SCHOTT PHARMA

The Next Generation of Infuse

Redefining Efficiency, Stability, Speed, and Security

Over the past decade, the pharmaceutical industry has experienced rapid growth in using new and advanced ideas. Prefilled syringes have become a popular method of drug delivery to treat an increasing number of patients suffering from chronic diseases, cancers, or autoimmune diseases due to increased safety, ease in usage, convenience, accuracy in clinical use, and the ability for self-injections. Moreover, they gained strong acceptance for chronic conditions requiring repeated medication administration.[2,3] A prefilled syringe (PFS) is filled with one or more active medicines at the required concentration and volume and correctly labelled before it enters the final clinical area, where it can be administered immediately without further preparation.

One of the recent reports, published in November 2024 by Fortune Business Insights, shows the global prefilled syringe market is expected to continue experiencing exceptional growth over the next eight years. The global prefilled syringes market size was $7.91 billion in 2023 and is projected to grow from $8.70 billion in 2024 to $20.62 billion by 2032, exhibiting a CAGR of 11.4% during the forecast period 2024–2032. Europe dominated the prefilled syringe market with a market share of 40.33% in 2023. North America is likely to hold the second-largest market share after Europe, owing to the rise in several chronic diseases, such as diabetes and rheumatoid arthritis. These diseases are likely to enhance the demand for prolonged drug administration at an accurate dosage.[4]

In hospital settings, where decisions must be taken more quickly or under stress (i.e., operating theatres, during urgent interventions, emergency department, ICUs), medication error rates in preparing injectable drugs from vials and ampoules are substantially higher. These errors can result from standard human factors and resource constraints, leading to Adverse Drug Events (ADEs). Such ADEs can substantially increase hospital operating costs. Several literature reports suggest that PFS can ensure sterility and help reduce medication errors associated with mislabelling, dosing errors, and related expenses. It's also reported that usage of PFS can also benefit drug/disposables/packaging waste reduction and medication preparation time reduction by more than 50%.

WHO has identified unsafe medication practices and medication errors as leading causes of injury and avoidable harm in healthcare systems across the world, with an estimated associated cost in the range of $42 billion annually. Often, medication errors occur when weak medication systems and/or human factors take effect, such as fatigue, poor environmental conditions, or staff shortages. These can all impact the preparation and administration of injectable drugs and result in severe harm to patients (Medication Without Harm, WHO).

Errors Related to IV Administration

The highest error rates involve intravenously administered drugs (48%–81%), mainly related to the complexity of preparation, administration, and monitoring.[4] These medication error allied problems appear to be mainly in clinical settings (e.g., during emergency interventions, emergency rooms, intensive care units, and operating rooms), where there are many possible human factor error steps in medicine preparation and administration, and decisions are made quickly or under stress.[5] IV medication errors pose an increased risk of patient harm due to the medication's immediate bioavailability, narrow therapeutic window, and challenges involved in reversing systemic effects. These errors can negatively impact both patients and nurses.[10]

Challenges Faced by Healthcare Providers

Ensuring safe injection practices is one of the most significant challenges for the healthcare system in developing countries. Unsafe disposal and reuse of contaminated syringes are standard. Interventions with the active involvement of several stakeholders are essential to address the problem. Many healthcare industry challenges stem from a need to respond to external forces from regulators, competitors, or cybercriminals. Inefficient workflows for documenting patient appointments, submitting insurance claims, and normalising unstructured data add to organisations' expenses. Hospitals and health systems face looming questions about deploying technology to improve the patient experience without further burdening clinical staff, from telehealth to electronic health records.

Challenges Faced by Healthcare Workers

It was prevalent during the COVID-19-induced pandemic, which has had a psychological, emotional, and physical impact on healthcare workers, including pharmacists and nurses. Hospital pharmacists have been playing a crucial role during the pandemic. They had found themselves facing particularly stressful factors, such as working extra hours to ensure a sufficient supply of medication to intensive care units and to mitigate drug shortages and disruptions in the supply chain. The latter faced the suffering and death of an extraordinary number of patients and the work overload caused by the shortage of personnel. Many were asked to work in unfamiliar clinical areas, hurriedly set up to deal with the patient overload. The contagious virus forced all healthcare personnel to wear extra personal protective equipment (PPE), which undoubtedly limited movement, restricted vision, constrained communication, and reduced speed of action. It followed an increased risk of errors during the preparation and administration of drugs.[5,6]

The Role of the Prefilled Syringe in Solving Those Challenges

The role of PFS, with specific reference to situations of heavy workload and high stress, such as those experienced during the COVID-19 pandemic, has recently been reviewed by a systematic review of several authors and reported by observational studies, surveys, case reports, and risk analysis.[5] The use of PFS provides the following advantages:[5]

1. Reduced number of preparation steps and associated cognitive complexity
2. Simpler use (no labelling needed on the point of care, as it is already correctly labelled)
3. Reduced infection (reduced microbiological contamination)
4. Reduced drug, disposables, and packaging wastage
5. Reduced nursing time allocated to the preparation and administration of drugs
6. Quicker to administer in an urgent crisis

7. Reduced the likelihood of medication errors
8. Reduced needlestick injuries
9. Overall cost savings (although more money is spent to purchase PFS, the use of PFS led to significant cost savings)

Like all businesses, hospitals try to reduce costs as much as possible. Labour costs and product waste are two areas where the right drug delivery product can impact their bottom line. For example, patients in medical and surgical units receive an average of 10 injections daily. PFS products have been shown to reduce preparation and administration time significantly.

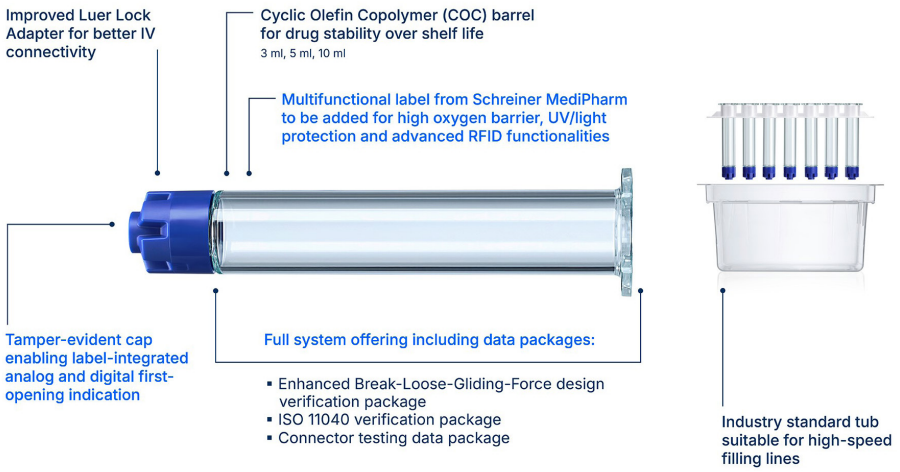

Figure 1: SCHOTT TOPPAC® infuse – the next generation

Figure 2: A. Traditional blister packaging; B. SCHOTT TOPPAC® infuse blister-free packaging.

The Next Generation of SCHOTT TOPPAC® infuse Syringes Redefines the Benchmark

Preparing anaesthesia trays requires manual checks of each syringe's shelf life and medication. Additionally, syringes in anaesthesia trays often lead to drug waste, as not all drugs are used during a single procedure, and the syringes do not indicate if they have been used. Space in hospital environments is also limited, so product packaging should be as compact as possible.

The next generation of SCHOTT TOPPAC® infuse prefilled polymer syringes features a new cap and label design that covers the entire shoulder of the syringe, providing a first opening indication to reduce drug waste. This design also forms the basis for a new blister-free packaging concept that can offer additional protection, such as from light or oxygen, guaranteed by the label instead of a blister. The label can be equipped with an RFID chip for seamless traceability and a digital-first opening indication, increasing the efficiency of anaesthesia tray preparation from 20 minutes to just 1 minute. Existing verification packages and connector tests can expedite the time to market for new and existing customers. The syringe features:

- First-opening indication: Ensuring the syringe has not been compromised or used before.
- Protection from contamination: Dust, moisture, microorganisms
- Protection against mechanical stress: Precise product fixing
- Gas Barrier: Protection against moisture, O_2, etc.
- Visibility identification: Ability to inspect and see the expiration date
- UV/Light protection: Shielding the product from environmental factors such as light
- User-friendly: Separation of single units via perforation or blister with tear tab

Secure and Blister-free Packaging

We must question and revolutionise traditional packaging methods to minimise environmental impact and maximise efficiency. While once ubiquitous, blister packaging poses significant challenges regarding waste generation and logistical complexity.

The new blister-free packaging concept that was created together with the Alliance to Zero members, SCHOTT Pharma, Schreiner MediPharm, and Körber Pharma, was enabled by the new cap and label of the SCHOTT TOPPAC® infuse syringe. It minimises waste and reduces space by containing 20% more syringes per container, resulting in up to 58% lower CO_2 footprint during transport. 3 times less storage space is required in hospitals and 500 kg less plastic and packaging waste is generated (All numbers are valid for 151.200 units of one sort for a 5 ml SCHOTT TOPPAC® syringe. Given values are valid for best-case scenarios. PCF data are not considered).

Using Labels to Add Relevant Functionalities

Labels in pharma packaging are the most common way to provide the relevant information directly on the primary container of a pharmaceutical product. However, as stated, labels offer many more options to add value to pharma packaging. They can contribute significantly to patient safety or user experience, provide a strong first-opening indication, or represent the interface for track and trace solutions and the digital world. Since a label covers a significant part of the primary container's surface, they are predestined to add additional protection to the packaging system, such as UV/light protection or gas barrier.

The Label Technology for the SCHOTT TOPPAC® infuse Syringes

Increasing Security and Efficiency

Since the Commission Delegated Regulation (EU) 2016/161 (Source: Delegated regulation – 2016/161 – EN—EUR-Lex) supplementing the falsified medicines directive 2001/83/EC became effective in February 2019, tamper

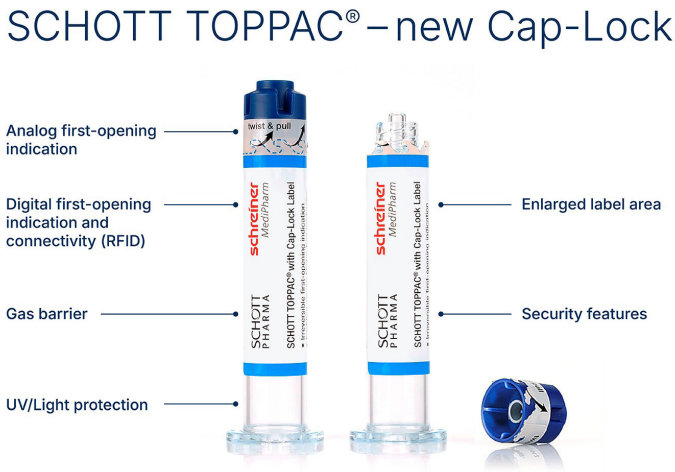

Figure 3: Overview of label-based functions for the next generation of SCHOTT TOPPAC® infuse syringes

indication on secondary medicine packaging has become mandatory in Europe, making tampering much more difficult for criminals. Illegal medicines inflict considerable damage on the pharmaceutical industry, but above all, they pose a massive risk to patient safety. The unauthorised use of medicines, e.g., in hospitals, or re-use of empty original medicine syringes with original labels from waste containers, pose a growing and significant threat: whenever criminals refill the container with ineffective or even harmful substitutes and put these adulterated medicines back into circulation in an uncontrolled way, patients are exposed to acute health risks. Thus, appropriate security solutions should be implemented on the primary container level to achieve comprehensive product and patient safety due to a consistently secured supply chain. This includes tamper-evidence and anti-counterfeiting technologies, together with unique serial codes.

The current standard packaging for syringes consists of a standard syringe without an integrated first-opening indication, plus a standard label packed in blister packaging sealed with lidding foil. Thus, the blister packaging takes over the crucial irreversible first-opening functionality on the secondary packaging level. If the blister is removed from the packaging concept at all or during the last mile to the patient (for space-efficient storage), this crucial functionality is removed, and the syringe is unprotected.

PFS are one of the most frequently used means of primary packaging, in addition to vials. Most standard syringes do not allow for a convenient label-based sealing up to the cap due to the different radii of closure and syringe barrel. The next generation of SCHOTT TOPPAC® infuse features a unique design to allow for label-based sealing and reliable first-opening indication on the primary container level. The new Cap-Lock Label wraps around the entire cap and the syringe like a second skin, thus securing the integrity of the syringe until the injection is performed. Use of the label is easy and safe: The syringe can be opened in a single move, opening the syringe and label simultaneously. This purposefully destroys the label, clearly and irreversibly indicating that the syringe has been opened and is no longer sterile.

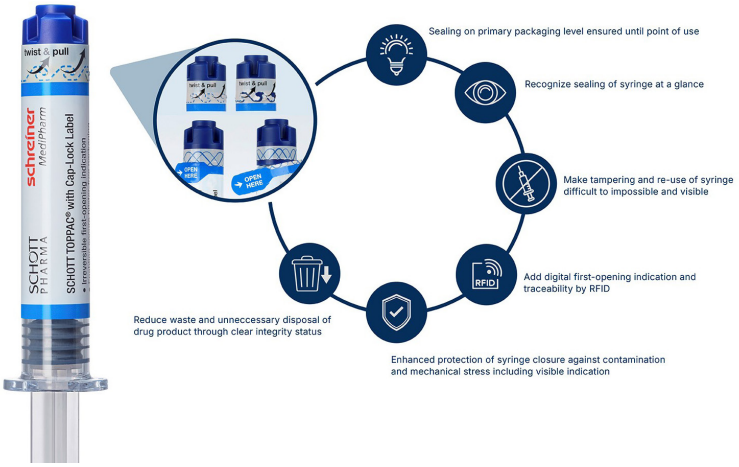

Figure 4: First-opening and re-capping indication via label, which covers both the syringe body and closure

Special security die-cuts and print layers result in the intended partial destruction of the label upon opening and prevent reclosing it unnoticeably, even after authorised opening. An initially covert warning message or colour can be integrated as an additional feature to enhance visibility. Healthcare staff can immediately detect whether the syringe has been tampered with or opened. This enhances supply chain security, minimises insider threats in hospitals, and contributes to the unnecessary disposal of drug products. Integrating an RFID chip can be considered to improve the functionality and security of the solution.

The new label offers an up to 25% larger label area as it uses the extra space on the top and above the transparent inspection window. Thus, there is more design flexibility to include customised branding, written information, or colour coding.

The security label can be applied to the syringe in conventional dispensing processes in pharmaceutical production, thus in a process without heat, so the SCHOTT TOPPAC® infuse syringe plus Cap-Lock Label combination is suitable even for sensitive substances. This combined solution approach helps ensure the syringe's sterility and integrity until its use.

Increasing Drug Stability

Light-Protect-Labels

Many drugs are degraded by exposure to light, which can have serious consequences for the formulation and, ultimately, for the patient, e.g., altered efficiency, loss of efficiency, or an adverse biological effect. Therefore, light protection is needed for various formulations such as biologics, biosimilars, and many vitamins and minerals.

The new SCHOTT TOPPAC® infuse syringe's advantages, as a ready-to-use solution with irreversible first-opening indication, can also be fully exploited for light-sensitive formulations.

Using functional films, optionally combined with printing, label solutions can be provided with a specific UV and light protection profile based on three protection levels. To the formulation in the SCHOTT TOPPAC® infuse syringe, Cap-Lock Label LP 1 adds protection against UV light (< 370 nm), Cap-Lock Label LP 2 against UV and violet/

Figure 5: Cap-Lock Label LP combines multi-level UV and light protection with first-opening indication

blue light (< 480 nm), and Cap-Lock Label LP 3 against the whole spectrum of UV and visible light. Customised protection levels can also be achieved by adapting functional films and printing inks.

Any deviation from the test procedures or conditions may lead to different results. Consequently, test results cannot be transferred to individual customer applications without testing. Deviations may also occur due to different printing techniques.

The next generation of SCHOTT TOPPAC® infuse syringes, combined with Light-Protect labels, prevents light from entering from the top of the syringe, allowing maximum light protection.

All Light-Protect-Labels have an inspection window to enable a complete, true-colour inspection. This window allows for easy examination of discolouration or particles through the transparent primary container.

Gas-Protect-Labels

Medical polymer containers made of COC have the disadvantage of low barrier properties, as they allow gaseous substances to pass through. Numerous medications, therefore, suffer from gas permeability, which may result in severe consequences such as adverse biological effects or a reduction of shelf life. Oxygen and the associated oxidation are a particular problem for many formulations.

To reduce permeation, Gas-Protect labels can be customised and applied flexibly to a container without changing the primary container. The adhesive is suitable for applications with a high migration risk and complies with FDA 175.105. Implementing Gas-Protect labels without any adjustments to the dispensing process is also easy. Cap-Lock Label GP for the SCHOTT TOPPAC® infuse syringe has the advantage that the irreversible first-opening indication of the label also allows for indication of the integrity status of the barrier function.

The 10 ml SCHOTT TOPPAC® infuse syringe (previous generation) with a Gas-Protect-Label (syringe barrel label) demonstrated a reduction in oxygen ingress of up to 86%. With the SCHOTT TOPPAC® infuse syringe, a higher degree of coverage is possible. Thus, an enhanced gas barrier function can be expected with the SCHOTT TOPPAC® infuse syringe (permeation tests with Cap-Lock Label GP are still being carried out).[11] The optimisation of the barrier performance of Cap-Lock Label GP is constantly being continued.

Increasing Traceability with RFID

RFID has fundamentally changed how inventory is managed, and goods are tracked along the supply chain. The ability to track products throughout their lifecycle – from production to shelf placement – has led to significantly greater visibility and efficiency. The technology allows retailers and manufacturers to track an item precisely (track & trace), minimising losses and optimising warehouse processes while reducing logistical costs and improving responsiveness in the supply chain. Global use has reached impressive numbers, with over 34 billion RFID inlays worldwide.[12] Even in drug management, RFID has made immense progress, with more than 250 million tagged drugs in over 750 hospitals in the USA.[13]

This is where RFID plays a key role in improving drug safety, efficiency, and traceability. Thanks to real-time data transmission, RFID enables up to 90% faster stocktaking than conventional, manual processes. Inventories can be recorded automatically and without direct visibility of the item, significantly reducing the workload and minimising the susceptibility to errors when recording data. Tracking medicines along the entire supply chain – from production to transportation to administration to the patient – ensures that the right medicine is in the right place at the right time. The automatic identification of medication also minimises the risk of mix-ups or incorrect administration, which is a key factor in patient safety.

To ensure an overview and, more importantly, the integrity of medication in everyday hospital settings, RFID technology

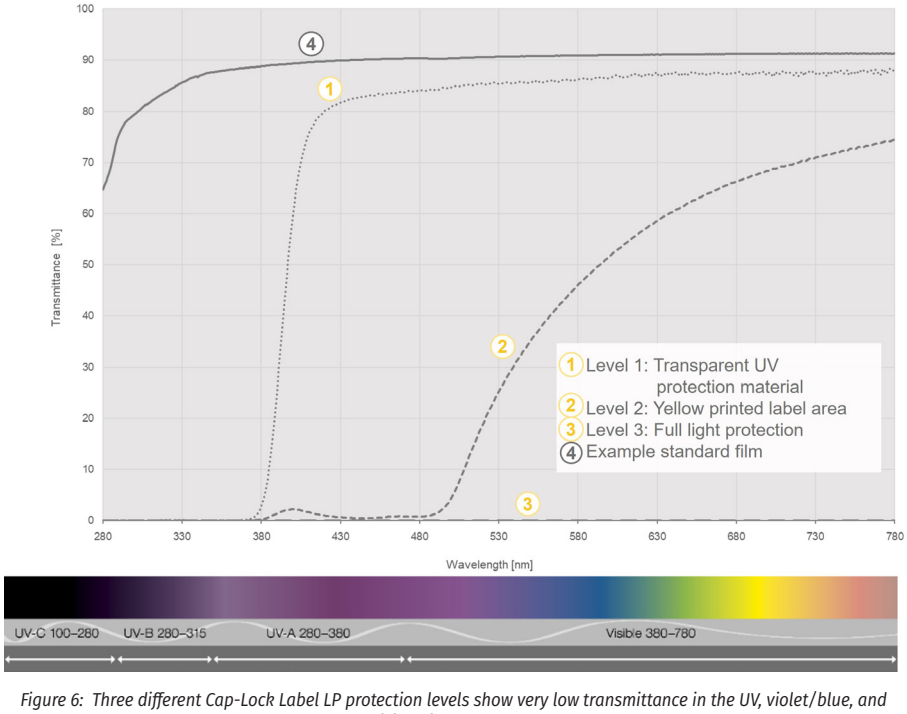

Figure 6: Three different Cap-Lock Label LP protection levels show very low transmittance in the UV, violet/blue, and visible light spectrum.

Figure 7: Digital First-opening functionality combined with Cap-Lock solution

for inventory can be expanded to include digital proof of initial opening. Thanks to its special design, it irreversibly indicates the first opening of the container and enables automated integrity tracking. It is no longer necessary to manually check whether the container has been opened. It optimises inventory management while making work easier for medical staff, as unused medication can be efficiently returned to stock. At the same time, possible diversions and the misuse of drugs can be monitored.

It is not only unique solutions that characterise Schreiner MediPharm's RFID labels. In addition, the label experts work on customised solutions to meet the special performance, implementation, and readability requirements, particularly in the pharmaceutical market. By individually adapting the RFID label to specific environments and applications, exceptionally high reading speeds and reliable detection can be achieved even under challenging conditions. The solution also greatly simplifies implementing RFID in existing systems, which means no costly machinery adjustments are necessary. As a result, an optimised RFID solution reduces operating costs and improves data accuracy and product traceability, leading to optimised operational performance and higher customer satisfaction.

Conclusion

In conclusion, the next generation of SCHOTT TOPPAC® infuse syringes represents a significant leap forward in addressing the challenges encountered in anesthesia tray preparation and pharmaceutical packaging. The innovative design, characterised by a cap and label that envelops the entire shoulder of the syringe, introduces a pioneering first-opening indication. This groundbreaking feature not only diminishes drug waste but also offers enhanced protection from light or oxygen, obviating the necessity for conventional blister packaging.

Moreover, by providing the option to integrate an RFID chip for seamless traceability, the efficiency of anesthesia tray preparation can be markedly improved, reducing the time required from 20 minutes to a mere 1 minute. Additionally, this advancement facilitates the expedited launch of new products for both new and existing customers, streamlining the overall process. The syringe's comprehensive array of attributes, including safeguarding against contamination, mechanical stress, and UV/light exposure, and its user-friendly single-unit separation, render it a cost-effective and space-efficient solution within hospital environments.

Furthermore, the integration of tailored functional labels for SCHOTT TOPPAC® infuse syringes serves to bolster security, efficiency, drug stability, and traceability, effectively addressing critical regulatory requisites and minimising environmental impact. This pioneering approach not only ensures the safety of patients and the integrity of products but also contributes to reduced waste generation, decreased CO2 emissions during transport, and enhanced operational performance. Ultimately, this innovation revolutionises traditional pharmaceutical packaging methods, setting a new standard for the industry.

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Add RFID to the PFS in existing processes

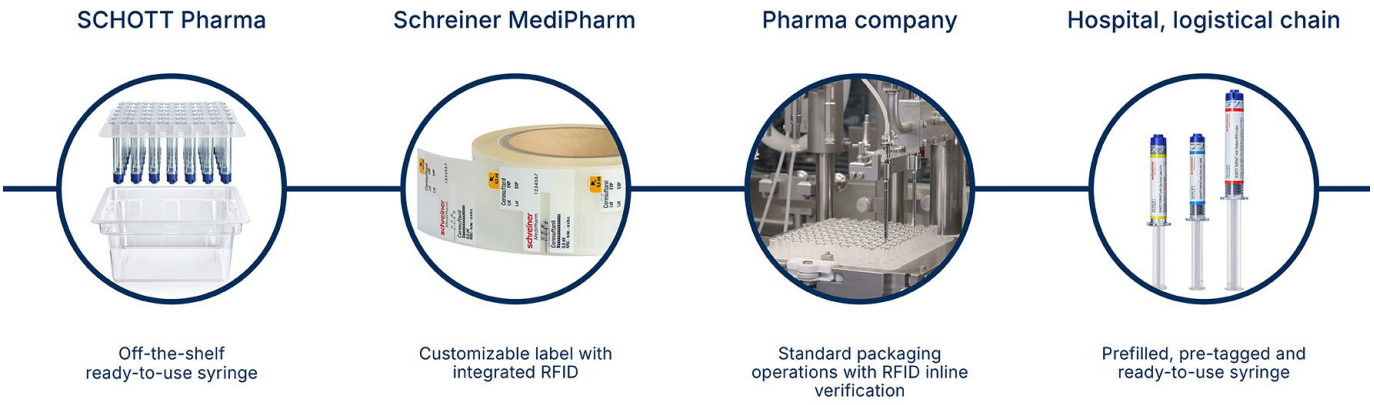

Figure 8: Added value of RFID along existing processes

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