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# EUROPE – REVISION OF EU GENERAL PHARMACEUTICAL LEGISLATION: Regulatory Exclusivities, Incentives, and Bolar Exemption

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The European Union ("EU") General Pharmaceutical Legislation is the cornerstone of the EU regulatory system for medicinal products. It consists of:

- Directive 2001/83 that regulates, on the one hand, the placing on the market, manufacturing, import, export, supply, distribution, control, use, and advertising of all medicinal products and, on the other hand, the decentralized/mutual recognition of marketing authorization procedures and pharmacovigilance for medicinal products to be authorized at the national level ("Directive").
- Regulation 726/2004 that regulates the centralized marketing authorization procedure and pharmacovigilance for medicinal products to be authorized at the EU level and establishes the European Medicines Agency ("EMA") ("Regulation").

On April 26, 2023, the European Commission published legislative proposals for an updated: (i) Directive on the Union code relating to medicinal products for human use ("Future Directive"); and (ii) Regulation setting out the centralized procedure and establishing the EMA ("Future Regulation"), which will replace the current Directive and Regulation, respectively.

This note explains the changes to the regulatory exclusivities that are currently afforded to companies under the Directive and the Regulation as well as under the Orphan Regulation and the Paediatric Regulation (both of which will be merged with the Future Regulation and, to some extent, the Future Directive). It also discusses the Bolar exemption.

The proposals reduce the basic data exclusivity period but provide more possibilities of prolongation. The same goes for orphan exclusivity. However, the conditions for being granted those prolongations, and thereby benefit from the same regulatory protection as under the former legislation, are too stringent to be realistic for most companies, especially those holding centralized marketing authorizations. Pediatric exclusivities remain the same except that the exclusivity specific to orphan products (2 additional

years of orphan exclusivity) is abolished. On the other hand, incentives are added for repurposing of known active substances and antimicrobials.

The legislative process will likely be completed in 2025 at the earliest (as new European elections will take place in 2024). The legislative process will provide stakeholders with opportunities to impact the proposed changes.

**Regulatory Data Protection (Data Exclusivity)**

- Basic protection: ***6 years of data exclusivity + 2 years market protection*** from the date of the initial MA.
  - Also applies in the Member States where the medicinal product is not/no longer authorized.
  - For MA that belong to the same global MA, the data exclusivity period starts from the date of the initial MA.

- Several prolongations of the data exclusivity period are provided, subject to a request by the MA holder and a scientific evaluation by the relevant competent authority.

Politics will most probably influence the application of the legal provisions on prolongations. Indeed, the Future Regulation allows Member States representatives to request the EU Commission to discuss issues related to the practical application of these provisions in the Pharmaceutical Committee, and the EU Commission may invite bodies responsible for health technology assessments or national bodies responsible for pricing and reimbursement to participate in the deliberations of the Pharmaceutical Committee.

- ***+2 years*** in case of ***launch in all the Member States where the product is authorized***.
  - Within 2 years from the date of the MA or 3 years for SMEs, not-for-profit entities, and companies/groups of companies not holding more than 5 centralized MA.
  - "Launch" means when the product is released and continuously supplied into the supply chain in a sufficient quantity and in the presentations necessary to cover the needs of patients in the Member States where the MA is valid.
  - Application for a variation (to prolong the data exclusivity period) must be filed between 34 and 36 months (46 and 48 months for SMEs, not-for-profit entities, and companies/groups of companies not holding more than 5 centralized MA) after the date of the initial MA. The application contains documentation from the Member States either to confirm that the conditions are met in their territory or to waive the condition in their territory (for example, when the launch is materially impossible). Positive pricing and reimbursement decisions amount to a confirmation.

- ***+6 months*** if, at the time of the initial MA, the company demonstrates that the medicinal product addresses an ***unmet medical need***.
  - Unmet medical need means that: (i) at least one of the therapeutic indications relates to a life threatening or severely debilitating condition; (ii) no medicinal product is approved in the EU or a medicinal product is authorized but high morbidity or mortality remains; and (iii) the use of the medicinal product results in a meaningful reduction in disease morbidity or mortality for the relevant patient population.

Designated orphan medicinal products are considered as addressing an unmet medical need.

  - This extension does not apply in cases of conditional MA, unless the conditional MA is transformed into a definite MA within 4 years.

- ***+6 months*** for medicinal products containing a new active substance if the clinical trials submitted in the initial MAA use a ***relevant and evidence-based comparator*** in accordance with the EMA's scientific advice. The EMA will adopt scientific guidelines on the criteria for proposing a comparator for a clinical trial after consultation with the EU Commission and health technology assessment authorities or bodies.

- ***+1 year*** if, during the data exclusivity period, a ***new therapeutic indication bringing a significant clinical benefit*** in comparison with existing therapies is approved. This extension may only be granted once.

- The ***1-year*** data exclusivity for the ***switch from prescription-only medicinal product to OTC*** is maintained.

- When a compulsory license is granted by a relevant authority in the EU to address a public health emergency, data and market protections are suspended for the duration of the compulsory license.

- Data exclusivity applies in parallel to orphan exclusivity and the other incentives, unless otherwise expressly provided by law.

- The Future Directive provides that reference medicinal products for which the MAA has been submitted before its date of application (18 months after entry into), are subject to the provisions on data exclusivity periods set out in the Directive as applicable on the date of application of the Future Directive until the date of application of the Future Directive… This must be a mistake since the Future Regulation provides that the periods of data exclusivity do not apply to reference medicinal products for which an MAA has been submitted before the date of application of the Future Regulation.

## Incentives

Incentives already existed for the development of orphan and pediatric medicinal products. The incentive system is extended to repurposing of known active substances and antimicrobials.

### Orphan Medicinal Products

- New concept of "high unmet medical need" ("HUMN")

– Criteria: There is no existing treatment or the product presents an exceptional therapeutic advancement and a meaningful reduction in disease morbidity or mortality. This last criterion is meant to ensure that only the most effective medicinal products are covered.
– Relevant evidence to be included in the marketing authorization application ("MAA").
– Does not apply in cases of bibliographic MAA.
– Assessment by the CHMP.
– May benefit from PRIME, which the Future Regulation codifies (Art. 60).

- Duration of Orphan Exclusivity

– ***10 years*** in case of a medicinal product addressing an ***HUMN***.
– ***5 years*** in case of a medicinal product approved based on a ***bibliographic MA***.
– ***9 years*** for all ***other*** medicinal products.

– ***+1 year*** if the medicinal product is ***launched*** (i.e., 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) within 2 years of the MA, ***in the Member States where the MA is valid*** (i.e., in all Member States given that designated orphan medicinal products are authorized through the centralized procedure).
The launch period is 3 years for SMEs, not-for-profit entities, and companies/groups of companies that do not hold more than 5 centralized MA.
The prolongation does not apply to orphan medicinal products authorized on the basis of a bibliographic MA.

– ***+1 year*** if a ***new orphan MA*** is granted at least 2 years before the expiration of the orphan exclusivity period. This incentive is available twice but may not accumulate with the + 1 year data exclusivity arising from the approval of a new indication which brings a significant clinical benefit in comparison to existing therapies.

– No more 2 additional years of orphan exclusivity in case of completion of a pediatric investigation plan (PIP).

- Application of the concept of "global" orphan MA: No new orphan exclusivity for a new orphan MA granted for the same active substance. The orphan exclusivity of all next orphan MA starts from the date of the first orphan MA.
- The legal definition of "clinically superior", which is one of the conditions for breaking orphan exclusivity, is now defined by reference to a substantial part of the target population.

### Access to Market – Similar, Generic/Biosimilar

- Submission of an MAA or granting of MA for a generic or biosimilar of an expired orphan medicinal product may not be prevented by orphan exclusivity of a similar medicinal product.
- The MAA for a similar medicinal product (innovative or generic/biosimilar) may be submitted 2 years before expiration of the orphan exclusivity.

**Pediatric Development**

- ***6-month SPC extension***.
- No more specific reward for orphan medicinal products (+2 years orphan exclusivity).
- Data exclusivity and marketing protection for PUMA.

**Repurposing of Known Active Substances**

- Repurposing refers to the development of known active substances for new therapeutic indications.
- Specific data exclusivity protection is provided:
  - ***4-year*** protection
  - New therapeutic indication which is not authorized in the EU and is of significant clinical benefit in comparison with existing therapies.
  - Medicinal product has not previously benefited from data exclusivity or 25 years have passed since the initial MA.
  - Only once for any given medicinal product.

**Antimicrobials**

- "Antimicrobial" is defined as any medicinal product with a direct action on micro-organisms used for treatment or prevention of infections or infectious diseases, including antibiotics, antivirals, and antifungals.

- The development of certain antimicrobials is incentivized:

  - ***Transferable data exclusivity voucher (+1 year data exclusivity).***
  - Only for a priority antimicrobial (i.e., preclinical and clinical data underpin a significant clinical benefit with respect to antimicrobial resistance and the product has at least one of the following characteristics: (i) it represents a new class of antimicrobials; (ii) its mechanism of action is distinctly different from that of any authorized antimicrobial in the EU; or (iii) it contains an active substance not previously authorized in a medicinal product in the EU that addresses a multi-drug resistant organism and serious or life threatening infection).
  - Only one transfer and for the benefit of a centrally authorized medicinal product.
  - The MA of the priority antimicrobial has not been withdrawn.
  - Value of the transfer to be disclosed to the EMA and be made public.
  - 10 vouchers will be available over 15 years.
  - Granted if requested by the company when applying for MA.
  - The Company must: (i) demonstrate its capacity to supply the priority antimicrobial in sufficient quantities for the expected needs of the EU market; and (ii) provide information on all direct financial support received for research related to the development of the priority antimicrobial.
  - A voucher is no longer valid where: (i) the EU Commission extends the data exclusivity of the receiving medicinal product; or (ii) it is not used within 5 years from the date it was granted.
  - The EU Commission may revoke the voucher before its transfer if a request for supply, procurement, or purchase of the priority antimicrobial in the EU has not been fulfilled.

**Bolar Exemption**

The scope of the Bolar exemption is further specified to better harmonize the application of the exemption in the EU and address outstanding issues.

The following actions are expressly not considered as patent/SPC infringements:

- Studies, trials, and other activities conducted to generate data for an MAA of a generic/biosimilar and hybrid/bio-hybrid, health technology assessment, and pricing and reimbursement;

– Activities conducted exclusively for those purposes, including the submission of the MAA and the offer, manufacture, sale, supply, storage, import, use, and purchase of patented products or processes, including by third party suppliers and service providers.

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King & Spalding's regulatory Life Sciences lawyers can help you better understand the changes that may result from the Revision, and anticipate their impact on the development and, in the future, marketing of products in Europe.

Companies involved in the development of orphan and pediatric medicinal products, as well as antibiotics, should closely follow future discussions around revision of the legislative framework and, whenever needed, be involved in those discussions.

Companies also should anticipate evolution of the EU legal framework and its impacts on current development and investment.