

Adaptive Licensing and Facilitated Regulatory Pathways: A stakeholder perception survey

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Introduction

It has become apparent that in most countries, as healthcare budgets need to be managed, novel medicine development paradigms that can facilitate regulatory reviews must also address the needs of payers and HTA bodies. Therefore, new approaches to medicine development are being assessed that address both the regulator's and payer's needs; these could potentially provide a streamlined, more cost- and time-effective approach to accelerate patient access to important new medicines.

Despite the active interest and investigation into the development and use of these pathways there appear to be divergent perceptions regarding their definitions, key elements, benefits, barriers, implementations and complexities. No research has sought to develop a stakeholder perception profile of novel adaptive licensing (AL) pathways and currently available facilitated regulatory pathways (FRPs).

Purpose of the study

To develop a baseline understanding of AL and FRP perceptions among key stakeholders in the medicine development, regulatory and access process.

Objectives

- ❖ Gain insights into personal opinions of currently available FRPs
- ❖ Gain insights into personal opinions of AL pathways
- ❖ Characterise the key elements of AL pathways
- ❖ Understand the barriers to implementing AL pathways
- ❖ Provide guidance about stakeholder interest, acceptance or concerns about AL pathways to those who are developing and seeking to implement these novel pathways

Methodology

Definitions

A variety of terms have been used to describe novel approaches to medicine development, review and access. For this survey, we used the following:

Adaptive Licensing (AL): Novel pathways to transforming the medicines development process are being designed and tested. These pathways go by a variety of names, most typically Adaptive Licensing, Staggered Approvals or Medicines Adaptive Pathways. Several novel pathways have been proposed and all share common elements: an early and controlled initial release following a shortened testing period in a limited number of patients; this is followed by a period of intensive real-world monitoring with progressive data collection to more completely define the medicine's profile and manage the uncertainty about the products benefits and risks; this leads to a follow-on full approval, an approval restricting use in a selected population, or a withdrawal. Active involvement of regulators, prescribers, patients and HTA/Payers is a hallmark of Adaptive Licensing pathways. Some Adaptive Licensing pathways could work within the context of current laws and regulations, while others will require a transformation of the legal environment, with a change in the risk-acceptance mind-set of all stakeholders, including regulators, payers, prescribers and patients.

Facilitated Regulatory Pathways (FRPs): Used in this survey to describe currently available regulatory and/or HTA/payer pathways that have been designed to accelerate submissions, reviews and patient access to medicines. Pathways that fall in this category include, but are not limited to Accelerated Assessment (EMA), Conditional Marketing Authorisation (EMA), Accelerated Approval (US), Breakthrough Therapy (US), and Fast Track (US). These pathways often involve more comprehensive interactions between stakeholders during development, set specific review timelines, are used primarily for products that address unmet medical needs and are implemented within the context of existing laws and regulations. Elements of some FRPs are observed in AL (i.e., a conditional license followed by data collection and conversion to a full license)

Survey Development and Distribution

The survey was developed by LL with advice and in collaboration with the other authors. The survey consisted of statements relating to the respondent's current understanding of AL pathways and FRPs as well as questions around their perception of the strengths and limitations of these pathways. The survey was organised in two main sections: Adaptive Licensing Pathways (9 statements regarding stakeholder support and environment for implementation; patient and prescriber perceptions of products approved by AL pathways; challenges to implementing AL pathways; and Facilitated Regulatory Pathways (3 statements). A free text comment section was provided. The survey was piloted among 6 potential participants and their feedback was used to develop the final survey. Survey recipients were randomly selected from the CIRS contact database; some were selected to ensure geographic diversity and a mix of respondent affiliations.

Results

252 individuals representing 90 organisations were invited to participate in the survey. 80 (32%) individual responses were returned (Figure 1); some responses reflected consolidated ideas for a single organization. Overall 50 (56%) of invited organisations responded. Respondents were from 14 countries, most commonly the USA (29), UK (14), Canada (7), Germany (5), Switzerland (5), Sweden (4), and Singapore (3).

- ❖ FRPs at FDA were generally considered fit-for-purpose (63%) when compared to EMA (13%) and PMDA (7%) (Figure 2).
- ❖ FDA Priority Review, Accelerated Approval and Breakthrough Therapy were FRPs considered fit-for-purpose by more than one-third of the respondents; only 15% rated the EMA Conditional Marketing Authorisation or Exceptional Circumstances pathways fit-for-purpose.
- ❖ Therefore, a need for alternative pathways at the EMA was identified by 74% of respondents and by 55% for the FDA.
- ❖ Key foundational building blocks for implementing an AL approach were: agreement on common evidentiary requirements; stakeholder alignment to accepting balance between early access and trade-offs of uncertainties of benefits and harms; the need to integrate patient voice throughout the process.
- ❖ Main barriers to implementing AL were: divergent regulatory and HTA requirements; insufficient infrastructure to monitor post-approval benefits and harms; limited legislative/regulatory frameworks; uncertainty as to how to "disinvest" a product that does not meet expectations; IP protection limitations.
- ❖ A perceived lack of commitment on the part of some regulatory and HTA agencies to implementing AL was observed as a barrier.
- ❖ Most respondents did not believe it likely that a fully implemented AL approach (integrating regulatory, patient, prescriber and HTA/payer needs) in a major jurisdiction (e.g. US, EMA, Japan) would occur within the next 5 years

Figure 1: Respondents' background (n=80)

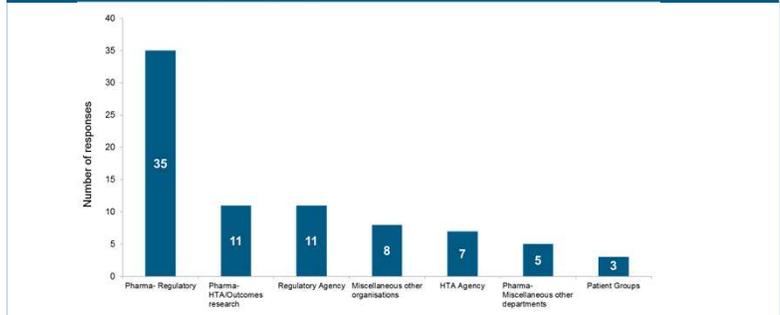


Figure 2: Usefulness of current FRPs

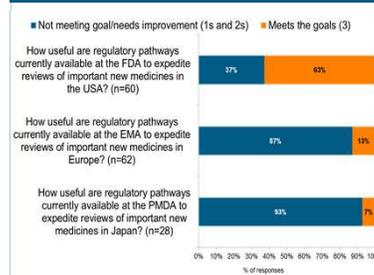


Figure 3: Likelihood of implementing AL

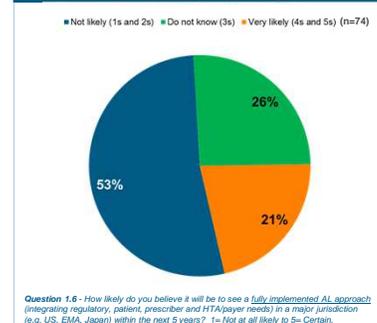
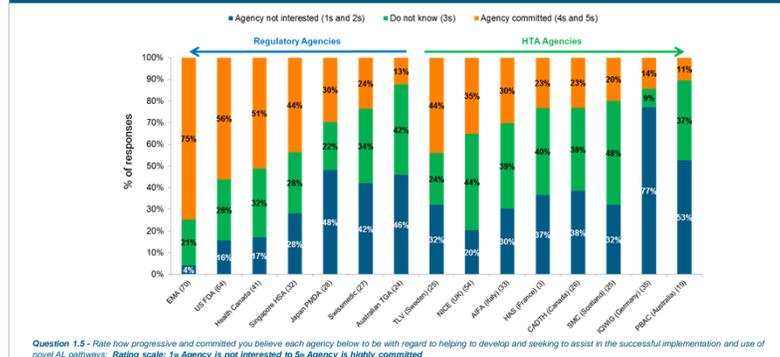


Figure 4: Are agencies committed to AL?



Conclusion

Current FRPs in the EMA and PMDA are considered less fit-for-purpose than at FDA; nevertheless, more than half of the respondents did not believe an alternative novel AL pathway would be successfully implemented in the near future in any major jurisdiction. Although key foundational AL building blocks have been identified, barriers to implementation exist. This study provided insights into perceptions regarding FRPs and the potential for implementing AL; the observations are not conclusive with regard to any agency's FRP performance or the ultimate ability of agencies to maximise the benefits of their FRPs or to implement an AL pathway. These findings support the need for further research into the key elements of successful FRP and AL pathways, and to determine solutions to overcome barriers to their implementation.

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