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European Confederation of Pharmaceutical Entrepreneurs AISBL

INITIAL INTEL ON THE EU PHARMA PACKAGE

ON THE REVISION OF THE GENERAL PHARMACEUTICAL LEGISLATION AND THE OMP AND PAEDIATRIC REGULATIONS

OVERVIEW

The EMA Regulation No. 726/2004, the OMP Regulation No. 141/2000 and the Paediatric Regulation No. 1901/2006 will be merged into one "Master Regulation". Also, the Human Medicinal Products Directive 2001/83/EC will be repealed by a new Directive. **Both the new Regulation and Directive are part of the same Pharma Package**. The dual pathway is therefore maintained, for central authorization procedure (via the Regulation) and decentralized and mutual recognition procedure (via the Directive).

The Commission is currently undergoing its inter-service consultation of the pharmaceutical package, which will last until 14 February. It is important to note, changes can still follow as a result of the inter-service consultation. The proposals are then expected to be published on **28 March 2023**.

The Regulation and the Directive will apply 18 months after their entry into force (and, accordingly, Member States will have up to 18 months to transpose the Directive).

GENERAL PHARMACEUTICAL LEGISLATION

In a nutshell: the revision is in line with the expectations that EUCOPE was reporting. There will be a reduction of Regulatory Data Protection (RDP), attached with conditions on market launch and Unmet Medical Needs (UMN). Transparency on public funding for clinical trials will be required. Report obligations on shortages will be introduced. Some measures to reduce the regulatory burden, especially for SMEs, will be adopted.

Regulatory Data Protection

The Commission's proposal will **reduce the current Regulatory Data Protection (RDP) to a baseline 6-years.** Additional RDP can be obtained upon conditions, but with **a maximum of 8-years RDP**:

- +**1 year on market launch** in all EU Member States, within 2 years from Marketing Authorization (MA) and, in case of SMEs (*as defined in Recommendation 2003/361/EC*), within 3 years from MA; the medicinal product should be released and continuously supplied in a sufficient quantity and in the presentation necessary to cover the needs of the patients in the Member States in which the marketing authorization is valid;
- +**1 year addressing unmet medical needs** (UMN);
- **+6 month, conducting comparative clinical trials**.

On top of this, **+1 year of RDP if the Marketing Authorization Holder (MAH) obtains authorization for new therapeutic indication with significant clinical benefit**. After the expiry of RDP, **two (2) years of Market Protection are guaranteed**.

The proposal will introduce **four (4) years RDP for repurposed medicinal products**, but only once for each product, if it provides significant clinical benefit in comparison to existing therapies.

Definition of UMN and HUMN

A medicinal product is **designated as UMN** if it addresses certain conditions at product and disease levels: **at least one of its indications relates to a life-threatening or severely debilitating conditions; and no medicinal products is authorized in the EU or it does not offer satisfactory method; and the use of a medicinal product results in reduction of morbidity or mortality.** All OMPs are designated as UMN, and some of them as Highest Unmet Medical Need (H)UMN.

Medicine Shortages and security of supply

Regarding **medicine shortages**, we understand the proposal will require the Marketing Authorization Holder (MAH) to **prepare and keep updated a shortage prevention plan (SPP)**. MAH shall notify a Member State on the: the intention to cease marketing of a medicinal product (12 months before last supply); the intention to temporarily suspend marketing of a medicinal product (6 months before temporary disruption); the request to withdraw MA (12 months before last supply); temporary disruption in supply (as soon as MAH is aware and no less than 6 months before expected disruption). In case a MAH wants to permanently withdraw a MA, it shall first offer to transfer MA to a third party.

A list of critical medicinal products will be established by the EMA. MAH of critical medicinal products shall provide any additional information requested by EMA and take relevant measures to address EMA recommendations to ensure security of supply.

Regulatory changes

- **Post-marketing authorization safety studies may be imposed on MAH**, if there are concerns about safety of a medicinal product. This can also concern environmental risk assessment (ERA).
- The EMA will only have a **limited number of permanent committees** (one of which being the CHMP), but will have the ability to create scientific committees to support the work of the CHMP. The COMP and CAT are not among the permanent committees.
- To **reduce regulatory burden**, measures related to electronic submission of MA, as well as the abolishment of the renewal and sunset clause, will be introduced. **Specific support schemes for SMEs** will be adopted (e.g., for MA application, scientific advice, fee reduction or waivers).
- Provisions related to adapted clinical trials and **use of RWE** will be included.
- The Commission is establishing a **'regulatory sandbox'**, by which new technologies can be approved on temporary basis if the existing regulatory framework is not appropriate in order to adapt to new technologies.
- The EMA will allow for phased review (i.e., rolling review) in cases of exceptional therapeutic advancement.
- Products will no longer need to meet the GMO requirements, but will instead be taken up centrally as part of the ERA.

Additional provisions

- If compulsory licensing is issued by a relevant authority in the EU due to a public health emergency, **also RDP and market protection shall be suspended during the period of compulsory licensing**.
- **6-month SPC extension remains in place as reward for the PIP completion**.
- The Commission will also introduce a notification to report public funding for transparency of R&D costs. **MAH shall list public funding or financial support to conduct any clinicals trial relevant to MA**, and this report shall be accessible to public.

OMP REGULATION

In a nutshell: The proposal appears to be more balanced with both upward and downward modulation and a more permissive understanding of HUMN. While orphan designation (OD) will remain at 5/10,000 a more restrictive definition of significant benefit is introduced and active substances will only receive a single period of orphan market exclusivity (OME).

Overall, EUCOPE's advocacy efforts have helped drive the conversation in a positive direction as elements are not as negative as feared, yet there remains room for improvement.

Orphan designation

- Orphan designation **remains at 5/10,000** with no reference to incidence.
- A **new definition of significant benefit** is introduced: clinically relevant advantage or a major contribution to patient care of an orphan medicinal product if such an advantage or contribution benefits a substantial part of the target population.

HUMN

- The regulation **does introduce a definition of HUMN but it is not as restrictive as feared**, with no reference to cure.
    - To qualify, at least one of the products indications diagnoses, prevents or treats an orphan condition for which:
        - no satisfactory diagnosis, prevention or treatment method exist;
        - a satisfactory diagnosis, prevention or treatment method exists and it has been demonstrated by the applicant that such a product will bring exceptional therapeutic advancement.
    - In both cases, the product must meaningfully reduce disease morbidity or mortality for the relevant part of the population.
    - Products authorized on biographical data will not quality as HUMN.
    - The EMA will develop additional scientific guidelines.

OME – effective protection can reach 12 years for HUMN

- OME will be modulated **both upwards and downwards:**
    - 10 years for products addressing HUMN;
    - 5 years orphan products authorized at national/decentralized approach;
    - 9 years all other orphan products.

- OME can be extended by +1 year on two occasions if the MAH obtains a MA for one more new therapeutic indications for a different orphan condition.
- OME will take on a similar characteristic as the Global Marketing Authorisation. If a single MAH holds more than one authorisation for the same active substance, there will be only one period of exclusivity for that active substance.
- The orphan paediatric incentive has been removed.

Launch Conditionality

- OME can be extend by +1 year if they are "released and continuously supplied into the supply chain in a sufficient quantity and in the presentation necessary to cover the needs of the patients in the Member States in which the marketing authorization is valid".
- If a product receives the extended OME from expanding into new indications, it **will not** be able to receive the benefit from launching in all Member States.

A more extensive assessment will be provided at a later stage.