EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Adaptive Pathways: concept and critical issues

EMA, London, December 2016

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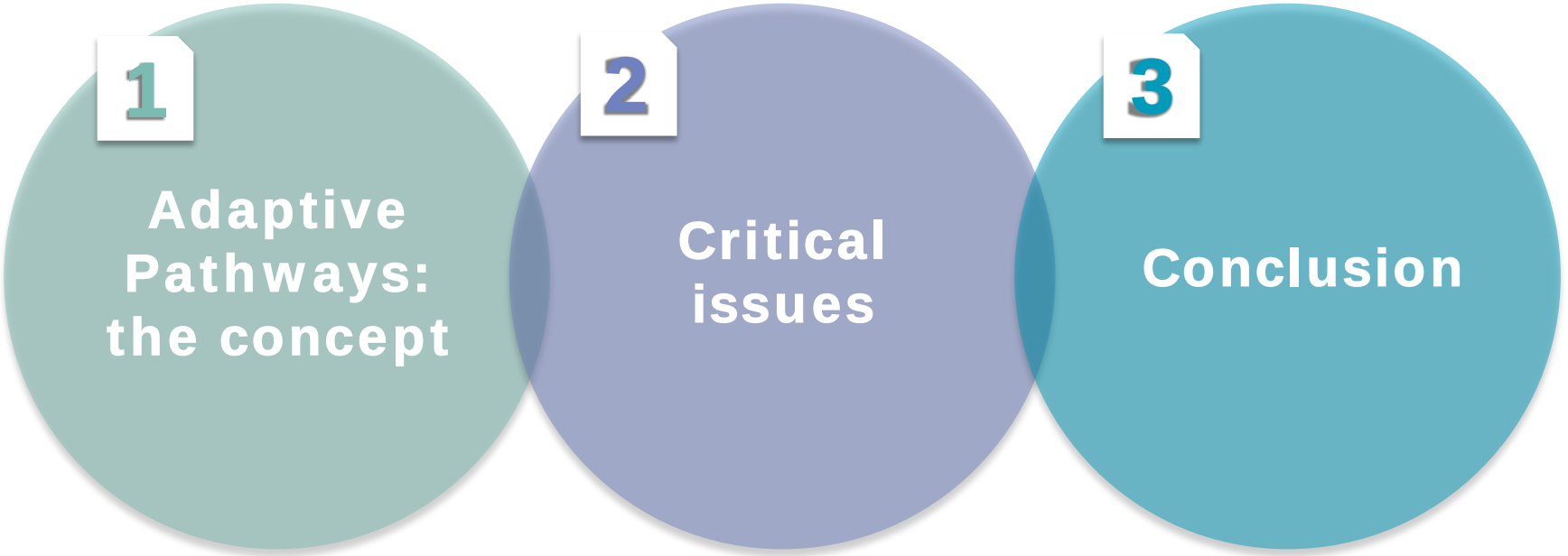
Agenda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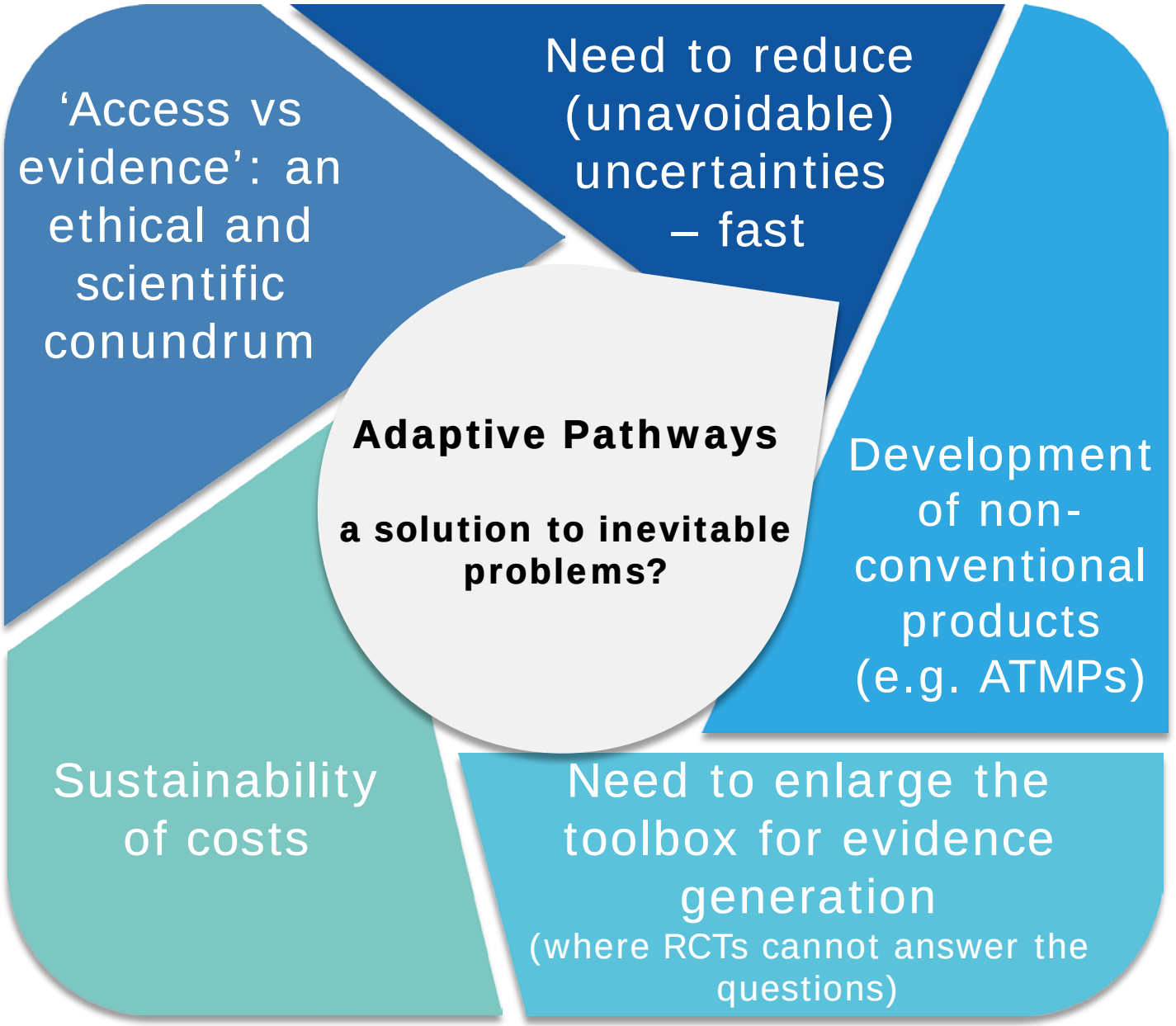
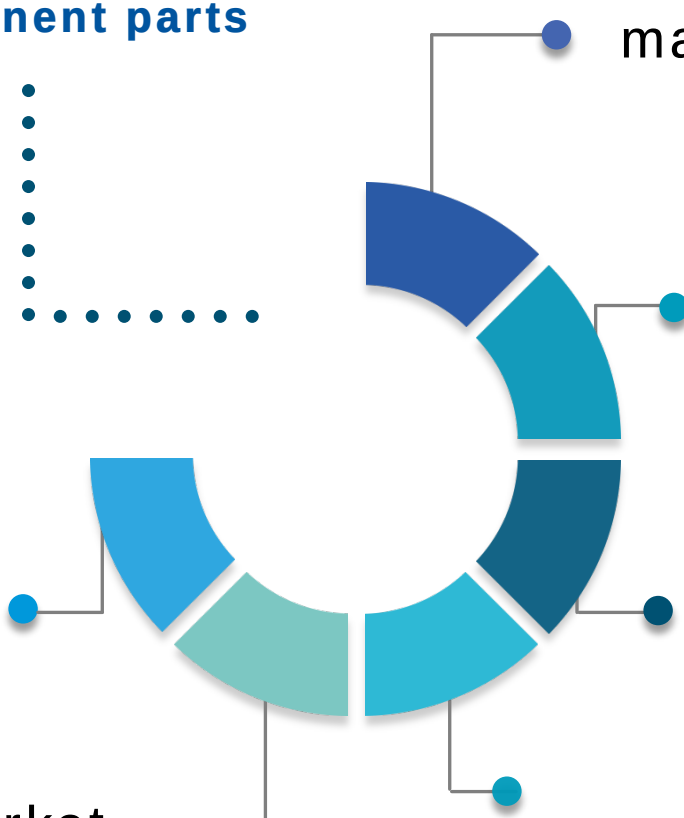

‘Access vs evidence’: an ethical and scientific conundrum
Need to reduce (unavoidable) uncertainties – fast
Development of non-conventional products (e.g. ATMPs)
Need to enlarge the toolbox for evidence generation
(where RCTs cannot answer the questions)
Sustainability of costs
Adaptive Pathways
a solution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

Adaptive Pathways

- component parts



Focus on high unmet need (sub-)population first, and on products likely to have major impact for patients

Reduce uncertainty as fast as possible; react to incoming data (iterative development; rapid cycle analysis)

Pre-plan, across entire life span (incl. post-marketing)

Use entire tool box for knowledge generation

Manage on-market utilisation

Leverage multi-stakeholder collaboration

Adaptive Pathways – harnessing existing tools

Conditional marketing authorisation (in EU legislation)

Post-marketing commitments; Risk Management Plans (in PharmacoVigilance Regulation)

Multi-stakeholder scientific advice

Registries, other data sources

Adaptive pricing/reimbursement (managed entry agreements)

Agenda

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Critical issues

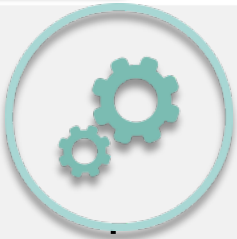
- Need and unmet need?
- Lowering the standards
- RCT and RWD
- Promises, compliance, exits
- On-market utilisation

Need and unmet need

Early access
– is it worth it?

Addressing 'unmet need'; focus on:

Conditions with major impact on quality of life / life-shortening / debilitating



Credible promise of relevant improvements in patient-relevant outcome(s) → an acceptably high probability of a relevant effect size

Lowering the standards?

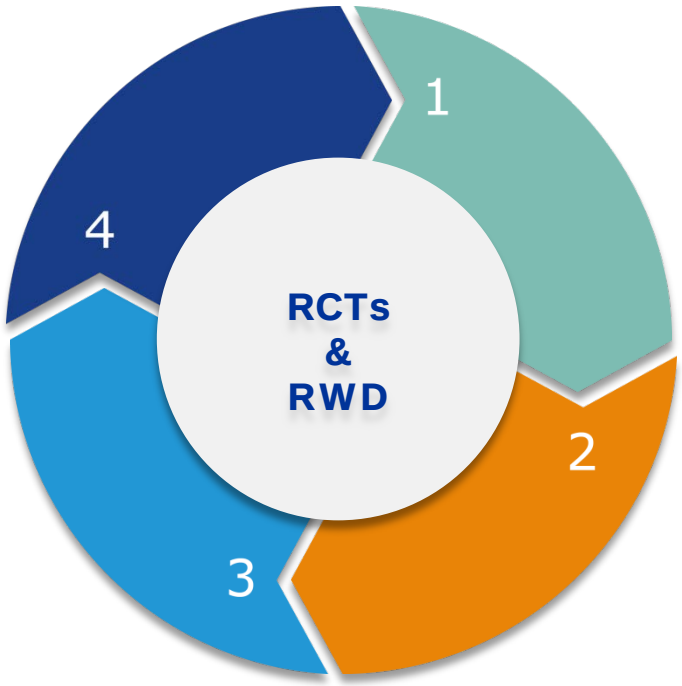
Benefit-Risk must be positive for treatment-eligible population

Access versus evidence conundrum has always been acknowledged:

… where, “the **benefit** to public health **of the immediate availability** on the market […] **outweighs the risk** inherent in the fact **that additional data are still required**”

[Regulation (EC) No 507/2006]

Randomised Controlled Trials (RCTs) and Real World Data (RWD)



1. RCTs are the methodology with the highest internal validity (≠ 'gold standard', not black & white)

2. For efficient increase of knowledge of benefits and risks: embrace the full evidence spectrum (RCTs, pragmatic trials, observational studies)

3. RWD complements rather than replaces RCTs. The right study type for the right question – where feasible

4. Pre and post-licensing evidence generation are not two different lives, it's one continuous life

Promises, compliance, exits

Promised data may not be forthcoming, “post marketing commitments might not be honoured”

Compliance with legally binding post marketing studies generally good (but start of studies slow). Regulatory system is robust*; supported by recent experience (post 2012)

* http://ec.europa.eu/health/files/pharmacovigilance/pharmacovigilance-report-2012-2014_en.pdf

Promises, compliance, exits

Subsequent data may not confirm initial promise of high effect size

For regulators, not a new scenario

For payers, plan ‘exit’ (or ‘adaptive disengagement’) scenarios upfront

Payers can get incentives right: limited initial label with prospect of widening, flexible conditions of reimbursement

On-market utilisation

Regulators can provide some (!) steer on appropriate prescribing (Risk Management Plans)

Payer action will be helpful but heterogeneity across EU member states is acknowledged

Right incentives (for companies) will help

Access to local healthcare data / drug utilisation review will facilitate appropriate utilisation – where feasible

Conclusion

Adaptive Pathways is an attempt to solve inevitable problems and conundrums in an imperfect world

We believe that these can be successfully addressed by way of adequate pre-planning, and collaboration of stakeholders

EUROPEAN MEDICINES AGENCY

Thank you

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#AdaptivePathways