How can unit-level traceability of primary packaging improve pharma operations?

Access Partnership

Important Notice on Contents

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The challenge: Improving operational efficiency and resilience in the complex pharmaceutical supply chain

The pharmaceutical industry operates within a complex ecosystem, facing ever-increasing demands for higher capacity and improved efficiency and quality. To thrive in this landscape, pharmaceutical operations need to overcome several challenges, including enhancing Overall Equipment Efficiency (OEE), ensuring a robust supply chain with no drug shortages, adapting to evolving regulatory frameworks, and embracing technological advancements like Pharma 4.0.

Growing demand for healthcare, accelerated by the COVID-19 pandemic, has created a need for pharma manufacturers to rapidly increase their capacity. However, this is not easily achievable without significant investment and planning, and even then, it is unlikely that capacity could be ready in time to deliver the market demand.[1] Therefore, optimizing OEE is a critical imperative for pharmaceutical manufacturers aiming to maximize productivity and minimize waste using existing capacity. Research has found that OEE of sterile manufacturing sites has decreased by 2.7 per cent over the last five years, with a median value of only 23 per cent.[2] This is less than half of the best-in-class sites, and improved OEE is critical to enhancing the resiliency of the pharmaceutical supply chain.

At the same time, the overall pharmaceutical supply chain is intricate, involving numerous stakeholders and processes. Ensuring a seamless flow of drugs, free from shortages and disruptions, is paramount for the manufacturers. To address these concerns, regulatory bodies are developing new frameworks which go beyond the simple adherence to Current Good Manufacturing Practice (CGMP) requirements, such as Quality Management Maturity (QMM),[3] that could impose additional constraints on manufacturing operations. While these regulations are essential for the industry, they may introduce complexities and necessitate innovative approaches to compliance and operational excellence.

To address these challenges, the pharmaceutical industry is embracing the transformative potential of Pharma 4.0,[4] integrating digital technologies and advanced analytics to optimize processes and drive informed decision-making. It is, therefore, critical for manufacturers to understand the benefit of technologies before implementing them. However, as of May 2021, while 93% of pharma companies believe that their current business model requires a digital and analytics transformation to survive, only 17% are moving towards these aspirations due to a lack of a clear business case before undertaking the transformation.[5]

Unit-level traceability of primary packaging could be a foundation of Pharma 4.0 by offering unprecedented visibility and control throughout the supply chain. By tracing individual units, rather than relying on batch-level information, manufacturers can unlock efficiency gains, mitigate risks, enhance inventory management, and ensure seamless product traceability. Prefilled syringes, with their unique characteristics and critical role in healthcare delivery, serve as an ideal test case to explore the benefits of unit-level tracking. By delving into the specific context of prefilled syringes, the industry can gain valuable insights into the broader applicability and transformative potential of unit-level identification in pharmaceutical operations.

1 McKinsey (2023), “How sterile pharma manufacturers can grow capacity without capital investment”, Available at: https://www.mckinsey.com/industries/life-sciences/our-insights/how-sterile-pharma-manufacturers-can-grow-capacity-without-capital-investment

2 McKinsey (2023), “How sterile pharma manufacturers can grow capacity without capital investment”, Available at: https://www.mckinsey.com/industries/life-sciences/our-insights/how-sterile-pharma-manufacturers-can-grow-capacity-without-capital-investment

3 FDA (2022), “Quality Management Maturity: Essential for Stable U.S. Supply Chains of Quality Pharmaceuticals”. Available at: https://www.fda.gov/media/157432/download

4 ISPE (2017), “Pharma 4.0™”, Available at: https://ispe.org/initiatives/pharma-4.0

5 McKinsey (2021), “Leveraging digital and analytics in biopharma operations: Six principles”. Available at: https://www.mckinsey.com/capabilities/operations/our-insights/leveraging-digital-and-analytics-in-biopharma-operations-six-principles

The solution: Unit-level traceability of primary containers can help to improve operational efficiency

Unit-level traceability of primary containers provides real-time visibility and tracking of individual units throughout the supply chain, from production to distribution to the end-user. Recent research by Parenteral Drug Association (PDA)[6] has found that 68% of pharmaceutical companies considered marking primary containers to facilitate internal tracking of filling lines on a unit level. However, while some technologies exist for tracing primary containers, these have not yet been implemented at a large-scale manufacturing standard.[7] Unit-level traceability can improve the overall equipment efficiency (OEE) of manufacturing sites and throughput by making time-consuming operations (such as reconciliation) faster and identifying the causes of line stops and deviations at the unit level. By implementing unit-level traceability of prefillable syringes, the risks associated with counterfeits and diversions can also be reduced.

This chapter aims to help the pharmaceutical industry and regulatory agencies understand how unit-level traceability can benefit prefillable syringes. It also provides insight into the discussions that may occur at the unit level to improve controls and traceability of prefillable syringes from production to the patient, both before and after filling.

BOX 1

WHAT IS UNIT-LEVEL IDENTIFICATION AND TRACEABILITY?

Unit-level traceability (compared to batch-level traceability) refers to using product identifiers to track products electronically at the individual packaging level,[8] while serialization refers to the process of applying unique serial numbers to products for identification purposes. Some standard technologies used to ensure unit-level traceability include barcodes, data matrices and radio-frequency identification (RFID).

Unit-level traceability can be applied to both primary and secondary packaging. When applied to the secondary packaging at the end of the manufacturing line, individual packaging units can be identified and traced as they get dispatched to pharmacies, hospitals, and patients. Unit-level traceability needs to be applied to primary containers to identify and trace syringes throughout the supply chain. However, most existing serialization mandates limit traceability to the secondary packaging and the primary packaging is not individually traceable during the manufacturing process.

[6] PDA is an international non-profit industry trade group for pharmaceutical and biopharmaceutical manufacturers

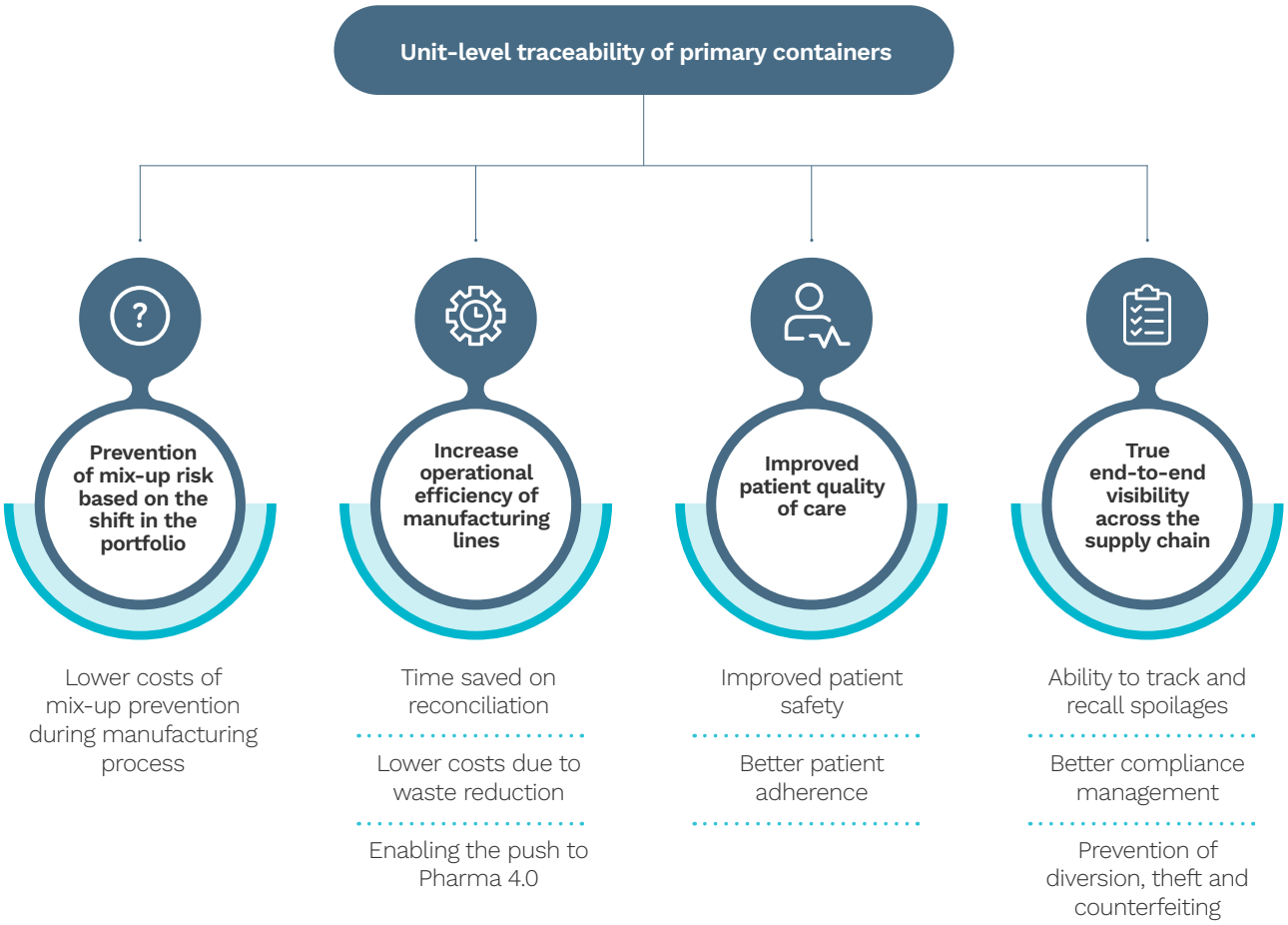
[7] ISPE (2021), Unique Identification on Primary Containers to Drive Product Traceability & Quality. Available at: https://ispe.org/publications/papers/unique-id-primary-Containers-drive-product-traceability-quality

[8] RFXCEL (2023), “DSCSA 2023: The Future of Pharmaceutical Traceability in the United States”. Available at: https://rfxcel.com/dscsa-2023/

The benefits of unit-level traceability of primary containers from four key operational areas have been identified based on a literature review and interviews with experts in the pharmaceutical manufacturing industry (Exhibit 1).

EXHIBIT 1

UNIT-LEVEL TRACEABILITY BRINGS ABOUT BENEFITS IN FOUR KEY OPERATIONAL AREAS:



Source: Access Partnership analysis

Prevention of mix-up risk based on the shift in portfolio

Unit-level traceability of primary containers allows manufacturers to better manage the risk of mix-ups to ensure safety and resilience of the supply chain. Manufacturers tend to use the same production lines for different drugs, and the same drug formulation in prefillable syringes can exist in up to 16 dosages,[9] increasing the risk of mix-ups happening due to a lack of traceability during the manufacturing process. Even with the current regulations which focus on unit-level traceability at the secondary container level post-production,[10] there are a high number of batch mix-ups being observed (refer to Box 2). Therefore, there is a significant risk in the manufacturing process where mix-ups of a single syringe can happen (Exhibit 2). In particular, during the packaging process, reconciliation issues can arise as often as once a week, leading to downtimes of up to an hour or two each time as time is needed in investigating the source of reconciliation. For instance, syringe(s) from another batch might be mixed with syringes from a new batch during the packaging process, resulting in reconciliation issues after the packing.[11]

[9] Voldrich et. al (2009), Encoding and reading of codes on glass containers for pharmaceutical and diagnostic products. Available at: https://www.ondrugdelivery.com/wp-content/uploads/2018/11/Jan2010.pdf

[10] Based on interviews with experts working in the pharmaceutical manufacturing industry and the filling machine manufacturing industry.

[11] Based on interview with an expert working in global platforms for parenteral networks at a global pharmaceutical company.

In the event of a mix-up, it becomes challenging to locate and identify the suspected item, and manufacturers will have to adopt a "full batch write-off" policy, incurring substantial financial costs. As a result, manufacturing companies have implemented multiple processes and protocols to prevent mix-ups, which requires additional resources and time. Implementing unit-level traceability at the primary container level has the potential to simplify these processes needed to avoid mix-ups (e.g., traceability at the nest level and quality protocols at different stages of the manufacturing line to ensure that instances of single syringe mix-up are reported, and the risk is significantly reduced),[12] leading to greater time savings and operational efficiency for firms. In addition, with unit-level traceability, individual units identified as problematic can be discarded separately rather than throwing out a whole batch, reducing the financial costs in the event of a mix-up.[13] Among pharmaceutical manufacturing companies considering implementing traceability of primary containers, 79% stated mix-up avoidance as a critical reason for doing so,[14] suggesting that the potential improvements in operational efficiency are significant.

EXHIBIT 2

UNIT-LEVEL TRACEABILITY FOR PREFILLED SYRINGES IS LACKING DURING THE MANUFACTURING PROCESS

Filling	Visual Inspection	Assembly	Labeling & Packaging
Automated process where syringes are placed in nests to be filled and stoppered by filling machines.	Visual inspection, which can be done by machines to detect any foreign particles	Includes assembling syringe components by ensuring sterility/ maintenance of sterility	Packing syringes in secondary packaging, which are serialized to be distributed
No unit-level traceability	No unit-level traceability	No unit-level traceability	Good unit-level traceability after the packaging but not before

Source: Access Partnership analysis

[12] Based on interview with an expert working in packaging solutions at a global pharmaceutical company.

[13] ISPE (2021), Unique Identification on Primary Containers to Drive Product Traceability & Quality. Available at: https://ispe.org/publications/papers/unique-id-primary-Containers-drive-product-traceability-quality

[14] PDA (2019), 2019 PDA Traceability of Primary Packaging Survey. Available at: https://www.pda.org/bookstore/product-detail/5467-2019-traceability-packaging-survey

BOX 2

CASES OF MIX-UPS DETECTED DURING THE INSPECTION PROCESS[15]

Since 2008, FDA has observed 881 cases of mix-ups during inspections of manufacturing facilities, including 22 cases in 2022. The mix-ups occurred due to various reasons, including (i) inadequate size for operations, which would be necessary to prevent contamination or mix-ups; (ii) facilities not adequate to ensure the prevention of mix-ups that could reasonably be expected to have an adverse effect on product quality; (iii) deficient separation or defined areas to prevent contamination or mix-ups during the storage of in-process materials as well as during the packaging and labelling operations; (iv) insufficient spatial or physical separation from operations and other drug products to prevent mix-ups and cross-contamination; and (v) buildings lacking the adequate space for the orderly placement of equipment and materials to prevent mix-ups between drug products and labelling. While the share of mix-ups as cause for citations is small (0.4% of all citations), the number remains significantly higher than zero. In addition, currently, the reported mix-ups are full batch mix-ups. With the current processes, a mix-up of an individual unit is almost impossible to detect, and therefore, is likely to be underreported.

Case study 1: Container labelling mix-ups[16]

In 2017, a pharmaceutical firm recalled more than 203,136 prefillable, single-use syringes at the hospital level due to incorrect labelling. They were reportedly mislabelled as Midazolam, a sedative used to relax patients before surgeries or medical procedures, but contained Ondansetron, which treats nausea and vomiting. This mix-up was labelled as a Class I recall.

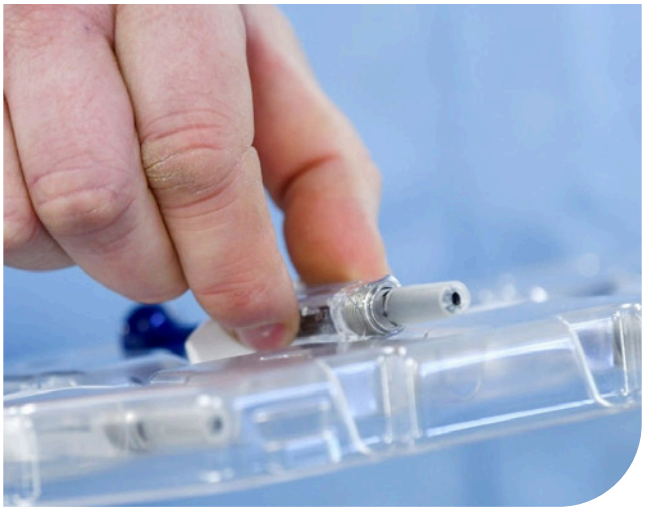
Case study 2: Manufacturing labelling mix-ups[17]

In December 2022, a pharmaceutical firm recalled a single lot of Daptomycin for Injection 500 mg/vial, and Daptomycin for Injection 350 mg/vial product contained in cartons. The company received a product complaint report from a hospital pharmacy that vials labeled as "Daptomycin for Injection 500 mg/vial" were found in cartons labelled as "Daptomycin for Injection 350 mg/vial".

Increase operational efficiency of manufacturing lines

Time saved on reconciliation

As part of the manufacturing process, manufacturers need to ensure that the same number of prefillable syringes are present at the start and end of the production process. This process, called reconciliation, is a process to prevent mix-ups and is an important part of asset tracking. Unit-level traceability at the primary container level would enhance the visibility of prefillable syringes during the filling process and reduce the amount of resources needed to trace missing syringes in the event of a reconciliation issue. Fast-tracking and simplifying the reconciliation process, especially in case of issues, could potentially increase the OEE, which would reduce the need to invest in new capacity to meet the demand.



[15] This was analysed using US FDA's Inspectional Observation Datasets for 2022, available at: https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/inspection-references/inspection-observations

[16] Based on the U.S. Food and Drug Administration Recall Information Search. Recall ID: D-0152-2018. Available at: https://www.accessdata.fda.gov/scripts/ires/

[17] Based on the U.S. Food and Drug Administration Recall Information Search. Recall ID: D-0131-2023. Available at: https://www.accessdata.fda.gov/scripts/ires/

Lower costs due to waste reduction

Another potential advantage of unit-level traceability would be to improve efficiency and minimize waste. Unit-level traceability helps to identify the units affected by an issue and therefore scrap only the targeted units instead of the whole batch. In addition, ensuring a data-driven approach using unit-level traceability can reduce waste by highlighting unexpected issues and expected faults in the manufacturing process before they occur, which may result in reduced yield. Analyzing unit data can highlight areas where most waste is produced to allow manufacturers to make adjustments and avoid breakdowns, batch scrappage and unnecessary energy consumption.

Enabling the push to Pharma 4.0

Pharma 4.0 focuses on improving the operations of manufacturing sites through integration of advanced technologies like the Internet of Things (IoT), big data analytics, and artificial intelligence. Such digital transformation has the potential to reduce production costs and cycle times. To achieve this, Pharma 4.0 requires end-to-end traceability of the entire supply chain, from raw materials to finished products. In the fill/finish, unit-level traceability of primary container is critical to this and helps pharma manufacturing companies by identifying quality issues at an early stage. This allows companies to take corrective action before the product reaches consumers, quickly identify and address safety concerns, and optimize supply chain operations.

Improved patient quality of care

Improved patient safety

Patient safety is a key aspect of quality healthcare systems. Unit-level traceability at the primary container level can improve patient safety by creating a fully transparent supply chain traceability system. For example, with unit-level traceability, syringe contents are verified and labelled at the filling point and remain fully traceable until patient administration. Issues that arose from the manufacturing of prefillable syringes can, thus, be detected in time before releasing to patients. Any defective products (e.g., due to spoilage and mix-ups) can be recalled in time, reducing the potential risks to patients exposed to these products. This also reduces the risk of administering wrong or expired medication to the patient in the event that the secondary packaging gets misplaced or discarded. From the perspective of healthcare delivery, unit-level traceability improves process efficiency and productivity through highly coordinated scheduling and planning and by increasing the ability to detect errors.[18]

Better patient adherence

One obstacle in achieving therapeutic goals is patient non-adherence with the medication regimen. Improving patients' levels of information concerning the specifics of their regimens and arranging for the continued monitoring of the patient's subsequent treatment compliance could help improve the adherence.[19,20] Unit-level traceability can provide patients with complete, secure, and easily accessible proof of a product's provenance and a map of its entire supply chain journey. In addition, product verification can be implemented for patients through a unique identifier, with corresponding validation data available at a central repository that can be easily retrieved once patients enter the unique identifier.[21]

[18] The Axia Institute (2022), RFID Uses, Benefits, and Costs: Literature Review and Key Informant Interviews. Available at: https://axia.msu.edu/rfid-uses-benefits-and-costs-literature-review-and-key-informant-interviews

[19] Seminars in dialysis (2020), Breaking the adherence barriers: Strategies to improve treatment adherence in dialysis patients. Available at: https://onlinelibrary.wiley.com/doi/full/10.1111/sdi.12925

[20] Therapeutics and Clinical Risk Management (2005), The challenge of patient adherence. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1661624/

[21] World Health Organization (2021), Policy paper on traceability of medical products. Available at: https://www.who.int/publications/i/item/policy-paper-on-traceability-of-medical-products

True end-to-end visibility across the supply chain

Ability to track and recall spoilages

Better unit-level traceability would mitigate reputational risks and reduce the financial loss arising from spoiled drugs that have been released for use. Each year, over $35 billion dollars' worth of pharmaceutical products are wasted due to inadequate temperatures or delays that make them pass their shelf lives.[22] Through unit-level traceability of primary containers, crucial information such as product code, lot number, expiration date, and serial number can be given to each unit. In the event of spoilage, recalls of medications are time-consuming and costly and usually involve wholesale removal of a product in order to isolate the relatively small number of potentially spoiled products. By providing visibility across the entire supply chain, unit-level traceability makes recalls faster and reduce the scope of the recalls, allowing users to locate and remove only affected items immediately and saving financial losses for the pharma companies.

Better compliance management

Notably, health authority inspections increasingly focus on product traceability in pharmaceutical operations related to the US FDA's 21 CFR 610.14, which became effective in April 2014. According to CFR 610.14 (identity), *"The contents of a final container of each filling of each lot shall be tested for identity after all labelling operations shall have been completed"*. By documenting the drug filling batch at the container level, it makes it easier to ensure the identity of each container through the fill/finish process and confirm the identity at each manufacturing site.

FDA has also proposed developing a rating system to incentivize drug manufacturers to invest in achieving Quality Management Maturity (QMM) instead of simply adhering to CGMP to improve supply chain resilience and minimize drug shortage. In a recent series of pilots, FDA evaluated six practice areas, namely, a) Leadership and governance; b) Continual improvement; c) Stakeholder engagement and satisfaction; d) Knowledge management; e) Workforce engagement; and f) Operations.[23] Unit-level traceability could be a critical driver for manufacturing units to achieve QMM by helping in continual improvement, knowledge management, and operational efficiency.

In Europe and the United States (US), regulations in the pharmaceutical industry have also increasingly emphasized the importance of ensuring traceability during the various stages of the supply chain. For instance, the 2016 EU Falsified Medicines Directive (FMD) mandates the use of standardized product data.[24] More recently, the US Food and Drug Administration (FDA) held a virtual meeting in 2022 to discuss Implementation and Readiness efforts for the Drug Supply Chain Security Act (DSCSA). As part of DSCSA 2023, traceability requirements from 2023 onwards will focus more on package-level traceability.[25] Implementing unit-level traceability, especially at the primary container level, reduces compliance risks that might arise for pharmaceutical manufacturing companies.

Prevention of diversion, theft, and counterfeiting[26]

Diversion, theft, and counterfeiting pose reputational risks for pharmaceutical manufacturers based in the EU and US exporting these prefillable syringes to other countries, especially if the mismanaged products get exposed to hospitals and administered to patients.

With unit-level traceability, especially using technologies that allow location tracking, manufacturers have the ability to trace prefillable syringes down to the individual product even after they have left the production country and be alerted to lock down the product at the first signs of diversion or theft. In cases like this, traceability on primary containers becomes more important, as it would prevent traceability from being lost after release (for instance, if the secondary packaging came off or if a counterfeiter replaced the label).[27] In addition, down the supply chain, hospitals and patients will be able to verify syringes (usually through a local repository) at the point of entry, identifying syringes that are counterfeited or stolen.

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22 Sykes, C. 2018. Time- and Temperature-Controlled Transport: Supply Chain Challenges and Solutions. P&T. March 2018. Vol 4, No.3.

23 An Official Journal of the American Association of Pharmaceutical Scientists (2023), Lessons from CDER's Quality Management Maturity Pilot Programs. Available at: https://link.springer.com/article/10.1208/s12248-022-00777-z

24 The EU Falsified Medicines Directive (FMD) (Directive 2011/62EU).

25 RFXCEL (2022), DSCSA 2023: The Future of Pharmaceutical Traceability in the United States. Available at: https://rfxcel.com/dscsa-2023/

26 Based on an interview with an expert working in a global pharmaceutical company. Expert has experience working on projects related to supply-chain traceability across both developed and developing markets.

27 Based on interview with an expert working in quality assurance in a global pharmaceutical company.

The approach: RFID is emerging as the most optimal solution for implementing unit-level traceability at manufacturing sites

The ready-to-use (RTU) format is the most common primary container format used in prefillable syringes' fill-and-finish process, with a large number of glass syringes taking this form. Under the RTU format, empty sterilized syringe containers arrive in a sealed tub containing a nest. The entire filling process is automated, where the tub is taken out of its bag and unsealed at the start of the filling line by the filling machine, and, in most cases, the entire nest of empty syringes is filled and stoppered by the filling machine without de-nesting.

A common technique to prevent mix-ups involves using color-coded labels applied at the exit of the visual inspection stations to syringe barrels to help identify the drug formulation based on colors. However, color-coding is prone to reading errors, as colors are becoming less discernable due to large number of products and therefore challenging for cameras to distinguish. Given newer mechanisms that not only prevent mix-ups but also provide traceability in prefillable syringes, manufacturers are evaluating other mechanisms.

Two preferred mechanisms and their viability for unit-level traceability in primary containers are explored in this section; these include optical marking using Data Matrix Codes (DMC), as well as radio frequency identification (RFID) (Exhibit 3).

EXHIBIT 3

MECHANISMS DIFFER IN FEATURES AND THEIR DESIRABILITY TO BE USED FOR UNIT-LEVEL TRACEABILITY

▼ Disadvantage ▲ Advantage

DESIRABLE FEAURES FOR UNIT-LEVEL TRACEABILITY OF PREFILLED SYRINGES	OPTICAL MARKING USING DMC	RFID
Quantities of information stored	▼ Limited space to print large DMC	▲ Ability to encrypt and store large amount of data
Ability to conduct mass reading	▼ Not possible in DMC	▲ Possible with RFID
Ability to rewrite/reencode information	▼ Data cannot be rewritten or recoded	▲ Flexibility to rewrite or recode with password protection
Ability to read through an auto-injector/ secondary device	▼ Not possible as it needs line-of-sight reading	▲ Possible as no line-of-sight requirement
Simplicity of implementation	▼ Need to denest to read, need to add a rotational step, may require cameras inside the isolators	▲ No need to denest
Adherence to current process	▼ Potential changes to the process to use DMC	▲ Minimal impact on current process— Ability to read up to 1000 units/min
Efficiency of capital expenditure	▼ Requires specific camera systems, equipment to denest and rotate syringes	▲ Only requires RFID readers
Efficiency of direct operational costs	▲ Low cost of DMC	▼ Empty syringes with RFID chips may cost more
Efficiency of total cost of ownership (TCO)	▼ High due to the impact on the process and the limited scope of use cases	▲ Low TCO due to high number of use cases and low impact on process

Source: Literature review, Expert interviews, Access Partnership analysis

Optical marking using DMC

Optical marking uses a two-dimensional barcode that consists of data encoded in black and white as a grid called a Data Matrix Code (DMC). A key advantage of DMC is the high fault tolerance with an automatic error correction mechanism, such that up to 30% of the coded surface can be destroyed without affecting traceability.[28] However, as DMC requires line-of-sight reading, it is essential that syringes are well-positioned to ensure readability. Glass syringes with glossy surfaces tend to impede readability due to sub-optimal reflection of light.[29] For prefillable syringes in RTU formats in particular, readability is a challenge during the filling process, as syringe containers are placed in a nest to be transported to a nest-fixing frame, putting the syringes in a fixed position for filling. Readability under DMC tends to be limited here, given that syringes cannot be lifted out of the nests to be scanned.[30] Placing the DMC at different areas of the primary container poses different challenges: placing it on the side of the glass influences visual inspection and requires rotation of individual syringes within the nest, while placing it at the top of the syringe will require cameras to be placed on the top of the machine, obstructing airflow needed to maintain a sterile environment.[31] In addition, DMC are susceptible to bad prints, especially when the printer ink is low. Based on the experience of serialization of secondary packaging, it is estimated that around 1% of syringes get rejected in the industry during the inspection process due to a lack of readability of DMC.[32]

Radiofrequency identification (RFID)

RFID tags use radio waves to communicate information to RFID readers, which have antennas to receive signals.[33] This allows for real-time tracking of medications and equipment, including syringes. RFID can automatically track product receipt/transfer and inventory management, increasing efficiency over standard barcode technology by reading multiple tags at once. Tags are able to store more information per chip than a barcode, and scanners have the ability to instantly identify and capture data when within scanning range.[34] RFID has the following advantages:

- Does not require line-of-sight reading. Unlike color-coding and DMC, information can be read and processed under RFID without requiring line-of-sight reading.[35] For prefillable syringes, RFID tags ensure that the syringes do not have to be de-nested, and the positioning of the reader could be flexible. In addition, Ultra-High Frequency (UHF) RFID tags facilitate mass reading all at one go,[36] allowing for unit-level traceability without having to individually scan items. A pilot study by a pharma machine maker using samples provided by Becton Dickinson (BD) is reported to have found that RFID tags are less prone to unreadability than DMC.[37]

- Continuous supply chain due to two-way communication. Compared to DMC, which are non-rewritable, RFID provides flexibility. RFID allows locking any re-writes or re-writing with a password protection to prevent malicious attacks. For prefillable syringes, this is ideal as information can be added to the tags as it moves along the supply chain. Information can be codified from the start of the filling process up till the point of patient administration, allowing for greater traceability and patient safety.

- Low training and simplified process. While the RFID technology might be new to employees along the supply chain, the process of reading RFID tags is straightforward, and employees can be easily trained to adopt this technology.[38]

- Safer information storage in greater quantities. RFID generally has high data storage capacities, and a memory organization allowing an easy and interoperable data exchange. RFID chips contain a specific memory bank that cannot be altered which is helpful to confirm the tag's authenticity.[39] In the case of prefillable syringes, this helps prevent the possibility of counterfeiting.

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28 Weber Marking (2019), Data Matrix Code: a barcode with special skills. Available at: https://www.weber-marking.com/blog/data-matrix-code-a-barcode-with-special-skills/

29 Innovating Automation (n.d.). DMC vs. RFID in Manufacturing. Available at: https://www.innovating-automation.blog/dmc-vs-rfid-in-manufacturing-2/

30 ISPE (2021), Unique Identification on Primary Containers to Drive Product Traceability & Quality. Available at: https://ispe.org/publications/papers/unique-id-primary-Containers-drive-product-traceability-quality

31 Based on interviews with experts working in the filling machine manufacturing industry.

32 Based on interview with an expert working in a global pharmaceutical company. Expert has experience working on projects related to supply-chain traceability across both developed and developing markets.

33 U.S. Food and Drug Administration. Radio Frequency Identification (RFID). Available at: https://www.fda.gov/radiation-emitting-products/electromagnetic-compatibility-emc/radio-frequency-identification-rfid

34 Paaske, S., Bauer, A., Moser, T. et al. (2017). The Benefits and Barriers to RFID technology in Healthcare. Online Journal of Nursing Informatics, 21(2). Available at: https://www.proquest.com/openview/246b89e011c35482a3103c9de7c592fb/1?pq-origsite=gscholar&cbl=2034896

35 Innovating Automation (n.d.). DMC vs. RFID in Manufacturing. Available at: https://www.innovating-automation.blog/dmc-vs-rfid-in-manufacturing-2/

36 Automation Insights (n.d.) DMC vs. RFID in Manufacturing. Available at: https://automation-insights.blog/2018/04/04/dmc-vs-rfid-in-manufacturing/

37 Based on interviews with experts working in the pharma inspection machine manufacturing industry.

38 Based on interviews with experts working in the filling machine manufacturing industry.

39 GS1 (2022), EPC Tag Data Standard (TDS). Available at: https://ref.gs1.org/standards/tds/

While RFID signals are, in certain cases, subject to environmental interference due to their reliance on radio waves,[40] pilot studies are reported to indicate that such interference could be negligible for prefillable syringes during the filling process.[41] Moreover, successful feasibility of the technology has been demonstrated in both syringe supplier and pharmaceutical commercial production environments.[42]

While RFID would increase the cost of the container, the implementation of RFID in manufacturing is less complex and overall requires lower capital expenditure. Experts have also highlighted that, if the pharmaceutical company can internally manage data via a local repository, the data management cost will likely be lower than the syringe manufacturers managing the data. [43]

40 Core RFID (n.d.). RFID and interference. Available at: https://www.corerfid.com/rfid-technology/technology-issues/rfid-and-interference/

41 Based on an interview with the senior global marketing manager of the Digital Traceability Platform, BD.

42 Novartis (2022), "PFS Traceability: Case Studies on RFID Based Solutions for PFSs".

43 Based on interviews with experts working in the filling machine manufacturing industry.

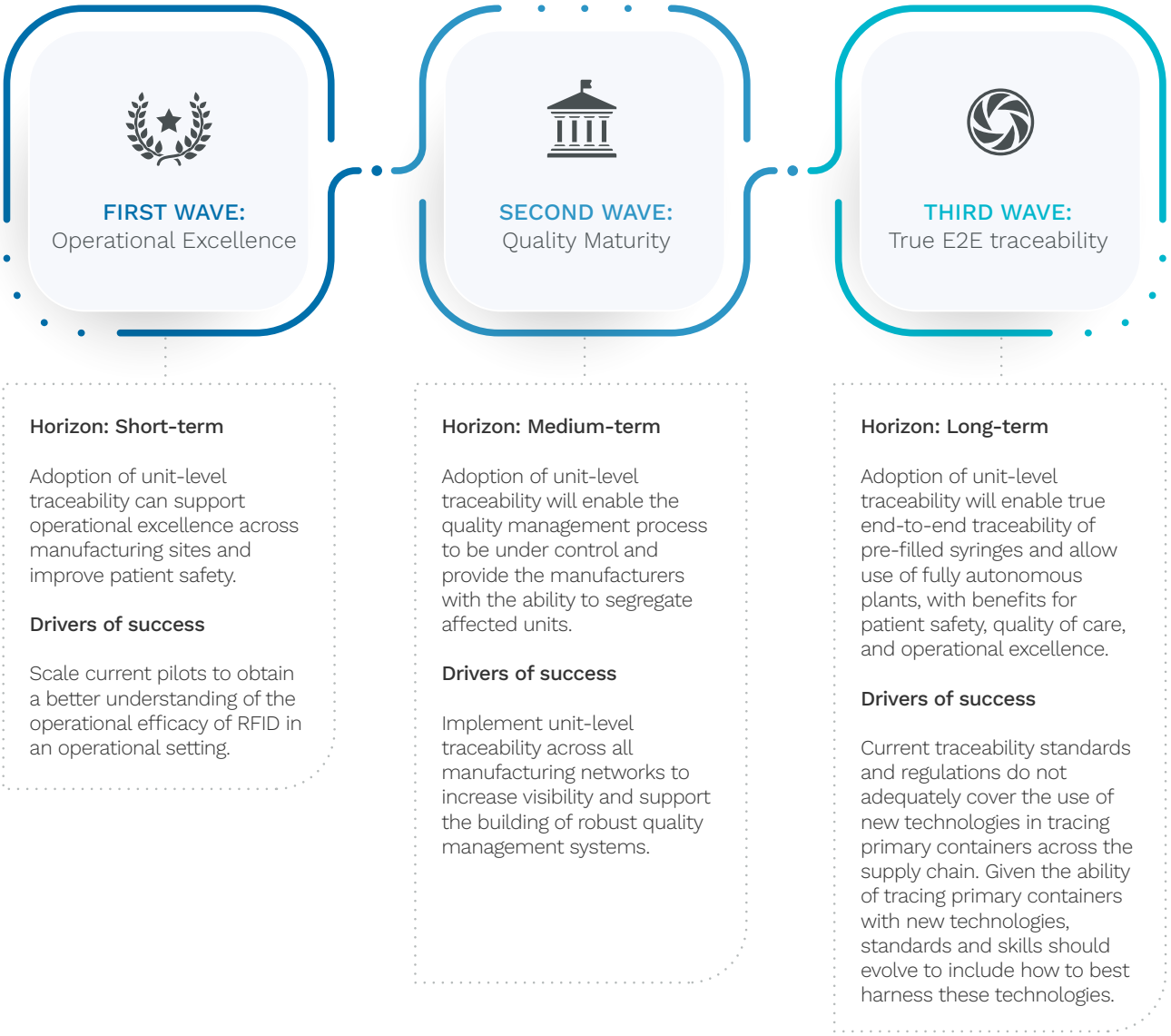
The conclusion: Unit-level traceability has the potential to play a significant role in the future success of pharma operations

Unit-level traceability has the potential to successfully improve operational excellence without significant investment in new capacity. It can prevent mix-ups, improve patient safety and accelerate changeovers. As a result, it will help to ensure supply chain resilience. Among the different solutions to implement unit-level traceability for prefillable syringes, RFID is emerging as the most optimal solution.

Exhibit 4 outlines potential waves of opportunity on the path to fully harness the opportunities from implementing unit-level traceability at the primary container level for prefillable syringes.

EXHIBIT 4

POSSIBLE WAVES TO FULLY HARNESS OPPORTUNITIES OF UNIT-LEVEL TRACEABILITY FOR PREFILLED SYRINGES



Source: Access Partnership analysis

The ability to track prefillable syringes at the unit-level, together with the capability to analyze the quality data, would bring substantial benefits to the pharma operations. At the same time, linking this ability with patient outcomes would trigger additional value for the global healthcare supply chains.