

Outcome of public consultation on ICH Reflection Paper on Patient-Focused Drug Development (PFDD)

Summary report of comments received during the public consultation

1. Background and consultation

The PFDD Reflection Paper was endorsed by the ICH Assembly in November 2020. It identifies key areas where incorporation of the patient's perspective could improve the quality, relevance, safety and efficiency of drug development and inform regulatory decision making. It also presents opportunities for development of new ICH guidelines to provide a globally harmonized approach to the inclusion of the patient's perspective in a way that is methodologically sound and sustainable for both regulated industry and regulatory authorities.

The PFDD Reflection Paper (RP) was published on the ICH and other ICH Regulators' websites for public consultation up to March 2021. ICH would like to thank all the commenters for their input. This document, to be read in conjunction with the updated and final version of the reflection paper, presents a high-level overview of the comments received with indications on how these will influence the next steps in this ICH strategic priority area.

2. Contributors

In total, 313 individual comments were received from 38 stakeholders including:

- 12 private companies
- 11 learned societies
- 7 patient organizations
- 3 ICH Members
- 3 individuals (patient/patient advocate/academia)
- 2 industry associations

3. Summary of main points raised during the consultation

Generally, there was strong support for the initiative and for the development of the guidance as outlined in the reflection paper. This support was received across the broad range of stakeholders responding. Some examples:

"This is a very timely and needed paper"

"High appreciation for ICH taking the initiative to acknowledge importance of patients perspectives."

"As a community, we believe in working with patients, patient organizations and health charities to ensure their views, perspectives, and voices are part of the drug development process from start to finish. We believe this approach will lead to medicines better designed for patients and their particular needs."

"The reflection paper is very well written, structured and covers the key issues to prepare the implementation of an important novel instrument in drug development"

ICH Reflection Papers are intended to articulate ideas for potential future harmonisation work, lay out an area where harmonisation work is needed, or make proposals for a series of future topics for harmonisation. As harmonisation is achieved through the development of ICH guidelines via a process of scientific consensus, ICH has considered the current consultation by categorising the majority of the input / comments into **3 areas**:

1. Modifications proposed within the reflection paper, including mechanisms for engagement of non-ICH stakeholders in the ICH process
2. Recommendations for the development of the proposed guidance,
3. Recommendations on the use of existing tools / research / initiatives.

A large number of the comments received can be attributed to more than one of the above categories.

3.1 Text modifications proposed to the reflection paper

Comments proposing changes to the reflection paper itself were considered. In most instances, proposals for amending the reflection paper were complemented by detailed rationale and considerations that, though valuable, go beyond the scope/level of detail intended for ICH reflection papers. The paper has been revised under this assumption and considering ICH's scope of activities and membership. As stated in the first RP version, concept papers and business plans of the intended guideline drafting activities will include specific plans for public consultation and engagement.

3.2 Recommendations for the development of the proposed guidance

ICH has identified a series of overarching themes and intends these to be further considered, in conjunction with the underlying comments, in the intended upcoming guideline activities:

Criteria for data robustness and quality

Several comments requested that the guidance should include a clear outline of what constitutes acceptable and/or desirable criteria for qualitative data; "what level of 'robustness criteria' is acceptable for regulators" (e.g. how endpoints suggested by patients can be robust enough, how many patients needed for their preferences to be considered relevant and 'patient focused?', how to select patient population). In this line, guidance is also requested on how patient preferences are weighed and incorporated into wider evidence base for decision making, together with an overview of quality and good practice standards to guide sponsors & regulators to improve standard and confidence in this type of evidence. Finally, a comment emphasised that PROs and patient preferences, collected in a robust systematic manner, should be given same weight as clinical data.

Terminology / definitions

There were numerous comments received requesting clarification on the terminology used; define terminology as there are too many different terms used; harmonisation is needed to avoid miscommunication, e.g. 'patient' / 'patient centricity', 'patient experience data', 'PFDD', PPI, patient engagement vs patient involvement, patient preferences, etc.

There were recommendations to refer to specific existing definitions and to potentially include a glossary in the guidance. It was also recommended to maintain the use of generic terms, e.g. rigour, bias-free, which are not so usual in qualitative research.

Inclusion criteria

Many comments highlighted the need to consider the following groups when collecting patient data:

- All disease areas and disease states (including late stage)
- All ethnic groups (culturally validated PROMs are under-representative of ethnic minorities)
- Children, adolescents and young adults in all studies when ethically appropriate
- Caregivers (e.g. mental health, minors)
- Older adults in all trials with therapeutics that are primarily taken by older adults
- Different communities to address diversity - patient needs different in different communities
- All fields, e.g. gene therapy, vaccines, non-drug therapies, personalised medicine
- Design trials that support patient equality regardless of disease stage, age or geography

Involvement of patients/carers

Several comments emphasised the importance of engaging with patients at the start of drug development when defining goals, and to continue all along the drug lifecycle. Too much focus on disease progression, not on patient experience and AEs not fully understood from patient perspective

- need to engage in dialogue with patients.

Patients/public should be involved in development of all new standards/tools to assess QoL during treatment (e.g. questionnaires). Collection of patient information should be transparent and understood by patients and guidance should include how and when patients should be kept informed, and how best to explain benefit/risk (text/graph etc). It was suggested that the information collected should derive from expert patients, i.e. people who know in-depth the pathophysiology, clinical expression, complications and multi-disciplinary management of their disease and are familiar with drug development processes and policies.

Research methodology

Various comments related to methodological aspects for consideration in the proposed guidance;

- include all types of COAs with a move towards concepts rather than current 'instrument led' approach. COAs should be agreed among all stakeholders and they are equally valuable as patient preferences. Include therapies that cannot be measured by short term COAs, but impact on QoL due to route of administration etc.
- Mixed method research best suited to generate patient centred evidence and novel methodologies / test theory approaches should be acknowledged/included.
- Consider how to evaluate patient outcomes in progressive conditions, or with no historical data and how to link to bio clinical measures.
- Systematic patient preference studies may not be necessary in many clear-cut situations but when they are, methods should follow agreed standards and consider how to account for variability of patient preferences.
- Include issue of defining clinically meaningful within-patient score changes, and collection, analysis, and interpretation thereof, at different stages of the clinical trials and in consultation with patients.
- Patient insights should be collected throughout development, not only during CT.
- including PROs in trials from phase I would complete reliable data generation.

- Focus on limited number of (existing/new) patient preference methods (not be over-ambitious).
- Include ethical aspects (i.e. when ethics committee should be consulted).

Real world evidence

Several comments included the need to include PROs generated in a real-world setting with guidance on tracking patient outcomes in this context, and to ensure that 'field experience' i.e. from pharmacists / primary care is included.

Novel approaches

Input received highlighted the need to include all types of data collection, especially novel approaches, such as social media listening, wearables, remote monitoring, e-consent, home visits. BYOD technology, AI, machine learning etc. Interactive monitoring can be effective strategy to continuously engage with patients - to enhance adherence, safety and enable tailored modifications. The increasing use of devices to measure/monitor patients in a decentralised manner requires clear requirements in the approval process of patient data perspectives obtained through a device.

Non-health benefits

It was highlighted to include non-health related benefits for patients, e.g. convenience, choice of drug formulation, dosing, packaging, devices, etc, also beyond disease factors (e.g. psychosocial aspects).

Bias

Several comments mentioned bias, such as how to select the right patients to provide input, without selection bias is a challenge, how to prevent cherry picking the patients whose opinions are preferred and how to handle different types of patients having different opinions?

Requirements

Some comments addressed potential requirements, e.g. preference information should be made mandatory by regulators (esp. for borderline data) especially for rare diseases. Will there be new requirements for sponsors? Aim should be to improve quality but no unrealistic expectations.

Flexibility

A few comments asked to ensure the guidance be flexible and adaptable with appropriate patient perspective measures for different conditions / treatments. Standards should not be too complex and time-consuming to delay / prevent benefits of patient perspectives included.

Sustainability

It was mentioned several times to address sustainability of the guidance and avoid future duplication.

Data use / transferability

Several aspects related to data use were included, such as how will data be scored / coded, and to consider transferability of data between diseases and that the data collected must fall within FAIR principles.

Harmonisation

One comment highlighted that all COAs developed should ultimately be automatically accepted in all ICH regions.

Societal benefits

The importance to highlight the benefits for society, not only individuals was mentioned.

3.3 Recommendations on the use of existing tools / research / initiatives

Comments frequently emphasised the need to align, harmonise or build upon existing tools and guidance, where appropriate, and not to 'redo' standardised methodologies that exist. Existing methodologically sound, safe and easy to use collection tools can provide predictive capabilities for further enhancement. Many references to existing initiatives, tools, research and guidance were provided. These, in conjunction with the underlying comments, are intended to be flagged in the upcoming guideline activities for expert consideration.

4. Overall Summary

Overall, the feedback received from a broad range of stakeholders widely supports the initiative for the development of guidance for inclusion of the patient's perspective into drug development and inform regulatory decision-making. There were no major objections raised or significant obstacles foreseen for the development of guidance. Substantial feedback highlights the momentum and encouraged ICH to initiate the work as soon as possible, and to also engage appropriately with non-ICH stakeholders throughout the process.

The updated, and final, version of the reflection paper reflects the comments accepted by ICH. The feedback received taking the form of tangible recommendations / proposals for the guidance development considered to fall in the scope of ICH activities will be considered when guideline work commences, as will be the numerous references to existing tool and guidance.