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Medicines Adaptive Pathways to Patients (MAPPs):

Guiding Principles for IMI2 Projects

European Federation of Pharmaceutical Industries and Associations

www.efpia.eu

Guiding Principles for IMI2 Projects

- The objective of this presentation is to provide an overview for SGGs as to what should be considered for inclusion into IMI2 projects from the perspective of MAPPs

Presentation Topics

- What is MAPPs?
- Possible IMI2 Enablers/Tools for MAPPs
- Next steps
- Case studies of effective IMI projects to develop MAPPs

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What is MAPPs - Medicines Adaptive Pathways To Patients?

MAPPs refer to flexible development and access pathways within the current regulatory framework that balance early patient access, public health and societal benefits.

How is MAPPs different from Current Pathways?

- An early authorisation of a product in a well-defined and targeted patient population with a clear safety and efficacy profile
- The target population is adjusted as additional evidence becomes available
- MAPPs may integrate adaptive clinical trial design, patient centric benefit/risk assessments and continuous re-evaluation as new evidence becomes available
- MAPPs relate to the entire life cycle of a medicine from development, through licensing to patient access

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MAPPs – What are the Potential Benefits?

- MAPPs respond to advances in technology
- MAPPs provide new medicines to patients sooner and potentially at a lower cost to all stakeholders
- MAPPS provide better effectiveness data sooner to regulators and payers

MAPPs – What are the remaining challenges?

- The agreement by stakeholders (patients, regulators, HTA/payers, practitioners, industry) on the evidence package required for early regulatory approval, reimbursement, and access for patients
- The willingness of patients, payers and industry to operate with increased uncertainty
- The IT infrastructure needed to provide the real world evidence base

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MAPPs: Effective for all industry players, regardless of size

"An increasingly adaptive development and licensing environment. . .improves outcomes for all key stakeholders, a rare piece of good news in health care policy..."*

***Comparison of Stakeholder Metrics for Traditional and Adaptive Development and Licensing Approaches to Drug Development**

Lynn G. Baird, Mark R. Trusheim, Hans-Georg Eichler, Ernst R. Berndt, and Gigi Hirsch

May 9, 2013 http://dij.sagepub.com/content/early/2013/05/09/2168479013487355

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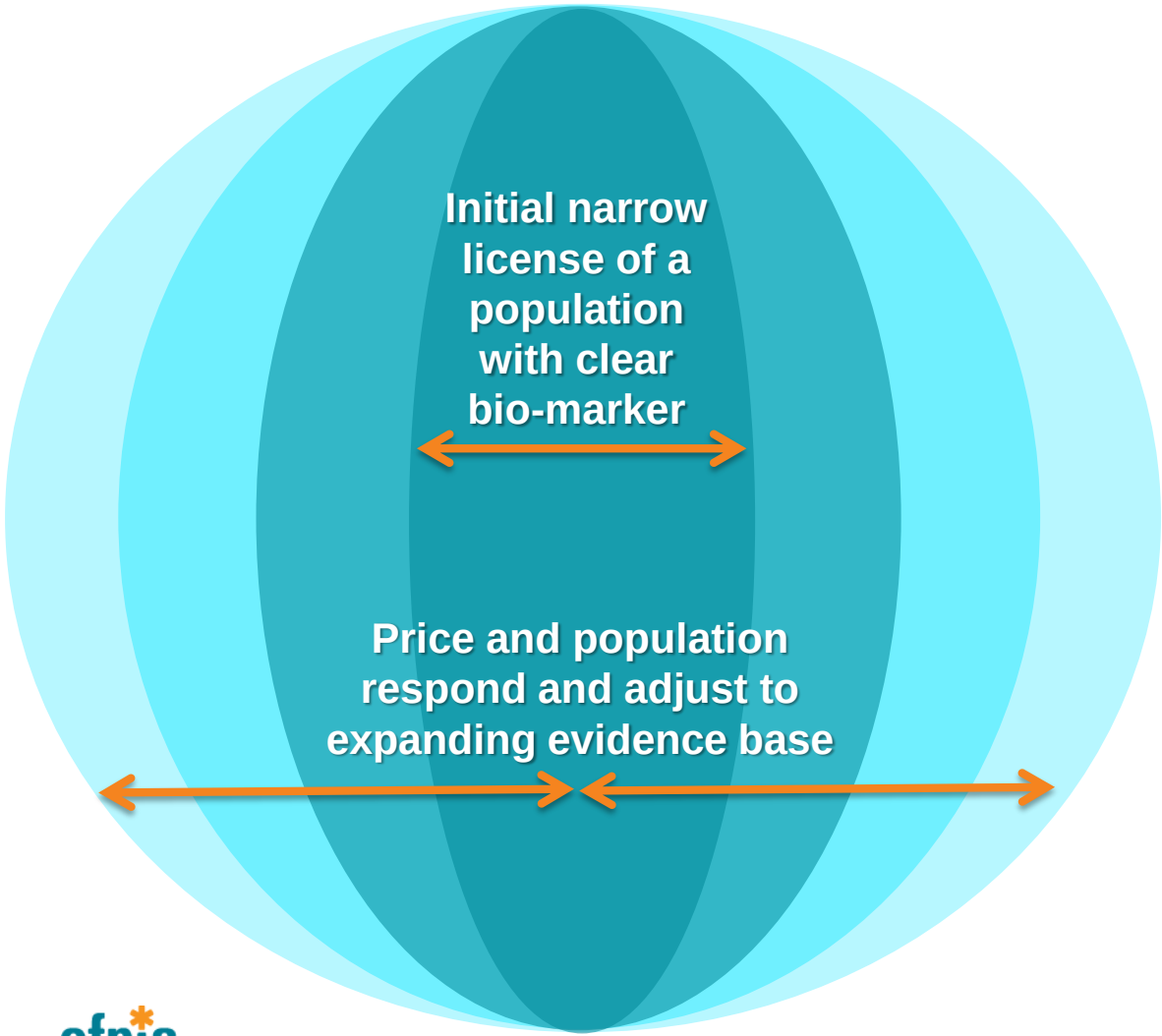
An Example of a Theoretical MAPPs Pathway



Managing uncertainty:

1. Robust capture of real-time data of the actual trial experience
2. All key stakeholders (patients, regulators, practitioners, industry) are aligned with the process starting at the design stage
3. Target population responds and adjusts to expanding evidence base
4. Price responds to evidence, can go up or down

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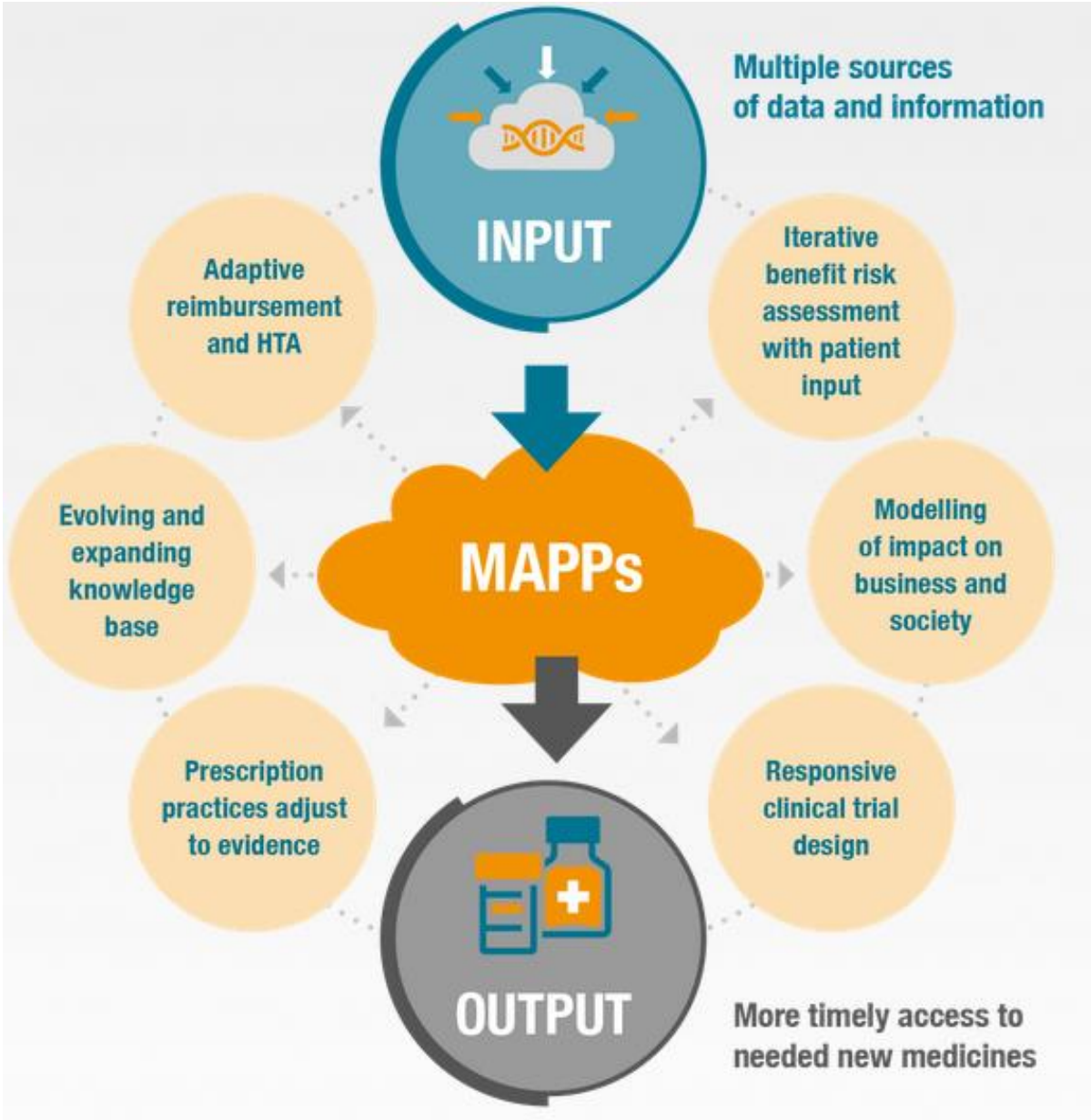
NRDD vol. 10, July 2011

The MAPPs Ecosystem



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IMI – An Opportunity for MAPPs

- MAPPs Deliverables:
  - How can efficacy and safety be determined at an earlier stage?
  - How can data capture and processing using e- and m-technologies be enhanced ?
  - How can MAPPs manage post-launch obligations?
  - Can MAPPs support off-label data collection?
  - Define business models that secure business and healthcare budget sustainability
- IMI can be used as a platform to develop and test new methodologies and tools to optimise the following:
  - Development, licensing, access pathways, adaptive clinical trial design
  - Patient centric benefit/risk assessments, continuous re-evaluation with expanding evidence base

SGGs and MAPPs – Project Scoping

- In order to integrate MAPPs into IMI projects, SGGs in therapeutic areas, data & knowledge management and translational safety should consider:
  - **For new IMI2 projects**: the MAPPs enablers described in this Presentation
  - **For ongoing IMI projects**: identify potential MAPPs enablers to include in regulatory science or policy activities at EFPIA

MAPPs Enablers for Adaptive Development

- Tools for stratifying patient population
- Pre-clinical evidence of impact on primary or secondary endpoints
- Innovative trial design (e.g. adaptive, Bayesian), modelling, and simulation
- Iterative benefit/risk methodologies aligned with HTAs, patients, regulators, payers, and industry
- Real World Evidence (RWE) quality/reliability
- Methodologies to evaluate multiple sources of targeted datasets
- Predictive preclinical tools for benefit/risk at iterative time-points
- Sustainable databases, health registries and monitoring systems for evidence

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MAPPs Enablers for Adaptive Pathways

- Safety and risk minimization programmes to balance uncertainty based on smaller data sets
- Feasibility of collecting data, follow-on RCTs, or confirmatory data to expand the initial license
- Processes and procedures for collecting, analysing and presenting evidence
- Tools for regulatory reassessment
  - Definition of reassessment criteria and the evidence base acceptable to regulators
    - periodic benefit risk evaluation report (PBRER)
    - Post-authorisation Safety Studies (PASS)
    - Post-authorisation Efficacy Studies (PAES)
  - Processes to remove medicines from the market post-authorisation

MAPPs Enablers Access (HTA, Pricing & Reimbursement)

- Methodologies for pricing and volume adjustments, both up and down, based on the evolution of the MAPPs' evidence
- Models to test the assumptions made in MAPPs pricing/reimbursement for accurate value proposition
- Modelling of HTA/pricing/reimbursement/regulatory frameworks to simulate and measure uncertainties at launch
- Tools for HTA reassessment
  - Develop or test infrastructure(s) for companies, payers, and regulators to meet post-launch obligations
  - Development and testing of tools/methodologies to evaluate the risk of broad off-label prescriptions

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NEXT STEPS: Continued dialogue

IMI2 MAPPs Coordination and Support Action (CSA)

The CSA will establish a platform with relevant stakeholders for the coordination of MAPPs related activities within IMI2:

- **gap analysis**: identify challenges and opportunities for implementation of MAPPs, taking account of tools, methodologies and infrastructures developed in IMI and other initiatives;
- **informing research activities**: facilitating inclusion of MAPPs enablers in new IMI2 activities based on the gap analysis;
- **knowledge management**: horizon scanning on non IMI activities relevant to MAPPs to create a comprehensive repository of knowledge and opportunities for coordination.

→ Operational in Q2 2015, in the meantime MAPPs TF as reference point.

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APPENDIX

CASE STUDIES

Case Study 1: DIRECT - Diabetes Research in Patient Stratification (*ref: draft IMIPACT report 22 Sept 2014*).

Aim: Identify biomarkers that will define subtypes of rapid diabetes development and those who will respond to therapy. Identify, develop and validate surrogate response biomarkers that reflect the underlying disease progression in clinical trials.

Relevance to MAPPs:

- Predictive biomarkers of rapid glycaemic decline and the response to drugs which will allow selection of patients
- The innovative clinical trial designs that may also offer value in the MAPPs agenda if they are submitted for early joint EMA/HTA evaluation
- The cost implication of screening thousands of patients when only a few may be 'positive' with HTAs and payers
- The governance of biomarker sampling to be in line with ISO standards will need to be addressed before introduction to clinical practice;
- The ability to limit / restrict prescribing to a clearly defined cohort through wide-scale physician and patient education.

Case Study 2: Get Real (*ref: IMIPACT report 22 Sept 2014*)

Aim: incorporate estimates of relative effectiveness early in drug development and to enrich decision-making by regulatory authorities and HTA bodies simultaneously.

Relevance to MAPPs:

- The results should help to reduce the uncertainty about medicines at the moment of marketing authorisation and initial reimbursement
- The initial license would need to consider a data package with a different composition than is currently the case
- Pragmatic trials will need to give sufficient confidence to HTA bodies to make an assessment about the added value of treatment
- HTA assessment could also be informed by evidence from other sources, such as network meta-analysis and observational data
- GetReal aims to provide the evidence to support the need and feasibility for these changes.