World Health Organization

Policy paper on traceability of medical products

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Contents

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Key points

This policy paper outlines the features of existing traceability systems and provides guidance on developing workable traceability regulation. In the light of the widely varying needs, capacity, and resources of Member States, the risk mitigation and sustainability strategies embedded in implementation efforts will vary. Given the range of possible implementation pathways, a set of guiding principles will assist Member States in establishing systems best suited to their needs and constraints.

For this purpose, Member States are encouraged to:

- establish a suitable governance process for their traceability system based on the analysis of national specificities (e.g. regulatory environment, supply chain management), taking into account the impact of the different forms of governance on interoperability, cost, security, regulatory control and access to safe, quality medical products;

- include a costing analysis as well as a sustainability mechanism in their traceability system planning to prevent costs from negatively impacting patients, government, supply chain stakeholders, and ultimately, access to medical products; and

- use global standards for product identification, production identification, automatic identification, and data capture and data exchange to reduce set-up and operating system costs and maximize national and international interoperability.

Glossary

This glossary was developed in consultation with the International Coalition of Medicines Regulatory Authorities. It is not intended to be an exhaustive list.

Aggregation	The documented parent/child relationships between uniquely identified items and the uniquely identified outer container that they are contained within for the purposes of improving the efficiency of serialization business processes involving data exchange and/or regulatory requirements.
Authentication	The act of determining the authenticity of a product or a system user.
Authenticity	The quality of a product and labelling, establishing that they are unquestionably genuine.
Automatic identification and data capture	The processes used to automate the assignment, marking and capturing (reading) of product identification, through the use of carrier technologies such as barcodes and radio frequency identification tags.
Barcodes	A symbol that follows a data carrier standard that allows it to encode a finite amount of data, which may be read repeatably and reliably to extract the data it contains. There are generally two types of barcodes used in commercial supply chains around the world: linear and two-dimensional.
Batch number/lot number	An identifier assigned to a homogeneous quantity of a product that has identical manufacturing and packaging characteristics, including raw materials, manufacturing processes and timing. The batch or lot number associates an item with production information that the manufacturer considers relevant for the traceability of the trade item. The data may refer to the trade item itself or to items contained in it.
Data capture	The process of collecting data about product instances. This includes data to be encoded into a data carrier to be affixed to an instance of a product package, as well as data read from existing data carriers on one or more product instances at any level of packaging.
Data carrier	One of several technologies used to encode and present product identification data on a product package. There are many specific types of data carriers but those used in medical product supply chains generally fall into these categories: linear barcodes, two-dimensional barcodes and radio frequency identification tags.
Data exchange/information exchange	The sharing/movement of structured data from one party to one or more other parties. To be successful, all parties must agree in advance on the structure and the data transmission protocol. This is normally the subject of global standards.

Data ownership	The recognition of the party that retains ownership rights to a given set of data.
Data standard	A published standard that describes the characteristics of a set of data for a particular purpose.
Decommissioning	1. The act of documenting the disassociation of a unique identifier from a specific instance of an object class, typically when the object no longer exists or reaches the absolute end of its life cycle (i.e. after destruction or consumption of a product). 2. A type of "visibility event" defined in the GS1 EPCIS standard[1] that documents the decommissioning as defined in 1 above.
Expiry date	The latest date that the manufacturer of a product is confident a given instance of the product will meet the published/regulated application.
Falsified	Products that deliberately/fraudulently misrepresent their identity, composition or source.
Global data standards/"family" of standards	A set of standards specifically defined to work together coherently to facilitate a specific purpose, i.e. secure commerce within a supply chain.
Globally unique	Adjective describing something with a characteristic that it is unique throughout the world.
Global/globally unique product identifier	A product code that cannot be assigned to more than one product throughout the world because it is defined by elements that are controlled via a global assignment agency and the manufacturer.
Governance	The process of developing and enforcing technical rules intended to enable secure product supply chains.
Grandfathering exception	An exception to a traceability regulation granted explicitly by that regulation applies to products already in the supply chain on the day the new regulation comes into effect because they were packaged prior to that date and therefore cannot be expected to comply. These products are said to be "grandfathered".
Inference	The process of determining the unique identifiers on objects contained inside of outer containers like cases, totes and pallets, using aggregation data rather than opening the containers themselves. The unique identifiers found are said to be "inferred" from the aggregation data because their accuracy depends on the accuracy of the aggregation data and the integrity of the outer container since the actual objects and their identifiers are not visible.
Interoperability	The ability to exchange product traceability information accurately, efficiently, and consistently among trading partners in a supply chain and/or authorized regulators.
Legal supply chain	The supply chain paths and participants that are recognized and authorized by the government(s) of jurisdiction. Also sometimes referred to as the "legitimate supply chain".
Marketing authorization holder	The legal entity that has been authorized to place specified medical products on a regulated market by the national regulatory authority.

[1] See GS1 website: https://www.gs1.org/standards/epcis (accessed on 21 September 2020).

Packaging levels	The hierarchy of product packaging. Each level includes a specific way of protecting and identifying the product during different types of handling. Recognized levels include "primary", "secondary" and "tertiary".
Pack	The packaged product that moves through a supply chain and is sold/administered/dispensed to the end patient and that is typically the subject of serialization requirements.
Pharmaceutical product	Any material or product intended for human or veterinary use presented in its finished dosage form or as a starting material for use in such a dosage form, that is subject to control by pharmaceutical legislation in the exporting state and/or the importing state.
Point of dispense verification	A recognized traceability architectural model that aims to limit the points in a supply chain where a drug must be verified to the point where it is dispensed or administered to a patient. Also referred to as a "book-end approach" because it usually requires manufacturers at one end of the supply chain to apply a unique identifier to drug packages, and dispensers at the other end of the supply chain to perform the verification step. The European Union Falsified Medicines Directive (Directive 2011/62/EU) as defined by the Commission Delegated Regulation (EU) 2016/161 is an example of a system that implements point of dispense verification.
Primary pack	The product packaging that touches the dose, i.e. a blister pack, a vial. If no secondary pack exists, then the primary pack is usually the lowest saleable pack.
Product	Usually a drug, biologic, vaccine or other health-related consumable that is regulated and moves through a supply chain from manufacturer to consumer.
Product code	A numeric or alphanumeric sequence of characters that is registered as an identifier for a class of objects (e.g. a trade item).
Product identifier	A numeric or alphanumeric sequence of characters that is registered as an identifier for a class of objects (e.g. a trade item) or an instance of an object (e.g. a logistic unit).
Product master data	Data that describe various characteristics of a specific product to differentiate it from all others.
Real-time	A qualifier of an event or process that occurs so fast in response to a trigger that it appears to happen immediately or even simultaneously. "Near real-time" describes an event or process that occurs rapidly in response to a trigger but not fast enough to be considered "real-time".
Secondary pack	A package that contains one or more primary packages. A secondary pack in most, but not all, markets is the lowest saleable pack in the supply chain, when it exists. Sometimes referred to as the "finished pack", "finished product" or "sales pack".
Serial number	1. A unique numeric or alphanumeric code that, when associated with a product code, identifies a single instance of a product. 2. (Colloquial) A unique number that identifies a single instance of a product.
Serialization	The processes and results of defining, assigning and affixing unique serial numbers to product packaging at any level.

Stakeholder funding model	A method of funding the construction and management of the technology infrastructure necessary for a national traceability system that relies on the companies that are regulated (the "supply chain stakeholders") to pay for all or part of it.
Substandard	Also called "out of specification", these are authorized products that fail to meet either their quality standards or specifications, or both.
Supply chain	Two or more companies that buy and/or sell products, starting with the manufacturer and ending with the entity that supplies or administers the products to the end patient.
Supply chain stakeholders	Companies, including nongovernmental organizations and aid agencies, that participate in the supply chain of medical products, including, but not limited to, manufacturers, third-party logistics providers, importers, distributors, wholesale distributors, logistics companies, pharmacies, hospitals, clinics, etc.
Tertiary pack	A third level of packaging or higher, usually including logistic units like shippers, cases, totes and pallets.
Trace	The ability to know where a product has been within a supply chain prior to its current location.
Traceability	The capability to trace something. In some cases, it is interpreted as the ability to verify the history, location, or application of an item by means of documented recorded identification.
Traceability data/traceability information	Data that document where a product, or products, has/have been within a supply chain.
Traceability model	A well-defined approach to capturing, sharing and storing traceability data.
Traceability system	A systematic implementation of a traceability model.
Track	The ability to know where a product is right now.
Track and trace	1. A type of traceability model that attempts to track and trace products through a supply chain. 2. (Colloquial) A term used to refer to any and all traceability models.
Trade item	A product or a homogeneous grouping of a product that is identified so that it may be treated as a "quantity one" unit for the purpose of registration, listing, marketing, sales, shipment, billing and other value chain and supply chain applications. Not all homogeneous groupings are trade items.
Trading partner	Supply chain stakeholders that engage in the purchase, sale and donation of products between each other.
Transactional data	Data that describe one or more transactions, whether financial or supply chain (product change of ownership), or both.
Transactional interoperability	A transaction in one system is extended automatically to another system.

Unique identifier	A unique serial number in combination with a product code. A unique identifier identifies a single instance of a product.
Unique number	A numeric or alphanumeric sequence of characters that identifies a single instance of a product such that no other instance has the same sequence associated with it.
Unregistered/unlicensed	Medical products that have not undergone evaluation and/or approval by the national regulatory authority for the market in which they are marketed/distributed or used, subject to permitted conditions under national or regional regulation and legislation.
Verification	The process of determining that the unique identifier on a product is valid.

Introduction

As a result of the growth and globalization of trade, medical products[1] nowadays are manufactured and distributed in complex supply chains. Products pass through many entities on their journey to the patient, often being manufactured in one country and shipped across borders to be subsequently marketed or sold in other countries. As distribution spreads geographically and the supply chain becomes more fragmented, the oversight capacity of national regulatory authorities becomes stretched. Effective oversight of the supply chain is thus weakened, raising the risk of substandard and falsified medical products entering the market and increasing the likelihood of inefficiencies emerging such as stockouts or expired products. This can lead to a loss of public confidence, which eventually results in hesitancy, reduced adherence and under utilization of health programmes. It is therefore vital to address these vulnerabilities and strengthen the integrity and efficiency of the supply chain, with patient safety at the forefront.

Traceability technologies, as described in this document, offer the technical possibility to trace medical products along the supply chain – from final stage manufacture to the point of dispensing, or the ultimate place where the medical product is administered to a patient – with a view to strengthening the near real-time monitoring of the integrity of a given pack. There is global recognition that traceability systems can be leveraged as useful tools to ensure the integrity and improve the efficiency of supply chains. Traceability may not be able to completely block falsified medical products from entering the supply chain but implemented alongside the considerations contained in this policy paper, it can minimize the risk and allow for earlier detection and response.

In recent years, Member States have called on the World Health Organization (WHO) to facilitate the exchange of experiences, lessons learned and information gained about traceability technologies, methodologies and models. *(1)* The WHO Member State mechanism on substandard and falsified medical products has prioritized work around this issue and has published technical documents that strengthen the understanding of the current landscape, including the experiences in countries. *(2)* A global framework or guidelines have however yet to be developed. There is also limited peer-reviewed evidence on the implementation of traceability systems available to support policy development.

This policy paper therefore aims to bring together the available knowledge around existing traceability systems to guide national regulatory authorities in their efforts to ensure the traceability of medical products.

[1] In this document, "medical products" include finished pharmaceutical products, including medicines and vaccines.

Methodology

A working group composed of members of the WHO Member State mechanism – with balanced and diverse regional representation from Member States – was convened to draft a policy paper on traceability designed primarily by regulators, for regulators.

The following 19 Member States were members of the working group:

WHO African Region	Benin Ethiopia Kenya Liberia Mozambique Nigeria United Republic of Tanzania
WHO European Region	Russian Federation Spain Ukraine
WHO Eastern Mediterranean Region	Iraq
WHO Region of the Americas	Argentina Brazil Chile Mexico United States of America
WHO South-East Asia Region	India Indonesia
WHO Western Pacific Region	Republic of Korea

The working group also included participation from the International Coalition of Medicines Regulatory Authorities and the European Directorate for the Quality of Medicines.

A review of numerous national and international implementation efforts and technical resource documents was conducted, which included a case study approach whereby the actual Member State implementers systematically shared their views through surveys, discussions and interviews. In an effort not to duplicate efforts and ensure coordination, the working group members also engaged with other regional and international regulatory bodies as well as external experts, industry stakeholders, and standard-setting organizations, where appropriate.

Scope

The policy paper covers pharmaceutical products, including medicines and vaccines, as finished products in the supply chain from the point of manufacture to receipt by the dispenser (e.g. pharmacist) or administrator (e.g. hospital or clinic).

The following product streams will be excluded from the scope of this paper: active pharmaceutical ingredients, compounded preparations, medical devices including in vitro diagnostics, blood and blood products (except plasma-derived medicinal products which are medicines), organs, tissues and cells, personalized medicines, traditional medicines (except those registered as medicines), food supplements and veterinary products.

This policy paper is not automatically and entirely applicable to medical devices as there are wide differences in the regulatory requirements and supply chain environments for medical devices when compared to pharmaceuticals/vaccines. However, a situation analysis is provided in Annex 1[1] and future iterations of this policy paper may consider traceability for medical devices.

With respect to the level at which this policy paper is applicable, this document responds to questions of national or regional implementation (when several Member States in one region decide collectively to develop an integrated traceability system within their respective region). For information on interoperability between several national or regional systems, and in an effort not to duplicate efforts, WHO encourages Member States to refer to the upcoming guidance developed by the International Coalition of Medicines Regulatory Authorities on interoperability, to be published in 2021.

This policy paper covers the supply chain and its legitimate stakeholders that are appropriately registered, licensed or authorized, from manufacturers of finished products (lot/batch release) until the point of dispense of the medicine (e.g. pharmacies) or the point of administration (e.g. hospitals or clinics). Movement of medicines beyond these boundaries fall outside the scope of this document, thus excluding traceability of active pharmaceutical ingredients used to manufacture finished products. However, a section on patient verification is included, which uses traceability features to enable patients to verify medicines after dispensing (Nigeria and Kenya).

In terms of depth, this policy paper is designed to offer guidance to Member States on policy and regulatory approaches, particularly regarding the governance of traceability systems and their data management. Once Member States have set up the appropriate policies and regulatory environment for traceability, separate guidance and support will be needed to strengthen regulatory capacities and ensure the seamless integration and suitable enforcement

[1] For Annex 1 on traceability systems for medical devices, including in vitro diagnostic medical devices, please see: https://mednet-communities.net/sf (accessed 28 September 2020).

of the subsequent implementation measures. Country-level implementation will require Member States and all supply chain stakeholders to reference other guidance, particularly on the multiple data standards that exist for the traceability of medical products.

This policy paper does not aim to provide an analysis of, or identify a preference among, currently available technology or data standards.[1,2] It focuses instead on the benefits and scenarios that impact the implementation of the standards chosen by Member States and the value of standardization across systems.

With respect to the use of traceability systems, the policy paper covers supply chain integrity and efficiency. While the drafting committee discussed pharmacovigilance and product reimbursement, these topics were not considered to an extent that allowed for the drafting of specific recommendations. These areas therefore remain out of the scope of this paper. Member States should be aware of the global discussions surrounding the use of the International Organization for Standardization (ISO) Identification of Medicinal Products standards, designed to provide a global framework for the identification of substances, medicinal products and packaged products, and their corresponding regulatory approval status in each implementing country or region.

Intellectual property issues also fall outside the scope of this policy paper. However, should a traceability system be used for purposes such as product reimbursement or trade (e.g. at the customs level), health authorities are advised to liaise with other relevant authorities to ensure the right use of, and access to, traceability data handled by the system.

The scope described above pertains to this policy paper. National regulatory authorities responsible for devising traceability regulations should determine the scope of their regulation, which may include some of the topics in this policy document as well as other topics that are not. Each national regulatory authority should clearly define that scope in its respective regulation to remove any ambiguity.

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[1] The examples provided by Member States participating in the working group are based on the implementation of the set of standards known as GS1. GS1 is a trademarked name for data standards, owned by GS1 as an international non-profit standards development organization registered in Belgium. It was unintentional, but not unexpected that all the examples were based on this particular standard. While it is broadly understood that the GS1 standards are the most commonly used for medicines, including use by numerous United Nations agencies, it should be noted that WHO as a practice does not endorse brands.

[2] For Annex 2 on global standards organizations, please see: https://mednet-communities.net/sf (accessed 28 September 2020).

Opportunities and risks of traceability systems

Potential opportunities

The successful implementation of a traceability system can facilitate strengthened supply chain integrity and efficiency, with the ability to trace where a product has been at any given moment. Near real-time information and appropriate data access can provide visibility of products and can expedite regulatory responses to safeguard patients and the supply chain, including by:

1. Ensuring only authorized products, registered or approved, circulate in the legal supply chain;
2. Preventing the distribution and/or dispensing of falsified, expired, prohibited or recalled products;
3. Facilitating efficient and fast market recalls;
4. Enabling efficient inventory management at all levels; and
5. Identifying shortages and monitoring the reasons for shortages and stockouts.

The challenges posed by increasingly complex manufacturing processes and trade flows are likely to grow, with current estimates indicating that one in ten medical products are substandard or falsified in low- and middle-income countries. *(3)* Strong regulatory oversight can help mitigate supply chain vulnerabilities and risks, and facilitate increased prevention, detection and response to substandard and falsified medical products. Traceability systems can help prevent the entry of falsified medical products into regulated supply chains, detect any falsified medical products that are circulating in-country, and assist regulators to respond quickly and proportionately to any substandard and falsified incidents that are detected.

These potential opportunities, if realized, can offset the costs of traceability systems. The hidden costs of not investing in traceability in preparedness for resilient supply chains may end up being considerably higher.

Potential risks

The inception and deployment of traceability systems require significant investment and involve high costs that can disproportionately burden low- and middle-income Member States. Regulatory authorities already struggle from low-resource or weak regulatory environments and additional initiatives may further constrain budgets, programmes and workforces. The consequences of poorly managed implementation and weak enforcement measures also impact supply chain stakeholders and could overwhelm or divert limited resources to move forward and resolve issues – which may have a long-term impact on the affordability of medical products and therefore patient access to those products. At the same time, some markets do not suffer in a significant way from substandard and falsified medicines so, in those areas, the risks of implementing traceability systems may outweigh the benefits.

Some Member States have issued traceability regulations that are currently implemented, or on the way to being implemented; while others are assessing various implementation alternatives, or have not yet approached the topic. Without coordination and guidance, there may be variability in the requirements and standards used. New traceability initiatives should consider harmonization of standards to ensure the continuity and sustainability of the system once implemented.

The deployment of technologies is an inherent part of traceability, but if there is limited technological capacity at ports of entry, distribution centres and pharmacies, particularly in remote areas – where internet connectivity, cellular data service, etc. are weak – there may be gaps in the information collected and delays in the exchange of information. Sustainability concerns also go hand in hand with a lack of clear and workable regulation. As a mitigation measure, Member States should formulate phased and long-term transition and continuity plans that factor in risk management and are coupled with realistic time frames.

Strong collaboration and dialogue are needed with key stakeholders, including those donating/providing medical products, such as international donors, international procurement agencies or nongovernmental organizations. Any weaknesses or lack of robustness in the technical settings of a traceability system, its governance or its data management policy, may lead to breaches in the system, including access by non-registered or rogue users, misuse of data and attempts to disrupt service. These risks are amplified due to the sensitivity and value of the data handled by traceability systems relating to the identity and near real-time location of products at item level, where applicable. As such, ensuring data security as part of enforcement plans is of utmost importance to guarantee that the security expectations of stakeholders are met.

All traceability models require a robust definition of interoperability standards to achieve traceability throughout the supply chain. Transfers of the physical product and corresponding data require strict alignment and efficient transmission between entities to eliminate errors and streamline operations.

Various features of traceability systems, including governance

Outlined opposite are nine common features of traceability systems that have been implemented by Member States, including key considerations. Some of the features are mutually exclusive, while others are not. It should be noted that implementation of the following features largely depends on the existing regulatory system maturity, national resources and local context of the implementing Member State. Member States are encouraged to assess the potential feasibility of each of these features, including implementation and sustainability opportunities and risks.

Feature 1
Identification

Feature 2
Use of global standards

Feature 3
Lot/batch-level traceability

Feature 4
Unit-level serialization

Feature 5
Aggregation data

Feature 6
Verification

Feature 7
Full track and trace vs point of dispense verification

Feature 8
Patient verification

Feature 9
Detection and response, including reporting

FEATURE 1

Identification

To successfully trace products through a supply chain, it is necessary to identify the following four key elements in a standardized way: (a) products; (b) stakeholders; (c) subsets of products based on manufacturing/production; and (d) locations.

- This should start with the master data unambiguously identifying products, including distinguishing features such as the product name, active ingredient, strength, pharmaceutical form, packaging, and often the pre-established market destination, following the principles defined in the ISO standards on Identification of Medicinal Products. *(4)* Medical products need to be identified at the secondary packaging level (see glossary), or, if there is no secondary level, at the primary packaging level.[1]

- The quantity of units of manufacturing/production uniquely identified will inversely determine the granularity of the tracing possible.

- Locations and stakeholders must be identifiable so that product movements between buyers and sellers can be documented in the traceability system.

Consideration

Batch-level identification is suitable for implementing product recalls and pharmacovigilance, but unit-level serialization would likely be more suitable for other purposes, including investigations of substandard and falsified incidents and cargo theft and diversion. Member States relying on implementing partners for part of their supply of medical products should consider establishing an exception, exemption or waiver (see Strategy 8: Exemptions, exceptions and waivers) for tracing products composed of the same components (e.g. the same molecule) imported under different names without being registered in the destination market.

[1] Identifying products with a product code, lot and expiration date within a single data carrier offers benefits beyond traceability, including bed-side scanning and automated recall detection and expiration date checking.

FEATURE 2

Use of global standards

The use of global standards offers the following benefits over locally defined approaches:

- robust governance and clear procedure for updating;
- fewer limitations when traceability regulations change in the future;
- third party support available globally to all stakeholders;
- wide familiarity and acceptance by medical product manufacturers and their economic operators (agents, distributors, authorized representatives) and logistics companies globally;
- large set of choices for application, with future expandability built-in;
- enhanced opportunity for the interoperable exchange of pharmacovigilance data with many countries using the same set of standards; and
- widely available off-the-shelf hardware and software technology designed to work with such standards.

These benefits result in lower start-up and operational costs and smoother operation for national authorities and supply chain stakeholders throughout the life cycle of individual medical products. *(5)* Some commonly used standards include:

- The GS1 standards that are currently the global family of standards in wide use globally for pharmaceuticals.
- The ISBT 128 standard from the International Council for Commonality in Blood Banking Automation (ICCBBA) that is widely used to identify medical products of human origin (including blood, cell, tissue, milk, and organ products).

However, mere use of global standards alone will not automatically result in interoperability. Careful attention must be given to the choice of standards and how they are applied.

Consideration

Standardized identification across the supply chain is vital to the success of traceability regulation and continued access to supply from global markets. Member States are encouraged to make use of international global standards for product, stakeholder, production and location identification for medical products, as well as for any mandated automatic identification and data capture elements such as barcodes or radio frequency identification tags. Application of global standards consistent with other Member States can enable the international interoperability necessary for international vigilance.

3 Lot/batch-level traceability

A limited form of traceability can be accomplished using only product codes and lot/batch numbers, but the efficiency and accuracy of information capture is low and the introduction of falsified medical products into the supply chain cannot be detected. At most, a regulatory system can keep track of which lot/batch numbers have been where, which may be sufficient for recall execution and vigilance.

Consideration

Although limited in information capture, some countries have used lot/batch-based tracing of medical products in a phased approach as a first step towards their ultimate goal of unit-level tracing, in an effort to spread the costs over multiple budget cycles (see Feature 4: Unit-level serialization).

FEATURE 4

Unit-level serialization

Unit-level tracing requires unit-level serialization. Unit-level serialization requires the placing of a unique identifier – a unique serial number in combination with a product code – on every saleable unit of a class of medical products. The saleable unit is the level of packaging that would normally be distributed (sold or donated) to a pharmacy or hospital in the supply chain. The unique identifier is normally applied to the secondary level packaging, where the primary packaging level (packaging that touches the dose itself) is contained inside. If there is no secondary level of packaging, then the unique identifier would be placed on the primary packaging (See Fig. 1).

Serialization and tracing at the unit-level is considerably more complex and therefore necessarily involves challenges that are well beyond lot/batch-based traceability. Consequently, packaging costs are considerably higher for manufacturers working under a serialization mandate. These costs include, but are not limited to, new packaging equipment, new business processes, slower production line speeds, more repackaging or rework, and more rejects. Costs are also higher for downstream trading partners in the supply chain when required to incorporate operational changes, such as reading the product identifiers, handling and managing the data, and taking actions mandated by regulation on the unit-level unique identifiers, including initiating investigations on suspect substandard and falsified medical products, reporting activity to a government portal, verifying authenticity, etc. Member States often overlook these additional costs because the potential benefits are so great, namely that such unit-level serialization can help to detect the introduction of falsified medical products into the supply chain.

Automatic identification and data capture coding as well as data standards should be defined so that they enable interoperability and remove ambiguity of unit-level serialization and/or other levels of packaging.

The unique identifier allows for verification of the pack. Verification can be enhanced if it is paired with tamper-evident packaging, ensuring that the verification of the identifier on the pack refers to the content of the pack.[1]

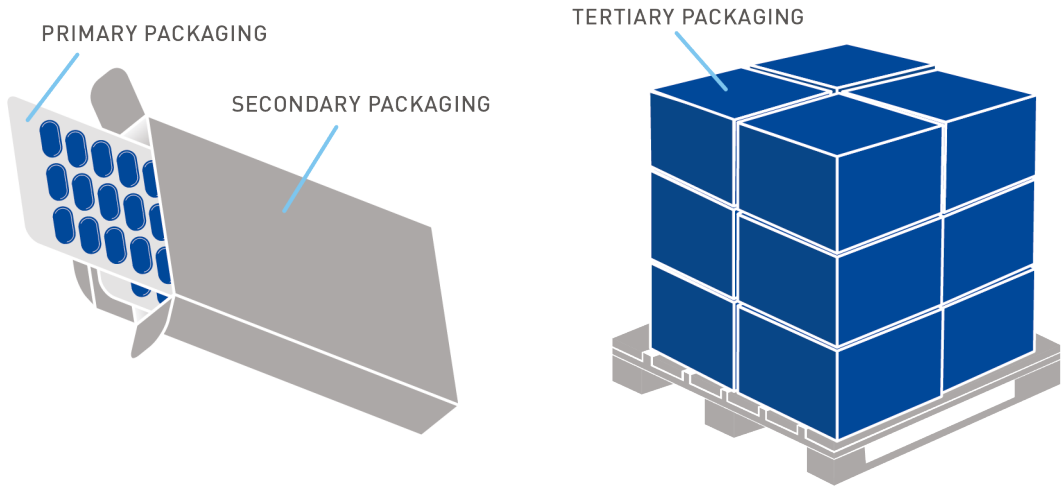
Consideration

Traceability regulations should clearly specify the levels of identification required, i.e. down to unit-level serialization or not, and in the former case, who and at which level – and which trading partners in the supply chain should verify or capture identification data. This requirement should be complemented by the requirement for tamper-evident packaging in order for the verification of the pack identifier to be valid for the contents, i.e. the actual medicine. Traceability regulations should integrate measures to help prevent falsification (copying) of the unique identifiers. These may include randomization (European Union), external documentation proving the chain of ownership (United States of America), verification (Turkey), and/or crypto-codes (Russian Federation). These measures may be useful tools for preventive efforts in combination with other strategies.

[1] For appropriate tamper verification features, please consult ISO 21976:2018 (Packaging – Tamper verification features for medicinal product packaging).

Fig. 1

The three levels of packaging. Primary packaging always touches the product. When it exists, the secondary packaging contains the primary package(s). Tertiary levels of packaging are reserved for shipping products.



For example, in the Egyptian market, each unit-level package must encode a GS1 Global Trade Item Number (GTIN), Application Identifier (AI)=01, a serial number unique to that GTIN (AI=21), the lot/batch number (AI=10), and the expiration date (AI=17). This information is encoded using GS1 standards into a GS1 DataMatrix barcode (See Fig. 2). *(6)* Each of those elements are specified clearly in the implementation guideline published by the Egyptian Ministry of Health and Population.

Fig. 2

Example of a DataMatrix barcode and human readable contents accepted in Egypt for serializing drug products

(01)10534890175010
(10)12345678
(17)121023
(21)12345678901

FEATURE 5

Aggregation data

Whenever multiple levels of packaging are serialized, aggregation data may be valuable for accurate, efficient tracing, and in some markets, for decommissioning of large shipments in hospitals and hospital pharmacies. Aggregation data are data that document the parent-child relationships between serialized containers (the "parents") and the serialized units inside the containers (the "children") (See Fig. 3). That data can be used throughout the supply chain to "infer" the contents of the containers. Aggregation data must be captured at the time the serialized child packages are inserted into the serialized parent packages/containers. Such data are especially useful later in the handing of the parent packaging/containers to identify the unique identifiers that are contained inside, without opening the parents and reading the unique identifiers on the children. The need for this inference might occur in several different supply chain business processes – anywhere in the supply chain where verification of the children may be necessary, including shipping, receiving and processing returns.

The regulations in some countries mandate the collection and use of aggregation data (Argentina, Pakistan, Russian Federation, Saudi Arabia). Others mandate actions by members of the supply chain that can only be accomplished efficiently when aggregation data are captured by the manufacturer or repackager but do not mention the capture of such data as an explicit requirement (European Union, United States of America). *(7)*

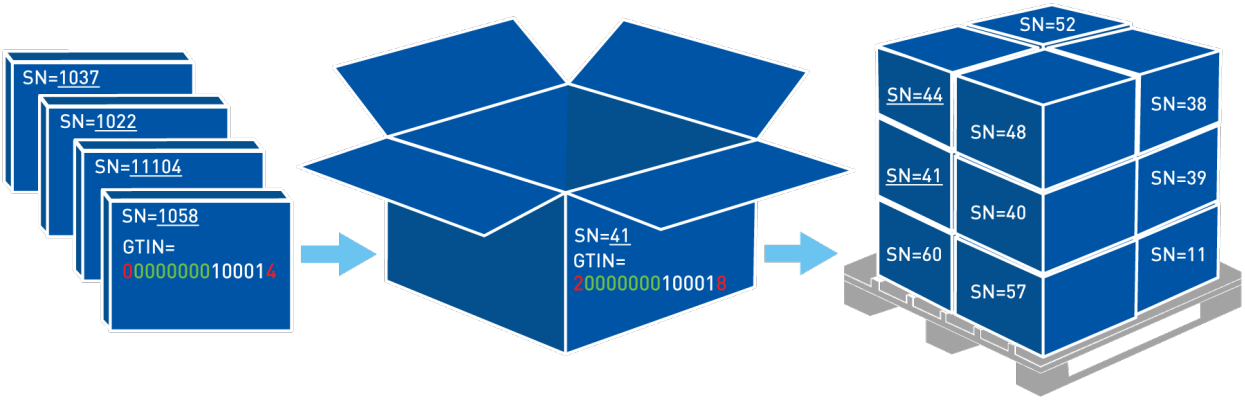
Mandating unit-level serialization without also requiring aggregation data capture during packaging risks slowing down the supply chain with intolerable manual verification and data capture. However, the use of aggregation data and the inference that it allows requires the overall system to be tolerant of unintended errors and their results.

Consideration

Weighing the high-cost impact of capturing and maintaining aggregation data using local supply chain capabilities (e.g. the capability of the distributors and wholesalers to manage the demanding task of maintaining a complete chain of custody along the supply chain as aggregation data changes) against the actual expected benefits (such as not needing to scan every unit at a wholesaler or hospital and the potential improved knowledge of supply chain events) is recommended before mandating such a requirement.

Fig. 3

Aggregation of serialized secondary packages into a serialized tertiary package (case) and then onto a serialized pallet. Aggregation data are shown in the table below.



AGGREGATION DATA

Carton SGTINs (with AIs)	Case SGTINs (with AIs)	Pallet SSCC (with AI)	
01 00000000100014 21 1037	01 20000000100018 21 41	00 000000000000002530	Depicted in the drawing above
01 00000000100014 21 1022			
01 00000000100014 21 1104			
01 00000000100014 21 1058			
01 00000000100014 21 235	01 20000000100018 21 44		Not shown in drawing
01 00000000100014 21 236			
01 00000000100014 21 237			
01 00000000100014 21 238			
01 00000000100014 21 239			

Note: Drawing shows GS1 standards in use. Adapted from drawing by Dirk Rodgers.

FEATURE 6

Verification

Verification is a technique that allows stakeholders, patients and/or regulatory or enforcement agencies to check the likely authenticity and authorization of products within the supply chain or, under regulations that allow it, in the hands of patients. Each traceability model (see Fig. 4) offers one or more ways to implement the verification of the product identifiers and/or production identifiers (unit-level unique identifiers).

- In the centralized model, where all traceability data are stored in a single database or repository, verification can be performed by national regulatory authorities, members of the supply chain, health care professionals and/or patients communicating with the central repository to verify the identifiers.

- In the semi-centralized model, where traceability data are spread among a small number of repositories, verification can be performed by communicating with one of the regional repositories.

- In the distributed model, where each member of the supply chain holds its own traceability data, verification can be performed by communicating with the original manufacturer. Owing to the frequency of verification required in most cases, these communications should be standardized, web-based messages between systems.

The type of governance required for verification varies widely and depends on which traceability model is in place. Verification success is highly dependent on technical specifications because it requires the user to read the unique identifier on products and transmit it to a remote server. Improperly configured reading equipment will likely cause false alerts

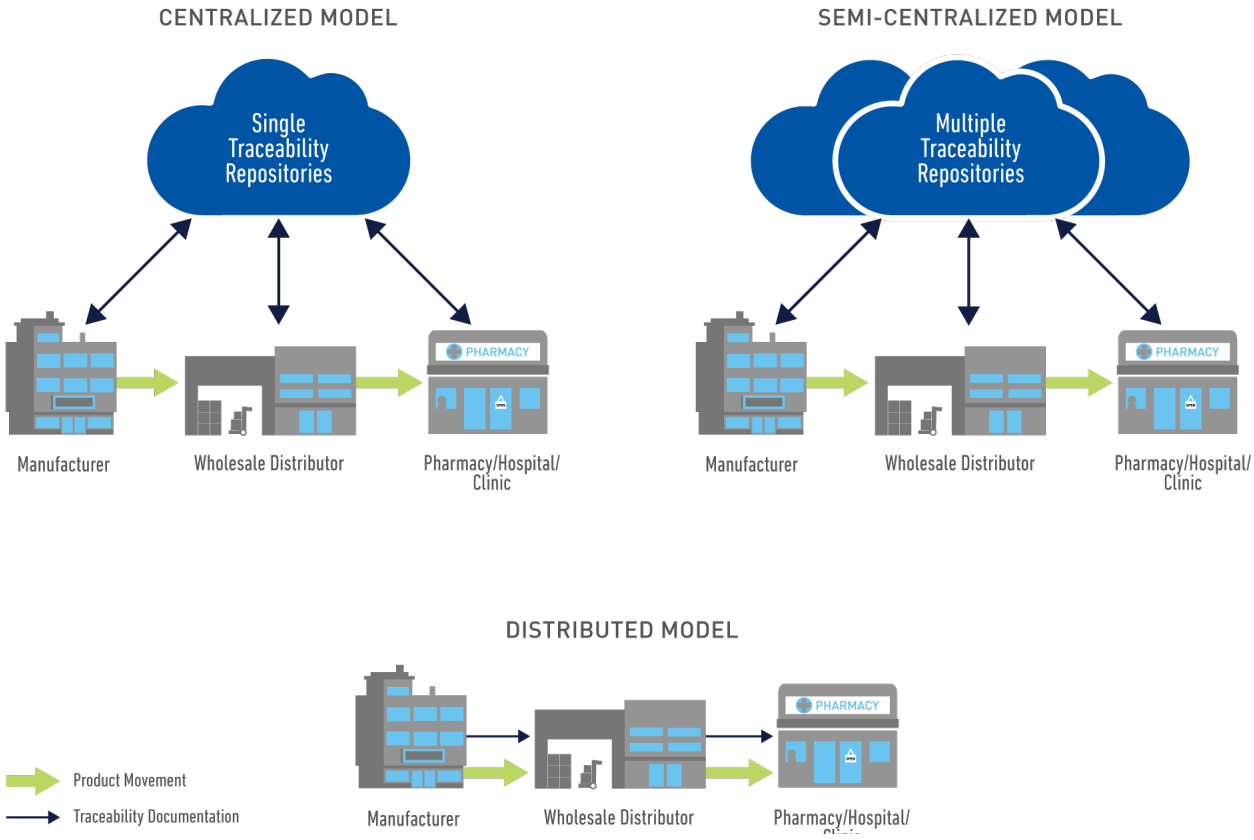
Consideration

Regardless of the model chosen,[a] it should be noted that verification techniques cannot check the authenticity of the chemicals, the drug or the active pharmaceutical ingredient inside the package; rather, they confirm the use of genuine unique identifiers and, if applicable, the corresponding status, as stored in the corresponding database against which the verification takes place.

[a] The drafters of new traceability regulations must choose a traceability model, taking into account many considerations including the operational details of their specific medical product supply chain, complexity, implementation and operational costs, and the ability to address the problems faced. The traceability regulation should identify the model selected.

Fig. 4

The three primary traceability models are differentiated by where the traceability data are stored and how verifications are performed.



Note: Adapted from drawing by Dirk Rodgers.

FEATURE 7

Full track and trace vs point of dispense verification

Two approaches exist in medical product traceability today (see Fig. 5).

- The full track and trace approach involves some form of traceability documentation or verification being completed for each change of ownership in the supply chain. The goal is to detect the introduction of falsified medical products in the supply chain as early as possible so that they can be detected and withdrawn quickly. The drawing shows two approaches to this type of traceability.

- The point of dispense verification approach involves medical products being verified only at the end point of dispense (e.g. a pharmacy) or use/administration (e.g. a hospital or clinic), and optionally, at some point prior to that moment. It can also be used during the reimbursement process to help to reduce fraud. The goal of this type of verification is to protect patients from harm at the point of dispense/administration while minimizing costs along the supply chain.

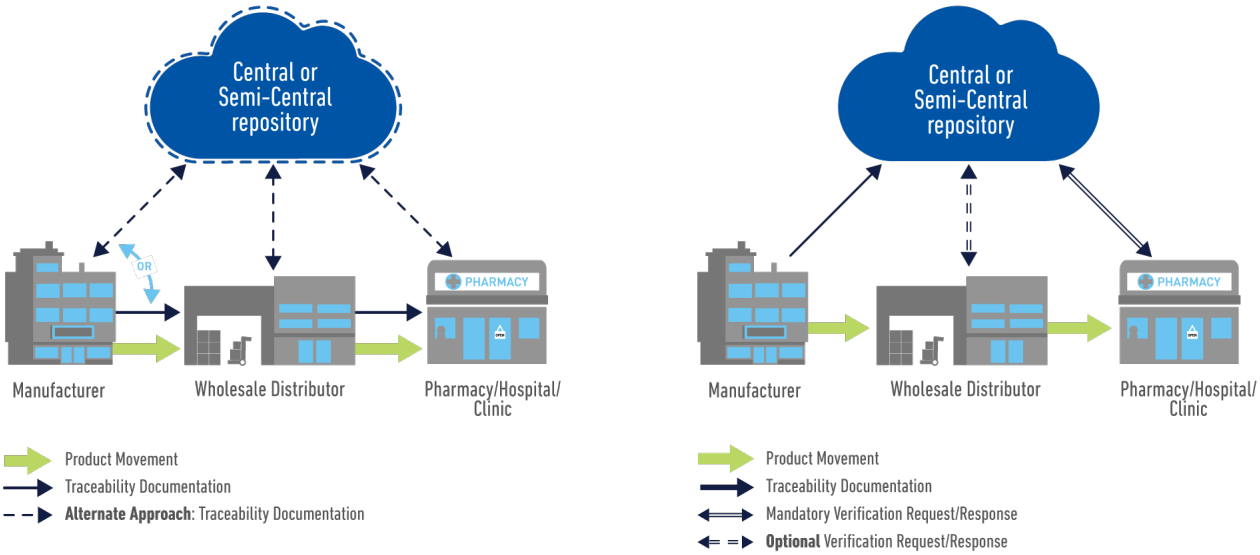
Countries that have enacted regulations using the full track and trace approach include Argentina, the Republic of Korea, the Russian Federation, Turkey and the United States of America. The European Union has enacted regulation using the point of dispense verification approach in its market.

Consideration

Regulators can specify clearly in their traceability regulation the frequency of verification, in particular with respect to point of dispense vs full track and trace verification, based on the maturity of the local supply chain, the capability of the stakeholders to efficiently fulfil the verification requirements, their objectives and the cost implications.

Fig. 5

One approach to full track and trace is shown on the left with solid black lines and the alternate approach shown in dashed black lines. Point of dispense verification is shown on the right.



Note: Adapted from drawing by Dirk Rodgers.

FEATURE 8

Patient verification

Where supply chains are complex but funding is minimal to non-existent, patient verification can serve as a last resort for performing a measure of product verification. This feature is usually implemented with a unique identifier applied to each product package and the corresponding validation data held in a central repository. In the existing systems, patients can send a SMS text message or a photo containing the unique identifier to the repository which looks for the corresponding data. The repository responds with the result of the verification operation.

Patient verification may be most useful as a feature added on top of a full supply chain traceability system rather than as a stand-alone solution. However, patient confidentiality should be taken into consideration when setting up such a system to ensure that either patients are not personally identifiable or that patient information is safeguarded and not accessible to unauthorized persons. Since the service must be available to all patients, security can be problematic. For privacy reasons, the patient-accessible service does not authenticate the user, and therefore could be more susceptible to hacking and falsification.

Consideration

Regulators are cautioned that patient verification efforts should be balanced with strong monitoring and enforcement measures and should not be used as the sole way of determining whether a product is safe. Rogue actors have been known to replicate regulatory services that respond to all verification requests with a positive result. For example, in one incident, although falsifiers had included a greyed-out area on the fake packaging that imitated a scratch-off authentication device, it was not actually scratchable. Manufacturers may be exposed to liability claims if patients submit verification requests improperly. In any case, no access should be given to patients to the system itself to preserve its integrity and patients should be made aware that such a feature is not a definitive and absolute protection against substandard and falsified medical products.

9 Detection and response, including reporting

Active surveillance and monitoring should be established to ensure that the appropriate regulatory responses take place once substandard and falsified medical products are detected or there are authentication or verification failures. All supply chain stakeholders should clearly understand the system and reporting process to the national regulatory authority as well as the relevant actions to be taken, including quarantining the suspected product, storing it in appropriate conditions, etc. Once substandard and falsified medical products are confirmed, the national regulatory authority should respond accordingly to protect public health, including by issuing rapid alerts or notifications for increased vigilance.

The system should be designed so that the evidence of the failed verification should be retrievable for enforcement purposes, where the evidence data are located in the system or in client systems.
There are likely many beneficial uses of traceability data and the identifiers needed for such a system. These are beyond the scope of this policy paper, but national regulatory authorities are encouraged to seek them out when justifying the cost of a proposed regulation.

Consideration

National regulatory authorities should designate trained focal persons tasked with handling and responding to incidents of substandard and falsified medical products using the evidence coming from the traceability system. Such focal points should have the ability to report to the WHO Global Surveillance and Monitoring System as well as to participate in the WHO Member State mechanism. *(8)*

Developing a workable traceability regulation

Developing appropriate regulation for traceability should take into account the compatibility of the requirements (e.g. the standards and identifiers used and the corresponding information systems, such as databases, repositories etc.) with other pre-existing or upcoming requirements, standards, identifiers or regulatory information systems used for registration, reimbursement, pharmacovigilance or monitoring of substandard and falsified health products. Medical product traceability regulation should be as practical and workable as possible, for governments and supply chain stakeholders alike. Practicality will help maximize acceptance, which will lead to wider adoption and success in solving the targeted problems. A practical, workable regulation is one that:

- explains the reasons for which it is being enacted;
- clearly sets out the governance of the system, defining roles and responsibilities between authorities, supply chain stakeholders and third parties involved in the system;
- assigns data ownership to the entity that created it;
- has achievable deadlines;
- includes appropriate exemptions, exceptions and/or waivers for special circumstances;
- incorporates compliance and enforcement activities;
- maintains a balance between costs and benefits across the supply chain;
- establishes clearly defined requirements; and
- has requirements that are achievable using global standards.

There are various elements that Member States can consider when developing regulations, including the adoption of strategies that focus on:

Strategy 1
Risk–benefit analysis

Strategy 2
Governance and fundings

Strategy 3
Standards

Strategy 4
Current state analysis

Strategy 5
Draft regulatory requirements

Strategy 6
Piloting systems and processes

Strategy 7
Deadlines

Strategy 8
Exemptions, exceptions and waivers

Strategy 9
Enforcement planning

Strategy 10
Publication

Strategy 11
Communications planningg

STRATEGY 1

Risk–benefit analysis

An early step in the consideration of a traceability regulation could be a risk–benefit analysis. Besides system development and operational costs, Member States should establish the effect of potential traceability requirements on the cost of health products and the impact on accessibility of medicines to patients in low-income settings.

Consideration

Each element of a traceability requirement provides identifiable benefits and results in quantifiable costs for manufacturers, distributors, hospitals, pharmacies, clinics and governments. Before finalizing a regulation, attempt to estimate these costs and weigh them against the benefits expected. Consider how these costs will likely affect the cost of medicines throughout the population. A risk–benefit analysis may help to expose the most effective mix of requirements at the least cost.

STRATEGY 2

Governance and funding

How and who funds the different implementation stages of a traceability system and how its inception, development and functioning should be governed are important decisions that must be taken early.

- Some countries have opted for a "stakeholder model", which means that a large part of the infrastructure necessary for stakeholder compliance is paid for and operated by the stakeholders themselves (European Union). Other countries are also leaning in that direction (China, Ukraine).

Consideration

To gain a comprehensive overview of all the costs involved and their impact on the supply chain, Member States should consider the investment costs of developing a traceability system, the operational costs of running such a system (including costs for implementing the system, particularly in hospitals and hospital pharmacies), and the corresponding return on investment (e.g. increased supply chain efficiency for inventory management). The governance of traceability is similarly linked to those costs and their division between the different parties (governmental organizations, stakeholder organizations, third parties). Thus, when selecting the type of governance to be used, similar considerations should be taken into account. In all cases, including in terms of data capture and verification, regulators should clearly define and oversee the execution of the governance responsibilities of supply chain stakeholders involved in day-to-day operations at all levels.

Despite the lower costs borne by governments using this approach, Member States may have less control over the implementation and upholding of regulation, particularly when governance of the technology is delegated to stakeholders. To ensure the smooth day-to-day operation of the infrastructure, regulation must contain clear provisions enabling stakeholders to make certain decisions without the need for prior consent from the authorities.

- Stakeholder funding is not unique to a centralized traceability model. Distributed traceability models can also adopt a stakeholder funding approach. In this case, large investments by the government or by stakeholders are not necessary. Costs relating to implementation and compliance automatically fall to each supply chain participant. The costs borne by the government are limited to those necessary for enforcement. This model however requires the establishment of robust and clear governance from the outset.

- The most common alternative to the stakeholder funding model is a government model, typically associated with a centralized traceability model (Argentina, Egypt, India, Republic of Korea, Pakistan, Saudi Arabia, Turkey). This can be expensive for the government and may require new revenue sources to be found. This approach also necessitates authorities developing internally, or acquiring, the required technical expertise and capabilities at the government/authority level.

- Some countries fund the operation of their government-run centralized traceability system partly by requiring manufacturers to obtain a physical or digital asset from the government before the products are packaged and charging a fee, i.e. a cryptographic code based on the product unique identifier (Russian Federation), a hologram (Malaysia) or a unique identifier (Italy).

STRATEGY 3

Standards

Before publishing traceability regulation, governments should decide which global data and coding standards will be required. These include product, stakeholder, production and location identifier standards, coding standards for data carriers, such as barcodes and/or radio frequency identification tags[1] and data exchange, as necessary. WHO encourages the use of internationally recognized global standards – preferably a single "family" of supply chain standards[2] that work together as a whole to ensure logical consistency and interoperability, allowing data exchange between the different elements of the system – for example, the users' client systems such as enterprise resource planning systems and core systems such as the database(s) storing the data.

The technical standards for operating traceability systems may be complemented by data integrity standards as well as other standards appropriate for all sectors connected to the traceability system. These kinds of standards ensure data integrity by specifying the rules and requirements for data management (e.g. data access, data use) of the different elements of the system (i.e. the databases and repositories storing the data and their interface with users' client systems) among the multiple users holding different access rights.

In cases where regulation relies on a global standard, the published standard should not be modified or customized. Any change to a published standard undermines the robustness of the standard and the efforts to standardize the data or processes.

Consideration

By specifying the standards that must be adhered to in the published regulation, stakeholders can begin to formulate their compliance plans immediately. If it is not possible to specify the family of standards in the regulation itself, a document tied to the regulation should be published as soon as possible to provide the relevant guidance to the industry.

[1] Radio frequency identification tags are mentioned here because such technology is in use in two countries for medical product traceability, but it has been found to be problematic. Member States should make sure that they understand the issues before selecting it for inclusion in new regulation.

[2] Examples of "families" of supply chain standards include the GS1 and the Health Industry Business Communications Council (HIBCC) standards. For certain product classes, special standards may be more appropriate. For example, ICCBBA standards are not a true "family" of standards, but they are appropriate for human donor-based medical devices because they have the unique ability to keep track of the donor on a blinded basis.

STRATEGY 4

Current state analysis

Before drafting a medical product traceability regulation, it is important to study the operation of the existing supply chain. A current state analysis should then be performed. The evaluation should assess supply chain maturity, including the levels of local manufacturing and imports, national medicines lists or formularies, the national inventory management system, including potential interoperability issues between current systems, and future traceability systems. This analysis should reveal existing security elements, and most importantly, what is missing in the current supply chain regulations and systems, as well as what is necessary to raise the security of the supply chain to the desired level. For example, existing licensing/registration requirements for marketing authorization holders and importers may need to be enhanced to support a new traceability regulation. By identifying vulnerabilities early in the process, regulators are able to proactively coordinate and collaborate with those who are or should be equipped to take the necessary actions.

Consideration

Regulatory requirements can be itemized from the results of the current state analysis.

STRATEGY 5

Draft regulatory requirements

In order to minimize disruption to patient care, draft regulatory requirements should be carefully formulated to reflect the results of the current state analysis, the traceability model selected, the standards chosen, the deadlines set, and the overall design and operability of the traceability system. National regulatory authorities should assess their existing capabilities and sustainability to enforce the requirements imposed by their draft regulations with the planned funding. Some countries have published draft regulations for comment by stakeholders and the public before finalizing them (Brazil). Others have published final regulations without inviting public comment, only to have to withdraw or significantly change those regulations due to foreseeable complexities. This approach has the effect of penalizing early adopters who attempt to adhere to the original regulation and results in a loss of confidence among supply chain stakeholders.

In the scope of the draft regulations, products and transactions that are not covered by the regulation should be explicitly excluded to remove ambiguity, as is the case in the European Union with non-prescription medicines. All products within the scope of the regulation should be subject to the same traceability requirements to ensure harmonization with the standards and the system used.

The draft regulatory requirements should be written in a way that avoids the need for frequent or annual updates. Instead, national regulatory authorities should issue supplemental regulatory documents that contain pertinent guidance for the industry, thereby allowing for flexibility in terms of updating the information when needed.

Consideration

National regulatory authorities are highly encouraged to publish draft regulations and invite comment from stakeholders before finalizing them. It is best to consult with all major stakeholders before finalizing draft requirements to help with rationalization and eliminate unnecessary complexity. Stakeholders need to be confident that their development of systems and adoption of process changes will meet the requirements and that they can do so without penalty for early adoption. Ensuring workability and practicality for supply chain stakeholders will result in wider acceptance and greater adherence to the requirements moving forward.

STRATEGY

6

Piloting systems and processes

Conducting pilot(s) using the draft regulatory requirements can help to inform all stakeholders of the relevant regulatory provisions as well as detect where difficulties may arise during the final implementation stage. A pilot may consist of using a subset of products and a small number of participants throughout the supply chain. After completing the pilot(s), the draft regulatory requirements can be adjusted if the difficulties are related to unnecessarily complex or restrictive requirements, before moving to wider implementation. While pilots involve time and resources, the difficulties or issues that they highlight can provide invaluable information for regulatory authorities and supply chain stakeholders. The outcomes of a pilot can push regulators to establish more feasible requirements and encourage greater adoption by industry, resulting in a more successful implementation phase.

Consideration

Conducting pilot(s) before finalizing a traceability regulation has led to improved requirements in a number of Member States (Brazil, Russian Federation, United States of America). Pilots work well as one step in a phased implementation approach.

STRATEGY 7

Deadlines

Establishing deadlines in the regulation that are workable for supply chain stakeholders and enforcement agencies is very important. Setting tight deadlines for the industry or agencies to prepare often leads to fragmented adoption, loss of acceptance, loss of interoperability, confusion, frustration, and, inevitably, extensions to the deadline that are likely to have a lower success rate than if the original deadline had been set for those dates.

Compliance deadlines should be based on the publication of clear guidance with detailed explanations and the provision of the necessary training, where appropriate. Implementation should be phased in over time based on the risk of the products concerned. The implementation phase should factor in enough time for compliance at each stage.

When setting deadlines for new systems and processes to meet the current requirements, sufficient time should be allocated for the testing, verification and validation of the systems and interfaces involved with the different stakeholders within the supply chain.

Grandfathering provisions should be considered for manufactured products already stored in manufacturers' warehouses or in distribution in the supply chain on the effective date so as to minimize the impact on available supplies and the costs to industry for implementation changes.

Consideration

As a risk mitigation strategy, some countries have adopted a phased approach where multiple deadlines for various parts of the traceability requirements are spread across a period of time (United States of America). This approach enables stakeholders to spread the cost of necessary conversions to their technology and processes across multiple budget cycles while enjoying some of the benefits early and increasing the likelihood of acceptance and wider on-time adoption.

STRATEGY 8

Exemptions, exceptions and waivers

Member States should consider a pathway for exemptions, exceptions or waivers of certain requirements for products or scenarios that may not be suitable for the typical traceability model or may not need additional requirements due to existing supply chain provisions. For example, a number of existing pharmaceutical serialization and tracing regulations around the world exempt radiopharmaceuticals because they are already the subject of existing, and more rigorous, tracing regulations owing to their radioactivity (European Union, Russian Federation, United States of America). Other examples include: non-prescription (over-the-counter) medicines, contrast media, free samples to doctors, and new and not yet authorized medicinal products intended for use in clinical trials. A grandfathering provision is an example of an exception. Some countries include exceptions for packages that are too small to accommodate the required barcode and/or human readable text (European Union, United States of America). Some countries allow stakeholders to file special requests for a waiver of some parts of the requirements due to extenuating circumstances. Such requests must typically be reviewed and granted by the regulator before the supply chain entity receives the exemption, exception or waiver (United States of America).

Consideration

Exemptions, exceptions and waivers can help to increase acceptance and adoption because they demonstrate a recognition of the difficulties imposed by the regulation and the fact that those difficulties can be greater for products and stakeholders with certain uncommon characteristics. For example, exemptions or waivers for implementing partners should be considered if the organization can justify the exemption or waiver, namely by demonstrating that supply chain integrity is maintained through its own end-to-end supply chain operating in the country. In some circumstances – for example, natural disasters and humanitarian crisis – margins of flexibility within existing regulations should also be considered. Exemptions, exceptions and waivers should be communicated widely to avoid confusion and the appearance of non-compliance between supply chain participants.

STRATEGY 9

Enforcement planning

National regulatory authorities planning a new traceability regulation should incorporate compliance and enforcement activities (e.g. planning inspections of the traceability systems by regulatory inspectors or involving customs authorities in the enforcement of the regulation). As part of devising enforcement efforts, consider performing a cost-effectiveness evaluation, including an assessment of the national regulatory authority's capacity to respond to problems/violations detected through the traceability system. Proactive planning will rationalize the requirements and ensure that adequate capabilities and the resources needed are in place at a reasonable and predictable cost, including the use of regulatory or criminal law sanctions, if needed, for non-compliance of stakeholders (e.g. fines, withdrawal from circulation).

Consideration

Proactive compliance and enforcement planning is an essential step for regulators to identify additional requirements and costs and to ensure their preparedness to respond to potential risks in a transparent, consistent and proportionate way.

STRATEGY 10

Publication

When a draft or final traceability regulation or guidance document is enacted or published, it should ideally be published on the Internet on an official government website in a portable document format (PDF) that contains text rather than scanned images of the printed pages. This will allow the relevant stakeholders to find these documents and search and translate them quicker and with fewer errors, which will promote faster and wider adoption.

Consideration

When a new regulation or guidance document related to medical product traceability is published in a local language, consider also posting additional official translations to eliminate confusion and errors in interpretation which will ensure faster adoption for global stakeholders.

STRATEGY 11

Communications planning

Communications planning should cover the development of the draft regulation, the running of pilots, and the confirmation of the final regulation and its subsequent publication. Putting a communications plan in place will help to raise awareness of the process among stakeholders and the public and will ensure that they are able to provide valuable feedback at each stage. A good communications plan should include regular status updates, links to official documents and translations, announcements of exceptions, exemptions and waivers, and in-person or live web-based updates that offer question and answer sessions. These ensure that the solution (technical and business process) is designed to meet the aim of the regulation and there are no gaps due to misinterpretation.

Consideration

A good communications plan, developed as one of the first steps and adhered to throughout the development and deployment of a new traceability regulation, will help to promote better implementation, adoption and acceptance of the new process by stakeholders. Engaging the public through regular communications will also help to generate support and raise awareness of the purpose and operation of the system.

Implementation of tracebility

The world has never been better equipped to ensure the quality, safety and efficacy of medical products through to the "last mile" of the supply chain. Effective technologies, standards and tools to facilitate the traceability of medical products now exist with the potential for adoption in even resource-limited settings. With the potential to trace where a given product is at any given moment, regulators will assume the additional responsibility of being data stewards. While this policy paper outlines the main features of existing traceability systems and provides guidance on developing workable regulation, it does not presume to tackle all aspects of traceability in depth. It serves more as a starting point for Member States in their regulatory and implementation efforts.

Prior to implementation, Member States should consider best practices and lessons learned from other Member States. As part of a phased approach, establishing voluntary pilots to test draft regulations before finalizing them (Brazil, Egypt, India, Russian Federation, United States of America) can help to reveal unexpected complexities, missing requirements and unnecessary stages. Such incremental steps can ensure greater performance accountability moving forward but should be balanced with active monitoring and evaluation systems or frameworks. Taking stock on a real-time basis and taking timely corrective actions can maximize the benefits and minimize the risks of traceability, improving the chances for sustainability in the system over the long-term.

THE WORLD HAS NEVER BEEN BETTER EQUIPPED TO ENSURE THE QUALITY, SAFETY AND EFFICACY OF MEDICAL PRODUCTS THROUGH TO THE "LAST MILE" OF THE SUPPLY CHAIN.

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Annex 1
Traceability systems for medical devices, including in vitro diagnostic medical devices

Note: Medical devices are not specifically covered in this policy paper, but this annex is included to provide information on traceability of medical devices.

Background

The traceability system proposed for medical devices, including in vitro diagnostic medical devices (IVDs), builds on the Unique Device Identifier (UDI)[1] system for medical devices promulgated by International Medical Device Regulators Forum (IMDRF). The IMDRF[2] is a voluntary group of medical device regulators who have come together to accelerate international medical device regulatory harmonization and convergence. Current Members are: Australia, Brazil, Canada, China, Europe, Japan, Russian Federation, Singapore, Republic of Korea, and the United States of America with WHO as an official observer.

The UDI is a series of numeric or alphanumeric characters that is created through a globally accepted device identification and coding standard. It allows the unambiguous identification of a specific medical device on the market.

The UDI is composed of two parts: Device Identifier (UDI-DI) + Production Identifier (UDI-PI):

- UDI-DI identifies a manufacturer's specific product and package configuration. Examples of the UDI-DI include GS1 GTIN (Global Trade Item Number), HIBC-UPN (Universal Product Number), or ICCBBA ISBT 128-PPIC (Processor Product Identification Code).
- UDI-PI identifies the unit of device production when one or more of the following is included on the package label of the device: lot number, serial number, expiry date, date of manufacture, version number, etc.

"Globally accepted ISO/IEC coding standards implemented by global organizations, such as GS1, HIBCC and ICCBBA, meet the criteria of the UDI and manufacturers shall be permitted to choose which system to use. These organizations have responsibility for maintaining the global uniqueness of their coding systems."[1]

[1] Unique Device Identification system (UDI system) Application Guide IMDRF/UDI WG(PD1)/N48

[2] IMDRF website http://www.imdrf.org/

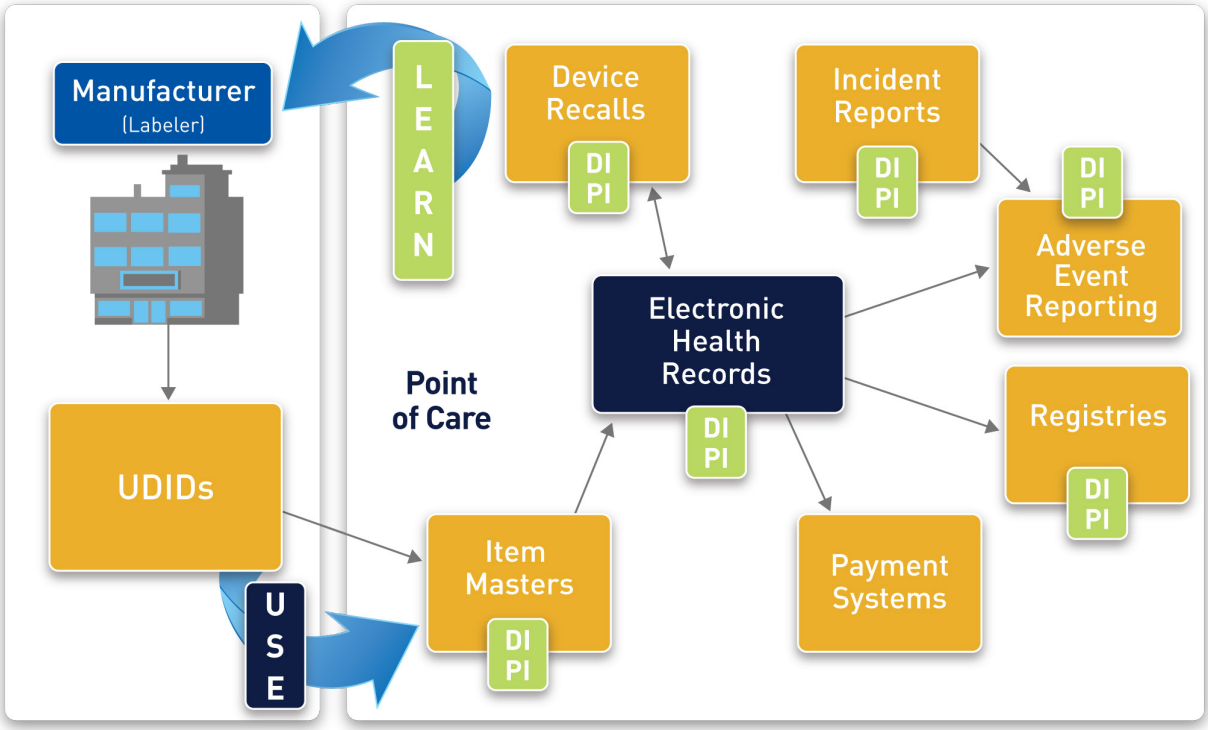
The UDI Carrier shall be on the label or on the device itself and on all higher levels of device packaging. Higher levels do not include shipping containers. The UDI and UDI carrier are fundamental parts of UDI system requirements and should be based on global standards[1]. Manufacturers are responsible for creating and maintaining globally unique UDIs for their medical devices. Distributors, importers, healthcare providers and users significantly contribute to enhance the potential of the UDI as a key standard to facilitate adequate medical device identification through distribution and use on patients.

How would UDI be used?

A global UDI system is intended to provide a single, globally-accepted system for identification of medical devices, but also serves for post-market surveillance, vigilance, market surveillance, reimbursement, inventory management as shown in Fig. A1.1

Fig. A1.1

Different uses for UDI throughout the life cycle of a medical device
(adapted from IMDRF/UDI WG/N54 FINAL:2019)



Supply chain

The greatest challenge for the supply chain of medical devices is to deliver a valued product that relates not only to the design, safety and quality of the product but to all the health care environment where it is implemented and used. Many countries are reliant on importation, hence the efficient regulatory systems and the modernization of supply chains are key components to reduce cost and environmental impact, as well as increase safety and quality customer service. The main drivers are the high prices of medical devices that foster third party manufacturers to produce products at lower costs and then

[1] Unique Device Identification system (UDI system) Application Guide IMDRF/UDI WG(PD1)/N48

sell them through online auctions; the long and complex supply chains with poor traceability; and the increasing accessibility to technology that can be used to manufacture devices and print labels and even certification markings.

Implementing traceability of medical devices requires upfront investment that is compensated by improving efficiency in the whole value chain, it helps in the inventory management and incites the application of automation for refurbishment and reverse logistics, together with enhancement of the post-market surveillance. Medical devices are returned and exchanged due to five main reasons: product replacement (based on patient needs changing), manufacturer recalls, faulty devices, product maintenance or obsolescence. However, the complexity to the supply chain means that product is not just pushed out but also must handle small and frequent shipments, tracking returns and processing exchanges.

Regulation

Marketing authorization (pre-market assessment for sale and use)

Use of UDI Data Elements across different "IMDRF Jurisdictions", also to provide a useful tool to worldwide operators when confronting with UDI compliance in several jurisdictions. The IMDRF table of contents allows for the harmonized standards for submission of regulated products for regulatory assessment.

Post-market surveillance (feedback, notification of incidents)

- Manufacturers of medical devices and their economic operators should implement an effective system for post-market surveillance (user feedback, field safety corrective actions, and post-market performance follow-up) with active and passive collection of post-market information. The UDI will allow manufacturers to have more control over their product once is enters the supply chain.

- National regulatory authorities conduct market surveillance through ensuring healthcare professionals notify complaints for medical devices circulating within their jurisdiction to the manufacturer or their economic operators and by ensuring capacity for testing of IVDs by competent and proficient testing laboratories. The UDI will act as an important reference for regulators to be aware of products that may require field safety corrective actions.

UDI and WHO prequalification

WHO prequalification of IVDs is a comprehensive assessment of individual branded products through a standardized procedure aimed at determining whether the product meets WHO prequalification requirements for quality, safety and performance. In dossier assessment, is an element of the product dossier/table of contents (linking submitted information to a specific product); in quality management system is used for identification of lot numbers; and in post-prequalification activities is used in the tracking changes to a product, and in linking complaints or adverse events to a product and identification of affected lot numbers.

Annex 2
Global Standards Organizations

GS1

GS1 is a global, neutral, non-profit standards organization that introduced the barcode in 1974, providing a common language to the industry. Supply chain family of standards, including identification, data capture and sharing. GS1 standards commonly used in healthcare supply chains include:

- Global Trade Item Number (GTIN)
- Global Location Number (GLN)
- Serial Shipping Container Code (SSCC)
- DataMatrix barcode
- Application Identifiers (AI)
- Electronic Product Code Information Services (EPCIS)
- Core Business Vocabulary (CBV)

WEBSITE https://www.gs1.org/industries/healthcare
EMAIL ulrike.kreysa@gs1.org

HIBCC

Health Industry Business Communications Council (HIBCC). Non-profit standards development organization. Supply chain family of standards aimed at health products. HIBCC standards commonly used in medical device supply chains include:

- Labeler Identification Code (LIC)
- Health Industry Number (HIN)
- Health Industry Bar Code (HIBC)

WEBSITE https://www.hibcc.org/
EMAIL info@hibcc.org

HL7

Health Level Seven International (HL7). Not-for-profit, ANSI-accredited standards developing organization dedicated to providing a comprehensive framework and related standards for the exchange, integration, sharing, and retrieval of electronic health information that supports clinical practice and the management, delivery and evaluation of health services. HL7 standards commonly used in healthcare supply chains include:

- V2 Messaging Standard (V2)
- Clinical Document Architecture (CDA)
- HL7 Fast Healthcare Interoperability Resources (FHIR)

WEBSITE http://www.hl7.org/index.cfm
EMAIL hq@HL7.org

ICCBBA

International Council for Commonality in Blood Banking Automation (ICCBBA). Non-profit international standards organization. ICCBBA standards commonly used in healthcare supply chains include:

- ISBT 128 Standard

WEBSITE https://www.isbt128.org/
EMAIL iccbba@iccbba.org

ISO

International Organization for Standardization (ISO). An independent, non-governmental international organization with a membership of 164 national standards bodies. ISO standards underpin many of the standards offered by the other standards organizations listed here and elsewhere, including IT, communications, barcode, security and quality standards.

WEBSITE https://www.iso.org/home.html
EMAIL central@iso.org

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https://www.who.int/health-topics/substandard-and-falsified-medical-products#tab=tab_1

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