



Lars Olsen, Global
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THE RACE AGAINST THE

serialization deadline

Serialization will soon become a legal requirement and contract manufacturing clients have to comply with the EU Falsified Medicines Directive Safety Features Delegation Regulation. The new regulations mean a lot of work for companies to comply with the demands, as well as large investments and new work routines. The biggest challenge is however to get everyone ready in time.

TEXT ANNELI HIDALGO

IN ORDER TO counteract the huge, ongoing problem of falsified medicines, increased legal demands are being introduced in the European Union and the US. At the beginning of 2019 the European Union will introduce stricter regulations on serialization, as pharmaceutical companies have to comply with the EU Falsified Medicines Directive Safety Features Delegation Regulation. As of 9 Feb 2019 thousands of pharmaceutical companies serving the EU market (in the United States as of November 2017) have to connect to the system, transfer all data to the European hub and make sure that all pharmaceuticals are authentic. The EU Falsified Medicines Directive orders obligatory, harmonized safety details on all human prescription drugs packaging (with some exceptions). The safety details consist of a 2D data matrix barcode that contains four different elements. In Sweden, for example, this means a product code, an expiration date, a batch number and the unique serialization number. The company gathers all the serial numbers that are sent to the European hub and data is then transmitted to the countries that are included in that transmission. On the distributor side there will sometimes be some risk based controls, checking if the product is in the database or not.

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Anita Finne Grahnen,
Manager Policy at LIF

When the pharmacies sell the product they scan the code and a request goes out to the system to check if the product is registered.

The safety details also include an anti-tampering device, which leaves marks to indicate if a package has been opened. Another part is aggregation, where all package levels are linked in a parent/child relationship. This will however not be included in the European legislation system, although a company can choose to include it.

Challenges for the industry

The companies have a lot of work ahead of them to ensure serialization readiness on a massive scale and full compliance readiness for a complex set of reporting requirements. The biggest changes are all the new work routines that have to be implemented and the rooting of ownership and responsibility going forward, as a natural part of daily routines and job descriptions, according to Lars Olsen, Global Technology Partner at NNE within Assembly and Pack. This is crucial for an effective integration but is often underestimated or misunderstood, he says.

“A problem is that many companies are treating this like a project that has an A to Z characteristic. There are projects elements to consider, such as the IT angle and packaging, but these are sub-projects in the whole aspect of mobilizing. Serialization is here to stay and the companies have to understand that. This is not just a EU issue, it is a worldwide matter. There are more than 40 countries where there are different variants of the regulations, and the companies have to be compliant with all of them and make sure to update whenever a new country comes up.”

A large investment

One of the major issues is a high increase in production costs.

“We’re talking about half a million to one and a half million Euros in average for a full packaging line and increased cost of the products over time. A lot of expensive, hard work for the companies, while the return for the manufacturers is zero,” says Lars Olsen.

Anita Finne Grahnen, Manager Policy at LIF, the trade association for the research-based pharmaceutical industry in Sweden, also acknowledges large costs for the companies, however “as any new regulation, it implies new costs,” she says and continues, “In the European legislation, it is clearly stated that it is the manufacturers that shall pay. This means paying for what is made within the production of a company’s own products, but also for the data system on a European level as well as a Swedish level, for those who distribute on the Swedish market.”

ONE COMPANY THAT has tried to find a solution to the large investment expenses is the Swedish CDMO Recipharm. They have previous experience of providing serialized products in other places, such as Turkey, Korea and China, some of the countries that already have different types of regulations in place. The company decided to take that practice and go for a proactive approach before the regulations are implemented in the European Union and the United States. Recipharm will invest EUR 40 million in serialization technology. The company will offer their serialization services free of charge, beginning in 2017. Once serialization becomes a legal requirement they will begin charging clients with a fixed service fee per package. The grace period is designed to allow customers to clear early hurdles, calculate their individual requirements, and request customization prior to the deadline. This project will ensure that all of Recipharm’s contract manufacturing clients will comply with the EU Falsified Medicines Directive Safety Features Delegation Regulation.

“The main idea with the standard solution is to avoid the burden on our customers with any larger investment costs, but to spread out the costs for a number of years,” explains Staffan Widengren, Director Corporate Projects at Recipharm and the person leading the company-wide serialization project.



Staffan Widengren,
Director Corporate
Projects at Recipharm

RECIPHARM'S STANDARD SOLUTION does not include aggregation, however the company will offer it as well to accommodate certain customers, says Staffan Widengren. Recipharm has more than 250 clients and the CDMO expects that around 85 percent of the corporation's gathered production will require serialization. In the fall of 2016 the company introduced their clients to an up-close view of the company's solution by launching a showcase line at the French Fontaine office. Demonstrations allow the customers to view and trial the solution and include downloading serial numbers, serializing packages, and applying tamper-evident labels. The line also shows the manual tasks, including labeling of boxes and pallets and uploading data.

The clock is ticking

February 2019 might seem like it's still far away, but the time aspect is without doubt the biggest challenge, asserts everyone that Nordic Life Science has interviewed for this article.

"We have repeatedly stated that there will be a bottleneck situation. Still, many companies have reacted very slowly," says Lars Olsen. "In general it is sort of an awkward situation for the companies. Many of them think that they are the only ones that are having problems and don't want to be left behind and thus, the more conservative ones, don't open up about these issues with the authorities."

Anita Finne Grahnén says that a majority have been aware of the effort that is needed and are working intensively to meet the deadline. However, she agrees that the time frame is a huge concern, an issue that LIF has been clear on.

"Start now. That has been our main message that we have pointed out for a couple of years now," says Anita Finne Grahnén.

For Lars Olsen the probability that all companies will stick to the time frame remains doubtful.

"I think there will either be a delay or we will get a longer grace period of grant. Otherwise we'll have a situation where some companies are off the market," he says.

The boy who cried wolf

Besides the considerable amount of work and the substantial economic undertaking, Lars Olsen implies that another big problem is that there is a view on the introduction of these types of regulations that is colored by some previous negative experience. Olsen refers to an earlier case when a serialization law was about to be introduced in Italy back in the 1990s. A track and trace serialization law that brought on a lot of preparation and worry among the pharma companies. Unfortunately, it ended in somewhat of a disaster as the law was finally pulled off the chart and changed completely two weeks before it was supposed to have come into effect and the companies lost the time and money that had been invested. A few years later the industry saw another situation in 2004 as the state of California several times delayed new anti-counterfeiting and anti-diversion legislation (known as The California ePedigree Law).

"This is a classic case of the boy who cried wolf. Many companies have seen this coming over the past ten years. But due to the high costs and the experience of the Italian case, a lot of firms have decided to wait it out," claims Lars Olsen.

But the cautiousness can lead to nothing less than a disaster for a great deal of companies, Lars Olsen predicts.

"Some big companies are home safe. But for those with only one or two packaging lines that suddenly have to implement all of these changes it can have a huge impact. Some of these packaging lines are old fashioned with outdated



Recipharm will invest EUR 40 million in serialization technology

equipment that probably would benefit from an update. The problem is that there is still a belief among some of these smaller firms that it's just a matter of some new printers and visions, they have not understood the magnitude of the work that needs to be done. These late movers include many CMOs and small to midsize companies. In a worst-case scenario, this could pull the plug on their business. This can lead to a mass catastrophe, there's no doubt about that, unless a more gradually transition period is granted," he says.

Anita Finne Grahnen recounts that as a trade organization LIF has spent much time to enlighten the industry on what is required.

Effects of the regulations

The new measures are aimed to protect patients from falsified and low-quality medicines by guaranteeing authenticity and improving supply chain security, in

the end securing patient safety and reliability.

"The whole regulation is about preventing falsified medicines from entering the legal supply chain, a scenario that would mean a huge risk of patients losing confidence. Strengthening credibility will be the absolute biggest benefit with this regulation," says Anita Finne Grahnen.

For the industry, there will also be some supply chain transparency benefits, says Lars Olsen.

"What serialization will bring is more knowledge to a company's own operation. If you have an incident during an IPC control, for example, you will be able to narrow it down exactly to the individual samples that were affected. It will also be possible to have a much better case with authority inspection, with the exact serial number you'll be able to know when it occurred. That is a business advantage I have seen many companies benefit from."

Another possibility following the regulations that Lars Olsen brings up is generating an electronic compliance tool by a mobile application that shows batch number and expiration date, to give patients better information.

"This would be a really helpful tool as only 27% of medicines are used in the right way."

STAFFAN WIDENGREN AGREES with the notion that the regulations hopefully will eliminate any illegal activities on the legal supply chain. Unfortunately, this does not include all that is traded over the internet and will not get at the falsified medicines that are sold illegally, both he and Lars Olsen note.

"Most incidence of counterfeit medicine takes place in the illegal supply

chain, which will thus not be mitigated by these complex regulations. Only the very few lots that have been introduced by certain traders of medicine can be mitigated if systems are built and functioning without flaws and followed by everyone. These lots, by the way, were discovered in the legal supply chain anyway, because control already is strict. It's only a question of how soon you want to detect the suspect products. So, in the legal supply chain it will be helping, but it will be to a high cost and doesn't meet the actual needs here," says Lars Olsen.

However, as Staffan Widengren says, perhaps it can make those who buy medicines online only chose legal alternatives and also scare off fraudulent players on the market. Anita Finne Grahnen concurs that the problem with fraudulence most definitely will continue. "When it comes to online purchases it is the duty of our organization and others, such as the Medical Product Agency, to show how insecure it is to buy pharmaceuticals on unknown sites," she says.

Staffan Widengren also points to possible problems for companies.

"There might be some pharmaceuticals that can't bear the costs that serialization entails. Many generic drugs are very cheap, for example, and this could mean a significant cost increase for them."

A less costly and complex alternative

For Lars Olsen, who has been working in pharmaceutical packaging for the past 25 years and has spent the past decade dealing with the new regulations, it is difficult to see many positive sides of the directive.

"There are of course benefits following this directive but I believe it's important to highlight what has been overlooked by both top management and regulatory

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authorities. The more I've gone into the details of the technical complexity, the more I have realized that the whole thing has been side-tracked since the beginning and has become too complicated.”

THE ORIGINAL SERIALIZATION regulation is in fact made for taxation and reimbursement fraud, simply to mitigate economic fraud, but not for the end user, he maintains, pointing out that it all has originated from a misunderstanding.

“Some of the big pharma companies went down the road of serialization earlier. AstraZeneca, Pfizer and many others implemented it as a mean to mitigate some high profile products that could be counterfeited and decided to go for serialization for those particular products. So it derived from some unique situations that ended up being taken into a general interpretation and pushed toward all products, without seeing the end need or looking into the root cause.”

Olsen states further that the problem from the authorities' side is that they

often tend to be more technocratic and do not always have the view of the manufacturers in mind.

“I believe that they have unfortunately not been talking to the right people and don't see what this will lead to for companies and eventually the price of medicine. The authorities that are mandating these laws have not understood fully what they have started, what it will cost for the end users.”


Also, Lars Olsen describes another fundamental part of the problem is that the industry initially perceived the regulations as a much simpler system when the directive was presented, and therefore did not grasp the magnitude of the transition.

In the end, Lars Olsen says he would have preferred to see another alternative, something simpler and more straight to the point.

“A less costly system like e-lot tracking could have been introduced years ago without a huge cost for the industry – and ultimately the end-user – and would have mitigated the problems in the legal supply chain very efficiently,” says Lars Olsen.

Advice for late starters

For those companies that are still in a startup phase to adapt to the new regulations, Anita Finne Grahnén at LIF, recommends making an inventory of what you have, looking at the time frame for production, what needs to be communicated to authorities and how it will be handled on an internal level. Lars Olsen points to two things that need a key focus: an early involvement and awareness of all stakeholders for mobilization, and top management involvement.

“If this is handled correctly during the start-up period the rest of the ride would be less bumpy. It is very important to keep in mind that this is not a project going from A to Z. This is true change management.” 



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