessary to investigate the research question, including data on potential confounders and effect modifiers,* ***such as risk factors and environmental health elements****. A specific study may also require additional data collection from other sources if these data are not routinely collected in the registry'.*
Lines 17-21, p. 18 (Good Registry Practice)		Comment: In light of the importance given to registry design consultations with patient groups both, it would be necessary to specify how to ensure patients groups and advocates are part of the full registry process, and not just a token. Proposed change (if any):
Lines 37-41, p. 18 (Good Registry Practice)		Linked to this, EMA should clarify whether registries should differentiate between input data coming from **self-patient reports and/or medical reports**. This distinction is crucial not only for good registry management practice, but also to assess unmet care needs or inaccurate patient information, extremely important in chronic non-communicable diseases such as allergy, asthma and COPD, where patients may occasionally overestimate or underestimate their reaction and provide biased input. Proposed change (if any): [add another point] *'clarify whether registries should differentiate between input data coming from* ***self-patient reports and/or medical reports****. This distinction is crucial not only for good registry management practice, but also to assess unmet care needs or inaccurate patient information, extremely important in chronic non-communicable diseases such as allergy, asthma and COPD, where patients may occasionally overestimate or underestimate their reaction and provide biased input.'*
Lines 31-34,		Comment: It would be very valued to have EMA's recommendations to establish registry and enrolment criteria in view of

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p.18 (Good Registry Practice)		**highly prevalent diseases** e.g. allergy, asthma, COPD etc. EFA believes such recommendations would facilitate the patient selection and encourage their enrolment in registries. Proposed change (if any):
pp. 19-20 (Time elements)		Comment: Regarding the inclusion of the diagnosis event in the time elements, EFA would like to draw attention to the fact that **diagnosis timing** can be very vague or inaccurate in diseases such as food allergies and asthma. This uncertainty is frequently linked to the specialty of the person that is providing the diagnosis, and to the fact that access to a sound, science-based diagnosis might be considerably delayed. Furthermore, for diseases where timelines are not easy to establish due to factors such as wrong/delayed diagnosis, random appearance of symptoms, and treatment differentiation, EFA encourages EMA to consider recommending a **disease-specific patient registry framework** that takes these aspects into consideration. Proposed change (if any): Complete a comment: *'Date of definitive diagnosis - Depending on the disease, for ex. date of definite diagnosis using a validated method such as MRI, histology, cyto-genetic method, etc.* ***Moreover, accurate diagnosis is also linked to the doctor's specialty and the sub-type of disease, which influence the likelihood of wrong diagnosis and over-diagnosis.'***
pp. 20-21 (Core Data Elements)		Comment: There is a need for EMA to elaborate on the case of diseases where **co-morbidities** are a common feature, such as COPD. Co-morbidities may have an impact on the enrolment process, as well as the conclusions drawn from the clinical manifestations of the diseases. From EFA perspective, co-morbidities should be also subject to specific patient registries, this is one-disease registry, co-morbidities registry, to avoid yielding misleading population-based results. Proposed change (if any):
pp. 25-27 (Measures to Improve Data		Comment: In general, regulators should develop **scrutiny mechanisms to assess the independency and transparency of the patient registry data** that will be trusted and endorsed for regulatory purposes. Whether it is arguable who should be the registry manager (public authority, research institution, industry operator, non-for profit civil society organisations),

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Quality, Indicators of Data Quality)		EFA encourages EMA to elaborate on the conditions a regulator should assess prior to the use of a patient registry. Looking for potential bias, conflict of interests, or misleading interpretation of data, is fundamental to foster trust in registries as enablers of scientifically validated data. Such scrutiny is also a warranty for loyal practice for those patients that volunteer to cede their most personal health data. Proposed change (if any):
Lines 10-29, p. 31 (Data Ownership and Intellectual Property)		Comment: EFA is glad to see the Discussion Paper stressing that **patients remain in control** of the use of their data, and that they need to be fully aware of why, what, how, and by whom their data are collected, and with whom it is shared. Meanwhile, it is important that EMA acknowledges the need to take action towards the **harmonisation of consent forms** across all registries, and enable patient access and management through the establishment of an electronic system, to truly transfer the data ownership from data managers to patients. It would be more than welcome if EMA could provide further information on its views on informed consent in the context of this paper. Proposed change (if any): complete: '*Patients remain in the control of the use of their data. They may or may not consent for their use for clinical or research purpose and they may withdraw their previous consent.* ***For this, it is necessary to harmonise consent forms across all registries, making use of electronic tools'.***
p. 42 (Reporting of Study Results)		Comment: Those patients who give their data should be **informed on any results of research that their data is contributing**. In this way, their involvement would become more consistent and meaningful, contributing to an overall good experience for the participating patients. Proposed change (if any):
All		Comment: Overall, beyond scientific and observational purposes, registries could be structured in the future to also inform the ultimate **provision of health care**, especially in life-threatening situations such as during an asthma attack or an anaphylactic shock.

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		Proposed change (if any):

Please add more rows if needed.