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Chapter 16
Evaluation of the Mechanism of Action of Anti-fertility Treatment in Cases of Sexual Assault: Moral Certitude and Human Acts

Thomas J. Davis Jr.

16.1 Introduction

Anti-fertility treatment for victims of sexual assault is a first line defense in Catholic healthcare. However, respect for human life prohibits interventions that destroy nascent human beings. Consequently, concern about the mechanisms of action of proposed treatments focus on the potential for embryocide. Commonly utilized medication may, in some minority of cases, prevent fertilization and thereby prevent pregnancy. The most popular of these products is the emergency contraception [EC] drug levonorgestrel [LNG]. Another widely distributed emergency contraceptive is ulipristal acetate [UPA]. Because the anti-fertilization action of any treatment is only relevant in the narrow six-day fertile window, specific assessment of mechanism of action in that time period is critical. Although typically proposed as an anovulant, LNG rarely prevents pregnancy by suppressing ovulation when administered in the fertile window. Its impact on other pre-fertilization processes, including sperm motility, transport, and capacitation, and sperm-egg binding, is too negligible to account for its efficacy or is non-existent. Its principal mechanism of action for preventing pregnancy is unknown but does so in the face of extraordinarily high ovulation rates, raising evidence based suspicion that it operates as an abortifacient. Careful assessment of the scientific corpus cannot rule out significant post fertilization mechanism(s) of action and cannot establish the minimum level of confidence necessary for moral certitude that it is not abortifacient. UPA is a known contragestative that also manifests strong anovulant features. Although very early fertile window administration will be likely to suppress ovulation, it is not assured and a significant level of ovulation nonetheless occurs. Later administration, when pregnancy is more likely, adversely effects endometrial development and carries

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significant abortifacient risk. Rape treatment protocols designed to identify a safe window of opportunity for UPA administration are inadequate and it is not appropriate for Catholic health care providers to facilitate its use.

16.2 Moral Specification

EC is intended for prevention of pregnancy[1] following unprotected sexual intercourse or a known or suspected contraceptive failure. Various formulations exist. LNG is marketed under various proprietary names including, most popularly, "Plan B One Step," an over–the-counter 1.5 mg single dose synthetic progestin compound. Other LNG products include "Take Action," "My Way," and "Next Choice One Dose," as well two-dose generic 0.75 mg formulations. UPA is a selective progesterone receptor modulator, available only by prescription and marketed in the United States under the brand name "ella."[2]

The long-running dialogue in Catholic healthcare over the use of EC in treatment of victims of sexual assault has long been focused on the mechanism of action [MOA] of LNG. The central issues are addressed in the *Ethical and Religious Directives for Catholic Health Care Services* [ERDs], which provide in pertinent part:

> A female who has been raped should be able to defend herself against a potential conception from the sexual assault. If, after appropriate testing, there is no evidence that conception has occurred already, she may be treated with medications that would prevent ovulation, sperm capacitation, or fertilization. It is not permissible, however, to initiate or to recommend treatments that have as their purpose or direct effect the removal, destruction, or interference with the implantation of a fertilized ovum (n. 36).

[1] This essay does not address the debate over the definition of "pregnancy" and "conception" that some authors believe manipulate language in a manner that disguises some forms of abortion. Sufficient discussion of that topic is widely available (Davis 2010b; Gacek 2009; USCCB 2014). An excellent discussion of this issue is included in the position submitted by the Catholic Medical Association to the U.S. Supreme Court in *Sibelius v. Hobby Lobby* (subsequently decided by the court under the caption of *Burwell v. Hobby Lobby*, 573 U.S. ___ (2014)) (Zucker 2014). For the purposes of this essay the terms "pregnancy," "conception," and "fertilization" shall be treated as synonymous. Accordingly, the term "abortifacient" is applied to both interceptive and contragestative acts. Technical means that act after fertilization "are *interceptive* if they interfere with the embryo before implantation and *contragestative* if they cause the elimination of the embryo once implanted" (CDF 2008, n. 23). Both forms of embryocide are abortive.

[2] Other types of EC include compounds containing both progestin and estrogen, known as "combined EC," including many brands of daily low-dose birth control pills ingested at higher than normal doses (Office of Population Research and Health Professionals 2015). This method of combined progestin and estrogen treatment is not designed as EC but is essentially off-label use and is not a form of EC proposed in hospital rape treatment protocols. Another EC formula contains small doses of mifepristone, a known abortifacient, but is not available in the United States. *Id.* The Copper-T IUD is also used for EC but is a known abortifacient (USCCB 2014).

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As ERD n. 36 makes clear, MOA is at the heart of the EC debate. The embryo, even before implantation, is a human being with an absolute right to life. That teaching, definitively asserted by Pope John Paul II in *Evangelium vitae* [*EV*] n. 57, applies without exception:

> [B]y the authority which Christ conferred upon Peter and his Successors, and in communion with the Bishops of the Catholic Church, I confirm that the direct and voluntary killing of an innocent human being is always gravely immoral. This doctrine, based upon that unwritten law which man, in the light of reason, finds in his own heart (cf. Rom 2:14–15), is reaffirmed by Sacred Scripture, transmitted by the Tradition of the Church and taught by the ordinary and universal Magisterium.[3]

> Nothing and no one can in any way permit the killing of an innocent human being, whether a fetus or an embryo ... no one is permitted to ask for this act of killing, either for himself or herself or for another person entrusted to his or her care, nor can he or she consent to it, either explicitly or implicitly. Nor can any authority legitimately recommend or permit such an action.[4]

Accordingly, the critical distinction is between "pre" and "post" fertilization MOAs. Treatment that prevents fertilization—by suppressing ovulation, retarding sperm, or by some other modality—is a welcome intervention in cases of sexual assault. Such treatment does not implicate the intrinsic evil of contraception, which, properly defined in its moral specification, involves the intentional separation of the unitive and procreative significances of sexual intercourse "in which the husband and wife are intimately and chastely united to one another" (Paul VI, 1968, nn. 11–12). Where no reasonable doubt exists that an abortifacient MOA is operative, sexual assault treatment with EC does no harm to the values safeguarded by the Church's teaching on contraception.[5] Catholic doctrine holds that spousal love is designed to be procreative and unitive and that these two aspects must not be intentionally severed. But "unitive" in this context does not mean the mere joining of body parts. It refers to the complete interpenetration of being marked by a nuptial embrace that leads a couple on a spiritual ascent reflecting the mutual and total outpouring of being exchanged between the persons of the Blessed Trinity.[6] Rape

[3]The source cited in EV for the declaration's authoritative nature is Vatican II's Dogmatic Constitution on the Church, *Lumen Gentium*, n. 25, the definitive formulation of the infallible teaching authority of the Church on matters of faith and morals.

[4]Quoting (CDF 1980). This moral judgment also applies to the origins of the life of an embryo even before it is implanted in the mother's womb, which will protect and nourish it for 9 months until the moment of birth: "Human life is sacred and inviolable at every moment of existence, including the initial phase which precedes birth" (Benedict XVI 2006).

[5]Those values are drawn from "the fundamental nature of the marriage act" which unites the spouses and makes them "capable of generating new life" (Paul VI 1968, n. 12) posits the "inseparable connection, established by God" between those elements of conjugal relations and the preservation of "true mutual love and its ordination to the supreme responsibility of parenthood."

[6]John Paul II (1981, nn. 11, 13) captures the transcendent meaning of unitive love in: "As an incarnate spirit ... man is called to love in his unified totality. Love includes the human body, and the body is made a sharer in spiritual love." Reflecting on the "vocation of the human person ... to love" the Pope recalled the "most profound truth of man, of his being 'created in the image of

has none of those characteristics. It is an act of violence that proceeds from a radical rejection of unitive love. The procreative potential of biology is not a final value for Catholic thought, and in the case of rape it is never joined to a properly understood unitive significance. "Unitive" demands *consent* and its absence precludes concern over misunderstood nomenclature utilized in the teaching on conjugal love.[7]

God.'" This means, the pope taught, that "sexuality … is by no means something purely biological, but concerns the innermost being of the human person as such. It is realized in a truly human way only if it is an integral part of the love by which a man and a woman commit themselves totally to one another until death. The total *physical self-giving* would be a lie if it were not the sign and fruit of a *total personal self-giving*, in which the whole person … is present. … Conjugal love involves a totality, in which all the elements of the person enter – appeal of the body and instinct, power of feeling and affectivity, aspiration of the spirit and of will. It aims at a deeply personal unity, the unity that, beyond union in one flesh, leads to forming one heart and soul …" (emphasis added). The Pope references Tertullian's letter *Ad Uxorem* ("to my wife") in which the great early Father suggests the sweeping transcendence of unitive love: "How can I ever express the happiness of the marriage that is joined together by the church, strengthened by an offering, sealed by a blessing, announced by angels and ratified by the Father? How wonderful the bond between two believers, with a single hope, a single desire, a single observance, a single service! They are both brethren and both fellow servants; there is no separation between them in spirit or flesh. In fact they are truly two in one flesh, and where the flesh is one, one is the spirit."

[7] Paul VI (1968, n. 13) is explicit: "a conjugal act imposed on one's partner without regard for his or her condition or personal and reasonable wishes in the matter, is no true act of love, and therefore offends the moral order in its particular application to the intimate relationship of husband and wife." From this it is plain that nonconsensual sex, which is never a "true act of love," is not "unitive." For that reason it would be wise for Catholic healthcare facilities to avoid the term "emergency contraception" in rape treatment policies and for their spokespersons and Catholic officials to avoid describing EC as an exception to the church's teaching on contraception. It is no such thing and reference to it as such inevitably dilutes the force of the Church's teaching on the exceptionless nature of intrinsically evil acts and invites further attempts to erode the teaching in so-called "hard cases." Examples of the "exception" explanation have had high visibility, for example, a 2009 *National Review* online interview with Cumberland School of Law professor Leonard J. Nelson III in which he was asked about potential conflict between EC legislative mandates and Catholic teaching: "Should there be an emergency-contraception exception—for those who aren't Catholic, at least?" Nelson responded: "Under the principle of self-defense, the Church has provided for an exception to the usual prohibition on contraception in order to allow victims of sexual assault to use contraception to prevent fertilization" (Nelson, 2009). In 2007 the bishops of Connecticut issued a statement explaining their position of reluctant compliance with a state legislative mandate for EC in rape treatment which included the following: "Catholic moral teaching is adamantly opposed to abortion, but not to emergency contraception for victims of rape" (Archbishop Henry J. Mansell Writes About Plan B and Catholic Hospitals 2007). Archbishop Mansell had previously stated "We are not opposed to emergency contraception for women who are victims of rape" (Ibid.). While the bishops did not speak of an "exception" to the teaching on contraception, their acceptance of the language "emergency contraception" clouds a critical distinction between "contraception" and "anti-fertilization treatment" and suggests a misunderstanding of the precise moral meaning of the terms. A better approach is presented by Thomas Berg (2011) and others. They distinguish the moral object of preventing fertilization following nonconsensual sexual intercourse from contraception associated with consensual sex. However, their reliance on the concept of "self-defense" "to repel the unjust aggressor," which follows the rationale of ERD n. 36, seems superfluous and potentially dangerous. The action taken is not the same moral species as contraception. Thus, for example, should sexual intercourse occur between individuals, each of whom are incapable of consent, such as in the case of institutionalized and

It follows, as the ERD provides, that so long as embryonic life is not attacked in the process, EC may be a compassionate and morally sound intervention in rape treatment protocols. And therein lays the dilemma. While it is well established that LNG and UPA may in some cases prevent pregnancy, the MOA of the former is unresolved at best and the later almost certainly includes abortifacient outcomes. The chemical structure of UPA is similar to the abortion drug RU-486 (marketed as Mifeprex). Both RU-486 and UPA are selective progesterone receptor modulators that block progesterone essential to maintain implantation. Its MOA "in human ovarian and endometrial tissue is identical to that of its parent compound mifepristone" (Harrison and Mitroka 2011). While its anovulant action is undeniable, as is the case with RU-486, it is not limited to pre-fertilization outcomes.

In addition, the timing of administration within the menstrual cycle alters the probabilities of a particular MOA in a given case. The resulting absence of definitive evidence establishing the MOA resolves to a circumstance of imperfect knowledge. In the face of such ambiguity, some have concluded that it is reasonably likely that LNG is not an abortifacient in certain identifiable circumstances and may properly be administrated in Catholic healthcare facilities subject to a preliminary hormone test (Berg et al. 2011). Some maintain that the ambiguity is ephemeral and assert sufficient certitude precluding an abortifacient MOA. These authors would limit preliminary testing to a determination of pre-existing pregnancy (Cataldo 2009a; Hamel 2010b). Others reject outright any use as a likely or potential abortifacient. (Kahlenborn et al. 2015; Raviele 2014; Peck and Velez 2013b). Still others hold the view that the scientific corpus creates such substantial doubt as to whether an abortifacient MOA is operative that EC is precluded in most cases (Davis 2010b, 2015).

This intra-Catholic debate is not properly about theory but facts. While there appears to be substantial agreement that the standard to be applied in the case of imperfect knowledge is one of moral certitude, differing assessments of the scientific literature drive a split of opinion. Traditional and more recent teaching on moral

severally developmentally delayed individuals, it would be enough that the moral species of the anti-fertilization treatment does not separate the unitive and procreative significances of the act, no unitive aspect (properly understood) having ever been operative. In such circumstances, and assuming no post fertilization MOA, those charged with the care of such persons may licitly resort to appropriate treatment without resort to "self-defense" theory. When dealing with treatment responding to rape one danger associated with applying "unjust aggressor" theory to a non-choosing, non-volitional sperm cell is that it may open the door to a similar argument applied to a non-choosing, non-volitional embryo conceived through rape that presents some level of burden to health. This is, in fact, the misnomered "parasite" argument advanced by some abortion rights advocates. Oakham's Razor favors a simpler approach: we are not dealing with contraception. Alexander Pruss (2013) offers a superb reflection on the meaning of "one body" union. Reflecting on the communion of body and soul that constitutes a human person, he maintains that such a union presumes "a personal and psychological ... union" (pp. 52–3). Taking up Sacred Scripture's reference to sexual union he demonstrates that such unity, when freely chosen (i.e., consensual), is not merely physical but may properly be understood "as an image of the intra-Trinitarian love" (p. 138). That understanding of "unitive" precludes equating non-embryocidal post rape treatment with intrinsically evil contraception and avoids the danger associated with "unjust aggressor" theory.

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certitude of the imperfect kind requires a level of confidence about proposed courses of action that is simply not attainable based on the current level of scientific knowledge. Neither probabilism nor resort to the principle of double-effect can avoid one overriding fact: no one knows how Plan B prevents pregnancy in the vast majority of cases.

It had long been maintained by proponents of LNG that it prevented pregnancy primarily by suppressing ovulation. However, recent data has demolished that contention (Noé et al. 2010; Noé 2011). It is now certain that LNG is a poor anovulant in the late follicular phase, no more effective at preventing ovulation than a placebo (Brache et al. 2013). Nonetheless, when ovulation follows administration at that stage, it is 100% effective at preventing pregnancy. No one knows how. Even with earlier administration, its anovulant effect varies according to the timing of uptake from meager to more reliable, but never certain. While various theories have been proposed, none resolve reasonable doubt regarding the MOA. With respect to UPA, some proponents of LNG in Catholic rape treatment protocols readily acknowledge its clear potential for embryocide and therefore reject its use.[8] Others remain open to an evolution of data on its MOA (Hamel, 2014), but substantial empirical data, properly evaluated, precludes unrestricted use. While several rape treatment protocols employ various tests to assess the likelihood of the abortifacient potential of LNG or UPA in a given case, each has significant drawbacks.[9]

In order to assess properly the theories regarding MOA and the positions advanced by various schools of thought for or against use of LNG or UPA in rape treatment protocols, a review of the salient features of human reproductive biology and the data available from published studies is essential. Only on that foundation may a proper analysis be made, one that critically examines the scientific corpus, distinguishes objective data from subjective opinion, and correctly applies the principles concerning moral certitude, imperfect knowledge, and human acts.

[8] For example, Austriaco (2013d), a strong supporter of LNG-EC in rape treatment protocols, describes both UA and mifepristone as a "bona fide abortifacients." Cf. Austriaco (2010b): "Significantly, previous studies with guinea pigs and monkeys described in the manufacturer's report to the European Agency have demonstrated that Ulipristal acetate can act as an abortifacient" citing (European Medicines Agency 2009). For additional resources on the abortifacient properties of UA, see (Davis 2010b; USCCB 2014).

[9] The "ovulation" approach, for example the Peoria Protocol, calls for the administration of a pregnancy test and, if negative, testing to determine the imminence of ovulation, either by a quick urine Luteinizing Hormone (LH) test and/or by serum progesterone level testing. The "modified" Peoria Protocol would limit LH assessment to a quick urine dip strip test. The National Catholic Bioethics Center's position is set forth in (Hilliard 2016) and follows the modified Peoria Protocol. See further discussion of the Peoria Protocol and the NCBC position, see Peck and Velez 2013b, pp. 38–9). Another proposal addressing LNG in conjunction with a COX-2 inhibitor or for use of UA which involves considerable testing and careful assessment of various biological markers has been advanced by (Bonelli et al. 2014).

16.3 Essential Facts Related to Reproductive Biology

MOA must be assessed in relation to the narrow six-day fertile window of opportunity during a woman's menstrual cycle when coitus may result in pregnancy. The relevant biology begins with follicle maturation, the process by which finger-like projections on the ovary-containing oocytes (eggs) mature in preparation for release of an egg. This process occurs in the preovulatory or follicular phase. During this phase the pituitary gland in the brain secrets Follicle Stimulating Hormone, which is responsible for the maturation of the ovarian follicles, and Luteinizing Hormone (LH), which stimulates the follicle to secrete estrogen, which in turn influences the development of healthy endometrium, a blood vessel-rich glandular tissue layer lining the uterus. A leading or dominant follicle will develop containing the oocyte to be released at ovulation. On or about day 12 of the menstrual cycle estrogen peaks and LH acutely and sharply rises, reaching its peak within 24 h. This event is known as LH surge. This sudden increase in LH is a reliable marker that ovulation is imminent. It triggers an inflammatory response in the dominant follicle that results in the follicular stigma, or rupture, through which the oocyte is released into the fallopian tube. Follicular rupture (FR) marks the moment of ovulation, which occurs "about 36 hours after the surge" (Homburg, 2014). However, about 20% of women ovulate three or more days after urine LH surge, confirming significant variation in the duration between LH rise and ovulation (Stratton et al. 2010). Following FR a mass of cells called the "corpus luteum" forms from the ruptured follicle and produces progesterone essential to the further development of the endometrium. The dominant follicle differs from other antral follicles in size and rapid growth, increasing in diameter at a rate of 2 mm per day (Chizen and Pierson 2010).[10] The typical size of

[10]The dominant follicle destined for rupture typically appears in a secondary (or later) wave of growing follicles. The wave model of folliculogenesis presents challenges for identifying the dominant ovulatory follicle as large anovulatory follicles may appear that share critical traits of a typical dominant follicle near time of rupture. This inevitably complicates assessment of dominant follicle size in some proposed EC protocols. Chizen and Pierson describe the wave model as follows: "Each follicle wave is composed of a group of antral follicles with synchronous growth. Typically, one follicle grows to a larger diameter and becomes the lead, dominant follicle of the group. New follicle waves appear at regular intervals within cycles and each of the waves is preceded by a small increase in FSH. Within each cycle, the earlier waves are consistently anovulatory, whereas the final wave ends with ovulation. In this fashion, a two wave cycle begins with growth and regression of the first wave of follicles without ovulation; however, a second wave of follicles grow and a preovulatory follicle ovulates from the second follicle wave. In a three wave pattern, the first two waves are composed of only anovulatory follicles, but the final wave ends with ovulation of its dominant preovulatory follicle. Similarly, a five wave menstrual cycle has been documented. It was comprised of four waves that did not ovulate, but the final fifth growth wave terminated with ovulation. In anovulatory waves, follicles grow to a maximal diameter and regress. Anovulatory waves are classified as minor if antral follicles are small, <8 mm, or major if the largest follicle diameters are >10 mm. It is of clinical value to learn that the maximal size of many anovulatory follicles (14–20 mm) in (major) anovulatory waves that regressed spontaneously were comparable in size and echotexture to the preovulatory follicles that progressed to ovulation in a later wave. The natural history of follicle waves provides an explanation for persistence of large anovulatory follicles in the early follicle phase. A large anovulatory follicle may begin growth within a luteal phase wave and persist into the next menstrual cycle."

the dominant follicle at FR, which may be assessed by ultrasound, measures 21 and 23 mm, although the full range of variance is 18–29 mm (Moghissi et al. 2015)[11] with some reporting variance as high as 18–36 mm (Chizen and Pierson 2010).[12]

Sperm deposited in the vagina during coitus migrate into the fallopian tube where they encounter the egg. Sperm survival in that journey is affected by cervical mucus and the endometrial environment. During migration sperm cells undergo a complex series of changes known as capacitation, which enables the cell to undergo the acrosome reaction (AR). AR is the capacitated sperm cell reaction to molecular signals from the egg which enables it to bind to and penetrate the zona pellucida, the hard outer membrane of the egg, progressing to the fusion of the genetic material of the sperm and egg which constitutes fertilization. After fertilization the embryo undergoes multiple divisions as it migrates through the fallopian tube to the uterus. After additional cell divisions the embryo develops an outer shell and an interior fluid cavity and is known as a "blastocyst." When the blastocyst reaches the uterus it may implant in the endometrium.

The luteal phase of a menstrual cycle begins the day following ovulation and continues to the end of the menstrual cycle, typically 12 to 14 days. Blastocyst migration occurs in the luteal phase, as does further endometrium development under the influence of progesterone produced by the corpus luteum. Implantation occurs in the late luteal phase. If the luteal phase is abnormally short, implantation will fail. This is called luteal phase defect (LPD). LPD may be the result of abnormal progesterone production by the corpus luteum, irregular response to progesterone by the endometrium, disruption of normal balance and sequence of hormones necessary for endometrial development, as well as by other factors.[13]

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[11] "Ovulation is deemed to have occurred if the follicle reached a mean diameter of 18–25 mm and subsequently changed in size, shape, or sonographic density. … Disappearance or sudden decrease in follicle size has been found to be the most frequent sign of ovulation. … [T]he diameter of the dominant follicle increased from 12 to 23 mm over the 5 days preceding ovulation, and the range of diameter of follicles at ovulation was 18–29 mm."

[12] See also (Luque 2014): "Before ovulation occurs, the average diameter of the dominant follicle is 22 to 24 mm (range 18–36 mm)."

[13] LPD in the context of EC MOA is a one-time drug-induced condition. It must be distinguished from naturally occurring LPD. The link between naturally occurring LPD and infertility, while widely suspected, is still debated. In that context, "infertility" is a specific term of art and means a disease characterized by "not being able to get pregnant despite having frequent, unprotected sex for a year for most people and 6 months in certain circumstances." (Mayo Clinic 2013). The Practice Committee of the American Society of Reproductive Medicine (ASRM) recognizes an apparent link between naturally occurring LPD and "infertility", properly defined, but cautions some reserve, especially for clinical significance: "Although there appears to be an association with infertility, it has not been established that persistent [LPD] is a cause of infertility. Moreover, [LPD] is only clinically relevant if it is consistently present in most cycles" (ASRM, 2012). Those reservations are not applicable when speaking of a one-time drug-induced LPD, such as that which may result from late follicular phase administration of LNG. Such a transient inadequacy does not equate with "infertility." The ability of a chemically-induced distortion to deter pregnancy is not seriously questioned. For an exchange on this specific topic between Catholic ethicists and medical professionals, see Austriaco (2013b) and a reply by Davis et al. (2013).

In the process of sexual human reproduction there is a time-limited fertile window in which a woman may become pregnant. An egg released into the fallopian tube can survive and thus be available for fertilization for about 24 h. Sperm can live up to 5 days in the cervical crypts or the fallopian tubes, waiting to fertilize an ovum. The fertile window is thus limited to 6 days. For the remaining 22 days of a typical menstrual cycle coitus cannot result in pregnancy. The fertile window is typically referenced as day -5 through day 0 with day 0 being the day of ovulation.

16.4 History of LNG Product Labeling Regarding MOA

With the relevant facts related to reproductive biology in mind, and understanding the critical fertile window timeframe, examination of MOA appropriately begins with the history of LNG product labeling requirements imposed by the U.S. Food and Drug Administration (FDA).

Plan B, a two dose package of 0.75 mg LNG tablets to be taken 12 h apart, was originally approved for prescription distribution in the United States in 1999 with no labeling requirements (Davis 2010b). On December 16, 2003 two FDA advisory committees met jointly to consider application for over-the-counter (OTC) marketing of Plan B.[14] The sponsor's representative maintained that:

> Plan B works like other progestin only oral contraceptives and prevents ovulation. Plan B is an oral contraceptive, not an abortion pill. The direct evidence is highly in favor of the fact that the primary mechanism of action, if not the sole mechanism of action, is prevention of ovulation (U.S. Food and Drug Administration 2003).

After lively public hearings a majority of the committee agreed that disclosure of possible post-fertilization MOA was required (U.S. Food and Drug Administration 2003).[15] Subsequent application for FDA approval of OTC marketing of Plan B resulted in extensive review by the agency's Center for Drug Evaluation and Research, which concluded that Plan B may prevent pregnancy in some cases by post-fertilization MOA including prevention of implantation (Galson, 2005). The FDA granted limited OTC approval in 2006 with the requirement that the product carton contain the following statement:

> This product works mainly by preventing ovulation (egg release). It may also prevent fertilization of a released egg (joining of sperm and egg) or attachment of a fertilized egg to the uterus (implantation). See consumer information leaflet.

The FDA also required the consumer information leaflet to read:

> Plan B works like a birth control pill to prevent pregnancy mainly by stopping the release of an egg from the ovary. It is possible that Plan B may also work by preventing fertilization of an egg (the uniting of sperm with the egg) or by preventing attachment (implantation) to the uterus (womb), which usually occurs beginning 7 days after release of the egg from the ovary. Plan B will not do anything to a fertilized egg already attached to the uterus. The pregnancy will continue.

[14] For an extensive review of the primary source record of the FDA labeling application, scientific review, and public hearings, see Davis (2010b).

[15] For further discussion of the committee hearing, see Davis (2010b).

In 2009 the FDA approved Plan B One-Step, which is a single dose 1.5 mg LNG tablet. The FDA mandated prescribing information, consumer information insert, and "Drug Facts" label containing essentially the same information concerning MOA as required for Plan B.[16] The same year the FDA also approved Next Choice, a generic 0.75 mg two dose LNG and required product insert disclosure substantially similar to that required for Plan B and Plan B One-Step, including the statement that Next Choice "works mainly by stopping the release of an egg from the ovary. It is possible that Next Choice may also work by preventing fertilization of an egg (the uniting of sperm with the egg) or by preventing attachment (implantation) to the uterus (womb)" (see Davis (2010b)).

The conclusion of the FDA that LNG prevented pregnancy "principally" or "mainly" by suppression of ovulation was based on its reading of the medical research and scientific literature available in 2006 and 2009. However, correct reading of that record, along with more recently published research, demonstrates that LNG seldom prevents pregnancy by suppressing ovulation. The labeling of Plan B One-Step has now abandoned any claim that it prevents pregnancy *primarily* by preventing ovulation. It includes a subtle but significant variation:

> Plan B One-Step is believed to act as an emergency contraceptive principally by preventing ovulation *or fertilization* (by altering tubal transport of sperm and/or ova). In addition, it may inhibit implantation (by altering the endometrium). It is not effective once the process of implantation has begun (FDAd 2009: emphasis added).

The record now makes it indisputably clear that LNG efficacy is achieved *primarily* through one or more post-ovulatory MOA. While a final conclusion identifying which post-ovulatory mechanism(s) are operative cannot be definitively reached, reasonable doubt subsists precluding moral certitude that it does not included abortifacient modalities.

16.5 Discussion of MOA[17]

16.5.1 The Pre-2010 Data on LNG

Various studies prior to 2010 purported to establish LNG as a pre-fertilization contraceptive that worked principally by suppressing ovulation. The critical question is whether those properties are the reliable means by which pregnancy is avoided.

[16] For discussion of the labeling of Plan B One-step, see Davis (2010b).

[17] With the caveat that some of the following were written before the revolutionary data that emerged in 2010, the following offer a representative collection of specifically Catholic perspectives from the Plan B discourse: Hamel and Panicola (2002); Sulmasy (2006); Austriaco (2007); Davis (2007); Hilliard (2008); Austriaco (2008a); Yeung et al. (2008a); Austriaco (2008b); Yeung et al. (2008b); Austriaco (2008c); Yeung et al. (2009a), Cataldo (2009b), Cataldo (2009a), Yeung et al. (2009b), and Hilliard (2009); Reznik (2010); Hamel (2010a); Hamel (2010b); Austriaco (2010a); Austriaco (2010b); Davis (2010a); Davis (2010b); Raviele (2011); Austriaco (2011a);

In the case of LNG it has long been established that it may prevent or delay ovulation by abolishing or significantly blunting LH surge. However, that result is closely tied to the timing of administration. Studies show that the nearer in time to ovulation that EC is used, "the less likely it is to interfere with ovulation" (Leung et al. 2010, pp. 158–68). The reason is simple: the closer LNG is administered to ovulation, the greater the development of the dominant follicle and the more likely the ovulatory process has passed a point of no return. While pre-2010 studies have often been presented as definitively rebutting any post-fertilization MOA, that conclusion is not supported by the data. Excellent analysis of the principal studies of that vintage is provided by (Peck and Velez 2013b). A brief review of the earlier studies demonstrates the lack of resolution regarding MOA.

Hapangama et al. (2001) showed that of those women administered LNG in the preovulatory phase and who subsequently experienced normal ovulation (58%), there was a significant reduction in LH levels. However, the study also demonstrated that the same participants had a significantly shortened luteal phase, which the authors themselves recognized as potentially abortifacient: "it is possible that the shortened luteal phase observed was a consequence of reduced total LH and may have a contragestive effect" (Leung et al. 2010, p. 128); cf. Peck and Velez 2013b, pp. 13–14).

Durand et al. (2001) established a strong (80%) anovulant action for women who used LNG on cycle day 10, but that timing is either prior to or at the very beginning of the fertile window when the probability of conception is extremely low (Peck and Velez 2013b, p. 14) and therefore suggests only marginal avoidance of pregnancy with such early administration. All participants medicated at, or 48 h after, LH surge ovulated with no significant alteration of cycle length or luteal progesterone levels. However, all who were in the late follicular phase at administration, between day -5 and day -2,[18] ovulated and had significantly deficient progesterone production with a significantly shorter luteal phase (Durand et al. 2001, p. 230). As Peck and Velez (2013b, p. 15) note, "luteal deficiency impairs normal transformation of the endometrium so that if fertilization occurs, changes in the endometrium may impair implantation."

Croxatto et al. (2004) found that FR occurred in about half of all LNG-treated cycles observed and that "the further the woman was from the LH surge when she received [LNG], the more likely she was not to ovulate, whereas the closer she was to the LH surge, the more likely she was to ovulate" (Peck and Velez 2013b, p. 15). The data also showed blunted LH levels in FR cycles. Croxatto hypothesized that FR, preceded by blunted LH, resulted in the release of ova that were resistant to

Davis (2011); Austriaco (2011b); Rella (2013); Peck and Velez (2013a); Peck and Velez (2013b); Austriaco (2013a); Austriaco (2013b); Austriaco (2013c); Yeung and Harrison (2013); Davis et al. (2013); Harrison (2014); Mozzanega et al. (2014); Austriaco (2014); Berchelmann (2014); Peck and Velez (2014); Wills (2014); Davis et al. (2015); Kahlenborn et al. (2015); Catholic Medical Association (2015); Peck et al. (2016).

[18] Durand et al. (2001, p. 229) identified this group as medicated "3 ± 1 day prior to serum LH surge."

fertilization. Referring to the phenomenon as "ovulatory dysfunction," they proposed it as a sufficient explanation of LNG MOA in the face of FR. The concept referenced the work Verpoest et al. (2000), who studied *in vitro* fertilization rates at various LH levels. But Verpoest was not an LNG study and, as Peck and Velez (2013b, pp. 16–17) and others (Davis et al. 2013, p. 583; Kahlenborn et al. 2015; Peck et al. 2016) have shown, does not support the notion of ovulatory dysfunction:

> Verpoest's definition of fertilizable ova … was "the presence of two pronuclei at 24 hours and continued cleavage until embryo transfer at 2–3 days." Thus, they define as unfertilizable ova embryos which cannot continue to divide properly, which is actually a post-fertilization event. Moreover, Croxatto … failed to realize that the addition of [LNG] (itself a powerful progestin) would alter the proposed scenario of "low LH." In fact, progestins have been shown in animal studies to promote oocyte maturation and meiosis resumption in the absence of an LH surge (Siqueira et al. 2012; Borman et al. 2004), which indicate (at least in animal studies) that the addition of [LNG] (a progestin) would actually facilitate the ovulation process, even in the midst of a blunted LH environment (Peck et al. 2016).

Further, participants with reportedly low LH levels associated with ova that resisted fertilization, as defined by Verpoest, "had peak LH levels that were comparable to the healthy controls" in Croxatto (Peck and Velez 2013b, p. 17). Kahlenborn et al. (2015) also demonstrates that Croxatto neglected to factor the duration of LH surge, a factor others have found more significant than its height and which substantially affects pregnancy rates associated with low LH.[19] Croxatto (Brache et al. 2013) now concedes the conjectural nature of the theory that blunted LH preceding FR in LNG treated cycles alters the ovulatory process so as prevent pregnancy.

Data published by Durand et al. (2005) showed that when LNG is administered 3–4 days before the LH surge, it results in luteal phase progesterone insufficiency sufficient to inhibit implantation. In addition, the results showed decreased endometrial glycodelin-A staining. That is a significant indication of LNG-induced luteal progesterone insufficiency because glycodelin-A is progesterone-dependent. Glycodelin-A endometrial stains from this study provide tissue-level evidence of LNG-induced progesterone inadequacy. This reduced glycodelin-A staining, independent of progesterone-mediated effects, is itself is a possible abortifacient MOA since glycodelin-A is possibly another mediator needed by the developing embryo for its ability to help implantation through appropriate immunosuppressive activity.[20]

Okewole et al. administered LNG to eight women at day -3 and six at day -1 (Okewole et al. 2007). They reported significant delay in LH peak of 96–120 h in the first group. But when the data is examined independently, rather than as a mean, it shows that the delay was as small as 1 day (subject 7) or 2 days (subject 4). Two subjects had only a four-day delay (subjects 6 and 8). Thus, four of eight participants experienced delays that may not prevent fertilization. In addition, that group also had "significantly lower levels of estrogen and progesterone during their

[19] Cf. Cohlen et al. (1993): "Taking into account that the duration and height of the LH surge are correlated, it seems that duration is more important than height."

[20] Peck and Velez (2013b, pp. 23–4) develop this point.

follicular and luteal phases, and four of eight women had vaginal bleeding, suggestive of endometrial instability due to lower progesterone levels. Fertilization under such conditions could lead to impaired implantation because of endometrial changes" (Peck and Velez 2013b, p. 18). The other group experienced no effect on ovulation but had "statistically significant shortening of the mean cycle length in comparison with pretreatment cycles (20.2 vs. 25.1 days) and with a diminution of luteal mean progesterone levels" suggesting "that LNG impaired the corpus luteum" (Ibid.). Okewole et al. recognized the implication: "This shows that LNG administration at late follicular phase (Group B) did not interfere with the estradiol-mediated midcycle gonadotrophin surge and probably ovulation, but did alter progesterone production by the corpus luteum. It suggests that LNG might have caused premature degeneration of the corpus luteum" (Okewole et al. 2007, p. 375). If fertilization followed FR, such a process could produce inadequate luteal progesterone, a shortened luteal phase, and an abortifacient outcome.

A study by Novikova et al. (2007) confirmed that Plan B did not prevent pregnancy when administered after ovulation. Proponents offered that datum as proof that it did not prevent implantation. But the study also showed that no pregnancies resulted when Plan B was administered in the follicular phase, a result entirely consistent with FR and fertilization followed by interception or some other post-fertilization action, especially in view of the dubious data supporting inhibition of sperm migration.[21]

Tirelli, Cagnacci, and Volpe (2008) reported data on administration of LNG to women at various phases of their menstrual cycle. In a small subgrouping, seven of eight participants who took the medication in the late follicular phase did not experience FR. That was offered as proof that preovulatory LNG was a potent anovulant and not an abortifacient. However, Peck and Velez have shown that the mean size of the dominant follicle at the time of administration placed them outside the fertile window "when intercourse would not lead to pregnancy" (Peck and Velez 2013b, p. 20). What the data did indicate is that preovulatory LNG significantly shortens the luteal phase leading to the equivalent of a luteal phase insufficiency – a finding supportive of a potential post-fertilization MOA in the event of ovulation and fertilization.

Lalitkumar et al. (2007) reported successful *in vitro* human embryo attachment to mature endometrial tissue that was exposed to LNG. This was offered by some to support the view that LNG did not prevent implantation. But the study has nothing to say about the effect of preovulatory LNG on earlier endometrial development or the potentially causal relationship between preovulatory LNG and dysfunction of the corpus luteum. The endometrial tissue in the study was never exposed to LNG in the preovulatory phase, but only after it was harvested through biopsy.

Two studies reported by Meng et al. (2010) and Palomino et al. (2010) are sometimes offered to rebut the suggestion that Plan B may prevent implantation. In those studies, LNG was administered between days LH +1 and LH +4 (Meng) or on LH 0, the day of LH surge (Palomino). It was not administered during the preovulatory

[21] See discussion of effect on sperm *infra* at n. 24 and accompanying text.

fertile phase. While both studies provide some evidence that Plan B does not adversely affect endometrial receptivity when administered during the ovulatory phase, the results say nothing about its post-fertilization effect when it is administered during the fertile days preceding LH surge.

In another study by Durand et al. (2010) women received LNG 2 days before the LH surge. They reported "apparently normal" progesterone production during the luteal phase, which would suggest normal luteinization and corpus luteum function. The data also showed increased levels of glycodelin-A, which Durand suggested as an alternative MOA preventing sperm-egg binding. That theory largely collapsed under scrutiny as discussed *infra*. In addition, controversy over the accuracy of timing of administration, based on the size of the leading follicle, may mean LNG was actually administered later then presented (Peck and Velez 2013b, p. 25). What is clear is that ovulation occurred in two thirds of the women and "LNG treatment significantly reduced the mean cycle length (26.9 ± 0.5 vs. 29.2 ± 0.5 days, respectively; $p < .05$) in LNG-ov subjects" (Durand et al. 2010, p. 529). LH levels were markedly reduced but did not deter a high rate of ovulation (Peck and Velez 2013b, p. 24). When viewed in light of other studies confirming LNG-related shortened luteal phase, the ambiguity as to actual timing of administration, and Durand et al.'s (2005) data on reduced progesterone levels, Durand et al.'s (2010) contribution does not rule out post-fertilization MOA.

Reznik (2010) reviewed some of the scientific literature, including Croxatto and Novikova, and identified the MOA as "preventing ovulation and thickening cervical mucus" (p. 60). From that foundation she categorically asserted: "levonorgestrel acts to prevent pregnancy before, and only before, fertilization occurs" (Reznik 2010, p. 59). As with much in the Plan B debate, various of her assumptions were unfounded and her analysis lacked rigor.[22] In the months that followed additional data emerged undermining standard MOA assertions and revolutionizing the debate.

16.5.2 The 2010 Clinical Data on LNG

As the FDA labeling requirements and the preceding discussion suggest, prior to 2010 it was widely believed that LNG was primarily an anovulant. However, a startling development undermined that dogma when Noé et al. (2010) published data from a remarkable study. The article reports the findings of a clinical trial of LNG involving a substantial number of women who engaged in coitus during their fertile phase and were prescribed LNG. Eighty-seven test participants took the medication

[22] For a specific critique of Reznik, see Davis (2010b). Reznik's (2010, p. 59) assertion that LNG "causes thickening of cervical mucus" thereby limiting sperm migration has been thoroughly debunked; see n. 24 and accompanying text. Her claim that it is "virtually undisputed that levonorgestrel prevents ovulation" is misleading at best without reference to the fertile window, and within that time frame LNG is now recognized as a poor anovulant; see text accompanying and immediately following nn. 44–5.

between days -5 to -1. Thirty-five took it on or after the day of ovulation. In the first group, no pregnancies were reported (normal expected pregnancies = 13.2). In the second group six pregnancies were reported (normal expected pregnancies = 7.1). While at first blush that data may appear to support the view that Plan B is not an abortifacient because it did not prevent pregnancy when taken at or after ovulation,[23] careful analysis shows the opposite. Follow-up examination of those participants who took the drug on day -5 to day -1 reveals that in 80% transvaginal ultrasound detected FR. That means that 80% of the women taking LNG in their preovulatory fertile window actually ovulated, but none became pregnant despite a significant expected pregnancy rate. That data demolished the long-standing claim that Plan B prevents pregnancy primarily by suppressing ovulation. Even Noé et al. recognized the significance of the data and readily acknowledged its unavoidable implication: postovulatory MOA must be at work (Noé et al. 2010). They suggested as a likely explanation that Plan B impeded sperm migration, a claim frequently made by LNG proponents, and cited the seminal work of Kesserü et al. (Kesserü et al. 1974).

Kesserü examined intrauterine sperm concentrations and attributes at various intervals after a single dose of d-norgestrel and concluded that it produced significant interference with migration and function at all levels of the genital tract. If accurate, that would support a potential postovulatory, yet pre-fertilization, explanation for Noé data. But the Kesserü data is not correct. A more recent study, specifically designed to replicate Kesserü, and utilizing more modern methodology, contradicted their findings (do Nascimento et al. 2007). That study found that Plan B had no effect on sperm migration or on the quality of cervical mucus. It is now well established that Plan B does not have any significant role in the prevention of pregnancy by affecting sperm function, cervical mucus, sperm transport, or sperm capacitance, including AR (Gemzell-Danielson et al. 2013, p. 302).[24]

The exclusion of Kesserü as explanation for the Noé data led some to suggest impairment of sperm-egg binding, a potential pre-fertilization MOA, based on data from other studies showing elevated intrauterine glycodelin-A in women taking LNG in the preovulatory stage (Durand et al. 2010, pp. 526–33).[25] High levels of glycodelin-A have been shown to disrupt sperm-egg binding (Seppälä et al. 2002, pp. 401–30). However, it has been demonstrated that glycodelin-A can be displaced

[23] In fact, one well-respected Catholic theologian and bioethicist maintained that the data reported by Noé et al. (2010) "show that Plan B is not an abortifacient" (Austriaco 2010b). See also his letter in the same issue of *NCBQ*, in which he maintained that the Noé data "only strengthen the claim made by me and others that Plan B is not an abortifacient" (Ibid., p. 222).

[24] For an excellent discussion of claims related to cervical mucus, sperm transport, and sperm capacitance, including discussion of Kesserü and do Nascimento, see Peck and Velez (2013b, pp. 3–9). While the claim is still asserted by some, most LNG proponents now accept this conclusion. Noé et al. (2010), who cited Kesserü without any mention of do Nascimento, in an effort to explain the absence of pregnancy following the astoundingly high ovulation rate, subsequently acknowledged the significance of do Nascimento's study and conceded that Kesserü, at best, could only account for a "transient" MOA that vanishes shortly after uptake (Noé 2011, p. 491).

[25] Durand's et al. 2010 study was cited as support for the suggested sperm-egg binding inhibition by Austriaco (2011a, p. 213).

from spermatozoa when passing through the oocyte-cumulus cell complex by a cumulus isoform of glycodelin known as glycodelin-C. Chiu et al. demonstrated that such a process not only removes the zona pellucida binding inhibitory activity of glycodelin-A, "but that [in the process] spermatozoa acquired enhanced zona pellucida binding ability" (Chiu et al. 2007, p. 5378). In other words, exogenous glycodelin-A can be stripped from sperm as it encounters the oocyte and be converted to a different isoform, the net effect of which promotes rather than impedes sperm-egg binding. Moreover, even if glycodelin-A were elevated without conversion to a different isoform, the concentrations would be inadequate to explain the Noé data.[26]

Croxatto's "dysfunctional ovulation" theory continues to be advanced by some who maintain that LNG induces low LH surge resulting in defective eggs that are difficult to fertilize (Durand et al. 2010, pp. 526–33).[27] As demonstrated above, that claim is conjecture and its reliance on findings by Verpoest et al. is misplaced. Verpoest et al. (2000, p. 76) reported that eggs resisted fertilization in IVF procedures when they were conditioned by inadequate LH. However, their definition of "fertilization" required two pronuclei and continued cleavage for up to 72 h. That means oocytes that were actually fertilized but failed to sustain cleavage for the specified duration were deemed "unfertilized." That "unfertilized" oocytes included actual embryos on a path to early demise is further evidenced by reported LH levels. Some of the "unfertilized" oocytes were from women whose peak serum LH and follicular fluid LH concentrations fell within the ranges associated with oocytes that fertilized and sustained cleavage. Assuming for the sake of argument that this MOA actually occurs *in vivo*, it would constitute something monstrous – the predestined, preprogrammed early demise of human beings. But whether such events occur is suspect. Brache et al. (2013) searched for a pre-fertilization MOA to explain the absence of expected pregnancy despite follicular rupture evident in Noé et al. (2010), Noé (2011), a search necessitated by their acknowledgement that Noé's data established LNG as no more effective in suppressing ovulation than a placebo (Brache et al. 2013, pp. 611–18).[28] They plainly admit that whether "the abnormal

[26] Durand et al. (2010, p. 532) acknowledged that her study left "unknown whether the content of uterine glycodelin-A reached at midcycle is optimal to affect the fertilization process." In fact, concentration would have to reach 25 μg/ml if there is to be any significant inhibitory action, assuming *in vivo* conditions were to permit it at all. (Morris et al. 1996, pp. 32159–67). See also Durand et al. (2005, p. 455). The concentrations measured by Durand in her 2010 study ranged from much lower to slightly lower (17.7 ± 5.9 μg/ml) than the minimum necessary for a significant impact (Durand et al. 2010, pp. 529 and 532, fig. 6, panel A).

[27] This theory has been presented most prominently by Austriaco (2011b, p. 625; 2013b, p. 399) in which he identified it as an "especially attractive" explanation.

[28] The authors report that LNG- inhibited or delayed ovulation only 14% of the time when administered in the advanced follicular phase, the highly fertile 2–3 days preceding ovulation, a rate effectively no better than placebo. Significantly, Brache was one of the experts who previously maintained that inhibition or delay of ovulation as LNG's principal and possibly only MOA, making her acknowledgement that suppression or delay of ovulation is an insignificant player all the more significant (p. 617).

blunted or absent LH peak preceding follicular rupture in the LNG-treated cycles in which rupture occurs contributes to the alteration of the ovulatory process and has any clinical consequence is unknown." The most they can offer is that it is "biologically plausible," (Ibid.) a tepid response at best and one that abandons prior reliance on Verpoest. Moreover, the authority they cite to support "biological plausibility" is (Cohlen et al. 1993), which merely reported a higher successful pregnancy rate associated with normal LH. Finally, additional research suggests that a synthetic progestin, such as LNG, administered before ovulation may actually trigger the resumption of egg maturation and meiosis in the presence of blunted LH (Borman et al. 2004). This is an area warranting further study, but the hard-to-fertilize egg theory is an extraordinarily weak explanation for the absence of expected pregnancy in Noé and, even if true, would almost certainly entail a post-fertilization MOA.

Mozzanega and Cosmi presented an explanation of how LNG impacts ovulation, implantation, cervical mucus, and sperm function (Mozzanega and Cosmi 2011). They conclude that claims dismissing post-fertilization MOA in favor of inhibition or delay of ovulation are not supported by careful analysis of the data. Rather, after analysis of Hapangama, Durand, Croxatto, Okewole, and others, they make the following judicious observation: "short or inadequate luteal phase did follow ovulation and in some patients who did ovulate the luteal endometrium was out of phase; these observations cannot lead straight to conclusions, but they suggest some kind of difficulty for the implanting embryo" (Mozzanega and Cosmi 2011, pp. 439–42).

Three recent articles by Catholic medical professionals examined the scientific corpus and each makes the case that the scientific data does not preclude an interceptive MOA associated with fertile window follicular phase intake and that LNG is either an established or likely abortifacient.

Raviele (2014), emphasizing the timing of LNG administration, suggests that LNG is safe once LH surge is detected – but useless as it "would not prevent ovulation anyway and would not have an adverse effect on the conceptus or on implantation" (p. 124) – and maintains that it effects the conditions necessary for fertilization only if administered "at the beginning of the fertile window," correlating to day -5 (Ibid.). As to administration on day -4 to day -2, timing that cannot readily and reliably be assessed in an emergency room setting after rape, she maintains that "*the drug does not prevent ovulation or fertilization ... but is still highly effective in preventing a pregnancy, [and] it has to be action after fertilization has taken place*" (Ibid.).

Kahlenborn, Peck, and Severs (2015) similarly expressed grave concern over the potential post-fertilization potential of LNG. After dissecting the data they concluded that it "suggests that abortion is a likely mechanism of action. Therefore, the claim that moral certitude exists via [LNG]'s non-abortifacient action is currently indefensible" (p. 11).[29]

[29] Some of the authors collaborated on a "Statement on Emergency Contraception in Cases of Rape" adopted by the Catholic Medical Association (2015). Although a superb analysis of many of the prominent clinical research studies related to LNG and UA, the statement is subject to friendly critique. It maintains, with respect to LNG, that "[t]he medical literature claims that the drug works primarily by preventing ovulation." As shown above, that singular claim is dated and

Peck et al. (2016) offered quantitative estimates of MOA. They examined the effect of LNG on cervical mucus, sperm transport, and capacity to fertilize and found them negligible. They assessed inhibited sperm-egg binding associated with increased glycodelin-A as "doubtful" as a "credible MOA" (p. 41). With respect to effects of ovulation when administered in the peri-ovulatory days, they concluded that "the fraction of pregnancies prevented by the ability of the drug to inhibit or significantly delayed ovulation" at only 12.7% (Table 2 and p. 38). Presenting data on altered embryo transport through the fallopian tube,[30] corpus luteum dysfunction,

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has been abandoned by almost all responsible authors following publication of (Noé et al. 2010). The current claim most frequently encountered by LNG proponents is that LNG works primarily by preventing ovulation *or delaying* ovulation. While the former has been debunked and the later is doubtful, the significant point is that most proponents of LNG in the clinical community have broadened the MOA claim to include delayed ovulation. Second, it incorrectly claims "as of October 2013, it [Plan B] is available to anyone of any age in the United States without prescription." That is true for Plan B-One Step but not for the original two dose 0.75 mg. The original Plan B, and its generic copies, still requires prescription for women under the age of 17. The complex litigation that resulted in such an odd circumstance is accurately presented in summary at the Office of Population Research and Association of Reproductive Health Professionals (2016). For further discussion of the court ruling triggering the current perplexity on Plan B availability, see Davis (2013). Third, it maintains that LNG is "likely to act after fusion of the sperm and the egg." As I have shown, that claim may be true but it is not established and doubt as to MOA subsists. Moreover, the use of "likely" in this regard is unnecessary to the moral evaluation of LNG. It is sufficient that reasonable doubt precludes its unrestricted administration. The CMA statement compounds the dilemma by stating "LNG-EC does not prevent ovulation and fertilization when given during the fertile window." That is overstatement. As shown above, LNG does suppress ovulation in some percentage of cases when given in the early fertile window, even if that timing is of marginal help as it is also the point during the fertile window when pregnancy is least likely. Its advice, at least with respect to LNG, doubles down when it states: "[W]e must refrain form acting violently against innocent human life as the current approved drugs are known to do." In fact, the principal MOA is unknown – even if one were to conclude that interception is "likely." The critical analysis concerns moral certitude, which precludes unrestricted LNG in view of the reasonable doubts as to its abortifacient modality. Finally, and highly significant, is the selective presentation of the Durand data from 2005 and 2010. The statement correctly points out that Durand found that pre-LH surge LNG can trigger a premature spike glycodelin-A, which, in part, acts "to suppress the mother's immune system so that the blastocyst is not recognized as a foreign body." The statement reports Durand's findings that such early administration of LNG "altered the luteal phase secretory pattern of glycodelin in serum and endometrium and significantly lowered serum progesterone levels in the luteal phase" and that "[l]evels of glycodelin-A were low at the time of implantation, preventing the suppression of the mother's natural killer cells. This could result in a postfertilization effect." I agree. However, the statement did not adequately distinguish the 2005 and 2010 studies and did not report that Durand et al. (2010) found "apparently normal" luteal phase progesterone (P) following Pre-LH surge administration, a finding that would militate against a postfertilization effect tied to defective corpus luteum. Doubts exist regarding the expression "apparently normal" and the area under the curve calculations in that study and the data, taken as a whole, do not eliminate reasonably doubt as to MOA. The failure to report the apparently normal P data for 2010 may subject the statement to criticism for selective reporting of data with the implication of excessive advocacy.

[30]They cite Wanggren et al. (2008) and Mahmood et al. (1998), studies which note that LNG reduces tubal motility (Wanggren) and caused significant reduction in in the fallopian tube epithelial ciliary beat frequency (Mahmood). Peck et al. (2016, p. 44) suggests that "[g]iven the higher

and altered endometrial histology,[31] they maintain that administration in the preovulatory days "can be demonstrated to impair luteal function and may adversely affect the survival of the embryo" (p. 47).

A recent contribution by Mena (2014) suggesting a postovulatory yet prefertilization MOA focuses on inhibited contractions and retarded ciliary beating within the fallopian tube (FT) which are posited to impede migration of the oocyte thereby preventing fertilization at the ammpullary-isthmic junction (AIJ). While data supports the claim that LNG inhibits contractions and normal ciliary beating, the evidence is thin that the effect would only prevent fertilization. Mena himself acknowledges that his theory is but one of three possible results of such action. The others suggest a post fertilization MOA by which impeded migration of the early embryo prevents continued growth or delayed implantation. While he asserts that the latter MOAs are less likely, he cannot dismiss them. Moreover, his theory rests on the presumption that fertilization occurs at the AIJ. In fact, the structure of the ampulla, a segment of the FT averaging 5–8 cm, is thought to be the locus of most fertilization and early embryo development and is most often the site for ectopic implantation (Ghazal et al. 2014). "The most common location in the fallopian tube for ectopic pregnancies to occur is the ampulla (70.0%); other locations, such as the isthmus (12.0%), the fimbria (11.1%) and the cornua (2.4%), are less common" (Kulp and Barnhart 2008). This observation suggests that fertilization typically occurs near the ovary before migration to the AIJ and necessarily means that sperm penetrates well past the AIJ. Sperm is known to be present in the FT within 5 min after insemination and certainly within 2 h, suggesting that in cases of rape it is likely that sperm are present in the FT before treatment with LNG may be reasonable expected. Peck and Velez (2013b, p. 6) provide substantial documentation of rapid sperm transport and note, without conceding that LNG in fact impedes sperm migration, that "if sperm can arrive in the fallopian tubes in minutes, then the action of emergency contraception (even if taken within 24 h) would occur too late to affect this phenomenon." In view of the foregoing, Mena's speculative proposal

affinity of LNG for progesterone receptors, its effects on fallopian tube epithelial ciliary beat frequency could be significant at the doses of LNG used in EC."

[31] Ugocsai et al. (2002) studied endometrial surface changes by scanning electron microscope in women who intentionally took high doses of LNG (about four to six times the standard dose). They found that in comparison to controls, specimens displayed marked restructuralization of the endometrium and disappearance of pinopodia (necessary implantational structures). They concluded that the contraceptive effect of LNG was accomplished by alteration of the endometrial surface, and therefore, receptivity. See also Acache and Revel (2006), which found that the relationship between pinopods (implantational markers) and progesterone levels, pinopod formation, and regression were closely associated with increases and decreases respectively in serum progesterone concentrations. Pinopods are bleb-like protrusions found on the apical surface of the endometrial epithelium and are preferred sites of embryo-endometrial interactions. Endometrial pinopods' development is associated with the mid-luteal phase increased expression of leukemia inhibitory factor and its receptor progesterone. "Pinopods appear progesterone-dependent. Moreover, HOXA-10, a homeobox gene whose expression is necessary for endometrial receptivity to blastocyst implantation, has an essential role in pinopod development" (p. 732).

faces substantial barriers. However, what it does demonstrate is that the MOA remains unresolved thereby precluding moral certitude that it is not abortifacient.

16.5.3 Ulipristal Acetate

Ulipristal acetate poses strikingly clear risks for embryocide. It is effective in preventing pregnancy (defined as implantation) for 120 h after sexual intercourse, substantially longer than the 72 h window claimed the manufacturer of Plan B. As a result it is promoted as a superior EC. However, it is a selective progesterone receptor modulator, which means that it, like abortion pill RU-486 (mifepristone), attaches to the receptors to which progesterone normally attaches, preventing the hormone from having its normal effect on endometrial development. Its close structural chemical affinity to mifepristone, their common effects on folliculogenesis and endometrial differentiation, and similarities in dose and effect when treating fibroids, demands extreme caution. It poses a direct and substantial risk of rendering the endometrium inhospitable to nesting. Three significant sources confirm the risk:

The (U.S. Food and Drug Administration 2015) prescriber information on ella reads:

> When taken immediately before ovulation is to occur, **ella** postpones follicular rupture. The likely primary mechanism of action of ulipristal acetate for emergency contraception is therefore inhibition or delay of ovulation; however, alterations to the endometrium that may affect implantation may also contribute to efficacy.

The (U.S. Food and Drug Administration 2015) approved patient labeling information similarly reads:

> **ella** is thought to work for emergency contraception primarily by stopping or delaying the release of an egg from the ovary. It is possible that **ella** may also work by preventing attachment (implantation) to the uterus (Ibid.).

Finally, the distributor of ella in the United States maintains and online Patient Brochure which states:

> How does *ella work? ella* works by delaying or preventing ovulation (the release of an egg from the ovary). It's also possible that *ella* works by preventing attachment to the wall inside the uterus (Afaxys 2015).

These sources constitute sufficient evidence of a potential post fertilization mechanism such that UPA should be disqualified from unrestricted use in Catholic facilities. The scientific literature supports the conclusion that UPA can prevent or disrupt implantation. As with LNG, timing of administration is closely associated with potential mechanisms.

Brache et al. (2010) documented a strong anovulant mechanism for UPA when administered in the follicular phase preceding LH surge, suggesting its potential as a rape treatment drug. However, once LH surge commenced anovulant efficacy dropped to 78% and dwindled to a meager 8% at and after LH peak. This suggests that sufficiently confident anovulant action is limited to the least fertile fraction of the fertile window preceding LH surge. Should ovulation occur after LH begins to

rise, research indicates that any resulting embryo may be destined for an inhospitable endometrial environment. Stratton, Hartog, et al. demonstrated that an EC equivalent dose of UPA administered at mid follicular phase significantly delayed endometrial maturation (Stratton et al. 2000). Passaro et al. (2003) studied the effects of luteal phase administration of UPA and found that half of test participants administered a single EC equivalent dose experienced induced endometrial bleeding. Stratton, Levens studied the effects on the endometrium of early luteal phase administration and reported "significant reduction in endometrial thickness" at every dosage tested, including that used for EC. Moreover, they documented significant "decreased expression of peripheral node addressins, which are important L-selectin ligands found on the surface of endothelial cells" (Stratton et al. 2010, pp. 2040–1). Superb analysis of the data is offered by Mozzanega et al. (2014). They point out that endometrial epithelial cells "are unregulated during the implantation window, allowing the uterus to be more receptive to the trophoblast. Human blastocysts, in fact, utilize L-selectin to initiate implantation by binding to endometrial ligands. Their absence is associated with implantation failure" (p. 681). Further, they challenge the claim that UPA can delay ovulation when taken at LH peak (Brache et al. 2010) since the time delay between intake and FR was similar to placebo. "This indicates that when ... UPA was administered 1 or 2 days before ovulation, [its] effects on ovulation were null ... UPA can consistently delay ovulation only when taken on the first and, maybe, second fertile day" (Mozzanega et al. 2014, p. 681). Nonetheless, UPA prevents 80% or more of expected pregnancies regardless of which of the 5 days (120 h) it is taken after intercourse. Given the sharp decrease in anovulatory action as LH rises, its steady effectiveness necessarily suggests an additional mechanism. The obvious candidate is endometrial inadequacy, a conclusion adequately supported by the research data and strongly endorsed by Mozzanega et al. (2014, p. 682): "the high efficacy of Ella(One) in preventing the appearance of clinically evident pregnancies can be attributed to [endometrial effects] rather than ovulation delay, which is not observed in the most fertile days of the cycle." They also note that "UPA and mifepristone have been demonstrated to be capable of decreasing fibroid size with exactly the same schedule and dose" thereby further evidencing their similarities (Ibid.). Miech (2011, p. 392) identifies three UPA mediated abortifacient mechanisms related to interference with progesterone uptake: "(1) failure of the decidua to develop and become receptive to implantation of the blastocyst, (2) failure of secretions of uterine glands in the decidua to maintain and implanted embryo, and (3) the return of spontaneous uterine contractions." He proposes a fourth related to suppression of the selective immune tolerance of certain endometrial cells related to progesterone uptake. Absent that tolerance the implanting embryo may be rejected as a foreign body (p. 393). Finally, Keenan (2011) maintains that deleterious effects on the endometrium producing a post-fertilization mechanism account for the enhanced effectiveness of UPA compared with LNG. The conclusion that UPA is an abortifacient is sound and precludes unrestricted use of UPA in Catholic hospitals.[32]

[32] Recent suggestion has been made that a "consensus" has developed among researchers warranting reconsideration of UPA's general exclusion from Catholic healthcare facilities (Hamel 2014).

16.6 Moral Certitude

The typical MOA by which Plan B prevents pregnancy is unknown and that creates a moral dilemma. While no one claims that absolute certainty is necessary for human action, something more than "possibility" or even "probability" is required in view of the grave matter at issue. The critical issue is and always has been one of moral certitude. Where prudential doubt exists as to MOA – and that is the *minimum* at play here – LNG must not be utilized absent some means providing moral certitude of the imperfect kind precluding embryocide.[33] That level of certitude is a specific term well understood in Catholic thought and well explicated by Thomas Slater (1908):

> Certainty in general is a firm assent of the mind to something known, without the fear of mistake. In mathematics and in other branches of exact science we can often attain absolute certainty, which rests on the evident truth of the principles which are employed to arrive at it. … In the science of morality we have frequently to be content with a lower degree of certainty…We have to be content with what is called moral certainty; but this again is of various degrees. I am morally certain of the existence of Berlin, though I never saw the city. Any person who doubted of its existence would be thought to be insane. The grounds on which the judgment that Berlin exists are based are so many and so strong that they leave no room for prudent doubt in the matter. In such cases we have perfect moral certainty. In other cases I may be conscious that mistake is possible but not probable, as when a man has been condemned on evidence which has satisfied a jury of intelligent men. In such cases *if there can be no prudent doubt about the justice of the verdict I have moral certainty of an imperfect but real kind.* If I could not safely rely in guiding my conduct on such a degree of certainty, I should have to abstain from action altogether. Ordinarily greater certainty cannot be obtained in human affairs.
>
> In order to act lawfully and rightly, *I must have at least moral certainty of the imperfect kind that the proposed action is honest and right.* This degree of certainty will be sufficient, for ordinarily no greater can be had, as we have just seen. It is also required for right action; for *if I am not at least to this extent morally certain that my action is right, I am conscious that it may be wrong. In this case I am bound to pause, and satisfy myself that it is right before acting; for if I do not do so my will is ready to embrace what may be wrong: I am ready to*

Hamel, who had reviewed the emerging data on UPA on two prior occasions (Hamel 2010a, 2012), reviewed the principal original research and review studies and suggested that UPA may offer a morally sound treatment in rape cases. Crediting Mozzanega's analysis as leaving the matter nominally unresolved, Hamel nonetheless strongly inferred that "sufficient moral certitude" might now exist to permit such use. Brehany (2016), relying on Mozzanega et al. (2014), sharply challenged Hamel's analysis. Given the significant deleterious impact on endometrial thickness, the frequency of induced bleeding, and the decreased expression of peripheral node addressins, Brehany's intervention provides welcome ballast to the discussion of UPA which, like that related to LNG, appears destined to endure. However, resort to "consensus" opinion among the cohort of researches supporting the contraceptive pharmaceutical industry is unwise. Such reliance by Austriaco (2007) and Hamel (2010b) proved unwarranted with respect to LNG, resulted in unnecessary and prolonged confusion, and contributed to the debacle in Connecticut regarding a state law mandate that requires Catholic hospitals to provide Plan B. See Davis (2010b) and the long-running colloquy between Austriaco and Davis in *NCBQ* extending from 2010 through 2015.

[33] Some maintain that a negative LH surge test provides sufficient assurance while others maintain a negative test does not preclude pre LH surge fertile phase uptake. For more on that debate see Peck and Velez (2013b, pp. 37–9) and Berg et al. (2011, pp. 16–18).

> *do the action whether it is in right order or not. But such a will is malicious; it is not firmly set on doing what is right; and sin is thereby committed.*[34]

In other words, certainty precluding reasonable doubt is required for moral certitude of the imperfect kind. Pope Pius XII (1942) was explicit that "probability" is insufficient:

> Between the two extremes of absolute certainty and quasi-certainty or probability, is that moral certainty ... It is characterized on the positive side by the exclusion of well-founded or reasonable doubt, and in this respect it is essentially distinguished from the quasi-certainty which has been mentioned; on the negative side, it does admit the absolute possibility of the contrary and in this it differs from absolute certainty.[35]

Even Plan B champions readily acknowledge that moral certitude requires "that the agent has excluded *all reasonable possibility of error*" (Hamel 2010a, p. 65; emphasis added). With that standard firmly in mind, it may be confidently stated that unless all reasonable probability that Plan B is an abortifacient may be excluded, moral certitude warranting its unrestricted use is not established. Other formulations that linguistically discount the abortifacient potential of Plan B are sometimes offered as a basis for moral certitude. However, with reference to a possible post-fertilization MOA, words and phrases such as "unlikely," "not probable," "more probable than not," "the preponderance of evidence," and "the weight of the evidence" are inadequate. Even the term "solid probability," frequently employed in various moral systems, may set the bar too low if it is used to assert moral certitude that LNG does not have an abortifacient MOA.

The burden of proof rests with the proponents of Plan B. And the locus of the burden is critical. Clarity as to that presupposition was clouded by a statement of the Connecticut Catholic Bishops (2007) in response to a statutory mandate to provide prescription emergency contraception to female victims of sexual assault without any testing other than for pre-existing pregnancy.[36] They announced a position of reluctant compliance given "doubt about how Plan B pills and similar drugs work." They also stated: "If it becomes clear that Plan B pills would lead to an early chemical abortion in some instances, this matter would have to be reopened." That reverses the burden of proof, freeing proponents of the duty to establish moral certitude, and placing a burden of affirmative proof on those raising prudential doubts about MOA and is plainly erroneous. The proper test is whether the acting agent has precluded all reasonable doubt that Plan B is an abortifacient, not whether the evidence is "clear" that it is an abortifacient.

This assessment of moral certitude applies equally to UPA. Outside the first and perhaps the second day of the fertile window, UPA presents clear abortifacient potential. Even with respect to that apparently "safe zone" difficulties arise with respect to identifying a rape victim's current cycle date. Given its known chemical

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[34] Vol. I, bk. 2, ch. ii, "On the Certain Conscience," pp. 59–60; emphasis added. Heribert Jone (1962) holds, "For moral certainty it suffices that all reasonable fear be excluded" (Bk. I, pt. 3, ch. i, n. 85.II.3, pp. 38–9).

[35] This English language translation is from the official version of the Holy See's *Address of John Paul II to the Tribunal of the Roman Rota* on 4 Feb. 1980 in which he quoted the passage from Pius XII's 1942 address. https://w2.vatican.va/content/john-paul-ii/en/speeches/1980/february/documents/hf_jpii_spe_19800204_sacra-rota.html. Accessed 30 April 2017.

[36] Conn. Gen. Stat. §19a–112e.

properties and the data regarding endometrial effects, ovulatory process, and steady prolonged efficacy, unrestricted provision of UPA is precluded, as abortifacient effects cannot be rules out to a moral certitude. Indeed, they seem quite likely.

Several other considerations warrant brief attention. First, reference to the principle of double-effect is occasionally offered as a default justification for administration of LNG (Berg et al. 2011, p. 24). Resort to that principle is inappropriate since any given administration of Plan B "does not have two effects, but only one of two [or perhaps more] possible effects" (O'Donnell 1997, pp. 196–7). Double-effect requires that at least *two* effects be anticipated: one good and the other evil and, while foreseen, is not intended. That is never the case with Plan B. In any given administration it is either abortive or it is not. The two potentials are mutually exclusive.[37]

Second, ERD n. 36 provides that healthcare providers should "offer the person … accurate medical information." Fn. 16 in that ERD recommends that "a sexually assaulted woman be advised of the ethical restrictions that prevent Catholic hospitals from using abortifacient procedures." How can a Catholic healthcare provider who dispenses Plan B to rape victims – with or without LH testing – reconcile the duty to provide accurate information with the unresolved MOA apparent from the scientific corpus? How might such "accurate information" be incorporated into a discussion about the ethical restrictions related to abortifacient procedures? Those dilemmas may well be unresolvable, at least at the current level of scientific knowledge as to MOA and so long as Catholic hospitals fail to properly assess the proper standards related to determination of moral certitude.

16.7 A Note on Protocols and a Dilemma

Various protocols have been proposed in an effort to identify acceptable windows of opportunity for non-abortive anti-fertility treatment. Perhaps the best known is the Peoria Protocol, also known as the "ovulation" approach. It calls for the administration of a pregnancy test and, if negative, testing to determine the imminence of ovulation, either by a quick urine Luteinizing Hormone (LH) test and/or by serum progesterone level testing. A positive LH test would preclude provision of LNG. However, a negative LH test cannot rule out the possibility that the patient is in her preovulatory fertile phase, precisely the time that LNG administration may trigger

[37] Excellent summaries of the principle of double-effect are provided in O'Donnell (1997, pp. 32–4) and Grisez (1983, pp. 307–9). For additional discussion of the principle of double-effect in relation to LNG, see Peck and Velez (2013b, pp. 36–8). There is some debate among interpreters of the principle of double-effect whether both effects must be anticipated to occur or whether the negative effect may merely be *risked*. In the case at hand, the claim of the latter camp would be that one does not both prevent conception and prevent implantation; rather, one seeks to do the first while accepting the risk of the second. A representative of this view in relation to LNG is Sulmasy (2006); for a critique of this view, see Davis (2010b, pp. 766–7, n. 93).

postovulatory abortifacient MOA. For that reason the ovulation approach does not provide an adequate model for assessing LNG administration.

A more involved protocol for LNG and UPA has emerged from Austria. It proposes transvaginal ultrasound examination to measure the diameter of the leading follicle and thickness of the endometrium, along urine LH testing and macroscopic evaluation of cervical mucus. It would permit LNG, combined with a non-hormonal COX-2 inhibitor, if the leading follicle measured less than 14 mm, the endometrium thickness measured 8 mm or less, and both a LH urine test and evaluation of cervical mucus were negative. For UPA, administration would be permitted if the leading follicle measured less than 14 mm (Bonelli et al. 2014). While this proposal should be applauded for the effort to make non-abortive treatment available, it is more complex than the ovulation approach related to LNG and would require careful assessment of multiple indicia. As for UPA, it appears viable as it sets the follicle diameter low enough to provide relative assurance that breakthrough ovulation is extremely unlikely. The potential for human error in assessment is evident and in any event would only apply to a fraction of potential patients confirmed to be in first day or two of the fertile window. Perhaps it most important contribution is recognition that unrestricted administration of LNG or UPA is unacceptable in Catholic hospitals. Nonetheless, it is a proposal warranting additional evaluation in the United States.

The movement of LNG toward full over the counter (OTC) accessibility will soon precipitate a national confrontation. Some states, such as Connecticut, mandate the provision of EC to victims of sexual assault in all licensed healthcare setting were victims are treated or examined, including Catholic hospitals. Other states have similar mandates and proposals for a federal mandate have long circulated[38] and are sure to re-emerge. The three Connecticut Catholic hospitals currently provide Plan B without restriction to rape victims who test negative for pregnancy. However, should Plan B finally become fully OTC, as appears imminent, it will no longer satisfy the state mandate which requires provision of *prescription* EC.[39] That would leave UPA and perhaps RU-486, the so-call "abortion pill" which is also a powerful anovulant, as the alternatives. The state mandate would require one or the other without any testing protocol to determine cycle phase, diameter of the dominant follicle or other indication of post-fertilization MOA. This has long been the Trojan Horse of a concerted plan to introduce abortion into Catholic hospitals. The crisis, long approaching and frequently forewarned,[40] has arrived.

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[38] In 2005, then Senators James Corzine, Hillary Clinton, Patty Murray, Frank R. Lautenberg, Barbara Boxer, Maria Cantwell, Edward M. Kennedy, Daniel K. Inouye, and John F. Kerry proposed the Compassionate Assistance for Rape Emergencies Act which would have required any hospital receiving federal funds to provide FDA approved EC to rape victim. The proposal mandated that providers explicitly advise the victim that "emergency contraception does not cause an abortion" (Corzine et al. 2005).

[39] Connecticut General Statute, sec. 19a–112e, (a)(1) and (b)(3), http://law.justia.com/codes/connecticut/2012/title-19a/chapter-368a/section-19a-112e (accessed 18 July 2016).

[40] See Davis (2007, 2010b, 2013).

16.8 Conclusion

While no one knows with absolute certitude how LNG works in a given case, the suggestion that the scientific corpus establishes the MOA in the majority of cases is unfounded. Claims that post-fertilization MOA has been proven nonexistent or "rare" has passed onto the ash heap of history. But that has not precluded the sustained and erroneous assertion that Plan B operates primarily by suppressing ovulation.

The task of separating objective scientific data from the subjective opinion of researchers and commentators has yielded valuable insights and has thoroughly undermined prior claims of moral or scientific certitude about the MOA of Plan B. While resistance to the obvious has been entrenched, this much is certain: the Catholic tradition of moral analysis in cases of doubt, properly applied, prohibits the unrestricted administration of LNG. The same holds true with respect to UPA.

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