efpia
European Federation of Pharmaceutical Industries and Associations

Draft ☐ Final ✱

The path to improved access to medicines through alternative registration pathways

Date: 13/11/2017

EFPIA's position on reliance and expedited registration pathways in emerging markets

European Federation of Pharmaceutical Industries and Associations (EFPIA) is reaching out to regulators and/or legislators in emerging markets to **look at ways to build upon existing structures and other countries' experience in order to accelerate registration and patient access**, while fully respecting the legal authority of the National Regulatory Authority (NRA) to fulfill its public health mission.

Patients are demanding faster access to new medicines, especially in areas of high unmet medical need. Even though access does not only depend on regulatory approvals, this is an important element on the path towards access. Therefore, regulators play an important role in addressing the patients' needs by establishing appropriate registration pathways.

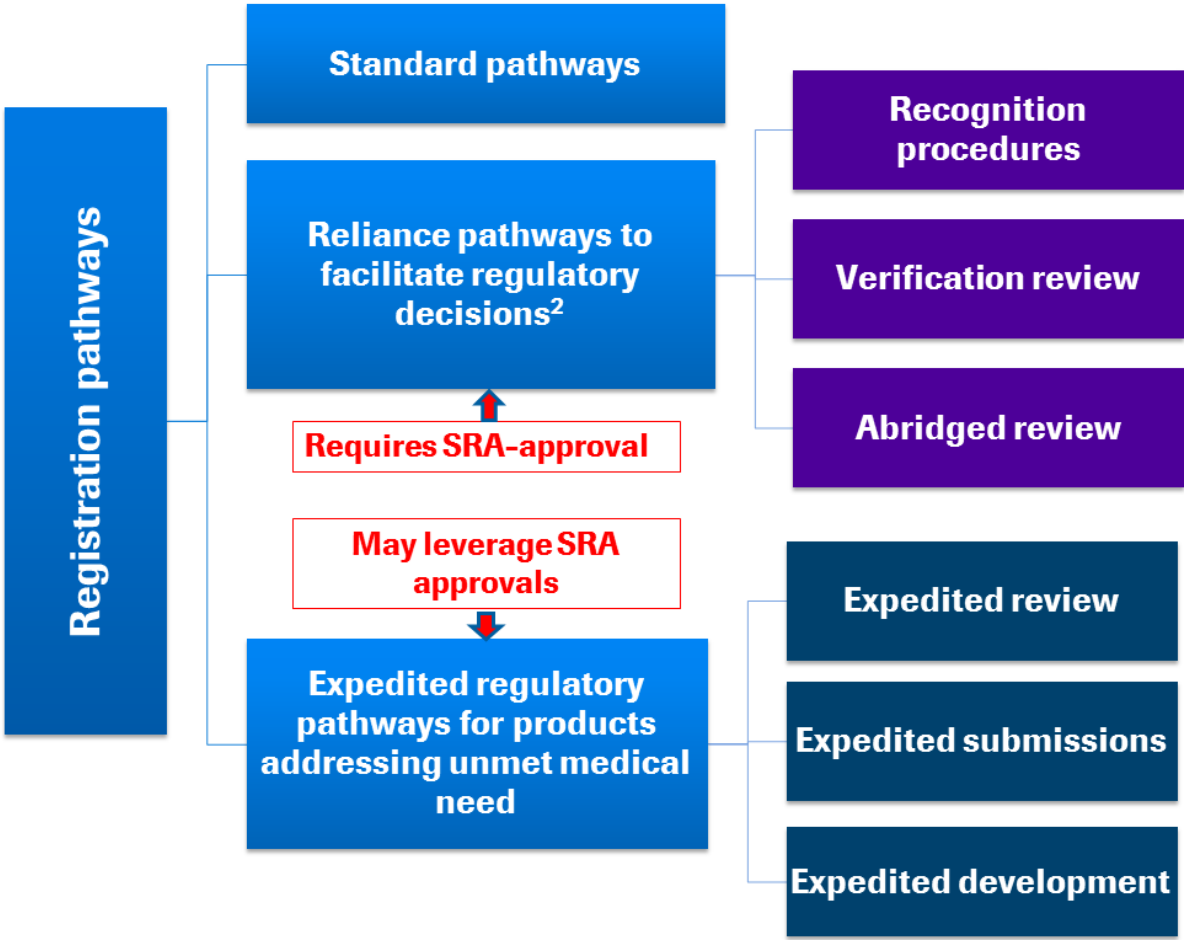
Several regulatory agencies have already started to address the need of the patients, by establishing new/alternative registration pathways that aim to speed up the development, submission **or** review of marketing authorizations of certain type of products.

We see the emergence of two types of alternatives to standard, full and independent registration pathways (see figure 1).

a) The continuous limitation of adequate resources within NRAs is driving implementation of risk-based evaluations, focusing on what is locally critical (i.e. value-added) versus what can be leveraged/relied upon Stringent Regulatory Authorities (SRAs) [see definition of terms]. In this position paper, we categorize such pathways as **Reliance pathways to Facilitate Regulatory Decisions**.
b) In addition, several regulatory authorities started to apply specific approaches to accelerate access to medicines for products that address an unmet medical need [See definition of terms]. In this position paper, we categorize such pathways as **Expedited Regulatory Pathways for medicines targeting unmet medical need.**


EFPIA Brussels Office
Leopold Plaza Building ✱ Rue du Trône 108
B-1050 Brussels ✱ Belgium
Tel: + 32 (0)2 626 25 55 ✱
www.efpia.eu ✱ info@efpia.eu

Figure 1. *An overview of alternative registration pathways*[1].



1 Naming presented in Figure 1 is the EFPIA preferred wording to categorize the different type of registration pathways.
2 These pathways can be used for any type of products, as long as there is a SRA approval.

In the interest of public health, EFPIA encourages regulators to strengthen their regulatory oversight in line with their capacity and capabilities and prioritize the development and implementation of such alternative registration pathways for the benefit of patients.

WHO guidance under development recommends that *any regulatory system should be science based, respect international standards and best practices, and adopt an approach that focuses on what cannot be done by others, while leveraging the work of trusted NRAs and regulatory networks for the rest* [WHO1].

On that basis, EFPIA encourages NRAs currently performing full dossier reviews of SRA-approved products, to embrace the concept of reliance [See definition of terms]**.** The latter can be done by establishing verification and/or abridged registration pathways to replace full dossier reviews for such products. This can include products approved by SRAs on the basis of expedited pathways.

When establishing new registration pathways, EFPIA strongly recommends considering the points listed in chapter 4 of the EFPIA white paper on *reliance and expedited registration pathways in emerging markets*. These considerations are focused on ensuring that the registration pathways encompass and address all the key elements in a given local regulatory environment.

A summary of EFPIA recommendations and points to consider:

We encourage every NRA to collaborate with other regulators and build upon existing regulatory frameworks and other countries' experience in order to accelerate registration and patient access. NRAs are encouraged to consider the following:

- Assess available regulatory capacity and identify opportunities for alternative registration pathways based on local needs.
- Apply principles of WHO draft guidelines on Good Regulatory Practice and Collaborative registration procedures when establishing alternative registration pathways.
- Look at all steps taken for regulatory approval as part of the new registrations pathways and consider certain waivers, including:
    - The need for local clinical trial data, outside of ICH E5 requirements, which could increase the development timeline
    - Analytical or batch testing requirements during regulatory review when the manufacturing source is the same as for the SRA approved site.
- Using reliance pathways for initial approvals as well as the management of post-approval changes and renewals to facilitate the supply of the medicine and timely safety information for patients.
- Establish the use of IT submission tools to facilitate efficient dossier submissions, that will speed-up manual, face-to-face, appointment based submissions.
- Focus submission documents on what is absolutely required for the purpose of the respective assessment that will be performed and avoid redundant or non-essential documentation (e.g. request the CPP before approval instead of at time of submission, or waive the requirement completely).
- Consider allowing pre-submission meetings with applicants to discuss the companies' product portfolio and overall filing strategies, especially for products addressing unmet medical need.
- Ensure confidentiality of the dossier, especially if details from the SRA approval process are provided.

Please note: *A topic not covered as part of this position paper are work-sharing and joint-assessment procedures, another tool for regulatory authorities globally to make best use of the often limited resources available. Through joint assessment procedures, a group of regulators from different countries shares the work related to the regulatory assessment of medicinal products. This can be especially valuable in situations where SRA approval does not exist and/or to resolve unmet medical needs which are only prevalent in certain regions and therefore never submitted to SRAs.*


EFPIA Brussels Office
Leopold Plaza Building * Rue du Trône 108
B-1050 Brussels * Belgium
Tel: + 32 (0)2 626 25 55 *
www.efpia.eu * info@efpia.eu

Definition of terms

Stringent Regulatory Authority
In this paper, a Stringent Regulatory Authority is referred to as a regulatory authority that is:

a) a member of ICH prior to 23 October 2015, namely: the US Food and Drug Administration, the European Commission and the Ministry of Health, Labour and Welfare of Japan also represented by the Pharmaceuticals and Medical Devices Agency; or
b) an ICH observer prior to 23 October 2015, namely: the European Free Trade Association, asrepresented by Swissmedic and Health Canada; or
c) a regulatory authority associated with an ICH member through a legally-binding, mutual recognitionagreement prior to 23 October 2015, namely: Australia, Iceland, Liechtenstein and Norway. [WHO2]

Reliance
In this paper, reliance is referred to as the act whereby the NRA in one jurisdiction may take into account and give significant weight to – i.e., totally or partially rely upon – evaluations performed by a stringent regulatory authority in reaching its own decision. The relying authority remains responsible and accountable for decisions taken, even when it relies on the decisions and information of others (definition adapted from WHOs definition in the draft Good Regulatory Practice guideline) [WHO3].

Unmet medical need
The definition of unmet medical need varies between countries and constituents. Even if many definitions may look similar, different constituents may apply different sets of criteria (such as epidemiology/prevalence, burden of disease, existence or not of a treatment, etc) depending on the context of use. Two examples of the definitions used by EU and US regulators are given below.

- **European Commission**: Commission Regulation 507/2006 on the conditional marketing authorization (CMA) for medicinal products for human use provides for four conditions for CMA to apply: positive risk/benefit balance, likelihood to provide comprehensive clinical data, unmet medical need and benefit to public health. For this purpose, unmet medical need means a condition for which there exists no satisfactory method of diagnosis, prevention or treatment authorized in the Community or, even if such a method exists, in relation to which the medicinal product concerned will be of major therapeutic advantage to those affected. [EC]
- **US FDA:** In FDAs guidance for industry, unmet medical need is defined as a condition whose treatment or diagnosis is not addressed adequately by available therapy. An unmet medical need includes an immediate need for a defined population (i.e. to treat a serious condition with no or limited treatment) or a longer-term need for society (e.g. to address the development of resistance to antibacterial drugs).[FDA]

Recognition procedures
A procedure in which authorities/organizations (offer to) review medicinal products intended to be marketed in countries or regions other than their own.

Verification procedure
This model is used to reduce duplication of effort by agreeing that the importing country will allow certain products to be marketed locally once they have been authorized by one or more SRA.

Abridged review procedure


This model relies on assessments of scientific supporting data that has been reviewed and accepted by SRA's, but includes an 'abridged' independent review of a certain part of the registration dossier of the product (e.g. relevant to use under local condition).

Expedited review
Regulatory authorities speed the review of certain products to enable faster approval. The review time of an expedited review is substantially shorter than the review time of a standard review.

Expedited submission
Expedited submission means that information and data-packages can be submitted and reviewed as they become available even before the official submission date. Expedited submissions are often being referred to as 'rolling submissions'.

Expedited development
Expedited development approaches allow for earlier submission and approval with a data set which may be less complete than from a standard development program.

References

[WHO1] Mike Ward (WHO). Presented at CIRS workshop entitled " Facilitating the review of new medicines through risk-based evaluations: How can a stratification process be utilised to achieve an effective use of resources?" (March 2017 – Sao Palo).

[WHO2] WHO, *Clarification with respect to a stringent regulatory organization as applicable to the stringent regulatory authority guideline*, WHO/PQT:Medicicines. Guidance Document (15 February 2017)

[WHO3] WHO, *Good Regulatory Practices: guidelines for national regulatory authorities for medical products.* WHO/DRAFT (October 2016)

[EC] Commission Regulation (EC) 507/2006 of 29 March 2006.

[FDA] www.FDA.drugs.gov


EFPIA Brussels Office
Leopold Plaza Building * Rue du Trône 108
B-1050 Brussels * Belgium
Tel: + 32 (0)2 626 25 55 *
www.efpia.eu * info@efpia.eu