PACKAGING, COSMETICS AND PHARMACEUTICALS

1. Introduction

The packaging industry is continuously evolving as medical and cosmetic product companies institute changes in the design, development, and manufacture of packaging systems. The industry must be aware of important packaging issues involving both design and manufacture as well as validating processes and equipment and the need for consistency and control of packaging. A package should protect the product during handling and shipping and from the environment and microorganisms until the package is opened. When the consumer is ready to use the product, it should be easy to open without compromising the quality. The consumer should also be able to detect easily whether the product has been tampered with. Cosmetics (qv) and Pharmaceuticals (qv) each have their own special packaging requirements. Each product must be analyzed for stability in the package being considered for use by the manufacturer; changes in container material, resin formulation, color, and closure system can all affect product stability. Although the distribution function of the packaging is always important, each product has other objectives that packaging components must achieve.

Cosmetic packaging, in addition to the above functions, is used to enhance the image of the product. This can be accomplished by frosting the container, graphics, proprietary design of the package, or use of metallized closures. The display package, or other secondary packaging, is also used to promote the image of the product. Principal products may have proprietary designs; smaller cosmetic manufacturers are able to distinguish their products through creative combinations of stock designs and graphics.

Although pharmaceutical packaging has the same basic objectives as cosmetic packaging, different parameters dictate product stability and safe packaging requirements. Both classes of products and their packaging are regulated by the U.S. Food and Drug Administration (FDA), but requirements for pharmaceutical packaging are more stringent because of product tampering prevention and child safety requirements of the FDA and the Consumer Product Safety Commission, respectively.

2. Packaging Design

Package design should be an integral part of the product development program. The package system should be considered with respect to the product characteristics, sterilization process if any, sealing, labeling, secondary packaging, handling, shipping, environment, storage, federal regulations and end use. Defective packaging and seals have been a major cause of medical device recalls. Recalls can be avoided by correct package design including validation of the packaging and sealing processes (1).

The following activities are important to maintain control of package design.

1. Planning for the design and development of packaging and defining responsibility for implementation of controls.
2. Establishing design input and output procedures, including review, documentation, signature, date, that are appropriate for the intended use and needs of the consumer.
3. Ensuring that the design review procedures for all appropriate stages of design development are conducted by qualified individuals.
4. Documenting design verification/validation to confirm that the design output meets the input requirements in the design history file.
5. Establishing and maintaining design transfer procedures that ensure the package design is correctly translated into product specifications.
6. Controlling changes after the design is accepted.
7. Establishing a design history file to demonstrate the design was developed and approved.

Protection of the public from product tampering is of major concern when considering a package design.

3. Product Tampering

In 1982, seven people died from consuming cyanide-laced Tylenol capsules. The incident resulted in a total product recall, massive negative publicity for the product, new requirements for safe packaging, and a federal statute making product tampering a crime (2). Since that time, the packaging industry has become visible to most consumers. This awareness has benefited the consumer by a reduction in loss of life due to consumption of adulterated products from tampering. Never before has an industry reacted so swiftly to resolve a problem.

There were incidents of product tampering prior to 1982, however, the exact number of incidents per year is unknown due to various methods of reporting. According to government figures, the problem peaked in the United States in 1986 when ~1800 claims of possible product tampering were reported. The number has decreased to around 500 per year. The decrease may be the result of better packaging or discouragement of potential violators by the penalties for violating product tampering laws. Most probably the decrease is caused by a change in the way claims are recorded.

Every developed nation has experienced product tampering incidents. The principal difference between domestic and foreign incidents is the motive of the tamperers. In the United States, typically random tampering without prior threat occurs; whereas outside the United States, extortion prior to injury occurs, with money appearing to be the primary motive. Most developed nations are either implementing or modifying their rules on the use of tamper-evident packaging. Some features as they are used in the United States would have to be modified or the use of a secondary feature required to meet the standards of various other countries.

In the late 1970s representatives from the U.S. FBI, Commerce Department, Defense Department, State Department, and CIA met to address the pro-

blem of state-sponsored terrorism in detail. One of the chief concerns was the threat of retail product tampering by a state-sponsored organization, ie, any group of terrorists supported financially, logistically, or with intelligence by the government body of any country. Protection against bioterrorism is still a concern. In certain countries that sponsor terrorist groups, training in retail product tampering, and how such acts can be used to further the cause, is being conducted. An example of the potential for disaster that exists if a tamperer has the resources available to build a complete packaging line and can print duplicate labels, occurred in South America when a drug organization bought a beverage plant in order to smuggle cocaine into the United States. At least one bottle in a specially marked case contained the drug in a liquid form, and when the contents of the bottle were distilled in the United States it yielded a powder that could be cut in strength and distributed to dealers. Unfortunately, one bottle was overlooked and sold to a consumer who died from a massive cocaine overdose.

4. The FDA's Role

The FDA has passed a rule (21 CFR 211.132) (3) requiring the use of tamper-evident packaging on all over-the-counter (OTC) drugs and some Cosmetics (qv), while ignoring other products they regulate (2). Table 1 offers examples of such packaging forms.

Product tampering is a possibility and manufacturers have a responsibility to protect consumers against such possible acts. If a product in an adulterated form could harm a consumer, manufacturers have the responsibility of protecting the product and consumer against such acts, meaning the use of tamper-evident packaging transcends FDA regulations.

The FDA has a procedure by which methods of providing protection that are not on the approved list may obtain approval on a case-specific basis. To obtain approval, samples of the complete package must be submitted to the FDA along with a written request for a waiver. The inclusion of a specific form of protection does not warrant that the feature will deter violation, nor does it prevent legal action in the event of a claim of injury related to product tampering. There are variances in designs and tooling of the same design that affects each feature. Any evaluation of a package relates to the exact components used in the test. Material from a different manufacturer usually results in a different level of effectiveness, much the same as using a different resin or closure liner affects a stability study.

Recent attention of the FDA was focused on retail cosmetic liquid oral products and vaginal products that were not contained in tamper-resistant packages. The FDA has the authority to establish a uniform packaging requirement for such products and acted on this problem. A package is considered tamper resistant if it has an indicator or barrier to entry, which if breached alerts the consumer that tampering has occurred. The indicator must be distinctive by design or appearance to preclude substitution. The tamper-resistant feature may involve the immediate or outer container. The package must also bear a prominently placed statement alerting the consumer to the tamper-resistant feature (5).

4.1. Law Enforcement Authority. For enforcement of the law, the FDA may conduct examinations and investigations of products, inspect establishments in which products are manufactured or held, and seize adulterated or misbranded products. Adulterated or misbranded products from foreign sources may be refused entry into the United States. To prevent further shipments, the agency may request a federal district court to issue a restraining order against the manufacturer or distributor. The FDA may also initiate criminal action against violators of the law (6).

5. Tamper-Evident Features

Selection of features to use should be done by objective testing during the package development stage. During the design stage, the package engineer should consider the function of the product and how the consumer intends to use it. Next, each tamper-evident feature that is usable on the package should be tested to determine which feature offers the greatest protection to the consumer. The test used should be objective, consistent, and replicable. Records of the test results should be retained indefinitely. If a feature selected for use achieves a lower value than others that were rejected, reasons for the selection should be recorded and retained with the test results. Cost should not be a factor in selecting which feature to use. It would be a false economy to accept less effectiveness to save a few cents when compared to the cost of potential injury to a consumer.

5.1. Testing. One form of testing the effectiveness of tamper-evident packaging is the Rosette protocol which measures the degree of difficulty in violating a specific package and restoring it to a near original condition. The Rosette protocol also measures increases in effectiveness through the use of multiple features. The value for a specific combination of features is not equal to the sum of each feature. Some factors cover the combination rather than each feature separately. For example, the knowledge factor is applied once. Regardless of the number of features in a combined package, only one knowledge level is required. Time is cumulative; if it takes 20 minutes to violate each feature, the time required is not the value for 20 minutes times the number of features used on the package. In this example, the time factor is the value for one hour. Only one category of equipment may be required if all tools or equipment required to violate the different features in the combination are in the same class. The feature visibility values for all used on multiple feature packages are multiplied; even the use of multiple features not shelf-visible increases the effectiveness of the package. The feature material is added for each feature replaced or reused to determine the feature material value. The value of the feature, used with the specific package components, on the specific product and form of product tested, is the sum of all the factors.

5.2. Child-Resistant Packaging. Under the Poison Prevention Packaging Act of 1970, any product that, if consumed by a child, could result in harm to the child must be packaged using components difficult for a child to open. This is referred to as child-resistant packaging.

The Consumer Product Safety Commission is responsible for administering the packaging rule under 16 CFR 1700, and the procedures for testing packages

to assure compliance with the rule are included in the Code of Federal Regulations (CFR) (7). In 1995 the Commission concluded hearings on changing the protocol to require child-resistant packaging be user friendly, that is, easy to open by senior adults. A search of the patent literature shows the interest in developing improved tamper proof lids and containers (see for example Refs. 8 and 9). The outcome of the change in this protocol is reflected in 16 CFR 1700 and the CFR should be reviewed for current testing requirements (7).

5.3. Effectiveness of Packaging. No single TE feature is best for all products. There are variations in effectiveness of similar features from different manufacturers, as well as variations in effectiveness where the product contributes to the effectiveness. An example is a metal can that is much more effective for a carbonated product than a noncarbonated product. The product can direct which feature provides the most protection, eg, products that can be adulterated effectively by penetration require a more rigid outer container than one that degrades visibly upon violation by penetration. The best feature for a product is the one that provides the greatest resistance to violation for the product in its current form and size. All features can be violated in some manner, but effective TE features provide greater difficulty in violating the product. In a particular instance a package was opened, the original product was replaced with a toxic substance, and no attempt was made to restore the package to its original appearance. The package worked as intended, ie, it showed it had been opened, but because there was no indication of violation to the actual product, the consumer still experienced injury.

6. Conclusion

Increased consumer awareness of packaging has led to an increase in the number of complaints of possible product tampering, although most are later dismissed as unfounded. Tamper-evident packaging prevents in-store tasting and violation, and if the feature is intact assures the consumer that the product is safe. Effective tamper-evident packaging acts as a deterrent to most persons who would commit such acts of violation and makes it difficult for others to violate the package and restore it to its original appearance. Effective tamper-evident packaging works, provided the consumer is aware of the feature and pays attention to what is being used.

Studies into consumer preferences for tamper-evident (TE) packaging have consistently revealed that consumers prefer products that are resistant to tampering and have shelf-visible features. The same studies have indicated that a consumer is willing to pay slightly more than a competing brand that is not TE, indicating consumer awareness of packaging.

When compared to the potential expense for defending a single claim of tampering, the cost of effective tamper-evident packaging becomes insignificant. Many firms simply cannot afford the cost of responding to product tampering claims, especially if the firm is a small one with a limited or totally related product line where the reputation of the entire product line can be affected by adverse publicity on one item. Liability insurance cannot return lost customer confidence.

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Table 1. **FDA Examples of Tamper-Resistant Package Forms**[a]

Type	Description
film wrappers	transparent film[b] with distinctive design wrapped securely around a product or product container
blister or strip packs	dosage units individually sealed[c] in clear plastic or foil
bubble packs	product and container sealed in plastic[d] and mounted in or on display card
shrink seals and bands	bands or wrappers with distinctive design are shrunk by heat or drying to seal union of cap and container
foil, paper, or plastic pouches	product enclosed in individual pouches[c]
bottle seals	paper or foil with distinctive design sealed[e] to mouth of container under cap
tape seals	paper or foil with distinctive design sealed[e] over all carton flaps or bottle cap
breakable caps	container sealed by plastic or metal cap[f] that either breaks away completely when removed from container or leaves part of cap attached to container
sealed tubes	mouth of tube is sealed and seal must be punctured to obtain product
sealed carton	all flaps of carton securely sealed and carton must be visibly damaged when opened to remove product
aerosol containers	inherently tamper resistant

[a]Refs. 3 and 4.
[b]Must be cut or torn to open container and remove product.
[c]Must be torn or broken to obtain product.
[d]Must be torn or broken to remove product.
[e]Must be torn or broken to open container and remove product.
[f]Must be broken to open container and remove product.