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**White paper on reliance and expedited registration pathways in emerging markets**

**Date:** 23/11/2017

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**Introduction**

Recent breakthroughs in science are driving the development of many innovative medicines addressing current unmet medical needs. To ensure that these drugs can be provided as quickly as possible to patients in need globally, appropriate registration pathways are needed to create a framework that is sustainable for all stakeholders. Especially for products where safety and efficacy have already been confirmed by Stringent Regulatory Authorities (SRAs), patients in other jurisdictions expect timely access facilitated by the regulatory process in the country.

For the above mentioned reasons, the European Federation of Pharmaceutical Industries and Associations (EFPIA) is reaching out to regulators in emerging markets **to strengthen their regulatory oversight in line with their capacity and capabilities and prioritize the development and implementation of alternative registration pathways for the benefit of patients.**

In this white paper, EFPIA presents their perspective regarding the need for optimized registration pathways and shares their recommendations on how such pathways can be established or their use be maximized.

**Regulators play an important role in ensuring the highest attainable** **standard of health**

As outlined in the constitution of the World Health Organization (WHO) “*the enjoyment of the highest attainable standard of health is one of the fundamental rights of every human being”.*

Among other stakeholders, regulators play an important role in achieving this. In resolution WHA67.20, the Sixty-Seventh World Health Assembly in 2014 recognized that:

* **Effective regulatory systems are an essential component** of health systems strengthening and contribute to better public health outcomes.
* **Regulators are an essential part** of the health workforce
* **Inefficient regulatory systems themselves can be a barrier to access to safe, effective and quality medical products.** [WHO4]

Conducting regulatory reviews in a timely manner should therefore be a major priority for all health authorities. At the same time, accelerating the review process should not compromise safety, quality and efficacy of medicines.

The expectation of patients to have timely access to medicinal products, in addition to the continuous limitation of adequate resources within NRAs have the potential to drive greater focus toward risk-based evaluations, focusing on what is locally critical (i.e. value-added in terms of resource/time investment) versus what can be leveraged/relied upon from decisions made by SRAs. Such risk-based evaluations lead to improved allocation of local resource, improved patient access and increased equity of access globally.

WHO therefore, proposes a scheme for NRAs in which registration and approval of medicines already approved by SRAs is facilitated. This scheme is outlined in the draft WHO guideline on ‘*collaborative procedure in the assessment and accelerated national registration of pharmaceutical products approved by stringent regulatory authorities’, March 2017* [WHO5]*.*

In addition to NRAs applying risk-based approaches, several regulators are developing ways to further accelerate access to medicines by establishing registration pathways that expedite the drug development process and/or the regulatory review timeline for products addressing an unmet medical need.

**Positive trend towards more efficient and tailored regulatory pathways globally**

Many regulatory authorities across the globe have already implemented registration pathways where the objective is to speed up the **development, submission and/or review** of marketing authorizations for certain type of products.

Often, these pathways are an alternative to standard registration pathways. They exist in many different types and formats. Some alternative registration pathways encourage early dialogue between the agency and pharmaceutical company, many aim to reduce the overall review time (e.g. by applying the reliance concept), while others introduce new dynamics in the regulatory process to allow patient access much earlier in the lifecycle of a medicine based on initial data with further confirmation of the product’s profile based on follow-up post-approval data generation.

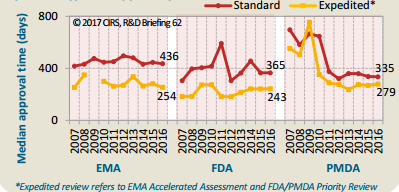
In this paper we organize alternative registration pathways into the following two categories:

* **Reliance pathways to Facilitate Regulatory Decisions:** Registration pathways used by NRAs or regional regulatory initiatives (RRIs) wherein their decisions regarding the approval of any type of product can be accelerated by the reliance on or recognition of prior reviews by stringent regulatory authorities[Liberti]
* **Expedited Regulatory Pathways for medicines targeting unmet medical need:** Registration pathways that speed the development, review and approval of a product which fulfills the national requirements for unmet medical need; typically implemented by a SRA, for a first non-dependent review, where no prior approval exists [Liberti].

Examples of NRAs that have developed and/or implemented reliance pathways are Singapore, Saudi Arabia, Panama and Taiwan. A complete overview of reliance pathways established globally can be found in [Appendix 1](#_Appendix_1).

Among regulatory authorities that have implemented expedited regulatory pathways are the European Medicines Agency (EMA), US Food and Drug Administration (FDA), Japanese Pharmaceuticals and Medical Device Agency (PMDA), China FDA and Swiss Medic. A complete overview of expedited pathways established globally can be found in [appendix 2](#_Appendix_2).

The positive effect on review timelines by the introduction of expedited pathways by EMA, FDA and PMDA over time is illustrated in Figure 1.



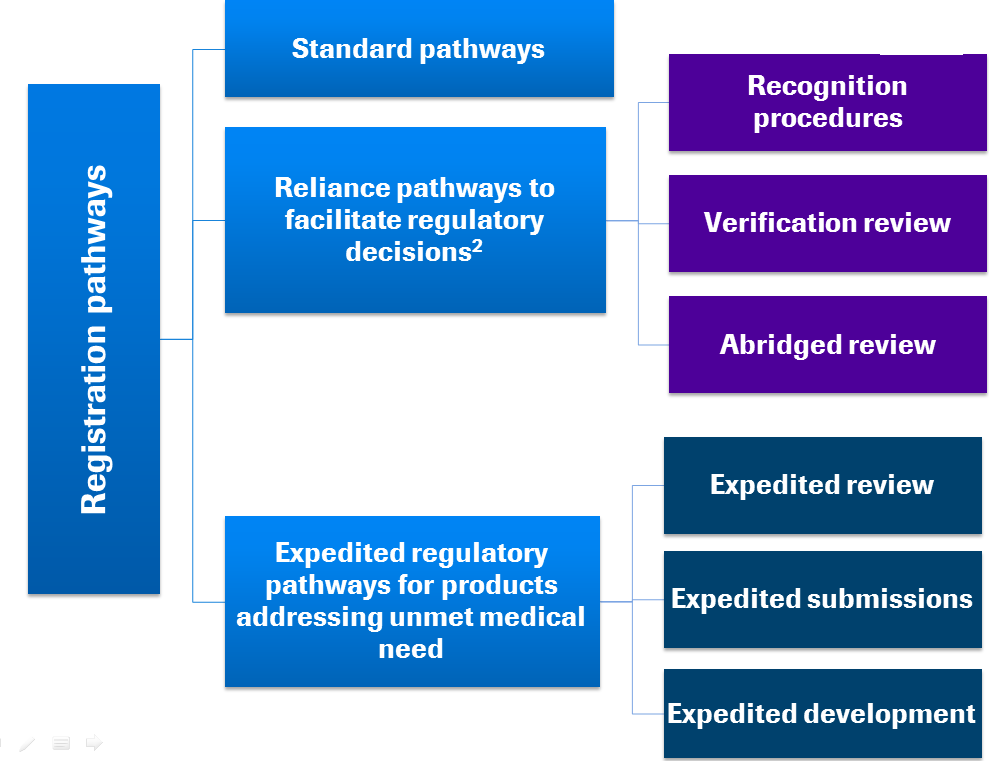
**Figure 1.** Median approval time for New Active Substances approved by ICH agencies by review type and approval year [CIRS]

**Regulatory pathways need to be tailored to the country situation**

Figure 2 shows an overview of the different types of alternative registration pathways. Figure 2 is followed by explanation of the aim and application of the different pathways.

Please note, terminology used to describe the different registration pathways varies per country. **The naming used in the figure 2 and the description underneath, is the preferred wording by EFPIA. NRAs are encouraged to apply this wording, in order to harmonize as much as possible and make sure the name of the procedure reflects its meaning.**

**Figure 2.** *An overview of alternative registration pathways1.*

**

**Requires SRA approval**

**Can leverage SRA approval**

*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.*

**Reliance pathways to Facilitate Regulatory decisions:**

1. **Recognition procedures**

*A model in which authorities/organizations (offer to) review medicinal products intended to be marketed in other countries or regions other than their own. Examples of such review procedures are EMA’s Article 58 procedure, Swissmedic’s Marketing Authorization for Global Health products and medicines reviewed through the WHO collaborative prequalification program [Liberti]). With such review procedures, the authority of the country/region where the product is intended to be marketed/used can directly recognize the outcome of this review.*

1. **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. The main responsibility of the NRA in the importing country is to ‘verify’ that the product intended for local registration has been duly registered by the SRA as declared in the application and that the product characteristics (use, dosage, precautions) for local registration conform to that agreed in the reference authorization(s). Additionally, there needs to be the assurance that the product is equal or similar to that approved by the reference agency [Liberti].*

1. **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). This might include a review of the pharmaceutical quality (CMC) data in relation to climatic conditions and distribution infrastructure and a benefit-risk assessment in relation to use in the local ethnic population, medical practice/culture and patterns of disease and nutrition.*

*As for the verification procedure, there needs to be the assurance that the product is equal or similar to that approved by the reference agency [Liberti].*

**Expedited Regulatory Pathways for medicines targeting unmet medical need:**

1. **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. A decision on which product to grant expedited review is normally based on its importance to public health aspects.*

1. **Expedited submission (rolling submissions)**

*Expedited submissions means that information and data-packages can be submitted and reviewed as they become available even before the official submission date. There is for example no need to wait for the availability of the full clinical data before submission of the earlier available pre-clinical data. This allows regulatory agencies to review available data sets as soon as they are available and may allow the shortening of regulatory procedures. Often ‘expedited submissions’ are being referred to as ‘rolling submissions’.*

1. **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. This approach is exclusively reserved for products which address a high unmet medical need in a serious or debilitating condition and where the data are nonetheless adequate to demonstrate a positive benefit-risk profile. The most common example of expedited development is* ***approval based on convincing Phase 2 clinical data and/or data based on well validated surrogate endpoints.*** *Such approvals (e.g. EMA Conditional Marketing Authorization, FDA Accelerated Approval pathway) are often only granted on the basis that the benefit-risk profile observed during clinical studies will be maintained post approval; furthermore, certain conditions, such as annual renewals will be required to be met. The success of such approaches depends on the ability of the regulatory agency to apply the principle of ‘regulatory flexibility’ in defining the regulatory requirements for a particular application. This can entail reduced data requirements, where justified, based on medical need, but can also rely on evolving scientific developments or new and innovative approaches to drug development (e.g. adaptive clinical trial designs, modelling and simulation, extrapolation)) .*

*Another approach that aims at expediting development is based on* ***greater collaboration with the regulatory agency to identify options for expediting development or at least ensuring the most efficient development strategy****. Examples include ‘Breakthrough Designation’ in the US , ‘PRIME’ in Europe and ‘Sakigake’in Japan. These schemes benefit from the early identification (designation) of a promising medicine in an area of high unmet medical need and the consequential prioritization and resources applied to that development both by the applicant and the regulatory agency.*

*Expedited pathway concepts are currently still being further developed and piloted by several regulatory authorities globally, including SRA’s like EMA. EMA, for example, is piloting an ‘adaptive pathways’ concept.*

See table 2 for an EFPIA recommendation on products that qualify for the registration pathways mentioned above and examples of countries having such pathways in place.

In many countries where regulators have established new registration pathways, a combination of several alternative pathways are being implemented. This approach gives regulators and marketing authorization applicants the flexibility to select the procedure that is most appropriate for the specific public health situation and medicinal product in focus.

**Considerations in relation to establishing new registration pathways**

When establishing new registration pathways, EFPIA strongly recommends consideration of the points outlined in box 1-3. These considerations are focused on ensuring that the registration pathways encompass and address all the key elements in a given local regulatory environment.

**Box 1.** Key points to consider in relation to reliance pathways

* 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.
* When using reliance pathways, it is important to understand that some of the SRA approved products are developed in an expedited manner and that the products might be approved on the basis of an abbreviated data-set, but with well defined post-authorisation commitments.
* Focus time and resources on the value-added and locally critical aspects of registration and leverage upon information available from SRAs where applicable:
  + E.g. waive GMP inspections, but rely on GMP certificate from a SRA
  + E.g. waive analytical or batch testing requirements during regulatory review when the manufacturing source is similar with SRA approved site.
* Align local regulatory requirements with global standards by gradually adopting internationally recognized technical guidances, standards and best practices. Such alignment is an important pre-requisite to facilitate reliance on the assessments and approvals by SRAs.
* Ensure confidentiality of the dossier, especially if details from the SRA approval process are provided.

**Box 2.** Key points to consider in relation to expedited pathways

* NRAs are recommended to use SRA decisions regarding products that qualify for expedited registration pathways (e.g. on the basis of unmet medical need and/or transformative clinical efficacy) as a basis for their decision regarding applicability of such procedures.
  + E.g. in the absence of or in addition to reliance pathways, products that were approved through a priority review pathway by a SRA, are recommended to be given priority review in the NRA as well (as long as it also addressed unmet medical need locally). The Chinese Health Authority is already applying this principle.
* When aiming to expedite the approval process for products addressing an unmet medical need, it is important to ensure that all elements (not only review time) are facilitated/expedited:
  + E.g. reduce waiting times to get an appointment slot to submit the marketing authorization application for products addressing an unmet medical need.
  + E.g. for countries that have requirements for clinical studies in their own territories/patient populations, waive this requirement for products addressing an unmet medical need in the country(or base initial approval on data from outside the region with a commitment to continue to study the drug further in the relevant territory). Some countries already allow local clinical data waivers for specific categories of products (e.g. South-Korea, India, Taiwan).
* Expedited development pathways which involve increased interactions between the health authority and applicants and an increased amount of post-authorization commitments can be labor-intensive for both the regulators andthe marketing authorization applicant. Therefore, such procedures should only be established by regulatory authorities who have the necessary resources available.  For regulatory authorities that do not have adequate resources available it is recommended to consider an approach which relies on the approvals achieved via expedited development pathways by stringent regulatory authorities.
* It is recommended to facilitate dialogue between the NRA and applicant during the registration procedure.
* In the case of limited epidemiologic data in the country of interest, it is recommended to rely on SRA assessments of unmet medical need (where possible).

**Box 3.** Key points to consider in relation to reliance and/or expedited pathways

* When assessing the possibility to establish alternative registration pathways, NRAs have to assess the need for specific legislation to create a legal basis for the pathway. If needed, legislators need to be involved.
* NRAs should provide clear guidance to applicants, describing the dossier requirements, eligibility criteria, timelines and processes for the registration pathway. Principles outlined in the draft WHO Good Regulatory Practice guidelines and WHOs recently published draft guideline on “the Collaborative Procedure in the accelerated assessment of national registrations” are recommended to be applied. Relevant stakeholders, including industry, should be involved as part of the process of developing such guidance.
* 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. Mechanisms to ensure a transparent decision making process (e.g. why does a product qualify for an alternative registration pathways, what is the basis for approval/rejection of the product) should be in place.
* Look at all steps taken for regulatory approval as part of the new registration pathways and consider certain waivers, including:
  1. The need for local clinical trial data, outside of ICH E5 requirements, which could increase the development timeline
* In countries where market access is governed by a further review process, such as Health Technology Assessment, then the Regulatory and HTA authorities/departments should increase collaboration during development of registration pathways in order to ensure gains made in the registration pathway are not lost at the next stage of assessment related to Market Access (Price and Reimbursement).
* Establish the use of IT submission tools to facilitate efficient dossier submissions, that will speed-up manual, face-to-face, appointment based submissions.
* Allowing applicants to have pre-submission meetings to present the companies’ product portfolio and discuss overall filing strategies are very much welcomed, especially to discuss products addressing unmet medical need.

**Criteria to qualify for an alternative regulatory pathway**

1. When assessing the possibility to establish alternative registration pathways, NRAs have to assess the need for specific legislation to create a legal basis for the pathway. If needed, legislators need to be involved.
2. NRAs should provide clear guidance to applicants, describing the dossier requirements, eligibility criteria and processes for the registration pathway. Principles outlined in the draft WHO Good Regulatory Practice guidelines and WHOs recently published draft guideline on “the Collaborative Procedure in the accelerated assessment of national registrations” are recommended to be applied. Relevant stakeholders, including industry, should be involved as part of the process of developing such guidance.
3. Documents required for submission should be tailored to the type of registration procedure used and be and kept to what is truly need for the type of assessment that will be performed. Redundancy of information should be avoided (e.g. CPPs should not be requested when full dossier reviews are being performed, as recommended by WHO (http://www.who.int/medicines/publications/druginformation/WHO\_DI\_30-3\_AdoptedGuidance.pdf?ua=1) ) .
4. Mechanisms to ensure a transparent decision making process (e.g. why does a product qualify for an alternative registration pathways, what is the basis for approval/rejection of the product) should be in place.
5. A holistic approach should be taken when developing alternative registration pathways. Meaning that all steps to the product getting regulatory approval are addressed as part of the new registration pathway.
   1. E.g. in countries where market access is governed by a further review process, such as Health Technology Assessment, then the Regulatory and HTA authorities/departments should increase collaboration during development of registration pathways in order to ensure gains made in the registration pathway are not lost at the next stage of assessment related to Market Access (Price and Reimbursement).
   2. e.g. establish the use of IT tools to effect and facilitate smooth and seamless dossier submissions, compared to the often available manual, face-to-face, appointment based submissions.
6. Allowing applicants to have pre-submission meetings to present the companies’ product portfolio and discuss overall filing strategies are very much welcomed, especially to discuss products addressing unmet medical need.

When defining which registration pathway to establish or use, it is important for regulators to ask themselves the following questions in relation to their public health mission:

* What resources are available for the majority of applications? If resource constrained, would it be possible to use assessments from reference agencies, in part or in whole, to ensure timely approvals and make best use of resources available?
  + Is there sufficient information available regarding the basis of regulatory decisions by SRAs?
* Given the situation, how can timely access and prioritization for those products which address a high unmet medical need be ensured?

Table 2 shows EFPIAs recommendations regarding product profiles required to qualify for certain registration procedures and summarizes the pro’s and cons of these procedures.

EFPIA strongly believes that the driver for establishing and using alternative registration pathways should be to efficiently meet patient needs and not economic reasons (e.g. expediting registration of locally manufactured products only). Of paramount importance, all registration pathways must have a benefit- risk assessment for patients and product quality approved to standards.

**Table 2. EFPIAs recommendations regarding product profiles required to qualify for certain registration procedures**

| Type of registration pathway | Profile of products that qualify | Pros and cons of the procedure |
| --- | --- | --- |
| Reliance pathways to Facilitate Regulatory Decisions | | |
| Recognition procedures | * Can be used for any product for which the quality and benefit-risk profile have been verified to an appropriate standard | **√** Accelerated access to patients1  **√** Saves resources  **×** Must wait for assessments by the respective authority/institution |
| Verification review | * Can be used for any product with approval by one or more stringent regulatory reference authorities. * Also applicable for line extensions, new indications and other post-authorization variations. | **√** Accelerated access to patients1  **√** Saves resources  **×** Must wait for prior approvals and/or documents (e.g. CPP, assessment report) from SRAs used as reference authorities. |
| Abridged review | * Can be used for any product with approval by one or more stringent regulatory reference authority. * Also applicable for line extensions, new indications and other post-authorization variations. | **√** Accelerated access to patients1  **√** Saves resources  **√** Allows independent review of product aspects within local context  **×** Must wait for prior approvals and/or documents (e.g. CPP, assessment report) from SRAs used as reference authorities. |
| Expedited Regulatory Pathways for medicines addressing unmet medical need | | |
| Expedited review | Can be used for any product, but especially new chemical entities and biologics addressing an unmet medical need (including orphan drugs, medicines to be used for pandemics and in emergency situations) with no prior approval history should qualify.  Assuming that only a selective amount of products can be reviewed through a priority review procedure, it is important to select the qualifying products on the basis of:   * The seriousness of the disease they are intended to threat * The potential medical impact the product has (as compared to Standard of Care) * The public health interest   Also applicable to line extensions and new indications, if meeting the qualifying measures above. | **√** Accelerated access to patients in highest need  **√** Resource prioritization to support important public health needs, if done in the right manner.  **×** Labour-intensive  **×** Risk of review being of poorer quality if adequate resources are not allocated |
| Expedited submissions | Can be used for any product. | **√** Accelerated access to patients in highest need  **√** Better resource allocation, if done in the right manner.  **×** Requires robust project management systems |
| Expedited development | Products for diseases and indications for which there are currently no satisfactory treatment options available and the treatment effect is sufficiently large to allow a greater uncertainty about the overall benefit-risk profile at time of approval. These products should be:   * Addressing a high unmet medical need (e.g. treating, preventing or diagnosing life-threatening or seriously debilitating conditions for which no satisfactory treatment exists). This can include orphan drugs, medicines to be used for pandemics and in emergency situations. * Disease transformative * Targeting a well-defined patient population.   Also applicable for new indications. | **√** Accelerated access to patients in highest need  **×** Labour-intensive and requires highly skilled agency  **×** Higher uncertainty about benefits and risks at the time of licensing. This uncertaintly could for example arise from use of surrogate/biomarker endpoints.  **×** Requires well established Pharmacovigilance System |

1 This only applies when the advantages of the procedure (shorter review timelines) outweigh the document requirements, as compared to the standard registration procedure. For example, if the standard registration procedure does not require a CPP and has relatively short timelines, a reliance procedure requesting 2 CPPs and Assessment Reports could lead to later approval of the medicinal product.

Even though registration pathways need to be tailored to the country situation, a certain degree of convergence between registration pathways established by different regulators is important. For example, regarding eligibility criteria for the different type of registration pathways and dossier requirements.

**Definition of terms**

**Stringent Regulatory Authority**

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

1. 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
2. an ICH observer prior to 23 October 2015, namely: the European Free Trade Association, as represented by Swissmedic and Health Canada; or
3. a regulatory authority associated with an ICH member through a legally-binding, mutual recognition agreement 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]

**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

[WHO4] resolution WHA67.20, the Sixty-Seventh World Health Assembly in 2014

[WHO5].WHO, *collaborative procedure in the assessment and accelerated national registration of pharmaceutical products approved by stringent regulatory authorities.* Working document QAS/17.704 (March 2017).

[Liberti] Lawrence Liberti, *Globally Applicable Facilitated Regulatory Pathways to Improve Equitable Access to Medicines.* July 2017.

[CIRS] Centre for Innovation in Regulatory Science, *The impact of the evolving regulatory environment on the approval of new medicines across six major authorities 2006-2015,* R&D Briefing 59 (2016).

**Appendices**

**Appendix 1 - overview of reliance pathways currently in place in emerging markets**

Overview last updated: November 2017

| Region/Country | Name of Pathway | Type of pathway according to EFPIA suggested naming | Key Criteria for Designation | Benefit(s) |
| --- | --- | --- | --- | --- |
| Albania | Accelerated procedure | Verification review | Products registered via EMA or FDA only | 1 month review time (in practice 9-12 months) |
| Argentina | Reliance Approval | Verification review | Small molecule products either imported finished products or products packed in primary container with a previous approval from the following countries: US, Japan, Sweden, Switzerland, Israel, Canada, Austria, Germany, France, UK, the Netherlands, Belgium, Denmark, Spain and Italy | Review within 6-8 months after the file is submitted. |
| Costa Rica | Recognition of clinical studies procedure | Abridged review | Recognition of clinical studies for new chemical entities and new biologics and post-approval changes approved by SRAs | Review within 5 months after the file is submitted |
| Dominican Republic | Simplified procedure | Abridged review | New chemical entities and new biologics, renewals and post-approval changes. The product must be manufactured and commercialized in the country in which it was approved by the SRA or PAHO Regional Level IV Authorities | Review within 3 months after the file is submitted. |
| Ecuador | Homologation Procedure1 | Verification review | Applicable to new registrations previously approved by EMA, FDA, TGA, HC, Japan, South Korea and PAHO Regional Level IV authorities | Shorter registration timelines than average (however, no standard registration timelines are provided) |
| Egypt | Verification procedure | Verification review | New chemical entities and new biologics registered by US FDA and EMA | Review within 30 days after the file is received |
| Egypt | Abridged Procedure | Verification review | New chemical entities and new biologics registered by US FDA or EMA | Review within 60 days after the file is received |
| El Salvador | Recognition of registrations | Abridged review | New registrations of products previously registered by SRAs and PAHO Regional Level IV authorities. | Review in 10 working days (in practice it currently turns out to be longer) |
| Indonesia | Abridged review | Abridged review | New registration (NCE or biological) or variation of new indication/posology approved in more than 3 countries with known good evaluation system | 150 days assessment instead of 300 days |
| Jordan | Fast Registration Pathway | Verification review | New chemical entities and new biologics registered by US FDA and/or EMA AND post-approval changes approved by US FDA and EMA. | Review within 60 days |
| Macedonia | Accelerated procedure | Verification review | Products registered via EMA only | 15 days review time (in practice 4-18 months) |
| Mexico | Equivalence agreements | Abridged review | New chemical entities and new biotech products registered by SRAs as US-FDA, EMA, TGA, Swiss Medic and Health Canada | Review within 3 months after the file is submitted and reviewed by a third authorized party (in practice currently takes longer) |
| Montenegro | Accelerated procedure | Verification review | Products registered via CP/MRP/DCP procedure in EU | 150 days review time (1-5 years in practice) |
| Panama | Abbreviated procedure | Abridged review | New registrations, renewals and post-approval changes of products registered by SRA and commercialized in the respective country. | * Shorter review timelines (max. 60 calendars days). * Waive of quality control analysis of registration samples previous to the registration procedure. |
| Saudi Arabia | Verification procedure | Verification review | New chemical entities and new biologics (excluding vaccines and blood products) registered by US FDA and EMA submitted to SFDA within 2 years of approval by the reference regulatory agencies. | Review within 30 days |
| Saudi Arabia | Abridged procedure | Verification review | New chemical entities and new biologics (excluding vaccines and blood products) registered by US FDA and EMA submitted to SFDA within 2 years of approval by the reference regulatory agencies. | Review within 60 days |
| Serbia/Bosnia-Herzegovina | Accelerated procedure | Verification review | MA according to accelerated procedure applies to products used in human medicine representing a  therapeutic innovation which are of major interest to public health.  -EMA approval gives access to this pathway | 150 days assessment instead of 210 days. |
| Singapore | Verification Route | Verification review | Any non-biological product that has been approved by at least two drug regulatory agencies2 at time of submission | A review within 60/120 working days (instead of the standard 270 working days) |
| Singapore | Abridged Route | Abridged review | Any product that has been approved by at least one drug regulatory agency2 at time of submission | A review within 180 working days (instead of the standard 270 working days) |
| Taiwan | Abbreviated Review | Abridged review | Products with approval by two of the three regulatory agencies (US FDA, EMA, or MHLW/PMDA) that have a bridging study waiver. | A review within 180 days |
| Thailand | Abridged Route | Abridged review | Product with approval by 1 reference authority. | A review within 200 days (150 days for live-saving medicines) |
| Ukraine | Simplified procedure | Abridged review | Effective for products registered in the following countries: USA, Japan, Switzerland, Canada, EU (in case of centralized procedure only) | A review in 20 working days instead of 210. |

1 A significant impact on the registration timelines for NDAs not yet seen in current practice.

2 Any of the following agencies are used as reference authorities: TGA, Health Canada, US FDA, EMA via the centralized procedure, UK MHRA via the national procedure or as the reference member state via the Mutual Recognition Procedure or De-centralized procedure.

**Appendix 2 – Current overview of countries with different types of expedited registration pathways1 for products addressing unmet medical need**

Overview last updated: November 2017

| Region/Country | Pathway | Type of pathway according to EFPIA suggested naming | Key Criteria for Designation | Potential Benefit(s) |
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| Australia | Priority Review | Expedited review | Serious condition; and comparison against existing therapeutic goods; and major therapeutic advance. | Shortened review time (150 working days instead of 255) |
| Australia | Provisional Approval | Expedited development | Promising evidence from early clinical data. | * Filing of an eligible drug submission earlier than normally possible * Shortened time to approval and market |
| Brazil | Priority review2 | Expedited review | Applicable to medicines that meet certain health, economic and social criteria. | Shortened review time |
| Brazil | Phase II submission (no official name) | Expedited development | Dossiers of synthetic and biological drugs can be submitted with Phase II data and Phase III studies initiated. There is no detailed guideline on this pathway and they are applied based on a case-by-case rationale. | Earlier submission of dossiers. |
| Canada | Priority Review | Expedited review | Serious, life-threatening or severely debilitating disease or condition for which there is substantial evidence of clinical effectiveness for unmet need OR there is a significant increase in efficacy and/or significant decrease in risk such that the overall benefit/risk profile is improved over existing therapies | Shortened review time |
| Canada | Notice of Compliance w/Conditions | Expedited development, expedited review | Serious, life-threatening or severely debilitating disease or condition for which there is promising evidence of clinical effectiveness based on the available data that the drug has the potential to meet an unmet need OR there is a significant increase in efficacy and/or significant decrease in risk such that the overall benefit/risk profile is improved over existing therapies | * Filing of an eligible drug submission earlier than normally possible * Shortened time to approval and market |
| China | Priority review | Expedited review | Priority review system started in Feb 2016 with scope including:   1. Drug with significant clinical value   For diseases prevention and treatment (including AIDS, TB, Hepatitis, Rare disease, Malignant tumor, Pediatric drug, Diseases with high incidence or unique in elderly people) and can show significant clinical advantage | * Shortened review time and conditional approval can be granted for marketing prior to the completion of phase III confirmatory clinical trial for new drugs for the treatment of life-threatening diseases for which no effective therapeutic methods currently exists and having great significance to meet clinical needs. |
| Egypt | Fast-track procedure | Expedited review | Drugs addressing an unmet medical need in Egypt, Drugs with an orphan drug desinations, Drugs for which no similar products (or of same class or same clinical value) are marketed in Egypt. | * The time frame of fast track registration is 15-18 months, instead of 24 months in the normal process. * Fast-track enables companies to skip queues and processing in registration steps in parallel to pricing. |
| EU/EMA | Priority Medicines Scheme (PRIME) | Increased HA collaboration to support expedited development and potential for expedited review | Innovative product for target conditions where there is an unmet medical need in relation to which the medicinal product concerned will be of major therapeutic advantage to those affected AND available data supports the claim that the product has the potential to bring a major therapeutic advantage to patients in a given indication, through a clinically meaningful improvement of efficacy, such as having an impact on the prevention, onset and duration of the condition, or improving the morbidity or mortality of the disease. | * Early appointment of CHMP rapporteur and dedicated EMA contact point * Dedicated and reinforced support * Enhanced dialogue to support development * Enable AA * Better use of existing regulatory procedural tools |
| EU/EMA | Accelerated Assessment | Expedited review | Medicinal products of major interest from the point of view of public health and in particular from the view point of therapeutic innovation | Shortened review time |
| EU/EMA | Conditional Approval | Expedited development | Seriously debilitating or life-threatening diseases OR use in emergency situations OR an orphan medicines AND   * benefit-risk balance of the product is positive; * comprehensive data will be provided; and * unmet medical needs will be fulfilled; | Approval may be granted at an earlier time point, subject to specific obligations for confirmatory studies |
| EU/EMA | Exceptional Circumstances | Expedited development | When comprehensive data on the efficacy and safety under normal conditions of use cannot be provided, because:   * rare disease/condition * scientific knowledge is not yet developed * unethical | Full data package not required |
| Indonesia | Priority review | Expedited review | Products that are life-saving, serve unmet medical needs and/or public health (incl. orphan drugs) | Shortened review time |
| Israel | Fast-track procedure | Expedited review | • One of the following categories should be met:  o The product is intended for unmet medical need.  o The product is part of a new therapeutic group and significant effectiveness was proven in comparison to the existing alternatives for a specific illness.  o Products that are categorized with high medical significance in comparison to the existing medical alternatives, such as: life extension, organ rescue, healing of severe illness or provides solution to a unique medical situation in Israel that was not resolved appropriately . | * Gives the possibilities to companies to register in Israel without SRA approval (product has to be submitted EMA/FDA/Swissmedic simultaneously and were categorized as indications with high medical significances in comparison to the existing medical alternatives) |
| Japan | Priority Review | Expedited review | Serious disease where there is there is no existing method of treatment, prophylaxis, or diagnosis AND there is therapeutic usefulness with respect to existing treatment from the standpoint of efficacy, safety, and reduction of physical and mental burden on the patient | Shortened review time (from 12 months to 9 months) |
| Japan | Sakigake | Increased HA collaboration to support expedited development and expedited review | In addition to Priority Review criteria, there is novel mechanism of action for life-threatening diseases that demonstrates prominent effectiveness and developed and planned for approval in Japan ahead of the rest of the world, or at least global simultaneous submissions | * Prior assessment by PMDA * Clinical trial consultations request notice period will be shortened from two months to one month * Shortened review period from 12 months to 6 months * Reexamination period potentially extended (longer market exclusivity). |
| Kuwait | Priority review | Expedited review | A new drug is considered as a priority review designation when its intended for the treatment of a serious (life threatening) condition, demonstrates the potential to address unmet medical needs, or as a breakthrough | Facilitate and expedite review |
| S. Korea | Priority Review | Expedited review | New products for serious, life threatening or rare disease with an unmet need or with no alternative therapy among locally developed NME, life-threatening drug | Shortened review time |
| S. Korea | Rolling Submission | Expedited submissions | New biotech like Cell therapy and Gene therapy and biosimilars | Expedited submission |
| S. Korea | Conditional Approval w/Phase 2 Results3 | Expedited development | Oncology products, orphan drugs, cell therapy for life-threatening or irreversible disease that use surrogate endpoints | Ability to base studies on phase 2 studies with surrogate endpoint |
| S. Korea | Full Approval w/Phase 2 Results | Expedited development | Unmet need and less than 2000 cases in a year | Ability to base studies on phase 2 studies with surrogate endpoint |
| Saudi Arabia | Priority review | Expedited review | Medicines for serious or life threatening conditions, medicines which demonstrate the potential to address unmet medical needs, medicines that fall under the Saudi FDA exempted list. | A reduction in the drug approval timeline from 18 months to 12 months. |
| Singapore | Priority Review4 | Expedited review | Serious life-threatening condition AND potential to address local unmet medical needs AND a significant improvement compared to available marketed products | Shortened review time |
| Switzerland | Fast-track | Expedited review | Promising therapy for a severe, debilitating or life-threatening disease AND unmet need And  a high therapeutic benefit is expected from using this new medicinal product. | Shortened review time (from 330 days to 140 days) |
| Taiwan | Priority Review | Expedited review | New molecular entity for serious disease AND unmet medical needs AND delivers major advance | Shortened review time to 240 days |
| Taiwan | Accelerate Approval | Expedited development | New molecular entity and Unmet medical need AND delivers major advance (or with ODD approved by a A10 country, or difficult to manufacture or import) AND uses a surrogate endpoint | Approval may be granted at an earlier time point, subject to specific obligations for confirmatory studies |
| Turkey | Priority evaluation | Expedited review | Innovative products addressing an unmet medical need  Other products can be designated as highly prioritized and prioritized according to their impact on public finance and production status. | A reduction in the drug review timeline and the possibility for parallel GMP inspections. |
| USA | Breakthrough Therapy Designation (BTD) | Increased HA collaboration to support expedited development + eligibility for expedited submission and review | Serious condition AND when early clinical data show a substantial improvement on a clinically significant endpoint (s) over existing therapy | * All Fast-track benefits, PLUS: * Intensive guidance on efficient drug development- timely and interactive, including potential for abbreviated or condensed development, i.e., potential for shorter, smaller trials * Meetings w/sponsors throughout development * Organizational commitment * Potential for Expedited review (even faster than ‘normal’ expedited review in USA) |
| USA | Fast-Track designation | Increased HA collaboration to support expedited development + eligibility for expedited submission | Serious condition AND nonclinical or clinical data demonstrate the potential to address unmet medical need OR a drug designated for a qualified infectious disease | * Actions to expedite development and review, including more frequent meetings and written correspondence and eligibility to submit data as it becomes available (rolling review) |
| USA | Accelerated Approval | Expedited Development | Serious condition AND a meaningful advantage over other therapies AND surrogate endpoint likely to predict benefit or on a clinical endpoint that can be measured earlier than an effect on IMM or other clinical benefit | * Approval based on surrogate or intermediate endpoint, allowing for shorter development time and earlier submission/ approval of MAA, with confirmation of benefit in a postmarketing confirmatory trial |
| USA | Priority Review | Expedited review | Serious condition AND will provide a significant improvement in safety or efficacy OR pediatric labeling change under Section 505A (voluntary pediatric development) OR drug for qualified infectious disease OR using a priority review voucher | Shortened review time |
| USA | Limited Population Pathway | Expedited development | Antibacterial or antifungal drug, or combination of, with one or more other drugs, AND serious or life threatening infection in a limited population of patients AND with unmet need | Approval based on smaller, targeted studies that demonstrate safety and effectiveness |
| USA | Regenerative Advanced Therapy Designation | A combination of expedited development and expedited review | Cell therapy, therapeutic tissue engineering product, human cell and tissue product, or combination of AND serious condition AND preliminary clinical data demonstrate the potential to address unmet medical need | * Accelerated approval benefits, if using surrogate endpoint * Expedited review, potential use of other pathways (i.e., Priority, BTD, FT) if criteria are met * Flexibility in types of evidence that may be used to meet post-marketing commitments |

1 Specific registrations procedures available for orphan drugs are not part of the overview.

2 ANVISA is currently revising this regulatory framework to comply with new legal provisions.

3 This procedure requires a CPP.

4 Can only be used in combination with abridged review procedures.