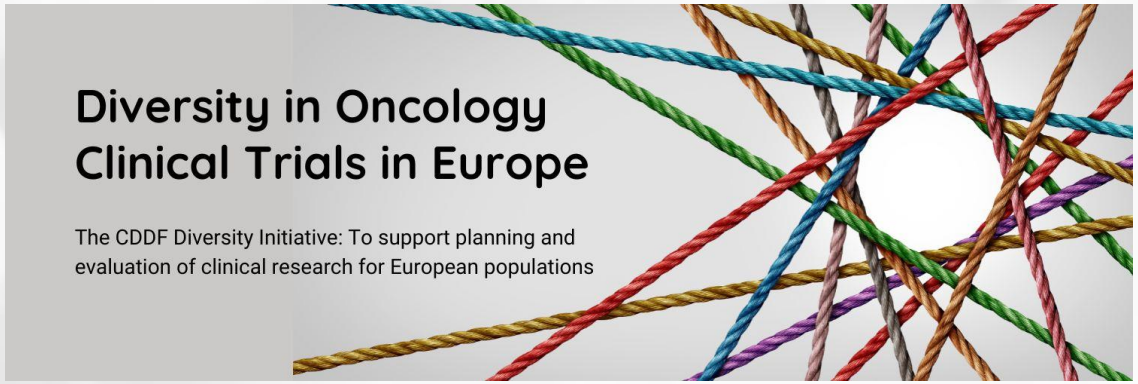
CDDF Annual Conference 2025

CDDF Cancer Drug Development Forum

CDDF Diversity in Oncology Clinical Trials

Fergus Sweeney

CDDF



Disclaimer

Retired, Clinical Trial expert

Member of WHO Technical Advisory Group on Development of Guidance on Best Practices for Clinical Trials

Project Scope and Objectives

- The need to assure that underrepresented groups are included in clinical trials and more broadly healthcare research is widely recognised as a necessary pillar of achieving healthcare for all
- This requires inclusion, of underrepresented groups - who are within the anticipated therapeutic target population of the medicine involved - in clinical trials and research in oncology
  - During development of medicines
  - Elaboration of therapeutic approaches – treatment optimisation/therapeutic guidelines
  - Ensuring patient focussed research and healthcare with a focus on therapeutic outcomes.

Inclusion of under-represented patient populations is recognised in the objectives of WHO and UN, Regulatory Science Strategy of EMA and strategies of other major regulators including MHRA. FDA has published draft guidance

Project Scope and Objectives

- CDDF Diversity Initiative - Diversity in Oncology Clinical Trials with impact on European patients
- CDDF-sponsored and directed project with a multi-stakeholder working group of regulators, patients, academic researchers, and pharmaceutical companies.
- This initiative aims to:
  - examine parameters of inclusion/diversity in clinical research,
  - support the planning and evaluation of clinical research, and the applicability of clinical trial outcomes which have an impact on Europe's diverse population – wherever in the world those trials may be conducted

Scope

- Clinical Trials (and observational studies) of oncology medicines carried out to support:
    - marketing authorisations in Europe
    - development of treatment optimisation and treatment guidelines whose outcomes are used in Europe
- CInical trials (and studies) conducted in Europe or elsewhere when results are used with impact on European patients
- Focused on the treatment of cancers, i.e. the patients have a cancer diagnosis.
- The project will not address impact of diversity on susceptibility to developing cancer per se.

White Paper on Diversity in Oncology Clinical Trials

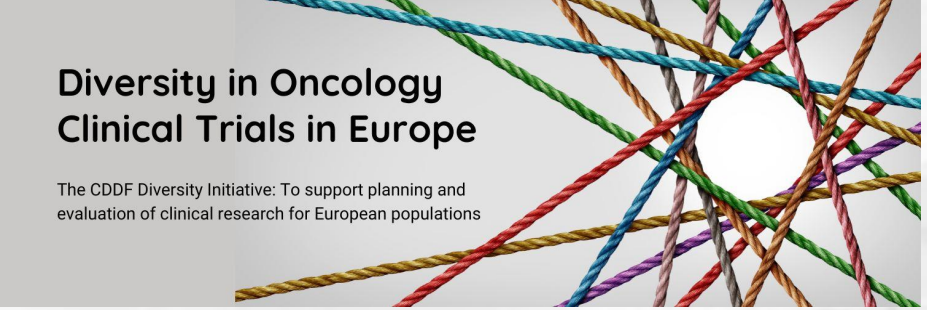
- Involve the perspectives of key stakeholders: patients, healthcare professionals, academia, pharmaceutical industry, and medicines regulators.
- Review and summarize existing research, guidance, and data on variables capturing diversity and representativeness relevant for oncology clinical trials.
- Describe a set of variables relating to diversity and representativeness that can serve to plan and evaluate oncology clinical trials for their applicability to Europe's population.
- Describe processes to assure inclusion through
  - planning/advice,
  - protocol design,
  - conduct/analysis,
  - evaluation of clinical trial outcomes, including for regulatory assessment / benefit-risk determination.

Benefits

- A white paper agreed upon by a cross section of key stakeholders setting out an approach and parameters for addressing EU patient diversity in oncology clinical trials and observational studies.

- In the absence of other guidance specific for the EU, it provides a reference point for developers, researchers and regulators when advising on, planning or conducting a clinical trial/study and when evaluating the clinical data produced with relevance to EU populations.

- It offers input to future guidance that may be developed at EU level on this topic.



Project Timeline

CDDF Cancer Drug Development Forum

Phase I
11/24-01/25

Phase II
Month 1-12
02/25-02/26

Phase II
Month 13-18
03/26-08/26

Participation
Workplan
Budget

Work Packages
F2F Meeting

White Paper
Add. Publications

	2024		2025											2026							
	November	December	January	February	March	April	May	June	July	August	September	October	November	December	January	February	March	April	May	June	July	August
Phase / Period	PHASE-I			PHASE-II - PERIOD-1													PHASE-II - PERIOD-2					
Preparation				X		X		X		X		X		X								
WP Meeting					1		2		3		4		5		6							
F2F Conference																⚑						
White Paper																		⚑				
Add. Publications																			X	(X)	(X)	(X)

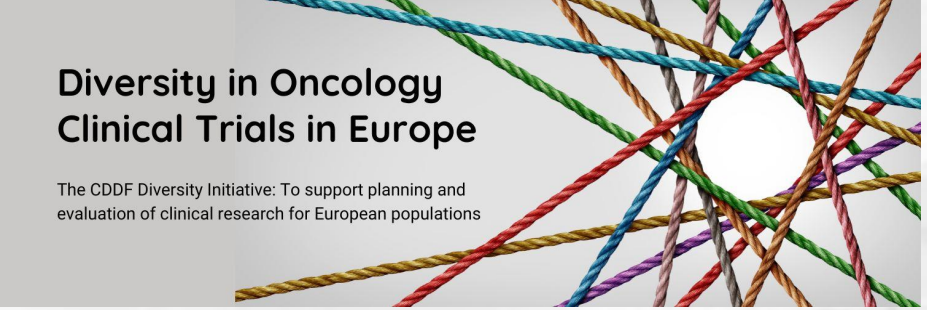
3 - 5 February 2025

Project Governance

- CDDF
- CDDF Board
- CDDF Diversity and Inclusion in Oncology CTs
  - Organizing Committee
  - Working Group
  - Academic partner

Multistakeholder involvement

- Project mandate is from CDDF and adopted by the CDDF Board who will also oversee progress and endorse outcomes for publication
- Project has a coordinating committee and a working group:
- Coordination committee:
  - Co-chairs. Axel Glasmacher and Fergus Sweeney both from CDDF Board
  - Members: Sushmita Sen (Roche), Birgit Wolf (Bayer), Harald Enzmann (BfArM), Marie von Lillenfeld-Toal (RUB)



Phase II Participants

CDDF Cancer Drug Development Forum

Regulators
H. Enzmann (BfArM)
F. Pignatti (EMA)
B. Sepodes (CHMP/Inframed)

Academic Partners
European Haematology Association
Inst. f. Diversity Medicine, Ruhr-Univ. Bochum

Patients / Patient Advocacy Groups
Melanoma Patient Network Europe
VHL Europe (EURORDIS)
WECAN
Youth Cancer Europe (pending)

Confirmed Industry Partners
Bayer
Bristol Myers Squibb
Genmab
Johnson & Johnson
Novartis
Roche
Ryvu

Cancer Drug Development Forum
Axel Glasmacher
Caroline Marissal
Fergus Sweeney

Participants are involved on their own basis and do not necessarily represent the views of their organizations or institutions.

Agreed information exchange:
Other diversity initiatives: ESMO, IHI-READI
Clinical trial design/regulation: EORTC

Project Working Group

- Members participate on the basis of their personal expertise and perspective
- Ad hoc experts will be invited as required (e.g. statistician, biomarkers, epidemiologists)

Regulatory perspectives

- EMA Regulatory Science Strategy:
  - Foster Innovation in Clinical Trials: *"…**Promote the inclusion of neglected populations** such as pregnant women, the elderly and those of diverse ethnicity in clinical trials. "*
- WHO Guidance on Best Practice for Clinical Trials:
  - *"…A further major challenge is that **clinical trial cohorts have often lacked diversity**, with under-representation of certain populations, resulting in them being underserved by clinical trials,…"*
  - *"..Guidance .. to **improve inclusion of underrepresented groups Decentralized or point-of-care trials may help .... by increasing trial accessibility.** In addition, diversification of trial staff can help to improve community engagement ..."*
- MHRA Draft Inclusion and Diversity Guidance
  - *"The purpose of the Inclusion and Diversity Plan (the Plan) is to **ensure clinical research is designed to include people who could be impacted by the findings**, and that **people often underserved by research are not overlooked**."*

Regulatory perspectives

- FDA – Draft guidance Collection of Race and Ethnicity Data in Clinical Trials and Clinical Studies for FDA-Regulated Medical Products - January 2024
- FDA – Draft Guidance Study of Sex Differences in the Clinical Evaluation of Medical Products – Jan 2025
- FDA – Draft guidance Diversity Action Plans to Improve Enrollment of Participants from Underrepresented Populations in Clinical Studies - June 2024
  - *"Consistent **implementation of actions to improve representativeness** in clinical studies can support **more equitable and timely access to medical discoveries** and innovations, **improve the generalizability** of results across the intended patient populations, improve our **understanding of the disease and/or medical product** under study, and inform the **safe and effective use of the medical product for all patients**. "*

Regulatory perspectives

- ICH E5 Ethnic Factors in the Acceptability of Foreign Clinical Data
  - Addresses intrinsic and extrinsic factors
  - *"…**permit adequate evaluation of the influence of ethnic factors** while minimizing duplication of clinical studies and **supplying medicines expeditiously to patients for their benefit**…"*

- ICH E8(R1) General Considerations for Clinical Studies
  - *"..**study population may be narrowly defined** to reduce the risk to study participants or to **maximise the sensitivity** …for detecting a certain effect. .*
  - *...it **may be broadly defined to more closely represent the diverse populations** for which the drug is intended. "*
  - *"..Studies conducted in the **later phases of drug development or post-approval are often more heterogeneous in study population definitions**. Such studies should involve participants who are representative of the diverse populations which will receive the intervention in clinical practice…"*

Regulatory perspectives

- ICH E6 (R3) Good Clinical Practice
  - *Principles 1.4 "When designing a clinical trial, the scientific goal and purpose should be carefully considered so* ***as not to unnecessarily exclude particular participant populations****. The participant* ***selection process should be representative of the population groups that the investigational product is intended to benefit, once authorised,*** *to allow for generalising the results across the broader population."* to be read in conjunction with ICH E8R1

- ICH E17 General Principles for Planning and Design of Multi-regional Clinical Trials
  - *"****MRCTs allow for an examination of the applicability of a treatment to diverse populations.*** *The intrinsic and/or extrinsic factors that are believed or suspected to impact upon responses to the drug can be further evaluated based on data from various regions using a single protocol. "*

Regulatory perspectives

- EMA/CHMP Nov 2023 Guideline on the Clinical Evaluation of Anti-Cancer Medicinal Products
  - *"[phase 3 trials]. **Depending on the objectives**, .. study should **generally be designed to include patients representative of those likely to be treated** ..in clinical practice. The study population is expected to be characterised by relevant tumour .., treatment …, and patient characteristics …. "*
- EMA/CHMP Jan 2029 Guideline on the investigation of subgroups in confirmatory clinical trials
  - *"6. **Implications for study planning**:*
    - *6.1. Considering heterogeneity within a target population*
    - *6.2. A strategy for selection and definition of subgroups for assessment*
  - *5. **Issues to be addressed during assessment***
    - *5.1. A strategy for the assessment of clinical trials"*

Key thoughts

- Think in terms of clinical development or research programmes, not just of single trials
- Planning is essential – design of trial, design of analysis, design of evaluation
  - Anticipate which populations are affected by the cancer and how that may impact the treatment benefit – risk
  - Which populations need to be included
  - What data is needed to identify the subpopulations and related outcomes
  - What analyses are proposed – prospective sub-group analysis and how this impacts the design and power of the trial

Key thoughts

- There is a trade-off between sensitivity and generalisability – recognise this – first we need to know can a drug have an effect then determine which groups can benefit from that effect
- We need to understand what to ask from MRCTs and how to interpret their data – all regulators face the issue that 70% or more of data on average is generated in other regions
- Enable visualisations of data to support evaluation - how subgroups are impacted and extrapolations where possible of results for other groups

Conclusion

- CDDF Diversity in Oncology Trials Project - Important challenge with impact for all patients
- Focused timeline leading to whitepaper in first half of 2026
- Multistakeholder involvement in discussion and in delivering whitepaper
- Envisage how clinical trials can be planned and analysed to assure that the needs of all patient groups can be addressed
- We will keep you all well informed as we progress - https://cddf.org/events/cddf-diversity-initiative/
- Assuring that poorly represented groups are included in the planning, conduct, analysis and evaluation achieving healthcare for all