efpia

European Federation of Pharmaceutical Industries and Associations

The Role of Innovation in Future General Pharmaceutical Legislation

European innovative industry's perspective






Sini Eskola

RSNN Annual Workshop

6 June 2023

THIS PRESENTATION CONTAINS EFPIA'S PRELIMINARY ASSESSMENT AND RECOMMENDATIONS OF SOME PARTS OF THE PUBLISHED GENERAL PHARMACEUTICAL LEGISLATION

Role of Innovation in Regulation

- Regulation can be a powerful stimulus to innovation and EU regulation matters at all stages of the innovation process.
- Pharmaceutical legislation has evolved in the past 20 years into a complex framework, and is an important modulator of the pharmaceutical innovation system.
- More prescriptive regulation tends to hamper innovative activity, whereas the more flexible EU regulation is, the better innovation can be stimulated. Lowering burden of red-tape has a positive effect on innovation.
- Evaluation principles proposed by EFPIA's Innovation leaders facilitate help balancing the scientific opportunity with costs and benefits, and include a series of questions e.g.:
    - Are there any elements that could limit innovation that are not easily amendable?
    - Is the proposed measure futureproof enabling enough freedom for the industry to operate efficiently?
    - Which policy instrument (hard/soft law) would be most impactful and would provide appropriate level of risk governance and degree of agility?
    - Are the conditions to bring medicines to a market competitive and attractive?

References:

- *Heikkinen I, Eskola S et al. Role of innovation in pharmaceutical regulation: A proposal for principles to evaluate EU General Pharmaceutical Legislation from the innovator perspective Drug Disc Today Volume 28, Issue 5, May 2023, 103526, https://doi.org/10.1016/j.drudis.2023.103526*
- *Pelkmans J and Renda A. How Can EU Legislation Enable and/or Disable Innovation, Jul 2014. https://ec.europa.eu/futurium/en/system/files/ged/39-how_can_eu_legislation_enable_and-or_disable_innovation.pdf*

EC legislative proposal – Key areas of change

1. Future proofing the EU regulatory system
2. Incentives for innovation
3. UMN
AMR
Competition: generic, biosimilar entry
Security of supply
OMP & Paediatric
Quality & manufacturing
Addressing environmental challenges

Pharmaceutical Regulation and Directive

Regulation 181 Articles + Directive 221 Articles = **402 Articles**

Supporting Innovation

- Scientific decision making

EFPIA's vision for streamlined and expertise-based decision making

Reconsider the committee structure to enhance Member States ability to bring forward their expertise. It is imperative that the EMA and the EU Regulatory network ensure the upskilling of staff expertise and are provided with the needed resources. The decision-making process from EMA approval to EC decision to be made more efficient.

Positives

- Only two high-level committees kept (CHMP and PRAC), the rest (PDCO, COMP, CAT) will support decision making by expertise-driven way (ensuring >50% MS reps, rest can be appointed experts in the relevant field) (Reg Art. 146 – 151)
- Decision on Orphan designation moved from EC to EMA (Reg Art. 138)
- Timelines for assessment changed from 210 to 180 days Reg Art. 6 (6), 150 days remain for accelerated assessment Art. 6 (7) Reg
- Timelines for decision-making: changed from 67d to 46d (Reg Art. 13, Recitals 49 & 50 Reg)
- Coordination between NCAs and EMA strengthened
- Strengthened international collaboration (Reg Art. 140 & 141)

CAVEATS:

- Timelines for decision making: Timelines (10 d) for Standing Committee Procedure not explicitly mentioned in the legal text, only in recitals (Art. 13, Recitals 49 & 50 Reg)

efpia
European Federation of Pharmaceutical Industries and Associations

Supporting Innovation - Expedited Regulatory Pathways Framework

EFPIA's vision for expedited regulatory pathways framework

Embed PRIME in legislation to ensure its optimal use and allocation of sufficient resources in the EU Medicines Regulatory network, including EMA permanent staff. Put in place A suite of effective ERPs should be put in place to be leveraged and combined as needed. Eligibility criteria should be consistent and apply to new indications/line extensions

Positives

- PRIME in legislation (Reg Art 60) ensuring resources for regulators BUT eligibility criteria lacking clarity (e.g HUMN/UMN)
- Phased review in cases of exceptional therapeutic advancement (Reg Art 6(2))
- New indications can be included in CMA (Reg Art 19)
- New Exceptional Circumstance Marketing Authorisation introduced (Reg Art 18)
- New Temporary Emergency Marketing Authorisation introduced (Reg Sect 3)

CAVEATS

- Phased reviews: The text in the Regulation is over-prescriptive. Important to introduce changes not to inadvertently limited in the future by detailed legislative text.
- Accelerated Assessment (AA): Timeline should be explicitly defined as a 'maximum' of 150 days to encourage even shorter assessment timelines than this and to ensure the AA pathway remains valuable as general timelines have shortened to 180 days. AA should also be available for new indications, consistent with other EU & global ERPs, as well as for associated marketing authorisation extensions.
- PRIME: Eligibility to PRIME is overly complex, limiting its value as an innovation tool, and is not consistent with other ERPs e.g. phased reviews. It is unclear whether it is open to new indications, and automatic eligibility to other tools such as AA is missing from the proposed provision.

Supporting Innovation - Regulatory Sandbox

EFPIA's vision for Regulatory Sandbox: Provide a transparent and tailored path for innovative solutions to emerge even in situations where gaps in the legislation exist, as they are impossible to predict today.

Positives

- Foresee EU-level sandboxes to be established via implementing acts (Reg Art 113-115)
- Both methodologies / approaches & products seem to be scope
- Foresees approval of solutions that enter the sandbox with a label reflecting this is under sandbox.
- Include provisions that foresee the need to consider other legislations within the EU which could be concerned by the sandbox when it comes to complying to requirements.
- Horizon scanning mechanism toward the establishment of sandbox includes possibility of discussion with stakeholders.
- Foresee consultation with stakeholders with regards to developing the sandbox plan based on data submitted by developers of eligible products
- (new) Further clarity provided in the sandbox role to set out a regulatory framework including scientific requirements for the development, clinical trial and approval (placing on the market)

CAVEATS

- Limiting the use of the sandbox to solely pharmaceuticals is clearly a missed opportunity. Crucial to expand the scope beyond pharmaceuticals as its use may be required specifically at the interplay with different sectoral legislations (e.g. MDR 2017/745, IVDR 2017/746 and CTR 536/2014)

Supporting Innovation - Drug-device & Drug-diagnostic combinations

EFPIA's vision for Combination Products: A new legal category is needed for combinations of medicines and medical devices and in vitro diagnostics (IVD) that are regulated as medicinal products. Extend to EMA's role in relation to companion diagnostics (e.g. consultation procedure) and to enable EMA to coordinate (co)development support (including multi-stakeholder Scientific Advice) for combinations of medicinal products and medical devices & medicinal products used with an IVD.

Positives

- Legal definition of combination products introduced (Reg Art 59)
- EMA taking the responsibility in the assessment and coordination, including offering scientific advice for combinations of medicinal products and medical devices

CAVEATS

- Missing the element of in vitro diagnostics - Scientific advice should be also offered for in vitro diagnostics used in conjunction with medicines.

Supporting Innovation - Electronic Product Information

EFPIA Vision: Ensure legislative readiness to transition from paper leaflets to ePI while considering the elderly population and those who may not have access to computers or mobile technology. Stakeholder to consider further improvements to health literacy by removing any barriers in the legislation.

Positives

- ePI envisaged in the future and prominently in legislation (Dir Art 63)
- Labelling provisions part of Annex (more flexible flexible to change)
- Published EC proposal shifts possibility for pan-EU implementation "five years following 18 months after the date of entering into force of this Directive" and no qualified majority of MSs required.
- Requirement to implement common standards for the electronic version of PIL, SmPC and Pack.

CAVEATS

- Gradual implementation driven by Member States readiness -> difficult to operationalise and “Member State by Member State” implementation phase should be kept as short as possible and consider the currently existing landscape of multi-country packs.
- Pan-European approach to apply ePI by product classes in phased approach not included in the proposal – Allowing Healthcare Professional administered products to be transitioned first with a short implementation window due to multiple positive pilot experiences already in place
- Find a solution in each country to make paper patient leaflets available to those who need them, as EFPIA and its members acknowledge that no patient should be left behind.

Cross-cutting themes – Emerging elements

Problem statement

- The Commission proposals for the general pharmaceutical legislation review have raised some additional challenges on cross-cutting themes: **1) Increased role of regulators in R&D process (including development, regulatory decision making pre and post authorisation) and 2) Potential for "double-standards" for evidence requirements**

KEY POINTS

Increased role of regulators

- Influence of regulators in decisions across the lifecycle management has increased (UMN, repurposing, use of RWE, modifications to PIP, OME designation) will pose challenges in terms of liability & MAH ability to control their own label
- **Consultative and collaborative process with MAH must be in place with open scientific discussion**

Evidentiary requirements

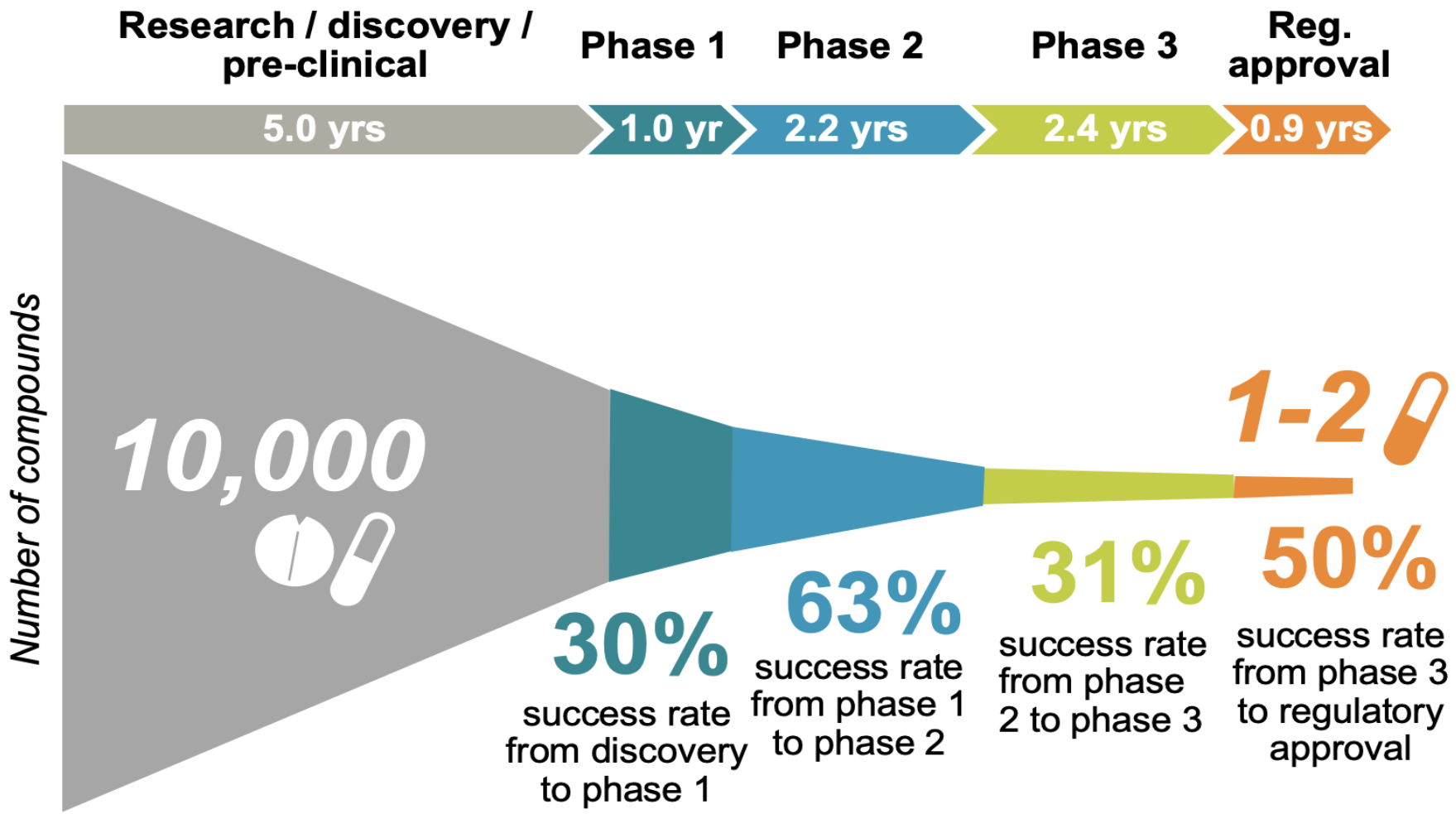
- Using raw data, epidemiological data/RWD, additional environmental data in isolation without a broader context runs contrary to principle that assessments should be based on the totality of the evidence
- **Standards of evidentiary requirements should be equal to all (MAHs vs Regulator vs 3rd party)**

Other Important Areas from Published Legislation Impacting Innovation

Advanced Therapy Medicinal Products (ATMPs)and hospital exemptions – Welcomed improvements to increase safety of patients (Dir Art 2-6) BUT legislation follow should ensure the use of hospital exemption stays true to its intended purpose -> **interpretation of 'non-routine basis'** needs to be ensured that a hospital exemption approval is only granted in cases when no authorised therapeutic alternative or clinical trial could satisfy the specific needs of the patient.

Active Substance Master File (ASMF) established to extend a more general Quality Master File, which could apply to any component of the finished medicinal product. Welcomed change BUT it leaves out the **key priority of a Platform Technology Master File (PTMF)**. Such master files (typically considered for manufacturing technologies) would be a significant enabler of innovative manufacture in Europe, e.g. manufacturing platforms for mRNA vaccines, oligonucleotide therapeutics, ATMP viral vectors or continuous tabletting platforms.

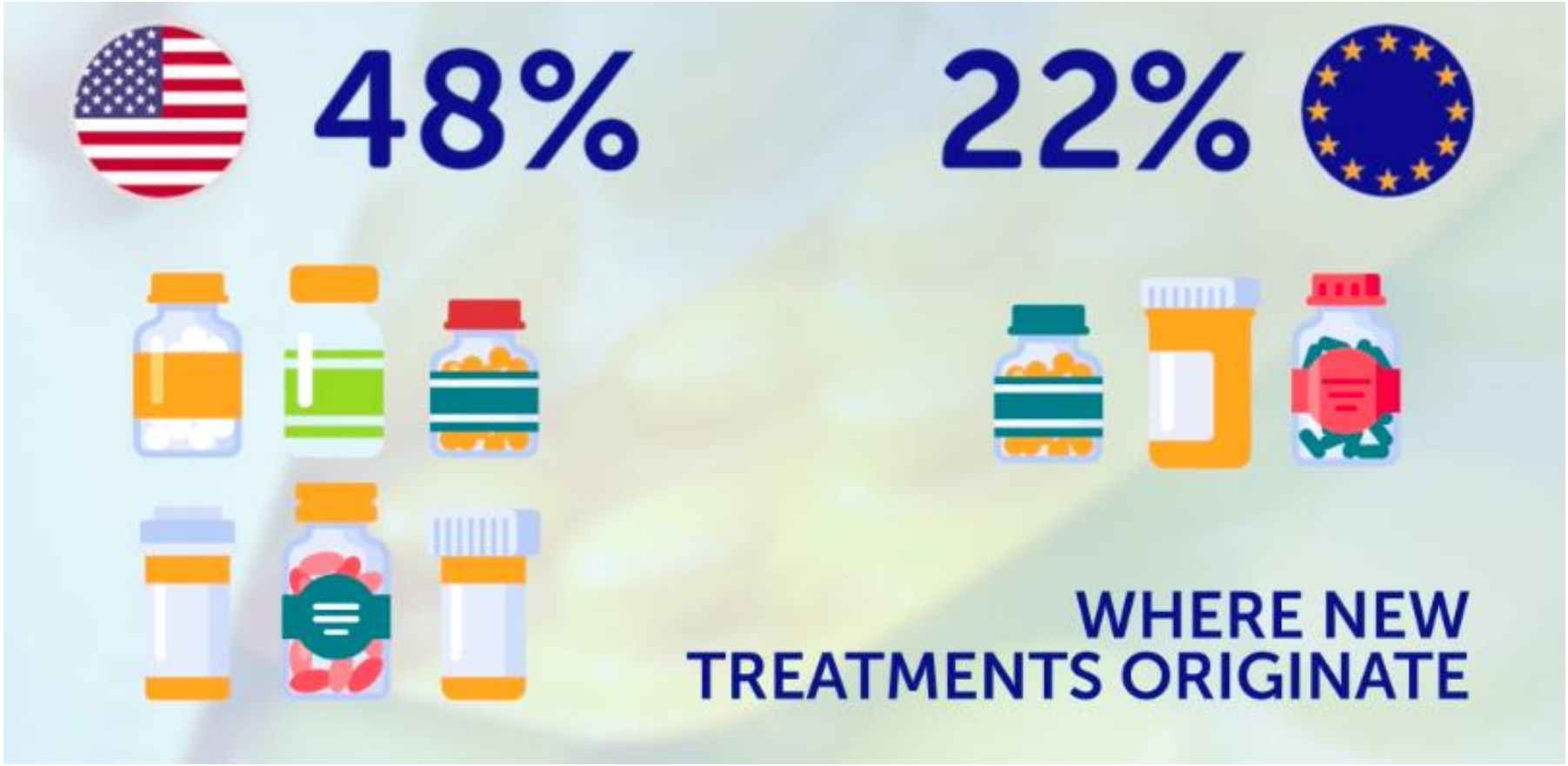
Drug development is a long, risky and costly endeavour



In 2020, the composite success rate (phase 1 – regulatory approval) was 9,8%*

efpia
European Federation of Pharmaceutical Industries and Associations

Most new therapies are no longer developed in Europe…

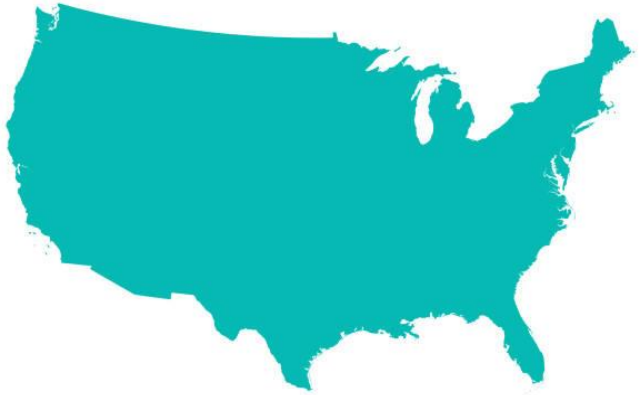


…putting Europe's strategic autonomy in a societally strategic and high-value sector at risk

efpia
European Federation of Pharmaceutical Industries and Associations

Launch and Availability of New Medicines Often Follows R&D Activity

Europe already lagging behind on availability of innovative medicines



85%

Availability of medicines launched between 2012 and 2021

Germany: 61%
France, Italy: 52%
…others even less

efpia
European Federation of Pharmaceutical Industries and Associations

Proposals in brief	Assessment
Regulatory Data Protection (RDP) lowered from 8 to 6 years	Reduces incentives for private investment in R&D
+ 2 year possible if medicine launched in all 27 MS within 2 years from EU authorisation and continiously supplied	Will not lead to improved access – condition is too challenging and unpredictable to be meaningful
+ 6 months possible if medicine fulfills criteria for Umnet Medical Need	Unclear how UMN criteria will interpreted
+ 6 months possible if data from comparative trials	Only possible for some therapies before MA + size of incentive unlikely to match time and costs

Proposal will not achieve objectives of improved access, but likely lead to less investment in R&D for unmet health needs

efpia
European Federation of Pharmaceutical Industries and Associations

How do we improve access to innovative medicines?

A commitment from the industry to file pricing and reimbursement applications in all EU countries no later than 2 years after EU market authorization.

The creation of a European Access Portal with information on the timing and processing of pricing and reimbursement (P&R) applications in the EU-27 countries, including the reasons why there is a delay in the P&R decision or why the MAH has not filed in a particular market.

A conceptual framework for Equity-Based Tiered Pricing (EBTP), to ensure that ability to pay across countries is considered in the prices of innovative medicines, anchored in a principle of solidarity between countries

Implementation of Novel payment and pricing models, to accelerate patient access, allowing payers to manage clinical uncertainty, budget impact and sustainability of the healthcare system, whilst providing sufficient incentives for innovation.

Contributing to achieving an efficient system of European assessments of relative efficacy at time of launch in the context of the implementation of the Health Technology Assessment (HTA) Regulation.

This requires real dialogue between Member States and all stakeholders

RDP and Unmet medical need/High unmet medical need
- Patient centricity forgotten?

Directive Art. 83: UMN	Regulation Art. 65: HUMN for OMP
Disease level life-threatening or seriously debilitating	**OMP are perceived as UMN**
AND	**AND**
Product level ○ absence of Tx, or if any still high mortality or morbidity ○ new Tx has to reduce meaningfully mortality or morbidity	**High UMN** ○ Absence of Tx or ○ In addition to significant benefit to show exceptional therapeutic advantage over existing Tx ○ new Tx has to reduce meaningfully mortality or morbidity

Assessment

- Products meeting UMN criteria, would be eligible to +0,5 y RDP or + 1y OME and regulatory incentives
- Difference of proposed articles is not clear
- Bar for UMN and HUMN <u>is unrealistic</u>
- Value judgments are not defined in any legal text, and were not subject to a stakeholder consultation

Much more dialogue and improvements in legislative proposal needed

efpia

European Federation of Pharmaceutical Industries and Associations

BACK-UP

Patents and additional protection periods ensures developers can get return on investment if successful – no investment in R&D would happen without it