EFPIA THEMATIC ANALYSIS ON CUMULATIVE LEGISLATIVE IMPACTS

CONSIDERATIONS ON THE CUMULATIVE IMPACT OF NEW AND UPCOMING EUROPEAN PHARMA, ENVIRONMENTAL, CHEMICAL, FOOD AND ANIMAL LEGISLATION ON THE HEALTHCARE SECTOR – PATIENTS AND THE PHARMACEUTICAL INDUSTRY

efpia

TABLE OF CONTENTS

EXECUTIVE SUMMARY

The pharmaceutical industry supports the EU's climate and environmental ambitions, while at the same time emphasizing the need for science-based, risk-sensitive approaches to avoid unintended disruptions, especially to medicine supply and innovation. Many new regulations will soon take effect – at the same time - creating pressure on industry and regulators. Concerns include administrative overload, potential conflicts between EU and global standards, and the unpredictability of cumulative regulatory impacts.

The regulatory inconsistencies within the EU and globally, as well as complex compliance requirements, may erode Europe's pharmaceutical competitiveness. Divergent EU standards could deter investment, especially in R&D and innovation. Regulatory changes risk disrupting the supply chain and patient access to medicines if certain chemicals or processes are restricted without suitable alternatives. This could lead to shortages of essential medicines. Furthermore, new mandates for environmental reporting may add significant costs, resource demands, and intellectual property risks, potentially diverting resources from research and innovation.

Our industry is committed to taking decisive actions to reduce our environmental impacts across the value chain[1]. Between 2020 and 2022, our members were able to cut by 10% scope 1 and scope 2 CO_2 emissions - equivalent to 1.5 million tons of CO_2 and was achieved despite a production increase. Furthermore, 95% of EFPIA companies engage with suppliers on climate action targets. Benchmarked against high-impact industry sectors (such as chemicals).[2] EFPIA members are further committed to the science-based phase-in of methods to replace the use of animals for scientific purposes and the deletion of animal tests which are obsolete or redundant.

This report gives an overview of how accumulation and combinations of legal requirements driven by pharmaceutical, environment, chemical, food and animal will affect the healthcare sector, including the pharmaceutical industry, regulators and patients. It identifies key legislative changes, timelines, and cumulative impacts to guide industry preparedness for future developments. By mapping out the pace of these changes and illustrating their impact across the value chain, the report offers a foundation for developing balanced policy recommendations. **The cumulative demands create a substantial regulatory and resource burden, impacting innovation, competitiveness, and patient access.** It will require a dedicated discussion of the healthcare sector's unique requirements and constraints to find solutions that prioritise patient needs, support industry innovation, and align with sustainability goals.

EFPIA urges alignment and coordination of policies impacting life sciences. We advocate for close collaboration between regulators and the industry, careful assessment of cumulative impacts, and sector-specific risk assessments. Such assessments should recognise that active substances in medicines are supposed to have a persistent or therapeutic effect. We further call for ongoing impact assessments, timely guidance, and enhanced communication among EU regulatory bodies and agencies like the EMA to manage legislative effects while maintaining patient access to essential medicines.

We suggest an EU Office for Life Sciences to monitor outcomes and ensure coherent policy development.

[1] https://www.efpia.eu/news-events/the-efpia-view/statements-press-releases/clear-steps-toward-a-greener-future-pharmaceutical-sector-s-environmental-sustainability-statement/

[2] https://www.efpia.eu/media/gtbncsjc/survey.pdf

2. BACKGROUND & OUTCOMES

Driven by the European Green Deal launched by the European Commission in December 2019, and other contemporaneous environmental policy initiatives, the European pharmaceutical industry is navigating a period of substantial legislative change. The Green Deal aims to achieve climate neutrality within the EU by 2050, focusing on areas such as climate action, zero pollution, sustainable chemicals, and a circular economy whilst ensuring economic growth. Industry supports the overall objective behind those policies, as they address legitimate environmental concerns. Sustainability actions are not new to the pharmaceutical industry, who always encourages appropriate use of evidence, science and risk-based approaches to environmental challenges and continually undertakes initiatives to promote greater environmental responsibility.

As many of the European Green Deal and related pieces of legislation enter their implementation phase, the European Commission has defined their strategic agenda for 2024 – 2029[3]. As well as a successful 'green transition' via the Green Deal, this also includes priorities for a prosperous and competitive Europe whereby they propose to bolster the EU's competitiveness. Europe's competitiveness was also the subject of a recent report by Mario Draghi[4], which identified the "complex EU regulatory framework" as a cause of the EU's "emerging competitive gap" within the pharmaceutical sector. However, Europe's pharmaceutical sector accounts for 5% of value added to the economy from all manufacturing, and plays a role in pharmaceutical innovation, with 77% of Active Pharmaceutical Ingredients (APIs) used within innovative medicines being sourced from the EU[5].

THE GREEN DEAL AIMS TO ACHIEVE CLIMATE NEUTRALITY WITHIN THE EU BY 2050, FOCUSING ON KEY AREAS SUCH AS CLIMATE ACTION, ZERO POLLUTION, SUSTAINABLE CHEMICALS, AND A CIRCULAR ECONOMY WHILST ENSURING ECONOMIC GROWTH.

[3] https://european-union.europa.eu/priorities-and-actions/eu-priorities/european-union-priorities-2024-2029_en

[4] *The Future of European Competitiveness, Part B | In-depth analysis and recommendations, Mario Draghi*, 9 Sept 2024

[5] *The Future of European Competitiveness, Part B | In-depth analysis and recommendations, Mario Draghi*, 9 Sept 2024

With the number and diversity of regulatory changes coming within a short period of time there are concerns regarding the potential for unintended consequences, particularly those that could disrupt the supply of medicines, ultimately impacting patients.

Many of these legislations, whilst specifically targeting chemicals, food or the environment, will also impact the pharmaceutical industry and healthcare systems, with some integrating medicines within their scope for the first time. This presents potential challenges to business continuity and the license to operate, particularly concerning decisions to restrict certain substances and technologies.

EFPIA and its members "recognise the urgent need to address climate change... given the profound impact on both human health and nature"[6] and "are committed to taking decisive actions to reduce environmental impacts across the value chain and contribute to building resilient and sustainable health system."[7]

While **environmental regulations aim to enhance sustainability, they may lead to unintended consequences for medicine availability, regulatory complexity, resource allocation, and competitiveness** within the EU pharmaceutical sector. By not considering those consequence when discussing environmental and chemical legislations, patients' access to innovative medicines will be jeopardized and Europe's focus on strategic autonomy and competitiveness will be undermined.

This report provides an analysis of how new and revised EU legislation will impact the pharmaceutical industry and patients, serving as a foundation for understanding industry and regulators challenges. The scope of inputs for this analysis included a non-exhaustive overview of recent new or revised environmental, chemical, food and animal legislations[8] for which EFPIA and its members have engaged in, referring to public or EFPIA position and briefing documents based upon or in response to these legislations, and information sessions with industry Subject Matter Experts (SMEs) from EFPIA's network.

Outcomes of the analysis

The European Green Deal presents the pharmaceutical industry with opportunities to follow through on their environment and sustainability goals. However, it may negatively influence the competitiveness of the EU and counter the opportunities for a more sustainable future to ensure continued access to safe and efficacious medicines for patients.

A fragmented legislative environment is leading to contradictory and incoherent policies that negatively affect life science

[6] https://www.efpia.eu/about-medicines/development-of-medicines/regulations-safety-supply/environment-health-safety-and-sustainability/

[7] Clear Steps Toward a Greener Future - Pharmaceutical Sector's Environmental Sustainability Statement (efpia.eu)

[8] (EU Taxonomy for sustainable activities (EUT), Corporate Sustainability Reporting Directive (CSRD), Corporate Sustainability Due Diligence Directive (CS3D), Carbon Border Adjustment Mechanism (CBAM), Industrial Emissions Directive (IED), Packaging and Packaging Waste Regulation (PPWR), UN Treaty on Plastic Pollution (UNTPP), General Pharmaceutical Legislation (GPL), Roadmap to phase out animal testing (RAW), One Substance, One Assessment (OSOA), Essential Use Concept communication (EUC), Regulation on the registration, evaluation, authorisation and restriction of chemicals (REACH), Titanium Dioxide (TiO_2), Per- and polyfluoroalkyl substances (PFAS), Talc (Talc), D4, D5, D6 (D4, D5, D6), Bisphenol A (Bisphenol A), PVC (PVC), Nitrosamines (Nitrosamines), F-gas Regulation (F-gas), Synthetic polymer microparticles (formally microplastics) (SPM), Classification, labelling, and packaging of chemicals (CLP): Urban Wastewater Treatment Directive (UWWTD), ground, surface Water Framework Directive (WFD)

companies operating in Europe. The life sciences sector is currently navigating a dynamic regulatory environment, with responsibilities split across multiple Commission services and European and national regulators. Possible inconsistencies across legislations' potential impacts were identified during this analysis; related to impacts of chemical, food or environmental legislation on the life sciences sector.

The imminent impacts of the legislations on the healthcare system, affecting both patients and the pharmaceutical industry, are due to these contributing factors:

1) THE PACE OF CHANGE

Many of the legislations covered in this analysis are expected to enter into force before or by 2027, with specific requirements becoming applicable over the next decade. Many of the regulations will result in regulatory filings; and the rapid pace of change will result in large spikes of regulatory activity impacting both industry and regulators. This creates a two-fold concern.

- The first is, the excessive number of new or updated legislations coming into force in a short period, some covering specific focus on pharmaceuticals for the first time;
- The second is, the roll-out of these legislative changes is over a 10-year period following entry into force, including development of various delegated and implementing acts, meaning that the impacts will be changing over that predicted decade of rollout and remain unpredictable.

The short timeframe during which many of the legislations are expected to enter into force, and the lack of clarity regarding implementation timelines creates uncertainty for businesses. Additional resources will be required to plan for and implement changes to comply with these legislations. To further complicate the matter, there are many identified cases where industry will be required to replace with alternative substances within dedicated timelines, where they don't yet exist with the uncertainty if there will be alternatives in the future.

2) GOVERNANCE

As responsibility does not lie with one authority but multiple driven by different imperatives, this creates uncertainties as to which rules take precedence and makes engagement and scientific dialogue very complicated. This creates a perception of complexity that is complicated for EU institutions themselves and that is completely opaque for the innovators.

3) INCONSISTENCIES BETWEEN NEW/ PROPOSED LEGISLATIONS

The EU's competitiveness may be impacted by the potential divergence of requirements across different legislations in the EU, or furthermore when compared to existing globally accepted standards.

The analysis identified inconsistencies between the set of legislations examined that would need to be addressed. These are categorised into three inconsistency types:

- Amongst the new/proposed EU legislations themselves;
- Between new/proposed EU legislations and other global (outside-EU) legislations;
- Of the specified intent of a given new/ proposed EU legislation compared to its potential impacts (including potential for unintended consequences).
- Amongst national legislations coming from transposition of EU legislation

These inconsistencies, where present, lead to increased administrative burden and resource needs on companies because of the additional resources to analyse the impacts to their portfolio to minimise the impacts on their ability to provide medicines in Europe. Regulators would also be further burdened, with resource constraints. In addition, the potential divergence of requirements in the EU compared to existing globally accepted standards may impact Europe's competitiveness.

4) CUMULATIVE IMPACTS

Several potential cumulative impacts of these legislative changes were identified and investigated, broadly grouped into four impact themes:

Patient Access: The legislative changes may have an impact on patient access to medicines, for example due to product withdrawals or supply chain disruption. Product withdrawals may arise from, for example, revocation of marketing authorisations due to unfavourable environmental risk assessments, or the banning/restriction of chemicals used in the R&D or manufacture of medicines. Additional requirements could disrupt supply chains and divert resources, potentially exacerbating shortages. Patient access could also be impacted if adherence is reduced due to possible changes in the appearance of medicines due to required reformulation or packaging changes.

Innovation & Competitiveness: Europe's competitiveness in pharmaceutical R&D and manufacturing could be impacted by complexity of new legislations leading companies to divert investment from Europe, or tighter timelines and costs to comply with legislative changes and potential divergence between new/proposed EU legislation and the global regulatory landscape.

60–70% OF ORAL DOSAGE FORM MEDICINES MAY BE DISCONTINUED OR IN SHORT SUPPLY IF TITANIUM DIOXIDE (TIO_2) IS BANNED IN MEDICINES[9], AS THERE IS CURRENTLY NO SUITABLE ALTERNATIVE NOR SCIENTIFIC JUSTIFICATION TO BAN.

UNCERTAINTY OF CERTAIN MEDICINES CONTINUITY AS DECISIONS BY REGULATORS TO WITHDRAW, REFUSE OR REVOKE MEDICINES MAY BE BASED ON AN IDENTIFIED ENVIRONMENTAL RISK ALONE.

Companies will face a difficult decision to focus resources on making changes to older medicine formulations and manufacturing processes or to invest in newer greener medicines. One path will lead to reduced patient access to existing medicines, the other path will lead to a reduction in development of innovative new medicines. Additionally, the potential for products to appear less sustainable due to proposed sustainability criteria may reduce the attractiveness of the industry for investment, as Environmental, Social and Governance (ESG) continues to play a more significant role in investment decisions.[10] This could reduce EU competitiveness, drive up costs, and limit innovation within Europe in the absence of reward or incentives for continued green transition investments by companies. Additionally, the requirement to meet all

[9] *European Regulatory Landscape: Impact of Access and Availability of Medicines*, EFPIA, 23 May 2024

[10] *Beyond Financial Performance: How ESG Factors Impact Companies and Investments*, Iris Carbon, 3 May 2023

PATIENT IMPACT ANALYSIS SHOWED THAT OVER 600 ESSENTIAL MEDICINES WOULD BE IMPACTED BY A PER- AND POLYFLUOROALKYL SUBSTANCE (PFAS) RESTRICTION[12], AS PFASS ARE A KEY COMPONENT OF APIS AND RAW MATERIALS AND IN MANUFACTURING, DELIVERY DEVICES, ANALYTICAL EQUIPMENT AND PACKAGING.

the proposed Technical Screening Criteria in order to define a product as 'sustainable' creates a risk that products may not appear as sustainable, whereas the EU Taxonomy regulation will only provide a limited presentation of the commitments to environmental sustainability from innovative pharmaceutical companies. This may reduce the attractiveness of the industry for investment, as ESG factors are becoming more significant in investment decision[11].

DATA AND IP CONFIDENTIALITY CONCERNS – MAINTAINING COMPLIANCE WITH REPORTING REQUIREMENTS RAISES CONCERNS. THE POTENTIAL RELEASE OF COMMERCIALLY SENSITIVE DATA, WILL IMPACT. THE QUESTION REMAINS WHO TAKES RESPONSIBILITY WHEN THERE IS A BREACH.

EU TAXONOMY REQUIREMENTS DO NOT REFLECT THE PHARMACEUTICAL INDUSTRY'S SUSTAINABLE PRACTICES WHEN EUROPE'S MEDICINES SECTOR IS MAKING REAL PROGRESS ON SUSTAINABILITY.

Environment & Sustainability: Uncertainty of medicines continuity is based on environmental impacts. There are concerns over Imminent withdrawal or refusal of medicines which do not comply with environmental standards or bans of chemicals over concerns over environmental impacts. Compliance with environmental reporting mandates may affect intellectual property protection, confidentiality, and data security. Long timelines for obtaining approvals for restricted substances could add business uncertainties, while reporting requirements might also demand significant resources, and may divert resources from R&D, innovation and investment in manufacturing. New Extended Producer Responsibility (EPR) fees lead to uncertainty of the cost implications may raise medicine prices and impact availability, while for example, not significantly reducing water pollution.

NEW LEGISLATION MAY NOT LEAD TO CLEANER WATERS – WHILE PHARMACEUTICAL AND COSMETIC SECTOR TO PAY BILLIONS TO UPGRADE WATER TREATMENT FACILITIES ACROSS EUROPE, THERE IS NO INCENTIVE TO OTHER POLLUTERS TO PRODUCE MORE SUSTAINABLE PRODUCTS.

[11] *Beyond Financial Performance: How ESG Factors Impact Companies and Investments*, Iris Carbon, 3 May 2023

[12] Evidence shows more than 600 essential medicines at risk, and manufacturing in Europe will 'grind to a halt' if wide-ranging chemical ban is implemented (efpia.eu)

The legislations can contain legal uncertainty (including for intellectual property which is at the core of the industry's ability to innovate) and feasibility uncertainty. Requirements mostly apply to the European market leading to differences to other global requirements would lead to diversity in products. Diverging opinions, generated by different methodologies of work between Commission services and agencies, cause uncertainty and unclarity for business operators.

Regulatory & Compliance: The scope and/or implementation of several legislations are unclear, and there are inconsistencies between multiple legislations. Compliance challenges arise due to stringent sustainability criteria for R&D investments, possible restrictions on chemicals like PFAS, and delays for new medicines due to unclear future restrictions and regulations. This causes uncertainty regarding the scale of impacts on patients and the pharmaceutical industry and requires additional resources to comply and to understand the impact on specific medicinal products. Delays in R&D investment[13], clinical research and manufacturing could also occur in anticipation of further clarity on proposed chemical restrictions and bans.

THREAT TO CLINICAL TRIAL CONTINUITY IN EUROPE WITHOUT CLARITY ON INCLUSION IN BAN ON SYNTHETIC POLYMER MICROPARTICLES AS MEDICINAL PRODUCTS INTENDED FOR CLINICAL TRIALS MAY FALL WITHIN THE ECHA RESTRICTION (SIMILARLY POSSIBLE FUTURE PFAS RESTRICTIONS WHERE MEDICINAL PRODUCTS CONTAIN PFAS APIs).

The legislations can contain legal uncertainty (including for intellectual property which is at the core of the industry's ability to innovate) and feasibility uncertainty. Requirements mostly apply to the European market leading to differences or conflicts with other global requirements would lead to differences in products. Diverging opinions, generated by different methodologies of work between Commission services, agencies and other regulatory bodies, cause uncertainty and unclarity for business operators. The complex and divergent EU requirements, also risk impacting global reliance mechanisms, at a time where several key stakeholders are making a concerted effort to leverage reliance mechanisms.

DIFFERENT MEDICINES IN EUROPE THAN THE REST OF THE WORLD! TITANIUM DIOXIDE REQUIREMENTS IN EUROPE WOULD DIVERGE FROM THOSE IN OTHER REGIONS - REGIONS WHICH TAKE A SCIENTIFIC RATHER THAN A POLITICAL APPROACH AS SEEN IN THE EU.

[13] *The role of regulators in mitigating uncertainty within the Valley of Death*, Jaime Bonnin Roca, Eoin O'Sullivan, 2022

3. WHAT'S NEEDED?

The EU must take leadership in the creation of strategic oversight, aligning EU policies affecting the sector across Member States and at EU level, including regular engagement with the industry. Europe is seeking open strategic autonomy, it needs to be a competitive place to research, develop and manufacture medicines, from the most innovative to the most familiar. Safeguarding access to medicines and mitigating shortages must be central to strategic oversight actions. The EMA (European Medicines Agency) must be engaged in legislation governing medicines and lead decisions, which the general pharmaceutical legislation taking precedence, specifically when the benefit/risk evaluation of medicinal products is impacted.

Awareness and mitigation of the potential cumulative impacts of legislative changes can contribute to the drive for a more sustainable future and continued patient access to safe medicines. There is a need to ensure coherence & streamlining of all policies that impact the EU's ambition of a Strategy for Life Sciences (as per Political Guidelines of July 2024), in particular pro-innovation policies, green deal and clean transition policies. EFPIA proposes an EU Office for Life Sciences in the EU Commission to ensure focus, coordination & track actual outcomes. Furthermore, there is a need for the commission to continuously evaluate (incremental and cumulative) impact of new and existing policies and regulatory proposals, on the competitiveness of the EU's Life Sciences sector. Furthermore, there is a need to consider the shortages/supply chain risks and work with regulators to minimise these risks.

The pharmaceutical sector is one of the most regulated in Europe and the world. Accordingly, the pre-approval of manufacturing plants, clinical trials and marketing authorisations should be given consideration when implementing and interpreting related elements of the new legislations. The long development timelines and highly regulated nature of this industry are fundamental aspects of the ability to react to changes in legislation (e.g. restriction of chemicals).

To respond to these potential effects of the legislative changes, the following considerations have been identified:

- As part of the Better Regulation processes, legislative proposals should be developed by taking into account their impact on competitiveness and health security (especially in times of geopolitical instability) and be sure that by aiming to achieve

important EU goals (such as the Clean Industrial Deal), other European objectives are not undermined. This will further improve policy coherence and avoid duplication of reporting and over-regulation[14].

- **Improved and continued impact assessments** of each newly proposed or revised legislation against existing legislative landscape (including legislations still in draft) to determine incremental and cumulative impacts of all relevant sectors taking into consideration EU competitiveness – and should involve consultation across a wide range of stakeholders and EU Agencies.
- Where possible, reconsider **implementation timelines** and closely monitor and adapt them as new evidence about feasibility or impact emerge.
- Develop **clear and timely guiding documents** for potentially unclear legislations and their implementation to increase clarity. Engage the relevant impacted stakeholders from a variety of sectors early on in the development process of guiding documents, to provide feedback on potential areas of focus to aid in understanding of the legislation and its implementation.

[14] Better regulation - European Commission (europa.eu)

- In order to safeguard **patient access to medicines**, consider potential derogations/ exemptions of medicinal products and their ingredients, packaging and processes, within legislations that are not primarily focused on medicines (i.e. those for food, chemicals or the environment), understanding that medicines are subject to stringent safety and regulatory requirements. Consider patient perspectives when making changes to products or packaging.
- Ensure the **EMA is systematically consulted** on proposals for new or amended legislation that could have an impact on medicines and is furthermore systematically involved in subsequent implementation and support innovator's journey through scientific advice in the absence of joint mechanisms for different agencies and their different mandates.
- Ensure a **proportionate** European Green Deal and balanced implementation through a resilient supply chain transition plan based on robust science that enables a level playing field in environmental and manufacturing standards and doesn't disproportionately impact innovation.
- **Proactive Industry-Regulator Collaboration**, such as with the EMA, EEA, EFSA and ECHA when developing and implementing legislation impacting medicinal products, and when proposing restrictions on substances used in medicinal products, to ensure the European Green Deal achieves its objectives whilst maintaining access to safe medicines; highlight potential consequences of legislation to patients and the pharmaceutical industry and healthcare systems early on and encourage specific considerations for continuity of medicine supply in chemical, food and environmental legislation. and healthcare systems early on. It is crucial to engage in consultations with the industry to ensure that the implementation of various regulations aligns with the objectives and needs of the affected sectors. This dialogue should occur before, during, and after the regulatory process. There is also a further need to **build capacity in terms of expertise and skills** specific to medicines development and regulations, within the other agencies.
- **Stakeholder Engagement**: Proactively communicate with other stakeholders, such as patients, academia and investors, to address any potential concerns for example where there are proposals for restrictions on substances to ensure an appropriate sector specific science and risk assessment is conducted leading to appropriate mitigation plan. Engage with suppliers to timely identify and develop alternative materials and technologies, to proactively mitigate potential supply chain disruptions.
- **Recognise the different characteristics and specificities of innovative therapies** (i.e. biological products such as ATMPs, plasma products, vaccines, radionuclides, etc.) and make sure that policy solutions are fit-for-purpose, targeting the specific issues they are designed for. Particularly in the context of the Critical Medicines Alliance recommendations, where supply chain vulnerabilities differ depending on the product characteristics.

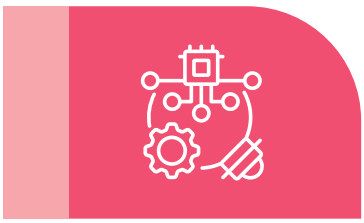
OUR VISION IS THAT EUROPE IS A NET GENERATOR OF INNOVATIVE HEALTH SOLUTIONS FOR PATIENTS AND HEALTH OUTCOMES. THE PHARMACEUTICAL INDUSTRY WILL AIM TO BE A PARTNER IN THIS PROCESS AND SUPPORT CHANGE MANAGEMENT

1. THE CREATION OF AN EU OFFICE FOR LIFE SCIENCES AND A DEDICATED COMPETITIVENESS STRATEGY FOR EUROPEAN LIFE SCIENCES:

- Despite efforts to streamline processes and improve market competitiveness, the lack of strategic coordination and oversight stands in stark contrast to Europe's global competitors, who view life sciences as a strategic asset. A dedicated office could steer and coordinate policymaking, with a vision to make Europe a world-leader in science, innovation and modern manufacturing.

2. A EUROPEAN ECO-SYSTEM THAT CAN TRANSFORM IDEAS INTO INNOVATION

- Europe needs an eco-system-based approach if it is to compete with the major US hubs including Boston and San Francisco and close an investment gap that has seen the US share of global R&D rise from €2 billion a year to €25 billion a year mor than Europe in 20 years.
- A European life science strategy should foster competitive European biotech and pharmaceutical clusters, support and retain European start-ups, and strengthen European venture capital. It should ensure that EU framework programs can foster partnerships with both big and small companies as well as partnering for European health security and reinforce internationally competitive Intellectual Property (IP) rights.



3. DEVELOP A GLOBALLY COMPETITIVE LOCATION FOR DEVELOPING AND MANUFACTURING NEW TECHNOLOGIES

- Europe needs to recruit and retain the best people and develop them. It needs policies and infrastructure that attract basic research and clinical trials

4. INVEST IN HEALTH

- With an ageing population, increased burden of chronic disease, a shrinking workforce, and the impact of climate change, the EU must support Member States in enhancing their healthcare systems by recognising health expenditure as an investment in the future, protecting health budgets and supporting strategic funding of infrastructure upgrades, prevention, digitalisation, national framework conditions and green practices. Facilitating the sharing of best practices among Member States in improving and modernising their healthcare systems is an often overlooked and incredibly valuable action that the EU Commission could take now.

5. SECURE EUROPE'S PLACE AS A RESILIENT GLOBAL BIOPHARMA PLAYER

- The strategy should ensure robust funding and resources for the EMA, enabling Europe to match the ambitions for a future-proof regulatory framework, making the region more attractive to launch medicines and the EMA a leader in setting regulatory standards internationally. It requires alignment with the US and other regulators to prevent delays to medicines access, ensuring EU companies can grow and compete.

[2] https://www.efpia.eu/media/677291/european-access-hurdles-portal-efpia-cra-report-200423-final.pdf

4. UPHOLDING THE COMPETITIVENESS OF THE HEALTHCARE SECTOR IN THE EU

There are many wide-ranging challenges facing Europe in healthcare and beyond. This includes an aging population, increasing numbers with chronic diseases like diabetes, cancer, cardiovascular disease, budget constraints and a depleted health workforce and geopolitical instability and climate change. Medicines should be seen as a solution to these problems.

There are many wide-ranging challenges facing Europe in healthcare and beyond. This includes an aging population, increasing numbers with chronic diseases like diabetes, cancer, cardiovascular disease, budget constraints and a depleted health workforce and geopolitical instability and climate change. Medicines should be seen as a solution to these problems.

European resilience relies on its ability to deal with future health crises and pandemics and its ability to innovate, its access to home-grown research and treatments, and not being reliant on other parts of the world. COVID-19 showed how important a strong pharmaceutical and life-science sector is in tackling health crises maintaining a healthy population. Only Europe's strong R&D eco-system, knowledge, and expertise in health platforms ensured the region was able to lead on the R&D and manufacturing scale up of vaccines during the pandemic – this must be maintained and supported.

INDUSTRY'S CONTRIBUTION VALUED AT THE ECONOMY[16]:

- €44.5bn investment in R&D in 2022 in Europe
- 865,000 employees
- Worth over €215bn to European economy
- The industry is the largest contributor to EU trade balance with a surplus of 175bn in 2022
- Innovative industry accounts for 80% of the pharmaceutical GVA in the EU

[16] the-pharmaceutical-industry-in-figures-2023.pdf (efpia.eu)

The innovative pharmaceutical industry is a critical pillar of the European economy, yet its position as a global leader is precarious as investors increasingly look elsewhere. The European Commission have recently defined their strategic agenda for 2024 – 2029[17] which includes priorities for a prosperous and competitive Europe whereby it proposes to bolster the EU's competitiveness. EFPIA therefore welcomed Mario Draghi's report[18], published by the European Commission, outlining proposals on how Europe can regain its competitive edge and the critical role of innovative industries in achieving this. It aligns with industry's ambition to once again make Europe the go to location for research, development and manufacturing of new diagnostics, treatments and vaccines.

It recognises the pharmaceutical sectors strategic importance to Europe as well as its uncertain future in the context of fierce competition of other leading regions of the world. In addition, it further underlines the need to harmonise and streamline practices and invest in infrastructure to improve the fragmented life science ecosystem that exists in the EU.

In the written answers[19] by Stéphane Séjourné to the questions raised by European Parliament before the hearings leading to his appointment as Executive Vice-President for Prosperity and Industrial Strategy, he notes the need for policy coherence, calling out specifically the European chemicals industry, which includes the pharmaceutical industry. He emphasizes that the chemicals industry is faced with an increasing number of regulatory requirements, which are justified on their own but may create inconsistencies and duplications between different pieces of legislation. He calls for better coordination at both EU and national levels and a more holistic approach to ensure that the cumulative burden does not hamper the EU's competitiveness and innovation potential. He further notes Europe has a strong manufacturing base and a strong position in global markets and confirms that the automotive, chemical, and pharmaceutical sectors are areas of excellence but are facing significant global competition.

Furthermore, recent concerns over medicines shortages in Europe, and the establishment of the Critical Medicines Alliance, is a positive step by protecting and enhancing the security of global supply chains and strengthening the region's manufacturing capabilities. The reasons for shortages are multifactorial and complex, with nuances between different actors in our sector and we look forward to working in partnership to address these challenges over the coming years. These must not be exasperated by misalignment with new legislations which could counter the ongoing actions to minimise medicines shortages.

If pharmaceutical companies are to catch up and compete on a level playing field, these recommendations should be actioned swiftly alongside a coherent and comprehensive life science approach and method.

[17] https://european-union.europa.eu/priorities-and-actions/eu-priorities/european-union-priorities-2024-2029_en

[18] https://commission.europa.eu/topics/strengthening-european-competitiveness/eu-competitiveness-looking-ahead_en

[19] https://hearings.elections.europa.eu/documents/sejourne/sejourne_writtenquestionsandanswers_en.pdf

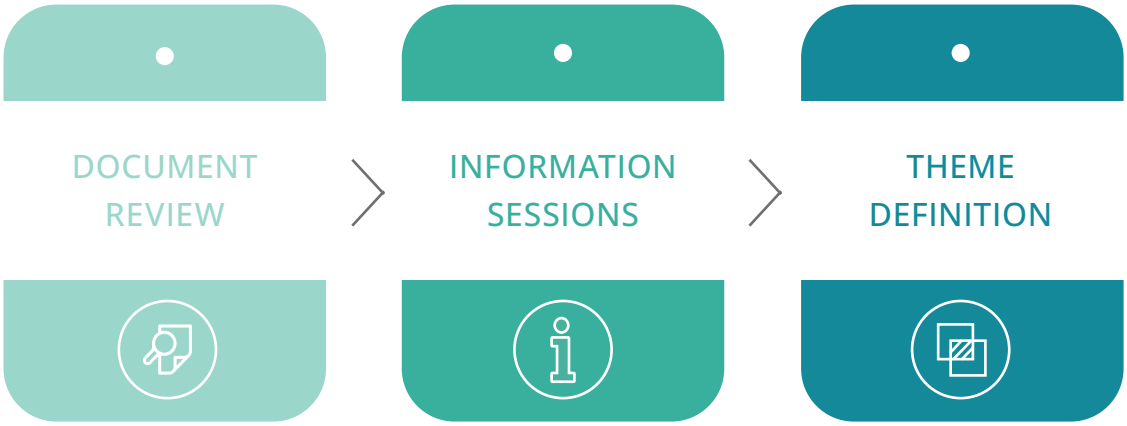
5. THEMATIC ANALYSIS APPROACH

A thematic analysis research method was used to identify, analyse and report patterns (themes) within the data. The impact themes uncovered by this work cut across the assessed legislations, revealing timeline concerns, cumulative impacts and inconsistencies amongst the legislative changes.

The specific legislations covered in this study were chemical, food and environmental legislations being revised/defined, and that are anticipated to have an impact on patients and the pharmaceutical industry within the EU. This list is not exhaustive and focuses on pieces of legislation where EFPIA had identified impacts. The revision to the General Pharmaceutical Legislation was integral, as it calls out many of the legislations and it will lead to further changes within the same period.

The **documents** consisted of research, feedback on public consultations, summaries of legislations, and other opinion documents produced by EFPIA. Please see Appendix for a list of legislations and documentation covered.

The impacts identified during the document review were validated with industry SMEs from EFPIA's network across a series of **information sessions**. The SMEs also provided additional context into impacts across the various legislations.



The impacts identified were mapped against the following pharmaceutical value chain areas, to highlight individual and/or cross-cutting impacts:

1. Research & Development: The discovery, development and testing of new medicines and/ or technologies.
2. Regulatory: Activities related to the submission and maintenance of marketing authorisations, and activities undertaken to comply with all relevant legislation.
3. Manufacturing & Supply: The production, packaging, and distribution of marketed pharmaceutical products.
4. Launch & Availability: Activities related to the initial launch, subsequent availability and continuity of supply of a medicinal product on the market.

The analysis identified the following **four themes** as having the potential for high-level cumulative impacts across the value chain areas:

1. Patient Access: Impacts on patients' access to medicines, including drug shortages, high medication prices, and reduced patient trust in/ adherence to medicines.
2. Regulatory landscape & Compliance: Impacts on companies' ability to apply and comply with the legislative changes.
3. Environment & Sustainability Reporting: Impacts related to the environment and/ or sustainability, particularly in relation to reporting of any required environmental related data.
4. Innovation & Competitiveness: Impacts on Europe's position as an innovator in pharmaceutical research, development and/ or manufacturing.

Potential impacts are presented in a heatmap (in Section 6.3.1.) showing the relevant legislation, impact theme and value chain area for each potential impact. This visual representation displays 'hotspots' of potential impact across these axes.

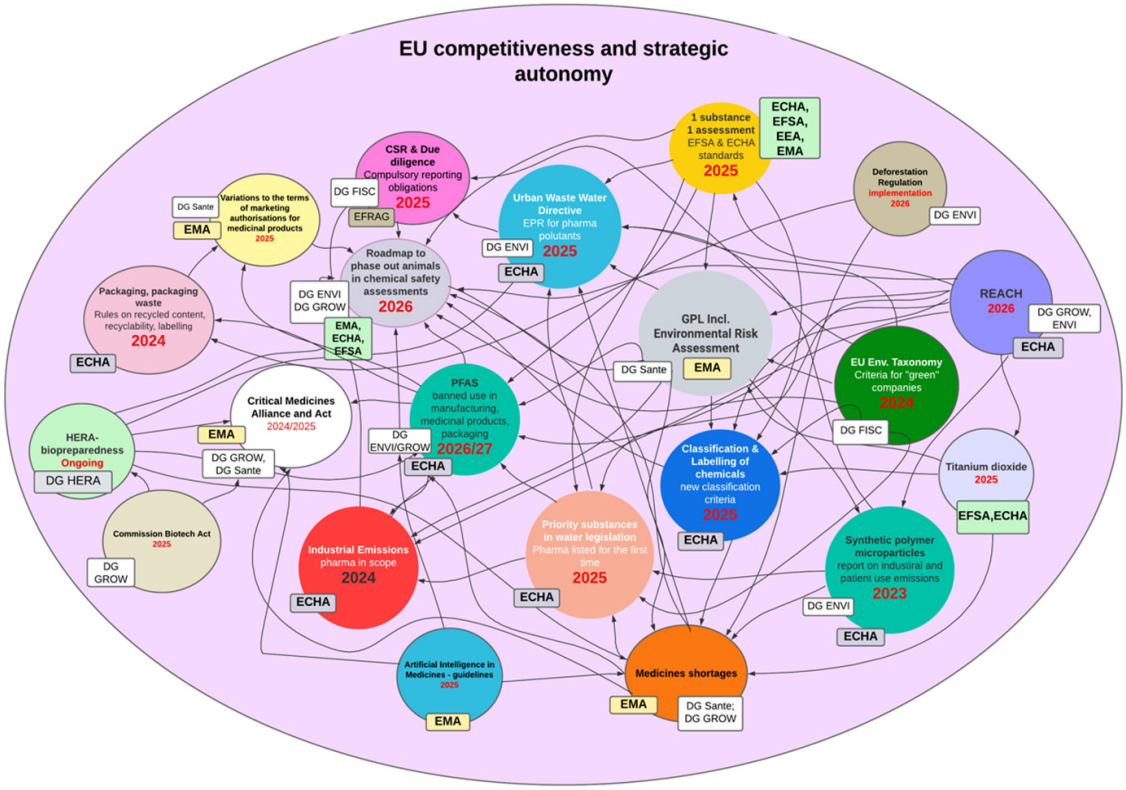
Considerations were identified to mitigate or prepare for these potential impacts, keeping in mind both the legislators as well as pharmaceutical industry stakeholders.

The findings from the analysis can be found in Section 6 of this report.

6. THEMATIC ANALYSIS

A thematic analysis research method was used to identify, analyse and report patterns (themes) within the data. The impact themes uncovered by this work cut across the assessed legislations, revealing timeline concerns, cumulative impacts and inconsistencies amongst the legislative changes.

There are significant linkages between pharmaceutical legislations, and those targeting chemicals, food and the environment as shown in the below figure. The figure demonstrates how it is more complicated for innovators and regulators to navigate the landscape with the multiple interplays and moving targets, whereby the EMA (European Medicines Agency) is not always in the lead, even if the Benefit/Risk evaluation of medicinal products is impacted. In addition, the cited pieces of legislation are developed and implemented by various Commission Directorates and led through by various EU agencies, all with differing mandates and expertise, thus adding more regulatory complexity to comply:



The review of new and revised pieces of legislation generated in the framework of the European Green Deal highlights several potential impacts amongst them on availability of medicines to patients, on the pharmaceutical industry's license to operate and on the competitiveness of Europe compared to other regions. When reviewed holistically, main contributing factors to these impacts are:

1. **The pace of change**: Many of the legislations analysed are anticipated to enter into force by 2027, some with specific requirements becoming applicable through to 2035. Both of these factors are a concern: the potential for up to 26 new legislations coming into force in a 5-year period, and the evolving nature of impacts over the ~10-year rollout period.

2. **Inconsistencies between new/proposed legislations**: Our analysis identified inconsistencies between the proposed legislations and other proposed/existing legislations, grouped into the following inconsistency types:

- Amongst the new/proposed EU legislations themselves;
- Between new/proposed EU legislations and other global (outside-EU) legislations;
- Of the specified intent of a given new/proposed EU legislation compared to its potential impacts (including potential for unintended consequences).

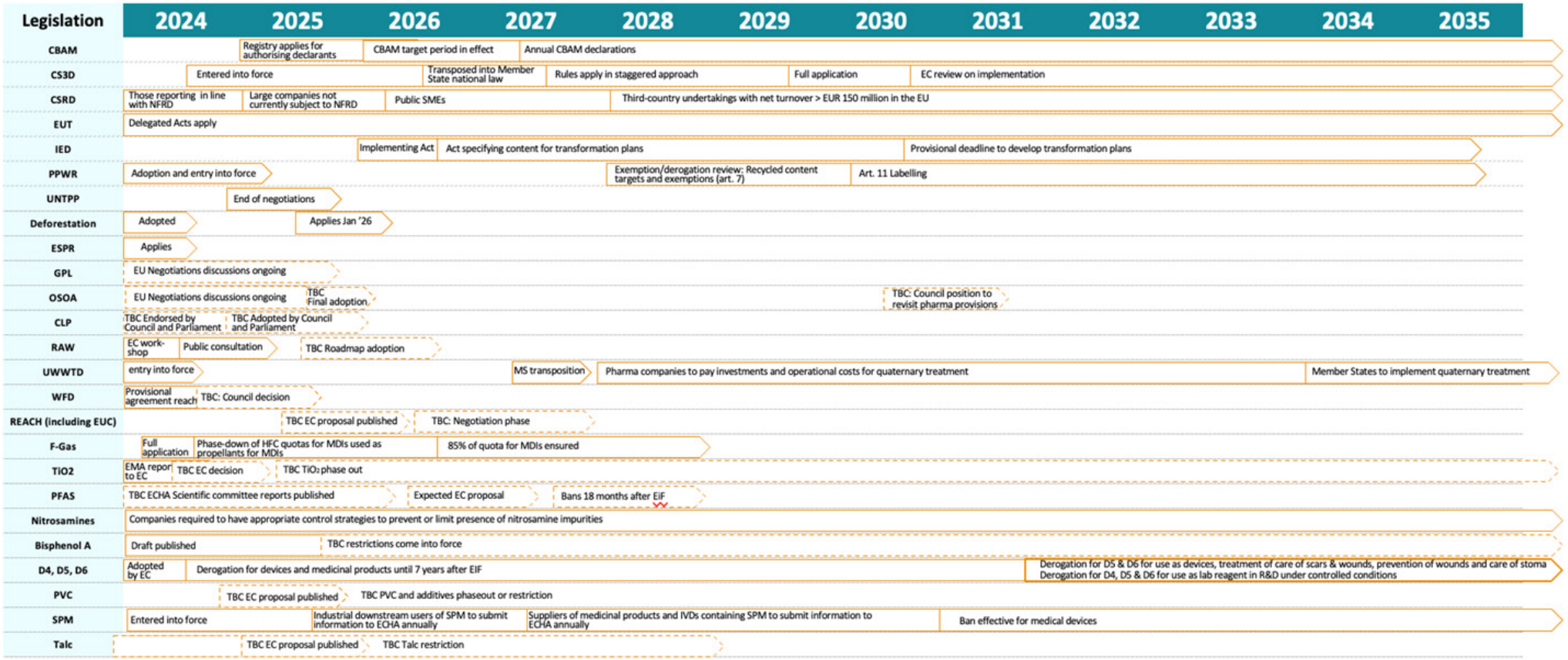
3. **Cumulative impacts**: When combined, proposed requirements from the individual legislations may lead to greater cumulative impacts.

6.1 Pace of Change

Where available, the anticipated/expected timelines of legislations covered in this analysis were plotted in the timeline below:

ALL AT THE SAME TIME - Many of the legislations covered in this analysis are expected to come into force within the next few years. However, they often have undefined final timelines for compliance with new requirements. This rapid pace of change and lack of clarity regarding timelines creates uncertainty for businesses. In some cases, it may lead to delayed authorisations and market access impacting on companies' exclusivity.

Many of the changes could require product reformulation, with potential impact on existing stability and performance characteristics of the products, process changes and eventual registration of the changes requiring additional resources and time. This would result in large spikes of activity for industry and regulators that could be unsustainable and could limit investment in innovative medicine.



These timelines are indicative at the time of writing; timelines with a dashed outline are uncertain.

6.2 Inconsistencies

Review of the legislations identified several inconsistencies. Some examples to illustrate these inconsistencies are called out:

1) Amongst new/proposed EU legislations

There are proposed requirements within some of the legislations analysed that read as inconsistent with those in other existing/proposed legislations, particularly where these legislations fall under the remit of different regulatory bodies.

In some cases, these inconsistencies are nuanced, such as the requirement to minimize packaging under the proposed Packaging and Packaging Waste Regulation (PPWR), and the additional labelling requirements under the PPWR, General Pharmaceutical Legislation (GPL) and the F-gas Regulation (F-gas), which would add to packaging. Such inconsistencies between EU legislations would require work to understand and address, thereby increasing the administrative burden on companies as they require more resources to analyse the impacts to their portfolios.

However, there is one example of a direct contradiction between the GPL focus on environmental risk assessment (ERA), under which a marketing authorization may be refused on environmental grounds, and the European Parliament's resolution on the Strategic approach to pharmaceuticals in the environment, which states that marketing authorisations should not be refused based solely on environmental impacts.

Inconsistencies identified

Legislation 1	Legislation 2
General Pharmaceutical Legislation (GPL): Environmental Risk Assessment (ERA) - EMA Possibility to refuse a marketing authorization on environmental grounds.	**Strategic approach to pharmaceuticals in the environment - EP** Marketing authorisations should not be delayed nor refused solely on the grounds of adverse environmental impacts[20].
Packaging and Packaging Waste Regulation - EC Requirement to minimize packaging as much as possible. Labelling within PPWR is not fully aligned with the sectorial legislation and not being encompassing of Business-to-Business packaging requirements.	**GPL - EMA** Requirement to add more information to packaging, such as disposal and recycling symbols.
	GPL In the Parliament revision of the GPL, the adopted text has a requirement to include additional serialization data for single dose blisters in a pack, particularly on variable data[21]. Manufacturers would need to increase the size of the package to comply with this requirement.
	F-gas - EC New labelling requirements to external pack and the leaflet.

[20] European Parliament resolution of 17 September 2020 on a strategic approach to pharmaceuticals in the environment (2019/2816(RSP)), TA MEF (europa.eu)

[21] Amendment 186 Proposal for a directive Article 66 – paragraph 2a (new). https://www.europarl.europa.eu/doceo/document/TA-9-2024-0220_EN.pdf

Legislation/s 1	Legislation 2
Urban Wastewater Treatment Directive (UWWTD) - EC Challenges on data relevant for toxicity or hazardousness that may require tests on animals.	**Roadmap to phase out animal testing (RAW) - EC** Proposal to phase-out animal testing.
Per- and polyfluoroalkyl Substances (PFAS) - ECHA Proposal to ban PFAS use in laboratory equipment/intermediates that are required for non-animal technologies, while there is no alternative[22]	
Classification, Labelling and Packaging of Chemicals (CLP) - ECHA Expected higher animal use requirements through inclusion of new hazard criteria[23]	
GPL: ERA - EMA Testing requirements of legacy APIs (those on the market prior to 2006) require animal tests[24]	
UWWTD - EC Producers of human medicines and cosmetic products required to pay for at least 80% of quaternary treatment of all micropollutants in wastewater, without consideration of contribution of other products[25].'Polluter Pays Principle' is not applied, and a free riding effect will be created.	**Art. 191(2) Treaty on the Functioning of the European Union** 'Polluter pays' principle[26].
One substance, one assessment package – ECHA The proposal for a regulation establishing a common data platform on chemicals suggests that business operators should notify all studies performed on chemicals that are being tested (Article 22).	**REACH** Substances for medicinal use, used in R&D are exempt from some obligations under REACH, including registration (article 9), therefore are not subject to study notification.

[22] https://echa.europa.eu/registry-of-restriction-intentions/-/dislist/details/0b0236e18663449b

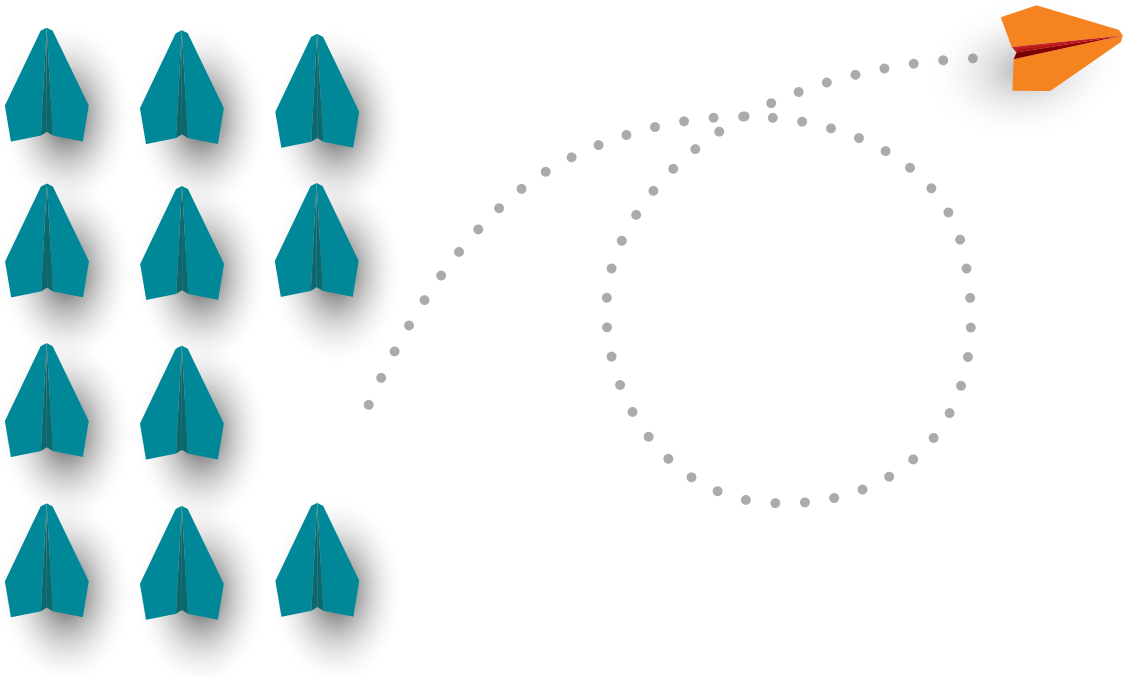
[23] Cruelty Free Europe (CFE) comments following the 45th Meeting of Competent Authorities for REACH and CLP (CARACAL-45) on 5-6 July 2022 (available on CIRCABC)

[24] European Commission proposal for pharmaceutical review – Managing the environmental impact of the medicine's lifecycle, EFPIA, 10 June 2024

[25] *EFPIA Memo Re The New Urban Wastewater Treatment Directive and Its Impact on Producers of Human Medicines*, 25 June 2024

[26] Consolidated version of the Treaty on the Functioning of the European Union - PART THREE: UNION POLICIES AND INTERNAL ACTIONS - TITLE XX: ENVIRONMENT - Article 191 (ex Article 174 TEC)

[27] Clear Steps Towaraceutical Sector's En



2) Between the proposed EU legislations and the global legislative landscape

Where proposed changes to legislations suggest divergence of requirements from those which are currently globally developed and accepted, impacts are expected on Europe's competitiveness.[27]

Inconsistencies identified

Legislation 1	Legislation 2
Proposed GPL:Good Manufacturing Practice (GMP) - EMA Proposed addition of new requirements for GMP inspections, such as environmental risks (adopted position of the European Parliament[28]). Proposal undermines mutual recognition and collaborative assessment initiatives reversing recent progress at efficiency in these areas.	**Current GMP** Globally accepted and recognized inspections[29].
Proposed RAW - EC Proposed phase-out of animal testing chemicals including for pharmaceuticals[30].	**Current global requirements** Require animal testing in other regions[31] or in ICH guidelines.

[27] Information Session 2 - General Pharma

[28] https://www.europarl.europa.eu/doceo/document/TA-9-2024-0221_EN.html

[29] *Good Manufacturing Practices (GMP) – important points to consider in current context of General Pharmaceutical Legislation (GPL) Revision*, EFPIA, 12 January 2024

[30] https://ec.europa.eu/info/law/better-regulation/have-your-say/initiatives/14281-Animal-testing-in-chemical-safety-assessments-Commission-roadmap-to-phase-it-out_en

[30] https://ec.europa.eu/info/law/better-regulation/have-your-say/initiatives/14281-Animal-testing-in-chemical-safety-assessments-Commission-roadmap-to-phase-it-out_en

Legislation/s 1

Proposed Chemical Bans & Restrictions

- Possible TiO_2 ban in medicines, as already adopted for food in EU[32].
- Possible PFAS ban on intermediates / manufacturing equipment/medicinal product/ packaging.
- Possible PVC and additives ban.

PPWR, Art. 7 - EC

Potential future revision of proposed derogation, possibly requiring recycled content in packaging of medicinal products.

Legislation 2

Global requirements

- Third countries' health authorities have opposed the TiO_2 ban and will not implement it as in the EU[33].
- Different definitions for PFAS in other global regions[34].
- European Pharmacopeia (EDQM – beyond only EU) and United States Pharmacopeia (USP) monographs include use of PFAS (Need for changes to the European Pharmacopeia monographs (e.g. PFAS reagents used in > 170 monographs. Of these, 100 prescribe the use of trifluoroacetic acid in the mobile phase of HPLC analytical methods. + More than 90% of EDQM reference standards (>2500 reference standards), are supplied in glass vials with a PTFE coated stopper or septum), PVC. Updating these monographs is a lengthy process[35].
- There's the possibility that, through mandatory reformulations, the EU product may be significantly different to the "global" product, meaning that reliance mechanisms would be difficult to implement. This deviates from the "one product, one submission" aspirations of global reliance.

FDA Guidance for Industry Container Closure Systems for Packaging Human Drugs and Biologics[36]

Prohibits use of recycled plastic in the production of immediate packaging[37].

[32] https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32022R0063&from=EN

[33] USE OF TITANIUM DIOXIDE AS EXCIPIENT IN HUMAN AND VETERINARY MEDICINES AND IDENTIFICATION OF ALTERNATIVES INDUSTRY FEEDBACK TO QWP EXPERTS/EMA QUESTIONS FINAL REPORT, FEB 2024 + https://www.ema.europa.eu/en/documents/other/annex-i-use-titanium-dioxide-excipient-human-medicines-industry-feedback-qwp-experts-ema-questions_en.pdf

[34] https://www.efpia.eu/media/3balrcsd/efpia-report-in-response-the-annex-xv-pfas-restriction-proposal.pdf

[35] EDQM presentation, Sustainability session, DIA Europe 2024 + EDQM submission to the public consultation at ECHA on the universal ban on PFAS proposal, September 2023

[36] Guidance for Industry: Container Closure Systems for Packaging Human Drugs and Biologics

[37] Response to the Commission Consultation on their proposal for a Regulation on Packaging and Packaging Waste (COM(2022) 677 final) - Pharmaceutical Industry considerations, EFPIA, April 2023

3)Between a legislation's intent and its potential impact(s)

Inconsistencies between the stated intent of a legislation and the potential impacts identified during this analysis may lead to unintended consequences of the legislation and a lack of clarity on its implementation.

Inconsistencies identified

Legislation	Legislation Intent (non-exhaustive)	Potential Impact
EU Taxonomy for Sustainable Activities (EUT) - EC	Facilitate sustainable investment[38]	The 'all or nothing' approach to sustainability scoring[39], complexity and uncertainty around what qualifies as a 'sustainable activity', and the challenges linking impact of sustainability actions with reporting[40], may cause Europe's pharmaceutical industry to appear less sustainable than other regions and industries[41]. This may divert investors to other regions or sectors deemed more sustainable[42].
UWWTD	Zero Pollution – cleaner waters	Directive fails to comply fully to the EU principles of proportionality, non-discrimination and polluter-paying. Only two sectors, human pharmaceuticals and cosmetics, are to pay for the pollution caused by others who fail to incentivise greener product development.
PFAS	Reduce environmental and human health impacts	With such a universal ban proposed, there may be regrettable substitution as every substance life cycle has complex environmental impact and changes in substance or sourcing may influence multiple aspects

[38] REGULATION (EU) 2020/852 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 18 June 2020

[39] EFPIA policy paper on Taxonomy Technical Screening Criteria 1.2

[40] Information Session 1 - Climate and Circularity

[41] *EFPIA Briefing: EU Taxonomy Delegated Acts*

[42] Information Session 1 - Climate and Circularity

6.3 Cumulative Impacts

When considered individually, each of the proposed legislations analysed may have an impact on patients, the pharmaceutical industry, or both. It is recognised as well, that in principle the drivers for these legislations are positive aiming to protect the environment for future generations. However, when these are considered collectively, hotspots of impact potential appear across the value chain for certain impact themes. These impact hotspots, and the specific impacts behind them, are detailed in the following section.

The potential way these impacts will manifest and their potential magnitude will depend on individual organisations' circumstances.

6.3.1 HEATMAP: ACCUMULATION OF REQUIREMENTS DRIVEN BY DIFFERENT LEGISLATIONS AT EVERY STAGE OF MEDICINES R&D AND SUPPLY

Value chain:		Research & Development				Regulatory				Manufacturing & Supply				Launch & Availability				
Theme		Patient Access	Regulatory landscape & Compliance	Environment & Sustainability Reporting	Innovation & Competitive-ness	Patient Access	Regulatory landscape & Compliance	Environment & Sustainability Reporting	Innovation & Competitive-ness	Patient Access	Regulatory Landscape & Compliance	Environment & Sustainability Reporting	Innovation & Competitive-ness	Patient Access	Regulatory Landscape & Compliance	Environment & Sustainability Reporting	Innovation & Competitive-ness	Potential cross-theme Impacts
Legislative Area																		
Climate & Circularity	EUT																	Lack of clarity; diversion of investment; admin and resource burden; reduced competitiveness
	CSRD																	Supply disruption; diversion of investment; hindrance of innovation; admin and resource burden
	CS3D																	Supply disruption; diversion of investment; hindrance of innovation; admin and resource burden
	CBAM																	Admin and resource burden
	IED																	Admin and resource burden
	PPWR																	Lack of clarity; reduced competitiveness; admin and resource burden; usability; adherence
	UNTPP																	Supply disruption; admin and resource burden
General Pharma	RAW																	Lack of certainty; testing and resource burden; reduced innovation and competitiveness
	GPL																	Product availability; supply disruption; reduced innovation and competitiveness; healthcare costs; admin and resource burden
Chemicals	OSOA																	Diversion of investment
	EUC																	Uncertainty; product availability; reduced attractiveness
	REACH																	Product availability; supply disruption; reduced innovation and competitiveness; admin burden
	B&R (TiO_2)																	Product availability; supply disruption; usability; adherence
	B&R (PFAS)																	Product availability; supply disruption; usability; adherence
	B&R (Talc)																	Product availability; supply disruption; usability; adherence
	B&R (D4, D5, D6)																	Supply disruption
	B&R (Bisphenol A)																	Lack of clarity, adherence
	B&R (PVC)																	Adherence
	B&R (Nitrosamines)																	Product availability
	B&R (F-gas)																	Product availability
	B&R (SPM)																	Supply disruption; admin and resource burden, lack of clarity
	CLP																	Supply disruption; admin and resource burden
Water	UWWTD																	Diversion of investment; admin and resource burden, cost, reduced innovation
	WFD																	Product availability; reduced innovation and competitiveness; admin and resource burden
Potential cross-legislation impacts		Diversion of resources	Development delay Lack of clarity	-Lack of clarity	Diversion of investment Hindrance of innovation	Supply disruptions	Admin burden Cost	Admin burden Lack of clarity	Diversion of investment Hindrance of innovation	Product availability	Cost	Supply disruptions	Diversion of investment Competitiveness	Product availability Usability	Launch delays	Lack of clarity, divergence-	Competitive-ness	

The heatmap suggests there are hotspots as are outlined below. Further details on specific potential impacts can be found in Section 6.3.2 Impact Details.

ORANGE CATEGORY

Unavoidable impacts: under the relevant proposed legislation or chemical ban, requiring redesign of products, packaging and/or manufacturing equipment/processes. Product withdrawals and/ or discontinuation could occur if no suitable alternative to a banned substance is available. Products may also be withdrawn if companies deem redesign economically unviable.

Product availability: Chemical bans and restrictions are drivers for patient access impacts such as availability of medicines. This is partly due to proposed bans / restrictions meaning that medicines, packaging or manufacturing equipment/processes would need to be redesigned to exclude or reduce banned/restricted substances. Where redesign is not possible due to lack of a suitable alternative substance or manufacturing process, products would be removed from the market. Product availability may also be impacted if redesign is not economically viable.

BLUE CATEGORY

Possible reduction in patient access: Potential supply disruption / product unavailability leading to reduced patient access to medicines.

Supply disruptions: The heatmap shows that supply disruptions may occur during the implementation of changes required by the legislations, for example if there are delays in obtaining additional regulatory approvals for product, process or packaging changes. Necessary timing for the implementation of new requirements does not take into consideration development work, data generation, regulatory submission and approval processes that are different in the pharmaceutical industry from other industrial sectors. They may also occur because of ongoing legislative requirements, such as the potential need to switch suppliers based on their sustainability performance (e.g. for Corporate Sustainability Due Diligence Directive (CS3D), Corporate Sustainability Reporting Directive (CSRD), EUT)[43].

BLACK CATEGORY

Other impacts: such as administrative burden, diversion of resources etc.

Innovation and competitiveness: Any increases in costs and timelines due to the proposed legislative changes, particularly for R&D and manufacturing, may reduce the competitiveness of Europe as an innovator and a manufacturing hub[44,45]. Investments may be diverted from European pharmaceutical R&D and manufacturing due to a possible perception that the industry is not as sustainable as others[46,47], or may provide a greater risk of the release and use of commercially sensitive data[48,49,50]. There is also a risk that resources could be diverted from innovation in order to try to comply with legislation changes.

[43] Information Session 1 - Climate and Circularity

[44] Information Session 1 - Climate and Circularity

[45] Information Session 3 - Chemicals

[46] Information Session 1 - Climate and Circularity

[47] Information Session 1 - Climate and Circularity

[48] Dolon analysis; EFPIA Pharma Review, October 2023

[49] Information Session 2 - General Pharma

[50] Information Session 4 - Water

Administrative and resource burden: Impacts on administrative burden and requirements for additional resources may include additional regulatory submissions (such as for variations required due to necessary product/equipment/packaging/process changes), generation and reporting of additional data (such as sustainability or shortage notification data), or additional analysis to understand the impact of specific legislations. Increases in administrative and resource burden may be limited to a legislation's implementation period, for example where additional submissions are required, or where analysis may be required to understand the impact of potentially conflicting requirements between legislations. These may be exacerbated by the fact that most of the assessed legislations are expected to come into force by 2027, with impacts phased over ~10 years.

Alternatively, maintaining ongoing compliance with a legislation (rather than the initial implementation) may cause an increase in administrative and resource burden, for example, where additional reporting is anticipated (such as for CSRD, CS3D, EUT, Carbon Border Adjustment Mechanism (CBAM), Industrial Emissions Directive (IED), Water Framework Directive (WFD), Bans & restrictions (Synthetic Polymer Microparticles (SPM)), GPL:ERA). Additionally, where there are new reporting requirements, there may remain ambiguity on the type and level of information requirements leading to misinterpretations if over or under reporting, or different formats used, as may be the case for Bans & restrictions (SPM) and/or UWWTD.

The impacts extend beyond the industry. The increased administrative and resource demands will also affect EU and national regulators, who face growing responsibilities across the assessed legislations. This heightened workload will strain resources and impact their core tasks, as legislative changes modify regulatory processes, increase the volume of assessments and registrations, and ultimately lead to greater uncertainty and ambiguity.

KEY LEGISLATIONS

As well as impact hotspots, the heatmap also shows specific legislations that could have impacts across multiple stages the value chain (i.e. EUT, PPWR, GPL, Bans & restrictions (TiO_2, PFAS), UWWTD and WFD).

6.3.2 IMPACT DETAILS

The cumulative impacts of the assessed legislations split into the four themes and four value chain areas described in the Approach section above, are detailed below.

Please note the following when reading this section:

- The order of the impacts follows that of the heatmap with regards to the value chain and impact themes; impacts are not listed in any order of importance or magnitude.
- Where impacts are applicable across multiple themes and/or value chain areas, they are included in all relevant tables below.
- The illustrative examples provided are not exhaustive. They are to give indications of some identified impacts; the full extent is expected to be far more impactful.

6.3.2.1 RESEARCH & DEVELOPMENT

This section provides examples of impacts identified across the four themes having the potential for high-level cumulative impacts on the R&D process - how they impact the discovery, development and testing of new medicines and/or technologies:

Impact	Illustrative examples
	
New requirements and obligations from the assessed legislations have the potential to affect patient access to medicines. **Impacts on access to medicines:** The Extended Producer Responsibility (EPR) scheme, established for example in the Urban wastewater treatment directive and the packaging and packaging waste regulation could lead to decreased medicine access and increased costs.	✱ **UWWTD**: According to the European Commission[51] in their impact assessment, the proposed EPR scheme could increase of 12-45% for paracetamol and 6-48% for metformin. Pharmaceutical and Water Industry estimates indicate that these estimates may be underestimated by a factor of 8 to 10. Some companies are concerned that some over-the-counter (OTC) medicines may be shifted to prescription only which could decrease patient accessibility and increase patient costs. ✱ **WFD**: Adding pharmaceuticals to the list of priority substances and monitoring may lead to the phase out of certain pharmaceuticals according to NGOs.[52] **Other relevant legislations: PFAS**

[51] https://environment.ec.europa.eu/document/download/0c65f57a-9db0-4665-b5e4-e2ba671de95d_en?filename=Impact%20assessment%20accompanying%20the%20proposal.pdf

[52] https://eeb.org/wp-content/uploads/2024/11/Joint-letter-to-rapporteurs_trilogue-timing-1.pdf

Impact	Illustrative examples

The assessed legislations have introduced new requirements for more sustainable medicines in the R&D process and complying with them presents challenges.

Linking investments to sustainability criteria: More sustainable products and manufacturing process will require new investments in R&D. However, linking these investments with the new sustainability criteria from the legislations is a challenge for the pharmaceutical industry.[53]

- The manufacture of APIs, active substances, and medicinal products are included in EUT Annex III Technical Screening Criteria[54]. **Annex III (2023) 3851 final to the Commission delegated supplementing Regulation (EU) 2020/852** which includes Manufacture of active pharmaceutical ingredients (API) or active substances and Manufacture of medicinal products for the first time.
- As per the **GPL:ERA** proposal, marketing authorisations could be refused or revoked on the basis of incomplete or insufficiently substantiated environmental risk assessment or if the risks identified in the environmental risk assessment have not been sufficiently addressed by the applicant[55]. There is no specific allowance for medicines included on the Critical Medicines List.
- **UWWTD**: Recital 20: '*...A system of extended producer responsibility is the most appropriate means to achieve this, as it would limit the financial impact on the taxpayer and water tariff, while providing an incentive to develop greener products*'. Changing the design of a pharmaceutical compound (e.g., make it more biodegradable) would require development work and new submissions. It could reduce the pharmacological efficiency and would take many years to lead to a market authorisation, while in the meantime there is a high chance investment for R&D is diverted to cover EPR cost.

Other relevant legislations: PPWR, WFD

[53] Information Session 1 - Climate and Circularity

[54] Annex to the Commission Delegated Regulation (EU) supplementing Regulation (EU) 2020/852

[55] https://health.ec.europa.eu/publications/proposal-directive-union-code-relating-medicinal-products-human-use_en

Impact	Illustrative examples

Delayed investments due to chemicals restrictions uncertainties: Chemicals restrictions are currently being assessed by EU agencies or the Commission. Uncertainty over these processes will delay investments for the development of new, and more sustainable, medicines or technologies use said chemicals.[56]

- Lack of clarity on scope of **PFAS restriction proposal**[57]. PFAS are used throughout the entire medicines' life cycle (from research to manufacturing to packaging and within the final medicinal product). In addition, a ban of PFAS impacting other sectors could cascade to a reduction of demands for suppliers, thus affecting the supply of said substances for the manufacturing of pharmaceuticals
- Lack of certainty of **proposed TiO_2 ban** in medicinal products. TiO_2 has unique properties and is used in pharmaceuticals as a colourant and opacifier. Furthermore, it ensures stability of medicines since it absorbs visible and UV light and, hence, protecting photosensitive ingredients from degradation and extending shelf life. It is estimated that around 90 000 medicinal products (human and veterinary) in the EU contain TiO_2[58].
- **Governance of the Essential Use Concept (EUC)** remains at the Communication stage and has not been confirmed[59]. It is uncertain for companies if they will be able to use certain substances, categorized as "most harmful substances" in medicines in the future.
- The present **REACH regulation** has demonstrated lengthy processes for the evaluation and authorisation of certain substances (used in medicinal products) that could potentially qualify as alternatives to substances under a restriction/ban.
- Any change in the formulation of medicines (through the use of an alternative substance) would need new approval by the EMA. The long development timelines, stability assessments and material qualification and highly regulated nature of this industry are fundamental (This requires significant resource input from EMA and other competent authorities in Europe on a variation-by-variation basis, putting more strain on them).
- **Relevant legislations: Bans and restrictions (PFAS, TiO_2, Nitrosamines, PVC), Regulation on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH)**

[56] Information Session 3 - Chemicals

[57] https://echa.europa.eu/-/echa-publishes-pfas-restriction-proposal

[58] https://www.ema.europa.eu/en/documents/other/annex-i-use-titanium-dioxide-excipient-human-medicines-industry-feedback-qwp-experts-ema-questions_en.pdf

[59] Joint Industry Response to 47th Meeting of the Competent Authorities for the REACH and CLP (CARACAL) – AP4 Outcome of Essential Use Study.

Impact	Illustrative examples

Regulatory Landscape and Compliance

Diversion of resources: New costs generated to comply with the regulatory requirements coming from the assessed legislation may lead pharmaceutical companies to redirect financial resources (i.e., away from R&D, especially in Europe.)	Under the **proposed Extended Producer Responsibility (EPR) scheme as part of UWWTD**[60], companies would be required to cover new costs for set up of quaternary systems. This is exacerbated by the lack of clarity on the cost allocations of the EPR[61]. ✱ EFPIA and AESGP have estimated the average product costs could increase by 2.8% to 4.9% as a result of the UWWTD[62]. ✱ Germany's Environment Agency estimates for quaternary treatment costs range from €885 to €1,025 million annually – four times higher than the Commission's figure of €238 million[63]. In the Netherlands, costs are up to six times more than the Commission's estimations. Estimates from EurEau, the European Federation of National Associations of Water Services, indicate costs ranging from three to over nine times higher than the Commission's numbers (between €3.6 and €11.3 billion per year). ✱ Requirements to develop more environmentally-friendly medicines (e.g., **GLP:ERA**, UWWTD) while covering the cost of future pollution at the same time are diverting investments away from R&D and innovation in Europe.
Divergence- National legislations vs EU: The assessed legislations have created regulatory requirements contradicting or diverging from national legislations. This creates uncertainty and a lack of clarity over how companies should comply with the requirements. In addition, the implementation of legislations (directives) or guidelines can lead to different national interpretations with some more stringent than others.	✱ While ECHA (European Chemicals Agency) is working on an opinion regarding a **PFAS restriction**, members states, such as France has already moved with their own actions plan for PFAS[64] and TiO_2[65]). This lack of harmonization and coordination brings greater uncertainty and unclarity for the industry. ✱ Complexity of legislation with short take- up timeframes with different regional interpretations poses additional burdens and stringent bureaucracy and administration efforts companies and regulators ✱ In the case of **UWWTD**, the implementation of the directive may vary vastly from one member state to the other, for instance regarding the number of sectors including the EPR scheme. Therefore, the proportion of financing coming from the pharmaceutical industry may vary vastly from one member state to the other, without any current way of anticipating such costs. ✱ Often for new regulations, there is a tendency to over comply when reporting ✱ Different interpretations of reporting obligations lead to artificial geographical boundaries for multinational companies that have to report on a global scale. **Other relevant legislations: Bans and restrictions (TiO_2); GPL-GMP, EUT, OSOA, CSRD, CS3D, SPM**

[60] Information Session 4 - Water

[61] Information Session 4 - Water

[62] EFPIA and AESGP feedback on the Commission Open Consultation on the Urban WasteWater Treatment Directive (UWWTD): https://ec.europa.eu/info/law/better-regulation/have-your-say/initiatives/12405-Water-pollution-EU-rules-on-urban-wastewater-treatment-update-/F3388408_en

[63] European Regulatory Landscape: Impact of Access and Availability of Medicines, May 2024

[64] https://www.ecologie.gouv.fr/sites/default/files/documents/2024.04.05_Plan_PFAS.pdf

[65] https://www.ecologie.gouv.fr/presse/france-continue-defendre-classification-du-dioxyde-titane-cancerogene-suspecte-niveau

Impact	Illustrative examples

Lack of experts, divergence between agencies: A number of the assessed legislations will be implemented through the activities of EU agencies, with some of the abovementioned requirements monitored by the agencies. However, some agencies will be tasked to make decisions and to monitor situations related to substances included in medicinal products and they don't hold the expertise in this regard.	✱ ECHA is tasked with preparing an opinion on the **universal PFAS restriction proposal**, this is done without consultation of the EMA or focus on benefit/risks assessment. ✱ Regarding **Bisphenol A**, the EFSA has issued an opinion setting minimal limits, the EMA has issued a diverging opinion. ✱ The proposal regarding the re-attribution of scientific and technical tasks and improving cooperation among Union agencies in the area of chemicals, as part of the **'One substance, one assessment' legislative package**, included the foundations for an improved cooperation between agencies, especially on diverging opinions, but limited resources and expertise available could jeopardize any efforts. **Other relevant legislations: Bans and restrictions (TiO_2, D4,5,6); OSOA: re-attribution of scientific and technical tasks to the European Chemicals Agency.**

Impact	Illustrative examples

Commitments to environment: Industry decisive actions to reduce our environmental impacts across the value chain and contribute to building resilient and sustainable health system go unnoticed leading to stricter restrictions	✱ **EUT** Industry led sustainable and environmental actions in the R&D phase of medicines development are not recognised through restrictive criteria set in the EU taxonomy. ✱ **GPL:ERA proposal** to withdraw or refuse a market authorisation based on environmental impacts of medicinal product does not take into account greener considerations taken in medicines development (greener solvents, more advanced technologies, shorter and cleaner API development methods etc).
Research and innovation impacted through bans on materials; equipment and technologies where use is in a controlled environment and where emissions or environmental impact are none or very low.	✱ **PFAS bans** apply to intermediates and equipment used during the R&D phase of medicines development. ✱ **TiO_2 ban or restrictions** impacts directly the pharmaceutical development of innovators, where equivalent performance solutions, alternative to this substance, seem to lack.

Impact	Illustrative examples

The assessed legislations have overall introduced obligations and requirements that would ultimately lead to a degradation of the innovation efforts and a decrease in the competitiveness of the industry in Europe. **Perception of lower sustainability:** The 'all or nothing' approach to sustainability scoring[66], complexity and uncertainty around what qualifies as a 'sustainable activity', and the challenges linking impact of sustainability actions with reporting[67], may cause Europe's pharmaceutical industry to appear less sustainable than other regions and industries[68]. This may divert investors to other regions or sectors deemed more sustainable[69].	✱ The **EU Taxonomy Regulation** requires medicinal products to be deemed an appropriate substitute for an existing product, which is incompatible with the strong focus of the innovative pharmaceutical industry on delivering new or significantly improved treatment options to patients, aiming to innovate with first in class or best in class medicinal products. Every product brought to the market by the innovative industry will therefore per se qualify as non-sustainable. ✱ This approach also disincentivises bringing to market a new product which is more sustainable than existing medicines in a category but does not meet all the criteria to be deemed sustainable. Improvement should be rewarded. **Other relevant legislations: Bans and restrictions (TiO_2, D4,5,6); OSOA: re-attribution of scientific and technical tasks to the European Chemicals Agency.**
EU-specific testing burden: animal testing requirements in other regions not aligned with EU ambitions[70].	✱ Some regions require animal studies to assess product quality, often referred to as "batch release" or quality control studies where the scientific value is highly questionable (South Korea, Russia and China) **Relevant legislation: RAW**
Data exclusivity: The reduction in Regulatory Data Protection (RDP) in the proposed GPL could have significant impacts on the pharmaceutical industry. With reduced RDP, there is less incentive to invest towards greener innovation.	✱ Data exclusivity is a key factor in determining R&D investments and is a driver of investment for approximately 1/3 of innovative medicines[71]. ✱ Modelling of the impact of RDP changes on products relying on RDP in Europe suggests that the proposed reduction in exclusivity period (**GPL:RDP**) may lead to a reduction of 22% of innovation in Europe; this equates to approximately 50 products foregone in the next 15 years[72]. ✱ The Regulatory Scrutiny Board states that the proposed reduction of RDP may impact European pharma's "capacity to finance future innovation and international competitiveness"[73].

[66] *EFPIA policy paper on Taxonomy Technical Screening Criteria 1.2*

[67] Information Session 1 - Climate and Circularity

[68] *EFPIA Briefing: EU Taxonomy Delegated Acts*

[69] Information Session 1 - Climate and Circularity

[70] Information Session 2 - General Pharma

[71] *Assessment of main provisions and key EFPIA recommendations on the revision of the pharmaceutical package*, EFPIA, October 2023

[72] Dolon analysis; EFPIA Pharma Review, October 2023

[73] *Assessment of main provisions and key EFPIA recommendations on the revision of the pharmaceutical package*, EFPIA, October 2023

6.3.2.2 REGULATORY

This section provides examples of how the assessed legislations impact the activities related to the regulatory requirements around submission and maintenance of marketing authorisations of medicines, with some impacts from R&D flowing over to the medicinal authorisation phase.

Impact	Illustrative examples
	
New regulatory requirements generated from the assessed legislations may impact the submission and maintenance of marketing authorisations of medicinal products and ultimately patient access to said products. **Refusal/revocation of Market Authorisations (MA):** MAs may be refused or revoked on environmental grounds under the proposed GPL:ERA[74]. This may impact the availability of medicines.	✱ Art. 47(d) of the proposal for a directive **GPL:ERA** states that a Marketing Authorisation may be restricted if ERAs are "incomplete or insufficiently substantiated […] or if the risks identified […] have not been sufficiently addressed"[75,76]. ✱ It is unclear on what would be considered '"incomplete or insufficiently substantiated" ✱ Art 95 of GPL: The competent authorities of the Member States or the Commission may suspend, revoke or vary a marketing authorisation if a serious risk to the environment has been identified and not sufficiently addressed. ✱ Complying with such new regulatory requirements could impact the availability of medicines. Furthermore, availability of medicines included in the EU Critical Medicines list may be affected.
Additional regulatory approvals: Manufacturing processes, equipment changes, product reformulation and/or packaging changes to adhere to new legislations would require additional regulatory approvals.[77] Costly and complex generation of data to demonstrate equivalence would be necessary. This can lead to disruptions in supply if approvals are not obtained in a timely manner.	✱ A **PFAS restriction** impacting different stages of the life-cycle of medicines would result in identifying alternatives, and thus launch the generation of data from toxicological, extractables & leachable, stability, and patient usability studies Such data generation may take over 10 years. Regulatory approvals for the same may take 6 – 24 months[78]. ✱ From the regulatory requirements and processes to find alternatives and get the necessary approval would take years following a PFAS restriction and would severely impact the availability of medicines and, hence, patient access to those medicines. ✱ Consideration would need to be given to regulatory strategies in other jurisdictions, especially where similar restrictions do not apply. **Other relevant legislations: Bans & restrictions, EUT, PPWR, UN Treaty on Plastic Pollution (UNTPP)**

[74] *European Regulatory Landscape: Impact of Access and Availability of Medicines*, May 2024

[75] *Regulatory messaging on Refusal of a Market Authorisation based on environment grounds alone*, EFPIA, 24 April 2024

[76] *European Parliament resolution of 17 September 2020 on a strategic approach to pharmaceuticals in the environment (2019/2816(RSP)*, TA MEF (europa.eu)

[77] Information Session 1 - Climate and Circularity

[78] *Human Health Medicinal Products Sector Survey - Impact of Proposed PFAS Restriction on Patient Access to Medicines & EU Strategic Autonomy: https://www.efpia.eu/media/b1rcqvlt/annex-2-patient-impact-survey_human-health-associations.pdf*

Impact	Illustrative examples

Diversion of resources: New regulatory requirements as part of the GPL propose to change shortage prevention plans to a) extend the notification period to six months, and b) include non-critical medicines. This would increase administrative burden , potentially leading to resources being diverted from critical issues .

- Risk that the shortages provisions increase the actual shortage situations, which would go against the **Critical medicine list/Act**.
- Imposing a shortage prevention plan (SPP) for medicines that are not critical is too resource-intensive for both manufacturer and competent authorities and is disproportionate. This might drive efforts, and waste time and resources, potentially hampering the prevention and mitigation of potential shortages for critical medicines.
- If the scope of the **European Shortages Monitoring Platform (ESMP)** is expanded to identify critical shortages, data reporting requirements would increase for MAHs and NCAs significantly. Hence, EFPIA calls for the monitoring/ reporting to be done through an interoperable IT monitoring/ prevention including the ESMP and the European Medicines Verification System (EMVS).

Relevant legislation: GPL:Shortages

[79] Information Session 2 - General Pharma

[80] European Regulatory Landscape: Impact of Access and Availability of Medicines, May 2024

[81] Article 122 of the Proposal for Regulation of the General Pharmaceutical Legislation. https://eur-lex.europa.eu/legal-content/EN/TXT/HTML/?uri=CELEX:52023PC0193 nformation Session 1 - Climate and Circularity

Impact	Illustrative examples

The new regulatory requirements from the assessed legislations may impact the regulatory activities undertaken from the industries. **Conflicting requirements:** There may be a lack of coordination between different regulatory bodies (across the EU (including Member States) and globally), which results in conflicting requirements for individual companies to adhere to[82] and requires increased analysis to understand the direct impact of legislations on marketed and pipeline products.	✱ Requirements regarding labelling within **PPWR** are not fully aligned with the sectorial legislation, in addition to not being encompassing of Business-to-Business packaging. As a result, these requirements would be not only costly but also potentially jeopardize patient understanding of relevant information regarding the product. ✱ **PPWR** sets requirements for minimal packaging for medicinal products which may contradict the requirements for display of information to consumers (Proposal GPL, Recital 129, Articles 65, 73). ✱ It has yet to be clarified by the commission if clinical research and clinical trials fall within the scope of the **SPM** restriction – where clinical trials are already on the decline in EU[83], or **future TiO_2, PFAS, PVC restrictions.** **Other relevant legislations: REACH, Classification, Labelling and Packaging of Chemicals (CLP), GPL, CBAM**
Administrative and resource burden: Additional resources to comply with the new regulatory requirements will be needed to prepare submissions for changes to products, packaging and/ or processes (e.g. variations or new marketing authorisations) to comply with upcoming legislation, particularly impacting companies with large portfolios.	✱ Changes to labelling on outer packaging and leaflets required by e.g.: the proposed **F-gas legislation** require regulatory approval. Most MDIs currently marketed are approved via national or decentralized procedures[84]. **Other relevant legislations: UWWTD, PPWR, Bans & restrictions, EUT, WFD, variations**

[82] Information Session 3 - Chemicals

[83] https://www.efpia.eu/news-events/the-efpia-view/statements-press-releases/60-000-fewer-clinical-trial-places-for-europeans-despite-global-surge-in-research-projects/

[84] *EFPIA Feedback on F-gases update of format of F-gas labels*, 4 June 2024

Impact	Illustrative examples

Increased timelines:
Authorisations required to utilise newly restricted chemicals can lead to business uncertainty, increase timelines to set up manufacturing in the EU, potentially reducing attractiveness of the EU compared to other markets that do not require these authorisations[85].

- The Authorisation process laid out in the **REACH regulation** is lengthy: it takes on average 24 months for a restricted substance to be authorised. In addition, multiple applications are launched for similar uses of the same substance, adding to the administrative and resource burden for companies, and there are uncertainties for the applicant over the entire process[86]
- The **essential use concept** governance has not been confirmed. If not carefully balanced and assessed, once integrated in a legislation, this concept could provide more uncertainty over the authorisation of a substance and reduce further the EU competitiveness.
- There is increasing regulatory burden and uncertainty, whereby REACH assessments can be incompatible with those from the EMA assessment (e.g. for specialised orphan medicinal product).
- Overall, there is a multiplicity of reviews and authorisations processes to go through (from agencies and notified bodies), increase the regulatory burden and the uncertainty as it is not always clear who takes the primacy.

Relevant legislations: REACH, EUC

[85] Information Session 3 - Chemicals

[86] https://echa.europa.eu/authorisation-process

Impact	Illustrative examples

The new regulatory requirements from the assessed legislations may impact sustainability reporting and the environmental performance of companies. **Perception of sustainability performance:** Companies may find it challenging to link their sustainability reporting with their overall business strategy[87], and demonstrating the impact of their sustainability actions if impacts of actions only materialise after 2-3 years. This may affect investor perceptions of companies' sustainability performance[88].	✱ Technical Screening Criteria within the **EUT** give a distorted picture of sustainable practices of companies. Thresholds required to be met by the pharmaceutical industry are not realistic nor achievable, because small molecules often cannot be replaced by biodegradable options, and the criteria dismiss current market conditions, which do not support the substantial R&D effort and cost of developing degradable alternatives for existing medicinal products. **Relevant legislations: CSRD, CS3D, EUT**
Data security & IP protection: Reporting and submission of additional data to maintain compliance with reporting requirements in legislations raises concerns around confidentiality, data security and intellectual property protection[89,90]. Over reporting remains a concern. The potential release of commercially sensitive data, whether intentionally (to comply with legislations), or unintentionally (due to data leak), may impact the competitiveness of Europe as a market if the perceived risk is too high[91,92]. If there are data breaches, it is unclear in many circumstances who is in the lead and where responsibilities lie.	✱ Potential requirement to provide actual quantities of products placed on the market to comply with **UWWTD**[93]. ✱ Potential requirement for multi-use chemicals if made available under the regulation establishing a common data platform on chemicals in **OSOA**[94]. ✱ Requirement to report on micropollutants contained within medicines under **SPM**. ✱ Possible requirement for data generated under the revised **SPM, UWWTD and PPWR legislations** to be included in the common data platform on chemicals under **OSOA**[95]. ✱ A study notification obligation without an R&D exemption (present REACH regulation, Recital 28 and Article 56) in **OSOA** will result in the disclosure of chemical identification information, on proprietary materials **Other Relevant legislations: CSRD, CS3D, EUT, REACH.**

[87] Information Session 1 - Climate and Circularity

[88] Information Session 1 - Climate and Circularity

[89] *April 2024 - Executive Summary OSOA common data platform analysis*

[90] *Executive summary OSOA common data platform – data requirements analysis*

[91] Information Session 2 - General Pharma

[92] Information Session 4 - Water

[93] EFPIA and AESGP feedback on the Commission Open Consultation on the Urban Waste Water Treatment Directive (UWWTD)

[94] *EFPIA response to the Commission public consultation on the proposal to establish a common data platform on chemicals*

[95] *EFPIA response to the Commission public consultation on the proposal to establish a common data platform on chemicals*

Impact	Illustrative examples

Member State interpretations: The lack of clarity and guidance on cost allocations for the proposed Extended Producer Responsibility (EPR) could disadvantage companies operating in EU countries with stricter interpretations or higher cost burdens[96] than other EU countries.	✱ **UWWTD**: Germany's Environment Agency estimates for quaternary treatment costs range from €885 to €1,025 million annually – four times higher than the Commission's figure of €238 million[97]. In the Netherlands, costs are up to six times more than the Commission's estimations. Estimates from EurEau, the European Federation of National Associations of Water Services, indicate costs ranging from three to over nine times higher than the Commission's numbers (between €3.6 and €11.3 billion per year). **Other relevant legislation: PPWR**
Administrative and resource burden: The generation, collection and reporting of additional environmental impact data will add an administrative and resource burden and cost to companies to maintain ongoing compliance with proposed legislations[98,99,100].	✱ Maintenance and audit of an Environmental Management System (EMS) under the proposed **IED**[101] ✱ Reporting to ECHA on SPM end uses, identity of polymers, estimated quantity of SPMs released into the environment and applicable derogations[102]. ✱ Data for approximately ~1000 APIs may need to be generated to satisfy the proposed **GPL:ERA** requirement to provide an ERA for medicinal products authorised prior to 2005[103]. ✱ Requirement for data generation in set up and functioning of the for EPR calculation system under the **UWWTD.** ✱ Resource issues need to be considered as of the availability of competent skills in the EU. ✱ The **CS3D** does not only require companies to perform due diligence over their own activities, but across their whole value chain. ✱ The **Taxonomy criteria** require companies to gather biodegradation data, e.g. for key human metabolites and their transformation products, which are very infrequently available. Such transformation studies come with very high costs, resource use and utilise valuable contract laboratory capacity. **Other relevant legislations: CSRD, CBAM, IED, WFD, Bans & restrictions (SPM).**

[96] Information Session 4 - Water

[97] European Regulatory Landscape: Impact of Access and Availability of Medicines, May 2024

[98] *EFPIA Briefing: REACH Restriction on synthetic polymer microparticles*, EFPIA, 25 September 2023

[99] Information Session 1 - Climate and Circularity

[100] Information Session 4 - Water

[101] *Revision of the Industrial Emissions Directive: Initial EFPIA Analysis*

[102] *EFPIA Briefing: REACH Restriction on synthetic polymer microparticles*, EFPIA, 25 September 2023

[103] *European Regulatory Landscape: Impact of Access and Availability of Medicines*, May 2024

Impact	Illustrative examples

Innovation & Competitiveness

The new regulatory requirements and processes may impact companies' investment in Europe and lead them to relocate elsewhere.

- Some restrictions (**PFAS**) are so far ranging that they make it impossible to manufacture APIs (30 % contain PFAS-moiety) or even comply with the analytical requirements for GMPs. Furthermore, PFAS ban on fluoropolymers would make manufacturing impossible resulting in manufacturing leaving Europe.
- Current **REACH Regulation**: First time use of a substance at EU-27 facility, past the sunset date - the Authorisation process has the potential to divert manufacturing operations away from EU facilities. In the case of OPE (e.g. octyl phenol ethoxylates used in biotechnology), the Authorisation process is diverting manufacturing operations to South Korea and North America

Other relevant legislations: CSRD, IED, WFD, Bans & restrictions.

6.3.2.3 MANUFACTURING & SUPPLY

This section provides examples of impacts identified across the four themes on manufacturing facilities, on the quality, production, packaging and distribution of marketed pharmaceutical products.

Impact	Illustration
	
New requirements from assessed legislations in the manufacturing and supply of medicines may impact patient access to said medicines. **Reduced treatment options:** The manufacturing processes to redesign medicinal products and packaging to comply with new regulatory requirements and (proposed) substances restrictions will be time and resources consuming. This may potentially lead to companies withdrawing some medicines from the market, possibly reducing treatment options for patients[104,105]. The availability of medicines may be impacted by proposed chemical bans/restrictions, including medicines on the EU Critical Medicines List.	✱ **Reformulation to remove TiO_2**, if possible, may take 3-5 years per product, and 7-12 years for the reformulation of a typical company's entire portfolio[106]. ✱ Over 600 essential medicines would be impacted by a **PFAS restriction**[107], as PFAS are a key component of APIs, raw materials and in manufacturing equipment, delivery devices, analytical equipment and packaging[108]. ✱ Many of the 60-70% of solid oral dosage form medicines that contain **TiO_2** may be discontinued or become subjects of shortages if a suitable alternative is not found[109,110]. If a suitable alternative is found, implications may exist on product's stability and, ultimately, shelf-life. **Other relevant legislations: Nitrosamines, F-gas.**
Medicines availability is impacted through restrictions and bans on materials; equipment and technologies	✱ In addition, **RAW - A recommendation from the joint Research centre of the Commission** to restrict the use of animal derived antibodies in the manufacturing process[111] will impact those critical therapeutics (including cancer treatments) and biomanufacturing that contain and require the use of animal derived antibodies[112].

[104] Information Session 3 - Chemicals

[105] Information Session 4 - Water

[106] https://www.ema.europa.eu/en/documents/other/annex-i-use-titanium-dioxide-excipient-human-medicines-industry-feedback-qwp-experts-ema-questions_en.pdf

[107] Evidence shows more than 600 essential medicines at risk, and manufacturing in Europe will 'grind to a halt' if wide-ranging chemical ban is implemented (efpia.eu)

[108] EFPIA Pharma Review, October 2023

[109] European Regulatory Landscape: Impact of Access and Availability of Medicines, May 2024

[110] Use of Titanium Dioxide as Excipient in Human and Veterinary Medicines and Identification of Alternatives: Industry Feedback to QWP Experts/EMA Questions Final Report Feb 2024

[111] https://publications.jrc.ec.europa.eu/repository/handle/JRC120199

[112] https://www.efpia.eu/media/580524/eara-efpia-antibody-report.pdf

Impact	Illustrative examples

New manufacturing and supply requirements may impact the sustainability reporting of medicines by companies and their environmental goals. **Supply chain vulnerability:** Bans and restrictions could affect the supply and use of raw materials[113], which can lead to manufacturers needing to rely on fewer suppliers, making the supply chain more vulnerable to disruption[114].	✱ A universal ban on **PFAS** based on environment and emission concerns will impact manufacturing[115] capabilities in Europe, as medicinal product manufacturing facilities are heavily dependent upon fluoropolymer components present in utilities, piping, equipment (process/utilities), & single use systems. **Other Relevant legislations: UNTPP, Bans & restrictions (SPM, Talc, PVC).**
Supply chain disruption: The potential reporting requirements for data or information requirements on materials from suppliers may temporarily disrupt the supply chain if there is a requirement to switch suppliers on this basis[116]. (There is also the potential for inaccurate data if not supplied by the supplier).	✱ As part of the **SPM restriction**, companies are required to report on their use of SPM and rely on suppliers to provide the information (end of use, generic information, quantity, estimated release in environment, etc). If suppliers (specifically non-EU) do not provide the necessary data or have the capacity to report the required information, companies may be required to swap suppliers and thus limiting the supply to various materials for the manufacturing of medicines. This may lead to disruptions in the supply chain. ✱ **Other relevant legislations: CS3D, CSRD, EUT, SPM**

[113] *A universal PFAS ban: availability of medicines, manufacturing, jobs and economic growth will be put at risk*, EFPIA

[114] Information Session 3 - Chemicals

[115] https://www.efpia.eu/media/jc1lcupo/annex-3_industrial-use-of-fluoropolymers-in-pharma-manufacturing_final.pdf

Impact	Illustrative examples

New requirements for the manufacturing and supply of medicines may affect innovation in Europe and competitiveness.

Increased costs and timelines: There may be higher manufacturing costs and timelines required to comply with proposed legislations, which could reduce the competitiveness of Europe as a manufacturing hub compared to other regions with a less burdensome regulatory landscape[117,118].

- The potential additional cost required for GMP inspections if MRAs are no longer valid under the proposed **GPL:GMP**[119,120].
- Testing of each packaging batch using recycled plastics under the proposed **PPWR**[121].
- Variations required where there are changes to manufacturing processes.
- Potential for unique product for Europe, increasing cost and decreasing flexibility.

Other relevant legislations: EUT, EQS, REACH, GPL

[116] Information Session 1 - Climate and Circularity

[117] Information Session 1 - Climate and Circularity

[118] Information Session 3 - Chemicals

[119] Information Session 2 - General Pharma

[120] *Good Manufacturing Practices (GMP) – important points to consider in current context of General Pharmaceutical Legislation (GPL) Revision*, January 2024

[121] *EFPIA White Paper on pharmaceutical packaging*

6.3.2.5 Launch & Availability

This section provides examples of impacts identified across the four themes on how the assessed legislations impact the activities related to the initial launch, subsequent availability and continuity of supply of a medicinal product on the market:

Impact	Illustration
New requirements from the assessed legislations regarding the launch and the availability of medicines to patients will impact their access to said medicines. **Reduced patient trust and usability:** changes in physical appearance, composition, and packaging for present and future medicinal products could reduce patient trust and effective usability.	✱ Changes in physical appearance of products (such as a colour change due to TiO_2 removal) could reduce patient trust in the product (possibly leading to reduced patient adherence)[122] ✱ Change in the product or product device (e.g., F gas metered dose inhalers) due to chemical bans and restrictions could reduce patient trust in the product. **Other relevant legislations: PPWR, Bans & restrictions (PFAS, PVC).**
Patient access to medicines could be reduced if companies are required to reduce population consumption to remain below environmental thresholds. ✱ Where limits are under consideration for specific active ingredients, companies may reduce quantity of medicines supplied to the European market to comply with the legislations and remain under the thresholds, thus impact access to medicines. ✱ Products may be removed from the market if marketing authorisations are revoked due to an unfavourable environmental risk assessment as part of the pharmaceutical legislation. Developing more sustainable products may not be scientifically feasible as active substances in medicines are supposed to have persistent or therapeutic effect, thus leading to exclusion of EU patients from an effective product. ✱ Complying with certain legislations may mean some products are no longer economically viable and may be withdrawn from the market.	✱ The **WFD (ground, surface water and Environment Quantity Standards) legislation** proposes to limit the total pharmaceuticals to very low threshold levels and also includes in the list for priority substances for the first time pharmaceuticals used as painkillers, anti-convulsants or antibiotics[123]. On a contradictory note, some of these are in parallel have been subject to recent shortages in Europe. ✱ **UWWTD** provisions exempt a producer from contributing to the EPR scheme where the total amount of substances contained in the products that that producer places on the EU market is less than 1000kg per year. Companies may reduce supply of those products to meet the minimum threshold and thus impact access to medicines. ✱ The costs generated by the **UWWTD EPR system** could mean that some products put on the market would no longer be economically viable and thus be withdrawn from the market. ✱ As part of the **GPL:ERA** medicinal products can see their marketing authorisation revoked due to an unfavourable environmental risk assessment.

[122] Information Session 3 - Chemicals

[123] https://environment.ec.europa.eu/topics/water/surface-water_en#:~:text=In%20October%202022%20the%20Commission,to%20nature%20and%20human%20health.

Impact	Illustration

Increased healthcare costs: Where over-the-counter medications are reclassified as prescription-only due to environmental concerns, healthcare costs could increase due to increased demand for healthcare professionals and accessibility to these medications could decrease[124,125].

- Article 51 of the **GPL** proposal requires medications to be subject to a prescription if it is antimicrobial or contains an active substance that is considered persistent, bio-accumulative, toxic and/or mobile (or a specific mix of 2-3 of those 4 conditions)[126].

Impact	Illustration

The new requirements from the assessed legislations related to the availability of medicines may impact the activities on sustainability reporting and the efforts to develop greener medicines.

A number of these requirement will affect medicinal products in the launch phase and after they have been put on the market. Some of them could lead to additional pollution, waste or larger climate impacts.

- **UWWTD**: The extensive set up and running of quaternary wastewater treatment facilities across the EU may increase greenhouse gas emissions
- Alternative materials to plastics, such as glass and paper, may have a higher carbon footprint or consume more water during production, such as paper. Finding materials and formats that meet recycling and lower carbon benefits is challenging.

Relevant legislation: PPWR, Restrictions and bans

[124] Assessment of main provisions & key EFPIA recommendations on revision of the pharmaceutical package, October 2023

[125] Information Session 2 - General Pharma

[126] Assessment of main provisions & key EFPIA recommendations on revision of the pharmaceutical package, October 2023

Impact	Illustration

New legislative requirements may impact the regulatory landscape of medicines. Diverging and conflicting legislative requirements with other global regions may affect continuity of supply on the market	✱ **PPWR** - Key markets like the USA do not accept using recycled materials in pharma; this may negatively impact exports and contradict collaborative drug approval efforts. ✱ **GPL** Proposed addition of new requirements for GMP inspections, such as environmental risks[127] undermines mutual recognition and collaborative assessment initiatives reversing recent progress at efficiency in these areas. ✱ Third countries' health authorities have opposed the **TiO_2 ban** and will not implement it as in the EU[128]. If the EU bans use in medicines, it will lead to global issues. **Other relevant legislations: Bans and restrictions (PFAS, PVC)**
Clear timely guidance – an increasing number of the regulatory provisions from the assessed legislations would require companies to monitor the use of certain substances once the product is put on the market. The current state of some of the guidance has led to uncertainty and unclarity for companies regarding what, when and where to report. Clear guidance is thus needed for companies.	✱ **SPM**: Commission is delayed in Q&A document to guide industries in the implementation of the new legislation. ✳ Ban in Regulation 2023/2055 could include intended for clinical trials. This effectively would prohibit clinical trials in Europe. This needs to be clarified ✳ Reporting: industry waiting for clarifications on requirements, what's in scope, Biodegradability and water solubility criteria etc ✱ **UWWTD**: guidance required on 'rapidly biodegradable', cost modulation etc ✱ **GPL:ERA**: Guidance on clarity on what can be interpreted as 'ERA is incomplete or insufficiently substantiated' or 'risk mitigation measures etc **Other relevant legislations: Bans and restrictions (PFAS, PVC)**

Perpetual Competitiveness concerns:
In addition to the above potential impacts, there are also possible impacts on investment decisions across the entire pharmaceutical value chain. Lack of clarity on certain legislations and their implementation (e.g. EUT, UWWTD, CSRD, CS3D), and the rapidly evolving legislative landscape within Europe may discourage investment in the life sciences industry[129,130,131,132]. Possible decreases in investment within the EU may potentially hinder pharmaceutical innovation in the region[133]. Expected reductions in perceived drivers of European competitiveness, such as data exclusivity and confidentiality, and increases in cumulative short timelines and costs of compliance may lead to a reduction in the competitiveness of Europe in pharmaceuticals.

[127] https://www.europarl.europa.eu/doceo/document/TA-9-2024-0221_EN.html

[128] https://www.ema.europa.eu/en/documents/other/annex-i-use-titanium-dioxide-excipient-human-medicines-industry-feedback-qwp-experts-ema-questions_en.pdf

[129] The role of regulators in mitigating uncertainty within the Valley of Death, Jaime Bonnin Roca, Eoin O'Sullivan, 2022

[130] Information Session 1 - Climate and Circularity

[131] Information Session 3 - Chemicals

[132] Information Session 4 - Water

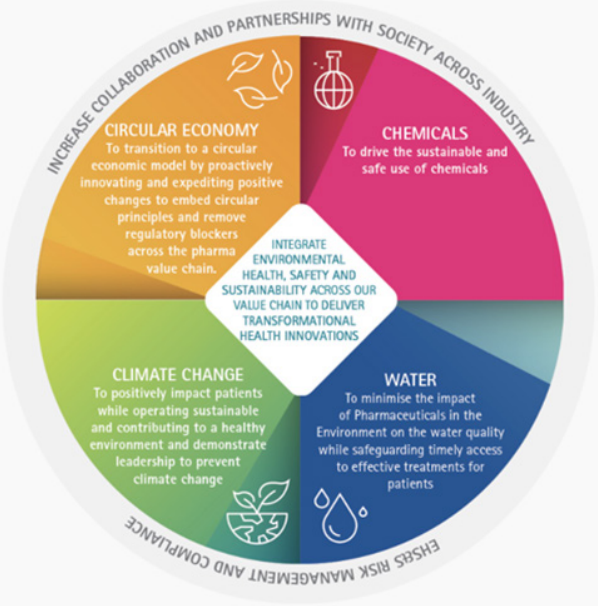
[133] Information Session 1 - Climate and Circularity

7. HOW INDUSTRY ALREADY RESPONDS TO SUSTAINABLE AND ETHICAL CHALLENGES

The innovative pharmaceutical industry supports the overall objective behind the European Green Deal policies as they address legitimate environmental or societal concerns. EFPIA member companies are already actively engaged in sustainability initiatives and always encourage appropriate use of evidence, science and risk-based approaches to environmental challenges and animal welfare. They also continually undertake initiatives to promote greater environmental responsibility.

CLEAR STEPS TOWARD A GREENER FUTURE

EFPIA and its members recognise the urgent need to address climate change and safeguard natural resources, given the profound impact on both human health and nature. We further acknowledge concerns of pharmaceuticals in the environment. It's essential to move away from traditional methods and adopt innovative practices that reduce our environmental impact. We strive to go beyond compliance on the targets set within the various EU legislative requirements as part of the EU Green Deal initiatives under the Zero Pollution, Circular Economy and Climate Action plans.



As leaders in the pharmaceutical sector, we are committed to taking decisive actions to reduce our environmental impacts across the value chain and contribute to building resilient and sustainable health system. We are leading the transition towards the decarbonisation in the pharmaceutical sector by setting ambitious science-based targets, investing in renewable energy, driving circularity, and collaborating with stakeholders.

How we commit to move forward:

- *Carbon Reduction Targets:* We pledge to set ambitious targets that are science-based to reduce our greenhouse gas (GHG) emissions across our operations and value chains while engaging our suppliers to do the same[134]. These targets will align with the goals outlined in the Paris Agreement to limit global warming. In addition, we strive to get these targets externally verified.

- *Invest in Renewable electricity and clean technology solutions:* We will improve energy efficiency and prioritise the transition to renewable energy sources to power our facilities and in the investment in low carbon clean tech solutions. We will explore opportunities for on-site renewable energy generation and investing in off-site renewable energy projects where feasible.[135]

- *Advance circularity[136]:* We aim to implement measures to improve resource efficiency and drive circularity throughout our operations and value chain. This includes designing products for reduced environmental impacts, optimising manufacturing processes and supply chains, improving waste management, fostering circularity solutions, prolonging the life of products, influencing the behaviours of patients, customers and stakeholders and implementing sustainable packaging and end of life solutions.

- *Collaboration and Knowledge Sharing:* We recognise that addressing climate change requires collective pre-competitive action. Therefore, we *aim to* identify opportunities to collaborate with other stakeholders, including other industry sectors, suppliers, authorities, regulators, academia, patients and civil society, to share best practices, research findings, and innovations in decarbonisation efforts. We will facilitate collaborative initiatives, such as industry-wide working groups and knowledge-sharing platforms, to foster innovation and collective problem-solving in decarbonisation efforts. We recognise the partnerships already established in the field of climate and health and aim to draw inspiration from this work.

- *Pharmaceuticals in the Environment:* We are committed to continue playing an active role in addressing concerns around risks associated with Pharmaceuticals in the Environment (PiE)[137]. Minimising the impact of medicines on the environment while safeguarding access to effective treatments for patients is a critical

[134] https://efpia.eu/media/gtbncsjc/survey.pdf

[135] https://www.efpia.eu/media/sydk5acr/white-paper-on-climate-change.pdf

[136] https://www.efpia.eu/media/htreo44j/white-paper-on-circular-economy.pdf

[137] https://www.efpia.eu/media/636524/efpia-eps-brochure_care-for-people-our-environment.pdf

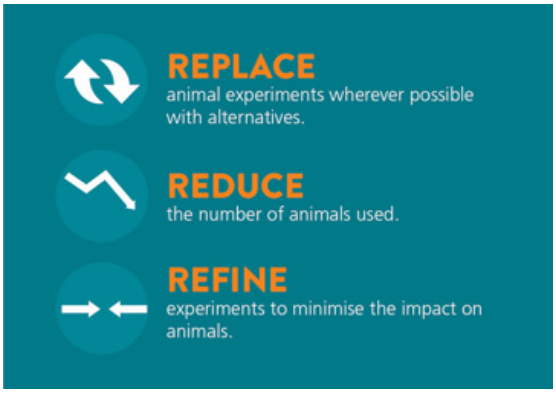
issue across all sectors of healthcare, environmental risk assessment plays an important role. We are continually engaging with stakeholders and across industry to enhance our processes and find new ways to detect the trace amounts of Pharmaceuticals in the environment, understanding their impact, prioritising APIs posing a potential risk to the environment and also further reducing discharges from manufacturing plants worldwide.

Industry supports an open dialogue and invites stakeholders including decision makers and regulators to progress on these commitments. EU medicines Regulators should prioritise the flexibility and support for innovation in the (re) development and supply of medicines to address climate, environment and sustainability targets.

TOGETHER, LET'S COMMIT TO THESE GOALS FOR A HEALTHIER PLANET.

COMMITMENT TOWARDS ANIMAL WELFARE

In addition to their environmental and climate commitments, EFPIA members are committed to the science-based phase-in of methods to replace the use of animals for scientific purposes and the deletion of animal tests which are obsolete or redundant. EFPIA members aim to lead progress on this by engaging in a wide range of practical activities to help drive the development, uptake and promotion of non-animal technologies (NATs) and new approach methodologies (NAMs) so that these can be phased-in as soon as it is scientifically possible to do so[138].



The pharmaceutical industry members of EFPIA:

- Are fully committed to the principles of 3Rs;
- Continue to support the objectives of the Directive 2010/63/EU on the protection of animals used for scientific purposes which has enhanced animal welfare standards and mandated the application of replacement, reduction and refinement across the EU while ensuring Europe remains a world leader in biomedical research;
- Will continue to strive to go beyond what is legally required and work to develop and validate systems leading to improved 3Rs, animal welfare and high-quality science and technologies in everyday practice and ultimately improve the lives of the people and animals that stand to benefit from the research. Training of staff will remain an essential element of good science and good welfare;
- Are committed to continue invest in collaborative research initiatives and projects to improve animal welfare and 3Rs, and support start-ups with expertise in new approaches under the Innovative Health Initiative (IHI);
- Will continue to work with regulators, the scientific community and civil society to improve implementation of the science and speed up regulatory acceptance of alternative methods in the EU and at a global level;
- Will strive to lead by example by disseminating beyond own department and own establishment to drive improvements in welfare and general quality of science;
- Will improve the systems in place working with academia, CROs, animal breeding and testing facilities to share good practices, new methodologies and lead by example by uptake of high 3Rs and animal welfare standards in the daily activities;
- Will be transparent in telling what we do and how we do it, to explain and justify where live animals are required and used and also inform on the work and commitment of companies to reduce the sectors reliance on animals;
- Will continue to identify, develop and implement their phase-in strategies and communicate on animal use through either dedicated webpages or CSR reports. Open communication and dialogue with the public are key to highlight our contribution to phasing-in replacement methods.

[138] https://www.efpia.eu/about-medicines/development-of-medicines/animal-use-and-welfare/

8. APPENDIX

8.1 Legislative areas

CLIMATE & CIRCULARITY

Legislations covered:

- EU Taxonomy for sustainable activities *(EUT)*
- Corporate Sustainability Reporting Directive *(CSRD)*
- Corporate Sustainability Due Diligence Directive *(CS3D)*
- Carbon Border Adjustment Mechanism *(CBAM)*
- Industrial Emissions Directive *(IED)*
- Packaging and Packaging Waste Regulation *(PPWR)*
- UN Treaty on Plastic Pollution *(UNTPP)*

GENERAL PHARMA

Legislations covered:

- General Pharmaceutical Legislation *(GPL)*
  a. Environmental risk assessment (GPL:ERA)
  b. Good Manufacturing Procedures (GPL:GMP)
- Roadmap to phase out animal testing *(RAW)*

CHEMICALS

Legislations covered:

- One Substance, One Assessment *(OSOA)*
- Essential Use Concept communication *(EUC)*
- Regulation on the registration, evaluation, authorisation and restriction of chemicals *(REACH)*
- Titanium Dioxide *(Bans & restrictions – TiO_2)*
- Per- and polyfluoroalkyl substances *(Bans & restrictions – PFAS)*
- Talc *(Bans & restrictions – Talc)*
- Octamethylcyclotetrasiloxane (D4), Decamethylcyclopentasiloxane (D5) and Dodecamethylcyclohexasiloxane (D6) *(Bans & restrictions – D4, D5, D6)*
- Bisphenol A *(Bans & restrictions – Bisphenol A)*
- Polyvinyl chloride *(Bans & restrictions – PVC)*
- Nitrosamines *(Bans & restrictions – Nitrosamines)*
- F-gas Regulation *(Bans & restrictions – F-gas)*
- Synthetic polymer microparticles (formally microplastics) *(Bans & restrictions - SPM)*
- Classification, labelling, and packaging of chemicals *(CLP)*

WATER

Legislations covered:

- Urban Wastewater Treatment Directive *(UWWTD)*
- Water Framework Directive *(WFD)*

8.2 Legislations and documents analysed

Legislation/ focus area	Abb.	Objectives of the legislations	Documents
Industry driven initiative			✱ Innovative pharmaceutical industry statement on COP28 Declaration on Climate and Health[139] ✱ Clear Steps Toward a Greener Future - Pharmaceutical Sector's Environmental Sustainability Statement[140] ✱ EFPIA public climate change survey[141] ✱ EFPIA Climate change white paper[142] ✱ EFPIA Circular economy white paper[143] ✱ Inter industry association eco-pharma-stewardship paper[144]
EU strategic agenda (European Commission Secretariat General)) **EU political priorities 2024 - 2029[145]** **EU competitiveness report[146]**		Sets out 3 priorities: A free and democratic Europe A strong and secure Europe A prosperous and competitive Europe ✱ bolstering the EU's competitiveness ✱ making a success of the green and digital transitions ✱ promoting an innovation- and business-friendly environment advancing together	EFPIA signs Antwerp declaration[147] EFPIA statement on competitiveness[148] EFPIA report on a competitiveness strategy for the life science sector[149]

[139] https://www.efpia.eu/news-events/the-efpia-view/statements-press-releases/innovative-pharmaceutical-industry-statement-on-cop28-declaration-on-climate-and-health/

[140] https://www.efpia.eu/news-events/the-efpia-view/statements-press-releases/clear-steps-toward-a-greener-future-pharmaceutical-sector-s-environmental-sustainability-statement/

[141] https://www.efpia.eu/media/gtbncsjc/survey.pdf

[142] https://www.efpia.eu/media/sydk5acr/white-paper-on-climate-change.pdf

[143] https://www.efpia.eu/media/htreo44j/white-paper-on-circular-economy.pdf

[144] https://www.efpia.eu/media/636524/efpia-eps-brochure_care-for-people-our-environment.pdf

[145] https://european-union.europa.eu/priorities-and-actions/eu-priorities/european-union-priorities-2024-2029_en

[146] https://commission.europa.eu/topics/strengthening-european-competitiveness/eu-competitiveness-looking-ahead_en

[147] https://efpia.eu/news-events/the-efpia-view/statements-press-releases/efpia-signs-the-antwerp-declaration/

[148] https://www.efpia.eu/news-events/the-efpia-view/statements-press-%20releases/efpia-swings-behind-council-s-call-for-a-european-%20competitiveness-deal/

[149] https://efpia.eu/media/fzkbhzoe/a-competitiveness-strategy-for-european-life-sciences.pdf

Legislation/ focus area	Abb.	Objectives of the legislations	Documents
Critical Medicines List[150] and Alliance[151] (HERA)	CMA	✱ Providing an inclusive and transparent consultative platform ✱ Focusing on critical medicines that face the greatest vulnerabilities, on the basis of the Commission supply chain vulnerability assessment[152] for a sub-set of substances listed on the Union list of critical medicines[153]. ✱ Identifying vulnerabilities in critical medicines supply chains. ✱ Pooling the expertise and resources of its members, to determine how vulnerabilities in the supply chains could be best addressed. ✱ Recommending priority actions and proposing new tools to address the identified challenges. In particular, the recommendations focus on mitigating structural risks and reinforcing supply by: ✳ encouraging diversification; ✳ boosting manufacturing. As such, the Alliance will play a key role in bolstering industrial competitiveness in the EU and strengthening its open strategic autonomy, in the best interest of EU citizens.	EFPIA joins Critical medicines alliance[154]

[150] https://ec.europa.eu/commission/presscorner/detail/en/ip_23_6377

[151] https://health.ec.europa.eu/health-emergency-preparedness-and-response-hera/overview/critical-medicines-alliance_en

[152] https://health.ec.europa.eu/publications/assessment-supply-chain-vulnerabilities-first-tranche-union-list-critical-medicines-technical-report_en

[153] https://www.ema.europa.eu/en/news/first-version-union-list-critical-medicines-agreed-help-avoid-potential-shortages-eu

[154] https://www.efpia.eu/news-events/the-efpia-view/statements-press-releases/critical-medicines-alliance-a-positive-collaboration-to-enhance-medicines-supply-chain-security-and-ensure-all-europeans-have-access-to-medicines-/#:~:text=Specifically%2C%20EFPIA%20will%20work%20within,therapies%2C%20MRNA%2C%20and%20bioproduction

Legislation/ focus area	Abb.	Objectives of the legislations	Documents
EU Taxonomy[155] for sustainable activities (DG FISC) Adopted Taxonomy legislation – 2020[156] Delegated acts adopted June 2022 Annex III[157] Publication of delegated acts in the Official Journal on 21 November 2023 and applied as of **1 January 2024**	EUT	Taxonomy is a transparency tool based on a classification system translating the EU's climate and environmental objectives into criteria for specific economic activities for private investment purposes	How the EU can incentivize environmental sustainability of new medicines[158] – blog by EFPIA
Corporate sustainability reporting directive (DG FISC) Adopted legislative act[159] in OJ (14 Dec 22) Adopted Delegated Act containing Agnostic reporting standards[160] (July 2023) Expected Delegated Act containing Sector Specific reporting standards, under development by the EFRAG (expected in 2025) Agnostic reporting standards[161] have been adopted as delegated act (July 2023) and apply since 1 January 2024 Sector specific standards are expected to be developed in 2025 and will apply as soon as adopted by the EU institutions (deadline 1 June 2026)	CSRD	The new rules will ensure that investors and other stakeholders have access to the information they need to assess the impact of companies on people and the environment and for investors to assess financial risks and opportunities arising from climate change and other sustainability issues.	

[155] https://finance.ec.europa.eu/sustainable-finance/tools-and-standards/eu-taxonomy-sustainable-activities_en

[156] https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex:32020R0852

[157] https://health.ec.europa.eu/publications/assessment-supply-chain-vulnerabilities-first-tranche-union-list-critical-medicines-technical-report_en

[158] https://www.ema.europa.eu/en/news/first-version-union-list-critical-medicines-agreed-help-avoid-potential-shortages-eu

[159] https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32022L2464

[160] https://eur-lex.europa.eu/legal-content/en/TXT/?uri=CELEX:32023R2772

[161] https://eur-lex.europa.eu/legal-content/en/TXT/?uri=CELEX:32023R2772

Legislation/ focus area	Abb.	Objectives of the legislations	Documents
Synthetic polymer microparticles (originally microplastics) (ECHA) Restriction legislation[162] adopted 25 September 2023 Legislation was officially adopted on 25 September 2023 and **came into force on the 17 October 2023** Still under preparation: Commission developing guidance on reporting member state consultation group kick off work in April 24	SPM	The restriction aims to restrict synthetic polymer microparticles - better known as microplastics - on their own or intentionally added to mixtures. ✱ Exceptions to the ban are granted to SPM used at industrial sites, in MP ✱ Reporting implications for medicinal products: ✳ Starting from 31 May 2027, suppliers of medicinal products and in-vitro devices containing SPM and being placed on the market for the first time, shall submit information to ECHA by 31 May of each year ✳ Starting from 17 October 2025, industrial downstream users utilizing SPM at industrial sites shall submit information to ECHA by 31 May of each year ✱ Medical devices included in restrictions There are concerns that there will be an impact on clinical trials as they may fall within the scope of the restriction	EFPIA position on microplastics 2019[163]
F-Gas (DG Climat) Adopted legislative act in OJ (7 Feb 2024) Guidance on the EMA website	F-Gas	Aims to: ✱ Reducing hydrofluorocarbons ✱ Expanding the quota system ✳ HFCs used in metered dose inhalers have been integrated into the quota system. Additional prohibitions on F-gas equipment, products and use of F-gases will apply in the future. ✱ Stricter rules to prevent emissions ✱ Facilitating better monitoring ✱ Capping EU production of HFCs	EFPIA submission (May 2024) to 'Have your say' consultation on F gas labelling[166]

[162] https://eur-lex.europa.eu/eli/reg/2023/2055/oj

[163] https://www.efpia.eu/media/554625/efpia-position-echa-microplastics-restrictions.pdf

[164] https://eur-lex.europa.eu/legal-content/EN/TXT/HTML/?uri=OJ:L_202400573

[165] https://www.ema.europa.eu/en/human-regulatory-overview/marketing-authorisation/product-information-requirements#labelling-requirements-for-metered-dose-inhalers-containing-fluorinated-greenhouse-gases-70134

[166] https://ec.europa.eu/info/law/better-regulation/have-your-say/initiatives/14209-F-gases-update-of-format-of-F-gas-labels/F3468695_en

Legislation/ focus area	Abb.	Objectives of the legislations	Documents
Carbon border adjustment mechanism Adopted legislative text[167] (10 May 2023)	CBAM	A CBAM aims to ensure equal treatment of domestic and imported goods by applying a charge to carbon emitted during the production of imported carbon-intensive goods, such as aluminium, cement, iron and steel. Its aim is to prevent carbon leakage	
Deforestation (DG Env) Adopted Legislative text[168]	EUDR	aims at banning import/trading/ export of specific commodities that might be linked to deforestation activities. Due diligence must be performed by importers, traders and exporters of these commodities. In case a product uses a commodity listed as ingredient, but it is not listed itself as commodity, the product is out of scope. Specific commodities with potential impact to pharm are: ✱ Pulp and paper derived materials e.g. printed paper/leaflets ✱ Palm oil and its derivatives ✱ Cattle derived blood ✱ Natural rubber	EFPIA signs Antwerp declaration

[167] https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32023R0956

[168] https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32023R1115&qid=1687867231461

Legislation/ focus area	Abb.	Objectives of the legislations	Documents
Pharma package (proposal for a directive on the union code relating to medicinal products for human use)[169] (GPL) (EMA) **Environmental Risk Assessment** **GMP** EP adopted reports (10 April 24): Directive[170] Regulation[171]	GPL GPL:ERA GPL:GMP	The European Commission has proposed revisions to the Pharmaceutical Legislation, with the view to bolster innovation in areas of unmet medical need, enhance the sector's global competitiveness, ensure timely, equitable and affordable access to medicines across the European Union (EU) and expand environmental protection	✱ Interassociation paper on extended environmental risk assessment[172] ✱ Responsible Manufacturing Effluent Management ✳ Interassociation Policy statement[173] on responsible manufacturing effluent management ✳ Technical guidance document[174] on responsible manufacturing effluent management ✳ Slide set on the guidance[175], including real world examples ✱ Eco-Pharmaco-Stewardship (EPS) initiative[176] – Care for people & our environment

[169] https://health.ec.europa.eu/medicinal-products/pharmaceutical-strategy-europe/reform-eu-pharmaceutical-legislation_en

[170] https://www.europarl.europa.eu/doceo/document/TA-9-2024-0220_EN.html

[171] https://www.europarl.europa.eu/doceo/document/TA-9-2024-0221_EN.html

[172] https://www.efpia.eu/media/677261/interassociation-paper-on-extended-environmental-risk-assessment.pdf

[173] https://www.efpia.eu/media/637030/policy-statement-iai-manufacturing-effluent-management.pdf

[174] https://www.efpia.eu/media/677262/technical-guidance.pdf

[175] https://www.efpia.eu/media/637032/iai-responsible-manufacturing-effluent-guidance-webinar.pdf

[176] https://www.efpia.eu/media/636524/efpia-eps-brochure_care-for-people-our-environment.pdf

Legislation/ focus area	Abb.	Objectives of the legislations	Documents
Urban Waste Water Treatment Directive **Corrigendum text[177] (ECHA)**	UWWTD	The Directive aims to protect human health and the environment from the effects of untreated urban wastewater. It aims to ✱ protect the environment from the adverse effects of urban wastewater discharges and discharges from certain industrial sectors ✱ ensure that domestic and industrial wastewater is effectively collected, treated and discharged Includes extended producer responsibility for the pharmaceutical sector ✱ From 2027 – 2033: pharmaceutical companies (along with the cosmetics sector) will have to pay the investments and the operational costs for the quaternary treatment across 27 MS. ✱ From 2033 - 2045: implementation of the quaternary treatment in the Member States.	EFPIA submission to Commission consultation on the legislative proposal[178] EFPIA press statement after vote in European Parliament Plenary[179]
Water Framework Directive. Priority Substances of pollutants surface and ground water (ECHA) COM 26 Oct 2022[180] EP Adopted report Sept 2023[181] Council adopted position on 19 June 2024[182]	WFD	Aims to update lists of water pollutants to be more strictly controlled in surface waters and groundwater. Pharmaceuticals included for the first time	EFPIA submission in response to the open consultation[183]

[177] https://data.consilium.europa.eu/doc/document/PE-85-2024-INIT/en/pdf

[178] https://ec.europa.eu/info/law/better-regulation/have-your-say/initiatives/12405-Water-pollution-EU-rules-on-urban-wastewater-treatment-update-/F3388408_en

[179] https://www.efpia.eu/news-events/the-efpia-view/statements-press-releases/efpia-response-to-the-european-parliament-endorsement-of-the-political-agreement-on-uwwt-directive/

[180] https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A52022PC0540

[181] https://www.europarl.europa.eu/doceo/document/TA-9-2023-0302_EN.html

[182] https://www.consilium.europa.eu/en/press/press-releases/2024/06/19/surface-water-and-groundwater-council-agrees-negotiating-mandate-to-update-list-of-pollutants/

[183] https://ec.europa.eu/info/law/better-regulation/have-your-say/initiatives/12662-Integrated-water-management-revised-lists-of-surface-and-groundwater-pollutants/F3388409_en

Legislation/ focus area	Abb.	Objectives of the legislations	Documents
Corporate sustainability due diligence directive (DG FISC) **On 25 July 2024, the Directive on (Directive 2024/1760[184]) entered into force**	CS3D	The aim of this Directive is to foster sustainable and responsible corporate behaviour in companies' operations and across their global value chains. The new rules will ensure that companies in scope identify and address adverse human rights and environmental impacts of their actions inside and outside Europe.	Joint statement[185]
CLP of chemicals - Classification, labelling and packaging[186] (ECHA) Corrigendum document Sept 24 Delegated act on new hazard classes (ED, PMT) published 19 Dec 2022[187]	CLP	With the CLP Regulation, the EU aims to protect workers, consumers and the environment as well as the free movement of substances, mixtures and articles. The regulation: ✱ requires manufacturers, importers or downstream users of substances or mixtures to classify, label and package their chemicals appropriately before placing them on the market ✱ establishes legally binding hazard identification and classification rules ✱ sets out common rules on labelling for consumers and workers to enable them to make informed decisions when purchasing or using dangerous products	EFPIA submission[188] to the public consultation EFPIA Survey results[189]

[184] https://eur-lex.europa.eu/eli/dir/2024/1760/oj

[185] https://www.amchameu.eu/system/files/position_papers/23-05-25_joint_business_community_statement_on_cs3d_proposal_-_due_diligence_0.pdf

[186] https://ec.europa.eu/info/law/better-regulation/have-your-say/initiatives/12975-Revision-of-EU-legislation-on-hazard-classification-labelling-and-packaging-of-chemicals_en

[187] https://environment.ec.europa.eu/publications/clp-delegated-act_en

[188] https://ec.europa.eu/info/law/better-regulation/have-your-say/initiatives/12975-Revision-of-EU-legislation-on-hazard-classification-labelling-and-packaging-of-chemicals/F3392022_en

[189] https://www.efpia.eu/media/676623/efpia-report-on-api-hazard-classes.pdf

Legislation/ focus area	Abb.	Objectives of the legislations	Documents
Industrial Emissions Directive[190] (ECHA) Sets out 3 priorities:	IED	Is the main EU instrument to reduce these emissions into air, water and land, and to prevent waste generation from large industrial installations and intensive livestock farms (pig and poultry). The latest rules will help promote innovation in new and emerging technologies and foster material efficiency and decarbonisation by encouraging greener practices. Covers the manufacturing of pharmaceutical products including intermediates	EFPIA signs Antwerp declara
Packaging and Packaging Waste Regulation (ECHA) COM proposal 30 Nov 2022[191] Provisional agreement[192]	PPWR	Legislation lays down measures to prevent the production of packaging waste, and to promote reuse of packaging and recycling and other forms of recovering packaging waste. pharmaceuticals in scope All packaging placed on the market in the Community and all packaging waste	EFPIA submission[193] to commission consultation

[190] https://environment.ec.europa.eu/topics/industrial-emissions-and-safety/industrial-emissions-directive_en

[191] https://environment.ec.europa.eu/publications/proposal-packaging-and-packaging-waste_en

[192] https://data.consilium.europa.eu/doc/document/ST-7859-2024-INIT/en/pdf

[193] https://ec.europa.eu/info/law/better-regulation/have-your-say/initiatives/12263-Reducing-packaging-waste-review-of-rules/F3405904_en

Legislation/ focus area	Abb.	Objectives of the legislations	Documents
One Substance, One Assessment (ECHA, EFSA, EMA) Horizontal legislative proposal in form of omnibus published 7 December: **Proposal for a Regulation** establishing a common data platform on chemical[194] **Proposal for a Regulation** re-attribution of scientific and technical tasks and improving cooperation among Union agencies in the area of chemicals[195] Proposal for a Directive re-attribution of scientific and technical tasks to the European Chemicals Agency[196] Waiting for adoption: Proposal for Regulation for a basic regulation of the European Chemicals Agency[197]	OSOA	This initiative aims to improve access to chemicals data by removing technical and administrative obstacles. This is based on the principle that data should be easy to find, share and reuse, as well as be interoperable and secure. The initiative will make it easier to access and use all available data and will increase transparency. It will also enable EU and national authorities, where necessary, to commission testing and monitoring of chemical substances as part of the regulatory framework	EFPIA response to the open consultation on the proposals[198]

[194] https://environment.ec.europa.eu/publications/proposal-regulation-establishing-common-data-platform-chemicals_en

[195] https://environment.ec.europa.eu/publications/proposal-regulation-re-attribution-scientific-and-technical-tasks-and-improving-cooperation-among_en

[196] https://environment.ec.europa.eu/publications/proposal-directive-re-attribution-scientific-and-technical-tasks-european-chemicals-agency_en

[197] https://ec.europa.eu/info/law/better-regulation/have-your-say/initiatives/13554-European-Chemicals-Agency-proposal-for-a-basic-regulation_en

[198] https://ec.europa.eu/info/law/better-regulation/have-your-say/initiatives/13459-Chemical-safety-better-access-to-chemicals-data-for-safety-assessments/F3461642_en

Legislation/ focus area	Abb.	Objectives of the legislations	Documents
Ecodesign for sustainable products regulation[199] (ECHA)	ESPR	The ESPR[200] aims to significantly improve the circularity, energy performance and other environmental sustainability aspects of products placed on the EU market. By doing so, a significant step will be taken towards better protecting our planet, fostering more sustainable business models and strengthening the overall competitiveness and resilience of the EU economy. A sustainable product is likely to display one or more of the following characteristics: ✱ Uses less energy, Lasts longer, Can be easily repaired, Parts can be easily disassembled and put to further use, Contains fewer substances of concern, Can be easily recycled, Contains more recycled content, Has a lower carbon and environmental footprint over its lifecycle	EFPIA signs Antwerp declara
UN Treaty on Plastic Pollution Main text: ✱ Zero draft text of the international legally binding instrument on plastic pollution, including in the marine environment[201] ✱ Revised draft text of the international legally binding instrument on plastic pollution, including in the marine environment[202]	UNTPP	There is currently no dedicated international instrument in place designed specifically to prevent plastic pollution throughout the entire plastics lifecycle. The aim is to develop an international legally binding instrument on plastic pollution, including in the marine environment, based on a comprehensive approach that addresses the full lifecycle of plastics.	IFPMA paper[203] (EFPIA has cosigned)

[199] https://commission.europa.eu/energy-climate-change-environment/standards-tools-and-labels/products-labelling-rules-and-requirements/ecodesign-sustainable-products-regulation_en

[200] https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32024R1781&qid=1719580391746

[201] https://wedocs.unep.org/bitstream/handle/20.500.11822/43239/ZERODRAFT.pdf

[202] https://wedocs.unep.org/bitstream/handle/20.500.11822/44526/RevisedZeroDraftText.pdf

[203] https://www.ifpma.org/wp-content/uploads/2024/04/2404_Position-Paper_Plastics-Instrument_INC-4_IFPMA.pdf

Legislation/ focus area	Abb.	Objectives of the legislations	Documents
Essential Use Concept (DG Grow, DG Env, ECHA) Commission communication published 22/4/24[204]	EUC	Communication defines and develops the "essential use concept" as part of the CSS. Defined as "A use of a most harmful substance is essential for society if the following two criteria are met: (1) That use is necessary for health or safety or is critical for the functioning of society, and (2) there are no acceptable alternatives. Presently there are no legal effects until specific legislation contains a legal definition of essential uses of substances. Currently, the concept is not part of the REACH Regulation (incl. PFAS Restriction proposal). Yet, its interpretation might support decision-making processes.	EFPIA paper on Essential use[205]

[204] https://op.europa.eu/en/publication-detail/-/publication/90926c62-0365-11ef-a251-01aa75ed71a1/language-en

[205] https://www.efpia.eu/media/636867/efpia-paper-on-essential-uses-oct-2021.pdf

Legislation/ focus area	Abb.	Objectives of the legislations	Documents
REACH legislation revision[206] (DG Grow, DG Env, ECHA) Revision expected in 2026	REACH	The REACH Regulation aims to: ✱ ensure a high level of protection of human health and the environment against harmful substances ✱ assess the safety of chemical substances in use in the EU ✱ promote innovation and competitiveness ✱ promote alternative (non-animal) methods for the assessment of the hazards of substances Present legislation: Pharmaceuticals in scope: R&D, Manufacture, placing on the market or use of substances and mixtures Under revision, Medicines expected to be impacted: Revision of the registration requirements; Simplifying communication in the supply chains; Revision of the provisions for dossier and substance evaluation; Reforming the authorisation process; Reforming the restriction process; and Revision of provisions for control and enforcement	EFPIA response to Commission roadmap on chemicals strategy for sustainability 2020[207]

[206] https://ec.europa.eu/info/law/better-regulation/have-your-say/initiatives/12959-Chemicals-legislation-revision-of-REACH-Regulation-to-help-achieve-a-toxic-free-environment_en

[207] https://www.efpia.eu/media/554626/efpia-response-to-commission-s-sustainable-chemicals-strategy-roadmap.pdf

Legislation/ focus area	Abb.	Objectives of the legislations	Documents
Roadmap to phase out animal testing (DG Grow, DG Envi, DG RTD, DG Sante, EMA, ECHA, EFSA) Commission Communication on roadmap[208] published 25/7/23 Roadmap to be published 2026	RAW	The commission will: ✱ continue to apply and enforce the animal testing ban in the framework of the EU Cosmetics Regulation; consider the need for legislative changes to further clarify the interface between the EU Cosmetics and REACH Regulations based on the outcome of an ongoing judicial review; ✱ kick off work on a roadmap towards replacing animal testing in chemical safety assessments, with multiple actions and a step-by-step path to replacing animal testing, involving all relevant stakeholders; ✱ initiate a series of actions to accelerate the reduction of animal testing in research, education and training, including exploratory workshops, and sustaining new training initiatives for early career scientists; continue to support research on alternatives to animal testing with EU funding.	EFPIA website: Animal Use and Welfare[209] Industry publication on 3Rs[210] Industry Pioneers the Contribution of Substance Data to decrease animal testing[211]
Titanium Dioxide (EFSA) Regulation 2022/63[212]	TiO_2	From 7 August 2022, bans the use in food The Commission shall, following consultation on the European Medicines Agency, review the necessity to maintain titanium dioxide (E 171) or to delete it from the Union list of food additives for the exclusive use as colour in medicinal products in Part B of Annex II to Regulation (EC) No 1333/2008 by Feb 2025	Industry report to EMA 2021[213] Industry report of Feb 2024 is not yet public

[208] https://single-market-economy.ec.europa.eu/publications/communication-commission-european-citizens-initiative-eci-save-cruelty-free-cosmetics-commit-europe_en

[209] https://www.efpia.eu/about-medicines/development-of-medicines/animal-use-and-welfare/

[210] https://www.sciencedirect.com/science/article/pii/S0273230024001247

[211] https://www.efpia.eu/news-events/the-efpia-view/statements-press-releases/industry-pioneers-the-contribution-of-substance-data-to-decrease-animal-testing/

[212] https://eur-lex.europa.eu/eli/reg/2022/63/oj

[213] https://www.ema.europa.eu/en/documents/other/annex-i-use-titanium-dioxide-excipient-human-medicines-industry-feedback-qwp-experts-ema-questions_en.pdf

Legislation/ focus area	Abb.	Objectives of the legislations	Documents
Per- and polyfluoroalkyl substances (ECHA) ECHA Restriction Proposal[214] published on 7 February 2023 Commission proposal expected in 2025	PFAS	Universal PFAS ban with some proposed derogations - all medical products, manufacturing, R&D, devices, packaging impacted	EFPIA submission 24 Sept 23 ✱ Report: EFPIA response to the ECHA consultation on the proposal for a universal ban on PFAS[215] ✱ Annex 1: EFPIA SEA report prepared by EPPA[216] ✱ Annex 2: Human Health Medicinal Products Sector Survey - Impact of Proposed PFAS Restriction on Patient Access to Medicines & EU Strategic Autonomy[217] ✱ Annex 3: ISPE_Industrial Use of Fluoropolymers & Fluoro-Elastomers in Pharmaceutical Manufacturing Facilities[218] ✱ PFAS Infographic[219]
Talc (ECHA) Proposal for Harmonised Classification and Labelling for Talc (Mg3H2(SiO3)4), CAS 14807-96-6. File dossier[220]	Talc	ECHA recommends the following classification ✱ Carcinogen 1B, H350 (may cause cancer); and ✱ STOT RE 1, H372 (a substance that causes damage to lungs through prolonged or repeated exposure via inhalation).	EFPIA signs Antwerp declara
Octamethylcyclo-tetrasiloxane (D4), Decamethylcyclopen-tasiloxane (D5) and Dodecamethylcy-clohexasiloxane (D6) (ECHA) Proposal to list in Stockholm Convention on Persistent Organic Pollutants Restriction under the REACH regulation[221]	**D4, D5, D6**	REACH - restriction ✱ bolstering the EU's compe	EFPIA signs Antwerp declara

[214] https://echa.europa.eu/hot-topics/perfluoroalkyl-chemicals-pfas

[215] https://www.ema.europa.eu/en/documents/other/annex-i-use-titanium-dioxide-excipient-human-medicines-industry-feedback-qwp-experts-ema-questions_en.pdf

[216] https://www.efpia.eu/media/52ipvgfi/annex-1-efpia_sea_pfas_final.pdf

[217] https://www.efpia.eu/media/b1rcqvlt/annex-2-patient-impact-survey_human-health-associations.pdf

[218] https://www.efpia.eu/media/jc1lcupo/annex-3_industrial-use-of-fluoropolymers-in-pharma-manufacturing_final.pdf

[219] https://www.efpia.eu/media/k24nszud/pfas-infographic.pdf

[220] https://echa.europa.eu/registry-of-clh-intentions-until-outcome/-/dislist/details/0b0236e186f6f6b2

[221] https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=OJ:L_202401328

Legislation/ focus area	Abb.	Objectives of the legislations	Documents
Bisphenol A (EFSA) EFSA Report April 2023[222] EFSA/EMA joint report on scientific divergence: April 2023[223]		EFSA significantly lowered the tolerable daily intake (TDI) for BPA (which would have had a significant impact on medicines)	
Polyvinyl chloride (ECHA) Commission request to ECHA 2022[224] for an investigation report on PVC and its additives ECHA investigation report[225] on PVC and its additives November 2023 + Appendix: Appendix A + B[226], Appendix C[227], Appendix D[228], Appendix E[229], Appendix F[230] Amendment to Annex XV: DEHP as PVC plasticizer (2018)[231] (bis(2-ethylhexyl)phthalate),	PVC		
Nitrosamines (EMA) EMA nitrosamine Impurities[232] EMA Q&A Nitrosamines[233]		Nitrosamines are chemical compounds classified as probable human carcinogens on the basis of animal studies. There is a very low risk that nitrosamine impurities at the levels found in medicines could cause cancer in humans	EFPIA nitrosamine workflows[234]

[222] https://www.efsa.europa.eu/en/news/bisphenol-food-health-risk

[223] https://www.efsa.europa.eu/sites/default/files/2023-04/ema-efsa-article-30.pdf

[224] https://echa.europa.eu/documents/10162/17233/mandate_pvc_and_additives_rev_en.pdf/a860fd87-4231-5ed4-157b-f6cda1ee5832?t=1655721970557

[225] https://echa.europa.eu/documents/10162/17233/rest_pvc_investigation_report_en.pdf/98134bd2-f26e-fa4f-8ae1-004d2a3a29b6?t=1701157368019

[226] https://echa.europa.eu/documents/10162/17233/rest_pvc_investigation_report_appendix_a_b_en.pdf/5a1e8057-b576-73fd-e163-4587874349d3?t=1701157496271

[227] https://echa.europa.eu/documents/10162/17233/rest_pvc_investigation_report_appendix_c_en.pdf/1447558b-568c-235c-bd7a-b79fcbbe564f?t=1701157496727

[228] https://echa.europa.eu/documents/10162/17233/rest_pvc_investigation_report_appendix_d_en.pdf/ad8f3a8c-04fc-e5c6-abb8-91f24cf2f7d7?t=1701157496954

[229] https://echa.europa.eu/documents/10162/17233/rest_pvc_investigation_report_appendix_e_en.pdf/d2c07da7-b67a-465c-9bff-ec57d0b26dcf?t=1701157497228

[230] https://echa.europa.eu/documents/10162/17233/rest_pvc_investigation_report_appendix_f_en.pdf/5614b916-35b4-21b1-089c-1a2c4dd3934a?t=1701157497434

[231] https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32018R2005

[232] https://www.ema.europa.eu/en/human-regulatory-overview/post-authorisation/pharmacovigilance-post-authorisation/referral-procedures-human-medicines/nitrosamine-impurities

[233] https://www.ema.europa.eu/en/documents/opinion-any-scientific-matter/nitrosamines-emea-h-a53-1490-questions-answers-marketing-authorisation-holders-applicants-chmp-opinion-article-53-regulation-ec-no-726-2004-referral-nitrosamine-impurities-human-medicinal-products_en.pdf

[234] https://www.efpia.eu/media/676632/efpia-nitrosamines-quality-risk-management-workflows-sep-2022.pdf

A universal PFAS ban: availability of medicines, manufacturing, jobs and economic growth will be put at risk

efpia

The pharmaceutical industry shares concerns about the environmental impact of PFAS[1]. However, PFAS is a broad non-specific term which does not inform whether a compound is harmful, and not all PFAS present the same risks[2] to the environment or health. The potential impact of a Europe-wide ban on PFAS in pharmaceutical products, packaging and operations is significant:

- The pharmaceutical industry relies on PFAS for **safe manufacturing, distribution and use** of medicinal products.
- The proposed derogation for PFAS Active Pharmaceutical Ingredients (APIs) does not derogate medicinal products, and only applies to **less than 10% of medicinal products in the EU market impacted by the ban[3]**.

We need strategic planning and alternative approaches to avoid disruptions in patient care.

Impact on patient access to medicines

98%
of the Market Authorisations of innovative medicines would need to be amended

93%
of the EU's active substance manufacturing relies on fluoropolymers[4]

>70%
of critical medicines in European Member States could be in short supply

Examples of the widespread impact:

R&D → **Manufacturing** → **Distribution & Use**

Laboratory
Equipment, Instruments, Piping

Chemicals
APIs, Starting materials, Intermediates, Process materials

Production equipment
Pipes, Gaskets, Caps, Valves, Injector, Degasser Filters, Refrigerants, Lubricants

Packaging
Stoppers, Blisters

Storage & transport equipment
Plastics, Coatings, Refrigerants

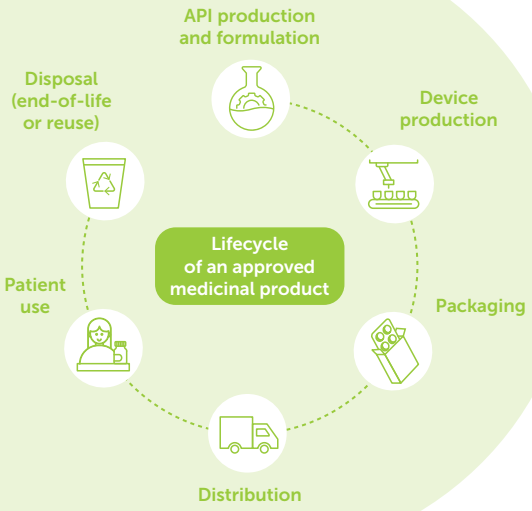
Application
Medical device, Drug delivery devices

Our recommendations

- Derogations until suitable alternative solutions are commonly agreed and qualified
- Develop partnerships throughout supply chains to better manage emissions
- Global health authorities expedite approvals of suitable fluorine-free alternatives

PFAS derogations ensure uninterrupted access to key medicines in pharmaceutical production and supply

The challenges



- Not all PFAS substances present **the same human health and environmental risk**.
- The basis for a restriction under REACH must be a profound hazard and risk assessment including socio-economic and risk-benefits. Restrictions on uses of substances which do not pose a risk is **not in line with the principles of REACH**.
- The scope of the EU Restriction deviates from other jurisdictions. This broad-brush approach impacts patients globally and puts EU-based companies and associated manufacturing at a **major competitive disadvantage**.
- Derogations do not allow **sufficient time** to identify suitable alternatives and further develop waste treatment technology and analytical methods.
- Pharmaceutical production in EEA will be impacted by **shortage of key raw materials** if suppliers cannot produce or import into the EEA.

Strategic Autonomy – strong pharmaceutical manufacturing footprint in Europe

1 million people
are working in the pharmaceutical manufacturing sector in the EU-27[5]

EEA production of medicinal products amounts to **€226.4 billion**. Europe is the 2nd largest market representing **22.4% share** of the world pharmaceutical (prescription) market[6]

Without an exemption for medicines and derogations for the supply chain, the proposed restriction contradicts other EU policy objectives.

Pharmaceutical industry supports substitution

Replacing PFAS-containing materials in a highly regulated sector like the pharmaceutical one is challenging:

- in most cases **no alternatives are currently available**;
- available alternatives must be analysed for their superior environmental performance and must not compromise patient safety;
- when a viable and scalable alternative is identified, **implementation will require time and collaboration** amongst different stakeholders in the value chain, including regulatory procedures.

Fluoropolymers[7] are highly resistant to heat, chemicals, and degradation. Potential replacements that provide the same benefits will be hard to find and may also be persistent in the environment.

Packaging materials and **drug delivery devices** specified in the marketing authorisation of a medicinal product may contain PFAS components. To ensure product quality, medicinal products regulation mandates toxicological evaluations, extractive and leachable studies, and product stability evaluations. Regulatory requirements will apply to any suitable alternative.

1 The PFAS (per- and polyfluoroalkyl substances) Ban or Restriction, which was created by five national authorities (Germany, the Netherlands, Sweden, Norway and Denmark) is currently being assessed by ECHA (European Chemicals Agency).
2 Certain PFAS have been identified as environmental pollutants, resulting in protective measures e.g., drinking water standards. This substance group, includes short and long chain fluorosurfactants or telomers.
3 Human Health Medicinal Products Sector Survey - Impact of Proposed PFAS Restriction on Patient Access to Medicines & EU Strategic Autonomy.
4 A wide range of therapeutic areas could be impacted e.g. cardiovascular disease, chronic respiratory disease, cancer, diabetes and mental health disorders but to name a few. The sector survey identifies over 600 medicines on the WHO Essential medicines list. Member State "Critical Medicines Lists" e.g. 78% of the critical medicines list in Norway could be impacted by the proposed Restriction.
5 Employment data for European countries can be obtained from Eurostat here: Statistics | Eurostat (europa.eu).
6 the-pharmaceutical-industry-in-figures-2023.pdf (efpia.eu).
7 "Fluoropolymers" represent a distinct subset of fluorinated polymers, based on a carbon-only polymer backbone with F atoms directly attached to it, e.g. polytetrafluoroethylene (PTFE); though some fluoropolymers also have Cl or O directly attached to the backbone. [Buck et al (2011) **Perfluoroalkyl and polyfluoroalkyl substances in the Environment: Terminology, Classification and Origins**]

Building a healthier and more environmentally sustainable future

efpia

A collaborative approach for the success of the EU Green Deal

The innovative pharmaceutical industry acknowledges the need to **address climate change and safeguard natural resources** ensuring well-being of the environment and human health.

We pledge to support the transition to circular economy for the pharmaceutical sector and reduce the industry's carbon footprint while safeguarding patient access to medicines and the future competitiveness of the industry.

Clear steps towards a greener future

Our members aim to take actions across all operations to reduce their environmental impact and contribute to **building resilient and sustainable health systems**.

Carbon reduction targets: Companies are setting targets to reduce their greenhouse gas emissions across our operations while engaging their suppliers to do the same.

- **Set climate policies**
- Annually and publicly **disclosed progress towards CO_2 emission reduction targets**
- Increase the **share of renewable energy**
- Set CO_2 reduction targets based on science
- Contribute to **reducing energy consumption** and **increased energy efficiency**

In only two years, EFPIA members[1] reduced their CO_2 emissions by **10%**

All companies indicate long-term targets for CO_2 emission reduction, and more than **60%** have short term targets

1. https://www.efpia.eu/media/gtbncsjc/survey.pdf

Investing in renewable electricity and clean technology solutions[2]: Companies are improving energy efficiency and prioritising the transition to renewable energy sources to power their facilities.

Advancing circularity[3]: Companies are implementing measures to improve resource efficiency and drive circularity throughout their operations and value chain. This includes designing products for reduced environmental impacts, optimising manufacturing processes and supply chains, and improving waste management.

Each year millions of injections pens are produced worldwide. After use many end up as waste. Novo Nordisk, Eli Lilly, Sanofi and Merck, together with 9 partners, collaborate on recovering injection pens from the Danish market. They are now expanding across other Member States.

Green-Collaboration and knowledge sharing: Companies are collaborating with other stakeholders to make healthcare systems more sustainable, including other industry sectors, suppliers, authorities, regulators, academia, patients and civil society, to share best practices, research findings, and innovations in sustainability efforts.

Pharmaceuticals in the environment[4]: Companies are taking steps into addressing concerns around risks associated with pharmaceuticals in the environment. Minimising the impact of medicines on the environment while safeguarding access to effective treatments for patients is critical. Industry proposes the extended environmental risk assessment to strengthen current processes.[5]

Several healthcare stakeholders (industry, healthcare professionals and student organisations) jointly developed **#medsdisposal.eu**, an online communication campaign aimed at raising public awareness on the appropriate use, storage and disposal of medicines

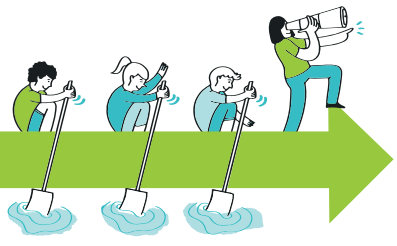
The IHI **PREMIER** project brings together a world-leading multi-disciplinary consortium composed of 25 partners from the public and private sectors working to contribute to a **sustainable future by proactively managing the environmental impact of medicines**.

A dedicated Competitiveness Strategy for European Life Sciences[6]

There have been an increasing number of environmental policies, legislative and non-legislative proposals, at EU-level stemming from the EU Green Deal package. **Industry supports the overall objective behind those policies**. However, these measures can have unintended negative consequences on highly regulated sectors, such as the pharmaceutical sector. Collaboration between policymakers and the industry is needed to ensure future measures drive sustainability efforts while not hindering the **availability of medicines to patients** or the **sustainability and strategic autonomy of Europe's pharmaceutical and healthcare sector**.

A **Strategy for European Life Sciences** would **ensure policy coherence** and help Europe regain its position of world-leader in life sciences.

Over the coming months, we look forward to working together towards building a **healthier and more environmentally sustainable future**.



2 https://www.efpia.eu/media/sydk5acr/white-paper-on-climate-change.pdf
3 https://www.efpia.eu/media/htreo44j/white-paper-on-circular-economy.pdf
4 https://www.efpia.eu/media/636524/efpia-eps-brochure_care-for-people-our-environment.pdf
5 https://www.efpia.eu/media/677261/interassociation-paper-on-extended-environmental-risk-assessment.pdf
6 https://efpia.eu/media/fzkbhzoe/a-competitiveness-strategy-for-european-life-sciences.pdf

Delivering treatments to patients: The medicines manufacturing journey

efpia

Manufacturing includes all the operations and the quality controls that are required to produce and distribute an Active Pharmaceutical Ingredient (API) and medicinal product. It is a highly regulated process: at each step, quality assurance confirmation ensures that the product has been manufactured and tested in accordance with marketing authorisation applications, regulations and commitments. Once all requirements are met, a final certification can be given to release the product for wholesale distribution.

Manufacturing facilities must operate to strict standards and are regularly inspected by competent authorities. Besides the unproductive time during cleaning, each facility is often shut down for 2-8 weeks each year to ensure maintenance, equipment qualifications and the implementation of innovations, e.g. for sustainability. Local regulatory requirements are part of the global manufacturing process. This means that the same manufacturing process delivers the same product to patients living in different parts of the World.

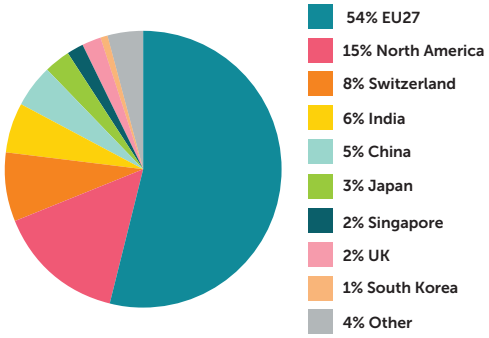
European manufacturing by the research-based pharmaceutical industry in figures

Today, the EU-27 is a leading location for the manufacturing of innovative medicines and related active ingredients, contributing to a trade surplus of 158 billion euros in 2023[1] and continued supply to patients. The changing policy environment may put this contribution at risk.

€363 billion (EFPIA total): The value of pharmaceutical production in Europe in 2022[2]

€158 billion: Trade surplus of medicinal and pharmaceutical products in 2023[3]

64% of APIs are manufactured in Europe (EU-27, Switzerland, UK)[4]



Innovative manufacturing is key to continue to meet patients' needs

Manufacturing enables access to medicines

The research-based pharmaceutical industry is constantly making investments in innovative manufacturing technologies such as continuous processing, automation, modular/mobile manufacturing for all medicines including vaccines, biologics, and advanced therapy medicines.

These innovations help improve supply reliability, meet regulatory requirements, as well as facilitating the green and digital transitions.

1,2,3 EFPIA, The Pharmaceutical Industry in Figures, 2024, https://efpia.eu/media/2rxdkn43/the-pharmaceutical-industry-in-figures-2024.pdf
4 EFPIA survey conducted in April 2021. Number of APIs (biological and chemical) sourced or manufactured per region of origin (irrespective of value/volume). A total of 16 EFPIA member companies submitted their input to the survey referring to in-patent and off-patent medicines
5 Deoxyribonucleic Acid
6 Physical separation of a chemical substance of interest from foreign or contaminating substances
7 Bulk materials include any materials that are dry, granular, powdery, or lumpy in nature

The Manufacturing process: Continuously optimised by implementing innovations

efpia

Our Commitment

Developing and manufacturing **high quality** and **greener medicines**.

Ensuring a stronger **European voice** while being at the forefront of developing and implementing **innovative products and processes**.

Defining a strategic vision to **proactively prevent medicines shortages** caused by disruptions to global manufacturing and supply chains.

Raw materials:

These are usually commercially available and sourced from plants, organic and inorganic compounds, oil, or DNA[5]. Many are sourced from the bulk chemical industry from suppliers all over the world, with the pharmaceutical industry representing a minor customer.

Starting material:
(12–28 weeks)

Some API starting materials may be commercially available; others may be manufactured/ modified for the specific use and require complex chemical transformations. For biotech products, a working cell bank is created from the master cell bank.

API manufacturing:
(1–10 weeks)

Manufacturing of the Active Pharmaceutical ingredient (API) from API starting materials is conducted in a carefully controlled manner which is critical to the production of high quality, safe, and efficacious medicinal product. API manufacturing may require many chemical and purification[6] steps. Each of these steps may be performed in a dedicated facility, and in a continuous or batch manufacturing mode. For many products, especially biological, manufacture may be in a sterile environment. Cleaning is necessary after each manufacturing cycle and may take additional 1-3 weeks.

Excipients, containers, and packaging materials added:

Usually commercially available from the chemical or food industry. They can also be designed and manufactured specifically for pharmaceuticals. Quality is controlled by adherence to pharmacopoeia or internal standards. Major changes in demand may take between 1–12 months to implement.

Pharmaceutical products:
(1–10 weeks)

These are manufactured from the API with excipients towards 'bulk'[7] material and further processed into containers or devices. Conditions to ensure sterility are applied when required (e.g., for injectable products).

Devices used:
(as applicable)

Devices (e.g., inhalers, pre-filled syringes, on-body injectors) may be used for better patient experience. Where medical devices are required, they are manufactured and controlled to predefined specifications.

Medicinal product:
(1–2 weeks)

The packaging step prepares the final drug product to be delivered to patients. This step is applied to comply to country specific rules, including labels, packaging, and specific content for each country, including leaflets. Repackaging might occur, e.g., if the product is needed in another country or there is a change in the leaflet.

Distribution to patients:
(1–4 weeks)

The finished product gets delivered to different owners (e.g., distributors, wholesalers, pharmacies or directly to local health authorities), ensuring all Good Distribution Practices are respected. The distribution chain of medicinal products needs careful maintenance to ensure their quality, potency, and purity.

Call to action

Promote a **policy environment that fosters R&D in Europe** – the first step to locating advanced manufacturing in the bloc.

Streamline and harmonize **regulatory requirements** to support innovation.

Build a collaborative, best-practice led approach to **sustainable manufacturing** to address environmental challenges.

efpia
European Federation of Pharmaceutical Industries and Associations

EFPIA Brussels Office
Neo Building,
Rue Montoyer 51,
1000 Bruxelles
Tel: + 32 (0)2 626 25 66
www.efpia.eu * **info@efpia.eu**