Report from the IMI-EMA-FDA Regulatory Science Summit – Collaborative research through public-private partnership in support to advancing regulatory science

Introduction

The Innovative Medicines Initiative (IMI) held its 5th IMI-EMA-FDA Regulatory Science Summit, organised in collaboration with the European Medicines Agency (EMA) and the US Food and Drug Administration (FDA) on 4th and 5th December 2017 in Brussels.

Over 40 representatives from the regulatory agencies [EMA, FDA, EU Heads of Medicines Agency, the Pharmaceuticals and Medical Devices Agency (PMDA)], the European Federation of Pharmaceutical Industry and Association (EFPIA), the European Commission (Directorates General Research and Innovation and Health and Food Safety), the IMI2 Scientific Committee and IMI Programme Office participated.

The overall goal of this meeting was to:

- get input on the proposed research priorities planned for 2nd half of IMI2 (2018-2020) – 'Think Big' topics;
- discuss questions/gaps of particular interest to regulatory agencies to further maximise the transformational impact of the IMI proposed topics on drug development and patients' access to innovation;
- share lessons learned and opportunities for enhanced and timely regulatory interactions.

This meeting was organised to enable all attendees to bring their perspectives into the discussion and exchange experiences and ideas through open dialogue. In particular the Summit offered an opportunity for regulatory stakeholders to come together and discuss in more depth the research questions in the broad topic areas that are relevant from regulatory science and public health perspective, and to help in shaping the 'Think Big' IMI topics under consideration.

The meeting was opened with keynotes from the lead representatives of IMI, FDA, EMA and EFPIA on the vision for future innovation in drug development and patients' access.

The high-level discussion provided key messages that are outlined below around the value of collaboration, the evolution of science and its impact on regulatory science, the existing gaps to be addressed and the need for tangible and impactful outputs.

These key points also set the scene for a more in-depth discussion on the proposed research topics under consideration in the following four 'Think Big' areas: Big Data & Digital Health, Clinical Trials and Regulatory Pathways, Immunology & Microbiome and Antimicrobial Resistance. Since the Summit, the vast majority of the proposed topics discussed were launched through the IMI2 Call for proposals published in 2018.

Key outputs

Throughout the discussion considerations were given on how to ensure maximum impact of the IMI-funded projects for European patients and global health, and how regulatory stakeholders could help in ensuring they engage effectively for better outcomes. The need for open and transparent stakeholder dialogue was felt to be an important enabler to achieve these objectives. The innovative pharmaceutical industry stressed its readiness to play its part and committed to working together to collectively deliver value for patients and society.

Nature of collaboration

- Collaboration is key. The ability to succeed in step-changing medicines innovation is contingent on partnerships in vibrant ecosystems. We need to derive new ways of generating evidence through sharing of data and knowledge, using novel approaches such as Master Protocols, Clinical Trial Networks, Adaptive Designs, Bayesian Approaches, Real World Data and Evidence, Developing and Qualifying Predictive Biomarkers and PRO Instruments to understand what patients care about most. We should work together on such efforts.
- More intra-sector collaboration but also inter-sector collaboration is required. This in turn requires safe harbours such as IMI to facilitate collaboration between different stakeholders, build the trust and pilot new ideas. It is therefore important to identify areas where we must work together to develop new approaches for realising the full potential of new technologies and innovation. All of us have a responsibility and accountability to make the best use of taxpayer funded-research, and define the value proposition accordingly.
- Cultural barriers exist in industry and in the regulatory system that need to be overcome to embrace a much needed radical change in the way drugs are developed.
- Regulatory practice should support the R&D opportunities. Technology moves fast, regulatory changes are slow. Change in regulatory practice does not necessarily need change of framework but regulatory practice should be adapted to support advances in innovation and technologies. It therefore requires collaboration and partnership between regulators and industries which, in the context of IMI, may need slightly more, or different, emphasis than what exists in the routine interactions (such as in marketing authorisations and post-authorisation procedures). Continued and early dialogue help increase mutual understanding and expectation setting between regulators and IMI project partners, which should result in better availability and acceptability of study outcomes for the benefit of public health. The emphasis in this context is on confluence of interest rather than conflicts of interests.

Evolution of science and impact on regulatory science

- Basic science is advancing at a fast pace and is driving product development forward; even regulators (who are usually ‘the last to know’) see very clearly that new development paradigms are progressing with an unprecedented speed. We need to translate basic sciences into clinical use.
- We are breaking new ground in ways never seen before. With over 7 000 medicines currently in development, the exciting new wave of medical innovation will play a key role in addressing the challenges faced by patients and healthcare systems. At the same time, the technology changes are faster and faster, making it difficult to keep up. Rapid digitalisation in healthcare and new technologies offer even more potential to go for an integrated healthcare delivery but also entail challenges causing disruption in established systems that must be addressed.
- There is a vast range of complex and challenging products being explored that need to be developed, manufactured, evaluated and made available to patients. What we see in Europe sometimes with these complexities is that, unfortunately, very innovative and potentially ground-breaking products or methodologies may ‘fall through the cracks’ due to the range of national and European regulations around medicines, devices, cells and tissues, manufacturing, data privacy, and so on.
- Regulatory pathways cannot be a barrier to such advancement. In addition, in the not-too-distant future, we can foresee that it will be difficult to distinguish for instance a medicine from a device or a transplant, and perhaps to define data. We therefore need to develop a much more modern approach to our benefit-risk assessment and lifecycle approach to medicines evaluation.
- Although the regulatory world is not the fastest to change, there is still progress made and therefore it is important to ensure our approach is robust and that it has taken into consideration the feedback from and is supported by all stakeholders.

- The role of regulators has changed from ‘control-only’ to enablers of better population health. Regulators should take a new role at the crossroad between science and national healthcare systems: in order to promote public health in the current environment, they can no longer be just a gatekeeper between those two worlds; they need to become a catalyst, or enabler, for science to be translated into patient-centred healthcare and to fit into the reality of healthcare systems today and in the future.
- A reflection at an international level is needed to prioritise and recommend cooperation in innovative areas, if we want to ensure that the regulatory framework, or insufficient cooperation between the relevant stakeholders, do not paralyse innovation.
- Ultimately, we need to develop and implement a regulatory science strategy. Such a regulatory science strategy should draw from a variety of sources, within the regulators network and from the experiences and views of developers, academia, industry for instance. It should utilise a purposefully collaborative approach, with continuous feeding into and feeding from horizon-scanning activities, detecting, triaging information, assessing it for impact on European public health and on regulators’ own workload, and prioritising any resulting actions appropriately.
- The strategy should reflect the need to adapt and to be sufficiently agile to accommodate regulatory evaluation and assessment of innovative medicines.
- Related implementation activities and outputs range from development of guidelines and outreach actions, to regular discussions with the European Commission, in order to make sure that the regulatory framework is interpreted and adapted in line with the evolution of science.
- Leveraging collaboration at EU and global level with partners is important for ensuring stakeholder engagement to avoid self-referential outcomes, and identifying ‘hot spots’ in the current regulatory science discussions.
- Health systems must also prepare and reform to provide rapid, effective and sustainable patient access to new innovations and technologies. With good forecasting, healthcare systems should be able to project how scientific developments will impact patient outcomes, healthcare delivery, and society. The adoption of breakthrough technologies becomes much less disruptive for a system if their impact is understood and their introduction is planned well and in good time.

Gaps to be addressed

- There should be focus on translational science.
- Cross-disciplinary research involving diagnostics, devices, etc. or other areas like food should be encouraged.
- Similarly, research should be encouraged to shift focus from disease management to health management, from treating to preventing and intercepting diseases, and from vertical integration to externalisation and open innovation.
- Opportunities for learning from each other and knowledge sharing in order to accelerate these areas should be more fully taken advantage of.
- It is key to define together what the clinical need is, from a pull-and-push mechanism with clear emphasis on the public health perspective.
- New competences are needed for the regulatory and public health systems, both for the evaluation of health interventions, including but not limited to medicines, and for the delivery to patients. To build the expertise to evaluate increasingly complex products, regulators need to reach out to many stakeholders and interact with new players outside the health arena. Likewise, to help ensure maximum public health impact, such stakeholders need to engage proactively with regulators in all stages of the lifecycle of a product.
- In addition to the suggested shift from disease management to health management, there is also a shift from treatment of symptoms to potentially curative medicines. This will require entirely new approaches to benefit / risk and value assessment, as well as payment and financing – and all this is in a context of constraints that are driving the strategic allocation of resources.

- One example given where research and technology meet when there is a market opportunity is of 3D printing comprising an automated process, with minimal operating costs, and which has the potential to print out within a short time frame, a product impacting personalised medicine. Potential applications of 3D printing are one of the emerging trends seen for medicines, for drug-device combinations, and for tissues and cells, or even entire organs – both as transplant and as advanced therapies. With this, the 3D printed tablet is a reality. It is a welcome reality, expected to benefit patients, but one that poses interesting challenges for regulators when making decisions on how best to handle these products from a regulatory perspective.
- Looking forward, we need to continue to move towards more seamless and convergent regulatory approaches (not just studies but the whole development approach) where we integrate traditional clinical trials with real-world evidence generation. This would also mean moving eventually from ‘a point in time' regulatory filing approach to a much more continuous and seamless regulatory review of data while adapting access to the right patient populations.
- In a holistic systemic change, we need to reinvent each element of an integrated healthcare delivery – healthcare financing, de-siloing social security budgets, focus on outcomes, intellectual property protection to enable innovation.

Towards tangible and impactful outputs

- There should be a focus on concrete tangible results (‘low hanging fruits’) that could be achieved in the short term and then looking at the strategy to maximise impact.
- Early engagement with regulators is critical for them to know what is in early development as well as to enable early dialogue regarding innovative medicine development to help enable mutual expectation setting. Regulators are not here to drive innovation but have a role as enablers. Regulators should understand and be ready to integrate innovative approaches in the regulatory pathways and developers need to engage with regulators to help enhance mutual understanding.
- Embracing this changing role, these interactions through the existing mechanisms are meant to help ensure maximum impact of research on innovative medicines.
- There was a clear message from EMA that they want to see many more of the IMI outputs delivered into the public domain, for example through qualification of methods. This is why in the design of projects, IMI should ensure that applicants are encouraged to come and share their intelligence and their plans for innovative medicines development. This not only educates regulators, but also helps ensure the right regulatory interaction at the right time to help enhance impact for patients.
- Medicines development is a long, complex and costly process with high failure rates, requiring significant long-term, high-risk investment. Pharmaceutical incentives have been instrumental in delivering innovative medicines. There should be consideration for incentives and protection to continue promoting medical innovation and delivering significant advances in areas of unmet medical need.
- Public funding is an opportunity but there is a great responsibility to ensure that EU public resources are invested in a way that maximises impact for patients in areas of major importance to EU public health.