

INTERNATIONAL COALITION OF MEDICINES REGULATORY AUTHORITIES (ICMRA) SUPPLY-CHAIN INTEGRITY PROJECT

Recommendations on Alignment of Existing and Planned Track and Trace (T&T) Systems to Allow for Interoperability

Adopted by the ICMRA on 25th October 2017

1. Background

ICMRA participating regulatory authorities work together to:

- address current and emerging human medicine regulatory and safety challenges globally, strategically and in an on-going, transparent, authoritative and institutional manner;
- provide direction for areas and activities common to many regulatory authorities' missions;
- identify areas for potential synergies;
- wherever possible, leverage existing initiatives/enablers and resources.

ICMRA also provides a global architecture to support enhanced communication, information sharing and response to crisis and address regulatory science issues among health regulatory authorities.

Supply-chain integrity was identified in November 2015 as an ICMRA priority. ICMRA's focus is currently on the alignment of existing and planned Track and Trace (T&T) systems, with a view to facilitating their future interoperability, as to date, existing T&T systems for medicines have been designed with a national or regional focus only.

Building on the work undertaken on this topic by WHO through its Member State Mechanism on SSFFC Medical Products, ICMRA has collected additional information among ICMRA members and the mechanism participating authorities on several technical and regulatory aspects of existing and planned T&T systems. A summary of the results obtained is presented in annex 1.

These results provide a global overview of how existing and planned T&T systems for medicines have been planned and designed so far. The analysis and recommendations presented in this paper are informed by these results, the work of WHO and the expertise of the working group members.

2. Objectives

The rapid exchange of regulatory information among national authorities is integral to the protection of the supply chain integrity and to the protection of patient safety. T&T systems enable such rapid exchange of information among regulatory authorities along the supply chain.

T&T systems allow tracing transactions resulting in a change of ownership of a given health product thus showing the supply chain lineage of health products. By establishing a common language among the supply chain regulatory and industry actors, it directly supports the identification and management of risks associated with counterfeit or substandard health products and enables enhanced pharmacovigilance. It can also contribute to further mutual reliance in risk-based decision-making as it increases certainty about the health product and the industry party at stake in particular health and safety risk situations (e.g. facilitation of recalls, detecting fraud, monitoring internet sales).

Interoperability is defined, for the purpose of this paper, as the ability of T&T systems to exchange information and make use of the information received from other systems. Interoperability is paramount to achieve outcomes associated to T&T systems, and the global advantages for regulators associated with such systems only go as far as the level of interoperability of systems put in place by the different national and regional authorities. In the absence of global alignment on technical recommendations, there is a proliferation of different T&T systems which impacts interoperability.

Differences in national and regional T&T systems add additional complexity in tracking products globally in the event of a defect, a pharmacovigilance problem or a falsified product. It also imposes an additional burden on the industry which needs to adapt to multiple national or regional T&T requirements for product distributions.

The objective of this paper is to provide recommendations and strategic direction to improve the alignment of national and regional T&T systems for medicines in order to establish the conditions for the interoperability of systems already developed or being planned.

Once interoperable, T&T systems should complement other systems of exchange of information in place such as the Rapid Alert System for the PIC/S Member Countries, the WHO Drug Alert System or adverse drug reaction monitoring and reporting systems. While alert systems allow for the exchange of some detailed information about the risk associated with a specific product (e.g. root cause of a defect, kind of adverse reaction involved in a pharmacovigilance case, detection of falsified products etc.) T&T systems allow for real time exchange of information and can support the regulators community in taking coordinated actions to more efficiently mitigate the risks by providing traceability of the products involved.

This paper does not focus on the review of current alert systems and such review remains outside the scope of this paper. In the future however, as interoperability of T&T systems materialise, ways to enhance interactions between interoperable T&T systems and alert systems and related technical aspects should be considered further.

3. Scope

In determining the scope, it has been considered that:

- several T&T systems are already in place or in the final stage of planning and focus on human medicines;
- interoperability among T&T systems is dependent on the establishment of a set of minimal common global features or standards;
- different rules around confidentiality of business information and legal ownership of information may pose limitations on interoperability and transparency of information to be shared among jurisdictions via T&T systems.

Based on the above considerations, the scope of these recommendations focusses on:

- T&T systems for medicinal products for human use;
- exchange of information limited to cases where there is a serious threat to public health¹;
- full T&T systems (systems which allow full traceability of the product transactions from beginning to end of its supply-chain, including the agents in the middle e.g. distributors), end-to-end systems (systems which allow verification of the product status only at the beginning and at the end of its supply-chain) and systems in-between (partial verification between the beginning and the end of its supply-chain, in addition to end-to-end).

4. Identified challenges

The main challenges to interoperable T&T systems for medicines are technical in nature. Systems should be developed based on agreed common technical features or standards in order to enable interoperability.

In addition, information stored in the T&T systems databases is often confidential and in many cases cannot be exchanged freely among regulators.

Cost associated with the development of these systems has also been identified as a challenge by a number of jurisdictions.

¹ In order to overcome limitations due to differences in rules around confidentiality and legal ownership of information, it is envisaged that only information limited to cases where there is a serious threat to public health will be exchanged among regulators through interoperable T&T systems. A definition of serious threat to public health is outside the scope of this paper, which sets general principles to be followed to allow for interoperability; the detailed sort of information that will be exchanged among the T&T systems will be the subject of further discussion.

Finally, like any multi-jurisdiction initiative, political consensus will be needed if interoperability between T&T systems is to be achieved.

5. Prospective public health benefits of interoperability of national and regional T&T systems

Interoperability of national and regional T&T systems could allow traceability of products and batches throughout the global supply-chain and minimise patients exposure to risk associated with defective health products through immediate notification of products and batch numbers related to a serious safety incident throughout the interoperable systems.

- Enhanced traceability

There are many cases where regulators can benefit from knowing where the product has been before reaching their jurisdiction and/or from real time localisation of products outside their jurisdiction. For example, this can support regulators in identifying the origin of quality and safety issues associated with a product, and informing health risk mitigation measures.

Traceability information can also support investigation of a suspect quality defect, pharmacovigilance or falsified incidents, and real time localisation of products can support regulators in addressing drugs shortages, as they would be better positioned to localise in real time where similar products are.

- Minimising patients exposure to risk associated with defective health products

Immediate notification through T&T systems has the potential to minimise patients' exposure to defective and counterfeited products, by facilitating the identification of falsified or substandard products through the use of standardised product codes and batch numbers along the supply chain.

Once the immediate notification of a product quality and safety issue has gone in real time through the systems, regulatory authorities are better positioned to take fast actions in their jurisdiction and concerted risk mitigation actions with regard to this products across all the markets where the product is distributed, and as appropriate at the different points of the supply chain. For example, at the end of the supply chain pharmacists scanning a product which has been the subject of a notification can receive a warning message at the time of dispensing the products and can take action to comply with regulatory requirements in place.

Some examples of possible scenarios which illustrate and explain the benefits arising from interoperability of T&T systems are presented as annex 2.

6. Recommendations on common technical T&T systems features to enable interoperability

Described below are common technical features recommended for T&T systems for medicines, which would enable interoperability between T&T systems.

- Standardized information included in the carrier

Every pack of medicinal product on the market should carry some common standardised information, including: an International Common Product Identifier, International Batch Number and expiry date.

Further information (e.g. serial numbers, reimbursement numbers etc.) can be included according to national/regional requirements, but are not essential as regards interoperability of the systems. Information is exchanged among the systems at batch level; exchange of information at pack level (serial numbers) would make the recommended common technical features burdensome without adding much value from a global public health point of view.

- International Product Identifier (independent from name of product in the various regions)

A common international product identifier should be established in order to identify the same product (same active substance, pharmaceutical form, dosage, Marketing Authorisation/Registration Holder), independently of the commercial (brand) name used in different countries/regions. It is recommended that the common international product identifier is based on internationally recognised standards, such as the ISO Identification of Medicinal Products (IDMP) standards.

- International Batch Number

Together with the International Product Identifier, a common International Batch Number would allow for unequivocal identification of a batch among the interoperable systems, when information is shared.

- Expiry date

Information on the expiry date of relevant batches should be exchanged among the interoperable systems, to avoid expired batches being dispensed, e.g. in case batches packaged in different languages (maybe using different alphabets) travelling from one jurisdiction to another in case of shortages.

- Common global data coding standards

A data coding standard is the data structure, syntax and semantics allowing identification, capture and sharing of data. It is essential for interoperability of T&T systems that a common global data coding standard is used. Systems should be based on a single internationally agreed data coding standard or on coding standards that allow for interoperability.

- Common data carrier

It is recommended that the same kind of data carrier is used throughout the interoperable systems. The 2D data-matrix code is one of the economical solutions in use in most of the current and planned T&T systems and appears to be the most cost-effective solution.

7. Next Steps

ICMRA has the potential to add value to the development of interoperable T&T system supporting the integrity of the global supply chain by:

- building consensus among its members on the above common technical features as a prerequisite to the establishment of new national and regional T&T systems aligned for becoming interoperable;
- identifying the appropriate technical international fora that can bring together technical experts to undertake further work on the development and adoption of common standards for T&T systems and identify technical solutions to enable interoperability among systems;
- identifying synergies with other related initiatives such as big data and pharmacovigilance, the adoption of IDMP standards, ongoing discussion in other fora such as the WHO SSFFC Member States Mechanism, Australia-Canada-Singapore-Switzerland (ACSS) Consortium, the International Pharmaceutical Regulators Forum (IPRF)², MEDICRIME Convention etc.

It is recognised that existing systems cannot be easily modified to comply with the principles in this document, so solutions should be identified in order to allow interoperability of existing systems. Evolving technologies should be used as an opportunity for convergence of the systems when they are updated.

Therefore, it is proposed that as next steps ICMRA discusses and identifies a technical expert body to enable implementation of the principles in this paper, with the mandate to:

- develop more detailed guidance on common technical features for enabling interoperability of T&T systems;
- develop capacity building tools for jurisdictions wishing to implement T&T systems;
- develop solutions/tools for both new systems (designed and built according to the principles in this paper) and already existing systems (built or designed before this paper was published, and therefore only partially complying with the principles) to become interoperable;
- examine further technical aspects related to implementation of interoperability among T&T systems and interactions between alert systems and T&T systems;
- identify solutions related to obstacles to exchange of information between different T&T systems including data ownerships and confidentiality issues.

² As of January 2018, the International Pharmaceutical Regulators Forum (IPRF) will be merged with the International Generic Drug Regulators Programme (IGDRP) to form the International Pharmaceutical Regulators Programme (IPRP).

Annex 1

ICMRA – T&T QUESTIONNAIRE – SUMMARY OF RESULTS

General information

The ICMRA drafting group received answers on the questionnaire from **22** authorities: Argentina, Australia, Brazil, Canada, China, Costa Rica, Denmark, EMA-EC, Fiji, Ireland, Italy, Japan, Mexico, Nigeria, Russia, South Africa, Spain, Sweden, Switzerland, UK, Uruguay, USA.

4 of these authorities are non-ICMRA countries: Argentina, Costa Rica, Fiji, and Uruguay.

Of the 22 responses received, **5** indicated that no T&T system is existing or planned in their jurisdiction (Australia, Costa Rica, Fiji, Switzerland and Uruguay).

It should also be noted that answers to the questionnaire received from 6 EU agencies (EMA-EC, Denmark, Ireland, Spain, Sweden and UK), refer to the same EU-wide T&T system under implementation. Although Italy is an EU country, there is a national system already in place in Italy, which will converge into the EU one by 2025. The response received from Italy refers to the already implemented system. Taking all this into account, the answers received to the questionnaire refer to **12** existing or planned systems in: Argentina, Brazil, Canada, China, European Union, Italy, Japan, Mexico, Nigeria, Russia, South Africa and USA.

Q1. Is a T&T System for the tracking of medicines through the supply chain in place or planned in your country/region?

Of the **22** answers received, **5** indicated that a system is already in place (Argentina, Canada, Italy, Japan and US).

5 responses indicated that currently there is no plan for a T&T system to be implemented (Australia, Costa Rica, Fiji, Switzerland and Uruguay), although it was indicated by some of these countries that some discussion on the possibility of having a T&T system are on-going.

In the other jurisdictions a system is planned (**12** responses, corresponding to **7** systems by grouping the EU answers).

Q2. What is its primary purpose of the system?

The primary purpose of **11** existing or planned T&T systems have been described in the responses received.

Although described with different terminology, the common primary purpose of most of the systems (**9** systems) is/will be the prevention of illegal medicinal (drug) products entering the distribution supply chain, after manufacturing or importation.

The aim of **1** system will be more oriented at facilitating follow-up of marketed products (recall, inspections, quality monitoring), while another **1** will be implemented in order to monitor and detect availability of medicines.

Q3. Is the system regulated?

12 respondents answered that their system is regulated (corresponding to **8** systems grouping the answers received from the EU), while **4** systems are not/will not be regulated.

Q4. What is the date of implementation? (Established or estimated).

The answers received indicate that most of the planned systems are either already implemented (**5** systems) or will be implemented in the next 2 years (**4** systems). Implementation of **1** planned system will take longer (up to 5 years) and for **2** planned systems the implementation date has not been established.

Q5. Are the coding standards which are used/planned for the system global or domestic standards?

8 responses indicated the use of global standards (grouping responses for the EU system) and 4 indicated the use of domestic standards.

Among the global standards in use/to be used, compliance with ISO standards 16022 (Data Matrix) are mentioned several times, as well as the use of the GS1 code for identification of products.

Q6. What is the data carrier/data matrix used/planned (e.g. linear barcode, 2D barcode etc.)?

Responses were received for 12 existing or planned systems (grouping responses for the EU system). 4 responses indicated the use of 2D barcodes, 2 indicated the use of either 2D or linear barcodes, 1 the use of 2D/linear barcodes or RFID and 1 linear barcodes. 3 responses refer to the use of the GS1 coding standards and 1 to the European Article Numbering Code 13 (EAN 13) being used as an accepted standard.

Q7. Please provide information on the database(s) in use/planned to be used in the context of traceability systems for medicines, including ownership, management framework, any other information that could be useful for the purpose of this survey

Responses were received for 11 existing or planned systems (grouping responses for the EU system). Regarding the database ownership, responses indicated that in 6 cases the owner will be the regulatory agency or other governmental organisation. In 2 cases the ownership will be with stakeholders (pharmaceutical industry, wholesalers). 3 responses indicated that this decision has not yet been made. Regarding management of the database, in 3 cases the agency or government will manage the database, in 1 case it will be managed by stakeholders with agencies supervision and in 1 case it is indicated that the management of the database will be outsourced. In the other cases this info was not provided.

Q8. Please provide information on ownership of data and access to data (e.g. for regulatory agencies, pharmaceutical companies etc.)

Of the 22 countries surveyed replies were received from 16 of these. Five responses should be considered together as they related to the system being introduced across the EU. Responses were related to 12 existing or planned systems (grouping responses for the system planned in the EU).

While in 2 jurisdictions the data ownership was yet to be decided, 6 responses indicated that government agencies owned the data storage system whilst 7 were established by the pharmaceutical industry (2 grouping the answers received from the EU).

In many cases comments were received that in the majority of systems data access was restricted to either the regulatory body or at least to the entity who generates the data within the system (11 responses). In 2 cases the data are publicly available and 2 countries have yet to determine who will be able to access the data. In 1 response the data were said to be able to be accessed by the regulator, the industry and members of the public.

Q9. Provide any further available information on the software in use/planned for the implementation of the T&T system which could be useful in the context of this survey

Of the 22 countries surveyed 12 responses were received (9 grouping responses received from the EU). The majority of them (10 responses, 7 grouping responses received from the EU) indicated that no further information could be supplied as the systems had yet to be determined.

Oracle systems and links to these were mentioned in 2 responses.

Q10. Provide information on the products covered by the system (e.g. all medicines for human use, prescription medicines only, medicines for human and veterinary use, medical devices, and other products)

Of the 22 countries surveyed 16 (12 grouping responses related to the EU system) responded to the question.

7 respondents (3 grouping responses related to the EU system) have indicated that only medicines available on prescription will be impacted. 5 respondents said that the system being introduced would impact on all human medicines, while 2 respondents said all medicines (human and veterinarian) and medical devices. 1 country had indicated that they were still considering the scope of the scheme being introduced and 1 country said that the scheme would start with high cost medicines (currently one third of all medicines on the market) and would increase coverage in a gradual manner.

Q11. Are there obstacles to sharing of data in the T&T database with other T&T systems (e.g. legal, operational etc.)?

There were 15 responses to this question from the 22 countries surveyed. Each country did not necessarily respond under each heading.

Under the “legal obstacles” category, while some countries are still in discussion regarding this, the key issue to emerge was that of data access and data confidentiality (9). 4 respondents were still looking at what issues may emerge.

Under the “operational obstacles” category views appeared to be polarised with 4 saying there would be no problems and 4 that interfaces and data-exchange would be problematic. Those who believed there were operational problems with what was required felt that political will to harmonise systems would be a big feature. 4 further responses said that this was still to be considered.

Q12. What costs are envisaged by the implementation of a T&T system, who will be impacted by the costs and will this influence the ability of patients to access medicines?

There were 15 responses received from the 22 countries surveyed. Concerning the system and hardware costs 7 respondents indicated that there would be substantial costs associated with the implementation of T&T systems. 8 respondents indicated that there would be associated costs throughout the pharmaceutical supply chain. 5 respondents indicated that the costs will be borne by the pharmaceutical industry.

In relation to the ongoing availability of medicines 3 replies indicated that this could have a negative impact whilst 1 respondent felt that the system would increase patients’ access to medicines. 4 respondents indicated that no or limited effect on availability is foreseen.

1 respondent indicated that government will oversee the introduction of the system whilst allowing the industry to play a full part in the development.

Q13. Further information

Please provide any further information on T&T systems for medicines in your country/region which are not covered by the questions above but could be useful in the context of the ICMRA supply-chain project e.g. practical use of the traceability system to date, problems/issues that may have arisen but have been prevented by the system, impact on different actors in the supply chain (this list is not exhaustive).

12 responses were received to this question. Many of these raised similar issues which would need to be considered. These covered:

- Small containers could be difficult to apply 2D data matrix codes to.
- Complexity of the medicines supply chain could be a barrier
- Aggregation of codes was needed
- Documentation for everyone in the supply chain was important
- Interoperability of systems was mentioned
- Timeframes being manageable
- Capacity planning was important in all sectors of the medicines supply chain
- Security of the system.

Annex 2

- Scenario 1

A product is produced in country A, and exported to countries X, Y and Z.

Regulators from country X discover during inspection of the manufacturer that batches of the product have been produced with a counterfeited active substance.

Information is input from country X in the system, and shared in real time with regulators in countries A, Y and Z. Pharmacists dispensing the affected batches to patients in countries X, Y and Z receive an alarm message when scanning the barcode.

- Scenario 2

Same as above but the counterfeit is discovered by country A (where the manufacturer is located).

- Scenario 3

There is a serious quality defect or Ph.Vig. problem that makes recall of all batches of a product from a certain manufacturer necessary at all levels. The information is input by the country where the product is manufactured in its system and shared in real time with all the other systems. Supply to patients is stopped immediately, while the procedures for the recall are started.

- Scenario 4

There is a shortage of a product in a certain country. Regulators in this country can query the system and get information in real time on where batches of the same product (independently of the brand name) are located.