

/ **AGGREGATION** IN PHARMA: THE FUTURE-PROOF SOLUTION



SERIALISATION IS JUST THE BEGINNING

According to the World Health Organization (WHO) up to one percent of all drugs circulating in the industrialised countries are counterfeit. This figure rises in Asia, Africa and Latin America up to 10 percent of all medications in the market. This starts with lifestyle drugs and goes all the way through to medicines for cancer therapy or treating HIV and diabetes. In recent years, there has also been an increase in the number of cases involving pills that contain no active substances at all.

In the coming year, the bar for counterfeiters will be set considerably higher due to the entry into force of the Falsified Medicines Directive 2011/62/EU and Commission Delegated Regulation (EU) No. 2016/161 which aims to protect patients in the legal supply chain from falsified drugs.

This could also have a positive impact on further harmonisation of the different laws, regulations and directives applicable worldwide. Compliance with the requirements of good manufacturing practice for medicines (GMP) is becoming more difficult than ever in the wake of globalisation: Production facilities are spread worldwide and the complexity of distribution channels increases.

Today, new technical solutions are needed for the manufacturing process as well as up-to-date IT structures to enable even closer integration of GMP and GDP for distribution along the entire supply chain. Serialisation, which is linked to an enormous amount of effort within com-

panies, is certainly a step in the right direction. But what is going to happen in coming years as globalisation continues to increase? The process is unstoppable and there will be more dismantling of trade barriers. Regulatory framework conditions will have to be further harmonised worldwide – international production and distribution methods will be increasingly closely interwoven. It's only a matter of time until mechanisms like serialisation are no longer sufficient. Companies that have already set the course to serialisation¹ can proactively make a further contribution by means of additional aggregation. What may still look like a (small) technical advantage – compared to competitors – can become a decisively unique selling point as globalisation progresses. But why aggregation is a future-proof solution?▲

WHY SHOULD PHARMACEUTICAL COMPANIES AGGREGATE BEFORE THEY MUST?

BENEFITS OF THE AGGREGATION TECHNOLOGY

Proactive pharmaceutical companies are finding significant cost savings in the deployment of traceability and aggregation technology. A large part of these cost savings are coming from improvements in process and supply chain efficiency. Many companies now view this technology as a major competitive advantage in today's global economy.

Flexibility to meet Track & Trace requirements of multiple countries



Aggregation is required or will be required by different countries as a part of their national Track & Trace regulations. Due to globalisation, manufacturers can achieve a long-term success only if they can quickly adapt to new export markets.

Optimisation of warehousing and supply chain activities



Aggregation simplifies reporting and verification of the product at one or more stops along the supply chain. By scanning the barcode, all the necessary data can be obtained in a matter of seconds, which leads to significant time and resource savings.

Fast decommissioning of shipping cases and pallets



Shipment pallets could be decommissioned in bulk from the cloud system. In case the whole pallet or a part of it has been damaged during transportation, aggregation will significantly simplify booking out the damaged products from the system.

Efficient product re-calls or returns



Aggregation technology facilitates the ability to manage the entire process of inventory returns better. It also helps manufacturers perform targeted recalls of specific product units instead of an extensive, unnecessary amount.

/ PHARMACEUTICALS – THE LONG ROAD FROM PRODUCTION TO PATIENT

With the new Serialisation Directive, every packaging unit of a prescription-only drug in Europe will have a distinct identity due to a globally unique individual number. Based on these numbers, it will be possible to trace which manufacturer this packaging has come from later in the pharmacy. If this serial number has already been dispensed at another pharmacy, this could be proof that the product in question is a counterfeit. The disadvantage of this solution is undoubtedly that all intermediate stages in the supply chain are ignored.

These intermediate stages make the trade of drugs more complex while providing counterfeiters with an advantage. Unlike in the past, a medicine does not simply go from the pharmaceutical company to the pharmaceutical wholesaler and from there to the pharmacy. Today, there are also re-import medicines which are manufactured in one country and then exported initially to another one for re-import at a later date.

Parallel imports² are also common. Drugs are manufactured abroad, purchased at lower prices by a pharmaceutical importer and subsequently exported from there to a designated country. All this makes expens-

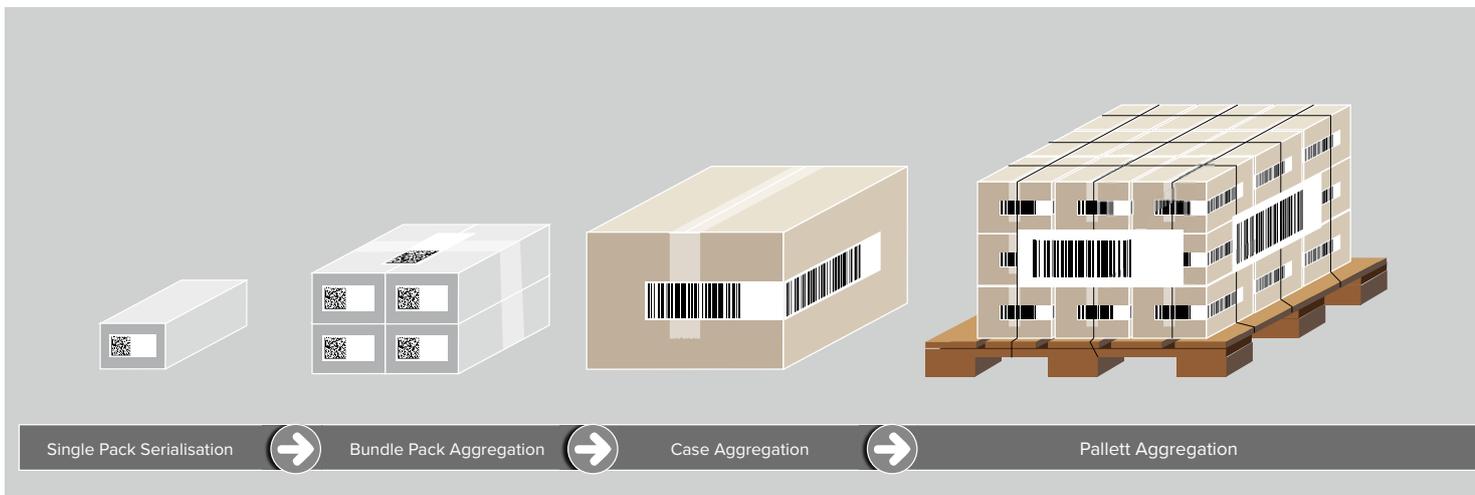
ive medicines cheaper, provided that genuine medicines are crossing the counter. ▲



Parallel Importation



Re-importation of medicines



Aggregation according to the parent-child principle:
from folding box to pallet

/ AGGREGATION – HOW DOES IT WORK?

Aggregation enables companies to seamlessly trace the origin of their products according to the parent-child principle. When a blister pack is placed in a folding box (child), its serialisation code is scanned. If several folding boxes are packaged into a bundle (parent) in the next step, the folding boxes are placed in a relationship with this (parent) bundle. Then, in turn, these aggregated bundles are linked and placed in a relationship with the shipping box (again a higher-ranking parent level) in which they are stored in the interim. The parent-child dataset is linked in a further step to palletising data.

These are in turn part of a delivery and an important part of the logistics process which is now beginning. To sum up, aggregation means a process in which each

participant in a supply chain takes over the information from the predecessor and additionally supplements it with its own data. This begins with the manufacturer, travels via the packaging to the logistician, on to the wholesaler, etc. Each data aggregate is saved in a database before being passed on to the next participant in the supply chain and can be called up anywhere and at any time. This is why the aggregation of primary, secondary and tertiary packaging is reminiscent in its logic of the blockchain which, among other things, aims to increase transparency in the finance industry. ▲



THE SUPPLY CHAIN NEEDS TO BECOME EVEN MORE TRANSPARENT

By aggregation and use of databases, it is possible to generate valid data as described and place them in a logical relationship with each other. They can be called up at any time and increase transparency in the pharmaceutical supply chain. Thanks to the new serialisation guidelines and the end-to-end principle, pharmacists can prove the authenticity of a medicine relatively easily. Due to aggregated packaging, a pharmacist could completely retrace the entire supply chain of a drug if any abnormalities were to emerge. This is especially important when it comes to clarifying by which direct route or via which detours a drug has reached their pharmacy.

Pharmaceutical companies gain additional advantages due to aggregation: They can collect and analyse a large number of parameters for the medicine produced on their premises. Standing and turnaround times at customs can also be recorded for re-imports, as can the length of stay at the wholesaler before being issued to the pharmacies.

Aggregation should also be seen as a pioneering part of supply chain visibility. For manufacturers, this creates potential for making their own processes more efficient and for checking downstream steps, such as logistics, for weak spots.

Example: delivery damage that has occurred during unloading of a pallet. Where previously it was necessary to book out the individual products of this defective pallet manually, now it is enough to scan the pallet to make the information about the damaged medicines visible to all authorised persons along the supply chain.

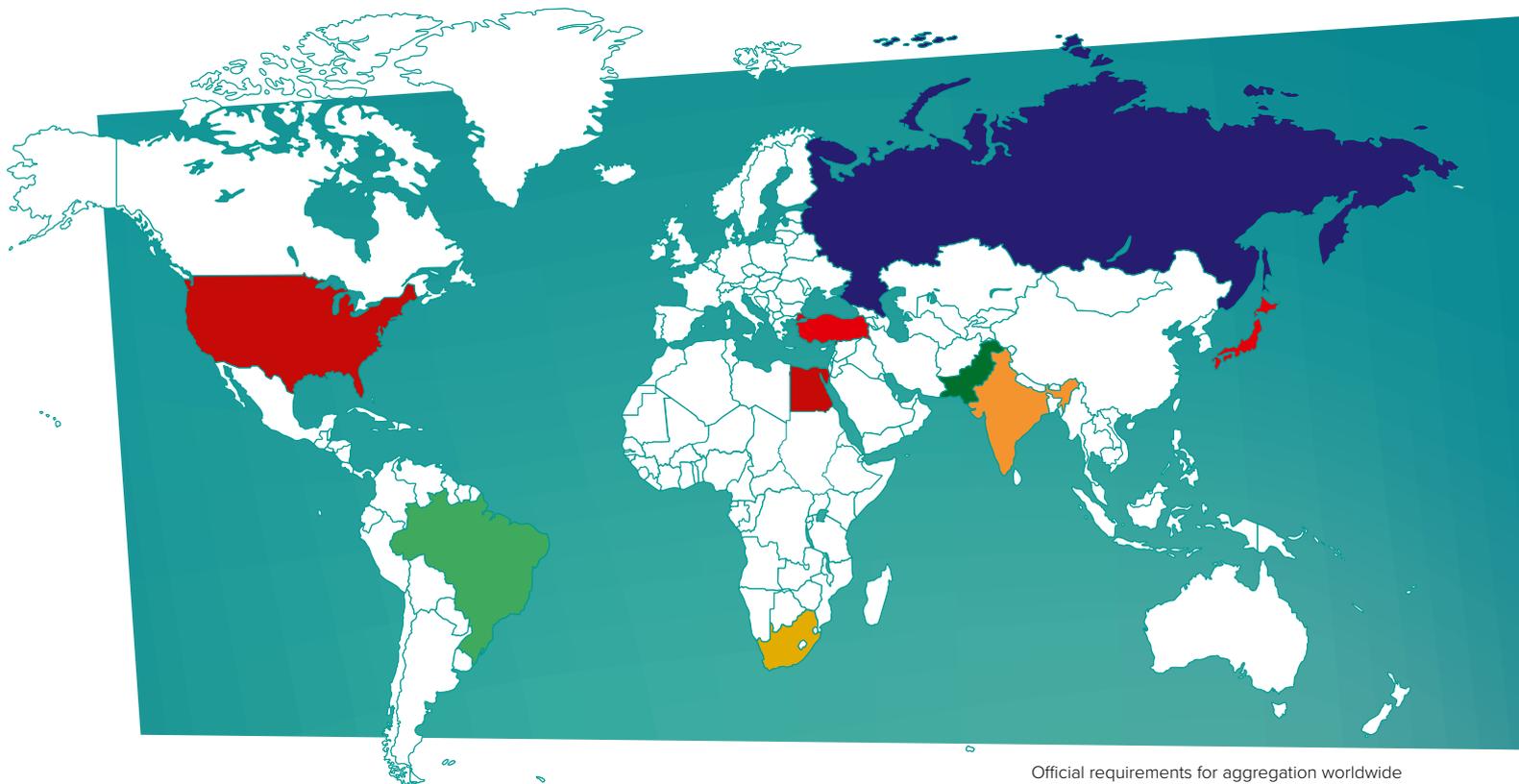
Aggregation and the data management associated with it therefore results in traceability from the birth of a drug up to the moment when damage is detected or theft leads to disruption of the data flow – including all the information that add up to the drug. This includes the product GTIN, the serial number and batch number and also the expiry date and all the master data of a medicine.

Thus, at the same time aggregation is also an up-to-date tool for improving all processes because every step is meticulously recorded. This applies to logistics or warehouse management and, of course, also at the end of the chain, in case it becomes necessary to notify the pharmacist about a recall.

Even companies that are currently looking at the conversion of a production line should consider implementing aggregation technology at an early stage. The same applies to those that are relocating

old plants abroad or to other locations³. There, too, it may make sense to use re-installation with subsequent qualification and validation to upgrade or retrofit aggregation systems or modules. ▲

GLOBALISATION REQUIRES A HIGHER TECHNICAL LEVEL



Official requirements for aggregation worldwide

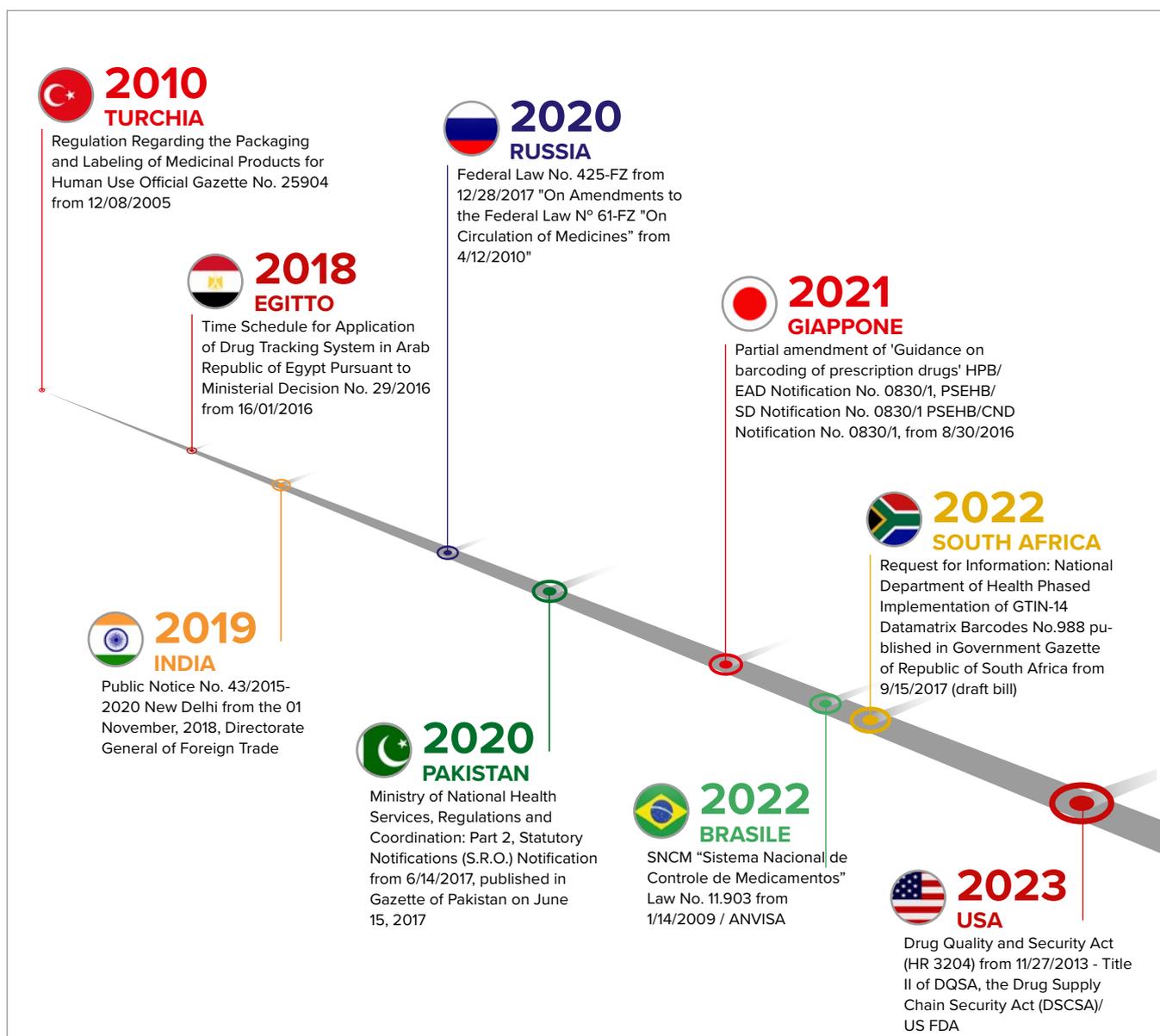
Those choosing aggregation today, set themselves apart from the competition. New markets can be opened up based on regional needs without being subject to restrictions imposed by government agencies or wholesalers. Thus, anyone aggregating now is exceeding current requirements and as a result becomes significantly more flexible in their trade relations. Anyone delivering more than expected does not run the risk that potential new clients will not actually want to conclude contracts due to regulatory deficiencies. The fact is

that, as globalisation progresses, manufacturers will only remain capable of acting in the long term if they can adjust very quickly to new export markets.

For example, pharmaceutical companies that export to Turkey have considerably better conditions for increased competitiveness because it has been necessary to aggregate drugs for the Turkish market since 2012. Those who know the regulated environment know that the mills grind slowly but steadily. Egypt will follow in 2018. The situation is similar for deliveries

to India whose government will require aggregation from July 2019. From January 2020, aggregation will become obligatory in Russia, in Pakistan from December 2020. Japan will follow in April 2021, Brazil a year later in April 2022, with South Africa shortly afterwards in June 2022. The USA will require full traceability from 2023 onwards.

All the countries mentioned are united by the fact that the government has made the aggregation of drugs mandatory. >>



Global aggregation timeline

Lack of aggregation is synonymous with an export ban. In places where governments are not involved in the procedure, it is wholesalers who are making corresponding demands on suppliers. Thus, Korean or US wholesalers accept product aggregation from their supplying pharmaceutical companies without the legislative authority expressing any opinion whatsoever.

It is clear from this dynamic that developments and decisions in these countries are subject to mechanisms that today – where serialisation is the norm – are not yet foreseeable but can at best

be speculated upon. In the course of globalisation, new questions about drug safety⁴ and packaging will also continue to crop up and require clarification. ▲

APPROPRIATE INTERFACES AND EASY OPERATION



TQS Fast Track from left to right: TQS-SP for the serialisation of single packs; TQS-HC-A serialisation, tamper-evident labelling and weighing, TQS-CP for aggregation

Companies that want to make the shift from serialisation and tamper-evident to aggregation require appropriate interfaces that can provide data for aggregation. The compatibility of these data formats is important when choosing an aggregation solution. Open and standardised interfaces ensure unrestricted use with regard to all machines and components already in use at a manufacturer's premises. At best, the aggregation equipment with all peripherals should be modular and therefore easy to integrate in an existing line. Manual aggregation of bundles or cases should be quick and easy for the machine operator and can be implemented with ergonomic design on the smallest footprint.

Taking the requirements into account, WIPOTEC-ocs has developed the Traceable Quality System (TQS). This solution is a highly flexible modular Track & Trace platform that enables manufacturers to implement the latest legal requirements in a straightforward way and can easily be integrated in packaging lines. It is suitable for existing as well as newly constructed lines that are yet to be qualified and validated.

The TQS has a modular structure. In addition to serialisation and checkweighing, the individual modules can also be used for tamper-evident labelling. All steps in the serialisation and aggre-

gation process are recorded and the data are read in and stored according to the parent-child principle. In addition to introducing or complying with the soon-to-be legally binding serialisation requirements, the technology enables simple and secure aggregation of all packaging data. ▲

/ CONCLUSION

The counterfeiting industry is a dedicated industry and, like all others, is constantly evolving. However, serialisation and aggregation can set the bar so high that the falsification of drugs becomes significantly more complicated and therefore less economically attractive. New technologies such as TQS can signify “the end”, particularly for the so-called backyard kitchens. Aggregation can therefore make a valuable contribution to patient safety and can also reduce bureaucracy in the long term – whether by preventing costly product recalls or detecting counterfeiters. Aggregation is also an effective way of further harmonising the various international standards in the course of globalisation and of further reducing economic damage to health systems worldwide. ▲

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