Whitepaper on the Deployment of Advanced Primary Pack Coding Techniques for Generic Medicines in Europe

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1. Abstract

The advent of new technologies in the pharmaceutical packing industry provide exciting and innovative ways to improve patient safety, reducing dispensing errors and waste, leading to increased availability of medicines where they are needed most.

This document seeks to introduce, discuss and propose pragmatic solutions to the operational issues which could be associated with the introduction of advanced coding techniques on primary medicinal packs.

Drawing on experience of the fundamentals of the pharmaceutical packing process, the interplay of quality and regulatory requirements, this document proposes a set of simple measures which will allow manufacturers to meet the expanding requirements of their customers.

The final section of this document defines urgent actions which must be taken in order to avoid unnecessary complexity, divergence of standards and most importantly, reduction in the availability of medicines.

2. Introduction

Advances in the capability of pharmaceutical packing equipment have brought about significant new flexibility of function compared to the simple, traditional application of pre-printed lidding foils and product labels. Arguably the most important of these advances is the ability to print increasingly compact and data rich coding at primary pack level. This can be used to print product and batch information, in both human and machine-readable formats, on primary packs and even at unit dose level.

Examples of this primary packaging are tablet blister packs and strip packs, vials containing liquid products and sachets containing powders. In practice, particularly in healthcare institutions, it is often the case that these primary packs are split from their secondary container (often a carton), with the latter being disposed of often some time before the product is administered to one or more patients.

The most prominent benefit of upgrading primary pack coding relates to packs used in healthcare institutions. In these settings it is often the case that primary packs are separated from their secondary container (for example a collation of two blisters are removed from their carton, or a single vial removed from a box containing five units). These primary packs are then loaded into containers destined for specific wards and patients, multiple times a day as dictated by medical and operational needs. Often, even blisters are subdivided into individual doses of product, so that no more than the medicines needed at that specific point must be transported around the facility, eliminating the need for extensive ‘returns’ to the pharmacy area. A significant learning from other areas of the supply chain is that occasions where standard product flows are diverted, or reversed, provide the most significant risk of human error and falsification. As such, any opportunity to eliminate them should be welcomed.

While legislation provides for these activities to take place under the supervision of trained staff, many healthcare institutions are seeking to simplify or remove this process, by receiving packs of medicine which are better suited to their needs. In doing so, risks relating to the pack splitting process, where a blister is subdivided into individual doses, can be reduced considerably. Moving from a blister pack with just a single print of LOT and Expiry

information to blisters supplied with *multiple* repeats of the data over each pocket means that this traceability is assured down to unit dose level.

New technologies in the dispensing environment also benefit from provision of data rich, machine-readable coding at primary pack level. Integration of computerised patient records with pack data allows the scanning of individual product pockets or sachets in order to verify that the product in hand is correct for the patient, guarding against dispensing errors. Enhanced traceability is also possible where records of specific batch information are maintained, improving patient safety with monitoring of adverse events and in recall situations.

These same traceability benefits allow enhanced control of medicines within healthcare institutions with monitoring of stock levels being instantaneous, ensuring that medicines can always be available when and where they are required.

In 2019 the European Falsified Medicines Directive (FMD) Safety Features legislation came into force, and care must be taken not to confuse the traceability requirements of FMD with the features discussed in this document. There is no reporting or alerting functionality proposed for primary packs, nor is it envisaged that any form of aggregation be applied in terms of packaging hierarchy (the same product code printed on the outer package is repeated on the primary). We do however seek to further leverage the ubiquity of the GS1 coding 'normalised' by FMD for additional patient benefit.

However, it should be noted that for all these benefits, the adoption of these new coding standards brings new challenges which require evaluation from a different perspective to that provided by current medicines regulation. While manufacturers of generic products are keen to explore and work with customers to maximise patient benefit, these advances must not come at the expense of the flexibility, reliability and cost effectiveness these organisations have come to provide for European healthcare systems. This document seeks to address these challenges and propose pragmatic solutions to the benefit of patients, governments and manufacturers alike.

3. Methods

At factory level, operatives enter data to the 'line' system based on information stored on batch records, or possibly an integration with a resource planning tool.

The human and machine-readable codes themselves are similar to those applied for FMD, with the significant exception that there is no serialised element present. Commonly used primary pack code elements are given below:

Human Readable	**Machine Readable (AI*)**
Lot Number	LOT (10)
Expiry Date	EXP (17)
Product Code	GTIN (01)

*GS1 Application Identifier

The use of standardised coding terminology and GS1 application identifiers ensures interoperability between codification, scanning and processing systems and gives predictable input data for systems which are configured to process the information contained within, for example, Data Matrix or Databar codes. Examples of these codes are given below:

GS1 Data Matrix:

LOT: AB123
EXP: 10/2023
PC: 12345678912345

GS1 DataBar:

It is anticipated that application of batch coding information using inkjet, thermal transfer or laser coding would replace existing coding methods in some cases, i.e. the use of embossing characters or printing of only the human readable elements on the primary pack. This is a significant benefit since these technologies are significantly less sensitive to variability of the surface onto which the data is printed, compared to embossing.

4. Discussion

Recent developments in technology and the increased awareness of the safety and efficiency advantages the use of advanced codification bring significant opportunity to manufacturers, the medicines supply chain and end users. FMD has driven a substantial upgrade of coding at finished pack level and the industry should now be working to capitalise on this opportunity at primary pack level too.

There is a significant patient safety benefit to the use of advanced coding techniques at primary pack level. The GS1 coding standard allows the automated analysis of product information to ensure that the right medicine is reaching the right patient, furthermore that the pack is within its expiry date and not subject to any quality defect. Medicines supply chains can be optimised to ensure that stock levels are maintained, safeguarding patients against the risk of shortages.

A pragmatic discussion is needed on the challenges associated with implementing advanced coding, not least considering the challenges in terms of available space on the very smallest product packs. There is a significant risk that by following current guidance around font sizes many of the efficiencies enjoyed by users of generic medicines may be eroded or reversed, leading to:

- adverse environmental impacts from increasing pack dimensions
- increased costs due to materials usage and re-tooling requirements
- reduced availability of medicines caused by additional manufacturing constraints and lower machine output.

In particular, font size restrictions for batch coding data and general design would overly restrictive when it is considered that in many cases, coding is currently applied using embossing, resulting in highly variable results which are heavily dependent on the type and specification of the materials and equipment used. In general, inkjet and laser coding technologies guarantee legibility of the coding at smaller sizes than would be possible with embossing.

In the document ‘Guideline on the Readability of the Labelling and Package Leaflet of Medicinal Products’ published by the European Commission, Section B Point 8 details provisions made specifically with regards to ‘Small Containers’, and states:

“*The criteria for small container status would normally apply to containers of nominal capacity of 10ml or less. However, other factors may need to be taken into account such as the amount of information which has to be included and the font size necessary to ensure the legibility of the information*”

It would logically follow that the majority of immediate packaging being described in this document would fit into the category of ‘Small Containers’, therefore manufacturers should be able to rely on pragmatism and flexibility from regulators when designing labelling to include advanced coding features, even in scenarios where it is necessary to reduce font sizes in order to achieve a workable design.

Use of the abbreviation ‘PC’ for Product Code both saves space and is more flexible than variably using GTIN or NTIN dependant on target market. LOT and EXP should become universally acceptable in place on lengthy local market translations which are not possible to print in space constrained areas.

The complexity of producing packs in this way is likely to mean that use of this coding is restricted only to settings where it is required, i.e. hospital environments where machine reading is likely to replace the need for a human to study the print on the pack. Furthermore, with medicines in these situations being handled exclusively by HCPs, it is not necessary for the readability guideline to account for such a wide variety of end users, it being designed to accommodate the poor eyesight of elderly patients who will not have to handle this type of pack.

Finally, it is useful to consider the part which additional, complex features such as the high-quality printing of machine readable coding play in creating a barrier for entry to the casual counterfeiter. While they are not *technically* security features (no government data reporting or alert handling requirement is implied), their replication in order to imitate a genuine pack presents another challenge for rogue actors to overcome in order to introduce their products to the legitimate supply chain.

5. Conclusion

Further adoption of advanced coding practices at primary pack level offers significant advantages in terms of patient safety, supply chain efficiency and user friendliness of medicinal packs.

Their deployment is beginning to become a reality across various healthcare sectors in Europe and we should expect to see this trend accelerate as other organisations realise the benefits they bring.

Manufacturers of medicines are becoming ever better placed to support these initiatives and are, as always, keen to engage with their customers, competent authorities and industry associations to ensure that the most appropriate decisions are taken in order to capitalise on the opportunities available. Whilst doing this, we must safeguard the highly efficient nature of the medicines supply chain in Europe; continuing to supply the right products at the right times at the right cost.

6. Recommendations

We must act quickly! Manufacturers are already being asked to accommodate requests from health authorities and tender bodies. Without an open and pragmatic discussion across industry, we risk adoption of **multiple** standards for primary pack coding, in an area where FMD has already shown that a **single** standard is essential to project success.

Manufacturers should continue to approach pack coding as a core tenet of GMP compliance and see the adoption of advanced coding methods to improve GMP standards and the safety of their processes. At the same time, competent authorities should be should be minded to consider that primary level coding should be considered part of the 'Small Containers' provision of the EC Guideline on Readability, thus ensuring that existing manufacturing and supply chain arrangements can continue without introducing unnecessary inefficiency.

It should be left to healthcare professionals, healthcare institutions and their suppliers to determine where advanced primary coding is deployed, according to medical and operational need – no legal mandates should exist beyond those in place today. Indeed, not every supply chain will benefit from these additional features (for example where a patient is in receipt of a full pack of medicine at each dispensing point). Customers should have choice over when these features should be employed as an alternative to a traditional pack design.

Broadly speaking, we must:

1. Define a single standard for code formatting and the basic data elements
2. Clarify legibility requirements for primary packs
3. Agree core principle that the initiative ought not compromise current best practices regarding environmental impact and the efficiency of the medicines supply chain.

7. References

1. GS1 Position paper on the identification of the primary package level of drugs
2. European Commission Guideline on the readability of labelling and package leaflet of medicinal products for human use