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**Standfirst**

*Patients and our diverse society are beneficiaries of scientific discoveries, new technologies and improved medications; but they also can and should be able to contribute to these discoveries through participation in clinical studies, co-design of research and input into regulatory processes* **say Lee Aiyegbusi and colleagues.**

## The importance of Patient and Public Involvement and Engagement

The COVID-19 pandemic has generated greater public and government awareness of the importance of the life sciences and regulation of new interventions. Regulatory agencies play an essential role in independently evaluating the safety and effectiveness of interventions, in a robust and timely manner to determine if they should be approved for use to treat patients.

To deliver effective interventions, the public need to trust the regulatory processes. A lack of public trust has been highlighted through anti-vaccine campaigns. One way to promote patient and public trust in regulatory processes and ensure that regulations are responsive to their needs is through greater patient and public involvement and engagement (PPIE) in regulatory science initiatives and healthcare regulation.

Patients and the public provide unique insights based on their lived experiences which cannot be substituted by expert knowledge from other stakeholders. These insights and perspectives may influence the eventual success or failure of new discoveries and technologies.[1] Furthermore, in line with the widely used principles of biomedical ethics (i.e. autonomy, beneficence, non-maleficence, and justice) patients and the public should be actively involved and engaged in regulatory science and processes, which may affect them directly or indirectly.[2]

Here we highlight key PPIE initiatives by international regulatory agencies and regulatory science centres, provide patient perspectives on PPIE, and suggest strategic areas for improvement. Supplementary Figure 1 presents the key stakeholders in regulator science and Supplementary Box 1 provides the definition of key terms.

## Key PPIE Initiatives by international regulators

International regulators have undertaken PPIE initiatives and published strategic documents on PPIE. Here we highlight and briefly discuss some of their recent initiatives with further information provided in Supplementary Table 1.

The U.S Food and Drug Administration (FDA) recently convened a series of public workshops with patients/advocates, researchers, practitioners, and drug developers to inform the development of four patient-focused drug development (PFDD) guidance documents.[3] The documents are intended to provide methodological guidance to foster the systematic collection of useful patient and caregiver input to inform medical product development and regulatory decision-making process.[3]

Patient and consumer organisations were consulted during the development of the European Medicines Agency (EMA)'s regulatory science strategy 2025. They provided substantial input that shaped several strategic goals with core recommendations for patient relevance in evidence generation, innovation in clinical trials, benefit risk assessment, and market access.

Following the Independent Medicines and Medical Devices Safety (Cumberlege) Review, the UK's Medicines and Healthcare products Regulatory Agency (MHRA) has made substantial progress in integrating PPIE in its work. Its new delivery plan 2021/23 "Putting patients first – A new era for our agency" highlights the importance of engagement with patients and their outcomes which the MHRA have put at the heart of the delivery plan. The Patient & Public Involvement Strategy, published in September 2021, was informed by extensive public consultations, and sets out how the Agency will deliver the change across five key workstreams.

Work is underway to develop Health Canada's Patient Involvement Strategy, with the goal of integrating patient expertise in Health Canada's policy and regulatory decisions. Key areas of development revolve around structural and cultural changes to encourage patient involvement in Health Canada's regulatory work, potentially including, for example, new patient-focused guidance, and increased patient representation on relevant scientific and advisory committees.

## PPIE initiatives by public regulatory science centres

Academic/not-for-profit regulatory science centres play an important role in fostering PPIE in regulatory science and healthcare regulation. These organisations are often affiliated with university healthcare centres and interact directly with patients, collating and presenting their findings to regulators or policy makers.

The FDA's Centers of Excellence in Regulatory Science and Innovation (CERSIs) are collaborations between the FDA and academic institutions to advance regulatory science through innovative research, training, and scientific exchanges. In Europe, several Centres of Excellence exist. For example, the Copenhagen Centre for Regulatory Science aims to improve the drug regulatory system and contribute to an improvement in health of society and sustainable drug innovation. The UK's, Birmingham Health Partners Centre for Regulatory Science and Innovation (CRSI) works with multi-stakeholder groups, including patients, in the development of guidelines (Supplementary Box 2).

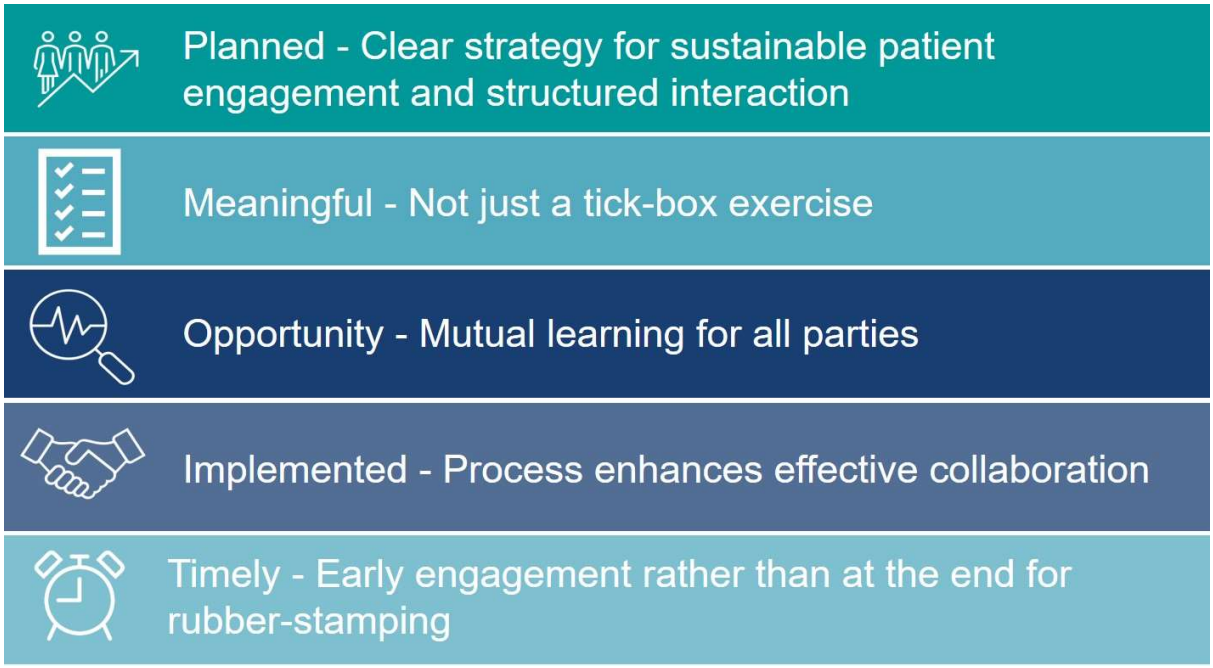
## Patient Advocacy perspectives

The key elements of PPIE proposed by Kathy Oliver, Patient Advocate and Chair of International Brain Tumour Alliance (IBTA), are presented in Figure 1. Elaine Manna, patient partner, and co-author of guidelines for artificial intelligence trials noted, *"It is vital for patients to be equally involved in their healthcare, to understand how decisions are made and to have agency in the decision-making process. Trust and nurturing are major factors for progress."*

*"Being informed is empowering and often re-assuring for patients and carers. Being given a voice can alter personal perceptions of oneself and others. Being heard can be a confidence building and uplifting experience. We can all learn from each other.*"

*"It is essential that patients and citizens have a voice and are accepted as* ***true partners*** *in these endeavours."*

**Figure 1: Elements of PPIE** (proposed by Kathy Oliver, Patient Advocate and Chair of IBTA)




## Strategic areas for development of PPIE in regulatory science

*International collaboration* - The potential benefits of PPIE could be leveraged by international collaboration and sharing of good practice by stakeholders including regulatory agencies, regulatory science centres and patient groups. Organisations such as the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) which bring together regulatory authorities and the pharmaceutical industry to discuss scientific and technical aspects of drug registration have a role to play. Continuously sharing best practices at forums such as the FDA/EMA Patient Engagement Cluster will ensure that the quality of PPIE in regulatory science is enhanced among stakeholders, reduce inefficiencies, and help optimise approaches. Independent nonprofit, public-private partnerships, can also play an important role such as the US Critical Path Institute or the work of SISAQOL-IMI providing a neutral environment for industry, academia, regulators, and other government agencies, to work together with patients and the public to accelerate and de-risk the medical product development process.

*Organisational approach* - PPIE is often conducted ad hoc on a project-by-project basis, limiting its effectiveness. Organisations whose activities are informed by regulatory science need to take a broader perspective, by embedding PPIE within

the wider infrastructure of the organisation.[4] There is a need for a strategy for systematic PPIE at an organisation level, which patient and the public contribute to and regularly review.[4] Appropriate training needs to be provided for staff, and multidisciplinary collaborative working should be encouraged. Practical considerations to facilitate PPIE are detailed in Supplementary Box 3.

*Inclusivity and diversity* - The views and input of all groups should be effectively captured and incorporated in regulatory processes to prevent the widening of existing health inequalities or creation of new ones. There is a tendency to focus on patients who are the immediate beneficiaries of medical research. However, the broader ramifications of medical research and drug development may affect everyone in society and so participation by members of the public should be encouraged. It is essential to engage with individuals from underserved groups, for example, minority ethnic populations, elderly, and teenage/young adult populations. As these individuals may be less engaged with PPIE, strategies to facilitate their involvement in PPIE activities should be co-designed with members of these groups.

*Communication* - Effective continuous communication channels with PPIE group members can help sustain engagement over time. Patients and the public should be regularly informed about how their feedback has been used to inform regulation. Effective communication and transparency could build trust and help demystify the regulatory process and correct patient and public misconceptions. Concerns raised by PPIE members should be addressed promptly.

*Measuring impact* - There is a need to develop effective methods to record PPIE and capture evidence of its impact. Regularly monitoring and reporting key performance indicators could facilitate the assessment of PPIE impact.[5] The GRIPP2 checklist, international guidance for reporting of PPI in health and social care research can be used to document evidence of PPIE.

## Conclusion

Patients and the public have a voice and several regulators, are listening. PPIE impacts the application of regulatory science in medicine and healthcare regulation. Patient and caregiver experiences of disease and treatment provide valuable insights and inform regulatory decision-making, alongside broader PPIE activities

throughout the medicine development lifecycle. It is ethically important as patients and the public are the end consumers of scientific discoveries and therapies. PPIE builds trust by enhancing patients' and the public's understanding of the activities of regulatory agencies, which could in turn improve the uptake of new therapies. There is an ongoing need to listen to and meaningfully involve patients and the public on a sustainable basis.

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**Conflicts of Interest**

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