efpia
European Federation of Pharmaceutical Industries and Associations

REGULATORY ROAD TO INNOVATION: DELIVERING A WORLD CLASS 21ST CENTURY REGULATORY FRAMEWORK

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Regulatory Road to Innovation – Introductory Words to Experts Insights

As part of the EU Pharmaceuticals Strategy, and lessons learned from the COVID-19 pandemic, the European Commission (EC) declared its plans to assess and revise the EU's general legislation on medicines for human use (Directive 1001/83/EC and Regulation 776/2004) to safeguard a future-proof and crisis-resistant medicines regulatory system. EFPIA has participated actively in the dialogue with all relevant stakeholders from legislators/regulators to patients and healthcare professionals, not to mention the different types of medicine developers, preceding these official steps. We have constantly evolved our goals on how to enhance the legislative framework in the EU and at the same time looked at how we can make improvements already now to support today's innovations and those for the future for the patient to reach them faster.

This is the Regulatory Road to Innovation (RRI) with the objectives to enhance the policy and regulatory environment in Europe to deliver safe, efficacious and high-quality treatments, vaccines and diagnostics to patients.

In order to highlight concretely on how the main priority goals of RRI could be reached, we partnered with industry topic leads to generate a blog publication for the EFPIA's blog page called "EFPIA View". The purpose was to create reader-friendly, timely, interesting and sometimes thought-provoking articles.

This blog collection comprises all these topics published between April 2022 to March 2023 on the following topics:

1. EU Regulatory Network - New architecture for a new era
2. Complex Clinical Trials - A decade of innovation in clinical research: from a Drug centric to a Patient centric approach
3. Supply Chains reshaping - How to respond to a crisis
4. The future treatment of patients - Combination Products and Companion Diagnostics
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6. Electronic Product Information (ePI) – Making the latest medicine's information available for patients without any delay
7. Digital endpoints for patient-focused health management
8. A sustainable environment for a healthy population[1]
9. Real-world data/evidence: How it can inform patient treatment and care decisions
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I would like to thank all the topic leads and blog authors who were involved in the generation of the blogs by providing their input and expertise and thus made this collection possible. A big thanks goes as well to Deloitte team for partnering with us in this project and providing project management support along the journey.

Sini Eskola
Director Regulatory Strategy
EFPIA

1 - The blog on environmental issues (focusing on key pillars of Eco-Pharmaco-Stewardship) is part of this blog series and whilst this is not (yet) formally part of the RRI, it is a key part both from non-legislative and legislative perspective of our preparedness for future changes.

2 - The blog on role of innovation in regulation (focusing on the proposal for evaluation principles for legislative text from the innovation point of view) is part of this blog series and whilst not formally part of the RRI, forms an obvious backbone to the policy work in terms of enhancements in the pharmaceutical legislation.

EU Regulatory Network - New architecture for a new era

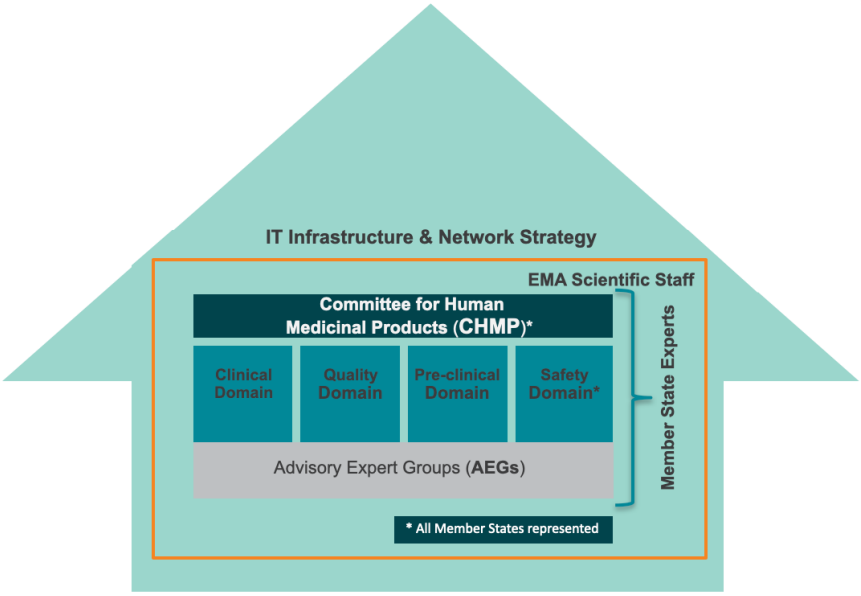
When we look at the current EU regulatory system which was established 27 years ago, and compare this with the house analogy, we see that structures, systems and processes have been added over time to address specific needs without revisiting the overall architecture. The EU has grown from a family of 15 to 27 Member State and moving within the framework is slow and difficult. The framework has become a complex and inefficient construction.

New science and technologies are evolving fast with integrated solutions for personalized healthcare. However, conventional processes coupled with complex governance within the EU regulatory network make it challenging for innovative therapies to rapidly make their way to patients. Europe is lagging behind other leading regulators in terms of agility and speed. The time to act is now[3] [4]: With the European Commission's evaluation of the pharmaceutical legislation as part of the EU pharmaceutical strategy[5], we have an unprecedented opportunity to reconstruct the EU's regulatory framework, processes and governance. Every house needs renovation at some point. What should the new structure look like so that it will fit current and future needs?

EFPIA's overall goal is to reinforce expertise-driven assessment and enable a more agile centralized authorization framework by facilitating Member States ability to bring forward their expertise and by removing unnecessary, burdensome interfaces between Committees and the European Commission.

To achieve this, EFPIA propose the following renovations:

- High-quality assessments need to be ensured and further strengthened by revising the governance framework, enabling the best expertise to be brought forward by the EU Member States in the areas where they can best contribute.
- The need for agility in the system requires us to rethink the current outdated committee and working parties structure for agility and efficiency gains.
- To address any resource gaps related to both current and future workload, as well as the implementation of forward-looking strategies, it will also be crucial to rethink funding and resourcing mechanisms for EMA and the Network.



The building blocks for a new model:

- **EMA Scientific Staff** will enable a strong interface between the different activities for consistency of managing benefit/ risk assessments. Beyond that, the EMA of future must utilise and maximise the potential of advanced technology
- **Committee for Human Medicinal Products (CHMP)**: The final scientific opinion will be adopted by a separate committee representing all Member States to create a collective and inclusive decision moment and ensure appropriate checks and balances.
- **4 Domains** are at the heart of the proposal for a stronger expertise driven assessment. The domains deliver the scientific assessment of products in the relevant areas and hence are the engine for delivering scientific opinions.
- **Advisory Expert Groups (AEGs)** established with clear governance to support assessments by the EMA, the domains and all parts of the regulatory network, including above product considerations and guidelines.
- Finally, EMA will have a strong role in fostering capability building of **Member State Experts** in the EU for their participation in the domains, committees, and expert groups.

3 - https://efpia.eu/media/636486/improving-regulatory-timelines-to-optimise-patient-access-to-innovative-oncology-therapies-in-europe.pdf
4 - https://www.efpia.eu/media/636564/evidence-mix_final-9-dec-2021.pdf
5 - https://www.efpia.eu/about-medicines/development-of-medicines/regulations-safety-supply/regulatory-road-to-innovation/

We spend years developing a drug, bringing our best experts to the table. Given the complexity of drug development, we need to move away from a few formalized meetings with regulators on scientific advice to more frequent dynamic interactions with best scientific and regulatory experts to create clarity on drug development expectations in a dynamic environment. Regulatory processes and governance of EMA and the Network need to support this, ultimately enabling an informed and streamlined assessment of marketing authorization applications.

The EU Regulatory Network response to the COVID-19 pandemic demonstrated that European stakeholders could work and collaborate together in order to significantly accelerate the regulatory approval process. We sense a strong will by all actors in the system to leverage and build on this experience, and at the same time a desire for urgent renovation. Through EMA and the EU Regulatory Network, Member States have been collaborating intensively for over 27 years. Now may be the right point in time to bring the trust established to another level.

Patients and healthcare professionals are waiting for new treatments; would they not expect an urgent renovation of the current house?

SABINE ATZOR
Head EU Regulatory Policies, F. Hoffmann-La Roche Ltd

EMMA DU FOUR
Head of International Regulatory Policy, AbbVie

Complex Clinical Trials - A decade of innovation in clinical research: from a Drug centric to a Patient centric approach

> **Patients with unmet needs are longing for innovative treatments to be approved. Especially rare disease patients, where only 5-6% have approved treatments, need a new strategy to speed up research and provide new opportunities to access innovative drugs. Complex clinical trials can be the change that patients want to see.**
>
> Claas Röhl, chair NF Patients United

'To ensure that patients have faster access to innovative and transformative therapies', that is the overall goal of EFPIA's Regulatory Road to Innovation. An important area for action within the existing legislative framework is the use of more advanced clinical trials in order for medicines to reach patients more rapidly. These types of clinical trials are called complex clinical trials (CCTs)[6].

The increased understanding of both human genetics, patients' DNA, and the genetics known to be associated to various diseases has created the current reality that traditional clinical trial designs are no longer suited to answer medical questions within the timeframe that the patients are expecting to gain access to new therapies[7]. Complex (and innovative) clinical trials can allow multiple new treatments to be investigated in parallel in various diseases or patient groups. This will enable more patients to be given the opportunity to join a trial and it will result in shorter timelines to get the data to decide if a medicine is effective and safe and considered by regulators to be approved. CCTs designs have been used for over a decade in drug development, examples include the application of master protocols covering platform, umbrella and basket trials; the enrichment of trial populations through the use of biomarkers, incorporating historical control arms and more advanced adaptive trial designs. CCT and innovation in trial designs have so far been used by 80% of EFPIA companies and have become a key component in generating clinical data[8,9].

The use of CCT should be encouraged but key stakeholders, such as regulatory agencies and Health Technology Assessment bodies, need to accept the use of CCTs for new treatments to find their way to the right patients in an efficient manner[2].

HOW DOES THIS BENEFIT THE PATIENT?

The decision to participate in CCTs is one that should be made by the patient in close communication with the physician. Patients in clinical trials play a key role in drug development and discovery; CCTs contribute important knowledge on potential new treatments for treating and preventing diseases.

First and foremost participants can help others who are suffering from the same medical conditions by contributing to medical research which has the goal to improve public health. Above all, patients who take part in a CCT may benefit from the treatment(s) they receive and will be seen regularly by a healthcare professional.

HOW CAN PATIENTS CONTINUOUSLY BE ENGAGED FROM BEGINNING TO END?

Since there is a desperate need for new and innovative treatments in areas of significant unmet medical need, it is crucial that CCTs, with innovative trial design, are broadly adopted to enable an acceleration of clinical trials in Europe and beyond[1,4]. The emphasis should not just be on data collected from patients regarding their medical conditions.

6 - https://www.efpia.eu/about-medicines/development-of-medicines/regulations-safety-supply/regulatory-road-to-innovation/
7 - https://www.efpia.eu/media/636599/workshop-report-_accelerating-ccts_final.pdf
8 - https://www.efpia.eu/news-events/the-efpia-view/blog-articles/make-the-regulatory-system-fit-for-the-future-of-medical-innovation/
9 - https://efpia.eu/media/541132/efpia_regulatory-road-to-innovation_leaflet.pdf

It is as equally important to understand the viewpoint of the patient and how their condition affects their everyday life. Moreover, patients need to feel comfortable in joining a CCT and need to be able to visualize how they are contributing to the bigger picture where their data could enable a potential new therapy to treat and/or prevent disease. CCTs design should recognize the needs and expectations of patients. The goal is for participants to experience more patient-friendly trials, from start to finish. Digital technologies can support this goal by making trial participation less burdensome and brings more options in how patient care is delivered. Ensuring positive experiences for patients facilitates participation and retention in CCTs[2,3].

HOW DO CCTS NEED TO EVOLVE?

CCTs have been increasing in their use in recent years, so it is important that lessons are learned from these recent experiences to further evolve CCTs. Building on the COVID pandemic and the use of master protocols to search new COVID therapies, identifies the need of fostering innovation in Clinical trials[2]. Moreover, COVID trials have shown that different stakeholders, including academics, Pharmaceutical Industry, regulators and HTAs can align on CCTs supporting innovative strategies for evidence generation[3]. New tools and technologies, and improved clinical trial processes will pave the way towards higher patient centricity including diverse patient populations and patient engagement strategies across the development ecosystem.

All of this together will enable patients to have faster access to innovative and transformative therapies that best fits their specific disease. Much progress has been achieved in recent years but there is more to be done to align all stakeholders to accept CCTs.

CHRISSIE FLETCHER
Vice President and Head for Speciality & Primary Care Statistics, GlaxoSmithKline

MIREILLE MULLER
Executive Regulatory Policy Director, Novartis

Supply Chains reshaping - How to respond to a crisis

> **Fear of disease kills more men than disease itself.**
>
> Mahatma Gandhi

After the COVID-19 pandemic, the medicines supply chains faced another huge challenge due to the crisis in Ukraine. These two crises have caused substantial challenges to medicines supply chains as well as economic losses. Supply chains are critical to European growth so solving any issues that impact them is vital to rebuilding economies after a crisis. A reshaping of supply chains is essential to make them more resilient and future ready.

INTRODUCTION

There are many stakeholders involved in medicines supply chains, which are complex. Their design is a long-term undertaking that starts long before the approval of a medicine. Once established, supply chains must be preserved and scaled up to keep up with advances in technology, growing clinical needs and rising environmental standards. Today, products in our hospitals and pharmacies, typically commenced their supply journey up to 2 years ago. However, for biological products, which includes vaccines, the process of manufacturing and distribution can be even more complex. Despite the preparation and planning that goes into this work, delays and shortages can still occur.

There are two extensive categories that can cause this: factors that companies can control, and those that are unforeseen, such as issues around unexpected increase of demand, global crisis, or economic policy. It is safe to say that the COVID-19 outbreak and crisis in Ukraine fit directly under the category of 'unforeseen events' and have exposed some of the vulnerabilities in the medicines supply chains in Europe[10]. Therefore, we need to draw the lessons and propose changes in the current legislation to implement a framework that will better respond to a future crisis.

COVID-19 PANDEMIC

Spring 2020 marked the beginning of the COVID-19 pandemic, and whilst fear of this novel virus was spreading like a fire across the global population, fear of extensive shortages of medicines was also portrayed all over the news. The companies reacted by making changes to work practices to ensure the safekeeping of employees while increasing production.

The restrictions on export were a major concern and concerned patients who stocked up on the medicines they required.

The element of fear was absolutely predominant back at the time given it was an unknown disease without medicines to treat it, requiring thus companies to respond in such a difficult environment and rise up to the challenge. Indeed, manufacturing sites and distribution centers showed that they were actually able to maintain supply. It was a hands-on assessment of global supply chain resilience and robustness in the face of a dramatic surge in patient need and demand, and the majority of the pharmaceutical sector in Europe rose to the occasion. Moreover, some medicines' supply increased to 800% of the normal volume to answer to the expanding requests for specific treatments. Furthermore, the pharmaceutical industry has been striving for equitable and broad access to advanced COVID-19 vaccines across the world to curb the pandemic. These vaccines were not only developed in record time, based on the decades long research, but delivered in a scale never seen before, supplying more than 12 billion doses11 globally in less than 18 months[1].

CRISIS IN UKRAINE

Whilst it was expected that the medicines supply chain disruption due to the COVID-19 pandemic would reach some kind of stabilization in 2022 and partly 2023, another global crisis, replaced COVID as a major risk for the medicines supply chains: the crisis in Ukraine.

Although this ongoing crisis is more localized, it is generating a similar fear amongst patients with medical need in Ukraine, Russia, neighboring EU Member States and other countries where access to medicines might be impacted. Indeed, the war is creating instabilities in some of the mechanisms of global medicines supply although current situation shows that there are no specific shortage reported nor anticipated in the EU. The demand did increase as a result of refugee movements to neighboring countries of Ukraine in Europe. Nevertheless, manufacturers do not expect any complications in the near future.

In Ukraine, however, there have been major issues with commercial supply chain because of transportation challenges. Companies have had to seek alternatives routes, via humanitarian organization and the Ukrainian Ministry of Health, to be able to provide medicines to match the patients' need. The companies have also experienced issues in moving the medicines in Ukraine, since warehouses and depots were closed.

10 - https://www.efpia.eu/news-events/the-efpia-view/blog-articles/drug-shortages-lessons-from-the-covid-19-crisis/
11 - https://www.efpia.eu/media/636989/efpia_vaccines-europe_covid-19-lessons-learned_may-2022.pdf

The deliveries to pharmacies and hospitals were also disrupted but has resumed in some areas. Currently, the delivery of medicines to Ukraine have been restarted wherever is possible and where the infrastructure is intact.

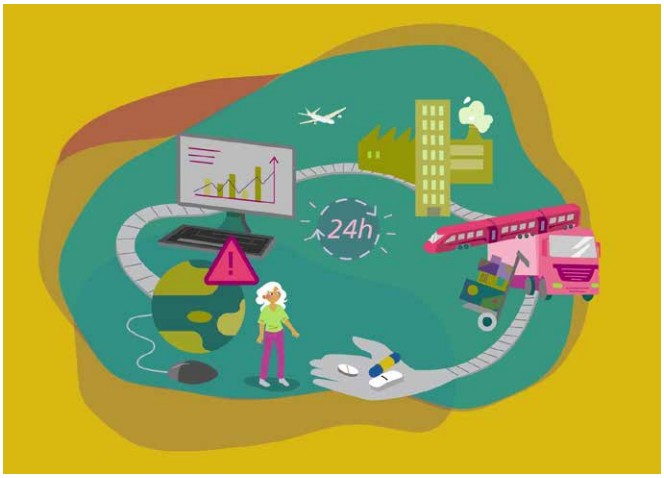
Regarding the supply to international markets like Asia, there have been shortages on specific products for several weeks as well. In general, there are increasing difficulties in the shipment of medicines, since products need to be shipped by road because of flight prohibitions. There is a growing amount of transporters that refuse to ship medicines to Northern Asia, which causes logistic times to be extended. Therefore, additional transportation methods are being considered.

So far, the main priority is to make sure that patients in need of medicines, wherever they are located, have access to medical aid. Thus, companies have responded to urgent product request with donations of various medicines to address the health needs of patients that are affected by the war. Currently, over 22 million doses of essential medicines have been offered as support[12].

LESSONS LEARNED AND FUTURE ACTIONS

Looking forward, there are long-term opportunities to learn from and to be better prepared when similar crises would occur again:

- Introduction of policies by the EU and national governments with the aim to strengthen global supply chains and support the production and free flow of such technologies.
- Joint procurement procedures should be limited to emergency situations, when the purchase and supply of medical countermeasures cannot be ensured by other means.
- Infrastructure should be developed in a way that there is capacity to get doses in the lower middle- and low-income countries.
- Actions should be coordinated at supranational level since companies run global supply chains and these are more likely to ensure continuous supply to all EU countries.
- Regulatory flexibilities could provide value for tackling future pandemics, and beyond emergency situations, particularly where the EU and Member States have aligned closely to provide a streamlined regulatory environment.
- EU-level coordination of procurement should guarantee coordination between Member States to fairly allocate initially limited supply quantities in a transparent manner, and the need to prevent issues related to national distribution channels, or the risk of inefficient stockpiling.



In conclusion, EMA and the EU Commission (EC) need to set up a reporting system, with a harmonized definition of a 'shortage'. The system should collect real time information and ensure a streamlined alert system. The data in the existing European Medicines Verification System could be used for such purpose. The European Centre for Disease Control (ECDC) could also help by releasing epidemiological modelling, patients' needs and hospital capacity data in the Member States to improve demand forecasting. Finally, special consideration and focus should be provided to a subset of critical medicines for manufacturers and regulators to efficiently cooperate over shortage prevention plans[13]. This is the way forward to ensure a future-proof supply chains process that releases patients from the fear of not have access to medicines wherever and whenever.

MARCO FARINELLI
Global Supply Chain & Strategy, Astrazeneca

FRANCOIS LAMÉRANT
Senior Manager, Country Support, EFPIA

12 - https://www.efpia.eu/news-events/the-efpia-view/efpia-news/pharmaceutical-industry-response-to-the-war-in-ukraine/
13 - https://www.efpia.eu/media/636798/efpia-regulatoryroadtoinnovation_triptych_v07-final-neworder_pbp.pdf

The future treatment of patients - Combination Products and Companion Diagnostics

INTRODUCTION

The development of science and technology is moving at an ever increasing rate, resulting in significant innovations in treatments. Currently, 20% of approved medicinal products are combination products, comprising of both a medicine and a medical device. However, Europe is lacking an integrated approach for the assessment of combination products, which represent more than 1 in 5 of current products in development. This creates uncertainty and puts European patients at a disadvantage when compared to the developments underway and regulatory pathways in other major territories for combination products, companion diagnostics and digital tools. With the rapid expansion of digital tools for personalized medicines, combination product manufacturers have become increasingly interested in making them available with their combination products. If Europe wants to catch this medical technology wave and ensure rapid access to innovative medicines for its patients, it needs to adapt its regulatory regime[14,15]. In particular to drive improved alignment and connectivity between the existing separate and distinct regulatory frameworks for medicines and medical devices.

WHICH CHANGES ARE NEEDED?

It is suggested that a clear legal basis and framework within the medicines legislation needs to be established that enables EMA to take responsibility and accountability for tasks concerning both combination products and companion diagnostics. This would reinforce EMA's role to facilitate the research, development, approval and monitoring of these products. Thus allowing EMA to manage (co)development support (including integrated Scientific Advice), qualification procedures, lead/coordinate policy development and issue procedural guidance.

A legal definition for "combination product" would encourage the conjunction of two detached and discrete legal frameworks to create the foundation of a clear regulatory pathway for combination products in Europe, putting European requirements on a similar level to other regions. This definition would not include companion diagnostics, as they are already defined in the In-Vitro Diagnostic (IVD) Regulation (2017/746)[16].

Furthermore, an extended responsibility would allow EMA to lead coordination of required stakeholder input in a timely manner thus ensuring an effective process for the consultation and approval of combination products as well as companion diagnostics. This would increase clarity and predictability for sponsors, European regulators and other stakeholders supporting the delivery of innovative medicines to patients. Moreover, the extension of EMA's responsibilities, suitably resourced with applicable medical device and IVD expertise, could be accomplished through a network of European experts selected by national Competent Authorities. This way, an aligned approach would be guaranteed together with optimal co-ordination of (co-)development aspects through all relevant stakeholders, including Notified Bodies.

CONCLUSION

In conclusion, a harmonised framework is required to enable a smooth and aligned development and authorisation of combination products and companion diagnostics. Furthermore, governance should permit flexibility and distinguish the diverse responsibilities regarding particular regulations to leverage those to best effect., These changes should be implemented with the ultimate goal that European patients are able to experience the transformation of modern medicine and have prompt access to innovative medicines.

TIM CHESWORTH
Senior Director, Global Regulatory Affairs, Devices & Digital Therapeutics, AstraZeneca

AMANDA MATTHEWS
Senior Director, Global Regulatory Affairs - Medical Devices and Combination Products, Pfizer R&D UK Ltd

14 - https://www.efpia.eu/media/636798/efpia-regulatoryroadtoinnovation_triptych_v07-final-neworder_pbp.pdf
15 - https://www.efpia.eu/media/636564/evidence-mix_final-9-dec-2021.pdf
16 - https://eur-lex.europa.eu/eli/reg/2017/746/oj

Expedited Regulatory pathways – a toolbox to provide innovative medicines to patients

> **The revision of the pharmaceutical legislation is a once in a generation opportunity. Leveraging this opportunity to enhance and future proof expedited regulatory pathways is essential to ensure the European regulatory framework can continue to support the development and regulatory approval of innovative medicines.**
>
> Nadège Le Roux, Senior Director Regulatory Policy & Intelligence at Bristol Myers Squibb

INTRODUCTION

Evidence generation for innovative medicines requires a global approach, both now and in the future, to meet regulatory requirements around the world. Evidence generation also continues long after the first registration of a new medicine. Some medicines benefit from increased support, such as enhanced regulator interactions, due to the level of complexity in development or unmet medical need and/or the ethical urgency with which a treatment should be integrated into best standard of care. Expedited regulatory pathways (ERPs)[17] were developed by multiple international authorities to respond to these needs, creating enhanced early and frequent interactions to support and facilitate innovative treatment development and rapid processes to increase efficiency and reduce time both in development and subsequent regulator assessment. ERPs can be considered a 'regulatory toolbox' that can be leveraged to best support the development and efficient assessment of important innovative treatments, so patients can receive them in a timely manner.

In recent years, ERPs have expanded worldwide (Real-time Oncology Review 'RTOR' and Regenerative medicine-advanced Therapy Designation 'RMAT' in US, China, Australia…) to better support development and improve the speed and efficiency of regulator review of new technologies. Furthermore, ERPs adding work-sharing processes or collaborative platforms (e.g. Innovative Licencing and Access Pathway 'ILAP' with project ORBIS) can deliver faster access to new therapies by remaining in the global first wave to innovation while helping to manage resource capacity and expertise[18]. EFPIA welcomes the ongoing reflexion on a futureproofed regulatory framework for ERP, and beyond[19].

The development, submission and/or regulatory review of innovative medicines is accelerated by ERPs, but use of this regulatory toolbox in Europe is limited compared to other regions. Consequently, Europe's ability to approve innovative medicines efficiently and rapidly to the market is reduced, resulting in delayed access for European patients. ERPs are a necessity for a future-proofed and viable regulatory framework that European patients can rely on for continued delivery of key treatment innovation. Importantly, ERPs are anchored on the same standards for treatment development with regards to safety, quality and efficacy. To ensure European patients continue to benefit from treatment innovations, the 'toolbox' needs to be reviewed, and our key proposals are outlined below.

CURRENT SITUATION

The current toolbox of European ERPs is used infrequently compared to similar international pathways. EMA had the second lowest percentage (37%) of medicines approved through an expedited review in comparison to five other major authorities in 202020. The FDA had the highest percentage of new medicines approved via expedited pathways (74%) followed by Swissmedic (61%), and Therapeutic Goods Administration (TGA) in Australia (56%). Moreover, the complexity of the EU regulatory ecosystem, organized in two layers (e.g. National and EMA/EU one), slows the potential of ERP tools.

The flexibility, agility and possibility of combining various ERPs in the EU needs to be enhanced. Some member states are hesitant about ERPs as they imply a more iterative evidence generation with a first registration based on a first dossier responding to the core benefit:risk that may not yet reflect the long-term need decisions of other downstream decision-makers. Health Technology Assessment and Pricing & Reimbursement authorities must focus on how to support delivery of treatments to patients who need them by engaging in a conversation on evidence generation, including generation beyond the first registration to further characterize the treatment and support access decisions. Important conversations on skills and resources are taking place currently within the EU Network and we would like to re-iterate the EFPIA position that innovative

17 - In the European Union, ERPs include PRIME, Accelerated Assessment and Conditional Marketing Authorisation.
18 - https://circsci.org/wp-content/uploads/dlm_uploads/2022/06/CIRS-RD-Briefing-85-NAS-list-v2.2.pdf
19 - ERPs include in the US 2 new tools e.g. RTOR and RMAT- in China, in addition to priority and special review pathway, NMPA introduced Breakthrough and Conditional Approval in 2020 to accelerate development and approval of drugs with significant clinical value. In Australia, in early 2022 TGA consulted on new Priority review pathway for biologicals including human cell and tissue therapies.
20 - https://circsci.org/wp-content/uploads/dlm_uploads/2021/06/CIRS-RD-Briefing-81-6-agencies-v5.pdf

industry is willing to pay more for the additional support provided by some key ERP components: iterative scientific advice, PRIME and dynamic regulatory assessment[21].

FUTURE PROOFING THE ERP TOOLBOX

ERP within the toolbox should be used flexibly to suit specific situations. ERPs include the following tools and methods that are not mutually exclusive and can be used on their own or combined to adapt to the context and support efficiently the expedited development and efficient treatment approval:

Expedited development:

- To actively support the development of ground-breaking medicines with enhanced and active iterative dialogue to align on appropriate evidence generation, needed for regulatory assessment and future decisions (e.g. for PRIME designated medicines).
- Facilitate early multistakeholder discussions across the EU network (EMA and NCAs) and other stakeholders as needed.
- Where appropriate, more agile and rapid scientific advice (SA) to efficiently support development.
- Where and when appropriate, earlier submission and approval with a dataset based at an agreed time point (e.g., surrogate endpoints, phase 2 data only), with robust commitments to continue with post licensing evidence generation (e.g. in context of Conditional Marketing Authorisation 'CMA'). A first time to registration is to support patient needs while the evidence generation is pursuing its pace to build the knowledge of the innovative medicine.

Expedited assessment (iterative/dynamic regulatory assessment):

- Rolling reviews were successfully used during the COVID pandemic, leading to greatly reduced development and authorisation timelines. Although this level of resource can only be released in rare public health emergencies, there are learnings that must be extracted from iterative release and assessment of data (also called Dynamic Regulatory Assessment 'DRA') and applied more broadly. DRA should be thoughtfully applied to ERP as an additional mechanism to support development and efficient regulatory approval, and we recommend beginning with a pilot of this concept as an action connected to the PRIME 5 year review[22,23], although the concept applies more broadly (see below). In a close future IT tools and digitization will facilitate smooth processes and connectedness that ERPs greatly need.

Expedited review:

- Regulatory authorities can speed up the review of certain products to enable faster approval with the ERP called Accelerated Access (AA).
- Leveraging iterative/dynamic regulatory assessment could be helpful in this setting thanks to a stagged approach. A pilot would help to discuss this in a concrete way.

21 - https://www.clinicaltherapeutics.com/article/S0149-2918(21)00456-2/fulltext
22 - https://cirsci.org/wp-content/uploads/dlm_uploads/2021/06/CIRS-RD-Briefing-81-6-agencies-v5.pdf
23 - https://www.ema.europa.eu/en/documents/report/prime-5-years-experience_en.pdf

Expedited or early submission:

- Evidence generation is a continuum and continues long after the first registration of a new medicine. CMA can facilitate early access to medicines, as seen in for e.g. COVID therapeutics/vaccines. In CMA, the benefit:risk of earlier regulatory approval is assessed taking into account the context of e.g. a seriously debilitating or life-threatening disease, public health conditions and the remaining uncertainty with regards to the ability to generate the required data. Part of the first approval is decided with a set of pre-approved commitments to subsequently generate the additional data needed towards a full marketing authorisation. Thoughtful evidence generation planning can support timely assessment for HTA/pricing reimbursement. The continuum knowledge on a product is a reality that each stakeholder of the EU ecosystem should embrace.

- ERP allows acceleration of the first registration, while evidence generated actively and rapidly continue to complement and confirm the initial knowledge of the product. It is important to state that post marketing evidence generation always continues in this setting and always in agreement with regulators.

GOING FORWARD

As recorded in the European Pharmaceutical strategy, PRIME ought to be incorporated in the regulatory framework to fully optimize the support and acceleration of innovative medicines being launched on the EU market. This tool will also be improved and invested in according to the EMA Regulatory science and HMA European Medicines Agencies Network Strategy to 2025. It will be crucial to align on the eligibility criteria for PRIME. For example too narrow definition of 'Unmet Medical Need' would further limit the use of this tool for patients' faster access and EFPIA stands firm that unmet medical need has to take into account patient, societal and health system perspectives[24]. Furthermore, rolling review is currently only being used to manage health emergencies like the COVID pandemic[25].

Learnings from rolling review and stakeholder experiences must be thoughtfully applied to a broader set of medicines, as has happened in similar countries and regions. A crucial component for effective ERP evolution is the implementation of effective knowledge management and institutional memory within the EMA and the EU Network (at large) to connect all activities within the EU Network.

The COVID pandemic has shown an urgent need for a fast approach to addressing unmet medical need during a health emergency and has given a glimpse of the possibilities European patients have been anticipating for other life-threatening diseases and conditions. For Europe to stand its ground amongst other international regulatory authorities, in an era of innovation and global development, it is crucial to evolve and future proof EU ERPs.

We believe this evolution can be done efficiently, without compromising on the safety, efficacy and quality of future medicines. Furthermore, we strongly need support from NCAs as we future-proof the EU's regulatory system to reclaim competitive advantage and continue delivering the treatments patients need now, and in future. The effectiveness of the EU system will need improved allocation of local and national resources, setting clear priorities for innovation in the EU network. These reflections ought to be addressed urgently if the EU wants to support and deliver innovative medicines within similar timeframe as other Global agencies to be part of the first global wave to innovation. In parallel, an important conversation is needed to optimize fees, expertise and resourcing capacity generally within the EU network as this underpins functioning of any future system[26].

ESTEBAN HERRERO-MARTINEZ
Director, Regulatory Intelligence and Policy, AbbVie

NADEGE LE ROUX
Senior Director Regulatory Policy and Intelligence, Bristol Myers Squib (BMS)

24 - https://www.efpia.eu/about-medicines/development-of-medicines/unmet-medical-need/
25 - https://pubmed.ncbi.nlm.nih.gov/35123802/
26 - https://efpia.eu/media/636798/efpia-regulatoryroadtoinnovation_triptych_v07-final-neworder_pbp.pdf

Electronic Product Information (ePI) – Making the latest medicine's information available for patients without any delay

> **Although the existing EU legislation states that the paper version of a medicine leaflet is obligatory, there are many studies of electronic product information (ePI) that present the feasibility and benefits of electronic information. ePI covers the most recent, regulatory approved information without any delay, which leads to increased patient safety, enhances health literary and adherence to the treatment.**
>
> Koen Nauwelaerts, Regulatory policy and innovation lead at Bayer

INTRODUCTION

The pandemic caused an acceleration in the digitalization of healthcare in Europe, and one feature of digitalization is the implementation of electronic product information (ePI27) for human medicines. The objective of ePI is the expansion of access to information on medicines and to enable access to the most updated regulator-approved information without a delay.

The provision of comprehensive, accurate and recent regulatory-approved information on medicinal products, both for patients and healthcare professionals (HCPs), is abundantly supported by the pharmaceutical industry. The conclusion from European Medicines Agency (EMA)/Heads of Medicines Agencies (HMA's) is that it is essential to discover alternate innovative pathways of distributing information electronically. The amendment of the forthcoming pharmaceutical legislation revision must be leveraged to seize the benefits of ePI and those benefits will require implementation for both Centrally and Nationally Authorized medicinal products. As the end users of medicinal products, the requests of all patients and healthcare professionals (HCPs) must be prioritized in the development and implementation of ePI[28,29].

BENEFITS FOR PATIENTS, HEALTHCARE PROFESSIONALS AND ULTIMATELY TO THE ENVIRONMENT

There are many stakeholders involved to make the transition from paper leaflets to ePI happen, but the needs of patients and HCPs must be leading the implementation, whereas the method itself would come from the European regulators (EU Commission (EC)/EMA/HMA).

There are numerous end-user benefits[30,31]:

- ePI has the potential to address patient and HCP needs for accessible, relevant information on medicines at the right time during treatment
- Accessibility to user with diverse abilities
- Provision of the latest information on a medicine's safety, benefits and conditions of use
- Informed decision-making by patient/consumer and HCPs
- Availability of ePI in multiple languages
- Attractive, presentable and user-friendly interface with other potential supportive features (e.g. user font modification) would motivate patients to take a more active interest in their health status
- Availability of additional materials to the statutory information: video and audio facilities accessible to support and improve health literacy and safe use of the product
- Alerts for major updates to the leaflet

27 - According to EMA-HMA-EC, ePI is authorised, statutory product information for medicines (i.e. SmPC, PL and labelling) in a semi-structured format created using the common EU electronic standard. ePI is adapted for electronic handling and allows dissemination via the world wide web, e-platforms and print. ePI fulfils the key principles.

28 - https://www.ema.europa.eu/en/documents/report/report-european-medicines-agency-ema/heads-medicines-agencies-hma/european-commission-ec-workshop-electronic-product-information-epi_en.pdf

29 - https://www.medicinesforeurope.com/wp-content/uploads/2021/02/IATF-ePI-report_final_complete.pdf

30 - https://www.ema.europa.eu/en/documents/report/report-european-medicines-agency-ema/heads-medicines-agencies-hma/european-commission-ec-workshop-electronic-product-information-epi_en.pdf

31 - https://aesgp.eu/content/uploads/2021/02/IATF-ePI-report_executive-summary.pdf

However, it is important to state that the implementation of ePI should not lead to health inequalities among citizens with limited access to electronic information. Moreover, it is crucial to empower patients by concentrating on the construction of an EU common standard for harmonized and structured PI, which could be implemented gradually across Member States, followed by the whole of Europe.

Finally, EU's Green deal and the EU Commission agenda to improve the environment would be supported with a great potential of ePI to reduce the volume of paper and ink (and all associated industrial activities) that are currently used to produce the paper leaflet. ePI will contribute to the decrease of the Carbon footprint.

CURRENT SCENE

Currently, multiple EU countries like Belgium, Luxembourg, Germany, Spain and the Baltics have ongoing initiatives relating to the implementation of ePI for some medicinal products. These initiatives include ePI pilots for some medicinal products[32].

e-PIL pilot in Belgium/Luxembourg

At the initiative of the pharmaceutical industry and with the support of the national competent authorities and the associations of hospital pharmacists, the electronic patient information leaflet (e-PIL) pilot project was launched on 1 August 2018 in Belgium and Luxembourg for an initial period of two years, with the aim to demonstrate that the electronic leaflet is equivalent to the paper leaflet.

The Pilot surveys recognized that when the respondent hospital pharmacists had to consult the e-PIL, 96% of them viewed the e-PIL online, with only 4% requiring a printout from the online source. Furthermore, for 98% of the respondent hospital pharmacists, the absence of the paper PIL did not affect their daily practice in a negative way, or in their obligation to respond to questions from doctors or other HCPs. The results also show that patients very infrequently demand the PIL of their medicine. Accordingly, 98% of the respondent hospital pharmacists would be in favor for the removal of the paper PIL from all hospital-only medicines.

Since the participating stakeholders (hospital pharmacists, other HCPs and pharmaceutical companies) believe that the experience gained in this pilot project is a valuable source of empirical evidence to support the policy initiatives in this area, the EC prolonged the pilot until August 2022. Furthermore, as there is currently potential to support the change in the EU general pharmaceutical legislation, another pilot extension request was made to include more products in the scope of the pilot. Since December 2020, a total of 42 products restricted to hospital use from 18 pharmaceutical companies are included in the e-PIL pilot project[33,34].

THE WAY FORWARD

The results of these initiatives could be used cooperatively to support the recognition of ePI and its use in the step-by-step elimination of paper leaflets starting with hospital medicines. Thus, the expansion of pilot projects investigating the benefit of replacing paper leaflets with ePI for hospital/HCP administered products, should be stimulated. Furthermore, the EC needs to ensure legislative readiness to convert to ePI by conducting legal framework analysis for the development of an ambitious ePI roadmap.

For patients and HCPs, educational campaigns should be organized to raise awareness on ePI. Also, discussions on how to secure safe and easy access to ePI for patients need to be held, while making sure that the elderly population and those who may not have electronic access, will not be left behind[35]. The future of better and timely information on medicines is knocking on the door – all stakeholders will hopefully open this door with a warm welcome!

KOEN NAUWELARTS
RA Policy and Innovation Lead, Bayer

PÄR TELLNER
Director, Regulatory, Drug development and Manufacturing, EFPIA

32 - https://pharma.be/nl/e-pil-soortgelijke-projecten-in-europa
33 - https://pharma.be/sites/default/files/2022-04/2021_E-PIL%20pilot%20project_one-pager_final.pdf
34 - https://pharma.be/sites/default/files/2022-06/rr-april-2022-e-pil.pd
35 - https://aesgp.eu/content/uploads/2021/02/IATF-ePI-report_executive-summary.pdf

Digital endpoints for patient-focused health management

> **What gets me excited about digitally derived endpoints is the many promises they offer to improve the way we measure a patient's lived experience with their disease and ultimately better inform regulatory and HTA decisions. I know there are gaps in the ecosystem, but I see us already working together to close these gaps. Initiatives such as DEEP or the newly launched IHI go absolutely in the right direction. I look to a future where pre-competitive collaborations and efficient regulatory procedures for novel endpoints are the norm and where patients directly benefit from it!**
>
> Lada Leyens, Senior Director Regulatory for Roche

INTRODUCTION

The growing trend of digitalization across the healthcare ecosystem has transformed medical research, diagnostics, and therapeutics. This digitalization has led the way to rapid developments in the expansion and implementation of Digital Health Technologies (DHT) by the healthcare sector. With the propagation of DHTs, the term 'digital endpoints' has been steadily used to define a wide-ranging collection of measurements.

Digital endpoints are a novel type of endpoint that are derived from DHT-generated data (e.g. from sensors), which is often collected outside of a clinical setting, such as in a patient's daily activities. Digital endpoints can capture a pool of participants and real-world experiences from which novel insights can be generated to understand disease and aid clinical decision making.. Besides providing more precise and accurate assessments, digital endpoints could significantly decrease the time and costs related to trial participation, predominantly for persons with physical or time limitations[36,37]. However, we still have gaps in the ecosystem to enable seamless development, validation, interpretation and regulatory acceptance of novel digital endpoints. We need to work together with a broad range of stakeholders to solve these gaps in order for these measures to become fully a reality and realise its impact to patients by advancing drug development and medical innovation.

DIGITAL ENDPOINTS AND PATIENT ENGAGEMENT

In order to select meaningful digital endpoints, early and often patient engagement is key to ensure the measure is meaningful to patients and the DHT is also patient friendly and not adding burden. Therefore, stakeholders are stimulated by regulators to have a patient focus but often a well-defined action plan for patient engagement is not present. This comes with a risk for stakeholders to create digital versions of outdated or non-meaningful assessments and generate diminished DHT tools that are not fit for purpose38, burdensome, and decrease both quality and effectiveness in clinical care and research.

Thus, it is critical to safeguard the development of digital health measures with high-quality and a patient-centric and fit for purpose approach. Particularly, how can we guarantee that effective digital measures are created to detect important alterations in patients' everyday lives?[39,40]

DIGITAL EVIDENCE ECOSYSTEM AND PROTOCOLS – DEEP

In order to increase the efficiency in development and acceptance of digital endpoints in research and healthcare, we need to prioritize in identifying and developing measures in areas of unmet measure need, with not-so-gold standards. At this time, there is a wide collection of digital measures in development across therapeutic areas, use cases, and populations leveraging a wide range of technologies; most of them focusing on mobility and around a small number of disease areas. The lack of pre-competitive collaboration in this space can lead to wasted resources, but more importantly to the difficulty of interpretation and comparison of outcomes of trials in one disease area.

The Digital Evidence Ecosystem and Protocols (DEEP) initiative has been ideated to cover gaps in the current digital endpoints development ecosystem. This solution is supported by EFPIA and addresses these gaps with three key components:

36 - https://www.nature.com/articles/s41746-022-00583-z
37 - https://medcitynews.com/2022/05/digital-endpoints-global-opportunities-and-clinical-data-protection-and-other-challenges/
38 - https://trialsjournal.biomedcentral.com/articles/10.1186/s13063-022-06707-w
39 - https://www.karger.com/Article/Fulltext/509725
40 - https://www.nature.com/articles/s41746-020-0305-8

1) catalogue component that enables re-use of (parts of) digital measures; 2) collaboration ecosystem that enables pre-competitive and multistakeholder collaboration on digital measure development and 3) and ecosystem of services to connect the relevant stakeholders and facilitate the connections[41]. Especially important is the component related to facilitation of regulatory interactions aiming to improve the qualification procedures enabling more dynamic and iterative interactions, better access to experts and increased transparency on the regulatory insights gained through these interactions. These concepts are being piloted with the EMA.

The DEEP solution offers the opportunity to advance:

- Patient-focused drug development with digital endpoints that reveal novel insights of real-world health settings
- Collaboration within and among the industry and regulators to share solutions and co-create multistakeholder interactions for faster qualification advice
- Development, validation and approval of digital endpoints
- Access to data and solutions in an agile approach
- Transparency among different stakeholders (regulators, industry, patients, HTAs and SMEs) in the digital measures landscape
- Visible and accessible publication of standards related to digital measures
- Presenting evidence in a consistent way to regulators and other parties
- Re-using measures across diverse disease areas

The DEEP ecosystem's workflow is currently being evaluated via use cases to establish collaborations and new ways of working.

COLLABORATIVE NETWORK: CASE-STUDIES

The Innovative Health Initiative (IHI), which was built on the successes of the Innovative Medicines Initiative (IMI), supports several projects that are working on health-related mobile and digital technologies and puts them into practice to advance research in various disease areas like MOBILISE-D and IDEA FAST:

MOBILISE-D

An important indicator of health is 'Mobility', however, in the real world, there lies a challenge in precisely measuring a person's mobility. The solution is MOBILISE-D, with the purpose to develop a wide-ranging system to examine mobility based on digital technologies, with the use of sensors worn on the body. The case-study concentrates on diseases that affect mobility, i.e. chronic obstructive pulmonary disease (COPD), Parkinson's disease, multiple sclerosis, hip fracture recovery, and congestive heart failure. Once MOBILISE-D is validated, the results will help to progress accurate measurement of mobility in clinical trials. Likewise, the mobility of patients will be easier to track by clinicians and thus add to better-quality, more personalised care[42,43,44].

IDEA FAST

The aim of IDEA-FAST is to recognize digital endpoints for fatigue and sleep disorders that will offer a more subtle, consistent measure of the severity and effect of these indications in a real life scenery. This will be done by detecting the features of fatigue and sleep disturbances and the digital endpoints that could enumerate them. Next, digital health technologies will be selected to measure and record the symptoms. Also, a secure digital management platform will be designed to support the acquisition, storage and analysis of the data. In addition, IDEA-FAST's results should dramatically improve the efficacy of clinical trials, and therefore speed up the development of innovative treatments for these chronic diseases[45].

CONCLUSION

The use of digital endpoints offers the opportunity to create improved and stronger evidence that is meaningful to the patient and can inform regulatory decisions as well as payer decisions. In the same spirit as real-world evidence, digital endpoints are likely to enhance clinical data by portraying a more objective image of what is essentially happening with patients and their disease. In this new field, we have reached the stage where developers of digital endpoints need to demonstrate how these endpoints can improve understanding of disease and ultimately lead to improve outcomes. Digital endpoints can be developed, assessed, adopted, and reused across different areas in the life sciences and healthcare industry; however we need to advance the ecosystem together with all relevant stakeholders to ensure we achieve the promise within and beyond drug development. Especially important is the connection to EFPIA's "Regulatory Road to Innovation" action plan as well as the EMA's "Regulatory Science to 2025" strategy. And thinking of the broader ecosystem, it will be important to also bring HTAs along the journey as well as other relevant stakeholders in healthcare systems.

LADA LEYENS
PhD, Senior Director in Regulatory, F. Hoffmann-La Roche Ltd

ANETA TYSZKIEWICZ
Senior Manager Digital and Data, EFPIA

41 - https://www.ispor.org/publications/journals/value-outcomes-spotlight/vos-archives/issue/view/november-2020-supplement-spotlight-on-europe/the-digital-endpoints-ecosystem-and-protocols-(deep)-initiative-a-collaborative-multi-stakeholder-approach-to-defining-and-developing-standards-for-digital-endpoints
42 - https://www.imi.europa.eu/news-events/newsroom/digital-biomarkers-initiative-help-researchers-navigate-new-reality-roles
43 - https://www.ema.europa.eu/en/documents/other/letter-support-mobilise-d-digital-mobility-outcomes-monitoring-biomarkers-follow_en.pdf
44 - https://www.mobilise-d.eu/
45 - https://www.ihi.europa.eu/projects-results/health-spotlights/impact-data-management

A sustainable environment for a healthy population

There is strong agreement between Bengt Mattson and Andreas Haener, chairs of the interassociation industry pharmaceuticals in the Environment task force (IAI PiE TF) – industry has taken big steps over the past decade to combat the impact of pharmaceuticals in the environment. Bengt in particular has worked in the industry over the past 30 years, and led the IAI PiE TF since its set up over 15 years ago, 'The industry has taken strides forward in minimising its emissions and driving environmental sustainability. Every stakeholder concerned must play its fair part and the industry has taken a leading role in this respect'.

Andreas, the environmental risk assessor for Roche, agrees wholeheartedly – 'a collaborative approach is essential. Look at the IMI PREMIER Project, it brings together world-leading multi-disciplinary partners from the public and private sectors working to contribute to a sustainable future by proactively managing the environmental impact of medicines together.'

INTRODUCTION

The pharmaceutical industry acknowledges the impacts medicines and medicine's development may have on the environment, that is why steps are being taken to ensure a healthier and environmentally more sustainable future. This can be accomplished by approaching an agile, innovative and evidence-based sustainability strategy to empower the industry to evolve in science, technology and society and to push sustainable, high quality medicines across the entire value chain[46].

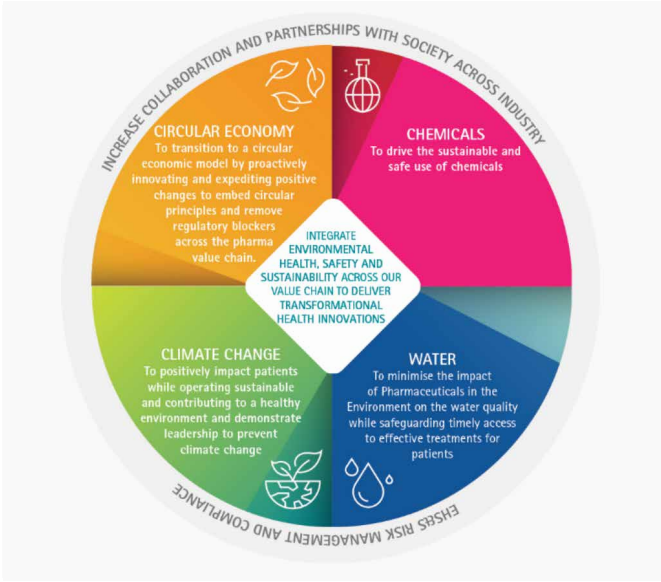
As we strive to move towards environmental sustainability, collaborating, coordinating, increasing conversations, listening, sharing, and learning with and from our partners is fundamental.

Therefore, at EFPIA, we believe a cooperative approach with broader stakeholders to be the way that will allow us to expand our common knowledge and comprehension on how to proactively handle any potential risks imposed by the existence of Pharmaceuticals in the Environment (PiE). Consequently, EFPIA along with AESGP and Medicines for Europe have established the Eco-Pharmaco-Stewardship (EPS) framework with the strong focus on PiE and is executed across the industry and with broader stakeholders in the healthcare and environmental sector[47].

Our members are devoted to making a positive impact on the lives of patients whilst functioning in sustainable ways. As we have a responsibility towards the health of the population, we are moving forward in making a beneficial impact to the society by actively addressing concerns and raise awareness around risks concerning the impact on the environment while responding to patient needs and ensuring access to life-saving medicines.

INDUSTRY ACTIONS AND THE EXTENDED ENVIRONMENTAL RISK ASSESSMENT CONCEPT

A risk-based approach is encouraged by the pharmaceutical industry to evaluate environmental challenges and thereby creating initiatives to endorse greater environmental responsibility across the industry and the society for water, chemicals, climate change and circular economy[48].



Although research driven pharmaceutical companies do not typically belong to high energy consuming companies, they are at the forefront of numerous ground-breaking initiatives to help reduce CO_2 emissions. They are committed to contribute responsibly to progress in mitigating climate change and transitioning to circularity across the medicines life-cycle with regard to CO_2 emission reduction targets, specifically addressing increased energy efficiency and lowered energy intensity across our value chains.

Furthermore, our members take responsibility for reducing environmental risks from both manufacturing emissions, through implementation of risk-based containment procedures in their manufacturing Effluent Management Programs and also extended producer responsibility (EPR) programs for waste pharmaceuticals and supporting the meds disposal campaign and other take-back schemes[49,50]

46 - https://www.efpia.eu/about-medicines/development-of-medicines/regulations-safety-supply/environment-health-safety-and-sustainability/
47 - https://www.efpia.eu/media/636524/efpia-eps-brochure_care-for-people-our-environment.pdf
48 - https://www.efpia.eu/more-than-medicine/responsible-innovation/
49 - https://www.efpia.eu/media/637030/policy-statement-iai-manufacturing-effluent-management.pdf
50 - https://www.efpia.eu/media/637031/responsible-manufacturing-effluent-management_technical-guidance.pdf

In the coming weeks, as part of the pharmaceutical legislative review, the Commission will adopt legislation looking at strengthening the environmental risk assessment for medicines. Minimizing the impact of pharmaceuticals in the environment, the extended Environmental Risk Assessment (eERA) concept was proposed by the pharmaceutical industry to address the challenges and strengthen the Environmental Risk Assessment (ERA) process in the EU.

We believe that the ERA should be reviewed and, if necessary, updated throughout a product's lifecycle to reflect the latest information on the medicine's potential impact on the environment, while avoiding duplications of submissions for off-patent drugs. However, the focus should be on the active pharmaceutical ingredients (APIs) entering the environment and not on each single product, as a single API can be used in multiple products. Regulatory, academic and industry resources and associated environmental mitigation strategies should be prioritised on those APIs that pose a potential risk to the environment. This is why we have been working on the eERA concept.

The refinement of the existing ERA process for medicines would ensure that they remain up-to-date and relevant, capturing new reliable environmental toxicity data and measured environmental concentration. Newly available data from research can play an important role in the refined ERA process, extending beyond marketing authorisation. The ERA of a medicine is currently performed by companies either as part of a new marketing authorisation, line extension or when marketing authorisation for an existing product is expected to increase the environmental exposure of the API. The ERA must be performed to evaluate potential risks of medicines to the environment and ensure adequate precautions are taken where specific unacceptable risks are identified[51,52,53].

In summary the eERA aims to provide the following benefits[54,55,56,57]:

- An API based ERA which better reflects the risks posed to environment from patient use
- Conduct robust and risk-based ERAs without compromising environmental protection or patient access to medicines
- Provision for the ability to automatically cross-reference ERA data in marketing authorisation applications
- Provide a mechanism for risk identification, refinement, and management during the MAA evaluation process
- Provide clarity on appropriate well-defined follow-up responsibilities for ERAs with no need for independent and duplicative risk identification and prioritisation processes under different legislations (e.g. Water Framework Directive)
- Updates to the ERA across the life cycle of the API in each medicinal product, with the latest environmental information
- A focus on risk that reduces the burden on regulators (i.e. oversight) and industry
- Reduction in the duplication of testing, delivering improved ERA consistency, proportionate use of testing resource, and bioethical benefits
- Increase the transparency of, and access to, ERA data

Furthermore, EFPIA members are committed to the science-based phase-in of methods to replace the use of animals for scientific purposes and the waiving of animal tests which are obsolete or redundant. Therefore, we believe that alternative and intelligent testing strategies such as the use of predictive in silico and in vitro tools can play an active role in reducing or avoiding unnecessary and particularly animal intensive testing required as part of the ERA. The prioritisation of testing of legacy APIs and development of intelligent testing methods has been, and continues to be, a significant research priority for the pharmaceutical industry and the European Commission through the Innovative Medicines Initiative (IMI).

CONCLUSION

The pharmaceutical industry is driven with motivation to advance human health and wellbeing in a sustainable way. Moreover, EFPIA welcomes and embraces the Commission's emphasis on the Green Agenda and a more sustainable Europe, and is engaging constructively on the roll-out of their policy priorities. There are many risks associated in the whole life-cycle of a medicinal product that impact the environment negatively. Further understanding of these impacts and the interface between the society, health and the environment is the key to guarantee that the pharmaceutical industry can form and execute actions. Next to these initiatives, we as industry should create awareness to the users/patients and support them to act sustainable by properly disposing medicines. This should be a team effort as the overall goal is to create a sustainable environment for a healthy population.

BENGT MATTSON
Lif, Pharmaceutical Industry Association and co-chair of EFPIA's task force on pharmaceuticals in the environment (PIE TF)

ANDREAS HÄNER
Environmental Risk Assessor, F. Hoffmann-La Roche Ltd

51 - https://www.efpia.eu/more-than-medicine/
52 - https://www.efpia.eu/more-than-medicine/responsible-innovation/
53 - https://www.efpia.eu/media/637068/putting-animal-welfare-principles-and-3rs-into-action.pdf
54 - https://www.efpia.eu/media/637033/eera-document_final.pdf
55 - https://www.efpia.eu/about-medicines/development-of-medicines/animal-use-and-welfare/#:~:text=EFPIA%20members%20are%20committed%20to,which%20are%20obsolete%20or%20redundant.
56 - https://www.efpia.eu/news-events/the-efpia-view/blog-articles/how-research-pharmaceutical-companies-are-contributing-towards-tackling-global-warming/
57 - https://www.efpia.eu/media/554662/white-paper-climate-change.pdf

Real-world data/evidence: How it can inform patient treatment and care decisions

> **Real world evidence is about generating insights that matter to patients sooner; embracing the possibilities offered by real world evidence for patient centred product development is an opportunity beyond obligation.**
>
> Álmath Spooner: Director Global Regulatory Policy and Intelligence at AbbVie

> **Realizing the potential of RWE will require collaboration across all stakeholders to deliver improved health information infrastructure and a regulatory regime that facilitates iterative scientific dialogue on evidence generation plans for faster, better decision making.**
>
> Karin Van Baelen: Head of Global Regulatory Affairs at Janssen, Pharmaceutical Companies of Johnson and Johnson

INTRODUCTION

Clinical evidence generation for healthcare products has advanced to include a range of approaches. Although clinical trials (CTs) remain the research modality most relied upon by regulatory authorities for establishing clinical safety and efficacy, the lifecycle of evidence generation for medicines and vaccines increasingly include real world evidence (RWE) as a valuable component for assessment both pre- and post- regulatory approval[58,59]. The key driver for the selection of a research methodology in healthcare product development is the underlying research question. Both clinical trials and RWE generation require robust research practices and their value in a particular case depends on their fitness to address the question posed.

The COVID-19 pandemic has highlighted the need to embrace the totality of evidence to accelerate epidemiological understanding of disease and the value of existing and new preventive and therapeutic interventions. The effectiveness of several COVID-19 mRNA vaccines was estimated at the population level in "real-world" settings by analyzing Electronic Health Records (EHR) and vaccination data. Importantly, this example illustrates a scenario where RWE can provide answers to scientific questions that might not otherwise be available from CTs. Real-world data (RWD) are data regarding the effects of disease (patient characteristics, clinical and economic outcomes; health related quality of life) and health interventions (e.g. safety, effectiveness, resource use) been collected through routine clinical practice. The evidence derived from the analysis (and/or synthesis) of RWD, known as RWE, provides insights that inform all aspects of drug development from discovery to outcomes research. Feedback loops from clinical care to research and development allow for better, faster decision making through product development to delivery of healthcare. The main advantage over data and evidence from CTs is that RWD and the resulting RWE reflect real clinical practice. RWD can enable a better view of the actual effectiveness and characteristics of a medical product or technology, and create new insights to improve health outcomes for patients and efficiency of healthcare systems.

RWE can enhance healthcare decision making, by demonstrating outcomes and value for patients, healthcare professionals, regulatory bodies, Health Technology Assessment bodies and payers. Consequently, RWE can play a key role in their decision-making process and, as such, has received increased attention over recent years by the healthcare community and policymakers. Changing expectations for the use of RWE in regulatory decision making has particularly catalyzed scientific dialogue on how to increase alignment on the fitness for purpose of RWE in a particular research scenario. As users and generators of RWE, the research-based pharmaceutical industry has called for clear principles from regulatory authorities for data quality and interoperability, governance frameworks that facilitate access to data, and pathways for iterative scientific dialogue to align on the relevance of data sources and the fitness for purpose of methodologies and analytical approaches.

Use of RWD offers unique potential to create a learning healthcare environment where individual patient care can be personalised, where transitions between research and clinical practice are more seamless and where understanding of patient experience is more holistic. To build multistakeholder confidence in RWE, the value proposition for all partners in the healthcare ecosystem must drive collective efforts to collaborate as part of a patient centered model for clinical evidence generation.

58 - Flynn R. Et al. Marketing Authorization Applications Made to the European Medicines Agency in 2018– 2019: What was the Contribution of Real- World Evidence? Clin Pharmacol Ther. 2022;111(1):90-7.
59 - https://ascpt.onlinelibrary.wiley.com/doi/full/10.1002/cpt.2462

CURRENT BARRIERS

While healthcare product developers and policy makers recognize the potential value of RWD/RWE, there is also acknowledgement that there are challenges that need to be addressed to realise this potential. The variety in research objectives, study designs, data and methods presents a challenge for standardization. Regulators and other decision-makers across the globe evaluating RWE hold different expectations regarding their use and fitness for purpose. This diversity within and across regions, including across and within stakeholder groups, persists, although efforts are underway to improve convergence where possible[60]. A reliable data ecosystem is essential to accomplish a basic level of quality, relevance and interoperability amongst health data with the ability to link different sources. In this context, a European Health Data Space (EHDS) is one of the main priorities of the European Commission[61].

Generating insights from RWD requires access to the data in manner that is sustainable, predictable and which robustly protects data privacy. The EHDS will have a robust system of data governance and exchanging procedures, to safeguard the quality of data, and to create strong infrastructures that guarantee complete interoperability. Besides supporting healthcare delivery, the EHDS will provide a more robust framework for using RWD for secondary research and to inform health policy making. Furthermore, the scheduled launch of DARWIN EU® in 2024, which is EMA's own combined network of RWD sets, will be added to the EHDS and utilized to advance regulatory decision making by performing RWD-related research. This will provide multiple stakeholders a unique opportunity to align on the composition of fit-for-purpose evidence in a specific context[62].

Alongside DARWIN EU, we already see the benefits of public-private partnerships to improve healthcare data infrastructure in Europe. The IMI European Health Data and Evidence Network (EHDEN) project was set up to build an open-science network for large-scale data sources, in order to allow the use of RWD to generate RWE that is applicable to a broad range of use cases[63].

Robust study design and data analysis are critical requirements for multistakeholder confidence in RWE. A shared confidence in methodologies requires platforms for discussion[64]. Additionally, a framework for iterative scientific dialogue will enable greater alignment on evidence generation plans.

CONCLUSION

RWD/RWE has the ability to characterize patients' unmet needs, expedite understanding of disease and inform decision making through the product lifecycle from discovery through to access. Realizing the potential of RWE will require collaboration across all stakeholders to deliver improved health information infrastructure and a regulatory regime that facilitates iterative scientific dialogue on evidence generation plans for faster, better decision making.

ÁLMATH SPOONER
Director Global Regulatory Policy and Intelligence, AbbVie

KARIN VAN BAELEN
Head, Global Regulatory Affairs, Janssen, Pharmaceutical Companies of Johnson & Johnson

60 - https://globalforum.diaglobal.org/issue/november-2022/right-time-for-roadmap-to-harmonizing-rwe/
61 - https://health.ec.europa.eu/ehealth-digital-health-and-care/european-health-data-space_en
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How regulation can boost the EU innovation?

Technology moves fast. An agile and streamlined innovation ecosystem would make Europe more competitive and bring breakthroughs to patients

We have reached an important moment for Europe's ambition to be a global leader in innovation. The pharmaceutical industry is a key source of technological advances that improve the lives of patients, as well as a major driver of growth, jobs and creativity in the wider economy.

Regulation plays a central role in the development and use of safe, effective and medicines with impeccable quality. The revision of the current EU regulatory framework for pharmaceuticals is a chance to create a predictable, clear and consistent environment.

The EFPIA Innovation Board took a deep dive into the ways regulation can accelerate or hamper pharmaceutical innovation. We have produced evaluation principles that policymakers can use to evaluate future regulations that govern pharmaceuticals (see below).

LIFE SCIENCES INNOVATION ECOSYSTEM

First, let's be clear what we mean by innovation and the challenges that arise for regulators. History tells us that tomorrow's innovations will be very different from today's technologies. Knowledge is doubling faster than ever, while scientific fields are converging. From nanoscience to artificial intelligence, and from software integration to big data, future advances may not fit comfortably within existing regulatory frameworks.

If healthcare systems struggle to adapt, innovation will outpace the ability of laws, regulations and healthcare practices to embrace progress. This poses problems for industry, while acting as a brake on patient access to the fruits of scientific progress.

The path forward is to devise pharmaceutical legislation with adequate agility to futureproof it for emerging scientific discoveries. Adaptability is essential. The ability of our system to adapt to the Covid-19 pandemic has shown what is possible. This experience illustrates the value of taking a risk-based approach, leaving the innovator the freedom to operate within a set of agreed boundaries.

It should be noted that alongside the radical innovation powered by breakthrough technologies, routine innovation also continues to address unmet need. For example, changing the formulation of a medication can allow it to be administered as a subcutaneous injection rather than by intravenous infusion – saving time and resources, while offering convenience and quality of life for patients. Well-designed policy instruments must account for all types of innovation.

PREDICTABLE, STREAMLINED LEGISLATION

An efficient regulatory ecosystem can provide value to patients and the health system but, as all regulation comes with costs for innovators (and for the system), it is important to get the balance right. A business's ability to innovate is framed by the innovation system in which it is embedded. Complying with multiple layers of governance at EU and national level can add time and costs to the process.

For example, the European system features multiple networks of decision-makers, including medicines regulators, Notified Bodies, and Health Technology Assessment bodies. These stakeholders have different ways of working, diverse needs, and a variety of expectations of innovators. Such complexities can add unpredictability and bureaucracy.

EU-level legislation should aim to simplify and streamline processes, while Member States must strive to avoid complication and contradictions in how rules are implemented. There is a clear need for regulatory convergence between jurisdictions to avoid inefficiencies.

What is needed is a system that is consistent, predictable, and adaptable. It is paramount for the innovators but also for the society, which will bear the cost of less research, less innovation and by that, decline or stagnation in welfare. Unless we get this right, Europe will suffer a decline in its capacity to attract international investment. Reduced global competitiveness would have significant impacts on economic growth and on the fortunes of patients awaiting access to innovative tools and therapies.

Table 1. Evaluation principles for future regulations that govern pharmaceuticals

Principle	Key considerations
PLASTICITY Anticipatory and agile	Does the policy measure accommodate different types of innovation as defined in Oslo Manual (radical, architectural, modular and incremental)? Are there any elements that could limit innovation that are not easily amendable? Is the proposed measure futureproof enabling enough freedom for the industry to operate efficiently?
Type of policy measure	Which policy instrument (hard/soft law) would be most impactful and would provide appropriate level of risk governance and degree of agility? (i.e., how hard it is to change to meet the product, process or organizational innovation)
FEASIBILITY Likeliness to meet the intended effect **Patient centricity**	Will patients continue to have access to effective, safe and high-quality medicine in a timely manner? Is there a positive impact at system or societal level, e.g., cost savings or additional health gains? Are the conditions to bring medicines to a market competitive and attractive? Will Europe reinforce its innovation ecosystem and position in the global market? Will the policy measure enable greater patient input where applicable? (Including unmet needs)
IMPACT Connectivity & unintended consequences	Is there a risk of unintended effects? Is the policy proposal considering adjunct policies or frameworks (e.g., multiple decision makers) and attempting to streamline rather than add bureaucracy? Have all the relevant adjunct policies been considered?
COST (direct/indirect)	Will the impacted organizations need to change current processes, infrastructure or increase in resources? Have they been consulted of the cost/benefit assessment? (a) the regulator (b) industry.
CONTEXT Impact on international competitiveness	How will the policy measure support future innovation in the region and support the innovation ecosystem? Does the policy measure create entry barriers, impact the ability to operate negatively, reduce attractiveness of the region or delay launch of new innovations?
RESOURCES for implementation	Who is needed to implement and monitor the impact of the regulation? Is funding needed and is it secured? How is the European regulatory network impacted and can they carry the proposed tasks? Are governance changes required?
EFFECTIVENESS MEASURE	Are novel therapies and vaccines reaching the patient faster? Are scientific breakthroughs translating into new therapies? Is the system improving and efficiently embedding findings from regulatory science? Are there any unintended effects observed?
System impact: gaps	Are other system reforms required to enable different types of innovation?

KEY FACTORS IN DESIGNING A REGULATORY FRAMEWORK

While continuing to rely on the precautionary principle of the pharmaceutical legislation, the EFPIA Innovation Board proposes in addition to the evaluation principles, actions for the European policymakers, to support a more streamlined regulatory system.

- **Adaptability:** Use guidance documents as soft law tools to enable agile adoption of new tools and methodologies in line with the fast-paced evolution of science and technology.
- **Regulatory science:** Strengthen further emphasis on regulatory science to inform how the regulatory system is performing and support fit-for-purpose assessment of tools and methodologies.
- **Effective patient focus tools:** Conduct a thorough cost/benefit assessment of the new regulatory tools to ensure they have an overall positive impact, particularly from the patient perspective, as the ultimate beneficiary but also from the system perspective, to be able to carry the tasks given to the regulator or avoid burdening the regulated industry unless clear benefits are gained.
- **Stakeholder engagement:** Leverage stakeholder consultations to ensure that the framework actively mitigates negative externalities or unintended effects for every type of innovation or different types of products, which are often unavoidable with regulation.

The beauty of a fast-moving innovative sector is that we cannot know for sure what the future will bring. We can, however, build a system capable of coping with change while consistently applying agreed principles that support safe and timely access to medicines.
There is a lot at stake. Europe must take this opportunity for active dialogue with industry experts on building a fit-for-purpose innovation ecosystem.

NOTE: This blog is based on the research article "Role of innovation in pharmaceutical regulation: a proposal for principles to evaluate EU General Pharmaceutical Legislation from the innovator perspective" by Heikkinen et al, available online as pre-proof before print, in Drug Discovery Today. LINK: https://doi.org/10.1016/j.drudis.2023.103526

INKA HEIKKINEN
Director of Global Regulatory Policy, MSD

SINI ESKOLA
Director Regulatory Strategy, EFPIA

and colleagues: Inkatuuli Heikkinen (MSD), Sini Eskola (EFPIA), Virginia Acha (MSD), Alan Morrison(MSD), Chris Walker (Amgen), Catherine Weil (BMS), Antoine Bril (Servier), Max Wegner (Bayer), Thomas Metcalfe (Roche), Salah-Dine Chibout (Novartis), Magda Chlebus (EFPIA)

Dynamic Regulatory Assessment will support more efficient treatment development for patients: the time to pilot is now

> **Dynamic Regulatory assessment has the potential to significantly increase the efficiency of development and assessment of medicines, without reducing the evidence bar.**
>
> Judith Macdonald – Global Policy Development Lead at Pfizer Global Regulatory Policy and Intelligence

BACKGROUND

The current European Union (EU) model for authorising medicines requires submission of a marketing authorisation application (MAA) with complete information on e.g. safety, efficacy and quality followed by a standard review procedure lasting 210 days, with additional time allotted for clock stops to respond to questions. For certain promising treatments, greater agility and support would result in more efficient development and faster approval, without compromising on the level of evidence. The EFPIA concept of Dynamic regulatory assessment (DRA) describes improved regulatory dialogue and knowledge building during medicine development, supported by data packet release and assessment at time points agreed by the developer and regulator. Piloting of the concept is possible using current processes and IT capabilities, although these would need to evolve for DRA to reach its full potential. DRA would drive increased efficiency by identifying gaps in evidence generation earlier, assessing released data packets to improve final assessment efficiency, and reducing uncertainty by supporting regulator familiarisation with the data and decreasing the risk of unexpected questions at assessment. Implementation of DRA would support more rapid approval of innovative medicines and faster access for patients to new treatments of life-threatening diseases, without decreasing the evidence bar[65,66].

EFPIA has prioritised DRA because the value of the approach has been proven e.g. with the part rolling review played in supporting the rapid development of the COVID-19 vaccines, and as the concept is already in place in other global regions. Rolling review was effective, but burdensome: a thoughtful updated approach is needed, leveraging shorter term projects to improve EU regulatory processes non legislatively and the European Commission (EC) Pharmaceutical Strategy[67] longer term. Moreover, Annex 1 of the recent EC consultation on EMA fees68 included a fee for this phased approach suggesting the EC and regulators are also considering the concept. It will take time to learn how to optimise this approach for the EU, however, so the time to pilot DRA for the EU is now to ensure the concept is effectively implemented into the regulatory framework to support development and efficient assessment of the most promising treatments for patients[69].

CURRENT SITUATION AND VISION

It will take several years for DRA to be fully considered and implemented in the EU, since this will require adjustments to policies, processes and IT that will need to be informed by practical experience. To support this, it is crucial to have an aligned EU vision on DRA.

Today, a product's benefit-risk profile is assessed by a regulatory submission dossier built at the end of the development process to authorise the treatment for an indication that can be extended as further data is generated and assessed. Early conversations with regulators and medicine developers can provide clarity on expected evidence generation and when packets of data could be released for assessment to support development, regulator familiarisation and ultimately more efficient assessment. This can start to be piloted now. This approach would apply across the medicinal product lifecycle, although the intensity of engagement may fluctuate depending on the type of data, lifecycle phase, and other considerations. Longer term, evolution in terms of data standards, process and IT development will increase the efficiency and benefit of the DRA approach.

Scientific dialogue is crucial for effective development as it supports mutual developer and regulator understanding on what evidence needs to be generated for regulatory approval. It can also support broader stakeholder engagement where appropriate e.g. connecting Member State advice at clinical trial approval, feedback on device components, patient perspectives and more. Release of discrete

65 - https://efpia.eu/media/541132/efpia_regulatory-road-to-innovation_leaflet.pdf
66 - https://www.clinicaltherapeutics.com/article/S0149-2918(21)00456-2/fulltext
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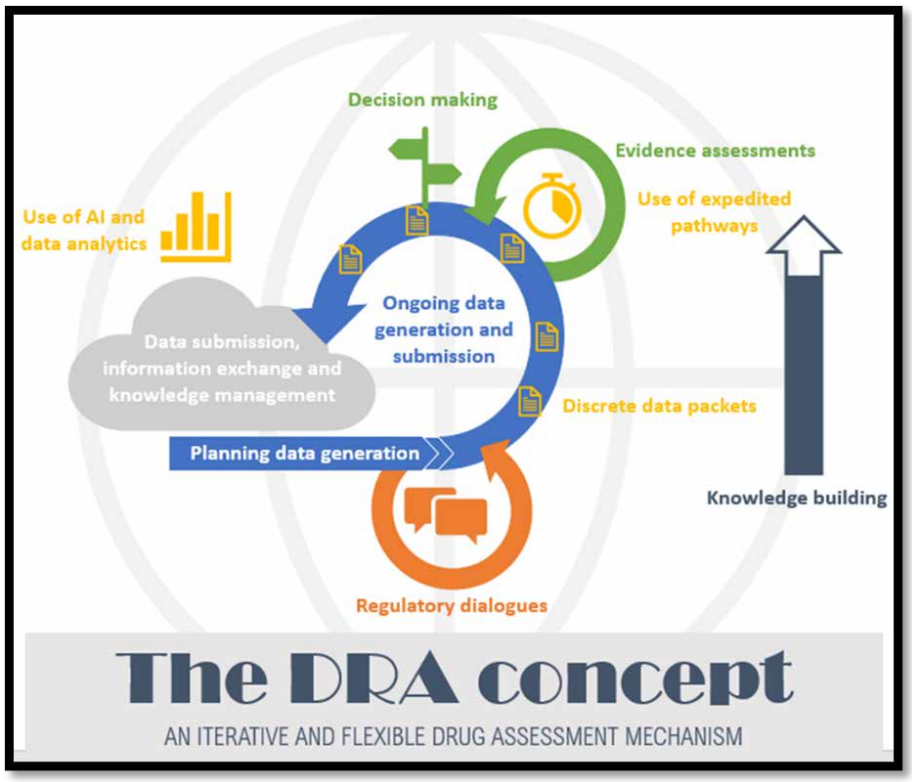

Figure 1: DRA concept outline

data packets under DRA will drive a connection between some of these disparate interactions, improving the building of knowledge management and corporate memory in the European Medicines Regulatory Network by better incorporating R&D product dialogue along the medicine life cycle.

Rolling reviews were successfully used during the COVID pandemic, leading to greatly reduced development and authorisation timelines. Although this level of resource can only be provided in public health emergencies, there are learnings that must be extracted from iterative release and assessment of data and applied more broadly. DRA should be thoughtfully applied to promising treatments as an important mechanism to support development and efficient regulatory approval.

CONCLUSION

Fully realising the potential of DRA would benefit from a short- and long-term roadmap, aligned across the relevant stakeholders. This will allow implementation of the process in a way that is beneficial to the developer, regulators and ultimately the patient. We recommend beginning the development of DRA for EU patients, with a pilot of this concept which we believe could be implemented now. In addition, the inclusion of a fee model adapted to support this process in the draft EC EMA fee consultation is welcomed as it will provide a framework for the approach to be financially viable.

Medicine development is global, and this approach would also support the EU's ambition to remain globally competitive as a region of choice for medicine development and approval.

ESTEBAN HERRERO-MARTINEZ
Director, Regulatory Intelligence and Policy, AbbVie

A modernised EU Variation Framework for enhancing the life of European patients

> **After more than 20 years since the last major revision, now is the time to update the regulatory framework for variations to simplify and adapt it to keep pace with scientific development. This will benefit patients by decreasing the risk for shortages and ensuring swifter access to innovative medicines and optimise life-cycle management to ensure the availability of safe, effective and innovative treatments to patients in a timely manner.**
>
> Pär Tellner, Simon Bennett & Markus Goese

BACKGROUND

The submission of information to regulators does not end with a medicine being approved. Medicine developers are required to continuously update the terms of their marketing authorisation to reflect the current understanding of the quality, safety and efficacy of a medicine. The current EU legal framework for managing these updates, the EU Variation Regulation and Classification Guideline70, is inflexible, outdated and is associated with a very high administrative burden both for industry and for regulators. Therefore, there is a pressing need to modernise the variation framework for human medicines in order to support future innovation in medicine development and manufacturing within the EU. Moreover, it should be a priority to revise the EU variation framework in the light of recent experience with the COVID-19 pandemic which underlined the necessity for a flexible and agile regulatory system in Europe that can rapidly respond to the needs of patients by guaranteeing the optimization of life-cycle management to deliver safe and effective treatments of high quality to patients[71].

THE TIME IS NOW

A comprehensive revision of the Variation Regulation (1234/2008) and the associated Classification Guideline (C(2013) 2804) is essential to deliver simplification, well-organized life-cycle management and to adapt to latest technological developments such as digitalization. This also includes addressing challenges that link to the increasing number of medicines associated with devices, as well as for novel and more complex therapies, such as cell- and gene/ advanced therapies (ATMPs). Meanwhile, for the EU, there is an opportunity to continue playing a leading role in driving international alignment across variation systems thereby improving lifecycle management at a global level. The time for action is now because:

* There are many challenges due to resource constraints within the EU regulatory network. Implementing a streamlined variation framework with accompanying advances in Information Technology to reduce the administrative burden for variations could release resources for use in other areas such as scientific advice and assessment of new medicines.
* The full incorporation of risk-based approaches to lifecycle management, together with potentially embedding some regulatory flexibilities adopted during the COVID-19 pandemic would support innovation in the EU, particularly in manufacturing and quality where advances in this area are often implemented via the variation framework. A very important modality to benefit from such full incorporation of a risk- and science-based approach would be well defined biologics (e.g. monoclonal antibodies), where industry has made significant progress over the last decades in terms of understanding the products and their manufacturing processes. The risk-based approach may also be extended beyond quality topics to include updates to labelling under certain circumstances.
* Lessons learned from the pandemic and expedited programs like PRIME have also demonstrated that post-approval lifecycle management continues to be a critical bottleneck under the current variation framework.
* On-going work on digital projects, portals, digital infrastructure and databases of the EMA and National Authorities serve as a building block for the future operational support to regulatory processes.
* Raising the modernisation of the variation framework as a priority now facilitates progress towards a future-state which could be aligned with modifications to the general EU pharmaceutical legislation.

70 - https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2008:334:0007:0024:EN:PDF
71 - https://www.medicinesforeurope.com/wp-content/uploads/2020/01/ESE_2019_Medicine-for-Europe_AESGP_Variation_WEB.pdf

GOING FORWARD

Going forward, it will be essential to build on experience and technical innovations to provide an EU variation framework that allows for efficient lifecycle management of medicines and vaccines today and which can also include future technological advances. Furthermore, revision to the EU change classification should incorporate all elements of the important international guideline ICH Q12 and accommodate developments of innovation and science to be "fit for the future". This should preferably happen via regulatory guidance, to allow for regular review and updating, rather than embed the detailed provisions in a regulation.

In parallel, advances in digital technology should be exploited to reduce the administrative burden associated with the oversight of minor variations that have no impact on safety, efficacy or quality of a medicine. In the near-term this may involve the development or extension of EU databases to maintain administrative information. In the longer term, advances in cloud-based technology could be employed to enable real-time maintenance and oversight of the dossier by regulators, thereby negating the requirement for any type of additional submission or data entry by regulators and industry. The present variation regulation needs however to be revised to fully benefit from such rationalization.

Lastly, the current and future needs of Regulators and Manufacturers should be reflected in a future variation framework through simplification, standardization and acceleration to certify optimal delivery of medicines to patients at a global level and reduce drug shortages. This can be achieved by redefining existing concepts such as work-sharing methods and grouping to decrease time for review and approval of the change and its subsequent implementation. Additionally, the concept of work-sharing and regulatory reliance with other regulatory agencies outside of EU, should be considered. These processes offer several benefits involving faster overall approvals, reduced regulator and industry resources and can support regulatory harmonization. This could result in rapid global implementation of changes, including in the EU[72].

CONCLUSION

EFPIA recommends that the EC and EMA fully implement the principles and tools described in ICH Q12 guidance in the future EU variation system and legislation. In addition, the future variation framework should assist a lifecycle management of medicines in being more efficient and tailored to new important modalities (e.g. ATMPs) and drug-device combination products as well as accommodate for the latest IT technological advances and digitalisation. In order to nurture European innovation, a revision of the EU variation framework needs to be tackled now. We owe it to European patients to ensure optimal and faster delivery of life-changing medicines throughout their lifecycle.

SIMON BENETT
Director, Global Regulatory Policy, Biogen

MARKUS GOESE
Head EU CMC Regulatory Policy,
F. Hoffmann-La Roche Ltd

PÄR TELLNER
Director, Regulatory, Drug development
and Manufacturing, EFPIA

72 - https://www.medicinesforeurope.com/wp-content/uploads/2020/01/ESE_2019_Medicine-for-Europe_AESGP_Variation_WEB.pdf

Biographies

SABINE ATZOR

HEAD EU REGULATORY POLICIES, F. HOFFMANN-LA ROCHE LTD

Sabine Atzor joined F. Hoffmann-La Roche Ltd in Basel as Head of EU Regulatory Policy in 2010. In this function she has been leading or contributing numerous discussions within Roche and EFPIA, e.g. EU Clinical Trial Regulation, adaptive pathways, incentives, real world data and in recent years on the EU Pharmaceutical Strategy and the revision of the EU Pharma Legislation. To support the industry association work, she was seconded to EFPIA from 2015-2016. Prior to joining Roche she worked for about 14 years in the public sector, of which almost 6 years in the Pharmaceuticals Unit of the European Commission, DG ENTR and later at DG SANCO. In this function, her focus was on the preparation of the Falsified Medicines Directive, management of the Influenza Pandemic in 2009, and agreements with third countries on GMP. Her earlier roles included head of the coordination unit for drugs for the German Länder at ZLG tasked with the setup of this unit and head of unit on pharmaceuticals and blood products at the regional Ministry of Health in Hesse.

MIREILLE MULLER

EXECUTIVE REGULATORY POLICY DIRECTOR, NOVARTIS

At Novartis, Mireille Muller currently focuses on clinical trials, advanced therapy medicinal products (cell and gene therapies), personalised medicines. She is also supporting efforts towards digitalisation in clinical research. She is involved in several IMI projects (IMI PREFER on patient preference elicitation for decision making by regulators and health technology bodies). Mireille is part of several EFPIA groups such as the Clinical Development Expert Group, expedited pathways (PRIME) and Scientific Advice (part of ERAO) group and is on the Personalised Medicine working group. She is part of the EuropaBio group on advanced therapy medicinal products, clinical trials and policy. She is also part of several other groups such as eClinical Forum, DIA patient engagement, all related in improving clinical research, patients' rights and well-being. Mireille is providing training on a regular basis both internally and at university level and chaired several sessions at DIA and other conferences.

CHRISTINE FLETCHER

VICE PRESIDENT AND HEAD FOR SPECIALITY & PRIMARY CARE STATISTICS, GLAXOSMITHKLINE

Chrissie leads a group of statisticians supporting the development and commercialisation of new and approved medicines in immunology, hepatology, gastrointestinal, renal, respiratory, cardiovascular, neuroscience, HIV, infectious diseases and global health. Chrissie has worked in the Pharmaceutical Industry for 30 years and has experience of developing and commercialising new medicines in a variety of clinical disease areas across all phases of clinical development. She previously worked at Amgen in a variety of leadership roles and began her career working at SmithKline Beecham.

Chrissie is actively engaged in statistical societies, pharmaceutical trade associations and initiatives relating to the Pharmaceutical Industry. Chrissie is the Chair of PSI, a Council member of EFSPI, and a member of various European and International Special Interest Groups. Chrissie is a member of the EFPIA Clinical Research Expert Group and is leading the Innovation in Clinical Trials team. Chrissie was the lead EFPIA representative for the ICH E9(R1) Working Group, and she set up the EFPIA/EFSPI estimand implementation working group where she continues to be an active member.

Chrissie is a Chartered Statistician of the Royal Statistical Society (RSS). Chrissie has an MSc in Applied Statistics and a BSc (Hons) in Statistics with Management Science Techniques.

MARCO FARINELLI

GLOBAL SUPPLY CHAIN & STRATEGY, ASTRAZENECA

Marco Farinelli is the Chair of the EFPIA Supply Chain Working Group and Drug Shortage Work Stream. He works in the Global Supply Chain function of AstraZeneca since more than 10 years, with responsibility over the market supply of all AstraZeneca's medicines and vaccines in several European countries. With a background in economics and business management, Marco has a PhD in Management Engineering at Politecnico di Milano.

TIM CHESWORTH

SENIOR DIRECTOR, GLOBAL REGULATORY AFFAIRS, DEVICES & DIGITAL THERAPEUTICS, ASTRAZENECA

Tim joined AstraZeneca in 2007 to lead a team responsible for developing delivery devices for AZ's new drug portfolio. This encompassed all dosage forms and had a significant focus on inhalation and injection devices.

Tim's current role is to lead the Devices & Digital Therapeutics group within AstraZeneca Global Regulatory Affairs. The group is responsible for developing and implementing regulatory strategies and processes for both new and existing medical devices and combination products. This encompasses conventional pharmaceuticals, biologics and AZ's increasing levels of activity in Digital Therapeutics. Tim is the chair of the EFPIA Medical Devices Regulatory Working Group, as well as an active member of a number of other groups and associations including the Combination Products Coalition and IPAC-RS. Before joining AstraZeneca, Tim led the Regulatory Affairs group at Valois Pharma (Part of the Aptar Group – a Manufacturer of Drug Delivery Devices) Tim was responsible for Valois' regulatory strategy and provided technical & regulatory input to new product development.

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AMANDA MATTHEWS

SENIOR DIRECTOR, GLOBAL REGULATORY AFFAIRS - MEDICAL DEVICES AND COMBINATION PRODUCTS, PFIZER R&D UK LTD

Amanda has 23 years industry experience working at Pfizer R&D UK, Ltd. Amanda's focus for the majority of those has been providing strategic support to global development programs and lifecycle management for a broad range of medical device, in-vitro diagnostic and drug-device combination products. Amanda is an active participant in a number of Industry Associations, including EFPIA where she is a co-chair on the ERAO and MQEG working groups relating to medical devices and drug-device products. Amanda is also a contributor to ICH working groups and several ISO standard technical committees, which included the ISO 20069 standard for Assessment of Changes to Drug Delivery Systems issued in 2019 and more recently the revision to ISO 11608 series. Her career started as an Analytical Chemist after obtaining a degree in Chemistry, before moving into a regulatory role in 2005.

ESTEBAN HERRERO-MARTINEZ

DIRECTOR, REGULATORY INTELLIGENCE AND POLICY, ABBVIE

Previously Director of Regulatory Intelligence and Policy at Daiichi Sankyo Development Ltd, lead for Pharmacovigilance & Regulatory Affairs at the Association of the British Pharmaceutical Industry (ABPI) and Pharmacovigilance Manager at P&G Pharmaceuticals. Education: Biochemistry BSc from Warwick University, Virology PhD from University College London, Virology postdoc at Imperial College London.

PÄR TELLNER

DIRECTOR, REGULATORY, DRUG DEVELOPMENT AND MANUFACTURING, EFPIA

Pär Tellner is Director at EFPIA since 2012. He is also a Member of the ICH Management Committee and -Assembly. Pär has previously been working as Compliance officer (marketing ethics) and Director of Veterinary Medicine, LIF Sweden and as Head of regulatory affairs for several pharmaceutical companies, e.g Octapharma, Biovitrum, Pharmacia Plasma Products and Novartis. Pär has also been working as Senior Pharmaceutical Officer for the Swedish Medical Products Agency. Pär graduated as a pharmacist at Uppsala University in 1986.

KOEN NAUWELAERTS

RA POLICY AND INNOVATION LEAD, BAYER

Koen Nauwelaerts holds a Master's degree in Pharmacy from Leuven University, Belgium and a PhD in Drug Development from the same university. Further he obtained an MBA degree from Vlerick Business School and completed the technology immersion program at MIT. Koen is currently working at Bayer as RA Policy and Innovation Lead. He joined Bayer as head of regulatory affairs and quality for the Belgium/Luxemburg region and previously has been active within MSD and Medicines for Europe in different roles in Regulatory Affairs and Quality.

Within his current role as RA Policy and Innovation Lead, Koen leads the internal global e-labeling initiatives at Bayer and is vice-chair of the Inter Association TaskForce (IATF) for ePI.

LADA LEYENS

SENIOR DIRECTOR REGULATORY, F. HOFFMANN-LA ROCHE LTD

Lada Leyens has a background in human genetics, health economics and personalised medicine. She has worked at Health Authorities for over 8 years, mainly as a clinical trial assessor and GCP inspector at Swissmedic. At EMA she was in the specialised disciplines office working in the centralised procedure and with the PKWP and PGWP. At Roche, Lada is the Senior Director in Regulatory, mostly working on digital endpoint development and clinical trial innovation. She co-leads the digital endpoint group of experts at EFPIA to advance the field in Europe. Globally, she is part of the transcelerate team and works with CTTI and DiME. In her role she is working to increase the use of fit for purpose innovations in our drug development programs and their acceptance by Health Authorities.

BENGT MATTSON

LIF - LÄKEMEDELSINDUSTRIFÖRENINGEN (THE SWEDISH RESEARCH-BASED PHARMACEUTICAL INDUSTRY)

Bengt Mattson began his career in Pfizer in 1994 as Research Scientist within the Packaging Development in Stockholm, Sweden. He became Manager of Environment & Risk Management in 1995. He was named Director of ESH & EMU (Environment, Safety and Health & Engineering, Maintenance and Utilities) in 2000 and worked as head of Corporate Social Responsibility & Environmental Affairs for Pfizer's operations in Sweden until April 2020. 2005 he became the chairman of the Environmental Committee of Lif, and has since Jan 2014 acted as co-chair of EFPIA's (the European Federation of Pharmaceutical Industries and Associations) task force on pharmaceuticals in the environment (PIE TF), today a joint initiative between the three industry associations AESGP, EFPIA, and Medicines for Europe. He is also a member of AESGP's and EFPIA's environmental, health and safety expert groups.

ANDREAS HÄNER

ENVIRONMENTAL RISK ASSESSOR, F. HOFFMANN-LA ROCHE LTD

Andreas Häner studied at ETH Zurich with a focus on biotechnology and did his doctorate and post-doctorate in environmental microbiology. He has 20 years of experience in consulting for the chemical and pharmaceutical industry and was head of the Ecotox Laboratory and the department of Product Stewardship. Since 2017, Andreas has been an environmental risk assessor at Roche in Basel in Group safety, Security, Health & Environmental protection (SHE). He co-chairs the Pharmaceuticals in the Environment Task Force of the three European pharmaceutical associations EFPIA, AESGP, and Medicines for Europe.

ÁLMATH SPOONER

DIRECTOR OF REGULATORY POLICY AND INTELLIGENCE, RA, R&D, ABBVIE

Álmath Spooner is a dual qualified pharmacist and barrister and earned her PhD at Trinity College Dublin. At AbbVie, she is global regulatory policy topic lead for real world evidence, patient focused drug development and pharmacovigilance and European regulatory policy topic lead for digital health. At EFPIA, Álmath is the Vice Chair of the Integrated Evidence Generation and Use (IEGU) Working Group, a member of the Digital Health Working Group (DHWG) and additionally co-chairs an EFPIA group devoted to increasing patient involvement in drug development and regulatory decision making. Álmath is the industry observer on EMA's DARWIN EU Advisory Board. Over her career, Álmath has worked in medicines regulation (HPRA/EMA's PRAC), legal practice, academia and clinical practice. She has represented the EU at ICH and has contributed to various international initiatives such as CIOMS, ICMRA, ISPE and DIA ACEMEA.

SINI ESKOLA
DIRECTOR REGULATORY STRATEGY, EFPIA

Sini Eskola is working as Team Leader and Director Regulatory Strategy at the European Federation of Pharmaceutical Industries and Associations (EFPIA) since February 2014. She has a degree in pharmaceutical sciences (MSc) from the University of Helsinki. In EFPIA her main focus areas are leading and coordinating regulatory policy and advocacy activities across vast spectrum of topics with emphasis on the regulatory science and EU legislation on medicinal products. She has previously worked at AstraZeneca R&D Global Regulatory Affairs in Sweden and prior to that as an Executive Director of Finnish Pharmacists' Society. She has vast experience as practicing community pharmacist. She is conducting a part-time professional PhD research at the University Utrecht Centre for Pharmaceutical Policy and Regulation and studying Real-World Evidence aspects in medicines development and regulatory decision making. Since 2011 she has been a member of the Executive Committee of Industrial Pharmacy Section of International Pharmaceutical Federation.

INKA HEIKKINEN
DIRECTOR OF GLOBAL REGULATORY POLICY, MSD

Inka Heikkinen is the global regulatory/HTA policy lead, specializing in regulatory-HTA interface topics as well as real-world evidence. Within EFPIA, she is a part of the core leadership team for the HTA Regulation, leading the EMA-EU HTA interface topics, focusing on intersection of HTA Regulation and General Pharma Legislation. She is also the lead of the RWE for HTA substream with IEGU and content team lead for EHDS workstream under Digital Health WG. Inka holds a MBA, Master in Health Economics and MSc in Food Policy from different European universities, and more than 12 years of experience in policy in pharmaceutical sector.

MARKUS GOESE
HEAD EU CMC REGULATORY POLICY, F. HOFFMANN-LA ROCHE LTD

Markus Goese holds a Ph.D. in Biochemistry/ Organic Chemistry from the Technische Universität München (Munich), Germany. He has more than 20 years of industry experience in various companies (Roche, DSM, Novartis) in Pharmaceuticals and Fine Chemicals Research, Development and Commercialization. For the last 15 years, he has been working in CMC Regulatory Affairs, initially on Biopharmaceutical Products in early- and late-stage development. In 2011, he took on the responsibility as EU Lead CMC Regulatory Policy for Roche Pharma Global Technical Operations. Markus is based in Basel, Switzerland. He is currently Chair of EFPIA's Manufacturing and Quality Expert Group (MQEG) and EFPIA Topic Lead for ICH Q12 (Technical and regulatory considerations for pharmaceutical product lifecycle management).

SIMON BENNETT
DIRECTOR, GLOBAL REGULATORY POLICY, BIOGEN

As Director of EU Regulatory Policy, Simon is responsible for developing and leading Biogen's European regulatory policy activities, including agenda-setting and prioritisation and representing Biogen in interactions with EU Trade Associations and regulators on key issues, including the European Regulatory Affairs and Operations (ERAO) Variations Subgroup. Simon began working for Biogen in 2003 within the clinical operations group, focusing on the initiation and management of clinical trial activities primarily in multiple sclerosis (MS) and other neurological conditions. In early 2008, Simon moved into Biogen's regulatory group and has undertaken a number of senior regulatory roles within that function. Prior to joining Biogen, Simon worked in medical communications and publishing in areas of schizophrenia and infectious diseases. Simon is a biologist by training with an MSc in medical parasitology.

EMMA DU FOUR

HEAD OF INTERNATIONAL REGULATORY POLICY, ABBVIE

Emma Du Four has a broad range of experience across all aspects of medicines and devices including research & development, evidence generation and marketing authorisation. Specific areas of expertise include clinical trials, biotherapeutics, real world evidence, paediatrics, pharmacovigilance, devices, regulatory policy and regulatory submissions. Emma leads an international team providing strategic guidance on the R&D regulatory environment, and its application to medicines and device research and development. She also provides external advocacy leadership on the R&D regulatory ecosystem. Emma has a Bachelor of Science (B.Sc. Hons) degree in Biology & Chemistry and a Masters degree in Business Administration (MBA). She is Chair of the EFPIA European Regulatory Affairs & Operations Expert Group and is a Fellow of 'The Organisation for Professionals in Regulatory Affairs' (TOPRA).

KARIN VAN BAELEN

HEAD, GLOBAL REGULATORY AFFAIRS, JANSSEN, PHARMACEUTICAL COMPANIES OF JOHNSON & JOHNSON

As the head of Global Regulatory Affairs (GRA) at Janssen, Karin Van Baelen leads an organization of approximately 900 highly-qualified colleagues who foster relationships with Health Authorities around the world and help Janssen deliver innovative healthcare solutions to patients. The GRA organization influences and interprets global regulatory requirements and enables Janssen to meet those guidelines. Karin oversees the development of regulatory strategy for products from all Janssen Therapeutic Areas, in addition to the delivery of high-quality, on-time regulatory submissions and approvals. Karin also engages in national and international policy development in the regulatory, biotechnology and clinical development arenas.

NADEGE LE ROUX

SENIOR DIRECTOR REGULATORY POLICY AND INTELLIGENCE, BRISTOL MYERS SQUIB (BMS)

Previously Global Regulatory Lead at Astellas Pharma. Regulatory and drug development Director in several Biotechs. More than 25 years in Regulatory & Drug development. Education: Post-Graduated research in Pharmacology/Pharmaco-dynamy at University of Marseille, PhD in Bioethics and public health from University of Necker – Paris Descartes.

FRANÇOIS LAMÉRANT

SENIOR MANAGER COUNTRY SUPPORT, EFPIA

François Lamérant works as Senior Manager Country Support at EFPIA as part of the Market Access and Social Affairs team. He leads the CEE country engagement efforts and is heavily involved in EFPIA's Shortages policy and mitigation activities. He has a Master Degree in Political Science from Sciences Po Lille.

ANETA TYSZKIEWICZ

SENIOR MANAGER DATA AND DIGITAL, EFPIA

Aneta Tyszkiewicz works as Senior Manager Data and Digital at EFPIA as part of the Science Policy and Regulatory team. She is main responsible support to EFPIA's Integrated Evidence and Generation expert group and to Digital Health working group. In recent years she has supported EFPIA's advocacy and policy activities in relation to European Health Data Space (EHDS) legislation, including industry's input to Darwin EU, as well as digital health activities. She has previously held positions as Policy Advisor in Council of European Dentists (CED), Public Affairs Coordinator in European Society for Radiotherapy and Oncology (ESTRO) and International Diabetes Foundation.

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European Federation of Pharmaceutical Industries and Associations

EFPIA
Leopold Plaza Building * Rue du Trône 108
B–1050 Brussels * Belgium
Tel.: +32 (0)2 626 25 55
www.efpia.eu * info@efpia.eu