Patient Labeling 101

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Patient Labeling

Consists of:

- Medication Guides (MG)

- Patient Package Inserts (PPI)

- Instructions for Use (IFU)

Medication Guides

Part 208 of 21 CFR

MG required if FDA determines one or more circumstances exist:

1. patient labeling could help prevent serious AEs

2. serious risks: could affect patient's decision to use

3. patient adherence to directions crucial to effectiveness

Medication Guides

FDA-approved patient labeling and a component of REMS

- Primarily for outpatient Rx products with serious & significant public health concerns

- Based on (not in conflict with) Professional Information (PI)

- Format and content
  - At least 10 point font
  - Written in nontechnical language
  - Specified section headings (Q & A)
    - relevant to drug product

Medication Guides

Distribution Requirements

- Mfrs must provide sufficient #s of MGs or means for the dispenser to produce
- Dispenser required to provide MG when product is dispensed

Medication Guides

- **In the past, a Medication Guide was approved and considered only part of labeling**

- **Now, any drug that requires a new Medication Guide is considered to have a REMS**

  – Some drugs with existing MGs may convert to a REMS if FDA determines that there is new safety information

A Few Words About Consumer Medication Information (CMI)

Consumer Medication Information (CMI):

- is information that is developed by third party companies, such as **First Databank Wolters Kluwer Health, and others.**

- is not part of FDA-approved labeling and is not reviewed by the Agency

Patient Labeling Review Process

- A collaborative effort between OND and OSE/DRISK

- DRISK is generally consulted by OND

- DRISK provides a formal review of patient labeling with recommended revisions

- DRISK works with OND to negotiate Patient Labeling with Applicants

Package Insert (PI)

MG = Medication Guide
PPI= Patient Package Insert
PIFU = Patient Instruction for Use

- Patient Labeling Reviewers rely on the PI to provide the basis for information that is included in patient labeling (PPI, MG, or PIFU)

- Review goal for PPI, MG, PIFU:
  - should be scientifically accurate, specific, and comprehensive, and *should not conflict* with PI information
  - weight given to and placement of information within patient labeling must be **consistent** with the weight given to and placement of information in the PI

Enhancing Readability of Patient Labeling Materials

General approaches to enhance readability:

- Patient labeling should be written at a 6 to 8th grade reading level

- Use of certain fonts: Verdana, Arial, or APHont size 11 or greater for better visibility

- Use of text boxes, bold font, and underlining to highlight important concepts

- Good use of white space, chunking, and bulleted formatting to enhance cognition

Patient Representative Q & A

We appreciate the questions that were forwarded to us for consideration.

Patient Representative Q & A (continued)

Many of the questions fall outside the scope of the Patient Labeling Team and should be addressed with OND. Examples:

- The PRO Guidance
- Inclusion of patient input regarding labeling
- Inclusion of quality of life issues in labeling
- Ensuring timely posting of updated labeling materials on the FDA web site, or timely distribution of updated printed materials

Patient Representative Q & A (continued)

Questions from Patient Representatives:

- Several Patient Representatives asked about including percentages of side effects and clinical trials statistics in patient labeling.

Patient Representative Q & A (continued)

- "Many of the materials are printed in pt. 2 type (or smaller!). Can FDA force the providers to make them legible w/o magnifying glasses?"

Patient Representative Q & A (continued)

- "Most patients do not read the labels if their doctor explained the drug and the side effects. Is there a way to print the label is such a way that it is Attractive to the reader?"

Patient Representative Q & A (continued)

- "Simply keeping track of the nomenclature (brand name, trade name, generic name, proprietary name, chemical name, etc.) is very confusing, even to professionals. FDA is making a real effort to remove such conflicts, but patients feel overwhelmed at times. Has any thought been given to creating some new system?"

Patient Representative Q & A (continued)

- "…how does this new drug I am about to start taking interacts with drugs I am already taking? In other words you should not take this drug with drugs X, Y, and Z."

Patient Representative Q & A (continued)

- "…I think it would be good to know, definitively, the process these pieces of information go through, the intended audience for each piece of information and then, ultimately how or if PRs (or anyone, for that matter) can weigh in and advocate for changes to be made to these informative pieces. …in my field of interest, asthma, there are PPIs which exist where there is no consistency whatsoever. In one paragraph, this word or that phrase is used and in the very next paragraph, a different word or different phrasing is used. While this is not so difficult for one who is immersed in this disease and in the lingo, I know that this would be difficult for the average person to try and follow when the words and phrases change over and over w/in the same document. Not to mention those persons when English is not their first (or second) language."

Thank you for your attention !

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Prescription Drug Information

- Human Prescription for Drug and Biological Products

- A prescription drug product label is a compilation of information about a product written by the manufacturer and approved by FDA

- Final Rule, Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products became effective in June 2006

Adverse Event Reporting

Adverse Event Reports Comes IN to FDA

Safety Information Goes OUT to the Public

MedWatch History

FDA Safety Information and Adverse Event Reporting Program
1993 to 2009

2009 - MedWatch, The FDA **Safety Information** and Adverse Event Reporting Program

1998 - MedWatch, The FDA Medical Products Reporting and Safety Information Program

1993 - MedWatch, The FDA Adverse Event Reporting Program

Introducing MedWatch, DA Kessler, MD, *JAMA*, 269 (21): 2765, June 2, 1993.

"Our **goal is to…more widely disseminate information** of the FDA's actions that have resulted from adverse event and product problem reporting.."

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FDA Website
www.fda.gov/medwatch

MedWatch Safety Information Out
MedWatch-issued product specific alerts

- FDA website
  - "your Internet gateway for timely safety information…."
- MedWatch Safety Alerts
  - Product-specific, timely and actionable alerts for drugs, biologics, devices and special nutritional products
- Monthly Drug Safety Labeling changes
  - 40-50 drugs with 80-100 changes/month to Boxed Warnings, Warning, Contraindications, Precautions, Adverse Reactions, Medication Guides

Monthly Safety Labeling Changes

- Clinically important safety labeling updates, including changes to the following labeling sections:
    - Boxed Warnings
    - Contraindications
    - Warnings and Precautions
    - Adverse Reactions
    - Patient Package Insert & Medication Guide
- In 2008:
    - 1157 safety changes
    - 561 PI's
    - 56 boxed warnings
    - 60 Medication Guides

Monthly Safety Labeling Changes

U.S. Food and Drug Administration

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Safety

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Home > Safety > MedWatch The FDA Safety Information and Adverse Event Reporting Program > Safety Information

MedWatch The FDA Safety Information and Adverse Event Reporting Program

Safety Information

Safety Alerts for Human Medical Products

Drug Safety Labeling Changes

Xenical (orlistat) capsules

Detailed View: Safety Labeling Changes Approved By FDA Center for Drug Evaluation and Research (CDER) – May 2010

Summary View

PRECAUTIONS
General

- There have been rare postmarketing reports of severe liver injury with hepatocellular necrosis or acute hepatic failure in patients treated with orlistat with some of these cases resulting in liver transplant or death. Patients should be instructed to report any symptoms of hepatic
  dy
  qu
  me   **PATIENT PACKAGE INSERT**
  le   **What are the possible risks of XENICAL?**
  ADVE
  Othe   • Xenical has been shown to reduce the absorption of certain vitamins. You should take a
          multivitamin containing vitamins D, E, K, and beta-carotene once a day at least 2 hours before
          or after the administration of Xenical, such as at bedtime.
- Ra   • Some patients taking Xenical may develop an increased risk for the development of kidney
  se   stones. Promptly report any symptoms of back pain or blood in the urine.
  of
  or   • Some patients prescribed Xenical may already be at increased risk for the formation of gall
  sy   stones. Weight loss with Xenical can increase the risk of gall stones. Promptly report any
  Ve   symptoms of pain in the upper right portion of the abdomen. The pain may be accompanied by
  in   nausea and vomiting.
  pa
  an   • There have been rare reports of severe liver injury in patients taking Xenical. Promptly
  orl   discontinue Xenical and contact your healthcare provider if you develop symptoms suggestive
  po   of liver impairment, such as loss of appetite, itching, yellowing of the skin, dark urine, light
  pa   colored stools, or right upper quadrant pain.

Drugs@FDA

Drugs@FDA
FDA Approved Drug Products

Start Over | **Back to Search Results** | **Back to Details**

Label and Approval History

Drug Name(s)	ZETIA (Brand Name Drug)
FDA Application No.	(NDA) 021445
Active Ingredient(s)	EZETIMIBE
Company	MSP SINGAPORE

Go to Approval History

Label Information

What information does a label include?
Note: Not all labels are available in electronic format from FDA.

View the **label approved on 07/21/2009 (PDF)** for ZETIA, NDA no. 021445

- To see older, previously-approved labels, go to the "**Approval History**" section of this page. Older labels are for historical information only and should not be used for clinical purposes.

Approval History
NDA 021445

Note: Not all reviews are available in electronic format from FDA.
Older labels are for historical information only, and should not be used for clinical purposes.
Approval dates can only be verified from 1984 to the present.

Click on a column header to re-sort the table:

Action Date	Supplement Number	Approval Type	Letters, Reviews, Labels, Patient Package Insert	Note
07/21/2009	026	Labeling Revision	Label (PDF) Letter (PDF)	
07/21/2009	027	Labeling Revision	Label (PDF) Letter (PDF)	
01/27/2009	025	Package Change	Label (PDF) Letter (PDF)	

Other FDA-approved safety information

- DailyMed Current Labeling

    – An FDA/National Library of Medicine collaboration

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

Patient Medication Information (PMI – aka CMI)
The Single-Document Solution

PMI — Giving Patients the Information They Need

- Patients need easy access to prescription medication information (PMI) that is clear, concise, current, accurate, actionable, and accessible

- 2008 Evaluation of Consumer Medication Information
  - 94% consumers received information with new prescriptions
  - 75% met the criteria for usefulness
  - Demonstrating the PMI need is not being met

Current System

- **Patient Package Inserts (PPI)** - prescription information developed by manufacturers, approved by FDA and dispensed with specific products, e.g. oral contraceptives, estrogen-containing products

- **Consumer Medication Information (CMI)** - prescription drug information developed by pharmacies or an outside company, voluntarily distributed to consumers by pharmacies

- **Medication Guides** - prescription drug information for certain medications that "pose a serious and significant public health concern," developed by the manufacturer, approved by FDA, and required to be distributed to consumers each time the medication is dispensed

A New Paradigm —
The Single-Document Solution

- Over 22,000 marketed products requiring PMI

- Eliminate PPIs, CMI, and Medication Guides

- FDA will propose a new regulation

  - Require all prescription drugs to have a single PMI document

  - Describe the content and format

  - Define evaluation criteria and standards

  - Require manufacturers to consumer-test

- Source of PMI document – FDA approved professional labeling

- Manufacturers must develop, test, and submit PMI to an electronic repository

PMI Activities

- Feature *Rheutopia*, fictitious drug for RA and other conditions
  - Multiple indications and multiple serious risks
  - Unique administration (injection)

- Myriad of issues to be addressed, including:
  - Design Quality Management System for monitoring/evaluation with enforcement authority
  - Processes for evaluation
  - Submission and distribution
  - PMI repository and access
  - Interim solutions for phased-in implementation strategy

The Prototypes

DRAFT PROTOTYPE 1
PATIENT INFORMATION
Rheutopia™ [Roo-toh-pee-ah] (also known as arixalate)

Important Warning: Serious Infections
- Rheutopia affects the immune system. It can lower your ability to fight infections. Do not use Rheutopia if you have an active infection.
- People taking Rheutopia have gotten serious infections including tuberculosis (TB) and infections caused by viruses, fungi, or bacteria. Some people have died from these infections.

What Does Rheutopia Treat?
- Rheumatoid arthritis in adults. Rheutopia reduces painful and swollen joints, slows joint damage, and improves mobility and the ability to do physical activities.
- Polyarticular juvenile rheumatoid arthritis (JRA) in people older than 4 years of age who did not have good results from other medicines. Rheutopia reduces pain, improves mobility, and decreases the number of painful joints.
- Ankylosing spondylitis. Rheutopia reduces back pain, swelling, and improves mobility.
- Plaque psoriasis in adults who may benefit from taking medicine or receiving phototherapy (using ultraviolet light). Rheutopia improves or clears up areas of skin with psoriasis.

What Should I Tell My Doctor?
Before using Rheutopia, tell your doctor if you:
- have an infection, are being treated for an infection, or think you have an infection (such as a cold, flu or skin infection).
- have TB or have been near someone who has TB.
- lived in or traveled to other countries.
- have any nervous system or heart problems.
- are taking the medicine Kineret (anakinra).
- are scheduled to receive a vaccination. (including a flu shot). You should not get a vaccination while taking Rheutopia.

When Should I Call My Doctor?
Stop using Rheutopia and tell your doctor right away if you develop:
- Fever, cough, flu-like symptoms, skin infection (red, warm, painful skin or open sores).
- Numbness, tingling, weakness, vision problems, or dizziness.
- Chills, swollen lymph nodes, night sweats, fever, or weight loss.
- Bruising, bleeding, and pale skin.
- Shortness of breath, swelling of ankles or feet, or sudden weight gain.
- Chest discomfort or pain, shortness of breath, joint pain or a rash on your cheeks or arms.

What Are Some Common Side Effects?
- Redness, rash, swelling, itching or bruising where the shot was given.
- Headache
- Runny nose

Tell your doctor about any side effect that does not go away in a few days or gets worse.

How Do I Use Rheutopia?
- Rheutopia is an injection (shot). Do not use Rheutopia until you have been shown how to give a shot.
- Store Rheutopia in the refrigerator. Do not shake or freeze.
- If you forget to take a dose, take it as soon as you remember. Take your next dose at your regularly scheduled time.
- Your doctor will tell you how often to use Rheutopia. Do not use Rheutopia more often than prescribed.

Where Can I Get More Information?
- Visit www.fda.more-information.gov
- Call 1-800-(manufacturer).

DRAFT PROTOTYPE 2
PATIENT INFORMATION
Rheutopia™ [Roo-toh-pee-ah] (also known as arixalate)

Important Warning: Serious Infections
- Rheutopia affects the immune system. It can lower your ability to fight infections. Do not use Rheutopia if you have an active infection.
- People taking Rheutopia have gotten serious infections including tuberculosis (TB) and infections caused by viruses, fungi, or bacteria. Some people have died from these infections.

What Does Rheutopia Treat?
- Rheumatoid arthritis in adults. Rheutopia reduces painful and swollen joints, slows joint damage, and improves mobility and the ability to do physical activities.
- Polyarticular juvenile rheumatoid arthritis (JRA) in people older than 4 years of age who did not have good results from other medicines. Rheutopia reduces pain, improves mobility, and decreases the number of painful joints.
- Ankylosing spondylitis. Rheutopia reduces back pain, swelling, and improves mobility.
- Plaque psoriasis in adults who may benefit from taking medicine or receiving phototherapy (using ultraviolet light). Rheutopia improves or clears up areas of skin with psoriasis.

What Should I Tell My Doctor?
Before using Rheutopia, tell your doctor if you:
- have an infection, are being treated for an infection, or think you have an infection (such as a cold, flu or skin infection).
- have TB or have been near someone who has TB. You may be tested and treated for TB.
- lived in or traveled to other countries. There is more risk for getting TB or other infections in certain countries.
- have any nervous system or heart problems.
- are taking the medicine Kineret (anakinra). The risk of serious infections increased when used with Rheutopia.
- are scheduled to receive a vaccination (including a flu shot). You should not get a vaccination while taking Rheutopia.

When Should I Call My Doctor?
Stop using Rheutopia and tell your doctor right away if you develop:
- Fever, cough, flu-like symptoms, skin infection (red, warm, painful skin or open sores). These can be symptoms of a serious infection.
- Numbness, tingling, weakness, vision problems, or dizziness. Symptoms of nervous system diseases, like multiple sclerosis, may develop or get worse.
- Chills, swollen lymph nodes, night sweats, fever, or weight loss. You may have a higher chance of getting lymph node cancer.
- Bruising, bleeding, and pale sk[...] may not make enough blood ce[...] infection or to help stop bleedi[...]
- Shortness of breath, swelling o[...] sudden weight gain. These are [...] failure that may develop or get [...]
- Chest discomfort or pain, short[...] joint pain or a rash on your che[...] These may be symptoms of an [...] with lupus-like syndrome.

What Are Some Common [...]
- Redness, rash, swelling, itchin[...] the shot was given.
- Headache
- Runny nose

Tell your doctor about any side e[...] go away in a few days or gets wor[...]

How Do I Use Rheu[...]
- Rheutopia is an injection (shot[...] Rheutopia until you have been [...] a shot.
- Store Rheutopia in the refriger[...] or freeze.
- If you forget to take a dose, tak[...] remember. Take your next dos[...] scheduled time.
- Your doctor will tell you how [...] Rheutopia. Do not use Rheuto[...] prescribed.

Where Can I Get More In[...]
- Visit www.fda.more-informati[...]
- Call 1-800-(manufacturer).

You may report side effects to (manufacturer) at (phone # and web address) or FDA at 1-8[...]

Appendix B: Single Document Prototypes   **DRAFT PROTOTYPE 3**

Drug Approved by FDA: 2005
Date of Leaflet: May 2009

Rheutopia [Roo-toh-pee-ah]

Active ingredient: arixalate

Uses
- Rheumatoid arthritis (adults and children older than 4): reduces painful swollen joints, slows joint damage and improves mobility
- Ankylosing spondylitis: reduces back pain, swelling, and improves mobility
- Plaque psoriasis in adults: clears up areas of the skin with psoriasis

Warnings

Important Warning: Serious Infections
Do not use Rheutopia if you have an active infection. Rheutopia affects the immune system and can lower your ability to fight infection. Some people have died from an infection such as tuberculosis (TB) when taking Rheutopia.

Ask your doctor before using if you
- have any signs of infection (fever, cough, flu-like symptoms)
- have a skin infection (warm, red, painful skin or open sores)
- have tested positive for tuberculosis (TB) or have been near someone who has TB
- have a problem with your nervous system
- have recently been vaccinated or are scheduled to be vaccinated
- have lived or traveled outside the country
- have a problem with your heart
- are taking Kineret (anakinra)

Stop use and call your doctor right away if you
- have an infection (fever, chills, cough, flu-like symptoms)
- have a skin infection (warm, red, painful skin or open sores)
- have a skin rash
- have numbness (can't feel your skin) or tingling skin
- have changes in your vision
- have swollen lymph nodes, night sweats
- took more Rheutopia then you were told to take
- have weakness in your arms or legs
- feel faint or light headed
- easily bruise or bleed
- get short of breath
- get swollen (fat) ankles
- have chest pain
- have sudden weight loss or gain

Report side effects to FDA at 1-800-FDA-1088.

Common side effects
- redness, rash, swelling, itching, or bruising where the shot was given
- headaches
- runny nose

Tell your doctor about any side effect that does not go away in a few days or gets worse.

PMI Activities, *cont.*

- Fall 2010 – Initiate public process on PMI Single-Document Solution

- Planned public workshop in conjunction with Brookings Institution

- Consumer Testing
  - FR Notice research protocol published 5/4/10; comment period closed 7/6/10
  - Initiate study following OMB approval Spring 2011
  - Test content compression, format and order of information
  - 150 face-to-face pre-screening encounters with consumers
  - Experimental design – 900 consumers with RA
  - Follow-up internet study – 200 consumers with RA
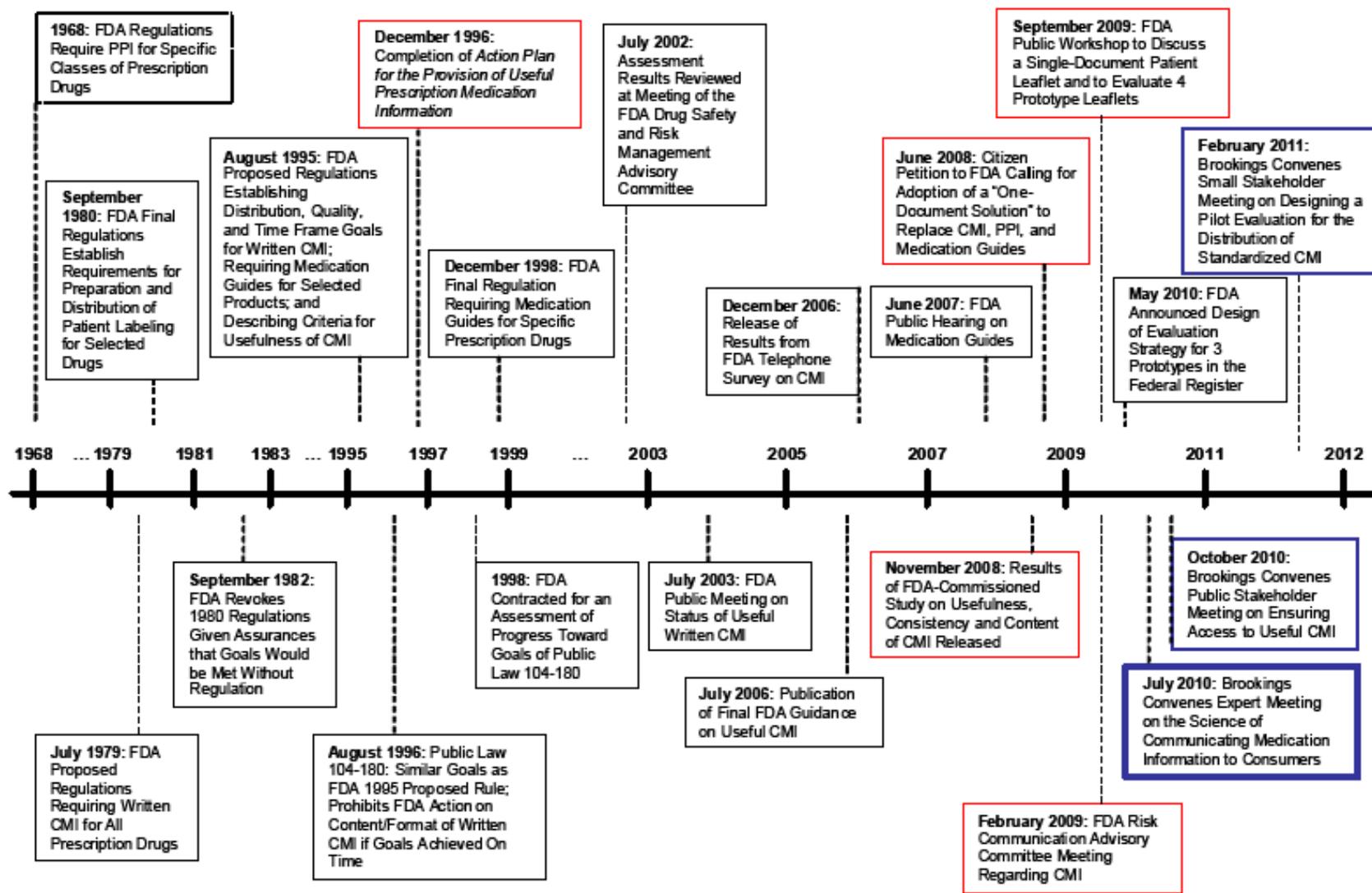
July 2010: Englewood Center for Health Care Reform at Brookings

http://www.brookings.edu/~/media/Files/events/2010/0721_CMI/Final%20CMI%20discussion%20guide%2007191 0.pdf *accessed 8/30/2010*

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Moving Forward

- Access and distribution – preliminary recommendations
    - Central e-repository of up-to-date leaflets
    - Permit e-receipt by the pharmacy
    - Pharmacy cannot change content or format
    - Permit the option for patients to receive leaflet electronically or in paper form (or other formats?)
- Process
    - Public/private consortium
    - Interim pilot solutions

Development and Distribution of Patient Medication Information for Prescription Drugs

- Register for the public hearing
  - email registration information to *PMIpublicmeeting@fda.hhs.gov*.
- Submit electronic comments
  - *http://www.regulations.gov*.
- Submit written comments
  - Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852
- A live webcast of this hearing will be viewable at
  - September 27 *https://collaboration.fda.gov/p15d109272010/*
  - September 28 *https://collaboration.fda.gov/p15d209272010/*

[Docket No. FDA–2010–N–0437]