EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA Scientific Advice on FIH studies

The new FIH EMA guideline: disruptive or Constructive?
EUFEMED 1st discussion forum

Presented by Stefano Ponzano on 19 September 2018
Clinical Pharmacology and Non-clinical Support Office

Methodology & Results

- Searched for the following key words in the EMA SA database: FIH, First-in-human, Phase 1, Phase I
- Time range: 2017-2018

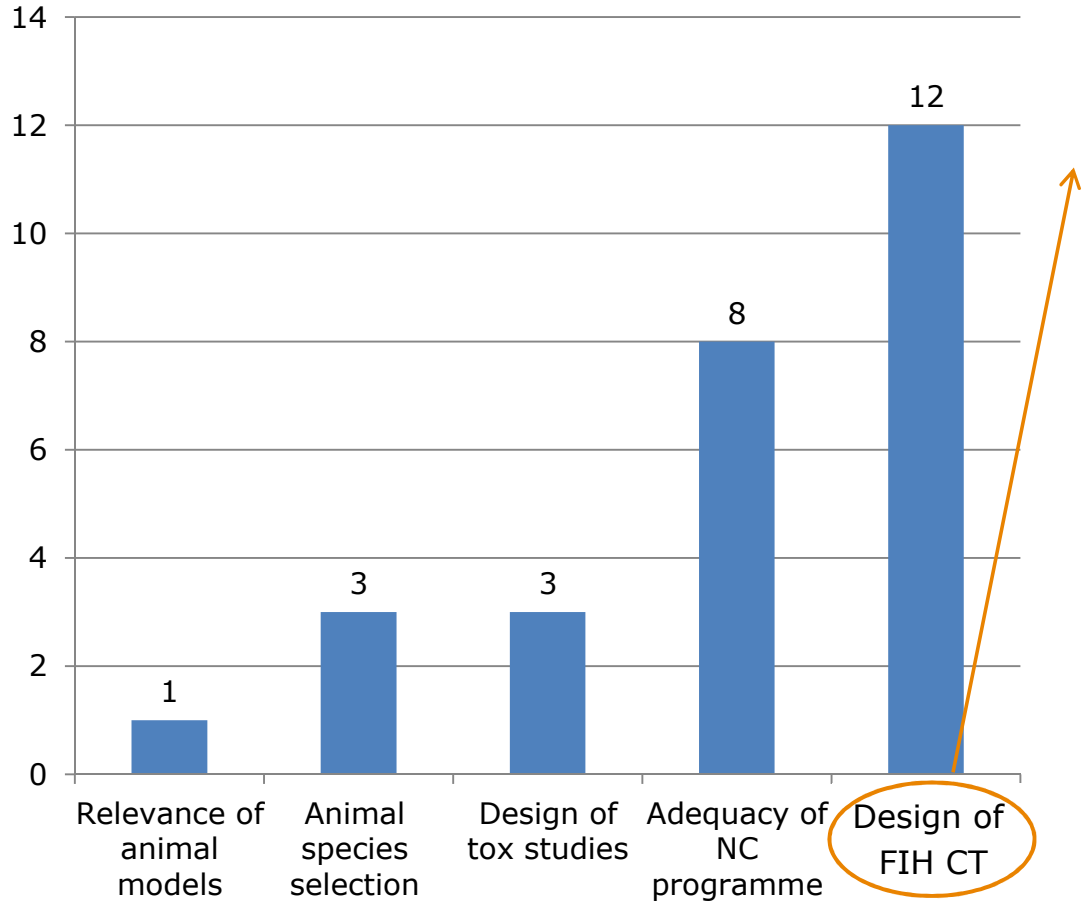
Results:

Since 2017 16 EMA centralised SA have been requested with questions related to FIH studies

ATMP	4
Biological	8
Chemical	4
Grand Total	**16**

Limited data to draw any conclusions on the impact of the revision of the FIH guideline

Type of SA questions related to FIH studies



Design of FIH CT covers:

- Target population
- Choice of endpoints
- Dose selection
- Approach to determine the starting dose
- Safety monitoring
- Stopping criteria
- Safety measures
- Defined criteria to move from HV to patients under integrated protocol

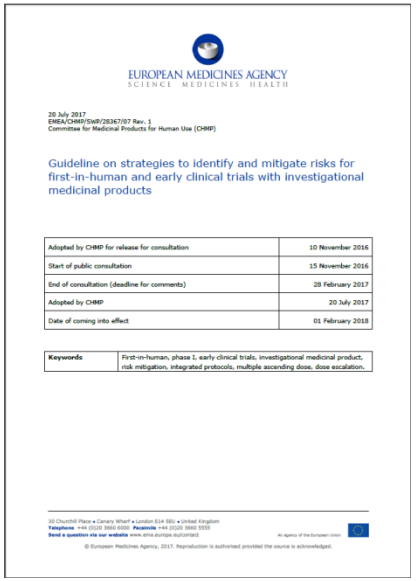
CHMP Recommendations

- Further in vitro studies to better define:
  - Proof of concept
  - relevance of animal species before moving to in vivo
- Dose Selection for FIH CTs
  - Starting dose (level of uncertainty →NOAEL, MABEL and PAD)
  - Maximum dose beyond pharmacodynamic dose range (provide more justification –> less aggressive dose escalation)
  - Transition from HV to patients under integrated protocol (different sensitivity of subjects should be considered for dose selection)
  - Justification for the use of a MTD

Harmonisation of FIH CTA- How can we support?

- EU Network training centre (NTC) **Assessors Training on Early Phase Clinical Trial applications** (March 2017)
- CTFG proposed training on **Clinical assessment training for NCA's and ethics committees on FIH guideline** (2019)
- Implementation of the new **clinical trial portal and database** (access to clinical trial applications and authorisations within the EU)
- Close interaction **EMA-CTFG-NCAs** (detect/address issues, Q&A?)

- FIH Guideline



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20 July 2017
EMEA/CHMP/SWP/28367/07 Rev. 1
Committee for Medicinal Products for Human Use (CHMP)

Guideline on strategies to identify and mitigate risks for first-in-human and early clinical trials with investigational medicinal products

Adopted by CHMP for release for consultation	10 November 2016
Start of public consultation	15 November 2016
End of consultation (deadline for comments)	28 February 2017
Adopted by CHMP	20 July 2017
Date of coming into effect	01 February 2018

Keywords	First-in-human, phase 1, early clinical trials, investigational medicinal product, risk mitigation, integrated protocols, multiple ascending dose, dose escalation.

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Thank you for your attention

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