EU Pharmaceutical reform

DG SANTE

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EU Pharmaceutical reform

Builds on the **Pharmaceutical Strategy** for Europe (2020)

Supports EU citizens and industry

Addresses **long-standing challenges and public emergencies**

Marks a **European Health Union milestone**

European Commission

A 4-part package

Chapeau communication

New Regulation

- Specific rules for the most innovative medicines such as orphans, antimicrobials
- Rules on shortages and security of supply
- EMA governance

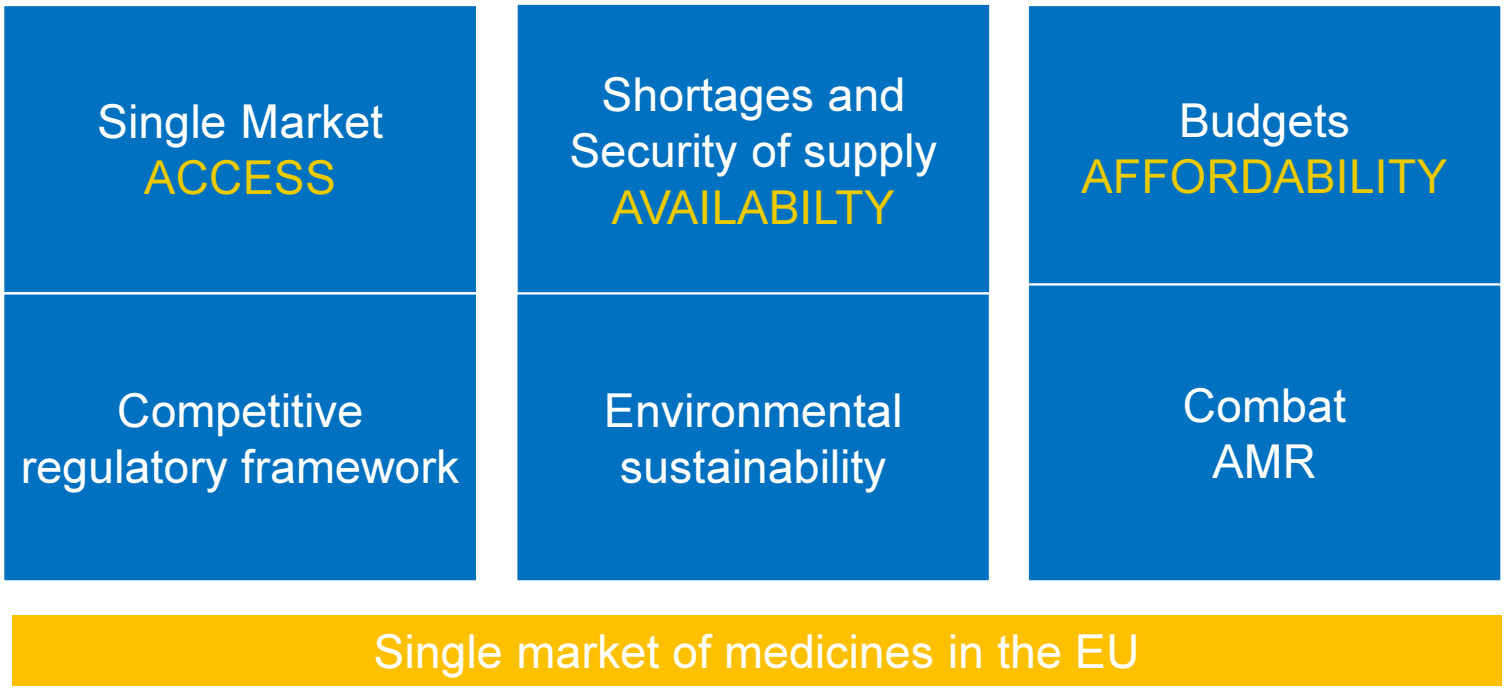
New Directive

- Placing on the market of all medicines
- Authorisation and labelling requirements
- Strong incentives for access

Council Recommendation on AMR

European Commission

6 Key political objectives



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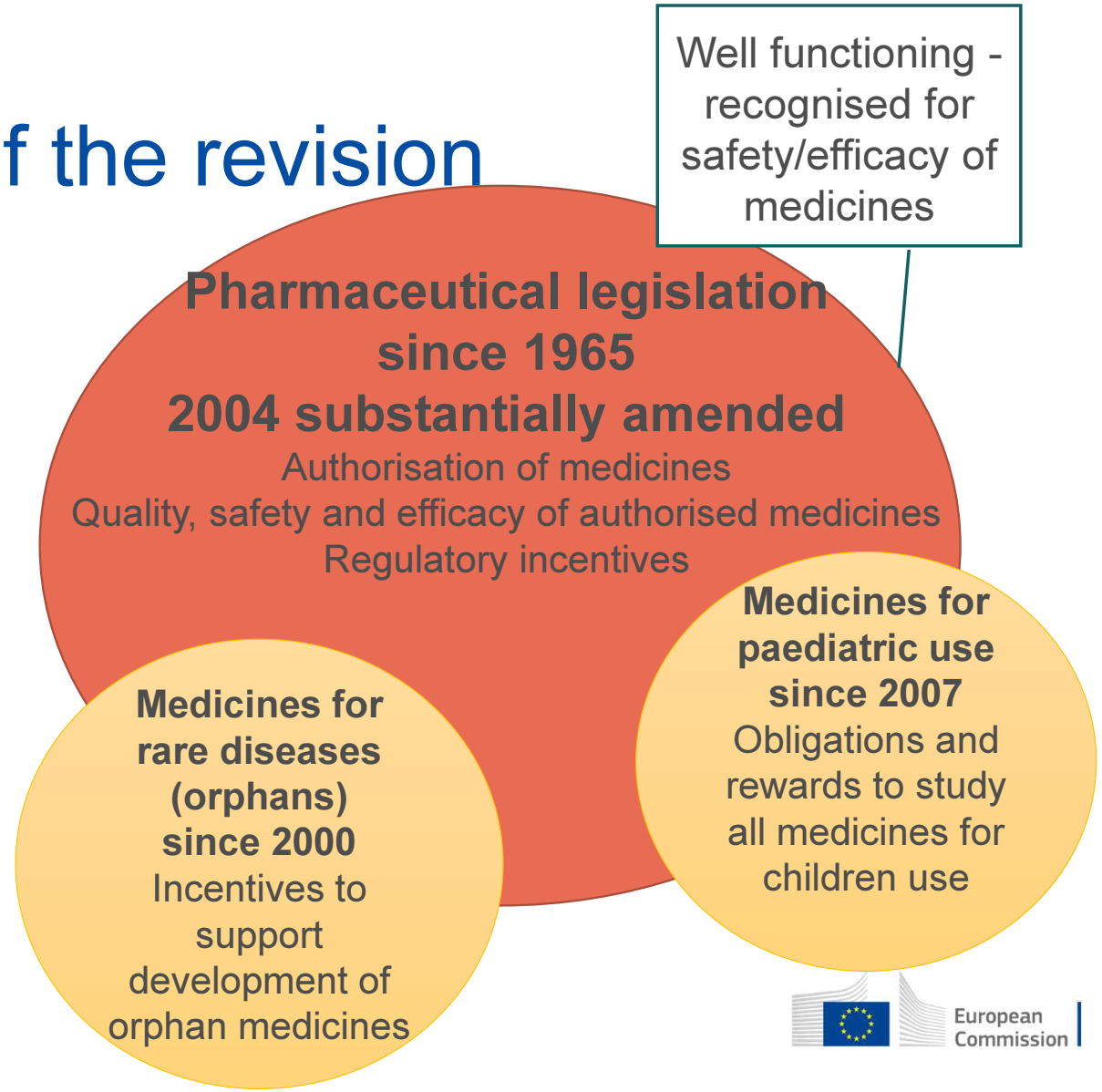
Quantitative facts of the revision

ESTIMATION

- **Directive 2001/83**: 13/14 titles revised – about 60-70% of 191 articles concerned
- **Regulation 726/2004**: 4 titles revised – about 70% of the more than 65 articles concerned.



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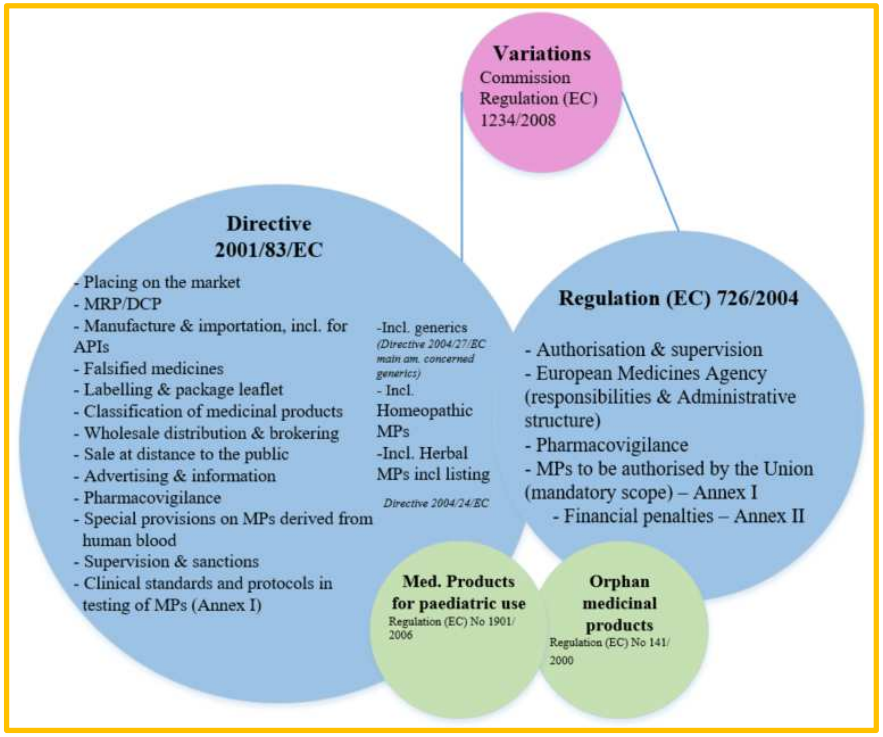
Structure of the revision



Areas not changed in substance

- Homeopathic medicines
- Herbal medicines (exception: herbal committee)
- Falsified medicines
- Sale at distance to the public
- Financial penalties

Areas with minimum intervention

- Pharmacovigilance
- Wholesale distribution
- Advertising

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Interplay between two proposals

Directive

- General principles for the MA (Ch I, Sec 1)
- Dossier requirements and legal basis (Ch I, Sec 2&3, (full or abridged MAA), categories of MAs, new types of MPs
- Specific dossier requirements common to national and centralised MAs (ERA, excipients, ASMF)
- Adapted frameworks
- Only the national procedures (purely national, MRP, DCP)
- Regulatory data & market protection rules
- PhV, manufacturing, supply and distribution, advertising, supervision
- Annex I → Annex II (after adoption by DA)

Regulation

- Centralised procedure/EMA governance (Ch XI)
- Mandatory/optional scope (Annex I)
- Orphan & paediatric medicines (Ch VI & Ch VII)
- Security of supply of all medicines (Ch X)
- Temporary Emergency Marketing Authorisation (Ch II Sec 3)
- Incentives for developing priority antimicrobials – vouchers (Ch III)
- Pre-Authorisation support – parallel scientific advice, PRIME, decision on regulatory status (Ch V)
- Sandboxes (Ch IX)

Access

Modulation of incentives

European Commission

Access to medicines

Current challenges

Access is not timely and differs across Member States:
90% variance between Northern and Western European countries and Southern and Eastern European countries

Average waiting time across the EU is from 4 months to 29 months

Proposed solutions

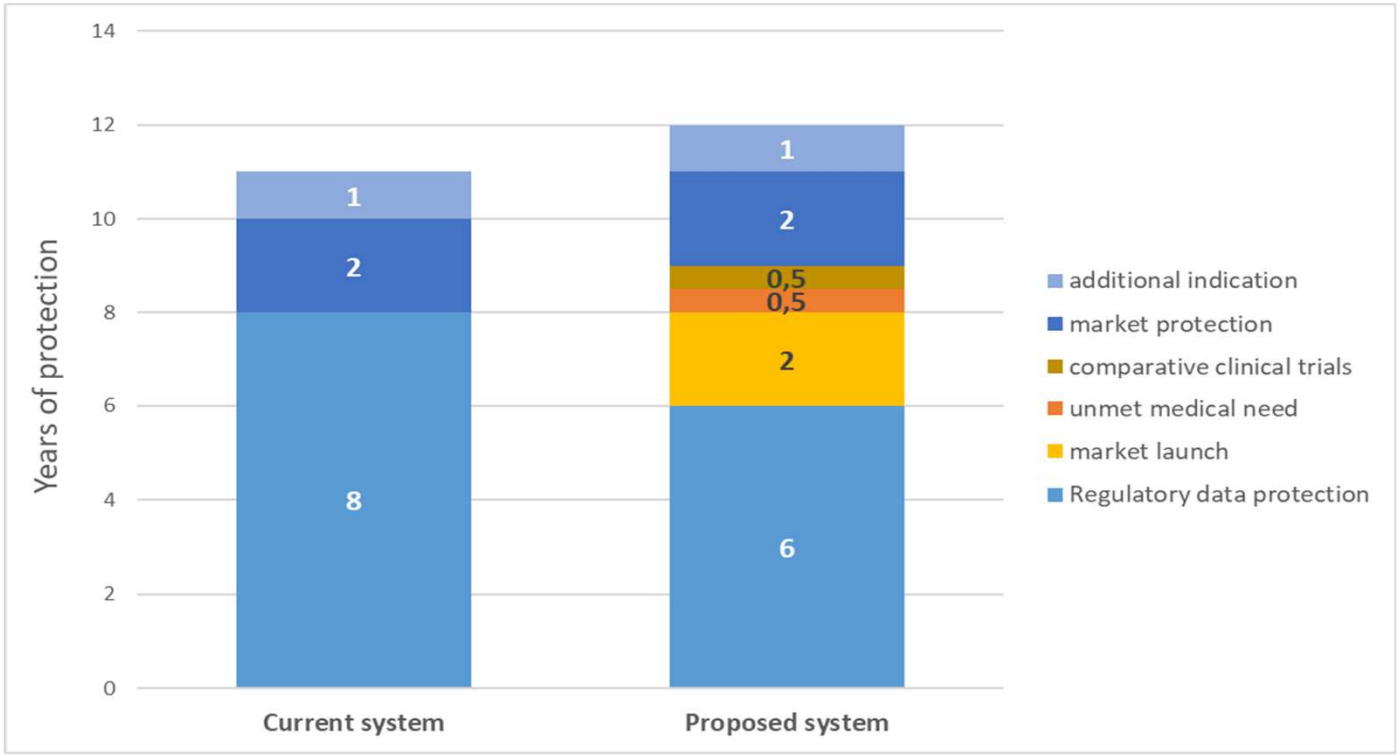
Incentives for innovation and access: Targeted approach vs current “one-size-fits-all” with 8 years of unconditional data protection

Earlier market entry of generic and biosimilar medicines

- Faster authorisation
- Pre-authorisation support

Modulation for the majority of innovative medicines

Regulatory data and market protection today and as proposed



Current system, max 11 years protection

Proposed system, max 12 years protection

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Access

- **Regulatory protection periods and modulation of data protection incentive -** market launch (+24m), unmet medical need (+6m), comparative clinical trials (+6m), additional therapeutic indication (+1yr) (DIR Art 81)
- **Market launch incentive modalities -** Incentive given if product launched in all MS covered by the marketing authorisation (*not necessarily in all 27* in cases of decentralised applications) (DIR Art 82)
- **Unmet Medical Need** criterion based on defined criteria
- **Repurposing incentive:** +4 years DP with respect to additional indication not authorised in Union, off-patent or innovative medicines (DIR Art 84)
- **Broadened BOLAR exemption:** Exemption to cover HTA and P&R activities in addition to studies/trials conducted for a MA (DIR Art 85)
- EMA **consultation process with downstream actors** and stakeholders

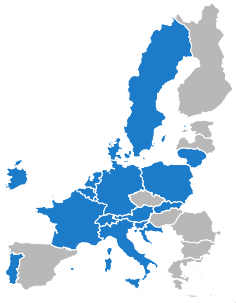
Modulation of incentives and EU competitiveness

- IP rights outside scope of pharmaceutical legislation will not be affected
- Ability to have the same regulatory protection as today
- EU system of regulatory incentives is already one of most generous (table)
- The incentives apply equally to all products, regardless of where they are developed – in the EU or elsewhere

Country	Protection	Duration
Canada	New Chemical Entity+ Market Protection	6+2 years
EU	New Chemical Entity+ Market Protection	8+2+1 years
Switzerland	New Chemical Entity	10 years
USA	New Chemical Entity (small molecule)	5 years
USA	Biosimilar Application Approval Exclusivity (biologic)	4+8 years
Israel	Market Protection	6 or 6.5 years
China	New Chemical Entity	6 years
Japan	New Chemical Entity	8 years

Market launch conditions

- Launch in all Member States where the marketing authorisation is valid (CP and DCP)



- **Actual placing** on the market and continuous supply for the needs of the patients in each MS (incl. presentations, quantities)
- **MS has 4+1 options**:
  - Positive/negative confirmation of actual supply
  - Waiver
  - Tacit [or]
  - positive pricing and reimbursement decisions (Transparency Directive)

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Access

Orphan and paediatric medicines

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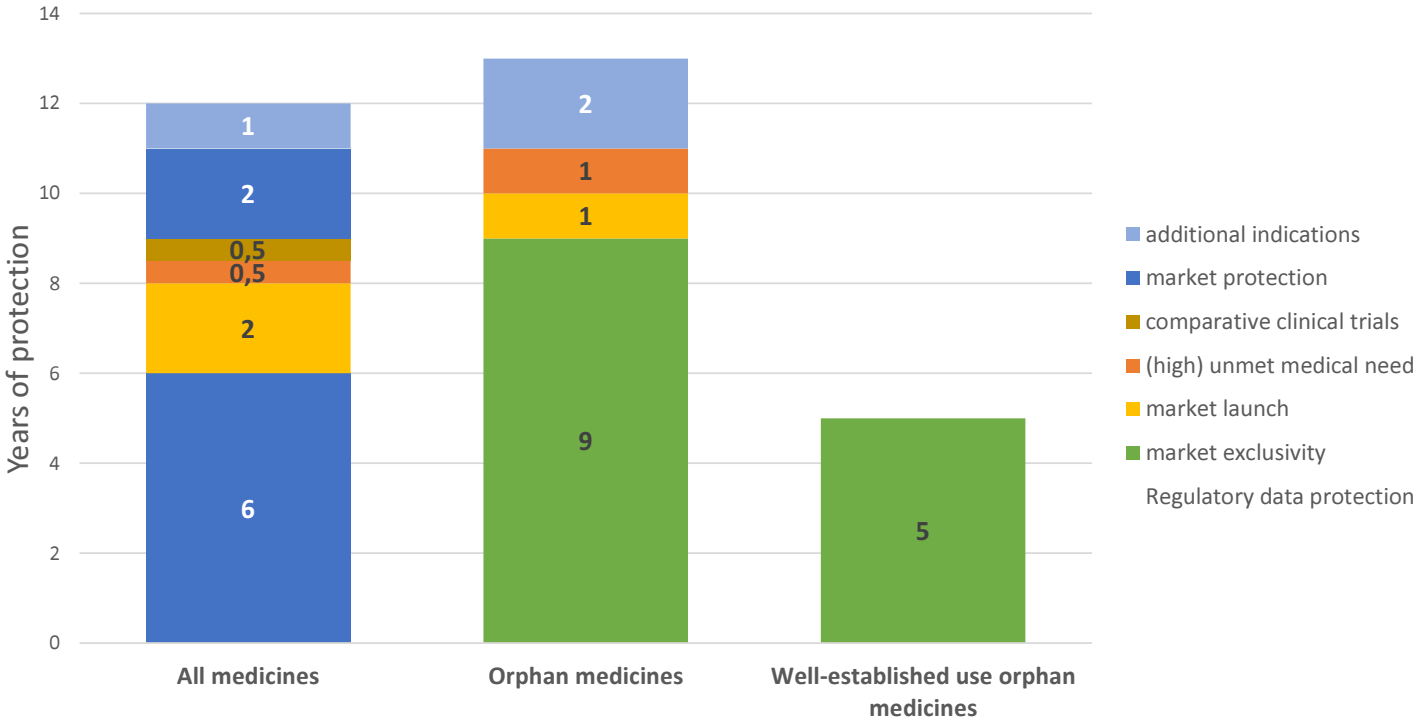
Modulation of incentives for orphan medicines

Modulation of data protection

Modulation of market exclusivity



max. 12 years protection

max. 13 years protection for orphan medicines

List of changes

- Default **market exclusivity** is 9 years (from 10 today)
- MPs addressing **HUMN** get +1 year market exclusivity = 10 years
- Launching in all MS adds +1 year **market exclusivity**
- Well-established use orphan medicines (application based on literature without trials) = 5 years of **market exclusivity** (from 10 today)
- **Data protection (left bar)** applies also to orphans, including modulation, e.g. 6m for comparative clinical trials. However, for market launch orphans benefit from 1 year market exclusivity only.
- To note, well established use products do not benefit from data protection as literature-based applications are not protected by data protection.

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Orphans – main changes (1)

- **Orphan medicinal products - Chapter IV of REG**
- **Market exclusivity modulation** – *improving access* (REG Art 71 and 72)
- **High unmet medical needs concept** – *innovation* (REG Art 70)
- **Orphans addressing High Unmet Medical Needs** would benefit from 10 year market exclusivity (REG Art 71(2)) and enhanced scientific and regulatory support ((PRIME) REG Art 60(1)(a))
- **Non-accumulation of market exclusivity periods** (for products with the same active substances) – 'global market exclusivity' - and other measures aimed at *faster access of generics* REG Art 71(3),(5),(6)

Orphans – main changes (2)

- **Specific criteria for orphan designation** for scientific reasons by a delegated act when prevalence criterion not appropriate (possibility of **incidence** criterion) - *adjustment to scientific progress* (REG Art 63(2))
- *DELETION:* **No 'insufficient return criterion/ sufficient profitability '** neither as a criterion for designation nor as a reason for reducing the market exclusivity
- **Competence on orphan designation** (and also the Register of designated orphan medicinal products) transferred from the Commission to EMA – *procedural simplification* (REG Art 64 and 67)
- **Validity of orphan designation** – 7 years (or until a MA granted), no validity period in current Orphan Regulation - *procedural simplification* (REG Art 66)
- **Other changes:** distinction between the designated orphan medicinal product and orphan medical products, definitions from implementing acts/guidelines (REG Art 2(2)-2(8))

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Paediatrics – main changes (1)

- Paediatric provisions **both in Regulation** “Chapter VII” and **in Directive** (Art 4, 6, 48, 49, 59, 60, 86, 94)
- Centralised MA procedure **compulsory for PUMA** medicines, optional for paediatric only MPs (REG Annex 1 & Art 3(2))
- Step-wise PIP, simplified PIP (REG Art 74(2), Art 85(2))
- **Mandatory PIP** on the base of the mechanism of action of a MP (same therapeutic area – REG 75(1))
- **Temporary waiver** from PIP obligation during public health emergencies for medicines relevant for the public health emergency (DIR Art 6(5) & REG Art 83).

Paediatrics – main changes (2)

- Cap to the **length of deferrals** (extendible) (REG Art 75(3))
- EMA responsible for agreeing on PIP, when appropriate CHMP for PIP compliance (REG Art 77, 86 & DIR Art 48)
- **6 months SPC extension** following PIP completion **also for orphan medicines** (DIR Art 86)
- **Increased transparency** on PIP conducted for discontinued medicines - REG Art 88
- Multi-stakeholders discussions about **prioritisation of paediatric R&D** in a pre-competitive environment (REG Art 95)
- Amendment of **Clinical Trials Regulation** to reflect the current timing of publication of summary of results of paediatric CT (6 months after the end of the trial) (REG Art 177)

Availability

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Availability – shortages of all MPs and supply

Shortages: Multiple root causes

Quality and manufacturing issues

Commercial reasons, incl. market withdrawals, and unexpected increases in demand

EU dependency on non-EU countries for medicines for supply of certain pharmaceutical ingredients.

Current challenges

Growing concern for **all EU countries**

- **Critical shortages** of medicines; current examples thrombolytics, antibiotics
- Security of supply of **critical medicines**

Ad hoc processes for dealing with **critical shortages**

Proposed solutions

Improved **coordination, monitoring and management** of shortages, in particular critical shortages (MS and EMA); **Earlier** and **harmonised notification** of shortages and withdrawals (industry) (REG Art 116)

Shortage Prevention Plans

Union list of critical medicines

Stronger coordinating role for **EMA &** more powers for **MS** and **Commission**

Outside pharma package

- Other **Commission initiatives**, including the work of **HERA**
- **Joint Action** on shortages
- **IPCEI** in the area of health
- **National measures** e.g. State aid
- **EMA mandate extension** (Regulation (EU) 2022/123)

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Shortages of all medicines (1)

- Obligation on **MAHs and wholesalers** to ensure **appropriate and continued supplies** (DIR Art 56 and 167)
- **Shortage prevention plans** for **all medicines** (REG Art 117) and **Shortage mitigation plans** for shortages (REG Art 119, Annex IV)
- **Notification of market cessations (decision), withdrawals, suspensions and shortages** (temporary disruptions) (REG Art 116, Annex IV)
- **Shortage monitoring** by both NCAs and EMA based on MAH notifications REG Art 118 (all shortages), Art 124 (critical shortages)
- **MSSG list of critical shortages and recommendations** (REG Art 123)
- **MAH obligations to provide information, based on MSSG recommendations, comply with national and Union level measures and report on measures taken** (REG Art 118, 125, Annex IV)
- **Commission role** in implementing measures, taking MSSG recommendations into account (REG, Art 126)

Shortages of all medicines (2)

- Possibility for **wholesale distributors and other actors to report shortages** can provide any information on shortages requested by NCAs or EMA (REG Art 120)
- **NCA requests for information and information sharing with EMA** and **SPOC working party activities** to allow for **improved coordination and management of critical shortages** (REG Art 121)
- **EMA requests for information, collaboration with SPOC working party and reporting to MSSG and the Commission** to allow for improved coordination and management of critical shortages (REG Art 122,124)
- EMA establishment of **criteria** to adopt and review **critical shortages list**, **specification of tools, methods and criteria** to be used in **monitoring and reporting of critical shortages** and methods for MSSG recommendations and development of guidance on risk assessments (REG Art 122)
- **Publication** of shortages by NCAs and EMA (REG, Art 121,124)

Security of supply of critical medicines

- MS (national competent authority) identification of critical medicines at national level and MS, EMA and Commission preparation for **Union list of Critical Medicinal Products** (REG Art 127)
- **MAHs and other actors** shall **submit information** on critical MPs (REG Art 129,131)
- **MSSG recommendations** on appropriate security of supply measures to MAHs, the Member States, the Commission or other entities (REG Art 132)
- Responsibility of **MAHs** to **take MSSG recommendations into account, comply with measures taken at EU or national level** and **report on measures** they have taken (REG Art 133)
- Role of the Commission, including a provision on **Commission** adoption of an **implementing act to improve security of supply of certain medicines on the Union list of Critical Medicinal Products,** directed towards on MAHs, wholesale distributors or other relevant entities (REG Art 134)

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Affordability

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Affordability

Current challenges

Pricing, reimbursement and procurement of medicines is a **national** competence

High prices endanger national health systems' sustainability **& restrict patient access**

Lack of **transparency of public funding** is a growing issue

Scope to increase/strengthen cooperation among NCAs

Proposed solutions

Earlier market entry of generics/biosimilars to increase competition and reduce prices

Increased **transparency on public contribution** to R&D

Comparative Clinical Trials to support national decisions on pricing

Further support for **information exchange** between MSs (cooperation on pricing, reimbursement and payment policies)

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Measures to support generics and biosimilars

- **Earlier access** to the market (DIR Art 81)
- **Broaden and harmonise the Bolar exemption** (DIR Art 85)
- **Risk management plan** is not required for generics (DIR Art 21)
- **Active substance master file –** harmonised EU assessment (DIR Art 25)
- Facilitate **the repurposing of off-patent medicines** (DIR Art 84)
- **Simplification** of procedures for all medicines (higher impact on generics and biosimilars): e-PL (DIR Art 63), abolish renewal and sunset clause
- **Recognition of interchangeability of biosimilars** with their biologic counterparts in recitals promotes uptake of biosimilars (DIR Rec 27).

Comparative clinical trials

Additional 6 months of data protection for medicines containing a **new active substance** if the pivotal clinical trials submitted use a **relevant comparator**
(DIR Art 81)

Objectives:

- Support early engagement with EMA on scientific advice (parallel scientific advice)
- Helps to align the design of CTs between regulators and HTA bodies
- Incentivise the compliance with scientific advice
- Provide meaningful clinical trial data to HTA and pricing authorities
- Avoid duplications of clinical trials

Transparency on public funding

Scope (DIR Art 57)

- All direct financial support provided by any **public authority or publicly funded body**
- Received for the **R&D** of the medicinal product
- Irrespective of the legal entity that received that support

Procedure (DIR Art 57, REG Art 138)

- **Electronic report by MAH** listing the amount, date, source & receiving entity
- **Audited** by independent external auditor
- Accessible on **MAH webpage**
- Link shared with EMA/NCA, **published in Union database for medicines for human use**
- Yearly update, as necessary
- **Harmonised** reporting (template → implementing act).

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Competitive regulatory framework

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A streamlined regulatory framework

Current challenges	Proposed solutions
Longer approvals times than in other regions (US 244 days)	**Faster autorisation:** a) **180**D standard procedure; b) 150D accelerated procedure **Regulatory efficiency:** simplified procedures, better use of data and digitisation, regulatory sandboxes
Administrative burden and compliance costs for the industry	**Pre-authorisation support** to promising medicines to accelerate development and attract investments
The clock stop mechanism	**Lower regulatory burden** (especially important for SMEs and not-for-profits)

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Future proofing

- Regulatory **sandbox** to test new innovative therapies (REG Art 113-115)
- Strengthening the **early regulatory support** by EMA (part. for promising medicines under development for unmet medical needs (REG Art 59))
- Adapted frameworks with specific regulatory requirements tailored to the characteristics of certain novel medicines (DIR Cpt II Sec 5)
- Scientific and regulatory support for priority medicines ('PRIME') (REG Art 60)
- Scientific recommendation on regulatory status (REG Art 61, 62)
- Facilitate use of **real-world evidence**, and of **health data** for regulatory purposes (REG Art 6(1), Art. 166+169)
- Promote use of new methodologies to reduce animal testing (DIR Art 6 and 44, REG Art 6(5),8,12(4)(m),138)

Regulatory simplification (1)

- Improved **clarity on the interplay** between EU legislative frameworks (e.g. medical devices, substances of human origin) (DIR Cpt I, REG Cpt V)
- Introduction of possibility for a scientific recommendation decision on **regulatory status** of a medicinal product under development (REG Art. 61 and 62)
- **Adapted frameworks** with specific regulatory requirements tailored to the characteristics of certain novel medicines (DIR Cpt II Sect 5)
- Reduction of assessment and **approval time** from 277 days to 226 days (DIR Art 30, REG Art 6,12,13)
- Possibility for regulators to reject **immature applications** to limit clock stops that delay the decision (DIR Art 29(3), REG Art 10(2))

Regulatory simplification (2)

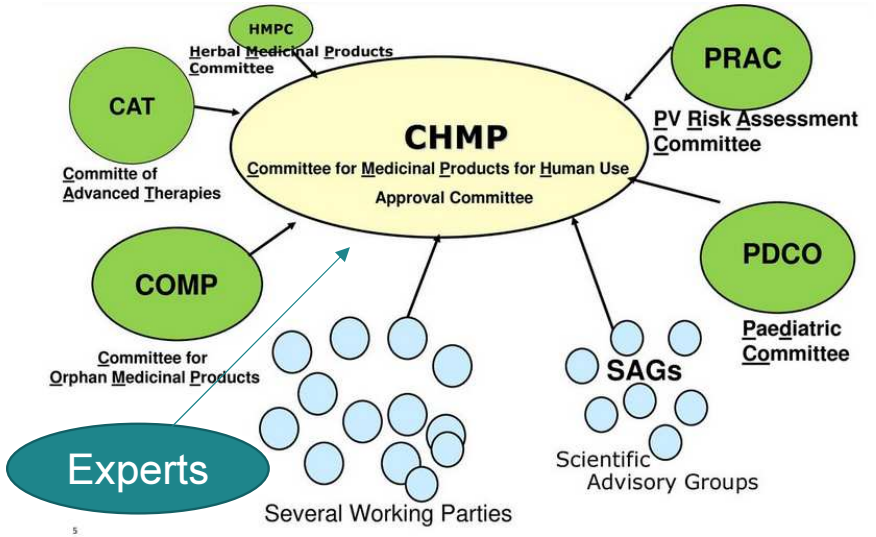
- **Electronic submission** of applications (DIR Art 6, REG Art 5(3),6(1))
- **Facilitate the use of electronic product information and multi-language packages** (DIR Art)
- **Facilitation of repurposing** through a mandatory variation on the basis of data submitted from not-for-profit entities for repurposing of authorised medicinal products (REG Art 48)
- Strengthening the **early regulatory support** by EMA, part. for promising medicines under development for unmet medical needs (REG Cpt V)
- **Risk management plan** not required for off patent medicines (DIR Art 21)
- **Conditional marketing authorisation (**REG Art. 19)
  Accelerated assessment (DIR Art. 6(7))
- Marketing authorisation in **exceptional circumstances** (REG Art. 18/DIR Art. 45)

Optimisation of procedures

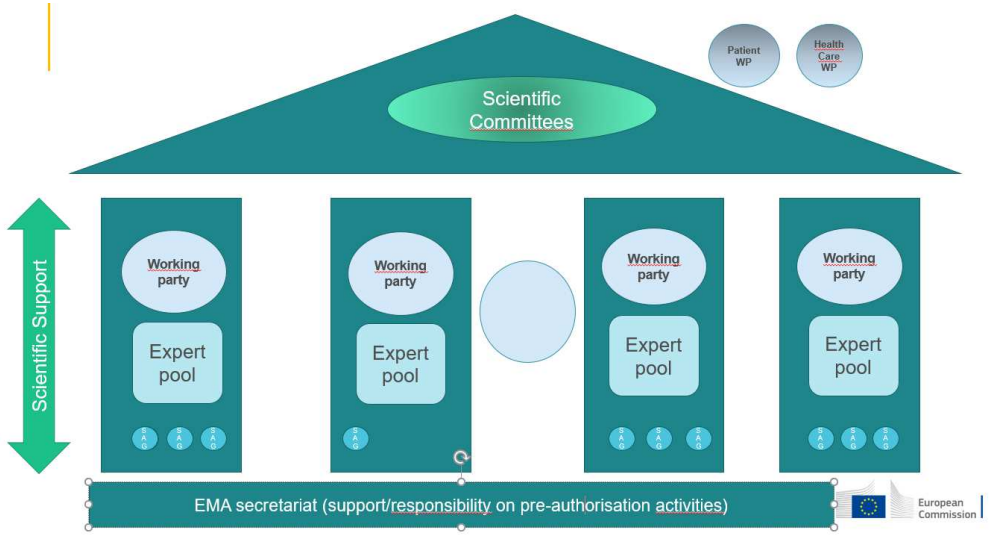
- Possibility for EMA to review **data in phases**, as they become available (rolling or phased review) (REG Art 6(2))
- **Active substance master file** to avoid duplication of assessment of chemical active substances (DIR Art 25)
- **Optimising EMA's structure and simplifying regulatory procedures** (REG Cpt XI Sec 2) → streamlining the procedures, shorter deadlines

EMA structure – today and tomorrow

Today



Tomorrow



Principles maintained in the future structure	
Full MS representation in EMA committees	Maintained
Rapporteurship	Maintained (no impact on fees)

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Simplification of DCP&MRP procedures

- Duration of procedure is 180 days (shortened deadline for agreement → 60 days, deadline for evaluation remains) (DIR Art 30)
- Applicant shall inform **all** MSs of its application, MS that are not Member State Concerned, may request to enter the procedure **on public health grounds** (DIR Art 33(3), 36(4))
- **Simplification** of 'repeat use procedure' → if MSs do not request the update of assessment report, RMS shall provide the AR within 30 days (instead of 90 updated AR) (DIR Art 36(5))
- If the application dossier is not of sufficient quality or maturity for the completion of the examination, it can be terminated within 90 days (DIR Art 34(4)).

Competitive regulatory framework

Supervision, controls and inspections

European Commission

System of supervision (1)

- NCAs to put in place a system of supervision (SoS) including announced/unannounced on-site inspections, remote inspections, compliance control measures and the effective follow-up (DIR Art 188(1))
- NCAs and EMA to exchange info on the on-site inspections and remote inspections (DIR Art 188(2))
- NCAs to ensure that measures included in the SoS are carried out at an appropriate frequency based on risk; and at premises or activities of certain entities (DIR Art 188(3))
- What to take in account to determine the appropriate frequency based on risk (DIR Art 188(4))
- Under which conditions and at the premises or activities of which entities the measures included in the SoS can be carried out (DIR Art 188(5)).

System of supervision (2)

- Possibility for the Agency to request that activities associated with the SoS are carried out (DIR Art 188(6))
- NCAs to empower its official representatives to carry out certain activities (DIR Art 188(7))
- NCAs to ensure that on-site inspections and remote inspections are carried out in compliance with principles developed by the Commission (DIR Art 188(8))
- How to carry out and conclude inspections and issue inspection report (DIR Art 188(8)-188(11))
- **NCAs - require a manufacturer of a medicinal product or of an active substance established in a third country to submit to an inspection** (DIR Art 188(12))
- NCAs to issue a certificate of compliance or a statement of non-compliance and to enter it in the relevant Union database (DIR Art 188(13)-188(16))
- Pharmacovigilance inspections (DIR Art 188(17)).

Cooperation on Inspections & Inspections guidelines

- NCAs and Agency, under certain conditions, to jointly carry out measures included in the SoS at the premises or activities of certain entities (DIR Art 188(3)-188(5)) (**joint inspections**, DIR Art 189(1)-189(5))
- NCAs, under certain conditions, possibility to request another NCA or the Agency to carry out measures included in the SoS at the premises activities of certain entities (DIR Art 188(3)-188(5), 189(6)-189(8))
- Commission to lay down **principles applicable to SoS**, **joint inspections**, **exchange of information** and **trusted non-EU regulatory authorities** (DIR Art 190(1))
- Commission to establish the form and content of: manufacturing authorisation, wholesale distribution authorisation, compliance report, certificate of compliance (DIR Art 190(2)).

Inspection capacity of the Agency

- Participation in inspections or carrying out of **inspections in third countries** by the Agency at the request of an NCA (REG Art 52(1))
- **Decision making** of the Agency following a request from an NCA (REG Art 52(2)-52(5), Annex III))
- Setting up and requisites of the inspection capacity of the Agency (REG Art 52(6))

- **International inspections**

- Agency to coordinate a structured cooperation on inspections in third countries between MSs, the EDQM, WHO and trusted international authorities, by means of **international inspection programmes** (REG Art 53(1))
- Agency to adopt **guidelines** laying down **principles applicable to international inspection programmes** (REG Art 53(2)).

Joint Audit Programme

- The inspection working group of the Agency to establish, develop and supervise the **joint audit programme** (JAP) (REG Art 54(1))
- Requisite for participation of the Member States in the JAP (REG Art 54(2))
- The JAP is an integral part of the quality system of the inspectorates (REG Art 54(3))
- Audit reports and follow-up actions of audits (REG Art 54(4))
- Role of the Agency in the JAP (REG Art 54(5)-54(6))
- Financing of the JAP (REG Art 54(7))
- Establishing the inspection working group (REG Art 142(k)).

Competitive regulatory framework

Manufacturing

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Relevant measures

Manufacturing and import of medicinal products

- Requisite of manufacturing authorisations for sites manufacturing medicinal products in the EU/EEA **with the exception of decentralised sites** (DIR Art 142)
- Requirements, granting and changes to manufacturing authorisation (DIR Art 143 –146)
- Obligations of the manufacturing authorisation holder (DIR Art 147)
- **Registration and listing process of decentralised sites** (DIR Art 148)
- Conditions related to the safety feature and falsified medicinal products (DIR Art 149-150)
- Availability, qualification, responsibilities and professional code of conduct of qualified person (DIR Art 151-154, Annex III)
- Certificate for export of a medicinal product (DIR Art 155).

Environmental sustainability

European Commission

Environmental sustainability

Current challenges	Proposed solutions
Pharmaceuticals in environment can **harm environment and human health**	Better enforcement of the current rules on **Environmental Risk Assessment** (part of the application)
Presence of antimicrobials in the environment contribute to the emergence and spread of AMR	Extending ERA requirements to **medicines already on the market before 2005 considered harmful to the environment**
Weak enforcement of current ERA rules in the MA of medicines	Adding AMR as a new protection goal for ERA, including the risks for AMR from manufacturing of antimicrobials

Relevant measures (1)

- Definition of environmental risk assessment (ERA) for MPs (use and disposal) and for MPs with an antimicrobial mode of action (manufacturing, use and disposal) (DIR Art 4(33))
- Applicant to prepare the ERA + **ERA requirements** (incl. compliance with scientific guidelines) (DIR Art 22(1)-22(4))
- **Agency to draw up scientific guidelines to specify technical details regarding the ERA requirements** (DIR Art 22(5))
- Applicant to submit the ERA (DIR Art 6(2)), **MAH, if new info, to update the ERA + ERA requirements** (DIR Art 22(6))
- Specific provisions for ERA of generic, hybrid, biosimilar, bio-hybrid medicinal products (DIR Art 22(7))
- National MA subject to conditions → to conduct post-authorisation ERA studies (DIR Art 44)
- MA to be refused if the ERA is incomplete or insufficiently substantiated by the applicant or if the risks identified in the ERA have not been sufficiently addressed by the applicant – NCAs (DIR Art 47) or Agency (REG Art 15).

Relevant measures (2)

- **After granting a marketing authorisation, possibility to impose obligation on the holder to conduct a post-authorisation environmental risk assessment study – NCAs** (DIR Art 87) or Agency (REG Art 20)
- Possibility for Commission to amend ERA requirements (DIR Art 22(1)-22(6),213)
- The European public assessment report to include a summary of ERA studies and their results as submitted by the marketing authorisation holder and the assessment of the ERA (REG Art 16)
- Agency to set up and maintain a register of ERA studies conducted for the purpose of supporting an ERA for medicinal products authorised in the Union, unless such information is made public in the Union by different means (REG Art 104)
- The CHMP may establish an ERA working party and other scientific working parties, as necessary (REG Art 150)
- **Suspending, revoking or varying the terms of marketing authorisations (DIR Art 195)**
- **Prohibition of supply or withdrawal of a medicinal product from the market (DIR Art 196)**.

Other measures to address environmental issues

Catching-up procedure for MPs before 30 Oct 2005	Monographs
▪ Agency to establish a programme for ERA of medicinal products authorised before 30 October 2005, that have not been subject to any ERA and that the EMA has identified as potentially harmful to the environment (DIR Art 23(1))	▪ NCAs and Agency to set-up an active substance-based review system of ERA data (ERA monographs) (DIR Art 24(1)-24(4))
▪ Agency to set scientific criteria for the identification of the medicinal products as potentially harmful to the environment and for the prioritisation of their ERA, using a risk-based approach (DIR Art 23(2))	▪ Possibility for Commission to specify the content and format of ERA monographs, the procedures for adopting and updating the ERA monographs, the procedure for submission of information, studies and data, the risk-based prioritisation criteria, the use of ERA monographs in the context of new MAA (DIR Art 24(5)).
▪ MAH to submit the ERA of medicinal products identified in the programme (DIR Art 23(3)-23(4))	

Combat AMR

European Commission

Combatting AMR

Current challenges

AMR causes **37000 deaths per year** in the EU.It amounts to +/- 1.5 bn EUR per year in healthcare costs

By 2050, **10 million deaths globally each year**

Current market failure/lack of effective antimicrobials

Lack of market incentives
0,5 bln EUR cost of a new antibiotic

AMR toolbox

Measures on **prudent use of antimicrobials** – prescription, restricted quantities, education etc.

Regulatory incentives with **transferable exclusivity vouchers** under strict conditions

Financial incentives with **procurement mechanisms** (HERA) 5 Targets, incl on the total **EU consumption of antibiotics for humans** (ECDC) → reduction by 20% by 2030 (Council Recommendation)

AMR voucher

Additional year of regulatory data protection

Strict conditions (only novel antimicrobials, full transparency of all funding, obligation of supply, max 10 vouchers in 15 years, review after 15 years, etc.)

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Description: transferable data exclusivity voucher

- Transferable **regulatory data protection** voucher allows the developer of a novel antimicrobial product that fights AMR to benefit from additional **data protection (+12 months)** on that product, on another product in their portfolio or sell the voucher to another company to use (REG Cpt III)
- **Selling only permitted once** → powerful incentive that may boost development of new antimicrobials
- **Conditions of granting the voucher** → PRIORITY antimicrobial (not cumulative):

− new class
− new mechanism of action (different from any other authorised in EU)
− new active substance that addresses a multi-drug resistant/serious infection
+ priority antimicrobial must present preclinical and clinical data that underpin a significant clinical benefit with respect to AMR
− MAH has a capacity to supply in sufficient quantities for needs of Union market
− transparency of all (private and public) direct funding received for R&D → information to be made public

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Conditions of use and transfer, validity

- Can only be used once in relation to a single medicinal product
- Receiving product: Use only in first 4 years of its data protection → 2 years legal certainty/preparation for generics and biosimilars
- Use possible only if priority antimicrobial is **still on the market** (not withdrawn)
- Transfer possible **only once** → obligation to inform EMA (information will be published on EMA website): (1) who the new bearer is and (2) the value of the transaction
- Voucher ceases to be **valid**:
  a) once it is used
  b) if not used within 5 years of granting
- Commission can **revoke** a voucher [prior to its transfer] if a request for supply or procurement of the priority antimicrobial in the EU is not fulfilled
- In case a priority antimicrobial if is **withdrawn** → immediate access to generics and biosimilars
- Measure only available for **15 years from entry into force** of the Regulation **OR** [whichever is earliest] **10 vouchers** available in total.

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Prudent use measures

- **Antimicrobial stewardship plan** (risk mitigation measures, monitor and report) (DIR Art 17)
- Special information requirements for antimicrobials (**educational materials** to HCPs, **awareness card**) (DIR Art 69)
- Special **ERA for antimicrobials** (DIR Art 22(4))
- All antimicrobials are subjects to the **medical prescription** (DIR Art 51)
- **Pack size** of the antimicrobial shall correspond to the usual posology and duration of treatment (DIR Art 17)
- **Additional obligations** if the risk mitigation measures contained in the antimicrobial stewardship plan is unsatisfactory (DIR Art 17)

Thank you

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