RX GPS
THE ALLIANCE FOR GLOBAL PHARMACEUTICAL SERIALIZATION

August 13, 2020

Ms. Jenny Burnett
Director, Scientific Operations Management Section
Therapeutic Goods Administration
Via email: 2dbarcodes@tga.gov.au

Re: Consultation on the new Therapeutic Goods Order 106 - Data matrix codes and serialization of medicines.

Dear Ms. Burnett,

I write to you on behalf of an organization called RxGPS regarding the Therapeutic Goods Authority's (TGA) consultation for data matrix codes.

RxGPS (http://www.rxgpsalliance.org/) is a coalition of multinational pharmaceutical supply chain stakeholders with a common interest in developing consensus strategies and policy recommendations that advance global alignment of supply chain serialization and data sharing requirements to enhance patient safety, supply chain security, and drug availability around the world. RxGPS brings together senior supply chain and policy leaders who have strategic insights, technical expertise, and policy expertise. The group has worked together for more than seven years, and includes representation from multiple supply chain sectors (e.g., innovator and generic manufacturers, wholesalers, logistics providers, and pharmacies) to provide the broadest possible perspective.

RxGPS has produced an extensive public toolkit of resources, including a serialization implementation roadmap, model regulation and packaging levels position statement to assist markets that are in the foundational stages of developing such capabilities. The documents in the toolkit are not specific to any individual country regulation and represent the collective insights and best practices gleaned from years of experience implementing serialization in dozens of markets around the work. They are available on our website http://www.rxgpsalliance.org/resources/:

- Patient Level Verification Position Statement
- Packaging Level Position Statement
- Principles for Using Serialization Position Statement
- Serialization Implementation Roadmap & Model Regulation
- Position Statement: Benefits and Complexity of Common Serialization Models
- Position Statement on Unit Identifier

We are happy to discuss any of these documents and nuances they describe in more detail should that be of interest.

RxGPS is aligned with the vision and benefits outlined in Therapeutic Goods Order 106. We appreciate the role Australian regulators will play in the global supply chain to reduce medication errors, adverse events and maintain a safe and secure supply chain for patients for exported pharmaceuticals. Methods to enable interoperable exchange of information using GS1 standards and a 2D data matrix will allow confidence for both consumers and regulators. Further, RxGPS supports utilizing a 2D data matrix for serialization of pharmaceutical products and the use of serialization data to secure the legitimate supply chain. Understanding TGA's goals are broader than supply chain security, we hope the comments below will assist TGA in understanding how to best utilize serialization and serialized data to secure the legitimate supply chain and how to assess the utility of serialization to accomplish the broader goals that TGA has put forth.

In addition to the general comments above, we offer the following specific comments for your consideration.

TGA Should Embrace A Phased Implementation

RxGPS appreciates the work of TGA regarding serialization in Australia. We believe serialization and data applications that leverage it are effective tools for securing the legitimate supply chain when it is implemented effectively. Our members can draw on implementation experiences from many international markets to provide a broad and deep understanding of effective approaches to serialization. For example, we have learned that appropriately phasing in implementation dates over time leads to a more effective system and reduces errors and costs.

A point-of-dispense verification system is efficient and effective. At the most basic level, a verification model has only two components. First, manufactures must affix a serial number to a product package, commission this event, and maintain a repository of the serial numbers they commission. This is done by manufacturers as part of the serialization process, and those databases established by each manufacturer can be used for verification. Second, a mechanism by which data can be shared in order for dispensers to verify serial numbers against those manufacturer databases is needed. As a result, a verification model limits the number of stakeholders that must integrate their data systems. Other supply chain partners (i.e., wholesale distributors, 3PLs) are not required to scan, upload, transmit, or otherwise connect to a data communication pathway in an end-point verification model.

A traceability (i.e., recreating the historical path of a package from the current entity/owner back to the manufacturer) or track and trace (i.e., identifying the current owner of the product and the pathway the product has taken to get to its current location) model provides some added level of security to the supply chain beyond verification. For example, in the event that a counterfeit product enters the supply chain; a verification model is likely to identify that product as counterfeit and prevent it from being dispensed to a patient. The addition of traceability or track and trace will also facilitate an investigation of where that product penetrated the legitimate supply chain. This is a modest benefit to patient safety and supply chain security, but it comes at a significant cost.

A traceability or track and trace system is significantly more complex to implement than verification. First, traceability or track and trace requires the capture and maintenance of significantly more data. As noted above, a verification model requires only the manufacturer to capture and maintain information about each individual serialized unit—an activity a manufacturer must already do as part of any serialization process. A traceability or track and trace system, however, requires that every company that owns a package (manufacturers, wholesalers, and dispensers) capture and maintain[1] data about each serialized unit. This is a significant operational burden to scan and capture the data, and a significant information technology burden to maintain the related data repository.

Second, a traceability or track and trace model significantly increases the number and complexity of data connections that are needed. As noted above, a verification model requires a communication mechanism by which a dispenser may query against manufacturer data sets. This includes the appropriate functionality, specifically for dispensers receiving product from multiple manufacturers, to ensure that verification requests are routed to the appropriate manufacturer's database. Traceability or track and trace, however, requires that every member of the supply chain connect to some type of data exchange, not just manufacturers and dispensers. This adds to an already complex system of communication by drastically increasing the number and type of connections needed.

The drastic increase in data capture obligations, data volumes, and complexity of data connections needed for a traceability or track and trace system means that the minimal benefit of such system is realized only at significant cost. Implementation is significantly more complex, which requires more testing, results in more implementation challenges, and increases the likelihood of failure. All of this adds to the time needed, by all companies that take ownership of a product within the supply chain, to for implementation, and delays realization of the benefits

Adoption and implementation of any traceability or track and trace system should be phased in over time, starting simple and achieving benefits before considering additional functionalities. The pharmaceutical supply chain is a complex, interconnected network of manufacturers, wholesale distributors, pharmacies, and other service providers, and a supply chain security system must account for a variety of elements and environments across this diverse array of stakeholders. Phased implementation leverages existing infrastructure and shared learnings across the supply chain to promote efficiencies as industry moves from one implementation phase to the next. A phased approach also allows for assessment of supply chain security at each phase and prior to implementation of a costly and complex traceability system.

A phased approach has been shown globally to yield valuable time for assessment and testing. The requirements should be broken down in manageable segments, including reasonable time to assess the effectiveness following each stage as measured against regulatory goals. Where possible and appropriate, we also believe regulators should consider an attempt to harmonize

[1] In the traceability context, data "capture" refers both to the scanning of a physical product serial number, as well as the exchange of data, often via Electronic Data Interchange (EDI). These data must then be recorded, or "maintained," for future query, such as under a product investigation.

requirements with other nations in their region to allow for a more efficient implementation, particularly where no requirements currently exist. Regional strategies composed of similar economies and cultures allow for more secure and consistent implementation of crucial safeguards.[2] RxGPS suggests a phased approach to meet long term TGA goals for machine-readable labels, taking into account the current level of readiness in Australia and adequate implementation timelines to leverage existing infrastructure and shared learnings. Our Serialization Implementation Roadmap & Model Regulation provides an example of how such a phased approach could be designed.

TGA Should Evaluate the Risks and Benefits of Patient-Level Verification

TGA is considering the use of consumer and patient access to medication data. It is important to note that patient-level verification of products has garnered discussion and interest worldwide. Proposals in some jurisdictions have included verification by the patient via a mobile phone application. While the benefits of patient-level verification may include incremental patient autonomy and peace of mind, there are significantly more challenges associated with patient-level verification that should be balanced against potential benefits.

Patient-level verification has the potential to create significant data security concerns, and the process of serializing primary packaging is extremely complex and costly. Further, testing has not yet occurred to determine the level of patient interest in verifying their medicines. Not only does authentication by the dispenser, rather than by the end user (patient), facilitate product checking by professional and informed pharmacists and physicians at the point of dispensation, it ensures the best opportunity for authentication of intact packaging, which might otherwise be destroyed after the patient has received the product. Additionally, patient-level systems are unlikely to be automated and may not include the required scanning capabilities. In instances where less sophisticated systems are available, patients may be more likely to manually type in the serial number than to scan it, increasing the level of inaccuracy or errors and inadvertently creating false negatives on patient verification attempts for otherwise good product. For these reasons there has not yet been a market to successfully implement patient-level verification of product serial numbers. Some markets, such as Turkey, have implemented scanning technology for the end user, but the patient only gains access to ancillary information about the product (e.g., manufacturer, location of dispense) rather than traceability data for product authentication. Given the numerous challenges with patient-level verification RxGPS supports limiting verification to supply chain entities; if patients are permitted to scan product, the information they receive should only include ancillary product information not related to traceability.[3] A dispenser has processes and procedures for dealing with suspect product while a patient does not. Authentication of product is best managed by the professionals within the supply chain.

RxGPS requests TGA consider all aspects of patient access to data, looking to other international examples, prior to making a final decision.

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[2] For additional information and recommendations on phased implementation, please see the RxGPS position statement: https://www rxgpsalliance.org/wp-content/uploads/2017/06/RxGPS_Serialization-Models-Position-Statement-010917.pdf

[3] Please also see the RxGPS Patient Level Verification Position Statement, https://www.rxgpsalliance.org/wp-content/uploads/2019/06/Patient-Level-Authentication-061319_Final.pdf

Align Packaging Level Terminology

Upon evaluation, TGA's Order 106 utilizes terms that would benefit from clarification/modification when viewed across the global supply chain. For example, page 4 of the Guidance for TGO 106 reads:

> Primary Pack has the same meaning as in the Act. Note that a primary pack is distinct from primary packaging. Primary packaging, as used in GS1 and GMP guidance, is the packaging which directly contacts the medicine (injection vial, tablet blister etc.). The Act refers to this as the container. The primary pack as defined in the Act is usually secondary packaging in GS1 and GMP guidance. Sometimes the primary pack is also primary packaging, such as a bottle of fish oil capsules with no further packaging. (p. 4 Guidance for TGO 106)

The term primary pack is used differently in other global markets, the TGO definition is closer to the common U.S. defined term of container, allowing for confusion among companies accustomed to that definition. Additional confusion remains around TGA's distinction and definition of a primary pack and primary packaging. Members of RxGPS who frequently rely on GS1 standards to operate their global operations are unclear how to follow these requirements.

Frequently, global regulators utilize the terms "primary," "secondary," and "tertiary" to distinguish between common packaging levels and to dictate which packaging level must bear a unique identifier for purposes of verification and/or tracing.[4] However, this terminology (ISO Terminology 21067-1:2016) is not aligned with the standard units of trade across the pharmaceutical industry. A lack of consistent terminology within and across markets has led to significant confusion and has resulted in situations where product barcodes are misplaced, repetitive, etc. This type of confusion impedes compliance with any market's regulations and, rather than promoting supply chain security, can actually introduce additional risks as well as potential product delays, which can be harmful to patients. TGA definitions and operational requirements should not stray from global standards and create additional confusion.

The chart below uses specific examples of packaging scenarios to align the "primary," "secondary," and "tertiary" packaging level terminology commonly used in regulatory language to the trade terminology more commonly used across the pharmaceutical supply chain. This chart is not meant to be an exhaustive list of packaging scenarios, but rather provides some illustrative examples that can be extrapolated to related packaging scenarios. The goal of the chart is to illustrate how utilizing trade terminology eliminates unnecessary confusion regarding the appropriate level of packaging on which to apply a serial number. For example, the trade

[4] The three levels of packaging that are generally addressed in serialization laws and regulations worldwide:
• 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 the packaging containing one or more primary packages. In some instances (e.g., a bottle of tablets without an outer carton), the primary package and the secondary package can be the same.
• 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
RxGPS, Packaging Levels Position Statement, https://www rxgpsalliance.org/wp-content/uploads/2019/05/RxGPS_Packaging-Levels-Position-Statement.pdf

terminology of "salable unit" directly maps to the serialized salable unit for every packaging scenario.

Example Packaging Scenario	Packaging Hierarchy	ISO Terminology 21067-1:2016	Trade Terminology	Serialized salable unit	Higher level serialized package (sGTIN) for aggregation purposes	Package labeled with SSCC
24 60-count bottles of tablets are placed in a corrugated cardboard case. 72 cases are put on a pallet.	Pill bottle	Primary	Salable Unit	X		
	Case	Secondary	Shipper | Case		Identify with sGTIN OR SSCC depending on market dynamics	
	Pallet	Tertiary	Logistical Unit			X
Four 60-count bottles of tablets are placed in a placed in a logistical inner pack (e.g., plastic wrap). Six such inner packs are placed into a corrugated cardboard case. 72 cases are put on a pallet.	Pill bottle	Primary	Salable Unit	X		
	Inner pack	Secondary	Logistical Unit			
	Case	Tertiary	Shipper | Case		Identify with sGTIN OR SSCC depending on market dynamics	
	Pallet	Tertiary	Logistical Unit			X
One 60-count bottle of capsules is placed in a Regulator-approved and medically labeled carton. Four mono-cartons are placed in a logistical inner pack (e.g., plastic wrap). Six such inner packs are placed into a corrugated cardboard case. 72 cases are put on a pallet	Pill bottle	Primary	Primary pack			
	Mono-carton	Secondary	Salable Unit	X		
	Inner pack	Tertiary	Logistical unit		Identify with sGTIN OR SSCC depending on market dynamics	
	Case	Tertiary	Shipper | Case		Identify with sGTIN OR SSCC depending on market dynamics	
	Pallet	Tertiary	Logistical unit			X
5 pre-filled syringes are placed in a Regulator-approved and medically labeled carton. Four cartons are placed in a logistical inner pack (e.g., plastic wrap). Six such inner packs are placed into a corrugated cardboard case. 72 cases are put on a pallet.	Pre-filled syringe	**Primary**	**Primary pack**			
	Carton	Secondary	Saleable unit	X		
	Inner pack	Secondary	Logistical unit		Identify with sGTIN OR SSCC depending on market dynamics	
	Case	Tertiary	Shipper | Case		Identify with sGTIN OR SSCC depending on market dynamics	
	Pallet	Tertiary	Logistical unit			X
5 blister packs of 6 tablets are placed in a labeled carton. 30 cartons are placed in a logistical inner pack (e.g., plastic wrap). Six inner packs are placed into a corrugated cardboard case. 72 cases are put on a pallet.	Blister Pack	Primary	Primary pack			
	Carton	Secondary	Saleable unit	X		
	Inner pack	Secondary	Logistical unit		Identify with sGTIN OR SSCC depending on market dynamics	
	Case	Tertiary	Shipper | Case		Identify with sGTIN OR SSCC depending on market dynamics	
	Pallet	Tertiary	Logistical unit			X
120 60-count bottles of tablets are placed in a mixed tote.	Pill bottle	Primary	Saleable unit	X		
	Mixed tote/ carton	Tertiary	Logistical unit			X

The first column in the chart describes, in detail, a potential packaging scenario. The second column depicts the packaging hierarchy described in the scenario. Each level of packaging is then mapped in the third column to the commonly utilized (and often confusing) ISO

terminology. The fourth column recommends the appropriate trade terminology that should be used for each packaging level to help avoid confusion. Then, using the trade terminology, the chart demonstrates where serialization should occur across three (potential) serialization levels:

1. The serialized salable unit
2. A higher-level serialized package (sGTIN) for aggregation purposes (e.g. a case)
3. The highest-level package labeled with an SSCC (e.g. a pallet)

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 disparate systems are interconnected but serialization data can be leveraged across the supply chain to improve patient health.

Industry and regulators would benefit from more global alignment with current industry practices and standards. Harmonization to global standards streamlines processes and reduces unnecessary implementation costs for manufacturers, which facilitates international trade in a global market. RxGPS believes that the success of serialization and traceability at the global level is dependent on harmonization to global standards. Defining primary pack in a separate and distinct manner than GS1 is problematic. RxGPS requests TGA reconsider definitions throughout TGO 106 to align with global standards.

Serial Number Aggregation Concerns and Confusion

On page 9 of the Guidance for TGO 106 V1.0 June 2020 the language states:

> "Where serialised units are packed into shippers, pallets etc. the machine-readable codes on these logistic units must allow the serialised contents to be identified. This allows every serialised unit to be accounted for in the time and place that each time the logistic unit is scanned."

As written the language outlines an approach to capture all the information for each unit contained in larger containers such as shippers and pallets. It is unclear if aggregation is required or suggested in this situation, allowing for full view of parent-child relationships. Our assumption is that identification of units within a sealed shipping container would be through the data relationship that is reported only, and not through placing unit serial numbers on the shipping label. The latter would be a security risk where verifiable serial number information could be copied by bad actors without opening the shipping container. Aggregation, or capturing and maintaining the parent-child relationships between separate packaging levels of a product, is a commonly used system but generally not a regulatory requirement. RxGPS requests further TGA and review consideration of this approach.

QR Codes and 2D Datamatrix on The Same Package Will Cause Confusion

Page 11 of the Guidance for TGO 106references QR Codes and 2D Datamatrix on the same package.

> "QR codes are permitted to be present on the same labelling as a data matrix code and may contain the same information as the data matrix code, some of same information, or none of it. However if the QR code contains a number or link that is unique to the unit of medicine it is printed on, the unit is considered to be serialised and a DataMatrix must be printed containing the serial number."

RxGPS understands that existing QR codes are used to link to product information pertaining to a product identified by its GTIN. Linking information to the product information repository could be embedded in the 2D datamatrix in order to save label space by having all information in one barcode. This could also eliminate confusion among downstream owners of the package as to which barcode should be scanned. Additionally, this would further place the serialization information, as well as links to product information into a globally standard GS1 format, the 2D datamatrix. RxGPS requests TGA investigate linking information to the product information repository embedded in the 2D datamatrix.

Conclusion

Serialization is a tool that, if leveraged appropriately, can have great benefits to supply chain security and patient safety. Pharmaceutical packaging scenarios can be complex and varied across global markets. This complexity can lead to confusion when regulatory requirements requiring serialization and traceability do not clearly distinguish the packaging levels that are required to be identified, verified, and traced. Utilizing trade terminology in global regulations, while providing the flexibility for manufacturers to respond to in-market dynamics, will minimize confusion and promote successful, efficient global trade.

RxGPS would welcome the opportunity to share our experiences with you and discuss TGA's plans for pharmaceutical product labelling and data exchange. If you are willing to have such a conversation, please contact me and we can arrange a time to discuss this important issue.

Best regards,

[redacted]

Eric Marshall, Advisor to RxGPS

[redacted]