Medicines for Europe Factsheets on
Market and regulatory reforms to ensure availability and resilience of the supply chain

Medicines for Europe is committed to improving access to medicines for all Europeans. Yet, many patients across Europe face restricted access to medicines which undermines public health. The 2019-2024 EU legislature should reshape pharmaceutical policy by prioritising **equitable access to essential medicines** for all Europeans. Equitable access is an achievable goal as the majority of essential medicines are already generic or biosimilar medicines.

It is important to tailor regulatory pathways for maintenance, approvals and regulatory learnings as well as enabling multi-source competition at loss of exclusivity of the reference drug. Amendments to the Variations Regulation and Variations Classification guidelines are needed to reflect the science and telematics tools to optimise the regulatory process, avoid duplication and enable a faster reaction to shortages or emergencies (via Target Operating Model). Current limitations to broader use of the CP, DP and RUP should be removed.

To prevent continued consolidation of the market and manufacturing, supply chain resilience should be strengthened via procurement reform that includes criteria other than price and encourages multiple manufacturers to supply the market. Imposing stronger obligations to supply and subsequent penalties will increase demands on manufacturers with no reward thus increasing consolidation. Any stockpiling of medicinal products must be done rationally: clear demand, financing and management of the stockpile, preventing strain on manufacturing capacities and potential wasteful disposal of unused medicines. Uncoordinated national stockpiling demands should be rejected as this will fragment the internal market, increase costs and undermine EU solidarity.

This document develops Medicines for Europe key priorities that should be reflected in the Pharmaceutical Strategy for Europe.

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1. Procurement and security of supply

Problem statement

Since the 2009 financial crisis, European Member States have introduced policies to reduce medicines prices to balance healthcare budgets. These cost-containment measures have typically taken the form of reference pricing (internal or external), mandatory price reductions, procurement practices, rebates, clawback or a similar contribution system and payback measures. Across Europe, the current procurement practices have generated a number of undesired effects, namely reduced competition, price erosion, supply constraints (e.g. need to have stock in house to bid) and consequently medicine shortages. On top of this, most procurement processes do not take into account the unique characteristics of pharmaceutical manufacturing operations (e.g. lead times, accurate volumes, etc.), do not promote an adequate number of participating suppliers in tenders and do not guarantee competition as soon as market exclusivity period ends. Developing optimal procurement practices is an opportunity to create healthy competition and guarantee patient access to medicines, by increasing the number of manufacturers in the market and thereby reducing the risk of medicine shortages.

Policy recommendations

The existing procurement process should be optimised to ensure the security of supply by:

- Adjusting the number of procurement winners according to the market, product and country characteristics
    - Multi-winner tenders are preferred to guarantee multiple manufacturers in the market and prevent supply issues.
- Using selection criteria that consider other factors than price and ensure fair competition by implementing MEAT criteria.
    - These criteria should not put any access barriers in place for generic, biosimilar and value added medicines.
    - Procurement criteria should consider product-specific characteristics.
    - Procurement criteria that consider other factors than the lowest price should ensure fair competition, such as:
        - Environmental criteria
        - Supply reliability and manufacturing resilience criteria
        - Product characteristics criteria
    - The non-price tender criteria should award a bonus, where the weight attributed to these criteria reflects the policy objectives.
- Guaranteeing that the procurement processes reopen after the entry of the first multisource medicine to ensure a competitive and predictable supply to patients.
- Using extended lead times that guarantee a predictable supply of medicines to patients.

- Lead times should be adapted to the product characteristics as well as the requested volumes to be supplied, to guarantee a predictable supply.

- Preventing disproportionate penalties to encourage a sustainable supply of medicines to patients.
  - Penalties should be proportionate to the contract value to ensure competition in the procurement process.
  - Before the application of penalties, there should be some flexibility to find solutions for the interruption in supply.
- Accurate estimates of volume and volume commitments to be provided should guarantee a continuous supply.

Example good practice

Italy:

- Regional authorities are now obliged to re-open the supply agreements within 60 days after the entrance of the biosimilar medicine to the market.
- If there are more than 3 competitors on the market, it is mandatory to select 3 preferred products.

Germany:

- By law, there need to be 6 months between the award of a tender and the first delivery, ensuring sufficient lead time.

Relevant documentation

- Position paper on best procurement practices
- Official letter Medicines for Europe and EFPIA on second wave pandemic preparedness: procurement principles
- Infographic Hospital Tendering

2. Supply chain security and resilience

Background

Pharmaceutical manufacturing and supply chains are complex, increasingly globalised and sometimes not sufficiently diversified. In principle, the generic medicines use should encourage the diversity of production and suppliers as it is a multisource competitive market. However, pharmaceutical policies in Europe only encourage competition at market formation. Once the competition is established, most countries apply cost-containment policies to the generic sector which drives consolidation and globalisation to lower production costs.

Multiple manufacturers can be involved in the various production steps for a single ingredient. Upwards of 350 components are needed to be produced in house or procured to produce a final medicinal product. Because of the consolidation of supply chains especially related to API manufacturers, for a substantial amount of medicinal products the API is manufactured and supplied by a small number of API manufacturers. The Marketing Authorisation Holders (MAHs) are transparent on their supply chains via the details included in the Marketing Authorisation Dossier as submitted to the National Competent Authorities (NCAs) or EMA. However, the Covid-19 pandemic showed that public authorities are unable to access this information about the structure of the manufacturing and supply chains.

The European market for prescription medicine is dominated by government (direct or indirect) purchasing based on obtaining the lowest price for most off-patent medicines. This jeopardises the strong manufacturing footprint in Europe, disincentivises investments in European manufacturing and supply chain resilience measures and generates market or manufacturing chain consolidation. Meanwhile, new regulations (e.g. FMD, Brexit, nitrosamines review, Pharmaceuticals in Environment, GMP annexes) require a manufacturer to invest more in manufacturing and supply chain regulatory compliance which reduces the possibility to invest in more manufacturing diversity.

By integrating security of supply into EU pharmaceutical policy, the EU could reverse the trend of consolidation. The EU public procurement directive and transparency directive could be amended to include security of supply in procurement and reimbursement policies. Pharmaceutical regulation could be amended to encourage rather than discourage manufacturing investment in resilience and contingency measures. For example, dual sourcing can bring additional resilience into the supply chains, but establishing and maintaining multiple active API sources into a regulatory dossier has a significant cost factor from a compliance and regulatory point of view. While it is essential to provide full oversight and transparency of the supply chain and product flow to the competent authorities, the current way of handling the maintenance of API related information discourages companies from registering more alternative API suppliers to mitigate shortages. The simplification of this process would bring huge benefit and will reduce duplication in the system and waste of resources on both the industry and authorities' sides. To encourage manufacturing in Europe, EU structural funds could encourage investments in new technology to maintain a competitive and sustainable production footprint.

The EU Structured Dialogue on manufacturing and resilient supply chains is an opportunity to align manufacturers, stakeholders and the EU on a coherent strategy to improve the security of supply of medicines for European patients.

Policy recommendations

- Based on the structured dialogue, pursue policy reforms to increase manufacturing security and resilience.
- Reward manufacturers for investing in supply resilience like double sourcing or inventory strategy
- The EU can rebalance the market toward investment by legally rewarding resilience and security of supply or other relevant most economically advantageous tender (MEAT) criteria into the implementation of Public Procurement and the Transparency Directives.
- NCAs to assess vulnerabilities in consolidated supply chains based on data submitted by MAHs in the regulatory dossiers and provide feedback on the highly consolidated products with limited approved suppliers (mainly API). The NCAs or EMA should create interoperable IT systems to identify those medicinal products having a highly consolidated supply chain and communicate this information back to the pharmaceutical industry.
- Procedural simplifications to lower expenditures are needed to encourage companies to register multiple API suppliers
- The EU should set an ambitious goal to restore Europe to its former position as the leading global manufacturing region for the finished product (medicine) and active pharmaceutical ingredients (API) for both the EU and the global market. Financial support should be combined with market incentives (value added medicines, green or multi-winner procurement market options that consider long-term volume and price certainty) to ensure that these investments are ultimately financed by markets.

3. Optimizing the regulatory procedures

Introduction:

Each medicine, before reaching the patient, needs to be approved by competent authorities. The regulatory framework of Marketing Authorisation (MA) is critical to achieve the twin objectives of timely patient access to medicines and assuring the sustainable long term development of the industry to meet patient needs in the future. The current system of MA is built on two main pillars: the Centralised Procedure (CP) when the assessment is led/ coordinated by the EMA; the Decentralised Procedure (DCP) when the assessment is led by the Reference Member State (RMS).

Issues:

From the perspective of 50 years of pharmaceutical legislation, enormous progress has been made to achieve better quality, safety and efficacy of medicinal products. Significant effort has been made to build a strong European regulatory structure and harmonised European standards. However, the **current regulatory systems** and their implementation **do not always support the objectives of timely access and operational efficiency.** The weakness of the current system has been recognised and the revision of the MA framework has been announced in the Pharmaceutical Strategy:

A study on the authorisation and monitoring of medicines for human use will inform the evaluation of the regulatory framework to simplify and streamline procedures and reduce costs.*

Although the outcome of the study is pending (to be published in 2021), Medicines for Europe recommends some improvements to the operational aspects of EU marketing authorisation procedures to facilitate timely access to generic and biosimilar medicines. †

Centralised MA procedure

T**he Centralised Procedure (CP) was not designed with generic and biosimilar medicines in mind, leading to some cumbersome and constraining steps for those medicines** (i.e. duplicate MAs due to use patents, naming policy, eligibility etc) This has limited the use of the CP by generic manufacturers compared to DCP applications. While the CP procedure is mandatory for biosimilar medicines and optional for generic medicines, these constraints have limited the appeal and therefore the optimal use of the CP for patient access.

Recommendation for CP procedure	What is needed to achieve optimal CP processes?
To remove the limitations of the Centralised Procedure for generic and biosimilar medicines	• Reinterpret the eligibility criteria to broaden access to generic medicines. • Address the inflexibilities that have limited generic medicine applications fully utilising the Centralised Procedure. • Address the issue of brand naming of duplicates agreed on use patent grounds to allow patient access to medicines in the cross-border healthcare setting and to avoid market hurdles at the expiry of patents.

* *Study on the experience acquired as a result of the procedures for authorisation and monitoring of medicinal products for human use* – to be published in 2021.

† *For deeper diagnosis of the current MA system, its weak and strong points and several detailed proposals for improvement, please refer to Medicines for Europe Regulatory Efficiency Report*

Decentralised Procedure (DCP)

The Decentralised Procedure is the main route for registering generic medicines in Europe. Over 85% of the medicines being registered in Europe through DCP every year are generic medicines. Therefore it is crucial to focus efforts on further improving this route to make these important medicines more widely and quickly available to patients and providing the value which sustains the EU healthcare systems.

Several suggestions have been made to **optimise the Decentralised** procedure for the regulatory approval of new generic medicines [‡]. The objectives of the proposed solutions are to **streamline procedures, eliminate unnecessary duplications** of approvals and enable rapid **reaction to patients' needs in new countries.** These improvements would more closely reflect the operation of the generic medicines industry and more importantly give the possibility to respond faster to patient and market needs.

Recommendations	What is needed to achieve an optimised Decentralised procedure?
To address weak points of the DCP (i.e. Repeat Use Procedures (RUP) in extending MA to new countries and meeting patient needs. timelines, duplications and inefficiency etc)	Refreshing the Decentralised Procedure by introducing "Backbone DCP"- inspired by the Centralised Procedure, where there would be a single harmonised assessment involving a rapporteur and co-rapporteur, endorsed by CMD(h). Another option: "Basket DCP" - Member State assessing a "full package/basket" of elements for a given product; with the Marketing Authorisation Holder choosing a tailored option for MA in each Member State.

Other areas for simplifications:

- Variations (addressed in the Pharma Strategy separately as an area for improvement and digitalisation)
- Assessment of the documentation for the active substance, used by multiple manufacturers of the finished medicinal products (addressed in the Pharma Strategy separately as an area for improvement)
- Further optimisation of the pharmacovigilance
- The digitalisation of the MA processes - switching from a document-based processes towards the submission, management and evaluation of structured data via a two-way common EU Regulatory submission gateway. Regulator data submitted once, as structured data and in one format only and reused by the authorities for various purposes

[‡] *For detailed proposals on simplification of the DCP, please refer to Medicines for Europe Regulatory Efficiency Report*

4. Telematics

Problem statement and background

There is an increasing trend in the proactive use of digital technology for wellbeing and health management. The Covid-19 pandemic has proven the importance of e-Solutions to save lives and provide EU citizens safe access to virtual medical services and information.

Digital initiatives and tools are anchored on the access of correct and relevant data, which includes data and information on medicines ("regulatory data"). To achieve complete and effective empowerment of patients and successful implementation of the Digital Health Agenda, regulatory data (such as product identification and authorised medicinal product data) and related medicines information must be a part of the Digital Health transformation. The simplification of regulatory management, interconnection and interoperability of data and systems will complete the digital patient journey by proving them access to significant information related to their treatments and medicines. It will also help regulators getting quality data more quickly and reacting faster to fulfil patient needs.

Today the EU medicines regulatory network is still based on a decentralised and fragmented regulatory setup. Fragmentation of data across national regulators and the complex architecture has resulted in silo databases which limit the potential use of the data.

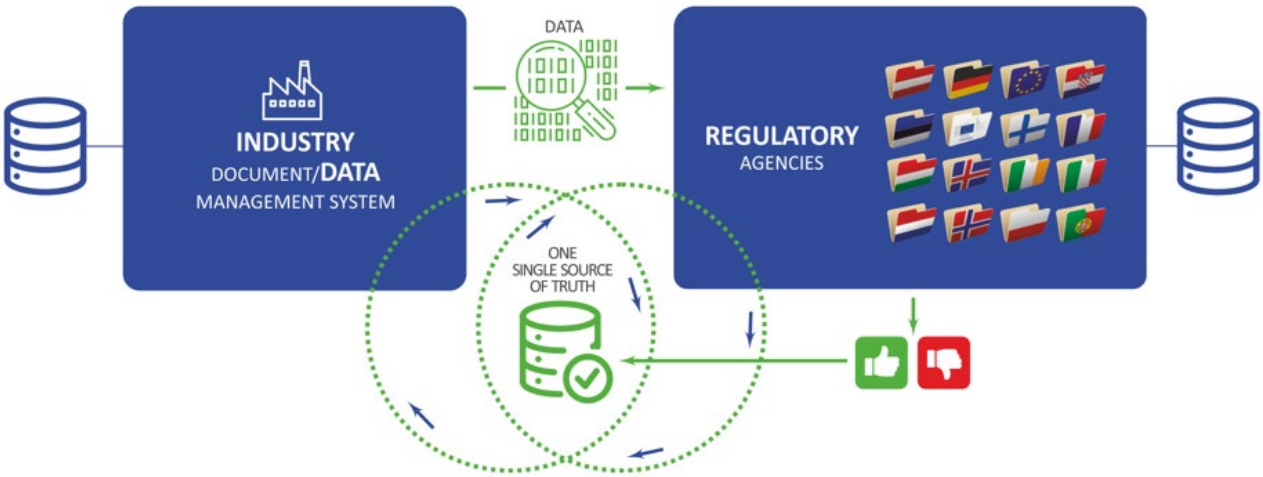
The pandemic demonstrated Europe's data weaknesses and gaps across all countries and at the EU level. The absence of useable data led to panic, hampered the ability of the EU to play its role in ensuring equitable access to medicines and weakened solidarity between member states. Industry-government cooperation enabled the EU and member states to develop ad-hoc solutions to medicines access challenges but we can clearly do much better in the future.

An effective digital regulatory system is an important first step to improve public health crisis management in Europe. Without harmonised standards, interoperability of systems and a data-driven regulatory process, the sharing of data amongst EU countries becomes challenging, as well as implementing protocols that enable change, when there are threats.

The creation of an interoperable digital medicine regulatory network is not a major technical challenge as digital tools exist and manufacturers are well-versed in shifting from paper to digital formats of data submission. The real challenge has been the lack of timely and consistent implementation of digitalisation and interoperability across EU member states.

Policy recommendations

To make Europe fit for the digital age, we need a **coherent digital regulatory infrastructure at national and European levels based on the interoperability of medicines agencies system. This would enable the collection and analysis of** regulatory data on authorised medicines appropriately and in a timely manner **while engaging minimal human resources to search for data (as opposed to the current almost manual approach used today)**



Objectives

- Accelerated exchange of regulatory data between medicine agencies in member states and industry in an automated way (structured data packets).
- Optimisation of regulatory processes to gain time and unify approach.
- Accelerate digital-telematics infrastructure to link regulatory and supply chain data for all medicines.
- Create the building block to implement and develop the electronic product information (ePI).

THE EU DIGITAL STRATEGY AND PHARMACEUTICAL STRATEGY OFFER CLEAR OPPORTUNITIES TO BRING THE EU MEDICINES REGULATORY NETWORK INTO THE DIGITAL AGE

INTEROPERABILITY-INTERCONNECTION ACROSS ALL DATA SOURCES

DIGITALIZATION OF THE MEDICINE AGENCIES SYSTEMS

E-INFORMATION TO PATIENT

RESILIENCE OF SUPPLY CHAIN

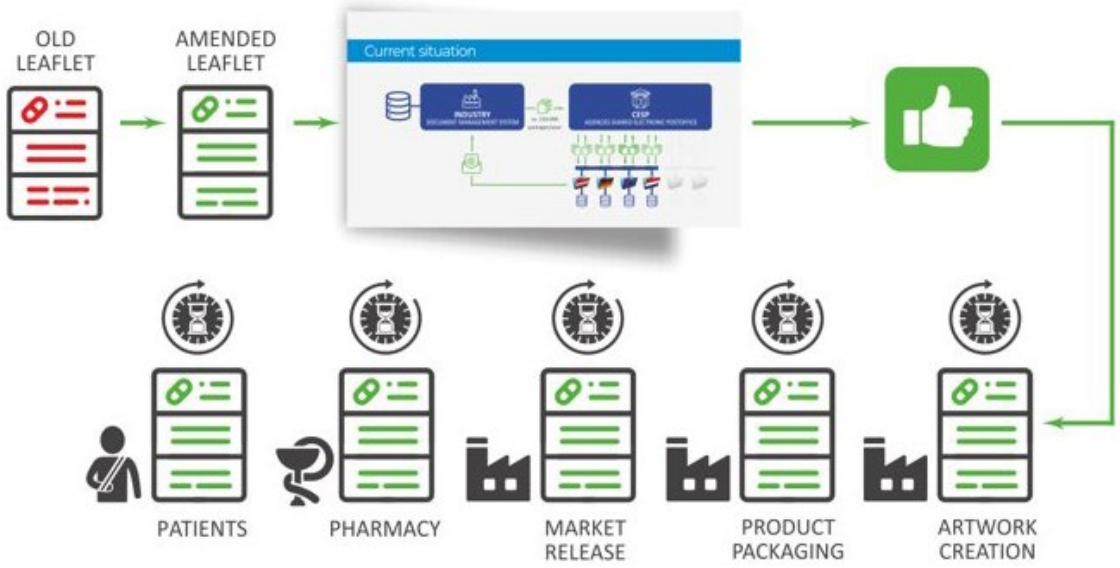
The EU4 Health program and other EU funding opportunity can speed up the digitalization process to invest in an EU-interoperable digital regulatory system as we seen the budgetary constraints have been a major factor of delay of digitalization so far.

Benefits

The digitalisation of the Regulatory Network infrastructure offers numerous benefits- i.e.

- better visibility of all parties in the supply chain, easier detection of potential supply issues having an EU-wide impact on access to medicines,
- optimisation of resources by automation of regulatory operations, incentives to maintain older, essential products on the market by simplifying their maintenance etc.
- One example of benefits that digitalisation of the European Regulatory network and interconnection of Medicines agencies system is related to the timely patient access to medicines information. Today, a change in the leaflet paper will reach the patients only when the new paper leaflet is embedded in the

medical package. In the future, with the digitalisation of the regulatory systems, patients and healthcare professionals can be alerted of leaflets updates almost in real-time after the Regulatory approval.



Policy recommendations

- Institutions and regulators should **prioritise the creation of an interconnected digital medicines regulatory system across the EU.** This is technically straightforward to implement and will improve access to essential medicines and vastly improve the EU's ability to avoid shortages.
- The European Commission can speed up the digitalization regulatory process by providing some EU **funding to member state medicines regulatory agencies to invest in an EU-wide digital regulatory system** as minor budgetary constraints have been a major factor of delay.

5. Variations system

Introduction:

Throughout its lifecycle, medicine will evolve and require a significant number of regulatory changes. Some changes (so-called: *Variations to the Marketing Authorisation*) might be significant (e.g. new indication, major change in manufacturing) when a deep assessment of the change is needed by the authorities to ensure quality, safety and efficacy of medicinal products. Some changes may be minor, quite often of an administrative nature, with no impact on the quality, safety and efficacy of the product (e.g. change of address of manufacturer) or need for a deep assessment by the authorities.

Issue:

The current regulatory framework for maintaining products on the market needs to evolve to better reflect scientific progress and operational efficiency in line with Better Regulation which aims to balance regulatory objectives with the need to reduce the administrative burden for companies and authorities[§]. Currently, disproportionate resources are allocated to the variations process in view of the overall benefit for patients and the entire regulatory system. The way of handling the process of changes needs to be digitalised to reduce resources used on administrative changes and to concentrate resources on activities that bring value to patients and public health. In addition, the variations system needs to be responsive to scientific & technological evolution and patient needs, as was also experienced during the COVID19 crisis.

Policy recommendations:

The weakness of the current system has been recognised in the Pharma Strategy:
"Review the variation framework for medicines, through changes in legislation and guidelines, to make the lifecycle management of medicines more efficient and adapted to digitalisation – 2021-2023"

The effective use of IT systems can be a powerful enabling tool for regulatory efficiency in the processing of variations across the EU Network. Regulation 1234/2008 was adopted at the time of relatively low digitalisation of the regulatory operations. Over the last 10 years, the regulatory environment has evolved significantly with regards to available IT tools and ongoing telematics projects – it is **time to move to digital solutions.** The simplification will reduce duplication in the system and save resources for both industry and authorities.

Recommendation for digitalisation of variations	**What is needed to achieve it?**
To **digitalise the process of reporting changes** to the authorities by pharmaceutical companies	Switching from document-based processes to the submission, management and evaluation of structured data via a two-way common EU Regulatory submission gateway. Continuity and speeding up of on-going digital projects (so-called SPOR database at the EMA, Target Operating Model (TOM) Harmonised and fast implementation by all EU MSs at the same time

§ For deeper diagnosis of the current variations system, its weak and strong points and several detailed proposals for improvement, please refer to Medicines-for-Europe Variations Report

	Financial support by the EU funding to digitalise interconnectivity between the health authorities and the EU Regulatory network
To modernise the concept of reporting changes by reporting minor, mainly administrative changes directly only to the database (not to several MSs in parallel), with the Competent Authorities having full access to the content	Amendment to the legislation as a part of the review process by explicitly allowing the reference to the databases. Modernise the transfer of "information that has changed" in the MA dossier (supply chain, safety updates, administrative data handling) via digital innovation. e.g. responsible data owner updates the respective databases, which is accessible by each NCA (i.e. leverage the robust ISO IDMP data model via SPOR database).
To make a **link between the digitalisation of variations and future way of managing changes to Product Information** (i.e. indications, the safety profile in patients' leaflet) and keeping patients and health care professionals informed about changes to medicinal products via e-leaflet	Continuity of investing in the digital infrastructure of the EMA and National Authorities and in databases (SPOR and TOM), serving as a building block for the future model of electronic Patient information (e-leaflet). Investing in Electronic product information (ePI) is an integral part of the Regulatory efficiency concept. In particular, a strategic way of designing the ePI IT system would improve the Variation system as well.

Other (not IT related) recommendations for changes to the current Variations regulatory and legal framework:

Recommendations	What is needed to achieve it?
Make the variation system responsive to scientific & technological evolution and patient needs	Amendment to the pharmaceutical legislation, Variations Regulation 1234/2008 and the Variations Classification Guidelines
Revise current risk-based approaches to variation categorisation in view of knowledge learned last 10 years for well-known / well-characterised products, incl. biologics	
Facilitate the continual improvement of manufacturing processes and the adoption of innovative manufacturing technologies, especially in the context of global supply chains (i.e. ICH Q12).	
An efficient way of handling supply chain information and its changes via digital tools will allow faster reaction in case of a major issue with supply and risk of shortages (e.g. fast process to report changes to the active substance; API suppliers, etc). Procedural simplifications will encourage companies to register multiple API suppliers to prevent shortages.	

Facts and figures:

- Disproportionate resources are allocated to the variations process in view of the overall benefit for patients and the entire regulatory system:
    - • Based on data gathered from 2010-2018, the number of variations per MA and per year appears to have increased about 75% since 2010.

- • Over 50% of the total number of variations submitted to the Competent Authorities are minor changes (Type IA Variations and Notifications), engaging a lot of resources from both regulators and the industry, to process these minor, mainly administrative submissions without scientific assessment and without any real added value for patients.
- • By reducing the average time spent on the type IA notification process in general, as well as lowering the volume by changing the way of reporting, approx. 65% of the current effort could be saved/resources could be used differently on activities more meaningful for public health.