CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

022523Orig1s000

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:	January 25, 2010
To:	Donna Griebel, MD, Director Division of Gastroenterology Products
Thru:	Melina Griffis, RPh, Team Leader Denise Toyer, PharmD, Deputy Director Carol Holquist, RPh, Director Division of Medication Error Prevention and Analysis (DMEPA)
From:	Anne Crandall, PharmD, Safety Evaluator Division of Medication Error Prevention and Analysis (DMEPA)
Subject:	Proprietary Name Review
Drug Name(s):	Pancreaze (Pancrelipase) Capsule, 4,200 USP Units Lipase/17,500 USP Units Amylase/10,000 USP Units Protease, 10,500 USP Units Lipase/45,750 USP Units Amylase/25,000 Units USP Protease, 16,800 USP Units Lipase/70,000 USP Units Amylase/40,000 USP Units Protease, 21,000 USP Units Lipase/61,000 USP Units Amylase/37,000 USP Units Protease
Application Type/Number:	NDA # 022523
Sponsor:	Johnson & Johnson Pharmaceutical Research and Development
OSE RCM #:	2009-2253

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

CONTENTS

EXECUTIVE SUMMARY

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

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

1 BACKGROUND

1.1 INTRODUCTION

This review is in response to a request from Johnson & Johnson on November 10, 2009, for an assessment of the proposed proprietary name, Pancreaze, regarding potential name confusion with other proprietary or established drug names in the usual practice settings. A previously proposed proprietary name for this product, Pancrease MT, was found to be unacceptable (OSE review # 2009-1213) due to the presence of the United States Adopted Names (USAN) stem, '-ase', in the proposed name. Container labels and carton and package insert labeling were submitted by the Applicant and will be reviewed under OSE review # 2009-1215.

1.2 REGULATORY HISTORY

Pancrease MT 4, Pancrease MT 10, Pancrease MT 16, Pancrease MT 25 and Pancrease MT 32 have been available in the marketplace without an approved NDA. A Federal Register (FR) Notice dated April 20, 2004 notified manufacturers of pancreatic insufficiency products that FDA approval, via the submission of a new drug application (NDA), would be required by April 2008 (deadline has been extended to April 2010) for these products to remain in the US marketplace. In accordance to this FR notice, the manufacturer of Pancreaze submitted an NDA for this product on April 27, 2009.

The Agency has determined that all three ingredients (Lipase, Amylase and Protease) are active and will be included on labels and labeling with their respective strengths. Even though these products (including Pancreaze) contain three enzymes current dosing practices are only based on the lipase component.

1.3 PRODUCT INFORMATION

Pancreaze (Pancrelipase) Delayed-release Capsules are orally administered pancreatic enzymes indicated for patients with exocrine pancreatic insufficiency associated with cystic fibrosis, chronic pancreatitis, obstructive pancreatic ductal neoplasm, post-pancreatectomy or post-gastroenterostomy. The usual dose is individualized according to indication and should be determined by the amount of steatorrhea. Pancreaze cannot be interchanged with any other pancrelipase products. The recommended starting dose is as follows;

Infants and children (0 to < 5 years) dosage: Starting dose is 375 Units Lipase/kg/meal or feeding with infant formula or breast milk. Maximum daily dose is 10,000 Units of lipase/kg/day.

Adults and pediatric (>/= 5 years) dosage: Starting dose is 375 Units to 1,000 Units Lipase/kg/meal. Maximum daily dose is 10,000 Units/kg/day.

Pancreaze capsules are available as hard gelatin capsules containing enteric coated microtablets of porcine-derived pancreatic enzyme concentrate consisting of three enzymes: lipase, amylase and protease (see table 1).

Table 1 Available Strengths of Pancreaze

Active Ingredients	Dosage Strength	Dosage Strength	Dosage Strength	Dosage Strength
Lipase	4,200 USP Units	10,500 USP Units	16,800 USP Units	21,000 USP Units
Amylase	17,500 USP Units	43,750 USP Units	70,000 USP Units	61,000 USP Units
Protease	(b) (4) USP Units	25,000 USP Units	40,000 USP Units	37,000 USP Units

2 METHODS AND MATERIALS

Appendix A describes the general methods and materials used by the Division of Medication Error Prevention and Analysis (DMEPA) when conducting a proprietary name risk assessment for all proprietary names. Sections 2.1, 2.2, and 2.3 identify specific information associated with the methodology for the proposed proprietary name, Pancreaze.

2.1 SEARCH CRITERIA

For this review, particular consideration was given to drug names beginning with the letter 'P' 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.[1,2]

To identify drug names that may look similar to 'Pancreaze', the DMEPA staff also considers the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (nine letters), upstrokes (one, capital letter 'P'), downstrokes (none or one, 'z' if scripted), and cross-strokes (none). Additionally, several letters in Pancreaze may be vulnerable to ambiguity when scripted (see Appendix B). As a result, the DMEPA staff also considers these alternate appearances when identifying drug names that may look similar to Pancreaze.

When searching to identify potential names that may sound similar to Pancreaze, the DMEPA staff searches for names with similar number of syllables (three), stresses (PAN-cre-aze, pan-CRE-aze, pan-cre-AZE), and placement of vowel and consonant sounds. Additionally, the DMEPA staff considers that pronunciation of parts of the name can vary (See Appendix B). Furthermore, names are often mispronounced and/or spoken with regional accents and dialects, so other potential pronunciations of the name are considered.

DMEPA also considered that Pancre**aze** was marketed under the name Pancre**ase** MT for many years. Practitioners may still continue to write the name with an '-ase' ending as the sound of "AZE" and "ASE" are identical and practitioners are familiar with the '-ase' spelling, therefore both spellings were searched.

2.2 FDA ADVERSE EVENT REPORTING SYSTEM (AERS)

Pancrease MT tablets are currently marketed, therefore, DMEPA conducted a search of the FDA Adverse Event Reporting System (AERS) database on January 4, 2009, to identify medication errors involving Pancrease MT.

---

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

2 Kondrack, G and Dorr, B. Automatic Identification of Confusable Drug Names. Artificial Intelligence in Medicine (2005)

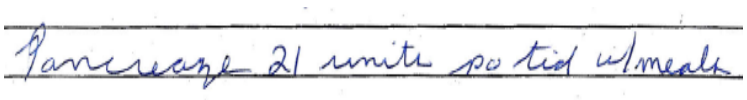
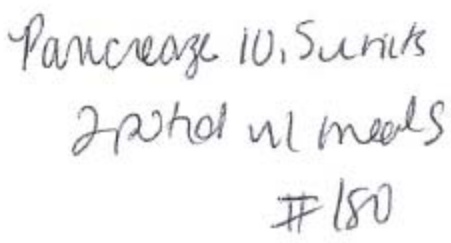
The MedRA High Level Group Term (HLGT) "Medication Errors", the High Level Term (HLT) "Product Label Issues" and the Preferred Term (PT) "Product Quality Issues" were used as search criteria for Reactions. The search criteria used for products was a verbatim substance search "Pancrease" as the name is not an approved name with a designated NDA number. No date limitations were set.

The reports were manually reviewed to determine if a medication error occurred. Duplicate reports were combined into cases. The cases that described a medication error were categorized by type of error. We reviewed the cases within each category to identify factors that contributed to the medication errors. If a root cause was associated with the name of the product, the case was considered pertinent to this review. Those reports that did not describe a medication error or did not describe an error applicable to this review (e.g. errors related to accidental exposures, intentional overdoses, etc.) were excluded from further analysis.

2.3 FDA PRESCRIPTION ANALYSIS STUDIES

In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, the following inpatient medication order, outpatient and verbal prescription was communicated during the FDA prescription studies.

Figure 1. Pancreaze Study (conducted on December 4, 2009)

HANDWRITTEN REQUISITION MEDICATION ORDER	VERBAL PRESCRIPTION
Inpatient Medication Order: 	Pancreaze 10 .5 Units 2 po tid with meals Number 180
Outpatient Prescription: 	

3 RESULTS

3.1 DATABASE AND INFORMATION SOURCES

The searches yielded a total of 14 names as having some similarity to the name Pancreaze.

Four of the 14 names (Danocrine, Pancuronium, Panocaps, and Parcaine) were thought to look like Pancreaze. Six of the 14 names (Pancrease, Pancrease MT, Pancreatin, Pancrecarb, Pancrelipase, and Panokase) were thought to look and sound similar to Pancreaze. The remaining names (Activase, Glynase, Patanase, and Puricase) were thought sound similar to Pancreaze.

A search of the United States Adopted Name stem list on December 28, 2009 did not identify any United States Adopted Names (USAN) stem within the proposed name, Pancreaze.

3.2 EXPERT PANEL DISCUSSION

The Expert Panel reviewed the pool of names identified by DMEPA staff (See Section 3.1 above) and noted no additional names thought to have orthographic similarity to Pancreaze.

DDMAC had no concerns regarding the proposed name from a promotional perspective.

3.3 FDA ADVERSE EVENT REPORTING SYSTEM (AERS) DATABASE

The AERS search conducted on January 5, 2009, yielded three cases. Two cases were excluded from further evaluation because the cases involved product complaints associated with labeled adverse events (excessive bloating, gas and weight loss) due to Pancrease therapy. There was no indication that an error had occurred.

The third case reported an error due to name confusion between Pancrease and Pacerone. A pharmacy technician misinterpreted the name Pancrease for Pacerone and typed that name in the computer, which was then filled with Pacerone. The pharmacist verified the prescription as Pacerone. The medication error reached the patient, however it is difficult, based on the report, to determine whether the patient took the medicine as it seems the error may have been discovered when refilling the medicine.

An additional search was run using the "interaction" function specifically focusing on the products Pancrease and Pacerone. The search used the verbatim "Pancrease%" and "Paceron%" and the tradename "Pacerone". No additional cases were found during this search.

3.4 FDA PRESCRIPTION ANALYSIS STUDIES

A total of 16 practitioners responded. Eleven (n=11) respondents interpreted the name correctly as 'Pancreaze', with correct interpretations occurring in written studies. The remainder of the responses misinterpreted the drug name. The majority of misinterpretations occurred in the voice study, mistaking 'aze' for 'ase'. One respondent in the inpatient study also misinterpreted 'aze' for 'ase'. Additionally, one respondent mistook 'aze' for 'zyme' in the inpatient study. See Appendix B for the complete listing of interpretations from the verbal and written prescription studies.

3.5 SAFETY EVALUATOR RISK ASSESSMENT

Independent searches by the primary Safety Evaluator identified no additional names that were thought to pose confusion with the proposed name. However, due to the AERS search results which revealed a medication error with Pacerone and Pancrease, Pacerone was added to the safety risk assessment.

Thus, a total of 15 names were identified as names with some similarity to Pancreaze.

3.6 COMMENTS FROM THE DIVISION OF GASTROENTEROLOGY PRODUCTS (DGP)

3.6.1 Initial Phase of Review

In response to the OSE e-mail on January 4, 2009 DGP did not forward any comments or concerns on the proposed proprietary name at the initial phase of the review.

3.6.2 Midpoint of Review

On January 6, 2009, DMEPA notified the Division of Gastroenterology Products via e-mail that we had no objections to the proposed proprietary name, Pancreaze. Per email correspondence from DGP on January 21, 2010, they indicated that they concur with our assessment of the proposed proprietary name, Pancreaze.

4 DISCUSSION

Neither DDMAC not the Division of Gastroenterology Products had concerns with the proposed name Pancreaze. DMEPA did not identify any issues that would render the name unacceptable other then names as potential sources of confusion because of their similar sound and appearance to Pancreaze.

DMEPA identified and evaluated a total of 15 names for their potential orthographic and phonetic similarity to the proposed name, Pancreaze. Two of the 15 names were removed from further analysis for the reasons identified in Appendix D. Therefore, 13 names were determined to have some orthographic and/or phonetic similarity to Pancreaze, and thus determined to present some risk for confusion.

Failure Mode and Effect Analysis (FMEA) was then applied to determine if the proposed name, Pancreaze, could potentially be confused with the remaining 13 names and lead to medication errors. This analysis determined that the name similarity between Pancreaze was unlikely to result in medication errors with any of the 13 products for the reasons presented in Appendices E through F.

5 CONCLUSIONS AND RECOMMENDATIONS

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

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

We are willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Nitin Patel, OSE Project Manager at 301-796-5412.

5.1 COMMENTS TO THE APPLICANT

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

The proposed proprietary name, Pancreaze, 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. The conclusions upon re-review are subject to change.

REFERENCES

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

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

2. Phonetic and Orthographic Computer Analysis (POCA)

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

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

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

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

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

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

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

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

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

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

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

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

USPTO provides information regarding patent and trademarks.

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

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

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

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

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

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

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

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

13. USAN Stems (http://www.ama-assn.org/ama/pub/category/4782.html)

USAN Stems List contains all the recognized USAN stems.

14. Red Book Pharmacy's Fundamental Reference

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

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

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

16. Medical Abbreviations Book

Medical Abbreviations Book contains commonly used medical abbreviations and their definitions

APPENDICES

Appendix A:

FDA's Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name and the proprietary and established names of drug products existing in the marketplace and those pending IND, NDA, BLA, and ANDA products currently under review by the Center. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. 3

For the proposed proprietary name, DMEPA staff search a standard set of databases and information sources to identify names with orthographic and phonetic similarity and hold a Center for Drug Evaluation and Research (CDER) Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name. DMEPA staff also conducts internal CDER prescription analysis studies. When provided, DMEPA considers external prescription analysis study results and incorporate into the overall risk assessment.

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

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. DMEPA bases the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proprietary name, and focuses on the avoidance of medication errors.

FMEA is a systematic tool for evaluating a process and identifying where and how it might fail. 4 DMEPA uses FMEA to analyze whether the drug names identified with orthographic or phonetic similarity to the proposed proprietary name could cause confusion that subsequently leads to medication errors in the clinical setting. DMEPA uses the clinical expertise of its staff to anticipate the conditions of the clinical setting where the product is likely to be used based on the characteristics of the proposed product.

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

Typical product characteristics considered when identifying drug names that could potentially be confused with the proposed proprietary name include, but are not limited to; established name of the proposed product, proposed indication of use, dosage form, route of administration, strength, unit of measure, dosage units, recommended dose, typical quantity or volume, frequency of administration, product packaging, storage conditions, patient population, and prescriber population. Because drug name confusion can occur at any point in the medication use process, DMEPA staff considers the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and monitoring the impact of the medication.[5] DMEPA provides the product characteristics considered for this review in section one.

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

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

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

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

Type of similarity	**Considerations when searching the databases**		
	Potential causes of drug name similarity	*Attributes examined to identify similar drug names*	*Potential Effects*
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	• Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication • Names may look similar when scripted and lead to drug name confusion in written communication
	Orthographic similarity	Similar spelling Length of the name Upstrokes Down strokes Cross-stokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	• Names may look similar when scripted, and lead to drug name confusion in written communication
Sound-alike	Phonetic similarity	Identical prefix Identical infix Identical suffix Number of syllables Stresses Placement of vowel sounds Placement of consonant sounds Overlapping product characteristics	• Names may sound similar when pronounced and lead to drug name confusion in verbal communication

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

1. Database and Information Sources

DMEPA staff conducts searches of the internet, several standard published drug product reference texts, and FDA databases to identify existing and proposed drug names that may sound-alike or look-alike to the proposed proprietary name using the criteria outlined in Section 2.1. Section 6 provides a standard description of the databases used in the searches. To complement the process, the DMEPA 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 DMEPA staff review the USAN stem list to determine if any USAN stems are present within the proprietary name. The individual findings of multiple safety evaluators are pooled and presented to the CDER Expert Panel.

2. CDER Expert Panel Discussion

DMEPA conducts an Expert Panel Discussion to gather CDER professional opinions on the safety of the proposed product and the proposed proprietary name. The Expert Panel is composed of Division of Medication Errors Prevention (DMEPA) staff and representatives from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The Expert Panel also discusses potential concerns regarding drug marketing and promotion related to the proposed names.

The primary Safety Evaluator presents the pooled results of the DMEPA staff 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 primary Safety Evaluator to supplement the pooled results, or general advice to consider when reviewing the proposed proprietary name.

3. FDA Prescription Analysis Studies

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

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

4. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

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

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

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

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

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

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

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

The answer to this question is a central component of the Safety Evaluator's overall risk assessment of the proprietary name. If the Safety Evaluator determines through FMEA that the name similarity would not ultimately be a source of medication errors in the usual practice setting, the primary Safety Evaluator eliminates the name from further analysis. However, if the Safety Evaluator determines through FMEA that the name similarity could ultimately cause medication errors in the usual practice setting, the Safety Evaluator will then recommend the use of an alternate proprietary name.

---

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

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

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

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

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

The threshold set for objection to the proposed proprietary name may seem low to the Applicant. However, the safety concerns set forth in criteria a through e are supported either by FDA regulation or by external healthcare authorities, including the Institute of Medicine (IOM), World Health Organization (WHO), Joint Commission on Accreditation of Hospitals (JCOAH), and the Institute for Safe Medication Practices (ISMP). These organizations have examined medication errors resulting from look- or sound-alike drug names and called for regulatory authorities to address the issue prior to approval. Additionally, DMEPA contends that the threshold set for the Proprietary Name Risk Assessment is reasonable because proprietary drug name confusion is a predictable and a preventable source of medication error that, in many instances, the Agency and/or Applicant can identify and rectify prior to approval to avoid patient harm.

Furthermore, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to rectify post-approval. Educational and other post-approval efforts are low-leverage strategies that have had limited effectiveness at alleviating medication errors involving drug name confusion. Applicants have undertaken higher-leverage strategies, such as drug name changes, in the past but at great financial cost to the Applicant and at the expense of the public welfare, not to mention the Agency's credibility as the authority responsible for approving the error-prone proprietary name. Moreover, even after Applicants' have changed a product's proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioners' vocabulary, and as a result, the Agency has continued to receive reports of drug name confusion long after a name change in some instances. Therefore, DMEPA believes that post-approval efforts at reducing name confusion errors should be reserved for those cases in which the potential for name confusion could not be predicted prior to approval. . (See Section 4 for limitations of the process).

Appendix B: Letters with possible orthographic or phonetic misinterpretation

Letters in Name, Pancreaze	**Scripted may appear as**	**Spoken may be interpreted as**
Capital 'P'	'R', 'D' or 'B'	"B"
Lower case 'a	'e' or 'o'	"AY"
Lower case 'n'	'm' or 'r'	"M"
Lower case 'c'	'o'	"CK" or "K"
Lower case 'r'	'v', 'n', or 's'	
Lower case 'e'	'i'	"EE"
Lower case 'z'	'g' or 'j'	"C", "S" or "SS"

Appendix C: FDA Prescription Study Responses

Inpatient Medication Order	Outpatient Prescription	Voice Prescription
Pancrease	Pancreaze	Pancrease
Pancreazyme	Pancreaze	Pancrease
Pancreaze	Pancreaze	Pancrease
Pancreaze	Pancreaze	
Pancreaze	Pancreaze	
	Pancreaze	
	Pancreaze	
	Pancreaze	

Appendix D: Unapproved proprietary name

Proprietary Name/ Established Name	Status
Puricase *** (Pegloticase)	DMEPA found primary name, Krystexxa*** acceptable. BLA still under review in the Agency.
Pancrecarb*** (Pancrelipase)	DMEPA found the name unacceptable. The Applicant has submitted a new name, (b) (4)***, which is under review

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

Appendix E: Products with no numeric overlap in dose or strength

Product name with potential for confusion	Similarity to Pancreaze	Strength	Recommended Dose
Pancreaze (Pancrelipase) Capsules		4,200 USP Units Lipase/17,500 USP Units Amylase/10,000 USP Units Protease, 10,500 USP Units Lipase/45,750 USP Units Amylase/25,000 Units USP Protease, 16,800 USP Units Lipase/70,000 USP Units Amylase/40,000 USP Units Protease, 21,000 USP Units Lipase/61,000 USP Units Amylase/37,000 USP Units Protease	**Usual Dose:** **Infants and children:** 375 Units Lipase/kg/meal by mouth up to a maximum of 10,000 Units Lipase/kg/day **Adults:** 375 Units to 1000 Units Lipase/kg/meal by mouth up to a maximum of 10,000 Units Lipase/kg/day
Pancuronium (Pancuronium bromide)	Orthographic	1 mg/mL, 2 mg/mL intravenous solution	Test dose in children : 0.02 mg/kg intravenously Adult dose: 0.04 mg to 0.1 mg/kg intravenously
Parcaine (Proparacaine hydrochloride)	Orthographic	0.5% ophthalmic solution	One drop each eye every 6 to 10 minutes for 5 to 7 doses, or 1 to 2 drops in each eye prior to procedure
Activase (Alteplase)	Orthographic	2 mg/vial lyophilized powder, 50 mg/vial, 100 mg/vial	Acute Myocardial Infarction: 100 mg intravenous (15 mg bolus, 50 mg over 30 minutes, then 35 mg over 60 minutes or 15 mg bolus, 0.75 mg/kg over 30 minutes then 0.50 mg/kg over 60 minutes or 60 mg intravenous in the first hour, 20 mg over second hour and 20 mg over third hour Arterial thrombosis: 1.5 mg/hour by transcatheter intra-arterial infusion Cerebrovascular accident: 0.9 mg/kg intravenous over 60 minutes Pulmonary embolism: 100 mg infused over 2 hours
Glynase (Glyburide)	Phonetic	1.5 mg, 3 mg, 6 mg oral tablets	0.75 mg to 12 mg by mouth daily, which may be given as a single dose or in divided doses
Patanase (Olopatadine)	Phonetic	0.665/spray metered nasal spray	1-2 sprays per nostril twice a day

Danocrine (Danazol)	Orthographic	50 mg, 100 mg, 200 mg oral capsules	100 mg to 800 mg by mouth in two divided doses per day 200 mg to 800 mg by mouth divided in two to three doses per day

Appendix F: Potentially confusing names that are unlikely to cause medication errors

Failure Mode: Name Confusion	**Causes (could be multiple)**	**Rationale**
Pancreaze (Pancrelipase)	**Orthographic and/or phonetic similarities** **Product characteristics**	**Factors that would prevent wrong drug selection.**
Panocaps, Panocaps MT (Pancrelipase) *Strengths:* *(Panocaps)* 4500 USP Units Lipase/ 20,000 USP Units Amylase/ 25,000 USP Units Protease *(Panocaps MT)* 16,000 USP Units Lipase/ 48,000 USP Units Amylase/ 48,000 USP Units Protease, 20,000 USP Units Lipase/ 56,000 USP Units Amylase/ 44,000 USP Units Protease oral delayed release capsules *Usual Dose:* 500 to 2500 units/kg/meal by mouth	*Orthographic similarities include the following:* Same beginning ('Pan') Similar length (Panocaps has 8 letters vs. Pancreaze has 9 letters) *Product characteristics that Pancreaze and Panocaps share:* Both products are pancreatic enzymes with the same directions for use (three times a day with meals) Both products will be used in the same population and prescribed by the same providers for the same diagnosis	The risk for medication error is decreased by the following factors: *1. Orthographic:* Pancreaze contains no downstrokes (unless the 'z' is scripted) vs. Panocaps which contains the downstroke 'p' Pancreaze contains four letter before the 'c' and five letters after the 'c' vs. Panocaps has four letters before the 'c' and four letters after the 'c' Pancreaze ends with an 'e' vs. Panocaps ends with 's' Based upon the Federal Register notice published by the FDA on April 30, 2004 all pancreatic insufficiency drug products must submit an NDA for review and be approved by April 28, 2010. If the drug product has not been approved by the FDA on April 28, 2010, the product will be pulled from the market. Per the Division of Gastroenterology Products, these products are not currently under review within the Agency therefore Panocaps and Panocaps MT products will be required to be removed from the market by April 28, 2010.

Failure Mode: Name Confusion	**Causes (could be multiple)**	**Rationale**
Pancreaze (Pancrelipase)	**Orthographic and/or phonetic similarities** **Product characteristics**	**Factors that would prevent wrong drug selection.**
Pancreatin (Pancreatin or Lipase, Amylase or Protease) *Strengths:* 325 mg, 500 mg, 1200 mg, 1400 mg, 1500 mg oral tablets (Strengths as listed in Micromedex) 100 gm, 500 gm and 1 gm oral powder (Strengths as listed in RedBook) 2,400 USP Units Lipase/ 30,000 USP Units Amylase/ 30,000 USP Units Protease oral tablet (Strengths as listed in Facts & Comparisons) *Directions for use:* Tablets taken by mouth with each meal	*Orthographic and phonetic similarities include the following:* Same beginning sound (”PAN”) Same middle syllable (”CREE”) *Product characteristics that Pancreaze and Pancreatin share:* Both products are pancreatic enzymes with the same directions for use (three times a day with meals) Both products will be used in the same population and prescribed by the same providers for the same diagnosis	The risk for medication error is decreased by the following factors: *1. Orthographic differences* - Pancreaze does not contain any cross-strokes or dotted letters versus Pancreatin which contains both a ‘t’ and and ‘i’. - Pancreaze is 8 letters vs. Pancreatin contains 10 letters making the scripted word appear longer *2. Product characteristics* - Pancreaze is available in strengths designated as 4,200, 10,500, 16,800 and 21,000 Lipase Units versus Pancreatin which has a strength of 5,550 Lipase Units. Based on these available strengths, there is no dose overlap between Pancreaze and Pancreatin. Based upon the Federal Register notice published by the FDA on April 30, 2004 all pancreatic insufficiency drug products must submit an NDA for review and be approved by April 28, 2010. If the drug product has not been approved by the FDA, the product will be pulled from the market by April 28, 2010. Per the Division of Gastroenterology Products, these products are not currently under review within the Agency therefore Pancreatin products will be required to be removed from the market by April 28, 2010.

Failure Mode: Name Confusion	**Causes (could be multiple)**	**Rationale**
Pancreaze (Pancrelipase)	**Orthographic and/or phonetic similarities** **Product characteristics**	**Factors that would prevent wrong drug selection.**
Panokase (Pancrelipse) *Strengths:* 8,000 USP Units Lipase/ 30,000 USP Units Amylase/ 30,000 USP Units Protease 16,000 UPS Units Lipase/ 60,000 USP Units Amylase/ 60,000 USP Units Protease oral tablets *Directions for use:* 500 to 2500 units/kg/meal by mouth	*Orthographic and phonetic similarities include the following:* Same beginning sound (”PAN”) Similar length (Pancreaze has 9 letters vs. Panokase has 8 letters) Same sounding end (”AZE” vs ”ASE”) *Product characteristics that Pancreaze and Panokase share:* Both products are pancreatic enzymes with the same directions for use (three times a day with meals) Both products will be used in the same population and prescribed by the same providers for the same diagnosis	The risk for medication error is decreased by the following factors: *1. Orthographic differences* -Pancreaze contains one upstroke provided by the ‘P’ vs. Panokase contains two upstrokes ‘P’ and ‘k’. -Pancreaze contains a ‘z’ in the ending ‘aze’ vs. Panokase ends in ‘ase’ -Pancreaze contains ‘cre’ in the middle of the name vs. ‘oka’ in Panokase *2. Product Characteristics* The dosing for Pancreaze products is reliant on only the Lipase component. The Lipase units do not directly overlap for Pancreaze (16,800 USP Units) vs. Panokase (16,000 USP Units). Based upon the Federal Register notice published by the FDA on April 30, 2004 all pancreatic insufficiency drug products must submit an NDA for review and be approved by April 28, 2010. If the drug product has not been approved by the FDA, the product will be pulled from the market. Per the Division of Gastroenterology Products, these products are not currently under review within the Agency therefore Panokase products will be required to be removed from the market by April 28, 2010.

Failure Mode: Name Confusion	**Causes (could be multiple)**	**Rationale**
Pancreaze (Pancrelipase)	**Orthographic and/or phonetic similarities** **Product characteristics**	**Factors that would prevent wrong drug selection.**
Pancrease, Pancrease MT (Pancrelipase) *Stengths:* **Pancrease MT 4** 4000 USP Units Lipase/ 12,000 USP Units Amylase/ 12,0000 USP Units Protease, **Pancrease MT 10** 10,000 USP Units Lipase/ 30,000 USP Units Amylase/ 30,000 USP Units Protease, **Pancrease MT 16** 16,000 USP Units Lipase/ 48,000 USP Units Amylase/ 48,000 USP Units Protease, **Pancrease MT 25** 25,000 USP Units Lipase/ 75,000 USP Units Amylase/ 75,000 USP Units Protease, **Pancrease MT 32** 32,000 USP Units Lipase/ 90,000 USP Units Amylase/ 70,000 USP Units Protease oral capsules *Directions for use:* 500 to 2500 units/kg/meal by mouth	*Orthographic Similarities:* Both names are nearly identical with only a 'z' vs. an 's' in the last component of the names *Phonetic Similarities:* Both names begin with "Pancre"; both names contain three syllables; both "aze" and "ase" are pronounced identically *Overlapping Product Characteristics:* Both are given orally Both are dosed with meals or as directed by physician	The risk for medication error is decreased by the following factors: Pancrease and Pancrease MT are the same products in this review undergoing FDA approval and will be marketed under 'Pancreaze' once approved. Pancreaze will be marketed with the stand-alone proprietary name 'Pancreaze' without modifier, MT, when it is approved. One strength, Pancrease MT 32, will not be marketed as the submitted NDA only contained the Lipase strengths 4,200 USP Units, 10,500 USP Units, 16,800 USP Units and 20,000 USP Units. Otherwise, there is no difference in formulation between what is currently marketed and what is undergoing FDA approval. In order to meet current standards, the proposed Pancreaze labels and labeling will be revised to accurately reflect the USP units for all three enzymes of the active ingredient, and to correctly reflect the amount of USP units contained in each capsule. While there may be a period of overlap when both products are available in the market, it is anticipated that the product labels and labeling will be sufficient to distinguish the two products during this overlap period. In addition, these products have slight differences in the Lipase strengths (e.g. 4.2 vs. 4). Therefore, if a provider were to write a prescription for 'Pancrease' instead of 'Pancreaze', he or she would still have to write the strength since these are not single strength products. Any discrepancies in ordered strength or missing strength selection would need to be clarified with the provider before dispensing and administering.

Failure Mode: Name Confusion	**Causes (could be multiple)**	**Rationale**
Pancreaze (Pancrelipase)	**Orthographic and/or phonetic similarities** **Product characteristics**	**Factors that would prevent wrong drug selection.**
Pancrelipase (various names) *Panocaps, Panocaps MT (Panocaps)* 4500 USP Units Lipase/ 20,000 USP Units Amylase/ 25,000 USP Units Protease *(Panocaps MT)* 16,000 USP Units Lipase/ 48,000 USP Units Amylase/ 48,000 USP Units Protease, 20,000 USP Units Lipase/ 56,000 USP Units Amylase/ 44,000 USP Units Protease oral delayed release capsules *Panokase* 8,000 USP Units Lipase/ 30,000 USP Units Amylase/ 30,000 USP Units Protease 16,000 UPS Units Lipase/ 60,000 USP Units Amylase/ 60,000 USP Units Protease oral tablets *Pancrease, Pancrease MT* *Pancrease MT 4* 4000 USP Units Lipase/ 12,000 USP Units Amylase/ 12,0000 USP Units Protease, *Pancreae MT 10* 10,000 USP Units Lipase/ 30,000 USP Units Amylase/ 30,000 USP Units Protease, *Pancrease MT 16* 16,000 USP Units Lipase/ 48,000 USP Units Amylase/ 48,000 USP Units Protease, *Pancrease MT 25* 25,000 USP Units Lipase/ 75,000 USP Units Amylase/ 75,000 USP Units Protease, *Pancrease MT 32* 32,000 USP Units Lipase/ 90,000 USP Units Amylase/ 70,000 USP Units Protease oral capsules	*Orthographic similarities* Both names have same beginning (‘Pancre’) *Overlapping product characteristics* All products are given orally All products are pancreatic enzymes with the same directions for use (three times a day with meals) All products will be used in the same population and prescribed by the same providers for the same diagnosis	The risk for medication error is decreased by the following factors: *Orthographic differences:* -Pancreaze contains 9 letters vs. Pancrelipase contains 12 letters which makes Pancrelipase look significantly longer. -Pancrealipase contains an upstroke, ‘l’ vs. Pancreaze has no upstrokes. -The down-stroke in Pancrelipase, ‘p’ has three letters that follow vs. if Pancreaze is scripted with down-stroke ‘z’ there is only one letter that follows. *Product characteristics* - The dosing for Pancreaze products is reliant on only the Lipase component. There is no direct strength overlap in the Lipase components for these Pancreaze and the other Pancrelipase products.

Failure Mode: Name Confusion	**Causes (could be multiple)**	**Rationale**
Pancreaze (Pancrelipase)	**Orthographic and/or phonetic similarities** **Product characteristics**	**Factors that would prevent wrong drug selection.**
Pacerone (Amiodarone hydrochloride) 100 mg, 200 mg oral tablets Loading dose: 800 mg to 1600 mg by mouth daily Maintenance dose: 400 mg to 800 mg daily as single or twice daily dose	*Orthographic similarities* Both names begin with 'Pa' Both names are similar in length *Overlapping product characteristics* Both are orally administered Capsule vs. Tablet dosage form	The risk for medication error is decreased by the following factors: Orthographic characteristics: - The 'z' in Pancreaze will have a downstroke, if scripted, which will help differ Pancreaze from Pacerone, which has no down-strokes. Product characteristics: - There is no dose overlap for Pancreaze and Pacerone (Pancreaze dose is now 4,200 USP Units Lipase vs. 100 mg, 200 mg, 400 mg or 800 mg for Pacerone). - Pancrease is dosed based on Lipase units, designated either as 'U' or units vs. Pacerone is dosed based on 'mg'. - Pancreaze is dosed three times a day with meals vs. Pacerone is dosed once or twice daily. The AERS case that was uncovered during the Pancrease MT search was due to orthographic similarity with Pacerone, as stated in the report. The reporter acknowledges that there is no overlap in the dosing schedules with Pancrease MT and Pacerone. No other cases were found in AERS between Pancrease MT and Pacerone. With the new spelling of Pancreaze (with the 'z') and the new doses of Lipase, there is less similarity and overlap with Pacerone, thereby making this error even less likely to occur.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22523	ORIG-1	JOHNSON & JOHNSON PHARMACEUTICAL RESEARCH & DEVELOPMENT LLC	Pancrelipase Microtablets

---

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

/s/

ANNE CRANDALL
01/25/2010

MELINA N GRIFFIS
01/25/2010

DENISE P TOYER
01/25/2010

DENISE P TOYER on behalf of CAROL A HOLQUIST
01/25/2010