Surrogate end-points for use in phase III clinical trials: their development and role in MAA approval:

EFPIA Position Paper Proposals

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Proposals in four specific areas

1. Collaborative working: Agencies, Industry and Academia -towards a global approach
2. Focus our efforts on surrogate validation
3. Guidelines on definitions and terminology
4. Regulatory framework to agree and progress surrogate evaluation plan

Collaborative Working

- Goal: biomarkers used for regulatory decision making
  - Readily interpretable and with clinical utility
- Industry, Regulatory Agencies and Academia
- Managing R&D costs
  - e.g. surrogates for long-term outcome measures
- Minimise divergent approaches (agencies or companies)
- Developing a Global Approach
  - Bipartite meetings progress to global workshops
  - Sharing output from consortia and initiatives
  - Coherent global plans for disease/class markers
    - Global Cross/ regional working groups with Agencies
  - ICH of value when concepts sufficiently well defined
  - Drug development is organised internationally

Focus our surrogate validation efforts

- EFPIA survey: biomarkers in development across a wide range of areas
- Surrogate endpoint may be critical to the development of progressive chronic disease treatment
- IMI proposes some key therapeutic areas for research
- Criteria for prioritising diseases and therapeutic areas would help to focus priorities for surrogates evaluation
  - Especially for collaborative projects

Guidelines on Definitions and Terminology

- Set of definitions and terminology required for surrogates evaluation
- Framework or development milestones for the validation process
- Building on existing work
- Joint Scientific Working Group should be formed

Different patterns for future surrogate end-point development projects

1. Single Company – proprietary funded research
2. Collaborative research
   - Company Consortia
   - Industry/Academic Collaborations
   - Public/private partnerships
   - Research in general disease areas not tied to specific products

Regulatory needs to be addressed

- Achieve scientific consensus across industry, regulators, academia & medical practice
- Early and on-going scientific dialogue & buy-in to validation plans from Agencies
- Data could be across products & not be related to a particular MA or holder
- Consensus & final agreement on validation status of a particular marker

Proposals/topics for Regulatory Framework

- Forum for early conceptual discussions
  - Across range of stakeholders
  - PGX “briefing meeting” model
- Agreed Surrogate Evaluation Plan
  - Scientific Advice – with role of SAG
  - Consider convening expert group
  - Inclusive of range of stakeholders for collaborative projects
  - Mechanism for follow up & modification of the plan
- Adapt processes for MAA review for collaborations e.g.
  - Master files of validation data – pre-approved for reference
  - Joint consortia responses to questions
- Conditional Authorisation route as an option

Next Steps: Establish a joint Agencies, Industry, Academia Working group to

- Initiate work on nomenclature, validation milestones and regulatory framework
- Establish links & collaboration with other surrogate marker initiatives in other regions
- Facilitate regulatory aspects of collaborative research projects
- Realise the potential to improve the clinical development process

Facilitating improved access to safe and efficacious therapies to address patients' needs