(1) Does the application adequately address the issue of the public health need for the medicine?

Yes ☑ No ☐

Please provide brief details:
The important role that family planning contributes toward advancing maternal and newborn health, and toward the achievement of UN Millennium Development Goal (MDG) 5, including reduced maternal mortality and universal access to reproductive health care, is well understood. Yet significant inequalities in access to modern contraception in developing countries continue, and unintended pregnancies, particularly those which are high-risk, remain a barrier to meeting the MDGs in many countries.

Long-acting reversible contraceptives (LARCs) are especially effective in preventing unintended pregnancies. With typical use, LARCs are the most effective at preventing pregnancy, the most cost-effective, and are associated with the highest levels of satisfaction and continuation of all reversible methods. In 2012, the UN Commission on Life-Saving Commodities for Women and Children prioritized implants as one of 13 life-saving commodities and the preferred long-term contraception method.

(2) Have all important studies that you are aware of been included in the application?

Yes ☑ No ☐

Please provide brief comments on any relevant studies that have not been included:

(3) Does the application provide adequate evidence of efficacy/effectiveness of the medicine for the proposed use?

Yes ☑ No ☐

Briefly summarise the reported outcomes (e.g. clinical, surrogate, other) and comment, where possible, on the magnitude of clinical benefit associated with use of the medicine:

No significant differences were found in the rate of pregnancies between IMPLANON and the other LARCs considered. All comparisons had ORs with 95% confidence intervals (CI) that included 1, or no pregnancies occurred in the studies.

No statistically significant differences in the rates of continuation were observed between IMPLANON and Norplant, nor between IMPLANON and Jadelle. Continuation rates for IMPLANON were significantly higher compared to DMPA within the first year of use (no data available beyond a year). No statistically significant differences in the rates of
continuation were observed between IMPLANON and Cu-IUD at Year 1 or overall. Continuation rates for IMPLANON were significantly lower compared to the Cu-IUD only at Year 2 and compared to LNG-IUD.

(4) Is there evidence of efficacy in diverse settings and/or populations?
Yes [ ] No [ ]

Please provide brief details:
Studies have been conducted in both developed (US, Finland, Sweden, France, Ireland, Slovakia, United Kingdom) and developing countries (Turkey, Thailand, Indonesia, Brazil, Chile, Dominican Republic, Hungary, and Zimbabwe).

(5) Has the application adequately considered the safety and adverse effects of the medicine? Are there any adverse effects of concern, or that may require special monitoring?
Yes [ ] No [ ]

Please provide brief details:
Bleeding patterns reported among continuing patients treated with IMPLANON were:
- Amenorrhea: 32% at the end of Year 1 and 35% at the end of Year 2
- Infrequent bleeding: 27% at the end of Year 1 and 24% at the end of Year 2
- Frequent bleeding: 3% at the end of Year 1 and 2% at the end of Year 2
- Prolonged bleeding: 8% at the end of Year 1 and 5% at the end of Year 2
The percentage of subjects using IMPLANON who discontinued due to bleeding issues over the full duration of studies was 0.07% due to amenorrhea and 5.5% discontinuing due to any bleeding issue

ADDITIONAL CONSIDERATIONS:

(6) Are there special requirements or training needed for the safe, effective and/or appropriate use of the medicine?
Yes [ ] No [ ]

Please provide brief details:
Insertion and removal need training. Insertion and removal of IMPLANON should be performed under aseptic conditions and only by a qualified health care provider who is familiar with the procedure. Insertion of the implant should only be performed with the preloaded applicator.

(7) Are there any issues regarding the registration of the medicine by regulatory authorities? (e.g., recent registration, new indications, off-label use)
Yes [ ] No [ ]

Please provide brief details:
IMPLANON is registered in over 115 countries across the globe, and is available in a further 14 countries without formal registration.

(8) Is the medicine recommended for use in a current WHO GRC-approved Guideline (i.e., post 2008)?

Yes ☐ No ☐

Please provide brief details:
Both IMPLANON and IMPLANON NXT are prequalified by the WHO.
IMPLANON is also included in the WHO Medical Eligibility Criteria for Contraceptive Use, where it is rated 1 (no restriction) or 2 (advantages outweigh theoretical or proven risks) for most of the conditions listed. It is also included in a host of other national guidelines, including the American College of Obstetricians and Gynecologists (ACOG), American Academy of Pediatrics, and the NICE LARC Guidelines published in 2014.

(9) Please comment briefly on issues regarding cost and affordability of this medicine.
In May 2013, building on previous partnerships, Merck and a group of public sector partners announced an agreement to further expand contraceptive access to women in some of the world’s poorest countries. Under the agreement, Merck reduced the cost of IMPLANON and IMPLANON NXT by approximately 50 percent for the next six years in the targeted poorest eligible countries of focus of the reproductive health community. Together, these countries account for 70+% of unmet need in the developing world.

(10) Any additional comments?

(11) Please summarise the action you propose the Expert Committee takes.
IMPLANON is a highly-effective long-acting reversible contraceptive (LARC) that provides excellent prevention of pregnancy (less than 0.058 pregnancy per 100 implants sold), and that is characterized by a rapid onset of action and a rapid return of fertility after removal.
IMPLANON is particularly well-suited for use in low-resourced settings. As a LARC, efficacy does not depend on daily, weekly or monthly administration. This reduces the potential administrative burden on women, and makes compliance user independent. The pre-loaded sterile, single-use applicator for IMPLANON makes it particularly beneficial for mobile clinics, settings with limited infrastructure and rural environments. In addition, it avoids the need for manual manipulation of the rods themselves. IMPLANON is effective for up to 3 years, which makes it ideal for birth spacing.
These features make IMPLANON a strong candidate for inclusion in the WHO List of Essential Medicines, in addition to the currently-listed levonorgestrel implant. The inclusion of more than one implant in the EML affords countries the opportunity to choose the implant that best meets their needs.