IMPLEMENTING INDIA'S DRUG SERIALIZATION AND TRACEABILITY REQUIREMENTS TO ADVANCE PATIENT SAFETY AND SUPPORT GLOBAL TRADE

MAY 2017

PRINCIPLES

Principle 1: Regulators should solicit stakeholder input early in the regulatory process (i.e., before the laws and regulations are developed) and throughout its implementation. Stakeholder input, both in policy formulation and in the subsequent adaptation after implementation, is critical to success. *(Page 5)*

Principle 2: A phased implementation schedule supports successful implementation of new regulatory requirements. *(Page 6)*

Principle 3: All regulatory requirements and systems should promote compliance and information integrity. *(Page 7)*

Principle 4: Technology solutions should be designed to meet regulatory requirements. Technology solutions should not dictate the requirements. *(Page 8)*

Principle 5: GS1 global standards and other global standards for barcoding are beneficial and achieve the intended effect only if they are implemented fully and without variation. *(Page 8)*

RECOMMENDATIONS

Recommendation 1: CDSCO and DGFT should delegate an independent body to undertake (i) an economic impact assessment for domestic serialization and traceability requirements under consideration, and (ii) a regulatory impact assessment of existing requirements for serialization and traceability of exports. *(Page 5)*

Recommendation 2: With regard to product exported to a country that has its own serialization requirements, the "tertiary package" should be considered the highest level of shipping container for export. For example, the pallet will typically be the tertiary package for exports to the United States or the European Union. The homogenous case would be the tertiary package for markets where the case is the highest level of container exported. All levels of packaging below the tertiary package (as defined here) should then be exempt from unique identifier and labeling requirements under the India serialization and traceability regulations. *(Page 10)*

Recommendation 3: DGFT should grant exemptions on a country-by-country basis, not a manufacturer-by-manufacturer or product-by-product basis. *(Page 10)*

Recommendation 4: Regulators should not define the GTIN indicator digit; it should be set by the manufacturer, as provided in the GS1 GTIN General Specifications. *(Page 11)*

Recommendation 5: NIC should revise the DAVA database and portal to:
- Segregate the portal interface for exports and domestic product.
- Eliminate the primary package serial number field, or at a minimum, permit the field to be left blank.
- Eliminate the pricing information field, or at a minimum, permit the field to be left blank.
- Eliminate the requirement to upload product photos.
- Permit a single manufacturer to repeat serial numbers for different GTINs.
- Provide the option and interface for automatic upload of data via web service.
- Prevent a company's data from being visible to other companies.

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Recommendation 6: NIC should maintain development and simulation environments to support revisions to the DAVA portal. *(Page 14)*

Recommendation 7: NIC should establish a clear, predictable process for communicating revisions to the DAVA portal. *(Page 14)*

Recommendation 8: In the initial phase of requirements for domestic product, CDSCO should require serialization of the saleable unit. *(Page 15)*

Recommendation 9: CDSCO should not require manufacturers to capture, maintain, or report any information related to the movement of products by downstream trading partners. *(Page 15)*

Recommendation 10: CDSCO should adopt a four-year, phased implementation timeframe for domestic requirements. *(Page 16)*

Recommendation 11: CDSCO and DGFT should consider alternative approaches that limit data volumes. *(Page 18)*

Recommendation 12: There should be a process for accrediting, certifying, or otherwise auditing serialization vendors. *(Page 19)*

India has emerged as a leader in the global pharmaceutical market. According to the India Brand Equity Foundation (IBEF), the Indian pharmaceutical market is the third largest in the world by volume and 14th largest by value (approximately 1.95 trillion INR, or 30 billion USD).[1] Dramatic growth is anticipated. The value of the Indian pharmaceutical market is expected to reach 3.6 trillion INR (55 billion USD) by 2020.[2] Foreign direct investment of nearly 916 billion INR (14 billion USD) since 2010 has helped stimulate this growth.[3] Today, pharmaceuticals manufactured in India account for approximately 10 percent of the world's pharmaceutical volume and are exported to more than 200 countries.[4]

A continued role as a leader in the global pharmaceutical market represents enormous value and opportunity for India. However, that role also carries tremendous responsibility to collaborate with global stakeholders to help ensure the security of the global pharmaceutical supply chain. Additionally, the adoption and implementation of global data standards and harmonized regulatory systems are critical to continued growth of the Indian market and the ability of Indian companies to expand trade networks.

India has taken important initial steps to do its part in helping to ensure the security of the global pharmaceutical supply chain. Its leadership in developing and implementing pharmaceutical serialization and traceability processes should be applauded. The benefits of India's efforts will be realized by all global pharmaceutical stakeholders, including most importantly, patients around the world.

Every new regulatory system encounters the need for adjustments, reforms, and modifications throughout the implementation process. As stakeholders—both public and private sector—implement new regulations, technical challenges and unforeseen issues arise. Regulators must recognize these challenges and have the flexibility to adjust requirements to achieve full, successful implementation. This reality is especially true with regard to pharmaceutical serialization and traceability due to its technical nature, its impact on international trade, and the dramatic increase in related regulatory requirements adopted by other countries over the past 5 years.

Implementation of India's serialization and traceability requirements for exported pharmaceuticals has sufficiently progressed to uncover technical challenges and unforeseen issues that require regulatory action to assure successful implementation and yield expected benefits. Industry's experience implementing the export requirements has also provided valuable insights that should be incorporated into the requirements currently under development for India's domestic market. A meeting, the *Stakeholder Consultation on Drug Serialization and Traceability in India* hosted by the Indian Council for

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[1] India Department of Pharmaceuticals, *Indian Pharmaceutical Industry—A Global Industry*, *available at:* http://pharmaceuticals.gov.in/pharma-industry-promotion.

[2] Indian Brand Equity Foundation, *India Pharmaceutical Industry*, updated March 2017, *available at*: http://www.ibef.org/industry/pharmaceutical-india.aspx.

[3] India Department of Pharmaceuticals, *Indian Pharmaceutical Industry—A Global Industry*.

[4] Indian Brand Equity Foundation, *India Pharmaceutical Industry.*

Research on International Economic Relations (ICRIER) and RxGPS[5], held on 3 March, 2017 in New Delhi commenced discussion of these issues.

The *Stakeholder Consultation* was attended by more than 60 representatives of the Indian and global pharmaceutical markets (including the Indian Drug Manufacturers' Association (IDMA)), patient and public health advocates (including the Partnership for Safe Medicines India and the World Health Organization), global regulatory authorities (including the U.S. Food and Drug Administration and the U.S. Department of Commerce), and Indian regulators (including the Central Drugs Standard Control Organization (CDSCO), the National Pharmaceutical Pricing Authority (NPPA), and Pharmexcil). A full list of participants is included in Attachment A.

During that meeting, the Indian regulators welcomed the preparing of a document to capture industry input for their consideration and potential future action. This white paper captures the dialogue and conclusions of the *Stakeholder Consultation* and sets forth a roadmap for strengthening the Indian pharmaceutical serialization and traceability system. Ultimately, the recommendations of this white paper will aid India in achieving its dual goal of remaining a leader in the global pharmaceutical market and advancing supply chain security for the benefit and protection of patients.

BACKGROUND

Serialization is the process by which products are marked with a standards-based unique identifier— typically a unique number or alphanumeric code—and is the enabling technology for systems and processes to enhance supply chain security. The unique serial number is typically encoded in a two-dimensional barcode that can be read electronically. Serialization of pharmaceuticals (*i.e.*, applying the unique identifier to medication packaging) itself provides virtually no benefit to the supply chain. Rather, it is the use of that serialized data in a manner to efficiently realize the goals of the system that enhances supply chain security. This complementary use of the serialized data is commonly referred to as "traceability" or "track-and-trace."[6] India has made great strides toward improved supply chain security through serialization requirements and the creation of a traceability system.

Serialization is one of many tools necessary to ensure quality, authentic products are delivered to patients. It does not, however, address all issues related to pharmaceutical quality and safety. In addition, when serialization information is not properly used or protected, that information can be used improperly to give substandard and falsified medicines the appearance of legitimacy, creating the exact security threats

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[5] RxGPS is a group of multinational pharmaceutical supply chain stakeholders who have a common interest in developing consensus strategies, policy principles, and policy recommendations that advance global alignment of drug serialization and tracing requirements in order to enhance patient safety, supply chain security, and drug availability around the world. Learn more at www.RxGPSalliance.org.

[6] For more information on serialization and traceability, including the distinction between tracking and tracing, see Attachment E. A glossary of relevant terminology is also included in Attachment C. In this paper, we do not generally distinguish between verification, authentication, tracing, and tracking, except where we specifically comparing those individual processes. Instead, for simplicity, we use "traceability" as a general term to describe the use of serialization data for any of those processes.

that traceability systems are intended to prevent. Breach of the pharmaceutical supply chain can have serious public health consequences from product shortages to medical complications, and in severe cases, even death.

India has established regulatory requirements for the serialization and traceability of pharmaceutical products intended for export from India. Draft requirements for serialization and traceability of product in the domestic Indian market have also been proposed, but have not been finalized.

EXPORT REQUIREMENTS

On January, 10 2011, the Directorate General of Foreign Trade (DGFT), announced the adoption and implementation of a track and trace system incorporating serialization for all pharmaceutical products exported from India. The stated purpose of the requirement is to "address counterfeit and ineffective product recall challenges, which effects the entire healthcare supply chain, from manufacturers all the way to patients, wholesalers, distributors, exporters and healthcare providers."[7]

Specifically, exported drug products must carry a one or two-dimensional barcode encoding a universal global product identification code in the form of a 14-digit Global Trade Item Number (GTIN),[8] along with the product's batch number, expiration date, and unique serial number. For all products manufactured on or after April 1, 2016, non-small scale industry (non-SSI) manufacturers must serialize the secondary and tertiary package. SSI manufacturers must serialize all product packages at the secondary and tertiary level on or after April 1, 2017. Serialization of the primary package is optional for exported products. Manufacturers must aggregate[9] lower-level packaging to higher-level packaging and upload this "parent-child" information to the Drugs Authentication and Verification Application (DAVA) database—a central, country-wide database for storage of serialization data developed and managed by the National Informatics Center (NIC).

An exception provides that serialization requirements for the primary and secondary packaging levels are not applicable to drugs exported to a country where the government of the importing country has mandated or formally notified its intention to mandate its own serialization requirements. Manufacturers must obtain written approval from the Indian government to avail themselves of this exemption. Regardless of exemption, all products must be serialized at the tertiary-package level using Indian standards, and tertiary-level data must be reported to the DAVA database. As a result, product subject to

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[7] Implementation Guidelines for Coding & Labelling Pharmaceuticals and Drugs Using Global Supply Chain Standards to Meet Directorate General of Foreign Trade's (DGFT) Authentication, Track and Trace Requirements, Version 1.3, at 5 (Aug. 2015).

[8] This is a recognized GS1 standard.

[9] Aggregation associates a set of "contained" or "child" objects (*e.g.*, cases) within a "containing" or "parent" entity (*e.g.*, pallet). The parent identifier identifies the aggregation and the "children" contained within the parent entity.

an exemption will carry a foreign identifier/serial number on the secondary package[10], and an Indian identifier/serial number on the tertiary package.

Ultimately, the purpose of the requirements is to allow serialized packaging to be verified or traced through the supply chain. When a barcode is scanned, the information encoded can be cross-checked with the DAVA database of known serial numbers. It is expected that the DAVA database will also be used for domestic product once requirements for such product are finalized.

DRAFT DOMESTIC REQUIREMENTS

On June 3, 2015, The Department of Health and Family Welfare issued a proposed amendment to the Drugs and Cosmetics Rules, 1945, to facilitate development of a system to "authenticate the genuineness of drugs."[11] The proposed rule amendment would require manufacturers to serialize each packaging level as follows:

- Primary Package: 2D barcode encoded with GTIN, batch, expiry date, and serial number.
- Secondary Package: 1D or 2D barcode with GTIN, batch, expiry date, and serial number.
- Tertiary Package: 1D barcode with GTIN, batch, expiry date, and serial number.

Manufacturers would also be required to maintain parent-child (*i.e.*, aggregation) data and information about the movement of their products through the supply chain. This data would be uploaded to the portal of Central Government before release of the drugs for sale or distribution. Responsibility for the correctness, completeness, and timeliness of data reported to the central portal would be assigned to the manufacturer.

GOOD REGULATORY PRACTICES

Serialization and traceability are advanced regulatory requirements to secure the pharmaceutical supply chain. A traceability system requires (i) an understanding of all products distributed through the supply chain, (ii) an understanding of all parties that participate in supply chain, and (iii) a mechanism for identifying and ensuring the good standing of all parties that participate in the supply chain (*e.g.*, through licensure or registration). Therefore, serialization and traceability necessarily builds upon other regulatory systems.

Serialization and traceability is a significant undertaking for regulators and industry. Implementation of the equipment and software necessary to generate, affix, and capture data related to the unique identifier can cost manufacturers millions of dollars, requires the reconfiguration (and thus suspension of

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[10] No country currently requires serialization of the primary package, except when the primary package is also the unit intended by the manufacturer for sale.

[11] Notification, Ministry of Health and Family Welfare, Department of Health and Family Welfare, New Delhi, June 3, 2015.

operations during that reconfiguration) of packaging lines, and takes months to install and validate.[12] Similarly, to achieve full traceability, downstream trading partners, such as wholesalers and pharmacies, must change their systems and processes for receiving, shipping, and dispensing product in order to capture information about each serialized package. Full traceability also requires serialized packages to be aggregated to cases, bundles, pallets, and other logistical units.[13] Finally, under the Indian requirements, regulators must bear the burden of developing and maintaining a constantly growing data repository of information about product movements (the DAVA database) and establish the systems and processes necessary to monitor and enforce compliance. All of this comes at a significant cost, which is ultimately passed on to patients and other purchasers. For this reason, regulators and industry typically aspire to implement serialization and traceability requirements in the most efficient manner possible and actually achieve their intended objectives.

> *Principle 1: Regulators should solicit stakeholder input early in the regulatory process (i.e., before the laws and regulations are developed) and throughout its implementation. Stakeholder input, both in policy formulation and in the subsequent adaptation after implementation, is critical to success.*
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> *Recommendation 1:* CDSCO and DGFT should delegate an independent body to undertake (i) an economic impact assessment for domestic serialization and traceability requirements under consideration, and (ii) a regulatory impact assessment of existing requirements for serialization and traceability of exports.

During the *Stakeholder Consultation*, regulators identified two shortcomings in development of the regulatory requirements for serialization and traceability of exported drug and the opportunity to improve upon those lessons in development of the domestic requirements. First, the importance of stakeholder input early in the regulatory process was emphasized to ensure the requirements can be implemented by industry in an efficient, effective manner that is consistent with their existing systems and processes. Serialization and traceability are complex requirements that must be built upon multiple systems and processes already used by manufacturers and other supply chain companies. The technical details of implementation require a deep understanding of those existing systems and processes, which can only be provided by those industry members. Successful and efficient implementation requires this input from impacted stakeholders early in the process when requirements are first being formulated and also through public comment on draft requirements. The *Stakeholder Consultation* was an important first step in collecting feedback. However, continued feedback from all impacted stakeholders, ideally through a multi-site progress monitoring program, will be critical to success.

Second, it was emphasized that an understanding of the full economic and regulatory impact of the requirements for serialization and traceability is important. Serialization can be leveraged in multiple different ways to advance supply chain security and achieve other objectives. For example, serialization

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[12] *See* Attachment B for more detail on a manufacturer's process for implementing serialization capabilities.

[13] Aggregation requires additional equipment, software, and processes and adds significant complexity, including greater challenges in ensure the accuracy of the data being relied upon.

can be used to verify the authenticity of a drug before it is dispensed to the patient. This approach, adopted in the European Union and often called "end-point authentication", provides patient safety with less burden on the supply chain and requires significantly less data to be collected and maintained. Traceability, which is proposed in the draft requirements for domestic products, provides some added benefit beyond authentication but imposes regulatory requirements on all members of the supply chain and requires the collection and maintenance of significantly more data. An economic impact assessment for domestic requirements under consideration will help regulators understand the full impact—both costs and benefits—of alternative approaches to serialization and supply chain security so a model that appropriately limits costs while also protecting patients can be implemented. A regulatory impact assessment for the serialization and traceability requirements currently in effect for exports will also help to understand the impact of those requirements.

> **Principle 2:** *A phased implementation schedule supports successful implementation of new regulatory requirements.*

As discussed above, successful implementation of any new regulatory system requires continuous feedback, evaluation, and adjustment. As the details are implemented, new and unforeseen issues are certain to arise. Throughout the implementation process, it should be verified that the systems are proceeding as anticipated and are actually capable of achieving intended objectives. The gradual or phased implementation of new regulatory requirements allows such feedback, evaluation, and adjustment. If phased correctly, this approach also allows industry and regulators to spread out costs and to control the costs of implementation by preventing investment in systems that ultimately have to be replaced.

A phased approach is especially important for implementation of serialization and traceability. First, as mentioned above, the process of generating and affixing the unique identifier is a complex, time-consuming, and expensive process. Additionally, a traceability system—by design—requires that each successive trading partner's data and systems build upon the prior trading partner's data and systems. Several countries, including China[14] and Brazil[15], have attempted to implement complete traceability in one phase, and as a result, both have experienced a slower, more resource-intensive implementation process. Both countries have been forced to shut down their initial systems and begin anew to address challenges from implementation of those initial systems. Other markets, such as the European Union,[16]

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[14] China Food and Drug Administration, *Circular on Issues Relating to Comprehensive Implementation of Electronic Supervision and Administration for Drug Production and Distribution Enterprises* (No. 1, 2015), January 4, 2015.

[15] Law No. 11,903, *Provides for tracking of the production and consumption of drugs through the capture, storage, and electronic data transmission technology*, January 14, 2009.

[16] Development of the European requirements has been a collaborative process over a period of more than 10 years.

the United States,[17] and Saudi Arabia[18] have provided long implementation periods that allow challenges to be addressed and learnings to be incorporated as the system is developed and implemented. The United States' requirements, in particular, are designed both to implement early protections while also allowing each sector of industry (first manufacturers, then wholesalers, then dispensers) to implement and learn before the next sector builds upon their experience and systems.[19]

> **Principle 3:** *All regulatory requirements and systems should promote compliance and information integrity.*

All regulatory structures, including serialization and traceability, should be built upon a sound regulatory foundation that demands and promotes compliance and the integrity of the systems used to implement the regulatory requirements. As discussed in more detail later in this paper, industry has been advised to generate "fictitious", "dummy", "virtual", or "fake" data for certain data elements built into the DAVA database. This notion entirely contradicts basic principles of good regulatory practices, where documentation is essential to tracking activity and the results of that activity. Current Good Manufacturing Practices require, as a core element, documenting the activity that takes place. Complete, consistent and accurate data supports regulator review, investigation of product quality issues, and continuous quality improvement. Requiring regulated industry to submit intentionally fake data creates, at a minimum, cognitive dissonance: on the one hand, maintenance of so-called "ALCOA" (attributable, legible, contemporaneous, original and accurate) data is required throughout the regulatory process. On the other hand, industry is directed to create, and submit to a regulatory agency, fake data which has none of those attributes. Furthermore, fake data presents an opportunity for fraud, deception, and illegal practices which undermines the entire system. For example, fake serial numbers uploaded to the DAVA database are a ripe opportunity for a counterfeiter. If a counterfeiter acquires those serial numbers and uses them to label counterfeit product, those counterfeit products would be verified by the DAVA database as being *legitimate*—allowing exploitation of the very system developed to curtail these types of activities.

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[17] The requirements in the United States are implemented over a ten-year period. The requirements are phased in by complexity (*e.g.*, tracing by lot first, then later by individual package) and by sector (manufacturers first, then wholesalers, then pharmacies).

[18] Saudi Arabia started with a requirement to encode the GTIN, expiry and batch number in a 2D GS1 DataMatrix, and later required the addition of a serial number.

[19] The United States' Drug Supply Chain Security Act (DSCSA), multiple requirement work in tandem to secure the supply over a ten-year period. Currently, supply chain trading partners are required to trace product at the batch level. In November 2017, manufacturers must serialize all product at the saleable-unit level. That serialization information is gradually used over the next 6 years for verification activities. In 2023, trading partners will begin to be required to exchange serialization information in an interoperable electronic manner, which is expected to necessitate aggregation.

> **Principle 4:** *Technology solutions should be designed to meet regulatory requirements. Technology solutions should not dictate the requirements.*

As discussed in more detail below, a number of operational challenges have arisen as a result of the way the DAVA portal and database were developed and structured. In many instances, the structure of the portal and database are forcing industry members to act in a manner that is not consistent with the regulatory requirements. Technology solutions should not dictate regulatory requirements or implementation. Technology solutions should instead be designed to meet relevant regulatory and business requirements. The data integrity issue identified above, for example, is a result only of the structure of the DAVA database. It is not a specific regulatory requirement, but has become a "requirement of regulators" because of the DAVA database construct.

IMPORTANCE OF GLOBAL STANDARDS

Global standards are critical to the development of regulatory systems that support and advance global trade. This is especially true with regard to serialization and traceability because it is based entirely upon the generation and exchange of data among multiple parties with regard to product handled by multiple entities, often across multiple countries. Global standards are designed to be flexible enough that they can be leveraged to implement serialization and traceability systems tailored to a given country, but they provide the globally harmonized foundation and structure necessary for product identification and the exchange of data. Effective implementation of traceability would be virtually impossible without the use of standards. As India has recognized, the GS1 global standards are broadly recognized as the preferred standard for pharmaceutical serialization and the exchange of serialization data.

An important benefit of global standards is that those standards can speed and ease implementation of serialization and traceability. Global standards promote efficiencies that reduce costs and simplify system development and compliance projects. This resulting efficiency and costs savings facilitates implementation and speeds up patient access to safe and secure product.

> **Principle 5:** *GS1 global standards and other global standards for barcoding are beneficial and achieve the intended effect only if they are implemented fully and without variation.*

Global standards facilitate international commerce through interoperability and promote competition and expansion. The use of country-specific standards—*including country-specific variations to global standards*—is a barrier to global trade. Standards create a common language among different systems which enables those systems to communicate in a common and understandable format. Global standards remove the disincentive associated with exporting to or from markets that would require conversion to country-specific systems, language, or formats. However, this efficiency is generated only if global standards are implemented completely and without any country-specific variation. Such variations undermine the very purpose and benefit of global standards.

DEVELOPING A SYSTEM THAT USES GLOBAL STANDARDS, ADVANCES GOOD REGULATORY PRACTICES, AND FACILITATES GLOBAL TRADE

To maintain its position as a leader in the global pharmaceutical market, it is critical that India's serialization and traceability requirements follow good regulatory practice and adopt global standards. This will facilitate global trade and effective implementation to ensure patients receive the desired benefit of a more secure supply chain.

PACKAGING LEVELS AND DEFINITIONS

The Indian regulations for exports define three packaging levels for serialization: primary package (the serialization of which is optional), secondary package, and tertiary package.[20] In many other countries, barcoding requirements are based on the discrete packaging levels driven by trade, including the saleable unit (*i.e.*, the smallest unit of trade intended by the manufacturer for sale to a dispenser) and homogenous case. In the United States, the saleable unit may be a primary package or a secondary package. In the European Union, the saleable unit is always the secondary package. Other countries have still different trade practices. As a result, a single packaging level is often understood and regulated differently in different countries.

The confusion related to packaging level terminology is especially challenging for product exported from India to a country that has its own serialization requirements. When granted, the Indian exemption that may be requested for exports to such a country provides some relief, but confusion remains with regard to what Indian requirements call "tertiary" packaging, which is not covered by such exemption. GS1 defines a tertiary package as the logistical unit that is shipped, the shipper, carton, case, pallet, or tote that contains one or more primary/secondary levels of packaging. This means different or multiple levels of packaging can be "tertiary" packaging. This has created significant confusion, and as a result, package labeling for product leaving India as "tertiary" packaging varies widely. In some instances, product exported from India to the United States has carried two different GTINs. In other instances, the same GTIN (which is intended to be specific to a single packaging level) is affixed to multiple packaging levels.

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[20]The *primary package* is the level of packing that is in direct contact with the product (e.g., blister card or vial). The *secondary package* is a level of packaging that may contain one or more primary packages, or a group of primary packages containing a single item. The *tertiary package* is the logistical unit that is shipped, the shipper, carton, case, pallet, or tote that contains one or more primary/secondary levels of packaging.

The primary, secondary, and tertiary package terminology is distinct from the terminology commonly used to refer to trade items. Units of trade are typically referred to as saleable units, cases (homogenous or mixed), bundles, pallets, etc. These two sets of terms do not always align in the same manner. The salable unit, for example, is the smallest container of package intended by the manufacturer to be sold to a pharmacy. In practice, the saleable unit could be a pill bottle (which is a primary package), a carton containing a blister strip (which is a secondary package), or even a ten-pack of individual vials that could be dispensed to a patient. The salable unit is based on the manufacturer's intent. Similarly, multiple levels of trade items (*e.g.*, case, bundle, pallet) could be the tertiary package at various times during the distribution process, but only one trade item should be considered tertiary at a given point in time.

The terms primary package, secondary package, tertiary package, and saleable unit are used in this manner throughout this paper.

The GTIN is the backbone of pharmaceutical trade, so these types of discrepancies can actually stop the movement of product and, in some instances, cause the return of the product. This is a significant barrier to trade and adds unnecessary cost to distribution. For products stocked in low volumes, this barrier to commerce can even prevent patients from receiving their needed medications entirely. Fortunately, India's exemption process provides an opportunity to address this confusion.

> *Recommendation 2: With regard to product exported to a country that has its own serialization requirements, the "tertiary package" should be considered the highest level of shipping container for export. For example, the pallet will typically be the tertiary package for exports to the United States or the European Union. The homogenous case would be the tertiary package for markets where the case is the highest level of container exported. All levels of packaging below the tertiary package (as defined here) should then be exempt from unique identifier and labeling requirements under the India serialization and traceability regulations.*

The goals and objectives of India's export requirement are met with this approach: the shipping container processed at customs is labeled with a unique identifier and is able to be verified to the DAVA database. This allows Indian customs to verify the authenticity of its exports. Defining the tertiary package as the highest level of shipping container for export and requiring a unique identifier (serialized GTIN or SSCC) to be affixed to that container enables this capability. Furthermore, this capability does <u>not</u> require that a unique identifier be affixed to any package level smaller than the highest-level shipping container. Instead, those smaller levels should be serialized and labeled according to the importing country's requirements. This also means that aggregation of smaller units to the highest-level shipping container is not necessary, which will reduce complexity and costs.[21] The exemption provision in the Indian regulation permits this structure, but (i) this definition of "tertiary package" needs to be communicated clearly and broadly, and (ii) the process for obtaining an exemption needs to be clarified.

> *Recommendation 3: DGFT should grant exemptions on a country-by-country basis, not a manufacturer-by-manufacturer or product-by-product basis.*

Products are not required to comply with the serialization requirement if intended for export to a country that has "mandated or formally notified its intention to mandate a specific requirement and the exporter intends to avail the option of printing the barcodes in their format."[22] At least 19 countries[23] and the European Union meet these criteria. Despite potentially broad applicability, the usefulness of the

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[21] The DAVA portal is currently set up for exporters to upload batch details (including the serial number information) and shipper and pallet detail (including SSCC number and number of packs) even without aggregation, which should be sufficient for tracing. Furthermore, if the importing country mandates for a specific requirement for aggregation then this will likely conflict with the DGFT/DAVA mandate for master data and it will be very difficult to modify.

[22] Para 2.89A(v) of the Handbook of Procedure, as revised by Public Notice 52/2015-2020.

[23] Argentina, Albania, Brazil, China, EU, Iran, Jordan, Nigeria, Saudi Arabia, Serbia, South Korea, Turkey, and the United States have mandated barcoding. In addition, the United Arab Emirates, Oman, Taiwan, Pakistan, Egypt, and Russia have stated an intent to implement serialization requirements.

exemption has been limited because each manufacturer must apply for its own exemption for its own products. As explained above, these exemptions are critical to the effective functioning of the export requirements and ensuring the continued distribution of Indian products.

If an importing country has mandated serialization, that will be equally true for any manufacturer exporting to that country. The current process only slows and complicates the issuance of the important exemption established by law. It is unclear why, as is currently required, each manufacturer must apply for an exemption for each of its products. The DGFT (or Pharmexcil, to the extent this authority has been delegated) should instead publish and maintain a list of countries that have mandated or formally notified its intention to mandate barcoding requirements. All exports, by any manufacturer, to those countries should then automatically be able to rely on the exemption from all requirements except barcoding for the tertiary package (as defined above). In addition to simplifying and speeding the exemption process, a country-by-country exemption applicable to all companies would significantly reduce DGFT's workload of processing many applications from many manufacturers for the same exemption.

FULL IMPLEMENTATION OF GS1 STANDARDS

As explained above, country-specific standards and country-specific variations to global standards impede global trade and add significant, unnecessary complexity to the serialization and traceability system. This challenge is proving true with regard to the India requirements for structuring the GTIN used in the unique identifier.

> **Recommendation 4:** *Regulators should not define the GTIN indicator digit; it should be set by the manufacturer, as provided in the GS1 GTIN General Specifications.*

The first digit of any GTIN is commonly referred to as the "indicator digit." According to the GS1 General Specifications, the GTIN indicator digits "have no meaning. The digits do not have to be used in sequential order, and some may not be used at all".[24] The standard provides that the value to be used for the indicator digit should be determined by the manufacturer, which is true of all aspects of GTIN allocation. Manufacturers around the world have developed their systems in accordance with the GS1 global standard and its guidance related to indicator digits.

Implementation guidelines from DGFT[25] and guidance posted on DAVA portal, however, contradict this use of the standard by requiring that specific digits must be used for the indicator digit.[26] Implementation of the specified indicator digits creates significant technology challenges for industry and adds unnecessary cost and complexity to the system. This is especially true for exported product because

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[24] Specifications v15, pg. 46 (Section 2.1.2.6.2. Trade Item Groupings of Identical Trade Items).

[25] *Implementation Guideline for Coding and Labelling Pharmaceuticals and Drugs Using Global Supply Chain Standards to Meet Directorate General of Foreign Trade's (DGFT) Authentication, Track and Trace Requirements*, Section 1.1.2.

[26] Notification, GS1 India, *Steps to be taken to comply with DGFT's Track & Trace Requirements*; Presentation, GS1 India, DAVA Portal Workshop, December 2015.

systems in the importing country have already been developed to use GTINs that are allocated according to the global standard (*i.e.*, with the indicator digit set by the manufacturer). In practical terms, systems have been established in numerous markets around the world based on a global GTIN that is structured according to the global standard, but the Indian requirement would force use of a different GTIN. For example, markets may be set up and already processing a given product with an assigned GTIN that starts with the digit "7", but according to the Indian requirements that product would be required to have a GTIN that starts with the digit "3." The result is conflicting GTINs for the same product, which is exactly contrary to the purpose and value of global standards.

Each manufacturer should be permitted to assign indicator digits at its own discretion, consistent with GS1 global standards. If it is necessary to the levels of packaging for a single product, DGFT could achieve that by allowing manufacturers to assign their own indicator digits and register the product master data in DAVA.

DAVA

As mentioned above, the DAVA database structure is driving regulatory requirements and implementation specifications. The DAVA database and portal should instead be structured to implement the regulatory requirements in a manner that is consistent with global standards.

> ***Recommendation 5:*** *NIC should revise the DAVA database and portal to:*
> - *Segregate the portal interface for exports and domestic product.*
> - *Eliminate the primary package serial number field, or at a minimum, permit the field to be left blank.*
> - *Eliminate the pricing information field, or at a minimum, permit the field to be left blank.*
> - *Eliminate the requirement to upload product photos.*
> - *Permit a single manufacturer to repeat serial numbers for different GTINs.*
> - *Provide the option and interface for automatic upload of data via web service.*
> - *Prevent a company's data from being visible to other companies.*

Six specific changes to the DAVA database and portal are needed to improve its functionality support efficient, effective compliance with reporting requirements.

First, several challenges with the DAVA structure appear to be driven by an attempt to design the DAVA database and portal in a manner that would allow it to be used for both export and domestic requirements. Although the requirements for domestic product have not yet been defined, it should be expected that those requirements will differ in at least some respects from the requirement for exported product given the differing goals and objectives of the two systems. Therefore, the portal should include different upload interfaces for exported product and domestic product.

Second, the primary package serial number field of the DAVA portal should be eliminated, or at a minimum, should be structured in a way that permits the field to be left blank. Serialization of the primary package is currently optional, but upload of data to the DAVA portal requires the primary package serial number field to be populated. As a solution, manufacturers have been advised to generate and upload

"dummy" or "fake" serial numbers. As discussed earlier in this paper, the generation and use of fake data entirely contradict good regulatory and business processes. The effective functioning of the traceability system is based on the ability to rely on the accuracy and integrity of the data input into the system. The inability to leave the primary package serial number field blank undermines the system.

Similarly, the DAVA should also be structured to eliminate the pricing information field, or at a minimum, allow it to be left blank. Price is not a master data element and should not be considered as part of master data. To the extent pricing information is included in the DAVA structure for purposes of domestic requirements, that should not dictate the structure for export requirements, especially given that the domestic requirements are still being developed. As with primary package serialization, inaccurate data should not be used to populate the pricing field.

Fourth, the DAVA portal should not require product photos to be uploaded. Again, to the extent this requirement is driven by anticipated domestic requirements, those unfinalized requirements should not generate additional requirements for exported product. In addition, high-resolution photos require significant data capacity, which exceeds the DAVA capacity. Compressing photos to the size currently required makes the photos virtually unusable. The requirement should therefore be eliminated.[27]

Fifth, a single manufacturer should be permitted to repeat serial numbers for separate GTINs. The global GS1 standard permits a manufacturer to repeat a serial number for separate GTINs because even in those instances, the combination of the GTIN and serial number is unique. Manufacturers' data systems are configured consistent with the global standard, and revisions to ensure unique GTINs across all of a manufacturer's products would be a significant and costly burden with no discernable benefit. Furthermore, the DGFT regulations and implementation guides do not indicate that serial numbers must be unique across all GTINs. The DAVA portal should be structured consistent with global standards and permit manufacturers to repeat serial numbers for different GTINs.[28]

Sixth, the process of manually uploading data files to the DAVA database adds unnecessary time and burden to the system. The upload process could be easily improved by developing the option and interface by which data could be automatically uploaded through a web service. This will improve the efficiency of the DAVA system.

Finally, data uploaded to the DAVA database should be made available only to regulators. Specifically, the data of one company should not be visible to other companies through the DAVA database. Data about a manufacturer's products is sensitive business information and could be used for anticompetitive purposes. In addition, access to such information could be used to attempt to legitimize fake product with legitimate serialization information. A formal, documented security risk assessment of the Portal,

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[27] We understand that, during the March 27, 2017 Interactive Meeting on Barcoding in Hyderabad, NIC indicated the photo upload is optional. If this is accurate, NIC should promptly publish this information in official guidance (*e.g.*, a Question and Answer document) and ensure the DAVA portal is structured accordingly.

[28] We understand that, during the March 27, 2017 Interactive Meeting on Barcoding in Hyderabad, NIC indicated serial numbers can be repeated for different GTINs. If this is accurate, NIC should promptly publish this information in official guidance (*e.g.*, a Question and Answer document) and ensure the DAVA portal is structured accordingly.

including penetration testing, should be conducted to ensure that the portal and its data is secure and not subject to external and internal threats.

> **Recommendation 6:** *NIC should maintain development and simulation environments to support revisions to the DAVA portal.*

The DAVA database and portal changes described above should be developed and implemented in accordance with Good Automated Manufacturing Practices (GAMP). At a minimum, NIC should maintain development and simulation environments for revisions. In addition to supporting effective design, this will also help maintain portal uptime which has been a significant challenge for manufacturers that have frequently found the DAVA portal to be unavailable when attempting to upload the mandatory data.[29]

> **Recommendation 7:** *NIC should establish a clear, predictable process for communicating revisions to the DAVA portal.*

Clear communication is important to successful implementation. Particularly with regard to exports, which directly impact stakeholders around the globe, it is difficult to distinguish draft concepts versus rumors versus final, binding requirements. Clearly documenting and publishing (*e.g.*, Question and Answer documents) requirements in a manner that can be easily accessed by all stakeholders will greatly support successful implementation.

One of the significant impacts of not having a development or simulation environment for the DAVA database is that all revisions to the DAVA portal require downtime for regulated industry (and regulators who need to use the system) and then any changes are implemented (or go "live") immediately. This is a significant challenge for companies trying to upload data on a routine basis. This makes compliance unnecessarily challenging, which has obvious risks, but more importantly can undermine the value of the system. NIC should establish a clear process for (i) communicating any downtime for the DAVA portal in advance, and (ii) communicating and explaining any revisions to the DAVA portal in advance.[30] Such a process will benefit all stakeholders. In addition, NIC should maintain a formal service desk for incident management and support of users who face issues with the uploads.

DRAFT DOMESTIC REQUIREMENTS

As discussed in the *Stakeholder Consultation*, now is the time for stakeholders to provide input on the design of a serialization system that best meets the needs of India, its industry members, and most importantly, its patients. This section provides three primary recommendations related to CDSCO's June 3, 2015, draft amendments to the Drugs and Cosmetics Rules, 1945 regarding the serialization. As discussed above, a phased approach to implementation will support the efficient and successful

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[29] We understand that, during the March 27, 2017 Interactive Meeting on Barcoding in Hyderabad, NIC indicated it is implementing the infrastructure necessary for a simulation environment.

[30] We understand that, during the March 27, 2017 Interactive Meeting on Barcoding in Hyderabad, NIC indicated it would establish such a process. If this is accurate, NIC should promptly publish the process it will use so that all stakeholders are aware of expectations.

implementation of the system this is ultimately mandated. This is particularly true with regard to the packaging levels to be serialized.

> **Recommendation 8:** *In the initial phase of requirements for domestic product, CDSCO should require serialization of the saleable unit.*

The proposal to mandate serialization of a product's primary package is unique to India—no other country requires serialization to this level—and would present several challenges for the supply chain. Product serialization at the primary level is costly. Many manufacturers estimate that it will cost up to an additional $1 million per packaging line to serialize primary packaging, and most manufacturers use many lines to package products (*e.g.*, different lines for different products). In addition, there is currently no accommodation for products for which there are logistical challenges with serialization (*e.g.*, small packages on which a serial number will not fit), or for products which would require approved changes in artwork before serialization is feasible.

Although product authentication is a significant objective for serialization of the primary package, serialization of the saleable unit (*i.e.*, the smallest unit of trade intended by the manufacturer for sale to a dispenser) is a better way to accomplish accurate product authentication and achieve optimum safety in the supply chain. Serialization of the salable unit will enable verification by the dispensing pharmacist or health care professional. Not only does authentication by the dispenser, rather than by the end user, facilitate product checking by professional and informed pharmacists and physicians at the point of dispensing, it ensures the best opportunity for authentication of intact packaging, which might otherwise be destroyed after the patient has received the product. Further, difficulties in scanning from small primary packaging or difficulties interacting with the verification portal may cause patients to discard good medicines.

To the extent that the dispensing of primary packages (when the saleable unit is a secondary package) such as individual blisters or blister strips is the reason serialization of primary packaging was proposed, industry and regulators should undertake serious dialogue regarding packaging sizes. When a package smaller than the saleable unit is dispensed, the patient loses access to critical information, such as directions for use, storage conditions, and warnings. Serialization should not be a fix for this. Instead, serialization should build on good regulatory practices that require dispensing of the saleable unit, and saleable unit package sizes should reflect patient needs.

> **Recommendation 9:** *CDSCO should not require manufacturers to capture, maintain, or report any information related to the movement of products by downstream trading partners.*

Draft rule 96(1)(viii)(B) requires manufacturers to maintain parent-child data for all three levels of packaging "and their movement in its supply chain." The phrase "and their movement in its supply chain" could be viewed as a requirement that manufacturers maintain information about subsequent product movements by downstream supply chain participants, such as stockists, distributors, and pharmacies. Such a requirement would be extremely burdensome for the supply chain. Supply chain requirements like these take several years to implement, require extensive detailed specifications and guidance from

regulators, raise significant concerns about data ownership, and place undue obligations on manufacturers for the accuracy of data over which they have no control. Similar requirements have created significant operational challenges and drawn extensive criticism and legal challenge in other markets, such as Brazil. Instead, each supply chain trading partner should be responsible for and control its own data about the product it handles. CDSCO should remove the phrase "and their movement in its supply chain" from draft rule 96(1)(viii)(B).

> *Recommendation 10: CDSCO should adopt a four-year, phased implementation timeframe for domestic requirements.*

As currently proposed, it would not be possible to comply with the requirements of the Draft Rules within 180 days of being finalized. Although some manufacturers are currently serializing product for export, many manufacturers either do not export product or have some packaging lines dedicated to the domestic Indian market. Serialization and the ability to establish parent-child relationships require significant changes to packaging lines, including shutting down those affected lines for a period of time to re-space and add new equipment and software, and then test those lines. These changes—especially the changes necessary to establish and capture parent-child relationships—can require significant time to implement, and most manufacturers must make these changes to many packaging lines. The chart in Attachment B shows the steps a manufacturer must undertake to implement serialization. Additional time and action is necessary for a manufacturer and other subsequent supply chain companies to implement systems for traceability, reporting, or verification.

A three-phase implementation process approach should be considered. The following three phases would support successful implementation:

1. **Serialization.** In the first phase, manufacturers and repackagers would be required to affix and encode serial numbers.[31] Manufacturers should be provided at least four years[32] from the date of publication of final, clear guidance to implement serialization. Serialization could be implemented in a single phase; however, the experience of manufacturers in other markets suggests that, for some smaller manufacturers with less serialization experience, it may be beneficial to implement codification (*i.e.*, encoding the GTIN, batch, and expiry in a 2D GS1 DataMatrix, but not necessarily including a serial number) in a separate phase prior to serialization. The addition of the serial number to these encoded data elements would then constitute a second phase of implementation. If this approach were taken, India should provide two years for codification and a subsequent two years for serialization. Furthermore, the

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[31] The content and format of the of the unique identifier with the encoded information should be the same as required for exported product (*i.e.*, GTIN, batch, expiry, and serial number in the same format), except for the changes related to uniqueness described in Recommendation 5 and permitting the manufacturer to determine the indicator digit as described in Recommendation 4. For more information on content and format, *see* http://www.rxgpsalliance.org/wp-content/uploads/2016/07/Position-Statement-Unit-Identifier-072816.pdf.

[32] *See* Attachment B for more detail on the need for this amount of time.

requirements for both codification and serialization should be released simultaneously so that manufacturers may choose to use a single phase of implementation.

2. **Verification.** In the second phase, dispensers would be required to verify each unit prior to dispensing. It would be appropriate for this requirement to take effect one year after serialization is required. This one-year timeline is necessary for sufficient testing of systems once serialization is in place. It will also allow a large volume serialized product to move through the supply chain to dispensers. This second phase should be limited to verification by the dispenser. More elaborate requirements, such as traceability provide modest additional value, yet drastically increase the complexity and time for implementation. A verification model, by contrast, is essential to the safety of the supply chain and also provides the highest return on investment, as depicted by the following graphic.
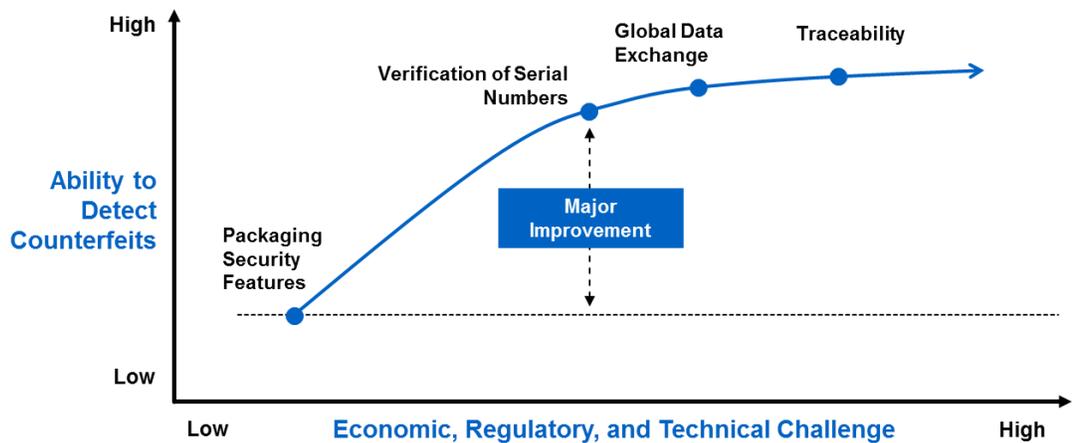
3. **Evaluate Traceability.** In the third phase, India could conduct an assessment of supply chain security following the implementation of the prior two phases. If there are additional goals such as to monitor supply chain velocity or to have visibility to the specific location of product within the supply chain, an interoperable system for traceability could be implemented. A traceability system requires that each member of the supply capture (*i.e.*, scan physical product) and maintain information about (1) from whom it bought the product, and (2) the person to whom it sold the product. While the prior steps would facilitate successful implementation of traceability, capture of this information for every unit is complex and requires significant change to existing processes. Further, additional necessary functionalities (*e.g.*, aggregation, stakeholder connections, interoperable means of communication) would require additional investment and time-consuming testing. If traceability were pursued, further phasing the implementation of those requirements by sector can be valuable. The United States and Turkey, for example, took a top down approach by first requiring manufacturers to act, then wholesalers, then pharmacies.

During the *Stakeholder Consultation*, regulators twice urged stakeholders to question the amount of data that is being generated for and by the DAVA system. This recommendation is consistent with concerns expressed by many in industry. Turkey and other countries have begun to understand firsthand just how complex management of an ever-growing data repository can be.

> *Recommendation 11: CDSCO and DGFT should consider alternative approaches that limit data volumes.*

The DAVA database is a repository of duplicate data sets already held by individual companies. By design, the size of the database continues to grow daily and will continue to grow for several more years. Management and maintenance of a database this size is expensive and difficult, at best. The DAVA model is commonly referred to a centralized database model, meaning a copy of all relevant information is sent to a shared database. An alternative approach, referred to as a distributed database model, does not require duplicate data to be sent and stored. Instead, each company continues to hold the data themselves, and a communication systems is established to allow authorized entities and regulators to query the data sets held by each company. This approach can be designed to provide the same functionality as a centralized database, but with many added benefits. A comparison of these two primary approaches is provided in the chart below. Hybrid approaches can also be used. These approaches should be evaluated fully to determine the approach that is most beneficial for India.

	Centralized Database Model	Distributed Database Model
Data Integrity	Data is duplicated and held in two locations	Single, initial source of data
Security	Data transmitted to central database Single layer of security Single point of potential breach for *all* data	Data remains in control of initial source Multiple layers of security No single breach point for *all* data
System Availability	Connection to data source must be available at time of data upload	Connection to data source must be continuously available for query
Cost Effectiveness	Requires development and maintenance of enormous databases to store duplicate data	Leverages existing data and blueprint for communication gateway
Flexibility	Requires development of database with single method of connection	Leverages existing data and Allows multiple methods of connecting and continued use of existing service providers
Interoperability	Data stored in separate centralized databases in each economy	Network allows multiple economies to use the same system

Ease of Implementation and Maintenance	Requires development and maintenance of enormous databases Requires single method of connection	Leverages existing data and blueprint for communication gateway Allows multiple methods of connecting and continued use of existing service providers

ASSURANCE OF VENDOR QUALITY

Many industry stakeholders have expressed concerns about the number of serialization vendors that have entered the market, and it is expected that the finalization of requirements for the domestic market would drive more new vendors into the market. Despite the significant number of vendors offering their services, GS1 India has identified only eight companies as approved vendors. Risks or breakdowns at any point along the supply chain jeopardize the security of the entire supply chain.

> *Recommendation 12: There should be a process for accrediting, certifying, or otherwise auditing serialization vendors.*

There should be a process for accrediting, certifying, or otherwise auditing serialization vendors to ensure they meet minimum standards, such as GAMP compliance. An approach such as this will make it easier for manufacturers select quality vendors and will help to ensure the integrity of an integrated supply chain traceability system.

NEED FOR ONGOING COLLABORATION

The pharmaceutical supply chain is a highly complex, interconnected web of companies, and serialization and traceability impacts all participants and requires their coordination. Collaboration among all supply chain participants, regulators, and patients is necessary for successful implementation and achieving the goal of supply chain security. The *Stakeholder Consultation* was an important first step in establishing a collaborative dialogue designed to promote efficient implementation for patient benefit. Ongoing dialogue will be critical.

The *Stakeholder Consultation* produced 16 specific recommendations set forth in this paper. It also surfaced a number of questions that remain to be answered:

1. How should serialization and traceability requirements apply to re-exports?
2. Should composition or intended use be a component of the information reported to the DAVA database?
3. Should placebos and clinical trial samples be subject to the serialization and traceability requirements?

4. Should bulk and semi-finished package be exempted from serialization and traceability requirements?[33]

Additional questions and challenges are certain to arise as implementation continues. Industry and regulators share the goal of securing the supply chain to advance patient protection, and they can achieve that goal by coming together in a collaborative manner to identify and address challenges in a manner that supports efficient implementation.

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[33] For proposed answers to these outstanding questions, please see Attachment D.

ATTACHMENT A

Stakeholder Consultation on Drug Serialization and Traceability in India
Attendee List

Abbott
Alembic Pharmaceuticals
Allergan
AmerisourceBergen
Cipla
Dr. Reddy's Laboratories
Eli Lilly and Company
Fresenius Kabi Global
Glenmark Pharmaceuticals
Johnson & Johnson
Jubilant Cadista
Jubilant Generics
Lupin Pharmaceuticals, Inc.
Macleods Pharma
Mylan
Novartis
Roche Pharma
Strides Shasun
Zydus Cadila
Indian Drug Manufacturers' Association (IDMA)
Pharmexcil
Partnership for Safe Medicines India
Central Drugs Standard Control Organization (CDSCO)
National Pharmaceutical Pricing Authority (NPPA)
United States Department of Commerce
United States Food and Drug Administration, India Field Office
World Health Organization

Implementation Timeline for Manufacturer Serialization of Salable Units*
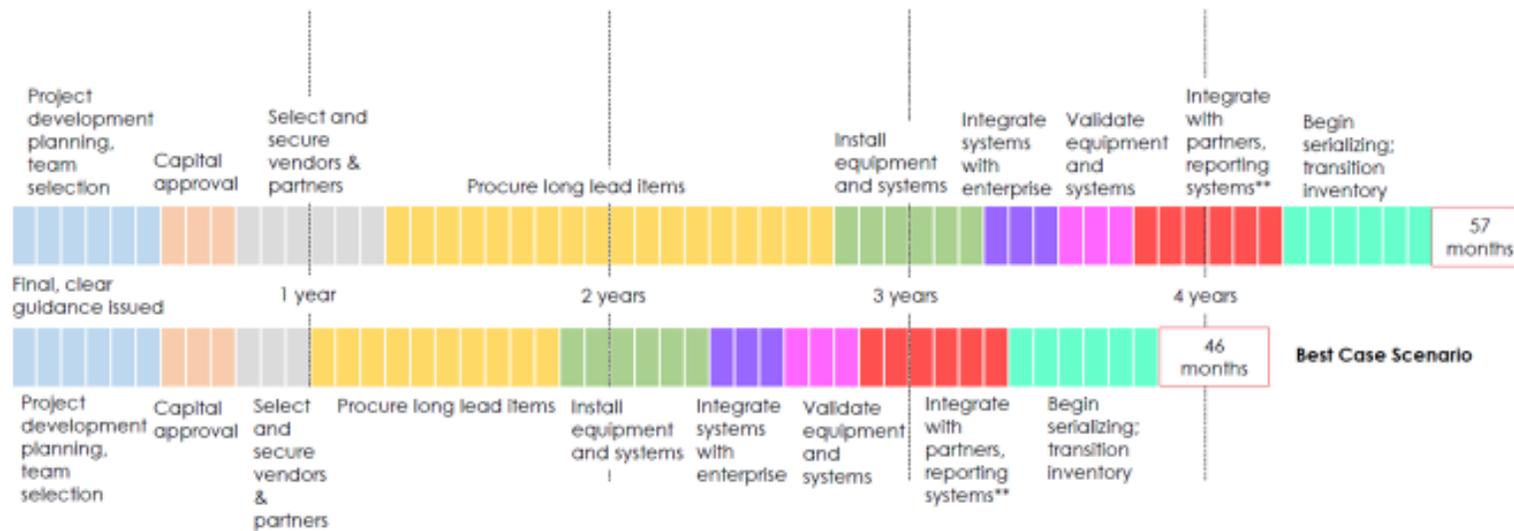
* This timeline assumes the use of global standards; because no markets require serialization of the primary package, this timeline assumes that serialization is occurring at the salable unit level. The timeline would be much longer in the case of primary package serialization.
** This assumes that external connections for reporting systems are finalized.

ATTACHMENT C

Glossary of Terms

ABBREVIATIONS

ALCOA – Attributable, Legible, Contemporaneous, Original, and Accurate

CDSCO – Central Drugs Standards Control Organization

DAVA – Drugs Authentication and Verification Application

DGFT – Directorate General of Foreign Trade

DSCSA – Drug Supply Chain Security Act

IBEF – India Brand Equity Foundation

ICRIER – Indian Council for Research on International Economic Relations

IDMA – India Drug Manufacturers Association

GAMP – Good Automated Manufacturing Practices

GTIN – Global Trade Item Number

NIC – National Informatics Centre

NPPA – National Pharmaceutical Pricing Authority

SSI – Small Scale Industry

GOVERNMENT OF INDIA (GOI)

Central Drugs Standards Control Organization (CDSCO) – the Central Drug Authority for discharging functions assigned to the Central Government under the Drugs and Cosmetics Act. Its major functions include: regulatory control over the import of drugs, approval of new drugs and clinical trials, meetings of Drugs Consultative Committee (DCC) and Drugs Technical Advisory Board (DTAB), and approval of certain licenses as Central License Approving Authority. CDSCO is a subdivision of the Indian Ministry of Health and Family Welfare.

Directorate General of Foreign Trade (DGFT) – an attached office of the Ministry of Commerce and Industry and is headed by Director General of Foreign Trade. DGFT is responsible for formulating and implementing the Foreign Trade Policy with the main objective of promoting India's exports, and also issues scrips/authorization to exporters and monitors their corresponding obligations. DGFT is a subdivision of the Indian Ministry of Commerce and Industry.

National Informatics Centre (NIC) – established in 1976, and has since emerged as a "prime builder" of e-Government / e-Governance applications up to the grassroots level as well as a promoter of digital opportunities for sustainable development. NIC, through its ICT Network, "NICNET", has institutional

linkages with all the Ministries /Departments of the Central Government, 36 State Governments/ Union Territories, and about 688 District administrations of India, and is a subdivision of the Ministry of Electronics & Information Technology. NIC built and manages the DAVA portal and database.

National Pharmaceutical Pricing Authority (NPPA) – NPPA is an organization of the Government of India which was established to revise the prices of controlled bulk drugs and formulations and to enforce prices and availability of the medicines in the country. The organization is also entrusted with the task of recovering amounts overcharged by manufacturers for the controlled drugs from the consumers, and monitors the prices of decontrolled drugs in order to keep them at reasonable levels. NPPA is a subdivision of Department of Pharmaceuticals, within the Ministry of Chemicals and Fertilizers.

INDUSTRY STAKEHOLDERS/NOT-FOR-PROFIT ORGANIZATIONS

ICRIER – ICRIER is an autonomous, policy-oriented, not-for-profit, economic policy think tank. ICRIER's main focus is to enhance the knowledge content of policy making by undertaking analytical research that is targeted at informing India's policy makers and also at improving the interface with the global economy.

Indian Drug Manufacturers Association (IDMA) – IDMA is an India-based trade association with membership of over 1000 wholly-Indian large, medium and small companies and State Boards (SB) in Gujarat, Himachal Pradesh & Uttaranchal, Haryana, Tamil Nadu, West Bengal, Madhya Pradesh, Telengana and Karnataka.

GS1 – GS1 is a not-for-profit, widely recognized global standards organization with nearly 40 years' experience in supply chain optimization. The GS1 system of standards now spans more than 20 industry sectors, over a million companies in 150 countries and facilitates more than six billion daily transactions. The GS1 system of standards provides an effective globally harmonized and integrated framework to manage supply chain information.

RxGPS – RxGPS is a group of multinational pharmaceutical supply chain stakeholders who have a common interest in developing consensus strategies, policy principles, and policy recommendations that advance global alignment of drug serialization and tracing requirements in order to enhance patient safety, supply chain security, and drug availability around the world. Learn more at www.RxGPSalliance.org.

TERMINOLOGY

Aggregation – associates a set of "contained" or "child" objects (*e.g.*, cases) within a "containing" or "parent" entity (*e.g.*, pallet). The parent identifier identifies the aggregation and the "children" contained within the parent entity.

Drugs Authentication and Verification Application (DAVA) – a portal for Indian Drugs Authentication, Track and Trace.

Drug Supply Chain Security Act (DSCSA) – The DSCSA enhances the security of the pharmaceutical supply chain by establishing a national system for tracing and serializing pharmaceutical products and

for establishing national licensing standards for wholesale distributors and third-party logistics providers.

End-Point Authentication – a use/application of serialization, adopted by the European Union, whereby serialization is used to verify the authenticity of a drug before it is dispensed to the patient. End-point authentication is one traceability option.

Global Trade Item Number (GTIN) – GS1 identification key used to identify types of products at any packaging level. Once a company has assigned a GTIN to a trade item, it provides a common language for all of its entities and trading partners worldwide to uniquely identify the item and easily communicate information about the item. A GTIN-14 has 14 digits and is composed of an indicator digit (1-9), GS1 Company Prefix, item reference, and check digit.

Good Automated Manufacturing Practices (GAMP) - A system for producing quality equipment using the concept of prospective validation following a life cycle model. Specifically designed to aid suppliers and users in the pharmaceutical industry.

Indicator Digit – the leftmost component of a GTIN-14. The indicators have no meaning. The digits do not have to be used in sequential order, and some may not be used at all. The GTIN-14 structure for trade item groupings creates extra numbering capacity. Indicators can be reused.

Primary Package - the level of packing that is in direct contact with the product (e.g., blister card or vial).

Salable Unit - the smallest container of package intended by the manufacturer to be sold to a pharmacy. In practice, the saleable unit could be a pill bottle (which is a primary package), a carton containing a blister strip (which is a secondary package), or even a ten-pack of individual vials that could be dispensed to a patient. The salable unit is based on the manufacturer's intent.

Secondary Package - the smallest unit intended by the manufacturer to be sold to the dispenser/pharmacy. In some instances (*e.g.*, a bottle of tablets without an outer carton), the primary package could become the smallest saleable unit.

Serialization – the process by which products are marked with a unique identifier—typically a unique number or alphanumeric code. The unique serial number, along with other related information, is typically encoded in a barcode that can be read electronically.

Tertiary Package - the logistical unit that is shipped, the shipper, carton, case, pallet, or tote that contains one or more primary/secondary levels of packaging.

Traceability/Track and Trace – the complementary use of serialized data. Tracking pharmaceuticals allows each stakeholder to identify the current owner of the product and the pathway the product must take to get to its current location. Tracing pharmaceuticals means recreating the path of a product, from the manufacturer to the current entity/owner. Tracing systems identify where the product has been and which entities have had ownership of the product.

ATTACHMENT D

RxGPS Proposed Answers to Outstanding Questions

1. **Should serialization and traceability requirements apply to re-exports?**

    No. Serialization and traceability requirements should not apply to re-exports. Several aspects of practical supply chain operation makes 100% reconciliation of each batch in DAVA Portal unachievable. Therefore, the portal would have a vast inventory of open items (promised vs. delivered), which gives opportunities to counterfeiters to take advantage of the portal gaps.

2. **Should composition or intended use be a component of the information reported to the DAVA database?**

    No. Composition or intended use should not be required to be reported to the DAVA database. These fields are non-standard, not part of current master data records, and not required for effective traceability. In addition, label claims for composition are already part of regulatory filings, and therefore are already appropriately monitored. Intended use of a drug should not be considered as part of the DAVA master data set because it is solely dependent on the physician, and all generic product information is already included as part of the product leaflet.

3. **Should placebos and clinical trial samples be subject to the serialization and traceability requirements?**

    No. All clinical trial products should be exempt from the serialization and traceability requirements because they are already subject to adequate, strict regulatory controls. Applying requirements to drugs for investigational use is neither necessary nor practical given that they are not introduced into the supply chain in the same unrestrained manner as commercial products. Additionally, clinical trial products may be required to be packaged and labeled in such a manner as to blind the identity of the drug. Imposing serialization and traceability requirements could also break the blind, thereby compromising the integrity of the study.

4. **Should bulk and semi-finished package be exempted from serialization and traceability requirements?**

    Yes. Only those products packaged for dispensing should be subject to serialization and traceability requirements. Serialization is intended to secure the pharmaceutical supply chain, and bulk and semi-finished package are not intended for commerce. Serialization and traceability requirements will apply to these products once they are packaged for commerce.

ATTACHMENT E

A Primer on Serialization

Introduction

Global pharmaceutical distribution networks and supply chains have become more complex and interconnected, quickening the pace of regulations that mandate pharmaceutical serialization and traceability. As pharmaceutical serialization gains momentum around the globe, it is important to understand the building blocks of traceability systems and how serialization data can be leveraged across the supply chain. Understanding serialization and the ways in which serialized data should be used is of primary importance.

Serialization is the process by which products are marked with a unique identifier—typically a unique number or alphanumeric code—and is beginning to be leveraged to enhance supply chain security. The unique serial number, along with other related information, is typically encoded in a barcode that can be read electronically. Serialization of pharmaceuticals (*i.e.*, simply applying a unique identifier) itself provides virtually no benefit to the supply chain. Rather, it is the use of that serialized data in some manner that enhances supply chain security. This complementary use of the serialized data is commonly referred to as traceability.[34]

The purpose of this primer is to explain the components of serialization, the use of serialization data, and the processes and systems necessary to leverage serialization data to achieve greater security and safety in the supply chain.

The Value of Serialization and Traceability

Breaches of the pharmaceutical supply chain can have serious public health consequences. The market for counterfeit medicines has expanded in recent years and increased globalization of trade. Counterfeit, medications pose a risk to patients as they are often substandard products that are physically indistinguishable from valid product. These counterfeit drugs may be inactive or incorrect, or contain improper dosages that are less, or more, potent than the legitimate drug.

The risk of medication diversion and theft is an additional supply chain security concern. Drug diversion is the transfer of any legally prescribed drug from the person for whom it was prescribed to any other person for illicit use, and includes the trading of drugs not legally available for sale in a given country. When drugs are diverted or stolen, the quality and safety of the product cannot be assured or maintained. These drugs may be intentionally altered or damaged due to improper storage or exposure to contaminants. If reintroduced to the market, these products may be ineffective, or may pose a risk of additional health complications for patients.

Traceability systems, which use the serialized data on each package, can authenticate product and/or trace the product's path through the supply chain. Although serialization requires large investments of time and resources, with the appropriate infrastructure and technology, the data acquired from

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[34] Depending exactly how the data are used, this may also be referred to as "tracking", "track and trace", or "authentication."

serialized product can be leveraged to address challenges, such as counterfeiting or diversion, faced by a country.

What is Serialization?

Serialization means that each individual package is assigned and marked with a standardized unique identifier that can be read and communicated across the supply chain. Though a straightforward concept, the process of serialization is much more complex than setting up packing lines with bar code printers and scanners. In addition to serial number and identification, serialization must include a process for:
1. Product Identification
2. Data Capture

Identification
A serial number is a code assigned to an individual item for its lifetime. To identify a unique individual item, serial numbers must be augmented with encoded product identifers. These encoded identifiers must be affixed to all products as they enter the supply chain. GS1, a global standards setting organization, has identified the standards below for identification of health care products. All of the identification standards listed are globally unique identifiers that may be utilized around the world.

For pharmaceuticals, GS1 has indicated that the product identifier should include, at minimum, the following three data elements:
1. Global Trade Item Number (GTIN)–A company (or regulator) may elect to use an 8-, 12-, 13-, or 14-digit GTIN code.
2. Expiration Date
3. Batch Number[35]

Given the unique safety concerns associated with counterfeit, diverted, stolen, and adulterated medications, the inclusion of the expiration date helps to prevent outdated product from being dispensed to patients. Furthermore, the association of expiration date and batch number with a serial number helps to distinguish between trade items with similar production and usage characteristics. Once a GTIN is assigned to a product, this information is uploaded to a live database. All of a company's entities and trading partners should be able to recognize a GTIN.

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[35] http://www.gs1.org/docs/traceability/Global_Traceability_Standard_Healthcare.pdf

As a product moves through the supply chain, additional data elements can provide more specific information about a product. These data elements include:

1. Serial Shipping Container Code (SSCC) – a SSCC can be used by companies to identify a "logistic unit," or combination of trade items packaged together for storage purposes. Examples include a case, pallet, or parcel.
2. Global Location Number (GLN) – a GLN can identify the physical location and legal and functional entities related to a product or involved in transactions.

Capture

The second component of serialization is the method of capturing serialized data (GTIN, expiration date, and batch). For efficiency, all serialized data must be encoded in a barcode that can then be read electronically and recognized further down the supply chain. While GS1 has endorsed several methods of data capture (see below), industry stakeholders have coalesced around the use of a 2D Data Matrix barcode for identification of individual packages of product. Cases or logistic units are typically encoded with a 2D Data Matrix or a linear barcode (*e.g.*, GS1-128).

The most common format for a 2D barcode is a square as this enables the encoding of the largest amount of data. A 2D Data Matrix, as pictured above, can encode up to 2,335 alphanumeric characters, or 3,116 numbers. Data Matrix symbols are typically read by two-dimensional imaging scanners or vision systems or by mobile phone applications.

Packaging Levels and Serialization

There are three main levels of packaging for pharmaceutical products moving through the supply chain. Each level has its own serialization requirements based on the contents of the package.

Primary level—the primary level of packaging is the first level. This package is in direct contact with the product. Examples include a medicine strip, vial, single therapy kit, or ampule. Industry consensus is that products should not be serialized at the primary level for cost, security, and logistical reasons. In many cases, the 2D matrix is not able to fit on primary packages, which are too small.

Secondary level—the secondary level is often the smallest level intended to be sold to the dispenser/pharmacy. This may be a package containing one or more primary packages, or a group of primary packages containing a single item. Industry consensus is that the secondary package is the smallest level of packaging that should be serialized.

Tertiary level—the tertiary package is the logistic unit, as described above. Tertiary packages are the shipper, carton, case, pallet, or tote that contains one or more primary/secondary levels of packaging. As noted, tertiary packages are serialized using a SSCC.

Traceability Models for Serialized Product

The true value of serialization lies in the use of serialization data to trace a specific product (unique identifier) through the supply chain or to validate that the product given to the patient is authentic and undamaged. As depicted in the flow chart below, there are two general approaches and four models for the use of serialized data.
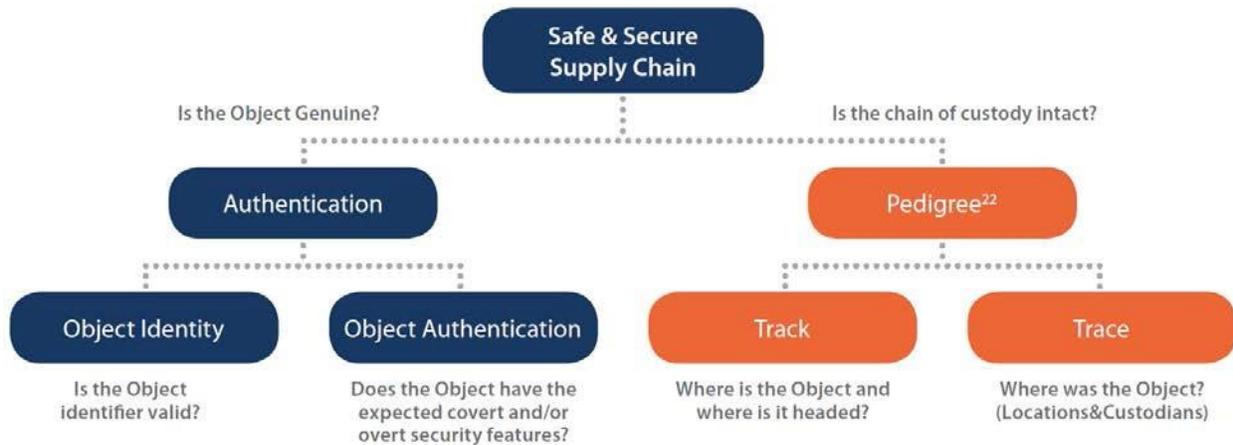
Authentication

Object Identity (Verification)
In an authentication model, supply chain stakeholders verify that the serial numbers used to identify a particular product were, in fact, affixed to the package by the manufacturer of that product. This is accomplished by cross-checking the product identifiers on a package with the database of existing serial numbers previously populated by the manufacturer and associating them to lot number and expiry date in the manufacturer's database. Additional indicators of product identity are the integrity of the product packaging and the presence of the brand insignia on the package.

Object Authentication
Serialization is implemented on product packaging, and not the product itself, and therefore verification of serialized data is necessary, but not necessarily exhaustive, to determine the authenticity of the product within the package. Once a product identifier is determined to be valid, an Authentication Model also includes a process for object authentication. While serial numbers play a role in determining the authenticity of a product, a check of the serialized data may be supplemented by checks of both overt and covert security features used for brand protection by manufacturers (*e.g.*, tamper-evident packaging).

Track & Trace

A drug track and trace system is intended to provide, in electronic form, the transaction history of a product including all changes of ownership of a given product. A query of an individual package outlines the movement of a given shipment throughout the supply chain from sale by a manufacturer, though

acquisition(s) and sale(s) by one or more wholesalers, manufacturers, or pharmacies, until final sale to a pharmacy or other person furnishing, administering, or dispensing the drug.[36]

Track
Tracking pharmaceuticals allows each stakeholder to identify the current owner of the product and the pathway the product must take to get to its current location.

Trace
Tracing pharmaceuticals means recreating the path of a product, from the manufacturer to the current entity/owner. Tracing systems identify where the product has been and which entities have had ownership of the product.

Importance of Standards

The implementation of a traceability system effectively requires the interoperable exchange of data. Stakeholders must have servers that can communicate with one another, and data must be transferable, without alteration or translation, from trading partner to trading partner. Global standards for data exchange allow products to be seamlessly followed across country borders and allow for global supply chain security. Utilizing data standards creates a common language among different servers which enables supply chain members to exchange data in a common and understandable format. System efficiencies and cost savings are created when trading partners adhere to standards for data exchange.

Data Sharing
A widely utilized standard for sharing event data is the Electronic Product Code Information Services (EPCIS) standard created by GS1. The goal of EPCIS is to enable disparate applications to create and share data between trading partners and internally about each product event (*e.g.*, the initial serialization or "commissioning" of a product, the shipment of a product, the dispensing of a product).[37] EPCIS can operate within diverse information technology (IT) environments to identify where products are and why they are there.

Conclusion

Serialization of pharmaceuticals involves assigning a unique identifier to a product for identification purposes, and also capturing that data in a barcode. While serialization of products is leveraged to promote supply chain security, serialization alone has no benefit for the supply chain. The traceability systems that use serialized data to verify, authenticate, track, or trace products in the supply chain are what truly help to secure the supply chain. For serialization to have the optimal benefit, countries should analyze the issues that they would like to address within their market and implement the most efficient method to use serialized data using global standards to be communicated clearly between both companies and countries to identify anomalies before that product is dispensed to the patient.

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[36] http://www.gs1.org/docs/healthcare/Wed_9h05_VirginiaHerold_ePedigree.pdf

[37] http://www.gs1.org/sites/default/files/docs/epc/epcis_1_1-standard-20140520.pdf