Policy brief on traceability of health products

Key points

With this policy brief, the World Health Organization (WHO) aims to outline the features of existing traceability systems and provide guidance on developing workable traceability regulation. Careful consideration should be given to Member States' (MS) unique needs, capacity and resources, with risk mitigation and sustainability strategies embedded in implementation efforts.

For this purpose, MS are encouraged to

- Establish a suitable governance for their traceability system based on the analysis of their national environment (e.g. regulatory environment, supply chain management), after evaluating how the different options for this **governance** will impact interoperability, cost, security and regulatory control;
- Integrate in their plan for a traceability system a costing of the system and a sustainability mechanism to prevent **costs** from negatively impacting patients, government, supply chain stakeholders, and ultimately access to medicines; and
- Use **global standards** for product identification, production identification, automatic identification and data capture (AIDC)[1] and data exchange to reduce creation and operating system costs and maximize interoperability.

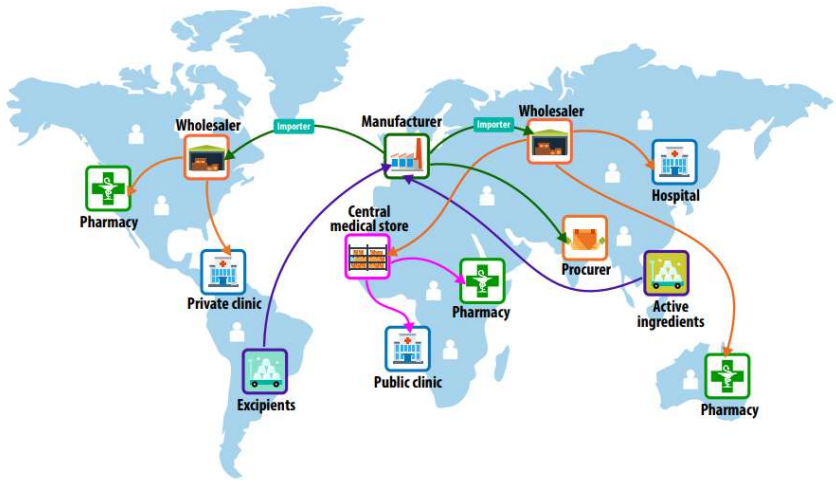
Introduction

What is the issue

Given the growth and globalization of trade, health products[2] are manufactured and distributed in complex supply chains. As illustrated in Figure 1, products pass through many entities in their journey to the patient, often being manufactured in one country and distributed across borders to be marketed or sold in other countries. As distribution spreads geographically and the supply chain becomes more fragmented oversight capacity of national regulatory authorities become stretched.[1] Effective oversight of the supply chain is thus weakened, raising the risk of substandard and falsified (SF) medical products and leading to inefficiencies such as stockouts or expired products (ref). These can lead to loss of public confidence, which eventually leads to hesitancy, reduced adherence and reduced utilization of health programmes (ref). There is a need to addresses these vulnerabilities and strengthen supply chain integrity and efficiency, with patient safety at the forefront.

[1] AIDC refers to technology used to automate the reading of product identification, such as barcodes, Radio Frequency Identification (RFID) tags and their reading devices.
[2] For the initial version of this document, "health products" include finished medicines, including vaccines and pharmaceuticals.

Figure 1: An example of a medicine's journey[3]



Traceability technologies, as described in this document, offer the technical possibility to track or trace health products along the supply chain – from their point of manufacture to the point of dispensing or the ultimate place where the medicine is administered to a patient – with a view to strengthen the real-time monitoring of the integrity of a given pack. There is global recognition that traceability systems could be leveraged as a useful tool to ensure the integrity and improve the efficiency of supply chains.

In recent years, MS have called on WHO to facilitate the exchange of experiences, lessons learnt and information about traceability technologies and methodologies and models.[4] The WHO Member State Mechanism on SF medical products has prioritized work around this issue and have published technical documents that strengthen the understanding of the current landscape including the experiences in countries,[5] but a global framework or guidelines have yet to be developed. There is also limited peer-reviewed published evidence on the implementation of traceability systems available to support policy development.

This policy brief was therefore designed to guide National Regulatory Authorities (NRAs) on the use of existing standards, to equip them with how-to guidance on where to start, and to provide guidance on the governance of the systems to be established in terms of data (use and ownership).

Methodology

A working group of MS that are members of the WHO Member State Mechanism, with balanced and diverse regional representation from MS that have and have not implemented traceability, was convened to draft a policy brief primarily "by regulators for regulators."

[3] WHO Global surveillance and monitoring system for substandard and falsified medical products, Geneva: World Health Organization;2017. Licence: CC BY-NC-SA 3.0 IGO.

[4] Workplan of the Member State Mechanism on substandard and falsified medical products (A67/29) (links and access date to be added)

[5] Existing technologies and "Track and Trace" models in use and to be developed by Member States (A69/41) (links and access date to be added)

The following MS were members of the working group:

AFRO	EURO	EMRO	PAHO	SEARO	WPRO
- Benin - Ethiopia - Kenya - Liberia - Mozambique - Nigeria - United Republic of Tanzania	- Russia - Spain - Ukraine	- Iraq	- Argentina - Brazil - Chile - Mexico - United States of America	- India - Indonesia	- Republic of Korea

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

A review of numerous national and international implementation efforts and technical resource documents was conducted. It relies also on a case study approach whereby the actual Member State implementers have systematically shared their views through surveys, discussions and interviews. In an effort not to duplicate efforts and ensure coordination, the drafting 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 brief will cover the following product streams: finished medicines, including vaccines and pharmaceuticals. The following product streams will be excluded from the scope: Active Pharmaceutical Ingredients (APIs), medical devices, blood and blood products (except plasma derived medicinal products, PDMPs, which are medicines), organs, tissues and cells (except those registered as medicines), traditional medicines and food supplements. This policy brief is not automatically and entirely applicable to medical devices as there are wide differences between the regulatory and supply chain environments of the two product streams. However, a situation analysis is provided in Appendix 1 and future iteration of this policy brief may include the traceability for medical devices.

With respect to the level at which this policy brief is applicable, this document responds to questions of national or regional implementation (when several MS in one region decide collectively to develop an integrated traceability system within their respective region). For the aspects of interoperability between several national or regional systems and in an effort not to duplicate efforts, WHO encourages MS to use the upcoming guidance developed by ICMRA on interoperability to be published in 2020.

This policy brief covers the supply chain and its legitimate and registered or licensed stakeholders, from manufacturers of finished products (batch release) until the point of dispense of the health product (e.g. a pharmacy) or its point of use (e.g. a hospital pharmacy). Movements of health products beyond these boundaries are out of scope of this document, thus excluding traceability of APIs used to manufacture finished products. However, some authorities may consider using traceability features to enable patients to verify health products after dispensing (e.g. in Nigeria, Kenya).

With respect to its level of depth, this policy brief aims at advising MS on policy and regulatory approaches, particularly regarding the governance of traceability systems and their data management. Once MS have set up the appropriate policies and regulatory environment for traceability, separate guidance and support will be needed to strengthen regulatory capacities to ensure seamless integration and suitable enforcement of its implementation measures. Country level implementation will require MS and other supply chain stakeholders to reference other guidance, particularly on the multiple data standards that exist for the traceability of medicines.

This document does not intend to provide an analysis or identify a preference among the data standards that are available. The examples provided by MS participating in the drafting group are based on 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 association registered in Belgium, and as such is considered to be a branded name. It was unintentional that all of the examples were based on this particular standard, but not unexpected. While it is broadly understood that the GS1 standard is the most commonly used for medicines, including use by numerous UN agencies, it should be noted that WHO as a practice does not endorse brands. In this case, the focus of the document is on the benefits and scenarios that impact implementation of the standards chosen by MS, and the value of standardization across systems.

With respect to the use of traceability systems, the scope of the document focuses on supply chain integrity and efficiency. Pharmacovigilance and product reimbursement aspects have been discussed between MS of the drafting, but not to an extent allowing to draft specific recommendations in these areas. Regarding pharmacovigilance, MS should be aware of the global discussions on the use of the Identification of Medicinal Products (IDMP) ISO standards for a global framework for the identification of medicines for pharmacovigilance purposes.

Intellectual property issues are also out of scope for this policy brief. However, should a traceability system be used for purposes such as product reimbursement or trade (e.g. at 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.

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 time. Real-time information and (data access and data ownership permitting) visibility of products can expedite regulatory responses to **safeguard patients and the supply chain**, including, but not limited to, the following scenarios:

1) ensuring only registered/approved products circulate in the legal supply chain;
2) preventing the distribution and/or dispensation of expired, prohibited or recalled products;
3) facilitating efficient and fast market recalls;
4) enabling efficient supplies management at all levels; and
5) minimizing and monitoring the reasons of shortages and stock outs.

The challenges posed by the complex manufacture and trade are likely to grow, and current estimates show that one in ten medical products are SF in low- and middle-income countries.[6] Strong regulatory oversight can help mitigate supply chain vulnerabilities and risks, and facilitate increased **prevention, detection and response to SF medical products**. Traceability systems can help prevent entry of SF medical products into regulated supply chains, detect any SF medical products that are circulating in-country, and assist regulators to respond quickly and proportionately to any incidents that are detected.

Potential risks

Inception and deployment of traceability requires **significant investment and high costs** that can disproportionately burden low and middle-income MS. 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 would extend to 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 health products.

Some MS have issued traceability regulations that are currently implemented or on the way to being implemented; whereas, others are assessing various implementation alternatives or otherwise have not approached the topic.[3] Without coordination and guidance, there may be **variability in the requirements and standards used**. New and existing traceability initiatives should consider harmonization of standards to ensure undisrupted systems continuity and sustainability. Deployment of technologies are an inherent part of traceability, but it there is **limited technological capacity** at ports of entry, distribution centers, and pharmacies, particularly in remote areas – where internet connectivity, cellular data service, etc. is weak – there may be gaps in the information collected and delays in the exchange of information." Sustainability concerns also go hand in hand with **lack of clear and workable regulation**. As a mitigation measure, MS should set phased and long-term transition and continuity plans, including risk management, coupled with realistic timeframes.

Strong collaboration and dialogue is needed with key stakeholders. 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 on identity and real-time location of products at item level. As such, ensuring data integrity as part of enforcement plans is of utmost importance to ensure to meet the security expectations of stakeholders.

Various features of traceability systems, including governance

Outlined below are the seven common features of traceability systems that have been implemented by MS, with information on relative cost and other 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, resources and local context of

[6] A study on the public health and socioeconomic impact of substandard and falsified medical products. Geneva: World Health Organization;2017. Licence: CC BY-NC-SA 3.0 IGO.

the implementing Member State. MS are encouraged to assess the potential feasibility, implementation and sustainability opportunities and risks of each of the features.

Feature 1: Identification (Product, Production, Location)

To successfully trace products through a supply chain, it is necessary to identify the following four key elements in a standardized way: 1) Products; 2) Stakeholders; 3) Subsets of Products based on manufacturing/production; and 4) Locations.

- This should start with the master data unambiguously identifying **products**, distinguished between them for their name, active ingredient, strength, pharmaceutical form, packaging, and often their pre-established market destination. Medicines need to be identified at the saleable package level (sometimes referred to as the lowest level of packaging for sale to a pharmacy or patient).
- The quantity of units of **manufacturing/production** uniquely identified will inversely determine the granularity of the tracking and tracing possible.
- **Locations** and **Stakeholders** must be identifiable so that product movements between owners and/or sites can be documented in the traceability system.

Consideration: Batch-level identification is suitable for implementing workable product recall and pharmacovigilance systems, but unit-level serialization would likely be more suitable for other purposes, including investigations of substandard and falsified product incidents and cargo theft and diversion.

Feature 2: Use of Global Standards

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

- robust design – Fewer surprise limitations when regulations change in the future;
- third party support available globally to all stakeholders;
- wide familiarity and acceptance by health product manufacturers, exporters and logistics companies globally;
- large set of application choices, with future expandability built-in;
- more opportunity for the interoperable exchange of pharmacovigilance data with many countries around the world that use the same set of standards;
- widely available off-the-shelf technology hardware and software designed to work with them.

These benefits result in lower startup and operational costs and smoother operation for governments and supply chain stakeholders throughout the lifecycle of individual health products.[7] For example, commonly used standards are referenced below:

- For pharmaceuticals, GS1 standards are currently the only international family of standards in wide use globally.

[7] Ref: GS1 "Cost Savings Through Standards", McKinsey & Company, "Strengthening health care's supply chain: A five-step plan", McKinsey & Company, "Strength in unity: The promise of global standards in health care", McKinsey & Company, "Building new strengths in the health-care supply chain"

- The ISBT 128 standard from ICCBBA is widely used to identify medical products of human origin (including blood, cell, tissue, milk, and organ products).

Consideration: Standardized identification across the supply chain is vital to the success of traceability regulation. MS are encouraged to make use of international standards for product, stakeholder, production and location identification for health products, as well as for any mandated AIDC elements such as barcodes and/or Radio Frequency Identification (RFID).

Feature 3: Batch-level traceability

A limited form of traceability can be accomplished using only product codes and batch numbers, but the efficiency and accuracy of information capture is low. At most, a regulatory system can keep track of which batch numbers have been where, which may be sufficient for recall execution and some vigilance programs.

Consideration: Although limited in information capture, some countries have used batch-based tracing of medicines in a phased approach as a first step toward their ultimate goal of unit-level tracing in an effort to spread the costs over multiple budget cycles (see below the section "Feature 4").

Feature 4: Unit-level Serialization

Unit-level tracing requires unit-level serialization – the placing of a unique serial number on every saleable unit of a class of health products. Serialization and tracing at the saleable unit level is considerably more complex and therefore necessarily involves challenges that are well beyond lot-based traceability. Consequently, packaging costs are considerably higher for manufacturers under a serialization mandate. These costs include new equipment, new business processes, slower line speeds, more re-work and more rejects. Costs are also higher for downstream trading partners in the supply chain when required to incorporate operational changes, such as reading (for every single pack in a Track and Trace model) and taking actions mandated by regulation on the unit-level serial numbers (i.e., initiate investigations on suspect SF product reports, report activity to a government portal, verify authenticity, etc.).

AIDC coding and data standards should be specified to ensure interoperability and to remove ambiguity of unit-level serialization and/or other levels of packaging.

The unique serial number allows verification of the pack. However, this verification has reduced value if it is not paired with a tamper proof seal ensuring that the verification of the identifier on the pack refers to the content of the pack.

Figure 2: Example from Egypt

For example, for the Egyptian market, each unit-level package must encode a GS1 Global Trade Item Number (GTIN), a serial number unique to that GTIN, the lot/batch number and the expiration date, all encoded using GS1 standards into a GS1 Datamatrix 2D barcode. Each of those elements are specified clearly in the implementation guideline published by the Egyptian Ministry of Health and Population (ref: Egypt pharma serialization implementation guideline).

Consideration: Traceability regulations should clearly specify the levels of identification required, i.e. down to until 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 another one for a tamper proof seal in order for the verification of the pack identifier to be valid for the content i.e. the actual medicine.

Figure 3: Preventing falsification

Traceability regulations should integrate measures to help prevent falsification (copying) of the unique serial numbers. These may include randomization (EU), external documentation proving authentication (USA), verification (Turkey) and crypto-codes (Russia). It should be noted that these are not fool-proof methods but can be useful tools for preventive efforts.

Feature 5: Aggregation Data

Whenever multiple levels of packaging are serialized, aggregation data may be valuable for accurate, efficient tracing. Aggregation data is data that documents the parent-child relationships between serialized containers (the "parents") and the serialized units inside the containers (the "children"). Aggregation data must be captured at the time the serialized child packages are inserted into the serialized parent packages/containers. This data is very 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. This need 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.

Some countries mandate the collection and use of aggregation data (Brazil, Pakistan, Russia). Others mandate actions by members of the supply chain that can only be accomplished efficiently when aggregation data is captured by the manufacturer or repackager, but do not mention it as an explicit requirement (EU, USA).

Consideration: It is suggested to balance the cost impact of aggregation with the 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 get changed) and the actual expected improved knowledge of the supply chain events before mandating such a requirement.

Feature 6: Verification

Verification is a technique that allows stakeholders, patients and/or enforcement agencies to check the authenticity and authorization of products within the supply chain or in the hands of patients. Each Traceability model offers one or more ways to implement verification of the product identifiers and/or production identifiers (unit-level serial numbers).

- In the Centralized model, where all traceability data is stored in a single database or repository, verification can be performed by members of the supply chain, healthcare professionals and/or patients communicating with the central repository to verify the identifiers.

- In the Semi-Centralized model, where traceability data is 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 their own traceability data, verification can be performed by communicating with the original manufacturer. Because of the frequency of verification in most implementations, these communications should be standardized web-based messages between systems.

Consideration: Regardless of the model chosen, 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, it checks the authenticity of the unique identifiers on the packaging.

Feature 7: Full Track and Trace (T&T) vs. Point of Dispense (PoD) Verification

Two approaches exist in pharmaceutical traceability implementations today.

- The full T&T approach is that some form of traceability documentation or verification must be performed at each change of ownership or custody in the supply chain. The goal is to detect the introduction of falsified medicines into the supply chain as early as possible so they can be detected and responded to quickly.
- The PoD Verification approach is that medicines are verified only at the point of dispense (e.g. a pharmacy) or use/administration (e.g. a hospital), or at some point prior to that moment. It can also be used during the reimbursement process to help reduce fraud. The goal of PoD Verification is to protect patients from harm without imposing costs all along the supply chain.

Figure 4: Differences in implementation

Countries that have enacted regulations using the full T&T approach include Argentina, Republic of Korea, Russian Federation, Turkey, and the United States of America. The market that has enacted a regulation using the PoD Authentication approach is the European Union.

Consideration: Regulators can specify clearly in their Traceability regulation the frequency of verification, in particular with respect to PoD vs full T&T, based on the maturity of the local supply chain and the capability of the stakeholders to efficiently fulfill verification requirements.

Feature 8: Patient Verification

Where supply chains are complex but funding is minimal to non-existent, patient verification can provide a last resort ability for patients to perform 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.

Consideration: Regulators are cautioned that patient verification efforts should be balanced with strong monitoring and enforcement measures. Rogue actors have been known to replicate regulatory services that responds to all verification requests with a positive result. For example in Uganda, although falsifiers had included a greyed-out area on the fake packaging that imitated a scratch-off authentication device, it was not actually scratchable[1]. In any case, no access should be given to patients to the system itself to preserve its integrity and the patients should be educated not to believe that such a feature is a definitive and absolute protection against SF products.

Feature 9: Detection and Response, including Reporting

Active surveillance and monitoring should be established to ensure the appropriate regulatory responses take place once substandard and falsified medical products are detected or there are authentication or verification failures. All SC stakeholders should clearly understand the system and process to report to the National Medicines Regulatory Authority and the actions to be taken, including quarantining the suspected product, storing it in appropriate conditions, etc. Once substandard and falsified medical products are confirmed, the NRA should respond accordingly to protect public health, including 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.

Consideration: NRAs should have trained focal persons with the core regulatory responsibility to handle these incidents using evidence coming from the traceability system and to respond to incidents of substandard and falsified medical products, including the ability to report to the WHO Global Surveillance and Monitoring System as well as participation in the WHO Member State Mechanism[1].

Developing a workable traceability regulation

Developing an appropriate regulation for traceability will enable the compatibility of the requirements (e.g. the standards and identifiers used and information systems, i.e. databases, repositories) with other pre-existing or upcoming requirements, standards, identifiers or regulatory information systems used for registration, reimbursement, pharmacovigilance or monitoring SF medical products. Health product traceability regulation should be as practical and as workable 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 the governance of the system, defining roles and responsibilities between authorities, supply chain stakeholders and third parties involved in the system
- has achievable deadlines;
- includes some exemptions, exceptions and/or waivers for special circumstances;
- incorporate compliance and enforcement activities;

- has clearly defined requirements; and
- has requirements that are achievable using international standards.

The following summarizes various implementation strategies that MS can take into account when developing regulation, with considerations to take into account.

Strategy 1: Governance & Funding

How and who funds different parts of the implementation of a Traceability system and how its inception, development and functioning is governed are important, early decisions.

- Some countries have imposed a "**stakeholder model**", which means that a large part of the infrastructure necessary for stakeholders to comply is paid for and operated by those stakeholders (ref: EU). Others are leaning in that direction (ref: China, Ukraine). Despite the lower costs borne by governments, MS may have less control over the implementation and operation of regulation. To help ensure smooth day-to-day operation of the infrastructure, this needs to be clearly specified in the governance so that stakeholders can make certain decisions without the need for a prior consent from the authorities.
- The most common alternative to the stakeholder funding model is a **government model**, typically associated with a centralized traceability model (ref: Turkey, Argentina, Republic of Korea, Egypt, Saudi Arabia, India, and Pakistan). This can be expensive for the government and may require new revenue sources. This also requires authorities to develop internally or to acquire the needed technical expertise and the capabilities at governmental/authority level.
- Countries that have adopted a **distributed traceability model** do not require a large investment by the government or by a group of stakeholders (ref: USA). Costs for implementation and compliance automatically fall on each supply chain participant. The costs borne by the government can be limited to those necessary for enforcement. This model makes the need for setting up a robust and clear governance even more pressing.
- One MS is funding the operation of their government-run centralized traceability system by requiring manufacturers to obtain a cryptographic code based on the product unique identifier from the government before the products are packaged and charging a fee for each crypto-code issued (ref: Russian Federation).

Consideration: To establish a comprehensive overview of all costs and their impact on the supply chain, MS should consider investment costs to develop a traceability system, operational costs for running such systems, and return on investments (e.g. increased supply chain efficiency for stock management). The governance of traceability will be linked with the costs and with their division between the different parties (governmental organizations, stakeholder organizations, third parties), therefore the choice of the governance should also be made with similar considerations. In all cases and with data capture and verification, regulators should clarify and oversee the execution of governance responsibilities at all levels of supply chain stakeholders involved in the day-to-day operations.

Strategy 2: Standards:

Before publication of a traceability regulation, governments should decide which data and coding standards will be required. These include product, stakeholder, production and location identifier standards, coding standards for barcodes and/or RFID and data storage, access and exchange, as necessary. WHO encourages the use of international standards--preferably a single "family" of supply chain standards that work together as a whole to ensure logical consistency and interoperability, allowing data exchange between the different elements of the system, e.g. the users' client systems such as Enterprise Resource Planning (ERP) systems and core systems, such as the database(s) storing the data. Examples of "families" of supply chain standards include GS1 and HIBCC. For certain special 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.

The technical standards for operating traceability systems need to be completed by data integrity standards, such as Good Automated Manufacturing Practice (GAMP) and Good Distribution Practice (GDP). This kind of standard ensures data integrity by specifying rules and requirements for data management (e.g. data access, data use, etc.) between the multiple users with different access rights of the different elements of the system, i.e. the databases and repositories storing the data and their interface with users' client systems.

Consideration: By specifying the standards that must be used to meet the regulation in the published rule itself, stakeholders can begin making their compliance plans immediately. If it is not possible to include the specification of the family of standards in the regulation itself, then it is suggested to publish a guidance document tied to the regulation as soon as possible.

Strategy 3: Gap Analysis

Before creating a health product traceability regulation, it is important to study the operation of the existing supply chain, make the decisions listed above, then perform a gap analysis. The evaluation should assess the level of supply chain maturity, including potential impact on local manufacturing and national medicines lists or formularies, and review the supply management system, including potential interoperability issues between current systems and the future traceability systems. This analysis is intended to expose existing security elements, and most importantly, what is missing in the current supply chain regulations and systems and what is necessary to elevate the security of the supply chain to the desired level. For example, existing licensing/registration requirements for marketing authorization holders (MAHs) and importers will need to be enhanced to support a new traceability regulation. By identifying vulnerabilities early on in the process, regulators are able to proactively coordinate and collaborate with those who are or should be equipped to take necessary actions.

Consideration: Regulatory requirements can be itemized from the results of the gap analysis.

Strategy 4: Draft Regulatory Requirements

The draft regulatory requirements you create should be based on the gap analysis, model, the standards you wish to enable the deadlines and many other elements of the Traceability system. NRAs should assess their existing capabilities and sustainability to enforce the requirements imposed by their draft regulations with the expected funding. Some countries have published draft regulations for comment by stakeholders and the public before finalizing them (ref: China, India). Some have followed up their publication of "final" regulations with changes in response to criticisms from stakeholders and others.

Consideration: NRAs are highly encouraged to publish the draft regulation and to collect comments from stakeholders before finalizing it. Ensuring workability and practicality for supply chain stakeholders will enable wider acceptability and greater adherence to requirements moving forward.

Strategy 5: Deadlines

Establishing deadlines to include in your regulation that are workable for stakeholders in your supply chain and enforcement agencies is very important. Setting deadlines that are too soon for the industry or agencies to properly prepare often leads to fragmented adoption, loss of acceptance, loss of interoperability, confusion, frustration, and, inevitably, extensions to the deadline that now become less likely to be successful than if the original deadline were set for that later date.

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 (ref: USA). This approach can allow stakeholders to spread the cost of necessary conversions to their technology and processes across multiple budget cycles, increasing the likelihood of acceptance and wider on-time adoption.

Strategy 6: Exemptions, exceptions and waivers

Not every health product is suitable for the typical traceability regulation and so exemptions, exceptions and waivers are likely to be necessary. For example, a number of existing pharma serialization and tracing regulations around the world exempt radiopharmaceuticals because they are already the subject of existing, and more rigorous tracing regulations due to their radioactivity (ref: Russia, EU, USA). Some countries include exceptions for packages that are too small to accommodate the required barcode and human readable text (ref: EU, USA). Some countries allow stakeholders to file special requests for a waiver of some part the requirements due to extenuating circumstances. The requests typically must be reviewed and granted by the regulator before the supply chain entity receives the exemption, exception or waiver from those requirements. (ref: USA).

Consideration: Exemptions, exceptions and waivers can help elevate acceptance and adoption because it demonstrates a recognition of the difficulties imposed by the regulation and that those difficulties are greater for products with certain uncommon characteristics. In exceptional circumstances (e.g. natural disasters), margins of flexibility within existing regulations should also be considered.

Strategy 7: Enforcement plan

NRAs 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 this regulation). As part of developing an enforcement plan, consider performing a cost-effectiveness evaluation, including an assessment of the NRA capacity to respond to problems/violations detected through the traceability system. Proactive planning will rationalize the requirements and ensure adequate capabilities and 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 ensure preparedness to respond to potential risks in a transparent, consistent and proportionate way.

Strategy 8: Publication

When a draft or final traceability regulation or guidance document is enacted or published, it is encouraged to publish it 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 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 health 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.

Implementation of traceability

The world has never been more equipped to ensuring the quality, safety and efficacy of health products through to the “last mile” of the supply chain. Effective technologies, standards and tools to facilitate the traceability of health products now exist with the potential for adoption in even resource limited settings. With the potential to trace where a given product is at a given time, regulators will assume the additional responsibility of being data stewards. Whilst this policy brief aims to outline the features of existing traceability features and providing guidance on developing workable regulation, this remains only a starting point for MS.

Prior to implementation, MS 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 (ref: Brazil, Egypt, India, Russia, USA) can help expose unexpected complexities, missing requirements and unnecessary steps. Such incremental steps can ensure greater performance accountability moving forward but should be balanced with active monitoring and evaluation systems or frameworks. Taking real-time pulses and timely corrective actions can maximize the benefits and minimize the risks of traceability, improving the chances for sustainability in the long-term.

Appendix 1. Traceability systems for medical devices, including in vitro diagnostic medical devices

Background

The traceability system proposed for medical devices, including in vitro diagnostic medical devices (IVDs), builds on the Unique Device Identifier (UDI)[8] system for medical devices promulgated by International Medical Device Regulators Forum (IMDRF). The IMDRF[9] 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.

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[10]. 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.

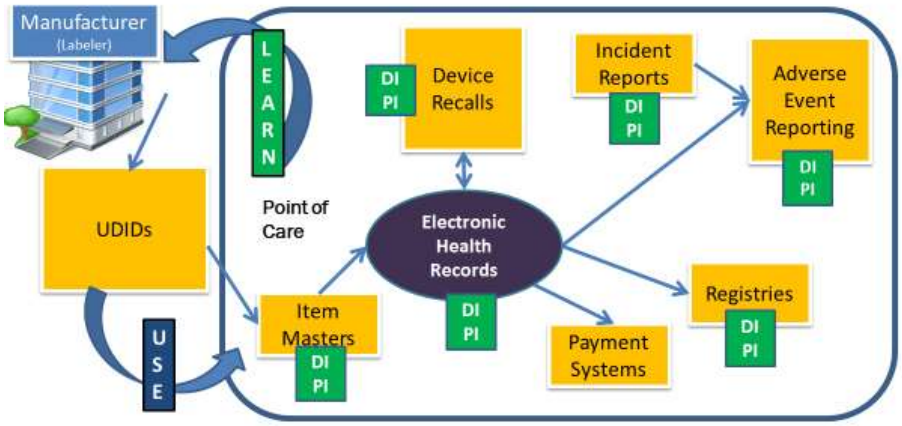
"*Globally accepted ISO/IEC coding standards implemented by global organizations, such as GS1, HIBCC and ICCBBA, meet the criteria of the UDI and manufacturers shall be permitted to choose which system to use. These organizations have responsibility for maintaining the global uniqueness of their coding systems.*"[11]

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, reimbursement, inventory management as shown in Fig. A1.1

[8] Unique Device Identification system (UDI system) Application Guide IMDRF/UDI WG(PD1)/N48
[9] IMDRF website http://www.imdrf.org/
[10] Unique Device Identification system (UDI system) Application Guide IMDRF/UDI WG(PD1)/N48
[11] Unique Device Identification system (UDI system) Application Guide IMDRF/UDI WG(PD1)/N48

Figure A1.1 – Different uses for UDI throughout the life cycle of a medical device. (Ref)



- 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 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 I 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 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 (complaint handling, vigilance of adverse events)
        - Manufacturers of medical devices and their economic operators should implement an effective system for post-market surveillance (complaint handling, field safety corrective actions, and post-market performance

follow-up) with active and passive collection of post-market information. The UDID will allow manufacturers to have more control over their product once is enters the supply chain.

- National regulatory authorities conduct market surveillance through ensuring end-users 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 UDID 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 IVDs 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.

Appendix 2. Traceability Models

TBC: Existing Technologies and Traceability Models In Use and To Be Developed by MS

Explanation of many aspects of medical product traceability aimed at national and/or regional regulatory authorities to consider when developing a regulation.

Appendix 3. Global Standards Organizations

TBC: Insert contact information (website and email) for each:

- GS1
- HIBCC
- ICCBBA
- HL7
- ISO

Appendix 4. Links to existing medical product traceability regulations

TBC: Existing Regulations (pharma/vaccine T&T, UDI, etc)

- Argentina
- Australia (UDI)
- Brazil
- China
- Columbia (UDI)
- Egypt
- European Union
- India
- Republic of Korea
- Pakistan
- Russian Federation
- Saudi Arabia
- Turkey
- United States of America