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October 24, 2007

Division of Dockets Management
Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane
Room 1061
Rockville, MD 20852

CITIZEN PETITION

The undersigned submits this petition under the Federal Food, Drug, and Cosmetic Act, Chapter 5, Subchapter B (more commonly known as the Orphan Drug Act), and in accordance with the procedural requirements specified in 21 CFR 10.30, to request that the Commissioner of Food and Drugs (the Commissioner) revoke the Orphan Drug designation for Gestiva™, a product described as a long-acting, naturally-occurring form of progesterone, for which a New Drug Application (NDA, number 21-945) is currently under review, and, should this application be approved, refrain from granting Gestiva exclusivity of any kind due to the longstanding availability and use of the active ingredient in the indication being pursued and the lack of any research investment by the sponsor which merits compensatory protection in the marketplace.

A. ACTION REQUESTED

Sidelines National Support Network (Sidelines) requests that the Commissioner reconsider and revoke the Orphan Drug designation assigned to Gestiva and entered in the Cumulative List of Orphan Designated Products which was published on January 25, 2007 by the Office of Orphan Product Development (OOPD).

B. STATEMENT OF GROUNDS

Sidelines is a 501(c)(3) non-profit organization providing international support for women and their families experiencing complicated pregnancies and premature births. We also encourage mothers to investigate scientifically well-founded therapies targeted at reducing preterm birth, irrespective of the circumstances surrounding delivery (e.g., singleton births, multiple births, recurrent and first-time preterm delivery).

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According to the March of Dimes website¹ which cites final natality data for 2004 from the National Center for Health Statistics, there were 4,112,052 live births in the United States that year. Of these, 1 in 8 babies (12.5% of live births) was preterm (born before 37 weeks' gestation).² The rising incidence of preterm birth over the past decade (a nearly 14% increase between 1994 and 2004)³ underscores to an even greater extent the growing need for accessible and economically feasible treatment options for women facing high-risk pregnancies.

It was with great anticipation that we observed the May 4, 2006 press release from Adeza Biomedical Corporation (Adeza) revealing its submission of an NDA for Gestiva, also known as 17 alpha-hydroxyprogesterone caproate (or 17P) for the indication of "prevention of recurrent preterm birth." Although 17P has been a chief treatment option for over 25 years for mothers facing premature labor and delivery, FDA assessment of data (supported by the U.S. government via the National Institutes of Health) submitted for this drug in this underserved group appeared to be an opportunity to gain a greater and more specific knowledge of 17P activity via more widespread post-approval use. These *publicly-funded* data were reviewed at the Reproductive Health Drugs Advisory Committee (the Committee) meeting of August 29, 2006.⁴ At that time, a representative of Sidelines was among those who addressed the Committee and raised concerns, not about the efficacy of 17P, but about the implications of any inappropriate marketplace exclusivity, and particularly its potential status (upon approval) as an Orphan Drug.

The Orphan Drug Act (ODA) has at its foundation the concern that treatments for rare diseases or conditions will go uninvestigated or under-investigated due to the difficulty or cost involved in conducting the two adequate and well-controlled clinical studies demonstrating the safety and efficacy of the drug product customarily required for NDA approval, and the extended timeframe for recouping costs once that approval is granted. ODA provides protection of this extensive investment of time and resources in the form of market exclusivity for a seven-year period commencing at approval of a successful Orphan Drug application.

A number of unique circumstances argue against application of ODA to any 17P NDA.

First, there are substantial, unresolved issues as to what the final indication would be, should the Gestiva NDA be approved – with options ranging from the applied-for "prevention of recurrent preterm birth," to the OOPD designation of "prevention of preterm birth in singleton pregnancies," to some variant of these two -- and whether the number of patients in that final group would ever, however defined, total less than the statutory minimum of 200,000 individuals.

¹ <http://www.marchofdimes.com/peristats/tlanding.aspx?reg=99&top=2&lev=0&slev=1>

² <http://www.marchofdimes.com/peristats/tlanding.aspx?reg=99&top=3&lev=0&slev=1>

³ *ibid.*

⁴ Summary Minutes available at <http://www.fda.gov/ohrms/dockets/ac/06/minutes/2006-4227M1.pdf>

Second, any database search of the available literature shows an abundance of clinical investigations utilizing 17P to treat various subgroups of at-risk pregnancies. The ODA focus on stimulating research efforts, therefore, seems unnecessary for 17P. Unfortunately, no unequivocal portrait of the optimal patient profile or patient group has emerged, to date, from this research, a fact is recognized by the American College of Obstetricians and Gynecologists (ACOG), when it issued its opinion that “further studies are needed to evaluate the use of progesterone”⁵ in additional patient populations. Somewhat ironically, it is an NIH-based study⁶ that constitutes the backbone of the Gestiva NDA and which would slam the door on further investigation of 17P for treatment of pregnant women at risk of giving birth prematurely.

This leads to a third concern. Specifically, that should Gestiva be approved, it would have achieved that status and the attainment of a seven-year monopoly of the 17P market via utilization, not of its own original research, but of data licensed from a *government-funded* clinical trial.

The constraints a seven-year monopoly would impose on what is currently a free-flowing marketplace for 17P directs us to a fourth observation: while a 17P product approved for prevention of preterm birth in some, as yet, undefined subgroup of pregnant women may find more acceptance by prescribing physicians, if marketing exclusivity is assigned to that product, all chance of competitive pricing will be lost for the exclusivity period.

In summary, unless the Orphan status of the indication currently under consideration for Gestiva (or a subsequent NDA-based 17P product) is revoked, the provisions of the Orphan Drug Act, under which exclusivity could be granted, will have the completely unintended effects of reducing competition, reducing access, increasing price, and stifling research in this critical area of clinical endeavor.

C. ENVIRONMENTAL IMPACT

Petitions requesting “action on an NDA...if the action does not increase the use of the active moiety” are categorically excluded from the requirement to file an environmental assessment or environmental impact statement, per 21 CFR 25.31.

D. ECONOMIC IMPACT

A statement of the economic impact of the requested action will be provided if required by the Commissioner following review of this petition, per 21 CFR 10.30

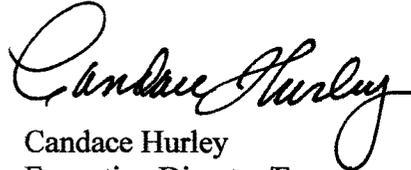
E. CERTIFICATION

⁵ ACOG Committee Opinion No. 291, Use of Progesterone to Reduce Preterm Birth, *Obstet. Gynecol.* 2003; 102(5):1115-1116.

⁶ Meis, P et al., Prevention of Recurrent Preterm Delivery by 17 Alpha-hydroxyprogesterone Caproate, *NEJM* 2003; 348(24): 2379-2385.

The undersigned certifies that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner which are unfavorable to the petition.

Respectfully submitted,

A handwritten signature in black ink, reading "Candace Hurley". The signature is written in a cursive style with a large, looping initial "C".

Candace Hurley
Executive Director/Founder
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