Log of Meeting

AUG 2 1 2003

Subject: Unit dose packaging

Date of meeting: July 30, 2003

Place: Room 714 CPSC Headquarters, Bethesda, MD

Log Entry Source: Suzanne Barone, Ph.D. HS

Commission Representatives: See attached sheet

Non-Commission Representatives: See attached sheet

Summary of meeting:

Representatives from Pfizer requested this meeting to discuss unit dose packaging, the HCPC petition (PP 03-1), and type testing. Rich Hollander from Pfizer stated that they did not take a position on the HCPC petition. However, he stated that packaging should be designed to keep the amount of product considered to be toxic from children.

Mr. Hollander presented an overview of how packaging decisions for drugs are made by Pfizer. Mr. Hollander stated that Pfizer has all child-resistant packaging they use tested. He stated that bottles are often chosen because unit packaging takes more time to develop and can be more costly due to iterative changes and testing. In his presentation, Mr. Hollander also highlighted benefits of unit packaging such as patient compliance and the decreased need for repackaging which can minimize errors. He showed several packages that Pfizer makes to increase patient compliance.

Pfizer suggested that wider usage of unit packaging could exist if there were clear standard definitions for various unit packaging types as exist for cap and vial packaging. They proposed the development of voluntary standards packaging specifications for various types of child-resistant features. Pfizer requested that the CPSC take the lead and promote the development of these voluntary standards through the ASTM. Concern about identifying all of the parameters that could influence the child-resistance of a packaging, including the influence of the medication itself, was voiced by the staff. The staff explained that although they were not averse to encouraging such standards development activity, the decision to expend staff resources on that project would be made higher in the organization.

A copy of Mr. Hollander's slides are attached.

8/21/03

CPSA 6 (b)(1) Cleared

____No Mfrs/PrvtLblrs or Products Identified

____Excepted by

____Firms Notified,

Comments Processed

CPSC Staff Meeting With Pfizer
July 30, 2003
Room 714, 10:30am

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16 CFR 1700 and Its Impact on Pharmaceutical Distribution

CPSC July 2003

Rich Hollander
Sr. Director, Packaging Services

Agenda

- Pfizer Comment to Docketed Petition
- Understanding of Package Design Decisions
- Alternative Recommendations for Consideration

Comments to Docket

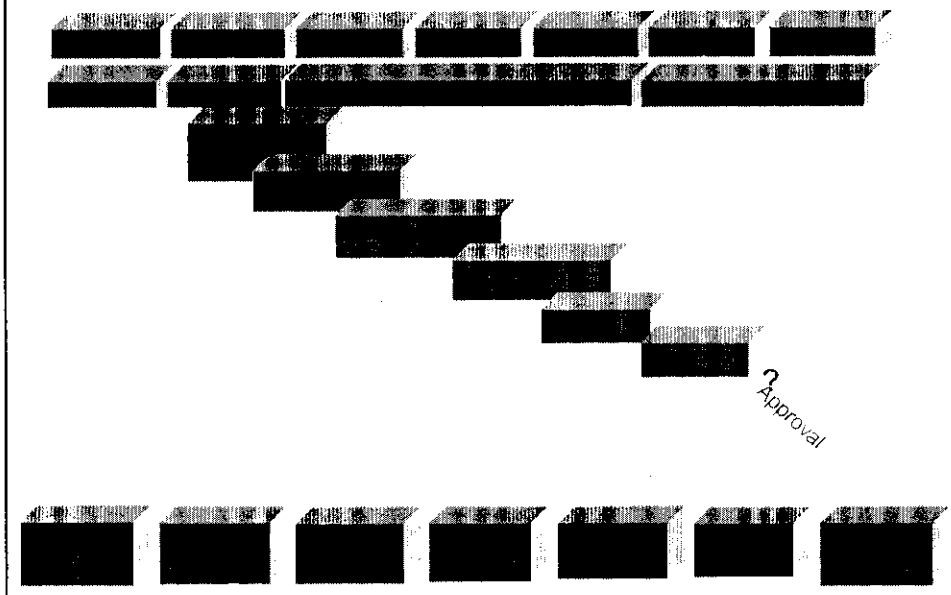
- Pfizer Does Not Take a Position on the HCPC Proposal Petition to Rely Solely Upon a Numerical Standard (for Determining the Failure Level for Regulated Products Packaged in a Non-Recloseable Package).
  - An evaluation of Each Product's Toxicity Profile is Required Prior to Designing a CR Package
  - Such Packages Should be Designed to Keep the Amount of Product Considered to be "Toxic" from Children
- Change/Guidance is Needed to Remove Unwarranted Obstacles & Clarify Expectations for Use of Non-Reclosable Packages

Package Design Decisions

Understand the Drivers:

- **Container Closure System Needs (Product)**
  - Protect the Product - Temperature and Humidity
    - ICH and the Four Climactic Zones
      - Hot and Dry, Hot and Humid, Cool, etc.
    - Shipment
    - Do Not Interact with the Product
    - 2-5 Year Expiration Dating
- **Patient Needs (Product and Patient)**
  - Indication: Acute vs. Chronic
  - Target Population
  - Compliance
  - Safety
- **Drug Product Distribution Chain (Supply Chain)**
  - Global Sourcing Strategies
  - Wholesale Operations
  - Retail Operations
  - Repackaging Operations

Package Development Process



Standard Package Options Approved in NDA

Registration Programs for Bottles:

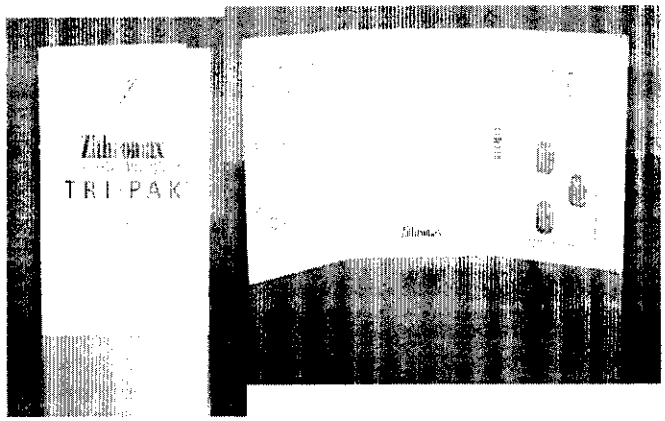
- **Infinite Number of Bottle-Closure Combinations to Choose From**
  - Size, Shape, Style Closure, Liner, Supplier
- **2, 30, 100, 300 and/or 500s with CR or non-CR Closures**
  - Bracketing Strategies Deployed
    - Sponsor Unclear on Final Dosing/Strengths Sample Strategies Unclear
    - Agency Allows
- **Regulatory Strategies**
  - Relatively Complex to Setup Initial Packaging
  - High Degree of Flexibility Once Approved

Standard Package Options Approved in NDA

Registration Programs for Blister Packs:

- **Constrained by Film and Foil Choices**
- **Each Foil Supplier has Unique Heat Seal Lacquer**
- **Each PVC Film also Unique**
- **Package Styles Supported:**
  - Carded Blisters
  - Push Through
  - CR Blisters (Separate, Peel, Push)
  - Hospital Unit Dose (Peelable)
- **Regulatory Strategies**
  - Relatively Straightforward For Initial Setup
  - Low Degree of Flexibility Once Approved
    - Product Contact Surfaces Raise Stability Concerns

Compliance Packages - Trade



Product less than 8 Tablets and does not Contain Harmful Dose

Compliance Packaging - Starters

Starter Package F>8

What is The Right Package?

A Variety of Dispensing Pharmacy Types Exist

- **Mail Order, Hospitals, Large Retail, Independent Pharmacy, Government, VA**

What is the right count?

- **30 or 90 for Chronic?**
  - Driven by Health Insurance Provider
- **What about Acute Indications?**
  - Driven by Indication
  - Highly Variable
- **Retailers have Strong Desire to Stock Only One Trade Package**
  - Driven by Inventory Costs
- **All but Hospital and Long Term Care Facilities Typically Dispense CR Packages**
  - Hospitals Make Strong Use of Blister Packs
    - Reduce Dispensing Errors
    - Compliance (Long Term Care)

Hospital Unit Dose Blister Packages

Non-CR Blister

Bar-coded Product, Lot Number and Expiration Date

Repackagers

- Repackagers Bridge Gap Between Drug Manufacturers and Dispensing Pharmacy
- Types of Repackgers
  - Repackagers for Resale
    - Generally Large Operations
    - Registered with FDA
    - Inspected by FDA
  - Repackagers Pursuant to a Prescription
    - Large, Medium and Small Operations
      - Back of Pharmacy is Repackaging
    - Governed by State Board of Pharmacy
    - Follow USP Guidance on Repackaging
- Packages Used
  - Back of Pharmacy – Bottle (CR or non-CR)
  - Mail Order Pharmacy – Bottle (CR accompanied with non-CR)
  - Long Term Care Facility – Bingo Blister Cards (non-CR)
  - Hospital – Hospital Unit Dose Packages (non-CR)

Perils of Repackaging

- Repackaging Adds Risk to Drug Product Distribution
  - Changing Primary Container Closure System with No Supportive Data
  - Dispensing Errors
  - Labeling Errors
  - Cross Contamination
  - Opportunity for Counterfeit Product to Enter Supply Chain
- Prevalent Usage of Blister Packs Would Render the Need for Repackaging Inefficient and Less Likely

Package Design Dilemma

- We Know A Lot About Blister Packs…
  - Significant Time, Effort and Money Spent Determining Optimal Container Closure Systems for Drug Product Packaging During Drug Product Development
    - ICH Stability Requirements
    - High Barrier Films and Foils (e.g., PCTFE, COC, PVdC, Alu/Alu)
  - Sponsors Often Prefer Blister Packs Over Bottles Due to Consumer Benefit
    - Compliance
    - Patient Education
  - FDA Sometimes Mandates
    - Patient Education
- … But Usage Can Be Challenging as CR Protocol Poses Hurdles to Designers as it Relates to Blister Packs
  - Subjective Toxicity Determination
  - Design Pack
  - Testing Requirements
    - We Panel Test Each New Package
    - Compliance
  - Iterative, Timely and Costly Process
  - Translation:
    - Sufficient Challenges to Refute Blisters and Use Bottles

Time and Effort Required to Develop a CR Blister Pack

General Rule of Thumb –

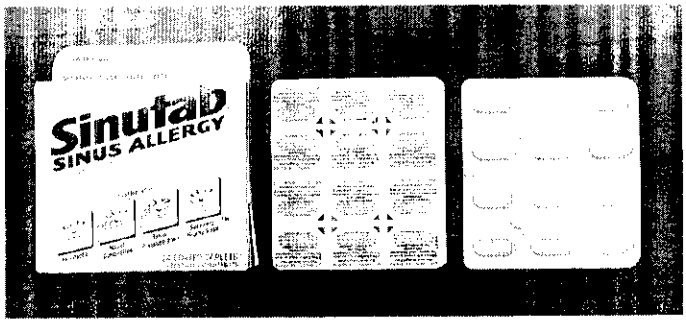
- **Nine-Ten Months Once Design is Finalized**
  - Tooling Lead-times
    - Done on Production Equipment
    - Thermoforming Tooling Lead-time of 16 weeks
  - Protocol Test Time
    - Dependent on Time of Year
      - Availability of Children
  - Iterative Process
    - Driven by Product Toxicity
    - "Learn" (if new design)
    - Choose Different Design
- **Cost – Upwards of $100,000 per Dosage/Pack**
  - Tooling
  - Protocol Testing
  - Production Time

Package Design Dilemma

Does the same barrier exist for OTC Products?

- **Blister Packs Preferred Design for Solid Oral Dosage Forms Across Many Indications**
  - Compliance
  - Patient Education
  - Product (Brand) Loyalty
- **Ease of Compliance with PPPA**
  - Toxicity Well Understood
  - Often contain Half of The Prescription Strength
  - Many OTC Medicines Not Regulated by PPPA

OTC Products



F=3

OTC Products vs. Prescription Products

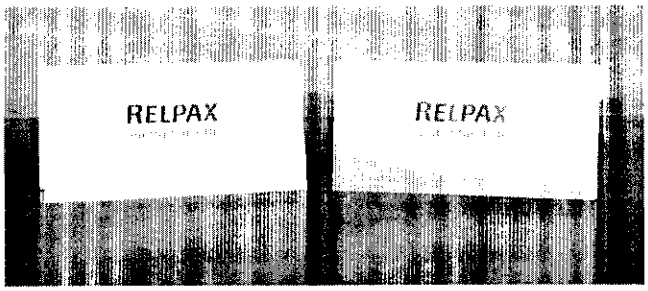
- Brand Name Recognition
- Indication Recognition

Slide Originated by Wal-Mart

Type Testing

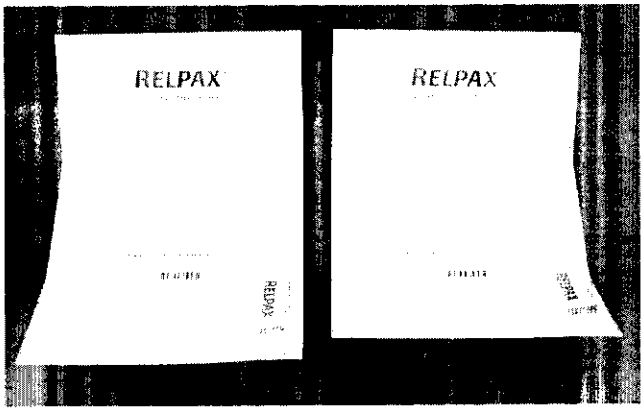
- **Component Manufacturers and Drug Manufacturers do Apply "Type Testing" to Some Reclosable Packages**
  - Standard Bottle and Closure Finishes
  - American Society for Testing and Materials (ASTM) Classifies "Types" and Describes "Some" Performance Tests for Certain Types
- **Manufacturers do NOT Generally Apply "Type Testing" to Non-Reclosable Packages**
  - Perceived Need/Expectation for Testing Governs
- **What is "Type Testing" for Non-Reclosable Packages?**
- **Manufacturers (and Agency) Need Clarity in How to Apply "Type Testing" to Non-Reclosable Packages**

Compliance Packages - Trade



- **Migraine Medication:**
  - 20mg F=5
  - 40mg F=3
  - Identical CR Features
    - Board Stock Caliper
    - Heat Seal Coating
    - Minimum Edge Distance

Compliance Packages - Trade



- F=3
- Passed Child - 92%
- Passed Adult – 100%

- F=5
- Passed Child - 94%
- Passed Adult – 100%

What Can Be Done?

- **Goal:**
  - Reduce the obstacles preventing wider usage of non-reclosable packages WITHOUT compromising public safety. Need clear regulatory expectations, definitions.
- **Proposal:**
  - For a Protocol Proven Package –
    - Detailed Design of Child Resistant Features
    - Specific Performance Tests
    - Evaluation Criteria
  - Utilize ASTM to Recognize CR Package Specifications and Make These Publicly Available
    - CPSC Should Participate in Standard Setting Process
    - CPSC Should Develop a Guidance that Defers to ASTM Specifications Regarding Good-faith Reliance on Recognized ASTM Standards

Example

Separate, Peel, Push Blister

- **Protocol Data Demonstrating Passing Results at F=4**
- **CR Features:**
  - Minimum 10 mil PVC
  - 10mm Unsealed Area
  - 5mm Kiss Cut
  - Cavity Shapes and Sizes
  - Detailed Drawing for Reference
- **Test Methods:**
  - Burst Strength of Film and Foil
  - Tensile Strength of Supported Foil
- **Evaluation Criteria:**
  - Film: Between x and y in. lbs.
  - Foil: Between x and y in. lbs.
  - Supported Foil: Between x and y in. lbs.

Benefits

- **Overall Increase in Safety**
  - Approval Process for Technical Specifications Governed by Industry Experts
    - Better Designs Established
  - Available for Wide Reference
  - Performance Tests
    - Package Qualification
    - In Process Controls
    - Elimination of Need for "Periodic Retest"
- **Wider Use of Blister Packaging**
  - Improve Patient Compliance
  - Reduce Opportunities for Repackaging
    Improving Product Protection
    - Decreasing Dispensing Errors

Questions?