



Workshop report: The seamless pathway and decision making

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The work leading to these results was conducted as part of the ADAPT SMART consortium (Accelerated Development of Appropriate Patient Therapies: a Sustainable, Multi-stakeholder Approach from Research to Treatment-outcomes). For further information please refer to www.adaptsmart.eu. This paper is the result of the collective input from working group D2.05 and D3.02 and only reflects the views of the authors.

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1. Introduction

In February 2016, the ADAPT SMART consortium hosted a multi-stakeholder workshop on the *'selection criteria for applicability of MAPPs'*. In order to continue the instructive discussions, a joint (D2.05 and D3.02) multi-stakeholder workshop on, 'The seamless pathway and decision making' was held on 6th July 2016. More than 30 representatives including; European regulators, Health Technology Assessment (HTA) bodies, the pharmaceutical industry, patient organizations, health care professionals and academics attended the workshop.

More information on adaptive pathways can be found at the European Medicines Agency (EMA) website.

2. Workshop summary

The workshop was opened by Sue Forda (Eli Lilly) and Richard Barker (CASMI). Michael Berntgen (EMA) summarized the rationale for Adaptive Pathways. André Broekmans (Lygature) introduced the ADAPT SMART project and consortium. Finally, Angelika Joos (MSD) provided updates on the selection criteria for MAPPs and Jacqueline Bouvy (NICE) reported on the 5th July 2016 workshop on managed entry agreements (MEAs).

Participants then joined two consecutive breakout sessions. The first reviewed the conceptual framework for a proposed MAPPs pathway; the second discussed the implications and resource commitments for an adaptive process. The day concluded with an open exploratory discussion on 'exit' strategies - the terminology, what was understood by it, and by which stakeholder. The detailed stakeholder input will be used to update the various work stream deliverables.

Break out 1 - Seamless Pathway

- When applicable for some medicines, MAPPs should be understood as a new development pathway with several cycles of evidence generation and assessments [iterative development]. The pathway uses the same existing legislation but in a continuous iterative process with multistakeholder consultation, which permit product and EU member state specific nuances.
- MAPPs involves a notable upstream shift in prospective planning and discussions on topics such as: design of the development plan, identifying sources of real world data (RWD) and how they can be best utilized in combination with registries and RCTs, budget impact estimates, reimbursement and prescribing conditions, and resource planning.

Participants commented on a pre-read including a graphic representation of the pathway.

Overall, the participants agreed on the core MAPPs development/access milestones within the 5 development stages [Drug discovery, Preclinical, Clinical Trials, Review, Patient Access]. However, the representation of the MAPPs model could be simplified and more iterative, including the possibility for a product in the MAPPs pathway to return to a more traditional development pathway.

- Although a formal multi-stakeholder discussion is not foreseen at the drug discovery stage, general inputs from stakeholders including therapeutic contextual assessments are still anticipated as part of companies' definition of development priorities.
- For a product that fits the MAPPs criteria modifications to CMC (Chemistry, Manufacturing and Control) development paradigm should be considered at an early phase (eg already during the preclinical phase). A more adaptive and flexible CMC process throughout development is critical to ensure reliable supplies of the product
- Patient preferences should be explored early on – this is already possible in the preclinical stage.
- Clinical trials plans and outcomes are expected to satisfy all stakeholders (including patients). The views of payers on potential outcomes could also be considered at an earlier stage reflecting later concerns on budget and pricing decisions. The question remains of who should be 'the coordinator' of the multi-stakeholder interactions.
- MAPPs is a continual development plan and dialogue, thus there is no need to define separate pre- and post-authorization development stages for multi stakeholder interactions.
- Considerations of MEAs need to be initiated prior to marketing authorization.
- In addition to a moment for 'reassessment' (based on additional data collected in the post marketing phase) of an authorized indication, a separate decision point is needed to reflect the moment of reviewing a possible new indication or population.

Break out 2 - Impact of decision making on resource requirements and commitments

Participants were asked to share their views on the resources they would need at the different moments on the pathway.

- Trust in the MAPPs process is an essential success factor: stakeholders should be confident at entry into the MAPPs pathway that commitments by all parties will be met. This may argue for a more formal concordat or agreement that the stakeholders enter into. This concept requires further in-depth exploration as to its nature and how it would be sympathetic to each stakeholder.
- Additional time, relevant expertise, and access to lay-term information will be required at each

decision moment.

- For some stakeholders this type of engagement may be beyond their current legal mandate. If so, it may require political support to allocate the resource and to hire the experts (for example, a fund or fee-for-service for the early engagement steps).
- An early indication by all stakeholders of a potential MAPPs product could signal an R&D opportunity, and the early multi-stakeholder dialogue act as an incentive for sponsors.
- Conflicts of interest for all stakeholders vary along the pathway and need careful consideration to ensure sufficiently resourced, unbiased input can be fully utilized.
- Post-marketing RWD collection should, wherever possible optimize the use of digital solutions and eHealth, so that as part of a composite with registries and RCTs , reduce resource burden and address each stakeholder's questions. As a consequence of the mixed nature of these data sources there might be different standards and regulatory requirements for their collection and use, which requires further reflection.
- Multi-stakeholder access to, and creation of, disease-specific registries offer a vital resource for prospective assessment of; unmet needs, patient population(s), RWD collection, and early cross stakeholder collaboration.
- Stakeholders should be assured that a satisfactory infrastructure to enable the sustainable collection and analysis of post-marketing evidence is available, and a mechanism for cost-sharing is agreed.
- Concerns over intellectual property and regulatory data exclusivity periods could hinder decision making. As part of its work in IMI ADAPTSMART is exploring possible scenarios and options to minimize any disincentives.
- Patient perspective should be considered in reassessments.

Exchange of views on 'Exit' (or 'disinvestment') strategies

The terminology 'exit' strategy was considered confusing and alternative term (s) could be more useful for all stakeholders moving forward. There was also as yet no common understanding of the intent and implications of 'exits' from the MAPPs pathway, which could arise for a number of reasons for example; i) MAPPs pathways ceases to add value, ii) post MA commitments are not satisfied or, iii) product development is terminated.

There would be a need for a transparent commitment and agreement by all stakeholders up front as to what constitutes a 'yes' or 'no' decision to continue along the MAPPs pathway, and that a mechanism is available for this to occur. Exploration of these concepts very early on would reduce

potential conflicts later on.

Patients need to give input throughout so that all possible outcomes and alternatives within the MAPPs pathway are understood from the patient perspective.

As part of its work in IMI, ADAPTSMART is exploring the terms of 'exit' and 'disinvestment' and their implications in various scenarios, across all stakeholders and a number of work streams.