EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

BOS1 Regulatory Discussant Theme 3

Efthymios Manolis, EMA

Outline

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Role of regulators in early development

Regulatory experience and status

- Translational M&S
- M&S to support early clinical development

Gaps and Room for improvement

Open Questions

Role of Regulators

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Mission statement: The mission of the EMA is to foster scientific excellence in the evaluation and supervision of medicines, for the benefit of public and animal health

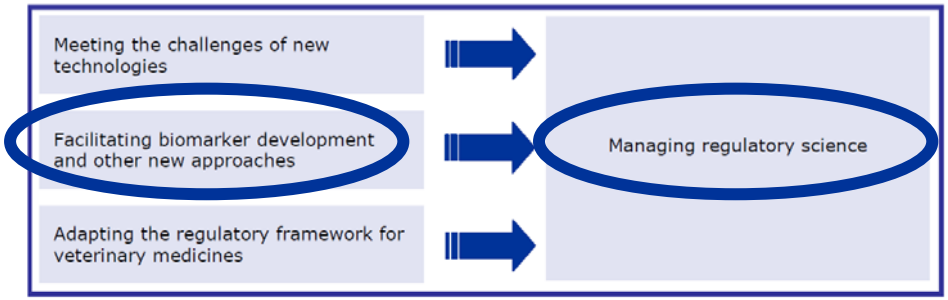
EMA Road Map 2015

Three priority areas:

1. Addressing public health needs

..Facilitating new approaches to

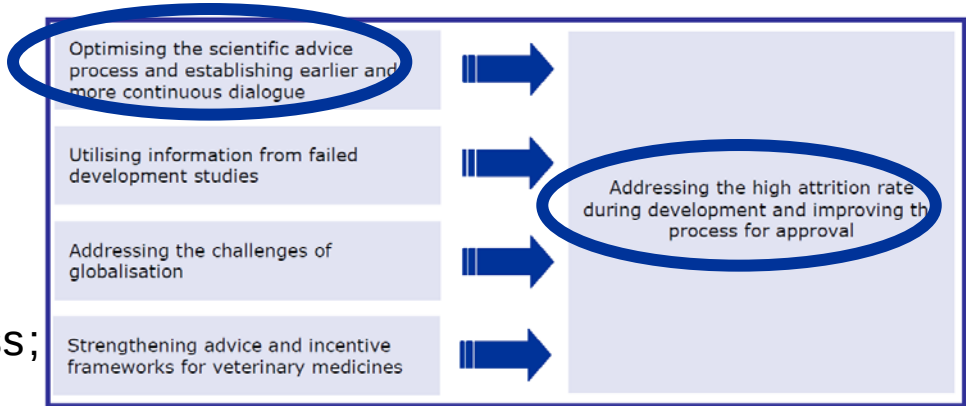
medicine development; …



2. Facilitating access to medicines

…Addressing the high attrition rate

during the medicine-development process;



3. Optimising the Safe Use of Medicines

http://www.ema.europa.eu/ema/index.jsp?curl=pages/about_us/general/general_content_000292.jsp&mid=WC0b01ac05800293a4&jsenabled=true

Role of Regulators

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Tools available to regulators to foster innovation in drug development and regulatory review

- Guidelines
- Scientific Advice and other regulatory procedures
- Qualification of Novel Methodologies (Advice and Opinion)
- Informal meetings with regulators (ITF, pipeline meetings)
- Participation in consortia (e.g. IMI)
- Workshops and meetings with external stakeholders

Translational M&S

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M&S to translate from in vitro-preclinical data to human. Experience in scientific advice

Translation of activity. Usually in vitro data and preclinical disease animal models are used with M&S methods to support range of doses to be tested in patients

Very limited experience with use of models to support **translation of safety findings** from preclinical to clinical. In this case conservative exposure margins are used to support safe doses to be tested in human

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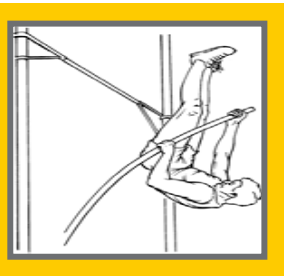
Regulatory scrutiny

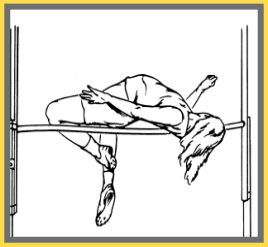
High impact

Scientific Advice **(+)** Documentation **(+++)**



Medium impact

Scientific Advice **(±)** Documentation **(++)**



Low impact

Scientific Advice **(?)** Documentation **(+)**

Translation of Safety

Translation of activity

Impact on regulatory decision

M&S in early clinical development

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M&S to support early clinical development. Experience in scientific advice

M&S is encouraged but not required by regulators

M&S is well perceived for optimisation of studies, data analysis, reporting and decision making

Proper exploratory development reduces uncertainties in benefit/risk assessment

“The extend of confirmatory phase III data needed will depend upon what is established for the product in earlier phases, and what is known about related products” Points to Consider on Application with 1. Meta-analyses; 2. One Pivotal study

Gaps and Room for improvement

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Move focus from single target to the whole system

•Systems Pharmacology very promising but not integrated in drug development and regulatory review

•Modelling and Simulation should be accompanied by advancements in biomarkers (BMs), in vitro techniques and preclinical animal models

•Lack of mechanistic understanding of safety (off target toxicity). Develop databases, safety BMs and Models

Regulators should be more involved in early development

•In communication with agencies, break the vicious circle of internal decision vs. regulatory review issues

Share data and models and aim at qualification advice and opinion

Open Questions

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Are the tools available to regulators to foster use of M&S in early drug development and regulatory review adequate?

How to establish uniform standards for M&S analysis and reporting, especially when data comes from various sources (in vitro, preclinical, literature, clinical) and different kind of models are used (e.g. PBPK-PD, POP-PK-PD, mechanistic models, disease models)?

Data/Model sharing in a competitive environment and the role of regulators