Congress of the United States
Washington, DC 20515

August 2, 2010

The Honorable Margaret Hamburg
Commissioner
U.S. Food and Drug Administration
Rockville, MD 20687

Dear Commissioner Hamburg:

On June 3, 2010, you received a Congressional letter requesting information regarding questions and concerns about the approval of Ulipristal Acetate, marketed as *ella,* and to date you have not replied. Furthermore, these questions and concerns were not adequately addressed during the June 17, 2010 Reproductive Health Drugs Advisory Committee meeting regarding *ella.*

While the drug is being presented as a five day "emergency contraceptive" – preventing ovulation, fertilization, or implantation – there is evidence that Ulipristal Acetate (*ella*) may also kill or injure an unborn child after implantation. If this is the case, classifying *ella* as an "emergency contraceptive" would be deceptive. Women deserve to know if *ella* can cause an abortion so they can make informed decisions. We are also concerned about the potential for adverse health effects on women and girls who take this new drug.

Ulipristal Acetate and the abortion drug Mifepristone (RU-486) are both selective progesterone receptor modulators (SPRM). SPRMs block progesterone, which is necessary to maintain pregnancy.[1] According to the Food and Drug Administration (FDA), if approved, *ella* would be the first SPRM available in the United States for the indication of "emergency contraception (EC)."[2] Alternatively, the FDA approved "emergency contraceptive" Levonorgestrel (Plan B or NextChoice) is classified as a progestogen, not an SPRM.

Given *ella*'s similar chemical makeup to RU-486, we were disappointed that the advisory committee did not insist on evidence demonstrating that *ella*'s modes of action do *not* include abortion, especially in light of information showing that *ella* causes abortions in animal studies and that data are "too limited to draw any definitive conclusions regarding the effect of ulipristal on an established pregnancy or fetal development."[3] If *ella* will be marketed as an emergency contraceptive, women deserve to see evidence demonstrating that *ella* will not destroy or harm an unborn child. Similarly, we are deeply disturbed to learn the advisory panel dismissed the manufacturer recommendation for a pregnancy test to rule out an existing pregnancy prior to dosing.

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[1] "Ulipristal acetate prevents progesterone from occupying its receptor, thus the gene transcription normally turned on by progesterone is blocked, and the proteins necessary to begin and maintain pregnancy are not synthesized." European Medicines Agency, "CHMP Assessment Report for EllaOne," (Doc.Ref.: EMEA/261787/2009), p. 8.

[2] FDA Background Document for Meeting of Advisory Committee for Reproductive Health Drugs NDA 22-474 Ulipristal Acetate (Proposed trade name: ELLA) HRA Pharma (June 17. 2010), pg 8

[3] FDA Background Document for Meeting of Advisory Committee for Reproductive Health Drugs NDA 22-474 Ulipristal Acetate (Proposed trade name: ELLA) HRA Pharma (June 17. 2010), pg 10-11

manufacturer recommendation for a pregnancy test to rule out an existing pregnancy prior to dosing.

Another issue that has not been adequately addressed is the potential for off-label use and the possibility of adverse effects to women and their children if *ella* is used off-label. There are compelling reasons to believe that *ella* could be used off-label to intentionally or unintentionally induce an abortion expecially if dispensed off-label after the time indication included in the FDA approved dosing regimen. In order to give women adequate informed consent, the FDA must ensure that the approved dose or higher doses cannot be used to induce an abortion.

We also have significant concerns about the safety of *ella*. The FDA summary indicates that the clinical study was too limited to draw any meaningful conclusions about risks associated with ectopic pregnancy[4]. Since *ella*'s chemical make-up and mode of action are very similar to RU-486, which causes serious adverse health risks such as severe bleeding, ruptured ectopic pregnancies, serious infections, and even death, further study is necessary to ensure *ella* is safe for women, particularly if it is used off-label. Limited to no data is available about *ella*'s effect on minors or its interaction with other drugs, such as hormonal birth control.

In light of these significant concerns, we urge you to ensure that additional research is conducted to ensure *ella* is safe for adult women and minor girls when used as approved or off-label. We also believe that *ella* should not be approved unless there is significant evidence that it does not pose a risk to unborn children after implantation. Without such evidence, it certainly should not be categorized as "emergency contraception."

We respectfully request a response to the concerns raised in this letter no later than August 13, 2010. Thank you for your consideration and attention to this important matter.

Signatories to Letter to FDA Regarding Ulipristal Acetate

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Chris Smith
Collin Peterson
Dan Lipinski

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George Radanovich
Mike McIntyre
Todd Tiahrt
Jim Sensenbrenner
Nick Rahall
Walter Jones
Pete Hoekstra

[4] FDA Background Document for Meeting of Advisory Committee for Reproductive Health Drugs NDA 22-474 Ulipristal Acetate (Proposed trade name: ELLA) HRA Pharma (June 17. 2010), pg 46

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