ENCODING AND READING OF CODES ON GLASS CONTAINERS FOR PHARMACEUTICAL AND DIAGNOSTIC PRODUCTS

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In light of ever increasing demands for documentation and monitoring, advanced methods for product identification are of great interest to the pharmaceutical industry, especially with regard to guaranteeing patient safety and preventing mix-up. In the case of disposable syringes, the following requirements can be formulated.

Patient safety

The European Federation of Pharmaceutical Industries and Associations (EFPIA) recommends an identification solution in the form of a data matrix barcode.[1] Consequently, new measures for guaranteeing patient safety were presented by the European Commission in December 2008.[2] Specific marking of the primary packaging should guarantee that it can be tracked and traced. By placing an individual code on each separate syringe, the pharmaceutical product can be tracked to 100% over the entire process chain.

Each glass container shall bear such individual identification which can be read during syringe manufacture, filling and packaging. Using a database, the data can be compared and retraced. This enables the medication to be tracked and traced from consumer back to manufacturer, in conjunction, for example, with the endeavors to introduce an electronic pedigree system (e-pedigree).

Avoidance of mix-up

There is also a demand for improved identification systems in the context of avoidance of mix-ups within the process chain of filling and packaging.

Pharmaceutical active ingredients and diagnostic presentations are available in many dosages. Parenteral medications, for example solutions for injection, are distributed worldwide in prefilled glass syringes (disposable syringes) in up to 16 different dosages.

Today, coloured rings on the barrels of the glass syringes facilitate quick identification of the different dosages.

On account of the coloured rings already in use, further colour-coding options cannot be pursued since the range of colours is limited and depends on the energy input in the stress-relieving furnace (gas or electric heating). Furthermore, the effects which arise from heating during the sterilisation and baked-on siliconisation process cause the colours of the rings on the glass to change. Mechanical colour identification must therefore incorporate increased colour variance in order to guarantee clear assignment of the colours. With 16 colours such a method reaches its limits. Hence, the development of a novel method was the aim.

Requirements for the quality of machine-readable product coding

The optimal solution is to apply an individual, machine-readable code to each manufactured syringe. In line with the present state of technology, the data matrix barcode is perfectly suited to such an application. Very stringent requirements are placed on the fact that the code must be of a consistently high quality, in order to guarantee a high level of readability over the entire process.

Standards ISO/IEC 15415 and 16022 are used as the basis for evaluating the quality of the data matrix barcode, although they in fact apply to flat, printed paper which has been printed with ink, for example.

In this project the translucent codes have been engraved by a laser technique on the transparent curved glass surface. Project-specific guidelines for quality assessment, similar to the said standards, therefore had to be developed.

Evaluation of different marking systems

The following criteria were to be considered when evaluating different systems for marking single glass containers and selecting the most appropriate method:

- no influence whatsoever from the product (drug formulation)
- readability and durability of the code
- mechanical stability of the glass unchanged after coding

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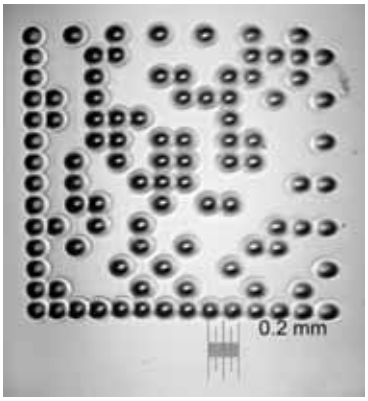


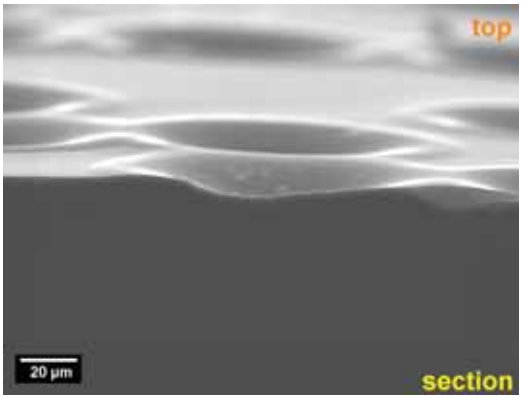


Figure 1: Left – Matrix code produced by CO_2 laser on heated glass guarantees there are no cracks. Right – SEM/BSE of the cross-section of a code enlarged 700-fold. The intact glass matrix is clearly identifiable.

A value benefit analysis was performed to ultimately select the preferred solution. The many variables to be considered were weighted according to their importance. An extensive evaluation process produced a shortlist containing several possible solutions, such as various laser, inkjet and pigment-transfer methods.

One possibility for identification was the ablation of a single layer or multiple coloured layers using a laser. High-contrast codes could be produced with such a method, but it would entail additional production stages. A further identification system for selection was the firing of cold glass with a CO_2 laser (wavelength 10.3 µm), although cracks appeared as a result.

The development of cracks is prevented by heating the glass to the transformation temperature. The selected method with CO_2 laser irradiation on hot glass thus guarantees that no cracks are generated during encoding (see Figure 1).

This laser method, further developed on the basis of a procedure for identifying special glass tubes for technical and pharmaceutical applications [4,5], was fully integrated into the process of syringe manufacture. The data matrix barcode is engraved thereby onto the hot glass barrel. Such a method has certain challenges: to apply a durable, easily readable code as well as to protect the glass matrix from microcracks during laser engraving.

METHODS

Content, structure and quality of the code

The coding is applied to empty glass syringes below the finger flange (see Figure 2), guaranteeing unimpeded transillumination when reading the code.

The content of the square code – unique to each glass syringe – involves a sequence of 16 symbols containing packaging data (glass type, syringe format, labeling site, production line, date of manufacture, batch number) and a serial number. The Data Matrix ECC 200 measuring 14x14 with a perimeter length of 2 mm was chosen as the barcode symbology.

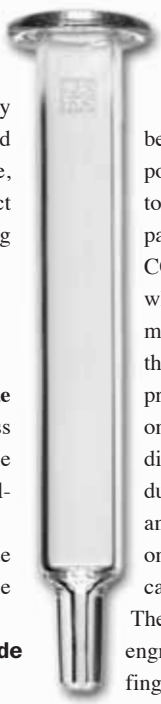


Figure 2: Position of data matrix code below the finger flange.

Laser coding process

SCHOTT FIOLAX® clear glass tubing was used in this project as the starting material for the syringes to be filled. It is made of borosilicate glass of hydrolytic class I, with a transformation temperature of 565°C.[3] An already established laser method [4,5] was further developed within the syringe forming process and the coding device integrated into the existing manufacturing equipment. This entails the commercially available rotary indexing machine for syringe manufacture.

To optimise the laser process in terms of readability of the code, the long-wave CO_2 laser (wavelength 10.6 µm) was programmed to 20% of laser output power. The glass matrix to be marked was heated with burners and the achieved temperature recorded and controlled during the laser process using a pyrometer.

The scan head guarantees that the laser beam is accurately focussed at the desired position on the syringe barrel. In addition to the exact position, it also specifies the pattern of the data matrix barcode. The CO_2 laser head also produces laser pulses which are directed at the glass material by means of scan optics. The pulse length of the CO_2 laser is between 50 and 70 µs and produces temperatures locally of >2,000°C on the surface of the glass. Spots with a diameter of approximately 100 µm are produced on the hot glass by the laser firing, and result solely from the thermal effect on the surface of the glass. This process can be detected indirectly (see Figure 3). The entire data matrix barcode of 2x2 mm is engraved on the cylindrical section below the finger flange (Figures 2 & 3).

If the transition temperature of the glass is not achieved during the laser process, the syringe is rejected immediately thereafter. This is to ensure that only crack-free, coded material is conveyed further.

In order to relax the thermal tension of the glass barrel induced by the manufacturing process, the syringes are ultimately conveyed through the tensile stress relieving furnace. The temperature in the furnace corresponds to the transition temperature of the glass.

The geometric, cosmetic and qualitative properties of the coded syringe are then subjected to visual inspection and several quality control tests.

Optical reading of the code

The 14x14 data matrix barcode is optically read from the surface of the glass syringe. Thus it is possible to produce a variable number of images of the syringe surface. A special image processing system was designed for multiple imaging, comprising illumination, camera and synchronisation to the handling of the syringe barrel.

The images were taken using LED flashlight. The code was backlit (transmitted light method) and the camera delivered a black and white image to the image processing software. Maximum reflection causes the cavities produced by the laser process to appear as white spots on a black background. This is a result of the effect of the lens on local deformations (Figure 5 on page 16).

Figure 3: The process of applying the matrix code. A light can be seen at the point of impact of the laser.

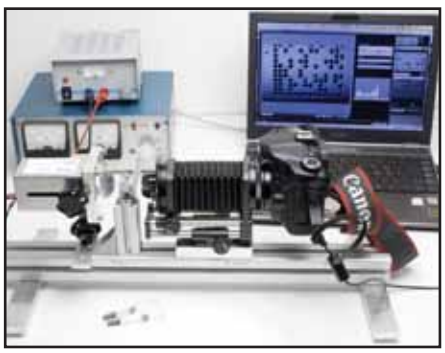


Figure 4: The testing station

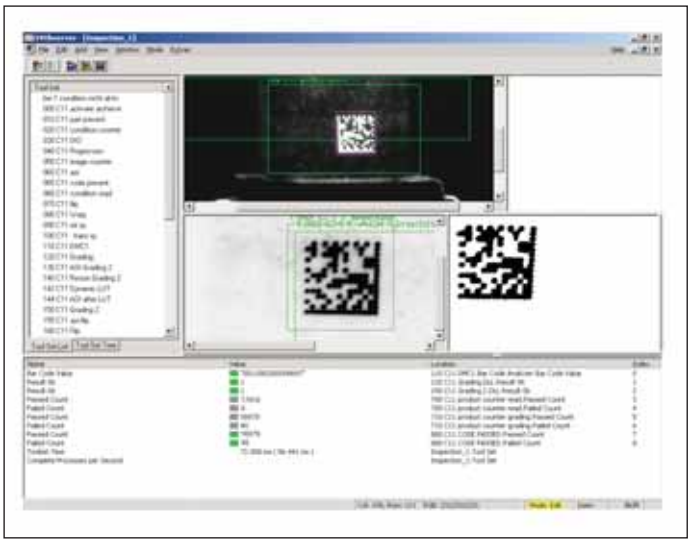


Figure 5: Screenshot of SVObserver with analysis of the code.

The total processing time of the reading phase, including data transfer, is between 20 and 200 milliseconds per syringe, from the point of localisation of the code on the glass. Software (SVObserver, Seidenader) then reads and analyses the 14x14 data matrix barcode. Special filters and additional tools are used to optimise the evaluation of the code.

Based on the scanned image data, the data matrix barcode is decoded and the data saved as well as the quality of the code checked. The glass barrels are then sorted according to quality criteria and released into the filling process. The data saved from the scanned code are transferred via a qualified interface to a superordinate ERP system (PI server).

The clear correlation between data set and medication takes place at the time of filling the solution for injection into the glass syringe.

During the entire production chain of the preparation on the filling and packaging line, the glass barrel undergoes two scanning and assessment steps. The first scanning step ensues prior to siliconisation and sterilisation of the glass syringes. At the end of the filling line the syringes are scanned a second time.

Quality controls

With a view to technological development, tests were carried out to check the quality of the coded glass syringes as well as the code itself.

The syringes were exposed to thermal stress: resistance to high temperatures was tested for 30 minutes at 230°C, and resistance to low temperatures for a week at -20°C and -40°C.

The syringe and code were exposed to mechanical loads: the glass syringe barrels were subjected to hydrostatic burst testing (constant pressure at a rate of 10 bar/sec until rupture) and the resulting fractographic tests analysed (SCHOTT Research). Distilled water was used as the pressure medium.

In order to expose the data matrix barcode to high frictional loads, the parameters were selected in such a way that limit samples emerge. The code was subjected to a friction test using a crockmeter (Mathis) with an abrasive of semi-friable aluminum oxide and silicon carbide with a grain size of P2500 with 50 strokes.

The code was examined on the surface and, after cutting the syringe across the coded area, the cross section analysed for microcracks. A polarised light microscope (PLM) and scanning electron microscope (SEM) with a magnification of up to 625x were used for these tests.

RESULTS

The integration of the coding process into the production line was successful and produced high-quality patterns which later could be successfully read, both before and after the pharmaceutical filling process.

Aside from SCHOTT FIOLAX® clear, two other types of glass were coded successfully, including SCHOTT BORO-8330™.

Reading of the code

To ensure that the code is visible on the syringe barrel, images are taken of the whole circumference of the syringe (see figure 5). To this aim the syringe is rotated while being conveyed by the apparatus past the camera station. Multiple images are produced in the visual field of the camera. Depending on the synchronisation of the rotation, distance and imaging, a variable number of images can be produced to cover the entire circumference of the syringe barrel.

High expectations were placed on the performance capabilities of the reading systems.

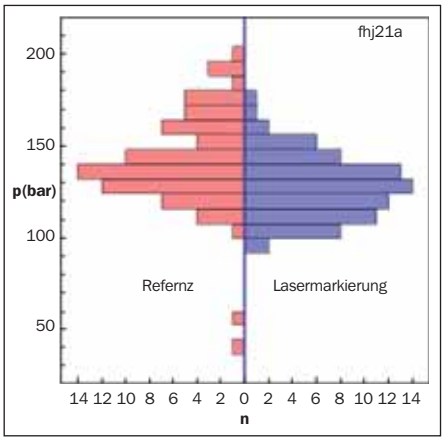
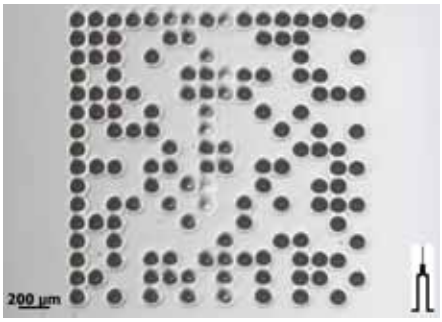


Figure 6: Double histogram of burst pressure testing.



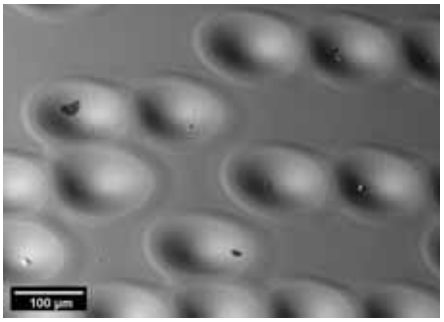
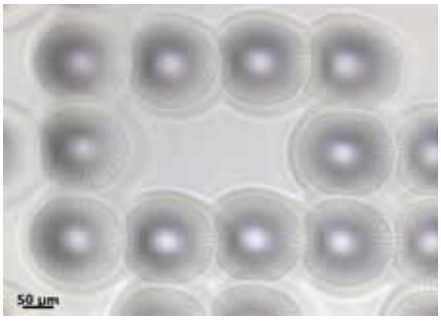


Figure 7: Left – total view of code enlarged 62.5-fold using polarised light microscope, non-analysed transmitted light (PLM/LPNA). Right – 200-fold enlargement of code using SEM/BSE.



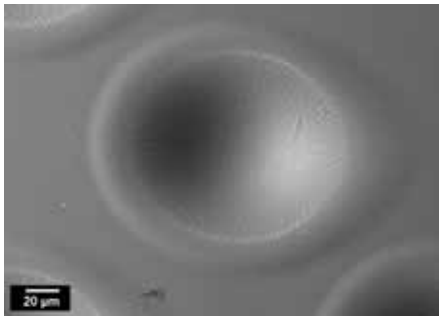


Figure 8: Left – section of code enlarged 250-fold using PLM/LPNA. Right – a code element enlarged 500-fold using SEM/BSE.

The coded syringe barrels were required to pass the test run to 99.9% before entering the packaging line.

To guarantee the prevention of mix-up, syringes of a second batch were deliberately intermixed. These samples differed only by their coded batch number.

The test run was successful. The run lasted 62 minutes, and 17,019 syringes were analysed. Of these, 1,474 items were rejected. This means all of the intermixed syringes were clearly identified. In 40 syringes the code had become contaminated, but was readable once cleaned.

Thus, avoidance of mix-ups is guaranteed and the proof of concept substantiated.

Quality controls

At a thermal load of 230°C, the readability of the samples was satisfactory. The low-temperature resistance testing at 20°C and 40°C did not reveal any damage to the glass resulting from the laser process.

During burst pressure testing, ruptures attributable to the laser marking were not detected. Defects causing breakage therefore were not produced under the applied parameters. No significant differences could be identified at these points between the laser-marked and non-marked syringes (reference). That is, the laser-marking process does not cause any defects in the support points (see Figure 6).

When measuring the data matrix code quality of samples submitted to abrasion tests 90% were readable but 10% of the samples did not fulfill the quality requirements as defined in ISO 16022.

The samples subjected to optical testing revealed no cracks (see Figures 7-8). The quality testing reveals that the coded glass syringes were free of cracks, the mechanical stability of the glass barrels guaranteed and the quality of the coding sufficient.

CONCLUSIONS & PERSPECTIVES

It can be concluded that avoidance of mix-ups was guaranteed and the proof of concept substantiated. The glass barrels also passed all quality inspections. In particular, the glass matrix revealed no microcracks or mechanical damage due to the laser process. The described technology can be used for other types of glass pharmaceutical containers such as ampoules, vials and cartridges, in addition to syringes. Hence we have a promising, industrially proven process for the identification of glass containers.

The newly developed process described here for encoding and reading a data matrix barcode on glass pharmaceutical containers fulfills all the criteria for tracking and tracing, as well as prevention of cross-contamination. In order to be able also to apply this code in the prevention of counterfeits, a random number rather than a serial number should be used as the code. Such technology can also be used commercially to prevent drug counterfeiting.

REFERENCES:

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[5] *A Witzmann, U Trinks, „Verfahren zum Markieren von Glas“ [A method for marking glass], Patent DE 10234002*