Steps for preventing tampering in OTC drug and food products.

INTRODUCTION
Most people are quick to associate tampering with the food industry when, in fact, it is not the food industry that has suffered the first notorious case of tampering, but the pharmaceutical industry. Although food tampering is more frequent, its severity is much lower, thanks to the nature of the product itself. Unusual sight, taste and smell usually alerts the consumer to detect and identify a potential food tampering. But, what happens when the tampering is not easily detectable, as is the case with OTC drug products?

This Risktopic is intended to draw attention to and suggest ways to prevent an often underestimated risk: the tampering of over the counter products (OTC). Although much of the discussion in this paper focuses on OTC drug products, it also applies to contamination and tampering risk for food products.

THE TYLENOL CASE
The first time a pharmaceutical company faced a case of tampering was in late September 1982 in the Chicago area where seven people died from ingesting Tylenol capsules laced with cyanide. At the time, the authorities promptly figured out that someone had opened the capsules and replaced some of the acetaminophen with cyanide and had returned them to the store shelves. However, to this day no party had been found responsible for this action. The Tylenol case triggered many events and brought up issues that changed the packaging requirements for the pharmaceutical industry.

During years that followed, a number of copycat tampering incidents occurred involving other OTC products with serious consequences, including fatalities. The Food and Drug Administration (FDA) reported 270 cases of suspected product tampering in the months following the Chicago poisoning cases in a wide range of products from pain relievers to eye drops to nasal sprays and even candy.

To prevent future tampering and restore the public’s shattered confidence in the products, Congress, the Food and Drug Administration and pharmaceutical manufacturers turned to the problem of securely packaging non-prescription drugs.
ANTI-TAMPERING REGULATIONS

In the U.S. in 1983, as a result of the Chicago-area Tylenol poisonings, the Federal Anti-tampering Act (FATA) was passed. The FATA outlaws:

- Tampering with any consumer product or its labeling or container
- Tainting any consumer product or rendering its labeling or container materially false or misleading with intent to cause serious injury to the business of any person
- Knowingly communicating false information that a consumer product has been tainted, if such tainting would create a risk of death or bodily injury to another person
- Knowingly threatening to tamper with a consumer product, its labeling or container
- Conspiring to tamper with a consumer product, its labeling or container

For each conviction under the FATA, there is a specific fine or custodial sentence. For example in the case of communicating false information, the guilty party shall be fined and/or imprisoned for a maximum of 5 years; if death of an individual results from tampering, the guilty party shall be fined or imprisoned for any term of years, for life, or both.

Less than a month after the Tylenol poisonings, the FDA enacted regulations that required manufacturers of the majority of over the counter drug products (OTC), some cosmetics and liquid oral hygiene products to package their products in tamper-resistant packages (TRP).

According to FDA regulations, “a tamper-resistant package has one or more indicators or barriers to entry that, if breached or missing, can reasonably be expected to give consumers visible evidence that tampering has occurred.”

Further, the regulations require a labeling statement on the container to alert the consumer to the specific tamper-resistant feature(s) used. The labeling statement is also required to be placed so that it will be unaffected if a TRP feature is breached or missing.

Most products only require one tamper-resistant packaging feature, while two-piece, hard gelatine capsules require at least two tamper-resistant packaging features. A series of tamper-resistant technologies were developed and became more widely used in recent years. These include, for example, film wrappers, bubble packs, heat shrink band or wrappers, bottle mouth-seal covers, tape seals, and blister packaging, breakable and tear-away caps.

In the U.S., producers of OTC are required to use tamper-resistant packaging. If a company does not comply with the regulation, it could be subject to several penalties, including product seizure, injunction and criminal prosecution.

FDA regulations do not mandate a specific type of tamper resistant packaging. Manufacturers and packagers are free to use any packaging system as long as the tamper-resistant requirements in the regulation are met. Examples of packaging technologies capable of meeting the TRP requirements include the following:

- **Blister or strip packs:** Dosage units (e.g., tablets or capsules) are individually sealed in clear plastic or plastic compartments with foil or paper backing. The individual compartment must be torn or broken to obtain the product. The backing materials cannot be separated from the blisters or replaced without leaving visible evidence of entry.

- **Breakable caps:** The container (e.g., bottle) is sealed by a plastic or metal cap that either breaks away completely when removed from the container or leaves part of the cap attached to the container. The cap or a portion of it must be broken in order to open the container and remove the product. The cap cannot be reapplied in its original state.

- **Sealed metal tubes or plastic blind-end heat-sealed tubes:** The bottom of the tube is heat-sealed and the mouth or blind-end must be punctured to obtain the product.

Many packaging technologies do not meet the TRP requirements in FDA regulations. Examples of packaging technologies not capable of meeting TRP requirements included the following:

- **Polystyrene foam container mouth seals:** these seals applied with pressure-sensitive adhesive are no longer considered effective tamper-resistant features as they can be removed and reapplied in their original state with no visible evidence of entry.

- **Tape seals:** Tape seals relying on an adhesive to bond them to the package are not capable of meeting the TRP requirements because they can be removed and reapplied with no visible evidence of entry. However, the Agency recognizes that technological innovations may produce adhesives which do not permit the removal and reapplication of tape seals.
Sealed cartons: Paperboard cartons sealed by gluing the end flaps are not capable of meeting the TRP requirements. However, the Agency recognizes that technological advances may provide sealed paperboard packages that meet the requirements of the TRP regulations.

The regulation concerning TRP has been recently applied across other countries after the main standard was imposed by the U.S. authority.

**Australia** – In June 2003, The Therapeutic Goods Administration published, on behalf of the Industry Government Crisis Management Committee, the Code of Practice for the Tamper-Evident Packaging (TEP) of Therapeutic Goods (Edition 1). “Although the Code is not currently mandatory the Australian therapeutic goods industry is encouraged to continue to comply with the Code of Practice on a voluntary basis in anticipation of it becoming a mandatory standard. The Code of Practice was developed to reflect the world’s best practice in the TEP of therapeutic goods, with the intention that it be regularly reviewed and amended as appropriate to accommodate packaging innovations and new information on packaging performance”. There are no significant deviations from the FDA regulation.

**Europe** – The code related to medicinal products for use by humans was put into force by the Council Directive 2001/83/EC, which was then amended by the Council Directive 2004/27/EC. However, the rules and regulations related to the selling of Over the Counter Products vary from country to country.

In order to assess the risk of tampering, it is very important to understand how the OTC drug products are sold in the store. Once an OTC pharmaceutical product is sold directly from the shelf, it is like any other kind of product sold. However, the risk and consequences of tampering an OTC drug product are much higher.

In a number of European countries, it is possible to sell OTC products in supermarkets without any further supervision. These countries include the United Kingdom, Holland, Switzerland, Ireland, Norway, Denmark, and Austria. In other countries, such as Italy, Portugal, and Spain, the regulations require a pharmacist nearby along with a dedicated pharmacy department. Since the selling of medicinal products directly on the store shelf is still a relatively new concept in these countries. There are currently no “specific” significant regulations like those in the U.S. in force.

**TYPES AND EFFECTS OF PRODUCT TAMPERING**

Product tampering can be classified into five types:

- **Criminal tampering**: An offender places one or more contaminated products on the shelf so that the consumers may purchase and consume the adulterated product without knowing.

- **Staged tampering**: An offender contaminates a product to simulate that the manufacturer has been the victim of true tampering. An example is the Seattle case where staged tampering was used to cover a murder. This kind of tampering is also used in suicides to try to gain money for their family and cover the true manner of death.

- **Extortion tampering**: An offender threatens to tamper with a product if their demands are not met. These demands are usually for substantial amount of money.

- **Faked tampering**: Offenders alert the media, law enforcement, relevant manufacturers, or others of a nonexistent tampering. Many of the alerts are merely hoaxes for entertainment.

- **Suspected tampering**: Consumers alert the manufacturer when a package has been compromised, when a product appears unusual, or when they suffered particular symptoms after the consumption of the product. The consumer complaints usually refer to quality defects due to machinery failures rather than tampering, for example burns on package seals, packaging containing not the right quantity of the product, damage to the packaging caused by careless opening of cartons in retail stores. It has been reported that the number of complaints due to suspected tampering increase following a true case of tampering as the consumer anxiety is much higher. In this case, many complaints are received about irregularities that would ordinarily go unreported.

Cases of true tampering are very critical for the manufacturer because, according to product liability laws, companies have the responsibility to protect consumers against “foreseeable possibility” of tampering. Following the Tylenol case, product tampering can now be considered a “foreseeable possibility,” and manufacturers therefore have a legal responsibility to protect consumers against it.

A consumer or his family can file a civil suit demanding compensation from the manufacturers if a tampered product results in injury or death. “In the Tylenol case, the families’ lawyers contended that the manufacturer (McNeil Consumer Products Company, a division of Johnson & Johnson) had been careless in its packaging and that it should have foreseen that the product could have been tampered with before putting it into the stream of commerce”.

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In general, product liability litigation involving a product tampering case may involve one or more legal theories, including the following:

- **Product liability:** The injured accuses the manufacturer of making a product that was defective and unreasonably dangerous because of inadequacy in packaging. Such a defect can include a failure to design or manufacture packaging properly to prevent tampering, or failure to make tampering evident to the consumer. Thus, it is important for the manufacturer to select the appropriate packaging technology that provides the required protection consistent with regulations and product use.

- **Negligence:** To show that a company was negligent, the plaintiff must prove that the manufacturer failed to act with a level of care that a reasonably prudent person would have done under the circumstances. In this case, it is critical what the company did to design and employ packaging technologies to prevent foreseeable tampering or make it evident to the consumer.

- **Breach of warranty:** Sale of a product may include an implied, or explicit, product warranty from the manufacturer. If a product reaches a consumer in tampered condition, the consumer may contend that the warranty was breached.

**REDUCING THE RISK OF PRODUCT TAMPERING**

In order to prevent and reduce the risk of tampering following points should be considered:

- Implement Good Manufacturing Practice (GMP).
- Apply appropriate tamper-evident packaging consistent with regulations and product use.
- Reinforce and provide an effective product recall strategy.
- Apply the right strategy in case of tampering in respect of media and communication.

**Good manufacturing practice**

Focusing on the manufacturing process, there are several stages where a product can be tampered with or contaminated. Product contamination can occur at the beginning of the process. If a raw material is contaminated without an effective quality control process, it could be processed and transformed, affecting the quality of the final product.

According to the GMP, “Upon receipt and before acceptance, each container or grouping of containers of components, drug product containers, and closures shall be examined visually for appropriate labeling as to contents, container damage or broken seals, and contamination.” Moreover, “Components, drug product containers, and closures shall be stored under quarantine until they have been tested or examined, as appropriate, and released.”

A line operator, a contractor or an external visitor could also tamper a product during the production process. It is therefore good practice for the manufacturer to strengthen the controls among the employees. It is crucial to complete a background check and to supervise all employees.

The operations teams should only have access to specified areas. This access should be limited to those areas and portions of the operations room, which are necessary and relevant to the functioning of their role. The levels of access should also be reassessed periodically for all employees.

Operators should be prevented from bringing personal items, and atypical behavior should be kept under surveillance.

Although not strictly a case of tampering, it is important to note that during the production process a product can be contaminated by a failure of the machinery. In November 2006, the FDA announced that a company in Michigan was conducting a voluntary recall for 383 lots of acetaminophen 500mg caplets manufactured and distributed under a variety of store-brands due to microscopic metal pieces found in some of these caplets. The recall involved nearly 11 million bottles containing different quantities of acetaminophen 500mg caplets. This contamination was due to the tableting equipment wearing down prematurely.

At this stage, quality control is very important and just as important as a good preventive maintenance plan.

Products could also be tampered with during the shipment. It is crucial to test that public storage warehousing and shipping (vehicles and vessels) implement appropriate security measures and random inspections should be done on the storage facilities, vehicles, and vessels. Moreover, missing stock or any other irregularities should be examined in detail and local law enforcement should be alerted of any unsolved issues.
**Tamper-evident packaging**

Packaging is a very important element in product safety. Besides its main function of protecting the product inside against physical and microbiological contaminants and oxygen ingress, packaging also provides brand recognition, product differentiation in the marketplace, coupled with the ability to protect the consumer against tampering (Cliona Reeves, 2004).²

A tamper-evident packaging feature is very important as it allows the consumer to notice immediately whether a package has been tampered with or altered in any way. In case of anti-tampering packages it is more appropriate to say “tamper evident” rather than “tamper proof” or “tamper resistant” as a package is meant to be opened by a consumer in the same way it can be opened by a tamperer.

What is crucial and can point out the effectiveness of a package is its ability to resist violation and the difficulty that a potential tamperer encounters in trying to restore the package to its original condition. The only way to enhance its effectiveness is during the package design phase. At this point various tests can be carried out to verify the quality of the packaging against tampering and highlight its possible weaknesses. The design and product development is a very important element for product liability prevention as deficiencies can easily be corrected at this stage.³ Another important factor is the labeling of a product. By reading the label a consumer must be able to notice immediately if the packaging has been tampered with.

Examples of label statements⁴:

<table>
<thead>
<tr>
<th>Tamper-evident feature</th>
<th>Suggested wording</th>
</tr>
</thead>
<tbody>
<tr>
<td>Film wrappers</td>
<td>- Do not use if film wrapper is damaged or missing.</td>
</tr>
<tr>
<td>Blister or Strip packs</td>
<td>- Do not use if blister seal is broken.</td>
</tr>
<tr>
<td></td>
<td>- Do not use if blister backing is damaged.</td>
</tr>
<tr>
<td>Bubble packs</td>
<td>- Do not use if blister seal is broken.</td>
</tr>
<tr>
<td>Heat shrink bands or wrappers</td>
<td>- Do not use if seal (around cap/under lid, etc.) is broken or missing.</td>
</tr>
<tr>
<td></td>
<td>- Do not use if tape (band) around cap is damaged.</td>
</tr>
<tr>
<td></td>
<td>- Band around cap must be present to ensure package security.</td>
</tr>
<tr>
<td></td>
<td>- The seal over/around the cap is your assurance that the package has not been opened.</td>
</tr>
<tr>
<td></td>
<td>- For your protection, this bottle has an imprinted seal around the neck.</td>
</tr>
</tbody>
</table>

Consumer education is extremely fundamental to the proper effectiveness of tamper-evident packaging. Therefore, warning consumers to be aware of the correct appearance and configuration of a specific product is very important. If consumers were taught to look out for the color of a package, a logo, and also the shape and design of the product itself, they would search for evidence to prove the authenticity of a product. Responsiveness and the education of consumer is, and will always be, the most important element in any security plan. True tamper-evident packaging must make it unequivocal at first sight that the product has been tampered with. (Eric F. Greenberg, 2004)⁵

**Products recall strategy**

In cases of tampering, it is very important to act promptly. J&J was able to recover from the Tylenol poisonings quickly due to its successful product recall strategy. The chemical/pharmaceutical company recalled the capsules within days (the recall included approximately 31 million bottles, with a retail value of more than 100 million dollars) and subsequently introduced tamper-resistant tablets shaped like capsules within months (coupled with significant price promotions), which set a standard for the industry. Whereas at the time of the scare the market share of Tylenol collapsed from 35 to 8 percent, it recovered in less than a year, thanks to J&J's prompt and aggressive reaction.⁶

As in most cases, the easiest way to respond promptly is to plan ahead. Every company should have a recall plan which provides information on “who” “what” “where” and “how”. Failure to prepare adequately for a product safety recall can
result in considerable and permanent damage to a company’s brand and reputation. Developing a plan before a recall hits is key to minimizing damage should one occur. Although a company may recall their product for a variety of reasons, the recall due to tampering is very critical for an industry and needs to pay special attention. The detailed steps of the recall may vary depending on the cause; the basic process for any recall is usually the same:

- Nominate a person or a team to examine the problem, assess the risk and co-ordinate the recall.
- Identify the steps that need to be taken to address the problem.
- Identify which models or batches are affected (by serial number, batch marking), when these were produced and where they have been distributed.
- Notify distributors, wholesalers, importers agents and retailers.
- Prepare and undertake a publicity campaign to ensure all users of the product are aware of the recall.
- Monitor the recall.  

COMMUNICATION

Effective communication is another key element in a successful corrective action program. A fast and efficient action plan may even enhance the reputation of a company with the consumers. The communication program should include the following elements:

- A central communication center with free telephone number (hotline)
- A list of audiences to be contacted
- A list of media to be used
- Draft communications for different media and audiences

Recall advertisement should be placed in the most relevant newspapers in each country to reach the targeted audience. It is important to have a trained spokesperson that can prioritize the corrective action and handle any media enquiries. In case of tampering, companies should try to respond in a proactive, open way with the press during a marketplace crisis and give accurate information as quickly as possible. This helps to avoid speculation, to ease the tension and to keep control of the information reaching the public.

CONCLUSION

Today the risk of tampering is foreseeable. This risk can be minimized if specific precautions are followed in design and manufacturing and consumers are properly educated by proper labeling.

Although the level of consumer awareness can vary following significant events, their consciousness should always be kept alert to avoid cases like Tylenol from repeating itself. For example, in order to enhance consumer attention, it could be useful to provide a notice on the shelf dedicated to the entire range of OTC products. This could be used as a secondary reminder to the customer to ensure that the individual product has not been adulterated by looking for the tamper resistant feature(s).

Currently the likelihood of tampering is low, but the severity of its consequences, should tampering occur, is very high. Companies may suffer significant and irreparable damage to their brand and reputation if their product is tampered with and they are found unprepared to deal with an eventual crisis.

With adequate precautions, planning and preparation, manufacturers will be able to reduce any potential damage to themselves and their consumers.
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