

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

022205Orig1s000

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**

Proprietary Name Review--Final

Date: January 26, 2012

Reviewer(s): Anne Crandall Tobenkin, PharmD
Division of Medication Error Prevention and Analysis

Team Leader Lubna Merchant, PharmD, M.S.
Division of Medication Error Prevention and Analysis

Division Director Carol Holquist, RPh
Division of Medication Error Prevention and Analysis

Drug Name(s) and Strength(s): Giazio (Balsalazide Disodium) Tablets, 1.1 g

Application Type/Number: NDA 22205

Applicant/sponsor: Salix

OSE RCM #: 2012-189

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

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1 INTRODUCTION

This re-assessment of the proposed proprietary name, Giazio, is written in response to the anticipated approval of this NDA within 90 days from the date of this review. DMEPA found the proposed name, Giazio, acceptable in OSE Review # 2010-79 dated April 1, 2010.

2 METHODS AND DISCUSSION

For re-assessments of proposed proprietary names, DMEPA searches a standard set of databases and information sources (see section 4) to identify names with orthographic and phonetic similarity to the proposed name that have been approved since the previous OSE proprietary name review. For this review we used the same search criteria described in OSE Review #2010-79. Since none of the proposed product characteristics were altered we did not re-evaluate previous names of concern. The searches of the databases yielded six new names (b)(4) Ziana, Cimzia, (b)(4) (b)(4), thought to look or sound similar to Giazio and represent a potential source of drug name confusion. Failure mode and effects analysis was applied to determine if the proposed proprietary name could potentially be confused with Giazio and lead to medication errors. This analysis determined that the name similarity between Giazio and the identified names was unlikely to result in medication error for the reasons presented in Appendices A and B.

Additionally, DMEPA searched the USAN stem list to determine if the name contains any USAN stems as of the last USAN updates. The Safety Evaluator did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, as of January 20, 2012. The Office of Prescription Drug Promotion OPDP re-reviewed the proposed name on January 26, 2012 and had no concerns regarding the proposed name from a promotional perspective.

3 CONCLUSIONS

The re-evaluation of the proposed proprietary name, Giazio, did not identify any vulnerabilities that would result in medication errors with any additional names noted in this review. Thus, DMEPA has no objection to the proprietary name, Giazio, for this product at this time.

DMEPA considers this a final review; however, if approval of the NDA is delayed beyond 90 days from the date of this review, the Division of Gastroenterology and Inborn Errors should notify DMEPA because the proprietary name must be re-reviewed prior to the new approval date.

If you have further questions or need clarifications, please contact Nitin Patel, OSE Project Manager, at 301-796-5412.

4 REFERENCES

1. *OSE Review # 2007-1800, Giazio Proprietary Name Review. Smith, Diane.*
2. *OSE Review # 2008-1483, Giazio Proprietary Name Review. Smith, Diane and Governale, Laura.*
3. *OSE Review # 2010-79, Giazio Proprietary Name Review. Chan, Irene. April 1, 2010.*

4. *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.

5. *USAN Stems (<http://www.ama-assn.org/ama/pub/physician-resources/medical-science/united-states-adopted-names-council/naming-guidelines/approved-stems.page?>)*

USAN Stems List contains all the recognized USAN stems.

6. *Division of Medication Error Prevention and Analysis Proprietary Name Consultation Request*

Compiled list of proposed proprietary names submitted to the Division of Medication Error Prevention and Analysis for review. The list is generated on a weekly basis from the Access database/tracking system.

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

Proprietary Name	Active Ingredient	Similarity to Giazio	Failure Preventions
(b) (4)			

Appendix B: FMEA Table

Proposed name: Giazio (Balsalazide Disodium) Strengths and Dosage form: 1.1 g oral tablet Usual Dose: 3 tablets by mouth twice daily	Cause of Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	Prevention of Failure Mode: Orthographic/Phonetic/Product Characteristic Differences
Ziana (Clindamycin and Tretinoin) - 1.2%/0.025% topical gel - Apply a pea-sized amount to face at bedtime	Orthographic similarities - Letters strings, ‘iazo’ and ‘iana’ appear similar when scripted - Both names are similar in length Overlapping product characteristics - Single strength	Differing product characteristics - Dose (3 tablets or 3.3 grams vs. pea-sized amount) - Frequency of administration (twice daily vs. once daily)
Cimzia (Certolizumab pegol) - 200 mg for injection - 400 mg (two injections) subcutaneously once followed by 200 mg at weeks two and four and then 400 mg every 4 weeks	Orthographic similarities - ‘G’ and ‘C’ appear similar when scripted - Both names have a ‘z’ in the middle of the name Overlapping product characteristics - none	Orthographic differences - Giazio has 5 letters and appears shorter when scripted vs. Cimzia which has six letters Differing product characteristics - Frequency of administration (twice daily vs. every other week) - Dose (3 tablets or 3.3 g vs. 200 mg or 400 mg)

**Proposed name: Giazio
(Balsalazide Disodium)**

**Strengths and Dosage
form: 1.1 g oral tablet**

**Usual Dose: 3 tablets by
mouth twice daily**

**Cause of Failure Mode:
Incorrect Product
Ordered/
Selected/Dispensed or
Administered because of
Name confusion**

**Prevention of Failure Mode:
Orthographic/Phonetic/Product
Characteristic Differences**

(b) (4)

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/s/

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01/26/2012

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01/26/2012

CAROL A HOLQUIST
01/26/2012



**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 1, 2010

To: Donna Griebel, MD, Director
Division of Gastroenterology Products

Through: Melina Griffis, RPh, Team Leader
Denise P. Toyer, PharmD, Deputy Director
Division of Medication Error Prevention and Analysis (DMEPA)

From: Irene Z. Chan, Pharm.D., BCPS, Safety Evaluator
Division of Medication Error Prevention and Analysis (DMEPA)

Subject: Proprietary Name Review

Drug Name(s): Giazio (Balsalazide Disodium) Tablets 1.1 gram

Application Type/Number: NDA 022205

Applicant: Salix Pharmaceuticals, Inc.

OSE RCM #: 2010-79

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

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1 INTRODUCTION

This re-assessment of the proprietary name is written in response to a notification that NDA 022205 may be approved within 90 days. The Division of Medication Error Prevention and Analysis (DMEPA) found the proposed proprietary name, Giazo, acceptable in OSE Review #2008-1483, dated April 8, 2009.

The Division of Gastroenterology Products did not have any concerns with the proposed name, Giazo, and the Division of Drug Marketing, Advertising and Communications (DDMAC) found the name acceptable from a promotional perspective as noted in OSE Review #2007-1800.

2 METHODS AND RESULTS

For the proposed proprietary name, DMEPA staff searched a standard set of databases and information sources (see section 4) to identify names with orthographic and phonetic similarity to the proposed name that have been approved since the previous OSE proprietary name review. We used the same search criteria that were used in OSE Review #2007-1800 for the proposed proprietary name, Giazo. Since our last review, the indication was changed to treatment in males only; therefore, we re-evaluated previous names of concern since any changes in the product characteristics of the proposed drug can affect our assessment. Additionally, DMEPA searched the USAN stem list to determine if the name contains any USAN stems as of the last USAN updates. DMEPA bases the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proposed proprietary name, and focuses on the avoidance of medication errors.

The searches of the databases yielded no new names thought to look similar to Giazo and represent a potential source of drug name confusion. Additionally, the change in indication did not affect the results of our analysis of previous names of concern. DMEPA staff also did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name Giazo, as of March 29, 2010.

3 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Giazo, is not vulnerable to name confusion that can lead to medication errors nor is the name considered promotional. Thus, the Division of Medication Error Prevention and Analysis (DMEPA) has no objection to the proprietary name, Giazo, for this product at this time.

DMEPA considers this a final review; however, if approval of the NDA is delayed beyond 90 days from the date of this review, the Division of Gastroenterology Products should notify DMEPA because the proprietary name must be re-reviewed prior to the new approval date.

4 REFERENCES

1. OSE review #2007-1800 Proprietary Name Review of Giazio; Smith, Diane C.
2. OSE review #2008-1483 Proprietary Name Review of Giazio; Smith, Diane C. and Governale, Laura
3. *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.
4. *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.
5. *Division of Medication Error Prevention and Analysis proprietary name 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.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22205	ORIG-1	SALIX PHARMACEUTICA LS INC	BALSALAZIDE DISODIUM TABLETS

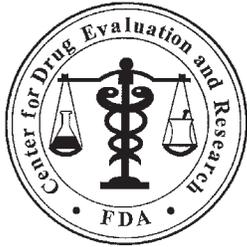
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/s/

IRENE Z CHAN
04/01/2010

MELINA N GRIFFIS
04/01/2010

DENISE P TOYER
04/01/2010



**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 8, 2009

To: Donna Griebel, M.D.
Director, Division of Gastroenterology Products

Through: Todd Bridges, RPh, Team Leader
Denise Toyer, PharmD, Deputy Director
Carol Holquist, RPh, Director
Division of Medication Error Prevention and Analysis

From: Diane C. Smith, PharmD, Safety Evaluator
Division of Medication Error Prevention and Analysis

Laura Governale, Pharm.D., MBA
Drug Use Analysis Team Leader
Division of Epidemiology

Subject: Proprietary Name Reconsideration

Drug Name: Giazio (Balsalazide Disodium) Tablets 1.1 Gram

Application Type/Number: NDA #22-205

Applicant: Salix Pharmaceuticals, Inc.

OSE RCM #: 2008-1483

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EXECUTIVE SUMMARY

The Division of Medication Error Prevention and Analysis (DMEPA) previously evaluated the name Giazio, in OSE Review 2007-1800, and did not recommend the use of the dual trade name, Giazio, because the product could be concomitantly administered with the currently marketed product Colazal. Subsequently, the Applicant submitted a Failure Mode and Effects Analysis (FMEA) conducted by (b) (4) a subsidiary of the (b) (4) (b) (4). Their FMEA indicated the primary prescribers for Colazal and Giazio will be gastroenterologists, which reduces the risk for concomitant therapy. After reviewing their FMEA and obtaining drug utilization data on March 25, 2009, DMEPA concurs with the (b) (4) conclusion regarding the prescribing population.

Upon evaluation of the aforementioned information, we reverse our initial decision, and find the proprietary name, Giazio, acceptable.

1 BACKGROUND

This review was written in response to a request from the Division of Gastroenterology Products (DGP) to review the Failure Mode and Effects Analysis (FMEA) of the proposed name, Giazio, submitted by the Applicant on September 8, 2008.

2 REGULATORY HISTORY

The Division of Medication Errors and Analysis (DMEPA) objected to the proposed proprietary name, Giazio, in OSE Review 2007-1800, dated May 20, 2008. After discussing the potential for concomitant administration with the Division of Gastroenterology (DGP), rather than use a dual proprietary name, DMEPA and DGP recommended the use of a single proprietary name, Colazal, for all balsalazide disodium products marketed by the Applicant because it would lessen the potential for concomitant therapy.

Subsequently, the Applicant was issued a discipline review letter on May 22, 2008; in which the Agency recommend the use of a single proprietary name, Colazal, for all balsalazide disodium products marketed by Salix. On June 9, 2008, the Applicant met with DGP and DMEPA, and DMEPA recommended the Applicant conduct a FMEA to support the use of a dual proprietary name for the tablet formulation of balsalazide disodium.

On September 8, 2008, the Applicant submitted a Failure Mode and Effects Analysis (FMEA) that evaluates the use of the proprietary name, Colazal, versus the dual proprietary name, Giazio, for the proposed formulation of balsalazide disodium.

3 MATERIALS REVIEWED

We reviewed the Applicant's rebuttal letter, their independent FMEA from (b) (4) (see their conclusion in Appendix A) and OSE review 2007-1800, which contains our FMEA. The conclusions of the two analyses were compared. Since the applicant's FMEA noted the primary prescribers for Giazio and Colazal would be gastroenterologists, DMEPA obtained drug utilization data.

4 DRUG UTILIZATION DATA BY PRESCRIBING SPECIALTY***

Dispensed prescriptions for Colazal by prescribing specialty were obtained from the SDI, Vector One®: ***National (VONA) database (See Appendix B for database description) for year 2008 (Table 1)***. SDI's VONA*** measures retail dispensing of prescriptions or the frequency with which drugs move out of retail pharmacies into the hands of consumers via formal prescriptions. The Vector One®*** database integrates prescription activity from a variety of sources including national retail chains, mass merchandisers, mail order pharmacies, pharmacy benefits managers and their data systems, and provider groups. Prescriptions are captured from a sample of approximately (b)(4) pharmacies throughout the US. The pharmacies in the database account for nearly all retail pharmacies and represent nearly half of retail prescriptions dispensed nationwide.

During year 2008, nearly (b)(4) of dispensed prescriptions for Colazal were prescribed by Gastroenterologists (Table 1). (b)(4)

Table 1. Total number of dispensed prescriptions for Colazal from U.S. outpatient retail pharmacies by prescribing specialty, Year 2008.

	2008	
	TRxs N	Share % (b)(4)
[Redacted Data]		

Source: SDI Vector One®: National. Year 2008. Extracted 3/09.
File: VONA 2008-1483 Colazal MD 3-25-09.xls

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5 DISCUSSION

The Applicant submitted an external analysis conducted by (b)(4) performed an FMEA that compared the risk of marketing balsalazide disodium under two different proprietary names (Colazal and Giazol) vs. marketing the product under a single proprietary name (Colazal). (b)(4) concluded it would be safer to market the product under two different names. (b)(4) rationale is based upon three main points: 1) The primary prescribers for these products will be gastroenterologists, therefore it is unlikely patients would receive concomitant therapy; 2) The higher risk of patients receiving the wrong strength because of the new 1.1 g strength; and 3) There is an additional risk to pediatric patients with the use of one trade name. Our assessment of the data is discussed below.

5.1 PRESCRIBER POPULATION

(b)(4) concluded that gastroenterologists are primarily the prescribers for these products; therefore, it is unlikely that a patient would receive Colazal from one physician and Giazol from another. Our analysis of drug use data examining dispensed prescriptions by prescribing specialty confirmed that gastroenterologists were the primary prescribers of Colazal in year 2008, accounting for approximately (b)(4) of dispensed prescriptions. Although this does not account for all prescriptions, consultation with the clinical team confirmed that general practitioners would not likely prescribe this product.

What is also unique about this product is that Colazal and Giazol are used for the same indication, whereas other products with dual trade names by the same manufacture have different indications of use. Having a limited prescribing population and the same indication of use reduces the risk of concomitant administration from different healthcare practitioners.

5.2 INTRODUCTION OF A NEW COLAZAL STRENGTH INTO THE MARKETPLACE

The (b)(4) FMEA noted there is an increased risk of confusion associated with the use of the name Colazal for the tablet formulation of balsalazide disodium when the product is first introduced into the marketplace. Their FMEA maintains that because Colazal has existed since 2000, as a single-strength product, healthcare practitioners did not have to indicate the strength when prescribing. They maintain that with introduction of a new dosage form and strength, healthcare practitioners are likely to confuse the 750 mg capsule dosage form with the proposed 1.1 g tablet. DMEPA concurs that there is a risk for confusion when a product line is expanded to include a new strength or dosage form. However, similar confusion may occur when any new product is marketed, as may be the case when Giazol is first marketed especially if the products are prescribed using their established name. Thus, the strength is not considered a reason to allow the use of two names.

5.3 PEDIATRIC POPULATION

The FMEA submitted by the Applicant states there is an additional risk, in pediatric patients with the use of one name, Colazal, for both formulations because the currently marketed 750 mg capsule has a pediatric indication whereas the proposed 1.1 gram tablet will not. Thus, they contend that a prescriber that is unfamiliar with the difference in the indicated patient populations between the two products may prescribe Colazal 1.1 gram tablet for a pediatric patient. They conclude that this error would result in an overdose or the patient may not receive therapy if they are unable to swallow the tablet.

However, as noted in Section 5.1, the utilization data indicates that gastroenterologists, write the majority of prescriptions for balsalazide disodium. These prescribers are more likely to be familiar with the differences in the dosing for the patient populations for Colazal and Giazio respectively.

6 CONCLUSIONS AND RECOMMENDATIONS

We reverse our initial decision and find the proprietary name, Giazio, acceptable based on the specialty prescribing and same indication of use, which will minimize the risk of concomitant administration.

We would be willing to meet with the Division for further discussion, if needed. Please copy DMEPA on any communication to the Applicant with regard to this review. If you have further questions or need clarifications, please contact Nina Ton, OSE Project Manager, at 301-796-1648.

7 COMMENTS TO THE APPLICANT

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

The proprietary name, Giazio, will be re-reviewed 90 days prior to the approval of the NDA. If we find the name unacceptable following the re-review, we will notify you.

If any of the proposed product characteristics are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review.

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/s/

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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 20, 2008

To: Donna Griebel, MD, Director
Division of Gastroenterology Products

Thru: Todd Bridges, RPh., Team Leader
Denise Toyer, PharmD, Deputy Director
Carol Holquist, RPh., Director
Division of Medication Error Prevention

From: Diane C. Smith, PharmD, Safety Evaluator
Division of Medication Error Prevention

Subject: Proprietary Name, Label, and Labeling Review for Giazio

Drug Name(s): Giazio (Balsalazide disodium) Tablets 1.1 gram

Application Type/Number: NDA 22-205

Applicant: Salix Pharmaceuticals, Inc.

OSE RCM #: 2007-1800

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EXECUTIVE SUMMARY

The Division of Medication Error Prevention does not recommend the use of the tradename, Giazo, as a dual trade name for this product. We believe that marketing this product with two different strengths with differing frequencies and total daily dose can be safely managed under one proprietary name. We recommend the use of the single tradename, Colazal, that is used for the currently marketed Balsalazide Disodium product marketed by this Applicant.

1 BACKGROUND

1.1 INTRODUCTION

This review was written in response to a request from the Division of Gastroenterology Products to review the proposed proprietary name, Giazo, to determine if the name could be potentially confused with other proprietary or established drug names. The applicant states the rationale for the new name is because this product differs in dosing regimens, product strength and total daily dose (see Appendix D). The labels and labeling were reviewed for their potential to contribute to medication errors.

1.2 PRODUCT INFORMATION

Giazo is an aminosalicylate indicated for the treatment of mildly to moderately active ulcerative colitis in patients 18 years of age and older. The usual starting dose of Giazo is three 1.1 gram tablets twice a daily (6.6 g/day). Giazo will be available as a 1.1 gram tablet in bottles of 180 and 500 count tablets.

Giazo, the tablet formulation of balsalazide disodium, will be an addition to the product line of the currently marketed Colazal (see Appendix A) for comparison of products.

2 METHODS AND MATERIALS

This section consists of two sections which describe the methods and material used by the Division of Medication Error Prevention staff conducting a proprietary name risk assessment (see 2.1.4 Proprietary Name Risk Assessment) and label, labeling and/or packaging risk assessment (see 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, Giazo, 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.

For the proprietary name, Giazo, the Division of Medication Error Prevention staff 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 a CDER Expert Panel discussion to gather professional opinions on the safety of the proposed names (see 2.1.1.2). We also conduct internal CDER prescription analysis studies

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

(see 2.1.2), and, when provided external prescription analysis studies results are considered and incorporated into the overall risk assessment.

The Safety Evaluator assigned to the Proprietary Name 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. Our Division 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, we consider 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 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 letter ‘G’ when searching to identify potentially similar drug names, as 75% of the confused drug names reported by the United States Pharmacopeia-Institute Safe Medication Practices Medication Error Reporting Program involve pairs beginning with the same letter.⁴⁵

To identify drug names that may look similar to Giazio, the 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 (five letters), upstrokes (one capital letter G), downstrokes (one, lower case ‘z’), cross-strokes (none), and dotted letters (one, ‘i’). Additionally, several letters in Giazio may be vulnerable to ambiguity when scripted, including the letter ‘G’ may appear as ‘J’ or ‘S’, lower case ‘i’ may appear as

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

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)

‘e’, ‘l’ or ‘r’, lower case ‘a’ may appear as ‘o’ or ‘c’, lower case ‘z’ may appear as ‘g’, ‘j’ or ‘y’; and lower case ‘o’ may appear as ‘a’ or ‘c’. As such, the Staff also considers these alternate appearances when identifying drug names that may look similar to Giazio.

When searching to identify potential names that may sound similar to Giazio, the medication error staff search for names with similar of syllables (three), stresses (GI-AZ-o, gi-AZ-o or gi-az-O), and placement of vowel and consonant sounds. In addition, several letters in Giazio may be subject to interpretation when spoken, including the letter ‘G’ may be interpreted as ‘gee’ or ‘je’; the letters ‘az’ may be interpreted as ‘as’; and the last syllable could be misinterpreted as ‘zoo’. The sponsor’s intended pronunciation of the proprietary name, Giazio, was expressed in the proposed name submission (pronounced “jē-Ā-zō”). This information will be taken into consideration, in the analysis.

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 prevention staff was provided with the following information about the proposed product: the proposed proprietary name (Giazio), the established name (balsalazide disodium), proposed indication (treatment of mildly to moderately active ulcerative colitis), strength (1.1 g), dose (three 1.1 g tablets), frequency of administration (twice a day), route (oral) and dosage form of the product (tablet).

Appendix A provides a more detailed listing of the product characteristics the Medication Error Staff general take into consideration.

Lastly, the Medication Error Prevention 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 Data base and information sources

The proposed proprietary name, Giazio, was provided to the Division of Medication Error Prevention 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 Giazio 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, 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 Prevention Staff reviews the United States Adopted Names 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 medication error staff to gather CDER professional opinions on the safety of the product and the proprietary name, Giazio. 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 Staff and representatives from the Division of Drug Marketing, Advertising, and Communications (DDMAC).

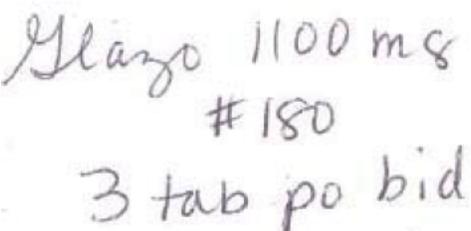
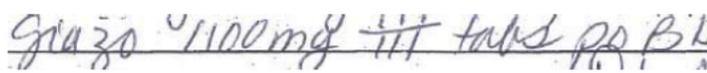
The pooled results of the medication error staff were presented to the Expert Panel for consideration. Based on the clinical and professional experiences of the Expert Panel members, the Panel may recommend the addition of names, additional searches by the Safety Evaluator to supplement the pooled results, 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 Giazio 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 Giazio 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. Giazio Study (conducted on September 13, 2007)

HANDWRITTEN PRESCRIPITON AND MEDICATION ORDER	VERBAL PRESCRIPTION
<p><u>Outpatient Prescription:</u></p> 	<p>Giazio 1100 mg # 180 3 tablet by mouth bid</p>
<p><u>Inpatient Medication Order :</u></p> 	

2.1.3 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 from a look and sound-alike perspective and evaluate the risk associated with marketing this product under a different name given the differences in dosing regimens, product strengths and total daily doses. 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 *Giazo* convincing similar to another drug name, which may cause practitioners to become confused at any point in the usual practice setting?” Additionally, for this name, we also asked “Does marketing this product under a different name cause confusion at any point in the usual practice setting?” An affirmative answer indicates a failure mode and represents a potential for *Giazo* to be confused with another proprietary or established drug name because of look- or sound-alike similarity and the availability of the product under two names. 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 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?” We also asked “Is it less confusing to market this product under the same name or two different names?” The answer to these questions are 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.

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

The Division of Medication Error Prevention staff 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. We identify 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 a United States Adopted Names 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 another drug product.

In the event that we object to the use of the proposed proprietary name, based upon the potential for confusion with another proposed (but not yet approved) proprietary name, we 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 the medication error prevention staff will recommend that the second product to reach approval seek an alternative name.

If none of these conditions are met, then we will not object to the use of the proprietary name. If any of these conditions are met, then we 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 for Medicine, The World Health Organization, The Joint Commission, 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, we believe 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 (e.g. new form introduced like Lamisil) (see limitations of the process).

If we object 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. Our Division is likely to recommend that the Sponsor select an alternative proprietary name and submit the alternate name to the Agency for review by our Division. However, in rare instances FMEA may identify plausible strategies that could reduce the risk of medication error of the currently proposed name, and so we 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 container labels and carton labeling 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 medication error staff analyzes reported misuse of drugs, the staff are able to use this experience to identify potential errors with all medication similarly packaged, labeled or prescribed. We use FMEA and the principles of human factors to identify potential sources of error with the proposed product labels and insert labeling, and provided recommendations that aim at reducing the risk of medication errors.

For this product the Applicant submitted on March 10, 2008, the following labels and labeling for us to review (see Appendices H and I):

- Container Label (6 sample count, 180 and 500 trade tablet count)
- Carton Labeling (6 tablet Professional sample (b) (4))
- Package Insert Labeling (no image)

3 RESULTS

3.1 PROPRIETARY NAME RISK ASSESSMENT

3.1.1 Database and information sources

We 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 Giazto to a degree where potential confusion between drug names could occur and result in medication errors in the usual clinical practice settings. In total, 5 names were identified as having some similarity to the name Giazto.

Four of the five names that were thought to look like Giazto, which include: Gingko, Gemzar, Solage, and Tiazac. One name Vidaza was thought to sound similar to Giazto.

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

Additionally, the Division of Medication Error Prevention did not identify any USAN stems in the name, Giazio, as of March 11, 2008.

3.1.2 CDER Expert panel discussion

The Expert Panel reviewed the pool of names identified by the Medication Error Prevention Staff (see section 3.1.1. above), and noted no additional names thought to have orthographic or phonetic similarity to Giazio.

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 CDER Prescription analysis studies

A total of 38 practitioners responded, but none of the responses overlapped with any existing or proposed drug names. About one-fourth of the participants (n=10) interpreted the name correctly as “Giazio,” 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 first vowel in Giazio reported as ‘e’ instead of ‘i’ and the constant ‘G’ reported as ‘J’. In the outpatient written prescription study, eleven respondents misinterpreted the name as “Glazo” as the letter ‘i’ was interpreted as lower case ‘l’. Additionally, in the inpatient written prescription study the letter ‘i’ was interpreted as ‘r’ by four respondents. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

3.1.4 Safety Evaluator Risk Assessment

3.1.4.1 Analysis of look and sound alike similarities

Independent searches by the primary Safety Evaluator did not identify any additional names thought to look and sound-alike similar to Giazio. Because the applicant proposes to market this product as a dual trade name, Colazal, was considered in the risk assessment. As such, a total of six names were analyzed to determine if the drug names could be confused with Giazio, and if the drug name confusion would likely result in a medication error.

Five of the names were determined to have some orthographic and/or phonetic similarity to Giazio, and thus determined to present some risk for confusion. The sixth name was considered in the assessment to determine if this product could be safely used under two proprietary names. Failure modes and effects analysis was then applied to determine if the proposed name, Giazio, could potentially be confused with any of the six products and lead to medication error.

This analysis determined that the name similarity between Giazio and the 5 name identified was unlikely to result in medication errors for five products. Two names (Solage and Vidaza) were not considered further because they lack convincing orthographic and/or phonetic similarities with Giazio (see Appendix E). For two names identified (Tiazac, Gingko), FMEA determined that medication errors were unlikely because the products do not overlap in strength or dose with Giazio and have minimal orthographic and/or visual similarity to Giazio (see Appendix F).

One name (Gemzar) had some numerical overlap with Giazio in either dosage or strength, but analysis of the failure mode did not determine the effect of this similarity to result in medication errors in the usual practice setting (see Appendix G).

Colazal was further evaluated to evaluate its potential for confusion and medication errors in the usual practice setting.

3.1.4.2 Analysis of Dual Trade Names

Giving consideration to the product differences in dosing regimens, product strengths and total daily dose, as part of the FMEA, this analysis determined that having this product marketed as both a single name or dual names provided opportunity for failures that could lead to confusion in the usual practice place. However, this analysis determined the presence of two names offered an additional failure mode than seen with the single name. This failure mode could result in the concomitant administration of balsalazide disodium (see section 4 for full discussion).

3.2 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 container labels and carton labeling appear to be vulnerable to confusion that could lead to medication errors.

3.2.1 Container Labels and Carton Labeling

1. Two different colors fonts are utilized for the letter ‘g’ in the proprietary name and the letter looks the number ‘8’. Additionally, two different font types are used in the proprietary name.
2. The established name appears to be smaller than half the size of the trade name.
3. The product strength is too small to read.
4. The dosage form “tablets” follows the product strength.
5. The NDC number appears in the bottom left corner of the container label and the bottom right corner of the carton labeling.
6. The net quantity has more prominence than the product strength.

3.2.2 Container Label

The large “swoosh” graphic on the principal display panel of the container label is too prominent.

3.2.3 Professional Sample Carton Labeling

There are no directions for the use for (b) (4) on the labeling.

4 DISCUSSION

4.1 PROPRIETARY NAME RISK ASSESSMENT

When evaluating the newly proposed name from a look and/or sound-alike perspective, we did not find the name vulnerable to confusion. However, when assessing if the name could be safely marketed using two different names, FMEA determined that marketing this product with dual trade names increases the risk of concomitant therapy because of the dosing error (e.g., overdose and underdose) that might arise could go undetected. This type of error would likely be undetected because patients and practitioners may not realize that the products contain the same active ingredients (see Appendix A). Additionally, the differences of administration may help to contribute to the assumption that the two products are different drugs. Thus, the error may go undetected unless an adverse event occurs.

In a meeting with the Division of Gastroenterology, on March 31, 2008, the Division of Medication Error Prevention presented the FMEA finding for the two balsalazide disodium products managed under two different proprietary names (Colazal and Giazol) as compared to management of two products under one proprietary name. The division reviewed the FMEA finding which determined a greater risk of medication errors with the use of dual trade name, and expressed concerns with the potential for

concomitant administration with dual trade names. Although they were unsure of the potential clinical consequences with concomitant therapy; the division agreed that the risk of medication errors, including concomitant therapy, could be mitigated if one proprietary name is used.

Marketing this product under one name will allow for increased education on the new strength and dosing frequency. This approach is not different than that seen in other products that market a higher strength requiring a decreased dosing interval. The differences in dosage form are not relevant because both are oral dosage forms.

4.2 LABEL AND LABELING RISK ASSESSMENT

The most prominent information on the primary display panel should be the proprietary name, established name, dosage form and product strength. However, when evaluating the labels and labeling, we noted the applicant uses two different color fonts for the letter 'g' in the proprietary name. As presented in the current font and two colors, the letter looks like the number '8'. Using one color would harmonize the appearance of the name and avoid ambiguity that could lead to possible misinterpretation.

The established name is small and difficult to read. It appears less than ½ the size of the proprietary name which is not in accordance with 21 CFR 201.10(g)(2). Additionally, the dosage form doesn't immediately follow the established name and doesn't appear in the same font as the established name. This appearance decreases the size and importance of this information.

Additionally, the product strength is presented before the dosage form and is too small to read. The prominent use of multiple colors (i.e., burgundy, turquoise and gold) for the trade dress distracts from the readability of the established name, dosage form and product strength which are presented in a light weight black font and are small in comparison to the colors for the trade dress.

The net quantity statement is more prominent than the product strength. The product strength is usually presented prominently below the established name. Increasing the prominence of the product strength and relocating the net quantity away from the product strength will increase the readability and give more attention to the number corresponding to the strength.

The NDC number appears at the bottom of the principle display panel. This placement is not in accordance with 21 CFR 207.35(b)(3)(i).

The applicant currently utilizes a (b) (4)
(b) (4)

Since both products will be marketed with the same proprietary name it would be reasonable for the manufacturer to place a new strength and dosing (b) (4) on the container and carton labels to aid in distinguishing the product strength and educate about the new strength and dosing interval.

5 CONCLUSIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Giazio, appears to be vulnerable to confusion that could lead to medication errors because of the risk of concomitant administration of both Giazio and Colazal. As such, we object to the use of the proprietary name Giazio, as a dual trade name for this product. We believe that the two balsalazide disodium products can be safely managed under one proprietary name.

Our Label and Labeling Risk Assessment found the presentation on the proposed labels and labeling vulnerable to confusion that could lead to medication errors. We believe the risks identified can be addressed and mitigated prior to drug approval, and provide recommendations in Section 6.

6 RECOMMENDATIONS

6.1 COMMENTS TO THE DIVISION

6.1.1 Proprietary Name

The Division of Medication Error Prevention does not recommend the use of the tradename, Giazo, as a dual trade name for balsalazide disodium. We believe that the two different balsalazide disodium strengths with differing frequencies can be more safely managed under one proprietary name. Rather than use a dual tradename, we recommend the use of a single tradename, Colazal, for all Balsalazide Disodium products marketed by this Applicant.

Based upon our assessment of the proprietary name, labels and labeling, we have identified areas of needed improvement. We have provided recommendations in Section 6.2 and request this information be forwarded to the Applicant.

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 Cheryle Milburn, OSE Project Manager, at 301-796-2084.

6.2 COMMENTS TO THE SPONSOR

6.2.1 Proprietary Name

The Division of Medication Error Prevention does not recommend the use of the tradename, Giazo. The results of the Proprietary Name Risk Assessment found that the proposed name Giazo, is confusing and misleading because the product may be concomitantly ordered and administered with the currently marketed product Colazal. Rather than use a dual tradename, we recommend the use of a single tradename, Colazal, for all Balsalazide Disodium products marketed by this Applicant.

6.2.2 Labels and Labeling

A. Carton and Container Labels

1. Revise the color scheme for the proprietary name so that the entire name is presented in one color and one font style.
2. Ensure that the established name is at least ½ the size of the proprietary name and the strength is proportional to the proprietary and established name.
3. Relocate the dosage form to ensure it immediately follows the established name (e.g., balsalazide disodium tablets)
4. Relocate the NDC number to the top one-third of the principle display panel, to be in accordance with 21 CFR 207-35(b)(3)(i).
5. Revise to include a statement on the container label and carton labeling noting the “new strength” and “dosing interval”. This statement should not appear on the labels and labeling for a period to exceed 6 months.

B. Container Label

1. Relocate the dosage form to ensure it immediately follow the established name (e.g., balsalazide disodium tablets).
2. Relocate the net quantity to the lower 1/3rd of the label and ensure the prominence is less than the product strength.

C. Carton Labeling (Sample)

1. Revise to include a statement on the container label and carton labeling noting the “new strength” and “dosing interval”. This statement should not appear on the labeling for a period to exceed 6 months.
2. Revise the color scheme for the proprietary name so that the entire name is presented in one color font and font type.
3. Ensure that the established name is at least ½ the size of the proprietary name and the strength is proportional to the proprietary and established name.
4. Relocate the dosage form to ensure it immediately follows the established name (e.g., balsalazide disodium tablets)
5. Increase the size and prominence of the product strength.
6. Relocate the NDC number to the top one-third of the principle display panel, to be in accordance with 21 CFR 207-35(b)(3)(i).

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 DMETS, 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 and Technical Support proprietary name consultation requests*

This is a list of proposed and pending names that is generated by DMETS 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.

Use standard format for citations for previous OSE reviews; literature.

APPENDICES

Appendix A: Overlapping and differentiating product characteristics

Product Characteristics	Colazal	Giazo
Indication	Treatment of active mild to moderate ulcerative colitis	Treatment of mildly to moderately active ulcerative colitis in patients 18 years of age and older.
Strength	750 mg	1.1 G
Usual Dose	3 capsules	3 tablets
Dosage Form	Capsule	Tablet
Frequency	Three times daily	Twice daily

Appendix B:

The Medication Error Staff consider the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. The Division of Medication Error Prevention 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 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 lead 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, we 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 Medication Error Prevention Staff 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 Cross-strokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	<ul style="list-style-type: none"> 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	<ul style="list-style-type: none"> Names may sound similar when pronounced and lead to drug name confusion in verbal communication

Appendix C:

Prescription Study Responses

Outpatient Prescription	Voice Prescription	Inpatient Medication Order
Glazo	Giazza	Grazo
Glazo	Giazza	Grazo
Glazo	Geazo	Grazo
Glazo	Jazzo	Giazo
Glazo	Giazo	Giazo
Glazo	Geazo	Ziazo
Glazo	Jazzo	giaz
Glazo	Geazo	Giazo
Glazo	Giazo	Grazo
Glazo	Geazo	Giazo
Glazo	Jazo	Giazo
	Giazo	Giazo
	Jiazo	
	Giaso	
	Ziazo	

Appendix D: Applicant's rationale for two Dual Trade Names



August 16, 2007

Daniel Shames, MD
Acting Director
CDER, Division of Gastroenterology Products
5901-B Ammendale Road
Beltsville, MD 20705-1266
Attention: Kristen Everett, Regulatory Project Manager

**Subject: Proposed Trade Name
NDA 22-205
Balsalazide Disodium Tablets, 1100 mg**

Dear Dr. Shames:

Please note the above referenced pending New Drug Application (NDA) for balsalazide disodium tablets submitted July 16, 2007 in accord with Section 505(b)(1) of the Federal Food, Drug and Cosmetic Act for the treatment of mildly to moderately active ulcerative colitis in patients 18 years of age and older.

Additional reference is made to the pre-NDA meeting with the Division on April 27, 2007 and the proposal by Salix to provide a new trade name and separate package insert for the tablet dosage form of balsalazide disodium. Salix proposes the following trade name for consideration:

Proposed Trade Name: Giazio (pronounced "jē-Ā-zō")

Further reference is made to the draft package insert text provided in Module 1.14.1.3 of the pending NDA for balsalazide disodium tablets. Salix requests a separate package insert for the tablet dosage form based on the following rationale:

1. A separate package insert would minimize potential consumer confusion between the capsule and tablet dosage forms. Important differences between the dosage forms include:
 - Different dosing regimens (3 capsules 3 times a day vs 3 tablets 2 times a day).
 - Different active amounts per unit (750 mg balsalazide disodium per capsule vs 1.1 g balsalazide disodium per tablet).
 - Different total daily doses (6.75 g per day for capsules vs 6.6 g tablets per day for tablets)

Based on the dosing regimen and active amount of each dosage form, confusion between the capsule and tablet could lead to incorrect administration of up to 9.9 g balsalazide disodium per day (tablet taken on capsule regimen) or as little as 4.5 g balsalazide disodium per day (capsule taken on tablet regimen).

2. In the case of Visicol[®] (NDA 21-097) and OsmoPrep[™] (NDA 21-892), the Division allowed separate package inserts when the active amounts were identical (1.5 g sodium phosphate per tablet) and the dosing regimens were different (40 Visicol[®] Tablets vs 32 OsmoPrep[™] Tablets).

Appendix E: Names that lack orthographic and/or phonetic similarity to Giazio.

Proprietary Name	Similarity to Giazio
Solage	Look
Vidaza	Sound

Appendix F: Products with no numerical overlap in strength and dose.

Product name with potential for confusion	Similarity to Giazio	Strength	Usual Dose (if applicable)
Giazio (Balsalazide disodium)		1.1 g tablets	Usual dose: 3 tablets (1.1 g) twice daily
Tiazac	Look	120 mg, 180 mg, 240 mg, 300 mg, 360 mg	120 mg to 240 mg once daily
Gingko	Look	60 mg, 120 mg	120 mg to 240 mg daily

Appendix G: Potential confusing name with numerical overlap in strength or dose

Giazio (Balsalazide Disodium)	1.1 g	Usual dose: 3 tablets (1.1g) bid
Failure Mode: Name confusion	Causes (could be multiple)	Effects
Gemzar (Gemcitabine) 1 g Powder for Injection; 200 mg Powder for Injection	Orthographically similar have downstroke 'z' and similar length of name Numerical overlap in strength (1 g vs. 1.1 g)	Strength or dose will be required for Gemzar <i>Rationale:</i> Gemzar available in two strengths, thus Gemzar prescriptions will contain a dose while Giazio prescriptions don't have to include a strength or dose. Gemzar is indicated for advanced or metastatic non-small cell lung cancer. Gemzar dose is individualized based on body surface area (1000 mg/m ²). The usual dosing schedule for Gemzar is on days 1, 8, and 15 of a 28-day cycle. Gemzar will be written on a chemotherapy order form.

2 pages of draft labeling has been withheld in full as B(4) CCI/TS immediately following this page

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/s/

Diane Smith
5/20/2008 04:04:00 PM
CSO

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DRUG SAFETY OFFICE REVIEWER

Carol Holquist
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