Unpacking the pharmaceutical and patent packages

OVERVIEW

On Wednesday 26 April, the European Commission published its long-awaited pharmaceutical package after five delays. The package consists of the following:

1. **A Directive on the Union code relating to medicinal products for human use** (amending and replacing Directive on the Community code relating to medicinal products for human use and incorporating and amending relevant parts of the Regulation on medicinal products for paediatric use)
2. **A Regulation outlining Union procedures for the authorisation and supervision of medicinal products for human use and establishing a European Medicines Agency** (amending and replacing the Regulation on laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency, Regulation on orphan medicinal products and Regulation on medicinal products for paediatric use)
3. **Two non-binding documents:**
    - **A Commission Communication on Pharmaceutical Reform and Antimicrobial Resistance (AMR)** *(please note the Communication is not being considered with the scope of this update)*
    - **A Commission proposal for a Council Recommendation** on stepping up EU actions to combat antimicrobial resistance in a One Health approach (based on this, the Swedish Council Presidency will work on the Recommendation and aim to finalise the text before the end of its Presidency in June 2023) *(please note the proposal is not being considered with the scope of this update)*

In addition to the publication of the pharmaceutical package, it is important to note that the Commission was also expected to publish the patent package, which includes supplementary protection certificates, compulsory licensing and standard essential patents. Contrary to expectations, the patent package was not published on Wednesday 26 April but should be published on 27 April. Please note FTI Consulting was able to view draft documents of the package and, therefore, is sharing initial considerations.

In this document, which follows our update on the press conference announcing the publication of the pharmaceutical package, we provide key considerations on:

- **I: Pharmaceutical package:** Overview of the core issues of the Directive and the Regulation (we will follow-up on the AMR pieces separately)
- **II: Pharmaceutical package**: Initial Member State and European Parliament positions
- **III: Patent package**: Supplementary protection certificates and compulsory licensing (standard essential patents are not covered in this document)

TABLE OF CONTENTS

KEY CONSIDERATIONS

I: PHARMACEUTICAL PACKAGE: OVERVIEW OF THE CORE ISSUES OF THE DIRECTIVE AND THE REGULATION

The pharmaceutical package outlines 14 issues overall ranging from manufacturing to paediatrics to advanced therapy medicinal products and hospital exemptions. Based on our assessment of the key changes, we have identified seven areas that could have substantial impacts on the biopharmaceutical sector: (1) incentives, (2), antimicrobial resistance, (3) shortages and security of supply, (4) reporting on publicly funded financial support, (5) environmental risk assessment, (6) regulatory procedures, (7) manufacturing.

1. INCENTIVES

The proposed changes in the incentives framework relate to: (i) regulatory data protection, (ii) market exclusivity, (iii) launch across EU Member States, (iv) unmet medical need, and (v) high unmet medical need. Please see more information on each in the sections below, which are further sub-divided along three elements (where relevant): proposed measures, current situation, and how the proposed measures vary from the March 2023 draft proposal.

i. Regulatory data protection (RDP) and market protection (MP) for medicinal products

Proposed measures

For medicinal products, the European Commission proposes reducing the baseline regulatory data protection (RDP) for medicines that are granted a marketing authorisation in the EU from 8 years to 6 years. To this baseline, additional RDP can be added if certain conditions are met up to a maximum of 10 years of RDP:

- +2 years if 'sufficient supply' (launching in all EU Member States) is met in all EU Member States within 2 years, or 3 years for SMEs, not-for-profits and undertakings that received not more than 5 centralised marketing authorisations (more detail in section on launch across all EU countries)
- +6 months if an unmet medical need is addressed (more detail in section on unmet medical need)
- +6 months if comparative clinical trials were conducted (the European Medicines Agency to set scientific guidelines to propose a comparator)
- +1 year if during the data protection period an authorisation for an additional therapeutic indication was obtained showcasing a significant clinical benefit compared to existing therapies (can only be granted once)

Market protection (MP) will extend protection for 2 years from the expiry of the RDP. This leads to a maximum of 12 years, when combining the maximum RDP and MP, compared to a maximum of 11 years currently.

Medicines with a conditional marketing authorisation can only receive an additional 6 months of RDP for an unmet medical need (UMN) in case the product is granted a full marketing authorisation within 4 years of obtaining the conditional marketing authorisation.

Current situation

Currently, RDP is granted for 8 years at the time of marketing authorisation, extended by 2 years of MP. An additional year of MP can be granted in case a new therapeutic indication is approved for the same medicine.

How the proposed measures vary from the March 2023 draft proposal

Compared to the draft proposal, the benefit that would be gained by meeting 'sufficient supply'/launch in all EU Member States has increased from 1 year to 2 years of additional RDP. Addressing UMN has been reduced from 1 year to 6 months of additional RDP. Finally, RDP, which was capped to 8 years in the draft, is no longer capped in the proposal.

ii. Market exclusivity (ME) for Orphan Medicinal Products (OMP)

Proposed measures

The baseline ME granted for OMP will be reduced from 10 years to 9 years. More specifically:

- 9 years of ME will be granted for all OMP that do not address a high unmet medical need, or are not well-established use cases
- 10 years of ME will be granted for orphan medicinal products that address a high unmet medical need (HUMN, more detail in section on HUMN)
- 5 years of ME for well-established use cases (meaning if the active substances of the medicinal product have been used within the EU for the same therapeutic use and route of administration for at least ten years)

Notably and to prevent 'evergreening' of medicines, if marketing authorisation holders (MAH) hold more than one marketing authorisation for the same active substance, they will not enjoy separate ME periods. Additionally, if an OMP has less than two years of ME left, a submission for a marketing authorisation for a similar medicinal product, generics and biosimilars, can take place. However, a similar medicine will only be able to enter the market after the expiry of the ME period.

On top of this, the ME of OMP can be extended if the following conditions are met:

- +12 months in case of 'sufficient supply' (launching in all EU Member States)
- +12 months if a marketing authorisation for a new indication for a different orphan condition is obtained (can be granted twice, though for a different orphan condition)

In cases in which ME is extended for a new therapeutic indication, RDP will not be granted for this new therapeutic indication.

Current situation

OMP receive 10 years of marketing exclusivity and 2 years of additional ME in cases including a paediatric investigation plan (PIP). Protocol support and reduced fees are available for paediatric medicines. Today for each medicinal product, even if they have the same active substance, they can have separate exclusivity periods. This will no longer be the case with the proposed changes.

How the proposed measures vary from the March 2023 draft proposal

There are no changes.

iii. Launch across all EU Member States—'sufficient supply'

Proposed measures

The proposal grants MAH an additional two years of RDP if the medicinal product meets the condition of 'sufficient supply', something that does not currently exist in the legislation. This means that when a medicine is 'released and continuously supplied into the supply chain in a sufficient quantity and in the presentations necessary to cover the needs of the patients in the Member States in which the marketing authorisation is valid.' (Directive, Article 82.1)

To obtain these additional two years of RDP, the MAH needs to apply for a variation of the marketing authorisation. This application needs to be submitted between 34 and 36 months after the granting of the marketing authorisation and will need to demonstrate that within two years the 'sufficient supply' condition was met. Non-profits, SMEs and undertakings that have received not more than five centralised marketing authorisations, will have 46 to 48 months to apply for this prolongation and will need to demonstrate they met the condition in three years.

As part of the application for a variation, Member States will need to respond within 60 days of the request from the MAH. In this context, Member States have three options:

- Confirm compliance
- Make a reasoned statement of non-compliance
- Provide a statement of non-objection to prolonging the period of regulatory data protection—in the case that there is no response within 60 day, it will be regarded as non-objection

Importantly, as the term 'sufficient supply' is rather vague, Member States are expected to discuss the practical application of this Article in the Pharmaceutical Committee. Furthermore, for this discussion on practical application, the Commission can invite payers—such as health technology bodies (HTA) bodies or national bodies responsible for pricing and reimbursement—to be part of these meetings. Based on the input from Member States, the Commission will likely adopt implementing measures.

Current situation

There are currently no measures in place to incentivise new medicines to be launched across EU Member States within a short time period.

How the proposed measures vary from the March 2023 draft proposal

Compared to the draft version, a new category of companies can benefit from the extended time to launch in all markets, namely undertakings which have received five or fewer centralised marketing authorisations. This allows these companies—who would not meet the SME criteria but still likely have smaller teams in markets—to have more time for market access applications and launch across EU Member States. Furthermore, in the discussion of how to apply this legislation at the national level, HTA and pricing and reimbursement bodies can be invited to participate in the meetings of the Pharmaceutical Committee. This means that national payers are likely to influence how this new provision will be applied in the Member States, and what criteria will define 'sufficient supply'.

iv. Unmet medical need (UMN)

Proposed measures

The Commission proposes that medicinal products receive an additional six months of RDP if they address an UMN. To meet this definition, at least one of the product's therapeutic indications needs to relate to a life threatening or severely debilitating disease. Importantly, this will only meet the criteria if:

- There is no other medicinal product in EU for such a disease, or, where despite a treatment, the disease is associated with a remaining high morbidity or mortality
- The new medicine will provide a meaningful reduction in disease morbidity or mortality for the relevant patient population

OMP are considered to be addressing an UMN by default.

Current situation

While UMN is used for faster regulatory approval, it is not linked to receiving RDP.

How the proposed measures vary from the March 2023 draft proposal

The draft version used the same terminology that European Medicines Agency (EMA) is using today to describe a UMN, talking about 'no satisfactory method of diagnosis, prevention or treatment'. In the new version, UMN only refers to medical products and the reference to diagnosis and prevention has been removed.

v. High unmet medical need (HUMN)

Proposed measures

In its proposal, the Commission suggests recognizing all OMPs as meeting UMN, thereby gaining 6 months of RDP. Building on that, OMPs can be granted an additional year of ME if they meet the criteria of HUMN. To do so, the following criteria need to be met:

- There is no medicinal product for such a condition or where, despite a treatment, the new OMP can demonstrate significant benefit that will bring exceptional therapeutic advancement *(FTI note: this concept is not defined)*
- The new OMP results in a meaningful reduction in disease morbidity or mortality for the relevant patient population

For medicinal products in well-established use (for the same therapeutic use and route of administration, for at least ten years), these will not be considered to address a HUMN.

The EMA will adopt scientific guidelines on the application of these measures.

Current situation

The concept of unmet medical need currently is used for faster regulatory approval, the term high unmet medical need is not used in current regulatory processes in EMA.

How the proposed measures vary from the March 2023 draft proposal

There are no changes.

2. ANTIMICROBIAL RESISTANCE (AMR)

Proposed measures

The Commission proposes the introduction of 'transferable data exclusivity vouchers' (TEV), which would be granted to manufacturers of a 'priority antimicrobial'. To qualify, at least one of three specific criteria are fulfilled:

- The antimicrobial needs to represent a new class of antimicrobials
- The antimicrobial's mechanism of action needs to be distinctly different from that of any authorised antimicrobial in the EU
- The antimicrobial needs to contain an active substance not previously authorised in medicinal product in the EU that addresses a multi-drug resistant organism or a serious or life-threatening infection

In addition, the Commission proposes that the EMA should take the WHO's priority pathogens list for R&D of new antibiotics or a European level list *(FTI note: this does not exist yet)* into consideration when making an assessment on the voucher.

To obtain a voucher, the manufacturer must fulfil two additional criteria, namely:

- Demonstration of capacity to supply the priority antimicrobial in the EU in sufficient quantities (sufficient quantity not defined)
- Provision of information regarding all direct financial support received for research related to the development of the priority antimicrobial, which needs to be made public 30 days after the marketing authorisation is granted (i.e., this is broader than the provision in the package on publicly funded support)

If obtained, the developer of the antimicrobial that meets the TEV criteria would be granted one additional year of RDP (this can only be received once) if requested within the four-year period following the market authorization of said antimicrobial.

Notably, this can be applied on the antimicrobial itself or on any product that has marketing authorization from the manufacturer. Alternatively, the voucher could also be sold to another MAH, but then will not be able to be transferred again (only change from March 2023 draft).

Once used, the voucher loses its validity. If the TEV remains unused, it will lose its validity after five years from the day the voucher was granted. The proposal outlines that a maximum of 10 vouchers will be made available for a duration of a 15-year period.

Current situation

TEVs do not currently exist at the EU level. As such, this new provision can be understood as the Commission's effort to combat the current market failure connected to AMR drug development.

Other jurisdictions, such as the United States, have established transferable vouchers for rare paediatric disease products or other eligible neglected diseases, to accelerate Food and Drug Administration review

process. However, these do not apply to regulatory intellectual property extensions (e.g., see: FDA guidance on Rare Pediatric Disease Priority Review Vouchers)

How the proposed measures vary from the March 2023 draft proposal

On the sale of TEV, the draft proposal outlined the possibility to transfer the voucher an unlimited number of times. This has been changed in the final proposal to prohibit further sales once the voucher has been transferred to a third MAH.

3. SHORTAGES AND SECURITY OF SUPPLY

Proposed measures

In its proposal, the Commission sets new definitions connected to shortages:

- 'Shortage'—a situation where the supply of a medicinal product does not meet the demand for that medicinal product
- 'Critical shortage in the Member State'—a shortage for which no appropriate alternative medicinal product is available on the market in the Member State and the shortage cannot be resolved
- 'Critical shortage'—a critical shortage in a Member State where coordinated EU action is considered necessary

Additionally, the Commission also proposes several new requirements for MAH:

- Once marketing authorisation is granted, MAH would be required to prepare and keep up to date a shortage prevention plan (SPP) for medicinal products
- In the case of a potential or actual shortage, MAH would be required to submit a notification of the EMA and Member State competent authorities
- Once a shortage notification is submitted, MAH may be required to provide Member State competent authorities with a shortage mitigation plan (SMP), and additional information—competent authorities will be able to set deadlines for the submission of requested information
- In the case of critical shortages, MAH will be obliged to comply with Commission and Member State actions to address such critical shortages

The EMA will have a central role in overseeing shortage monitoring and mitigation of shortages. More specifically it will:

- Provide guidance on how to develop the shortage prevention plan and the SMP, as well as on what information should be included
- Provide country-specific recommendations on shortage mitigation measures
- Adopt, review and update, via the EMA's Executive Steering Group on Shortages and Safety of Medicinal Products (also called 'the Medicines Shortages Steering Group', MSSG), a Union list of critical shortages of medicinal products and ensure monitoring of those shortages. The MSSG will also provide recommendations on measures to avoid shortages
- Collaborate and work in a coordinated manner with national competent authorities when critical shortages are identified, to manage those critical shortages, whether the medicinal product concerned by the critical shortage is covered by a centralised MA or a national MA

Current situation

The proposal is a strong move by the European Commission towards ensuring security of supply and avoiding future shortages and is a substantial change from the current framework creating new requirements for MAH and new responsibilities for EMA and Member State authorities. Presently MAH are only required to submit a notification of a product being taken off the market and ensure 'appropriate and continued supplies' of medicines.

How the proposed measures vary from the March 2023 draft proposal

Compared to the draft proposal, the final proposal provides definitions for 'shortage', 'critical shortage in the Member State', and 'critical shortage'.

4. REPORTING ON PUBLICLY FUNDED FINANCIAL SUPPORT

Proposed measures

The Commission introduces the responsibility for MAH to report on publicly funded financial support for a product obtaining a national or centralized marketing authorisation. MAH need to declare any direct financial support from public authorities or publicly funded bodies concerning any activities for the R&D for the medicinal product. A report will need to be submitted within 30 days following the granting of the MA. The electronic report will need to be audited by an independent external auditor and be available to the public.

Current situation

This requirement currently does not exist.

How the proposed measures vary from the March 2023 draft proposal

The obligation to report has been broadened to include any activities related to the R&D of the product, while before it was restricted to clinical trials. However, the scope of funding to be disclosed is limited to direct financial contributions (such as direct grants or contracts), and does not include instruments, such as R&D tax incentives.

5. ENVIRONMENTAL RISK ASSESSMENT

Proposed measures

The proposal sets out that the marketing authorisation application should be refused if the environmental risk assessment (ERA) is not complete or does not address risks identified in a sufficient matter. More specifically, it highlights:

- With regards to AMR, that the ERA will need to cover AMR-specific risks through its entire lifecycle including manufacturing, use and disposal of medicinal products
- With regards to medicines containing genetically modified organisms, that the ERA will need to identify and evaluate potential adverse effects of the genetically modified organisms on human health and the environment

In addition, the EMA will have to publish an assessment report on the medicinal product, in which a summary of the studies carried out for the ERA by the MAH and the assessment of the environmental risk assessment of the agency needs to be included.

The manufacturer will also be required to update the ERA if new information occurs that could lead to a change of the ERA conclusion.

For approved medicinal products prior to 2005, an ERA submission programme should be set up for products that are identified as potentially harmful to the environment. The programme is to be made public.

Finally, the EMA may also impose obligation on the MAH to conduct a post-authorisation ERA study to further investigate risks to the environment or public health due to the release of medicinal product in the environment, if new concerns emerge in the medicinal product or other medicinal products containing the same active substance. A joint ERA study could be done if this obligation applies to several medicinal products. Finally, a register of conducted ERA studies should be set up by the EMA and publicly accessible unless restrictions are necessary to protect commercially confidential information.

Current situation

While an ERA has been obligatory since 2006, this assessment currently does not impact the EMA's decision to grant an application for a marketing authorisation. The proposal changes this significantly and provides EMA with additional power to link the MA on the potential impact of a drug on the environment.

How the proposed measures vary from the March 2023 draft proposal

Environmental considerations have been strengthened in the final proposal, in particular the possibility to refuse MA based on the ERA has become more stringent. In the previous version of the proposal, it was outlined that the MA 'may be refused'. In contrast, the final proposal stresses that MA 'should be refused' if the ERA is incomplete or insufficiently addresses environmental risks.

6. REGULATORY PROCEDURES

These proposed changes to regulatory procedure relate to the (i) European Medicines Agency and (ii) e-leaflets and labelling. With regards to the EMA, our considerations focus on five changes: EMA's structure, pre-authorisation regulatory support, drug device combination, Temporary Emergency Marketing, and regulatory sandbox.

i. European Medicines Agency

EMA Structure

Proposed measures

Regarding the structure of the EMA, the Commission's proposal outlines two key changes on: (i) EMA's Committees and (ii) inclusion of patient representatives.

Regarding EMA's Committees, the proposal outlines the role of Agency's two key scientific committees, the Committee for Medicinal Products for Human Use (CHMP) and the Pharmacovigilance Risk Assessment Committee (PRAC), which are to retain their functions. Thus, the CHMP will be responsible for all activities

connected to submission, granting, variation, suspension, or revocation of marketing authorisation of a medicinal product while the PRAC Committee will cover risk management aspects of the use of medicinal products for human use.

In addition to these two Committees relevant for human health, scientific working parties and advisory groups can be established to support their tasks (e.g., a scientific advice working party or an ERA working party).

Regarding the inclusion of patient representatives, the proposal outlines that EMA is to create a consultation process with relevant national authorities and bodies, responsible for HTA and pricing and reimbursement at the national level. This may also be extended to patients, medicines developers, healthcare professionals, industries, or other stakeholders as relevant.

Current situation

EMA has seven scientific committees and several working parties and related groups.

The CHMP is the EMA's committee responsible for human medicines, in charge of conducting the initial assessment of all MA applications, assessing modifications or extensions ('variations') to an existing MA.

There are limited flexibilities and often delays to issuing regulatory MA.

How the proposed measures vary from the March 2023 draft proposal

There are no changes.

<u>Pre-authorisation regulatory support</u>

Proposed measures

The proposal outlines measures across the text for increased pre-authorisation regulatory support. As such, scientific pre-authorisation regulatory support will be strengthened by the provision of:

- Scientific advice to developers or not-for-profit organisations, with additional consultation support by Member States experts with clinical trials or medical device expertise for those developing medicinal products involving a medical device (i.e., combination products)
- Parallel scientific advice by EMA upon request by developers or not-for-profit organisations should they wish to receive additional scientific advice parallel to the joint scientific consultations as carried out by the Member State Coordination Group on Health Technology Assessment (HTACG)
- Enhanced scientific and regulatory support for priority medicinal products (PRIME) if these fulfil following conditions:
    - Medicinal product to address an unmet medical need
    - Medicinal product is an orphan medicinal product and is likely to address a high unmet medical need
    - Medicinal product is of major public health interest specifically regarding therapeutic innovation or an antimicrobial
    - Medicinal products which are tackling a disease that could cause a serious cross border health threat may also fall into the area of enhanced scientific and regulatory support

- Scientific recommendation on regulatory status: Developer or a competent authority of the Member States may submit a request to EMA for a scientific recommendation to determine whether the product is a 'medicinal product' or an 'advanced therapy medicinal product' respectively
- Regarding timelines, the reduction of the marketing authorisation procedure is outlined from 210 days to 180 days

Current situation

Currently, the EMA provides scientific advice or protocol assistance to developers (i) before the marketing authorisation submission throughout the development stage or (ii) during the post-authorisation stage. While scientific advice is provided for innovative medicines, or medicines that tackle an unmet medical need, topics such as advanced therapy medicinal product classification or PRIME eligibility are currently outside the scope of the scientific advice.

Not-for-profit organisations and academia are currently able to receive tailored scientific advice only in the context an EMA's pilot project on supporting not-for-profit organisations and academia in repurposing authorised medicines for an indication outside its existing authorised indication(s).

Lastly, marketing authorisation procedures by the EMA are currently completed in 210 days.

How the proposed measures vary from the March 2023 draft proposal

The provision on tailored scientific advice for not-for-profit entities and medicinal products has been removed, as well as the selection criteria for enhanced scientific regulatory support for priority medicines.

<u>Drug devices combination</u>

Proposed measures

The Directive includes measures for both types of drug-device combinations: integral combinations of medicinal products and medical devices (the medicinal product and device form a single product), and medicinal products in exclusive use with a medical device (the medicinal product is separate from the medical device, but both are presented in a same package).

The overall emphasis of the Commission is on ensuring consistent and coherent applicability of the EU medical device and medicinal product legislation as well as ensuring all data is submitted jointly for authorization of combination products, ensuring that authorities have information covering both the pharmaceutical and the medical device to undertake the product assessment.

In both cases, safe and effective use will have to be demonstrated. Authorities will assess the benefit-risk balance and the overall suitability of use and they can request the marketing authorisation applicant to transmit any additional information needed.

However, the Directive does not provide for a specific role by EMA in the coordination of co-development and authorization aspects, as it refers to the role of competent authorities more generally.

Current situation

Combination products are addressed by different legislative frameworks (Medical Devices Regulation and the EU general pharmaceutical legislation). The limited alignment and between both regulatory processes create fragmentation and delays in access for patients while impacting innovation.

How the proposed measures vary from the March 2023 draft proposal

There are no significant changes.

Temporary Emergency Marketing Authorisation (TEMA)

Proposed measures

The Commission proposed a new temporary emergency marketing authorisations (TEMA) to tackle public health emergencies. A TEMA can be granted if:

- There is no other satisfactory method of treatment, prevention or diagnosis authorised or sufficiently available. The availability of the new medicinal product will address a public health emergency
- EMA issues an opinion concluding that the medicinal product could be effective in treating, preventing or diagnosing the disease or condition connected to the public health emergency
- The benefit of the medicinal product's immediate availability would outweigh the potential risks (based on limited data at that point in time)

The manufacturing of the medicine must comply with good manufacturing and pharmacovigilance practices.

A TEMA is deemed invalid when the Commission terminates the recognition of a public health emergency. The TEMA marketing authorisation holder can submit an application to obtain a marketing authorisation, which would in reference to regulatory protection data be considered as part of the same marketing authorisation as the previously granted TEMA ('same global marketing authorisation)'

Current situation

Currently, the EMA offers conditional marketing authorisation, which is meant to tackle unmet medical need but can also be used in public health emergencies. With the provision of the TEMA, a separate tool is now existent to tackle public health emergencies specifically. While the new TEMA may only be granted after the recognition of a public health emergency and will stay valid if there is a health emergency, the existing conditional marketing authorisation is conditional to specific criteria related to unmet medical need, valid for 1 year and must be renewed annually.

How the proposed measures vary from the March 2023 draft

There are no significant changes.

Regulatory sandbox

Proposed measures

The pharmaceutical package outlines measures for a so-called 'regulatory sandbox', a tool to accelerate and test out product development under specific conditions.

As such, a regulatory sandbox may be set up by the EMA when following conditions are fulfilled:

- It is not possible to develop the medicinal product or category of products in compliance with medicinal products requirements due to scientific or regulatory challenges due to product characteristics or methods used

- The aforementioned characteristics contribute distinctively to the quality, safety or efficacy of the medicinal product or products category or provide major advantage connected to patient access to treatment

EMA will monitor the emerging medicinal products area to identify potential stakeholders. Once a likely candidate has been identified, EMA is to provide a recommendation listing eligible products/category of products to the Commission, as well as a sandbox plan, which sets out clinical, scientific and regulatory justification for a sandbox and needs to include proposed timeline and duration of the sandbox. Products that are in advanced development stage shall not be recommended.

Regarding the regulatory sandbox's characteristics, the proposal outlines that it will set out a regulatory framework, including scientific requirements for the development, clinical trials (if applicable) and access to markets.

The sandbox is under supervision of the competent authorities of the Member States concerned to ensure compliance with the requirements and an annual report needs to be provided by the EMA on the results of the regulatory sandboxes.

Current situation

A regulatory sandbox is a new provision under the pharmaceutical package.

How the proposed measures vary from the March 2023 draft

There are no significant changes.

ii. E-leaflets & labelling

Proposed measures

<u>E-leaflets</u>

The pharmaceutical package proposal puts forward provisions allowing the Commission to make electronic product information (ePI) for medicinal products mandatory via delegated legislation. The final proposal includes the right for patients to receive a printed copy of the electronic package leaflet free of charge in cases where the package leaflet is only available electronically. Additionally, the Commission is empowered to set common standards for the electronic version of the package leaflet, the summary of product characteristics (SmPC) and the labelling, taking into account available technologies.

<u>Labelling</u>

The Commission proposal allows for additional exemptions from the labelling and package leaflet requirements, namely where there are space constraints due to packaging/package leaflet size or multiple languages, in the context of a public health emergency, or to facilitate access to medicines in Member States. For antimicrobials in particular, the Commission proposes new requirements for marketing authorisation holders of antimicrobials who would need to:

- Ensure availability of educational materials to healthcare professionals detailing the appropriate use of diagnostic tools, testing and other diagnostic approaches
- Develop an 'awareness card' today

- Be included in the packaging of antimicrobials, which contains specific information about antimicrobial resistance, appropriate use and disposal

Current situation

E-leaflets

Text-heavy paper-based patient information leaflets (PIL).

Labelling

The proposal allows for greater labelling and packaging flexibility and introduces a new antimicrobial awareness card. This shows the Commission's ambition to create greater flexibility to allow quicker reactions to public health emergencies and facilitate access, as well as raising awareness of AMR.

How the proposed measures vary from the March 2023 draft proposal

Changes are minor. With regards to the E-leaflets, the final proposal removes the 2035 mark as the earliest year when a delegated power to make electronic product information mandatory for Member States could be adopted by the Commission. Instead, it states that delegation of powers shall apply five years following 18 months after the date of entering into force of the new Directive.

7. MANUFACTURING

Proposed measures

The proposal requires that the manufacturing, import and export of medicinal products are subject to a manufacturing authorisation granted by a Member State.

The application will outline the details of the manufacturing and ensure that the applicants have sufficient resources, both technical and facility focused, to meet the requirements.

The manufacturing authorisation holder needs to comply with the principles of good manufacturing practice (GMP) for medicinal products and only use active substances (API) that were manufactured in accordance with the GMP and distributed according to the good distribution practice (GDP) of active substances.

In order to manufacture, import and distribute active substances, including those intended for export, the active substances need to be manufactured according to the GMP.

Compliance with these requirements will be ensured through a system of supervision and controls by Competent Authorities and EMA, including through inspections and review of relevant documentation.

Third countries can be recognised as having a level of public health protection equivalent to that of the Union.

Current situation

Currently the GMP are not applicable to the import of active substances but only regarding medicinal products.

How the proposed measures vary from the March 2023 draft proposal

There are no significant changes.

II: PHARMACEUTICAL PACKAGE: INTIAL MEMBER STATE AND EUROPEAN PARLIAMENT POSITIONS

In this section, please find key considerations on initial positions of select Member States (outlined in informal non papers, drafted before the publication of the package, which FTI Consulting was able to see and is sharing with this update) as well as relevant Members of the European Parliament (MEPs).

1. MEMBER STATES

In this section we provide a brief overview of: (i) the Danish non-paper, (ii) the non-paper written by a group of six Member States: Austria, Estonia, Hungary, the Netherlands, Poland, and Slovakia, (iii) the French non-paper, (iv) the German non-paper and (v) a press statement from Irish Ministers. Additionally, we understand that Italy has also drafted a non-paper. Notably, there are no known positions from the two forthcoming Council Presidencies (Spain and Belgium) on the broader package.

Key issues discussed in the non-papers include:

- Regulatory data protection: Denmark, Germany and France warn against shortening the period of regulatory data protection stating that the uncertainty created by alterations could drive away investment while the group of six Member States are in favour of a more conditional approach to incentives
- Launch conditionality: Both Denmark and France support a more nuanced approach to the launch conditionality, taking into account gradual capacity building for supply in all Member States
- Supply chain security and shortages: While Denmark calls for balancing administrative burden for industry with transparency, France calls for the shortage monitoring and reporting requirements to go even further

Please note that these initial positions (aside from the Irish press statement) are based on a draft proposal of the pharmaceutical package and are likely to change once countries have assessed the European Commission's final proposal.

i. Danish non-paper

Positive elements

- Highlights the opportunity to address some of the critical challenges facing Europe – such as access, innovation, and security of supply

Areas of concern

- Highlights concerns around reducing the period of RDP for companies, fearing that this could have adverse impacts including creating uncertainty for companies' investments, leading to fewer new medicines, and making Europe less attractive to industry

Suggestions

- Puts forward the concept of establishing a principle of shared responsibility, instead of the requirement to launch in all Member States, which they believe will not improve access for patients. The principle of shared responsibility would include:
    - For industry:

        - The obligation for companies to report their national marketing authorisation plans for products for which they have not taken steps to market in all EU countries in a reasonable time, **OR**
        - The obligation for companies to file for pricing and reimbursement in all Member States—supported by efforts to ensure better transparency on reimbursement and launch status
    - For Member States: the requirement to ensure sufficient competent authority capacity to streamline national pricing and reimbursement procedures (including early advice to support companies) and enable collaboration on best practices amongst national authorities and proper implementation of shared health technology assessments
- Highlights that to keep Europe at the forefront of global innovation, the regulatory framework has to set competitive and predictable conditions which support development and approval of medicines, whilst simultaneously protecting and developing the European economy, to:
    - Ensure predictability in the Regulation's protection periods, as conditional regulatory protection periods create great uncertainty
    - Simplify and streamlined approval procedures and flexibility to allow for adaptation to scientific and technological developments-- including through closer, earlier and ongoing public-private collaboration in the regulatory phase
    - Timely and effectively implement health technology assessments to decrease the burden on national authorities
    - Ensure earlier scientific advice and, particularly for SMEs to overcome barriers related to market launch
- Notes that security of supply is an increasing issue, due to vulnerable global supply chains and actions around this should balance administrative burden for industry with transparency, more specifically, considering transparency regarding expected need and actual use of medicines in national health care systems and supply capacity of companies, diversification of production sites and supply chains, and use of electronic patient information leaflets

ii. Austrian, Estonian, Hungarian, Dutch, Polish and Slovakian non-paper

Positive elements

- Welcomes the proposal to link incentives to data protections for health priorities, stating that the EU incentives to pharma are 'lavish' (i.e., provide more protection compared to other regions)
- Supports an approach under which companies can attain ten years of data and market protection if their product addresses health priorities
- Supports allowing earlier generic competition to increase accessibility and affordability of medicines

Areas of concern: N/A

Suggestions

- Calls for a more patient-centric approach, which is designed to reward medicines meeting unmet medical needs and allows for earlier entry of generics
- Cautions against letting competitiveness concerns overshadow broader needs

iii. French non-paper

Positive elements

- Supports the minimal obligation for companies to present a supply shortage management plan for critical medicines
- Welcomes the proposal for a harmonised shared life-cycle assessment to be made public, and suggests assessing the potential use of existing tools including PBT (persistence, bioaccumulation, toxicity), as well as looking at carbon footprint

Areas of concern

- Emphasises that whilst concerns around antimicrobials are shared, France does not support the creation of the TEV, as it would have an important financial impact, instead would favour incentives and financial support to public health priorities *(FTI note: France was among the 14 signatories of the non-paper arguing against the transferable exclusivity voucher published at the end of 2022)*
- Highlights concerns around the reduction of data protection from eight to six years as this could hinder attractiveness of the EU for innovation

Suggestions

- Calls for marketing authorisations to be simplified and fast track processes to be facilitated for medicines that cover severe disease and present a clinical benefit compared to alternatives
- Highlights that orphan and paediatric medicines need to be supported by promotion of European coordination of clinical data collection and obligations to carry out paediatric investigation plan (PIP), as well as an introduction of a general framework for off-label use of medicines in paediatrics by EU authorities
- Suggests the creation of a temporary marketing authorisation rather than a conditional marketing authorisation, to overcome the challenges that medicines with conditional marketing authorisations have in accessing the EU market, as HTA bodies cannot assess their value due to not having access to the full set of clinical evidence. Under the temporary marketing authorisation, companies would be obliged to collect real data on patients receiving the treatment, until the marketing authorisation is confirmed, therefore monitoring patients receiving the treatment and generating additional data to support the re-evaluation by the EMA and HTA bodies
- States that the framework for promoting EU access must be pragmatic and consider supply chain capacities of companies and financial implications for Member States
- Proposes conditions for the unmet medical needs including: a mechanism to account for the progressive capacity of companies to supply all EU Member States, a Member State mechanism to opt out in cases where difficulties in accessing medicines are not foreseen, and a clarification of general conditions around an acceptable offer
- Suggests the creation of a more comprehensive framework for drug shortages including a common definition of supply tensions and shortages, harmonised obligations for companies to report to national competent authorities 12 months before supply ceases within markets, and the obligation for the holder to immediately report foreseeable shortages of medicines and commit to a remediation plan
- Proposes close examination of incentives to invest in and develop production lines in the European Union, for raw materials, Active Pharmaceutical Ingredients, and finished products; with fast tracks offered to relocation projects which require substantive modifications to marketing authorisations

- Calls for the pharma package to be coherent with environmental regulations, therefore calls coherence between GMP and environmental standards

iv. German non-paper

Positive elements

- Welcomes the package will contribute to improvements such as more flexible and faster authorisation procedure and lessen administrative burden, such as the number of EMA scientific committees and removing the obligation for marketing authorisation holders to renew marketing authorisation after five years
- Supports the Commission's intention to differentiate the existing incentive structures and to avoid inefficient incentives, however, highlights that these must be designed in a way that ensures transparent and feasible requirements for research and industry, and does not create obstacles to innovation. Therefore, the system created must be easy to navigate, and provide clear definitions for terms such as 'well-established use orphan products' and the criteria for 'high unmet medical need'

Areas of concern

- Emphasises the risks of reducing the data protection period by two years, as the current regulatory protection periods play a key role in incentivising development of new and innovative medicinal products; warning that it is necessary to maintain an overall balanced system and attractive conditions for industrial investment
- Highlights that the current approach is not fit for purpose as predictability is key for an effective system of incentives, and that data protection that is conditional on supplying adequate amounts to all Member States is problematic. Furthermore, suggests that the voluntary commitment of companies which are members of the European Federation of Pharmaceutical Industries and Associations to submit an application for pricing and reimbursement in all Member States is more appropriate as an initial step
- Clarifies that different availability of new medicinal products across different Member States is not linked to data protection periods but rather multifactorial causes, and that uncertainty around data protection periods could lead to significant reduction in investment

Suggestions: N/A

v. Irish press statement

Following the pharmaceutical package publication, the Minister for Health Stephen Donnelly and the Minister for Enterprise, Trade and Employment Simon Coveney published a press statement, summarised below:

- Welcome the publication of the package, stating: (i) the importance of balancing accessibility and affordability of products with the need to foster innovation and competitiveness; (ii) the need to ensure access to innovative medicines, and to ensure continued access to off-patent medicines; (iii) that the proposal 'offers the opportunity to small Member States to potentially enhance market and patient access, through exploration of the use of technological adaptive solutions, such as electronic product and patient information, and multi-country packs'. Moreover, Donnelly notes that the Department of Health is chairing a national Working Group which will aim to support Ireland's

response to the package. Furthermore, Coveney underlines the role of the Irish companies in developing innovative treatments and investing in R&D and innovation, as well as committed to ensuring that the EU and Ireland can remain 'patent-generating and patent reliant business activities' locations

2. EUROPEAN PARLIAMENT

At this stage we understand that the European Parliament Committee on Environment, Public Health and Food Safety (ENVI) will lead on the file negotiations, with the possibility that the Committee on Industry, Research and Energy (ITRE) could either co-lead or be assigned exclusive competence over specific provisions of the legislative proposals.

With regards to what MEPs will lead on the drafting of the Parliaments position, we understand that the European People's Party (EPP, centre-right) is likely to have rapporteurship (i.e. lead drafter) of the proposed Regulation, and the Socialists & Democrats (S&D, centre-left) likely to have rapporteurship of the proposed Directive. As for ITRE, we understand that Renew Europe (RE, liberals) is pushing to have rapporteurship, in case the Committee is granted a co-leading role.

Whilst political discussions can be expected to take place for several weeks before Committee roles, rapporteurs and shadow rapporteurs are officially assigned, there are several MEPs who are frontrunners for a leading role in the negotiations:

- EPP group: MEPs Pernille Weiss (Denmark), Dolors Monserrat (Spain), Stelios Kympouropoulos (Greece), Peter Liese (Germany) and Christian Ehler (Germany) are likely to have a prominent role in the review of the proposal
- S&D group: MEPs Tiemo Wölken (Germany), Sara Cerdas (Portugal) and Nicolás González Casares (Spain) have also been vocal on the legislative proposals and are likely to obtain an official role in the negotiations
- Renew group: Véronique Trillet-Lenoir (France), Frédérique Ries (Belgium), Ondřej Knotek (Czechia) and Susana Solís Pérez (Spain) will seek to play a role in the negotiations, most likely pushing to obtain rapporteurship in the ITRE Committe

On Wednesday 26 April, following the publication of the pharmaceutical package, MEPs were able to address questions to Commissioner for Health and Food Safety Stella Kyriakides during a presentation of the package in the ENVI Committee. Some of the above-mentioned MEPs asked questions, including MEPs Liese, Weiss, Wölken, Cerdas, González Casares, Trillet-Lenoir and Susana Solís Pérez. Please find an overview of these questions below (FTI can provide the full list if of interest):

- Peter Liese, EPP, Germany: Noted that while the European Parliament and stakeholders have long waited for the pharmaceutical package, the published text is much stronger than previous drafts. He recognises the important role of the pharmaceutical package for support innovation in the EU and stresses the importance of Transferable Exclusivity Vouchers (TEV) for antimicrobial resistance (AMR), and strongly supports the measures intended to support launch of medicines in the 27 Member States. On this latter point, he asks for clarification on responsibilities of industries and Member States and what would happen if only one Member State is blocking the launch of the medicine. Additionally, he

asks to clarify which role other Directorate-Generals in the European Commission and Member States will play in tackling medicines shortage

- Pernille Weiss, EPP, Denmark: Asked for clarifications on proposed measures to tackle shortages, and particularly what role will the European Medicines Agency (EMA) play
- Tiemo Wölken, S&D, Germany: Highlighted that shortages of medicines are the major issue and asks for clarification on the suggested approach in the proposal, as well as whether the pharmaceutical package envisage an EU stockpiling of medicines and what the Member States' position on medicines stockpiling in. Additionally, he stresses the importance for the EU to play a role in regulating medicines pricing, taking measures to improve affordability and access. Lastly, he asks for clarification between the different incentives included for AMR
- Sara Cerdas, S&D, Spain: While welcoming this important proposal, she stressed the need for a stronger focus on accessibility of medicines and asked to clarify which measures are directly aiming to improve access across the EU
- Nicolás González Casares, S&D, Spain: Welcomed the proposal and particularly asked to Commissioner Kyriakides to clarify the measures and approach to tackle medicines shortages in the EU and the role of different EU institutions involved
- Veronique Trillet-Lenoir, Renew, France: Welcomed the proposal put forward by the European Commission and recognises its importance to improve affordability and access to medicines to patients. She asks for clarification of measures on transparency of public investments for R&D and how the European Commission is planning to supervise and monitor the implementation of the different incentives to manufacturers
- Susana Solís Pérez, Renew, Spain: Stressed that the proposal is aiming to balance patients' needs and perspective and the need to support R&D for pharmaceuticals in the EU

III: PATENT PACKAGE: STANDARD SUPPLEMENTARY PATENTS AND COMPULSORY LICENSING

In addition to the pharmaceutical package, the Commission also adopted an EU patent package. The below is based on a draft, which will be officially published on 27 April.

The patent package consists of multiple proposals, which span across different regulatory areas, two of which are most relevant for health and life sciences:

- **Supplementary Protection Certificates (SPCs):** The proposals introduce a centralised procedure for granting (unitary) SPCs for medicinal products. The proposals do *not* amend the substantive elements of the current SPC regime, i.e., the conditions for obtaining SPCs or their legal effects. Only procedural provisions are changed
- **Compulsory licensing:** The aim of the proposal is to create an EU-level compulsory licensing system to address crises at EU-level by ensuring the supply of crisis-relevant products

Please note that the analysis below does not cover the proposal on Standard Essential Patents, which are also covered under the patent package.

1. SUPPLEMENTARY PROTECTION CERTIFICATES

Current situation

Currently, supplementary protection certificates (SPC) are regulated under Regulation on SPCs for medicinal products and are granted at national level in accordance with national procedures, on the basis of a national application and an analysis conducted by national authorities. The current proposal is intended to tackle the fragmentation that exists due to the inconsistencies between national procedures for granting SPCs and to improve the concerns with transparency which makes it difficult to identify for which products and in which Member States SPC protection exists. For unitary patents, no unitary SPC currently exists.

Proposed measures

Based on the unofficial drafts we received on 26 April, the Commission is expected to table two proposals. These are:

- Proposal for a Regulation of the European Parliament and of the Council on the supplementary protection certificate for medicinal products (recast) and
- Proposal for a Regulation of the European Parliament and of the Council on the unitary supplementary certificate for medicinal products, and amending Regulation (EU) 2017/1001, Regulation (EC) No 1901/2006 as well as Regulation (EU) No 608/2013

Notably, the proposals do *not* amend the substantive elements of the current SPC regime, i.e., the conditions for obtaining SPCs or their legal effects. Only procedural provisions are changed. Instead, they focus on (i) definitions; (ii) existing provisions; (iii) new provisions defining the new centralised procedure; (iv) final provisions. Please find further details below on the centralised procedure and the unitary SPC.

Centralised procedure

The proposals introduce a centralised procedure for granting SPCs for medicinal products. This would allow applicants to receive SPCs in relevant Member States (subject to having marketing authorisation in each of

them) by filing a single centralized SPC application. The application would undergo an assessment conducted by a centralized authority at EU level, but SPCs would be granted by relevant national authorities based on the binding opinion of the central examination authority. The proposal puts forward the EU Intellectual Property Office (EUIPA) as the central examination authority, which would be supported by national offices.

Unitary SPC

Building on the new unitary patent system (which enters into force on 1 June 2023), the proposal introduces the unitary SPC. The granting of a unitary SPC is based on the same centralised examination procedure described above. The unitary SPC application would only be available based on a unitary patent as a basic patent and would have legal effect uniformly in all the Member States in which the basic patent has unitary effect (i.e., the 17 participating Member States).

2. COMPULSORY LICENSING

Current situation

The current Regulation (EC) No 816/2006 of the European Parliament and of the Council of 17 May 2006 on compulsory licensing of patents relating to the manufacture of pharmaceutical products for export to countries with public health problems sets out an EU-level procedure for granting compulsory licenses for patents and supplementary protection certificates related to the manufacture and sale of pharmaceutical products when these products are intended for export to eligible importing countries that need these products to address a public health problem. There is currently no EU-level compulsory licensing framework for the domestic market. Instead, Member States have their respective national frameworks for compulsory licensing applicable to their national territory.

Proposed measures

Based on the unofficial drafts we received on 26 April, the Commission is expected to table a proposal for a regulation of the European Parliament and of the Council on compulsory licensing for crisis management and amending Regulation (EC) 816/2006.

The aim of the proposal is to create an EU-level compulsory licensing system for addressing crises with a cross-border dimension within the EU by ensuring the supply of crisis-relevant products. The system proposed would have its own triggers, procedure and conditions, leaving national compulsory licensing systems (used for purely domestic crises) untouched. More broadly, the proposal aims to ensure coherence with the EU's other crisis and emergency instruments[1] and is compliant with the Agreement on Trade-Related Aspects of

[1] Proposal for a Regulation establishing a Single Market emergency instrument ('SMEI');
Regulation (EU) 2022/2371 of the European Parliament and of the Council of 23 November 2022 on serious cross-border threats to health and repealing Decision No 1082/2013/EU ('SCBTH'); Council Regulation (EU) 2022/2372 of 24 October 2022 on a framework of measures for ensuring the supply of crisis-relevant medical countermeasures in the event of a public health emergency at Union level ('Emergency Framework Regulation'); Proposal for a Regulation of the European Parliament and of the Council establishing a framework of measures for strengthening Europe's semiconductor ecosystem ('Chips Act').

Intellectual Property Rights ('TRIPS Agreement') which sets out the international framework for compulsory licensing. Please find further details below on the relevant provisions on scope and procedure.

Scope

The proposal provides for compulsory licensing of patents, utility models and supplementary protection certificates. Compulsory licensing would be applied to 'crisis-relevant products' which the proposal only defines in general terms: 'products or processes that are indispensable for responding to a crisis or emergency or for addressing the impacts of a crisis or emergency in the Union'. In the same vein, no definition of a crisis or emergency is provided. Overall, the proposal leaves the scope—both the triggering of an emergency and the relevant product identification – to the 'other' EU crisis instruments. In the area of health, the Regulation on serious cross-border threats to health provides that the Commission, based on the advice of the Health Security Committee, can declare a public health emergency at the EU level. If this happens, this proposal would enable the Commission to issue a compulsory license after having consulted the Health Security Committee. Notably, the proposal is not limited to medicinal products—the Annex provides for the procedure for other types of crises for example for semiconductors and gas products.

Procedure

The compulsory licensing instrument would be triggered by an EU-level decision activating crisis mode or declaring an emergency under an existing EU crisis instrument (e.g. the Regulation on serious cross-border threats to health or the Emergency framework regulation). According to the exploratory memorandum, the procedure could also be used to respond to crises with a cross-border dimension that do not reach the activation threshold of EU crisis instruments. The Commission, based on the non-binding opinion of a relevant advisory body, would adopt an activation measure granting a compulsory licence, applicable so several EU Member States or the whole EU. The license could be used both intra-EU as well as for exports.