CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

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PROPRIETARY NAME REVIEW(S)

Department of Health and Human Services
Public Health Service
Food and Drug Administration Center for
Drug Evaluation and Research Office of
Surveillance and Epidemiology
Office of Medication Error Prevention and Risk Management

Memo for Proprietary Name- Aveed

Date:	2/14/14
Reviewer:	Justine Harris, RPh Division of Medication Error Prevention and Analysis
Drug Name and Strength:	Aveed (Testosterone undecanoate) Injection 750mg/3 mL (250 mg/ mL)
Application Type/Number:	NDA 22219
Sponsor:	Endo Pharmaceutical Solutions, Inc

*** This document contains proprietary and confidential information that should not be released to the public.***

DMEPA found the proposed name, Aveed, acceptable in OSE Review # 2013-2995 dated March 14, 2013. In this review we indicated the proposed proprietary name must be re-reviewed prior to approval of the NDA. However, DMEPA no longer re-reviews proposed proprietary names within 90 days of the anticipated application approval, unless there is a change in the proposed product characteristics.

Since none of the proposed product characteristics were altered, our conclusion that the proposed proprietary name is acceptable has not changed since the aforementioned review. DMEPA has no objection to the proprietary name, Aveed, for this product at this time.

If you have further questions or need clarifications, please contact Shawnetta Jackson, OSE project manager, at 301-796-4952.

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/s/

JUSTINE HARRIS
02/14/2014

LISA V KHOSLA
02/14/2014

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology
Office of Medication Error Prevention and Risk Management

Proprietary Name Review

Date:	March 14, 2013
Reviewer(s):	Alison Park, Pharm.D., Safety Evaluator Division of Medication Error Prevention and Analysis
Team Leader	Zachary Oleszczuk, Pharm.D., Team Leader Division of Medication Error Prevention and Analysis
Division Director	Carol Holquist, RPh, Division Director Division of Medication Error Prevention and Analysis
Drug Name(s) and Strength(s):	Aveed (Testosterone Undecanoate) Injection 750 mg/3 mL (250 mg/mL)
Application Type/Number:	NDA 022219
Applicant:	Endo Pharmaceutical Solutions, Inc.
OSE RCM #:	2012-2995

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CONTENTS

1 INTRODUCTION

This review evaluates the proposed proprietary name, Aveed, from a safety and promotional perspective. DMEPA found the proposed name, Aveed, conditionally acceptable in OSE Review #2009-958 dated July 29, 2009. None of the product characteristics changed since that review. However, DMEPA re-evaluated the names identified in that review to ensure that our findings from that review have not changed due to lessons learned through postmarketing. The sources and methods used to evaluate the proposed name are outlined in the reference section and Appendix A, respectively.

1.1 REGULATORY HISTORY

This is the third review cycle for this New Drug Application (NDA) 022219. The original Applicant, Indevus Pharmaceuticals, received an Approvable Letter on June 27, 2008 due to a chemistry, manufacturing and control (CMC) deficiency and due to safety concerns related to immediate post-injection adverse reactions. On March 2, 2009, the Applicant submitted a Complete Response which addressed the CMC deficiencies but did not address the safety issues related to post-injection adverse reactions. On December 2, 2009, the current Applicant, Endo Pharmaceuticals Solutions Inc, received a Complete Response (CR) for this NDA due to the reports of serious, immediate, potentially life-threatening post-injection adverse reactions.

The proposed name, Aveed, was found conditionally acceptable in OSE Review #2009-958 dated July 29, 2009, and the Applicant, Endo Pharmaceuticals Solution Inc, was notified via letter on August 7, 2009. The NDA received a CR on December 2, 2009. A proprietary name request had been submitted for Aveed (NDA 022219) for this review cycle on December 20, 2012.

1.2 PRODUCT INFORMATION

The following product information is provided in the December 20, 2012 proprietary name submission.

- Active Ingredient: Testosterone Undecanoate
- Indication of Use: Replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone (i.e., primary hypogonadism and hypogonadotropic hypogonadism).
- Route of Administration: Intramuscular injection into the gluteal muscle
- Dosage Form: Sterile injectable solution
- Strength: 750 mg/3 mL (250 mg/mL)
- Dose and Frequency: Inject 3 mL (750 mg) intramuscularly at initiation, at 4 weeks, and every 10 weeks thereafter. Following injection, the patient should remain in the health care facility or physicians office for 30 minutes in order to provide for early recognition and management of an anaphylactic reaction or an injection-based pulmonary oil microembolism.
- How Supplied: Single-Use amber glass vial containing 750 mg/3 mL testosterone undecanoate sterile injectable solution.

- Storage: Controlled room temp 25°C (77°F); excursions permitted to 15-30°C (59-86°F)
- Container and Closure Systems: Amber glass, single use vial with silver-colored crimp seal and gray plastic cap.
- Schedule III

2 RESULTS

The following sections provide the information obtained and considered in the overall evaluation of the proposed proprietary name.

2.1 PROMOTIONAL ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined the proposed name is acceptable from a promotional perspective. DMEPA and the Division of Urologic and Reproductive Products (DRUP) concurred with the findings of OPDP's promotional assessment of the proposed name.

2.2 SAFETY ASSESSMENT

The following aspects were considered in the safety evaluation of the name.

2.2.1 United States Adopted Names (USAN) SEARCH

The January 4, 2013 search of the United States Adopted Name (USAN) stems did not identify that a USAN stem is present in the proposed proprietary name.

2.2.2 Components of the Proposed Proprietary Name

The Applicant indicated in their submission that the proposed name, Aveed, has no intended meaning or derivation. The intended pronunciation provided by the Applicant is "Uh-Veed." This proprietary name is comprised of a single word that does not contain any components (i.e., a modifier, route of administration, dosage form, etc.) that are misleading or can contribute to medication error.

2.2.3 FDA Name Simulation Studies

Seventy-seven practitioners participated in DMEPA's prescription studies. The interpretations did not overlap with or appear or sound similar to any currently marketed products. In the written study, eleven out of 54 practitioners (20.4%) interpreted the name correctly as "Aveed." The most common misinterpretation was the letter 'l' instead of 'e' in the 4th position of the name Aveed (n=14) and the letters 'n' or 'r' in the 2nd position of the name Aveed instead of 'v' (n=12 each). In the verbal study, one practitioner out of 23 practitioners (4.3 %) interpreted the name correctly as "Aveed." The most common misinterpretation was the letter string '-ede' instead of '-eed' in the 2nd syllable of the name Aveed (n=4) and the letter 'i' instead of '-ee-' (n=3). We considered the misinterpretations in our searches and evaluation of similar names. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

2.2.4 Comments from Other Review Disciplines

In response to the OSE January 15, 2013 e-mail, the Division of Reproductive and Urologic Products (DRUP) did not forward any comments or concerns relating to the proposed name at the initial phase of the proprietary name review.

2.2.5 Failure Mode and Effects Analysis of Similar Names

Appendix B lists possible orthographic and phonetic misinterpretations of the letters appearing in the proposed proprietary name, Aveed. Table 1 lists the names with orthographic, phonetic, or spelling similarity to the proposed proprietary name, Aveed, identified by the primary reviewer, the Expert Panel Discussion (EPD), and other review disciplines. Table 1 also includes the names identified from the FDA Prescription Study or by (b) (4) not identified by DMEPA and require further evaluation.

Appendix G lists the names with orthographic, phonetic, or spelling similarity to the proposed proprietary name, Aveed, that was reviewed in the previous OSE Review #2009-958 dated July 29, 2009. These names were re-evaluated to ensure our findings of the previous review have not changed based on postmarketing experience. Our evaluation found that we still agree with the previous findings of those names, and therefore, won't be included in further analysis.

Table 1: Collective List of Potentially Similar Names (DMEPA, EPD, Other Disciplines, and (b) (4) External Study) (n=19)

Look Similar					
Name	***Source***	***Name***	***Source***	***Name***	***Source***
Alesse	External	Amoxil	External	Anaids	FDA
Anexia	External	Anusol	FDA	Arava	FDA
Aricept	External	Avastin	FDA	Avea	FDA
Avodart	FDA	Avosil	FDA	(b) (4)	FDA
Diuril	FDA	Evacet	FDA	Evamist	FDA
Ancef	FDA				
Look and Sound Similar					
Name	***Source***	***Name***	***Source***	***Name***	***Source***
Aveed***	FDA	Hivid	FDA	Avinza	External

Our analysis of the 19 names contained in Table 1 considered the information obtained in the previous sections along with their product characteristics. We determined 19 names will not pose a risk for confusion as described in Appendices D through E

2.2.6 Communication of DMEPA's Final Decision to Other Disciplines

DMEPA communicated our findings to the Division of Reproductive and Urologic Products via e-mail on February 20, 2013. At that time we also requested additional information or concerns

that could inform our review. Per e-mail correspondence from the Division of Reproductive and Urologic Products on February 21, 2013, they stated no additional concerns with the proposed proprietary name, Aveed.

3 CONCLUSIONS

The proposed proprietary name is acceptable from both a promotional and safety perspective.

If you have further questions or need clarifications, please contact Shawnetta Jackson, OSE project manager, at 301-796-4952

3.1 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, Aveed, and have concluded that this name is acceptable. However, if any of the proposed product characteristics as stated in your December 20, 2012 submission are altered, the name must be resubmitted for review.

Additionally, the proposed proprietary name must be re-reviewed 90 days prior to approval of the NDA. The conclusions upon re-review are subject to change.

4 REFERENCES

1. **Fava, W., OSE Review #2009-958, Proprietary Name Review for Aveed, July 29, 2009**

2. ***Micromedex Integrated Index (http://csi.micromedex.com)***

   Micromedex contains a variety of databases covering pharmacology, therapeutics, toxicology and diagnostics.

3. ***Phonetic and Orthographic Computer Analysis (POCA)***

   POCA is a database which was created for the Division of Medication Error Prevention and Analysis, FDA. As part of the name similarity assessment, proposed names are evaluated via a phonetic/orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. Likewise, an orthographic algorithm exists which operates in a similar fashion.

4. ***Drug Facts and Comparisons, online version, St. Louis, MO (http://factsandcomparisons.com)***

   Drug Facts and Comparisons is a compendium organized by therapeutic course; it contains monographs on prescription and OTC drugs, with charts comparing similar products. This database also lists the orphan drugs.

5. ***FDA Document Archiving, Reporting & Regulatory Tracking System [DARRTS]***

   DARRTS is a government database used to organize Applicant and Sponsor submissions as well as to store and organize assignments, reviews, and communications from the review divisions.

6. ***Division of Medication Errors Prevention and Analysis proprietary name consultation requests***

   This is a list of proposed and pending names that is generated by the Division of Medication Error Prevention and Analysis from the Access database/tracking system.

7. ***Drugs@FDA (***http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm***)***

   Drugs@FDA contains most of the drug products approved since 1939. The majority of labels, approval letters, reviews, and other information are available for drug products approved from 1998 to the present. Drugs@FDA contains official information about FDA approved brand name, generic drugs, therapeutic biological products, prescription and over-the-counter human drugs and discontinued drugs and "Chemical Type 6" approvals.

8. ***U.S. Patent and Trademark Office (*http://www.uspto.gov*)***

   USPTO provides information regarding patent and trademarks.

9. ***Clinical Pharmacology Online (www.clinicalpharmacology-ip.com)***

   Clinical Pharmacology contains full monographs for the most common drugs in clinical use, plus mini monographs covering investigational, less common, combination, nutraceutical and nutritional products. It also provides a keyword search engine.

10. ***Data provided by Thomson & Thomson's SAEGIS ™ Online Service, available at (www.thomson-thomson.com)***

    The Pharma In-Use Search database contains over 400,000 unique pharmaceutical trademarks and trade names that are used in about 50 countries worldwide. The data is provided under license by IMS HEALTH.

11. ***Natural Medicines Comprehensive Databases (www.naturaldatabase.com)***

    Natural Medicines contains up-to-date clinical data on the natural medicines, herbal medicines, and dietary supplements used in the western world.

12. ***Access Medicine (www.accessmedicine.com)***

    Access Medicine® from McGraw-Hill contains full-text information from approximately 60 titles; it includes tables and references. Among the titles are: Harrison's Principles of Internal Medicine, Basic & Clinical Pharmacology, and Goodman and Gilman's The Pharmacologic Basis of Therapeutics.

13. ***USAN Stems (http://www.ama-assn.org/ama/pub/about-ama/our-people/coalitions-consortiums/united-states-adopted-names-council/naming-guidelines/approved-stems.shtml)***

    USAN Stems List contains all the recognized USAN stems.

14. ***Red Book (www.thomsonhc.com/home/dispatch)***

    Red Book contains prices and product information for prescription, over-the-counter drugs, medical devices, and accessories.

15. ***Lexi-Comp (www.lexi.com)***

    Lexi-Comp is a web-based searchable version of the Drug Information Handbook.

16. ***Medical Abbreviations (www.medilexicon.com)***

    Medical Abbreviations dictionary contains commonly used medical abbreviations and their definitions.

17. ***CVS/Pharmacy (www.CVS.com)***

    This database contains commonly used over the counter products not usually identified in other databases.

18. ***Walgreens (www.walgreens.com)***

    This database contains commonly used over the counter products not usually identified in other databases.

19. ***Rx List (www.rxlist.com)***

    RxList is an online medical resource dedicated to offering detailed and current pharmaceutical information on brand and generic drugs.

20. ***Dogpile (www.dogpile.com)***

    Dogpile is a Metasearch engine that searches multiple search engines including Google, Yahoo! and Bing, and returns the most relevant results to the search.

21. ***Natural Standard (http://www.naturalstandard.com)***

    Natural Standard is a resource that aggregates and synthesizes data on complementary and alternative medicine.

APPENDICES

Appendix A

FDA's Proprietary Name Risk Assessment considers the promotional and safety aspects of a proposed proprietary name. The promotional review of the proposed name is conducted by OPDP. OPDP evaluates proposed proprietary names to determine if they are overly fanciful, so as to misleadingly imply unique effectiveness or composition, as well as to assess whether they contribute to overstatement of product efficacy, minimization of risk, broadening of product indications, or making of unsubstantiated superiority claims. OPDP provides their opinion to DMEPA for consideration in the overall acceptability of the proposed proprietary name.

The safety assessment is conducted by DMEPA. DMEPA staff search a standard set of databases and information sources to identify names that are similar in pronunciation, spelling, and orthographically similar when scripted to the proposed proprietary name. Additionally, we consider inclusion of USAN stems or other characteristics that when incorporated into a proprietary name may cause or contribute to medication errors (i.e., dosing interval, dosage form/route of administration, medical or product name abbreviations, names that include or suggest the composition of the drug product, etc.). DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. [1]

Following the preliminary screening of the proposed proprietary name, DMEPA gathers to discuss their professional opinions on the safety of the proposed proprietary name. This meeting is commonly referred to the Center for Drug Evaluation and Research (CDER) Expert Panel discussion. DMEPA also considers other aspects of the name that may be misleading from a safety perspective. DMEPA staff conducts a prescription simulation studies using FDA health care professionals. When provided, DMEPA considers external proprietary name studies conducted by or for the Applicant/Sponsor and incorporates the findings of these studies into the overall risk assessment.

The DMEPA primary reviewer assigned to evaluate the proposed proprietary name is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name. DMEPA bases the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proprietary name and misleading nature of the proposed proprietary name with a focus on the avoidance of medication errors.

DMEPA uses the clinical expertise of its staff to anticipate the conditions of the clinical setting where the product is likely to be used based on the characteristics of the proposed product. DMEPA considers the product characteristics associated with the proposed product throughout the risk assessment because the product characteristics of the proposed may provide a context for communication of the drug name and ultimately determine the use of the product in the *usual* clinical practice setting.

Typical product characteristics considered when identifying drug names that could potentially be confused with the proposed proprietary name include, but are not limited to; established name of

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[1] National Coordinating Council for Medication Error Reporting and Prevention. http://www nccmerp.org/aboutMedErrors html. Last accessed 10/11/2007.

the proposed product, proposed indication of use, dosage form, route of administration, strength, unit of measure, dosage units, recommended dose, typical quantity or volume, frequency of administration, product packaging, storage conditions, patient population, and prescriber population. DMEPA considers how these product characteristics may or may not be present in communicating a product name throughout the medication use system. Because drug name confusion can occur at any point in the medication use process, DMEPA considers the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and monitoring the impact of the medication.[2]

The DMEPA considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA compares the proposed proprietary name with the proprietary and established name of existing and proposed drug products and names currently under review at the FDA. DMEPA compares the pronunciation of the proposed proprietary name with the pronunciation of other drug names because verbal communication of medication names is common in clinical settings. DMEPA examines the phonetic similarity using patterns of speech. If provided, DMEPA will consider the Sponsor's intended pronunciation of the proprietary name. However, DMEPA also considers a variety of pronunciations that could occur in the English language because the Sponsor has little control over how the name will be spoken in clinical practice. The orthographic appearance of the proposed name is evaluated using a number of different handwriting samples. DMEPA applies expertise gained from root-cause analysis of postmarketing medication errors to identify sources of ambiguity within the name that could be introduced when scripting (e.g.,"T" may look like "F," lower case 'a' looks like a lower case 'u,' etc). Additionally, other orthographic attributes that determine the overall appearance of the drug name when scripted (see Table 1 below for details).

Table 1. Criteria Used to Identify Drug Names that Look- or Sound-Similar to a Proposed Proprietary Name.

Type of Similarity	**Considerations when Searching the Databases**		
	Potential Causes of Drug Name Similarity	*Attributes Examined to Identify Similar Drug Names*	*Potential Effects*
Look-	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	• Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication • Names may look similar when scripted and lead to drug name confusion in

[2] Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006.

alike			written communication
	Orthographic similarity	Similar spelling Length of the name/Similar shape Upstrokes Down strokes Cross-strokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	• Names may look similar when scripted, and lead to drug name confusion in written communication
Sound-alike	Phonetic similarity	Identical prefix Identical infix Identical suffix Number of syllables Stresses Placement of vowel sounds Placement of consonant sounds Overlapping product characteristics	• Names may sound similar when pronounced and lead to drug name confusion in verbal communication

Lastly, DMEPA considers the potential for the proposed proprietary name to inadvertently function as a source of error for reasons other than name confusion. Post-marketing experience has demonstrated that proprietary names (or components of the proprietary name) can be a source of error in a variety of ways. Consequently, DMEPA considers and evaluates these broader safety implications of the name throughout this assessment and the medication error staff provides additional comments related to the safety of the proposed proprietary name or product based on professional experience with medication errors.

1. Database and Information Sources

DMEPA searches the internet, several standard published drug product reference texts, and FDA databases to identify existing and proposed drug names that may sound-alike or look-alike to the proposed proprietary name. A standard description of the databases used in the searches is provided in the reference section of this review. To complement the process, the DMEPA uses a computerized method of identifying phonetic and orthographic similarity between medication names. The program, Phonetic and Orthographic Computer Analysis (POCA), uses complex algorithms to select a list of names from a database that have some similarity (phonetic, orthographic, or both) to the trademark being evaluated. Lastly, DMEPA reviews the USAN stem list to determine if any USAN stems are present within the proprietary name. The individual findings of multiple safety evaluators are pooled and presented to the CDER Expert Panel. DMEPA also evaluates if there are characteristics included in the composition that may render the name unacceptable from a safety perspective (abbreviation, dosing interval, etc.).

2. Expert Panel Discussion

DMEPA gathers gather CDER professional opinions on the safety of the proposed product and discussed the proposed proprietary name (Expert Panel Discussion). The Expert Panel is composed of Division of Medication Errors Prevention (DMEPA) staff and representatives from the Office of Prescription Drug Promotion (OPDP). We also consider input from other review disciplines (OND, ONDQA/OBP). The Expert Panel also discusses potential concerns regarding drug marketing and promotion related to the proposed names.

The primary Safety Evaluator presents the pooled results of the database and information searches to the Expert Panel for consideration. Based on the clinical and professional experiences of the Expert Panel members, the Panel may recommend additional names, additional searches by the primary Safety Evaluator to supplement the pooled results, or general advice to consider when reviewing the proposed proprietary name.

3. FDA Prescription Simulation Studies

Three separate studies are conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of the proposed proprietary name with marketed U.S. drug names (proprietary and established) due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. The studies employ healthcare professionals (pharmacists, physicians, and nurses), and attempts to simulate the prescription ordering process. The primary Safety Evaluator uses the results to identify orthographic or phonetic vulnerability of the proposed name to be misinterpreted by healthcare practitioners.

In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, inpatient medication orders and/or outpatient prescriptions are written, each consisting of a combination of marketed and unapproved drug products, including the proposed name. These orders are optically scanned and one prescription is delivered to a random sample of participating health professionals via e-mail. In addition, a verbal prescription is recorded on voice mail. The voice mail messages are then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants record their interpretations of the orders which are recorded electronically.

4. Comments from Other Review Disciplines

DMEPA requests the Office of New Drugs (OND) and/or Office of Generic Drugs (OGD), ONDQA or OBP for their comments or concerns with the proposed proprietary name, ask for any clinical issues that may impact the DMEPA review during the initial phase of the name review. Additionally, when applicable, at the same time DMEPA requests concurrence/non-concurrence with OPDP's decision on the name. The primary Safety Evaluator addresses any comments or concerns in the safety evaluator's assessment.

The OND/OGD Regulatory Division is contacted a second time following our analysis of the proposed proprietary name. At this point, DMEPA conveys their decision to accept or reject the name. The OND or OGD Regulatory Division is requested to provide any further information that might inform DMEPA's final decision on the proposed name.

Additionally, other review disciplines opinions such as ONDQA or OBP may be considered depending on the proposed proprietary name.

5. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

The primary Safety Evaluator applies his/her individual expertise gained from evaluating medication errors reported to FDA, considers all aspects of the name that may be misleading or confusing, conducts a Failure Mode and Effects Analysis, and provides an overall decision on acceptability dependent on their risk assessment of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.[3] When applying FMEA to assess the risk of a proposed proprietary name, DMEPA seeks to evaluate the potential for a proposed proprietary name to be confused with another drug name because of name confusion and, thereby, cause errors to occur in the medication use system. FMEA capitalizes on the predictable and preventable nature of medication errors associated with drug name confusion. FMEA allows the Agency to identify the potential for medication errors due to orthographically or phonetically similar drug names prior to approval, where actions to overcome these issues are easier and more effective than remedies available in the post-approval phase.

In order to perform an FMEA of the proposed name, the primary Safety Evaluator must analyze the use of the product at all points in the medication use system. Because the proposed product is has not been marketed, the primary Safety Evaluator anticipates the use of the product in the usual practice settings by considering the clinical and product characteristics listed in Section 1.2 of this review. The Safety Evaluator then analyzes the proposed proprietary name in the context of the usual practice setting and works to identify potential failure modes and the effects associated with the failure modes.

In the initial stage of the Risk Assessment, the Safety Evaluator compares the proposed proprietary name to all of the names gathered from the above searches, Expert Panel Discussion, and prescription studies, external studies, and identifies potential failure modes by asking:

> ***"Is the proposed proprietary name convincingly similar to another drug name, which may cause practitioners to become confused at any point in the usual practice setting? And are there any components of the name that may function as a source of error beyond sound/look-alike?"***

An affirmative answer indicates a failure mode and represents a potential for the proposed proprietary name to be confused with another proprietary or established drug name because of look- or sound-alike similarity or because of some other component of the name. If the answer to the question is no, the Safety Evaluator is not convinced that the names posses similarity that would cause confusion at any point in the medication use system, thus the name is eliminated from further review.

In the second stage of the Risk Assessment, the primary Safety Evaluator evaluates all potential failure modes to determine the likely *effect* of the drug name confusion, by asking:

> ***"Could the confusion of the drug names conceivably result in medication errors in the usual practice setting?"***

The answer to this question is a central component of the Safety Evaluator's overall risk assessment of the proprietary name. If the Safety Evaluator determines through FMEA that the name similarity would not ultimately be a source of medication errors in the usual practice

[3] Institute for Healthcare Improvement (IHI). Failure Mode and Effects Analysis. Boston. IHI:2004.

setting, the primary Safety Evaluator eliminates the name from further analysis. However, if the Safety Evaluator determines through FMEA that the name similarity could ultimately cause medication errors in the usual practice setting, the Safety Evaluator will then recommend the use of an alternate proprietary name.

Moreover, DMEPA will object to the use of proposed proprietary name when the primary Safety Evaluator identifies one or more of the following conditions in the Overall Risk Assessment:

a. OPDP finds the proposed proprietary name misleading from a promotional perspective, and the Review Division concurs with OPDP's findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a PROPRIETARY name or otherwise [21 U.S.C 321(n); See also 21 U.S.C. 352(a) & (n)].

b. DMEPA identifies that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].

c. FMEA identifies the potential for confusion between the proposed proprietary name and other proprietary or established drug name(s), and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.

d. The proposed proprietary name contains an USAN (United States Adopted Names) stem.

e. DMEPA identifies a potential source of medication error within the proposed proprietary name. For example, the proprietary name may be misleading or, inadvertently, introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug and another drug product but involve a naming characteristic that when incorporated into a proprietary name, may be confusing, misleading, cause or contribute to medication errors.

If DMEPA objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the primary Safety Evaluator uses the FMEA process to identify strategies to reduce the risk of medication errors. DMEPA generally recommends that the Sponsor select an alternative proprietary name and submit the alternate name to the Agency for review. However, in rare instances FMEA may identify plausible strategies that could reduce the risk of medication error of the currently proposed name. In that instance, DMEPA may be able to provide the Sponsor with recommendations that reduce or eliminate the potential for error and, thereby, would render the proposed name acceptable.

In the event that DMEPA objects to the use of the proposed proprietary name, based upon the potential for confusion with another proposed (but not yet approved) proprietary name, DMEPA will provide a contingency objection based on the date of approval. Whichever product, the Agency approves first has the right to use the proprietary name, while DMEPA will recommend that the second product to reach approval seek an alternative name.

The threshold set for objection to the proposed proprietary name may seem low to the Applicant/Sponsor. However, the safety concerns set forth in criteria a through e above are supported either by FDA regulation or by external healthcare authorities, including the Institute of Medicine (IOM), World Health Organization (WHO), the Joint Commission, and the Institute for Safe Medication Practices (ISMP). These organizations have examined medication errors

resulting from look- or sound-alike drug names, confusing, or misleading names and called for regulatory authorities to address the issue prior to approval. Additionally, DMEPA contends that the threshold set for the Proprietary Name Risk Assessment is reasonable because proprietary drug name confusion is a predictable and preventable source of medication error that, in many instances, the Agency and/or Sponsor can identify and rectify prior to approval to avoid patient harm.

Furthermore, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to rectify post-approval. Educational and other post-approval efforts are low-leverage strategies that have had limited effectiveness at alleviating medication errors involving drug name confusion. Sponsors have undertaken higher-leverage strategies, such as drug name changes, in the past but at great financial cost to the Sponsor and at the expense of the public welfare, not to mention the Agency's credibility as the authority responsible for approving the error-prone proprietary name. Moreover, even after Sponsors' have changed a product's proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioners' vocabulary, and as a result, the Agency has continued to receive reports of drug name confusion long after a name change in some instances. Therefore, DMEPA believes that post-approval efforts at reducing name confusion errors should be reserved for those cases in which the potential for name confusion could not be predicted prior to approval.

Appendix B: Letters and Letter Strings with Possible Orthographic or Phonetic Misinterpretation

Letters in Name, Aveed	Scripted May Appear as	Spoken May Be Interpreted as
Capital 'A'	H, O, N, S, ce, Fl, ci	o, u, i, e
lower case 'a'	Cl, el, ci, d, u, o, i, e	
lower case 'v'	u, r, n, i. w	b, f
lower case 'e'	u, i, l, o, a, p	ee, ea, ie, y, i
lower case 'd'	cl, u, ci, a, ol, b., il, el	t, b, v
Letter strings		
'Av'	Cin-	
've'	w	
'ee'	u, a	ie, ea, y
'ed'	ul	
'eed'		ede, id

Appendix C: Prescription Simulation Samples and Results

Figure 1. Aveed Study (Conducted on January 4, 2013)

Handwritten Requisition Medication Order	Verbal Prescription
Medication Order: Aveed inject 3 ml IM at each [illegible]	Aveed Take to the doctor's office Disp: #1
Outpatient Prescription: Aveed #1 Take to MD [illegible]	

Study Name: Aveed

As of Date 2/4/2013

190 People Received Study

77 People Responded

Study Name: Aveed

Total	26	23	28	
INTERPRETATION	**INPATIENT**	**VOICE**	**OUTPATIENT**	**TOTAL**
ANCED	0	0	1	1
ANEED	5	0	0	5
ANEID	1	0	0	1
ANEID INJECTION	1	0	0	1
ANELD	2	0	0	2
ANELD INJECT	1	0	0	1
ANILD	1	0	0	1
ARCED	0	0	4	4
AREAD	0	0	1	1
AREED	0	0	7	7
AVCED	0	0	1	1
AVED	0	0	3	3
AVEDE	0	3	0	3
AVEED	5	16	6	27
AVEEDE	0	1	0	1
AVELD	7	0	5	12
AVELD INJECT	1	0	0	1
AVELID	1	0	0	1
AVID	0	1	0	1
AVIDE	0	2	0	2
AVUD	1	0	0	1

Appendix D: Proprietary names not likely to be confused or not used in usual practice settings for the reasons described.

No.	Proprietary Name	Active Ingredient	Similarity to Aveed	Failure preventions
1.	Alesse	Levonorgestrel/Ethinyl Estradiol	Look alike	The pair have sufficient orthographic and/or phonetic differences.
2.	Anexsia	Hydrocodone Bitartrate/Acetaminophen	Look alike	The pair have sufficient orthographic and/or phonetic differences.
3.	Aricept	Donepezil Hydrochloride	Look alike	The pair have sufficient orthographic and/or phonetic differences.
4.	Avastin	Bevacizumab	Look alike	The pair have sufficient orthographic and/or phonetic differences.
5.	Avodart	Dutasteride	Look alike	The pair have sufficient orthographic and/or phonetic differences.
6.	Evamist	Estradiol	Look alike	The pair have sufficient orthographic and/or phonetic differences.
7.	Aveed***	Testosterone Undecanoate	Look and sound alike	Subject of this review. Name found conditionally acceptable in OSE Review 2009-958, dated July 29, 2009 for NDA 022219.
8.	Avinza	Morphine Sulfate	Look and sound alike	The pair have sufficient orthographic and/or phonetic differences.
9.	Anaids	Calcium Carbonate/Phenobarbital 300 mg/9 mg	Look alike	Identified in Red Book. Deactivated as of 12/12/95. No therapeutic equivalents are available and the name does not appear in common internet searches such as Google.com.
10.	[redacted]			(b) (4)

Appendix D: Proprietary names not likely to be confused or not used in usual practice settings for the reasons described.

No.	Proprietary Name	Active Ingredient	Similarity to Aveed	Failure preventions
11.	Evacet	Doxorubicin Liposomal	Look alike	This name is was registered with the USPTO on January 13, 1998 by Liposome Company, INC but is currently Abandoned. While there are other Doxorubicin Liposomal products (e.g., Doxil, Lipodox), there is no indication that the name Evacet is currently being used in any prescription in the United States based on usage data.

Appendix E: Risk of medication errors due to product confusion minimized by dissimilarity of the names and/ or use in clinical practice for the reasons described.

PROPOSED NAME: **Aveed** **(Testosterone Undecanoate)**		**STRENGTH:** **750 mg/3 mL** **(250 mg/mL)**	**USUAL DOSE:** **Inject 3 mL (750 mg) intramuscularly at each injection**
FAILURE MODE: Name Confusion		**CAUSES:** (Potential reasons for name confusion that could lead to medication error)	**PREVENTION OF FAILURE MODE** (Reasons why the risk of medication error is minimized)
1	Amoxil (Amoxicillin) Tablets 500 mg, 875 mg; Chewable Tablets 125 mg, 250 mg; Capsules 250 mg, 500 mg; Oral Reconstituted Suspension 125 mg/5 mL, 200 mg/ 5 mL, 250 mg/5 mL, 400 mg/5 mL <u>Usual Dosage</u> *Adults:* 500 to 875 mg by mouth every 12 hours or 250 to 875 mg every 8 hours. *For gonorrhea:* 3 g as a single dose. *For H.pylori:* 1 g BID or TID for 14 days. *Children:* 25 to 45 mg/kg/day in divided doses every 12 hours or 20 to 40 mg/kg/day in divided doses every 8 hours.	<u>Orthographic</u> Both names contain similar number of letters (6 vs. 5), begin with the letter 'A', and contain 2 upstrokes in similar positions. Additionally, the letter string '-il' in the Amoxil may appear similar to the letter 'd' in Aveed when scripted. <u>Route of Administration</u> Both available as a single route of administration <u>Achievable Dose Overlap</u> Both may be prescribed as 750 mg or 3 mL	<u>Orthographic</u> The letter string '-mox-' in Amoxil appears longer than the letter string '-vee-' in Aveed due to the rounded parts of the letters 'm' and 'o' which makes the name Amoxil appear longer. <u>Product Strength</u> Single strength vs. multiple strengths which must be specified <u>Frequency of Administration</u> One injection at initiation, at 4 weeks, and every 10 weeks vs. Every 8 to 12 hours or BID or TID

PROPOSED NAME: **Aveed** **(Testosterone Undecanoate)**		**STRENGTH:** **750 mg/3 mL** **(250 mg/mL)**	**USUAL DOSE:** **Inject 3 mL (750 mg) intramuscularly at each injection**
FAILURE MODE: Name Confusion		**CAUSES:** (Potential reasons for name confusion that could lead to medication error)	**PREVENTION OF FAILURE MODE** (Reasons why the risk of medication error is minimized)
2	Anusol (Pramoxine Hydrochloride/Zinc Oxide) Ointment 1%-12.5% Anusol-HC (Hydrocortisone Acetate) Rectal Suppository 25 mg; Rectal Cream 2.5% <u>Usual Dosage</u> *Suppositories:* One suppository per rectum morning and night for 2 weeks. *Cream/Ointment:* Apply to affected area 2 to 4 times daily depending on the severity of the condition.	<u>Orthographic</u> Both names contain similar number of letters (6 vs. 5), begin with the letter 'A', and contain 2 upstrokes in similar positions. Additionally, the letter strings 'Anu-' and '-ol' in the Anusol may appear similar to the letter string 'Avee-' and letter 'd' in Aveed, respectively, when scripted. <u>Product Strength</u> Both available in a single strength or combination strength per dosage form <u>Dosage Form</u> Both available in a single dosage form (ointment vs. IM injection) <u>Route of Administration</u> Both available in a single route of administration per dosage form	<u>Orthographic</u> The letter 's' between the letter strings 'Anu-' and '-ol' in Anusol gives the name a longer appearance vs. no additional letter between the letter strings 'Avee-' and 'd' in Aveed. <u>Frequency of Administration</u> One injection at initiation, at 4 weeks, and every 10 weeks vs. Every morning and night or BID <u>Usual Dosage</u> 750 mg or 3 mL or one injection vs. Apply or Use <u>Modifier</u> The modifier 'HC', if included, may help differentiate Aveed and Anusol-HC when scripted.

PROPOSED NAME: **Aveed** **(Testosterone Undecanoate)**		**STRENGTH:** **750 mg/3 mL** **(250 mg/mL)**	**USUAL DOSE:** **Inject 3 mL (750 mg) intramuscularly at each injection**
FAILURE MODE: Name Confusion		**CAUSES:** (Potential reasons for name confusion that could lead to medication error)	**PREVENTION OF FAILURE MODE** (Reasons why the risk of medication error is minimized)
3	Arava (Leflunomide) Tablets 10 mg, 20 mg <u>Usual Dosage</u> 100 mg by mouth once daily for 3 days as a loading dose, then 20 mg once daily. If 20 mg/day is not well tolerated, may decrease to 10 mg daily.	<u>Orthographic</u> Both names contain 5 letters and begin with the letter 'A'. Additionally, the letter string '-ra-' and ending letter 'a' in Arava may appear similar to the letter string '-vee-' and the ending letter 'd' in Aveed, respectively, when scripted. <u>Dosage Form</u> Both available as a single dosage form <u>Route of Administration</u> Both available as a single route of administration	<u>Product Strength</u> Single strength vs. multiple strengths which must be specified <u>Usual Dosage</u> 750 mg or 3 mL or one injection vs. One tablet or 10 mg or 20 mg
4	Avea (Tumeric roots extract/mineral water/ethanol) Oral Solution <u>Usual Dosage</u> Place 5 to 10 drops in a glass and add 120 mL (4 oz) of water, then wait one minute before drinking. Take 3 times per day or as recommended by your healthcare provider.	<u>Orthographic</u> Both names consist of similar number of letters (5 vs. 4) and contain the letter string 'Ave-' in the same position. Additionally, the ending letter 'a' in Avea may appear similar to the ending letter 'd' in Aveed when scripted. <u>Product Strength</u> Both available as a single strength product <u>Dosage Form</u> Both available as a single dosage form <u>Route of Administration</u> Both available as a single route of administration	<u>Orthographic</u> The name Avea appears shorter than the name Aveed when scripted due to the extra letter 'e' in the 4th position. <u>Setting of Use</u> Herbal product unlikely to be written on a prescription. Therefore, there is no expectation that confusion would occur with Aveed.

PROPOSED NAME: **Aveed** **(Testosterone Undecanoate)**		**STRENGTH:** **750 mg/3 mL** **(250 mg/mL)**	**USUAL DOSE:** **Inject 3 mL (750 mg) intramuscularly at each injection**
FAILURE MODE: Name Confusion		**CAUSES:** (Potential reasons for name confusion that could lead to medication error)	**PREVENTION OF FAILURE MODE** (Reasons why the risk of medication error is minimized)
5	Diuril (Chlorothiazide) Oral Suspension 250 mg/5 mL <u>Usual Dosage</u> *Adults:* 0.5 to 1 g (10 to 20 mL) by mouth once or twice a day. May adjust dose up to 2 g (40 mL) a day in divided doses. *Children:* 10 to 30 mg/kg/day in single or 2 divided doses	<u>Orthographic</u> Both names consist of similar number of letters (6 vs. 5) and contain 2 upstrokes in similar positions. Additionally, the beginning letter string 'diu-' and ending letter string '-il' in Diuril may appear similar to the letter string 'Ave-' and the ending letter 'd' in Aveed, respectively, when scripted. <u>Product Strength</u> Both available as a single strength product <u>Dosage Form</u> Both available as a single dosage form <u>Route of Administration</u> Both available as a single route of administration <u>Achievable Dose Overlap</u> 750 mg	<u>Frequency of Administration</u> One injection at initiation, at 4 weeks, and every 10 weeks vs. once or twice daily

PROPOSED NAME: **Aveed** **(Testosterone Undecanoate)**		**STRENGTH:** **750 mg/3 mL** **(250 mg/mL)**	**USUAL DOSE:** **Inject 3 mL (750 mg) intramuscularly at each injection**
FAILURE MODE: Name Confusion		**CAUSES:** (Potential reasons for name confusion that could lead to medication error)	**PREVENTION OF FAILURE MODE** (Reasons why the risk of medication error is minimized)
6	Hivid* (Zalcitabine) Tablets 0.375 mg, 0.75 mg <u>Usual Dosage</u> 0.375 to 0.75 mg by mouth 3 times daily * Voluntarily Withdrawn FR effective 06/18/2009 due to stopped marketing of the drug product. No Therapeutic Equivalents.	<u>Orthographic</u> Both names contain 5 letters, contain 2 upstrokes the same position, and end in the letter 'd'. Additionally, the letter string 'Hiv-' in Hivid may appear similar to the letter string 'Ave-' when scripted. <u>Phonetic</u> Both names contain 2 syllables in which the second syllable begins with the 'v' sound and ends with the 'd' sound. <u>Dosage Form</u> Both available as a single dosage form <u>Route of Administration</u> Both available as a single route of administration <u>Overlapping Product Strength in Written Order</u> 750 mg vs. 0.75 mg	<u>Phonetic</u> The beginning syllable 'Uh' in Aveed sounds distinct from the beginning syllable 'Hi' in Hivid when spoken. <u>Product Strength in Verbal Order</u> Single strength vs. multiple strengths which must be specified in a verbal order (i.e., 0.375 mg or 0.75 mg) <u>Frequency of Administration</u> One injection at initiation, at 4 weeks, and every 10 weeks vs. three times daily

PROPOSED NAME: **Aveed** **(Testosterone Undecanoate)**		**STRENGTH:** **750 mg/3 mL** **(250 mg/mL)**	**USUAL DOSE:** **Inject 3 mL (750 mg) intramuscularly at each injection**
FAILURE MODE: Name Confusion		**CAUSES:** (Potential reasons for name confusion that could lead to medication error)	**PREVENTION OF FAILURE MODE** (Reasons why the risk of medication error is minimized)
7	Ancef* (Cefazolin Sodium) Injection 250 mg/vial, 500 mg/vial, 1 gm/vial, 5 gm/vial, 10 gm/vial *Ancef, NDA 050461, Withdrawn FR effective 06/18/2009, but generics available on the market. <u>Usual Dosage</u> *Adult Range for Infection:* 250 mg to 1.5 g IM or IV every 6-12 hours. *Renal dosing:* As low as 125 mg to 250 mg every 18to 24 hours. *Preoperative prophylaxis:* 1 gm IV or IM administered 30 min to 1 hr prior to the start of surgery. *Children for Infection:* 25 mg to 50 mg/kg/day divided into 4 doses.	<u>Orthographic</u> Both names contain 5 letters, begin with the letter 'A', contain the letter 'e' in the 4th position, and contain 2 upstrokes in the same positions. Additionally, the letter string '-nc-' in Ancef may appear similar to the letter string '-ve-' in Aveed when scripted. <u>Dosage Form</u> Both available as injectable dosage forms <u>Route of Administration</u> Both available as IM injections <u>Frequency of Administration</u> Both may be given as "one injection" <u>Usual Dose</u> Both available as 750 mg dose	<u>Orthographic</u> The upstroke 'f' in Ancef looks distinct from the upstroke 'd' in Aveed when scripted either due to the down stroke in the letter 'f' if written in cursive or the cross-stroke if written in print vs. no down stroke or cross-stroke in the letter 'd'.

PROPOSED NAME: **Aveed** **(Testosterone Undecanoate)**		**STRENGTH:** **750 mg/3 mL** **(250 mg/mL)**	**USUAL DOSE:** **Inject 3 mL (750 mg) intramuscularly at each injection**
FAILURE MODE: Name Confusion		**CAUSES:** (Potential reasons for name confusion that could lead to medication error)	**PREVENTION OF FAILURE MODE** (Reasons why the risk of medication error is minimized)
8	Avosil* (Salicylic Acid) Topical Ointment *OTC <u>Usual Dosage</u> Apply 1/8 inch layer on scars twice daily and occasionally in between to control itching.	<u>Orthographic</u> Both names consist of similar number of letters (5 vs. 6), begin with the letter string 'Av-', and contain 2 upstrokes in similar positions. Additionally, the ending letter string '-il' in Avosil may appear similar to the letter 'd' in Aveed when scripted. <u>Product Strength</u> Both available in a single strength. <u>Dosage Form</u> Both available as a single dosage form <u>Route of Administration</u> Both available as a single route of administration	<u>Orthographic</u> The letter string '-os-' in Avosil appears longer than the letter string '-ee-' in Aveed due to the rounded part of the letter 'o' and the position of the letter 's' which makes the name Avosil appear longer. <u>Frequency of Administration</u> One injection at initiation, at 4 weeks, and every 10 weeks vs. BID

Appendix G: Names identified in OSE Review #2009-958 Name Review, dated July 29, 2009, that were re-evaluated by the Safety Evaluator to ensure our findings have not changed (n=31).

Table 1: Collective List of Potentially Similar Names (DMEPA, EPD, Other Disciplines, and External Name Study)

Look Similar					
Name	***Source***	***Name***	***Source***	***Name***	***Source***
Acuvail	2009	Amfed	2009	Aredia	2009
Asacol	2009	Avandia	EPD/2009	Avelox	EPD/External/ 2009
Avitene	2009	Axert	EPD/2009	Duoneb	2009
Evista	2009	Veetids	External/2009	Vfend	2009
Sound Similar					
Name	***Source***	***Name***	***Source***	***Name***	***Source***
Auranofin	2009	Avage	2009	Avar	2009
AVD	2009	Aviane	2009	Halothane	2009
Look and Sound Similar					
Name	***Source***	***Name***	***Source***	***Name***	***Source***
Advil	External/2009	Aleve	EPD/External/ 2009	Avail	EPD/2009
Avalide	EPD/External/ 2009	Avapro	EPD/External/ 2009	Avedis	2009
Aveeno	EPD/External/ 2009	Avena	EPD/2009	Avita	EPD/2009
Axid	External/2009	Oveen	2009	Ovide	EPD/2009
Viread	2009				

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

ALISON J PARK
03/14/2013

ZACHARY A OLESZCZUK
03/14/2013

CAROL A HOLQUIST
03/14/2013

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology

Date:	July 29, 2009
To:	Scott Monroe, MD, Director Division of Reproductive and Urologic Products (DRUP)
Thru:	Carlos Mena-Grillasca, R.Ph., Acting Team Leader Denise Toyer, Pharm.D., Deputy Director Carol Holquist, R.Ph., Director Division of Medication Error Prevention and Analysis (DMEPA)
From:	Walter Fava, R.Ph., Safety Evaluator Division of Medication Error Prevention and Analysis (DMEPA)
Subject:	Proprietary Name Review
Drug Name(s):	Aveed (Testosterone Undecanoate) Injection 750 mg/3 mL (250 mg/mL)
Application Type/Number:	NDA#: 22-219
Applicant/Applicant:	Endo Pharmaceuticals Solutions, Inc.
OSE RCM #:	2009-958

***** This document contains proprietary and confidential information that should not be released to the public.*****

CONTENTS

EXECUTIVE SUMMARY

Aveed is the proposed proprietary name for testosterone undecanoate injection. This proposed name was evaluated from a safety and promotional perspective based on the product characteristics provided by the Applicant. We sought input from pertinent disciplines involved with the review of this application and considered it accordingly. Our evaluation did not identify concerns that would render the name unacceptable based on the product characteristics and safety profile known at the time of this review. Thus, DMEPA finds the proposed proprietary name Aveed conditionally acceptable for this product. DMEPA considers this a final review; however, if approval of the NDA is delayed beyond 90 days from the date of this review, the proposed proprietary name, Aveed, must be re-evaluated.

Additionally, if any of the proposed product characteristics as stated in this review are altered, DMEPA rescinds this finding and the name must be resubmitted for review. The conclusions upon re-review are subject to change.

1 BACKGROUND

1.1 INTRODUCTION

This review is in response to a request from Endo Pharmaceuticals Solutions Inc. for an assessment of the proposed proprietary name, Aveed, regarding potential name confusion with other proprietary or established drug names in the usual practice settings. The Applicant submitted an external study in support of their proposed proprietary name. Container labels, carton and insert labeling were also submitted, but will be reviewed under separate cover (OSE Review #2009-510).

1.2 REGULATORY HISTORY

The proposed (b) (4) was originally reviewed by DMEPA in OSE Review #2007-2317, dated May 13, 2008. DDMAC objected to the name at that time (b) (4), however, the Division did not concur and instructed DMEPA to review the proposed (b) (4) for this product. In a subsequent review, DDMAC again objected (b) (4) and the Division concurred with their objection. Therefore, the Applicant submitted the alternative proposed proprietary name, Aveed, for this product.

1.3 PRODUCT INFORMATION

Aveed (testosterone undecanoate) is indicated for testosterone replacement therapy in males for conditions associated with a deficiency or absence of endogenous testosterone, e.g., primary hypogonadism or hypoganadotropic hypogonadism. It is administered by healthcare professionals as an intramuscular injection. The initial dose administered is 750 mg followed by a second dose of 750 mg four weeks later, and then every 10 weeks thereafter. Aveed will be supplied in single use vials containing 750 mg/3mL, which will be individually boxed. Aveed will be a Schedule III controlled substance.

2 METHODS AND MATERIALS

This section describes the methods and materials used by the Division of Medication Error Prevention and Analysis (DMEPA) when conducting a proprietary name risk assessment (See 2.1 Proprietary Name Risk Assessment). The primary objective for the assessment is to identify and remedy potential sources of medication error prior to drug approval. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. [1]

2.1 PROPRIETARY NAME RISK ASSESSMENT

FDA's Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name and the proprietary and established names of drug products existing in the marketplace and those pending IND, NDA, BLA, and ANDA products currently under review by the Center.

For the proposed proprietary name, DMEPA staff searched a standard set of databases and information sources to identify names with orthographic and phonetic similarity (See 2.1.1 for details) and held a Center for Drug Evaluation and Research (CDER) Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name (See 2.1.1.2). DMEPA staff also conducts internal FDA prescription analysis studies. When provided, external prescription analysis studies results are considered and incorporated into the overall risk assessment.

The Safety Evaluator assigned to the Proprietary Name Risk Assessment is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name (See 2.1.5 for details). The overall risk assessment is based on the findings of a Failure Mode and Effects Analysis (FMEA) of the proprietary name, and is focused on the avoidance of medication errors.

FMEA is a systematic tool for evaluating a process and identifying where and how it might fail. [2] FMEA is used to analyze whether the drug names identified with orthographic or phonetic similarity to the proposed proprietary name could cause confusion that subsequently leads to medication errors in the clinical setting. DMEPA uses the clinical expertise of its staff to anticipate the conditions of the clinical setting where the product is likely to be used based on the characteristics of the proposed product.

In addition, the product characteristics provide the context for the verbal and written communication of the drug names and can interact with the orthographic and phonetic attributes of the names to increase the risk of confusion when there is overlap or, in some instances, decrease the risk of confusion by helping to differentiate the products through dissimilarity. Accordingly, the DMEPA staff considers the product characteristics associated with the proposed drug throughout the risk assessment because the product characteristics of the proposed may provide a

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[1] National Coordinating Council for Medication Error Reporting and Prevention. http://www.nccmerp.org/aboutMedErrors.html. Last accessed 10/11/2007.

[2] Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

context for communication of the drug name and ultimately determine the use of the product in the *usual* clinical practice setting.

Typical product characteristics considered when identifying drug names that could potentially be confused with the proposed proprietary name include, but are not limited to, established name of the proposed product, proposed indication of use, dosage form, route of administration, strength, unit of measure, dosage units, recommended dose, typical quantity or volume, frequency of administration, product packaging, storage conditions, patient population, and prescriber population. Because drug name confusion can occur at any point in the medication use process, DMEPA staff considers the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and monitoring the impact of the medication.[3]

2.1.1 Search Criteria

The DMEPA staff considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted as outlined in Appendix A.

For this review, particular consideration was given to drug names beginning with the letter 'A' when searching to identify potentially similar drug names, as 75% of the confused drug names reported by the USP-ISMP Medication Error Reporting Program involve pairs beginning with the same letter.[4, 5]

To identify drug names that may look similar to Aveed, the DMEPA staff also considers the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (5 letters), upstrokes (two, capital letter 'A' and lower case 'd'), downstrokes (none), cross-strokes (one, upper case 'A'), and dotted letters (none). Additionally, several letters in Aveed may be vulnerable to ambiguity when scripted, including capital letter 'A' may appear as capital 'H', 'O', 'N', and 'S'; lower case letter 'a' may appear as the letters 'Cl'; lower case 'v' may appear as lower case 'u', 'r', 'n', or 'i'; the lower case letter 'e' may appear as lower case 'u', 'i', 'l', or 'o'; and the lower case letter 'd' may appear as lower case 'cl' or 'u'. As a result, the DMEPA staff also considers these alternate appearances when identifying drug names that may look similar to Aveed.

When searching to identify potential names that may sound similar to Aveed, the DMEPA staff searches for names with similar number of syllables (two), stresses (A-veed or a-VEED), and placement of vowel and consonant sounds. Additionally, the DMEPA staff considers that pronunciation of parts of the name can vary such as the letter 'a' may sound like 'o', 'u', 'i', or 'e'; the letter 'v' may sound like 'b' or 'f'; the letter 'd' may sound like 't'. The Applicant's intended pronunciation of the proprietary name, 'a'veed' was provided with the proposed name submission and, therefore, was taken into consideration. Moreover, names are often mispronounced and/or spoken with regional accents and dialects, so other potential pronunciations of the name are considered.

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[3] Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006.

[4] Institute for Safe Medication Practices. Confused Drug name List (1996-2006). Available at http://www.ismp.org/Tools/confuseddrugnames.pdf

[5] Kondrack, G and Dorr, B. Automatic Identification of Confusable Drug Names. Artifical Inteligence in Medicine (2005)

The DMEPA staff also considers the product characteristics associated with the proposed drug throughout the identification of similar drug names, since the product characteristics of the proposed drug ultimately determine the use of the product in the clinical practice setting. For this review, the following information was provided about the proposed product to the DMEPA staff: proposed proprietary name (Aveed), proposed established name (testosterone undecanoate), proposed indication of use (testosterone replacement), strength (750 mg/3 mL), dose (750 mg), frequency of administration (every 10 weeks), route (intramuscular) and dosage form (parenteral). Appendix A provides a more detailed listing of the product characteristics the DMEPA staff general takes into consideration.

Lastly, the DMEPA staff also considers the potential for the proposed proprietary name to inadvertently function as a source of error for reasons other than name confusion. Postmarketing experience has demonstrated that proprietary names (or components of the proprietary name) can be a source of error in a variety of ways. Consequently, these broader safety implications of the name are considered and evaluated throughout this assessment and the DMEPA staff provides additional comments related to the safety of the proposed proprietary name or product based on professional experience with medication errors.

2.1.1.1 Database and Information Sources

The proposed proprietary name was provided to the DMEPA staff to conduct a search of the internet, several standard published drug product reference texts, and FDA databases to identify existing and proposed drug names that may sound-alike or look-alike to the proposed proprietary name using the criteria outlined in Section 2.1.1. A standard description of the databases used in the searches is provided in Section 6. To complement the process, the DMEPA staff used a computerized method of identifying phonetic and orthographic similarity between medication names. The program, Phonetic and Orthographic Computer Analysis (POCA), uses complex algorithms to select a list of names from a database that have some similarity (phonetic, orthographic, or both) to the trademark being evaluated. Lastly, the DMEPA staff reviewed the USAN stem list to determine if any USAN stems are present within the proprietary name. The individual findings of multiple safety evaluators were then pooled and presented to the CDER Expert Panel.

2.1.1.2 CDER Expert Panel Discussion

An Expert Panel Discussion is held by DMEPA to gather CDER professional opinions on the safety of the proposed product and the proposed proprietary name. The Expert Panel is composed of Division of Medication Error Prevention and Analysis (DMEPA) staff and representatives from the Division of Drug Marketing, Advertising, and Communications (DDMAC). Potential concerns regarding drug marketing and promotion related to the proposed names are also discussed.

The pooled results of the DMEPA staff were presented to the Expert Panel for consideration. Based on the clinical and professional experiences of the Expert Panel members, the Panel may recommend the addition of names, additional searches by the Safety Evaluator to supplement the pooled results, or general advice to consider when reviewing the proposed proprietary name.

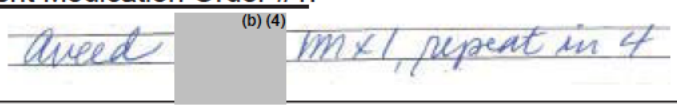
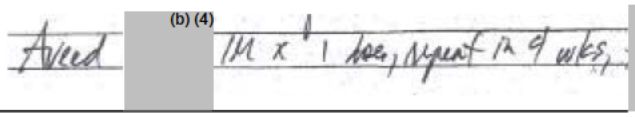
2.1.2 FDA Prescription Analysis Studies

Three separate studies are conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of the proposed proprietary name with marketed U.S. drug names (proprietary and established) due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. The studies employ a total of 123 (one hundred twenty-three) healthcare professionals (pharmacists, physicians, and nurses), and attempts

to simulate the prescription ordering process. The results are used by the Safety Evaluator to identify any orthographic or phonetic vulnerability of the proposed name to be misinterpreted by healthcare practitioners.

In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, inpatient medication orders and outpatient prescriptions are written, each consisting of a combination of marketed and unapproved drug products, including the proposed name. These orders are optically scanned and one prescription is delivered to a random sample of the 123 participating health professionals via e-mail. In addition, a verbal prescription is recorded on voice mail. The voice mail messages are then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants send their interpretations of the orders via e-mail to DMEPA.

Figure 1. Aveed Study (conducted on April 13, 2009)

HANDWRITTEN PRESCRIPITON AND MEDICATION ORDER	VERBAL PRESCRIPTION
Inpatient Medication Order #1: 	'Aveed (b) (4) x1 dose, repeat in 4 weeks, then every 10 weeks'
Inpatient Medication Order #2: 	

2.1.3 External Proprietary Name Risk Assessment

For this product, the Applicant submitted an external evaluation of the proposed proprietary name. The Division of Medication Error Prevention and Analysis conducts an independent analysis and evaluation of the data provided, and responds to the overall findings of the assessment. When the external proprietary name risk assessment identifies potentially confusing names that were not captured in DMEPA's database searches or in the Expert Panel Discussion, these names are included in the Safety Evaluator's Risk Assessment and analyzed independently by the Safety Evaluator to determine if the potentially confusing name could lead to medication errors in usual practice settings.

After the Safety Evaluator has determined the overall risk assessment of the proposed name, the Safety Evaluator compares the findings of their overall risk assessment with the findings of the proprietary name risk assessment submitted by the Applicant. The Safety Evaluator then determines whether the Division's risk assessment concurs or differs with the findings. When the proprietary name risk assessments differ, the Division of Medication Error Prevention and Analysis provides a detailed explanation of these differences.

2.1.4 Comments from the Division of Reproductive and Urologic Products

The regulatory division is contacted following our analysis of the proposed proprietary name. At this point, DMEPA conveys their decision to accept or reject the name. The regulatory division is requested to concur/not concur with DMEPA's final decision.

2.1.5 Safety Evaluator Risk Assessment of the Proposed Proprietary Name

Based on the criteria set forth in Section 2.1, the Safety Evaluator Risk Assessment applies his/her individual expertise gained from evaluating medication errors reported to FDA to conduct a Failure Mode and Effects Analysis and provides an overall risk assessment of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.[6] When applying FMEA to assess the risk of a proposed proprietary name, DMEPA seeks to evaluate the potential for a proposed proprietary name to be confused with another drug name as a result of the name confusion and, thereby, cause errors to occur in the medication use system. FMEA capitalizes on the predictable and preventable nature of medication errors associated with drug name confusion. FMEA allows the Agency to identify the potential for medication errors due to orthographically or phonetically similar drug names prior to approval, where actions to overcome these issues are easier and more effective than remedies available in the post-approval phase.

In order to perform an FMEA of the proposed name, the Safety Evaluator must analyze the use of the product at all points in the medication use system. Because the proposed product is not yet marketed, the Safety Evaluator anticipates the use of the product in the usual practice settings by considering the clinical and product characteristics listed in Appendix A. The Safety Evaluator then analyzes the proposed proprietary name in the context of the usual practice setting and works to identify potential failure modes and the effects associated with the failure modes.

In the initial stage of the Risk Assessment, the Safety Evaluator compares the proposed proprietary name to all of the names gathered from the above searches, expert panel evaluation, and studies, and identifies potential failure modes by asking:

> ***"Is the name Aveed convincingly similar to another drug name, which may cause practitioners to become confused at any point in the usual practice setting?"***

An affirmative answer indicates a failure mode and represents a potential for Aveed to be confused with another proprietary or established drug name because of look- or sound-alike similarity. If the answer to the question is no, the Safety Evaluator is not convinced that the names possess similarity that would cause confusion at any point in the medication use system, then the name is eliminated from further review.

In the second stage of the Risk Assessment, all potential failure modes are evaluated to determine the likely *effect* of the drug name confusion, by asking:

> ***"Could the confusion of the drug names conceivably result in medication errors in the usual practice setting?"***

The answer to this question is a central component of the Safety Evaluator's overall risk assessment of the proprietary name. If the Safety Evaluator determines through FMEA that the name similarity would not ultimately be a source of medication errors in the usual practice setting, the name is eliminated from further analysis. However, if the Safety Evaluator determines through FMEA that the name similarity could ultimately cause medication errors in the usual practice setting, the Safety Evaluator will then recommend that an alternate proprietary name be used. In rare instances, the FMEA findings may provide other risk-reduction strategies; for example, product reformulation to avoid an overlap in strength or an alternate modifier designation may be recommended as a means of reducing the risk of medication errors resulting from drug name confusion.

[6] Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

DMEPA will object to the use of the proposed proprietary name when one or more of the following conditions are identified in the Safety Evaluator's Risk Assessment:

1. DDMAC finds the proposed proprietary name misleading from a promotional perspective, and the Review Division concurs with DDMAC's findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a proprietary name or otherwise. [21 U.S.C 321(n); see also 21 U.S.C. 352(a) & (n)].
2. DMEPA identifies that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].
3. FMEA identifies potential for confusion between the proposed proprietary name and other proprietary or established drug names, and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.
4. The proposed proprietary name contains an USAN (United Sates Adopted Names) stem, particularly in a manner that is contradictory to the USAN Council's definition.
5. DMEPA identifies a potential source of medication error within the proposed proprietary name. For example, the proprietary name may be misleading or, inadvertently, introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug and another drug product.

In the event that DMEPA objects to the use of the proposed proprietary name, based upon the potential for confusion with another proposed (but not yet approved) proprietary name, DMEPA will provide a contingency objection based on the date of approval. Whichever product is awarded approval first has the right to the use the name, while DMEPA will recommend that the second product to reach approval seek an alternative name.

If none of these criteria are met, then DMEPA will not object to the use of the proprietary name. If any of these criteria are met, then DMEPA will object to the use of the proposed proprietary name. The threshold set for objection to the proposed proprietary name may seem low to the Applicant; however, the safety concerns set forth in criteria 1 through 5 are supported either by FDA regulation or by external healthcare authorities, including the Institute of Medicine (IOM), World Health Organization (WHO), Joint Commission on Accreditation of Hospitals (JCOAH), and the Institute for Safe Medication Practices (ISMP), who have examined medication errors resulting from look- or sound-alike drug names and called for regulatory authorities to address the issue prior to approval.

Furthermore, DMEPA contends that the threshold set for the Proprietary Name Risk Assessment is reasonable because proprietary drug name confusion is a predictable and preventable source of medication error that, in many instances, can be identified and remedied prior to approval to avoid patient harm.

Additionally, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to remedy post-approval. Educational and other post-approval efforts are low-leverage strategies that have proven to have limited effectiveness at alleviating medication errors involving drug name confusion. Higher-leverage strategies, such as drug name changes, have been undertaken in the past but at great financial cost to the Applicant and at the expense of the public welfare, not to mention the Agency's credibility as the authority responsible for approving the error-prone proprietary name. Moreover, even after Applicants have changed a product's proprietary name in the post-approval phase, it is difficult to eradicate the

original proprietary name from practitioners' vocabulary, and as a result, the Agency has continued to receive reports of drug name confusion long after a name change in some instances. Therefore, DMEPA believes that post-approval efforts at reducing name confusion errors should be reserved for those cases in which the potential for name confusion could not be predicted prior to approval (See Section 4 for limitations of the process).

If DMEPA objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the FMEA process is used to identify strategies to reduce the risk of medication errors. DMEPA is likely to recommend that the Applicant select an alternative proprietary name and submit the alternate name to the Agency for DMEPA to review. However, in rare instances FMEA may identify plausible strategies that could reduce the risk of medication error of the currently proposed name. In that instance, DMEPA may be able to provide the Applicant with recommendations that reduce or eliminate the potential for error and, thereby, would render the proposed name acceptable.

3 RESULTS

3.1 PROPRIETARY NAME RISK ASSESSMENT

3.1.1 Database and Information Sources

The searches yielded a total of 22 names as having some similarity to the name Aveed.

Twelve of the names were thought to look like Aveed. These include Axert, Aveeno, Avena, Aleve-D, Axid, Veetids, Aredia, Avandia, Duoneb, Acuvail***, Asacol, and Avelox. Five names, Aviane, Avage, Avail, Avar, and AVD, were thought to sound like Aveed. The remaining five names were thought to look and sound similar to Aveed. These include Avedis Avalide, Avita, Ovide, and Oveen.

Additionally, DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, as of May 15, 2009.

3.1.2 Expert Panel Discussion

The Expert Panel reviewed the pool of names identified by DMEPA staff (See Section 3.1.1. above), and noted no additional names thought to have orthographic or phonetic similarity to Aveed.

DDMAC had no concerns regarding the proposed name from a promotional perspective, and did not offer any additional comments relating to the proposed name.

3.1.3 FDA Prescription Analysis Studies

A total of 28 practitioners responded but none of the responses overlapped with any existing or proposed drug names. Twenty one of the participants (75%) interpreted the name correctly as "Aveed," with correct interpretation occurring in the verbal study (n=5) and both inpatient written studies (n=16). The remainder of participants misinterpreted the drug name in the voice study. The most common misinterpretations involved the end portion of the name, 'ede' as 'ide' or 'id'. See Appendix B for the complete listing of interpretations from the verbal and written prescription studies.

3.1.4 External Study

In the proposed name risk assessment submitted by the Applicant, the Drug Safety Institute (DSI) identified and evaluated a total of 22 drug names thought to have some potential for confusion with the name Aveed.

Eleven of the 22 names were identified in the DMEPA staff searches, the Expert Panel Discussion, or FDA prescription studies. The eleven remaining names identified by the DSI as having some similarity (phonetic or orthographic) to Aveed were: Advil, Aleve, Amfed, Auranofin, Avapro, Aveenobar, Avitene, Evista, Halothane, Vfend, and Viread. These names are assessed in Section 3.1.6.

3.1.5 Comments from the Division of Reproductive and Urologic Products (DRUP)

On May 15, 2009, DMEPA notified DRUP via e-mail that we had no objections to the proposed proprietary name, Aveed. Per e-mail correspondence from DRUP on May 18, 2009, they indicated that they concur with our assessment of the proposed proprietary name, Aveed.

3.1.6 Safety Evaluator Risk Assessment of the Proposed Proprietary Name

Independent searches by the primary Safety Evaluator resulted in no additional names which were thought to look or sound similar to Aveed and represent a potential source of drug name confusion. Thus, thirty-three names were analyzed to determine if the drug names could be confused with Aveed and if the drug name confusion would likely result in a medication error. Besides the potentially similar names there were no other issues identified that would render the name unacceptable.

4 DISCUSSION

Neither DDMAC nor the Division of Reproductive and Urologic Products have concerns with the proposed name. DMEPA identified and evaluated a total of thirty-three names for their potential similarity to the proposed name, Aveed.

Thirteen of the thirty-three names lacked orthographic and/or phonetic similarity and were not evaluated further (see Appendix C).

Failure mode and effects analysis (FMEA) was then applied to determine if the proposed name, Aveed, could potentially be confused with any of the remaining twenty names and lead to medication errors. This analysis determined that the name similarity between Aveed and the identified names was unlikely to result in medication errors with any of the twenty products identified for the reasons presented in Appendices D through H. This finding was consistent with and supported by an independent risk assessment of the proprietary name submitted by the Applicant.

5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Aveed, is not vulnerable to name confusion that could lead to medication errors. Thus, the Division of Medication Error Prevention and Analysis (DMEPA) has no objection to the proprietary name, Aveed, for this product at this time. Our assessment supports the findings of the External Study submitted by the Applicant.

However, if any of the proposed product characteristics as stated in this review are altered prior to approval of the product, DMEPA rescinds this Risk Assessment finding and the name must be resubmitted for review. In the event that our Risk Assessment finding is rescinded, the evaluation of the name on resubmission is independent of the previous Risk Assessment, and as such, the conclusions on re-review of the name are subject to change. If approval of the NDA is delayed beyond 90 days from the date of this review, the proposed proprietary name must be re-evaluated.

We are willing to meet with the Division for further discussion, if needed. If you have further questions or need clarification, please contact Maria Wasilik, OSE Project Manager, at 301-796-0567.

5.1 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, Aveed, and have concluded it is acceptable.

If approval is delayed beyond 90 days from the date of this review, the proposed proprietary name must be re-evaluated. If we find the name unacceptable following the re-review, we will notify you.

6 REFERENCES

1. Micromedex Integrated Index (http://csi.micromedex.com)

Micromedex contains a variety of databases covering pharmacology, therapeutics, toxicology and diagnostics.

2. Phonetic and Orthographic Computer Analysis (POCA)

POCA is a database which was created for the Division of Medication Error Prevention and Analysis, FDA. As part of the name similarity assessment, proposed names are evaluated via a phonetic/orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. Likewise, an orthographic algorithm exists which operates in a similar fashion.

3. Drug Facts and Comparisons, online version, St. Louis, MO (http://factsandcomparisons.com)

Drug Facts and Comparisons is a compendium organized by therapeutic Course; contains monographs on prescription and OTC drugs, with charts comparing similar products.

4. AMF Decision Support System [DSS]

DSS is a government database used to track individual submissions and assignments in review divisions.

5. Division of Medication Error Prevention and Analysis proprietary name consultation requests

This is a list of proposed and pending names that is generated by the Division of Medication Error Prevention and Analysis from the Access database/tracking system.

6. Drugs@FDA (http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm)

Drugs@FDA contains most of the drug products approved since 1939. The majority of labels, approval letters, reviews, and other information are available for drug products approved from 1998 to the present. Drugs@FDA contains official information about FDA approved brand name and generic drugs and therapeutic biological products; prescription and over-the-counter human drugs and therapeutic biologicals, discontinued drugs and "Chemical Type 6" approvals.

7. Electronic online version of the FDA Orange Book (http://www.fda.gov/cder/ob/default.htm)

The FDA Orange Book provides a compilation of approved drug products with therapeutic equivalence evaluations.

8. U.S. Patent and Trademark Office (http://www.uspto.gov)

USPTO provides information regarding patent and trademarks.

9. Clinical Pharmacology Online (www.clinicalpharmacology-ip.com)

Clinical Pharmacology contains full monographs for the most common drugs in clinical use, plus mini monographs covering investigational, less common, combination, nutraceutical and nutritional products. It also provides a keyword search engine.

10. Data provided by Thomson & Thomson's SAEGIS ™ Online Service, available at (www.thomson-thomson.com)

The Pharma In-Use Search database contains over 400,000 unique pharmaceutical trademarks and tradenames that are used in about 50 countries worldwide. The data is provided under license by IMS HEALTH.

11. Natural Medicines Comprehensive Databases (www.naturaldatabase.com)

Natural Medicines contains up-to-date clinical data on the natural medicines, herbal medicines, and dietary supplements used in the western world.

12. Stat!Ref (www.statref.com)

Stat!Ref contains full-text information from approximately 30 texts; it includes tables and references. Among the database titles are: Handbook of Adverse Drug Interactions, Rudolphs Pediatrics, Basic Clinical Pharmacology, and Dictionary of Medical Acronyms Abbreviations.

13. USAN Stems (http://www.ama-assn.org/ama1/pub/upload/mm/365/stem-list-2-09-update.pdf)

USAN Stems List contains all the recognized USAN stems.

14. Red Book Pharmacy's Fundamental Reference

Red Book contains prices and product information for prescription, over-the-counter drugs, medical devices, and accessories.

15. Lexi-Comp (www.lexi.com)

Lexi-Comp is a web-based searchable version of the Drug Information Handbook.

16. Medical Abbreviations Book

Medical Abbreviations Book contains commonly used medical abbreviations and their definitions.

APPENDICES

Appendix A:

The DMEPA staff considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA also compares the spelling of the proposed proprietary name with the proprietary and established names of existing and proposed drug products because similarly spelled names may have greater likelihood to sound similar to one another when spoken or look similar to one another when scripted. The DMEPA staff also examines the orthographic appearance of the proposed name using a number of different handwriting samples. Handwritten communication of drug names has a long-standing association with drug name confusion. Handwriting can cause similarly and even dissimilarly spelled drug name pairs to appear very similar to one another. The similar appearance of drug names when scripted has led to medication errors. The DMEPA staff applies expertise gained from root-cause analysis of such medication errors to identify sources of ambiguity within the name that could be introduced when scripting (e.g.,"T" may look like "F," lower case 'a' looks like a lower case 'u,' etc), along with other orthographic attributes that determine the overall appearance of the drug name when scripted (See Table 1 below for details). In addition, the DMEPA staff compares the pronunciation of the proposed proprietary name with the pronunciation of other drug names because verbal communication of medication names is common in clinical settings. If provided, DMEPA will consider the Applicant's intended pronunciation of the proprietary name. However, DMEPA also considers a variety of pronunciations that could occur in the English language because the Applicant has little control over how the name will be spoken in clinical practice.

Table 1. Criteria used to identify drug names that look- or sound-similar to a proposed proprietary name

Type of similarity	Considerations when searching the databases		
	Potential causes of drug name similarity	Attributes examined to identify similar drug names	Potential Effects
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	• Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication • Names may look similar when scripted and lead to drug name confusion in written communication
	Orthographic similarity	Similar spelling Length of the name Upstrokes Downstrokes Cross-strokes Dotted letters	• Names may look similar when scripted, and lead to drug name confusion in written communication

		Ambiguity introduced by scripting letters Overlapping product characteristics	
Sound-alike	Phonetic similarity	Identical prefix Identical infix Identical suffix Number of syllables Stresses Placement of vowel sounds Placement of consonant sounds Overlapping product characteristics	• Names may sound similar when pronounced and lead to drug name confusion in verbal communication

Appendix B: Aveed Prescription Study Responses

Inpatient Medication Order #1	Voice Prescription	Inpatient Medication Order #2
Aveed	Avide	Aveed
Aveed	Aveed	Aveed
Aveed	Avid	Aveed
Aveed	Avide	Aveed
Aveed	Avide	Aveed
Aveed	Avide	Aveed
Aveed	Aveed	Aveed
Aveed	Aveed	
Aveed	Avede	
	Aveed	
	Avide	
	Aveed	

Appendix C: Names lacking convincing orthographic and/or phonetic similarities with Aveed

Proprietary Name	Similarity to Aveed
Avena	Look
Duoneb	Look
Avelox	Look
Veetids	Look
Aviane	Sound
Avage	Sound
Avar	Sound
Auranofin	Look and Sound
Avapro	Look and Sound
Avitene	Look and Sound
Halothane	Look and Sound
Vfend	Look and Sound

Appendix D: Proprietary Names with Similarity to Aveed Withdrawn by FDA Commissioner

Proprietary Name	Similarity to Aveed	Status
Avedis	Look and Sound	Withdrawn by Commissioner July 1970

Appendix E: Proprietary Names with similarity to Aveed for discontinued products that have no generic therapeutic equivalents available

Proprietary Name	Strength, Active Ingredient(s), Dosage Form	Similarity to Aveed	Status
Oveen	(b) (4)	Look and Sound	Discontinued
Amfed	75 mg phenylpropanolamine capsule	Look and Sound	Discontinued

Appendix F: Abbreviations for Chemotherapy Regimens with similarity to Aveed

Proprietary Name	Strength/Active ingredient(s)/Dosage Form	Similarity to Aveed	Usual Dose	Differentiating Product Characteristics
Aveed	**750 mg/3 mL injection**		**750 mg intramuscularly x 1 dose, repeat in 4 weeks, then repeat every 10 weeks thereafter**	
AVD	Dactinomycin, Doxorubicin, and Vincristine injection	Sound	Dactinomycin 15 mcg/kg/day days 1 to 5 of weeks 0, 13, 26, 39, 52, and 65 Doxorubicin 60 mg/m^2 day 1 of weeks 6, 19, 32, 45, and 58 Vincristine 1.5 mg/m^2 day 1 of weeks 1 to 8, 13, 14, 26, 27, 39, 40, 52, 53, 65, and 66	**Route of administration** Intramuscular vs Intravenous **Frequency of administration** One dose repeated in 4 weeks and then every 10 weeks thereafter vs specific dosing regimen listed for each drug **Practice setting** General medicine and endocrinologist vs Oncology The letters 'AVD' would not be used to order chemotherapy for patients. 'AVD' was found in Lexicomp but is not a recognized medical abbreviation in the medical abbreviations dictionary for any drug product. As a medical abbreviation 'AVD' represents 'aortic valve disease', 'apparent volume of distribution', arteriosclerotic vascular disease', atrioventricular delay cerebrovascular accident'.

Appendix G: Proprietary names with similarity to Aveed, but have no overlapping strength, dose, and/or route of administration

Proprietary Name	Strength/Dosage Form	Usual Dose
Aveed	**750 mg/3 mL injection**	**750 mg intramuscularly x 1 dose, repeat in 4 weeks, then repeat every 10 weeks thereafter**
Avandia	2 mg, 4 mg, and 8 mg tablets	Take 4 mg by mouth in single or divided doses. Do not exceed 8 mg per day.
Aredia	30 mg/vial, 60 mg/vial, and 90 mg/vial pamidronate disodium	*Hypercalcemia:* 60 mg to 90 mg IV infusion over 2 to 24 hours *Paget's disease:* 30 mg IV infusion over 4 hours on 3 consecutive days
Axid	150 mg, 300 mg nizatadine capsules; 15 mg/mL oral solution	*Active Duodenal Ulcer*: Take 150 mg by mouth twice a day or 300 mg at bedtime *Maintenance Duodenal Ulcer:* Take 150 mg by mouth at bedtime
Advil	200 mg tablets and oral gelcaps; 50 mg chewable tablets; 100 mg/5 mL oral suspension; 50 mg/1.25 mL oral drops	200 mg by mouth every 4 hours as needed for pain
Avalide	150 mg/12.5 mg; 300 mg/12.5 mg; 300 mg/25 mg hydrochlorothiazide/irbesartan tablet	Take one tablet by mouth daily
Axert	6.25 mg and 12.5 mg almotriptan tablets	Take one to two tablets by mouth daily.

<u>Appendix H:</u> Proprietary names of single strength products with similarity to Aveed, with multiple differentiating characteristics

Proprietary Name	Strength/Active ingredient(s)/Dosage Form	Similarity to Aveed	Usual Dose	Differentiating Product Characteristics Aveed vs Similar Proprietary Name Product
Aveed	**750 mg/3 mL injection**		**750 mg intramuscularly x 1 dose, repeat in 4 weeks, then repeat every 10 weeks thereafter**	
Aveeno	1% colloidal oatmeal; lotion	Look	Apply daily as needed	**<u>Dosage forms</u>** Injectable vs Lotion **<u>Route of administration</u>** Intramuscular vs Topical **<u>Frequency of administration</u>** One dose repeated in 4 weeks and then every 10 weeks thereafter vs daily as needed **<u>Setting of use</u>** Administered by practitioner in a clinic vs applied by patient/caregiver
Aveenobar	Colloidal oatmeal, sulfur, salicylic acid	Look and Sound	Apply one to two times a day	**<u>Dosage forms</u>** Injectable vs soap **<u>Route of administration</u>** Intramuscular vs Topical **<u>Frequency of administration</u>** One dose repeated in 4 weeks and then every 10 weeks thereafter vs one to two times a day **<u>Settings of use</u>** Administered by practitioner in a clinic vs applied by patient/caregiver
Aleve	220 mg naproxen sodium tablets	Look and Sound	Take one tablet by mouth two to three times a day	**<u>Dosage forms</u>** Injectable vs tablet **<u>Route of administration</u>** Intramuscular vs oral **<u>Frequency of administration</u>** One dose repeated in 4 weeks and then every 10 weeks thereafter as needed vs two to three times a day **<u>Setting of use</u>** Administered by practitioner in a clinic vs self-administered by patient/caregiver

Avail	Multiple vitamins with Calcium	Look	Take one tablet by mouth once a day	**Dosage forms** Injectable vs Tablet **Dose** 750 mg vs 1 tablet **Route of administration** Intramuscular vs oral **Frequency of administration** One dose repeated in 4 weeks and then every 10 weeks thereafter as needed vs once a day **Setting of use** Administered by practitioner in a clinic vs self-administered by patient/caregiver
Avita	0.025% tretinoin; gel and cream	Look and Sound	Apply once a day	**Dosage forms** Injectable vs cream and gel **Route of administration** Intramuscular vs Topical **Frequency of administration** One dose repeated in 4 weeks and then every 10 weeks thereafter vs once daily **Setting of use** Administered by practitioner in a clinic vs applied by patient/caregiver
Ovide	0.5% malathion; lotion	Look and Sound	Apply to wet scalp x 1	**Dosage forms** Injectable vs Lotion **Route of administration** Intramuscular vs Topical **Frequency of administration** One dose repeated in 4 weeks and then every 10 weeks thereafter vs one time **Setting of use** Administered by practitioner in a clinic vs applied by patient/caregiver
Acuvail***	0.45% ketorolac tromethamine ophthlamic solution	Look	*Patient dosing;* Instill 1 drop into affected eye twice daily beginning one day prior to surgery, continued on the day of surgery and through the first two weeks of the postoperative period	**Dosage forms** Injectable vs ophthalmic solution **Route of administration** Intramuscular vs Ocular **Frequency of administration** One dose repeated in 4 weeks and then every 10 weeks thereafter vs twice daily or every 20 minutes x 3 doses prior to procedure

Asacol	400 mg mesalamine	Look	Take 2 tablets by mouth three times a day	**Dosage forms** Injectable vs tablet **Route of administration** Intramuscular vs Oral **Frequency of administration** One dose repeated in 4 weeks and then every 10 weeks thereafter vs three times a day
Aleve-D	200 mg naproxen sodium/120 mg pseudoephedrine	Look	Take one caplet every 12 hours	**Dosage forms** Injectable vs Extended-Release Tablets **Route of administration** Intramuscular vs oral **Frequency of administration** One dose repeated in 4 weeks and then every 10 weeks thereafter vs every 12 hours
Evista	60 mg raloxifene HCl tablet	Look and Sound	Take one tablet by mouth daily	**Dosage forms** Injectable vs tablet **Route of administration** Intramuscular vs Oral **Frequency of administration** One dose repeated in 4 weeks and then every 10 weeks thereafter vs once a day
Viread	300 mg tenofovir disoproxil fumarate	Look and Sound	Take one tablet by mouth once a day	**Dosage forms** Injectable vs Tablet **Route of administration** Intramuscular vs Oral **Frequency of administration** One dose repeated in 4 weeks and then every 10 weeks thereafter vs once a day

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/s/

WALTER L FAVA
07/29/2009

CARLOS M MENA-GRILLASCA
07/29/2009

DENISE P TOYER
07/30/2009

CAROL A HOLQUIST
07/30/2009

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology

Date:	April 15, 2009
To:	Scott Monroe, MD, Director Division of Reproductive and Urologic Products
Through:	Carlos Mena-Grillasca, R.Ph., Acting Team Leader Division of Medication Error Prevention and Analysis
From:	Walter Fava, R.Ph., Safety Evaluator Division of Medication Error Prevention and Analysis
Subject:	Proprietary Name Review
Drug Name(s):	[redacted] (b) (4) (Testosterone undecanoate) Injection 750 mg/3 mL
Application Type/Number:	NDA 22-219
Applicant:	Indevus Pharmaceuticals, Inc.
OSE RCM #:	2009-508

2 Pages have been Withheld in Full as b4 (CCI/TS) immediately following this page.

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/s/

Walter Fava
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Carlos M Mena-Grillasca
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Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology

Date:	May 13, 2008
To:	Scott Monroe, M.D., Director Division of Reproductive and Urologic Products
Thru:	Linda Kim-Jung, PharmD., Team Leader Denise Toyer, PharmD., Deputy Director Division of Medication Error Prevention
From:	Walter Fava, R.Ph., Safety Evaluator Division of Medication Error Prevention
Subject:	Proprietary Name, Label, and Labeling Review
Drug Name(s):	(b) (4) (Testosterone Undecanoate)
Application Type/Number:	NDA #: 22-219
Applicant:	Indevus Pharmaceuticals, Inc.
OSE RCM #:	2007-2317

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/s/

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Linda Kim-Jung
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Denise Toyer
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