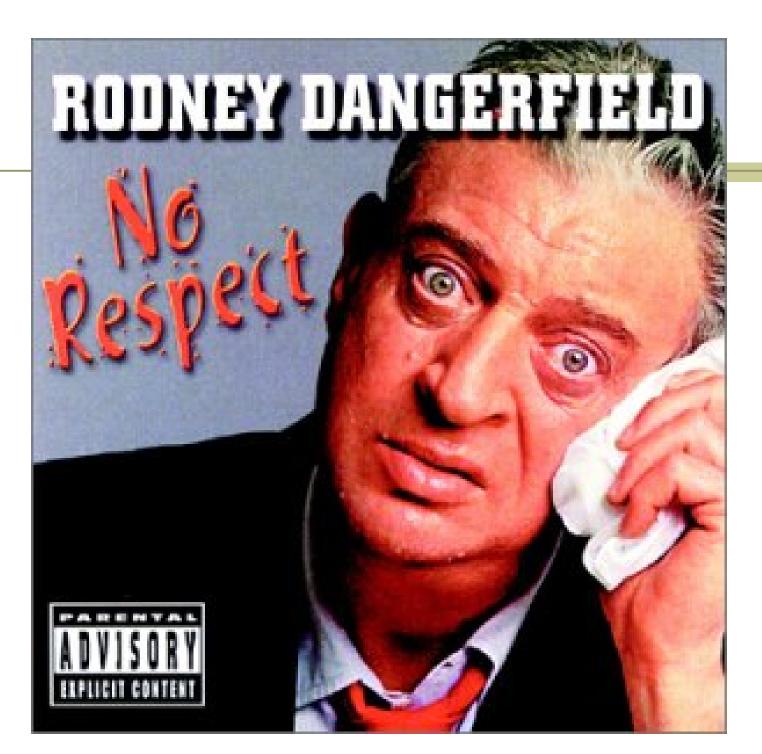


Generic Labeling 2006

CDR Koung Lee, RPh, USPHS

Labeling Review Branch
Division of Labeling & Program Support/Office of Generic Drugs
Center for Drug Evaluation & Research/U.S. Food & Drug Administration
(301)-827-7336 E-mail koung.lee@fda.hhs.gov



Page 2

"I think labeling is a complete waste of time,"... "It's much beloved by industry, it's much beloved by FDA and it's much beloved by lawyers, but it's worthless nonetheless."

The Pink Sheets
January 23, 2006
Volume 68 | Number 004 | page 8

"...studies show that fewer than one in 10 physicians routinely read drug labels, which provide the most complete information about a drug's dangers and uses."

The New York Times

"New Drug Label Rule Is Intended to Reduce Medical Errors"

By Gardiner Harris | January 19, 2006

Changes in Labeling

- Best Pharmaceuticals for Children's Act
- The Electronic Labeling Rule
- Structured Product Labeling
- Physician Labeling Rule

"Same As" Principle

- 505(j)(2)(A) An abbreviated application for a new drug shall contain-
 - (v) information to show that the labeling proposed for the new drug is the same as the labeling approved for the listed drug referred to in clause (i) except for changes required because of differences approved under a petition filed under subparagraph (C) or because the new drug and the listed drug are produced or distributed by different manufacturers.

21 CFR 314.94(8)

Such differences between the applicant's proposed labeling and labeling approved for the reference listed drug may include differences in expiration date, formulation, bioavailability, or pharmacokinetics, labeling revisions made to comply with current FDA labeling guidelines or other guidance, or omission of an indication or other aspect of labeling protected by patent or accorded exclusivity under section 505(j)(4)(D) of the act.

Pediatric Exclusivity Dilemma For Generics

When information protected by pediatric exclusivity is carved out, the generic product ends up misbranded because the labeling is not in compliance with 21 CFR 201.57(f)(9) which pertains the "Pediatric use" subsection of the PRECAUTIONS section.

Best Pharmaceuticals For Children's Act (BPCA)

Signed into law on January 4, 2002.

Amended the Federal Food, Drug, and Cosmetic Act to improve the safety and efficacy of pharmaceuticals for children.

Best Pharmaceuticals For Children's Act (BPCA)

- Section 11 of the Act addresses the prompt approval of drugs under section 505(j) when pediatric information is added to the label.
- Item (2) of this section states that the Secretary may require that the labeling of a drug approved under section 505(j) that omits a pediatric indication or other aspect of labeling... include –
 - "(A) a statement that, because of marketing exclusivity for a manufacturer-- (i) the drug is not labeled for pediatric use... and
 - (B) a statement of any appropriate pediatric contraindications, warnings, or precautions that the Secretary considers necessary."

Creating a Model Labeling For Generics under BPCA

- 1. Consults the pediatric committee.
- Incorporate the comments from the pediatric committee & consult the new drug reviewing division.
- 3. Incorporate both the pediatric committee & the new drug reviewing division's comments & consult Office of Chief Counsel (OCC).
- 4. Meet with representatives from the pediatric committee, new drugs, & OCC.

Consult to the Pediatric Committee

CONSULT TABLE: Comparison of Zofran Injection Labeling Previously Approved on November 24, 2004, Recently Approved on March 25, 2005, and OGD's Proposed Labeling for "Generic Zofran"

PREVIOUS INSERT TEXT SLR-034 (AP November 24, 2004) Uderline Indicates revisions in the new approved labeling	NEW INSERT TEXT with Pediatrio INFORMATION from 3-025 (APPROVED March 26, 2006) High ighted text indicates new approved language and highlighted text with strikeouts are proposed text for carve out.	OGD's Proposed Tex for "Generic Zofran Injection" proeucts.	COMMENTS, RECOMMENDATIONS & PROPOSED TEXT DRAFTED BY THE OFFICE OF GENERIC DRUGS (OGD)
Pharmacodynamics: Ondersetron is a selective 5-HTI receptor satisfying the While confidence of the S-HTI receptor satisfying the While confidence of the selection has not been fally characterized, it is not a departitude ecoeptor satisfying the section in cooptions of the 5-HTI, type are present both peripherally on vagal serve terminals and centrally in the characterized, it is not a departitude ecoeptor satisfying the selection in coeptors of the 5-HTI, type are present both peripherally on vagal serve terminals and centrally, in the other server is selected action in characterizery species of the serve posterize. It is not certainly, peripherally, or in both site. However, cytotrocic chemotherapy appears to be associated with release of secretian from the enterocheroratelia cells of the small intestine. In humana, univery 5-HIIAA (5-hydroxymidolescetic satis) excretion increases after cispheirs administration in pessible with the creat of sension. The released services may stimulate the vagal afferents through the 5-HII, receptors and initiate the ventiling reflex. In animals, the emetic response to cisplatin can be provented by protreatment with an inhibitor of secretion synthesis, bilateral abhorimal vagotomy and greater splanchraic nerve section, or perbestment with a serrotomin 5-HTI, receptor anlagenest. In normal volunteers, single LV, doese of 0.15 mg/kg of ordensetion had no effect on ecophageal motility, gastist motility, lower ecophageal splancher pressure, or email intestinal tensit time. In another study in six normal male volunteers, a life of the drug on certific contrast on the volunteers, blood pressure, or electrocardiogness (ECO), Multiday administratic transit in normal volunteers. Ondersetron has no effect on placems polacin concentrations.	CLINICAL PHARMACOLOGY Pharmacodynamics: Ondersetten is a selective 5-HT, receptor ortagorism. While endersetten in mechanism of action has not been fully characterized, it is not a departitio-receptor artagorism. Secotomic receptors of the 5-HT type are present both periphenelly or vagal nerve terminals and centrally in the chemoreceptor trigger zone of the area portreas. It is not certain whether endeaders in other properties action in chemotherapy-induced measure and ventiling is mediated centrally, periphenelly, or in both abe. However, cytotoxic chemotherapy appears to be associated with release of seroters from the enterocheromatin cells of the small intestine. In humans, uninary 5-HEA (5-hydroxyindelsecutic acid) exerction increases after cisplains administration in parallel with the creat of worsting. The released secretion improves and initiate the wenting reflect. In animals, the emotic response to cisplatin can be prevented by pretreatment with an infinitive through the 5-HT, receptors and initiate the wenting reflect. In animals, the emotic response to cisplatin can be prevented by pretreatment with an infinitive anythese, believed affected sugotomy and greater aplanches neave section, or pretreatment with a serotomic synthese, believed addressed sugotomy and greater aplanches neave section, or pretreatment with a serotomic synthese, believed addressed sugotomy and greater aplanches neave section, or pretreatment with a serotomic sintestinal tensit time. In acother study is six normal male volunteers, a figure does infused over 5 minutes showed no effect of the drug on cardiac culput, heart rate, stroke volume, blood pressure, or electrocardiogram (BCO). Multiday administration of ordersetors has been effect of the ore one offect on plasma prolactin concentrations.	CLINICAL PHARMACOLOGY Pharmacodynamics: Ondersetten is a selective 5-HT, receptor artagonist. While orderectored, it is not a department of action has not been fully characterized, it is not a department of proceeding of the period of the	"smatir" it replaced by "names and vomiting" No replacement statements necessary. "smatir" it replaced by "comiting". No replacement statements necessary.

Consult to New Drug Reviewing Division

CONSULT TABLE : Comparison of Zofran Injection Labeling Previously Approved on November 24, 2004, Recently Approved on March 25, 2005, and OGD's Proposed Labeling for "Generic Zofran"

PREVIOUS INSERT TEXT SLR-034 (AP November 24, 2004) Uderline Indicates revisions in the new approved labeling	NEW INSERT TEXT with Pediatric INFORMATION from S-025 (APPROVED March 25, 2005) Highlighted text indicates new approved language and highlighted text with atrikeouts are proposed text for carve out.	OGD's Version	Recommendation from the Division of Pediatric Drug Development	COMMENTS, RECOMMENDATIONS & PROPOSED TEXT DRAFTED THE OFFICE OF GENERIC DR (OGD)
CLINICAL PHARMACOLOGY Pharmacodynamics: Ondensetron is a selective 5-HT, receptor antegonist. While condensetron's mechanism of action has not been fully characterized, it is not	CLINICAL PHARMACOLOGY Pharmacodynamics: Ondenseron is a relective 5-HT, receptor antagonist. While ondenseron's mechanism of action has not been fully characterized, it is not	CLINICAL PHARMACOLOGY Pharmacodynamics: Ondanseron is a selective 5-HT, receptor antagonist. While ondanseron's machinism of action has not been fally characterized, it is not	CLINICAL PHARMACOLOGY Pharmacodynamics: Ondersetron is a selective 5-HT, receptor suragonist. While ondansecon's machanism of action has not been fully characterized, it is not	"emesis" is replaced by "nausea as
a dopamine-receptor antigonist. Seretonis receptors of the 5-HT, type are present both peripherally on usgal nerve terminals and centrally in the chemoreceptor trigger zone of the area posteren. It is not certain whether ondenseron's entirense textion in chemorherapy-induced-emests is mediated centrally, peripherally, or in both sites. However, cytotoxic chemotherapy appears to be associated with release of secrotonis from the enterochromatin cells of the small intestine. In humans, unitary 5-HLAA (5-hydroxyindelescetic acid) excretion increases after cisplatin administration in parallel with the onset of emests. The released secretonis may stimulate the wagal afferents through the 5-HT, receptors and initiate the womiting reflex.	a departite-receptor entragonist Serotomin receptors of the 5-HT, type are present both partiplearally on tragal nerve terminals and centrally in the chemorecoptor trigger sone of the area posteron. It is not certain whether outdensetron's antemetic action in chemotherapy-induced natures and womiting is mediated controlly, partiplearally, or in both sites. However, cytotoxic chemotherapy appears to be associated with release of serotomic from the auterochromatine cells of the small investine. In branens, writery 5-HTAA (5-hydroxyindoleacetic actid) excretion increases after cisplaint administration in parallel with the onset of tomiting. The released serotomin many stimulates the ungal afferents through the 5-HT, receptors and initiate the womiting reflex.	a deparatine-receptor antagonist. Sectionin receptors of the 5-HT, type are present both peripherally on vagal nerve terminals and centrally in the chemoreceptor trigger zone of the area postream. It is not certain whether outdensetron's antenset; action in chemotherapy-induced navases and vomiting is mediated centrally, peripherally, or in both sites. However, cytotoxic chemotherapy appears to be associated with release of service time from the enterochromatine realist of the small intestine. In humans, unitary 5-HIAA (3-hydroxyindoleacetic acid) excretion increases after cisplain administration in parallel with the onset of vomiting. The released service in may stimulate the wagal affectuals through the 5-HT, receptors and initiate the womiting reflex.	a deparatine-receptor antagonist. Seconomic receptors of the 5-HT, type are present both paripherally on ungal nerve terminals and contrally in the chemoreceptor trigger some of the area postrems. It is not certain whether condansatron's antemetic action in chemotherapy-induced natures and counting is mediated contrally, peripherally, or in both sites. However, cytoconic chemotherapy appears to be associated with release of seconom from the enterochemonifin calls of the small investine. In branans, writary 5-HTAA (5-hydroxyindoleacetic acid) excretion increases after cisplain administration in parallel with the onset of counting. The released seconomic may stimulate the ungal afferents through the 5-HT, receptors and initiate the womiting reflex.	"emests and nausea using the ipecacuanha model of emits. Both treatments were well tolerated by "no replacement statements necess "emests and nausea using the ipecacuanha model of emits. Both treatments were well tolerated" in replaced by "nausea and vomitis.
In animals, the emetic response to displatin can be prevented by pretreatment with an inhibitor of serotonin synthesis, bilasteral abdominal wagotomy and greater splanchnic nerve section, or pretreatment with a serotonin 5-HT, receptor antagonist.	In animals, the emetic response to displatin can be prevented by pestreatment with an inhibitor of secotomin synthesis, bilateral abdominal vegotomy and greater splanchmic nerve section, or pretreatment with a secotomin 5-HT ₃ receptor antagonist.	In animals, the emetic response to displatin can be prevented by pretreatment with an inhabitor of serotomin synthesis, bilateral abdominal vagotomy and greater splanchmic nerve section, or pretreatment with a serotomin 5-HT ₃ receptor antagonist.	In animals, the emetic response to displatin can be prevented by pretreatment with an inhibitor of serotonin synthesis, bilateral abdominal vagotony and greater splanchnic nerve section, or pretreatment with a serotonin 5-HT ₃ receptor antagonist.	replaced by nauses and volunting the ipecacuanha model of emeris." No replacement statements necess
In normal volunteers, single I.V. doses of 0.15 mg/kg of outdansetrou had no effect on esophageal motility, gastric motility, lower esophageal sphincher pressure, or small intestinal transit time. In another study in six normal male volunteers, a 16-mg dose infused over 5 minutes showed no effect of the drug on cardiac output, heart rate, stroke volume, blood pressure, or electrocardiogram (ECG). Multiday administration of ondensetron has been shown to slow colonic transit in normal volunteers. Ondensetron has no effect on plasms productin concentrations.	In normal volunteers, single LV, doses of 0.15 mg/kg of ondensetron had no effect on escoplaged motility, gastric motility, lower escoplaged motility, gastric motility, lower escoplaged sphincter pressure, or small intestinal transit time. In another study in six normal male volunteers, a 16-mg dose infused over 5 minutes showed no effect of the drug on cardiac output, heart rate, stroke volume, blood pressure, or electrocardiogram (ECG). Multiday administration of codensetron has been shown to slow colonic transit in normal volunteers. Oudensetron has no effect on plasma prolactin concentrations.	In normal volunteers, single I.V. doses of 0.15 mg/kg of ondemocron had no effect on ecophageal motality, gastric motality, lower ecophageal sphincter pressure, or small intestinal transit time. In another study in six normal male volunteers, a 16-mg dose infused over 5 minutes showed no effect of the drug on cardiac output, heart zee, stroke volume, blood prespagagopeler gocardiogram (ECG). Multiday administration of ondemocron has been shown to slow colonic transit in normal volunteers. Ondemocron has no effect on plasma profectin concentrations.	In normal volunteers, single LV, doses of 0.15 mg/kg of ondensetron had no effect on ecophageal motility, gastric motility, lower ecophageal sphincter pressure, or small intestinal transit time. In another study in six normal male volunteers, a 16-mg dose infused over 5 minutes showed no effect of the drug on cardiac output, heart rate, stroke volume, blood pressure, or electrocardiogram (ECG). Multiday administration of condensetron has been shown to slow colonic transit in normal volunteers. Oudansetron has no effect on plasma prolactin concentrations.	

Consult to Office of Chief Counsel

CONSULT TABLE: Comparison of Zofran Injection Labeling Previously Approved on November 24, 2004,
Recently Approved on March 25, 2005, OGD's Proposed Labeling for "Generic Zofran", Division of Pediatric Drug Development (DPDD) Recommendations and Division of Gastrointestinal and Coagulation Drug Products

PREVIOUS INSERT TEXT SLR-034 (AP November 24, 2004) Uderline indicates revisions in the new approved labeling	NEW INSERT TEXT with Pediatrio INFORMATION from 8-025 (APPROVED March 25, 2006) Highlighted text incloates new approved language and	Text with strikeouts are proposed for corve out and the underlined text are replacement statements recommended by OGD.	Revised based on Division of Pediatrio Brug Development Recommendation Memorandum dated June 6, 2006	Revised based on the Division of Gastrointestlanal	Comments	
CLINICAL PHARMACOLOGY	CLINICAL PHARMACOLOGY	CLINICAL PHARMACOLOGY	CLINICAL PHARMACOLOGY	CLINICAL PHARMACOLOGY		
Pharmacodynamics: Orderestron is a selective S-HT, receptor antagenist. While endanastron's mechanism of their has not been fully characteriorid, it is not a deparation-exceptor artisponist. Serotomin receptors of the S-HT, type are present both peripherally on vegal naive terminals and centrally in the chemoreospoter trigger zone of the sens postroma. It is not certain whether endanaetropy-induced-amounts is mediated centrally, peripherally, or in both sites. However, cytotoxic chemoflaterapy supports to be associated with release of serotoxin from the enterochromaffin cells of the small intestine. In humans, wiresey S-HIAA	Pharmacodynamics: Onderetron is a selective 5-HT, receptor autagonist. While condensation's mechanism of action has not been fully cheapterized, it is not a department of the 5-HT; type are present both peripherally on vagal rerve terminals and controlly in the chemoreospheritigar zone of the sea proteons. It is not certain whether endametron's artisensitic action in chemotherapy-induced transaction whether condensations artisensitic action in chemotherapy-induced transaction worthing is mediated centrally, peripherally, or in both sites. However, cyletoxic chemotherapy appears to be associated with release of according from the enterochromatin cells of the small intestine. In human, urinary 5-HIAA (S-hydroxyindeleasestic acid) encretion increases after cisplatin administration in sensite with the ones of varieties. The	Pharmacodynamics: Ondersetron is a selective 5-HT, receptor satisgment. While codessetror's mechanism of action has not been fully characterized, it is not a department of the 5-HT, type are present both puriphenelly on usual narve. Jerminals and continuity in the characteristic action in characteristic product of rances and comiting is medicate centrally, perspectively, or in both sites. However, cylotoxic characteristic action from the materiochromaffin cells of the small intestine. In human, uninary 5-HIAA (S-bydroxyinchlesserie acid) exception increases after cipitain administration in narollel with the const of ventical. The	Pharmacodynamics: Ordensetron is a selective 5-HT, receptor artisporist. While ordensetroris mechanism of action has not been fully characterized, it is not a departime exceptor artisporist. Sectomin receptor of the 5-HT, type are prisont both peripherally on regulatorial terminals and centrally in the characteristic action in characteristic posterior. It is not certain whether ordensetroris entirentic action in characteristic protection in characteristic protection in the continuity of the continuity and continuity or in both sites. However, cytotoxic characteristics are described in the centerochromeffin cells of the small intestine. In humans, trinary 5-HIAA (5-hydroxyinsdescribe actid) exception increases after citipatin administration in seculal with the most of vomiting The	Pharmacodynamics: Ordensetron is a selective S-HT, receptor suragonist. While ordensetron's mechanism of action has not been fully characterized, it is not a dopartime-receptor sattagonist. Serotomin receptors of the S-HT, type are possibled particularly in the chemoreceptor temper zone of the area postures. It is not certain whether ordensetron's entiremental and certainly in the chemoreceptor trigger zone of the area postures. It is not certain whether ordensetron's entiremental action in chemotherapy induced reasons and ventiting in mediated certainly, peripherally, or in both sites. However, cytotoxic chemotherapy appears to be associated with release of serotomin from the enter-chromatin cells of the small intestine. In humans, urinery S-HIAA (S-hydroxyindelsectic acid/exerction increases after cisplatin administration in received with the center of vention. The	"emedi" in replaced by "names and namefring". No replacement statement necessary. "emedi" in replaced by "comiting". No replacement statement	
(5-hydroxyindeleacntic acid) exerction increases after cirplatin administration in perallel with the onset of ensess. The released servicein may stimulate the vagal affects through the 5-HT ₁	released serotonin may stimulate the vagal afferents through the 5-HT, receptors and initiate the vomiting reflex. (Percellimate paragraph in the	released services may stimulate the vagal afferents through the 5-HT ₁ receptors and initiate the ventring reflex. (Penultimete paragraph in the	released seretoein may stimulate the vagal afforests through the 5-HT ₁ receptors and initiate the ventting reflex. (Penultimate paragraph in the	released services may stimulate the vagal affects through the 5-HT, receptors and initiate the vocating reflex. (Penultimate paragraph in the	"emerit and	
receptors and initiate the verniting reflex. (Penultimate paragraph in the "Pharmacodynamics" subsection) In a gender-balanced pharmacodynamic study (n = 56), ordametres 4 mg administered intervenously or infrastructularly was dynamically similar in the prevention of generic and names using the incommon small of amenical subsections of the common study of the prevention of generic and subsections.	"Pharmacodynamics" subsection) In a gender-balanced pharmacodynamic study (n = 56), orders etcon 4 mg administered introvencently or intransacciarly was dissented by intransacciarly was dissented in the prevention of names and voniting using the ipocacuants model of enterior.	"Pharmacodynamics" subsection) In a gooder-balanced pharmacodynamic study (n = 56), codusection 4 mg administered influencesoly or intramacodisely was dynamically similar in the prevention of natures and vomiting using the iperacuarba model of emais.	"Pharmacodynamics" subsection) In a gender-balenced pharmacodynamic study (n = 56), ondersetron 4 mg administered intravenously or intravenously the dynamically similar in the provention of nauses and vomiting using the specacusaha model of ensein.	"Pharmacodynamics" subsection) In a gender-balanced pharmacodynamic study (n = 56), ordersetten 4 mg administred introvencusly or inframacolacty was dynamically similar in the pervention of natures and vomiting using the ipecacuscha model of ornesis.	inecacusaha model of emit. Both treatments mane well telerated" in replaced by "names and ventifing using the inecacusaha model of ement." No replacement statement	

TIME

- Creating the Model Labeling is time consuming.
 - Preparing Consults
 - Waiting for the completed reviews of the consults.
 - Scheduling meetings
 - Preparing the final model labeling
 - Disseminating the model labeling
- Usually takes months to create the model.
- OGD is working to streamline this process.

The Electronic Labeling Rule

- Effective June 8, 2004
- Requires that "the content of labeling be submitted electronically in a form that FDA can process, review, and archive".

Portable Document Format (PDF) Attributes

- Can be used in Adobe for comparison
- Can be used to submit final printed labeling in place of 12 paper copies.

PDF Limitation



Structured Product Labeling (SPL)

- Implemented on October 31, 2005
- It is the electronic form that FDA has adopted to process, review, and archive the insert labeling.
- SPL is the content of labeling in a standardized electronic file format with tagged blocks of text and data elements in XML.

Purpose of SPL

- Improve patient safety through accessible drug product information
- Support initiatives to improve patient care by better management of health care information
 - Electronic prescribing
 - Possibly the electronic health record (EHR), which will provide health care providers, patients, and other authorized users access to patient information in electronic format
 - The DailyMed, a new way to distribute up-to-date and comprehensive medication information in a computerized format for use in health care information systems.
 - Decision support systems
- Meets the mandate in Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (Public Law 108-173)

SPL Advantages over PDF

- The exchange of labeling changes with SPL will become much easier and more efficient for both FDA and manufacturers. For example, with SPL, only the sections or data elements of the labeling that are changed needs to be submitted rather than the entire insert labeling.
- SPL can be used to exchange information needed for drug listing, thus eliminating redundant data collection and improving efficiency.

Status of SPL Submissions

- Number of SPL loaded in the ELIPS is____.
- Approximately 80% of SPLs are rejected due to validation problems.
- For generics that are not listed as the reference listed drug, the option to submit SPL within 30 days after the RLD SPL is posted on the DailyMed website is still in effect.

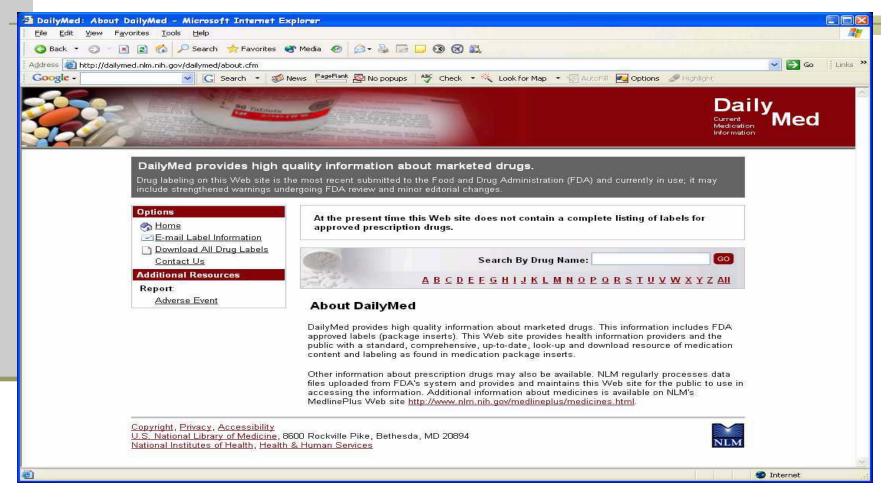
ELIPS

- Electronic Labeling Information Processing System (ELIPS)
 - Designed and constructed by Northrop-Grumman
 - Contracted & Implemented by OIT
 - ELIPS is the system the labeling reviewers will use to review and process SPL.

ELIPS

- Scans Electronic Document Room (EDR)
 - Every 5 minutes
 - Validation (Tier 2) of SPL
- Validates the labeling for SPL standards
- Puts copy of SPL into ELIPS label repository
- Assigns Label Coordinator and Reviewers to Labeling
- Allows editing of the SPL
- Allows transmission of SPL to the National Library of Medicine

DailyMed Web Site

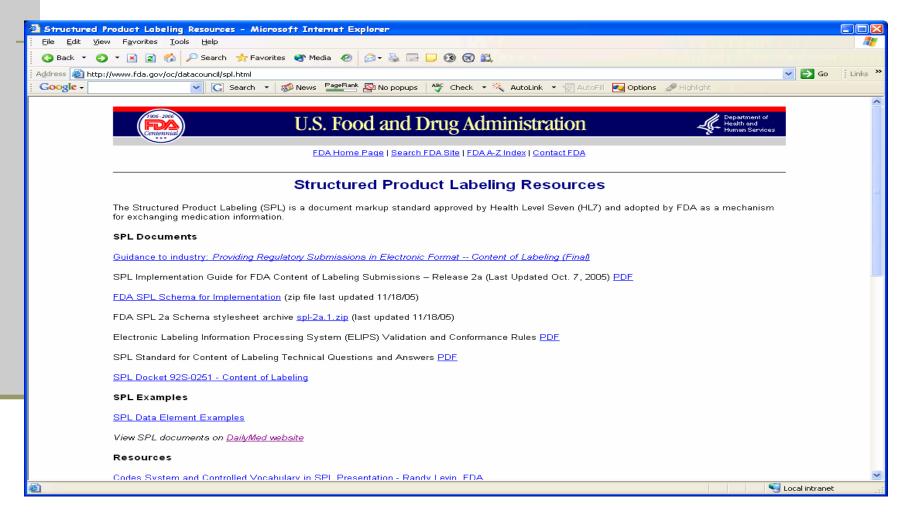


http://dailymed.nlm.nih.gov/dailymed/about.cfm

Things to Remember When Submitting SPL

- Place the electronic media immediately after the cover letter.
- Continue submitting side by side annotated labeling.
- Continue submitting final printed labeling for approval.
- Continue submitting a MS Word version of the insert labeling.

SPL Resources



http://www.fda.gov/oc/datacouncil/spl.html

Physician Labeling Rule

- Effective on June 30, 2006
- PLR is the first major change in the insert labeling in 25 years.
- It is designed to make the insert labeling easier to read and understand.
- Addition of Highlights and Table of Contents
- Revision and Reorganization of the section of the insert labeling.

Highlights

- Recent Labeling Changes
- INDICATIONS AND USAGE
- DOSAGE AND ADMINISTRATION
- HOW SUPPLIED
- CONTRAINDICATIONS
- WARNINGS AND PRECAUTIONS
- MedWatch phone number for patients to report adverse drug reactions

Example of Fictional Highlights of Prescribing Information Based on Physician Labeling Rule

(spurilous hypothetic chloride) Tablets or Capsules for oral use [fictional drug]
RECENT LABELING CHANGES
Adjunct therapy with a sulfonylurea to lower blood glucose in patients with Type 2 diabetes whose hyperglycemia cannot be controlled by die and exercise (1.1)
Initial dose is 100 mg once every morning and may be titrated up to 300mg (2.1)
Tablets: 100 mg (3) Capsules: 100 mg (3)
WARNINGS/PRECAUTIONS

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Hepatic dysfunction leading to acute liver failure may occur, typically within 3 months of initiation (5.2)

Evaluate liver function prior to initiating Ocracephalose and monitor weekly for 3 months. Discontinue if LFTs increase > 3 times upper limit of normal (5.2)

Severe depression with suicidal ideation occurred in 2% of patients. Discontinue Ocracephalose or initiate antidepressant therapy if depression occurs (5.3)

Hypoglycemia can occur with insufficient caloric intake and use of alcohol (5.5, 6.2)

Most Common Adverse Reactions (> 5%) (8)

somnolence, dry mouth, nightmares, and sexual disorders

To report SUSPECTED SERIOUS ADRs, call (manufacturer) at (phone#) or FDA's MedWatch at 1-800-FDA-1088

------DRUG INTERACTIONS------

Domecattus reduce domecattus dose by one-half (5.4, 6.1) Alcohol: increases incidence of hypoglycemia (6.2)

-----USE IN SPECIFIC POPULATIONS-----

Hepatic impairment: Contraindicated in patients with hepatic impairment (4, 7.6)

---See P for PATIENT COUNSELING INFORMATION and --Ocracephalose's approved patient labeling

These highlights do not include all the information needed to prescribe Ocracephalose safely and effectively. See Ocracephalose's comprehensive prescribing information provided below.

Revised: 12/2003

Effect of PLR on Generics

- Generics still need to be the same as the RLD.
- PLR will most likely be posted in SPL

PLR Implementation Plan

TABLE 5 .-- IMPLEMENTATION PLAN

Applications (NDAs, BLAs, and Efficacy Supplements) Required to Conform to New Labeling Requirements	Time by Which Conforming Labeling Must Be Submitted to the Agency for Approval
Applications submitted on or after June 30, 2006	Time of submission
Applications pending on June 30, 2006 and applications approved 0 to 1 year before June 30, 2006	June 30, 2009
Applications approved 1 to 2 years before June 30, 2006	June 30, 2010
Applications approved 2 to 3 years before June 30, 2006	June 30, 2011
Applications approved 3 to 4 years before June 30, 2006	June 30, 2012
Applications approved 4 to 5 years before June 30, 2006	June 30, 2013
Applications approved more than 5 years before June 30, 2006	Voluntarily at any time

What Next? Do we need FPL?

YES! However...

Challenges For the Labeling Review Branch

1. Increased workload

2. SPL: Learning new system, reviewing data elements and managing the release of SPL to NLM

3. Complicated patent and exclusivity issues

Challenge # 1

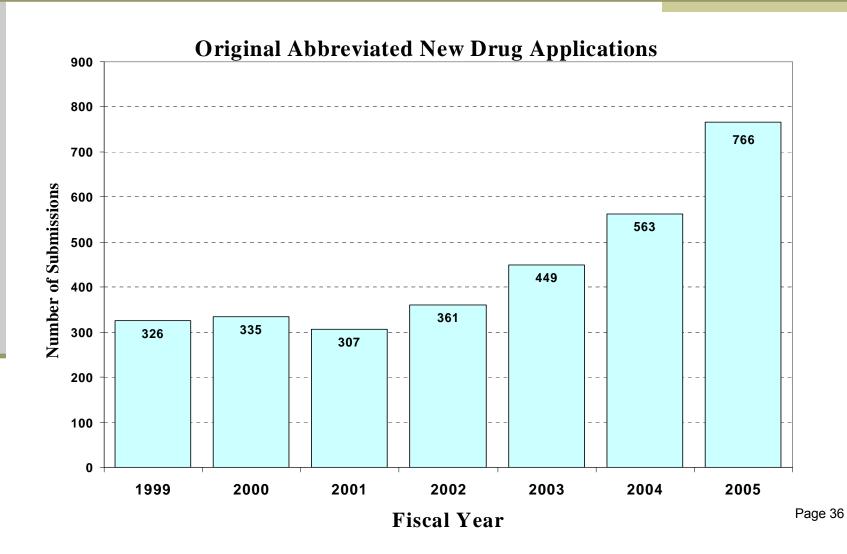
washingtonpost.com

Generic Drugs Hit Backlog At FDA

No Plans to Expand Review Capabilities

By Marc Kaufman Washington Post Staff Writer Saturday, February 4, 2006; A01

Workload



OGD Labeling Review Branch

John Grace (Team Leader)

- Angela Payne
- James Barlow
- Ruby Wu
- Postelle Birch
- Beverly Weitzman
- Ann Vu

Lillie Golson (Team Leader)

- Adolph Vezza
- Chan Park
- Jacqueline Counsel
- Melaine Shin
- Michelle Dillahunt
- Koung Lee

Challenge # 2

- SPL
 - Learning how to use ELIPS
 - Processing SPL
 - Managing SPL
 - Establishing SPL Legacy Labeling

Challenge # 3

- Patent and Exclusivity
 - Complicated
 - Time Consuming
 - PLR

How Can Industry Help?

- Submit SPL
- Submit all labeling electronically
- Submit supporting labeling information electronically
- Notify labeling reviewers when amending patent certifications
- Submit Side by Side annotated labeling with detail explanation of the differences.
- Check Drugs@FDA website

Supporting Labeling Information

- Component and Composition
- Patent certification and Exclusivity statement
- Conditions used to collect stability data (e.g.,Temperature and RH)
- Container/Closure system (including light transmission test if applicable)
- Provide an accurate description of the solid oral dosage form or provide a picture or image depicting actual size and color.
- Identify the manufacturer

SUMMARY

Significant Changes in labeling at the turn of the century have created an environment to improve dissemination of updated drug information and allow for better utilization of that information.

The Labeling Review Branch has challenges but with new technology, new regulations, and support from industry and upper management, I think we'll be able to review labeling more efficiently and help approve generic applications when they become eligible for approval.