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The Scientific and Public Health Need for Emergency Contraceptive Pills to be Available Over-the-Counter

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As an obstetrician/gynecologist and member of Physicians *for Reproductive Choice and Health*® (PRCH), I strongly encourage the United States Food and Drug Administration to grant emergency contraceptive pills (ECPs) unrestricted over-the-counter status.

PRCH is a national, nonprofit organization of nearly 6,000 physician and non-physician members committed to ensuring that all people have the necessary knowledge and freedom of choice to make reproductive health decisions. We firmly support universal access to safe, effective, and evidence-based reproductive health care.

I thank the Food and Drug Administration for this opportunity to testify regarding the safety and efficacy of ECPs, and to verify the urgency of unfettered access. I also applaud both Advisory Committees for their recognition of the scientific and medical data presented by experts in the field.

I am currently an Associate Professor at Mount Sinai Medical Center in New York City. Given the extremely high rate of unintended pregnancy in the United States, the extensive scientific research on ECPs, and my clinical experience, I believe that over-the-counter (OTC) status will remove unnecessary and harmful barriers to a highly effective and entirely safe product.

Unintended Pregnancy in America

The majority of American women use contraception. Of the 60 million women aged 15-44, 64 percent practice contraception.[1] Nearly all – ninety-three percent – of women aged 18-44 who are sexually-active, non-sterile, and not attempting to conceive use a form of contraception.[2] Most of these women – 61 percent – use reversible contraceptives like condoms or the pill, and the remaining women rely on male or female sterilization.[3] Overall, women use their contraception responsibly and effectively, as actual-use studies show success rates from 88 to 99.6 percent for reversible methods, and more than 99 percent for non-reversible methods of contraception.[4]

Contraception, regrettably, is neither universal nor fail-proof. Unintended pregnancies occur in both the small percentage of women who don't use contraception, and in women for whom contraception fails. Forty-eight percent of women who had an unplanned birth in 1994 had been using a contraceptive method during the month they became pregnant, as had 58 percent of those who had abortions. Of all the women who experienced an unintended pregnancy, more than half – 53 percent – were using contraception at the time of conception.[5] We must increase patients' access to, and knowledge of, correct contraception utilization while confronting the occurrence of unprotected intercourse; broken, slipped, or leaking condoms; dislodged or broken diaphragms; incorrect use of cervical caps; un-melted spermicide tablets; missed birth control pills; expulsion of intrauterine devices; late injection of subcutaneous contraceptives; rape; and simple statistical failure of birth control, among others.[6]

Despite being the wealthiest nation in the world, the United States has the highest rate of unintended pregnancy among industrialized nations.[7] As of 1994, nearly half – 49 percent – of all pregnancies in America were unintended, and more than half – 54 percent – of those ended in abortion. Among women aged 15-44, 28 percent have had an unplanned birth, and 30 percent have had an abortion.[8] These numbers are problematic, as unintended pregnancy is associated

with both high maternal morbidity and economic costs.[9] Fortunately, unintended pregnancies are largely preventable, and increasing use of effective contraception has led to an overall decline of unintended pregnancies since 1987.[10] Health experts estimate that widespread use of emergency contraceptive could prevent as many as 1.7 million unintended pregnancies each year.[11]

Medical Information about ECPs

Emergency contraceptive pills can prevent pregnancy after intercourse by providing a concentrated dose of the same hormones found in daily birth control pills. As with daily birth control, ECPs are available as either progestin-only or combined estrogen-progestin pills. Both types of ECPs are available as a two-dose regimen, in which the first dose should be taken as soon as possible after unprotected intercourse, and the second dose taken 12 hours after the first.[12]

Documented use of ECPs began in the 1960s, as physicians helped sexual-assault survivors reduce their risk of pregnancy.[13] In 1974, a Canadian physician named A. Albert Yuzpe first published studies showing his eponymous two-dose regimen of ECPs to be both safe and effective. By the 1990s, nearly one-third of ECP prescriptions were for rape survivors, and the medical community began to recognize that ECPs should be available to all women.[14] Since then, the FDA has recognized the extensive data on ECP safety and efficacy by endorsing the use of combined estrogen-progestin pills as emergency contraception in 1997, approving the first dedicated ECP in the United States in 1998, and approving the first progestin-only ECP in 1999.[15] Despite ECPs' unique ability to reduce unintended pregnancy rates, they have been vastly underused and misunderstood. A 2003 survey found that only 17 percent of gynecologists and 9 percent of general practice physicians routinely discussed emergency contraception with their clients. Thirty-two percent of women aged 18-44 still do not know there is something a woman can do to prevent pregnancy immediately after intercourse.[16]

ECPs and Existing Pregnancy

Both patients and providers have misconceptions about ECPs, their methods of action, and how they differ from mifepristone – the medical abortion pill. ECPs and mifepristone are unrelated medications. ECPs do not induce abortion in an already-pregnant woman; they prevent pregnancy.

Mifepristone (also known as RU-486) terminates an early, established pregnancy when taken within 63 days of a pregnant woman's last menstrual period. A mifepristone regimen interrupts the hormone necessary for fetal development, causing the uterus to contract and empty. In contrast, ECPs work by *preventing* a pregnancy before it even begins. ECPs are not abortion pills, do not contain the same chemical ingredients as mifepristone, and do not affect a pregnancy once it has been established. Instead, ECPs use estrogen and progestin to prevent a pregnancy by inhibiting ovulation, fertilization, or implantation. Pregnancy begins with the implantation of a fertilized egg into the uterine lining, typically six to seven days after intercourse. Emergency contraception acts within this one-week window to prevent the pregnancy from beginning.

Certain ECP opponents focus on this last mechanism – preventing implantation of a fertilized egg – and contend that it is analogous to abortion. This argument is scientifically and legally fallacious. The Medical Dictionary of Obstetric and Gynecologic Terminology, the United States Code of Federal Regulations, the National Institutes of Health, and the United States Department of Health and Human Services are among the many official sources that define pregnancy not by fertilization, but by implantation.[17,18,19]

It is both scientifically inaccurate and inconsistent to argue that implantation inhibition by ECPs is a form of abortion, as many standard contraceptive methods may have the same mechanism of action: daily birth-control pills, birth-control shots, and intrauterine devices (IUDs) may all prevent the implantation of a fertilized egg into the uterine lining. Even breast-feeding has a contraceptive effect that may work by inhibiting ovulation and/or implantation, particularly within six months of delivery.[20] More than half of all fertilized eggs are never implanted in the uterus, but flushed out of the body during menstruation.[21]

Additionally, the most recent analyses of ECPs offer no evidence of implantation interference, but do support pre-fertilization contraceptive effects.[22] Since ECPs work during the week after intercourse, they may either prevent the initial encounter of spermatozoa with the ovum or impede complete fertilization once gametes come in contact. Fertilization in humans is already an inefficient process: in *ideal* circumstances (when intercourse occurs during a woman's six most fertile days of the menstrual cycle), there is only a 50 percent chance of fertilization.[23] Minor changes in the processes leading to fertilization can significantly reduce the chances of gametes meeting, as has been confirmed experimentally with ECP alterations to pre-fertilization

events.[24] In contrast to such data supporting pre-fertilization mechanisms, only one post-fertilization mechanism – decreasing uterine receptivity – has been investigated. At least four studies have suggested that synthetic progestins from ECPs (e.g., levonorgestrel) have negligible effects on the uterine lining.[25,26,27,28] Analysis of synthetic progestins suggests that both the 25 percent failure rate of certain ECPs and the fact that efficacy is highest immediately after intercourse are additional reasons for doubting that these products prevent pregnancy via post-fertilization events.[29]

Some people have errantly expressed concerns about ECPs' effects on an already-established pregnancy or on a pregnancy that may develop despite ECP use. Several major studies show that high-dose hormonal contraceptives neither interrupt pregnancy nor harm a developing fetus.[30,31,32,33] Forty years of extensive studies support this data and confirm that hormonal contraceptive use during early pregnancy will not damage an embryo. The FDA removed label-warnings of possible teratogenic effects from oral contraceptive pills several years ago, and FDA-approved ECP labels do not carry such warnings. For this reason, guidelines from the FDA, the American College of Obstetricians and Gynecologists (ACOG), and the Program for Appropriate Technologies in Health do not require a pregnancy test before ECP treatment.[34] Although ectopic pregnancy may still occur after ECP use, research indicates that the product does not increase that risk.[35]

Efficacy and Safety

Multiple studies on ECPs demonstrate that they are highly-effective at preventing pregnancy when taken immediately after intercourse. The risk of pregnancy without contraception is 8 percent. The combined estrogen-progestin ECPs may reduce this overall risk to 2 percent, and the progestin-only product may reduce it to 1 percent.[36] Studies of the progestin-only regimen indicate that ECPs can reduce pregnancy risk by 95 percent when taken within 24 hours of unprotected intercourse, and by 89 percent when taken within three days.[37] After three days, ECP-efficacy is cut in half for every 12 hours of delay, even though the regimen may still work as a contraceptive up to 120 hours (five days) after unprotected intercourse.[38,39,40,41] Given these efficacy rates, our responsibility as medical professionals is to make ECPs available to all women as soon as possible after unprotected intercourse – preferably within the first 12 hours.

Extensive research also demonstrates that ECPs are extremely safe, including when self-administered. The hormones in ECPs have been used for more than thirty years as daily birth control by tens of millions of women, and serious complications have been extremely low. The World Health Organization's Task Force of Postovulatory Methods of Fertility Regulation conducted the largest study of the two FDA-approved ECP regimens to date, and found the most common side-effects to be nausea, breast tenderness, lower abdominal pain, fatigue, headache, irregular menstruation, dizziness, vomiting, and diarrhea.[42] Although no deaths have ever been attributed to ECP use, approximately 300 women die each year from overdoses of other OTC medications such as analgesics, antipyretics, and antirheumatics.[43] In contrast, research suggests that the most serious effects of intentional ECP overdose would be nausea and irregular menses.[44]

Although the current package-labels for ECPs list a number of contraindications, none of these are medically or scientifically-supported for hormonal emergency contraceptives. Rather, the lists are adapted from daily birth control labeling and, according to both ACOG's Practice Patterns and the Consortium for Emergency Contraception, are unlikely to apply to ECPs because of variant use and duration.[45] From this list, pregnancy is a contraindication to ECPs because the product is ineffective during pregnancy, not because of any safety concerns.

With such documented safety, ECPs do not require professional supervision or monitoring. The treatment duration with ECPs is only 12 hours, the hormones are not addictive, and side-effects are mild and limited. All women take the same dose of each regimen, and no harmful drug interactions are known to exist with ECPs. Although certain medications (like rifampin, some anticonvulsant drugs and St. John's Wort) may reduce ECP efficacy, there is no evidence how – or if – ECP dosage should be altered to accommodate these drugs.[46] Researchers assert that, contrary to popular belief, there is also no credible evidence that commonly-used antibiotics, including penicillins[47] and tetracyclines,[48] reduce the efficacy of oral contraceptive pills. Small-scale studies have revealed no relevant effects of common antibiotics on serum levels of contraceptive steroids.[49]

Concerns Regarding OTC Use

Actual Use

In addition to evaluating the safety and efficacy of ECPs, scientific research has also addressed actual-use questions specific to OTC availability. Common concerns include whether women will be less likely to use regular contraception, more likely to become repeat ECP-users, and/or more likely to engage in risky sexual behavior. At least six major studies on four continents have addressed these points. Results from these studies indicate that easier availability of ECPs neither undermines use of consistent contraception (like condoms and birth-control), nor increases the incidence of unsafe sexual behavior.[50] Studies of advanced provision do, however, show that women with easier access are much more likely to use ECPs when necessary.[51,52,53,54] Only a small proportion of studied ECP-users needed the product more than once or twice a year, which suggests that repeat use will not be a problem because consumers understand ECPs are not first-line contraceptives.[55,56,57]

Nevertheless, clear consumer information discouraging use as the sole method of contraception is important, as pregnancy risk is significantly higher when ECPs are used as a primary contraceptive. Product branding and marketing strategies have actively promoted this message by terming dedicated products "*emergency* contraceptive pills." The brand name of the current progestin-only product, Plan B®, likewise suggests that it is not a first line of contraception, and a major public education campaign out of Princeton University is named *Back Up Your Birth Control*. Available research indicates that such efforts are, and will continue to be, effective in promoting this product with its dedicated, "emergency" purpose. ECPs can be likened to fire extinguishers. They exist in case something goes wrong, but every home should have one. Buying a fire extinguisher does not increase the likelihood of, or incentive to, cook recklessly simply because an emergency solution is available.

Label Comprehension

Label-comprehension and actual-use studies for ECPs demonstrate that women, including adolescents, can use OTC ECPs safely, effectively, and appropriately. The label-comprehension study of a prototype-product revealed that 97 percent of participants understood to use the product as soon as possible or within 72 hours of unprotected intercourse, and 94 percent understood that it provided no protection against HIV or other sexually-transmitted infections.[58] The actual-use study found an extremely low incidence of contraindicated use (1.3 percent, based on labeled contraindications) in a study population broadly representative of women likely

to use ECPs. In addition, 93 percent of subjects took the first pill within 72 hours of unprotected sex and the second pill within 16 hours of the first. None of the participants reported serious side-effects, and less than 2 percent of the subjects became pregnant.[59] Over-the-counter provision of progestin-only ECPs abroad has been very successful, and women have not had problems understanding usage instructions.[60]

Adolescent Use

At least six major scientific studies have focused specifically on adolescents and ECPs. The conclusions uniformly report that adolescents will use the product correctly and infrequently.[61] Findings from a University of Pittsburgh study indicated that adolescent girls given an advanced supply of ECPs were more likely to use it when needed, and reported fewer unintended pregnancies and sexually-transmitted diseases.[62] Other studies confirmed that teens' use of regular contraceptives like condoms do not decline with ECP use,[63,64] and a study of young women in Britain found that using ECPs following a pregnancy scare may actually make women *more* likely to use an effective, ongoing contraceptive method.[65] Facilitating adolescents' access to ECPs is particularly important, as teenagers often have significant trouble gaining access to reproductive health information and care. Research shows that in settings as diverse as Scotland and Hong Kong, adolescents know more about emergency contraception and use it more frequently than in the United States.[66] Currently, condoms and spermicides are widely available to minors over-the-counter. As a product that could drastically reduce the rate of unintended pregnancy among adolescents, ECPs should share their OTC status.

ECPs Meet FDA Criteria for OTC Products

In the wake of overwhelming scientific data supporting OTC-ECPs' efficacy and safety, prescription-only status is medically unjustified and indefensible. When we consider each of the four FDA criteria for OTC status, ECPs meet them all:

- *First, treatment must be self-diagnosable.* No one is more likely to diagnose contraceptive failure (or failure to use contraception) than the woman herself.
- *Second, treatment must be effective when self-administered.* Correct administration of ECPs relies only on how much time has elapsed since intercourse. All patients receive

the same dose of ECPs, and any drug interactions would be harmless and unlikely to seriously affect efficacy.

- *Third, treatment must be safe when self-administered.* ECPs are nontoxic to women, as well as to a developing fetus in case of established pregnancy. The product has a low risk of abuse and few, minor side-effects.
- *Fourth, labeling must be clear for self-administration.* As demonstrated by research, ECP instructions are simple, clear, comprehensive, and easy-to-follow.

Prescription Status Creates Detrimental Access Barriers

In addition to being medically unjustified, prescription-only status of ECPs erects harmful barriers to access. Emergency contraceptive pills are unique in that their efficacy is extremely time-sensitive, and waiting for a prescription to be filled wastes precious moments. Most women seek emergency contraception on weekends or after normal business hours, and thus have difficulty obtaining a physician's prescription. Many women do not have a regular healthcare provider, and a study conducted by the Reproductive Health Technologies Project found that 14 percent of calls made to the ECP hotline (1-888-Not-2-Late) resulted in failure to get an appointment or prescription for ECPs within 72 hours.[67]

It is imperative that sexual assault survivors have immediate, private, and unhindered access to ECPs – a goal facilitated by OTC-access. Years of research suggest that women who have been sexually-assaulted do not always seek healthcare or feel comfortable discussing the episode immediately afterwards. According to the Alan Guttmacher Institute, there are an estimated 32,000 rape-related pregnancies each year in women over 18 years of age.[68] In the case of women who do present in emergency rooms post-sexual-assault, studies have found that the majority of hospitals do not routinely offer emergency contraception to rape survivors, nor do they have standard protocols for offering the treatment. A number of religiously affiliated – and even some secular – hospitals do not provide ECPs under any circumstances. Currently, only six states mandate that emergency rooms provide information about, and access to, ECPs for sexual-assault survivors.[69] Over-the-counter access to ECPs is especially critical for the well-being of sexual-assault survivors.

Prescription-only status of ECPs is deeply frustrating for both patients and healthcare providers. As a physician, supplying an unnecessary, immediate prescription for this product

adds to an already-busy practice. I often feel as though I'm racing against time while my patients overcome great hurdles to access a treatment for which my approval and guidance are gratuitous. A majority of my colleagues and our professional organizations share these sentiments. The American College of Obstetricians and Gynecologists has officially stated that ECPs "can meet the FDA criteria for OTC availability," and that "substantial barriers exist to women obtaining this fallback contraceptive method that must be used within 72 hours after unprotected intercourse."[70] Similarly, the American Medical Organization (AMA) declares that it will work to improve access to ECPs while promising to "support and monitor the application process of manufacturers filing for OTC approval of ECPs with the Food and Drug Administration."[71]

While considering improved ECP access, we must keep in mind that only a slim minority of women realize that this product exists: a 2003 survey revealed that only 6 percent of women in the United States who would need emergency contraception have ever used it (up from 1 percent in 1997).[72] Women who *are* aware of ECPs must locate a provider, obtain a prescription, fill it at a local pharmacy, and take the pills within 72 hours. This deleterious delay of treatment exists despite the fact that ECPs are time-sensitive, safe, and easy to self-administer.

Financial Implications of OTC-Status

Current Insurance Policies **(this section to be included in written testimony only)**

Some proponents of ECPs are apprehensive about the financial consequences of OTC status, and the potential consequences of limited access. Achieving OTC status may potentially involve a price increase and eliminate insurance coverage, making access particularly difficult for low-income women. However, so few women of any socio-economic status have current access to ECPs that OTC status could only benefit universal access.

Since 1973, individual states have been required to cover family-planning services for Medicaid beneficiaries. Nevertheless, only half the states currently have legislation requiring contraceptive coverage, 15 of which include exemptions for employers based on religious beliefs.[73] As of 2003, 23 states still do not cover emergency contraception as a family-planning service under Medicaid, and four states provide only conditional, case-based coverage.[74] Aside from Medicaid, many private insurance plans do not cover the costs of birth control (including emergency contraception). A 2001 Kaiser Family Foundation Survey found that only 41 percent

of insured employees had coverage of all reversible contraceptives, despite the fact that 98 percent of insured employees had coverage of prescription drugs in general.[75]

If we shelve the issue of time-sensitivity with emergency contraceptives for the moment, these numbers alone demonstrate an enormous access barrier. They tell us that even if women could get immediate access to ECPs, few of them would have an insurance plan that covers the cost. The trick is to provide all women the benefits of OTC access without denying the financial benefits of insurance coverage. There are two possible ways to do this. First, although insurers do not typically pay for non-prescription medications, some state Medicaid programs have made exceptions for certain OTC contraceptives like condoms. If ECPs were to go OTC, state governments and private-insurers could theoretically maintain this option.[76] Second, healthcare providers could continue to provide a prescription for women who need the financial support of insurance services. We have seen this OTC/prescription duality with allergy medications that recently have been granted OTC status, but for which providers may still write an alternate prescription. Upon weighing the question of insurance-coverage against the possibilities for widespread access and use, the switch to OTC-status appears fully justified, especially since fiscal impacts on insurance coverage are difficult to predict.

Cost Savings of Improved Access to and Use of ECPs

We know that currently, ECP dedicated products are available to public health clinics for $4 or less per dose, while women who purchase the same medication without insurance coverage pay $18-$50.[77] The projected commercial cost of an OTC ECP is estimated to be $25-$35, and research indicates that most women will use ECPs only once or twice each year. While $30 for a single dose of ECPs seems rather expensive (and may even be a deterrent for repeat use), we must hold this amount against the comparatively enormous costs of either continuing a pregnancy or having an abortion. The average cost associated with the birth of a healthy baby (including prenatal care, delivery and newborn care for a year after birth) is about $10,000, according to a 1993 special report in *Business and Health*.[78] The average cost of having a medical abortion ranges from $350 to $575, and a surgical abortion, $225 to $575.[79]

Studies in both Canada and the United States have shown that ECPs are significantly cost-saving to the payer, whether provided in advance or immediately following unprotected intercourse.[80,81] Advanced-provision of ECPs to American women using barrier contraceptives,

spermicides, withdrawal, or periodic abstinence was particularly lucrative, saving between $263 and $498 in personal medical costs annually by averting unintended births.[82] Researchers conclude that increased use of ECPs could reduce the considerable medical and social costs associated with unintended pregnancy.[83] In addition, the Comptroller of New York State released a cost-savings analysis of ECP provision on November 6, 2003.[84] His careful analysis points to a $452 million savings in Medicaid and private health care spending in New York State from effective ECP provision. The Comptroller's report thus demonstrates that ECP provision can be a significant cost-saver for government insurance plans, private insurers, and individuals.

Conclusion

Medical decisions should be rooted firmly in scientific evidence. Research on emergency contraception – including numerous randomized trials, data on actual use, and label-comprehension studies – has revealed that prescription-only status of ECPs is both gratuitous and harmful. Prolific research on ECPs documents their safety, efficacy, and ease-of-use, along with the economic benefits of OTC status for individuals, institutions, and public systems. The Institute of Medicine has claimed that establishing "evidence-based" medicine should be at the forefront of modern medicine's agenda, and has advocated in favor of aggressive efforts to reduce unintended pregnancy rates in America.[85] The FDA can bring the medical community one step closer to reaching both goals by acknowledging the overwhelming evidence and granting OTC status to ECPs.

Professional and public support of the OTC switch is obvious, as more than 70 organizations are signators to the 2001 Citizen's Petition for Status Change for Emergency Contraception. Among the numerous medical and public health organizations supporting the switch are: the AMA, ACOG, the Association of Reproductive Health Professionals, the American Academy of Pediatrics, the American Medical Women's Association, the American Nurses Association, the National Association of Nurse Practitioners in Women's Health, the American Public Health Association, Planned Parenthood Federation of America, the Black Women's Health Imperative, Advocates for Youth, the American Pharmaceutical Association and *Physicians for Reproductive Choice and Health®*.

Numerous other countries currently allow for non-prescriptive ECP provision, including Morocco, the United Kingdom, Norway, Sweden, Finland, Israel, France, Belgium, Denmark,

Portugal, South Africa, Albania, and provinces within Canada.[86] In the past 30 years, more than 700 products have been switched from prescription to OTC status in the United States.[87] ECPs clearly meet all requisite criteria to join their ranks. As our capacity to make scientifically-sound judgments increases, so does our responsibility to make proven safe, effective, and easy-to-use treatments available OTC to the general public.

As the nation's only physician-led organization dedicated to universal reproductive health, *Physicians for Reproductive Choice and Health*® firmly endorses over-the-counter status of ECPs. Over-the-counter status would facilitate access for women who have experienced contraceptive failure, been sexually-assaulted, or had unprotected intercourse. Medical studies clearly demonstrate the safety and efficacy of dedicated ECP products. Considering the high unintended pregnancy rate in America and the time-sensitive nature of ECP access, establishing OTC availability of this product is a crucial public-health imperative.

The Alan Guttmacher Institute. Facts in Brief: Contraceptive Use. Accessed 11/21/03 at: http://www.agi-usa.org/pubs/fb_contr_use.pdf.

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[4] Specific success rates are as follows. For reversible methods: cervical cap, 82 percent; diaphragm, 82 percent; condom, 84 percent; the pill, 94 percent; the IUD, 96 percent; and injectables, 99.6 percent. For non-reversible methods: tubal sterilization, 99.5 percent; vasectomy, 99.8 percent; and implants, 99.95 percent. Statistics from: The Alan Guttmacher Institute. Facts in Brief: Contraceptive Use. Accessed 11/21/03 at: http://www.agi-usa.org/pubs/fb_contr_use.pdf.

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