**Prescrire response to**
European Commission public consultation on the
Roadmap/Inception Impact Assessment on the
**Evaluation and revision of the general pharmaceutical legislation**

27 April 2021

We are glad to take the opportunity to provide initial thoughts on the European Commission objectives and policy options pointed out in the roadmap/Inception Impact Assessment relating to the announced revision of the general pharmaceutical legislation.

We would like to stress that due to the scarce and limited explanations for some policy options, we were unable to get a clear insight on the Commission intentions for the up-coming revision.

## 1. Prescrire comments on suggested policy options

***Simplify legislation and create regulatory attractiveness aiming to reduce regulatory approval times and costs while keeping high standards of robust assessment***

We **fully support** the need of **keeping high standards of robust assessment**.

Marketing authorisations should rely on reliable, robust evidence. Prescrire calls on the EU **to strengthen the regulatory standards and rules on drug evaluation**. **Solid evidence, based on comparative randomised double-blind clinical trials** versus the reference treatment **should be required for most marketing authorisations. These clinical trials should also be** designed to meet health needs with **relevant endpoints**.

Under current rules, the EMA CHMP is required to give an opinion on a marketing authorisation application within 210 days. For an accelerated assessment procedure, the time limit is 150 days. These time limits are already very tight and should not be further shortened.

Pharmaceutical companies blame EU Member States medicines appraisal systems and regulatory processes as the root causes of delayed market access. We do not agree with this argument. **The real barrier to access to medicines** is not caused by national differences in clinical assessments or duplication of assessments, **but by the exorbitant prices that are disconnected from added therapeutic value or R&D cost**. The real causes for delays in HTA assessments are linked to a lack of robust scientific evidence. To streamline the process and to make sure that HTA bodies can base their assessments on robust data, **comparative trial data should be available in marketing authorisations applications**.

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***Support and accelerate product development and authorization in areas of unmet need***

It should be reminded that mechanisms providing faster patient access to new medicines are already in place in the EU: the accelerated assessment procedure, approval under exceptional circumstances, the conditional marketing authorization and the PRIME scheme. In addition, "compassionate use" mechanisms are available in many Member States.

We are surprised by the Commission proposal to incorporate the EMA PRIME scheme in the regulatory framework. So far, EMA always stresses that this scheme complies with current legislation and doesn't require any legislative changes.

**Accelerated assessment procedures are legitimate when there is a real unmet health need**. But flexible **and accelerated authorisations increase the uncertainty regarding the clinical value and safety of the drugs authorised that way** and fail to guarantee better therapy. Some years ago, AIDS activists stressed that "*patients need knowledge – answers about the drugs they put in their bodies – not just access*". **The product labelling and patient information leaflets need to be improved** in particular for products authorised through an accelerated assessment procedure: **clearly stating what is known, what is unknown and what is still under investigation**, as well as report on the evidence and robustness of the data underlying the authorisation.

Accelerated authorisations lead to **a shift from pre-marketing approval evidence-collection to post-approval assessment**. However, years of experience have shown that manufacturers often fail to honour post-marketing commitments. **Failure to respect post-marketing commitments and requirements should not be tolerated** any longer: it should lead to a withdrawal of marketing authorisation. The revision of the pharmaceutical legislation needs to tackle this problem, in the interest of public health and patient safety.

Great hope is placed by some on the use and utility of "real life data", "big data" and artificial intelligence to accelerated approvals yielding to faster access for patients. We call on for caution and urge European and national regulators not to weaken marketing authorization requirements by shifting the provision of real and strong evidence before authorization to hypothetical and biased real world data after marketing authorization. As experienced during the Covid-19 pandemic (retraction of study in The Lancet) it is of outmost importance to consider very carefully the source and quality of big data, and to ensure access to the basic data and to the process used to analyse them. Once marketing authorization has been granted, it can take years before studies of sufficient methodological quality are obtained; and when a drug is proven to have severe or even fatal effects, it often takes months, if not years, to withdraw its marketing authorization.

**Accelerated marketing authorisations should only be used as an exception, in severe situation without proper treatment, so as to prevent unnecessary exposure to avoidable harm.**

***Introduce elements of flexibility that allow future proofing of the legislation***

The scarce and limited information in the roadmap doesn't provide clear ideas on the intentions of the Commission.

As already pointed out, we consider that marketing authorisation flexibilities enabling early access to medicines should only apply to true unmet medical needs while protecting patients' safety. Pre-market efficacy and safety evidence is an important health protection measure as it protects patients from a potentially harmful exposure to medicines without solid scientific evidence of a benefit to patient.

***Revise the system of incentives***

We **welcome a revision of the current incentive system to restore a balance with public needs and interests**. A tailored incentive system linked to real unmet medical needs and the linkage of rewards to obligations regarding availability, transparency (on costs and clinical data) and affordability is the way forward.

***Development of new classes of antimicrobials***

We are not convinced that the creation of specific incentives would improve the current situation. Market failures (e.g. the lack of new antimicrobials, neglected diseases) show that the current pharmaceutical business model does not provide solutions for all public health needs. Policy makers should take this into account and explore other business models and solutions to support R&D projects related to public health needs, such as: collaboration with European academia centres, independent clinical research and the not-for-profit sector (e.g. DNDi).

***Enhance security of supply, oversight of the supply chain, revision of manufacturing and distribution provisions***

In addition to the need for **diversification of supply chains**, the Commission should **recall and clarify the legal obligations of marketing authorisation holders** in respect to a timely delivery of critical medicines orders (Directive 2001/83/EC, article 81). If needed these rules should be reinforced. In case of non-respect of the obligations, appropriate sanctions should be applied.

The Commission should come up with **legislative proposals touching upon the supply of medicines** (minimum stock levels, potential alternative production sites, transparency on the supply chain) and **the prevention and management of shortages**, putting the interest and safety of patients at the centre of policy action.

## 2. Missing points

***Management and improvement of safety, including safety for medicines already on the market***

Prescrire calls on the Commission to include strengthened safety requirements of medicines in the legislative revision, by including the following:

- Ensure that the European pharmacovigilance system can sustainably cope with the surveillance of marketed medicines, both in normal times and in crisis situations. It must be foreseen and ensured that the system has sufficient financial and human capacity to handle this mission in a sustainable manner.
- Public funding should be secured to conduct and operate independent public pharmaco-epidemiological studies.
- The assessment and monitoring of the effects of drugs taken during pregnancy and the possible consequences on unborn children must be improved (cf. Depakine°, DES). EMA should make it a priority to assess possible long-term effects related to drug exposure.
- Mock-ups and packaging specimen of medicines should be made publicly available together with the EPAR. A safety assessment report of the naming, packaging and labelling should be part of the EPAR, as it is the case by the US Food & Drug Agency.
- Better prevention of errors related to the use of existing medicine products, notably through better quality packaging and product information (e.g. adapted packaging for specific patient categories like elderly people or children; safe dosing devices,…).
- Better prevention of the adverse effects of existing drugs through more effective and transparent pharmacovigilance.
- In order to ensure the non-commercial identification of authorized medicine products, improvement or, at least, strict compliance with the use of INNs in mandatory documents, such as the EPAR (too often only using brand names); and the incentive to apply for new INNs when the changes in the properties of an existing substance are substantial and putting patient safety at risk.
- Improved labelling and patient information leaflets by providing more useful information for clinical practice including comparative information with other treatment options.

***Affordability of medicines***

Sustainable access could be supported by:

- requiring total transparency on the prices paid and discounts granted; transparency on cost of R&D;
- European cooperation on HTA. HTA plays an important role in the decision-making process on pricing and reimbursement of health technologies. HTA should be based on a robust methodology, rely on high standards and be carried out in an independent and transparent manner;
- reducing waste by increasing the use of generic drugs and biosimilars and encourage rational use of medicines.

***Strengthened transparency and independence of the EMA***

Public trust relies on full transparency. Strengthened transparency standards and measures relating to the EMA working bodies and clinical data assessed for the evaluation and surveillance of medicines are paramount to gain and upheld public trust. The Commission has the duty to **ensure that the EMA has sufficient public funding and human capacity to sustainably cope with its transparency policy and obligations** as well as to respond to the general public access to documents requests, both in normal times and in crisis situations. The resumption of publication of clinical study reports is desperately needed as it includes safety information reported in no other source.

Without further delay the EMA and the Commission should strive to a **swift application of the clinical trials Regulation**.
The EU and the Member states should guarantee adequate public funding for the core missions of the EMA to ensure that the business interests of pharmaceutical companies do not override public health interests. The announced revision of the European Medicines Agency ("EMA") fee system is an excellent opportunity to put in place **public funding for the EMA**. The current funding system based on industry fees undermines the independence of the agency. To guarantee EMA's independence, and prevent sustainability issues due to fewer applications and subsequent fluctuations in fee revenues, any direct financial relationship between the Agency and the pharmaceutical industry should be avoided.

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