SEX AND GENDER IN RESARCH INVOLVING HUMANS ACCORDING TO THE HRA

ISSUES TO CONSIDER

This document reflects the swissethics *recommendations* on sex and gender in research involving humans according to the HRA

The integration of sex and gender (referred to as *"sex/gender"*) in biomedical research has recently gained significant attention among researchers and clinicians[1-4], which impacts on how Research Ethics Committee (REC) review the documents that are submitted[5]. biomedical research should strive to include participants from diverse sex/gender backgrounds whenever relevant. There is still a persistent underrepresentation of women and sexual *and gender diverse persons (SGDs*), and more broadly of sex/gender issues in biomedical research: investigators tend to ignore or dismiss this topic [6], not only in the way they develop their design and define the study population, but also in how they analyse, interpret and publish their results. This contradicts the declaration of Helsinki, which states (art 13) that "Groups that are underrepresented in medical research should be provided appropriate access to participation in research"[7].

Sex relates to the biological attributes that distinguish women and men or males and females, based on chromosomal identification, reproductive organs, hormonal exposure. However, a number of studies have shown that the distinction between male and female is far more complex and not reduced to a binary view that the sex category would suggest, for example for individuals with variation of sex development (intersex). *Sex assigned at birth* refers to the sex (male, female, intersex) assigned to a child at birth, most often based on the child's external anatomy[10]. In health research, sex assigned at birth is often used as a proxy for sex, as it is often readily available through administrative documents.

Gender refers to the roles, behaviours, expressions and identities built socially among girls, women, boys, men, and gender diverse people. Gender operates at different levels influencing health of individuals. For example, the distribution of power and resources in a given society (structural level) affects access to care; gendered social norms influence health behaviours such as risk taking or health-seeking behaviour, but also exposure to health risks and hazards in relation to the gendered division of labour (interactional level). In addition, gender identity manifests itself along a continuum and can change over time, reflecting the growing recognition of sexual and gender diversity (SGD), and of individuals defining themselves as LGBT+ or LGBTQQIP2SAA (lesbian, gay, bisexual, transgender, queer, questioning, intersex, pansexual, two-spirit (2S), androgynous, and asexual).

There are projects for which the component of sex/gender may not be relevant. If this seems irrelevant, the principal investigator should provide convincing arguments for avoiding the exploration of sex/gender in the research protocol. In most studies, all the documents submitted to RECs should address the issue of sex and gender, following the steps described in the next page, inspired by the SAGER guidelines[10][1]. The following grid or checklist has been elaborated to guide researchers in the writing of their documents: *researchers need to know that the check-up grid below will be used by RECs' members to review all protocols and related documents*.

[1] On March 4th 2024, the World Health Organization has officially disclosed the adoption of the SAGER guidelines

ISSUES
1. TOPIC OF THE STUDY
Are sex/gender (S/G), respectively sexual and gender diversity (SGD) issues relevant to the topic and aim of the study?
2. INTRODUCTION
2.1. Are S/G and SGD dimensions developed (genetic and/or biologic or social mechanisms at play)?
2.2. If appropriate, do the objectives include the question on S/G and/or SGD?
3. METHODS
3.1.: Is the study population correctly described regarding S/G (including sexual and gender diversity)?
3.2. Eligibility criteria: does it ensure representativeness of all the S/G and SGD dimensions? Is there a selection bias regarding S/G distribution?
3.3. Recruitment of participants: does the process of obtaining the data ensure an adequate distribution of S/G and SGD?
3.4. Definition of S/G and SGD dimensions: do they capture sex dimensions (hormonal levels, gene expression, etc.) and/or gender dimensions (identities, norms…) and/or sexual orientation dimensions (sexual attraction, romantic attraction…)?
3.5. Statistics (incl. sample size): if S/G and SGD are of primary interest, does the sample size estimation integrate this aspect? Are the statistical analyses appropriate?
4. INFORMED CONSENT & OTHER DOCUMENTS
4.1. Informed consent form & other documents: is the content of information written in an inclusive manner?
4.2. Informed consent form: Does the information cover the study's aspect related to sex/gender and SGD appropriately?
4.3. Informed consent form: If applicable, is the issue of contraception and pregnancy fully and clearly presented? does the document address the issue of potential extra costs that may deter women/parents to participate in the study, e.g. child care and custody?
4.4. In questionnaires, interviews: is the language and content inclusive? is the possibility to cover the sexual and gender diversity open (e.g. in an open box)?
5. PUBLICATION AND DISSEMINATION POLICY
Do the publication and dissemination plans include the presentation of disaggregated results by S/G and SGD?

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