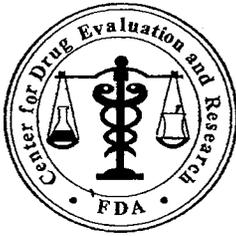


**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

NDA 22-185

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**

Date: April 24, 2008

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From: Walter Fava, R.Ph., Safety Evaluator
Division of Medication Error Prevention

Subject: Proprietary Name, Label, and Labeling Review

Drug Name(s): Taclonex Scalp (Calcipotriene Hydrate and Betamethasone
Dipropionate 0.005%/0.064%) Suspension

Application Type/Number: 22-185

Applicant: LEO Pharmaceuticals Ltd.

OSE RCM #: 2007-2028

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EXECUTIVE SUMMARY

The results of the Proprietary name Risk Assessment found that the proposed name, Taclonex Scalp, does appear to be vulnerable to potential confusion with Taclonex. However, approving the name, Taclonex Scalp, for this product line extension is the least error prone option for this product. Thus, the Division of Medication Error Prevention does not object to the use of the proprietary name, Taclonex Scalp, for this product.

The results of the Label and Labeling Risk Assessment found that the presentation of information and design of the proposed container labels and carton labeling appears to be vulnerable to confusion that could lead to medication errors.

The Division of Medication Error Prevention believes the risks we have identified can be addressed and mitigated prior to drug approval, and provides recommendations in Section 6 that aim at reducing the risk of medication errors.

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1 BACKGROUND

1.1 INTRODUCTION

This review was written in response to a request from the Division of Dermatology and Dental Products (HFD-540), for assessment of the proprietary name, Taclonex Scalp, regarding potential name confusion with other proprietary or established drug names. Taclonex Scalp is an extension of the Taclonex product line.

1.2 REGULATORY HISTORY

Taclonex was approved in January 2006. Taclonex is an ointment which is also indicated for the treatment of psoriasis vulgaris and contains calcipotrient 0.005% and betamethasone 0.064%.

1.3 PRODUCT INFORMATION

Taclonex Scalp is indicated for the topical treatment of psoriasis vulgaris of the scalp in adults aged 18 years and above. The usual adult dose is one application to affected areas of the scalp once a day for up to 8 weeks, _____ Each gram of Taclonex Scalp contains 52.18 mcg of calcipotriene hydrate (equivalent to 50 mcg calcipotriene) and 0.643 mcg betamethasone dipropionate (equivalent to 0.5 mg betamethasone). The maximum weekly dosage is 100 grams. Taclonex Scalp will be available in 15 gram, 30 gram, 60 gram bottles, as well as a package of 2 x 60 gram bottles.

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2 METHODS AND MATERIALS

This section consists of two sections which describe the methods and materials used by the Division of Medication Error Prevention medication error staff conducting a proprietary name risk assessment (see 2.1 Proprietary Name Risk Assessment) and label, labeling, and/or packaging risk assessment (see 2.2 Container, Carton Label, and Insert Label Risk Assessment). The primary focus for both of the assessments is to identify and remedy potential sources of medication error prior to drug approval. The Division of Medication Error Prevention 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, Taclonex Scalp, and the proprietary and established names of drug products existing in the marketplace and those pending IND, NDA, and ANDA products currently under review by the Agency. We also considered the appropriateness of the modifier, 'Scalp'. This modifier was also assessed for resemblance to and misinterpretation as any numbers, dosing instructions, or medical abbreviations, and for the potential of omission of the modifier.

For the proprietary name, Taclonex Scalp, the medication error staff of the Division of Medication Error Prevention search a standard set of databases and information sources to identify names with orthographic and phonetic similarity (see Sections 2.1.1 for detail) and held an CDER Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name (see 2.1.1.2). The Division of Medication Error Prevention also conducts internal CDER prescription analysis studies (see 2.1.2), and, when provided, external prescription analysis studies results are considered and incorporated into the overall risk assessment (see detail 2.1.4).

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 detail 2.1.4). The overall risk assessment is based on the findings of a Failure Modes 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 look- or sound-alike similarity to the proposed name could cause confusion that subsequently leads to medication errors in the clinical setting. The Division of Medication Error Prevention uses the clinical expertise of the medication error staff to anticipate the conditions of the clinical setting that the product is likely to be used in 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. As such, the Staff considers the product characteristics associated with the proposed drug throughout the risk assessment, since 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 drug name include, but are not limited to established name of the proposed product, the proposed indication, 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, the Division of Medication Error Prevention considers the

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.

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 Medication Error Staff consider 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 letters ‘T’ and ‘S’ 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.⁴⁵

To identify drug names that may look similar to Taclonex Scalp, or Scalp, the Staff also consider the other orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name, Taclonex Scalp, (13 letters), upstrokes (four: capital letters ‘T’ and ‘S’ along with the two lower case letters ‘l’), downstrokes (one: ‘p’), cross-strokes (two: ‘t’ and ‘x’), and dotted letters (none). Additionally, several letters in Taclonex Scalp may be vulnerable to ambiguity when scripted, including the letter ‘T’, which may appear as ‘F’, ‘J’, ‘L’; lower case ‘t’ appear as a lower case ‘l’ or ‘d’; lower case ‘n’ may appear as a lower case ‘v’, ‘r’, or ‘m’ and ‘cl’ may appear as the lower case letter ‘d’. The letter ‘S’ may appear as ‘G’, ‘I’, ‘g’ or ‘j’. As such, the Staff also consider these alternate appearances when identifying drug names that may look similar to Taclonex Scalp. In this case, we also considered the name ‘Taclonex’ alone in the event that prescribers omit the modifier ‘Scalp’. Taclonex alone has 8 letters, two upstrokes (‘T’ and ‘l’), no downstrokes, and two cross-strokes (‘t’ and ‘x’). Reviewing Taclonex alone did not change the search strategy outlined above for evaluating its vulnerability for ambiguity with similarly scripted letters.

When searching to identify potential names that may sound similar to Taclonex Scalp, or Scalp, the Medication Error Staff search for names with similar number of syllables (4), stresses (tac-LO-nex scalp or TAC-lo-NEX scalp), and placement of vowel and consonant sounds. For example, the letter ‘T’ may sound like the letter ‘D’ when pronounced, and the vowels ‘a’, ‘o’ and ‘e’ may be pronounced as long vowels such as ‘ay’, ‘oh’, and ‘ee’ or as soft vowels such as ‘ah’, ‘uh’, and ‘eh’. Our primary focus in identifying phonetic vulnerabilities was primarily on the root name, ‘Taclonex’, rather than ‘Taclonex Scalp’. The Sponsor’s intended pronunciation of the proprietary name could not be expressly taken into consideration, as this was not provided with the proposed name submission.

The Staff also consider 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 Medication Error Staff were provided with the following information about the proposed product: the proposed proprietary name (Taclonex Scalp), the established name (calcipotriene hydrate and betamethasone dipropionate), proposed indication (psoriasis vulgaris of the scalp), strength (0.005%/0.064%), dose, frequency of administration (daily), route (topical) and dosage form of the product (Suspension). Appendix A provides a more detailed listing of the product characteristics the Medication Error Staff general take into consideration.

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. Artificial Intelligence in Medicine (2005)

Lastly, the Medication Error Staff also consider the potential for the proposed 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. As such, these broader safety implications of the name are considered and evaluated throughout this assessment and the Medication Error Staff provide additional comments related to the safety of the proposed name or product based on their professional experience with medication errors.

2.1.1.1 Database and information sources

The proposed proprietary name, Taclonex Scalp, was provided to the medication error staff of the Division of Medication Error Prevention 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 Taclonex Scalp using the criteria outlined in 2.1.1. A standard description of the databases used in the searches is provided in Section 7. To complement the process, the Medication Error Staff use 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 Medication Error Staff review the USAN stem list to determine if any USAN stems are present within the proprietary name. The findings of the individual Safety Evaluators were then pooled and presented to the Expert Panel.

2.1.1.2 CDER Expert Panel Discussion

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

The pooled results of the medication error 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 CDER 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 Taclonex Scalp 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 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 Taclonex Scalp 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 prescriptions are optically scanned and one prescription is delivered to a random sample of 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 the medication error staff.

Figure 1. Taclonex Scalp Study (conducted on October 10, 2007)

HANDWRITTEN PRESCRIPTION AND MEDICATION ORDER	VERBAL PRESCRIPTION
<p><u>Outpatient Prescription:</u></p> <p><i>Taclonex Scalp Gel #1 bottle</i> <i>Apply to scalp daily</i></p>	<p>Taclonex Scalp Gel #1 bottle Apply to scalp daily.</p>
<p><u>Inpatient Medication Order :</u></p> <p><i>Taclonex Scalp Gel Apply to Scalp daily</i></p>	

2.1.3 AERS Selection of Cases

The AERS database was searched for combination products using the active ingredients ‘calcipotriene’ and ‘betamethasone’ and the search criteria “medication errors” as the HLGT. An additional search was conducted using the tradename, ‘Taclonex’, and the verbatim term, ‘Tac’ with the search criteria “medication errors” (HLGT).

2.1.4 Safety Evaluator Risk Assessment of the Proposed Proprietary Name

Based on the criteria set forth in Section 2.1.1, the Safety Evaluator Risk Assessment applies their individual expertise gained from evaluating medication errors reported to FDA to conduct a Failure Modes and Effects Analysis and provide an overall risk 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, the Division of Medication Error Prevention seeks to evaluate the potential for a proposed name to be confused with another drug name as a result of the name confusion and 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 look- or sound-alike 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 Taclonex Scalp convincing similar to another drug name,

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

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 Taclonex Scalp 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 name possesses similarity that would cause confusion at any point in the medication use system and 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 ultimately not 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, such as 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.

The Division of Medication Error Prevention will object to the use of proposed proprietary name when the 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 trade name or otherwise. [21 U.S.C 321(n); see also 21 U.S.C. 352(a) & (n)].
2. The Division of Medication Error Prevention 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 stem, particularly in a manner that is contradictory to the USAN Council’s definition.
5. Medication Error Staff identify a potential source of medication error within the proposed proprietary name. 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 name and another drug product.

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

If none of these conditions are met, then will the Division of Medication Error Prevention not object to the use of the proprietary name. If any of these conditions are met, then the Division of Medication Error Prevention will object to the use of the proprietary name. The threshold set for objection to the proposed

proprietary name may seem low to the Sponsor; 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, the World Health Organization, the Joint Commission on Accreditation of Healthcare Organizations, and the Institute for Safe Medication Practices, 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, the Division of Medication Error Prevention 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 efforts and so on are low-leverage strategies that have proven to have limited effectiveness at alleviating the 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 Sponsor, and at the expense of the public welfare, not to mention the Agency's credibility as the authority responsible for the approving the error-prone proprietary name. Moreover, even after Sponsor's have changed a product's proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioner's vocabulary, and as such, the Agency has continued to receive reports of drug name confusion long after a name change in some instances. Therefore, the Division of Medication Error Prevention 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 limitations of the process).

If the Division of Medication Error Prevention 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. The Division of Medication Error Prevention is likely to recommend that the Sponsor select an alternative proprietary name and submit the alternate name to the Agency for the Division of Medication Error Prevention to review. However, in rare instances FMEA may identify plausible strategies that could reduce the risk of medication error of the currently proposed name, and so the Division of Medication Error Prevention may be able to provide the Sponsor with recommendations that reduce or eliminate the potential for error would render the proposed name acceptable.

2.2 LABEL AND LABELING RISK ASSESSMENT

The label and labeling of a drug product are the primary means by which practitioners and patients (depending on configuration) interact with the pharmaceutical product. The carton and container labels communicate critical information including proprietary and established name, strength, form, container quantity, expiration, and so on. The insert labeling is intended to communicate to practitioners all information relevant to the approved uses of the drug, including the correct dosing and administration.

Given the critical role that the label and labeling has in the safe use of drug products, it is not surprising that 33 percent of medication errors reported to the USP-ISMP Medication Error Reporting Program may be attributed to the packaging and labeling of drug products, including 30 percent of fatal errors.⁷

Because the Division of Medication Error Prevention staff analyze reported misuse of drugs, the Division of Medication Error Prevention staff are able to use this experience to identify potential errors with all medication similarly packaged, labeled or prescribed. The Division of Medication Error Prevention uses FMEA and the principles of human factors to identify potential sources of error with the proposed product

⁷ Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006. p275.

labels and insert labeling, and provided recommendations that aim at reducing the risk of medication errors.

For this product the Sponsor submitted on June 19, 2007 the following labels and insert labeling to the Division of Medication Error Prevention for review (see Appendix F, G, H and I for images):

- Sample Container Label: 15 gram
- Sample Carton Labeling: 15 gram
- Trade Container: 15 gram, 30 gram and 60 gram bottles
- Trade Carton Labeling: 15 gram, 30 gram, 60 gram, and 2 x 60 gram bottles
- Prescribing Information (no image)

In addition, we also reviewed the container labels and carton labeling of the currently marketed Taclonex, obtained from the 2007 annual report submitted in March 2008, to identify any potential for product selection confusion which may result from look-alike carton labels and container labeling, between Taclonex and Taclonex Scalp (Appendix J).

3 RESULTS

3.1 PROPRIETARY NAME RISK ASSESSMENT

3.1.1 Database and information sources

The Division of Medication Error Prevention conducted a search of the internet, several standard published databases and information sources (see Section 7 References) for existing drug names which sound-alike or look-alike to Taclonex Scalp to a degree where potential confusion between drug names could occur and result in medication errors in the usual clinical practice settings. In total, 3 names were identified as having some similarity to the name Taclonex Scalp.

Two of the three names were thought to look like Taclonex Scalp, which include, tacrolimus and baclofen, both of which are established names. The third name, Taclonex, was thought to look and sound similar to Taclonex Scalp.

Additionally, the Division of Medication Error Prevention did not identify any United States Adopted Name (USAN) stems in the name Taclonex Scalp as of April 3, 2008.

3.1.2 CDER Expert Panel Discussion

The Expert Panel reviewed the pool of names identified by the Division of Medication Error Prevention staff (see section 3.1.1. above), and noted one additional name, Lactinex, which was thought to have orthographic and phonetic similarity to Taclonex Scalp and have the potential for confusion. The Expert Panel also noted that despite orthographic similarity of the letter 'T' with the letters 'F', 'J', 'L', and 'S' in some handwriting samples, no other names beginning with those letters were included in the pool. The Expert Panel recommended that independent searches consider the potential for confusion with drug names beginning with these letters.

DDMAC had no concerns regarding the proposed name from a promotional perspective, however, because they reviewed the proposed name as 'Taclonex Scalp Gel', they made the following comment: "There was concern that the name could read 'Taclonex Scalp Gel gel' since the dosage form should be included with the trade name".

3.1.3 CDER Prescription analysis studies

'Taclonex Scalp Gel' was inadvertently used in the CDER Rx Studies. However, this does not appear to have many any significant impact in the Rx Study results. A total of 34 practitioners responded, but none of the responses overlapped with any existing or proposed drug names. About half of the participants (n=14) interpreted the name correctly as "Taclonex Scalp Gel", with correct interpretation occurring more frequently in the written studies. The remainder of the responses misinterpreted the drug name. The majority of misinterpretations occurred in the phonetic prescription study, with the vowel 'o' in Taclonex Scalp reported as the letter 'i' in all seven of the responses. In the written prescription studies, the letter 'T' was misinterpreted as the letter 'J' by three respondents, and as the letter 'L' by another respondent. Also, three respondents interpreted the letter 'x' as the letter 'k', and one respondent interpreted the letters '-cl' as the letter 'd'. Five respondents omitted the modifiers 'Scalp Gel' and responded with the root name or variations of the root name, 'Taclonex'. See Appendix B for the complete listing of interpretations from the verbal and written prescription studies.

3.1.4 AERS Selection of Cases

Our search of the AERS database identified one case of overdose involving the use of Taclonex ointment (see Appendix K).

3.1.5 Safety evaluator risk assessment

Independent searches by the primary Safety Evaluator identified no additional names thought to look similar to the established name of Taclonex Scalp, and represent a potential source of drug name confusion. Careful evaluation was afforded to drug names beginning with the letters 'F', 'J', 'L', and 'S' in accordance with the Expert Panel's recommendations, but no drug names beginning with these letters were thought to have the potential for confusion with Taclonex Scalp. As such, a total of four names, Lactinex, tacrolimus, baclofen, and Taclonex were analyzed to determine if the drug names could be confused with Taclonex Scalp. Of the four names identified, two names, Lactinex and Taclonex are tradenames, whereas baclofen and tacrolimus are established names.

All of the four identified names were determined to have some orthographic and/or phonetic similarity to Taclonex Scalp, and thus determined to present some risk for confusion. Failure modes and effects analysis determined that it is unlikely for the proposed proprietary name, Taclonex Scalp, to be confused with three of the identified names and lead to medication errors as described below.

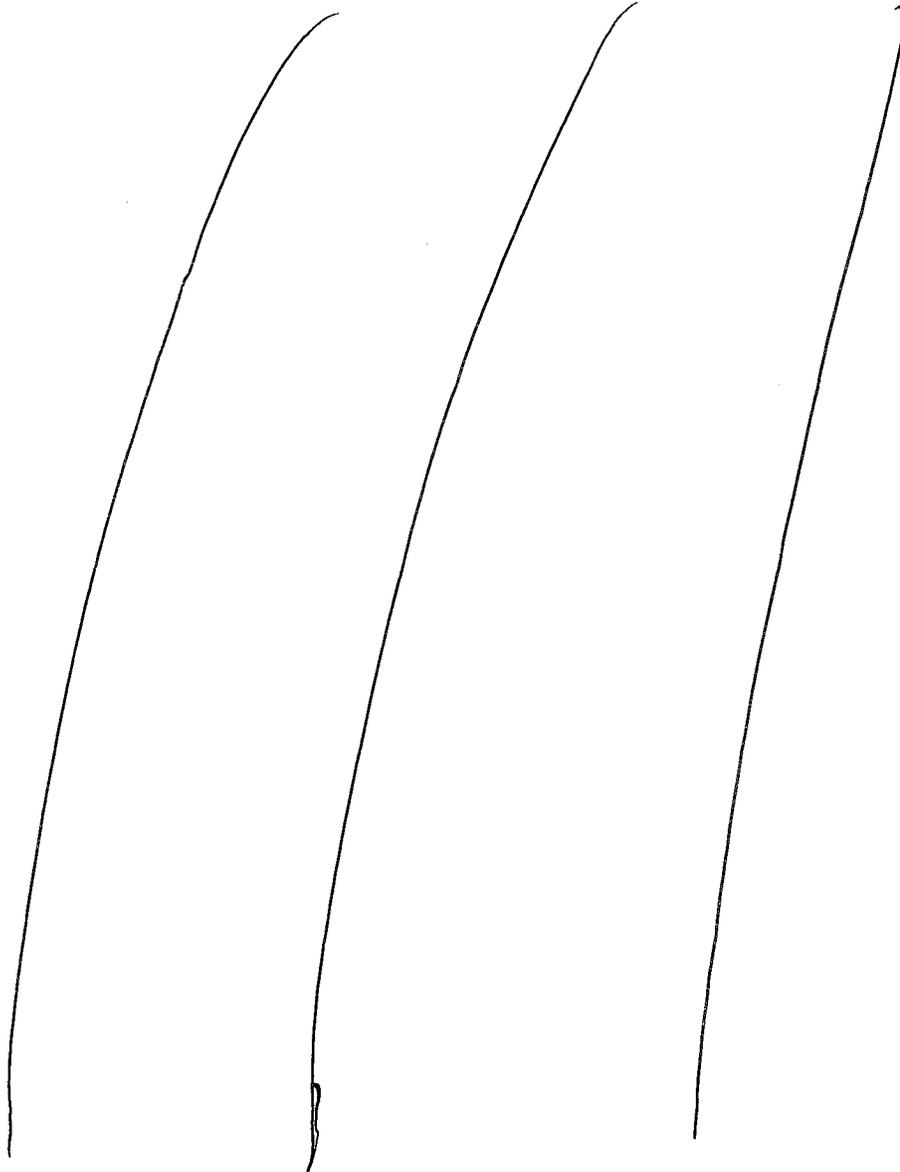
The analysis determined that the established names, tacrolimus (Prograf and Protopic) and baclofen (Lioresal and Kemstro) are unlikely to result in errors despite sharing similar numerals in their strength and having overlapping routes of administration (see Appendix C).

Lactinex has a different dosage form and is also a non-prescription product compared to Taclonex Scalp, and therefore it is unlikely confusion will occur between these names that would result in medication errors (Appendix D).

FMEA determined the remaining name Taclonex was vulnerable to confusion and medication errors due to orthographic and/or phonetic similarities in addition to overlapping product characteristics (see section 4 for full discussion).

3.2 LABEL AND LABELING RISK ASSESSMENT





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4 DISCUSSION

4.1 PROPRIETARY NAME RISK ASSESSMENT

The results of the Proprietary Name Risk Assessment found that the proposed name, Taclonex Scalp, is vulnerable to name confusion with the currently marketed product Taclonex and this vulnerability could lead to medication errors.

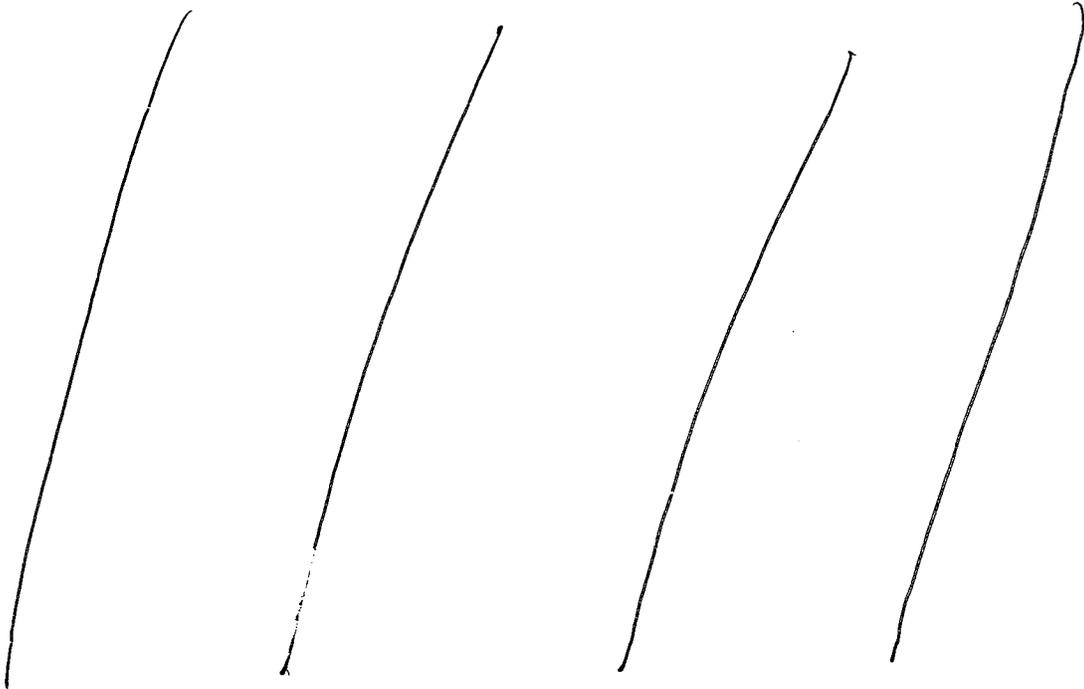
Introduction of a new product into an established product line is often a source of confusion. Errors introduced by product line extensions are multi-factorial in nature, and can stem from the timing of the product launch because of the similarity of product names, and overlapping product characteristics

coupled with the low level of awareness or knowledge of the product profile by healthcare professionals and patients. In this case, Taclonex Scalp Suspension and Taclonex Ointment have identical product characteristics except for dosage form (suspension vs. ointment) and location of administration (head vs. body). See Appendix E.

Post marketing evidence has shown that modifiers, such as Scalp, are often omitted by prescribers, leading to confusion. In this case if prescribers omits the modifier, 'Scalp' on orders for Taclonex Scalp, it is likely that Taclonex ointment will be dispensed especially if the dosage form 'suspension' is not included. However, since these products have the same active ingredients the adverse event profile will be similar minimizing the safety concerns if the wrong product is dispensed. Additionally, we also considered the possibility of the proposed product coming in with an entirely different proprietary name to in order to minimize name confusion. However, the FMEA determined that having a different name may cause concomitant administration of the proposed product resulting in possible overdose. Therefore, we have determined that it would be less error prone to use the name, Taclonex Scalp for the proposed product. Despite the minimal risk from medication errors between Taclonex Scalp Suspension and Taclonex Ointment, an educational campaign on the new dosage form may further mitigate the potential name confusion.

4.2 LABEL AND LABELING RISK ASSESSMENT

The results of the Label and Labeling Risk Assessment found that the presentation of information and design of the proposed carton and container labels appears to be vulnerable to confusion that could lead to medication errors.



The Division of Medication Error Prevention believes the risks we have identified can be addressed and mitigated prior to drug approval, and provides recommendations in Section 5 that aim at reducing the risk of medication errors.

Overall, our Risk Assessment is limited by our current understanding of medication errors and causality. The successful application of Failure Modes and Effect Analysis depends upon the learning gained from a spontaneous reporting program. It is quite possible that our understanding of medication error causality would benefit from unreported medication errors; and, that this understanding could have enabled the Staff to identify vulnerability in the proposed name, packaging, and labeling that was not identified in this assessment. To help minimize this limitation in future assessments, we encourage the Sponsor to provide the Agency with medication error reports involving their marketed drug products regardless of adverse event severity.

5 CONCLUSIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Taclonex Scalp, does appear to be vulnerable to potential confusion with Taclonex. However, since these products have similar adverse event profiles our safety concerns are minimized. Therefore, the Division of Medication Error Prevention does not object to the proposed proprietary name, Taclonex Scalp.

The Label and Labeling Risk Assessment findings indicate that the presentation of information and design of the proposed carton labels and container labeling introduces vulnerability to confusion that could lead to medication errors.

6 RECOMMENDATIONS

The Division of Medication Error Prevention believes the risks we have identified can be addressed and mitigated prior to drug approval, and provides recommendations in Section 6.2 that aim at reducing the risk of medication errors.

We would appreciate feedback of the final outcome of this review. We would be willing to meet with the Division for further discussion, if needed. Please copy the Division of Medication Error Prevention on any communication to the Applicant with regard to this review. If you have any questions or need clarification, contact Janet Anderson, Project Manager, at 301-796-0675.

6.1 COMMENTS TO THE DIVISION

1. The Division of Medication Error Prevention has no objections to the use of the proprietary name, Taclonex Scalp, for this product.
2. If any of the proposed product characteristics as stated in this review are altered prior to approval of the product, we rescind the Risk Assessment finding, and recommend that the name be resubmitted for review.
3. If the product approval is delayed beyond 90 days from the date of this review, the proposed name must be resubmitted for evaluation.

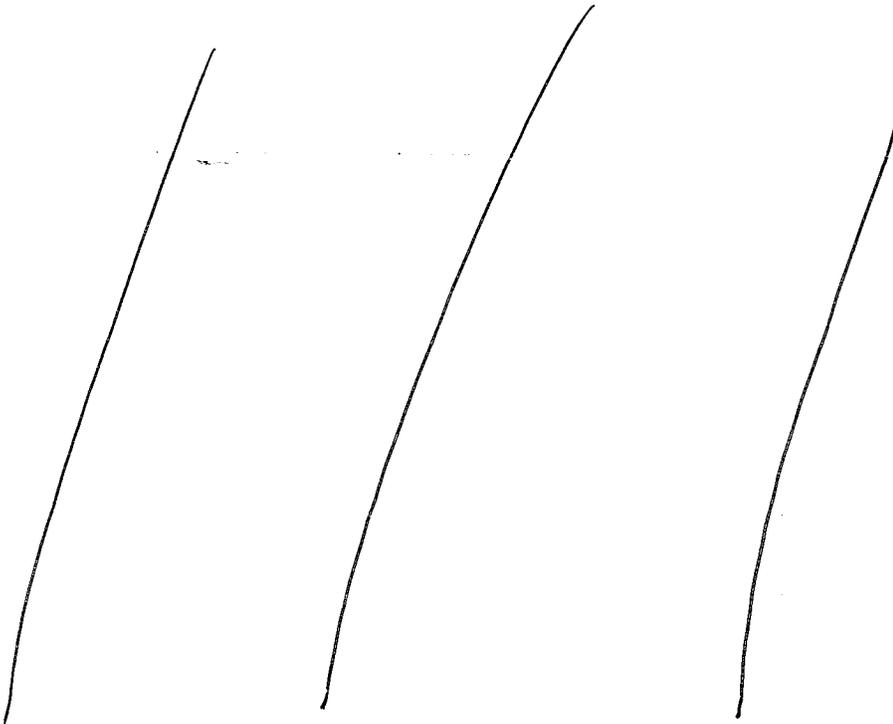
6.2 COMMENTS TO THE APPLICANT

6.2.1 *Proprietary Name*

1. The Division of Medication Error Prevention has no objection to the use of the proprietary name, Taclonex Scalp, for this product.
2. If **any** of the proposed product characteristics as stated in this review are altered prior to approval of the product, we rescind this Risk Assessment finding, and recommend that the name be resubmitted for review.

6.2.2 *Labels and Labeling*

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7 REFERENCES

1. *Adverse Events Reporting System (AERS)*

AERS is a database application in CDER FDA that contains adverse event reports for approved drugs and therapeutic biologics. These reports are submitted to the FDA mostly from the manufactures that have approved products in the U.S. The main utility of a spontaneous reporting system that captures reports from health care professionals and consumers, such as AERS, is to identify potential postmarketing safety issues. There are inherent limitations to the voluntary or spontaneous reporting system, such as underreporting and duplicate reporting; for any given report, there is no certainty that the reported suspect product(s) caused the reported adverse event(s); and raw counts from AERS cannot be used to calculate incidence rates or estimates of drug risk for a particular product or used for comparing risk between products.

2. *Micromedex Integrated Index (<http://weblern/>)*

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

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

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. This is a database which was created for The Division of Medication Error Prevention, FDA.

4. *Drug Facts and Comparisons, online version, St. Louis, MO (<http://weblern/>)*

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

5. *AMF Decision Support System [DSS]*

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

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

This is a list of proposed and pending names that is generated by The Division of Medication Error Prevention 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 and generic drugs and therapeutic biological products; prescription and over-the-counter human drugs and therapeutic biologics, discontinued drugs and “Chemical Type 6” approvals.

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

Provides a compilation of approved drug products with therapeutic equivalence evaluations.

9. **WWW location** <http://www.uspto.gov>.

Provides information regarding patent and trademarks.

10. **Clinical Pharmacology Online** (<http://weblern/>)

Contains full monographs for the most common drugs in clinical use, plus mini monographs covering investigational, less common, combination, nutraceutical and nutritional products. Provides a keyword search engine.

11. **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.

12. **Natural Medicines Comprehensive Databases** (<http://weblern/>)

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

13. **Stat!Ref** (<http://weblern/>)

Contains full-text information from approximately 30 texts. 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.

14. **USAN Stems** (<http://www.ama-assn.org/ama/pub/category/4782.html>)

List contains all the recognized USAN stems.

15. **Red Book Pharmacy's Fundamental Reference**

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

16. **Lexi-Comp** (www.pharmacist.com)

A web-based searchable version of the Drug Information Handbook.

17. **Medical Abbreviations Book**

Contains commonly used medical abbreviations and their definitions.

APPENDICES

Appendix A:

The Division of Medication Prevention Error Staff consider the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. We also compare the spelling of the proposed proprietary name with the proprietary and established name 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 Medication Error Prevention Staff also examine 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* dissimilarly spelled drug name pairs to appear very similar to one another and the similar appearance of drug names when scripted has led to medication errors. The Medication Error Staff apply their expertise gained from root-cause analysis of such medication errors to identify sources of ambiguity within the name that could be introduced when scripting (i.e. “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 detail in Table 1 below). Additionally, since verbal communication of medication names is common in clinical settings, the Medication Error Staff compare the pronunciation of the proposed proprietary name with the pronunciation of other drug names. If provided, the Division of Medication Error Prevention will consider the Sponsor’s intended pronunciation of the proprietary name. However, because the Sponsor has little control over how the name will be spoken in practice, the Division of Medication Error Prevention also considers a variety of pronunciations that could occur in the English language.

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	<ul style="list-style-type: none"> 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	<ul style="list-style-type: none"> Names may look similar when scripted, and lead to drug name confusion in written communication

		<p>Cross-strokes</p> <p>Dotted letters</p> <p>Ambiguity introduced by scripting letters</p> <p>Overlapping product characteristics</p>	
Sound-alike	Phonetic similarity	<p>Identical prefix</p> <p>Identical infix</p> <p>Identical suffix</p> <p>Number of syllables</p> <p>Stresses</p> <p>Placement of vowel sounds</p> <p>Placement of consonant sounds</p> <p>Overlapping product characteristics</p>	<ul style="list-style-type: none"> Names may sound similar when pronounced and lead to drug name confusion in verbal communication

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Appendix B:

CDER Prescription Study Responses

Outpatient Prescription	Voice Prescription	Inpatient Medication Order
Jaclonek Scalp Gel	Taclonex Scalp Gel	Taclonex
Taclonex Scalp Gel	Taclonex Scalp Gel	Taclonex Scalp Gel
Jacklonek Scalp Gel	Taclonex Scalp Gel	Taclonex Scalp Gel
Jacklonek Scalp Gel	Taclonex	Taclonex Scalp Gel
Taclonex Scalp Gel	Taclonex Scalp Gel	Taclonex Scalp Gel
Taclonex	Taclonex Scalp Gel	Taclonex Scalp Gel
Ladonex Scalp Gel	Taclonex	Taclonex Scalp Gel
Taclonek Scalp Gel		Taclovex Scalp Gel
		Taclonex Scalp Gel
		Taclonex Scalp Gel
		Taclonex Scalp Gel
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		Taclonex Scalp Gel

Appendix C: Names with numerical overlap in strength and/or route of administration

Taclonex Scalp® (calcipotriene hydrate and betamethasone)	0.005%/0.064%	Usual dose: Apply to affected areas daily
Failure Mode: Name confusion	Causes (could be multiple)	Effects
<p>tacrolimus (Prograf – trade name)</p>	<p>Orthographic similarities, numerical overlap in strengths</p> <p>(0.005% vs 0.5 mg and 5 mg tacrolimus capsules)</p> <p>(0.005%/0.064% vs 5 mg/ml injectable solution)</p> <p>Both names have similar letters at the beginning of the names, ‘tac’ vs ‘trac’, both names have the letters ‘l’ and ‘o’.</p>	<p>Wrong Drug</p> <p><i>Rationale:</i></p> <p>Orthographic differences include the upstroke letter ‘L’ in different positions, and tacrolimus appearing longer in length when scripted. Although they share similarity, in numbers, ‘5’, the placement of the five in the strength is different with different units of measure. It is unlikely prescribers will order Taclonex Scalp using only one of the required strengths. Additionally, Taclonex Scalp is a combination product and including the strength is not required to dispense the product, thus practitioners may write Taclonex Scalp prescriptions without the strength.</p>
<p>tacrolimus (Protopic – tradename)</p>	<p>0.03% and 0.1% tacrolimus ointment</p>	<p>Wrong Drug</p> <p><i>Rationale:</i></p> <p>Orthographic differences include the letter ‘L’ in different positions, tacrolimus appearing longer when scripted, and different appearance in the ending letters ‘mus’ vs ‘nex’. Also, these products have no overlapping strength and have different frequency of administration (twice a day vs once a day). Taclonex Scalp is a combination product and it is unlikely prescribers will indicate a strength on orders for Taclonex Scalp.</p>
<p>baclofen (Trade names: Lioresal and Kemstro)</p>	<p>Name confusion and overlapping numbers in the product strengths:</p> <p>(0.005%/0.064% vs 0.05 mg/mL)</p> <p>10 mg and 20 mg tablets</p> <p>10 mg and 20 mg orally disintegrating tablets</p> <p>0.05 mg/mL,</p> <p>10 mg/20 mL, and 10mg/5 mL</p>	<p>Wrong Drug</p> <p><i>Rationale:</i></p> <p>Orthographic differences between the names such as the three upstroke letters ‘b’, ‘l’, and ‘f’ in baclofen vs two upstroke letters ‘t’, ‘l’, in Taclonex Scalp, will help minimize orthographic confusion. Additionally, depending on how the letter ‘f’ is scripted, baclofen may have a downstroke in the middle of the name, whereas the downstroke letter ‘p’ is at the end of Taclonex Scalp. The similarity due to the numerical overlap in strength is minimized by the fact that Taclonex Scalp is a combination product and it is unlikely prescribers will only indicate the strength for only one ingredient on orders for Taclonex Scalp.</p>

Appendix D: Names with no overlapping strength or dosage form

Proprietary Name (Established name)	Strength	Dosage Form	Prescription Status
Taclonex Scalp® (calcipotriene hydrate and betamethasone)	0.005%/0.064%	Gel	Rx only
Lactinex	1,000,000 CFU/tablet	Tablet	OTC (over-the-counter)

Appendix E: Taclonex and Taclonex Scalp Comparison of Product Characteristics

Proprietary Name	Taclonex	Taclonex Scalp
Active Ingredient	calcipotriene hydrate and betamethasone	calcipotriene hydrate and betamethasone
Strength	0.005%/0.064%	0.005%/0.064%
Dosage Form	Ointment	Suspension
Indication of Use	Treatment of psoriasis vulgaris in adults 18 years of age and above for up to 4 weeks. Maximum weekly dose should not exceed 100 g. Treatment of more than 30% of body surface area is not recommended	Treatment of psoriasis vulgaris in adults 18 years of age and above for up to 8 weeks. Maximum weekly dose should not exceed 100 g.
Frequency	Once Daily	Once Daily
Route of Administration	Topical	Topical
Application Site	External (Doesn't specify)	Scalp

(Differences highlighted in yellow)

5 Page(s) Withheld

 Trade Secret / Confidential (b4)

 ✓ Draft Labeling (b4)

 Draft Labeling (b5)

 Deliberative Process (b5)

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Also signing for Walter Fava.

Denise Toyer
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