Medicines for Europe

factsheets

2021

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better access. better health.

Abstract

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.

Generic, biosimilar and value added medicines are key drivers for access to medicines. Generic medicines provide for almost 70% of dispensed medicines in Europe and have doubled access to medicines for patients with diabetes or cardiac conditions. Biosimilar medicines are drastically increasing access to biological therapies for cancer and auto-immune conditions such as rheumatoid arthritis or psoriasis. Value added medicines are increasing patient quality of life for chronic diseases and offer significant benefits to the healthcare community.

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

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generic medicines

better access. better health.

e.g. Cardiovascular, Hypertension,Diabetes, Depression, Epilepsy, Mental Disorder, Gastrointestinal, Infections, Critical and cronical diseases

+100% PATIENT ACCESS
OVER 10 YEARS

HIGH QUALITY MEDICINES
TO OVER
500 MILLIONS
PATIENTS

biosimilar medicines

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e.g. Cancer, Auto-immune diseases (arthritis, psoriasis, lupus)

BIOSIMILAR FILGRASTIM
+44% PATIENT ACCESS
IN THE EU (2006 - 2013)

A GROWING OPPORTUNITY
FOR HEALTHCARE BUDGETS
A €78 BN MARKET
WILL OPEN TO
COMPETITION BY 2020

value added medicines

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e.g. Respiratory (asthma, COPD), neurology (MS), Oncology

BETTER
ADHERENCE
AND QUALITY OF LIFE
OF **PATIENTS**

50%
OF PATIENTS
FACE CHALLENGES WITH
MEDICATION ADHERENCE

Content

Equitable Access **to medicines**

Generic Medicines Uptake

factsheet

- ☐ Problem Statement
- ☐ Clear recommendations
- ☐ Covid-19 suspension of cost-containment measures

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Generic Medicines Uptake

factsheet

The sustainability of healthcare systems is a challenge for many European governments. Multiple factors, such as a growing and ageing population, increased chronic disease burden, the introduction and increased cost of new innovative medicines, have put **pressure on healthcare budgets** across Europe. Increased utilisation of generic medicines presents an opportunity to improve healthcare system value, either by providing access for substantially more patients at the same spending level (higher cost-effectiveness) or by decreasing expenditure at equal treatment rates. However, not all European countries have a high level of generic medicine penetration, so more can and should be done to increase the use of generic medicines and increase the efficiency of healthcare systems

Clear recommendations

Ensure a cohesive generic policy to increase generic use and patient access.

Medicines for Europe encourages governments to focus on **measures to support the use of generic medicines rather than short-term and drastic cost-containment measures**, which endanger medicines supply reliability and ultimately patients' health. Generic medicines are now 70% of prescribed medicines in Europe while only accounting for less than 30% of pharmaceutical expenditure. Governments need to focus their attention on optimising generic use ensuring long-term competition rather than further lowering their price.
Ensure long-term competition.

Ensure long-term competition

- **Reform procurement processes**, moving away from price-only tendering to the inclusion of MEAT criteria – procurement specialists should take a holistic view when designing procurement processes to safeguard that competition is guaranteed in the long run. A well-functioning system would ultimately lead to a more competitive market environment that benefits patients, healthcare professionals and payers.

- **Rethink generic pricing mechanisms to ensure market sustainability** – External Reference Pricing (ERP) and Internal Reference Pricing tools that encourage permanent downward price spirals are not a suitable price control mechanism for ensuring an appropriate and competitive environment for generic medicines and are drivers of market unsustainability.

- **Prevent the application of short-term cost-containment measures** – policy measures such as clawback and payback mechanisms, mandatory discounts and rebates and recurrent or arbitrary price cuts are creating extremely difficult market conditions for generic medicines. These measures, often applied in conjunction, lead to unsustainable price levels and are drivers of market consolidation and consequently increase the risk of medicines shortages.

Ensure fast competition.

- Guaranteeing that the **procurement processes reopen** after the entry of the first multisource medicine to ensure a competitive and predictable supply to patients.

- **Accelerating the timelines** for pricing and reimbursement of generic and biosimilar medicines

- National authorities should comply with EU law and immediately remove any form of **patent linkage**, as well as refrain from introducing it in the future.
  - Patent linkage significantly delays market entry of generic and biosimilar competitors, has a negative impact on patient access, and results in additional costs to be sustained by national healthcare systems, by the generic industry and ultimately by citizens.

Covid-19 suspension of cost-containment measures

During the COVID-19 pandemic, generic medicine manufacturers have worked around the clock to ensure that the supply of medicines to patients continues without interruption. At the onset of the health crisis, many countries either suspended or halted cost containment measures scheduled, giving a clear indication that governments are perfectly aware of the influence these measures may have on supply of generic medicines. Governments must therefore rethink their approaches to ensure that pharmaceutical policy helps drive generic penetration while ensuring long-term competition to guarantee the long-term sustainability of healthcare systems.

Biosimilar medicines Uptake

factsheet

- ☐ Problem Statement
- ☐ Policy recommendations
- ☐ Sustainability examples
- ☐ Relevant documentation

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Biosimilar medicines Uptake

factsheet

Problem Statement

The sustainability of healthcare systems is a challenge for many European governments. Multiple factors, such as a growing and ageing population, increased disease burden, the introduction and the high cost of new innovative medicines, have put **pressure on healthcare** budgets across Europe. Biologic medicines take an important part of the pharmaceutical budget and a growing number of new pharmaceutical therapies are biological molecules. Biosimilar medicines have offered patients increased access to these life-altering biologic therapies. 15 years after the first biosimilar approval in Europe, we have reached more than 2 billion patient treatment days of safe clinical experience, accompanied by a growing trust in these more affordable biologic medicines.

Over the next 10 years, many biological medicines are set to lose market exclusivity. This represents an opportunity for the market to harness more competition in the biologic medicines market and offer invaluable opportunities for healthcare systems to **improve patient access, improve healthcare budget sustainability and significantly reduce equity gaps** across Europe. The reduction of treatment costs with biosimilar medicines frees up resources which can then be **reinvested** into better care for patients and sometimes make previously unaffordable innovative therapies, more affordable.

Policy recommendations

- Implement **thoughtful biosimilar medicine policies** that balance the benefits of competition, biosimilar use to increase patient access where necessary, and increase the affordability of treatments allowing reinvestments in health care.
- Design a **biosimilar policy framework** capable of delivering value for all stakeholders, building on the vast European experience. The **core components** of such framework are outlined here:
  - Political vision, will, action and targets towards healthier communities.
  - Involvement of all relevant stakeholders to build trust.
  - Implementation roadmaps allowing time for tangible results.
  - A coordinated and holistic design with multiple comprehensive policies.
  - A biologic market driven by level-playing field competition.
  - Resilience and continuous improvement reflecting contextual changes.
- Strengthen **shared decision making** and the **physician-patient relationship** has a central role throughout the course of biologic treatment (therapy selection, patient information/education and clinical oversight over time).

POLICY AREA	SUSTAINABILITY MEASURE	SUSTAINABLE MARKET STATUS
Regulatory environment and clinical guidelines	Time from EMA approval to first biosimilars sales	Instant or very short market entry after approval
	Treatment guidelines for biosimilar use	Publication of multiple guidelines on usage and protocols prior to first biosimilar entry
	Physician switching policies	Authorisation and guidance of physician-led ability to switch to a biosimilar medicine at entry of first biosimilar on the market
	No biologic pharmacy substitution	No biologic pharmacy substitution allowed
Awareness and education	Comprehensive training / education for patient	Access to comprehensive and unbiased training or education prior to first biosimilar entry
	Comprehensive training / education for physician	
Incentives	Patient incentives to promote biosimilar use	Incentives in place to encourage use of most economically advantageous product upon introduction of competition
	Prescription quotas or financial incentives for providers that do not restrict physician choice	An incentive or quota that does not restrict physician choice
Pricing rules and dynamics	Originator price not subject to mandatory price cuts	No forced originator price cuts by central authorities required, market forces to determine price
	Molecule pricing not subject to reference price	No reference price determined by central authorities, market forces to determine price
Purchasing mechanisms	Length of contracts	12- to 24-month contracts ensure market competitiveness and avoid patients are switched often
	Tender timing relative to biosimilar availability	Tender opens upon introduction of competition
	Time from tender award to delivery	4-6 months lead time to allow necessary preparations and stock build-up
	Number of winners	Consistently award multi-winner tenders to allow of market sustainability
	Winner decision criteria beyond price	Decision based on the most economically advantageous tender offers (e.g. incorporating sustainability, price,

Sustainability examples

- In **Denmark**, Amgros (secures the supply of drugs to public hospitals) divided the country into two different regions when procuring Adalimumab after biosimilar market entry. This allowed two competitors to supply the market, reducing market reliance on a single manufacturer while maintaining fast biosimilar medicines uptake, helping to ensure long-term competition and supply reliability for patients.

- In **France**, authorities set a national target for biosimilar use and created opportunities to implement policies to increase biosimilar prescription. France's objective is to achieve 80% biosimilar market penetration by 2022. In addition, France started piloting policy measures to increase biosimilar penetration in October 2018. While the project is scheduled to run for 3 years, policymakers are already looking to preliminary results based on defined KPIs and assessing and implementing alternative measures (e.g. incentives targeting hospital purchasing and for outpatient prescribers) to reach the target biosimilar penetration.

Relevant documentation

- IQVIA BIOSIMILAR SCORECARD 2020
- Positioning Statements on Physician-led Switching for Biosimilar Medicine
- Medicines for Europe Position on biologic pharmacy substitution

Biosimilar competition

factsheet

- ☐ Problem Statement
- ☐ Policy recommendations
- ☐ Sustainability examples

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Biosimilar competition

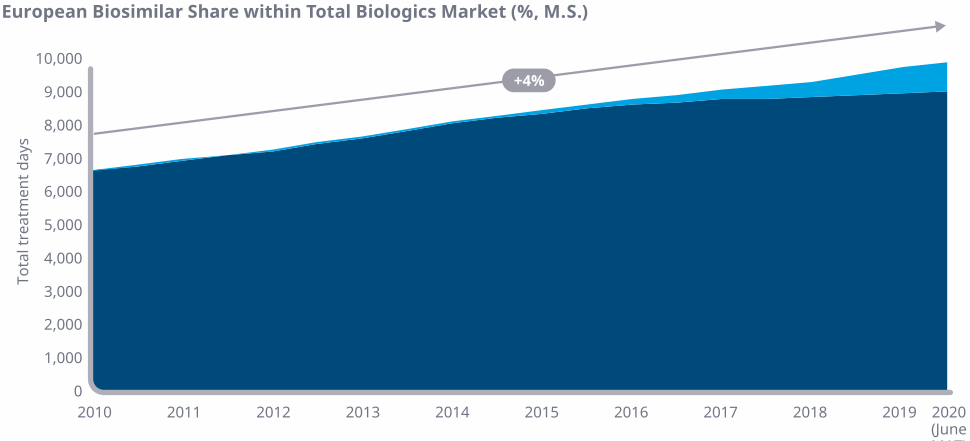
factsheet

Problem Statement

Biologic medicines represent a growing share of the pharmaceutical budget and many new pharmaceutical therapies are biological substances. Over the next 10 years many biological medicines are set to lose market exclusivity. This represents an opportunity for the market to harness more competition in the biologic medicines market and offer invaluable opportunities for healthcare systems to **improve patient access, improve healthcare budget sustainability and significantly reduce equity gap**s across Europe. IQVIA estimates that biosimilar medicines can contribute to close to 50% of future savings opportunities if the EU supports competition and uptake.

The level of biosimilar competition in each national market is directly affected by the country's biosimilar policy framework, the education of healthcare professionals and patients and relevant benefit sharing for key stakeholders. Measuring the competition level can be challenging and the number of biosimilar competitors present in a market does not provide the full picture. The Herfindahl-Hirschman Index (HHI) provides additional insight by considering the market shares of each competitor. The table below shows that the opportunity for an optimal competition level thanks to biosimilar medicines use is not yet fully grasped by all European countries.

European Biosimilar Share within Total Biologics Market (%, M.S.)



Segment	%M.S.	5yr CAGR
Biosimilars	9%	58%
Other biologics	91%	2%

Source: IQVIA MIDAS®June MAT 2020
Notes: Total market view including inaccessible market

MOLECULE	Adalimumab	Infliximab	Etanercept	Insulin Lipro	Insulin Glargine	Rituximab	Trastuzumab
Denmark	4	1	2	N/A	2	5	3
France	3	5	4	N/A	1	4	4
Germany	5	5	5	4	2	5	5
Hungary	1	1	N/A	N/A	2	4	5
Italy	4	5	4	1	4	5	5
Netherlands	4	5	4	N/A	4	4	5
Norway	3	3	4	N/A	1	2	4
Poland	4	5	5	4	4	1	4
Romania	1	4	1	N/A	1	1	1
Spain	4	5	4	N/A	2	5	4
Sweden	4	5	4	4	4	5	4
UK	5	5	4	N/A	2	4	4

Source: IQVIA MIDAS, 12 months of data ending MAT Q1 2020. HHI calculated using volume treatment days.
Chart notes: N/A = Not applicable due to unavailability of biosimilars within a market.

Policy recommendations

- Implement **thoughtful biosimilar medicine policies** that include (1) the benefits of competition, (2) biosimilar use to increase patient access where necessary, and (3) treatment affordability and accessibility that frees resources that can be reinvested.
- Ensure that **pricing policies incentivize competition** and do not create reference price groups.

  Ensure that **purchasing and procurement mechanisms** encourage long-term competition rather than short term cost containment:

  - **Re-opening tenders** at market entry of initial biosimilar competition.
  - **Encouraging the plurality of the offer** e.g. awarding multi-winner tenders in consolidated procurement systems.
  - **Visibility and predictability in terms of volume and tender execution**
  - Winner selection based on the **most economically advantageous tender** (MEAT) offers which recognise the long-term benefit of sustained competition over price only.
- **Harmonisation & Enlargement of the Bolar exemption** to include all the actions allowed for biosimilars to be ready to enter the market on day-1 after IP expiries, incl. API supply and administrative processes (e.g. Marketing Authorisations, P&R listing, tender bids, etc.).

- Make sure that national **pricing & reimbursement as well as tender procedures do not unduly delay biosimilar market entry by linking such procedures to the status of patents**, as this delays competition. The Commission committed to "strictly enforce the applicable rules [and] act against patent linkage" in the 2009 Pharma Sector Inquiry.
- Monitor and enforce competition rules to ensure that there is **no denigration/misleading information or market practice (incl. anti-competitive pricing strategies) to delay biosimilar competition**.
- Shape a **fit-for-purpose a multi-source environment for orphan biologic medicines** of which 28 are set to lose market exclusivity by 2028. Current biosimilar regulatory and market frameworks are not yet designed to address the **new competition challenges** posed for this future biologic portfolio.

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Sustainability examples

- As early as 2016, **Italy** reviewed its procurement law to ensure that tenders occur maximum 6 months after biosimilar market entry to guarantee the market is not blocked to competition after the expiry of the exclusivity period of the originator biologic. In addition, when more than 3 competitors operate in the market, regions should award multiple tender winners to ensure long-term competition.

- In **Sweden**, the division of the country in 10 procuring regions allows for multiple manufacturers to participate in the Swedish market.

- With its Commissioning framework for biological medicines (including biosimilar medicines), the **UK**'s NHS created a framework with clear implementation and monitoring roadmaps and guidance to different actors, with division of responsibilities and well established KPIs

- In the Westfalen-Lippe region, **Germany**, updated information to physicians and agreed quotas for biosimilar prescription make this region one of the top-performers in terms of biosimilar use in the entire country.

- **France** started piloting policy measures to increase biosimilar penetration in October 2018, while the project is scheduled to run for 3 years, policymakers are already looking to preliminary results based on defined KPIs and assessing and implementing alternative measures (e.g. incentives targeting hospital purchasing and for outpatient prescribers) to reach the target biosimilar penetration.

- In **Portugal**, tenders re-open as soon as the first biosimilar medicine is available on the market.

Barriers to generics and biosimilar competition

factsheet

- ☐ The importance of timely competition
- ☐ The barriers to timely competition of generic & biosimilar medicines
- ☐ Policy recommendations

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Barriers to generics and biosimilar competition

factsheet

The importance of timely competition

In the Health Council Conclusions of 2016, Member States stressed "*the importance of timely availability of generics and biosimilars*". In 2017, the European Parliament Resolution on Access to Medicines also urged to ensure timely and effective generic & biosimilar competition.

In the Pharmaceutical Strategy, the European Commission highlights the importance of "*greater generic and biosimilar competition, based on the sound functioning of the single market" and is ready to work for "the removal of barriers that delay their timely entry to market and increased uptake by health systems*".

It also stresses how "*originator companies sometimes implement strategies to hinder the entry or expansion of the more affordable medicines of their generic and biosimilar competitors" and that "this lack of competition thus inhibits price savings once innovative products lose their market exclusivities*".

The barriers to timely competition of generic & biosimilar medicines

Quality of patents – Divisionals – Patent related issue

For healthcare systems to function, it is fundamental that the patent system guarantees the **highest quality of patents** and **of patent granting procedures**. The risk, otherwise, is the creation of a multitude of secondary - often 'weak' - patents ('**patent thickets**') covering one product, with the effect of keeping competitors off the market. The EC Pharma Sector Inquiry of 2009 shows that individual medicines are covered by around 100 patent families, with up to 1300 patents and/or pending applications across EU countries.

Currently, the **patent granting process at the European Patent Office (EPO) allows a misuse of divisional patent applications…**

> i.e., whereby the patent holder, after filing a "parent" patent application, files a multitude of divisional patents, with new divisionals popping up right before the previous patent is invalidated. In this way, 'weak' patents are kept alive in order to enforce them in Court and unduly delay generic/biosimilar market entry.

…and this is considered an anticompetitive practice by the Commission in its EC Pharma Sector Inquiry.

Patent linkage – Regulatory related issue

Competition is further delayed by the practice of **patent linkage**…

> i.e., whereby regulatory/market access decisions (marketing authorisations/P&R decisions/tender bids, etc.) for a generic/biosimilar product are linked to the status of patents of the reference product.

…that, despite being considered "unlawful" by the Commission in its Sector Inquiry Report of 2009, exists in several Member States where generic/biosimilar medicines are systematically delayed. The European Parliament Resolution on Access to Medicines in 2017 urged the Commission to end patent linkage to ensure immediate market entry for generic/biosimilar competitors. This would be in line with the objective of the EU Bolar to "ensure that a generic could enter the market as soon as possible after the expiry of patent/SPC protection […] based on the basic rationale that free competition should be allowed as soon as protection expires" (European Commission Impact Assessment on the SPC manufacturing waiver).

Market or pricing or procurement related issue

Competition may also be delayed via **market strategies**…

> e.g., cases in which originators, by using their position of power on the market, change formulation or presentation (e.g. intramuscular, cutaneous/transdermal, sub-cutaneous, etc.) of a product to shift patients to the new version and reduce the accessible market for competitors, preventing head-to-head competition of similar products.

...or **pricing strategies**...

> e.g., aggressive price cuts to make the market unattractive or unprofitable for upcoming competitors, with a reduction of competition, as new entrants will struggle to penetrate the market. Reduced or absent competition result in price increases in the medium-long term.

...or **procurement policies**...

> i.e., any form of discrimination of biosimilars vs the originator, which may take the form of slots reserved for originators, with long litigation and subsequent loss of the market for the biosimilar.

Policy recommendations

Medicines for Europe urges the Commission to ensure effective competition in the pharmaceutical sector and immediate (i.e. Day-1) generic and biosimilar market entry as soon as IP protections expire. This is the only way to guarantee sustainable healthcare systems.

The European Union is encouraged to:

- Ensure **accountability of the EPO** and the **highest quality of patents**
- Immediately urge the EPO to change its internal rules to **stop the abuses of divisional patents**
- **Ban patent linkage in EU legislation** as it systematically delays timely (i.e. Day-1) competition
- Constantly **monitor the market to tackle marketing or pricing strategies or procurement policies** aimed at or with the effect of delaying generic/biosimilar entry
- Introduce a **mechanism for national authorities to systematically claim damages caused to national healthcare systems**, in compensation for overpaying due to the lack of competition caused by the conduct of dominant companies delaying off-patent entry
- Ensure **EU harmonization of the IP Enforcement Directive on damages** to be paid to companies suffering from practices delaying competition

The EU Bolar Exemption

factsheet

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- ☐ The objective
- ☐ The issue
- ☐ What's already been done
- ☐ The recommendations
- ☐ The Benefits
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The EU Bolar Exemption

factsheet

The 'Bolar'

The Bolar exemption was introduced in Europe in Art. 10(6) of the Directive 2001/83/EC.
It allows companies, during the patent/Supplementary Protection Certificate (SPC) protection of the reference product, to conduct studies, trials and the subsequent practical requirements necessary to obtain regulatory approvals for generic and biosimilar medicines, without this being considered patent/SPC infringement. The Bolar also exempts from infringement certain experimental research activities to develop new medicines.

THE BROAD AND HARMONISED BOLAR EXEMPTION SHOULD COVER

THE CONDUCT
of the necessary studies and trials by all partners for the purpose of seeking marketing authorisation in the EU

THE OFFER
manufacture, sale and purchase of patented APIs for the purpose of seeking marketing authorisation and for R&D purposes

THE SUBSEQUENT ADMINISTRATIVE ACTIONS
needed to effectively enter the market on day-1 after IP expiry

The objective

The primary objective of the Bolar is to "ensure that a generic could enter the market as soon as possible after the expiry of patent/SPC protection […] based on the basic rationale that free competition should be allowed as soon as protection expires". (European Commission Impact Assessment on the SPC manufacturing waiver, p. 15)

The objective

The primary objective of the Bolar is to "ensure that a generic could enter the market as soon as possible after the expiry of patent/SPC protection […] based on the basic rationale that free competition should be allowed as soon as protection expires". (European Commission Impact Assessment on the SPC manufacturing waiver, p. 15)

The issue

The Directive has been implemented in different ways across Member States, with some more restrictive and some more open national transpositions of the exemption. This fragmentation throughout the EU has led to legal uncertainty and confusion for generic, biosimilar, originator and Active Pharmaceutical Ingredients (APIs) developers around what is and what it not allowed by the Bolar. As a result, this has been a factor for driving investments on API development and production outside of Europe over the last 15 years.

What's already been done

The European Commission and Member States have expressed multiple times the intention to tackle the fragmentation in the implementation of an open Bolar exemption that delivers on competition as soon as protection expires:

- The 2015 Single Market Strategy for Europe identified enlargement & harmonisation of Bolar as a priority
- In 2016, the EC published a Charles River Associate study that highlighted the huge benefits for the entire pharmaceutical sector of an extension of the scope of Bolar
- In 2017, the EC Roadmap to optimise the IP legal framework explored the Bolar reform and its benefits
- In 2018 the Commission issued a Max Planck Institute study describing the willingness of EU Member States to harmonise the Bolar interpretation
- The 2020 pharmaceutical strategy includes Bolar as a priority issue for reform.

The recommendations

The Commission, in pursuit of the primary purpose of the Bolar to ensure that generic & biosimilar medicines can enter the market on day-1 after IP expiries, should build on all studies and assessments already conducted and propose a revised & harmonised Bolar covering the following actions:

- the conduct of **necessary studies and trials by all partners for the purpose of seeking EU marketing authorisation**, independently from who the final applicant/Marketing Authorisation holder is and where the medicine will be authorized (EU/ non-EU).
- the **offer, manufacture, sale (incl. by third party API suppliers) and purchase of patented APIs for the purpose of seeking marketing authorisation and for R&D purposes.**
- the subsequent **administrative actions needed to effectively enter the market on day-1 after IP expiry, i.e., Marketing Authorisations, pricing & reimbursement listing, tender bids, upload of serialised packs for compliance with pharmaceutical regulation against falsified medicines, etc.**

The Benefits

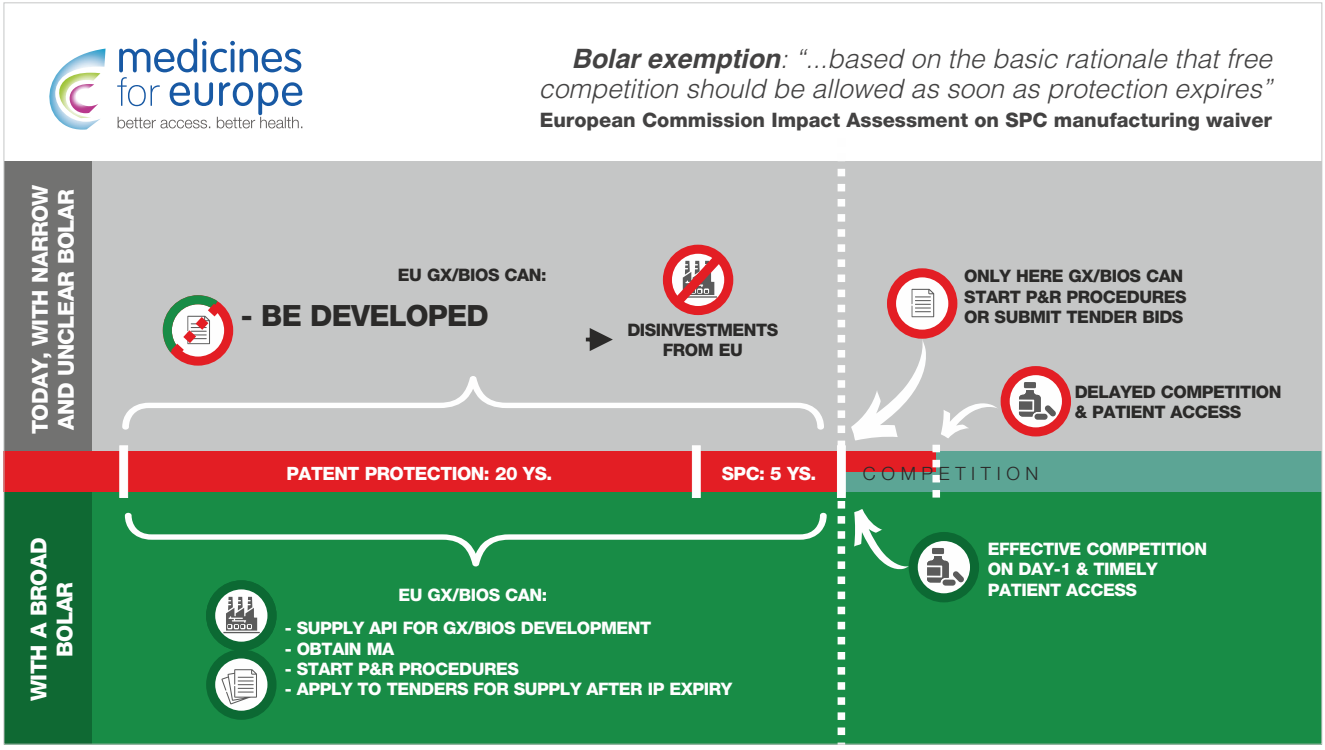
Harmonsation

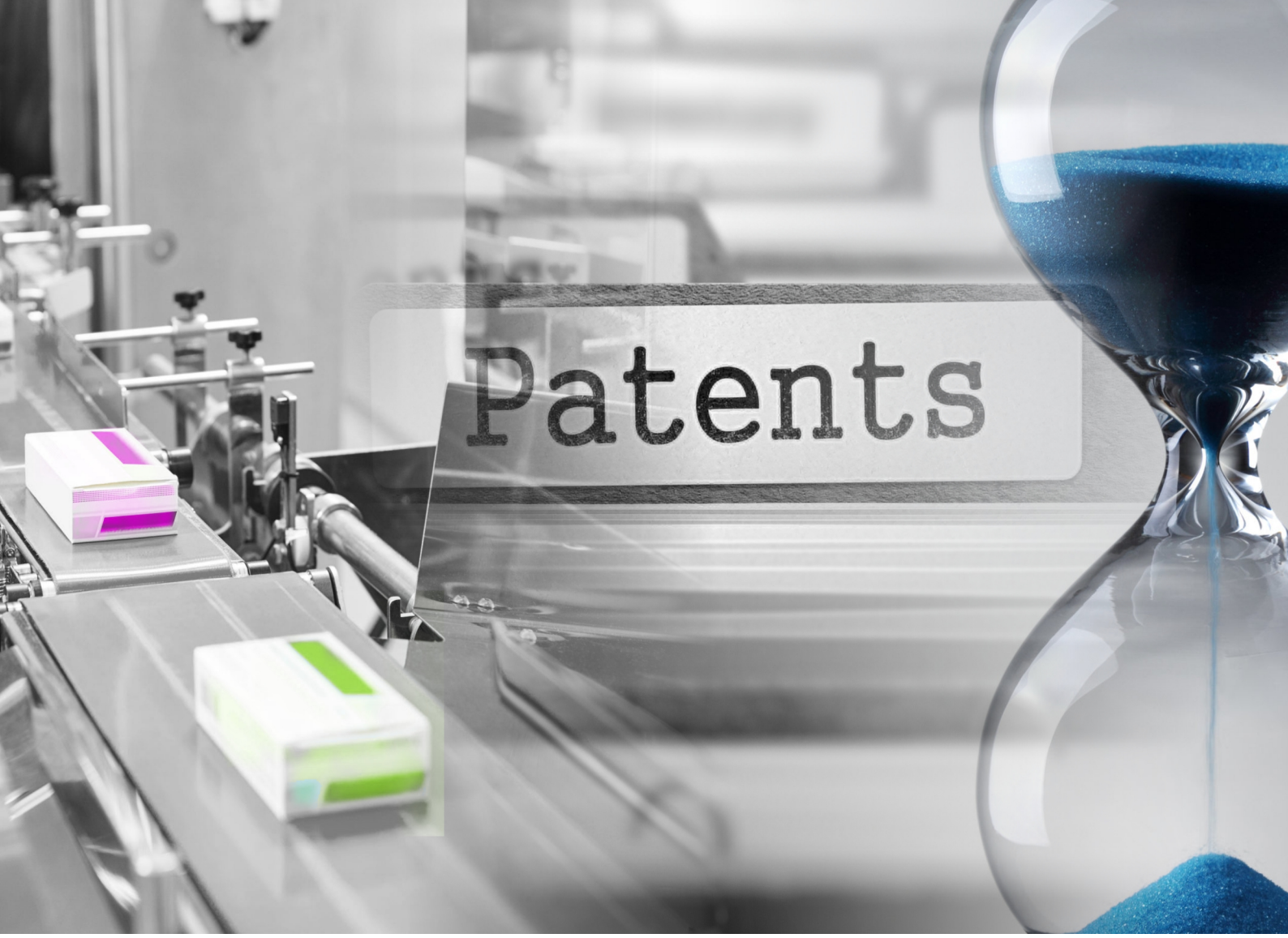
- More equitable distribution of API investments among MS
- Stability & predictability for the whole pharma sector
- More rational strategic business planning for European companies
- Reduced legal uncertainty

Extended scope

- More supply from European APIs suppliers
- Ready to access the market on day-1
- More investments in R&D & manufacturing of API in EU
- Wider choice of API suppliers for European companies

What it means in practice





The issue of divisional patent applications

factsheet

- ☐ What are divisional patents?
- ☐ The issue
- ☐ Good-to-know
- ☐ The EU competition law scrutiny of 2009
- ☐ What can be done: recommendations

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The issue of divisional patent applications

factsheet

What are divisional patents?

The current framework allowing unlimited filing of divisional patents opens the door to a widespread misuse of the patent system to artificially delay generic and biosimilar competition.

Divisional patent applications are those deriving from an earlier patent application (the "parent"), which the applicant splits into a sequence of divisional applications each claiming a single element of the same claimed invention.

Divisional applications, themselves, can give rise to further multiple divisional applications, without any limitation. Each divisional patent lasts until the expiry date of the parent patent, but is subject to new examination procedures and, if granted, new opposition periods independently from the outcome of the parent application.

The issue

Divisional patent strategies are often pursued by originator pharmaceutical companies at the European Patent Office (EPO)[1] to create legal uncertainty for generic/biosimilar medicines developers seeking to launch competitor products, resulting in delayed launches and, consequently, delayed patient equitable access to medicines.
The "divisional patent game" is the following:

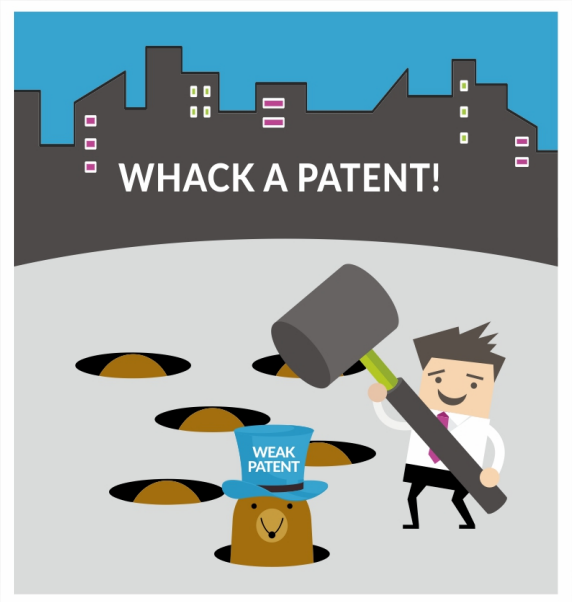
- (I) filing cascades of divisional patent applications at different times, related to the same weak parent application
- (II) defending such divisional patents in (EPO) opposition proceedings
- (III) enforcing such divisional patents in national courts, incl. via preliminary injunctions

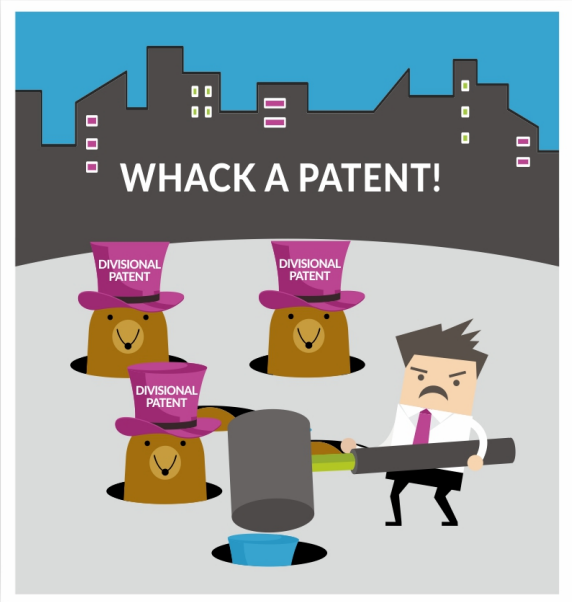
The EPO grants European patents, whose protection extends in the Member States picked by the patent owner. Such patents are then enforced and litigated in court at national level.

- (IV) strategically withdrawing any earlier patent from the family, just before an EPO decision confirming it is invalid, thus avoiding the negative effects on the other divisional members of the family
- (V) even when a parent patent is invalidated in Courts, there will still be a divisional patent application covering substantially the same subject matter, replicating the legal uncertainty and the clock starts ticking again

Good-to-know:

An opposition proceeding to invalidate a divisional patent can take 3-6 years until final resolution by EPO Technical Board of Appeal thus offering ample opportunity to artificially extend monopoly rights





The EU competition law scrutiny of 2009

In 2009, in the Pharmaceutical Sector Inquiry Report, the European Commission condemned the proliferation of divisional patent applications, noting that "examination of divisional applications continues even if the parent application is withdrawn or revoked, which can add to the legal uncertainty for generic companies", adding that: "filing divisional applications for the same secondary patent… can… be used strategically to create further uncertainty and delays for new entrants."

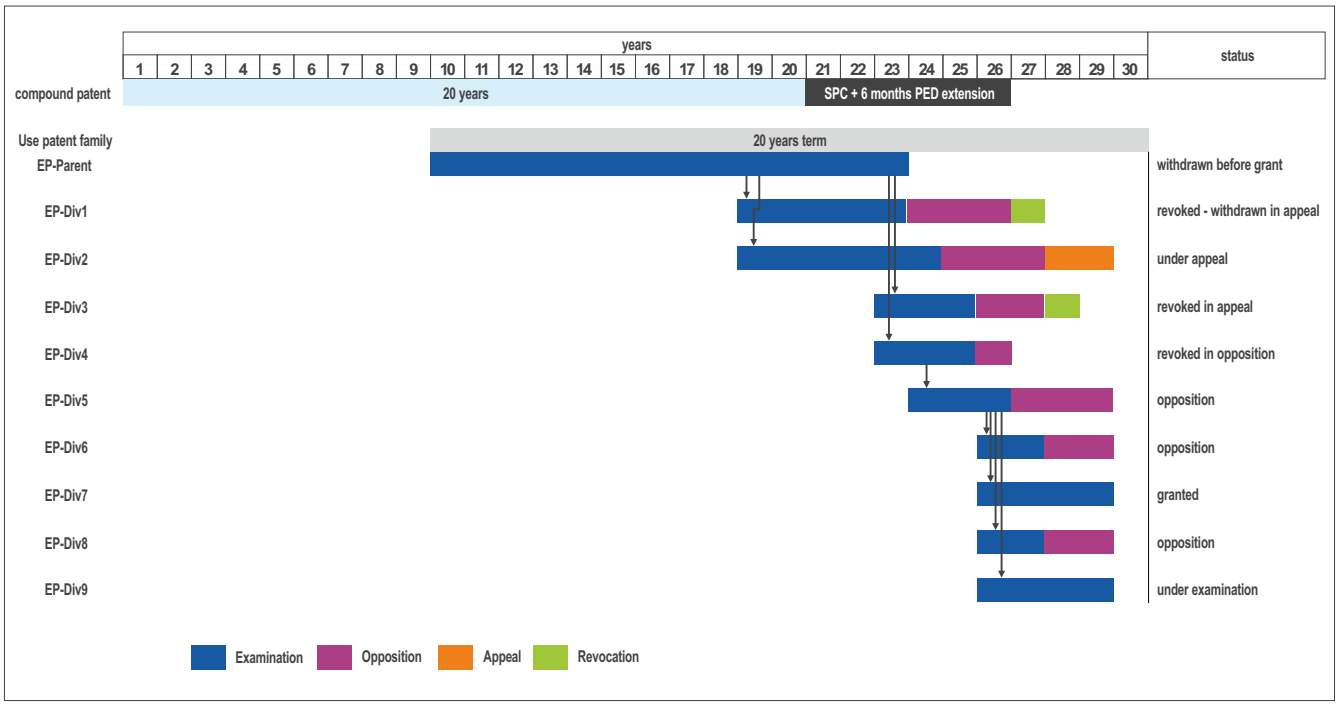
Due to the anticompetitive effects of this practice, Rule 36 of the European Patent Convention was amended in 2009 to set deadlines for filing divisional applications. However, due to limited EPO resources and some effective lobbying, the policy was changed in 2014 and the deadline was removed.

What can be done: recommendations

In line with the findings of the 2019 EC Sector Inquiry and seen the very direct impact it has on competition and public health expenditure, Medicines for Europe recommends:

- 1. Stricter requirements for filing and allowing new divisional applications.
- 2. Examination & opposition proceedings of patent applications from the same family should be heard together, incl. in relation to expedition of EPO procedures.
- 3. The withdrawal of a divisional application should be allowed only if duly justified and an EPO decision should be issued anyway.
- 4. Examination of divisional applications should be fast-tracked.
- 5. Divisional application/patent should not include any new experimental data or new facts that would overcome a patentability issue of an earlier application/patent.
- 6. The EPO should reaffirm the strict application of the prohibition of double patenting.
- 7. In addition, a 5-year deadline for the filing of any divisional applications should be re-introduced.

A real example of a "divisional patent game"



Unified SPC Grant Mechanism

factsheet

- ☐ What is an SPC?
- ☐ Where do we stand now?
- ☐ The objective
- ☐ Policy reccomendations

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Unified SPC Grant Mechanism

factsheet

What is an SPC?

A supplementary protection certificate (SPC) is an extension by up to 5 years of the market protection of a patented product conceived to compensate the time that it takes to develop a product from the filing of its patent until the authorisation to launch it on the market. The SPC regime is regulated by directly applicable EU law, but is a national IP title granted by national patent offices.

Where do we stand now?

In the 2015 Single Market Strategy, the European Commission proposed the introduction of a **Unitary SPC**. It is linked to and is intended to complement the unitary patent system and is part of a bigger package that includes the introduction of a Unified Patent Court (UPC). Due to the delays in the implementation of the UPC, the Commission has been considering a **unified mechanism for the granting of SPC titles** together with or instead of the Unitary SPC.

The objective

According to the IP Action Plan, the unified SPC grant mechanism would allow companies to file a single SPC application for multiple designated Members States. The main objective would be to reduce the burden on SPC applicants which would file one SPC application rather than multiple applications throughout EU Member States.

Policy reccomendations

The societal benefits of a unified SPC grant mechanism need to be further clarified. The current proposal seems to be aimed solely at reducing burdens for SPC applicants without due consideration for other critical issues like access to medicines. It requires in-depth analyses by institutions and stakeholders.

While it is still unclear how such a system would work and what would entail, several key elements need to be included in this mechanism for it to be balanced and coherent with a uniform SPC system in Europe:

European Parliament oversight of the granting body

The granting body should be **fully accountable** and **under the oversight of the European Parliament** to ensure quality of assessments and procedures

Coherent and unified SPC lifecycle

In line with the concept of EU uniformity justifying this measure, **the SPC lifecycle should be the same in all EU MS**:

- If an SPC is revoked in one country, the body should **automatically revoke the title in all the EU countries covered by the SPC**
- The **procedures for invalidating the SPCs (i.e. oppositions) should also be unified**

The Marketing Authorisation for SPC calculation

in line with the concept of EU uniformity justifying this measure:
It **should only cover products with European marketing authorisations**, otherwise the purpose of a uniform European mechanism would fail

Procedural transparency

There should be **the highest levels of transparency**, for the sake of legal certainty, on:

- the publication of SPC applications
- assessment procedures
- 3rd party observations & opposition periods

Biosimilar medicines interchangeability

factsheet

- ☐ Problem Statement
- ☐ Recommendations
- ☐ Mapping of existing biosimilar medicines positions by National competent authorities
- ☐ Relevant documentation

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Biosimilar medicines interchangeability

factsheet

Regulatory guidance and clarity on biosimilar interchangeability is a scientific decision and a key enabler for both uptake and competition

Problem Statement

European Member States continue to see wide disparities in use and access to biologic medicines, including biosimilar medicines, even 15 years after the first European biosimilar approval. While these disparities cannot be attributed to one single policy measure, a correlation can be made between the level of stakeholder awareness, their level of confidence in the regulatory framework, the clarity of national regulatory guidance and overall biosimilar use. While most countries in the EU are facing inequities, Central Eastern European countries count among the most pronounced challenges in terms of access to biologic medicines.

The limited or ambiguous national positioning contrasts with the vast scientific & regulatory data already available:

- Since 2006, regulators in Europe and globally have reviewed large data sets of scientific evidence with authorised biosimilar medicines which consistently and unambiguously supports the possibility to exchange one biologic medicine for another approved comparable biologic medicine[1]
- This experience includes the robust post-authorisation pharmacovigilance activities, which also converge towards the conclusion that a biologic reference product and its authorised biosimilar medicines behave similarly.
- In addition, Europe has cumulated over 2 billion patient treatment days of safe clinical experience with biosimilar medicines. Over that period, on average, clinical experience has doubled every 18 months.

(1) Kurki et al. (2017). Interchangeability of Biosimilars: A European Perspective. BioDrugs. 31. 10.1007/s40259-017-0210-0.

Reaching the point of trust with stakeholders has proven essential to enable shared decision making, to increase biosimilar use, design benefit-sharing and incentives schemes as well as to allow head-to-head competition (e.g., in tender procedures). For the market to harness more competition and offer invaluable opportunities for healthcare systems to improve patient access, improve healthcare budget sustainability and significantly reduce equity gaps across Europe, there needs to be clear and consistent regulatory guidance along with up-to-date data and evidence sharing. The absence of clear and consistent national regulatory guidelines on interchangeability and its implementation is associated with lower biosimilar medicines use.

In the European context of biologic medicines (biosimilar and reference), "it is important for healthcare professionals to be aware of the terminology to refer to interchangeability, switching and substitution practices in the EU. Interchangeability refers to the possibility of exchanging one medicine for another medicine that is expected to have the same clinical effect"[2].

Clear medicines agencies positioning has already enabled a number of EU Member States promoting confidence in the use of biosimilar medicines by both patients and physicians. Straightforward summary statements from these trusted sources can go a long way in achieving better uptake of biosimilar medicines. We therefore encourage all EU Member States to adopt such position statements as a significant enabler towards biosimilar medicines' adoption.

Policy recommendations

- Drive the European regulatory network of medicines agencies to issue **clear and aligned statements in support of biosimilar medicines interchangeability as defined by the European Medicines Agency (EMA)**, particularly in countries where no or limited guidance is available on interchangeability and its practical implication in the national context.
- Regulators should transparently and assertively share the latest **experience and data** (e.g., clinical and pharmacovigilance) gather as part of the current framework to inform regulatory positioning and provide continuous reassurance in the regulatory framework robustness.
- **Pro-actively engage in educational outreach with healthcare community stakeholders** in new therapeutic areas where biosimilar medicines are expected to be approved, such as ophthalmology, factoring in the learnings and experience to date from other therapy areas.

(2) https://www.ema.europa.eu/en/documents/leaflet/biosimilars-eu-information-guide-healthcare-professionals_en.pdf (Oct 2019) – "[…] Interchangeability refers to the possibility of exchanging one medicine for another medicine that is expected to have the same clinical effect. This could mean replacing a reference product with a biosimilar (or vice versa) or replacing one biosimilar with another. Replacement can be done by: 1.Switching, which is when the prescriber decides to exchange one medicine for another medicine with the same therapeutic intent. 2.Substitution (automatic), which is the practice of dispensing one medicine instead of another equivalent and interchangeable medicine at pharmacy level without consulting the prescriber"

Mapping of existing biosimilar medicines positions by National competent authoritiesRelevant documentation

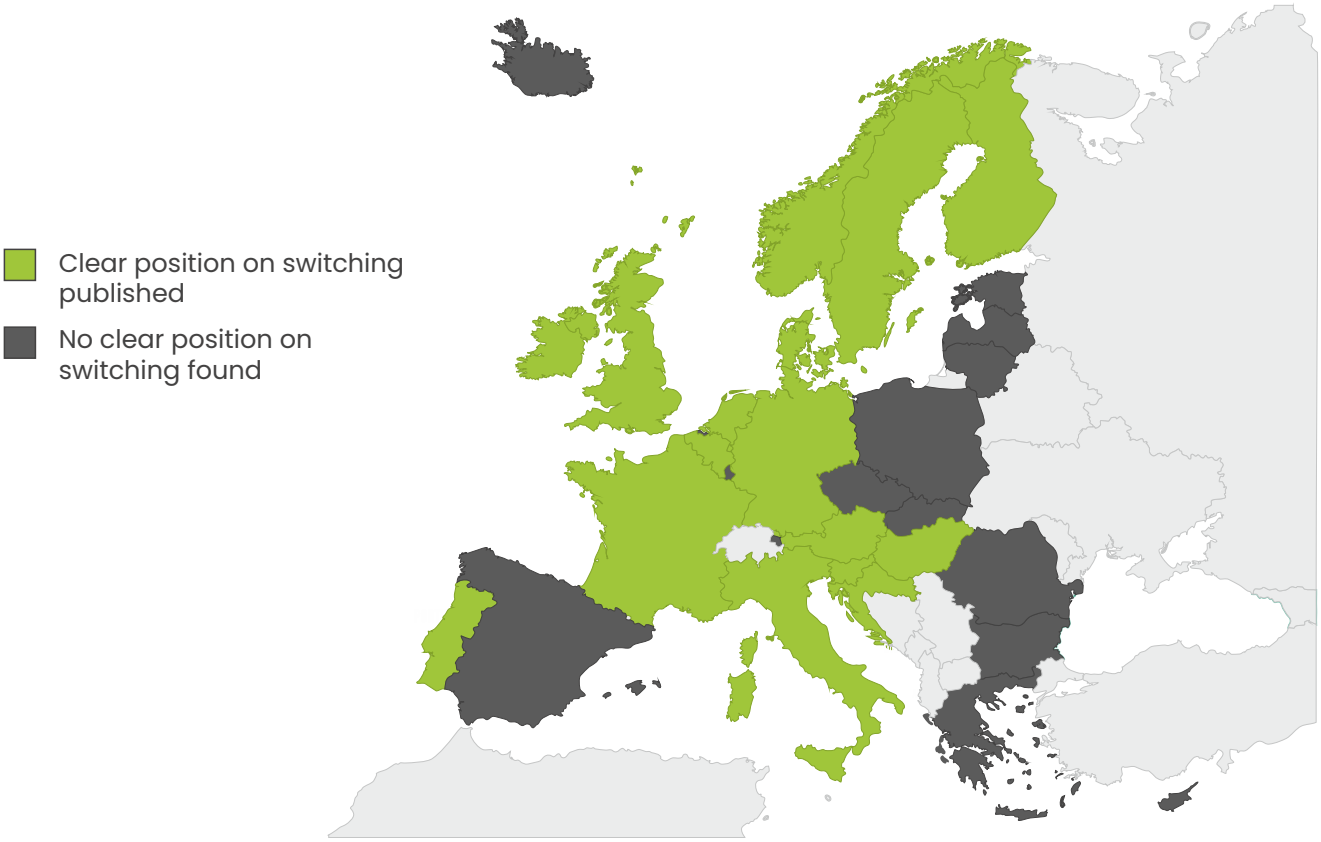

Figure 1 - Map of supporting statements for switching from reference to biosimilar medicines.

Available positioning statements from national competent authorities of the Member States of the European Union (EU) and the European Economic Area (EEA) responsible for human medicines, as well as other relevant national organisations. When multiple agencies or organisations for one country had released statements, those were all assessed, and positions merged. Light grey indicates countries that were not included in the analysis.

Relevant documentation

- https://www.ema.europa.eu/en/documents/leaflet/biosimilars-eu-information-guide-healthcare-professionals_en.pdf
- https://www.medicinesforeurope.com/docs/M-Biosimilars-Overview-of-positions-on-physician-led-switching.pdf
- https://www.medicinesforeurope.com/2020/10/01/positioning-statements-on-physician-led-switching-for-biosimilar-medicines/
- https://medicinesforeurope.com/docs/2020-biologic%20pharma%20substitution-position-FINAL.pdf

Unmet medical **needs**

Value Added Medicines

factsheet

- ☐ How can Value added medicines make a difference to patients and healthcare systems during a pandemic and beyond?
- ☐ Policy recommendations
- ☐ Relevant documentation

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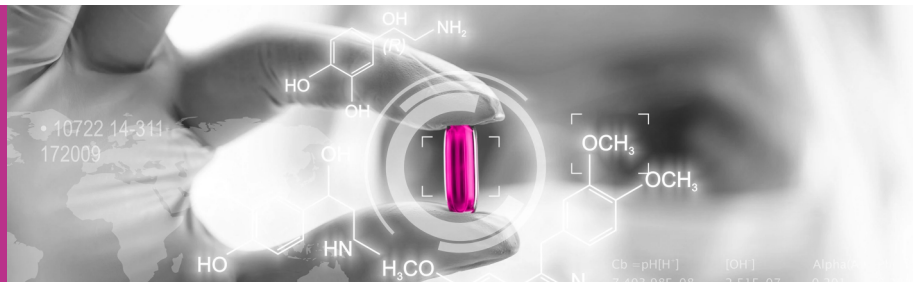
Value Added Medicines

factsheet



The Pharmaceutical strategy for Europe aims to address unmet health needs and the accessibility and affordability of medicines. Value Added Medicines are defined as an accessible, affordable innovation to address health needs that are especially important to larger patient populations in both, communicable and non-communicable disease management. We recommend the establishment of a new, simplified regulatory pathway for VAMs. By recognising VAMs as a category of innovation with a dedicated pathway and tailoring the system of incentives provided by the EU pharmaceuticals framework to support innovation throughout a molecule's lifecycle, we can achieve a complete and resource-efficient EU pharmaceutical industry while delivering medicines to satisfy the unmet need and improve the lives of patients in Europe.

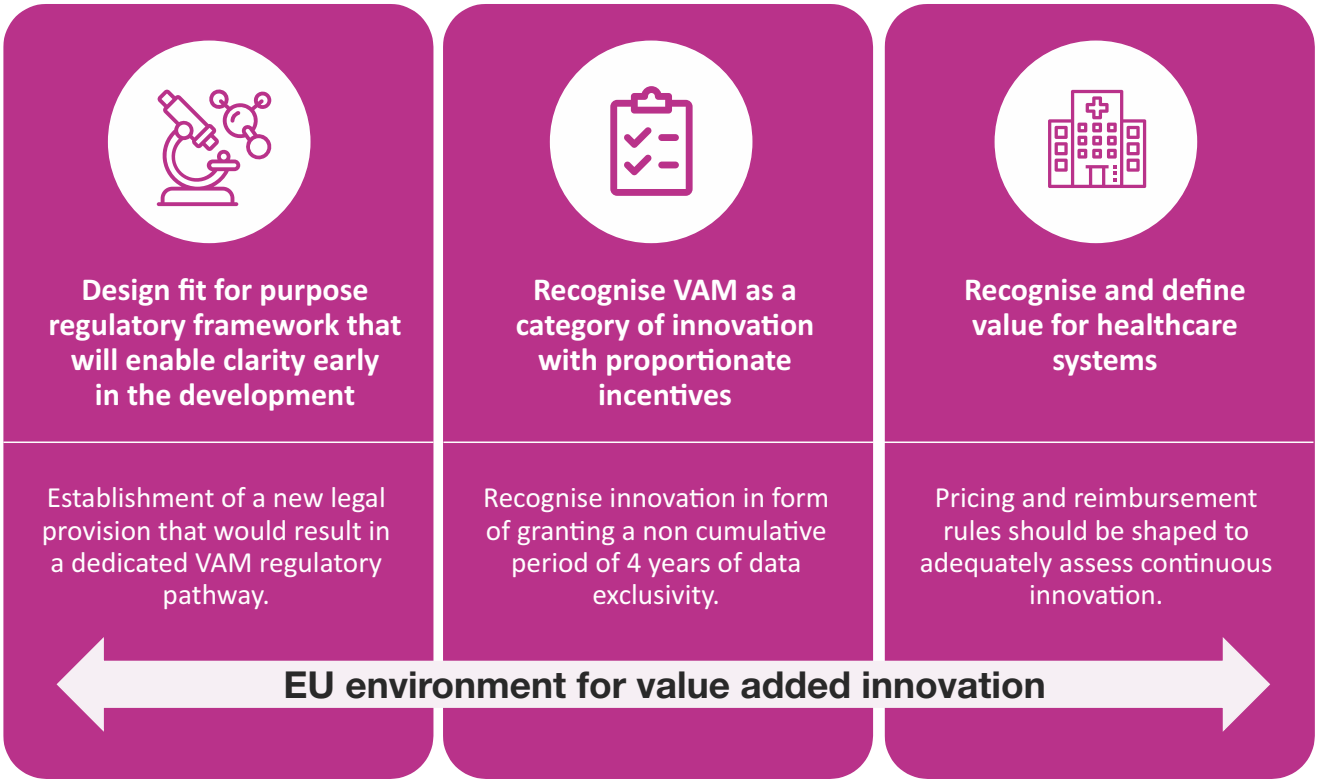
How can Value added medicines make a difference to patients and healthcare systems during a pandemic and beyond?

- **REPOSITIONING - FINDING NEW INDICATIONS TO ADDRESS UNMET MEDICAL NEED**
  Dexamethasone, an affordable steroid, repurposed for Covid-19 treatment, reduced deaths by 1/3 in hospitalised Covid-19 patients receiving mechanical ventilation.

- **REFORMULATION - FACILITATING PATIENT TREATMENT IN A HOME CARE SETTING**
  Covid-19 dramatically reduced accessibility of care and changed patients' needs in a number of ways. VAMs can support patient-centred reform of care with medicine reformulation and offer patients new ways to administer their own treatments at home and avoid in-person hospital visits.

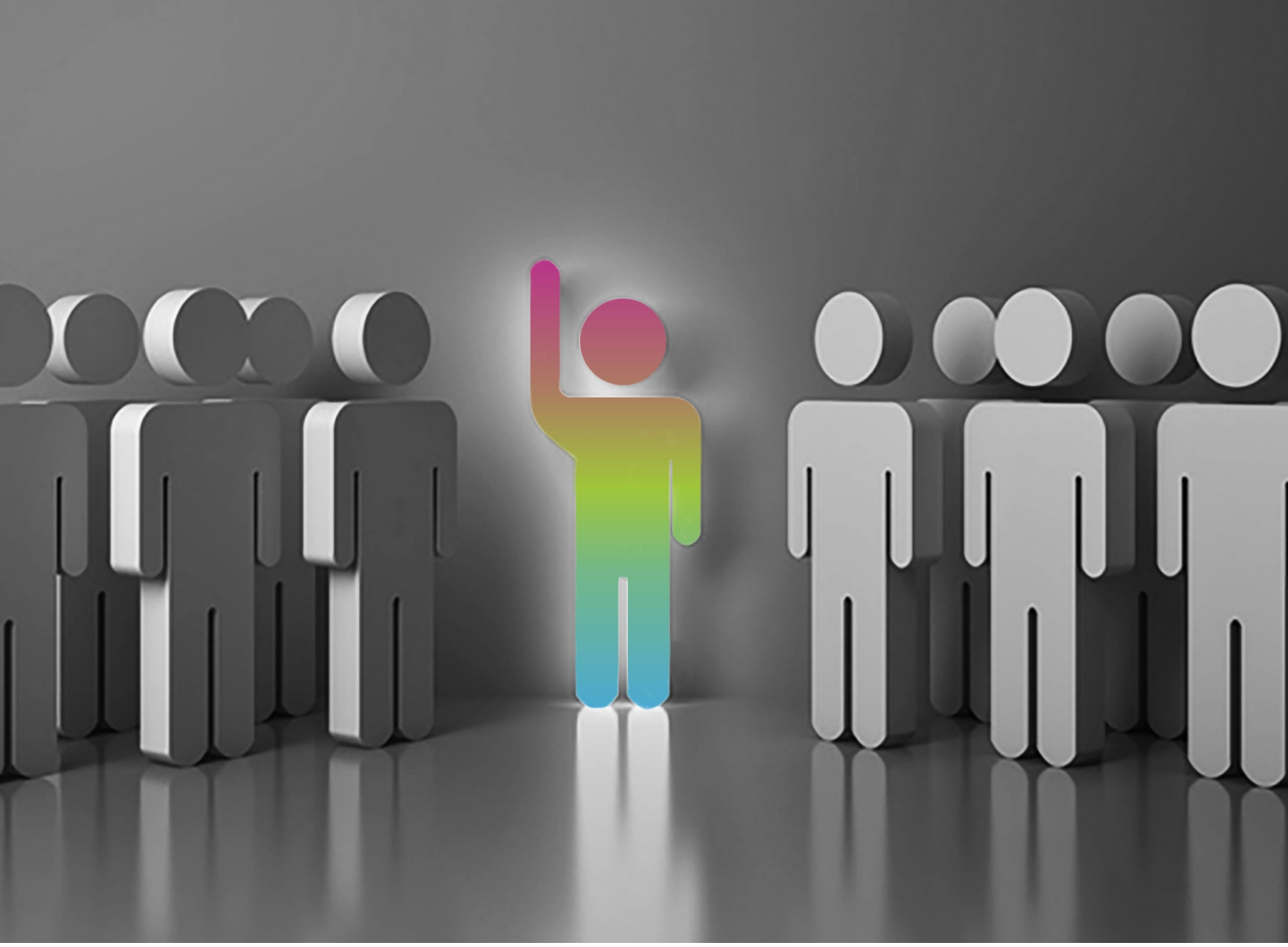
- **COMPLEX COMBINATIONS - UTILISING DIFFERENT RESOURCES TO DELIVER THERAPY**
  Digital Value Added Medicines, combine medicines with innovative technological solutions and can support the patient-HCP relationship and improve treatment adherence in a remote care setting.

Policy recommendations



Relevant documentation

- Medicines for Europe White Paper: Creating a European Ecosystem for safe, timely and affordable patient-centric innovation



Orphan & paediatric medicines incentives

factsheet

- ☐ Orphan & paediatric medicines incentives
- ☐ The scope of the review
- ☐ The recommendations

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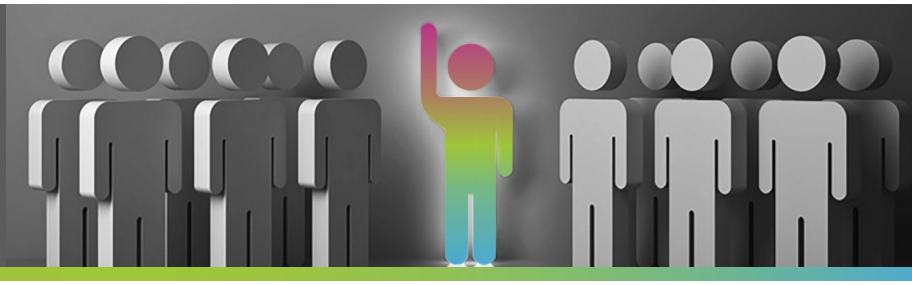
Orphan & paediatric medicines incentives

factsheet



Orphan & paediatric medicines incentives

EU Pharmaceutical legislation provides for 10-yr of market exclusivity for medicines for rare diseases (orphan) with free regulatory advice and fee reductions, and 6-month supplementary protection certificate (SPC) for paediatric medicines. For off-patent paediatric medicines development (PUMA), there is a 10-yr market exclusivity. For orphan/paediatric medicines, there is a choice between a 6-month SPC or an additional 2-yr orphan exclusivity.

The scope of the review

As urged in the Health Council Conclusions of 2016, in the context of the EU Pharmaceutical Strategy, the EC will propose amendments to the orphan & paediatric legislation in 2022 since there is:legislation.

- Insufficient development in areas of greatest unmet needs → 95% of rare disease still without treatment
- Limited availability & accessibility across Member States → incl. delayed generic & biosimilar competition
- Multiplication of rare diseases out of common diseases

The Health Council Conclusions of 2016 also called for timely access to generic & biosimilar medicines, which are fundamental to ensure budgetary sustainability.

To this end, the Commission proposed several options in its Inception Impact Assessment (IIA) on this legislation.

Recommendations

While incentives have generated some success, there is a need to **ensure incentives achieve the objectives originally intended whilst avoiding abuses/misuses of the system that delay generic/biosimilar competition**:

Orphan medicines

- The overlapping exclusivities blocking generic/ biosimilar competition could be tackled by **explicitly allowing in the legislation generics/biosimilars to enter the market** for any orphan medicine that has already benefitted from 10yrs of orphan exclusivity
- A **specific framework for value added medicines could be developed** with proportionate incentives & rewards for the effort invested so to address market failures related to repurposed products and continuous innovation (e.g. off-label prescribing)
- The EU should **address the risk of multiplication of exclusivity periods** ("salami-slicing" of indications)

Novel incentives via transferrable exclusivity vouchers should be excluded, also for paediatric medicines, as they would extend monopolies on more profitable products, increasing costs for HC budgets, legal uncertainty incl. on market formation dates & unduly delaying access to generics/biosimilars

Paediatric medicines

- While the proposals include the need to restrict the use of the 6-month SPC extension where no unmet need exists, it is **key for legal certainty to ensure early clarity on the upcoming paediatric SPC extensions**
- There is a **recognised market failure of the off-patent incentive (PUMA)**. As stressed in the pharma strategy communication, there is need to "stimulate innovation in particular in areas of unmet needs", incl. off-patent paediatric developments, where there is "absence of commercial interest". As is proposed for novel antimicrobials, **the reform should include pull incentives based on new P&R models to incentivise development of off-patent paediatric medicines, but also free pre-submission scientific advice (as for orphans) & clear framework for repurposed off-patent products for new indications for children only**

Use in combination of orphan/paediatric incentives

- A holder of a product with **orphan exclusivity should be prevented from withdrawing the orphan designation in order to obtain an SPC extension later** as this delays effective competition & patient access.

Incentives for follow-on orphans & off-patent paediatric products

To **stimulate faster competition from follow-on orphan developments** (ie. on day-1 of exclusivity expiry) & **investments in off-patent paediatric products**, the reform should:

- Tackle barriers to development by tailoring clinical requirements for biosimilars based on science & allow single development for multiple jurisdictions (comparable to international harmonisation of paediatric & orphan development of originator products).
- Facilitate access to reference product for clinical trials
- Remove barriers to day-1 launch after protections expire by banning patent linkage, harmonising the Bolar exemption & introducing uptake measures to stimulate competition
- Reduce timelines and obstructions to P&R decisions in line with Bolar
- P&R uptake measures to encourage investments in follow-on orphan development

Responsive regulatory **framework**

Optimizing the regulatory procedures

factsheet

- ☐ Problem Statement
- ☐ Policy recommendations

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Optimizing the regulatory procedures

factsheet

Problem Statement

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[1] 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[2].

(1) 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.
(2) 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

Policy recommendations

Centralised MA procedure

The 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.

Recommendations 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.

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[3]. 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.

(3) For detailed proposals on simplification of the DCP, please refer to Medicines for Europe Regulatory Efficiency Report

Recommendations 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

Telematics

factsheet

- ☐ Problem Statement
- ☐ Policy recommendations
- ☐ Objectives
- ☐ Benefits

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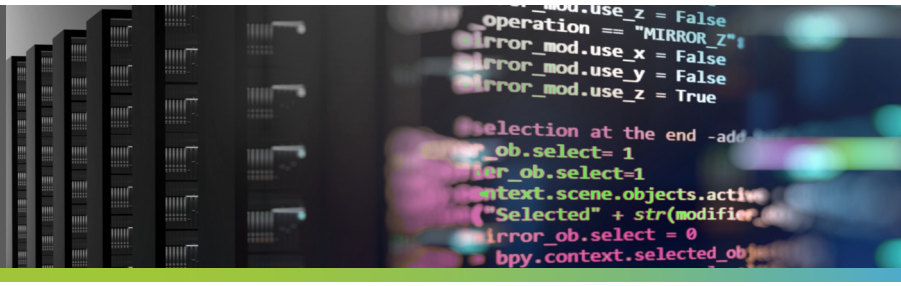
Telematics

factsheet



Problem Statement

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.

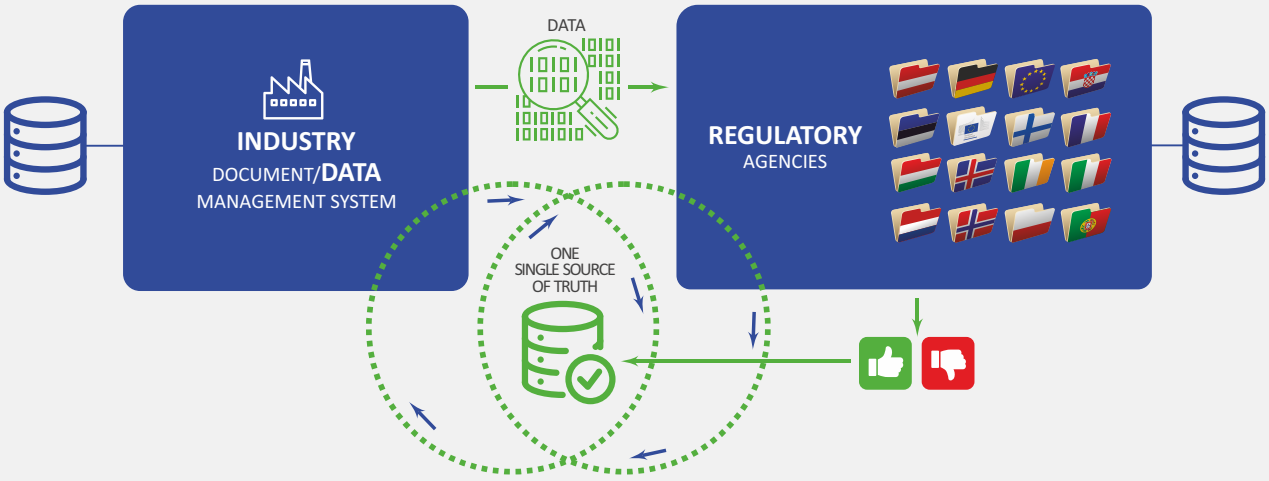
The pandemic demonstrated Europe's data weaknesses and gaps across all countries and at the EU level. The absence of useable data led to panic, hampered the ability of the EU to play its role in ensuring equitable access to medicines and weakened solidarity between member states. Industry-government 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

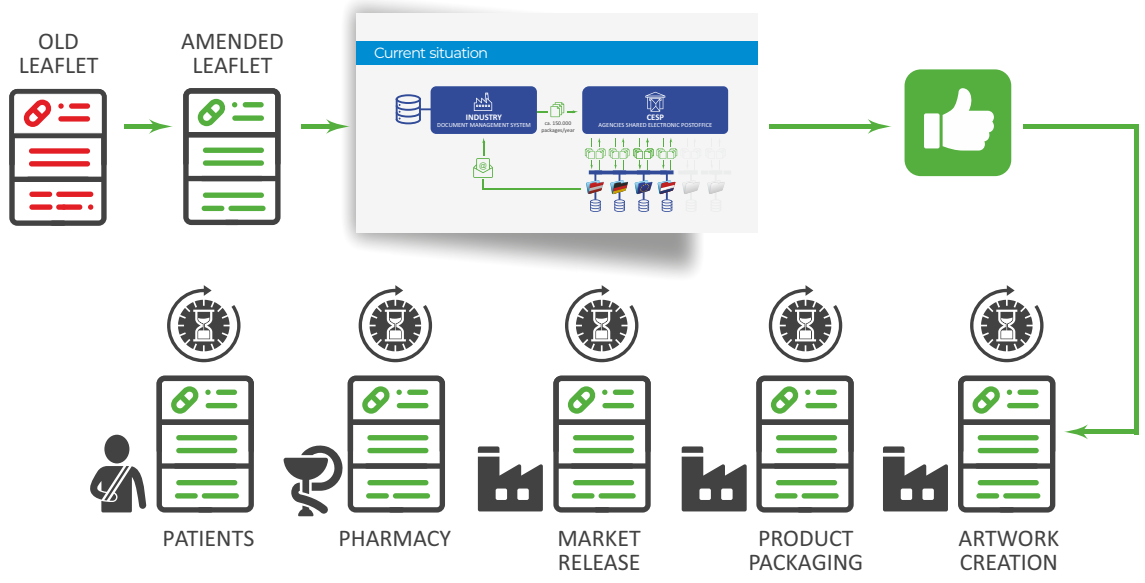
E-INFORMATION TO PATIENT

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.

Variations system

factsheet

- ☐ Introduction
- ☐ Issue
- ☐ Policy recommendations
- ☐ Facts and figures

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Variations system

factsheet

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. 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-	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	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.	

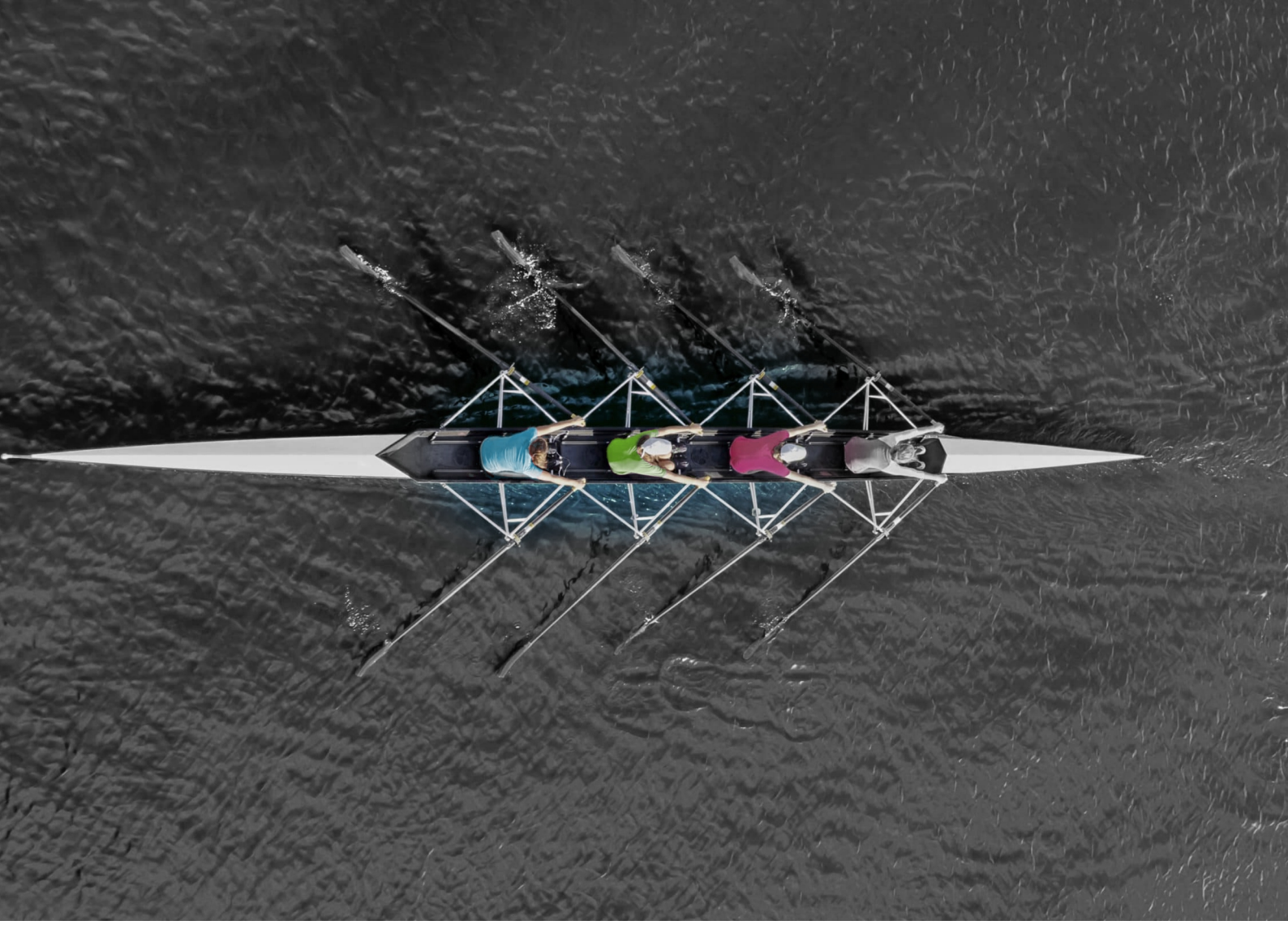
Facts and figures

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.



Off patent competition global development

factsheet

- ☐ Problem Statement
- ☐ Policy recommendations

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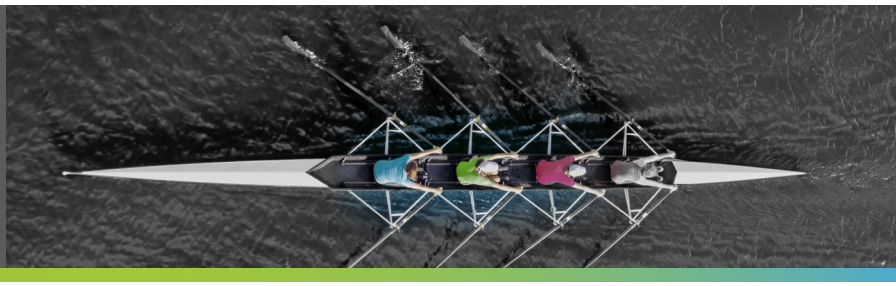
Off patent competition global development

factsheet



Problem Statement

Competition in the off-patent market is a major driver of greater access to important medicines for public health. Regulatory processes and requirements directly impact competition as requirements for marketing authorisation influence both development timelines and resources involved. The off-patent industry is largely global. Regional requirements and disparities further negatively affect development timelines and the resources involved.

Global development is a cornerstone of streamlined product development. It is essential for competition, especially for complex products. Conducting multiple clinical development programs for comparison with local reference products is not only time and resource-consuming, but also unethical, as it involves superfluous experimenting in human subjects with no added benefit.

Overall, this results in higher resource investment, extended timelines and delays in broader patient access to comply with these regional requirements.

Policy recommendations

Generic medicines aspects

- **Ask:** We call on the EU to take a leadership role in the development of strategies that may allow the use of foreign comparator products consistently across all medicines, which, together with the harmonisation of the scientific bioequivalence principles at ICH, will permit to pursue single global development for generic medicines. This will contribute to timely and efficient competition in the generic market and greater access to generic medicines.

- **Background**: Acceptability of the use of foreign comparators may be especially relevant in the cases where clinical development requires complex studies or studies in patient populations: under the current approach, for example for bioequivalence studies in patients, developers are sometimes required to prioritise development for one region over others in order not to compete in terms of recruitment. These delays access to affordable medicines to patients and decreases

- **1) Regulatory aspects**: For generic products, single global development depends on the harmonisation of scientific principles and acceptance of foreign comparator products in bioequivalence studies. International harmonisation of scientific principles to establish bioequivalence has already started at the International Council for Harmonisation (ICH).

  Generic medicine developers are generally expected to run multiple clinical development programmes that require comparison with local reference products. This means that multiple clinical studies are required, even if the reference product is the same in different regions.

  For biosimilar products, however, it is already acceptable to use comparator products from foreign sources.

- **2) Single global development in originator product development**: Single global development is the standard approach for the development of new originator products. As these are authorised, their clinical package is typically the same across highly regulated regions, where similar quality standards are also followed. Therefore, in many cases, it may be assumed based on certain analyses, that the reference products from different regions are actually the same product, making the repetition of the clinical development programme or other comparability exercises multiple times to compare with local references, unnecessary.

- **3) Acceptability of foreign comparators in other jurisdictions**: For the single global development of generic medicines to become a reality, acceptance of foreign comparators is required. This is not yet possible for generics in Europe although it has become very common e.g. biosimilar medicines development.

  However, other highly regulated regions already accept the use of foreign comparators (including but not limited to the UK, Switzerland, Singapore, and Canada). These regions have developed methodologies that allow establishing under which circumstances foreign comparators can be used (and from which territories), providing ideal conditions for thriving generic competition.

  Competitiveness, given that, to optimise resources, developers may opt to develop their products only for some of the regions.

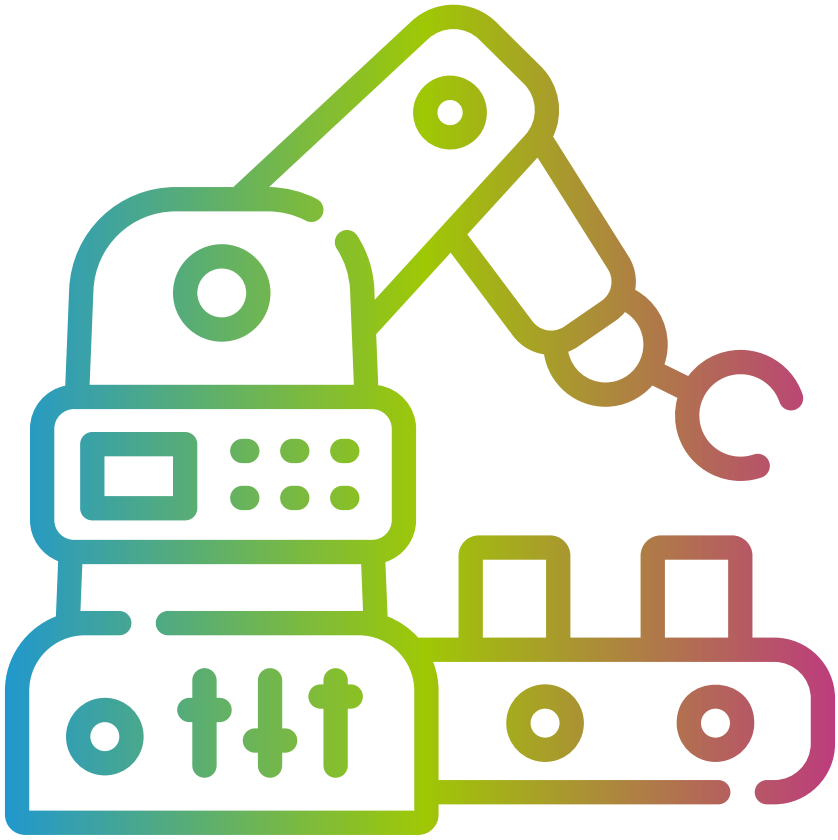
This could also play an important role in the development of generic versions of orphan drugs where development resources need to be used in an especially efficient manner.

Orphan biologic aspects

- **Ask**: We call on the EU to take a leadership role in designing a fit-for-purpose off-patent medicines global regulatory framework for the life-cycle of orphan and small population medicines: true global development should be enabled through acceptance of foreign reference data without bridging data, global convergence towards the scientific principles to streamline clinical comparability. This is essential to develop greater equity in access to these essential therapies.

- **Background:** By 2028, a total of 28 biologic orphan medicines will be eligible for biosimilar competition. However, the majority of orphan medicines do not have a follow-on product in clinical development. Only 11% of orphan biologic molecules have a biosimilar version in clinical development, as opposed to 23% for total biologic medicines.

  The development of follow-on products for these medicines certainly requires different approaches, as current biosimilar pathways did not foresee some of the challenges ahead.
  - Sourcing comparator product is restricted due to specific access schemes, small volumes, fewer product batches and prohibitive acquisition costs.
  - Clinical comparative studies may not be feasible. In particular, patient recruitment into studies may prove extremely slow given the low incidence of the disease, considerably slowing down the development. In addition, a recent consensus is emerging on the need for clinical comparability requirements to be waived as default requirements
  - The originator followed a global development pathway and was incentivised to mitigate and/or overcome the inherent hurdles to this field.



Leadership in medicines **manufacturing**

Manufacturing and open strategic autonomy

factsheet

- ☐ Problem Statement
- ☐ Policy recommendations

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Manufacturing and open strategic autonomy

factsheet

Problem Statement

Europe has a strong and competitive pharmaceutical industry. Together with other public and private actors, it serves public health and acts as a driver of job creation, trade and science. Our industry supplies close to 70% of prescription medicines in volume and employs close to 200000 highly skilled employees across over 400 factories and R&D centres in almost every country of the Union. The Pharmaceutical Strategy for Europe should build on these foundations to encourage more investment in manufacturing.

For many years, Medicines for Europe has been advocating for a more competitive framework for the manufacturing of medicines in Europe. The Commission is driven by the concern over Europe's increasing dependence on China and India for key aspects of medicines manufacturing.

The available data does confirm a considerable shift in API production from Europe, which used to be known as the pharmacy of the world, to Asia over the last 20 years. An examination of EDQM data on certificates of suitability (CEPs) shows that 62% originate from India and China. GDUFA (US law on generic medicine fees) shows that India has the most API manufacturing sites approved to supply the US but Europe (including Switzerland) is actually in second place whereas China is a smaller player. On the positive side, Europe still has a considerable manufacturing presence of both API and finished dosage forms according to EDQM and FDA data. Also, an in-house survey at Medicines for Europe related to API manufacturing showed that our members still have almost 58% of the API in house facilities located in the EU.

There is still a strong manufacturing base in Europe to boost our competitiveness with supportive policy measures, but these measures need to be seen from a global supply chain perspective. Such a global supply chain can come under pressure due to pricing policy pressures, FMD, administrative variations and costs, GMP topics included into regulatory

dossier leading to drop out of suppliers/manufacturer and hence consolidation which increases the risk of shortages.

The European Commission has approved a robust funding Plan to boost the recovery after the Covid virus crisis, there could be several opportunities for our industry indirectly via plan agreed with national Governments through the Next Generation EU, but also via directly industry participation in the EU4Health program that will finance actions aimed at (1) Overcoming health inequalities, (2) Improving crisis preparedness, (3) Strengthening EU manufacturing, (4) Innovating in the off-patent sector, (5) Addressing environmental challenges, (6) Leading the digital transformation of health systems.

Policy recommendations

- **Regulatory optimisation and enforcement** needed to reduce the cost burden associated with the filing and maintenance of regulatory files of API and medicines production by:
  - Taking GMP controlled information out of the regulatory dossier will increase adaptability, agility and resilience. Supply Chain Oversight maintained towards regulators via IT solutions, databases to achieve a leaner approach to the transparency of supply chain functions and actors.
  - Reducing administrative variations to be prepared and filled= lowering the costs
  - Including of multiple API sources into the approved dossier: Incentives or regulatory flexibility to lower fees, to bring this security into the supply chain
  - Stricting GMP enforcement in unregulated markets which do not enforce GMP locally.
  - supporting the digital transformation of healthcare systems or development of European monitoring, reporting and notification system for shortages of medicines and medical devices.
  - strengthening the manufacturing including the production of antimicrobials and essential APIs; diversifying supply chain production of active ingredients and generics within the Union to reduce the Member States' dependence on certain third countries;
  - Supporting actions to improve the environmental-friendly production and disposal of medicinal products and medical devices and support the development of medicinal products that are less harmful to the environment;
  - supporting actions that foster the production, procurement and management of crisis relevant products within the Union, ensuring complementarity with other Union instruments, to mitigate the risk of shortages.
- **Integrating security of supply into market policies:**
  - Considering incentives for products where there is limited competition
  - Incentivise API production in Europe with measures such as R&D investment tax deductions
  - Priority review and fee waiver for the introduction of API where an EU manufacturer would intervene in a shortage.

- Incentives to develop value added APIs
- Regulatory recognition of companies that choose to invest for EU security of supply
- Changes to EU procurement: The Commission could introduce guidelines on medicines procurement to include security of supply criteria – provided this is objective and based on open markets.
- Where substantial manufacturing investments would need to be made to increase the security of supply there could be a regulatory mechanism to trigger a price review at a national level for regulated (price reference) markets.

Funding: EU4 Health and recovery and resilience facilities

- Grants may be used in combination with financing from the European Investment Bank, national promotional banks or other development and public financial institutions, as well as in combination with financing from private-sector financial institutions and public or private sector investors, including through public-public or public-private partnerships.

Procurement and security of supply

factsheet

- ☐ Problem Statement
- ☐ Optimization of the procurement process to ensure security of supply
- ☐ Example good practice
- ☐ Relevant documentation

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Procurement and security of supply

factsheet

Problem Statement

Since the 2009 financial crisis, European Member States have introduced policies to reduce medicine 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.

Optimization of the procurement process to ensure security of supply

- 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.

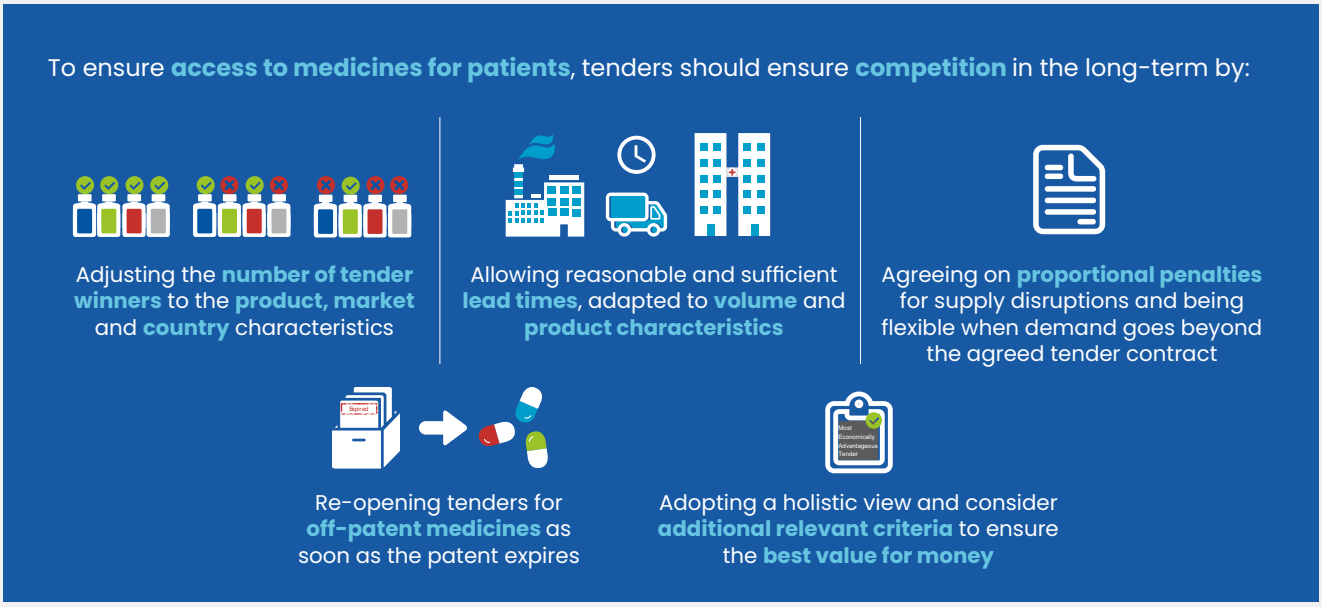
- Using selection criteria that consider other factors than price and ensure fair competition by implementing MEAT criteria.
  - These criteria should not put any access barriers in place for generic, biosimilar and value added medicines.
  - Procurement criteria should consider product-specific characteristics.
  - 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 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 needs to be 6 months between the award of a tender and the first delivery, ensuring sufficient lead time.

Relevant documentation

- https://www.medicinesforeurope.com/wp-content/uploads/2019/04/M-Best-procurement-practices-position-paper_final-version.pdf
- https://www.medicinesforeurope.com/wp-content/uploads/2020/08/31072020_procurement-principles-letter-final.pdf
- https://www.medicinesforeurope.com/wp-content/uploads/2018/05/Hospital_Tendering_Infographics_V.1.4_Final.pdf

Preventing shortages

factsheet

- ☐ Background
- ☐ Policy recommendations

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Preventing shortages

factsheet

Background

Shortages of medicines have been a concern in the EU for several years and have received increased attention during the COVID-19 pandemic. Shortages can compromise patient health and burden healthcare systems and healthcare professionals. Medicines shortages are increasingly reported for products that have been on the market for many years and are widely used. In a well functioning competitive market, generic medicines should be an opportunity to increase patient access and prevent medicines shortages through increased choice and availability of treatments. However, pharmaceutical policies that drive consolidation of multisource manufacturing undermines this benefit by reducing the number of marketing authoritisation holders or manufacturers that can supply medicines to patients.

Medicine shortages is a multi-factorial issue that can have **multiple root causes**:

Economic related issues

- The extreme pressure on prices due to cost containment measures such as price-only tendering, external reference pricing and payback mechanisms challenge the sustainability of our industry forcing the withdrawal of generic medicines from the market (or preventing the launch) and increasing the risk of medicines shortages.
- Pricing policies that are solely aimed at containing pharmaceutical expenditure rather than encouraging competition in a multisource setting.
- Tender practices: single-winner, price-only tenders that cause severe price erosion, reduce the number of suppliers in the market and poorly planned procedures (lead times, volume commitments) can create unnecessary disruptions.

Supply chain issues

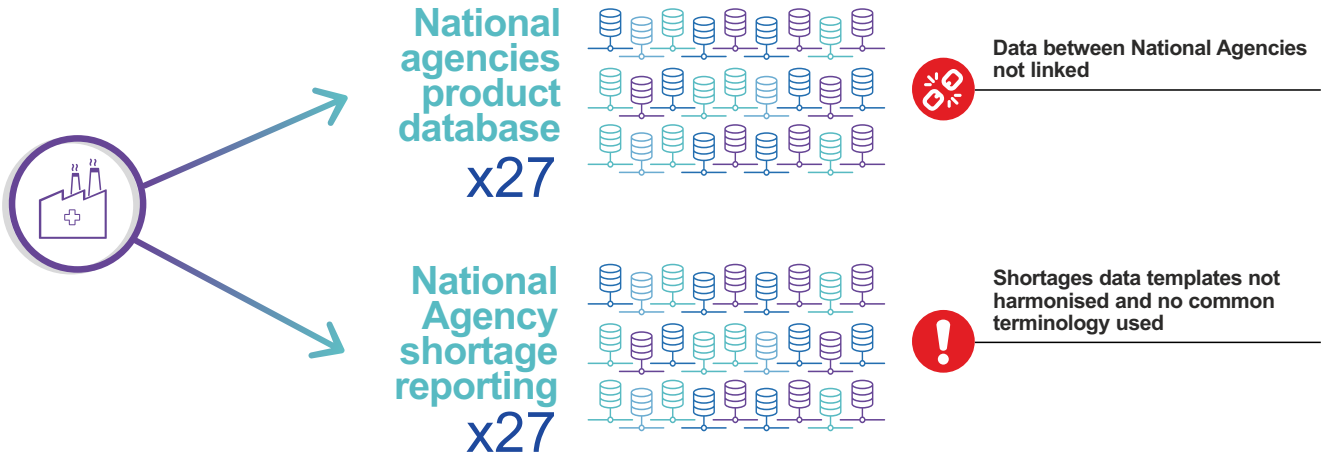
- Parallel trade: Parallel exports from lower income countries, often in Eastern Europe to wealthier countries in Western Europe can contribute to availability problems which undermine public health. Parallel trade will commonly target the reference product generating unexpected demand for the generic equivalent in the market.

Manufacturing and quality issues

- Consolidation of active pharmaceutical ingredients and raw material (API and excipient supply) production may reduce the number of suppliers on the market. EU pharmaceutical policy disincentivises investments in contingency measures such as multiple active API sources as this is not rewarded on the market although it adds materially to regulatory and production costs and challenges.
- Investments to comply with important and stringent regulatory/quality procedures are not rewarded
- Surges in demand in a crisis require industry to adjust production to meet the demand. There should be dialogue between industry and the Commission to tackle any legal or regulatory challenges to that scale-up.

The Commission launched a study to map the root causes of shortages and assess the legal framework. The study will inform the evaluation and revision of the current legislation. Prevention of shortages should be of great priority for our industry. An important lesson learnt from the COVID-19 outbreak was that a dialogue with industry and pragmatic regulatory flexibilities are crucial to prevent shortage occuring by allowing flexibilities on pack size and the introduction of electronic product information/e-leaflet.

MAH have the obligation to report potential shortages to national competent authorities via different portals which are hosted by the national agencies. This is resulting in multiple channels to submit similar data, but with differences in specific information to be provided depending on the different national requirments and due to these inconsistencies it finally is resulting in data quality issues and different interpretations by national agencies. The lack of harmonisation of a template for the data collection or use of master data leads to the impossibility of sharing information across National Competent Authorities and EMA.



During Covid-19 the i-SPOC system was created as additional reporting tool, resulting in a time-consuming manual process via Excel-based template and email exchange serving as the communication channel. By establishing the full implementation of SPOR by all stakeholders in all processes and all products and with the connection between existing systems (e.g. SPOR and EMVO) the national agencies would be in a position to better evaluate the impact on the supply chain (e.g. suppliers from specific regions/countries), evaluate availability of medicinal products within Europe (e.g. potentially tracking volume changes) and identify and signal shortages for critical products under the condition the definition of a shortage is amended toward the patient needs at national level. During Covid-19 it was clear that a defnition of a shortage should be around patient need and not as per current EMA defnition: 'A shortage of a medicinal product for human or veterinary use occurs when supply does not meet demand at a national level'. The current definition can artificially create shortages by stakeholders in the supply chain, hence the ban on parallel import during Covid-19. Via the creation of an early alert system to efficiently assess risk and identify mitigation mechanisms the majority of the potential shortages could be prevented or mitigated.

Policy recommendations

- 1) Definition of a shortage in relation to the patient is needed

- 2) Ensure market predictability:
  - A predictable and sustainable pricing and reimbursement environment will increase the number of manufacturers in the market guaranteeing that in case one of the manufacturers cannot supply other manufacturers in the market are able to supply the medicine
  - Prevent disproportionate sanctions that can increase the risk of medicine shortages or withdrawals
  - Revision and prevention of the application of short-term cost containment measures that discourage generic manufacturers from entering or staying on the market

- 3) Improve regulatory efficiency to reduce administrative and cost burden of keeping medicines in the market by Amending the EU Variations Regulation to ensure quick reaction is possible by allowing regulatory flexibilities
  - Implement flat fee structure for variations
  - Optimise the use of Centralised and Decentralised procedures for generic medicines
  - Increase flexibility to accept different pack sizes or multi-country packs to address market needs
  - Increase use of telematics tool (e.g. FMD, ISO-IDMP, Art. 57, etc.) for communication of changes currently requiring variation submission in large portfolios
  - Lower fees/costs for older molecules that still serve a healthcare need
  - Improvement management of API variations as this is critical in a shortage risk situation.

- 4) Manage available market stock information with non-coercive systems

- 5) Address negative healthcare impacts of parallel trade

- 6) (Regulatory) flexibility to mitigate shortages
  - Flexibility to accept different pack sizes at national level based on Marketing Authorization
  - Flexibility to accept multilingual packages (e.g. eLeaflet as a solution)
  - Efficient Repeat Use Procedure
  - Incentives for medically essential low price products

- 7) Harmonized shortages reporting format and content at national competent authority: develop streamlined electronic monitoring and reporting system(s) that establish a two-way communication between the Agency and the marketing authorisation holders

- 8) Need for a common repository for all medicinal products via SPOR data management supported by a Target Operating Model (TOM) to ensure data-quality and faster decision making in the EU Regulatory Network.

- 9) Strong legal framework to ensure unified implementation of digital systems and solutions by building appropriate telematics infrastructure to achieve an EU harmonized mechanism to monitor the entire value chain through interconnection of SPOR and EMVO-NMVs.

WTO Supply Chain Agreement

factsheet

- ☐ Background
- ☐ Recommendations

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WTO Supply Chain Agreement

factsheet

Background

The pharmaceutical sector supply chain is complex and global. The covid-19 crisis has shown the importance of a well-functioning global medicine supply chains and the industry has undertaken a sustained global effort to ensure continued access to medicines for patients throughout the crisis.

As underlined in the EU Pharmaceutical Strategy published on 25 November 2020, the Commission intention is to initiate a structured dialogue with the main actors of the pharmaceutical sector and it is willing also to "work directly with WTO members on an initiative that would aim to facilitate trade in healthcare products and contribute to an effective response to a health emergency. Such initiative would help to strengthen the resilience and robustness of supply chains in the EU and in all other WTO partners." Moreover, the Commission is also ready to: "Promote WTO-based actions to increase the resilience in global supply chains in essential goods."

Recommendations

Establishing a well-coordinated dialogue between the industry and WTO partners would be beneficial as often Institutions are not up to date about the complexity of manufacturing supply chains. In addition, thanks to a structured exchange it should be easier to identify a potential lack of diversity of the certain region to the supply of essential medicines and Active Pharmaceutical Ingredients (APIs). Given the important health and trade dimensions of this exercise, the WTO and the WHO should cooperate on this initiative to promote global solidarity and international cooperation. However, by undertaking this kind of initiatives it is important to bear in mind the following key elements:

- Understanding supply chains: an important first step of any agreement should be to understand the nature of pharmaceutical manufacturing supply chains across different segments: solid oral dose production (pills/capsules), sterile/aseptic production (injectable hospital medicines) and more complex medicine forms (biologics, vaccines, drug-device combinations). **Regulatory Convergence and Good Reliance Practices in Regulatory Decision-making for Medicinal Products:**
  - Foster regulatory international collaboration which plays a key role in strengthening the efficiency and effectiveness of regulatory authority bodies
  - Reduce or eliminate regulatory and other technical barriers
  - Promote the use of good regulatory practices and streamlined regulatory review
  - Eliminate duplicate actions and other barriers to reduce the time for approvals of both facilities and pharmaceutical products
  - Build trust and expand transparency, information-sharing and cooperation with participating governments and authorities
  - Encourage the negotiation of bilateral or plurilateral Mutual Recognition Agreements (MRAs) for Good Manufacturing Practices (GMPs)
  - Promote stronger regulatory cooperation in FTA negotiations
- **Tariffs:** eliminate tariffs on imports of pharmaceutical products and APIs.
- **Prevent protectionist measures:** The threat or use of export restrictions in various guises during a health crisis exacerbates panic in pharmaceutical production and markets and undermines the global solidarity that is often needed to overcome a global crisis. This was clearly the case for therapeutics and vaccines during the Covid-19 pandemic. While it may be necessary for governments to assist manufacturers in scaling up production and to ensure appropriate allocation to patients (instead of hoarding) in a crisis, there should be a clear proportion in interventions that re-direct production to serve home markets rather than global markets. Conversely, there should be counterweights to attempts by wealthier nations to hoard available supplies (wherever they are produced) at the direct expense of patients in less wealthy nations.

EU-US GPA and Single Development

factsheet

- ☐ Problem Statement
- ☐ Policy recommendations

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EU-US GPA and Single Development

factsheet

Problem Statement

Europe and the United States have a longstanding cooperative relationship with pharmaceuticals. Among other things, the two countries are part of the WTO Government Procurement Agreement (GPA), which facilitates reciprocal access to markets. Last August the US published an executive order which threatened the application of the WTO GPA agreement. On 21 April 2021, the US Government amended its policy to maintain its commitments under the WTO GPA agreement.

In addition, EU and US regulatory authorities cooperate through a Mutual Recognition Agreement on GMP inspections and have aligned a single development programme for biosimilar medicines with aligned Biosimilar Guideline/Guidance. Based on this positive experience, we strongly believe that regulatory cooperation should be extended to a single development for complex generic /hybrid medicines.

Single development is a cornerstone of streamlined product development. It is essential for competition, especially for complex products. Conducting multiple clinical development programs for the purpose of comparison with local reference products is not only time and resource-consuming, but also unethical, as it involves superfluous experimenting in human subjects with no added benefit. Overall, this results in higher resource investment, extended timelines and delays in broader patient access to comply with these regional requirements. Single development could be a stepwise process: first, there could be alignment on the use of reference product from either market; second, there could be alignment on regulatory guidelines/guidances specific to different product types – notably for scientific and clinical requirements.

Policy recommendations

Keep in place WTO GPA agreement

- Promote strong international collaboration
- Keep mutual trust in investments
- Do not disadvantage each or other country in local tenders
- Prevent protectionism

Go further with single development programmes

- Advance single development for orphan medicines
- Stimulate single global development of generic and complex generic medicines
- Develop methodologies for the acceptance of foreign comparator products

Crisis preparedness

Supply chain security and resilience

factsheet

- ☐ Problem Statement
- ☐ Policy recommendations

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Supply chain security and resilience

factsheet

Problem Statement

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.

European Medicines Agency (EMA) and shortages reporting

factsheet

- ☐ Background
- ☐ Current medicines shortages notification system
- ☐ Need to implement a robust harmonised digital shortage reporting system
- ☐ Policy recommendations

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European Medicines Agency (EMA) and shortages reporting

factsheet

Background

Shortages of medicines have been a serious concern in the EU for several years and have intensified during the COVID-19 pandemic due to sudden, unpredictably large demand surges. Shortages can compromise patient health and burden healthcare systems and healthcare professionals. They can lead to under-treatment and prolonged hospital stays. Shortages are increasingly reported for products that have been on the market for many years and are widely used which may reflect the increasing consolidation of the generic medicine market. The root causes are multifactorial: economic causes, industrial factors, regulatory burden, a sudden surge in demand[1].

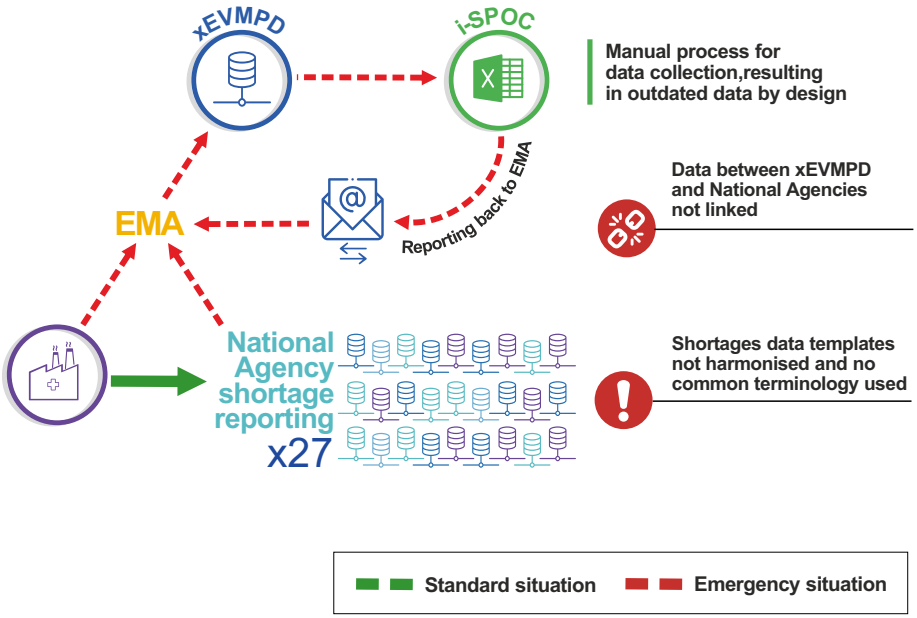
Current medicines shortages notification system

Marketing Authorisation Holders (MAHs) have the obligation to report potential shortages to National Competent Authorities (NCAs) via different portals. Due to a lack of harmonisation, companies submit different data depending on national requirements to multiple channels. The lack of a harmonised template for the data collection or use of master data makes it impossible to share information across National Competent Authorities and EMA. Consequently, the inconsistency of data and the different interpretations by national agencies make shortage reporting data irrelevant for crisis situations where multiple EU countries may be impacted.

During COVID-19, the EMA attempted to solve this issue by creating the i-SPOC system as an additional reporting tool, resulting in a time-consuming manual process via Excel-based template and email exchange serving as the communication channel.

(1) Infographic: medicines shortages: causes and recommendations explained

- Multiple channels between EU and National Regulatory authorities:
  - not interconnected
  - not interoperable
  - not harmonized
  - non identifiable
- **27 different data sets and interpretations** based on the national requirements
- During Covid-19 an additional system (i-SPOC) has been created with excel-based manual process



Impossible for regulators to exchange data on products that are:

- not harmonised
- not comparable or identifiable across countries
- in high risk of error in data population

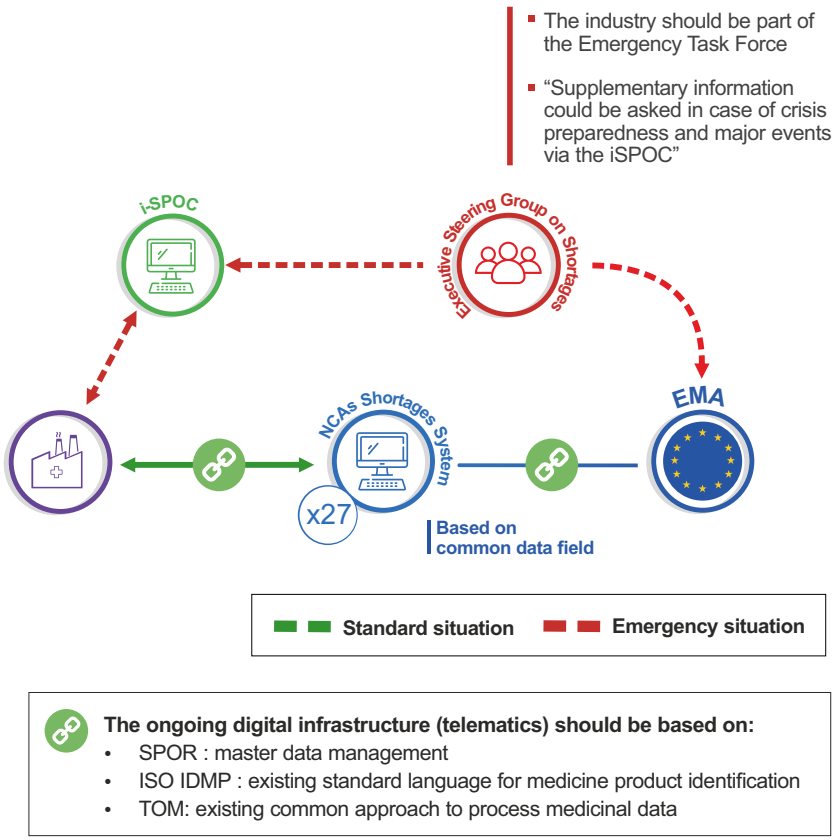
Need to implement a robust harmonised digital shortage reporting system

By establishing the full implementation of the ongoing master data management (SPOR) by all stakeholders for all processes and all products and through the connection of existing data systems (e.g. SPOR and EMVO) national and EU agencies would have access to better data to evaluate the impact on of major events on the supply chain (e.g. suppliers from specific regions/countries), evaluate the availability of medicinal products within Europe (e.g. potentially tracking volume changes) and identify and signal shortages for critical products. This would require a patient-needs definition of a shortage at the national level and at the European level[2] , to avoid the creation of artificial shortages (driven by hoarding or speculation in the market).

Indeed, COVID-19 underlined the critical importance of defining a shortage based on patient need as markets were quickly overrun with panic. This explains why most member states implemented strict oversight and control over pharmaceutical distribution (wholesalers, parallel traders, hospitals) during COVID-19. Based on a clear patient definition and by creating a more effective data collection system to efficiently assess risk and identify mitigation measures, many potential shortages could be prevented or mitigated.

(2) The current EMA definition does not integrate patient need: 'A shortage of a medicinal product for human or veterinary use occurs when supply does not meet demand at a national level.'

- The digital harmonised shortage reporting system would be implemented along with **existing digital infrastructure** and **ongoing digital projects**
- The shortage is notified by the Market authorisation holder (MAH) to all the relevant National Competent Authorities (NCAs) by **sharing data in harmonised digital format** to the interlinked NCA shortages reporting systems
- In case of large scale medicine shortage or pandemic, **the data can freely flow** between NCAs and EMA thanks to **interoperability of the digital systems**
- Opening **two-way communication** between EMA and MAHs to directly address the shortage and solve it



This system would enable regulators to respond promptly and adequately to any emergent large-scale crisis

In case of a public health emergency and the escalation of the shortage to the EU Executive Steering Group on Shortages and Safety of Medicinal Products at EMA, the relevant data submitted by MAHs would be captured into SPOR. Via the integration of SPOR and EMVO data and harmonizing shortages reporting on the EU level, NCAs would have access to relevant information about the availability of certain products in markets where the situation is acute. The harmonised and unique entry point of data by MAH will prevent duplication and confusion, this will also allow the Executive Steering Group on Shortages and Safety of Medicinal Products at EMA to:

- Evaluate the impact on the supply chain across all EU countries (e.g. suppliers from specific countries/regions)
- Evaluate the availability of medicinal products with all EU countries
- Identify and signal shortages for critical products for specific countries (based on active substance, indication)
- Create an early warning system to efficiently assess and identify mitigation mechanisms avoiding patient impact and EU wide shortages.

As emerged during the COVID-19 outbreak, the industry is an essential actor for medicine shortages response. Therefore, single points of contact from industry (iSPOC) should support the work of this steering group in case of shortage event, by enabling to rapidly provide input to questions related to production capacities and bottlenecks. There should also be a clear framework for interaction between the Commission and industry to take appropriate legal and regulatory measures to mitigate a shortage. To avoid reporting duplications requirement on product data, the EMA would be already in possession of all necessary information already submitted by MAH towards NCA via the harmonized NCA shortages system.

Policy recommendations

- Definition of a shortage based on patient need instead of markets.
- Build on the existing digital regulatory infrastructure and ongoing projects on data management - a common repository for all medicinal products via SPOR data management supported by a Target Operating Model (TOM)
- NCA shortages reporting system should be based on common data fields at the national level - harmonized shortages reporting format and content provided by the Market authorisation holders to all Member States.
- A strong legal framework to ensure unified implementation of interoperable digital systems between all EU NCAs as well as the EMA to achieve an EU centralised mechanism through the interconnection of SPOR and EMVO-NMVOs.
- The Medicines Steering Group should be supported in its work by a working party comprised of single points of contact related to shortages from industry (iSPOC) and involving iSPOCs in the consultation phase to determine the list of critical products and the determination of solutions to the public health emergency. At the same time, the Steering Group should maintain two-way communication with the industry throughout the public health emergency.
- Medicines Steering Group to extract relevant information from the product and shortage related data as submitted by MAH towards NCA via SPOR/NMVO and not to lead to double reporting of similar data via iSPOC, only supplementary information would be requested by EMA to industry via iSPOC system.
- In crisis situations, a clear legal framework should be established by the Commission to provide appropriate competition law and regulatory law guidance on actions to mitigate a shortage.

Joint procurement

factsheet

- ☐ Problem Statement
- ☐ COVID-19: Joint procurement of ICU medicines
- ☐ Procurement principles for generic medicines
- ☐ Relevant documentation

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Joint procurement

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Problem Statement

Joint procurement is not a suitable method to procure multi-source generic medicines, as it does not provide additional value to patients, healthcare professionals or payers. The application of joint procurement to generic medicines presents important challenges that defeat any perceived advantage of countries pooling resources to procure multi-source medicines.

Whether under the European Commission's Joint Procurement Agreement (JPA), or on a multi-lateral basis, cross-border procurement of generic medicines has many shortcomings, from which we highlight:

- Regulatory: Off-patent products usually have different national licences and different presentations and names.
- Legal: The legal frameworks for public and private contract laws are of national scope.
- Intellectual Property: Patent or trademark landscapes differ nationally.
- Healthcare system governance: Heterogeneity of healthcare systems organisation.
- Supply chain: Likelihood of driving market consolidation and increasing shortages risk.

COVID-19: Joint procurement of ICU medicines

On 17 June 2020, the European Commission and participating countries launched a "Call for tenders SANTE/2020/C3/29 for the supply of medicinal products used for intensive care patients subject to the novel coronavirus (COVID-19) disease" without prior industry consultation and proper definition of the purpose and rules of the procedure, contravening the spirit of the EU's own procurement directive. The European Commission shared the call for tenders with selected industry partners with a remarkably short deadline to present bids (initially 9 working days, later extended to 24 days due to lack of clarity and many technical questions being raised), with the selection process started in early July. It took,

however, several months for the decision to be made on the suppliers that presented the awarded offers. The decision was then followed by bilateral contract signature with participating countries – one per each tender lot and country – taking the timeline up until early December. This meant that the process took close to 6 months to secure the urgent supply of essential ICU medicines. Overall, the dialogue with organising entities was limited, giving rise to a high level of uncertainty, and creating difficulties to solve issues in the process.

Procurement principles for generic medicines

- **Minor adjustments to existing procurement frameworks are better suited for securing the supply of generic medicines due to the complexities of joint procurement:**
  - Guaranteeing that the procurement processes reopen after the entry of the first multisource medicine to ensure a competitive and predictable supply to patients.
  - Adjusting the number of procurement winners according to the market, product and country characteristics.
  - Using selection criteria that consider other factors than price and ensure fair competition by implementing MEAT criteria. We urge the Commission to support member states in the implementation of MEAT criteria, as this would contribute to ensure security of supply and manufacturing resilience in Europe.
  - Preventing disproportionate penalties to encourage a sustainable supply of medicines to patients.
  - Providing accurate demand estimates with clear volume commitments in tenders.
  - Using sufficiently long lead times that guarantee a predictable supply of medicines to patients.

- **If the European Commission and signatory countries of the Joint Procurement Agreement insist on utilizing the mechanism to address cross-border health threats:**
  - The scope for joint procurement shall continue to be exclusively in the context of cross-border health crisis and only to guarantee stability in an unpredictable environment.
  - The call for tenders should be transparent, open and communicated to all possible suppliers.
  - The procurement must follow the rules and principles in the Public Procurement Directive of the European Commission.
  - The procurement process, criteria, specifications and formalities must be transparent and workable.
  - A preliminary consultation phase involving potential participating manufacturers should take place to ensure issues with the procedure are addressed.

- The European Commission and participating countries ensure clear volume commitments irrespective of the selected supply modality.
- The participating countries need to commit not to procure the same medicines via other means and must honor pre-existing supply contracts with manufacturers.
- Joint procurement lead times should be aligned with manufacturers lead times.
- National authorities should apply certain regulatory flexibilities.
- Award criteria beyond price should be defined to ensure the joint procurement mechanism provides a suitable framework to procure medicines during a cross-border health threats.

Relevant documentation

- https://www.medicinesforeurope.com/wp-content/uploads/2020/08/31072020_procurement-principles-letter-final.pdf
- https://www.medicinesforeurope.com/wp-content/uploads/2019/04/M-Best-procurement-practices-position-paper_final-version.pdf

European strategic stockpile

factsheet

- ☐ Problem Statement
- ☐ Policy recommendations
- ☐ Examples

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European strategic stockpile

factsheet

Problem Statement

It is good practice for manufacturers, hospitals and the military to ensure good inventory levels to buffer demand fluctuations for medicines. However, during Covid-19, many Member States introduced counterproductive stockpiling measures that disrupted industry supply chains, threatened patient access and undermined EU solidarity. Disproportionate stockpiling requirements post-Covid-19 at national and/or EU level would further increase market consolidation and supply risks. Pharmaceutical companies already implement internal inventory policies (stocking critical materials needed to produce for demand variations) that covers API, bulk and finished products as part of their efforts to increase security of supply. Ill-conceived stockpiling medicines will generate the waste and destruction of medicines, which should be avoided as much as possible. Therefore, Medicines for Europe supports Commission policies to tackle national hoarding and other disproportionate restrictions to the free movement of goods and welcomes the structured dialogue to design EU-wide policies for resilient supply chains.

Medicines for Europe recognises the positive role that emergency reserves can play in crisis situations provided they are proportionate, based on industry recommendations for good stock management, aligned with the principle of EU solidarity and economically sustainable. However, EU stockpiling is challenging for multisource medicines because of licenses and different languages. Additionally, an EU stockpile is not suitable to address national shortages.

Policy recommendations

Regarding a possible future EU strategic reserve, we encourage the Commission to carefully design this policy together with medicine manufacturers.

Recommendations for fair, sustainable and practical stockpiling:

- European Strategic stockpiling should be **targeted** (based on a risk assessment to determine medicines or therapeutic focus areas) and **proportionate** (the size of the stockpiling should be defined per product to avoid overstocking waste).

- A stockpiling method should be adopted to absorb unforeseen market surges for a clear list of **essential medicines** for specific health emergency risks. Any European reserve should avoid distorting the normal functioning and sustainability of the Internal Market and prevent the wasteful destruction of unused medicines.

- **Facilitate the movement of stock** from one country to another within EU, especially for medicines approved under national procedures (referred to as DCP or MRP medicines – around 90% of medicine registrations in Europe) and avoiding expensive and time-consuming re-packaging.
  - Flexibility to accept eLeaflets and multilingual packages.
  - Flexibility to accept different pack sizes at national level based on Marketing Authorization.

- **Reduce the regulatory complexity** of managing a reserve of products which may have national licences (MRP/DCP) and labelling requirements.

- Establish clear **responsibility for the costs** associated with acquisition, distribution, storage and maintenance of these medicines.

- **Avoid the wasteful destruction** of medicines.

- Establish a **transparent process** to purchase these medicines, identifying who will place orders, purchase the goods, hold the reserve, call off deliveries and under which conditions these medicines can be used.

- Any European reserve should avoid distorting the normal functioning and sustainability of the Internal Market.

Examples

- Evidence from **Finland**, which has a stockpiling requirement for certain medicines, shows a decrease in the number of tender bidders inversely correlated with the months of obligation for stockpiling, leading to the consolidation of manufacturers and therefore contradicting the security objective of stockpiling.

- **UK strategic reserve**: From 2009 to 2019 the UK Government held a stockpile of approximately 400 essential medicines in the Essential Medicines Buffer Stock ("EMBS"). The list of medicines was drawn up by the DHSE, in conjunction with the NHS, and was designed to be key to prevent death or admission to hospital.
  - Awarded companies supplied stocks of medicines for one or more of approximately 400 lots of the essential/required medicines, which were purchased by the Department of Health.
  - The awarded company was required to store the stocks of Department of Health-owned medicines in the UK over the duration of the tender (4 or 5 years).
  - The awarded company was required to maintain a minimum shelf life for the relevant Department of Health-owned stock by releasing stock into the supply chain and replenishing with new stock.
  - In the event of a supply shortage caused by a pandemic or other emergency, the company was required to release stocks into the supply chain for supply to UK customers and for delivery to the NHS, with the object of lessening any shortages of such medicines, and the contractor was required to purchase such stocks from the Department of Health for the purpose of such release.

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