The Confluence of Accelerated Regulatory and Health Technology Assessment Access Pathways

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There is a growing interest in aligning accelerated regulatory pathways with flexible access and reimbursement pathways to expedite the equitable availability of high-quality, safe, and effective medicines that provide a value-based approach to meeting society's most important healthcare needs. The Centre for Innovation in Regulatory Science (CIRS) identified key issues regarding the confluence of regulatory and health technology assessment processes from discussions and presentations given by international regulators, health technology assessment bodies, payers, patient representatives, and multinational pharmaceutical company representatives on this topic at CIRS workshops held in 2014 and 2017 that focused on the commonalties and differences across these pathways. Recent publications have also been highlighted. The barriers to and opportunities for aligning stakeholder expectations and needs were investigated and recommendations provided. Early dialogue among the stakeholders is the process that will likely provide the greatest return on investment of time and effort to identify, develop, review, and recommend important new medicines, especially those that address an unmet medical need.

Healthcare stakeholders, including companies, regulators, health technology assessment (HTA) bodies, patients, providers, and payers generally agree that providing timely access to meaningfully better medicines at reasonable costs is an important aim of healthcare systems.[1] However, despite advances in clinical and regulatory sciences, the traditional development and regulation of medicine can take as much as 10 years.[2]

Therefore, a number of new regulatory initiatives to enable the flexible development and earlier licensing of innovative medicines have emerged. These include the US Food and Drug Administration Breakthrough Therapy Designation and Accelerated Approval pathway along with the US Congress 21st Century Cures Act to accelerate the development and delivery of new medicines.[3] In Europe, the Priority Medicines (PRIME) scheme was launched by the European Medicines Agency (EMA) to enhance support for the development of medicines that target an unmet medical need.[4] These emphasize enhanced interaction and early dialogue with developers of promising medicines to optimize development plans and speed up evaluation so these medicines can reach patients earlier. In addition, within jurisdictions such as the United Kingdom, experience is being gained with approaches such as the Early Access to Medicines Scheme.[5] The Early Access to Medicines Scheme focus is on evaluating the benefit-risk profile for a medicine's use in a restricted population in which unmet medical need is highest and decision making can be based on robust evidence. These facilitated regulatory pathways (FRPs) are playing an increasingly important role in regulatory approvals worldwide, especially for medicines that address an unmet medical need. FRPs have been designed to speed the progressive development, regulatory authorization, and access for important new drugs with a positive benefit–risk balance. Common elements of FRPs include facilitation of early stakeholder interactions and the early controlled release of needed medicines followed by real-world monitoring with progressive data collection to completely define the medicine's benefit–risk profile. This complete definition leads to the medicine's full approval, withdrawal, or limitation of use.

However, these medicines may be initially approved through the evaluation of surrogate markers of efficacy and subject to the collection of postauthorization data and stakeholders must, therefore, accept a degree of uncertainty around the safety and efficacy of the product at the time of marketing authorization. Although regulators do not consider product cost or comparative or incremental benefits in their assessments, these are key factors that characterize the value of the medicine for decision making by HTA bodies and payers.

Flexible access and reimbursement pathways (FARPs), on the other hand, provide options for managing the introduction of new medicines via pathways that include opportunities to decrease uncertainty present at the time of accelerated regulatory approval through the assessment of an increasingly robust practical experience database. FARPs can address the regulatory data limitations for translation to payer budgets and sponsors' return-on-investment expectations and can provide opportunities for managed disinvestment if the products do not meet clinical expectations.

Consequently, the outcomes of FRPs are not always widely embraced by the payers, due to the uncertainty around the effectiveness of new treatments that have received accelerated approvals and concerns as to whether their value to healthcare systems has

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been adequately demonstrated.[6] In addition, payers, although sympathetic to early access for truly unmet medical need, have shown reluctance to support use of accelerated pathways for a wider set of indications.[7] HTA bodies are also looking at how to better ensure that they are recommending facilitated coverage for medicines that are clinically or cost-effective by examining models, such as coverage with evidence development, managed entry schemes,[8] and new models around pay-for-performance. These FARPs include the HTA body and payer in the accelerated access process. FARPs provide options for managing the introduction of new medicines via pathways that build opportunities for both payers and sponsors to benefit from increasing certainty around the effectiveness of a product, relying on an increasingly robust database of experience following the regulatory approval, and initial introduction of a product. They can take any one of many forms to address the limitations of payers/budgets while providing opportunities for return-on-investment expectations of sponsors and for patient-centered managed disinvestment.

Therefore, the need to better define the relationship and alignment between FRPs and FARPs has emerged. Defining clinical certainty and translating it into a cost value is the primary source of tension between the two pathways. This tension might be mitigated to some extent if all parties agree to clearly define the initial target population that has the greatest and most urgent clinical need and for whom the medicine is likely to generate the greatest clinical benefit. However, challenges to implementing FRP and FARPs exist and include regulators' concerns regarding the controlled use of medicines approved through these flexible pathways, HTA bodies need to develop rules surrounding disinvestment for medicines that do not meet the burden of proof and industry's need to address competitive pricing, potentially tied to an agreed, genuinely adaptive pricing model.

There is a perceived disconnect in that regulator and payer evidence requirements and outcomes seem to be diverging rather than converging as regulators' approval of quality, safety, and efficacy evolves and becomes more flexible.[9] Conversely, others have found a relatively high degree of concordance between regulators and HTA bodies with regard to the parallel scientific advice given on development plans.[10] Faced with challenges of affordability, payers and some HTA bodies are becoming more stringent regarding evidence needed to justify the cost associated with incremental benefit.[8] Misalignments can occur when there is a lack of agreement around what is perceived as an unmet medical need among the stakeholders with HTA and payers using a nuanced approach that may consider gradations of "low" and high" unmet need,[11] whereas regulators and patients may focus on criteria that lead to a more binary (yes/no) approach.

In 2014, the Centre for Innovation in Regulatory Science (www.cirsci.org) (CIRS) held the workshop entitled "Medicines Adaptive Pathways: A Practical Strategy to Improve Patient Access to Medicines?"[12] Since this workshop, there has been an increased use of FRPs globally by regulators and the evaluation of different access schemes by HTA bodies and payers, as well as a narrowing of the gap between regulatory and HTA requirements.[13]

Therefore, in September 2017, CIRS held another workshop, "Flexible Regulatory/Access Pathways: Are We There Yet?"[14] This workshop brought together representatives from 5 regulatory agencies, 11 HTA and payer entities, 2 patient groups, and 6 university, nonprofit, and association groups, as well as 21 multinational pharmaceutical companies, to discuss current perspectives and opportunities for FRP/FARP alignment as part of the regulatory/HTA toolbox to enable earlier patient access, especially where there is high unmet medical need. Participants recommended how to evolve and ensure success of FRPs and FARPs for new medicines and the critical success factors to manage uncertainty, ensure their proper use, and interpret continuity with evidence generated during early phases of study. It was envisioned that, through this workshop, it could be determined how the predictability of regulatory success and of positive HTA recommendations could be improved and which activities would allow stakeholders to achieve their aims. A comprehensive report has been published as a CIRS Workshop report[14] and the key observations are described herein.

A 2014 multistakeholder study of FRPs and adaptive licensing (AL) approaches, assessed multiple varied stakeholder views on the knowledge of and perceptions around AL processes.[12,15] These results indicated that only 22% of respondents felt that it was likely that an AL approach would be fully implemented within the next 5 years (i.e., by 2019). When the survey was repeated by CIRS in 2017 by posing the question to workshop participants "By when do you think an aligned FRP/FARP pathway could be in place as a codified process within your geographic area of interest?" a more nuanced response was observed: 16% believed this was already in place, and almost a quarter indicated an expectation of having this in place in 1–2 years. Nevertheless, there remained skepticism, with 55% expecting it to take between 3 and 10 years for full implementation (**Figure 1**).[14] Participants cited a variety of barriers to implementation, which are discussed later in this summary.

THE FRP PROCESS

As noted above, FRPs may result in earlier and more frequent interactions between industry and regulators and increase the level of commitment between the parties by allocating regulatory resources to provide high-quality scientific and regulatory

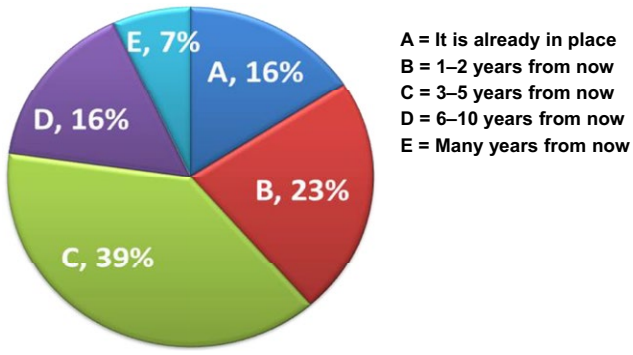

Figure 1 Survey question from September 2017 Centre for Innovation in Regulatory Science workshop: By when do you think an aligned facilitated regulatory pathway/flexible access and reimbursement pathway should be in place as a codified process within your geographic area of interest? Reprinted from Liberti *et al.*[14]

advice to sponsors, can give a larger role to effects on surrogate end points, and may move some of the burden of evidence generation from the preauthorization to the postauthorization phase. For patients, these expedited pathways can provide early access to medicines for severe diseases for which no or limited treatment options exist.

One example of a European FRP is the EMA PRIME scheme mentioned above, which is based on enhanced interaction and early dialogue with developers of promising medicines, to optimize development plans and speed up evaluation.[4] PRIME eligibility review is robust, with excellent collaboration across committees and rapid written decisions. The program includes iterative, enhanced multistakeholder scientific advice and enables early identification of potential issues. Kick-off meetings include broad discussion of development and regulatory strategy with multiple issues identified for future scientific advice and planning for postauthorization and stakeholder interactions. At the time of the workshop, of 130 requests for PRIME status, 28 products had been granted eligibility, mostly in rare diseases.

Evidence needs of regulators outside of the United States and the European Union are being influenced by evolutions in situational contexts and evidence generation innovations. FRPs that can narrow or shift the focus of research and influence the nature of the evidence produced can influence the decisions of these regulators because of potential gaps between their evidence needs and received evidence packages.

Potential panregulatory approaches to alignment include an assessment of the potential divergences expected across agencies and the management thereof; in these instances, there would be up-front decisions to address opportunities for generalizability and the applicability of the results from FRPs across multiple jurisdictions. Multiagency discussions and upfront alignment may promote a balance between evidence generation and product needs to avoid inefficiencies that increase time to decision and global decision diversity.

THE FARP PROCESS

Because healthcare expenditures are escalating to unsustainable levels in many countries, those payers would like to manage pharmaceutical costs as a way to maximize the use of their budgets; the use of flexible reimbursement mechanisms for pharmaceuticals, such as adaptive reimbursement, confidential national pricing, or agreement on mutually acceptable reference prices, could facilitate this process.

One integrated approach is the Medicines Adaptive Pathways to Patients (MAPPs) program that has sought to foster access to beneficial treatments for the right patient groups at the earliest appropriate time in the product lifespan in a sustainable fashion. MAPPs is a prospectively planned, iterative approach to medicines development and access pathways within the current regulatory framework, making the best use of existing tools and methods, such as conditional approval, scientific advice, and real-world data with multistakeholder engagement. However, as part of a movement for cost containment, payers would like to see programs, such as MAPPs, applied primarily to special cases, such as life-threatening diseases or where there is the need for urgent public health protection. The broader applicability of MAPPs, although scientifically justifiable, remains to be determined.

Moreover, although major health improvements may be expected to be gained through use of these processes, as the ultimate stakeholders, patients should be informed regarding the uncertainties in the efficacy and safety of medicines approved and made accessible through FRPs/FARPs and patients and physicians should agree in advance as to the possible withdrawal conditions and mechanisms for the medicine if results are not as expected. In these plans, reimbursement for the medicine would be decreased or increased according to mutually agreed observational results, and market authorization could be rescinded, or populations or indications can be altered, limited, or broadened.

HOW CAN FRPS AND FARPS ALIGN?

Flexible pathways are needed to achieve the possibly conflicting regulatory and HTA goals of innovation and affordability, but the required work is scientifically complex and labor intensive and more platforms, resources, and dialogue are needed. Participants in the 2017 CIRS workshop detailed some of the requirements for aligned flexible pathways.[14] These included: adequate capacity by the stakeholders for effective early dialogue, efficient mechanisms for the generation of postapproval evidence to address key uncertainties, and nimble mechanisms for policy revisions. Additional requirements specified for flexible reimbursement included a solid legal platform, early stakeholder agreement as to the level of evidence needed for initial access, and defining the criteria and process for determining acceptability of the study protocol for both regulatory and access needs.

In an interactive survey conducted at the 2017 workshop, 76% of participants said that early regulatory/HTA body involvement resulted in better meeting of downstream HTA and regulatory needs and was either always worth the effort or beneficial on a case-by-case basis. Perhaps reflecting the early stages of these types of interactions for some stakeholders, 23% thought it was still too early to assess the value to early planning interactions.

INCENTIVES FOR ALIGNMENT

FRPs provide regulators with tools to balance unmet medical need and the severity of a disease against any uncertainties about the medicine's efficacy and safety; for HTA bodies and payers, FARPs provide a pathway to reduce initial uncertainty about the expected value and comparative effectiveness of a new product. For these stakeholders, agreeing on expectations for drugs in development, conferring on mutual data requirements, explaining the rationale for divergent requirements for their respective decision making, and working toward the minimization of duplicative data assessments are goals of aligning FRPs and FARPs.

For industry, alignment incentivizes the development of innovative medicines by agreeing on the expected value and benefits of a new treatment modality early in development, thereby focusing development on the critical needs of the regulator and HTA/payer. In all cases, these stakeholders are seeking to determine how the new medicine can best address the unmet needs of patients in a clinically relevant and cost-effective manner.

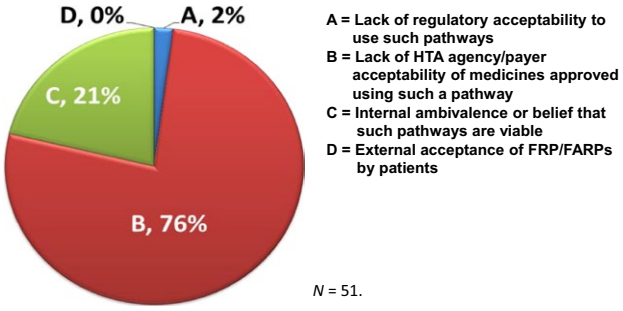

Figure 2 Survey question from September 2017 Centre for Innovation in Regulatory Science workshop: What do you think is the main stumbling block for the adoption of an aligned facilitated regulatory pathway (FRP)/flexible access and reimbursement pathway (FARP)? HTA, Health Technology Assessment. Reprinted from Liberti *et al.*[14]

This perspective was reinforced at the CIRS workshop by a representative of the European Patients Forum (EPF), an independent, nongovernmental umbrella organization providing a voice for 74 patients groups, European Union disease-specific organizations, and national patient coalitions. The EPF vision calls for equitable and timely access to high-quality, patient-centered health and social care for all European Union patients regardless of where they live in the European Union. The EPF has actively participated in Accelerated Development of Appropriate Patient Therapies, a sustainable, multistakeholder enabling platform (ADAPT SMART) for the coordination of MAPPs activities.[16] EPF participation in the ADAPT SMART program has assisted in the identification of gaps in patient involvement in medicines' development that need to be addressed. For example, a strong legal basis for FRPs and adaptive pathways is key for patients, particularly as it applies to the disinvestment in or withdrawal of new medicines, both of which have the potential to impact patient treatment options. Truly informed and comprehensive patient consent during development is also required, which includes an awareness of the trade-off in benefits and risks for the expedited access to new medicines.

BARRIERS TO ALIGNMENT

The sources of uncertainty around new medicines remain in the short term and that uncertainty combined with the increasingly specific requirements for alternative access models with evidence development involve a fundamental change in the relationship among companies, regulators, and funders for medicine development. Payers perceive that they are asked to share a growing proportion of the risks of the uncertainty and should expect that the budget consequences of that shared risk are recognized and compensated.

We observed that to some payers, MAPPs and aligned FRPs/FARPs are still concepts in development that require more discussion and research. For this group, the objective of FARPs is not necessarily early access but equitable access to important new interventions, and a perception of a lack of HTA body/payer acceptance of medicines approved using such a pathway has been recognized (**Figure 2**).

Another limitation to aligning these processes is the potential disconnect between expectations of completing postauthorization regulatory study commitments and their actual completion, resulting in a potential knowledge gap, especially when a refined value assessment needs to be based on these data. It has been reported that of 30 drugs that received conditional approval by the EMA from 2016–2016, 17 still maintain conditional status[17] and that of conditional approvals granted 2009–2010 at the US Food and Drug Administration, 25% of the commitments are still ongoing and 20% have yet to begin.[18] These statistics may understandably inspire caution among payers and uncertainties as to the safety and efficacy/effectiveness of new medicines may cause HTA bodies and payers to make initially conservative reimbursement recommendations. In addition, at present, obtaining meaningful data after licensing is challenging in most jurisdictions, and there are methodological problems in interpreting certain kinds of real-world data.

In considering other issues that might be impeding alignment of the FRP and FARP processes, CIRS 2017 workshop attendees cited the necessity for a flexible approach to characterize unmet medical need, mismatched evidentiary requirements and misaligned adaptive development expectations across regulators and HTA bodies/payers, and inconsistent approaches to exit and disinvestment strategies.

OPPORTUNITIES FOR ALIGNMENT

Much exciting work is taking place to identify opportunities to support the confluence of FRPs and FARPs. Possible solutions to observed barriers included convergence of legislative requirements, early involvement of all key stakeholders in designing clinical studies with patient relevant clinical and value outcomes, collaboration on aligning policy and processes, and beginning the development process with the ends of regulatory approval and equitable access in mind, all of which provide a direction for future research. **Figure 3** summarizes recommendations for the alignment of FRPs and FARPs put forth by workshop participants.

Expedited regulatory processes mean that products come to HTA agencies and payers sooner in their development cycle, typically with evidence that is fit-for-purpose for a regulatory decision but less mature for a value assessment. Therefore, further work is required to achieve consensus among HTA and payer agencies on some aspects of adaptive pathways, although these stakeholders are supportive in principle of pathways that allow patients early access to transformative medicines in a financially sustainable way.

For example, The National Institute for Health and Care Excellence has participated in some of this foundational work, including being active in the EMA Adaptive Pathways Pilots, designed to improve alignment of regulatory and HTA processes.[19] These have included ADAPT SMART,[16] which supports policy makers and national governments to further develop adaptive approaches to the development and reimbursement of medicines, and England's Cancer Drugs Fund, a source of funding for cancer drugs through which pharmaceutical companies, the National Health Service England, and National Institute for Health and Care Excellence address uncertainties surrounding the effectiveness of new cancer treatments, typically by the collection of additional data during a specified period of managed access.[20]

Recommendations to align facilitated regulatory and access pathways

Prioritizing important therapies– What are the criteria that will be used to determine which products should be considered for these pathways? How should they address evolving unmet clinical needs?

Consolidate, list, adapt

- ✓ Using a multi-stakeholder approach, develop a consolidated core list of factors to prioritize products for facilitated regulatory and access pathways. Adapt the list according to individual stakeholder needs.

Alignment – What are the elements needed to bridge the barriers and exploit the opportunities to promote convergence to ensure effectiveness and efficiency of the regulatory and HTA approaches?

Consult, discuss, define, recognize, accept

- ✓ Conduct earlier joint discussions among companies, regulators, and health technology assessors to develop agreements as to the core package for approval, evidence needs, and postauthorization effectiveness studies.
- ✓ Involve payers and health technology assessors to provide postauthorization expectations and input into risk management plans. With guidance from ICH M4, improve the description and understanding of uncertainty.
- ✓ Recognize that real-world data are an important element of evidence – develop agreements on requirements and approaches; include patient-reported outcomes as an important aspect of real-world evidence; embrace new technology to improve access and usability of these data.

Understanding stakeholder differences on views of outcome and success of flexible regulatory and access pathways: How can stakeholders bring the pathways to life?

Discuss, confide, acknowledge, plan, commit, accept, teach

- ✓ Conduct life-cycle spanning, multi-stakeholder dialogue in safe harbor spaces and include data protection and confidentiality. Acknowledge global differences in dialogue processes.
- ✓ Address issues in timing and compliance of commitments through earlier discussion, planning and agreement on postapproval commitments, including processes for enforcement and distinctions between commitments for FRPS vs FARPS.
- ✓ Remain open to the use of FRPs/FARPs, while understanding that they are still in the experimental phase. Make FRP experiences publicly available for global learning.

Figure 3 Syndicate discussion groups at the September 2017 Centre for Innovation in Regulatory Science workshop, recommended actions to align facilitated regulatory and access pathways. FARPs, flexible access and reimbursement pathways; FRPs, facilitated regulatory pathways; HTA, Health Technology Assessment; ICH, International Conference on Harmonization. Reprinted from Liberti *et al.*[14]

The uncertainties surrounding the evidence on which decisions for expedited medicines are based have resulted in challenges in pricing and reimbursement. In Sweden, for example, to meet this challenge, the HTA body, Tandvårds-och läkemedelsförmånsverket (TLV) has established a national platform for collaboration and dialogue with pharmaceutical companies and Swedish county councils. This three-party dialogue identifies and seeks ways to address risks, such as uncertainties about treatment populations and the duration and results of treatment. In addition, TLV revised its internal structure to allow for more therapeutic specialization and increased analytical capacity and adapted its processes to accommodate different types of applications. Finally, to meet the important challenges surrounding real-world data, TLV aims to run several pilots with regard to drug assessment and use of real-world data.

Unaligned regulatory and HTA views may lead to confusing signals and divergent outcomes, waste of resource, frustrated stakeholders, and delayed patient access. However, there are several ways that stakeholder decisions can become more agile while also being more predictable and reliable.

Among these is the use of real-world data to provide an appropriate standard of care or historical control and confirm the size of treatment effect after approval. Prices for the initial launch of a drug with confidential discounts would be adjusted over time as more evidence become available and data-driven schemes including pay-for-performance and outcomes-based agreements are explored and piloted more widely. However, implementing new payment models requires an appropriate infrastructure, including the ability to efficiently collect relevant data, compliant with data privacy and information technology regulations, and collective efforts are needed to invest in the appropriate infrastructure enabling outcomes-based agreements and an outcome-driven healthcare system. The appropriate procedures for analyses and interpretation to provide equitable compensation commensurate with the outcomes need to be further refined.

As discussed above, the ADAPT SMART Consortium has established a platform to facilitate and accelerate the availability of MAPPs to all healthcare stakeholders. MAPPs present stakeholders with an "evidence vs. access" conundrum; there are trade-offs between ensuring rapid access to promising treatments for unmet urgent need, balanced with ensuring that patients, healthcare professionals, and other decision makers possess adequate information on the benefits and risks at the time of launch.[21,22] Importantly, there is momentum behind the MAPPs concept with the ADAPT-SMART Consortium identifying four key stages for stakeholder alignment: preclinical, preliminary evidence generation, prelaunch, and postlaunch.[21]

In a recent summary of work undertaken by the Consortium, Bouvy and colleagues[23] identified challenges and opportunities to the use of aligned European adaptive pathways. They cited a continued lack of alignment between regulatory and HTA noting that from 2006–2016 outcomes-based managed entry agreements were not commonly used for products with a conditional marketing authorization or authorized under exceptional circumstances, important therapeutics for which an aligned adaptive pathway would be of most benefit where an unmet medical need exists. Difficulty in developing consensus around evidentiary standard and appropriate data collection process are areas that will benefit from alignment. Nevertheless, this is the momentum behind the MAPP concept. Moving forward, all stakeholders, whether from ADAPT SMART or other regulatory or HTA initiatives, must work together from the earliest stages of medicines' development and accept new paradigms to ensure the development of safe and effective innovative promising products of societal value that can fulfill unmet needs as early as possible.

To address regulatory harmonization and convergence, these efforts can be enhanced by focusing on regulatory processes, tools, trainings, and best practices that each regulatory authority could reference to ensure resources are efficiently managed by each regulator, between regulators, and by industry to support expediting patient access to innovative medicines. There are a number of existing tools through which regulatory convergence already happens, such as the International Council on Harmonization (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use Common Technical Document. Bilateral and multilateral agency collaborations occur through cluster and information-sharing practices and reliance and recognition agreements. Successful harmonization fora include the World Health Organization, ICH, and the Asia Pacific Economic Cooperation Centers of Excellence. Opportunities for future tools for regulatory convergence could include aligned clinical trial applications and common protocol templates. Technical guidelines to aid convergence could be developed around topics such as risk-based submission of chemistry, manufacturing and control information, and postapproval planning. Relevant to both regulators and HTA/payers would be the development of common approaches to terms, such as "life threatening," "serious," and "unmet medical need."

The European Network for Health Technology Assessment comprises 81 partnering national, regional, and not-for-profit agencies that produce or contribute to HTA. The European Network for Health Technology Assessment has undertaken a number of work streams to foster HTA alignment. Joint Action 3 aims to contribute to a sustainable model for the scientific and technical cooperation in HTA in Europe through a series of work packages (WPs). Parallel HTA consultations with the EMA as part of WP5A and linking to EMA PRIME might help to select the products that can most benefit from facilitated regulatory and access pathways and also clearly define what is needed in the research program. Joint relative effectiveness assessments conducted in parallel with EMA as part of WP4 may speed access to needed treatments and also ensure a more consistent relative effectiveness assessment perspective across Europe. Collaboration on additional data collection as part of WP5B can increase the number of patients included in registries and the robustness of registry data and ensure the use of standardized tools for data analysis. However, despite these HTA tools, it is likely that the management of pricing, reimbursement, managed entry, and exit schemes will remain for the foreseeable future at the national level.

The core observation from the 2017 workshop was that early dialogue among the stakeholders, including sponsors, regulators,

HTA bodies, payers, and patients, is the process that will likely provide the greatest return on investment of time and effort to identify, develop, review, and recommend important new medicines, especially those that address an unmet medical need.

In summary, there is a growing interest in aligning accelerated regulatory pathways with flexible access and reimbursement pathways to expedite the equitable availability of high-quality, safe, and effective medicines that provide a value-based approach to meeting society's most important healthcare needs. A variety of methodologies and procedures are being designed, piloted, and implemented, each with their own focus and emphasis. Identifying the common bestpractices across these procedures will work toward their confluence and the implementation of the most efficient development, regulatory, and access pathways.

METHODS

The results of discussions and presentations at two CIRS workshops conducted in 2014 and 2017 regarding the status of these processes and recommendations to move toward alignment were summarized. Workshop participants included thought leaders in the pharmaceutical industry and regulatory, HTA bodies and payers, as well as representatives from academia and patient organizations. A survey was conducted among the participants of the September 2017 workshop.[14] Participants (n = 51) used the MeeToo (www.meetoo.com) survey tool (by web or app) to respond to eight sequential questions posed by the moderator during an interactive response session. The questions were designed by CIRS staff and were piloted at a CIRS Technical Forum in 2016. All responses can be found in the CIRS full workshop summary.[14] The two questions illustrated herein were selected by the authors as the most germane to the topic of this paper. In addition, recent publications that could inform the workshop observations have been cited to provide context.[24]

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DISCLAIMER

The views expressed in this paper are the personal views of the authors and may not be understood or quoted as being made on behalf of or reflecting the position of any organization that participated in the workshops.

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