Belong

Inclusion of
People living with HIV
in non-HIV clinical trials

Clinical Trial Eligibility Criteria for Patients with HIV: Guidance on Improving Inclusion in Non-HIV Trials

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EATG European AIDS Treatment Group

Background

→ This guidance is part of a global effort to promote greater diversity and representativeness in clinical research.

→ Aims to improve the generalisability of findings and access to medicines for all populations.

Background

→ For use by industry, not-for-profit organisations, and other relevant stakeholders.

→ Applies to all drugs and biologics across all disease areas, with particular emphasis on conditions that disproportionately affect people living with HIV.

→ Complement existing guidelines and does not restate recommendations or best practices already detailed in ICH-GCP or other applicable clinical trial regulations.

Background

→ Careful consideration should be given to the inclusion and exclusion of people living with HIV in non-HIV clinical trials.

→ This requires that eligibility criteria (inclusion and exclusion) be intentionally developed to avoid the arbitrary exclusion of people living with HIV from research that may offer them potential benefit.

→ It is also important for this guidance to be clinically acceptable and implementable.

Guidance development

- Literature review
- Stakeholder interviews
- Online review
- Online consultation

Guidance structure

10-ponjts recommendations

Key guidance points to be reviewed (based on online survey)

Up to 15 minutes per topics

→ 1. Eligibility of people living with HIV must be based on sound scientific or clinical rationale

→ 6. Clinical Status

- 6.1 History of AIDS-defining illness
- 6.3 Timing, type and effectiveness of antiretroviral therapy
- 6.4 Comorbidities
- 6.2 Immune functions

→ 3. Relevance of the medical condition under investigation for people living with HIV

→ 9. Engaging with communities of people living with HIV

1. Eligibility of PLWH must be based on sound scientific or clinical rationale

→ Eligibility criteria should be proactively assessed.

→ Standardised protocol eligibility templates must not be used without clear justification.

→ Decisions on eligibility should be informed by the considerations outlined in this document.

→ Any exclusion must be documented and supported by a sound scientific and clinical rationale.

→ Risk assessments should be conducted to ensure safe and appropriate inclusion of PLWH.

→ Where concerns exist, study protocols should prioritise risk-mitigation strategies over exclusion.

2. Consider characteristics of the investigational product

→ When assessing eligibility, the properties of the investigational drug must be considered from multiple perspectives:

- Mechanism of action
- Existing safety data on the investigational drug or related drug classes
- Potential or suspected drug–drug interactions with antiretroviral therapy or treatments for comorbidities
- Feasibility and appropriateness of a temporary treatment switch (see Recommendations 6.3 and 6.4)

→ Protocols must explicitly state whether the investigational drug has a known or potential immunosuppressive effect, as this may in some cases justify exclusion of people living with HIV.

3. Consider the relevance of the medical condition under investigation for PLWH

→ Inclusion of people living with HIV in clinical trials should be encouraged where a medical condition poses increased risk or disproportionately affects them, provided this does not compromise participant safety or trial objectives.

→ Any exclusion of people living with HIV due to safety concerns or conflicts with study objectives must be clearly documented in the study protocol.

→ This approach promotes equity and accelerates the generation of evidence directly relevant to people living with HIV.

4. Ensure diversity within the study population

→ The literature on comorbidities associated with HIV is substantial but has significant limitations.

→ Existing research often focuses on narrow demographic groups, over-representing certain regions, genders, or age brackets.

→ This creates gaps in understanding how comorbidities vary and interact across gender, age, geography, and factors such as social determinants of health and life circumstances.

→ ICH-GCP recommendations and sponsor commitments to diversity and representation should extend to all people living with HIV.

→ Special attention should be given to gender and age, particularly when medical conditions may affect these subpopulations differently.

5. HIV testing

→ HIV testing should not be mandated as part of general eligibility for non-HIV trials.

→ If there is a suspected risk specifically linked to enrolling a person living with HIV, testing should be offered (see R2).

→ In trials addressing conditions that disproportionately affect people living with HIV, or where they may be at increased risk, testing should be offered as an option when HIV status is unknown.

→ This prevents unrecognised HIV infection from placing participants at risk. It also supports appropriate medical oversight, data interpretation, and access to testing.

→ Where HIV-positive status is not an exclusion criterion, the protocol should explicitly state that people living with HIV are eligible to participate.

→ HIV testing, when performed, must follow existing guidelines and best practices.

6. Clinical status

→ Several aspects of the participant's clinical status should be considered when assessing the inclusion of people living with HIV in non-HIV clinical trials.

→ These include:

- History of AIDS-defining illnesses.
- Immune functions.
- Timing, type and effectiveness of antiretroviral therapy
- Comorbidities.

→ These factors should inform both eligibility criteria and clinical monitoring during the trial.

6. Clinical status

6.1 History of AIDS-defining illness

→ **A participant's history of AIDS-defining illnesses should be evaluated in relation to:**

- Timing of the illness
- The investigational product under study
- The medical condition being investigated

→ People living with HIV without a history of AIDS-defining opportunistic illnesses should generally be considered eligible for non-HIV clinical trials.

→ **For those with such a history of AIDS-defining illnesses :**

- Inclusion decisions should consider the timing, control, and relevance of the illness to the trial.
- A distant, fully resolved illness should not generally preclude participation.

→ Uncontrolled AIDS-defining illnesses are a valid reason for exclusion. Participation may be reconsidered once the illness is adequately controlled.

→ The duration for defining "controlled" may vary:

- A 12-month period may be reasonable in some cases
- Shorter periods may be acceptable if the illness is clinically controlled and prophylaxis is adequate.

6. Clinical status

6.2 Immune functions

→ **CD4+ T-cell count and CD4+/CD8+ ratio** are important surrogate markers of immune function and should be considered when relevant to the clinical investigation. These markers should be evaluated in the context of:

- The investigational product
- The stage of clinical research
- The medical condition under study
- The potential of the intervention to prevent, cure, or mitigate the condition

→ Participants with **sustained CD4 counts ≥350 cells/µL and on suppressive ART** should generally be considered eligible for any study.

→ For participants **with CD4 <350 cells/µL**, eligibility may be considered based on additional factors such as:

- CD4+/CD8+ ratio
- Concomitant medical conditions
- ART history
- Other relevant immune surrogate markers

6. Clinical status

6.3 Timing, type and effectiveness of antiretroviral therapy (ART)

→ Exclusions based on ART duration or specific regimens must be justified and documented.

→ Enrolment should generally be limited to virologically suppressed patients; unsuppressed patients may be included only if benefits outweigh risks, with appropriate monitoring.

→ Exclusion due to specific ART should be applied only when there is a known or theoretical risk of toxicity and switching is not feasible.

→ ART regimen changes should be considered to manage drug–drug interactions or overlapping toxicities.

→ Short ART interruptions may be allowed, if necessary, with proper risk management, monitoring, participant input, and trial team training.

6. Clinical status

6.4 Comorbidities

→ Comorbidities should be considered, especially when they contribute to polypharmacy or increase the risk of drug–drug interactions.

→ The participant’s overall medical history and clinical management must be considered.

→ Switching to an alternative effective treatment for comorbidities should be considered when potential benefits outweigh risks, with appropriate risk management, clinical monitoring, and oversight.

→ When comorbidities can be effectively managed, standard-of-care interventions should be applied to enable safe participation of people living with HIV in non-HIV clinical trials.

7. Product development stage

→ Eligibility criteria should consider the stage of development of the investigational product or intervention.

→ In early-phase trials (Phase 1), where the primary focus is on safety, exclusion of people living with HIV may be justified.

→ From Phase 2 onwards, people living with HIV should generally be considered eligible if they meet other relevant criteria.

→ Regardless of development stage, people living with HIV should be engaged in research preparedness activities from an early stage (see R9).

8. Clinical design

→ Exclusion may be justified initially, but phased or stepped inclusion should be considered.

→ Flexible eligibility and innovative trial designs (staggered enrolment, stratification, subgroup analyses) can allow inclusion once safety is established.

9. Engaging with communities of people living with HIV

→ Engage people living with HIV early in the clinical development process, even if early-phase inclusion is not feasible.

→ Early engagement strengthens research relevance, acceptability, and effectiveness (aligned with MIPA principles).

→ Foster collaboration between the HIV community, regulatory agencies, and trial sponsors throughout development.

→ Emphasise inclusion benefits to sponsors to ensure products are safe and effective across broader populations.

10. Educate product developers and end-users

→ Promote training and capacity-building for non-HIV researchers and healthcare professionals on comorbidities and HIV coexistence.

→ Encourage and support the involvement of people living with HIV in non-HIV research.

→ Empower all patients to advocate for participation in research that may improve their care.