must be submitted within 90 days after the budget period ends. Final FSRs are due within 90 days of expiration of the project period. Standard Form 269 (long form for those reporting on program income; short form for all others) will be used for financial reporting.

Federal Cash Transaction Reports are due every calendar quarter to the Division of Payment Management, Payment Management Branch, Department of Health and Human Services at: *http://www.dpm.gov.* Failure to submit timely reports may cause a disruption in timely payments to your organization.

Grantees are responsible and accountable for accurate reporting of the Progress Reports and Financial Status Reports which are generally due annually. Financial Status Reports (SF–269) are due 90 days after each budget period and the final SF–269 must be verified from the grantee records on how the value was derived. Annual financial status reports must be submitted within 90 days after the end of the budget period. Final financial status reports are due within 90 days of expiration of the budget/project period. Standard Form 269 (long form) will be used for financial reporting.

5. Telecommunication for the hearing impaired is available at: TTY 301–443–6394

VII. Agency Contacts

For program information, contact Mr. Michael Berryhill, Office of Public Health Support, Division of Health Professions Support, 801 Thompson Avenue, TMP Suite 450A, Rockville, Maryland, 20852 (301) 443–2443.

For grant application and business management information, contact Ms. Denise Clark, Division of Grants Operations, Indian Health Service, 801 Thompson Avenue, TMP Suite 360, Rockville, Maryland 20852 (301) 443–5204.

Yvette Roubideaux,

Director, Indian Health Service.

[FR Doc. 2010–15423 Filed 6–24–10; 8:45 am]

BILLING CODE 4165–16–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2006–P–0089 (formerly Docket No. 2006P–0144)]

Determination That DELALUTIN (hydroxyprogesterone caproate) Injection, 125 Milligrams/Milliliter and 250 Milligrams/Milliliter, Was Not Withdrawn From Sale for Reasons of Safety or Effectiveness

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) has determined that DELALUTIN (hydroxyprogesterone caproate) injection, 125 milligrams (mg)/milliliter (mL) and 250 mg/mL, was not withdrawn from sale for reasons of safety or effectiveness. This determination will allow FDA to approve abbreviated new drug applications (ANDAs) for hydroxyprogesterone caproate injection, 125 mg/mL and 250 mg/mL, if all other legal and regulatory requirements are met. However, in considering whether to file an ANDA for hydroxyprogesterone caproate, future applicants are advised that they may not be able to obtain DELALUTIN (hydroxyprogesterone caproate) injection, 125 mg/mL and 250 mg/mL, for bioequivalence testing because the product has not been commercially available for a number of years. An ANDA applicant who is unable to obtain DELALUTIN (hydroxyprogesterone caproate) injection, 125 mg/mL and 250 mg/mL, for bioequivalence testing should contact the Office of Generic Drugs for a determination of what is necessary to show bioavailability and same therapeutic effect.

FOR FURTHER INFORMATION CONTACT: Nam Kim, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, rm. 6320, Silver Spring, MD 20993–0002, 301–796–3601.

SUPPLEMENTARY INFORMATION: In 1984, Congress enacted the Drug Price Competition and Patent Term Restoration Act of 1984 (Public Law 98–417) (the 1984 amendments), which authorized the approval of duplicate versions of drug products approved under an ANDA procedure. ANDA applicants must, with certain exceptions, show that the drug for which they are seeking approval contains the same active ingredient in the same strength and dosage form as the "listed drug," which is a version of the drug that was previously approved. ANDA applicants do not have to repeat the extensive clinical testing otherwise necessary to gain approval of a new drug application (NDA). The only clinical data required in an ANDA are data to show that the drug that is the subject of the ANDA is bioequivalent to the listed drug.

The 1984 amendments include what is now section 505(j)(7) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)(7)) (the act), which requires FDA to publish a list of all approved drugs. FDA publishes this list as part of the "Approved Drug Products With Therapeutic Equivalence Evaluations," which is generally known as the "Orange Book." Under FDA regulations, drugs are withdrawn from the list if the agency withdraws or suspends approval of the drug's NDA or ANDA for reasons of safety or effectiveness or if FDA determines that the listed drug was withdrawn from sale for reasons of safety or effectiveness (21 CFR 314.162). Under § 314.161(a)(1) (21 CFR 314.161(a)(1)), the agency must determine whether a listed drug was withdrawn from sale for reasons of safety or effectiveness before an ANDA that refers to that listed drug may be approved. FDA may not approve an ANDA that does not refer to a listed drug.

DELALUTIN (hydroxyprogesterone caproate) injection, 125 mg/mL and 250 mg/mL, is the subject of NDA 10–347 and NDA 16–911 held by Bristol-Myers Squibb Company (BMS). According to the latest version of the approved labeling for DELALUTIN (hydroxyprogesterone caproate) injection, DELALUTIN is indicated in non-pregnant women: for the treatment of advanced adenocarcinoma of the uterine corpus (Stage III or IV); in the management of amenorrhea (primary and secondary) and abnormal uterine bleeding due to hormonal imbalance in the absence of organic pathology, such as submucous fibroids or uterine cancer; as a test for endogenous estrogen production ("Medical D and C"); and for the production of secretory endometrium and desquamation.

FDA originally approved NDA 10–347 for DELALUTIN (hydroxyprogesterone caproate) injection based on a finding of safety in 1956. The indications section of the original labeling approved in 1956 states that DELALUTIN appears to be useful in conditions generally responding to progestogens and provided suggested dosing and administration for the following indications: primary and secondary amenorrhea; metropathia hemorrhagica

(functional uterine bleeding) not associated with genital malignancy; infertility with inadequate corpus luteum function; production of secretory endometrium and desquamation during estrogen therapy; premenstrual tension; dysmenorrhea; cyclomastopathy, mastodynia, adenosis, chronic cystic mastitis; habitual and threatened abortion; postpartum after-pains; test for endogenous estrogen production; and test for continuous endogenous progesterone production. In 1970, a supplement to NDA 10–347 was submitted for the additional indication of treatment of advanced adenocarcinoma of the uterine corpus (Stage III or IV). FDA reviewed this supplement as an original NDA (NDA 16–911) because it proposed a new indication, and approved it as both safe and effective in 1972. Both NDA 10–347 and NDA 16–911 reference the same drug product and utilize the same labeling.

The indications for DELALUTIN (hydroxyprogesterone caproate) injection, other than the indication for treatment of advanced adenocarcinoma of the uterine corpus (Stage III or IV), were reviewed for efficacy under the Drug Efficacy Study Implementation (DESI) program. In the **Federal Register** of September 9, 1971 (36 FR 18115), FDA announced that preparations containing hydroxyprogesterone caproate are effective for use in amenorrhea and abnormal uterine bleeding due to hormonal imbalance in the absence of organic pathology, such as submucous fibroids or uterine cancer; as a presumptive test for pregnancy; as a test for continuous endogenous progesterone production; and for production of secretory endometrium and desquamation—as a test for endogenous estrogen production (medical D and C). FDA also announced that preparations containing hydroxyprogesterone caproate are *probably* effective for habitual and threatened abortion and cyclomastopathies (mastodynia, adenosis, chronic cystic mastitis) and *possibly* effective for use in premenstrual tension and dysmenorrhea and disturbances of the menstrual cycle (hypomenorrhea, oligomenorrhea, irregular cycles). In addition, FDA announced that hydroxyprogesterone caproate lacks substantial evidence of effectiveness for use in postpartum afterpains and, when used alone, in deficiency syndromes (castration, primary ovarian failure, menopause, senile vaginitis, and pruritis vulvae). The notice announced that FDA was prepared to approve NDAs and supplements to previously approved NDAs under the conditions described in the notice, including the condition that the revised labeling include only the indications for which the drug was classified as effective or probably effective.

In the **Federal Register** of October 10, 1973 (38 FR 27947), FDA announced that it was modifying its prior conclusions with respect to the indications for DELALUTIN (hydroxyprogesterone caproate) injection that were determined to be probably effective and possibly effective. FDA stated that the additional information submitted by BMS to support use of DELALUTIN in threatened and habitual abortion does not constitute substantial evidence of effectiveness. In addition, the notice stated that data had become available which suggested a possible association of prenatal hormonal treatment of mothers with congenital heart defects in the offspring. The notice stated that the potential risk of teratogenic effects is considered high enough to warrant removal of pregnancy-related indications from the labeling of progestins currently marketed for systemic use, which are as follows: (1) Presumptive test for pregnancy, (2) treatment of threatened and habitual abortion, and (3) treatment of any abnormalities of pregnancy, including pregnancy complicating diabetes. The notice concluded that the labeling section given in the September 9, 1971, announcement for hydroxyprogesterone caproate should be amended to read as follows: "This drug is indicated in amenorrhea; abnormal uterine bleeding due to hormonal imbalance in the absence of organic pathology, such as submucous fibroids or uterine cancer; for production of secretory endometrium and desquamation; and as a test for endogenous estrogen production (Medical D & C)."

In the **Federal Register** of July 22, 1977 (42 FR 37646), FDA stated that reports during the past several years had indicated that the use of sex hormones during early pregnancy may seriously damage the offspring. FDA stated that in view of the adverse effects on the fetus that may be associated with its exposure to pregestational hormones, the labeling for all progestational drug products except those for use as contraceptives should be revised to include an additional contraindication and warning regarding the use of progestational agents during pregnancy. In the **Federal Register** of October 13, 1978 (43 FR 47178), FDA published a final rule requiring the labeling of progestational drug products to include warnings informing patients of an increased risk of birth defects associated with the use of these drugs during the first 4 months of pregnancy. In the **Federal Register** of January 12, 1989 (54 FR 1243), FDA published revised guideline texts for professional and patient labeling for prescription progestational drug products not including progestogen-containing oral contraceptive drug products. The notice revised the guideline texts by: (1) Deleting the warning about possible congenital heart defects and limb reduction defects, and (2) adding a warning stating that the use of progestational drugs in pregnancy may cause certain genital abnormalities.

In the **Federal Register** of November 16, 1999 (64 FR 62110), FDA revoked its regulation requiring such patient labeling for progestational drug products because it concluded, based on a review of the scientific data, that such labeling for all progestogens was not warranted. In the notice, FDA stated that the diversity of drugs that can be described as progestational and the diversity of conditions these drugs may be used to treat make it inappropriate to consider these drugs a single class for labeling purposes.

By letter dated September 13, 1999, BMS requested withdrawal of NDA 10–347 for DELALUTIN (hydroxyprogesterone caproate) injection and stated that the drug product had not been marketed for several years. In the **Federal Register** of September 13, 2000 (65 FR 55264), FDA announced that it was withdrawing approval of NDA 10–347 and NDA 16–911, effective September 30, 2000.

CUSTOpharm, Inc., submitted a citizen petition dated March 27, 2006 (Docket No. FDA–2006–P–0089), under 21 CFR 10.30, requesting that the agency determine whether DELALUTIN (hydroxyprogesterone caproate) injection was withdrawn from sale for reasons of safety or effectiveness and therefore is suitable for submission in an ANDA. After considering the citizen petition (including comments submitted) and reviewing agency records, FDA has determined that DELALUTIN (hydroxyprogesterone caproate) injection, 125 mg/mL and 250 mg/mL, was not withdrawn from sale for reasons of safety or effectiveness. The petitioner identified several publications discussing the potential teratogenic properties of DELALUTIN (hydroxyprogesterone caproate) injection over the years but asserts that recent studies indicate that with proper administration (beginning in the second trimester) in high risk patients these risks are minimal or not evident. In view of these studies, the petitioner

seeks a determination that DELALUTIN (hydroxyprogesterone caproate) injection was not withdrawn for reasons of safety or efficacy. FDA has reviewed the information submitted by petitioner and has independently evaluated relevant literature and data for adverse event reports for DELALUTIN (hydroxyprogesterone caproate) injection. Based on its evaluation, FDA does not consider this information to indicate that DELALUTIN (hydroxyprogesterone caproate) injection, 125 mg/mL and 250 mg/mL, was withdrawn for reasons of safety or effectiveness.

For the reasons outlined in this document, FDA determines that DELALUTIN (hydroxyprogesterone caproate) injection, 125 mg/mL and 250 mg/mL, was not withdrawn from sale for reasons of safety or effectiveness. Accordingly, the agency will continue to list DELALUTIN (hydroxyprogesterone caproate) injection, 125 mg/mL and 250 mg/mL, in the "Discontinued Drug Product List" section of the Orange Book. The "Discontinued Drug Product List" delineates, among other items, drug products that have been discontinued from marketing for reasons other than safety or effectiveness. ANDAs that refer to DELALUTIN (hydroxyprogesterone caproate) injection, 125 mg/mL and 250 mg/mL, may be approved by the agency as long as they meet all relevant legal and regulatory requirements for approval of ANDAs. If FDA determines that labeling for these drug products should be revised to meet current standards, the agency will advise ANDA applicants to submit such labeling.

In considering whether to file an ANDA for this drug product, future applicants should be advised that they may not be able to obtain DELALUTIN (hydroxyprogesterone caproate) injection, 125 mg/mL and 250 mg/mL, for bioequivalence testing because the product has not been commercially available for a number of years. An ANDA applicant who is unable to obtain DELALUTIN (hydroxyprogesterone caproate) injection, 125 mg/mL and 250 mg/mL, for bioequivalence testing should contact the Office of Generic Drugs for a determination of what showing is necessary to satisfy the requirements of section 505(j)(2)(A)(iv) of the act. If an ANDA is approved without a showing of bioequivalence, the approved product will not be considered therapeutically equivalent (i.e., granted an AB rating) in the Orange Book.

Dated: June 21, 2010.

Leslie Kux,

Acting Assistant Commissioner for Policy.

[FR Doc. 2010–15416 Filed 6–24–10; 8:45 am]

BILLING CODE 4160–01–S

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2010–D–0283]

Draft Guidance for Industry on Chemistry, Manufacturing, and Controls Postapproval Manufacturing Changes Reportable in Annual Reports; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a draft guidance for industry entitled "CMC Postapproval Manufacturing Changes Reportable in Annual Reports." This draft guidance provides recommendations to holders of new drug applications (NDAs) and abbreviated new drug applications (ANDAs) regarding the types of changes that may be reported in annual reports. Specifically, the draft guidance describes chemistry, manufacturing, and controls (CMC) postapproval manufacturing changes that FDA has determined will likely present minimal potential to have adverse effects on product quality and, therefore, may be reported by applicants in an annual report. (The draft guidance excludes positron emission tomography (PET) drug products.)

DATES: Although you can comment on any guidance at any time (see 21 CFR 10.115(g)(5)), to ensure that the agency considers your comment on this draft guidance before it begins work on the final version of the guidance, submit either electronic or written comments on the draft guidance by September 23, 2010.

ADDRESSES: Submit written requests for single copies of the draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, rm. 2201, Silver Spring, MD 20993–0002. Send one self-addressed adhesive label to assist that office in processing your requests. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the draft guidance document.

Submit electronic comments on the draft guidance to *http://www.regulations.gov*. Submit written comments, including comments regarding the proposed collection of information, to the Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Jon Clark, Center for Drug Evaluation and Research, Food and Drug Administration, Bldg. 51, rm. 4178, 10903 New Hampshire Ave., Silver Spring, MD 20993–0002, 301–796–2400.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry entitled "CMC Postapproval Manufacturing Changes Reportable in Annual Reports." This draft guidance provides recommendations to holders of NDAs and ANDAs regarding the types of CMC postapproval manufacturing changes that FDA has determined will likely present minimal potential to have adverse effects on product quality, and therefore, may be reported by applicants in an annual report under § 314.70 (21 CFR 314.70).

In its September 2004 final report, "Pharmaceutical Current Good Manufacturing Practices (CGMPs) for the 21st Century—A Risk-Based Approach" (Pharmaceutical Product Quality Initiative, *http://www.fda.gov/Drugs/DevelopmentApprovalProcess/Manufacturing/QuestionsandAnswersonCurrentGoodManufacturingPracticescGMPforDrugs/ucm137175.htm*), FDA stated that to keep pace with the many advances in quality management practices in manufacturing and to enable the agency to more effectively allocate its limited regulatory resources, FDA would implement a cooperative, risk-based approach for regulating pharmaceutical manufacturing. As part of this approach, FDA determined that to provide the most effective public health protection, its CMC regulatory review should be based on an understanding of product risk and how best to manage this risk.

The number of CMC manufacturing supplements for NDAs and ANDAs has continued to increase over the last several years. In connection with FDA's Pharmaceutical Product Quality Initiative and its risk-based approach to CMC review, FDA has evaluated the types of changes that have been submitted in CMC postapproval manufacturing supplements and determined that many of the changes being reported present very low risk to the quality of the product and do not need to be submitted in supplements.