Bar-codes, QR codes and Vaccine Vial Monitors in the context of COVID-19 vaccines

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Background

As vaccines, therapeutics and other health products for the prevention and treatment of COVID-19 become available, they will be distributed in exceptional circumstances. Questions have been raised about the best approach to leverage technologies for automated product traceability and information sharing. For the purposes of this document, the discussion includes two-dimensional (2D) bar-codes, quick-response codes (QR codes) and serialization technology. It also includes references to Vaccine Vial Monitors (VVMs). The focus is on the context of COVID-19 vaccines and possibly other products distributed to low- and middle-income countries (LMICs), where significant scaling up and investment towards functional systems to use such technologies would be needed. There are issues of costs, usability, risks and benefits to consider, which may change over time. As such, this will remain a working document.

This document provides a high-level position from WHO and it has been aligned with WHO regulatory resource documents. It intends to clarify an overarching position on the use of automated traceability technologies, including differentiating between various use cases, such as primary versus secondary packaging. The document considers the technologies in the context of supply chain traceability, regulatory requirements for labels and leaflets as well as use in operational research to support future applications of these technologies. It does not intend to supersede any current or future regulatory guidance on the subject(s) nor other official technical guidance or policies from Member States, UN agencies or WHO technical departments. Recognizing that other reference materials are available for that purpose, it does not attempt to define the various categories and sub-categories of digital identifier or information exchange technologies.

Definitions

For the purposes of this discussion, bar codes refer to 2-dimentional data matrix labels used for identification, information capture and verification of products in traceability systems. QR codes are a separate technology and have multiple applications; however, this discussion is focused on the use case of providing access to electronic versions of product information. Specific definitions of various bar code and QR code technology and are available through GS1[1] . Vaccine Vial Monitors (VVMs) are affixed to

[1] Glossary of Specifications, GS1, 23 October 2020:
https://www.gs1.org/sites/default/files/docs/barcodes/GS1_General_Specifications.pdf

vials and they provide an indication of cumulative temperature exposure over time to support cold chain management of vaccines[2].

In addition to the above clarifications on the technologies, it is also acknowledged that certain language may have multiple interpretations across the documents referenced herein. This document will not attempt to redefine language in those situations, but rather is focused on making the intent of the language clear for the purposes of this discussion. For example, a "preferred characteristic" in a procurement tender document allows for a proposal to be considered if it does not fully comply, while a mandatory characteristic would disqualify the proposal. In documents that describe programmatic needs, the use of language including "critical" versus "preferred characteristic" may refer to the degree of public health importance of a certain characteristic and would be used to guide product development and other decisions. The language may represent different interpretations, but in both cases, they support the same result i.e., the selection of a vaccine that to the degree possible has accounted for important characteristics.

For clarity, and in general, a "preferred" characteristic has significant public health impact, and all efforts should be made to include the preferred technology. "Optional" use would be a lesser priority and should be considered to the extent that a clear benefit could be achieved. "Encouraged" use would apply to applications that are low risk, low cost with potentially high value, subject to monitoring and evaluation of their use. Given that part of this discussion target vaccine vials, which are limited in size and readability, priority will be to ensure that statutory information is included. Prioritizing between optional technologies is not discussed here.

Summary

Four main position points and other discussion areas follow, including:

1) Use of 2D bar code technology on secondary packaging in the context of traceability systems as a preferred product characteristic;
2) Optional use of QR code technologies on primary and/or secondary packaging for supplemental electronic access to label and leaflet information, but not in lieu of related statutory requirements;
3) Use of Vaccine Vial Monitors (VVMs) as a preferred product characteristic;
4) Systematic approaches for the development of pilot evaluations or other operational research in the optional uses of these technologies, for example for safety monitoring.

The document does not define statutory label requirements COVID-19 vaccines, which will be addressed in separate documents.

[2] *What is VVM and how does it work,* WHO, https://www.who.int/immunization_standards/vaccine_quality/What%20is%20VVM%20and%20how%20does%20it%20work.pdf

Traceability systems

Traceability technology, including **bar coding is a preferred characteristic on the secondary packaging for vaccines.** This has been articulated by UNICEF in pre-tender discussions, where the specification is for the use of 2D bar codes containing information about the vaccine product and lot, as well as serial numbers to uniquely identify every individual secondary package. Recognizing the position of UNICEF as the primary procurement partner of COVID-19 vaccines, WHO supports UNICEF's position[3] to accelerate its existing plans to integrate the use of bar coding on secondary packaging of vaccines by adding this as a preferred characteristic in tender documents. For COVID-19 vaccines, the preferred data standard will include serialization capability, which accommodates validation through unique serial numbers. This may eventually apply to therapeutics and other products. The purpose of this preferred characteristic is to support ongoing efforts to scale up traceability systems in countries that receive COVID-19 vaccines, particularly for combatting distribution of any sub-standard or falsified products.

Including bar codes on primary packaging for traceability purposes remains optional. Acknowledging the interest in this innovation, as highlighted by Gavi's Vaccine Innovation Prioritization Strategy[4], inclusion on the primary packaging is optional; however, if implemented, they may not take the place of statutory information printed on labels or leaflets. There are multiple uses of bar codes and QR codes (see below); however, systems requirements to make use of bar codes on primary packaging for traceability are significant investments that take time to develop and they exist in very few markets. This use case has been limited to some high-income markets and some medical products, including devices and injectables.[5] Research on various uses of identifiers on primary packaging may be beneficial as discussed in the section below on pilot evaluations and tests.

Quick-response codes (QR codes) for label and leaflet information

The use of **QR codes on primary packaging is optional, but not in lieu of statutory requirements for printed information on vial labels.** QR codes are intended to provide rapid access to electronic versions of printed information, such as leaflets and labels, or to provide access to additional information that is not physically available on the package e.g., such as updated product information, expiration dates, or supplemental translations of leaflet information; however, it is noteworthy that this would be an unprecedented use of QR codes, particularly in LMICs.

Regarding vial labels, the route of administration, date of manufacture/expiration, batch number, doses per vial, dosage, temperature requirements, at a minimum, should remain visible on the primary container label to facilitate vaccine management. QR codes can be used to supplement this information for national regulators, but not as a replacement.

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[3] *COVID-19 Supplies,* UNICEF, September 2019. https://www.unicef.org/supply/stories/gavi-announcement-vaccine-manufacturer-gs1-compliance

[4] *The Vaccine Innovation Prioritization Strategy*, GAVI, September 2020. https://www.gavi.org/our-alliance/market-shaping/vaccine-innovation-prioritisation-strategy

[5] *Discussion paper on medicines identification requirements on primary level packaging using GS1 standards.* GS1, March 2019. https://www.gs1.org/docs/healthcare/position-papers/Discussion-paper-on-medicines-identification-requirements-on-primary-level-packaging-using-GS1-standards-final.pdf

Separate guidance will indicate the statutory label requirements, including communication of changes to label information, multi-language leaflets and other issues.

The inclusion of QR codes on secondary packaging is highly encouraged, and similarly, not in lieu of statutory information. The extent to which this would enhance supply chain management and provide enhanced access to leaflet information (e.g., for training purposes) has not been studied, but assuming that costs to add the information to secondary packaging would be minimal, it is encouraged. The specification for optional inclusion on secondary packaging is to be determined.

Regulatory implications

Regulatory implications are important considerations in the above recommendations. Bar codes (in their various technical forms) on secondary packaging for traceability are used in many markets and this use case is recognized by many stringent regulatory authorities. The above recommendations are generally consistent with existing use cases as well as the WHO draft guidance on traceability systems[6].

On the other hand, there are very few markets that require unique identifiers on primary packaging and to date, it remains limited to a small number of products. There is also an absence of regulatory support for substituting label or leaflet information with QR codes or 2D bar codes. The use of QR codes to supplement label and leaflet information is considered optional and only to the extent that it does not replace nor impinge on the usability or readability of other statutory information required on the label or leaflet[7]. Examples of considerations in this recommendation, include those below:

- A substitution of a QR codes for statutory printed information is not an established system, which creates liability risks, particularly around unauthorized use;
- Information provided in a QR code must be approved by the regulator in addition to printed labels and leaflets and may add to processing costs.
- Regulatory discussions are ongoing in considering the potential risks and solutions specific to COVID-19 vaccines.

Vaccine vial monitors (VVM)

The use of VVMs on vaccine vials is a preferred characteristic[8] for COVID-19 vaccines. This is consistent with the long-standing recommendations for the use of VVMs[9], including extensive training in health care workers in LMICs to monitor vaccine cold chain management before administration. Reference

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[6] *Policy brief on traceability of health products*, WHO, December 2019, https://www.who.int/medicines/regulation/traceability/7OCT19draft-WHO-policy-brief-on-Traceability-of-Health-Products.pdf?ua=1

[7] *Mobile scanning and other technologies in the labelling and package leaflet of centrally authorised medicinal products,* European Medicines Agency, November 2018. https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/mobile-scanning-other-technologies-labelling-package-leaflet-centrally-authorised-medicinal-products_en.pdf

[8] WHO Target Product Profiles for COVID-19 Vaccines, WHO, April 2020. https://www.who.int/blueprint/priority-diseases/key-action/WHO_Target_Product_Profiles_for_COVID-19_web.pdf

[9] Generic Preferred Product Profiles for Vaccines, v.2.1, WHO, March 2015. https://www.who.int/immunization/policy/committees/VPPAG_Generic_PPP_and_Workplan.pdf?ua=1

documents refer to this as a “critical” and in others as a “preferred” characteristic. The differences in language do not suggest that there are disagreements in prioritizing the use of VVMs. It is listed as a preferred characteristic in tender documents to acknowledge that there may be cases where the VVM technology may not be suitable, for example, where stability data of a candidate vaccine does not correspond to any existing VVM categories. It is important to note that the inclusion of a VVM is not a substitute for a well-monitored cold chain throughout the distribution process.

Language

Multi-language leaflets are expected[10]. The use of single language or QR codes to transmit national languages translations cannot substitute for multi-language leaflets where they are required. Using a QR codes to make approved translations more widely available is encouraged but not required. Languages other than those required by WHO may be required by National Medicines Regulatory Authorities (NMRA) in recipient countries. At present, it will be up to the NMRA how they accept translations and this subject will be addressed in other documents.

Bar codes or QR code in scale ups and demonstration projects

Expanding the use bar code and QR code innovations should be aligned and build upon existing initiatives, should be scalable and should contribute to future use of innovations. UNICEF has proposed a specification for a minimum basic traceability system to support countries that wish to scale out their use of these technologies, especially for the purpose of avoiding substandard and falsified medicines. The procurement requirements that UNICEF have published for 2D bar coding on secondary packaging as a preferred characteristic are consistent with the minimum system that has been proposed. Providing support to countries that have interest in expanding their use of traceability systems is encouraged.

Regulatory agencies in countries should be engaged and involved in considering the applicability of these technologies within national COVID-19 preparedness and response plans. Demonstration projects where bar codes and QR codes are used on primary packaging are under discussion. As this technology is of interest, demonstration projects could stimulate uptake in some contexts; however, the level of maturity across different markets is highly variable, which would affect the applicability of any innovation. It should also be noted that pilots and demonstration projects should be systematically managed, developed, and reported to avoid fragmenting national systems and efforts, and especially to prevent unauthorized uses of products and information. Additionally, pilots and demonstration projects should be developed with a view to contributing to specific, agreed goals and a pool of evidence that will systematically support the development of further innovations.

Costs of innovation

Cost information on implementing new systems, pilots and tests in countries that lack capacity should be developed. For countries that have no minimal viable solution for traceability in place, implementing new systems or pilots and tests can strain national resources. Estimating the end-to-end financial

[10] WHO Prequalification of Medicines, 2020. https://www.who.int/medicines/regulation/prequalification/prequal-vaccines/about/en/

requirements is important and should also address local technical capacities, reliability of infrastructure, personnel requirements and long-term operational costs to avoid fragmenting local resources. This area is critical in considering scaling out of existing systems as well as in pilots or tests of new applications of innovation.