

Institutional Review Board Oversight Points to Consider for IRB Reviewers¹ to assess DEI factors at Initial and Continuing Review

INTRODUCTION

IRBs are responsible for safeguarding the rights and well-being of participants in alignment with the foundational principles of respect for persons, beneficence, and justice – as detailed in the Belmont report. Federal Regulations (45 CFR 46) state that Institutional Review Boards (IRBs) have the authority to approve, require modifications in (to secure approval), or disapprove all research activities covered by the policy (45 §46.109 IRB review of research). This authority extends to requests that research protocols integrate study elements relevant to matters of diversity, equity, and inclusion (DEI), given the foundational research ethics principle of justice² and the regulatory requirement for IRBs to ensure that subject selection be equitable.³ IRBs have a responsibility to uphold these ethical standards to ensure that the protocols they review are inclusive and representative of those who will potentially benefit from the knowledge gained from the research.

Certain tools and resources, including protocol templates that incorporate DEI elements, have been developed to help the IRB support DEI efforts. The checklist below is an instrument that IRBs can utilize to evaluate whether the protocols they review incorporate DEI principles and optimize inclusion. The checklist offers a guidepost for IRBs during their review and deliberation of submitted protocols. For example, IRBs can incorporate some or all of the questions into existing reviewer checklists or use them to inform their continuing review or study close out application forms for investigators. Alternatively, there could be a designated DEI reviewer who conducts a pre-review of protocols using the checklist and flags important points to the committee. IRBs may even consider amending their protocol template, continuing review application, and close-out forms to incorporate some of the ideas below to prompt inclusion of this information in the protocol submission. When protocols fall short of DEI principles or ideals, then suggestions for improvements can be communicated to the investigator to require or suggest modifications as necessary. The list is not meant to be prescriptive or set out rigid norms that must be followed in all cases; rather, it is meant to aid IRBs in their ethical oversight to ensure DEI elements are included during initial review, continuing review, and study close out procedures.

¹ Adapted checklist from: Strauss DH, White SA, Bierer BE. Justice, diversity, and research ethics review. *Science*. 2021 Mar 19;371(6535):1209-11.

² [The Belmont Report](https://www.hhs.gov/ohrp/sites/default/files/the-belmont-report-508c_FINAL.pdf): Available from: https://www.hhs.gov/ohrp/sites/default/files/the-belmont-report-508c_FINAL.pdf

³ [Consideration of the Principle of Justice under 45 CFR part 46](https://www.hhs.gov/ohrp/sachrp-committee/recommendations/attachment-a-consideration-of-the-principle-of-justice-45-cfr-46.html): Available from: <https://www.hhs.gov/ohrp/sachrp-committee/recommendations/attachment-a-consideration-of-the-principle-of-justice-45-cfr-46.html>

INITIAL REVIEW:

Study Design and Intended Participant Population: *steps to ensure adequate feedback from participants/community have been attained.*

- Was participant and/or community input sought, collected, evaluated, and included in the design of the study?
 - Was the feedback and input solicited from representatives of the intended study population and or the condition under study? If not, was an explanation provided as to why not?
- Does the study background/introduction or study population section in the protocol application include information about the intervention and for whom it is intended?
- Does the study introduction include information on the epidemiology of the disease, including demographic and non-demographic factors⁴?
 - Do the demographics of the proposed study population reflect that of the population affected by the condition or for whom the intervention is intended?
 - If no, is the proposed research population adequately justified?
 - Does the protocol have a plan and/or proposal for what the intended population's demographic and non-demographic composition should look like in terms of age, race, ethnicity, sex, disability, comorbidities, etc.?
 - Is planned under- or over- representation by relevant factors (e.g., age, race, ethnicity, sex, disability, comorbidities, economic or educational disadvantage) in the sample scientifically justified?
 - If feasible, is there a statistical plan for examining heterogeneity in outcome or across subgroups?
- Is a feasibility assessment done for sites to assess their capacity to recruit the intended study population and achieve the clinical trial's objective?
- Is site selection informed by thoughtful, data-driven strategies that will reflect the intended study population and/or disease burden?

⁴ For this purpose, 'demographic factors' include variables, such as race, ethnicity, sex, and age. 'Non-demographic factors' are variables that are dynamic and able to change, such as gender identity, social determinants of health, co-morbidities, medications, etc.

Criteria for Inclusion and Exclusion: *steps to ensure eligibility criteria are as inclusive as possible and only as restrictive as necessary*

- Are the exclusion criteria justified by scientific, medical, ethical, and/or safety explanations?
- Have alternative approaches to minimizing risk that do not rely on exclusion been considered?
- Have approaches and accommodations to permit inclusion been proffered?
- Are upper and/or lower limits for age included? Is justification for these age limits explicit, adequate, and documented in the written protocol?
- Have normal values and reference ranges for routine laboratory tests considered race, ethnicity, geography, sex, age, and comorbidities appropriately, given potential natural variation in what counts as 'normal' ranges between these groups, so as not to exclude some groups unnecessarily during the screening process?
- Are participants excluded because of language proficiency or preference, cultural or religious beliefs and practices, socioeconomic status, or other factors? Are there documented scientific, medical, ethical, or safety reasons for exclusion?
- Does the protocol include provisions for accommodation or adjustments for different populations, such as: individuals with disabilities, individuals at the extremes of weight, individuals whose preferred language is other than English (or the preferred language of the region), individuals who are gender diverse?
- Will screen failure data be tracked and reviewed, to help determine if selection bias is operative and whether the resulting data is representative?

Recruitment: *steps to support inclusion of potential participants from diverse and/or underrepresented groups*

- Have recruitment procedures⁵ considered specific approaches to engage underserved populations?
- Have recruitment procedures and materials been reviewed by patients and/or potential participants who are diverse and representative?
- Are patient-facing recruitment materials culturally and linguistically appropriate?
 - Is the language gender neutral?
 - Is the language inclusive?
 - Is the language discriminatory against particular populations?
- Is the informed consent document available in a language(s) understandable to the anticipated participant populations or their legally authorized representatives (LAR)?
 - Are translation services readily available for participant recruitment and consent?

⁵ Mrctcenter.org. 2022. Available from: <https://mrctcenter.org/diversity-in-clinical-research/download/1081/>

- Are accommodations, including supporters for decision-making, assistive devices (e.g., screen readers, visual aids, wheelchairs), and other modifications, available for individuals who request or need them?

Study Conduct: *steps to ensure diverse and/or underrepresented groups are accommodated*

- Are in-person visits minimized and essential for study outcomes?
- If on-site visits are necessary, does the study conduct plan include features that enable access and/or participation to the research trial for all populations:
 - Have clinic hours been extended (beyond 8 am - 5 pm to early evenings and/or weekends)?
 - Will transportation be arranged? Does it minimize inconvenience?
 - Are virtual visits, use of local healthcare clinics, or home visits possible?
 - Is childcare or eldercare provided on site?
 - Is the study being conducted at sites that are accessible?
- Do all participant-facing materials conform to health literacy principles?
- Are all participant-facing materials accessible to people who are hearing or visually impaired?
- Are participant materials translated? According to institutional policies, is back translation necessary?
- If follow-up visits are scheduled, are translation services available for those who may need or want them?
- Are participant navigators available for participants who request them?
- Is data collection and acquisition minimized to that necessary for the study endpoint(s)?
- Can any research procedures, including laboratory tests or imaging procedures, be accommodated locally or more conveniently to the participant?
- Are there technology solutions that could be enabled and deployed?
 - Do all participants have access to such technologies?
 - Do all participants have the internet access, data plans, hardware, and software to utilize these technologies?
 - Has data privacy and security, including data collection, transfer, and storage, been considered, and reviewed?
- If technology or access to devices are required, will they be provided, or provided if necessary?
 - Will internet connectivity be provided?
 - Will costs for data plans be provided or reimbursed?
 - Will technical assistance be available, if required?

Payment: *steps to examine that participants are appropriately compensated for their time and effort*

- Is reimbursement for expenses and/or compensation for participants' time and burden, available for participating in the study?
- Will expenses of a necessary caregiver, guardian, or LAR be reimbursed?
- Have the processes for provision of payments be adequately simplified to minimize inconvenience and/or delay to receipt of funds?

Return of results: *steps to establish that participants are informed about the study results after the conclusion of the study*

- Is there an established procedure for the return of aggregate results to the participant, the community, and the public, in plain language and translated in a culturally and linguistically appropriate manner?
- Will individual results be returned? Is there an explanation of why or why not?
- Is there a description of how participant questions or need for follow-up medical evaluation or care will be addressed?

CONTINUING REVIEW:

- Has the sponsor and/or investigator reported to the IRB the demographic and non-demographic composition of the participants enrolled to date?
 - Is demographic distribution on track to approximate the study goals, as outlined in the initial protocol application?
 - If not, are adequate corrective actions described, sufficient, and likely to be successful?
- Have inclusion/exclusion criteria inadvertently or unnecessarily resulted in under- or over-representation of understudied subgroups?
- Can/does the study report the number of participants who have been withdrawn from the study by the relevant demographic and/or non-demographic data as compared to the intended study population? IRBs should ask investigators to include this information in their continuing review application, and patterns of systematic withdrawal reviewed.

STUDY CLOSEOUT:

- Did the study fulfill its enrollment and retention goals?
- Was the rate of completion of the study across subgroups within range of the intended study population?
- Was feedback of the clinical trial experience collected from participants?
- Has the study team reviewed study conduct to identify learning opportunities for the future?
- What changes will be made in community engagement, study design, conduct, reporting, or other methods or processes that will enhance inclusion?
- Have the results been, or will the results be, communicated to the participants and to the community?