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The future trade secrets directive in Europe:

more rights for companies, or more trouble?

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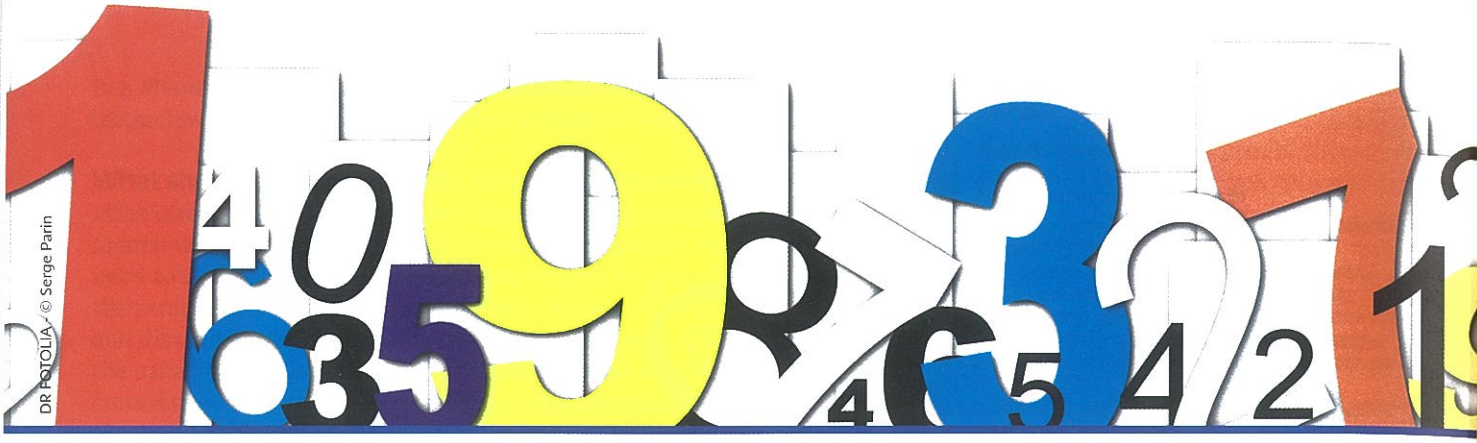

Serialization in Europe: a decisive step about to be taken

Focus on the European Commission's draft Delegated Regulation of August 12 - 2015, regarding the implementation of compulsory safety features for medicinal products.

By Cécile Théard-Jallu and Jean-Marie Job

The EU Directive 2011/62/EU[1] adopted on June 8, 2011 on the prevention of the entry into the legal supply chain of falsified medicinal products, introduced safety features to be displayed on the outer packaging of medicinal products to allow for the verification of their authenticity and avoid distribution of falsified products.[2] Two key safety features will be mandatory for all outer packages of medicinal products subject to prescription: a unique identifier and an anti-tampering device.

Among other delegated regulations linked to the fight against falsified products, Directive 2011/62/EU announced that one specific delegated regulation (the "Delegated Regulation") will set out the characteristics and technical specifications of the unique identifier to be used by pharmaceutical supply chain actors. It should also specify the modalities for verifying safety features, define the rules on the establishment, management and accessibility of the repository systems aimed at containing unique identifiers, list medicinal products or product categories covered by the new regime and identify notification procedures.

On August 12th, 2015, the European Commission eventually published this eagerly awaited draft Delegated Regulation, the final version of which should be officially released by the end of 2015.[3]

This major regulatory change will oblige stakeholders to both clearly identify their related rights and obligations towards each other and patients and secure & enhance the value of their assets.

It is now time to seriously think about it. Indeed, the draft Delegated Regulation of August 2015 is the result of a rather lengthy consultation period which makes it unlikely to be substantially modified before the official final release.[4] The new regime will then be enforceable in EU member states' laws within three years following the Delegated Regulation's official release. This period is very short considering the large financial, operational and legal investments required for actors to be ready to comply with the new rules at a global level.

Let us focus on the main provisions of this draft Delegated Regulation of August 12, 2015 and take the pulse of where things stand today and what will presumably need to be done in the near future.

Allocation of tasks among serialization stakeholders and major role given to serialization data repositories and related hubs: What are the draft Delegated Regulation's main features?

The Manufacturer will be in charge of initiating the serialization process at the beginning of the supply chain

Manufacturers (and not marketing authorization holders) will be compelled to place safety features on the outer packaging.[5] This means that when manufacturing is outsourced by the marketing authorization holder, the serialization responsibility will lie with the external manufacturer, i.e. the entity in charge of final batch release and identified as the manufacturer in the product's registration dossier.

The unique identifier to be displayed will be generated by means of a 2D data matrix code which should contain, for each product, such items as in particular, the product code, a serial number,[6] the national reimbursement number (if requested by the relevant Member State and if not already contained in the product code), the batch number and the expiry date of the product. The inclusion of such information will contribute to patient safety by facilitating recall, withdrawal, return procedures and pharmacovigilance. The unique identifier will be encoded using a standardized data structure and syntax fully harmonised across the EU so that it can be correctly recognized and decoded throughout its Member States by commonly-used scanning equipment. This data will be unique to a given pack until at least one year after the expiry date of the pack or five years after the release of the pack for sale or distribution, whichever period is longer.

No additional two-dimensional barcode will be displayed on the packaging carrying the abovementioned unique identifier.

Once this unique identifier is set for a given product, the marketing authorization holder will ensure that it is displayed in a readable way and contains the correct information. Before the product is released for sale or distributed, the marketing authorization holder will upload a set of information to the national or supranational repository or repositories corresponding to the country(ies) where the product is supposed to be marketed (see below).

Verification of the unique identifier: an end-to-end system

After the safety features have been displayed on the product packaging and controlled upon batch release by the manufacturer, the authenticity of the unique identifier and integrity of the anti-tampering device should be verified at the time when the medicinal product is dispensed to the public (e.g. at pharmacy or hospital level). This consists in verifying in repositories that they contain an active unique identifier with the product code and serial number that are identical to those of the unique identifier being verified. In principle, if the number has been decommissioned, the product may not be distributed.[7]

The authenticity of the unique identifier should be checked by comparing it with the legitimate unique identifier stored in the repositories system. The verification is meant to prevent products which are expired, recalled, withdrawn or indicated as stolen from being supplied to the public. While the medicinal product is dispensed to the public and once the above authenticity and integrity verification has been conducted, the person authorized to dispense the product will decommission the unique identifier in the repository.

At the hospital, this control may be conducted at any time when the product is in the physical possession of the healthcare institution, provided that no sale of the product takes place between the date when it is delivered to the healthcare institution on the one hand, and supplied to the public on the other hand.

Wholesalers themselves may, but are not bound to, verify such authenticity and integrity, unless medicinal products with high risks of falsification are at stake[8] in which case this verification becomes compulsory. This compulsory control by wholesalers may also be required by some Member States to comply with their specific local regulatory environment (in which case no authenticity control by healthcare institutions supplying products to the public, as the case may be, should be necessary, while integrity of the anti-tampering device must always be checked when the product is dispensed to the public).

When the person controlling the above safety features has reasons to believe that the product may not be authentic and/or that the integrity has been breached, the product must not be released to the public and this person must inform the relevant competent authorities forthwith.

Some medicines will be subjected to serialization, others not

As per the EU Directive 2011/62/EU, only medicinal products subject to prescription will be allowed to bear the safety features, whereas medicinal products not subject to prescription will not. Some medicinal products not subject to prescription and specifically listed in an Annex to the Delegated Regulation will also need to comply with this obligation. Conversely, some medicinal products subject to prescription and listed in another Annex will specifically be excluded from the scope of the new regulation. The idea behind this selection is to identify medicines that are particularly at risk in terms of potential falsification.

Also, Annexes to the Delegated Regulation will be filled in with great attention so that any specific regulatory constraints from one Member State to another are taken into account on a per-product basis.

Repositories will be set up at national or supranational levels and linked together through a dedicated hub

Data will be uploaded in national or supranational repositories located in the European Union and which should connect to each other and allow the exchange of data through a central information and data router ("Hub").

Each repository should be set up and managed by a non-profit legal entity established in the European Union by manufacturers and marketing authorization holders of products bearing the safety features. Other stakeholders such as wholesalers, pharmacists and healthcare institutions allowed to dispense medicinal products to the public may take part in the system on a voluntary basis and at no costs. Costs of each repository will be born by manufacturers.

The structure of the repositories system and format of data flows will need to ensure that medicinal product verification is possible throughout the Union and synchronized through the Hub, between national and supranational repositories serving the Member State or Member States where products are intended to be marketed.

These repositories will ensure the proper conduct of a number of tasks including, inter alia, reading 2D encoded data, verifying the authenticity of an active identifier on a repeated basis, triggering alerts, decommissioning unique numbers, giving access to data including to wholesalers and entities allowed to dispense medicinal products to the public, creating reports, informing on the decommissioned status of a unique number, and synchronizing with other repositories serving the same country.

The entire repositories system will be under the supervision of national public authorities, which may enter the management boards of the legal entities managing the repositories up to one third of the members of a given board.

Data will be generated and accessed by a variety of actors

Serialization data will be generated at all levels throughout the production and supply chain of the product up to dispensation. The general legal principle is that each person generating the data will be the holder thereof.

Once this data is uploaded in the repertories system, the repository manager will ensure the protection of personal data and confidential commercial information as provided for under European law.

Access to this data will be limited to what is strictly needed for any stakeholder to comply with its obligations (i.e. access limited to owned data plus some commonly accessible data expressly listed). In addition, the draft Delegated Regulation provides that national public authorities of a given Member State will automatically have access to all data contained in the corresponding national or supranational repository, so that they can supervise the proper functioning of the repository and investigate potential incidents of falsification, or handle reimbursement or pharmacovigilance or pharmacoepidemiology issues.

Serialization data, more especially dispensation data, will undoubtedly play a central role in the new serialization ecosystem given the high financial and strategic value that it will represent at all levels of the serialization chain.

Time schedule for the enforcement of the Delegated Regulation

If adopted in its current form, the Delegated Regulation will become directly enforceable in EU Member States' laws (i.e. same mechanism as a EU Regulation, unlike a EU Directive which requires the adoption of local legislation to be implemented in each Member State). The announced time schedule for the Delegated Regulation's entry into force is three years following its publication in the Official Journal of the European Union, i.e. presumably by the end of 2018, with an extended calendar provided for the benefit of a number of Member States that have already taken some form of serialization measures, such as Italy, Belgium or Greece.

What will be the impact of this major reform on contractual relationships?

First, sharing of responsibilities will need to be clearly established between the manufacturer and the marketing authorization holder. The current draft Delegated Regulation provides that manufacturers will be the ones bound to place serialization safety features on the product packaging, while marketing authorization holders will ensure that the unique identifier is uploaded to the repositories system, thereby depending on the manufacturer's serialization tasks.

Where the manufacturing tasks are outsourced by the marketing authorization holder, the consequences of those crossed responsibilities will be put down in writing in order to allow each party to fulfil its obligations in a secure way. A simple reference to the provisions of the Delegated Regulation will not be sufficient: appropriate contractual clauses will be needed and will undoubtedly generate discussions between the different actors.

Among those discussions and depending on the context, the marketing authorization holder may want the manufacturer to fill in the repositories system on its behalf. Conversely, the marketing authorization holder may decide to reinternalize the manufacturing or at least the final batch release step so as to be considered as the manufacturer from the standpoint of the registration dossier and the Delegated Regulation, and thereby to better control the generated data.

The opportunity of choosing this second option will be assessed in view of the actual feasibility of transferring industrial sites from the CMO to the marketing authorization holder and will therefore be highly context-dependent.

Also, the adaptation of production and distribution lines and related operation procedures, including the design, development, implementation and maintenance of new hardware and software equipment required to enable the display and control of safety features on the packaging of the medicinal products, will represent a substantial investment on the part of the manufacturer. The manufacturing cost of each box will necessarily increase, all the more so as the equipment will need to be adapted to an on-demand approach depending on the eligibility or non-eligibility of products for serialization, as mentioned above.

Therefore, the manufacturer may wish to try to transfer those extra costs to the marketing authorization holder, who may be tempted to refuse them, arguing that these new serialization tasks are legally imposed on the manufacturer.

With respect to agreements which have already entered into force, but which do not contain any clause related to serialization, parties should check whether the agreement contains any provisions relating to a required renegotiation in case of substantial economic change. If it does, then this clause will may apply. If it does not, then renegotiation will be subject to the intent of both parties.

In practice, manufacturing agreements generally provide that the manufacturer commits to comply with the current regulation. As a consequence, if the agreement is concluded after the entry into force of the Delegated Regulation, the manufacturer will implement safety features on the packaging of the products.

If the agreement has been signed before this date, due to the costs incurred, the manufacturer might be tempted to impose a renegotiation, although it would not be as easily in favour of the manufacturer if the agreement is dated after the adoption of Directive 2011/62/EU of June 8, 2011, since as from this date, actors knew about the coming regulations.

Note that under currently enforceable French law provisions, a revision of the agreement for "unforseeability" is not an option. The solution will be quite different from what will presumably be the provisions of Article 1196 of the forthcoming Order reforming French contract law, as according to their current draft version, they will allow for a revision of the agreement if its performance has become too expensive for any of the parties. Meanwhile, the contract manufacturer may be tempted not to perform the agreement. However, this would put it at risk of paying damages to the marketing authorization holder for any related prejudice the latter might suffer as a consequence of this non-performance.

In this context, we strongly recommend adapting existing agreements or agreement templates (especially warranty, liability, insurance and termination clauses) between manufacturers and marketing authorization holders so that they anticipate, as serenely as possible, the entry into force of the serialization reform, with controlled and predictable costs. For sure, the corresponding negotiations will be dense.

As well as manufacturers' and marketing authorization holders' relationships, many other contractual flows will or need to be generated or will be impacted...

New legal requirements will be generated for all stakeholders throughout the production and supply chain, including manufacturers, marketing authorization holders, as mentioned above, but also wholesalers, pharmacists and healthcare institutions as well as public authorities.

Among other issues, the new repositories system will trigger contractual engineering, design, drafting and negotiation work for the purposes of these repositories and for the Hub to be set up, operated, maintained and updated.

Serialization data will itself need to be protected and enhanced by using specialized services providers under conditions to be defined.

Also the new regulation will necessitate the modification of insurance policies or the subscription of new ones among other example of impacted documents.

All this being said, the draft Delegated Regulation leaves a number of issues unanswered...

The draft Delegated Regulation does not exhaustively cover all aspects of how serialization will be secured, by whom and at which levels.

Among other issues that will need to be clarified at the European Commission or State levels or in the field, there is the need to confront the Delegated Regulation's final rules with the specificities of each local Member State's regulatory landscape, operational organisation, culture and economic context.

The draft Delegated Regulation is also unclear as to who will carry out the serialization checking in the healthcare institutions allowed to dispense medicinal products to patients.

Another question is about the way the control of safety features will take place when the products are distributed online (in countries where this is allowed).

Last, as we saw above, under the new EU regime, eligibility for serialization is based on discrimination between medicines subject to prescription and those which are not. This prescription or non-prescription status is decided at each Member State's level including for products marketed in more than one country in the EU and which may additionally give rise to parallel imports. Neither the 2011/62/EU Directive nor the draft Delegated Regulation answer the question about the effective compatibility of this new regime with EU competition law rules as well as with the principles of the 2001/83/EU Directive related to parallel imports of medicinal products. Will manufacturers effectively be bound to

adapt their serialization equipment and procedures in order to align themselves with the abovementioned discrimination depending on the country of destination of the product batch? In other words, since a given product may not be subject to prescription in one given EU country (therefore not being possibly serialized) and may be subject to prescription in another EU (therefore having to be serialized), does this mean that for this same product, the manufacturer's serialization equipment will need to have the technical capacity to be put on hold when serialization features are not to be implemented or verified? What about the difficulties that this may cause for parallel trade?

In any event, a real and innovative legal drafting and assistance mission will need to be conducted to take this new regulatory landscape into account and accordingly enhance the value of the various stakeholders' related contract portfolios.

And again, this should be initiated rapidly. Indeed, the risk is that smaller but more flexible geographical zones or countries may implement in-the-field serialization rules quicker than the EU is able to do, then eventually impose these other zones' or countries' rules on the global market, including EU operators. ■

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Cécile Théard-Jallu has developed in-depth expertise as an attorney in private practice representing multinational corporations, including major US and European firms and organizations in the R&D and healthcare sectors. Cecile focuses primarily on complex transactions including IT, R&D and consortiums, technology transfers, licensing deals and other technological change related projects. She assists clients with their responses to project offers in the R&D and innovation sector in the context of public funding.

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He is also involved in issues related to the management of personal and commercial data. For fifteen years, he practiced in the legal department of a major pharmaceutical group before joining de Gaulle Fleurance & Associés in 2001.

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Notes

1. Directive 2011/62/EU of the European Parliament and of the Council of June 8th 2011 amending Directive 2001/83/EC on the Community Code relating to medicinal products for human use, as regards the prevention of the entry into the legal supply chain of falsified medicinal products (among other issues, introduction of a new Article 54 bis in the Community Code focusing on serialization aspects).
2. For more information, please refer to our previous article in PHARMAnetwork magazine – N°27 of May 2015, pages 55 to 59 and visit http://ec.europa.eu/health/human-use/falsified_medicines/index_en.htm.
3. http://ec.europa.eu/growth/tools-databases/tbt/en/search/?tbtaction=search.detail&num=306&Country_ID=EU&dspLang=EN&BASDATEDEB=&basdatedeb=&basdatefin=&baspays=EU&basnotifnum=306&basnotifnum2=306&bastypepays=EU&baskeywords
4. The final date for submitting comments on the draft Delegated Regulation through public consultation was October 11, 2015.
5. Or the immediate packaging if the product has no outer packaging.
6. The serial number should be generated according to specific randomization rules in order to have a negligible probability of being guessed by falsifiers.
7. However, decommissioning may be avoided in certain exceptional cases, e.g., products to be exported outside the EU or disposed of or which have been decommissioned before the display of safety features on the packaging or meant to be remitted to public authorities.
8. Returned medicines or medicines not being distributed directly by manufacturers, wholesalers holding the marketing authorisation or who are designated by the marketing authorization holder (with exceptions when the product remains in the physical possession of the same wholesaler or regarding distributions in a single member State between two warehouses of the same legal entity, without sale).