28 February 2019
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Inspections, Human Medicines, Pharmacovigilance and Committees Division

European Medicines Agency: Patient Registry Workshops

Follow-Up Survey of stakeholder actions following the workshops

1. Background

The Initiative for Patient Registries, launched in September 2015 by the European Medicines Agency (EMA), explores ways of expanding the use of patient registries by introducing and supporting a systematic and standardised approach to their contribution to the benefit-risk evaluation of medicines within the European Economic Area. Objectives of the Initiative include facilitating the use of existing patient registries as well as the establishment of new registries if none are available or adequate.

At a consultative meeting in October 2016, expert stakeholders who included registry holders, patients, health care professionals (HCPs), regulators, marketing authorisation holders and applicants (MAHs/MAAs), health technology assessment (HTA) and reimbursement bodies, and European Commission representatives participated in discussions to share their views on barriers and facilitators to registry use and on optimising the use of registries for regulatory assessments. Subsequently EMA hosted four disease-specific patient registry workshops: Cystic Fibrosis (14th June 2017), Multiple Sclerosis (7th July 2017), CAR T-cell therapy Registries (9th February 2018) and Haemophilia Registries (8th June 2018). These disease areas were chosen because there was ongoing product development with new products recently approved or undergoing assessment and registries had requested support for harmonisation.

Following each workshop, a report was published that included the recommendations and actions arising. Participants, who represented all of the stakeholder groups, contributed to the drafting of the reports.

During October-November 2018, a survey was conducted to assess the impact of the workshops on stakeholder registry-related activities and to identify further EMA activities that could be explored to facilitate stakeholders' work.

2. Aims of the survey

The aims were:

1) to determine if the recommendations and actions agreed in each of the workshops by the stakeholders had been achieved, were under consideration, or if stakeholders were actively working on measures to be put in place in the short/long term

2) to assess if views on the value of registries had changed following the workshops.

3. Methods

The EMA Patient Registries Initiative team drafted the survey and piloted it among regulatory colleagues who had attended at least one workshop. After revision, the survey was uploaded on the European Commission platform (EU Survey) and in October 2018, an invitation to complete it was sent to all participants from the four workshops.

The survey was anonymous. Participants were asked to provide their primary stakeholder group (registry holder, patient representative, regulator, marketing authorisation holder/applicant (MAH/MAA), health technology assessment (HTA) and/or reimbursement body) and the workshop attended.

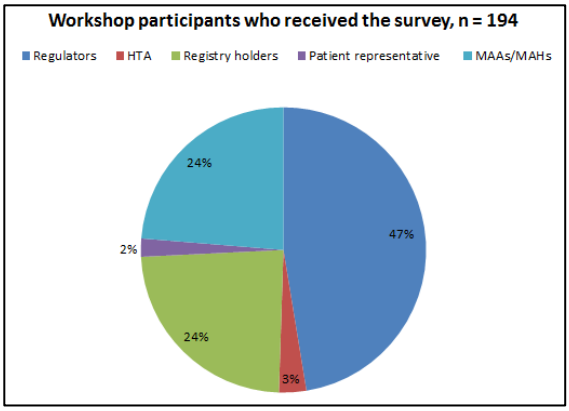
The survey consisted of common questions to be answered by all the participants and specific questions based on the stakeholder group and/or a specific workshop (Appendix). Most questions asked respondents to choose a single answer from a list of 3-5 options. Broadly, the questions enquired about the status of workshop actions and recommendations, impact on views about registries, and collaboration between stakeholders including any new alliances or early dialogue between registries and MAH/MAAs on studies or protocols. Free text space was provided for respondents to expand on their answers, for example, to explain why recommendations from the workshop had or had not been implemented.

Two weeks were allowed for completion with a reminder sent 1 week before the deadline. A further reminder and a one week extension were provided before the survey was finally closed.

The responses were extracted from the platform onto an Excel® file for analysis. Free text answers were analysed qualitatively by four members of the registries team and categorised according to themes.

4. Results

The survey was sent to a total of 194 participants and was completed by 60 (31%) of whom 18 had attended the CAR T-cell therapies registry workshop, 18 the haemophilia workshop, 12 the multiple sclerosis workshop and 10 the cystic fibrosis workshop. Figures 1a and 1b show the stakeholder groups and numbers responding.



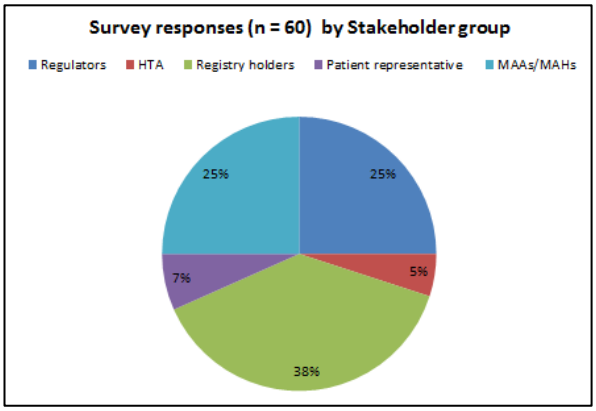


Figure 1a: Participants surveyed

Figure 1b: Survey respondents

Overall, 72% (n=43) of respondents said the workshop they attended was helpful in developing their understanding of the challenges faced by other stakeholders in managing or using patient registries while 25% (15) found it somewhat helpful and 3% (2 regulators) described it as somewhat unhelpful Figure 2 describes the individual stakeholder group responses.

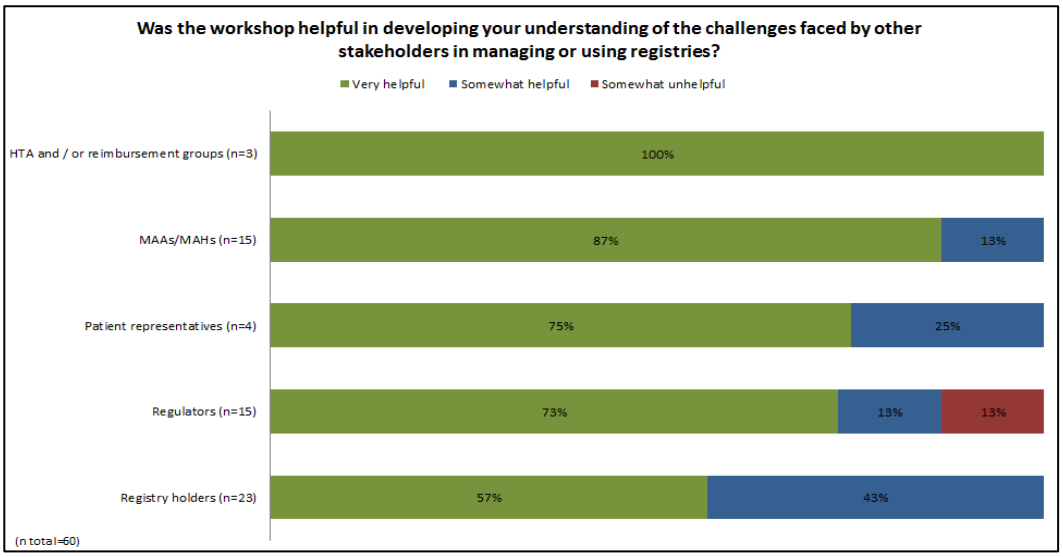


Figure 2: Workshop helpfulness for participant understanding of challenges faced by other stakeholders

All but one (regulatory) respondent agreed with all or many of the recommendations arising from the workshops (Figure 3).

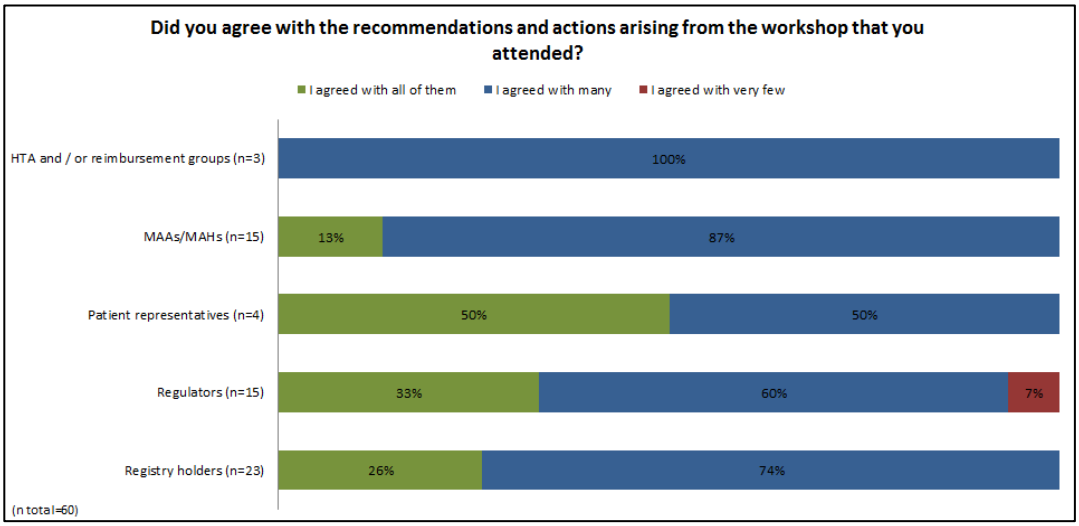


Figure 3: Participant agreement with workshop recommendations according to stakeholder group

Implementation of the workshop recommendations

Most respondents (95%) said that stakeholder implementation of the workshop recommendations would help to improve the use of registries in regulatory evaluations in future although three registry holders felt this would not be the case. Explanations of their views, provided by 58 respondents, fell into four categories: anticipation of benefits or utility that would follow implementation, affirmation of EMA's approach to facilitate improvements, description of existing limitations that would be improved and suggestions for implementing recommendations (Table 1).

Overall, 75% (n=45) of respondents had applied recommendations from the workshop in which they participated but 25% had not done so. MAAs/MAHs and registry holders were most active in this respect (Figure 4). Among 43 respondents providing details of their undertakings, 24 reported that revision was ongoing on matters including data elements, analyses and protocol development while 8 were considering moves to improve or increase collaboration with other partners. Six participants said they had already implemented some recommendations but five had not done so because it was too early for them (Table 1).

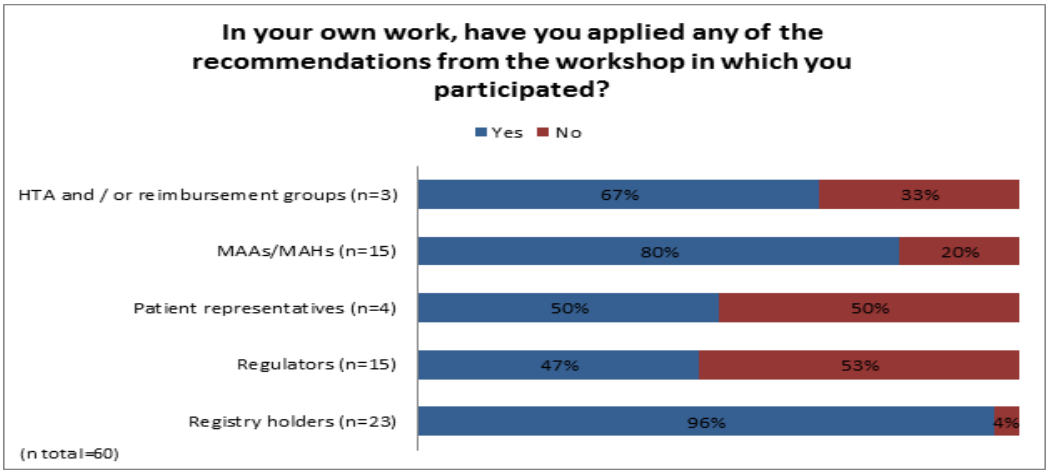


Figure 4: Participant application of workshop recommendations

Sixty-five percent of respondents (n=39), mainly registry holders and MAAs/MAHs, reported that the workshop had stimulated activities to promote the use of patient registries in their disease area but 23% were unaware if activities had occurred and 7% said that none had been undertaken. Figure 5 shows the details for the individual stakeholder groups.

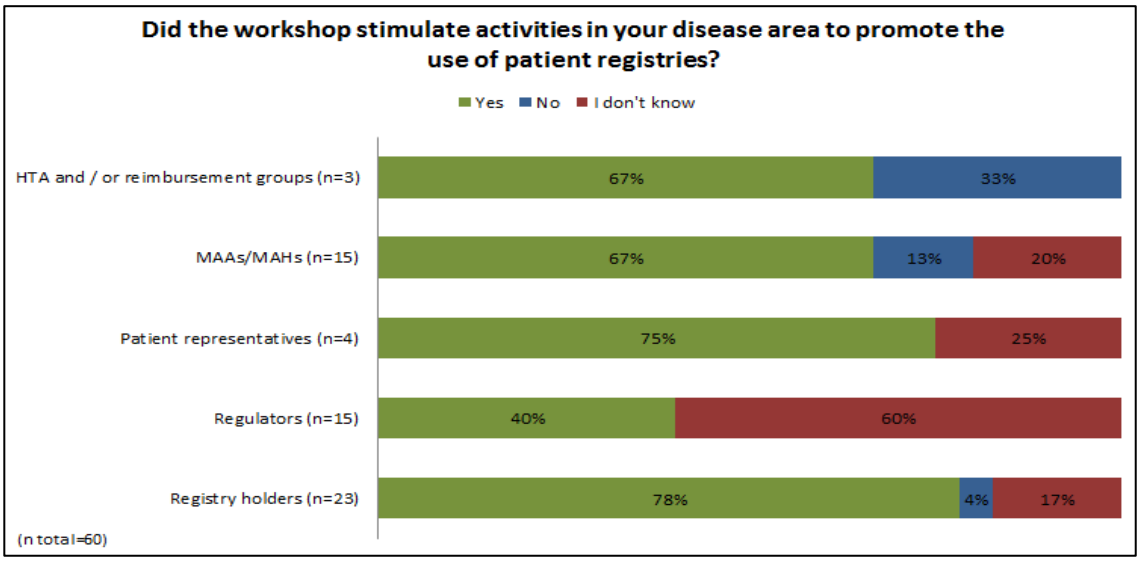


Figure 5: Workshop stimulation of activities to promote patient registry use

Views on patient registries

The workshops led to 53% of respondents changing their view on patient registries, becoming more positive in 50% (n=30) and less positive in 3% (n=2 regulators) while 47% (28) reported no change. The reasons for changed views included developing a more realistic or improved insight on registry data and its potential uses or on its benefits and limitations and the value of stakeholder co-operation (23 respondents), developing an appreciation of the value of the geographic spread of patients that could be evaluated through registry studies and the potential to collect HTA or patient reported outcome information (Table 1). Regulatory respondents whose views became more negative described concerns about the data quality and limits to the amount of clinical detail collected.

Among 11 respondents whose views were not changed, 8 were registry holders who said they already understood the value and limitations of registries. Seven respondents had a positive view of EMA actions and its openness to collaborate across the stakeholder groups (Table 1).

Actions needed from stakeholders

Participants were asked what needed to be done by both EMA and their own stakeholder groups to increase use of registries in supporting regulatory evaluations. Among 56 respondents who commented on EMA, fourteen felt the Agency needed to provide guidance on matters including study outcome measures, data access, harmonisation and quality (Table 1) while ten in each case said it needed to support new projects, methods or procedures that would promote registry use, enforce recommendations, and communicate about and promote registries via avenues such as qualification opinions or advice. Six respondents suggested EMA needed to provide funding or training and six had no new suggestions but expressed support for existing EMA activities.

Fifty respondents provided a stakeholder perspective on the actions required from their own groups. Thirteen thought stakeholders needed to consider registries early in product development and regulatory discussions while another 13 said improvements were needed in registry data collection and quality. Smaller numbers suggested current improvement activities should continue, that stakeholder communication and collaboration were necessary, and that harmonisation across registries in individual disease areas needed to be promoted (Table 1).

5. Discussion

The survey indicates that for the responding participants, the workshops were of value and the role of EMA in catalysing activities is welcomed. In providing an opportunity for different stakeholder groups to meet face to face, one effect of the workshops was to promote understanding of the differing perspectives on registries. This is likely to be especially helpful in fostering future collaborations as well as in planning registry-based studies built on information and data elements that can feasibly be collected in the registries.

There was broad agreement with workshop recommendations on actions needed to increase the use of registries for regulatory purposes and considerable ongoing activity already in implementing many of these, especially among MAAs/MAHs and registry holders.

In providing their views on the actions needed next to increase registry use, there was a clear desire from respondents for EMA guidance in respect of operational matters such as data quality and access as well as support for new projects, methods or procedures relating to registry use. Respondents were also realistic about actions they needed to take as stakeholders themselves. From MAAs/MAHs, this included consideration early during product development of the need for use of a registry while both MAAs/MAHs and registry holders recognised the necessity of improving data quality. The need for registries to have support, including financial support, in order to improve data collection, quality and access was widely noted.

A limitation of the survey is that although all of the stakeholder groups attending the workshops were represented in the responses, the survey is unlikely to be representative of the views and activities of all of the workshop participants. Participants who were active in implementing recommendations were probably most likely to respond and non-responders may have been less active. Nevertheless, the survey demonstrated that the workshops have stimulated activity to increase registry use and this is a positive impact.

It is important that all parties now sustain activities and collaborate to widen the circle of participants if the potential of registries as a whole to contribute to regulatory decision-making is to be realised. This applies especially in the case of products to treat rare diseases and /or needing long term follow-up but is limited currently by concerns about data quality, heterogeneity, governance and access.

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Categorisation of responses to free text questions									
If all stakeholders implement the workshop recommendations, will this help improve use of registries for regulatory evaluations? (All Yes) Explain your view		**Have you applied any of the recommendations ? Please say what you did or why you did not apply any of the recommendations**		**Did the workshop change your view on the potential value of registry data for supporting regulator evaluations? Briefly tell us why.**		**What do you think EMA needs to do next to improve registry use for regulatory evaluations**		**What actions are needed next from your side to improve registry use for regulatory evaluations?**	
Categorisation Summary	**Count: n=58 responses**	**Categorisation Summary**	**Count: n=43 responses**	**Categorisation Summary**	**Count: n=44 responses**	**Categorisation Summary**	**Count: n=56 responses**	**Categorisation Summary**	**Count: n=49 responses**
Benefits / Utility of implementing recommendations	**25 (42%)** (8MAH; 2HTA; 2Pt; 8regH; 5reg)	**Revision undertaken or ongoing: Data /analyses / protocol**	**24 (40%)** (16RegH; 6MAH; 2Pt;)	**Improved / more realistic insight on registry data & potential uses**	**16 (27%)** (5RegH; 8Reg; 2MAA; 1Pt)	**Provide guidance, eg, on study outcome measures, data access, harmonisation, quality, PRO/QoL**	**14 (23%)** (5 MAH; 5 RegH; 3 Reg)	**Increase registry use through early consideration & exploration of availability, data quality, access, protocols**	**13 (22%)** (5MAH; 5Reg; 1Reg; 2Pt;
Affirmation of EMA approach; Praise; Feedback	**15 (25%)** (7RegH; 6Reg; 2MAH)	**Considering moves to improve / increase collaboration with other partners**	**8 (13%)** (2 RegH; 2Reg; 4MAH)	**Already understand / have positive view on value of registry data**	**11 (18%)** (8 RegH; 2HTA; 1MAH)	**Support new projects, methods / procedures to mprove registry data use & standards**	**10 (17%)** (5 RegH; 2 MAH; 2 Reg; 1HTA)	**Improve data collection & quality control**	**13 (22%)** (9RegH; 2MAH; 1Reg; 1HTA)
Stating limitations +/- offering solutions	**14 (23%)** (4MAH; 8RegH; 1HTA; 1Reg)	**Already in place**	**6 (10%)** (4 RegH; 1MAH; 1Reg)	**Improved / more realistic insight on benefits / limitations & value of stakeholder co-operation**	**7 (12%)** (3MAH; 3RegH; 1Reg)	**Communication & promotion of registries, including on qualification, PROs & assisting stakeholder communication**	**10 (17%)** (3 Reg; 4 RegH; 2 Pt; 1MAH)	**Communicate, collaborate, educate**	**9 (15%)** (4MAH; 2RegH 1Reg; 2HTA)
Suggestions on implementing recommendations	**4 (7%)** (1 of each: RegH, Reg, MAH, Pt)	**Too early**	**5 (8%)** (3Reg; 1MAH; 1Pt)	**Positive view of EMA approach / openess**	**7 (12%)** (5MAA; 2RegH)	**Seeking EMA / regulator enforcement of recommendations**	**10 (17%)** (all h'philia; 5MAH; 4Reg; 1Pt)	**Proceed with measures to improve / assure quality, eg, audits, qualification**	**7 (12%)** (4RegH; 2MAH; 1HTA)
	2 (3%) N/A or N/C		**17 (28%)** N/A or N/C	**Appreciation of value of registry geographic spread & HTA / PRO potential**	**3 (5%)** (2Pt; 1MAH)	**Provide support for funding & training,**	**6 (10%)** (5 RegH; 1HTA)	**Promote harmonization across registries**	**5 (8%)** (2RegH; 2MAH; 1Pt)
N/C = no comment; N/A = not applicable; RegH = registry holder; Reg = regulator; MAH = marketing Authorisation holder; Pt = patient representative; QoL = quality of life				**Seeking EMA /Regulator guidance**	**2 (3%)** (2Reg)	**Expressed support for ongoing EMA activities, nil new suggested**	**6 (10%)** (3 RegH; 1Reg; 1Pt; 1MAH)	**Seeking mandatory registry inclusion of all patients; Highlighting funding need**	**2 (3%)** (1RegH; 1Pt)
					14 (23%) N/A or N/C		**4 (7%)** N/A or N/C		**11 (18%)** N/A or N/C

Table 1: Categorisation of respondents' free text comments to individual questions (DREAM link: https://docs.eudra.org/webtop/drl/objectId/090142b28427e1c4)

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Appendix

A. Stakeholder group

Please indicate the stakeholder group in which you belong

- HTA and/or reimbursement groups
- MAAs/MAHs
- Patient representatives
- Registry holders
- Regulators

B. Workshop(s) attendance

Please indicate the workshop(s) in which you participated:

- Cystic Fibrosis Registries (14 June 2017)
- Multiple Sclerosis Registries (7 July 2017)
- CAR T-cell Therapy Registries (9 February 2018)
- Haemophilia Registries (8 June 2018)

C. General questions

A. Was the workshop helpful in developing your understanding of the challenges faced by stakeholders in managing or using registries?

- Very helpful
- Somewhat helpful
- Somewhat unhelpful
- Very unhelpful

B. Did you agree with the recommendations and actions arising from the workshop you attended?

- I agreed with all of them
- I agreed with many
- I agreed with very few
- I agreed with none of them

C. If all stakeholders implement the workshop recommendations, will this help to improve the use of registries for regulatory evaluations of medicines in the future?

- Yes
- No

Please write a few words to explain your view (400 character(s) maximum)

D. In your own work, have you applied any of the recommendations from the workshop in which you participated?

- Yes
- No

Please say what you did or why you did not apply any of the recommendations (400 character(s) maximum)

E. Did the workshop stimulate activities in your disease area to promote the use of patient registries?

- Yes
- No

- I don't know

F. Did the workshop change your view on the potential value of patient (disease) registry data for supporting regulatory evaluations of medicines, for example, in post authorisation safety studies.
- Yes – I now have a more positive view of the value of registry data
- Yes – I now have a more negative view of the value of registry data
- No – it did not change my view on the value of registry data

G. What do you think EMA needs to do next to improve registry use for regulatory evaluations (indicate your stakeholder group) (400 character(s) maximum)
H. What actions are needed next from your side to improve registry use for regulatory evaluations? (Indicate your stakeholder group) (400 character(s) maximum)

D. Specific questions

Regulators

1. In the future, when you evaluate a medicinal product where the use of registry data could be considered, will you suggest this to the MAA/MAH concerned?
- Yes, I will advise the MAA/MAH concerned to consider registry use an to investigate potentially suitable registries
- No, it is up to the MAA/MAH, not the regulator, to propose the use of patient registry data in product evaluation
- No, randomized clinical trials are preferred option for regulatory evaluations and regulators should not encourage MAAs/MAHs to consider registry data

2. Has your Agency/Department developed plans to improve the use of patient registries in your regulatory evaluations?
- Yes, my Agency/Department is developing a plan to systematically consider whether registry data might contribute to product benefit-risk evaluations
- No, but we are aware of the EMA Patient Registries Initiative, so we can ask them if there are potentially useful registries that should be considered for individual evaluations
- No, we would like to improve registry use but we do not have enough resources for the extra work this would involve in our Agency
- No, we do not think that the Agency should encourage use of registries for regulatory evaluations

3. Have you established any plan/mechanism to facilitate communication between registry holders and MAAs/MAHs?
- Yes, within our department we identify registries that could be of value for certain product evaluations and advise MAAs/MAHs to explore this possibility
- No, but we are aware of the EMA Patient Registries Initiative, so we can ask them if there are potentially useful registries
- No, it would be too difficult to integrate it in our procedures
- No, we do not think that the Agency should encourage use of registries for regulatory purposes

4. Are you aware of any registry planning to go through the EMA qualification procedure?
- Yes
- No

5. Have you engaged with other initiatives exploring the potential use of registry data for regulatory or other public health type evaluations?
- Yes
- No

6. Have you facilitated contact between MAAs/MAHs and registry holders?
- Yes

- No

7. Before the workshop, were you aware of the EMA inventory of patient (disease) registries hosted at the ENCePP resources database?
- Yes
- No

8. Have you approached / supported registries in developing a policy on sharing aggregate / pseudo-aggregate or individual patient data and / or establishing a centralised process for requesting and obtaining data?
- Yes
- No

Registry Holders

1. Following the workshop, have you collaborated with any other registries in your disease area or specialty organisations in order to set-up or to join a registry network?
- Yes
- No

If yes, please indicate (e.g. European Reference Networks for Rare Diseases, contact with other registries in same disease area, moves to join a registry grouping, other)
2. Do registries in your disease area already collect a common set of data elements?
- Yes
- No

If NO, are you collaborating with other registries in your disease area to agree on common core data elements to be collected by everyone in order to support regulatory evaluations, for example, post-authorisation safety studies?
- Yes, we were already collaborating with other registries to establish a common core data-set prior to the workshop
- Yes, following the workshop, we have started collaborating with other registries to establish a common core data-set
- No, we believe our own registry has adequate data for regulatory studies and a common core data set is not needed
- No, we think it would be too difficult for registries in our disease are to agree on a set of common core data elements

3. Following the workshop, have you implemented common definitions for the core data elements collected by registries in your disease area?
- Yes, we were working on this prior to the workshop
- Yes, following the workshop, we have joined discussions with other registries in our disease area to agree and implement common definitions
- No, we think it would be too difficult for registries in our disease area to agree on common definitions for core data elements
- No, there is no need for common definitions for the core data elements in our disease area

4. Following the workshop, do you think you need to make any improvements to your registry quality assurance processes?
- Yes, in data consistency and accuracy
- Yes, in completeness
- Yes, in staff training measures
- Yes, in other processes (please specify below)
- No

Please specify any other quality assurance processes
5. Following the workshops, have you implemented changes in your data verification procedures?

- Yes
- No

Please provide further if you wish (400 character(s) maximum)

6. Have registries in your disease area agreed on a core protocol for doing post-authorisation safety studies or other post authorisation studies?
- Yes
- No

7. Are you considering seeking an EMA qualification for your registry?
- Yes
- No
- We have already obtained an EMA qualification opinion

8. Have you made or are you planning to make any change in your registry regarding data access or data sharing with regulators or MAAs/MAHs?
- Yes- patient consents need to be amended to facilitate access and sharing
- No – we are able to provide aggregated data and do not plan access to or sharing of more detailed data
- No –this would be too difficult

Please provide further if you wish (400 character(s) maximum)

9. Following the workshop, have any MAAs/MAHs contacted you about co-operating in a regulatory-related study?
- Yes
- No

If yes, how many MAAs/MAHs made contact? What kind of study was proposed?

10. Do you have a process for sharing aggregate and individual patient data?
- Yes, we already had a process in place before the workshop and we have made no changes to it
- Yes, we already had a process in place and following the workshop, we have amended it / plan to amend it
- No, but following the workshop we are developing a process for data sharing
- No, we do not have a process for data sharing

11. Do you have a policy for sharing aggregate and individual patient data?
- Yes, we had a policy in place before the workshop and we have made no changes to it
- Yes, we had a policy in place before the workshop and we have amended it following the workshop
- No, but following the workshop, we are developing our policy
- No, we do not have a data-sharing policy

12. Have you made contact with MAAs/MAHs with products in your disease area to let them know about the type and detail of data collected in your registry?
- Yes
- No

13. Have you added your registry information to the ENCePP registries inventory?
- Yes, we have already included the registry details in the inventory
- No, were/are not aware of the ENCePP registries inventory
- No, we are not interested in joining the ENCePP inventory
- No, we were/are not aware of the ENCePP registries inventory, but we will include our details

ONLY for Cystic Fibrosis Registries Workshop participants. What changes, if any, have you implemented following the EMA qualification opinion recommendations? Please write a few words in the box below to explain
ONLY for CAR T-cell therapy registries Workshop participants. What changes, if any, have you implemented following the EMA qualification opinion recommendations? Please write a few words in the box below to explain

MAAs/MAHs

1. Do you think data from patient registries have any place in supporting evaluations of products that are currently in your business pipeline?
- Yes
- No

Please provide a comment if you wish
2. Has your company ever used data from a patient registry to support regulatory evaluations of a product?
- Yes - for pre-authorisation studies
- Yes - for post-authorisation studies
- Yes - for both pre- and post-authorisation studies
- No
- I don't know

3. Is your company planning or conducting any studies currently using patient registry data?
- Yes, a study is under way currently
- Yes, we have developed / are developing a preliminary study protocol with a registry holder
- Yes, we have developed / are developing a preliminary study protocol for exploring with a regulator
- No, we are not planning or conducting any studies currently

4. Do you have a mechanism to systematically explore the use of suitable patient registries at any stage of your product development activities?
- Yes, we already had a mechanism in place before the workshop
- No, but following the workshop, we are putting a mechanism in place
- No, we would only consider the use of patient registry data if advised to do so by the regulator

5. Would an EMA qualification of a relevant patient registry encourage you to use data from that registry in post-authorisation studies of your company products?
- Yes - EMA qualification of the registry would provide assurance about the quality of the registry for doing a study
- No – Product registries are our preference for post-authorisation studies, not patient registries
- No – EMA qualification would not encourage us to use the registry for a study

Please provide further comment if you wish
6. Do you know about the EMA inventory of registries hosted at the ENCePP resources database?
- Yes
- No

Patient representatives

1. Have you engaged with registries in order to plan or improve communications with patients about the potential benefits and risks of sharing registry data to assist in medicines evaluations?
- Yes, I am already engaged with registries and we have a successful collaboration
- Yes, following the workshop, I have made contacts with patient registries about promoting the benefits and risks
- No, I have not explored the possibility

If yes, please indicate the name of the registry
2. Have you collaborated with any registry or network on Patient Reported Outcomes / Quality of Life measures that could be included in your disease area registries?

- Yes, I collaborated with a registry / network prior to the workshop
- Yes, following the workshop, I have started to collaborate on this with a registry network
- No, I have not explored the possibility

If yes, please indicate the name of the registry / network; add any other comments relevant
3. Have you had contact with any MAAs / MAHs about any aspect of patient input to registries?

- Yes – prior to the workshop, I have collaborated with MAAs / MAHs on patient-related aspects of registry data
- Yes – following the workshop, I have had contact with MAAs / MAHs on patient-related aspects of registry data
- No – but I would be glad to discuss this if I was approached by a MAA / MAH

Please add any views on contacts with MAAs / MAHs regarding patient input to registries

HTA and/or reimbursement groups

1. Have you collaborated with any registries regarding data elements to be included in the registry that would assist in health technology assessments (e.g. patient reported outcomes or quality life measures)?

- Yes, I have collaborated / am collaborating with a registry network
- No, I have not collaborated with registries but plan to explore registry use for data on relevant products in the future
- No, I do not think registries could provide necessary data

2. Have you contacted registries or patient representatives to explore the options for assessing patient reported outcomes or quality life data?

- Yes
- No

3. Are you aware of the EMA inventory of registries hosted at the ENCePP resources database?

- Yes
- No

Please use this area for any additional recommendations or observations you wish to make