

MEDICATION ERRORS: AN FDA PERSPECTIVE

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Pharmacotherapy Frontiers
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Objectives

- ✓ General Overview of Medication Errors
 - Define Medication Error
 - Describe and Recognize Contributing Factors to Medication Error
- ✓ Describe FDA's Proprietary Name Review Process to Minimize Name Confusion
- ✓ Describe FDA's Postmarketing Medication Error Review Process

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What is a Medication Error?

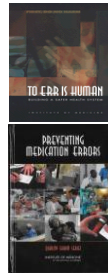
Any PREVENTABLE event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer.

FDA focuses on errors related to nomenclature, labeling and/or packaging of a drug product.

<http://www.nccmerp.org/aboutMedErrors.html>

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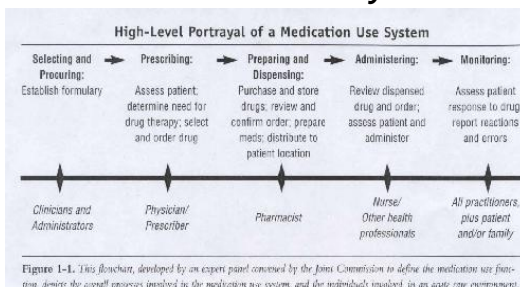
Exposing the Problem



- ✓ December 1999 IOM report
 - 48,000 to 98,000 people die yearly due to medical errors.
 - 7,000 of which are related to Medication Errors
- ✓ July 2006 IOM report
 - Major Problems with Naming Labeling and Packaging
 - Cause of 33% of medication errors, including 30% of fatalities

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Medication Use System

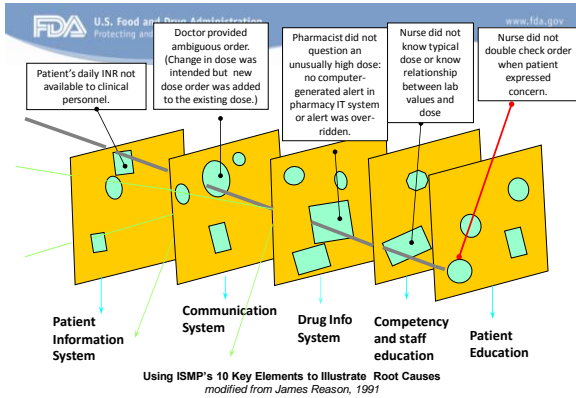


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Systems not People

- ✓ Errors are Multi-factorial
- ✓ Medication errors are property of the system as a whole rather than results of the acts or omissions of the people in the system
- ✓ Performance improvement requires changing the system, not changing the people

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Contributing Factors

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Environmental & Human Factors

- ✓ Stressful work environment
- ✓ Frequent interruptions & distractions
- ✓ Poor lighting
- ✓ Noise level

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Protecting and Promoting Public Health
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Confirmation Bias

- "IT AIN'T WHAT YOU KNOW THAT GETS YOU IN TROUBLE, IT'S WHAT YOU KNOW FOR SURE THAT AIN'T SO"
- Mark Twain

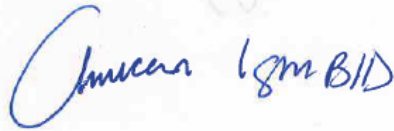
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PARIS IN THE THE SPRING

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Sound and Look-Alike Names

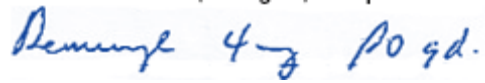


Amicar 1 gm BID

Amicar or Omacor?

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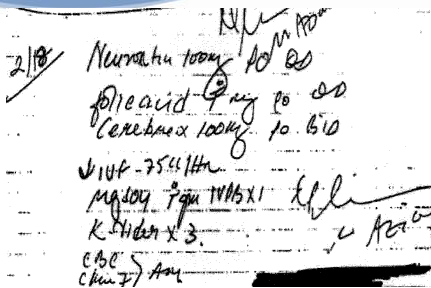
Sound and Look-Alike Names



Reminyl 4-8 PO qd.

Reminyl or Amaryl?

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2/18
Neurathu 100mg PO BID
folic acid 5mg PO qd
Cerebex 100mg PO BID
VIVE 750mg
Majora 3gm IVBx1
K. Hiden x 3
CABG
Chin 7) Am

Cerebyx or Celebrex?

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Transcription of Orders



morphine .5 mg

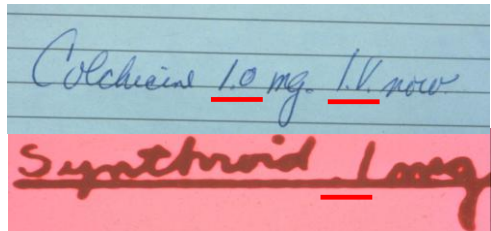
Morphine 0.5 mg

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	AM	1	2	3	4	5	6	7	8	9	10	11	12	PM	13	14	15	16	17	18	19	20	21	22	23	24
DATE	12	24	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
TIME	07																									
PROCESSED BY																										

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Use of Abbreviations & Trailing/Preceding Zeros



Colchicine 1.0 mg. 1.0 now
Synthroid 1.0 mg

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60 Regular INSULIN NOW

44 Rente Pork
44 Reg Pork

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OTC Brand Name Extensions



Aluminum Hydroxide,
Magnesium Hydroxide
& Simethicone

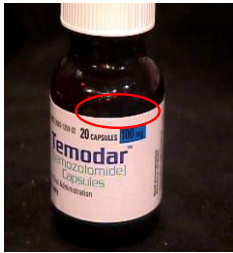
Calcium Carbonate
& Simethicone

Bismuth
Subsalicylate

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Placement and Prominence on Label

Before



After



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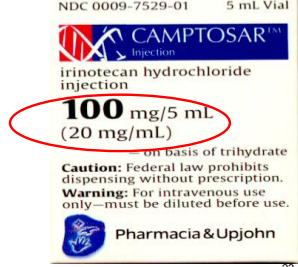
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Expression of Strength

Before



After



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Readability of Label



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Similar Packaging and Similar Trade Dress

Goldline	Goldline
NDC 0182-1494-89	NDC 0182-0555-89
HYDROXYZINE HCl TABLETS, USP	HYDRALAZINE HYDROCHLORIDE TABLETS, USP
50 mg	50 mg
Rx only	Rx only
100 COUNT UNIT DOSE TABLETS	100 COUNT UNIT DOSE TABLETS

For full prescribing information, see enclosed package insert.



Incorrect Dosing Frequency

Name: [REDACTED] Age: [REDACTED]
 Address: [REDACTED] Date: 3-30-04
 R

Effexor XR 75mg
 sig: TID BID
 #60

Refills: 0 1 2 3 6 12
 Label: Medication and Quality
 Dispense as written
 Voluntary Formula Permitted

M.D. [REDACTED]

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Packaging Configuration

[REDACTED] Date: 5/22/04

Quantity	Manufacturer	Strength	Form	Directions	Refills
1	Z-Pak	1	1	Take as directed	0
1	Plonoxone	1	1	Use as directed	2

PHARMACY FILING NUMBER: [REDACTED]
 PRESCRIPTION: [REDACTED]

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Abbreviated Name

ADDRESS: [REDACTED] DATE: 2/20/04
 R

EURA transdermal
 #12
 use as directed

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Advertising



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DMEPA Responsibility

- ✓ Post-Marketing Surveillance
- ✓ Review of Proprietary Names
- ✓ Label/ Labeling and Packaging Review
- ✓ Risk Communication/Risk Management of Errors

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Premarketing Proprietary Name Reviews

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Rationale for Proprietary Name Analysis

- ✓ Drug names are a critical “identifier” of the intended product in the U.S. market
- ✓ Drug name confusion or identification failures lead to error
- ✓ Medication errors have been shown to cause patient harm

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Primary Areas of Focus

- ✓ Promotional
 - Conducted by Division of Drug Marketing, Advertising, and Communication (DDMAC)
 - Opinion included in OSE review
- ✓ Safety
 - Conducted by Division of Medication Error Prevention & Analysis

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CDER Proprietary Name Analysis

- ✓ Review Begins:
 - IND (Phase II), NDA/BLA, or ANDA
 - Primary (1st choice)
 - Secondary (2nd choice)
- ✓ PDUFA IV Goal Dates
 - 90 days NDA/BLA
 - 180 days IND
 - No PDUFA IV goal for ANDAs
- ✓ Re-reviewed:
 - IND → NDA/BLA
 - 90 days prior to NDA/BLA/ANDA approval

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Proprietary Names Promotion

- ✓ Focus of review - “fanciful” names, false and/or misleading claims embedded in name
 - 21 CFR 201.10(c)(3) Regulation
 - Superiority claims
 - Claims for different or expanded indications
 - Claims for efficacy or safety not supported by data

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Proprietary Names Safety

- ✓ Focus of review - avoid medication errors
 - 21 CFR 201.10 (c.) “The labeling of a drug may be misleading by reason (among other reasons) of:
 - (5) “Designation of a drug or ingredient by a proprietary name that, because of similarity in spelling or pronunciation, may be confused with the proprietary name or the established name of a different drug or ingredient.”

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Proprietary Names Safety Considerations

- ✓ Prefixes or Suffixes
 - May be misinterpreted as a dosing schedule (e.g., QD, BID)
 - May not be understood by HCP or consumer
 - May be misleading from safety perspective
- ✓ Multiple proprietary names for products with same active ingredient
 - Potential for confusion, overdosing, concomitant administration, allergies, hypersensitivity reactions
- ✓ Misleading or ambiguous names
 - US Adopted Name (USAN) stem
 - Dosing interval (e.g., Name**BID**)
 - Dosage form/route of administration (e.g., Name**tabs**)
 - Medical and/or product name abbreviations

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Product Characteristics

- ✓ Drug name (Proprietary & Established name, Suffix, etc.)
- ✓ Indications
- ✓ Patient population, prescriber population
- ✓ Dose, strength(s), dosage form
- ✓ Unit of measure, typical quantity or volume
- ✓ Route of administration
- ✓ Frequency of administration
- ✓ Instructions for Use
- ✓ Product Packaging
- ✓ Physical attributes
- ✓ Storage conditions
- ✓ Setting of use
- ✓ Contraindications, etc.

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Directions For Use

“The evening before the colonoscopy procedure, 3 tablets should be taken with 8 ounces of clear liquids every 15 minutes for a total of 20 tablets. The last dose will be 2 tablets. The day of colonoscopy procedure, (starting 3-5 hours before the procedure) 3 tablets should be taken with 8 ounces of clear liquids every 15 minutes for a total of 20 tablets. The last dose will be 2 tablets.”

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The “Real” World

Use as directed

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Finding Similar Names

- ✓ Search strategy
 - Currently marketed drug names
 - Drug names pending approval
 - Other Medicinal Products
 - Commonly used medical abbreviations, medical procedures, and/or lab tests
- ✓ Databases
 - Literature
 - Textbooks
 - (e.g., Drug references)
 - Computer databases for existing or proposed names
 - (e.g., Internet, Saegis, POCA, etc.)

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Finding Similar Names

- ✓ Expert Panel Discussion
 - Safety Evaluators
 - Rely on clinical, regulatory, and professional experiences
- ✓ Name Simulation Studies
 - Studies are conducted with ~120 FDA volunteers
 - Provide qualitative information for predicting orthographic and/or phonetic vulnerability of a name

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Determining Potential Failure of Name

✓ Failure Mode and Effects Analysis (FMEA)

A systematic, proactive method for evaluating a process to identify where and how it might fail, and to assess the relative impact of different failures in order to identify the parts of the process that are most in need of change.

¹Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004

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Consider Entire Medication Use System

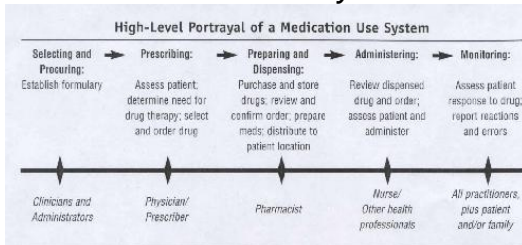


Figure 1-1. This flowchart, developed by an expert panel convened by the Joint Commission to define the medication use function, depicts the overall processes involved in the medication use system, and the individuals involved, in an acute care environment.

Intence (Etravirine) Tablets

- ✓ Indication – treatment of human immunodeficiency virus type 1 (HIV) infection in antiretroviral treatment-experiences adult patients.
- ✓ Usual Dose
 - 200 mg twice daily following a meal
- ✓ How Supplied
 - 100 mg tablets in bottles of 120
 - 200 mg tablets in bottles of 60

Intence (Etravirine) Tablets

- ✓ Look-Alike and Sound-Alike Letters

Letters in Name, Intence	Scripted may appear as	Spoken may be interpreted as
l	e, L	any vowel
n	v, r, s,	m
t	f, r, x	d
e	i, l	any vowel
l	b, e, h	
c	a, r	s

Intence (Etravirine) Tablets

- ✓ Prescription Study

HANDWRITTEN PRESCRIPTION AND MEDICATION ORDER	VERBAL PRESCRIPTION
<i>Intence 100mg tablets po bid after meals</i>	Intence 100 mg #240 tablets Take 2 tablets twice day following meals
Outpatient Medication Order: <i>Intence 100mg #240 Sig: 2 tabs po BID pc</i>	

Prescription Study Results

Inpatient Medication Order	Verbal Prescription	Outpatient Medication Order
Untence	Atalence	Intence
Intence	Intalents	Intence
Intence	Intellance	Intence
Intence	Intelance	Intence
Untence	Intela	Intence
Intence	Intellits	Intence
Intence	Intelants	Intence
Untence	Etalence	
Intence	Intellence	
	Talents	
	Talona	

Intence (Etravirine) Tablets

Intence vs. Invirase

- ✓ Invirase (Saquinavir Mesylate)
- ✓ Product Strength
 - 200 mg capsule
 - 500 mg tablet
- ✓ Dose
 - 1000 mg twice daily in combination with ritonavir 100 mg twice daily, both should be taken within 2 hours after a meal

Intelence (Etravirine) Tablets

Intelence vs. Invirase

- ✓ Orthographic Similarities
 - Both names begin with the letters 'In-'
 - Both names end with the same letter 'e'
 - Scripted Letters
 - 'i' and 'a' in Invirase may appear as 'e' and 'e' in Intelence
- ✓ Orthographic Differences
 - Intelence contains 2 additional upstroke letters ('t' and 'l') vs. Invirase

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Intelence (Etravirine) Tablets

Intelence vs. Invirase

- ✓ Product Characteristic Similarities
 - Solid oral dosage form
 - 200 mg
 - Frequency of administration (bid)
 - Overlapping patient (HIV) and prescriber populations (infectious disease practitioners)
- ✓ Product Characteristic Differences
 - Dose
 - 1000 mg vs. 200 mg

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Intelence (Etravirine) Tablets

- ✓ Risk Assessment
 - Orthographic differences include two upstroke letters ('t' and 'l') in Intelence vs. no upstroke letters in Invirase
 - The dose of these products differ
- ✓ Intelence was found acceptable with the product characteristics submitted

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DMEPA Post-Marketing Medication Error Surveillance

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Medication Error Safety Signals

- ✓ Sources
 - Adverse Event Reporting System (AERS), ISMP Datasources, Literature
- ✓ Focus
 - Confusion with product names
 - proprietary and established
 - Error prone product labels/labeling
 - Error prone product design, packaging or device

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Post-Marketing Medication Error Surveillance

- ✓ Monitor all medication error reports from
 - Manufacturers, Healthcare professionals, Consumers, and ISMP submitted to FDA via MedWatch
 - ≈1700 per month
 - ≈90% of medication error reports from practitioners
- ✓ Investigation of cases conducted
- ✓ Conduct a Root Cause Analysis
- ✓ Revise Labels and Labeling with CDER review division

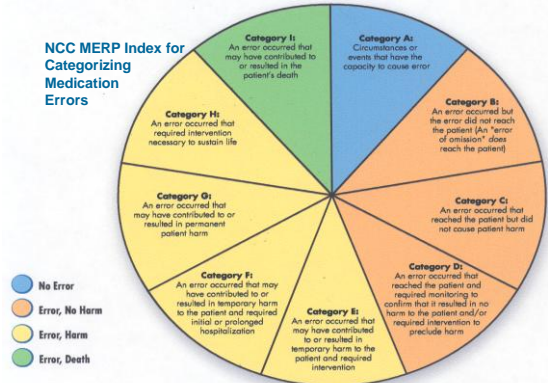
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<http://www.usd.edu/phys/courses/astronomy/images/Earth/Iceberg%201.jpg>

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NCC MERP Index for Categorizing Medication Errors



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Regulatory Approach: A Case Study

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Morphine Sulfate

✓ AERS Cases

- Oral solution strength confusion
 - 10 mg/5 mL & 20 mg/10 mL unit-dose cups
 - 20 mg/5 mL bulk bottles (100 mL & 500 mL)
 - 100 mg/5 mL 120 mL bottle
- Inventory numbering on unit-dose blisters
 - 15 mg & 30 mg

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Morphine Sulfate



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Morphine Sulfate

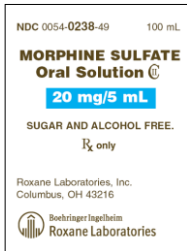
✓ Recommendations

- Unit-Dose Oral Solution
 - Differentiate strengths by using contrasting colors, boxing, or some other means
 - Express strength of concentrated solution as 100 mg/5 mL
 - Increase Prominence of product strength



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Morphine Sulfate



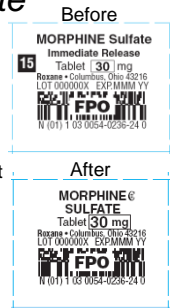
73

Morphine Sulfate

✓ Recommendations

➤ Unit-Dose Tablets

- Delete inventory numbering
- Increase prominence of product strength
- Include unit of measure (mg) in box
- Remove the term "Immediate Release"



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What can be done?

- ✓ Sharing our experiences through reporting
- ✓ Examine the various systems for causes and implement change
- ✓ Proactive risk assessment by considering error potential early in product development



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Practitioner's Responsibilities

- ✓ Provide Clear and Well Understood Rx
- ✓ Patient Involvement & Communication
- ✓ Agents for System Changes
- ✓ Reporting Errors to Local and National Reporting Systems
www.fda.gov/medwatch



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Patient Responsibilities

- ✓ Inquire and know the risks of treatment
- ✓ Expect and ask for medication counseling
- ✓ Report Errors to Local and National Reporting Systems
- ✓ www.consumermedsafety.org/



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Pharmaceutical Industry

- ✓ Clear & Concise Labeling
- ✓ Avoid Misleading or Confusing Proprietary Names
- ✓ Propose Packaging with Minimal Error Potential
- ✓ Swift Action When a problem occurs



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FDA's Responsibility

- ✓ Minimizing error potential PRIOR to approval
- ✓ Correcting problems quickly AFTER detection
- ✓ Risk Communication and Management
- ✓ Research

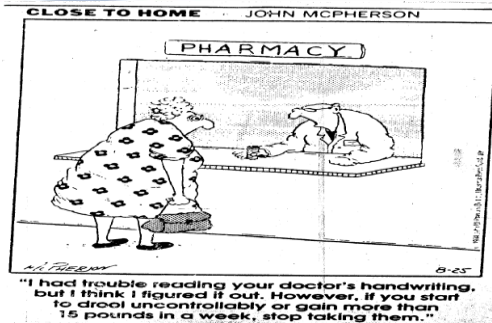


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Websites

- ✓ Food and Drug Administration
 - www.fda.gov
- ✓ Institute for Safe Medication Practices
 - <http://www.consumermedsafety.org>
 - <http://www.ismp.org>
- ✓ Joint Commission
 - <http://www.jointcommission.org>
- ✓ NCCMERP
 - www.nccmerp.org

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Questions?

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