Inside EU FMD and the Delegated Acts

A Compliance Primer

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INTRODUCTION

Falsified medicines represent a major public health threat, appearing in the market as legitimate, authorized product that can end up reaching patients across the EU and around the world.

In response to an increased risk of counterfeit medications, in 2013 the EU Commission enacted Directive 2011/62/EU—also referred to as the EU Falsified Medicines Directive (EU FMD). This legislation introduces tough laws that enable harmonized, European-wide measures to rigorously control the safety and supply of medicines for human use.

If you're at the beginning of your EU FMD journey, this guide is for you.

It provides foundational content on EU FMD, including what it is, how it will impact your company, key terminology, and how it compares to U.S. DSCSA.

If you're just starting to learn about serialization in general, download our eBook,
Serialization: Where to Begin.

On February 9, 2016, the Delegated Act on safety features was published. This part of EU FMD specifically outlines how the EU will track and trace medications using serialization, government reporting, and verification components. Companies have until February 2019 to comply with EU FMD.

If two years seems like a long time to prepare for compliance, it's not. If you're not ready by the deadline, you risk your medicines being rejected by government authorities and having your shipments stopped.

This seven-part eBook will arm you with what you need to begin on the road to 2019 EU compliance.

PART 1: EU FMD AND DELEGATED ACTS REQUIREMENTS

The Delegated Act on safety features for EU FMD has pharmaceutical companies, parallel importers, wholesalers, and pharmacies facing a tight legal timeline to address extensive serialization, compliance reporting, and verification requirements.

With an industry-wide effective date of February 9, 2019, EU FMD contains three major government requirements:

SERIALIZATION

Serialization must happen at the secondary or saleable-unit level in Europe. To enable verification, you need to first serialize product and send that serialized data to a central repository that can perform queries against it.

To enable serialization, verification, and government reporting, EU FMD requires that manufacturers mark packages with four data elements—a product identifier, serial number, lot or batch number, and an expiry date—all of which must be stored in a GS1 2D DataMatrix code.

A fifth data element may also be added to the package based on a particular member state's legal requirements, such as a national reimbursement number to help with reimbursement of drug product under a socialized medicine program.

To ensure that your product can accommodate the new code, you'll have to evaluate your product artwork. In Europe, this is particularly critical for multiple market packs that may have to meet disparate artwork regulations in different European countries. In some cases, for example, you may need to have two or more 2D matrixes included on one sales pack—one with the core product identifier and one with other information such as reimbursement conditions.

VERIFICATION AND SAFETY FEATURES

Verification – the process by which product must be verified at one or more stops along the supply chain. By law, this point-of-dispensation verification is required—pharmacy dispensers must verify drug product identity prior to dispensation. For example, the legitimacy of a barcode serial number on a sales pack in a pharmacy can be confirmed by comparing it to data that's stored

in a national repository serving that country.

Safety features – Elements such as anti-tampering devices and barcodes carrying product and pack data are incorporated into a medicinal product's packaging and identification to facilitate verification. Safety features under EU FMD contain two parts related to the packaging and identification of a medicinal product for human use:

- A unique identifier encoded in a 2D barcode enables identification and verification of each pack.
- Anti-tampering technologies determine whether product packaging has been compromised. The law does not specify which anti-tampering devices must be included on the pack.

COMPLIANCE REPORTING

On its journey from production to dispensation, a serialized drug package triggers certain compliance reporting activities for the marketing authorization holder (MAH). These focus specifically on the product and its market package, including product code, lot or batch number, expiry date, doses per pack, target markets, and serial number.

This information must be submitted to the European Medicines Verification System (EMVS) for all applicable medicine packs intended for sale in the market. In some cases, such as for parallel importation, reporting is also required by supply chain partners.

Data retention is also a key provision for the MAH, with EU FMD requiring that each MAH retain records of every operation that involves the unique identifier. Records must be available for a minimum of one year after the expiry date of the product, or five years after the pack has been released for sale or distribution, whichever is longer.

In terms of how information is shared with a government system, EU FMD compliance reporting for an MAH goes well beyond simply executing a file submission. For the EU, compliance reporting includes:

- The collection and preparation of master and serialized pack data.
- An understanding of how to manage notifications governing each target market for each product shipped into the market.
- Management of master data, serialized pack data, product status, and exceptions through the European hub.

AGGREGATION: WHAT IS REQUIRED UNDER EU FMD?

Under EU FMD, unique identity is defined at the package level. If you need to perform verification on a case of 100 packages, you'll need to do it at the individual pack level, regardless of the case packing they were sent in.

Even though case-level serialization and aggregation are not required by law in the EU, some pharma companies are choosing to aggregate product for the business enhancements it provides. The growing use of third-party logistics (3PL) providers by manufacturers illustrates a clear example. The manufacturer may want a precise inventory of the medicine in a batch that has been serialized and still sits at the packaging site, is currently in the inventory of a 3PL partner, and has been shipped into the supply chain. Without aggregation, this is a major challenge if the product is packaged in sealed cases or has been shipped in pallet quantities between locations.

Because aggregation will increase both the cost and complexity of serialization operations, budget is also a decision factor. Whether or not you aggregate product, and on which lines, will impact packaging processes, distribution operations, CMO conversations and more, so it's a determination best made early on.

For more information about aggregation and inference, download our eBook, ***Aggregation and the Life Sciences Supply Chain: Building Your Strategy.***

PART 2: HOW IS EU FMD GOVERNED?

EU FMD and the related Delegated Acts were designed by the European Parliament and EU regulators to provide a harmonized verification system—the EMVS—for adoption across EU member states in cooperation with national medicines verification organizations. The EMVS is managed by the European Medicines Verification Organization (EMVO), with specific criteria for how a system connection is developed and proven. EMVO oversees the following:

- The European hub.
- A blueprint system offered by EMVO-approved vendors.
- Service providers.
- Service-level agreements with national authorities.

WHAT IS THE EUROPEAN HUB?

EU compliance reporting requires collecting and preparing master data and serialized pack data, maintaining the status of such data, and enabling the ability to manage events such as recalls. The European hub is a cloud-based gateway for this data to travel by way of an approved communication link. It provides interoperability between different national systems, managing product status (decommissions, recalls) and exceptions (submission errors) throughout the life cycle of the product.

The European hub doesn't actually store serialization data like a repository. Instead, it acts as a single point of entry similar to a network switch or central router. The EMVS, composed of the European hub and a series of national repositories, is structured so that when an MAH reports product master data and pack data to the European hub, it passes the information straight through to the appropriate national repositories. These are the actual repositories containing the required package data and unique identifier for verification within member states.

Data that passes through the European hub is owned by the party that generates it, and cannot be accessed by other parties, except for verification purposes or when there is a specific agreement between partners.

By serving dozens of European countries, the European hub makes it easier for an MAH to:

- Connect and exchange data with multiple national systems.
- Maintain master data and pack status as product moves through the supply chain.

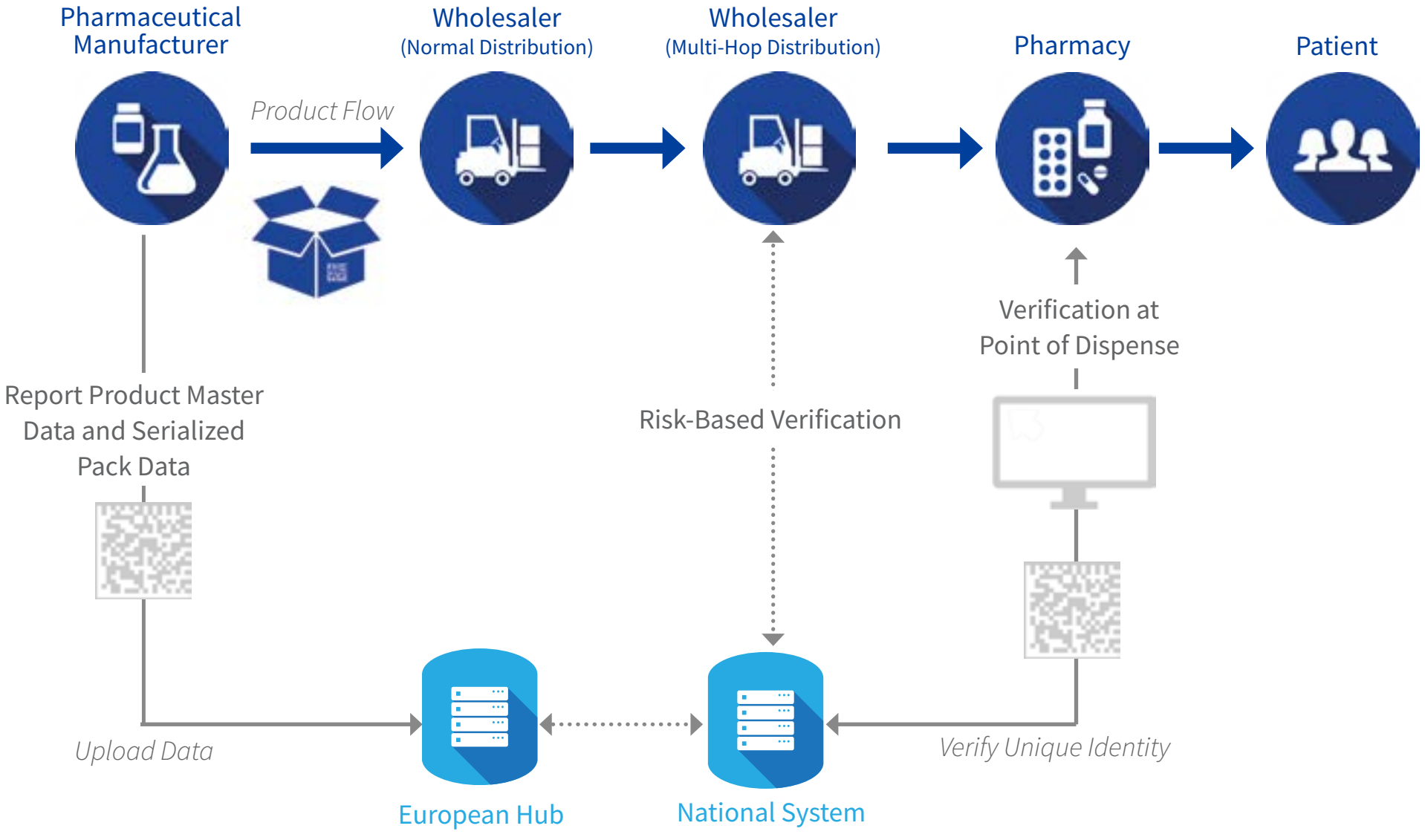
The European hub was specifically designed to facilitate the exchange of this information, while national repositories were designed for efficient local access to verification services.

Additional advantages of connecting to the hub include having basic reporting tools, the ability to query out-of-market packs, and a high level of connection security.

The European hub is not:

- **A central master data repository.** It does not hold pack-level data. Only a minimal data set is retained to identify clients and allow the hub to function. Master data challenges will be addressed in years to come through IDMP/SPOR standards.
- **A product registry.** The European hub is not a central register of all medicinal packs on the market. Pack data is abstracted to the national level, and is not retained at the hub after successful distribution.
- **A verification system.** National systems serve this purpose.

European Medicines Verification System



WHAT IS A NATIONAL SYSTEM?

A national system is set up and governed by national stakeholders to ensure a product's authenticity by verifying its safety features to prevent falsified products from entering the supply chain. National systems are supervised by member states using what EU FMD refers to as "competent authorities." These authorized supervisors ensure operations such as verification of a unique identifier's authenticity, decommissioning, providing an audit trail, and detecting potential incidents of falsification.

When national verification systems are connected to the European hub, information is pushed from the hub. A national system may also receive regulatory submissions directly from supply chain partners. All verification activities are performed within national systems of the EU member states. Risk-based verification, a requirement for wholesalers and parallel distributors, is also performed against a national system.

WHAT IS THE BLUEPRINT SYSTEM?

To interface with the European hub, the EMVO partners with qualified solution providers to offer individual countries the ability to select a standard blueprint template. While not an EU FMD requirement, the EMVO blueprint system is available to reduce time, risk, and cost. The blueprint addresses system capabilities based on specifications such as responsiveness to queries.

DO I NEED TO CONNECT TO THE EUROPEAN HUB?

MAHs, be they original manufacturers or parallel importers, must connect to the European hub and may not solely connect to a national system or repository. To meet EU FMD requirements, an MAH must establish a European hub account and connect to the EMVS to ensure that pharmacies, secondary wholesalers, and other stakeholders can verify its drug product as it travels through the European supply chain.

Under the Delegated Act on safety features, product master data may only be submitted by an MAH and not through a national repository system. Product master data must be provided to the European hub to ensure batch-information sharing, multi-market product movement, and secure parallel-trade activities across the market.

PART 3: WHAT ARE THE ROLES FOR DIFFERENT SUPPLY CHAIN SEGMENTS?

In addition to pharmaceutical manufacturers, wholesale distributors, packagers, and pharmacies are expected to comply with the EU FMD regulations by February 2019, although legal requirements may vary based on a company's role within the supply chain.

PHARMACY DISPENSER REQUIREMENTS

Pharmacy dispensers can determine whether they will perform verification at the point of dispense or elsewhere in their administrative operations. To verify a unique identifier, a dispenser scans the barcode and submits the information to the national repository. The national repository responds with information confirming the authenticity of the unique identifier.

WHOLESALE DISTRIBUTOR REQUIREMENTS

Wholesale distributors must support end-to-end serialization and compliance reporting by performing risk-based verification for product moving through the supply chain in one of two scenarios.

1. A wholesaler must verify a product by interrogating its safety features prior to resale when receiving medicines from a supplier that is not:

- The original manufacturer.
- The wholesaler holding the marketing authorization.
- The wholesaler designated by the MAH (by means of a written contract) to store and distribute products covered by the marketing authorization on behalf of the MAH.

2. A wholesaler that receives saleable returned product from a pharmacy or other wholesaler must verify the safety features prior to resale into the supply chain.

Verification and decommissioning may be required when a wholesaler distributes outside the normal supply chain, such as to healthcare practitioners or emergency responders. If product changes ownership but remains in the wholesaler's possession, or transfers between single-owner facilities within the same member state, verification is not required.

PARALLEL IMPORTER/DISTRIBUTOR REQUIREMENTS

To minimize the risk of diversion in Europe, EU FMD and the Delegated Acts codified the requirements for parallel importation, confirming its legality but with strictures on how it is performed. As a result, parallel importers have a complex set of serialization, verification, and reporting requirements.

When buying product on the open market that they intend to repackage or relabel (thereby covering or removing the original safety features), a parallel importer must first verify the identity of the original purchased product, decommission the serial number, and report the product to the verification system. All repackaged product must be appropriately serialized at the pack level.

Similar to an original manufacturer MAH, the parallel importer must also report the product master data and serialized pack data for these repackaged products before introducing them into the market.

Similar to wholesale distributors, parallel importers may need to perform verification and decommissioning of the medicine pack if the parallel importer is distributing that medicine to entities typically considered outside of the normal supply chain, such as medical practitioners and optometrists. These requirements will vary on a country-by-country basis.

PART 4: HOW EU FMD IS DIFFERENT FROM U.S. DSCSA

Pharmaceutical companies that must comply with the U.S. law are likely well underway with their serialization efforts. That's because in the U.S., the Drug Supply Chain Security Act (DSCSA) serialization deadline for manufacturers is in November 2017, 15 months ahead of EU FMD.

The U.S. and EU regulatory mandates share many common factors, such as the requirement for the four common data elements of product, batch/lot, expiry date, and serial number. They also share the primary goal of stopping the movement of counterfeit drugs through the supply chain.

However, there are deadline, market, and regulatory differences between EU FMD and U.S. DSCSA requirements. If you're a company selling product into both markets, you may be wondering how EU FMD compares to what you're already doing under U.S. DSCSA.

Here are seven of the top differentiators:

1. THE EU EMPLOYS A HARMONIZED REGULATION, BUT NOT STANDARDIZATION, FOR ALL COUNTRIES.

As an umbrella regulation, EU FMD treats required data elements differently from U.S. DSCSA. EU FMD allows country-specific requirements with no mandate to implement serialization in exactly the same way in different countries. This single harmonized process provides a measure of commonality across Europe—but not standardization.

In the U.S., DSCSA provides consistency across states, replacing the previous patchwork of state-specific regulations. In the EU, your business may be impacted by unique country requirements involving:

- **Product identifier** – The U.S. always requires the use of the national drug code (NDC) as part of the serialized product identifier, but EU countries do not follow a single approach for the product identifier. Some follow the global GS1 GTIN standard, while others mandate a unique national identifier.

- **Fifth data element** – In addition to product identifier, serial number, lot/batch number, and expiry date, an optional data element for a national reimbursement number may be required by different countries.

- **Multi-market packs** – These may require more than one product code or reimbursement number to be configured in the 2D barcode. If your business distributes into 10 EU countries, your serialization infrastructure may need to create and enable 10 different serialization approaches with similar but unique requirements.

2. THE REGULATIONS HAVE DIFFERENT LEVELS OF SERIALIZATION.

In the U.S., companies are required to serialize at the smallest saleable unit and at the sealed homogenous-case level. In the EU, companies must serialize at the secondary (saleable unit) level, but do not have to serialize at the case or transport level.

3. DIFFERENT POINTS OF VERIFICATION DRIVE UNIQUE OPERATIONAL CHALLENGES.

The EU is regulated as a point-of-dispense verification system, with verification of authenticity required at the pharmacy level, and on a risk-based basis elsewhere in the supply chain. In the U.S., on the other hand, verification of serialized identity isn't formally mandated at the pharmacy—instead, verification is required during saleable returns processing and during suspect product investigations.

4. PRESSURE FOR AGGREGATION IS GROWING IN THE EU, THOUGH NOT AS MUCH AS IN THE U.S.

While aggregation is not required by either system, the U.S. is seeing greater trade pressure to perform aggregation, primarily by the request of some wholesale distributors. Supply chain traceability is not a driving factor in the EU, although other issues, such as working with 3PLs, are increasing the pressure to aggregate.

5. REPACKAGING AND LABELING REQUIREMENTS ARE DIFFERENT.

In the U.S., repackaging tends to focus on converting the saleable unit as desired by the manufacturer into a saleable unit as desired by the point of dispense. Repackagers will break down product produced by the manufacturer and put it into other convenience package sizes. U.S. requirements for repackaging are not location-specific because the labeling of product is governed by federal law.

Across Europe, most drug products are already packaged at the point of manufacture in a "unit of use" form, thus removing much of the stimulus for repackaging for patient convenience. Still, EU FMD services a collection of independent countries, and because drugs are primarily regulated at the country level, one country may have different labeling and packaging requirements from another. An MAH initially distributes product into the supply chain with specific and approved target markets, and must follow the requirements of each of those markets.

To address the product integrity and patient-safety issues involved, EU FMD has extensive regulatory requirements governing labeling and packaging operations. When products cross country boundaries, the law may require a repackaging or relabeling process to meet the destination market's regulations, including reporting obligations to the EMVS.

6. DATA REQUIREMENTS HAVE DIFFERENT BUSINESS DRIVERS.

Here are some examples of how data requirements and practices are different between the two regulatory regimes:

- **Serial numbers** in Europe must be randomized by a specialized algorithm, and the manufacturer must ensure uniqueness for one year after the expiry date of the pack, or five years after the pack has been introduced for sale into the supply chain, whichever is longer. The U.S. has no legal specifications for the randomization of serial numbers, and no current rules for ensuring the uniqueness of serial numbers.
- **Data elements and fields** vary in the EU, where the number of elements you must encode in the product, the number of data fields, and how information is composed, can vary from one country to another based on national requirements. In the U.S., the product identifier at the saleable-unit level is always composed of the NDC, serial number, lot number, and expiry date.

- **Master data** must be reported to the European hub, along with serialized product pack data. It must include a list of intended target markets, as well as any downstream companies that act as agents on behalf of the manufacturer. This differs from the U.S., which handles master data and product pack data as part of transactional data sets exchanged between trading partners for regulatory or business purposes.

7. VOLUME IS 5X-7X LARGER FOR EU BASED ON PACKAGING AND POPULATION.

Medicines in Europe are generally packaged and sold at the "unit-of-use" level, so the volume of product, and the magnitude of transactions for serialization, will be five to seven times greater than what companies will handle in the U.S., where the saleable unit is distributed in larger bulk quantities.

Considering the larger population covered by EU FMD, the universe of data to be produced, managed, and reported in Europe will be massive, with the added complexity that each country has the flexibility to apply their own unique requirements.

In addition, product packaging in the EU centers on purchase by customers or health systems, whereas in the U.S., product is packaged into sizes intended to be purchased by the dispenser. Each of these unique distinctions will influence manufacturing decisions and operational processes, and affect system performance.

PART 5: OTHER UNIQUE EU FMD REQUIREMENTS

EU FMD compliance creates other challenges, such as how companies will address trade requirements in specific countries and when drug products are classified as prescription pharmaceuticals versus over-the-counter medicines.

WHAT ARE THE COUNTRY-SPECIFIC REQUIREMENTS OF EU FMD?

EU FMD provides general harmonized standards across the EU, while supporting the unique needs of individual member states. Member states have the flexibility to apply their own unique requirements for product, master, and company data. This flexibility allows for some member states to classify a drug product as a prescription pharmaceutical where other member states do not.

Countries that have extensive trade arrangements with the EU, and are expected to align with and follow EU FMD requirements for safety features, include Switzerland and the European Economic Area members of Norway, Iceland, and Liechtenstein. EU FMD provides considerable flexibility to each country to determine whether a medicine must contain safety features such as an identifier and on-package features (and thus require serialization/reporting). In addition, a given country may add data to the on-package and data carrier requirements. As a result, the same drug product may have quite different serialization and reporting requirements in two different target markets.

WHAT IMPACT WILL BREXIT HAVE?

As the U.K. negotiates their exit from the EU, they may still potentially use the European hub for pharmaceutical traceability. If they fully withdraw, what will that mean to manufacturers? Other member states will still use the European hub, so you will want a solution that ensures you are fully covered by your provider's integration into the European hub.

If the U.K. chooses not to participate in the European hub, they will draft specific laws with requirements defining how they want to perform traceability in their country. In this case, you will want a serialization solution that can track developments so you are able to support compliance reporting specific to the U.K. national system.

WHAT ARE THE GRANDFATHERING PROVISIONS?

Products packaged and released for sale on the market before the law takes effect may be distributed and sold until their expiry date. Grandfathering applies if such products are released for sale or distribution before their effective date in the member state where the regulation applies, and if they are not repacked or relabeled.

Countries with serialization and coding schemes already in place will get an additional six years of transition time to meet the EU FMD deadline. This includes:

- **Belgium** – expected to align with the EU 2019 deadline.
- **Greece** – considering aligning with the EU 2019 deadline.
- **Italy** – has indicated the country may use the full six-year extension.

COVERED VERSUS NON-COVERED PRODUCTS

A whitelist details certain prescription products that are exempted under EU FMD, including medical gases, solutions, solvents, and homeopathic medicines. Certain over-the-counter, non-prescription medicines are on a blacklist, meaning that although they are not prescription medicines, safety features must be applied to the products. Additionally, some products may be available only by prescription in one country but considered over-the-counter in another.

PART 6: NEXT STEPS

The advent of serialization and the larger track and trace laws will transform not just the pharmaceutical industry as a whole, but also many core operations at your company. And all that change needs to happen in a very short timeframe. The bottom line is that if you are not prepared to serialize by the February 2019 EU FMD deadline, you may not be able to sell product in the EU.

Now that you have a basic understanding of how these regulations can affect your pharmaceutical business, you are ready to start planning in earnest. Explore additional resources on aggregation, CMO relationships, 3PLs, and more, and contact TraceLink for a personal consultation on your serialization needs.

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