Developing Methods and Technologies to Ensure Safe and Effective Medicines

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Outline

• Who we are

• Drug safety
  • Current process / Why innovate?
  • Barriers / Progress to change

• Asks
Safer Medicines Trust

• An independent patient safety charity

• Our aim is to make medicines safer, by encouraging a change in the way they are tested, from a system based on animal tests to one based on human-relevant science

• See: www.SaferMedicines.org
Drug safety

..... the preclinical research process is patient free, relying on animal models of disease and toxicology as poor approximations of humans...

- Legacy processes and models are flawed with >90% of drugs failing
  - need to retool the R&D model
- Adverse drug reactions now 4th-6th leading cause of death in western world

Drug safety

• Many hundreds of licensed drugs cause undesired side effects in humans

• These cause many serious illnesses, including fatality (10,000 people in UK/year)…

• …and are not predicted by safety testing undertaken in animals, or in early clinical trials

• New drugs currently require prolonged testing in large numbers of people before they are licensed for use

Data from FDA labels:

WARNING: RISK OF HEMATOLOGICAL TOXICITY, MYOPATHY, LACTIC ACIDOSIS AND SEVERE HEPATOMEGALY WITH STEATOSIS
Zidovudine capsules have been associated with hematologic toxicity including neutropenia and severe anemia, particularly in patients with advanced HIV-1 disease [see WARNINGS AND PRECAUTIONS (5.1)].

WARNING: HYPERSENSITIVITY REACTIONS
Serious and sometimes fatal hypersensitivity reactions, with multiple organ involvement, have occurred with abacavir.
Human-relevant models

- Human-relevant experimental models use cells from human tissues, maintained under biologically relevant conditions

- Now used routinely to study many different human diseases, to explore disease susceptibility, and to design and test novel drug treatments

- **And** to predict and avoid human adverse effects of drugs that cannot be detected in animal studies

- Computational data analysis tools are used to enable accurate prediction of human in vivo responses from human-relevant models
Some human-relevant models

**COVID-19:**

**Inflammation in obesity:**

**Influenza and Staphylococcus aureus super-infection:**

**Hepatitis virus infection:**

**Cardiotoxicity of drugs:**

**Liver toxicity of drugs:**
Roadmaps to New Approach Methodologies (NAMs)

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Barriers to change

- Resistance to change
- Status quo bias
- Historical data
- Education

- Applicability domains
- Context of use
- QVIVE
- Regulation and implementation

- Multi billion £ animal supply industry
- Pharma liability protection
- Funding of NAMs vs animal methods

- Knowledge gaps (tox pathways, disease cause)
- Assay development
- Technology limitations

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Progress – Validation & Implementation

- Applicants encouraged to apply in parallel to the EMA and FDA
- Specify intended use, DD context, scientific rationale
- 6 weeks of public consultation. Publicly available 15 days after final opinion
- EMA/CHMP organise training and amend relevant guidelines
- ~190 day process
- MHRA process – Innovation Office
Accelerating the Growth of Human Relevant Life Sciences in the United Kingdom

A White Paper by the Alliance for Human Relevant Science

https://www.humanrelevantscience.org/white-papers/

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ASKs

Ability to challenge non fit-for-purpose regulations and propose new approach methodologies and solutions collaboratively

Clearly defined processes to enable adoption of innovative technologies into medicines regulation process

An agile system supporting innovation for safer medicines and regulatory processes reflecting this dynamic field

“Future proofing regulation”