



## *Which populations should be included in Phase 1 clinical trials?*

### **Sponsor's perspective**

Klaus Francke  
Joachim Höchel

EUFEMED Pre-conference workshop:  
The most suitable participant for  
phase 1 clinical trials – 21 May 2025



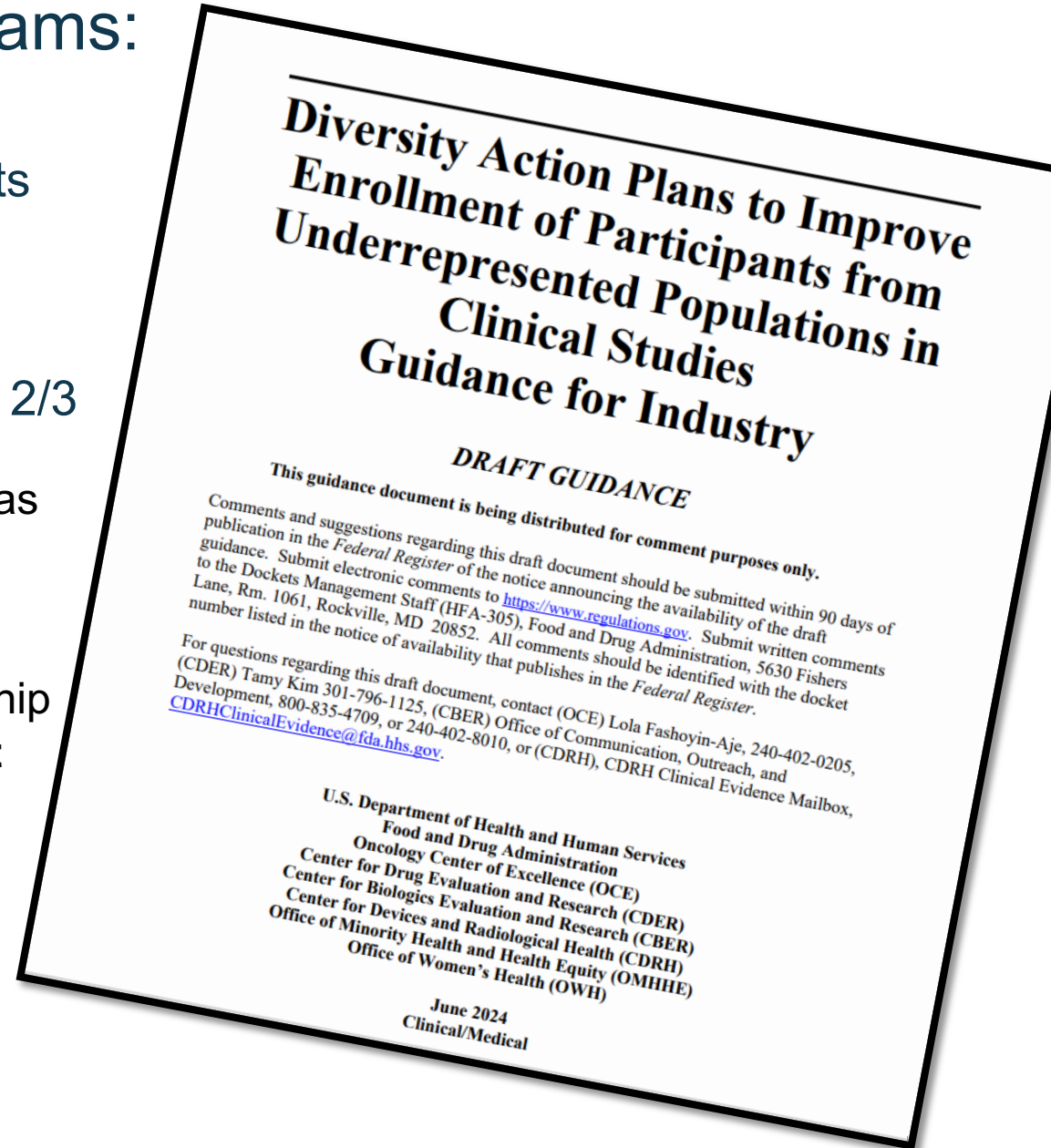


# Objectives of Phase 1 Clinical Programs:

Evaluate safety, pharmacokinetics (PK), and pharmacodynamics (PD) of new drugs or treatments

Key Outcome: relevant knowledge for informed conduct of subsequent clinical development Phase 2/3

- // Explore the pharmacology of the new drug candidate as far as possible unaffected from unexplained variability
- // Minimize the risk for study participants
- // Characterize the dose-exposure (-response) relationship with the subsequent trials and **representative patient population** in mind
  - // Race / ethnicity
  - // Sex
  - // Age
  - // BMI
  - // Concomitant disease(s)
  - // Co-medication(s)





# Paradigm Shift in Phase 1 Clinical Trials

## From

- // homogeneous study populations to minimize inter-subject variability
- // dose-response analysis limited to analysis of dose group effects (e.g., in FiH trial)
- // a primary focus on safety / tolerability and PK



## To

- // study populations representative for the target patient population
- // dose-exposure-response analysis allowing detection and consideration of modulating factors in individual study participants
- // detection of first signs of efficacy relevant for the future target population



# Considerations for Choice of Study Population

Scope: Healthy Volunteer Trials

High inter-subject variability...	
Relevant and beneficial	Exploration of dose-exposure-response relationship, e.g., FiH trial
Relevant but detrimental	Bioequivalence studies Parallel group comparisons, e.g., organ impairment studies
Less relevant	Intra-individual comparisons, e.g., DDI, rel. BA

// Other considerations, e.g.

// Safety of healthy trial participants, e.g., consequences of TEAEs

// Ethical obligation for equal opportunity for women and minorities to participate in clinical trials

// Scientific imperative to explore populations reflective of the population who will receive the approved drug



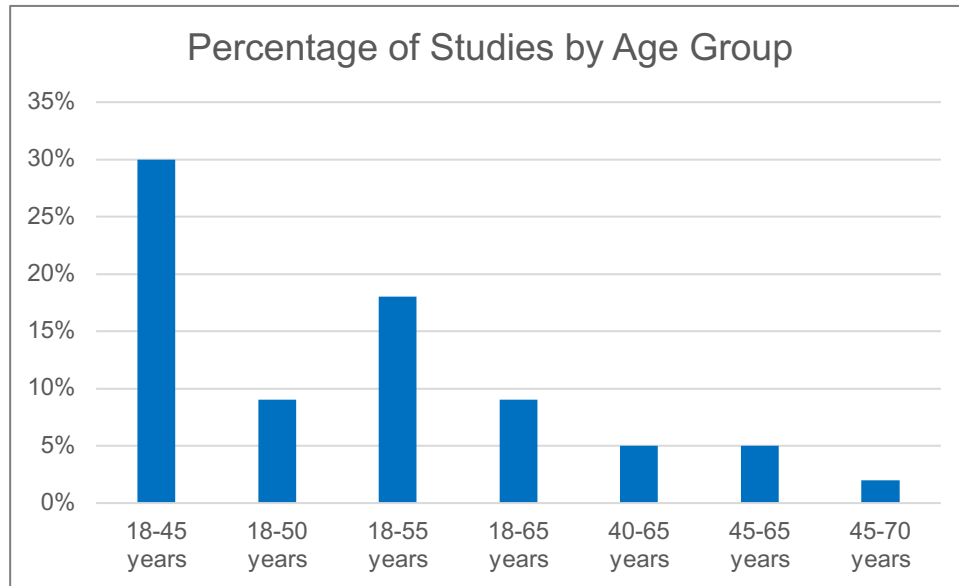
*Examples of changing  
populations participating  
in Phase 1 Clinical Trials:*

- Broadening of Age Range*
- Inclusion of Women*

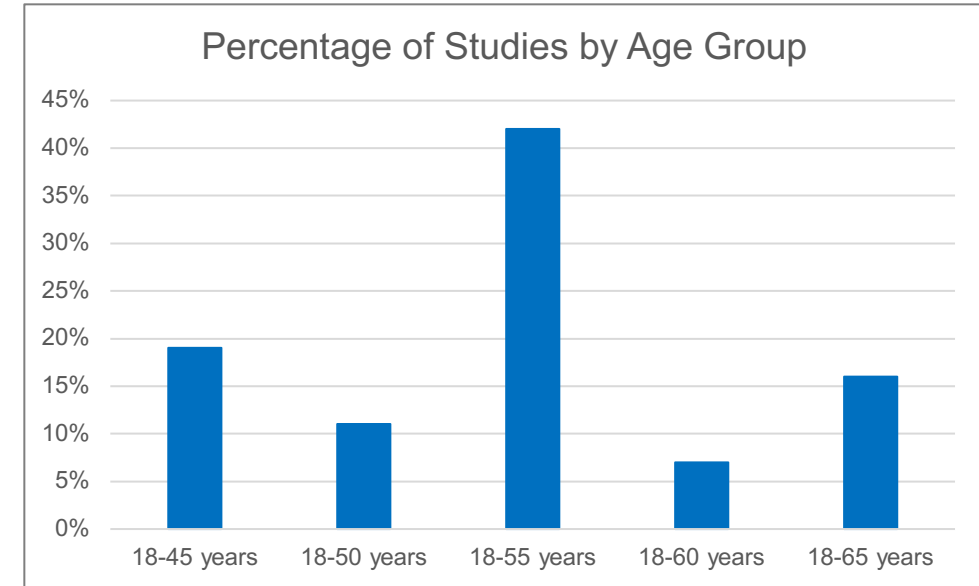


# Age Range of Participants in Phase 1 Studies

## Current Bayer Practice\*



## Current Industry Practice\*\*



Trend: Age ranges are expanding, with Phase 1 trials including participants up to 65 years

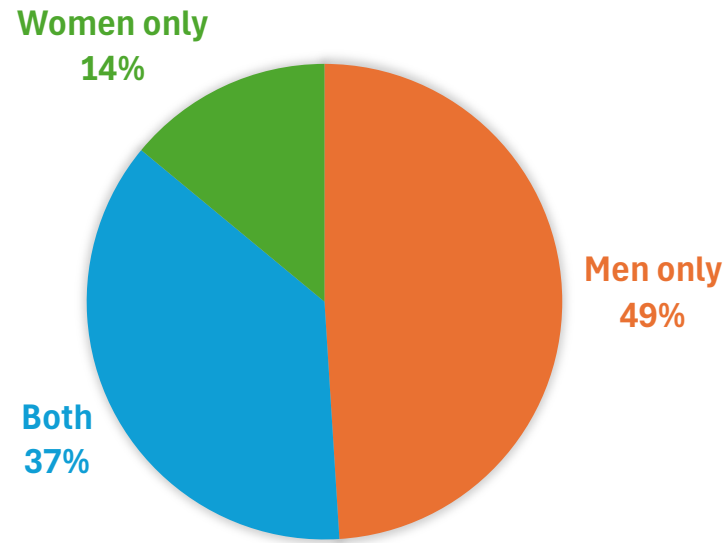
\* Based on 97 trials

\*\* Based on 5500 trials in ClinicalTrials.gov 2013-2023 sponsored by Bayer, BI, AstraZeneca, BMS, JnJ, or Pfizer

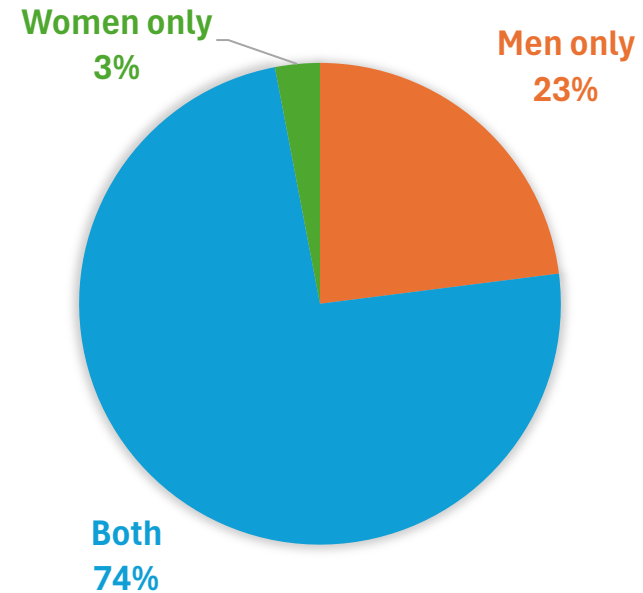


# Inclusion of **Women** in Phase 1 Clinical Trials

## Current Bayer Practice\*



## Current Industry Practice\*\*



Trend: Increasing inclusion of both genders in Phase 1 trials

\* Based on 97 trials

\*\* Based on 5500 trials in ClinicalTrials.gov 2013-2023 sponsored by Bayer, BI, AstraZeneca, BMS, JnJ, or Pfizer

# Toxicological Considerations (according to ICH M3(R2) 2009)

Regarding inclusion of men and women in clinical trials

- // **Men** can be included in Phase 1 and 2 trials before non-clinical male fertility study, as male reproductive organs are evaluated in repeated-dose toxicity studies in animals
- // **Women NOT of childbearing potential** (permanently sterilized, postmenopausal) can be included in clinical trials without reproduction toxicity studies in animals
- // **Women of childbearing potential** could be included in early clinical trials w/o (US) or with (EU) preliminary embryo-fetal development (EFD) studies in animals but with adequate safety measures\*
  - // Requirements for highly effective (user independent) contraception
  - // Frequent pregnancy testing
  - // Study conduct in a controlled environment where adherence to contraception measures incl. sexual abstinence can be guaranteed
  - // Education and informed consent of WOCBP participants



# Bayer's New Standard Approach Regarding Population in Phase 1 Clinical Trials

- // Recommended **age** range 18 – 55 years
- // Inclusion of Women of Non-Childbearing Potential (**WONCBP**) in Phase 1 study protocols as standard
  - // Exclusion of WONCBP is an opt-out from the standard, which requires a scientific rationale
- // Women of childbearing potential (**WOCBP**) can be included if regarded safe and scientifically meaningful
  - // incl. respective contraceptive measures and possibly initial data from embryo-fetal development studies
- // No restrictions regarding **race / ethnicity**





*Thank you!*

**Acknowledgements:**

Adriaan Cleton  
David Jung  
Klaus Francke  
Mira Pavkovic  
Pei Liu  
Yubin Sui



*What populations would you include in Phase 1 clinical trials?*

## **Breakout Session**

Moderated by  
Joop van Gerven  
Joachim Höchel

**Explore, debate, exchange, inspire new ideas on**

- // Whom to include in HV Ph1 trials in the context of the overall development program strategy
- // Differentiation between FiH vs. subsequent clinical pharmacology trials
- // Impact of trial population on addressing specific research questions most efficiently