



Tamper evidence solutions within the framework of EU Directive 2011/62/EU for pharmaceutical packaging

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Tamper-Evidence-Solutions under discussion

Tamper evidence solutions within the framework of EU Directive 2011/62/EU for pharmaceutical packaging

With the adoption of Directive 2011/62/EU on 8th June 2011, the EU set Europe-wide guidelines for making falsified medicinal products for human use more easily detectable for the purpose of protecting the health of patients. This amendment, also known as the „anti-falsification directive“, in the so-called EU pharmaceutical package is composed of two different regulations:

A serialised code on all packaging enables partners involved in the supply chain to verify packaging by means of a data base entry. Each package bears a unique code.

At the same time, the tamper evidence regulation makes manipulating packaging more difficult. The packaging is thereby sealed so that any premature opening or manipulation of the packaging is detected by partners in the supply chain, the supplying pharmacist for example. One of the purposes of this regulation is to prevent falsified medicinal products from being repackaged in valid packaging.

Both of these regulations are set out in the appended letter „o“ of article 54 of EU Directive 2011/62/EU:

„o) for medicinal products other than radiopharmaceuticals referred to in Article 54a(1), safety features enabling wholesale distributors and persons authorised or entitled to supply medicinal products to the public to:

- verify the authenticity of the medicinal product, and
- identify individual packs,

as well as a device allowing verification of whether the outer packaging has been tampered with.«

With these regulations the EU is reacting to the risk of falsified medicinal products appearing in original packaging from the drug manufacturer that has been manipulated. Such falsified medicinal products that have been put on the market within the EU by product pirates present an incalculable health risk for patients and also result in enormous damage to corporate image and financial losses in the pharmaceutical and supplier industry.

The required serialisation will most probably be carried out by means of a combination of a 2D barcode based on an ECC200 code and a row of readable code numbers (including a country code, manufacturer code, product code, sequential serial number, possibly a manufacture/best-before date, check digits, etc.) using an imprint procedure in an as yet unspecified standardised position on the packaging. Baumer hhs offers special solutions for the verification of this code.

In order not to go beyond the scope of this white paper, we mainly wish to focus on the subject of tamper evidence and, in this context, on the impacts of this Directive on the production of folding boxes.

»Tamper-Evidence« means a feature that enables unauthorised access to the product to be detected easily. This term must not be confused with „Tamper-Resistant“, a packaging attribute that is intended to make access to a product more difficult. Ultimately, unlawful access cannot be prevented; a folding box is not a safe. The aim is to ensure that the packaging is at least damaged enough when opened so that manipulation can be detected.

»Tamper-Evidence« is therefore a way of security that the packaging has not been opened.

Gluing the lid flaps: the most economical solution

A consequence of the „Tamper Evidence“ regulation is that, in addition to the gluing of the side seam, the folding box's lid flaps are also sealed. This sealing can be achieved by means of a seal, shrink wrapping packaging or gluing.

Gluing is by far the most economical sealing solution. Consumable costs of 1.5 - 2 Euros per 10,000 packages (2 lid flaps, each with 2 hot melt points - €5/kg for each hot melt) can be calculated for each packaging. In addition, when starting up the machine there are potentially the costs of set up and filling the hot melt systems.

Even doubling the amount applied, as is recommended later in this text, does not diminish the economic benefits of gluing. A cost comparison with the often propagated seal solutions is recommended.

With regard to processability, there are no limits with glue application. In modern folding carton machines, in which this technology is standard, several glue points are applied on each box at a machine capacity of 120,000 folding cartons per hour. This is an output that packaging plants are not yet able to achieve. Baumer hhs is a system provider for leading manufacturers of folding carton gluing machines.

Paradigm shift in the evaluation of gluing

The purpose of gluing was originally limited to just sealing packaging. In terms of the „tamper evidence guideline“ that now has to be met, in the future gluing will turn into a security feature, as packaging must not be capable of being opened at gluing points without a manipulation being apparent.

Two different situations must be distinguished between when it comes to gluing:

The gluing of the side seam and possibly the bottom (e.g. for an upright box) by a folding carton manufacturer

The gluing of the lid and possibly the bottom in a packaging plant

Tamper-Evidence-Solutions under discussion

The situation at the folding carton manufacturer

Gluing in folding carton manufacturing is generally only carried out using cold glue (also known as dispersion glue) or using a combination of hot melt and cold glue. Cold glues are physically bonding glues. With cold glues, the polymers involved in the formation of glue layers are in a watery dispersion agent. The glue layer develops after the liquid components are evaporated and absorbed into the packaging material. The spaces that become more tight in the joint thus create capillary force, which the polymer particles make into a homogeneous fusion due to their plastic characteristics. At the same time, static friction forces develop in the substrate surface, which, to a large extent, includes mechanical adhesion in the porous and rough surfaces of cardboard packaging material.

A solidified glue layer between two cardboard or paper joining areas with dispersion glues cannot be separated without damaging the fibres of the cardboard surface. Manipulating a glued point is extremely difficult because solidified cold glue cannot be restored to its original state, even by adding water or any other substances. Even a layman can easily identify the manipulation of a glued folding carton, if cold glue is used. After a box is opened by manipulation and reglued, the packaging will generally no longer be flat in the glued area. Weakening of the cardboard in the area of the folding carton's side seam can enhance the effect. Due to the easier detection of a manipulation, the requirement of the tamper evidence regulation is already optimally met and just has to be supported by a corresponding technical packaging design, which ensure complete gluing of packaging by means of outline perforations or similar elements.

The advantages of using cold glue lie in the cost-efficient adhesive, the lack of solvents and the good level of processability. The disadvantage is first and foremost the long setting time of the glue. The lines have to be mechanically compressed for a relatively long time. Press sections are therefore mostly integrated into folding carton gluing machines, through which the folded cartons are transported flat under pressure following glue application.

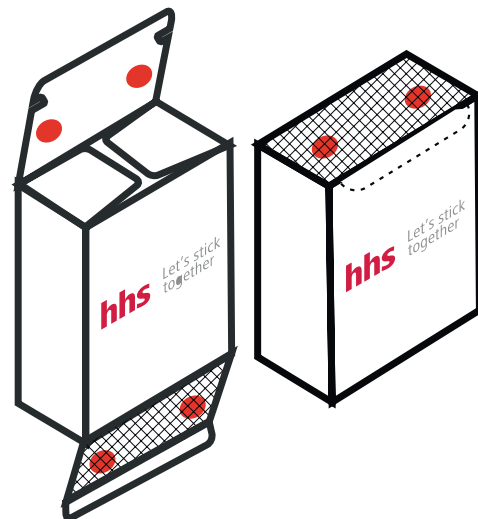
A combination of hot melt and cold glue is mostly used for objects with high restoring forces, e.g. folded down tabs on upright boxes. In so doing, the hot melt is used for assembly bonding for the initial bond. Hot melts set very quickly and hold the object in the desired position. The additionally applied cold glue is used for a lasting bond. It sets less quickly than hot melt, but cannot be unfixed by external manipulation (e.g. by heat application) after the drying process.

The situation in a packaging plant

In packaging plants, hot melt is generally used on packaging that require gluing due to its technical design. In the process, the hot melt demonstrates its full strength in speed. As the glue sets extremely quickly, high restoring forces on the lid and the high strains due to the packaged good during transport and the packaging process are countered. Only using cold glues is also not possible because press sections cannot be integrated into many packaging machines that lack counterpressure components with already upright folding boxes.

Gluing using hot melt is, however, not tamper-proof in every case within the meaning of Directive 2011/62/EU. Special hot melts must be used.

Hot melts are also physically bonding glues. They have a solid form at room temperature, are solventfree and are thermoplastics. They can be reversibly softened by adding heat and hardened again by reducing the temperature. A hot melt glue point can therefore be easily opened, for example using a heated blade, and resealed by adding heat, with no need to apply more new glue. Therefore, in industrial terms, it is conceivable that hot melt glue points could be manipulated without this being detected. However, special hot melts with modified recipes can be used. Baumer hhs provides the option of testing suitable solutions in its own hhs solution-centre.



Pic.1: Gluing with hot melt dots

Tamper-Evidence-Solutions under discussion

Reactive hot melts provide a tamper-proof alternative.

The reversibility of hot melt gluing can be prevented by using a special reactive hot melt. With these glues, the physical setting process is performed by means of a chemical reaction, which transforms the thermoplastic hot melt into an irreversible duroplast/elastomer. The best known example of this reactive hot melts are one component polyurethane hot melts. These have the advantage of linking durably. A disadvantage is the small amount of isocyanate that is present, however this does not cause any health impairments once the glue has cured.

Like conventional hot melts, PUR hot melts can also be applied to the lid. Baumer hhs has developed special product feeds that enable application with clear edges without tailing.

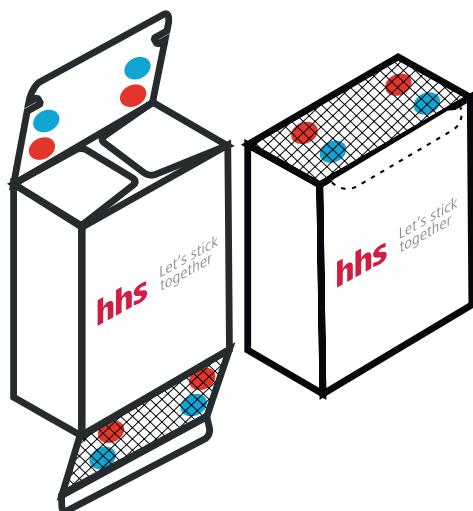
Due to the secondary chemical reaction, these glues provide tamper-proof adhesion. Our colleagues are also happy to test this type of gluing with you in the hhs solution-centre.

Combination gluing using hot melt and cold glue

Merely using cold glues in packing lines is not possible due to the long time required for setting. The restoring force on the folded glue flaps would be too high for a secure bond.

In terms of the Tamper Evidence regulation, it would also be ideal to use a combination of hot melt and cold glue in this case. The hot melt enables a spontaneous bond to be made, and the cold glue is used for a permanent, tamper-evident seal after filling. Folding box structures that prevent the cold glue from being smeared or removed in the packing line must be used.

Manipulation by means of heating or spontaneous cooling, to which the hot melt reacts critically, is not possible with combination gluing once the cold glue has set.



Pic.. 2: Gluing with Hot melt and Cold glue

Baumer hhs offers the possibility of operating both the cold glue and hot melt systems via a central control station. Machine operators can operate both systems while the machine is running without requiring any extra effort, they just have to keep an eye on the screen. The costs of the additional cold glue application are thus limited to the materials handling and the corresponding guns. These low additional costs are a clear plus point when it comes to security.

This solution can also be verified in our hhs solution-centre.

Quality assurance

In terms of „good manufacturing practice“, the packaging sealing will have to be checked within the framework of the new Directive in future, as this is now a security feature. The Baumer hhs portfolio contains several sensors suitable for monitoring glue application at the respective glue points. Baumer hhs recommends the tried and tested HLT-300 sensor for hot melt applications.

As soon as the operator has defined the tolerance of the sensor for the optimum amount of glue, the electronics in the sensor works autonomously. With the HLT-300, instead of sending minimal analogue signals via amplifier interfaces, the decision as to whether a product has been glued well or not is already made in the sensor the answer is purely digital. From here on, only purely digital signals are processed troublefree. Thus, the result is virtually free of the usual restrictions regarding product speed, point sequence or influences in the harsh industrial environment. Badly glued products are reliably detected according to the „fail safe principle“. It is therefore possible to conduct a 100% check on every box!

Baumer hhs developers have also integrated other useful aids for daily use into the approx. 20 x 40 mm small casing. A laser facilitates the mechanical gap adjustment, an integrated light barrier identifies the precise product length and digitally transmits this via a separate output to the superordinate control unit.

Baumer hhs' ULT-300 sensor measures the amount of cold glue immediately after application. In combination with Xtend control units, the sensor evaluates where glue must be and where it must not be, and signal processing in the customer's own PLC is also possible. ULT-300 detects narrow and flat glue applications as well as glue beads and dot applications. The signal processing is identical to that of the HLT hot melt sensor.

Solutions for complex glued products are possible with state-of-the-art camera technology, that has been specially developed by Baumer hhs. Baumer hhs also provides solutions that monitor the correct folding of the tuck-in flaps. Not only is glue application monitored, but also the correct closing of the box.

Tamper-Evidence-Solutions under discussion

All monitoring solutions work according to the »fail safe principle«.

By fail safe, merely a fail-safe switching of the sensor is not meant at Baumer hhs, rather the principle of evaluating a product as defective until it has been unequivocally evaluated as faultless or as a good part by means of all quality controls. Individual inspection stations are logically linked to each other, so that only a single fault in the chain (faultlessness not confirmed) prevents overall approval. Even if a sensor fails and thereby cannot confirm faultlessness, the overall process remains faulty and leads to a negative evaluation and thus to the removal of the folding carton concerned from the production flow. This dynamic fail safe principle has been used from the outset at Baumer hhs and ensures a high level of safety and quality in all systems used for the production of packaging.

Software for integration and quality control

All sensors involved in the checking processes (code reader, glue application controls, position monitoring, area and height determination) are linked by means of unique evaluation software.

For this, the individual signals are logically linked together and combined in an overall evaluation, which ultimately generates the control signal for the rejection mechanism.

As an integrated solution, the central controls offer numerous advantages. Rejected parts can be removed in the optimum location in terms of production technology as each part is individually recorded, identified and monitored throughout the entire process.

With Baumer hhs it is not necessary to allocate a discharge mechanism to every quality control station.

In any case, it is unnecessary to stop production as a whole for the removal of faulty products and this is prevented by the clever integration. Baumer hhs offers corresponding discharge mechanisms that are linked to the central control system and reliably remove the product.

In addition, the quality can be recorded over long periods, multiple cycles or batches or various production processes by means of statistical methods.

Seal monitoring

The checking of additionally applied seals and their correct placement is possible by means of Baumer hhs camera technology. Equally, this applies to transparent seals in a „non-label look“.

Fault concepts are necessary

If one packaging is identified as not being properly sealed, it must be removed from the product flow without stopping the machine. For serialisation this means that the identification number has to be deleted from the database or the packaging may have to be reprinted and refilled. For this, both EU Directives and company-specific production and quality assurance concepts must be developed. Close coordination between companies involved in production

and packaging and the distributing company is necessary in order to guarantee continuous traceability.

Alternative Tamper-Evidence-Solutions

In addition to the cost-effective variants, shown here, due to a special packaging design and simple gluing in accordance with the afore-mentioned guidelines, various sealing solutions are also under discussion. Here, the tuck-in flaps on the filled and sealed packaging should be fixed by means of adhesive seals that have to be destroyed before the box is opened. In our opinion, these seals cannot be designed as a simple label, as such labels can be removed by applying heat or water. Special labels and seals that are destroyed in the removal process so that they cannot be re-used would be required for this. However, poor processability and the high additional costs for this type of seal have to be taken into account. The seals must be attached and permanently fixed, and the gluing process must be controlled and documented by means of suitable checking processes and systems. Depending on the design of the seal, there is also always the risk that such a seal could be destroyed while being attached. This then inevitably leads to a reduction in packaging speed and increases costs.

A seal could also be made of paper strips, that are laid around the edge of the packaging like those used on cigarette packs. In order to prevent the seal being removed by manipulation, these seals must be glued using cold glue and the glue points on the folding box must be kept free of coating and ink during the printing process.

The combination of both the seal and packaging elements also always bears the risk of a mix-up and must be monitored according to good manufacturing practice (GMP) guidelines. An incorrect seal that is not associated with this production could be glued on. The packaging concerned must be removed from the production flow.

Of course, this risk does not exist if a standardised seal is used on all pharmaceutical packaging (e.g. a manufacturer's seal). However, a standardised seal limits the possibility of adapting the seal to the design of the packaging and developing the safety concepts that are adapted to the packaging. The security seal attached to the original packaging also reduces the chances of the packaging being securely resealed in a visually pleasing manner after it has been initially opened.

Also, in our opinion, the possibility of meeting the tamper evidence regulation by cellophane wrapping the whole surface of the filled folding box or by shrink-wrapping it in a film does not exist. A cellophane or film wrapping without introduced safety features can be replaced at any time and does not protect the actual product. A further disadvantage of a film wrapping is that the readability of the serialisation code put on the packaging is reduced and the risk of a misread increases. In addition, the film wrapping makes it more difficult to feel the compulsory Braille dots on the packaging.

Another more substantial disadvantage of the wrapping solutions is that the shrink-wrapping can be difficult for elderly or disabled people to remove. Also, the cellophane must be joined to the folding box, e.g. by gluing, so that the supplying pharmacist can recognise whether the wrapping has been removed from the packaging.

Tamper-Evidence-Solutions under discussion

Overall, cellophaning and shrink-wrapping are not recommended as the regulatory aim of tamper evidence cannot be achieved or can only be achieved by reducing the functionality of the folding box.

Conclusion

The efforts made by the EU to secure the majority of prescription and selected over-the-counter medicinal products intended for human use against manipulation by means of comprehensive and sustainable regulations in the European market are welcome. However, it must still be hoped that practical solutions are found that enable the lofty aims to be achieved and that can be realised in daily practice at all levels of production in the process chain. Baumer hhs would like to recommend itself as a partner of the pharmaceutical industry. The large set of solutions agreed with regard to glue application and quality assurance provide a good basis for this.

In our opinion, probably the most efficient and practical solution from a process perspective, is a glued all round seal of the cardboard packaging based on combinations of dispersion and hot melts with the additional design of cuttings with corresponding tear-off perforations. Baumer hhs offers several proven solutions for hot melt or PUR hot melt applications. Accept the offer of developing a sustainable and practical solution together with Baumer hhs.

No losses of process speed are expected for any gluing solutions and the process and material costs for glue application are considerably lower than the 6 Euro cents per folding box that is being discussed for a Tamper-Evidence-Solution. All required gluing technology and systems, including in terms of writing, reading and control systems required for quality assurance, are already available at Baumer hhs and can often be integrated into existing production and packaging lines without incurring large costs and additional effort. The EU also allows manufactures to decide whether to meet the provisions of 2011/62/EU section 54 »o« by using corresponding tamper evidence packaging concepts. This allows leeway for implementation approaches that are optimally adapted to the financial and technical circumstances of manufacturers and their suppliers.



Your contact partner for any questions concerning tamper evidence and hot melt applications:

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Baumer hhs GmbH headquarter in Krefeld

Baumer hhs GmbH

With its headquarters in Krefeld, Germany, Baumer hhs GmbH is an internationally operating manufacturer for industrial glue application systems in conjunction with quality assurance systems and camera control systems. They provide their customers with a carefully selected portfolio from the areas of hot melt and cold glue processing with guns, pumps and pressure tanks, as well as control and monitoring systems for quality assurance in glue application and adhesive application for factory automation.

Baumer hhs is part of the Swiss Baumer Group. With over 2,500 employees and production plants, sales offices and representations in 36 branches and 18 countries, the family business is always close to its customers. With high quality standards that remain constant across the world and an enormous innovation potential, the company provides customers from numerous industries with crucial advantages and measurable added value.

More information about Baumer hhs, to all products and other services are available on the Internet
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