This is my response to the FDA Resolution on Implanon (Etonogestrel) dated 10 November 2017. A part of the resolution stated that:

<table>
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<th>FDA RESOLUTION ON CASE NO. 2017-014</th>
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<td>Released on 10 November 2017, page 5</td>
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Based on the findings of FDA TWG, as supported by the findings of the Expert Review Group, Implanon, with generic name Etonogestrel, does not induce abortion. Its primary mechanism of action is inhibition of ovulation through the control of hormones both estrogen and progesterone, while its secondary mechanism of action is the thickening of cervical mucus and may cause the alteration of endometrial structure (thinning of endometrial lining).

The FDA resolution correctly stated the mechanisms of action of Implanon (Etonogestrel): (1) prevention of ovulation, (2) thickening of cervical mucus, and (3) thinning of endometrium. This mechanism of action is clearly stated in this review study:

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<th>EUROPEAN JOURNAL OF CONTRACEPTION AND REPRODUCTIVE HEALTH CARE</th>
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<td>“The contraceptive efficacy of Implanon: A review of clinical trials and marketing experience”</td>
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<td>Olivier Graesslin and Tjeerd Korver</td>
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<td>June 2008, Volume 13, pages 4-12</td>
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Beside inhibition of ovulation, etonogestrel also causes changes in the cervical mucus, which hinder the passage of spermatozoa, and thinning of the endometrium making it less suitable for nidation.
However, the FDA is erroneous in saying that Implanon does not induce abortion. In trying to prove that Implanon does not prevent implantation, the FDA resolution mentioned the following:

The FDA assertion that Implanon can cause thinning of the endometrium when the user is not ovulating but this effect will be reversed such that Implanon will suddenly “act to augment the endogenous hormones” when the user has breakthrough ovulation is absurd and defies medical knowledge! It ignores scientific facts!

These are the scientific facts:

1. The rate of implantation failure is higher with thin endometrium.
2. Other than thinning the endometrium, the molecular effects of implanon can further render the endometrium unsuitable for implantation.
3. Ectopic pregnancy rates are higher for implanon which proves that more breakthrough ovulation pregnancies fail to implant in the endometrium.

Evidence to support these three stated scientific facts shall be presented in this paper.
1. The rate of implantation failure is higher with thin endometrium.

It is common medical knowledge that the normal thickness of the secretory/luteal phase endometrium is 8-14 millimeters. The secretory/luteal phase endometrium transforms into the decidua during pregnancy on which the embryo will implant. Studies on in-vitro fertilization have shown that the cutoff endometrial thickness for successful implantation of an embryo is 9 millimeters. Research done on Implanon users showed that their mean endometrial thickness is 2.9 millimeters, markedly thinner than the thickness required for successful implantation.

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**REPRODUCTIVE BIOLOGY AND ENDOCRINOLOGY**

“The effect of endometrial thickness and pattern measured by ultrasonography on pregnancy outcomes during IVF-ET cycles”

Jing Zhao, Qiong Zhang and Yanping Li

2012, Volume 10, pages 1-6

The endometrial thickness predicts pregnancy outcome with high sensitivity and specificity. The cutoff value was 9 mm.

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**ULTRASOUND IN OBSTETRICS AND GYNECOLOGY**

“Ultrasoundographic features of the endometrium and the ovaries in women on etonogestrel implant ”


2002, Volume 20, pages 377-380

The mean endometrial thickness (ET) on ultrasound was 2.9 mm (standard deviation, 2.0).

The etonogestrel implant has direct effects on the endometrial progestin target sites and indirect effects by suppression of the hypothalamo–pituitary–ovarian axis leading to ovulation inhibition. This results in an inactive or weakly proliferative endometrium. Our findings confirm previous reports that the endometrial thickness on ultrasound scan does not usually exceed 4–5 mm.
2. Other than thinning the endometrium, the molecular effects of Implanon can further render the endometrium unsuitable for implantation.

These are the molecular effects of Implanon on the endometrium:

It is quite clear that the molecular effects of Implanon make the endometrium more fragile which predisposes it to bleed. The study has clearly established that Implanon damages the superficial blood vessels and the integrity of endometrial surface epithelium.

All of these molecular changes induced by Implanon effectively renders the endometrium less favorable to implantation of an embryo.
3. Ectopic pregnancy rates are higher for Implanon which prove that more breakthrough ovulation pregnancies fail to implant in the endometrium.

There are some studies that report an increase in the ectopic pregnancy rates for women using Implanon. This is further proof that implantation is affected by Implanon. Normal implantation is implantation of the embryo on the endometrium inside the uterine cavity. Ectopic pregnancy is abnormal implantation of the embryo outside of the uterus.

CONTRACEPTION
“Ectopic pregnancy with use of progestin-only injectables and contraceptive implants: a systematic review”
Rebecca Callahan, Irina Yacobson, Vera Halpern, Kavita Nanda
2015, Volume 92, pages 514-522

The only other progestin used in currently marketed implants (Implanon/Nexplanon) is etonogestrel. Only three studies of implants containing this progestin report any pregnancies; two of these studies were with the marketed product Implanon including a review of postmarketing surveillance data. While five of the 218 pregnancies reported in that review were ectopic, because of data limitations, it is unknown how many of them occurred among women who had the device in situ.

PERSPECTIVES ON SCIENCE AND CHRISTIAN FAITH
“The Oral Contraceptive as Abortifacient: An Analysis of the Evidence”
Dennis M. Sullivan
September 2006, Volume 58, pages 189-195

Progestin implants (e.g., Norplant) offer the advantage that compliance is not an issue. They are also more effective than Progestin-Only-Pills or POPs in preventing ovulation. However, for unclear reasons, the ectopic pregnancy rate is also statistically higher when (rarely) breakthrough ovulation does occur. These considerations, according to Crockett and colleagues, present unacceptable added medical risks to women, making both POPs and Norplant undesirable choices. In addition, the higher ectopic rate means that more breakthrough ovulation pregnancies fail to implant, which bolsters the ethical case that these agents are abortifacients.
CONCLUSIONS:

1. Implanon causes thinning of the endometrium and alteration of the endometrial lining at the molecular level. These two actions will render the endometrium unfavorable for implantation. Any drug that prevents implantation is classified as an abortifacient by the 1987 Constitution of the Republic of the Philippines and the Reproductive Health Law.

2. When an Implanon user has breakthrough ovulation and becomes pregnant, her ovaries will produce pregnancy hormones that will act on the endometrium. But Implanon is also simultaneously releasing hormones that will also act on the endometrium to thin it and alter it at the molecular level. There are no medical studies that can say whether the effect of pregnancy hormones is greater than the cumulative effect of Implanon. If the effect of pregnancy hormones is greater, pregnancy will be successful. But if the effect of Implanon is greater, pregnancy will fail because implantation of the embryo will not be possible. The FDA assertion that pregnancy hormones will prepare the endometrium for implantation despite the continued presence of Implanon cannot be proven with absolute certainty as there are no medical evidence to support such claim.

3. Some studies reported that ectopic pregnancy rate is increased with Implanon and other progestin-only implants. This further proves the assertion that Implanon predisposes to abnormal or failed implantation.

It is quite clear that medical literature is inconclusive on whether Implanon can prevent implantation or not. Some evidence say Implanon does not prevent implantation while the evidence presented in this paper clearly and categorically say that Implanon acts to prevent implantation which makes it an abortifacient.

In cases when medical evidence is inconclusive, the Supreme Court is quite conclusive and clear: “IN WEIGHING THE EVIDENCE, ALL REASONABLE DOUBTS SHALL BE RESOLVED IN FAVOR OF THE PROTECTION AND PRESERVATION OF THE RIGHT TO LIFE OF THE UNBORN FROM CONCEPTION/FERTILIZATION.”

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21 NOVEMBER 2017