Engaging patients in medicines regulation: a tale of two agencies

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The European Medicines Agency and the US Food and Drug Administration have committed to engaging patients in their regulatory processes to promote patient-focused medicinal product development, as well as improve transparency and trust in the regulatory system. Here, we highlight exchanges of experience between the agencies and some impacts on patient engagement.

The European Medicines Agency (EMA) and the US Food and Drug Administration (FDA) both consider that the voices of patients in medicines regulation are essential, as they bring the unique perspective of someone living with a disease, as a patient or carer. This perspective complements the medical and scientific information that is used when evaluating medicines for regulatory approval. For example, patients can highlight unmet needs for their condition that they consider to be particularly important, which might differ from the standard end points evaluated in clinical trials.

The EMA and the FDA also have a substantial history of collaboration with each other, and in 2009, terms of reference were agreed and exchanges formalised between the two agencies. In addition to hosting a permanent liaison official at each agency, visits and fellowship exchanges take place regularly through which staff can interact, participate in meetings and learn more from the corresponding department.

To further enhance interactions, approximately 30 'cluster' conference calls on specific areas that span the interest and work of both agencies are organised, including areas such as oncology, orphan medicines and vaccines. A cluster on patient engagement was established in 2016, resulting from reciprocal fellowship exchanges between the EMA and the FDA. The purpose of the fellowships was to gain an overall understanding of how each agency engages with patients, including practicalities such as how and when they are invited to collaborate, how they are selected and screened for potential conflicts and what training and support is provided to optimise participation. Here, we describe some of the learnings from these interactions, as well as examples of the impact so far of the two agency's efforts to improve patient engagement.

Mutual learnings and exchange of experience

During the patient engagement fellowship exchange and other interactions, staff at the EMA and the FDA identified several areas with similar objectives and different approaches where each agency could benefit from the other's experience. Three areas for each agency are highlighted here.

EMA. The first example is public hearings, which increase transparency, empower citizens, improve public understanding of the scientific and regulatory processes, and add value to the overall process. The FDA has extensive experience of leveraging public meetings and advisory committees to provide independent opinions and recommendations from outside experts and the public on specific diseases, as well as regulatory, policy and safety issues. The EU pharmacovigilance regulation introduced in 2012 enabled the EMA and its Pharmacovigilance and Risk Assessment Committee (PRAC) to begin holding public hearings, and the EMA has since held two public hearings, during which patients are given the opportunity to provide testimonies of their experience with the medicine under review.

Another example is the FDA's Patient Representative Program (see Related links), which comprises a pool of patients who provide input to inform the agency's decision-making on medical products. The unique aspect is that these patients and caregivers are appointed as Special Government Employees to serve the FDA on a temporary basis, and are trained and compensated for their involvement. The EMA already interacted with an extensive network of more than 300 patient organisations, and has now established a register for individual patients, who have the opportunity to be trained and involved in various aspects of the EMA's work on a voluntary basis (see Related links).

Thirdly, the FDA has training videos such as 'FDA Basics'. It also uses live chats and webinars to share information, and sends communications tailored to specific patient communities. The EMA has now also created 'EMA Basics' videos on fundamental aspects of the agency and its work (see Related links). In addition, the EMA produces a monthly newsletter with key information on human medicines, which it aims to expand to include more patient-specific themes.

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FDA. One example is direct involvement of patients in decision-making. Patients are involved throughout the medicines regulatory process at the EMA and have voting rights as members of four of the six EMA scientific committees for human medicines (the Committee for Orphan Medicinal Products (COMP), the Paediatric Committee (PDCO), the Committee for Advanced Therapies (CAT) and PRAC). In the Committee for Human Medicines (CHMP) and its Scientific Advice Working Party, patients are systematically invited to participate in discussions on benefit and risk with the applicant and early discussions on medicine development, respectively. FDA patient representatives may serve on FDA advisory committees, where they provide input directly to the committee and have voting rights or act as consultants early in the product development process for review divisions. In addition, listening sessions for patients with rare diseases have been established to further capture the patient voice in early-stage research and development (see Related links).

Another example is the EMA Patients and Consumers Working Party (PCWP), which is a forum for exchange of information that was created following adoption of a framework for interactions with patient organisations (see Related links). The PCWP meets 3–4 times a year and is consulted on a 'case-by-case basis', as needed. Topics of discussion have included Priority Medicines (PRIME), implementation of new EU legislation, and selection of a symbol for additional safety monitoring (a black triangle). Coinciding with the tenth anniversary of the PCWP, the FDA and the Clinical Trials Transformation Initiative (CTTI) announced their collaboration and launched a new work group called the Patient Engagement Collaborative (PEC), based on the PCWP model (see Related links). The PEC is patient-led group of patient organisations and individual representatives who discuss how to achieve more meaningful patient engagement in medical product development and related regulatory discussions at the FDA.

A third example is the review of documents. Prior to publication, patients review EMA documents destined for the public such as all package leaflets, safety communications and medicines summaries. This ensures the readability and appropriateness of the content and increases transparency. The FDA evaluated its 'For Patients' webpage, a resource for the patient community that allows patients and their caregivers to find trusted information directly from the agency, and is now leveraging PEC members and other patient organisations' input on updates being made to content specific to patients' interests.

Examples of input from patients

EMA. In one scientific meeting, patients with osteoporosis emphasized the importance of including wrist movement as an end point measure in addition to hip movement. Wrist movement was important as it would enable them to dress themselves, make a cup of tea and so on — benefits that were not considered by the company or other experts.

During a discussion on a medicine for soft tissue sarcoma, a patient challenged the company's choice to limit the target population to those with better prognosis, which resulted in further discussions regarding the level of homogeneity in inclusion criteria and interpretable trial data. The patient also provided insights regarding toxicity of the proposed treatment, including how it may be perceived by patients and the potential impact on trial enrolment and drop-out rate.

FDA. During a discussion around safety monitoring in a haemophilia gene therapy listening session, patients and caregivers present had consistent interest in prioritizing safety in clinical trials and were open to frequent safety monitoring visits to ensure risks are caught early and addressed quickly. The requirement for long-term follow-up procedures, including invasive procedures such as a liver biopsy, once a year was generally not considered burdensome.

In a Fabry disease listening session, patients and caregivers indicated enzyme replacement therapy (ERT) resulted in improved kidney function and helped to relieve fatigue. However, gastrointestinal symptoms were the most common symptoms mentioned by Fabry patients and caregivers at the meeting, and often did not improve significantly as a result of ERT.

Conclusion

For the EMA and the FDA, there is no question of the importance of patient engagement and the added value it brings to the regulation of medicinal products by promoting the development of treatment options that better reflect their needs and priorities.

It is also important to appreciate that citizens are frequently not aware of the existence or the precise role of the medicines regulator in their region and how they can be directly involved. One of the roles of the regulator is to ensure that public health is protected, and raising awareness of the agency as a source of trusted and reliable information can be part of this. Our responsibility is the same for all patients: to ensure that they receive the safest, most effective medicines and that, as much as possible, their needs and concerns are considered in the evaluation process. Given the global aspects of medicine regulation, collaborating and sharing experiences, information and resources between agencies is also vital, and exchanges such as those seen through the collaboration between the EMA and the FDA are helping to improve patients' trust in and understanding of the regulatory process.

Competing interests
The authors declare no competing interests.

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Getting involved with EMA: https://www.ema.europa.eu/en/partners-networks/patients-consumers/getting-involved
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