EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Report from the Adaptive Pathways workshop 8 December 2016

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The workshop

Organised upon request and in cooperation with the European Commission

Over 170 delegates in person, 155 logged in remotely

66% of participants non-industry

4 STAMP members participated

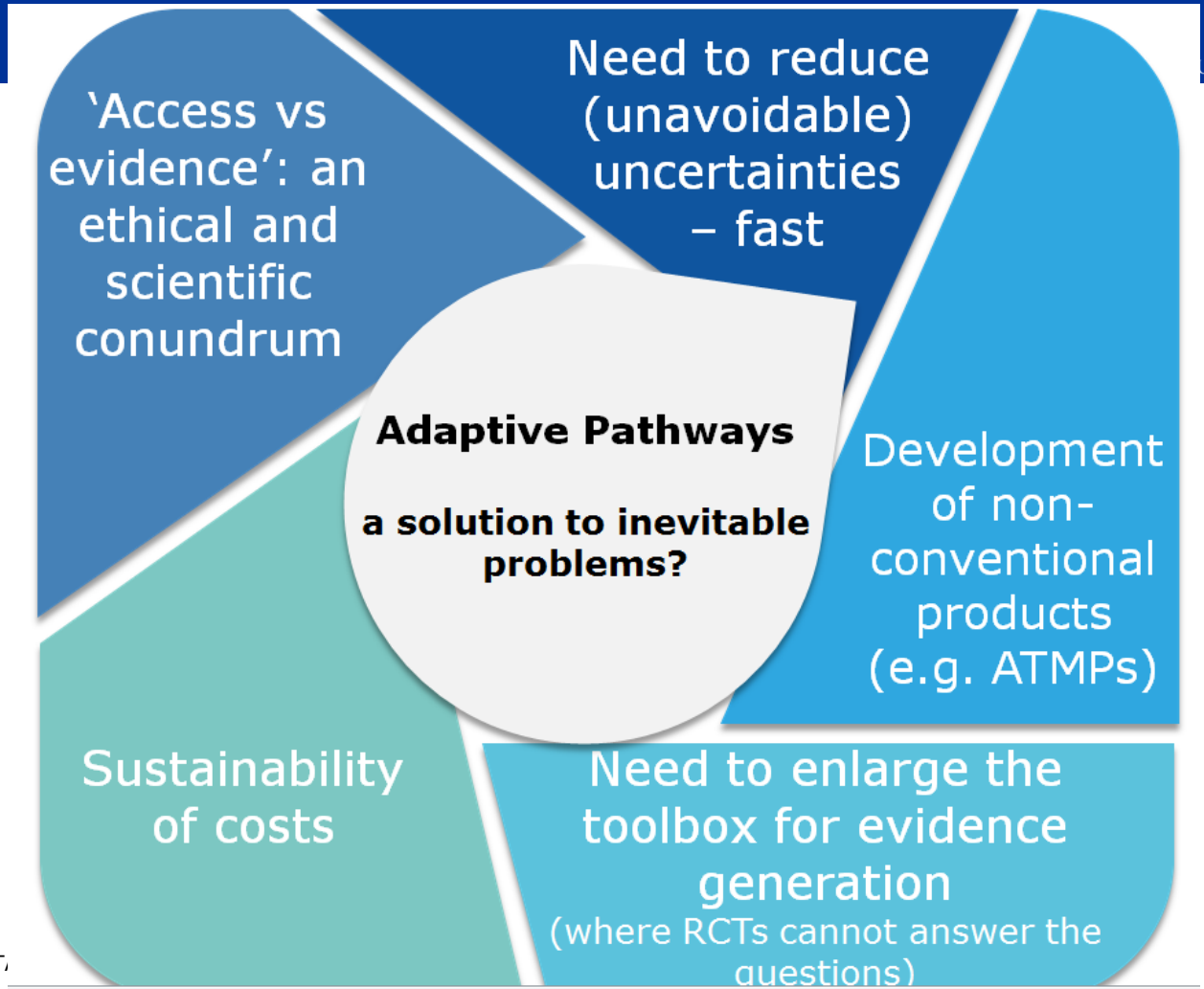
Report, briefing book and video available on EMA website (link)

To explore :

- Concerns raised by stakeholders
- Ways to implement the Adaptive pathways concept

Concerns raised by stakeholders

- ☐ How will **real world data** be used and defined?
- ☐ Will **standards** be relaxed?
- ☐ How will companies be made to **comply with data requirements** once their products are on the market?
- ☐ Will **restricted** medicines be restricted in practice?
- ☐ How will **high unmet medical needs** be defined?


'Access vs evidence': an ethical and scientific conundrum
Need to reduce (unavoidable) uncertainties – fast
Development of non-conventional products (e.g. ATMPs)
Need to enlarge the toolbox for evidence generation
(where RCTs cannot answer the questions)
Sustainability of costs
Adaptive Pathways
a solution to inevitable problems?

Submitted proposals *vs.* EU legal framework

(NB: no MAA expected before 2019)

Conditional MA: the most likely outcome of an AP. Good regulatory control tools available

Full MA: potentially possible if results *very* convincing at end of studies. Harder to enforce further studies

Accelerated Assessment: No proposals received (depends on final data package - PRIME).

Exceptional circumstances: No, as AP is based on further data acquisition. Proposals rejected from pilot.

Variations to MA: Expected in most cases following data collection. n No conditional variation possible on full MA.

ATMPs: Limiting step is often CMC. AP could be useful in balancing science and need

PhV/conditions: Registries already used in 30+ products outside AP. Foreseen in many proposals. Added benefit of early discussion on design

Real world data

Randomised controlled trials, if possible, would be the preferred way; but if it is not feasible, can we get data in another way?

The question is not how real world data can replace clinical trial data but how they can best support them

Cancer drugs examples raised at workshop show pros and cons: surrogate endpoints may fail to reflect clinical benefit, but also the population studied often does not reflect the real life population.

Methodology to generate data: how can it be improved.

Terminology: observational , everyday clinical practice

Drug development should be underpinned by the RCT principles

R	C	T
the most important design techniques for **avoiding bias** in clinical trials are blinding and randomisation	to allow discrimination of patient outcomes caused by the test treatment from outcomes caused by other factors	to ensure that groups are treated similarly in the course of the study to estimate effects **attributable to treatment**

Multi-stakeholder interactions

- Safe harbour talks were found useful by those who participated
- The devil is in the detail: advice request should follow, clarity on data expectations is important
- Patients should be routinely involved
- Clear selection criteria, unmet needs based
- Commitments should be met (refer to CMA report)
- EC and Council advocate increased cooperation
- Some framework changes may be required (e.g. pay per performance, flexible reimbursement)
- Resource and expertise challenge