

Multipurpose Prevention Technologies (MPTs)

An Introductory Factsheet

June 2016

This fact sheet provides basic information on multipurpose-prevention options. For more basic fact sheets in this series on emerging HIV prevention tools visit www.avac.org/intro.

The Need

Women need a variety of prevention strategies for different needs. They need protection against HIV and other STIs, as well as the prevention of unwanted pregnancies. Today only male and female condoms do both. But these methods require partner negotiation and cooperation which can be a challenge. Many women may not know the full range of options or be able to find them from trained providers. They may not be able to access or pay for them. Women have long asked for methods that meet HIV prevention and family planning needs and are easy to use—and work is underway to develop these “multipurpose prevention technologies”.

The Products

Multipurpose prevention technologies (MPTs)—most of which are still experimental—are designed to address two or more sexual and reproductive health concerns simultaneously; for example, combining protection against unintended pregnancy and at least one sexually transmitted infections. Both male and female condoms prevent against HIV, other STIs and pregnancy and so are important examples of MPTs that already exist. Additional choices that are not reliant on partner cooperation are needed for women to have more control of their sexual and reproductive health.

Effective, affordable, and widely available MPTs would save lives and money, improving the health of women and their families across the globe.

The good news is that there are nearly a dozen MPTs in clinical trials, with many other innovative technologies in earlier stages of development. MPTs in development include:

- Longer-acting vaginal rings
- Fast-dissolving films and tablets
- Innovative and effective gels
- Injectables that combine contraception and protection against infection
- Nanofiber delivery systems

The MPT product development box shows a variety of possible technologies. *Indication* lists possible health issues addressed by MPT. *Delivery Mode*: lists technology by type, e.g. vaginal gel, pill or injection. *Mechanism by action*: lists the range of biological action MPT can be designed to perform, e.g. physical barrier, hormonal contraceptive [HC]. *Dosage & Administration* lists methods to administer dosage, e.g. daily pill, topical application, sustained through the blood, taken around the time of sex (on-demand).

Resources and Links

AVAC www.avac.org

Initiative for Multipurpose
Prevention Technologies
www.theIMPT.org

CONRAD www.conrad.org

International Partnership
for Microbicides
www.ipm.org

Population Council
www.popcouncil.org

MPT Product Development: Many possibilities for MPT development

Indications	Delivery Modes	Mechanisms of Action	Dosage & Administration
BV*	Diaphragm*	Anti-microbial*	Oral daily*
Candida	Film*	Anti-fungal	Oral on-demand Gel*
Chlamydia*		Anti-viral*	Systemic sustained*
Gonorrhea*	Implant	Barrier*	Topical daily*
HIV*	Injection*	HC *	Topical on-demand*
HPV*	Intrauterine Device	Non-HC*	Topical sustained
HSV*	Oral pill*	Probiotic	
Pregnancy*	Ring (Non-IVR)		
Syphilis	Ring (IVR)*	*Currently being tested in human clinical trials.	
Trichomoniasis	Tablet*		

The Pipeline

The table below highlights a few products for both sustained-release and on-demand (peri-coital) products. Women will have different needs and preferences throughout their lives. A variety of products is key to meeting the needs of different women.

MPT Products in the Pipeline: Selected highlights	
Products not requiring daily-use	Products used around the time of sex
90-day IVR (LNG and tenofovir) An intravaginal ring (IVR) that stays in for 90 days and releases two hormones, levonorgestrel (LNG) for contraception and tenofovir for HIV and HSV-2 prevention. <i>(Developer: CONRAD)</i>	mapp66 (mAB)Film A combination of 3 monoclonal antibodies (mABs) delivered through a biodegradable film for protection against HIV and HSV-2. <i>(Developer: Mapp Biopharmaceutical, Inc.)</i>
90-day IVR (dapivirine and LNG) An intravaginal ring (IVR) that stays in for 90 days and releases a combination of dapivirine to prevent HIV and levonorgestrel-releasing hormone (LNG) to prevent pregnancy. <i>(Developer: IPM)</i>	Vaginal insert (tenofovir and TFV/FTC) Fast-dissolve vaginal tablets with tenofovir alone and tenofovir combined with emtricitabine (TDF/FTC) for HIV and HSV-2 protection. <i>(Developer: CONRAD)</i>

Acronyms

HC – Hormonal contraception

IVR – Intravaginal ring

LNG – Levonorgestrel-releasing hormone (hormonal contraceptive)

mAB – Monoclonal antibody

TDF – Tenofovir

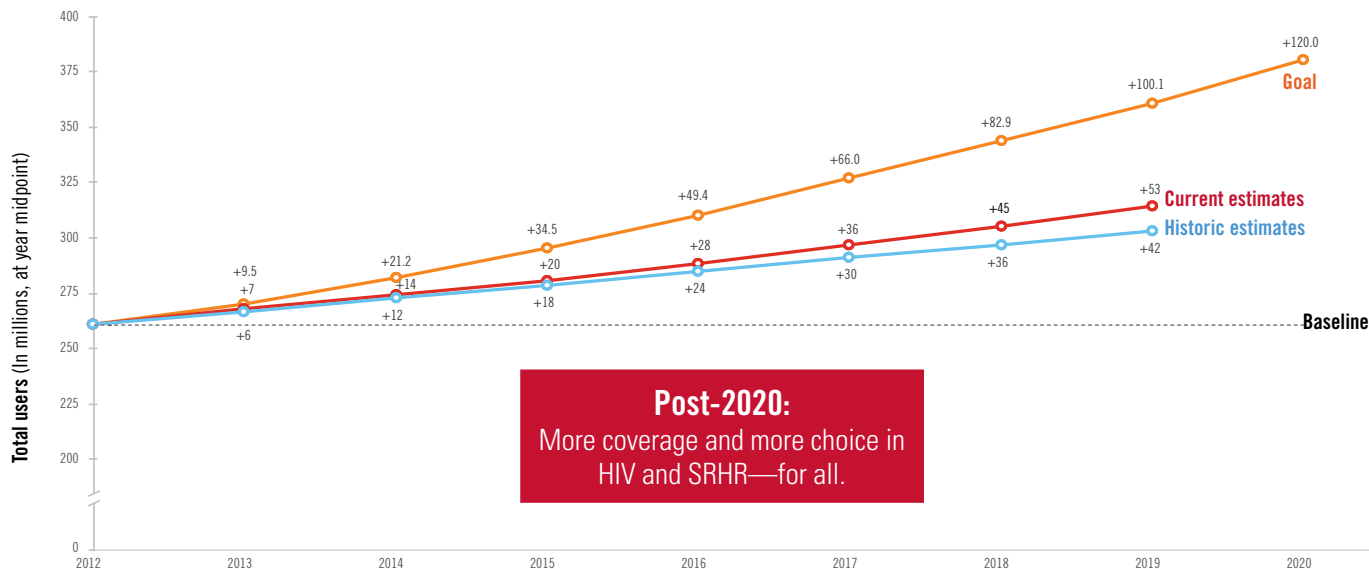
TDF / FTC – Tenofovir / emtricitabine

* There are mixed data regarding the impact of Depo-Provera (DMPA) on women's risk of acquiring HIV. A meta-analysis commissioned by the WHO recently found increasing concern, and research is ongoing. See www.avac.org/hc-hiv for more information on the state of the science, advocacy and research related to this issue.

About AVAC | AVAC is a non-profit organization that uses education, policy analysis, advocacy and a network of global collaborations to accelerate the ethical development and global delivery of new HIV prevention options as part of a comprehensive response to the pandemic. This fact sheet is part of the Women's HIV Prevention series, created to address HIV prevention strategies and the advocacy needed to bring them to reality.

Total and Additional Users of Modern Contraception, 2012-2019

In November 2019, FP2020 released "Women at the Center: 2018-2019" (<http://progress.familyplanning2020.org/>), its latest progress report from which this graphic is adapted. As its graphic below shows, coverage of modern contraception in the 69 low income countries that partner with FP2020 in tracking progress has increased since 2012, but not at the pace needed to meet the FP2020 goal. The group has also launched a post-2020 vision, and AVAC looks forward to working together towards an integration agenda.



Developing and Introducing a Dual Prevention Pill

Oral PrEP & oral contraceptive for HIV and pregnancy prevention

APRIL
2020

Background

A coalition of partners is developing a novel Dual Prevention Pill (DPP) for prevention of pregnancy and HIV acquisition in high-need countries. Women in sub-Saharan Africa are disproportionately affected by HIV compared to men, and 214 million women of reproductive age in the developing world have an unmet need for contraception.¹ In particular, young women ages 15-24 in sub-Saharan Africa account for 71 percent of new infections in their age group and 29 percent of new infections among adults in the region.² As the “youth bulge” results in millions of young people entering their reproductive years,³ it will impact efforts to end the HIV epidemic and reduce unintended pregnancies. It is critical to ensure all women have access to both contraception and HIV prevention.

The results of the Evidence for Contraceptive Options in HIV Outcomes (ECHO) Trial, released in June 2019, found that HIV incidence rates were alarming among women using widely available forms of contraception who were receiving a comprehensive HIV prevention package.⁴ The findings underscore the urgent need to optimize access to HIV prevention and contraception for African women.

Contraceptive multipurpose prevention technologies (MPTs) have the potential to overcome adherence and uptake challenges seen with oral pre-exposure prophylaxis (PrEP) and stigma associated with HIV service delivery. A DPP, an MPT comprising oral PrEP and an oral contraceptive, will offer significant advantages. It will be highly effective at preventing both HIV and pregnancy when used daily, feasible to deliver in various settings, with the potential to deliver public health impact by expanding choice and method mix. Adding an MPT to the available method mix could empower users with choices that better fit their needs and lives.

In the near-term, a DPP could increase the uptake of PrEP — decreasing new infections among women in high-burden settings — and reduce the number of unintended pregnancies. A DPP could also lay the groundwork for the development and rollout of other MPTs currently in the research pipeline, such as vaginal rings, injectables, implants and films.

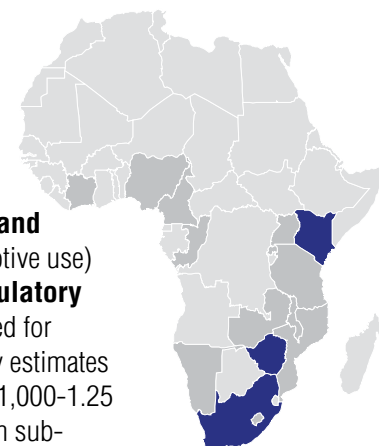
Project Goal

Rapidly and successfully introduce a daily oral pill for HIV and pregnancy prevention.

A coalition of organizations, including AVAC, the Clinton Health Access Initiative (CHAI), Mann Global Health, Mylan and the Population Council are implementing the DPP project. These efforts are supported by the Children's Investment Fund Foundation (CIFF), the Bill & Melinda Gates Foundation (BMGF), the U.S. Agency for International Development (USAID) and WCG Cares.

Geographic Scope

Settings that demonstrate **need** (high HIV incidence and high unmet need for modern contraception), **potential demand** (current oral PrEP and contraceptive use) and **enabling policy and regulatory environments** will be prioritized for early DPP introduction, but early estimates indicate a potential market of 251,000–1.25 million women in 15 countries in sub-Saharan Africa.⁵



PRIORITIZED COUNTRIES

INDICATOR	KENYA	SOUTH AFRICA	ZIMBABWE
HIV Incidence (per 1,000 population) ²	1.02	4.94	2.79
New HIV Infections, (# women 15+) ²	24,000	140,000	19,000
Unmet Need for Modern Contraception (%) ⁶	20.3	15	9.9
Unintended Pregnancies (#) ⁶	956,000	1,060,000	298,000
Oral Contraceptive Use (% of method mix) ⁶	14.1	12.3	56.5
Total PrEP Initiations (#) ⁷	56,000	44,304	17,588

¹ FP 2020, FP2020 Catalyzing Collaboration 2017-2018. <http://progress.familyplanning2020.org/>. 2019.

² UNAIDS 2019 data.

³ UNAIDS, The Youth Bulge and HIV. https://www.unaids.org/sites/default/files/media_asset/the-youth-bulge-and-hiv_en.pdf. 2018.

⁴ ECHO Trial Consortium, HIV incidence among women using intramuscular depot medroxyprogesterone acetate,

a copper intrauterine device, or a levonorgestrel implant for contraception: a randomised, multicentre, open-label trial, *Lancet* 2019; 394: 303–13.

⁵ Population Council, Oral cMPT Market Sizing Report. 2020 (forthcoming).

⁶ FP2020 Core Indicator Summary Sheet: 2017-2018 Annual Progress Reports.

⁷ AVAC, Global PrEP Tracker, Jan. 2020.

Key Milestones for Dual Prevention Pill Development



A single **co-formulated tablet** containing Truvada and combined oral contraceptive (COC) active pharmaceutical ingredients (APIs) is under development.

Conduct bioequivalence study to compare bioavailability of co-formulated tablet to Truvada and COC separately.

File dossier with SRA for regulatory approval.



To shape product development and demand creation strategies, **conduct human-centered design research** in South Africa and Zimbabwe on perceptions, barriers, and motivators of end users, providers and influencers as they relate to the DPP.

To inform clinical cross-over acceptability studies, **conduct formative research** to understand perspectives on the DPP among women, health care providers, community members and key opinion leaders.

Conduct clinical cross-over acceptability studies in South Africa and Zimbabwe to compare women's experiences using a DPP to two separate Truvada and COC pills.



Establish Advisory Board with leading research entities, normative agencies, donors, implementers and advocates working on HIV and SRHR to plan for and coordinate introduction of the DPP in parallel with product development activities.

Engage with policymakers, regulators, civil society and key opinion leaders in HIV and SRH **to generate buy-in, shape introduction plans, understand potential market size and inform regulatory strategies** for DPP introduction.

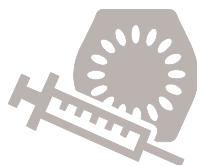
Develop a comprehensive Go-To-Market Strategy with global and national stakeholders.

2020	2021	2022	2023
<ul style="list-style-type: none"> Go-To-Market Strategy approved Investment case developed Human-centered design and formative research conducted 	<ul style="list-style-type: none"> Donor commitments secured to operationalize Go-To-Market Strategy Clinical cross-over acceptability studies begin 	<ul style="list-style-type: none"> Pilot introduction projects developed Bioequivalence study results available 	<ul style="list-style-type: none"> Target introduction in prioritized countries

* Timelines are subject to modification given funding, government buy-in, development feasibility, and regulatory requirements.

For inquiries, updates and resources on the development of the DPP, please visit prepwatch.org/dpp.





Hormonal Contraceptives and HIV

An Introductory Factsheet

June 2019

Information is constantly evolving on hormonal contraceptive methods, their impact on HIV risk in HIV-negative women, and their use in women living with HIV. We encourage you to supplement this factsheet with a visit to www.avac.org/hc-hiv for the most recent information.

What are the available data about hormonal contraceptive use and risk of HIV infection?

The data are mixed. Some studies suggest that use of certain hormonal contraceptives—particularly injectable progestogen-only methods like Depo-Provera (DMPA)-IM and NET-EN—increase women’s risk of HIV infection. Other studies do not show an association between hormonal contraceptives, particularly DMPA-IM, and HIV risk. Far more information is available on DMPA-IM than on NET-EN at the moment, and that information primarily comes from observational data. This refers to data derived from trials or studies originally designed to answer other questions. Observational data is hard to analyze since there are many variables that could have influenced or biased the outcome.

The Evidence for Contraceptive Options and HIV Outcomes Study, or ECHO, is a randomized clinical trial designed to compare the risks of acquiring HIV among women who used copper intrauterine device (IUD), a levonorgestrel (LNG); Jadelle implant, and DMPA-IM. Results are expected by July 2019.

Resources and Links

AVAC

www.avac.org/hc-hiv

WHO

www.who.int/reproductivehealth/publications/family_planning/HC-and-HIV-2017/en

How are available data being used to guide contraceptive use and programs?

As of March 2017, the World Health Organization’s (WHO) Guidance Statement on “Hormonal contraceptive eligibility for women at high risk of HIV” states that there “continues to be evidence of a possible increased risk of acquiring HIV” among women using DMPA, NET-EN and other progestogen-only injectables. The guidance states that women should be counseled about this risk, and that no woman should be denied her method of choice, regardless of HIV risk. Even with this possibility, DMPA and other injectables remain important options, including for women living with HIV.

What exactly do available data say?

As of July 2016, a WHO-commissioned systematic review of available data found “increased concern” regarding the impact of DMPA-IM on HIV-negative women’s risk of HIV acquisition.

A “systematic review” involves gathering all available evidence on an issue, evaluating the quality of that evidence and summarizing it to provide a reliable overview of knowledge on a topic. Such reviews are often conducted by teams of independent researchers who agree on search terms and criteria for identifying quality evidence. This was the approach used in the WHO publication.

Two previous systematic reviews concluded that there was uncertainty about the relationship between DMPA-IM and HIV risk. This latest review indicates concern but does not draw a firm conclusion. The key findings from the 2016 review are summarized below:

- Data on the oral contraceptive pill and levonorgestrel implants do not suggest an association with HIV acquisition, though data on implants are limited. *Right now, there’s no suggestion that hormonal methods other than progestogen-only injectables might impact HIV risk. But the information available on some methods is limited.*

- The 2016 review noted that a previous systematic review had suggested a possible association between NET-EN and increased HIV risk, but the updated review did not show this association. *In March 2017, WHO gave NET-EN a “MEC 2” rating indicating that there is a possible increased HIV risk among users, but emphasized that while women should be informed about this possibility, they should not be restricted from choosing this or another contraceptive method.*
- Newer, higher-quality observational data on DMPA-IM, added to previous information, increase concerns about DMPA-IM use and HIV acquisition in women. *The cumulative data strengthen concerns that DMPA-IM might be increasing women’s HIV risk.*
- The study states that, “Recent analyses contradict the hypothesis that differential over-reporting of condom use by HC users explains observed associations between HC use and HIV infection in some studies.” *The argument that women who use DMPA-IM also use fewer condoms than women who choose other methods has been suggested to explain previous data. It’s important to note that this review directly addresses this argument and supports research suggesting that it is not valid.*

What’s the difference between hormonal contraceptive methods?

All hormonal contraceptive methods contain synthetic versions of the hormones that orchestrate women’s menstrual cycles. These synthetic hormones change the normal cycle in ways that prevent pregnancy. Hormonal contraceptives differ by type of synthetic hormone(s), level of dosage or frequency of dosage, and they include pills, injections and implants. Not all contraceptives use hormones. Non-hormonal methods include the copper intrauterine device (IUD), diaphragms, male and female condoms and others. Right now, concern around HIV risk is focused only on hormonal methods because they affect the lining of the genital tract as well as the immune environment. Non-hormonal methods like the copper IUD and male and female condoms do not have the same effects on the genital tract.

Do all hormonal contraceptives have the same effects on the genital tract?

No. Different contraceptive methods contain different synthetic hormones and/or different doses of the same synthetic hormones.

Is the current discussion on potential increased HIV risk about all hormonal contraceptives?

When it comes to concern about impact on HIV risk, the main focus is on DMPA-IM. Extensive data on the oral contraceptive pill offers no indication of increased HIV risk. Data are available on these two methods because the oral pill and DMPA-IM are among the most widely used contraceptive methods in sub-Saharan Africa.

This doesn’t mean that other hormonal methods do not affect HIV risk—there just isn’t as much information about rates of HIV in women who use them. NET-EN is also classified as having a possible association with HIV risk, however there are fewer data on this specific method than there are on DMPA-IM. Many other gaps in the data exist. For example, there are no data on a hormonal contraceptive called Sayana Press (also known as DMPA-SC), which is being rolled out globally and uses the same hormone found in DMPA-IM but at a lower dose.

What are the primary concerns for women living with HIV?

Drug interactions are an issue for women living with HIV. Do antiretroviral therapy (ART) regimens undermine contraceptive efficacy or vice-versa? There is some evidence that the hormones found in some contraceptive methods interact with some antiretrovirals (ARVs). For example, the efficacy of implants containing the synthetic hormone called etonogestrel can be adversely impacted by ARV treatments containing efavirenz. There may be more method failure—increased pregnancy rates—in women taking etonogestrel and efavirenz. There is evidence of interactions between ARVs and some other synthetic hormones as well. This is one of many reasons why DMPA-IM and a full range of contraceptive options need to be available for all women. At this time, no evidence suggests any contraceptive method increases women’s risk of transmitting HIV.

Who is most impacted by the concern about DMPA-IM, NET-EN and HIV risk?

Over the past several years, the question of what to do if DMPA-IM impacts women's risk of HIV has been widely debated, as has the question of where action, if any, should be taken. These debates reflect a painful reality: in East and Southern Africa, DMPA-IM is often the only discreet, long-acting method available to women, and HIV incidence is especially high among adolescent girls and young women. In an ideal world, all women, including those in East and Southern Africa, would have access to a full range of contraceptive methods, along with HIV prevention and treatment. Providers would have adequate time for counseling, and supplies would be on the shelves at all times. In such a context, a finding about DMPA-IM or any other method would be relatively simple to respond to: change the counseling messages, inform women, let them make the choice. However, in today's context of restricted options, human resource gaps and siloed programming, this isn't possible—yet.

A woman-centered approach that expands method mix, integrates HIV and family planning programs, and supports women, peers and providers in conversations based on informed choice is needed everywhere. Funders, governments and policy makers must act affirmatively to protect contraceptive access, including access to DMPA-IM, as an option for many women, including HIV-positive women.

Will there ever be a clear answer about how different contraceptives affect HIV risk?

The Evidence for Contraceptive Options and HIV Outcomes Study, known as ECHO, is designed to compare the risks of acquiring HIV among women who used the copper IUD, a levonorgestrel implant (Jadelle), and DMPA-IM. From 2015-2018, the trial recruited 7,830 women in eSwatini, Kenya, South Africa and Zambia who were sexually active, HIV-negative, ages 16-35, seeking highly effective contraception and willing to be randomly assigned to use one of three contraceptive methods. All of the women received counseling about the risks and benefits of the study method they were assigned to, HIV risk reduction and, where available, were offered oral PrEP either at a study site or through a referral. Daily oral PrEP—a single pill containing a tenofovir-based drug—taken correctly and consistently reduces risk of HIV acquisition in women and men.

The trial's primary question is: what are the relative rates of new cases of HIV among HIV-negative women randomly assigned to either DMPA-IM, the Jadelle implant or the copper IUD? The findings of the study may clarify if one (or more) of the evaluated methods increase women's risk of HIV compared to the other methods in the trial. It's also possible that the trial won't provide definitive answers. The data are now being analyzed and results are expected by July 2019.

For the latest on ECHO, visit www.avac.org/hc-hiv.

What's needed now?

The following actions are of paramount importance to ensure informed choice and should be ongoing. Many of these are recommended or suggested by the March 2017 WHO guidance on hormonal contraception and HIV.

- **Programs, policies and messages should reflect women's *right to know* all available information regarding the contraceptive method(s) they are being offered.** Women weigh risks and benefits all the time. If properly delivered, information about hormonal contraceptives and HIV risk should not cause women to abandon contraception or their method of choice.
- **Investment in programs should provide women with choices in contraception and HIV prevention.** In most of East and Southern Africa, DMPA-IM is the only invisible, long-acting method available for women. The way to learn about preference is to increase the number of options that women can choose from (improve method mix), train providers and engage with women as experts on their own lives.
- **Ongoing engagement with women affected by these issues is essential.** Their perspectives and experiences must guide policy, programs and messaging.

Do hormonal contraceptives protect against HIV infection?

No. Hormonal contraceptives do not protect against HIV or other STIs. Currently, there are no contraceptives, with the exception of condoms (male and female), that protect against HIV. Women using hormonal contraceptives must also use a condom or take other measures to protect themselves against HIV.

What is the history of World Health Organization guidance regarding hormonal contraceptive use and HIV risk?

Since 1991, there have been data suggesting a possible link between some hormonal contraceptives and HIV. The WHO has been tracking the issue for many years and has reflected its analysis in the grading system it uses to classify contraceptive methods. This grading system is known as the Medical Eligibility Criteria, or MEC. For a plain language explanation of the MEC see AVAC's fact sheet, "What is up with DMPA and 'grades' for family planning?" available at www.avac.org/dmpa-grades.

In early 2012, the World Health Organization issued a "technical statement" on hormonal contraceptives and HIV risk that stated: "The World Health Organization should continue to recommend that there are no restrictions (MEC Category 1) on the use of any hormonal contraceptive method for women living with HIV or at high risk of HIV." However, the statement recommended a clarification that changed the grade to a MEC 1*. The clarification stated that

[B]ecause of the inconclusive nature of the body of evidence on possible increased risk of HIV acquisition, women using progestogen-only injectable contraception should be strongly advised to also always use condoms, male or female, and other HIV preventive measures. Expansion of contraceptive method mix and further research on the relationship between hormonal contraception and HIV infection is essential.

In 2014, WHO updated this technical statement. DMPA-IM and other similar methods remained a MEC 1* with the additional recommendation that women at risk of HIV selecting DMPA-IM be informed of the mixed data regarding that method's impact on risk of HIV acquisition. In March 2017, WHO updated guidance changes the MEC from a 1* to a 2.

WHO has said that immediately after ECHO results are released, it will release a statement to provide context for countries and other stakeholders on the next steps. After the statement, WHO will initiate its formal guideline review process to see how the ECHO trial impacts the current contraceptive guidance. This process can be lengthy; but WHO has committed to working on an accelerated timeline. African women impacted by the data must also be involved in this process.

AVAC | AVAC is a non-profit organization that uses education, policy analysis, advocacy and a network of global collaborations to accelerate the ethical development and global delivery of new HIV prevention options as part of a comprehensive response to the pandemic.