ECHO Consortium updates Q&A

2 August 2019—A Guideline Development Group (GDG) of experts convened by the World Health Organization (WHO) is reviewing the latest evidence on contraceptive use and the risk of HIV acquisition, including the results of the ECHO Study, to determine whether to recommend changes in WHO's Medical Eligibility Criteria (MEC) guidance. As the group considers the evidence, the ECHO Consortium has added information to the ECHO 'Q&A' fact sheet to provide additional background on the design and conduct of the trial.

The updates, summarised in this statement, provide clarification on how the research protocol was developed and the ethical safeguards built into that design.

The research protocol for the ECHO Study was designed over several years (2012-15) through an extensive consultative process. In 2012, as the trial was being proposed, formative research was conducted to assess what level of difference in HIV risk associated with a contraceptive would be likely to prompt changes in policies or programmes. This question was also among those discussed in meetings and teleconferences that the ECHO investigators convened with a range of stakeholders before and during protocol development. During this time, the available observational data in aggregate suggested a possible 50 percent increase in HIV risk with use of intramuscularly injected depot medroxyprogesterone acetate (DMPA-IM) compared to no method, and an observational study published in 2011 had associated DMPA-IM use with a doubling (100% increase) in the risk of HIV acquisition. However, these observational data were considered to be of low quality and subject to substantial biases.

The stakeholders consulted included researchers with expertise in HIV prevention and contraception, policy and programme officials in Africa and globally, ethicists, and HIV advocates and women's health advocates from the African region and from other global networks. The ECHO team also asked the Research Protocol Review Panel of WHO's Special Program of Research, Development, and Research Training in Human Reproduction and the Prevention Science Research Committee of the US National Institute of Allergy and Infectious Diseases, US National Institutes of Health, to conduct independent scientific and ethical reviews of the protocol. Through these consultations and reviews, a study design with the statistical power to detect a 50 percent difference in HIV risk between any pair of the three contraceptive methods studied was determined to be most appropriate.

This collaborative approach also helped the ECHO Consortium design and conduct the ECHO Study with careful attention to the rights and interests of participants. The motivation and driving force behind ECHO was a commitment to the health and wellbeing of women, and these same principles guided the conduct of the study.

The trial was collaboratively designed and implemented with joint African, WHO and U.S. scientific input, and began only after extensive scientific, ethical and community

consultation. Nine independent ethics review committees — including five based in African institutions — reviewed and approved the ECHO Study protocol.

Women participating in the trial engaged in a comprehensive informed consent process conducted in their respective local languages. The process involved multiple counselling sessions, testing of their understanding of the study before enrolment, formal reinforcement of the informed consent at each study visit, and documentation of written informed consent. After the WHO MEC categorisation for injectable contraceptives was changed in March 2017 (from a "1" to a "2" for women at high risk of HIV), the ECHO Consortium revised its informational materials and informed consent forms and discussed this change with each participant in the trial. The ECHO trial investigators respect and greatly appreciate the decisions made by the 7,829 women who chose to participate in the trial.

At each of the 12 study sites, the conduct of the ECHO Study was driven and monitored through a site-specific Good Participatory Practice plan. Every site had a Community Advisory Board (CAB), and the site teams communicated regularly with the CABs, providing updated information about the trial and receiving feedback from the community and its representatives. ECHO was also to our knowledge the first multi-country trial to have a Global Community Advisory Group (GCAG) that included advocates for women's health and rights from each of the countries where the study was conducted. GCAG members advised the study team on the study's protocol and its conduct before, during and after the trial was completed, including review of the informed consent process prior to study initiation and during the study when the informed consent process was modified.

Through commitment and adherence to the highest global standards for research ethics, human subjects' protection, Good Participatory Practice and rigorous clinical trial conduct — and with respect for and full engagement with the women who volunteered to participate —the ECHO Study achieved exceptionally high retention and continuation. The successful completion of a randomised trial on this important, complex topic has provided high-quality data that can be used to help women, first and foremost, make more informed decisions about their health and to develop policies and programmes that provide the options they need for HIV prevention and contraception.