Practical aspects of developing, implementing and using facilitated regulatory pathways in the emerging markets

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Background

- To expedite the review of new therapies, national regulatory authorities (NRAs) around the world have implemented expedited review pathways for products that address unmet serious public health needs.[1]
- These facilitated regulatory pathways (FRPs) are designed to accelerate development, submission, regulatory review and patient access to medicines, by providing alternatives to standard development and regulatory routes.[2]
- The importance of FRPs has also increased in low- and middle-income countries, where an expanding portfolio of products for neglected diseases[3] has resulted in the development of country-specific pathways to expedite the regulatory review of new treatments for unmet medical needs.
- While the characteristics of FRPs used by stringent regulatory authorities have been well characterised,[4] no systematic assessment has been conducted of these characteristics for emerging NRAs. This study assessed FRPs in emerging NRAs to understand their diversity and similarities.

Objectives

- Assess FRP characteristics used by NRAs in emerging markets
- Aid in the assessment and development of NRAs, and provide evidence to focus strategies for increasing regulatory capacity in emerging NRAs
- Inform the development of novel, globally aligned, accelerated development and regulatory pathways through the identification of common processes

Methods

- We identified NRAs with FRPs through Cortellis RI and NRA web sites.
- The respective NRA or a local specialist reviewed author interpretations.
- Characteristics were identified as procedural or substantive and based on 5 sequential regulatory activities.

Results

- We assessed 33 FRPs from 29 countries (Fig 1).
- We noted how often FRPs addressed a characteristic and the most common assessment for each characteristic (Table 1), the number and distribution of characteristics (Table 2), and provide a summary of the most frequently observed characteristics (Fig 2).
- The Middle East/North Africa (17) and Eastern Europe (17) addressed the most median characteristics. The Sub-Saharan African FRP addressed the fewest (9).
- All FRPs addressed at least twice as many procedural characteristics.
- A majority of FRPs provided opportunities for frequent interactions between sponsor and agency review team.
- Of the 24 FRPs for which a review target time was defined, all but one had a target of 180 days or less and 54% had a target of 90 days or less.
- Post-approval commitment requirements in the form of post-authorization studies (78%) and risk management plans (67%) were often required.

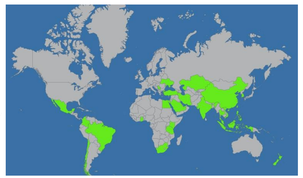


Figure 1. FRPs were assessed from 29 countries.

Results (continued)

Table 1 Most common response values for each facilitated regulatory pathway characteristic.

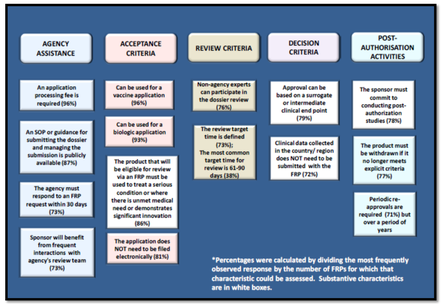
	Procedural or substantive	FRPs describing the characteristic, N (%)	Description	Assessment system classification	Most frequently observed assessment classification	FRPs describing the most frequently observed assessment classification, N (%)*
Agency assistance	Proc	30 (91%)	A standard operating procedure or guidance for submitting the dossier and managing the submission is publicly available	1=no 2=yes	2	26 (87%)
	Proc	30 (91%)	An SOP for how the dossier will be reviewed by the agency is publicly available	1=no 2=yes	2	20 (67%)
	Proc	27 (82%)	An application or processing fee required by agency	1=no 2=yes 3=yes but orphans excluded	2	26 (96%)
	Proc	26 (79%)	A product that uses the FRP will benefit from opportunities for frequent interactions of the sponsor with the agency's review team	1=no 2=yes	2	19 (73%)
	Proc	23 (70%)	The agency has established a special team/office to handle products that are submitted via the FRP	1=no 2=yes 3= ad hoc	1	14 (61%)
	Proc	15 (45%)	How quickly must the agency respond to a request for a designation for an FRP?	1=no/NA 2=within 30d 3=within 60d 4=within 90d	2	11 (73%)
Acceptance criteria	Subs	29 (88%)	The product that will be subject to an FRP must be used to treat a serious condition or where there is unmet medical need or demonstrates significant innovation	1=no 2=yes	2	25 (86%)
	Proc	29 (88%)	The FRP designation is requested or granted at the time of the NDA submission	1=no/NA 2=before 3=with 4=after	3	19 (66%)
	Proc	29 (88%)	The FRP can be used can be used for a biologic	1=no 2=yes 3=only if certain criteria are met	2	27 (93%)
	Proc	28 (85%)	The FRP can be used can be used for a vaccine	1=no 2=yes 3=only if certain criteria are met	2	27 (96%)
	Proc	27 (82%)	The FRP designation is requested or granted at the time of the IND/CTA application	1=no/NA 2=before 3=with 4=after	4	12 (44%)
	Proc	27 (82%)	The application must be filed electronically	1=no 2=yes	1	22 (81%)
	Proc	25 (76%)	The FRP can be used for any type of application (original or supplement)	1=no 2=yes	2	13 (52%)
	Proc	22 (67%)	A product that is designated an orphan product by this or another jurisdiction automatically is reviewed by the FRP	1=no 2=yes 3=only if certain criteria are met	1	15 (68%)
	Subs	19 (58%)	The sponsor must demonstrate that preliminary clinical evidence indicate that the drug might show substantial improvement on a clinically significant endpoint(s) in order to qualify for review via the FRP	1=no 2=yes	2	13 (68%)
Review process	Proc	24 (73%)	What is the target time (agency time) for the review [from submission to reaching regulatory decision for the FRP]?	1= no/NA 2=up to 60d 3=61-90d 4=91-120d 5=121-180d 6=181-240d 7=241-365d 8=>365d	3	9 (38%)
	Subs	22 (67%)	The application requires a certificate of pharmaceutical product (CPP) or other legalised document before product approval	1=no 2=yes 3=negotiable	2	15 (68%)
	Proc	21 (64%)	Non-agency experts may be asked to review the dossier and make recommendations	1=no 2=yes	2	16 (76%)
	Proc	16 (48%)	A "rolling review" of independent sections of the dossier submitted at different times is permitted	1=no 2=yes	1	10 (63%)
Decision criteria	Subs	25 (76%)	The product must have marketing experience in a prior market jurisdiction before it can be approved via an FRP by your agency	1=none required 2=less than one year 3=1y or less 4=more than 1 year 5=yes but time not specified	1	14 (56%)
	Subs	18 (55%)	Clinical data collected in your country/region must be a part of the application.	1=no 2=yes	1	13 (72%)
	Subs	16 (48%)	Does the agency recognise EMA article 58 approvals as a way to expedite approvals of important new medicines?	1=no 2=yes	1	12 (75%)
	Subs	14 (42%)	Approval can be based on an effect on a surrogate or intermediate clinical endpoint that is reasonably likely to predict a drug's clinical benefit	1=no 2=yes	2	11 (79%)
Post-authorisation activities and disengagement	Proc	28 (85%)	Does the product that has undergone review via an FRP need a periodic re-approval?	1=no 2= every year 3=other longer term	3	20 (71%)
	Proc	26 (79%)	The product must be withdrawn if it no longer meets explicit criteria set as a condition of approval.	1=no/NA 2=yes 3=provisional withdrawal	2	20 (77%)
	Subs	18 (55%)	The sponsor must commit to conducting post-approval studies to verify/address anticipated clinical benefit/effect	1=no 2=yes 3=negotiated	2,3	14 (78%)
	Subs	18 (55%)	A risk management plan is required as a condition of approval.	1=no 2=yes 3=negotiated	2	12 (67%)

Characteristics: Proc= Procedural ; Subs= Substantive; * Calculated as: The most frequently observed classification assessment /number of FRPs describing the characteristic.

Table 2. Analysis of distribution of FRP characteristics by country

		Name of FRP	Total rated characteristics	% of total	Procedural characteristics, N	Substantive characteristics, N
Latin America	Chile	High sanitary priority	19	70%	14	5
	Columbia abbreviated	Abbreviated route for biotechnology products	13	48%	9	4
	Columbia Exceptional Circumstances	Exceptional circumstance for identified patients for nonregistered medicines	9	33%	6	3
	Brazil	Priority review	16	59%	12	4
	Mexico	Accelerated marketing authorization	8	30%	6	2
		Median	13	48%	9	4
Eastern Europe	Ukraine	Priority review	13	48%	12	1
	Serbia	Abridged Procedure/Conditional Market Authorisation	17	63%	15	2
	Kazakhstan	Accelerated Pathway	18	67%	13	5
Middle East and North Africa	Israel	Priority review/Accelerated approval	11	41%	7	4
	Turkey	Fast Tracking of License Applications	6	22%	5	1
	Saudi Arabia	Accelerated approval/fast tracking	17	63%	12	5
	UAE	Fast track	17	63%	11	6
	Iran	No specific name	21	78%	12	9
	Egypt	Fast Track procedure	14	52%	12	2
	Tunisia	No specific name	18	67%	11	7
		Median	17	63%	11	5
Sub-Saharan Africa	Ghana	Based on WHO Prequalification Programme	9	33%	6	3
	Kenya	Fast-tracked registration (Locally manufactured and Priority Medicines)	9	33%	7	2
	Tanzania	Fast Track Evaluation	8	30%	6	2
	Uganda	No specific name	11	41%	6	5
	South Africa	Expedited Review Process	9	33%	8	1
	South Africa	Abbreviated Medicine Review Process	7	26%	6	1
		Median	9	33%	6	2
Asia	China	Special Review for innovative drug registration	18	67%	12	6
	India	Emergency	12	44%	9	3
	Taiwan	New drug priority review	16	59%	11	5
	Taiwan	Bridging Study Evaluation (BSE)	12	44%	8	4
	Korea	Fast Track review	20	74%	13	7
	Malaysia	Priority review	20	74%	12	8
	Philippines	Facilitation of Applications for Product Registration	20	74%	13	7
	Indonesia	No specific name	8	30%	8	0
	Thailand	Priority review /accelerated approval	8	30%	7	1
	Vietnam	Priority approval (accelerated approval)	9	33%	8	1
	New Zealand	Priority Assessment	13	48%	11	2
	New Zealand	Abbreviated Evaluation	11	41%	11	0
		Median	13	46%	11	4

Figure 2. Common facilitating practices in FRPs.*



Conclusions

- Emerging economies are developing country-specific FRPs to accelerate approval of medicines for serious and unmet medical conditions.
- Observed diversity in regional FRP characteristics suggests a role for further engagement with emerging NRAs in their design and implementation.
- FRPs can accelerate access to important new medicines and sponsors of products that may fulfil unmet, serious public health challenges should interact early with NRAs to address current requirements.
- These results and further research and experience may suggest FRP characteristics that could be successfully implemented by emerging NRAs.

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Disclosure

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