



## **Workshop report: Joint workshop on tools and systems used for prescription control & the ethical and legal aspects of adaptive decision making**

(London, 17 January 2017)

*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](http://www.adaptsmart.eu). This paper only reflects the views of the authors.*

*This project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking under grant agreement No 115890. This Joint Undertaking receives support from the European Union's Horizon 2020 research and innovation programme and EFPIA.*



## 1. Introduction

On the 17<sup>th</sup> of January 2017, as part of its Annual Meeting, the ADAPT SMART consortium hosted a multi-stakeholder workshop on *'Tools and systems used for prescription control and the ethical and legal aspects of adaptive decision making'*. The topic of this workshop related to two different deliverables: D2.07 (focused on prescription control) and D3.09 (focused on ethical and legal aspects of adaptive decision making).

The objectives of the workshop were:

1. To share an understanding of the in-depth analysis of the identified tools/systems to guide appropriate use, experience to date, and their feasibility and impact.
2. To share an understanding of the ethical and legal aspects of prescription control under MAPPs between all major stakeholders, with a special focus on patients and health care professionals.
3. To jointly explore potential recommendations to address the legal concerns, ethical concerns, how the current tools/systems can be sympathetic to and supportive of the MAPPs pathway, and any impact those solutions may have.

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](#). For more information about the Innovative Medicines Initiative (IMI) ADAPT-SMART project please click the link [here](#).

## 2. Workshop summary

The workshop was opened by André Broekmans (Lygature) who highlighted the objectives for the day and the agenda. This was followed by a presentation by Francesca Cerreta (EMA) on the concept of adaptive pathways and current development. This was followed by presentations from Jan van Emous and Stuart Faulkner introduced the work so far on ADAPT SMART deliverable D2.07 and D3.09 respectively.

Within deliverable D2.07 the focus is on a review of current tools and systems to guide the appropriate use by the targeted patient groups, both at the European and national level; tools such as the Summary of Product Characteristics (SmPC), the patient leaflet, delivery status, prescription guidelines, other drivers of utilization will be included in the work. This review will result in proposals for further study and in recommendations to the national health systems, EMA, European Commission, health care providers and patients.

During the day, Dr Rosa Giuliani, of the S.Camillo-Forlanini hospital in Rome presented her views on "the reality of early access today: current prescription tools in use and whom they affect". In her presentation, she highlighted the importance of the distinction between early approval, early market access and early access for patients. With regard to access for patients, significant differences exist in Europe - this was illustrated with a case study on medicines for metastatic melanoma. The differences between Western and Southern and Eastern Europe were

especially striking. Next, Dr Giuliani discussed different frameworks for assessing the values of new medicines, in particular those used by ESMO. Finally, real-world examples were presented from the Italian registry system for oncology medicines, and a number of recommendations were based on this. These recommendations include the need to focus on the quality of data, the need to coordinate across registries and avoid overlap/duplication of efforts. A key success factor for any registry is the buy-in and involvement of health care professionals.

Following this, Kevin Klein (Lygature) presented the results of a survey that was conducted among EFPIA companies in the period leading up to the workshop. With this survey, an overview was made of the tools/systems available to control prescribing in 12 different EU member states. Additionally, in the survey, respondents were asked to indicate their perceived or measured impact of a tool on guiding appropriate use, and the complexity of implementing the tool/system. All workshop participants received the results of the survey, as well as several key conclusions drawn from it. The survey showed that the tools/systems included in the survey were widely available throughout the twelve EU member states. Five tools/systems are available in all twelve Member States: treatment guidelines, DHPCs, restrictions by prescriber's specialty and registries followed by diagnostic tests, assessments of prior history and patient support programs. With regard to the evidence of the impact of the various tools, the survey concluded that there was limited scientific evidence available. Relating to implementation, restricting physician specialty, assessment of demographic characteristics and assessment of prior history were perceived to be most easily implemented. Patient Support Programs and registries were seen as more complicated to implement. The general conclusions of the survey were: large concurrence of tools/systems that are used to guide appropriate use in the EU exists; respondents indicated that restrictions at the level of assessing/diagnosing patients and prescribing have the highest impact, limited impact is expected from DHPC type communications; evidence on the impact of tools/systems is currently lacking, investments are needed. The authors of the report recommend national health systems and the European Commission to explore a number of these tools/systems in more detail, e.g. through disseminating a number of scenario for specific products.

The day continued with two break-out session. The first break-out session, in the morning, focused on the D2.07 report that was presented by Kevin Klein, in particular: the overall assessment of the report, whether any critical components were missing, which tools/systems were most relevant, how easy it was to implement them and what were any recommendations for future research and policy based on this.

To summarize, key outcomes from the discussions were:

- Overall, there was appreciation for the survey, within this context a number of recommendations were made, which can be found below.
- At the level of the member states, participants indicated that they would have like to have had more information about the enforcement mechanisms used in member states.
- Although the list of countries sampled was a diverse mix of EU member states, the authors could consider expanding the study beyond the 12 countries, but recognized that that would entail additional efforts.
- The idea of conducting studies with different scenarios was supported, this could provide additional insights in how member states would respond to different types of new medicines in a MAPPs context.

- The workshop participants highlighted the need to discuss in more detail the implications of the selection of EFPIA companies as respondents. To what extent may this have introduced bias? In addition, the authors could consider soliciting other perspectives (e.g. patients, payers etc.).
- The use of registries seemed especially promising to the workshop participants. It would be useful highlight the needs and pros and cons of registries (especially cross-border varieties). Exploring the use of registries further is an important recommendation for further research.
- The optimal tool may differ from product to product. It could be interesting to highlight what tools may best be used for which product (this is slightly out of the scope of the survey). This could also be the focus for future research.
- At this moment, a clear definition of what is appropriate use is lacking, this should be further defined. This could help to determine who is actually eligible for the use of a new medicine launched under a MAPPs pathway.

The second break-out session, in the afternoon, focused on which ethical and legal challenges that arise under MAPPs relating to prescribing and use in targeted populations (D3.09). Participants were asked to share their views on: what ethical and legal challenges arise under MAPPs, how, and to which stakeholder they might impact, and what mechanisms to mitigate these issues could be used.

- Managing patient expectations, understanding of benefit: risk and what happens if that changes were deemed to be important ethical issues for early and continual dialogue. MAPPs was seen to be positively influencing innovation to occur and healthcare systems to adapt. Also it could enable understanding a +ve benefit: risk in well-defined population, rather than less well understood benefit: risk in broad indication.
- Withdrawing treatment posed a critical ethical challenge in circumstances that patients fell outside an expanded indication, reimbursement is withdrawn (hence access too). There needed to be extra consideration for those populations that may have an alternative treatment options (however marginal) vs those that have no alternative treatment options.
- Differences in equity of access between EU MS and between those in public vs private healthcare systems is challenging. It is a fine judgement made by a HCP between, similar patients, as to who gets prescribed what treatment option. It was argued that patients with private healthcare may be able to bypass (some) prescription controls (i.e. off-label use) as this is very difficult to mandate in private healthcare practices.
- Whatever tools or mechanisms to control or guide more closely prescribing on-label and in the indications within the MA, they mustn't impact on the HCP duty of care for patients to provide the best possible treatment options.
- It was generally agreed that there were no new legal concerns around liability and the use of prescribing in targeted populations as this scenario occurs today. However many nuances remain. Legal challenges may occur from patients aiming to force a company to provide the medicine (either via initial access or continued access if withdrawal is recommended). The legal rights of patient 'responders', if the company withdraws the medicine, would need clarifying early on.
- There was concern of the political and legal implications that MAPPs may be widening the gap between those MS who are willing to engage or afford to vs those who can't or won't (i.e. IT infrastructure to support RWD). Legal challenges could occur between MS relating to responsibilities for RWD collection, PV follow-up of patients, and general costs for

implementation.

- There remained a strong voice as to the continuing legal responsibility of the HCP to 'do no harm' – who is really taking a risk? The common and differential considerations of the HCP and patient with respects to legality of risk and risk taking, needs to be accounted for.
- Some recommendations to mitigate against the ethical and legal issues should take account for any continued work under D2.07 and could also include the following:
  - Improved mechanism(s) of robust patient voice in the MAPPs process.
  - Education programmes to ensure regulators and decision makers (i.e. HCP, patients, policy) are well educated in order to make difficult decisions. Competent bodies could take a leading role here in continuing education and dissemination.
  - Explore mechanisms for informed and shared decision making (benefit: risk, uncertainty, expectations) - examples from UK's Managed Access Agreements could be incorporated as they address many of the difficult ethical and legal issues.
  - In combination with D2.07 exploration of case studies of MAPPs-like products were needed to understand which prescription tools were used, by who, how impactful they were, and what ethical and legal issues came out. This could offer the greatest learnings with respect to MAPPs and adaptive pathways.

The day closed with a plenary discussion of the key outcomes of the break-out sessions. The results from the day will be incorporated in the final deliverables for these activities in ADAPT SMART and will be published on the ADAPT SMART website.