Methodology in the regulatory landscape

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The views expressed are personal views and not necessarily the views of EMA

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Methodology in the regulatory landscape

- Introduce the new EMA Methodology Working Party.
- Support Innovation in drug development.
- Interaction with stakeholders.
- For discussion

But first……from regulatory statistics perspective

ICH Topic E 9
Statistical Principles for Clinical Trials

Step 5

NOTE FOR GUIDANCE ON
STATISTICAL PRINCIPLES FOR CLINICAL TRIALS
(CPMP/ICH/363/96)

But first……

Qualified Statisticians in the European Pharma Industry: Present and Future Directions

Zoe Williams*, Kit Roes, Nigel Howitt

(DIJ 2009)

OPEN LETTER

European regulatory agencies should employ full time statisticians

(BMJ, 2008)

But first……

Current Statistical Considerations and Regulatory Perspectives on the Planning of Confirmatory Basket, Umbrella, and Platform Trials

Olivier Collignon[1,*], Christian Gartner[2], Anna-Bettina Haidich[3], Robert James Hemmings[4], Benjamin Hofner[5], Frank Pétavy[6], Martin Posch[7], Khadija Rantell[8], Kit Roes[9] and Anja Schiel[10,*]

between the substudies. While trials governed by a master protocol can offer logistic and financial advantages, more experience is needed to gain a deeper insight into this novel framework.

(CP&T 2020)

But first……

High quality regulatory decisions in the interest of patients.

- *Key principles do stand the test of time…….*
- The world has changed: it is not necessarily possible, preferable or acceptable to patients anymore, to run the “same” RCTs we had in mind at ICH E9.
- Supporting innovation in drug development is an obligation.
- Complexity and diversity at odds with the level of experience desired for guidance.
- *Importance of regulatory (statistical) thinking & strong community of experts.*

Introducing the EMA Methodology Working Party

Within a dynamic context…

HMA-EMA Joint Big Data Taskforce Phase II report:

'Evolving Data-Driven Regulation'

Joint Action Towards the European Health Data Space – TEHDAS

The TEHDAS Joint Action project develops European principles for the secondary use of health data.

Raw Data Pilot

DARWIN EU

COVID-19

COVID-19: latest updates Share

The latest updates on the COVID-19 pandemic from the European Medicines Agency (EMA) are available below.

ACT-EU

Accelerating Clinical Trials in the EU

Introducing the EMA Methodology Working Party

- New entity, pulling together expertise from previous working parties and extending to expertise that was previously not organised or even available as such.

- In total 23 members across the different disciplines.

- *Previous working parties:*

  BSWP, M&S WP, PK WP, PGx WP.

- *Additional scientific disciplines:*

  Real World Evidence, Pharmaco-epidemiology, Artificial Intelligence, Data science,…..

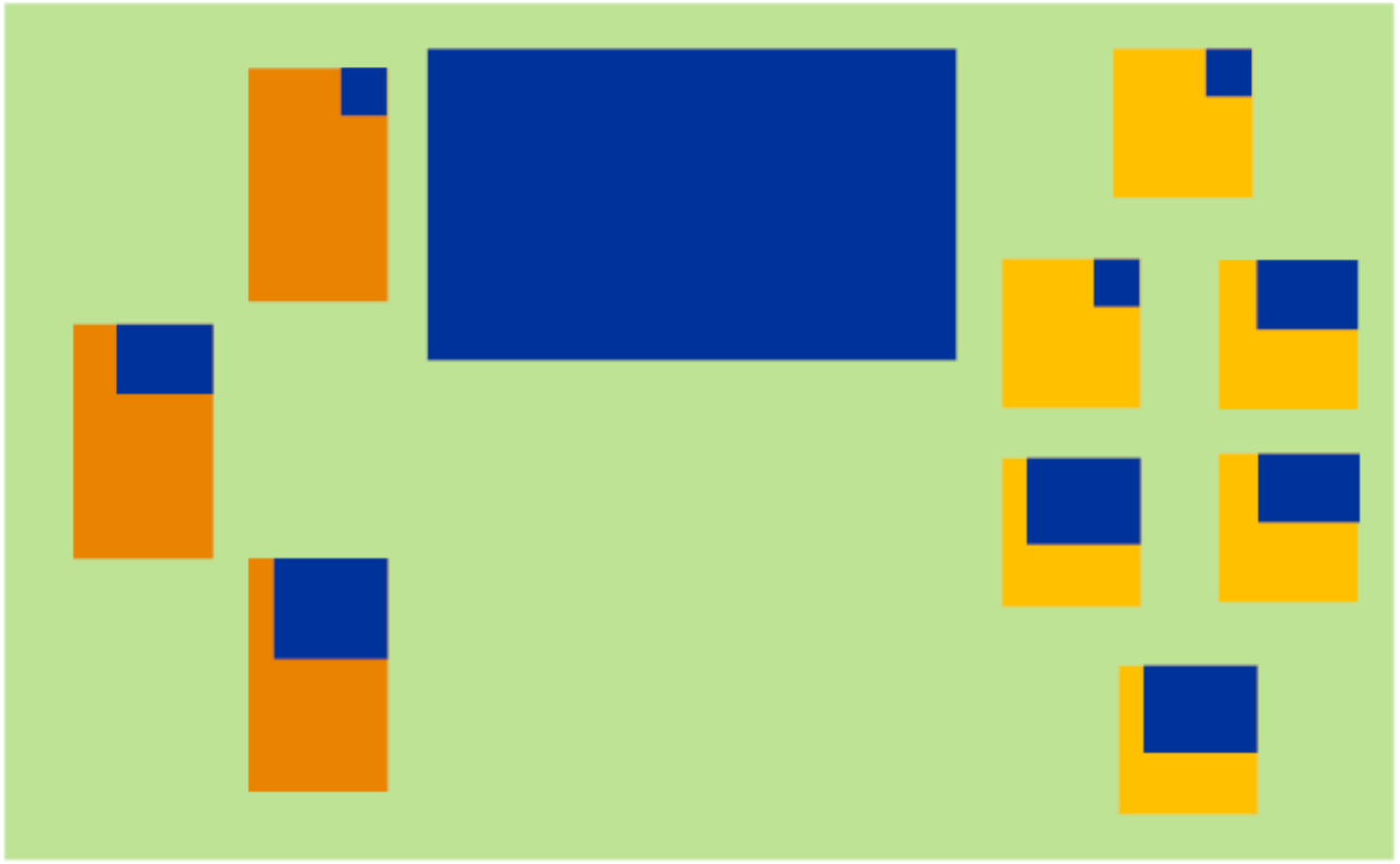
Methodology Working Party

- Leverage the cross-disciplinary expertise to:
  - Support methodological innovation in global drug development.
  - Support advice and interpretation of complex methodology across (clinical) drug development.

- Ensure agile processes supporting procedures & committees
  - Whether mono- or cross-disciplinary.
  - Making best use of the broad expertise across the system.

- Shape an effective *European Scientific Expert Community*
  - Disciplines are part of matching scientific ecosystems already (including global regulatory clusters).
  - Leverage academic interest for /involvement in regulatory process.

Basic groups & communities



European Scientific Expert Community

Methodology Working Party

Operational Expert Group

Temporary Drafting Group

Basic groups and communities

Working Parties

- Provide Rapid Product Support
- Provide Scientific Leadership

Temporary Drafting Groups

- Deliver Guidance Documents

Operational Expert Groups

- Deliver high volume predictable product support for Committees / SAWP

European Scientific Expert Communities (esp. for MWP)

- Strategic community to build the expertise and shape development.

Assignments for the new Working Parties

S

Strategic: Regulatory science & network

R

Reactive: ad-hoc requests from Committees

T

Tactical: Guidelines, reflection papers, primarily – ICH/non-ICH

E

Educational: training of assessors / network

O

Operational: procedure-specific support to Committees

S

Stakeholders: interaction with European and international stakeholders

A first view on priorities (work in progress)

- Build the ESEC(s), including Real World Evidence and AI and establish stakeholder interactions.

- Big Data SG priorities (including learning from raw data pilots).

- Reflection papers / guidance development (a selection):
  - Single Arm Trials, Real World Evidence (evidentiary standards,..,..).
  - Concept papers: AI, Master Protocols, Model informed bio-equivalence, Bayesian statistics.
  - Several PK and PFGx related guidances
  - Revision of Multiplicity & Non-inferiority (estimands & biologicals).
  - …….
- Develop training (guideline focused, as well as a.o. Big Data curriculum).

Interaction with stakeholders

Key principles for working party restructuring include:

- Towards greater transparancy of activities.
- Increase productive stakeholder interactions.

We will be actively seeking new & existing modalities – EFSPI remains important forum.

A birds eye view across “methodology”: the role of modeling

In 1995, the statistician Sir David Cox commented as follows.

“... it does not seem helpful just to say that all models are wrong. The very word model implies simplification and idealization. The idea that complex physical, biological or sociological systems can be exactly described by a few formulae is patently absurd. The construction of idealized representations that capture important stable aspects of such systems is, however, a vital part of general scientific analysis and statistical models, especially substantive ones, do not seem essentially different from other kinds of model.”

For discussion

- The role of & challenges with more advanced modeling in regulatory (confirmatory?) decision making.

- Regulatory guidance preferably built on substantial experience & speed and diversity of innovation: do we need to re-think what guidance needs to be about?

- Building strong expert communities capable of *regulatory statistical* (methodological) *thinking* likely key: suggestions for models?