because it would represent a substitution of current judgment for that of the prior adjudicator that the annuitant's impairment was medically disabling. The exception for error will not be applied retroactively under the conditions set out above unless the conditions for reopening the prior decision are met.

* * * * *

■ 14. In § 220.180 revise paragraphs (b) and (c) to read as follows:

§ 220.180 Determining continuation or cessation of disability.

* * * * *

(b) If the annuitant is not engaging in substantial gainful activity, does he or she have an impairment or combination of impairments which is medically disabling? If the annuitant's impairment(s) is medically disabling, his or her disability will be found to continue;

(c) If the annuitant's impairment(s) is not medically disabling, has there been medical improvement as defined in § 220.177(a)? If there has been medical improvement as shown by a decrease in medical severity, see step (d). If there has been no decrease in medical severity, then there has been no medical improvement; (See step (e));

* * * * *

§ 220.181 [Amended]

■ 15. In § 220.181 amend paragraph (i) by removing the word ''not'' and adding in its place the word ''no''.

■ 16. In § 220.186(c) amend the definition of ''Permanent impairment, medical improvement not expected'' by removing the phrase ''§ 220.178(c)(4)'' and adding in its place the phrase ''§ 220.178(c)(3)'' and revise paragraphs (1) through (3) of the definition to read as follows:

§ 220.186 When and how often the Board will conduct a continuing disability review.

* * * * *

(c) * * *

Permanent impairment medical improvement not expected—* * *

(1) Parkinsonian syndrome with significant rigidity, brady kinesia, or tremor in two extremities, which, singly or in combination, result in sustained disturbance of gross and dexterous movements, or gait and station.

(2) Amyotrophic lateral sclerosis, based on documentation of a clinically appropriate medical history, neurological findings consistent with the diagnosis of ALS, and the results of any electrophysiological and neuroimaging testing.

(3) Diffuse pulmonary fibrosis in an individual age 55 or older which reduces FEV1 to 1.45 to 2.05 (L, BTPS) or less depending on the individual's height.

* * * * *

Appendix 1 to Part 220 [Removed and Reserved]

■ 17. Remove and reserve Appendix 1 to Part 220.

Dated: November 20, 2009.

For the Board.

Beatrice Ezerski,

Secretary to the Board.

[FR Doc. E9–28453 Filed 12–3–09; 8:45 am]

BILLING CODE 7905–01–P

DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1300

[Docket No. DEA–285F]

RIN 1117–AB17

Classification of Three Steroids as Schedule III Anabolic Steroids Under the Controlled Substances Act

AGENCY: Drug Enforcement Administration (DEA), Department of Justice.

ACTION: Final rule.

SUMMARY: With the issuance of this final rule, the Deputy Administrator of the Drug Enforcement Administration (DEA) classifies the following three steroids as ''anabolic steroids'' under the Controlled Substances Act (CSA): Boldione, desoxymethyltestosterone, and 19-nor-4,9(10)-androstadienedione. These steroids and their salts, esters, and ethers are schedule III controlled substances subject to the regulatory control provisions of the CSA.

DATES: *Effective Date:* January 4, 2010.

FOR FURTHER INFORMATION CONTACT: Christine A. Sannerud, Ph.D., Chief, Drug and Chemical Evaluation Section, Drug Enforcement Administration, 8701 Morrissette Drive, Springfield, VA 22152, (202) 307–7183.

SUPPLEMENTARY INFORMATION:

I. Background Information

In a Notice of Proposed Rulemaking (NPRM) (73 FR 22294) published April 25, 2008, the DEA proposed the classification of three steroids as schedule III anabolic steroids under the CSA. These three steroids included boldione, desoxymethyltestosterone, and 19-nor-4,9(10)-androstadienedione. With the publication of this Final Rule, DEA classifies these three steroids as schedule III anabolic steroids. Background information in support of this Final Rule is provided below.

On November 29, 1990, the President signed into law the Anabolic Steroids Control Act of 1990 (Title XIX of Pub. L. 101–647), which became effective February 27, 1991. This law established and regulated anabolic steroids as a class of drugs under schedule III of the CSA. As a result, a new anabolic steroid is not scheduled according to the procedures set out in 21 U.S.C. 811, but can be administratively classified as an anabolic steroid through the rulemaking process by adding the steroid to the regulatory definition of an anabolic steroid in 21 CFR 1300.01(b)(4).

On October 22, 2004, the President signed into law the Anabolic Steroid Control Act of 2004 (Pub. L. 108–358), which became effective on January 20, 2005. Section 2(a) of the Anabolic Steroid Control Act of 2004 amended 21 U.S.C. 802(41)(A) by replacing the existing definition of ''anabolic steroid.'' The Anabolic Steroid Control Act of 2004 classifies a drug or hormonal substance as an anabolic steroid if the following four criteria are met: (A) The substance is chemically related to testosterone; (B) the substance is pharmacologically related to testosterone; (C) the substance is not an estrogen, progestin, or a corticosteroid; and (D) the substance is not dehydroepiandrosterone (DHEA). Any substance that meets the criteria is considered an anabolic steroid and must be listed as a schedule III controlled substance. DEA finds that boldione, desoxymethyltestosterone, and 19-nor-4,9(10)-androstadienedione meet this definition of anabolic steroid and is adding them to the list of anabolic steroids in 21 CFR 1300.01(b)(4).

Anabolic steroids are a class of drugs with a basic steroid ring structure that produces anabolic and androgenic effects. The prototypical anabolic steroid is testosterone. Anabolic effects include promoting the growth of muscle. The androgenic effects consist of promoting the development of male secondary sexual characteristics such as facial hair, deepening of the voice, and thickening of the skin.

In the United States, only a small number of anabolic steroids are approved for either human or veterinary use. Approved medical uses for anabolic steroids include treatment of androgen deficiency in hypogonadal males, adjunctive therapy to offset protein catabolism associated with prolonged administration of corticosteroids, treatment of delayed puberty in boys, treatment of metastatic breast cancer in women, and treatment of anemia associated with specific diseases (*e.g.,*

anemia of chronic renal failure, Fanconi's anemia, and acquired aplastic anemia). However, with the exception of the treatment of male hypogonadism, anabolic steroids are not the first-line treatment due to the availability of other preferred treatment options. DEA is not aware of any legitimate medical use or New Drug Applications (NDA) for the three substances that DEA is classifying as anabolic steroids under the definition set forth under 21 U.S.C. 802(41)(A). Moreover, DEA has not identified any chemical manufacturers currently using these substances as intermediates in their manufacturing process(es).

Adverse effects are associated with the use or abuse of anabolic steroids. These effects depend on several factors (*e.g.,* age, sex, anabolic steroid used, the amount used, and the duration of use). In early adolescence, the use of testosterone and other anabolic steroids that have estrogenic effects can cause premature closure of the growth plates in long bones resulting in a permanently stunted growth. In adolescent boys, anabolic steroid use can cause precocious sexual development. In both girls and women, anabolic steroid use induces permanent physical changes such as deepening of the voice, increased facial and body hair growth, and the lengthening of the clitoris. In men, anabolic steroid use can cause shrinkage of the testicles, decreased sperm count, and sterility. Gynecomastia (*i.e.,* enlargement of the male breast tissue) can develop with the use of those anabolic steroids with estrogenic actions. In both men and women, anabolic steroid use can damage the liver and can cause high cholesterol levels, which may increase the risk of strokes and heart attacks. Furthermore, anabolic steroid use is purported to induce psychological effects such as aggression, increased feelings of hostility, and psychological dependence and addiction. Upon abrupt termination of long-term anabolic steroid use, a withdrawal syndrome may appear including severe depression.

II. Evaluation of Statutory Factors for Classification as an Anabolic Steroid

With the issuance of this Final Rule, DEA is classifying boldione, desoxymethyltestosterone, and 19-nor-4,9(10)-androstadienedione as anabolic steroids under the definition set forth under 21 U.S.C. 802(41)(A). As noted previously, a drug or hormonal substance is classified as an anabolic steroid by meeting the following four definitional requirements: (A) The substance is chemically related to testosterone; (B) the substance is pharmacologically related to testosterone; (C) the substance is not an estrogen, progestin, or a corticosteroid; and (D) the substance is not DHEA.

(A) Chemically Related to Testosterone

To classify a substance as an anabolic steroid, a substance must be chemically related to testosterone. DEA discussed its evaluation of the chemical relationship of boldione, desoxymethyltestosterone, and 19-nor-4,9(10)-androstadienedione in the NPRM published April 25, 2008 (73 FR 22294). A Structure Activity Relationship (SAR) evaluation for each of the substances compared the chemical structure of the steroid to that of testosterone, as substances with a structure similar to that of testosterone are predicted to possess comparable pharmacological and biological activity.

Boldione is also known by the following chemical name: Androsta-1,4-diene-3,17-dione. DEA has determined that the chemical structure of boldione is chemically related to that of testosterone. The chemical structure of boldione differs from testosterone by only the following structural features: A ketone group at carbon 17 and a double bond between the carbon 1 and carbon 2. The human body would be expected to metabolize the ketone group at carbon 17 into a hydroxyl group that is present on testosterone (Payne and Hales, 2004; Peltoketo *et al.,* 1999; Moghrabi and Andersson, 1998). Furthermore, the scientific literature reports that the additional double bond at carbon 1 in boldione does not significantly decrease the anabolic activity of the substance (Vida, 1969). Boldione is an anabolic steroid precursor, being metabolized by the body into boldenone (Galletti and Gardi, 1971; Kim *et al.,* 2006), which is a schedule III anabolic steroid (21 *U.S.C.* 802(41)(A)(vi)).

Desoxymethyltestosterone (DMT) is also known by the following names: 17α-Methyl-5α-androst-2-en-17β-ol; and madol. DEA has determined that the chemical structure of desoxymethyltestosterone is chemically related to testosterone. The chemical structure of desoxymethyltestosterone differs from testosterone by the following four structural features: The lack of a ketone group at the third carbon, a double bond between the second and third carbon, the lack of a double bond between the fourth and fifth carbon, and a methyl group at carbon 17. Each of these four chemical features is known through the scientific literature not to eliminate the anabolic and androgenic activity of the substance (Brueggemeir *et al.,* 2002; Vida, 1969).

19-Nor-4,9(10)-androstadienedione is also known by the following chemical names: 19-Norandrosta-4,9(10)-diene-3,17-dione; and estra-4,9(10)-diene-3,17-dione. DEA has determined that the chemical structure of 19-nor-4,9(10)-androstadienedione is chemically related to testosterone. The chemical structure of 19-nor-4,9(10)-androstadienedione differs from testosterone by the following three structural features: A ketone group at carbon 17, the absence of a methyl group at carbon 19, and a double-bond between carbon 9 and carbon 10. The human body would be expected to metabolize the ketone group at carbon 17 into a hydroxyl group like that present in testosterone (Payne and Hales, 2004; Peltoketo *et al.,* 1999; Moghrabi and Andersson, 1998). Furthermore, the scientific literature reports that both the absence of the methyl group at carbon 19 and the additional double bond in 19-nor-4,9(10)-androstadienedione increase the anabolic activity of the substance (Vida, 1969).

(B) Pharmacologically Related to Testosterone

A substance must also be pharmacologically related to testosterone (*i.e.,* produce similar biological effects) to be classified as a schedule III anabolic steroid. The pharmacology of a steroid, as related to testosterone, can be established by performing one or more of the following androgenic and anabolic activity assays: Ventral prostate assay, seminal vesicle assay, levator ani assay, testicular atrophy assay, gonadotropin suppression assay, and androgen receptor binding and efficacy assays. These assays are described below.

Ventral Prostate Assay, Seminal Vesicle Assay, and Levator Ani Assay: The classic scientific procedure for examining the effects of a steroid as compared to testosterone is to perform the testosterone sensitive assays, ventral prostate assay, seminal vesicle assay, and levator ani assay in rats. Certain male accessory organs (*i.e.,* the ventral prostate, seminal vesicles, and levator ani muscle) specifically need testosterone to grow and remain healthy. Upon the removal of the testes (*i.e.,* castration), the primary endogenous source of testosterone is eliminated causing the atrophy of the ventral prostate, seminal vesicles, and levator ani muscle (Eisenberg *et al.,* 1949; Nelson *et al.,* 1940; Scow, 1952; Wainman and Shipounoff, 1941). Numerous scientific studies have demonstrated the ability of exogenous testosterone administered to rats following castration to maintain the normal weight and size of all three

testosterone sensitive tissues (Biskind and Meyer, 1941; Dorfman and Dorfman, 1963; Kincl and Dorfman, 1964; Nelson *et al.,* 1940; Scow, 1952; Wainman and Shipounoff, 1941). Thus, a steroid with testosterone-like activity will also prevent the atrophy of these three testosterone-dependent tissues in castrated rats.

Testicular Atrophy Assay: Administering testosterone to non-castrated rats causes a decrease in serum levels of gonadotropins (*i.e.,* luteinizing hormone [LH] and follicle stimulating hormone [FSH]) from normal levels. Gonadotropins are pituitary hormones that affect the size and function of the testes. The suppression of these gonadotropins by excess testosterone results in a significant decrease in the size and weight of the testes (Boris *et al.,* 1970; McEuen *et al.,* 1937; Moore and Price, 1938). Accordingly, a steroid with testosterone-like activity will also significantly diminish the size and weight of the testes.

Gonadotropin Suppression Assay: The castration of rats causes a substantial increase in the serum levels of gonadotropins (*i.e.,* LH and FSH) above normal levels due to the removal of the principal source of endogenous testosterone (Gay and Bogdanove, 1969; Swerdloff *et al.,* 1972, 1973; Swerdloff and Walsh, 1973). The administration of testosterone to castrated animals suppresses the increase in the serum levels of gonadotropins (Gay and Bogdanove, 1969; Swerdloff *et al.,* 1972; Swerdloff and Walsh, 1973; Verjans *et al.,* 1974). The administration of anabolic steroids with testosterone-like activity will also prevent this increase in serum levels of LH and FSH.

Androgen Receptor Binding and Efficacy Assay: Androgen receptor binding and efficacy assays are also used to demonstrate that the activity of a steroid is similar to that of testosterone. Testosterone produces its anabolic effects subsequent to binding to and activating the androgen receptor. Different cell-based assays can compare candidate steroids to testosterone for their ability to bind to and activate androgen receptors.

There are several different types of assays used to establish androgen receptor binding and efficacy. In one assay, C3H10T1/2 stem cells express androgen receptors and are used to assess steroids for their ability to bind and activate the androgen receptor (Jasuja *et al.,* 2005a,b; Singh *et al.,* 2003). In these stem cells, the translocation of the androgen receptor to the nucleus of the cell in the presence of the ligand (*e.g.,* testosterone or its active metabolite dihydroxytestosterone) confirms that the ligand bound to the androgen receptor and activated the downstream signaling cascade. When activated, the C3H10T1/2 stem cells differentiate into skeletal muscle cells as demonstrated by the increase in the expression of muscle specific proteins (*i.e.,* myogenic determination transcription factor [MyoD] and myosin heavy chain [MHC]). Another assay uses human breast cancer cells genetically altered to contain a specific reporter gene (*e.g.,* luciferase gene) regulated by androgen receptor activation (Hartig *et al.,* 2002; Wilson *et al.,* 2002). The expression of a bioluminescent protein (*e.g.,* luciferase) signals both androgen receptor binding and activation.

Results of the Androgenic and Anabolic Activity Assays: As discussed in the NPRM, in January 2006, DEA reviewed the published scientific literature for pharmacological data on the anabolic and androgenic activity of boldione, desoxymethyltestosterone, and 19-nor-4,9(10)-androstadienedione using the assays described above. As discussed further below, there was sufficient information on the pharmacology of desoxymethyltestosterone in the reviewed scientific literature to determine that desoxymethyltestosterone is pharmacologically related to testosterone (*i.e.,* produces biological effects similar to those of testosterone). However, the published literature contained insufficient pharmacological data to determine whether boldione and 19-nor-4,9(10)-androstadienedione were pharmacologically related to testosterone. Consequently, as discussed further below and in the NPRM, DEA sponsored pharmacological studies involving several different androgenic and anabolic activity assays to generate the data necessary to make this determination.

Androgenic and anabolic activity assay results indicate that boldione, desoxymethyltestosterone, and 19-nor-4,9(10)-androstadienedione have similar pharmacological activity as testosterone.

Boldione

DEA sponsored a study [1] by the Veteran's Administration Puget Sound Health Care System to determine the anabolic and androgenic effects of boldione in intact and castrated rats (Matsumoto and Marck, 2006). The results of these studies were compared to the results of a study by the same laboratory using a similar protocol to characterize the androgenic and anabolic effects of testosterone (Marck *et al.,* 2003). Boldione administered to castrated male rats by silastic capsules implanted under the skin prevented atrophy of the ventral prostate, seminal vesicles, levator ani muscle, and the rise in serum gonadotropin (LH and FSH) associated with castration. Boldione administration also produced testicular atrophy in intact rats. Another DEA sponsored study [2] at a laboratory at Boston University examined the ability of boldione to bind to the androgen receptor and to cause the differentiation of C3H10T1/2 stem cells into muscle cells (Bhasin, 2005). All of these effects caused by boldione in C3H10T1/2 stem cells were comparable to those of testosterone as established in experiments using the same or similar methodology (Singh *et al.,* 2003). Collectively, the evidence indicates that the pharmacology of boldione is similar to testosterone.

Desoxymethyltestosterone

Desoxymethyltestosterone was administered subcutaneously, orally, or intramuscularly to castrated rats (Dorfman and Kincl, 1963; Kincl and Dorfman, 1964; Nutting *et al.,* 1966). By all three routes of administration, desoxymethyltestosterone prevented the atrophy of ventral prostate, seminal vesicles, and levator ani muscle. Desoxymethyltestosterone also induced the expression of the bioluminescent protein luciferase in CAMA–1 breast cancer cells signaling androgen receptor binding and activation (Ayotte *et al.,* 2006). Collectively, the evidence indicates that the pharmacology of desoxymethyltestosterone is similar to testosterone.

19-Nor-4,9(10)-Androstadienedione

As discussed in the NPRM, DEA sponsored a study [3] by the Veteran's Administration Puget Sound Health Care System to determine the anabolic and androgenic effects of 19-nor-4,9(10)-androstadienedione in intact and castrated rats (Matsumoto and Marck, 2006). The results of these studies were compared to the results of a study by the same laboratory using a similar protocol to characterize the androgenic and anabolic effects of testosterone (Marck *et al.,* 2003). 19-Nor-4,9(10)-

[1] The study by the Veteran's Administration Puget Sound Health Care System may be found at *http://www.regulations.gov* in the electronic docket associated with this rulemaking.

[2] The study by Boston University may be found at *http://www.regulations.gov* in the electronic docket associated with this rulemaking.

[3] The study by the Veteran's Administration Puget Sound Health Care System may be found at *http://www.regulations.gov* in the electronic docket associated with this rulemaking.

androstadienedione administered to castrated male rats by silastic capsules implanted under the skin prevented the atrophy of the ventral prostate, seminal vesicles, levator ani muscle, and the rise in serum gonadotropins (LH and FSH) associated with castration. Another DEA sponsored study at a laboratory at Boston University [4] examined the ability of 19-nor-4,9(10)-androstadienedione to bind to the androgen receptor and to cause the differentiation of C3H10T1/2 stem cells into muscle cells (Bhasin, 2005). 19-Nor-4,9(10)-androstadienedione induced the translocation of the androgen receptor to the nucleus of the C3H10T1/2 stem cells, demonstrating binding affinity and efficacy for the androgen receptor. All of these effects caused by 19-nor-4,9(10)-androstadienedione in C3H10T1/2 stem cells were comparable to those of testosterone as established in experiments using the same or similar methodology (Singh *et al.,* 2003). Collectively, the evidence indicates that the pharmacology of 19-nor-4,9(10)-androstadienedione is similar to testosterone.

(C) Not Estrogens, Progestins, and Corticosteroids

As discussed in the NPRM, DEA has determined that boldione, desoxymethyltestosterone, and 19-nor-4,9(10)-androstadienedione are unrelated to estrogens, progestins, and corticosteroids. DEA evaluated the SAR for each of the substances. The chemical structure of each substance was compared to that of estrogens, progestins, and corticosteroids because the chemical structure can be related to its pharmacological and biological activity. DEA found that the three substances lacked the necessary chemical structures to impart significant estrogenic activity (*e.g.,* aromatic A ring) (Duax *et al.,* 1988; Jordan *et al.,* 1985; Williams and Stancel, 1996), progestational activity (e.g., 17β-alkyl group) (Williams and Stancel, 1996), or corticosteroidal activity (e.g., 17-ketone group or 11β-hydroxyl group) (Miller *et al.,* 2002).

(D) Not Dehydroepiandrosterone

Dehydroepiandrosterone, also known as DHEA, is exempt from control as an anabolic steroid by definition (21 U.S.C. 802(41)(A)). Boldione, desoxymethyltestosterone, and 19-nor-4,9(10)-androstadienedione are not dehydroepiandrosterone and are therefore not exempted from control on this basis.

III. Comments Received

On April 25, 2008, DEA published a NPRM (73 FR 22294) proposing to classify boldione, desoxymethyltestosterone, and 19-nor-4,9(10)-androstadienedione as schedule III anabolic steroids. The proposed rule provided an opportunity for all interested persons to submit their comments on or before June 24, 2008. In response to the NPRM, DEA received one comment from a consulting firm that described itself as ''[assisting] dietary supplement companies in understanding governmental regulations while facilitating their growth.'' These comments are summarized and responded to below.

Desoxymethyltestosterone: The commenter indicated that the scientific literature cited in the NPRM pertaining to desoxymethyltestosterone was sufficient to meet the four criteria that must be satisfied for DEA to designate the steroid as a schedule III anabolic steroid. DEA agrees with this conclusion. Therefore, DEA is placing desoxymethyltestosterone into schedule III as an anabolic steroid as proposed.

Chemical relationship of boldione and 19-nor-4,9(10)-androstadienedione to testosterone: The commenter claimed that DEA failed to show that boldione and 19-nor-4,9(10)-androstadienedione are chemically related to testosterone. The commenter claimed that both steroids were distinctly different from testosterone in that each lacks the 17β-hydroxyl, which is present in testosterone. The commenter noted that DEA did not provide any authority for the claim made that ''the human body would be expected to metabolize the ketone group at carbon 17 into a hydroxyl group that is present on testosterone.''

DEA Response: DEA disagrees with this comment. The presence of the ketone group at carbon 17 in boldione and 19-nor-4,9(10)-androstadienedione is consistent with both steroids being chemically related to testosterone, which has a hydroxyl group instead of a ketone group at carbon 17. The enzyme 17β-hydroxysteroid dehydrogenase is known to be responsible for catalyzing the conversion of the 17-ketone group to a 17β-hydroxyl group in steroids such as androgens and estrogens. This enzyme, in various isoenzymatic forms, has been documented in many body tissues in humans and various animal species (Payne and Hales, 2004; Peltoketo *et al.,* 1999; Moghrabi and Andersson, 1998; Melewich *et al.,* 1981). Considering the wide distribution of this enzyme in tissues of humans and animals, it is expected that this enzyme would convert the 17-ketone group found in boldione and 19-nor-4,9(10)-androstadienedione to the 17β-hydroxyl group, thereby producing boldenone and 19-nor-4,9(10)-androstadiene-3-one-17β-ol. Direct evidence that this conversion takes place comes from two studies showing that boldione is converted to boldenone, a schedule III anabolic steroid, in the human body (Galletti and Gardi, 1971; Kim *et al.,* 2006). Therefore, the presence of the ketone group at carbon 17 in boldione and 19-nor-4,9(10)-androstadienedione is consistent with both steroids being chemically related to testosterone.

DEA-sponsored studies regarding pharmacological relationship: The commenter claimed that the two studies sponsored by DEA were insufficient to justify determining whether boldione and 19-nor-4,9(10)-androstadienedione are pharmacologically related to testosterone.

DEA Response: DEA disagrees with this statement. The study using C3H10T1/2 cells demonstrates the ability of both steroids to act like testosterone in binding and activation of the androgen receptor resulting in protein synthesis and myotube formation. The second study reveals the ability of the steroids to act like testosterone in reversing the effects of castration of the rat on the size of selected androgen-selective organs (ventral prostate, seminal vesicles, levator ani muscle). This particular assay has been used in hundreds of studies within the scientific and industrial community to evaluate steroids for anabolic and androgenic activity similar to that found for testosterone (Vida, 1969). In addition, the effects of these two steroids on LH and FSH levels and testicular size in intact rats is also consistent with producing pharmacological effects similar to those of testosterone. Collectively, both studies demonstrate that boldione and 19-nor-4,9(10)-androstadienedione are pharmacologically similar to testosterone.

DEA-sponsored study at Boston University: The commenter claimed that the pharmacological analysis of boldione and 19-nor-4,9(10)-androstadienedione for androgenic activity using C3H10T1/2 stem cells did not show a pharmacological relationship. According to the commenter, this failure was due to: (1) Failure to obtain a random sample of C3H10T1/2 cells; (2) erroneously assuming that mere binding to an

[4] The study by Boston University may be found at *http://www.regulations.gov* in the electronic docket associated with this rulemaking.

androgen receptor and translocation to the nucleus is sufficient to show androgenic activity; and (3) the lower potency of boldione and 19-nor-4,9(10)-androstadienedione compared to dihydrotestosterone in the assay.

DEA Response: DEA disagrees with these comments. First, to conduct the study it was necessary, as provided in the protocol, to identify batches of C3H10T1/2 cells that had the potential to differentiate into myogenic cells when exposed to anabolic steroids. This was done and verified using the schedule III anabolic steroid dihydrotestosterone as a positive control. Second, this study did not simply examine androgen receptor binding and subsequent translocation of the bound receptor to the nucleus. Instead, with respect to boldione, 19-nor-4,9(10)-androstadienedione, and dihydrotestosterone, the study also demonstrated that this binding and translocation to the nucleus lead to the commitment of these cells to form muscle cells as evidenced by selected protein expression and the creation of myotubes. These various effects have previously been induced by exposure of C3H10T1/2 cells to the schedule III anabolic steroids testosterone, androstenedione, and tetrahydrogestrinone (Singh *et al.,* 2003; Jasuja *et al.,* 2005a,b). The fact that boldione and 19-nor-4,9(10)-androstadienedione were less potent than dihydrotestosterone at producing these effects does not preclude using this information to support the pharmacological similarity of these steroids to testosterone. It simply means that a higher dose of the two steroids is required to produce the effects.

DEA-sponsored study by the Veteran's Administration Puget Sound Health Care System: The commenter also asserted that DEA failed to show in the rat study that boldione and 19-nor-4,9(10)-androstadienedione produced androgenic and anabolic effects, thereby failing to show a pharmacological relationship to testosterone. The commenter indicated that this conclusion was based on the limited weight gain or lack of weight gain found in animals given these steroids compared to control animals not exposed to the steroids. Additionally, the commenter noted as evidence for a failure to demonstrate androgenic activity the statement in the study report that read ''[t]he direct androgenic and anabolic activity of 1,4-androstadien-3,17-dione in sham operated rats is less clear.''

DEA Response: DEA disagrees with this comment. DEA believes that using this assay, both steroids were found to produce pharmacological effects like that of testosterone. Although body weight was recorded in the study, it was not used as an endpoint for determining anabolic or androgenic effects. This was due to the fact that the regulation of body weight is complex, involving, among other factors, food intake, changes in fat mass, and changes in lean body mass. Instead, the androgenic and anabolic effects of both steroids were demonstrated by their ability to reverse the effects of castration of male rats on the size of the ventral prostate, seminal vesicles, and levator ani muscle, all three being androgen sensitive tissues. As discussed in the NPRM, numerous scientific studies have shown that exogenous testosterone administered to castrated rats can reverse the effects of castration on the ventral prostate, seminal vesicles, and levator ani muscle (Biskind and Meyer, 1941; Dorfman and Dorfman, 1963; Kincl and Dorfman, 1964; Nelson *et al.,* 1940; Scow, 1952; and Wainman and Shipounoff, 1941). This particular assay has been used extensively over the years by the scientific community, including the pharmaceutical industry, to evaluate steroids for anabolic and androgenic activity (Vida, 1969). The authors of the DEA sponsored study specifically conclude that ''In summary, we found that, 1,4-androstadien-3,17-dione (A0100) and 4,9-estradien-3,17-dione (E0160) demonstrated both androgenic activity, as evidenced by stimulation of the androgenic tissues (prostate and seminal vesicles) and anabolic activity, as evidenced by stimulation of the levator ani muscle growth in castrated male rats.''

In regard to androgenic activity comment, the commenter did not provide the full statement from the report which reads: ''The direct androgenic and anabolic activity of 1,4-androstadien-3,17-dione in sham operated rats is less clear because of the measured increases in serum T levels that could mediate the androgenic and anabolic activities of 1,4-androstadien-3,17-dione.'' This statement in the report mentioned the possibility that the pharmacological effects (reduction in LH and FSH levels and testes size) of 1,4-androstadien-3,17-dione could result indirectly by metabolism to an active steroid such as testosterone. As noted in the report, it was not possible to determine whether or not 1,4-androstadien-3,17-dione actually metabolized to testosterone or some other substance that cross reacted in the testosterone assay. Regardless of whether 1,4-androstadien-3,17-dione acts directly or serves as a prodrug, it still produced pharmacological effects similar to that of testosterone when administered to rats.

DEA has evaluated the comment received and finds that it does not provide any justification to dispute the determination that boldione, desoxymethyltestosterone and 19-nor-4,9(10)-androstadienedione are anabolic steroids.

IV. Conclusion and Impact of Final Rule

Conclusion

Therefore, based on the above, DEA concludes that boldione, desoxymethyltestosterone, and 19-nor-4,9(10)-androstadienedione meet the CSA definition of ''anabolic steroid'' because each substance is: (A) Chemically related to testosterone; (B) pharmacologically related to testosterone; (C) not an estrogen, progestin, or a corticosteroid; and (D) not DHEA (21 U.S.C. 802(41)(A)). All anabolic steroids are classified as schedule III controlled substances (21 U.S.C. 812(e) schedule III). Once a substance is determined to be an anabolic steroid, DEA has no discretion regarding the scheduling of these substances. As discussed further below, upon the effective date of this Final Rule all requirements pertaining to controlled substances in schedule III pertain to these three substances.

Impact of Classifying These Substances as Anabolic Steroids

The classification of boldione, desoxymethyltestosterone, and 19-nor-4,9(10)-androstadienedione as schedule III anabolic steroids makes these three substances subject to CSA requirements. Any person who manufactures, distributes, dispenses, imports, or exports boldione, desoxymethyltestosterone, or 19-nor-4,9(10)-androstadienedione, or who engages in research or conducts instructional activities with respect to these three substances, must obtain a schedule III registration in accordance with the CSA and its implementing regulations.

As of January 4, 2010, manufacture, import, export, distribution, or sale of boldione, desoxymethyltestosterone, and 19-nor-4,9(10)-androstadienedione, except by DEA registrants, is a violation of the CSA that may result in imprisonment and fines (21 U.S.C. 841 and 960). Possession of these three steroids, unless legally obtained, is also subject to criminal penalties (21 U.S.C. 844).

In addition, under the CSA, these three substances may be imported only

for medical, scientific, or other legitimate uses (21 U.S.C. 952(b)) under an import declaration filed with DEA (21 CFR 1312.18). Importation of these substances will be illegal unless the person importing these substances is registered with DEA as an importer or researcher and files the required declaration for each shipment. An individual who purchases any of these substances directly from foreign companies and has them shipped to the U.S. is considered to be importing even if the steroids are intended for personal use. Illegal importation of these substances is a violation of the CSA that may result in imprisonment and fines (21 U.S.C. 960).

Requirements for Handling Substances Defined as Anabolic Steroids

Effective January 4, 2010, boldione, desoxymethyltestosterone, and 19-nor-4,9(10)-androstadienedione are subject to CSA regulatory controls and administrative, civil, and criminal sanctions applicable to the manufacture, distribution, dispensing, importation, and exportation of a schedule III controlled substance, including the following:

Registration. Any person who manufactures, distributes, dispenses, imports, exports, or engages in research or conducts instructional activities with a substance defined as an anabolic steroid, or who desires to engage in such activities, must be registered to conduct such activities with schedule III controlled substances in accordance with 21 CFR part 1301.

Security. Substances defined as anabolic steroids are subject to schedule III–V security requirements and must be manufactured, distributed, and stored in accordance with 21 CFR 1301.71, 1301.72(b), (c), and (d), 1301.73, 1301.74, 1301.75(b) and (c), 1301.76 and 1301.77.

Labeling and Packaging. All labels and labeling for commercial containers of substances defined as anabolic steroids which are distributed on or after January 4, 2010, shall comply with requirements of 21 CFR 1302.03–1302.07.

Inventory. Every registrant required to keep records and who possesses any quantity of any substance defined as an anabolic steroid is required to keep an inventory of all stocks of the substances on hand pursuant to 21 CFR 1304.03, 1304.04 and 1304.11. Every registrant who desires registration in schedule III for any substance defined as an anabolic steroid shall conduct an inventory of all stocks of the substances on hand at the time of registration.

Records. All registrants are required to keep records pursuant to 21 CFR 1304.03, 1304.04, 1304.05, 1304.21, 1304.22, 1304.23.

Prescriptions. All prescriptions for these schedule III substances or for products containing these schedule III substances are required to be issued pursuant to 21 CFR 1306.03–1306.06 and 1306.21–1306.27. All prescriptions for these schedule III compounds or for products containing these schedule III substances, if authorized for refilling, are limited to five refills within six months of the date of issuance of the prescription.

Importation and Exportation. All importation and exportation of any substance defined as an anabolic steroid must be in compliance with 21 CFR part 1312.

Criminal Liability. Any activity with any substance defined as an anabolic steroid not authorized by, or in violation of, the Controlled Substances Act or the Controlled Substances Import and Export Act occurring on or after January 4, 2010 is unlawful.

Disposal of Anabolic Steroids

Persons who possess substances classified as anabolic steroids and who wish to dispose of them rather than becoming registered to handle them should contact their local DEA Diversion field office for assistance in disposing of these substances legally. DEA Diversion field offices will provide the person with instructions regarding the disposal. A list of local DEA Diversion field offices may be found at *http://www.deadiversion.usdoj.gov.*

Regulatory Certifications

Regulatory Flexibility Act

The Deputy Administrator hereby certifies that this rulemaking has been drafted in accordance with the Regulatory Flexibility Act (5 *U.S.C.* 601–612). This regulation will not have a significant economic impact on a substantial number of small entities. As of August 2008, DEA identified 61 dietary supplements promoted for building muscle and increasing strength that are purported to contain boldione, desoxymethyltestosterone, or 19-nor-4,9(10)-androstadienedione. Seven dietary supplements purport to contain boldione; twenty-three dietary supplements purport to contain desoxymethyltestosterone; and thirty-one dietary supplements purport to contain 19-nor-4,9(10)-androstadienedione. All 61 dietary supplements are marketed and sold on the Internet.

The manufacturers and distributors of the 61 identified dietary supplements purported to contain boldione, desoxymethyltestosterone, or 19-nor-4,9(10)-androstadienedione also sell a variety of other dietary supplements. DEA has identified a substantial number of Internet distributors that sell these dietary supplements. However, these distributors also sell a variety of other nutritional products. DEA did not receive any information regarding the percentage of revenues derived from these dietary supplements. DEA did not receive any comments regarding legitimate uses of these three substances. DEA has not identified any chemical manufacturers that are currently using these substances as intermediates in their manufacturing process(es).

As of August 2008, DEA identified 32 chemical manufacturers and distributors that sell at least one of the three substances. Most of the companies are located in China and sell a variety of steroids. DEA notes that, as the vast majority of entities handling these substances are Internet based, it is virtually impossible to accurately quantify the number of persons handling these substances at any given time. Further, DEA has no information regarding the percentage of revenue these substances constitute for each handler.

DEA has identified five companies based in the U.S. that are DEA registrants that manufacture and/or distribute at least one of these substances as reference products for testing laboratories. DEA notes, upon placement into schedule III, these substances may be used for analytical purposes. These companies are registered with DEA and are already in compliance with the CSA and DEA implementing regulations regarding the handling of schedule III substances.

Executive Order 12866

The Deputy Administrator hereby certifies that this rulemaking has been drafted in accordance with Executive Order 12866 section 1(b). It has been determined that this rule is a significant regulatory action. Therefore, this action has been reviewed by the Office of Management and Budget.

As discussed above, the effect of this rule removes products containing these substances from the over-the-counter marketplace. DEA has no basis for estimating the size of the market for these products. DEA notes, however, that virtually all of the substances are imported. According to U.S. International Trade Commission data, the import value of all anabolic steroids for the first eleven months of 2008 was $2.1 million. These three substances are

a subset of those imports. The value of anabolic steroid imports for the first eleven months of 2008 declined by 28.1 percent over the comparable period in 2007; the quantity imported during the first eleven months decreased by 60.1 percent over the comparable period in 2007. The total market for these products containing these substances, therefore, is probably quite small. Moreover, DEA believes that the importation of these three substances is for illegitimate purposes.

The benefit of controlling these substances is to remove from the marketplace substances that have dangerous side effects and no legitimate medical use in treatment in the United States. As discussed in detail above, these substances can produce serious health effects in adolescents and adults. If medical uses for these substances are developed and approved, the drugs will be available as schedule III controlled substances in response to a prescription issued by a medical professional for a legitimate medical purpose. Until that time, however, this action bars the importation, exportation, and sale of these three substances except for legitimate research or industrial uses.

Executive Order 12988

This regulation meets the applicable standards set forth in Sections 3(a) and 3(b)(2) of Executive Order 12988 Civil Justice Reform.

Executive Order 13132

This rulemaking does not preempt or modify any provision of state law; nor does it impose enforcement responsibilities on any state; nor does it diminish the power of any state to enforce its own laws. Accordingly, this rulemaking does not have federalism implications warranting the application of Executive Order 13132.

Paperwork Reduction Act

This rule regulates three anabolic steroids, which are neither approved for medical use in humans nor approved for administration to cattle or other non-humans. Only chemical manufacturers who may use these substances as chemical intermediates for the synthesis of other steroids are required to register with DEA under the CSA. However, DEA has not identified any chemical manufacturers that are currently using these substances as intermediates in their manufacturing process(es). Thus, DEA does not expect this rule to impose any additional paperwork burden on the regulated industry.

Unfunded Mandates Reform Act of 1995

This rule will not result in the expenditure by state, local, and tribal governments, in the aggregate or by the private sector, of $120,000,000 or more (adjusted for inflation) in any one year and will not significantly or uniquely affect small governments. Therefore, no actions were deemed necessary under the provisions of the Unfunded Mandates Reform Act of 1995.

Congressional Review Act

This rule is not a major rule as defined by Section 804 of the Small Business Regulatory Enforcement Fairness Act of 1996 (Congressional Review Act). This rule will not result in an annual effect on the economy of $100,000,000 or more; a major increase in cost or prices; or significant adverse effects on competition, employment, investment, productivity, innovation, or on the ability of United States-based companies to compete with foreign-based companies in domestic and export markets.

List of Subjects in 21 CFR Part 1300

Chemicals, Drug traffic control.

■ For the reasons set out above, 21 CFR Part 1300 is amended as follows:

PART 1300—DEFINITIONS

■ 1. The authority citation for part 1300 continues to read as follows:

Authority: 21 U.S.C. 802, 821, 829, 871(b), 951, 958(f).

■ 2. Section 1300.01 is amended in paragraph (b)(4) by:

■ A. Redesignating paragraphs (b)(4)(xiii) through (b)(4)(lx) as (b)(4)(xiv) through (b)(4)(lxi),

■ B. Adding a new paragraph (b)(4)(xiii),

■ C. Further redesignating newly designated paragraphs (b)(4)(xvii) through (b)(4)(lxi) as (b)(4)(xviii) through (b)(4)(lxii),

■ D. Adding new paragraph (b)(4)(xvii),

■ E. Further redesignating newly designated paragraphs (b)(4)(xlvii) through (b)(4)(lxii) as (b)(4)(xlviii) through (b)(4)(lxiii), and

■ F. Adding new paragraph (b)(4)(xlvii) to read as follows:

§ 1300.01 Definitions relating to controlled substances.

* * * * *

(b) * * *

(4) * * *

(xiii) boldione (androsta-1,4-diene-3,17-dione)

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(xvii) desoxymethyltestosterone (17α-methyl-5α-androst-2-en-17β-ol) (a.k.a., madol)

* * * * *

(xlvii) 19-nor-4,9(10)-androstadienedione (estra-4,9(10)-diene-3,17-dione)

* * * * *

Dated: November 20, 2009.

Michele M. Leonhart,

Deputy Administrator.

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[FR Doc. E9–28572 Filed 12–3–09; 8:45 am]

BILLING CODE 4410–09–P

DEPARTMENT OF HOMELAND SECURITY

Coast Guard

33 CFR Part 117

[Docket No. USCG–2009–0968]

RIN 1625–AA09

Drawbridge Operation Regulation; Automated and Remotely Operated Bridges

AGENCY: Coast Guard, DHS.

ACTION: Final rule.

SUMMARY: The Commander, Ninth Coast Guard District, is identifying all remotely operated or automated drawbridges in his area of responsibility in subpart B of this part. This rule identifies all the remotely operated or automated drawbridges in this district that currently open on signal to navigation. This rule does not revise the operating schedule or conditions for any of the identified drawbridges.

DATES: This rule is effective December 15, 2009.

ADDRESSES: Comments and material received from the public as well as documents mentioned in this preamble as being available in the docket, are part of docket USCG–2009–0968 and are available online by going to *http://www.regulations.gov,* inserting USCG–2009–0968 in the ''Keyword'' box, and