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Tamper-proof Pharmaceutical Packaging

The EU`s Falsified Medicines Directive and the Future of Closure Seals Standardization

1.   The EU`s "Falsified Medicines Directive"

There is hardly another product that reaches consumers or patients for which packaging requirements are as varied as for pharmaceutical products. The »Poisons Prevention Packaging Act« (PPPA) enacted in the United States back in 1970 addresses the issue of child-resistant packaging of substances that are potentially harmful to human health. In the EU, DIN EN ISO 8317 and DIN EN 14375 standards set out the requirements for child-resistant packaging. In the light of these demands, it is surprising that hardly any packs containing medicines are currently provided with tamper-proof seals. The implementation of the EU's "Falsified Medicines Directive" intends to change this.

On June 8, 2011, the EU Parliament and the Council of the European Union enacted Directive 2011/62/EU. It toughens the provisions of Directive 2001/83/EC for the production and distribution of medicinal products for human use and aims to prevent the introduction of falsified or altered pharmaceutical products into the legal supply chain.

The obligation to transpose this directive into national law was imposed on every EU member state at the beginning of 2013. As a result, the German Pharmaceutical Products Act (AMG) was amended on October 19, 2012. Section 10 AMG requires that pharmaceuticals for human use have security features, as well as the possibility to detect potential tampering, on their outer packaging.

Furthermore, finished medicinal products which are repackaged by another manufacturer must be provided with equivalent security and sealing features and allow the same type of inspection to be performed for authenticity and intactness of the outer packaging as the original product (Section 13, AMG).

2. An EU Standard to Define "Tamper Verification Features"

The new EU Falsified Medicines Directive requires the outer packaging of any medicine to be provided with the following features

1. "Security features which make it possible for wholesalers and persons who are empowered or authorized to dispense medicines to the public to verify the authenticity of the medicine and to identify single packs

2. As well as a device which makes it possible to check if the outer packaging has been tampered with."

But what is tamper-proof pharmaceutical packaging? A working group within the Packaging Standardization Committee (NAVp) of DIN e. V. was formed and tasked to formulate a clear definition. This working group has developed a standard proposal which, via the corresponding Mirror Committees, Working Group 12 "Marking" of the Technical Committee (TC 261), is to be adopted as an EU-wide CEN Standard (DIN EN 16679:2014) and/or as national standards of the member states.

The standardization serves to define the features used for tamper verification. These features should indicate that the outer packaging of a finished product has been opened or tampered with in order to prevent the unnoticed entry of falsified medicines into the legal supply chain.

The information provided by this standard primarily serves as guidance to pharmaceutical manufacturers and relevant approval and test institutes with respect to testing the suitability of seals, and lays down the following requirements:

- The tamper-proof seal must not impair the readability of the prescribed information.
- The prescribed packaging text must remain readable after the pack has been opened.
- The application of features to check tampering attempts may lead to an increase of the physical force required to open the packaging but must not substantially aggravate handling and opening the pack.
- The utilization of opening aids, such as special perforations or starter tabs, may be necessary.

Tamper verification is performed by wholesale distributors, persons authorized to dispense drugs, such as pharmacists or nurses, and other authorized personnel. These groups are enabled to carry out a visual inspection to verify the presence of the security feature and to demonstrate if the packaging has been tampered with.

The standard describes the scope of application, the requirements and features of tamper-proof pharmaceutical packaging, and provides specific recommendations for appropriate sealing.

3. Tamper-Proof Seals for Folding Boxes

Different methods have become established in field use for the purpose of reliably indicating the initial opening of folding boxes. Their effectiveness in providing tamper evidence varies.

3.1 Glue Dots

Gluing the tabs of the box using glue dots or labels is a technique that particularly suggests itself for this purpose. In this case, an adhesive—or combination of adhesives—or a label is applied to seal the packaging. This type of folding box may contain perforations which make it easier to open the box. To gain access to the product and to exchange the contents, the tabs or labels must be cut or torn, which visibly damages the box when it is opened for the first time.

3.2 Folding Construction

A specially constructed folding box is another conceivable option. The tabs and the body of this type of box are designed to "activate" the security feature when the tabs are inserted during the packaging process to seal the box. This technique leads to visible, irreversible damage when the box is opened for the first time. However, these delicate box constructions have not made their way into the marketplace to date because they must be handled with great care in the packaging and shipping process to prevent a premature opening of the box.

3.3 Self-adhesive Seals

Seal labels have proved to be particularly viable. Self-adhesive seals for first-opening protection provide an ideal combination of tampering and counterfeiting protection. The manufacturer's brand logo on the seal intensifies the recognition effect and improves the enforcement of legal brand protection rights. The seal labels have to ensure the intactness of the sealed component of the packaging. Inevitable visible and irreversible damage or alteration of the packaging and the label when opening the pack is the criterion for tamper verification.

3.4 Penetration Indicator

Closure seals with irregular die cutting geometries and protective varnish coatings to which a new label will not adhere are available as well. They ensure that tampering attempts by cutting through a label and subsequently covering it with a new seal will not go unnoticed. An integrated penetration indicator provides even more effective tamper evidence by causing serrated edges to curl up when cutting through the seal, which prevents an undetectable masking of the damaged seal.

① **Conventionally opened seal**

② **Seal has been cut through and box opened**

3.5 Tearing Fibers

Transparent seals that do not cover the inscription of the batch number and expiration date on the packaging tabs are in widespread use. Solutions which, due to their high adhesive strength cause the paper fibers to tear in a tampering attempt or—in the case of heavily varnished box surfaces—lead to "self-destruction" of the label are well-established in field use.

Seal unopened, opened and closed again

The standard recommends three examples of closure variants that prevent the unnoticed reclosing of packaging:

- Fiber-tear labels damage the cardboard box surface thanks to their strong adhesion.
- Void seals reveal a previously covert pattern or text after initial detachment.
- Seals with a zipper perforation show a conspicuous tear edge.

Other sealing techniques such as film wraps, blisters and sleeves today are playing only a minor part in secondary packaging of pharmaceuticals.

3.6 Void Effect

As very fragile label film stock may lead to dispensing problems so-called void films are typically used. They leave a warning message, a brand logo or a pattern on the surface, which is invisibly incorporated into the security seals through the integrated partial release of the film and adhesive. A non-adhesive starter tab makes it easier for the user to open the seal and also allows the box or wallet to be closed again. Multi-Seal labels effectively seal pharmaceutical packaging and allow multiple opening and closing of the packs. When the pack is opened for the first time a message emerges from a solid-colored area and effectively indicates any attempt to open the packaging. The message remains clearly visible even when the seal is reapplied in exactly the same place.

4. Conclusion

Manufacturers respond to the challenge of making pharmaceutical packaging safer with time-tested technologies. However, the qualification and implementation process should not be underestimated. In addition to established know-how, for instance in product development and purchasing logistics, the high quality criteria of "Good Manufacturing Practice" (GMP) must be maintained. Now, additional security requirements need to be observed: Have questions relating to security production and distribution been resolved? Have requirements concerning confidentiality and the approval process been established? Tampering and counterfeiting protection make detailed demands on security management. Even though legislators have formally "breathed leagal life" into the EU Directive by adopting the delegated legal act and granted a three-year transition period, manufacturers and packagers of medicines for human use should not wait and address the new requirements for their packaging lines now.

About Schreiner MediPharm

Schreiner MediPharm, a business unit of Schreiner Group GmbH & Co. KG based in Oberschleissheim near Munich, is a leading developer and manufacturer of innovative, multifunctional specialty labels and marking solutions with value-added benefits for the pharmaceutical and medical device industry. Thanks to its strong solutions expertise and specialized know-how Schreiner MediPharm has established itself worldwide as a highly capable development partner and reliable quality supplier to leading pharmaceutical companies.

In the field of pharmaceutical security, Schreiner MediPharm is supported by the security experts from the competence center Schreiner ProSecure. Schreiner ProSecure is a recognized specialist for authentication, tamper protection and track & trace.

The combination of these competencies enables the systematic realization of product requirements in the field of product and brand protection.