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REGULATORY ROAD TO INNOVATION

Europe's regulatory system is designed to ensure that new treatments for patients are safe and effective. It has helped to extend and improve the lives of millions of people across Europe and beyond. But to keep pace with developments in science and technology and to remain competitive in the face of fierce global competition, Europe's regulatory framework has to evolve.

WHAT HAS REGULATION ACHIEVED?

- **SERVING THE PATIENTS.** Since its foundation in 1995, the European Medicines Agency (EMA) has recommended the authorisation of over 1,400 medicines.[1] The regulatory system is an integral part of the medical innovation process that has transformed the lives of millions of Europeans living with diseases like cancer, heart disease, diabetes, HIV and Hepatitis C.

- **SUPPORTING INVESTMENT.** A stable and supportive regulatory system plays a key role in attracting the €35 billion that the pharmaceutical industry invests in European research and development every year.[2]

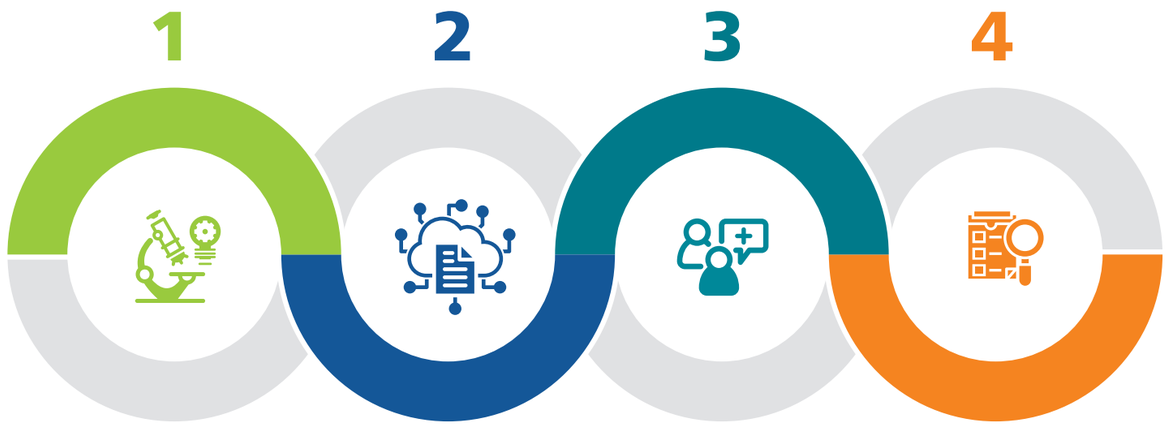
WHY DOES IT NEED TO EVOLVE?

To meet today's challenges, industry needs to work with multiple partners in the healthcare system to evolve and adapt the regulatory system within the existing legislation to deliver on the new opportunities science is offering to patients.

- **EVOLVING THE SYSTEM CAN HELP US DELIVER MORE FOR PATIENTS,** by adopting advances in technology, utilising real world evidence[3] and data analytics in regulatory decision making, and ensuring that Europe remains competitive in the face of fierce global competition.

TIME FOR ACTION

EFPIA, working with its members, has identified four areas for action **within the existing legislative framework** to deliver more treatments, safer, better, and faster.



SCIENCE IS TRANSFORMING THE LIVES OF PATIENTS, MAKING THE UNTREATABLE TREATABLE

Pharmaceutical R&D is driven by ground-breaking innovation which has transformed, and continues to transform, the development of new treatments and patient outcomes. Whereas early medicines were simple chemical compounds, many new medicines are now complex biotechnology products.

60 000 CLINICAL TRIALS

* There are almost 60,000 clinical trials ongoing in Europe.[4]

269 NGBs

* The total number of Next-Generation Biotherapeutics (NGBs) – defined as cell, gene and nucleotide therapies – in the development pipeline went from 120 in 2015 to 269 by the end of 2018.[5]

10% OF LATE-STAGE R&D

* NGBs make around 10% of the total late-stage R&D pipeline and have more than doubled in number over the past three years as new pathways for disease treatment and cure.[6]

143 NEW MEDICINAL ENTITIES

* Between 2015 and 2018, Europe approved 143[7] new medicinal entities compared to 172[8] in the USA. Developing the next generation of treatments raises new and challenging questions of our regulatory system, underlining the **need for new regulatory guidelines and policies to adopt these advanced technologies.**

436 DAYS TO ASSESS

* Today it takes an average of 436 days for the EMA to assess a new active substance, compared to 244 days in the USA, 323 in Japan, 348 in Canada, and 363 in Australia.[9] This results in a delayed access to innovative treatments for European patients.

FACING FIERCE COMPETITION STRIVING TO REMAIN AN INNOVATOR AND WORLD LEADER

2.5 M PEOPLE

€206 B GROSS

€35 B IN R&D

Europe's regulatory system supports a thriving European ecosystem of small and big pharmaceutical companies. Employing over 2,5 million people,[10] generating €206 billion in gross value added to the EU economy,[11] and investing €35 billion in R&D,[12] Europe is today the second largest pharmaceutical market in the world.[13]

However, this situation is gradually changing. Over the last 20 years there has been increasing competition from emerging economies to attract new products' launch[14] and, more recently, the EMA has lagged behind the Japanese PMDA and US FDA in approving new active substances.[15]

Europe should remain a world-leader in medical R&D, but needs to maintain an environment conducive to being at the forefront of the development of innovative treatments, by evolving its regulatory system.

1. INNOVATIVE CLINICAL TRIAL APPROACHES

ISSUE

Complex (and innovative) clinical trials (CCT) can enable several trials to be done in parallel to investigate the effect of a new medicine in different diseases or groups of patients. This gives **more patients the opportunity to join a trial** and can shorten the time needed to get the data to decide if a medicine can be licenced to treat a disease.

80% of EFPIA companies have used CCT designs to collect clinical data.[16] Encouraging the use of complex trial designs and their acceptance by Health Authorities will **help bring new treatments to patients earlier and more efficiently.**

RECOMMENDATIONS

EMA and the national authorities to lead a strategic initiative to broaden the appropriate use and acceptability of CCT, including the design of an IT platform for CCT application.

The European Commission to ensure the compatibility of CCT with the EU Clinical Trial Regulation.[17]

2. REAL WORLD DATA (RWD) / REAL WORLD EVIDENCE (RWE)

ISSUE

Industry and regulators recognise the value of using good quality RWD/RWE as additional sources of evidence for decision-making, since they allow to **consider real-life impact of medicines,** instead of standard effects as considered in traditional clinical trials. RWE has already shown its value[18] in medicine safety surveillance and for the development of medicines for rare diseases, when traditional clinical trials are impossible to conduct due to the low number of patients.

Aware of the potential to use RWD and RWE even more effectively and broadly to support medicine development and assessment of benefit and risk, the FDA is already developing a RWE regulatory framework.

RECOMMENDATION

EMA to develop and adopt guidance on a RWD/RWE framework with clear principles for data quality and interoperability, access, analysis and regulatory acceptance.

3. DYNAMIC REGULATORY ASSESSMENT

ISSUE

Today an application for approval of a new medicine needs a large amount of data to be collected over many years and then submitted as a single dossier to be evaluated. This means that any gaps in the data package may not be identified until a late stage in the medicine's assessment. An iterative scientific dialogue with Health Authorities during the collection of data will help **reduce the uncertainties and optimise the application process.** This would allow more rapid approval of medicines and faster access for patients to new treatments.[19]

Even though PRIME already allows for an early and ongoing dialogue, resulting in an accelerated assessment, criteria for PRIME eligibility are narrow. The EMA accepted only 22% of the 215 requests for eligibility.

RECOMMENDATIONS

EMA to design guidelines for a flexible regulatory pathway which includes an iterative process for seeking early and continuous dialogue on data, as they are generated.

The European Commission to accelerate the review of EMA recommendations for approval.

4.DRUG-DEVICE COMBINATIONS & BIOMARKER VALIDATION

ISSUE

1 in 4 medicines approved at EU level includes a device component.[20] In the EU, while medicines are assessed by the EMA, different authorities (notified bodies namely) are responsible for assessing the performance of medicines used in combination with medical devices and in vitro diagnostics. Experience gained by the FDA underlined the **importance of an integrated approach.**[21]

Advances in personalised medicine require additional regulatory requirements, such as biomarker validation. Current biomarker qualification process lengthens already **cumbersome procedures** thus jeopardising access of patients to innovation.

RECOMMENDATIONS

EMA to adopt an integrated EU pathway for the assessment of drug-device combinations and in vitro diagnostics.

EMA to incorporate best practices in order to include additional regulatory requirements coming from advances in science, such as biomarker validation, without overburdening existing procedures.