UPSTREAM MARKER FOR HEALTH

This Upstream Marker for Health is a learning tool for the foundation's upstream health investments. It is intended to be used by investment owners when designing and refining an investment and to spark conversation with grantees.

The purpose of this tool is to enable investment owners and teams to more intentionally integrate relevant considerations on sex as a biological variable (SABV) and sociodemographic characteristics.

For additional information on how to answer questions in this tool, please see the **Upstream Marker for Health Companion Resource**.

Considered	Responsive	Addresses Disparities in R&D
Possible sex and sociodemographic elements and their consequences are considered in investment design.	Sex and sociodemographic elements are accounted for, and representativeness is reflected in R&D plans.	Investment is responsive AND explicitly addresses a persistent disparity or inequity in the R&D field.

For non-upstream investments, use the downstream Gender Integration Marker here.

HOW TO USE THE UPSTREAM MARKER FOR HEALTH

STEP 1 **Input your general information.**

STEP 2 **Answer Questions 1–5 and explain your responses.**

STEP 3 **Count the number of 'YES' answers. If the count is 2 or less, the investment is *'considered'*; skip to Step 6. If the count is 3 or more, the investment is likely *'responsive'* or *'addresses disparities in R&D'*. Continue to Step 4.**

STEP 4 **Answer Question 6 and explain your response.**

STEP 5 **If you answered 'YES' to Question 6, the investment *'addresses disparities in R&D'*.**
If you answered 'NO' to Question 6, the investment is *'responsive'*.

This tool is informed by, and draws language from: the Sex and Gender Equity in Research (SAGER) Guidelines , the Women's Health Opportunity Map, and internal and external subject matter experts.

General Information

STEP 1 **Input your general information**

INVEST ID	
Is this a supplement	☐ **YES** ☐ **NO**
PO Completing Assessment	

Assessment

STEP 2 **Answer Questions 1 – 5 and explain your responses.**

Design incorporates end-user perspectives	
Question 1	**Will the design of the research, product, platform, or process be informed by specific perspectives, needs, and preferences of end-users?** End-users are defined as individuals who will use or receive the end-result of the product, platform, device, or policy, or will be subjects of research, including but not limited to: **patients/target population, health care workers, caregivers** who are responsible for or influence health behaviors and decisions, **manufacturing/laboratory personnel,** and **regulators**. *For example:* » Include a gender analysis when developing the iTPP with teams and the cTPP with partners to surface important distinctions in gender preferences for trade-offs between efficacy and tolerability, perceived barriers to access, preferred formulation, and other attributes that are critical to uptake and adherence. » In modeling investments, addressing differential exposure to a pathogen due to norms, roles, and behaviors, such as through labor migration or mobility constraints, that are influenced by sociodemographic characteristics which can be linked to sex-specific outcomes. » Ensuring that informed consent for participation is structured on local context and researchers use appropriate methods to communicate the study to participants.
☐ **YES** ☐ **NO**	*Please explain your response:*

Sampling is inclusive and representative of the target or reference populations	
Question 2	**Will the investment ensure that research samples, subjects, and/or participants are representative of the target or reference population? This could include sex* and other sociodemographic characteristics (e.g., age, socioeconomic status, or other characteristics).** *Select YES for single sex conditions (e.g., women's contraceptive technologies, maternal health). When possible, for single sex focused studies, ensure the diverse needs, preferences, and voices of women and girls are included. *In discovery investments, sex representativeness along cell lines may not be relevant. If not relevant, select no and describe why. *For example:* » In preclinical investments, consider sex-representative human tissue and/or animal models included in the design and testing based on the target/reference population. If sex-representative tissue/models are not used, explain why. » In clinical and epidemiological research investments, are study samples reflective of the target or reference population and are sex and other sociodemographic characteristics adequately represented in the sample? If not, what are the reasons for any exclusion, such as pregnancy and lactation, or study design interventions, contraception requirements?
☐ **YES** ☐ **NO**	*Please explain your response:*

Data management and analysis plan	
Question 3	**Does the investment's data management and analysis plan include collection and reporting on data disaggregated by sex* and sociodemographic characteristics (e.g., age, caste, etc.)?** *Select YES for single sex conditions (e.g., women's contraceptive technologies, maternal health). When possible, for single sex focused studies, ensure the diverse needs, preferences, and voices of women and girls are included. *For example:* » For cell biological, molecular biological, or biochemical experiments, the origin and sex chromosome constitutions of cells or tissue cultures are stated and, if unknown, the reasons are stated. » For in-vivo and in-vitro studies, the sex of the subjects or source donors is stated (except for immortalized cell lines, which are highly transformed). » For example, in vaccine trials, will data on adverse reactions be disaggregated by sex in order to understand sex-specific outcomes, such as effects on menstruation. » For disease modelling and epidemiology studies, are the effects of other exposures on health problems examined with sex and sociodemographic characteristics considered.
☐ **YES** ☐ **NO**	*Please explain your response:*

Mitigating unintended consequences	
Question 4	**Has the investment identified potential negative consequences that affect women and girls (and where relevant men and boys) and that may arise during implementation, and have appropriate mitigation strategies been developed?** *For example:* » Safeguard against retribution for participants' involvement/participation in research studies. Ensure confidentiality and privacy for participants to protect against stigma or backlash between couples/ within households or the potential to reveal sensitive information, such as STI diagnosis or use of contraception. » Women's participation in research can lead to increased time and financial burden. Identify and include measures that compensate and support women to participate. » For non-human investments, consider any potential future harms related to sex or other sociodemographic characteristics that could be associated with this investment
☐ **YES** ☐ **NO**	*Please explain your response:*

Additional considerations	
Question 5	**In addition to the previous questions, will the investment integrate any other sex and sociodemographic considerations? If yes, please provide examples.** Non-exhaustive examples of this integration might include: » Improving pathways to market for women's health solutions. » Strengthening regulatory and science policy frameworks covering all aspects of the R&D lifecycle for medical products and healthcare innovations. » Strengthening organizational practices and effectiveness. » Training and workforce development. » Filling data gaps on disease burden, calculating ROI in women's health R&D etc.
☐ **YES** ☐ **NO**	*Please explain your response:*

STEP 3 **Count the number of 'YES' answers. If the count is 2 or less, the investment is *considered*; skip to Step 6. If the count is 3 or more, the investment is likely *responsive* or *addresses disparities in R&D*. Continue to Step 4.**

YES	
NO	

STEP 4 **Answer Question 6 and explain your response.**

Addresses disparities in R&D	
Question 6	**Does this investment explicitly address a persistent disparity or inequality in the R&D field or does this investment contribute to an overarching portfolio that makes progress toward this goal?** *For example:* » Investing in solutions for women's health and improved quality of life that address conditions across the life course and across disease areas. » Contribute to developing sex as a biological variable (SABV) best practices, or advance R&D methodologies that help standardize sex and sociodemographic specific approaches. » Updating and expanding burden of disease metrics to better account for sex and other factors that differentially impact individuals, long-term sequelae, and sociocultural biases (including input data gaps, disability weighting, and duration assumptions) in order to more accurately measure and assess conditions for women and girls (and in some cases, boys and men). » Designing studies to address gaps in information for specific sub-populations (e.g., adolescent girls, women living with HIV, and pregnancy).
☐ **YES** ☐ **NO**	*Please explain your response:*

STEP 5 **If you answered 'YES' to Question 6, the investment should be marked as *'addresses disparities in R&D'*. If you answered 'NO' to Question 6, the investment should be marked as *'responsive'*.**

FINAL ASSESSMENT

STEP 6 **Mark the correct category based on this assessment.**

☐	**Considered**
☐	**Responsive**
☐	**Addresses Disparities in R&D**

Note for clinical trials

The GF Design Analyze Communicate (DAC) Team is a service available to all PSTs: DAC reviews clinical trial protocols and other types of clinical research studies to ensure sex, sociodemographic characteristics, and other considerations have been integrated and optimized for an informative outcome. Contact dactrials@gatesfoundation.org to learn more or request a review

Legal disclaimer

This tool is intended to support foundation learning and facilitate the integration of sex and sociodemographic considerations in investment design. Data collected will be aggregated by the foundation. Individual responses will not be used to influence decisions related to specific partners or investments.