Plastic Pre-filled Syringes: *Clinical Advantages, Technical Requirements, and Material Selection Criteria*

In the last decade, the use of plastic pre-filled syringes for parenteral administration has been steadily growing. In fact, the compound annual growth rate (CAGR) specific to the plastic segment is estimated to be between 11.5% and 13.8%.

This is understandable when considering and analysing the numerous advantages offered by pre-fillable syringes.

Firstly, contamination risks are reduced because fewer steps are required for medication preparation. This allows for direct drug administration to the patient, avoiding the stages of solution reconstitution and inoculation, and proceeding instead directly with administration. Secondly, pre-fillable syringes allow the operator to inject a dose of medication with high precision, as it is possible to fill the syringe with the exact amount needed for the treatment. This provides advantages in terms of both administration and dosage, avoiding drug waste and facilitating delivery operations.

Glass vs. Plastic Syringes

For decades, glass was the material of choice for pre-fillable syringes due to its high transparency, high chemical resistance, low alkali content, and barrier properties suitable for the long-term storage of vaccines and other pharmaceutical products. On the other hand, glass exhibits high sensitivity to cracking and breakage, as well as the risk of delamination, which constitutes a source of chemical and physical contamination for the drug or substance it contacts.

Furthermore, glass syringes present high levels of tungsten residue near the needle at the Luer Cone connection, which can lead to aggregation phenomena in the case of protein-based drugs. To address these issues, plastic solutions have entered the syringe market – and specifically the pre-filled syringe market – over the last decade.

The most commonly used polymers are:

- Polypropylene (PP)
- Polycarbonates (PC)
- COC (Cyclo-olefin copolymer)
- COP (Cyclo-olefin polymer)

The choice of which plastic to use for a product is directly related to its intended purpose and final use, as well as the intrinsic characteristics of the material. To select the suitable plastic type, one must first consider the final use and the type of solution it will contact.

For a proper evaluation, it is first necessary to identify the "intended use" of the solution or drug the pre-filled syringe will contain. In this initial phase, the syringe is considered primary packaging, and it is then considered a medical device once pre-filled with the solution or drug. To establish the suitability of the plastic, it is necessary to understand how the solution enters into contact with blood or tissues and the duration of exposure.

Based on these characteristics, the plastic must be evaluated for:

- Particulate release
- Biocompatibility

This is to understand the type of interactions that may be triggered, which could lead to drug degradation, protein precipitation (especially for protein-based drugs), decreased shelf-life, and a reduction in the activity of the active ingredient or other components of the solution. For this assessment, various chemical, physical, and biocompatibility tests must be performed to identify the material and particle content in the primary packaging and ensure biological compatibility for end-user safety.

Foreign Particulate Matter Testing

Tests aimed at identifying particulates follow Pharmacopoeia directives. According to regulations, particles of the following sizes are evaluated:

- ≥ 10 µm;
- ≥ 25 µm;
- ≥ 50 µm

The ranges vary based on the drug's intended use. Specifically, the reference standards for identifying particulate content are:

- USP <788> – Particulate Matter in Injections: Evaluates the presence of mobile, undissolved substances (other than gas bubbles) that may derive from various sources like contamination. In this case, particulate levels must be minimised and controlled regardless of type.

- USP <790> – Visible Particulate Matter in Injections: Concerns visible particulate matter. Its primary purpose is to define what is meant by an injectable pharmaceutical product being "essentially free" of visible particles. This is a critical safety standard, as foreign particles (such as glass, metal, or fibres) can cause serious medical complications, including embolisms or inflammatory reactions.

- USP <789> – Particulate Matter in Ophthalmic Solutions: Unlike USP <790>, this focuses on sub-visible particulate matter – particles too small to be detected by the human eye but potentially dangerous for ophthalmic solutions. These solutions have stricter directives due to the potential for endophthalmitis and corneal lesions.

It is therefore necessary to entrust the analysis of the primary packaging (syringe) to specialised laboratories to evaluate whether the particulate matter present complies with regulations. To increase performance, particularly for ophthalmic solution production, it is advisable to mould plastic components in ISO 7 classified cleanrooms to further limit particulate contamination.

Extractables and Leachables Testing

A second aspect to evaluate, based on the material's intrinsic properties in contact with the solution, are:

- **Extractables:** Chemical compounds that can be released from a contact material under aggressive or exaggerated laboratory conditions.
- **Leachables:** Compounds that can migrate into the drug during normal use.

- Reference can be made to the ISO 10993-18 standard or, specifically for

plastic materials, to USP <661.2>: Plastic Packaging Systems for Pharmaceutical Use. As with particulates, the release of these materials could compromise the stability of the solution, potentially modifying the pH, the activity of the active principle, or other components, thereby reducing the drug's efficacy and shelf life.

Biocompatibility Testing
The chosen plastic must be biocompatible. Reference is made to the ISO 10993 standard, which describes the biological evaluation of medical devices within a risk management process. This includes assessing aspects such as haemolysis, cytotoxicity, skin irritation, and toxicity.

In light of the cases described, it is important to choose the appropriate type of plastic for the specific solution and intended use:

Polypropylene (PP)
Polypropylene is widely used for its chemical and physical properties, as it resists erosion from various materials. Its performance remains optimal even in high-temperature and high-humidity contexts, which helps ensure instrument safety. It is compatible with several sterilisation methods, such as:

- Autoclave (cycles at 121°C)
- Gamma radiation
- EtO (Ethylene Oxide)

The choice of PP for syringes is also supported by its biocompatibility and cytotoxicity characteristics. PP syringes commonly contain generic drugs such as saline solution (e.g., pre-fillable syringes for flushing operations), heparin, atropine, and epinephrine in small volumes, and electrolytes like sodium bicarbonate in larger volumes for hospital and emergency use.

Cyclic Olefins (COC and COP)
While polypropylene remains the material of choice for low-cost drugs, diluents, and electrolytes, cyclic olefins have become the preferred plastic for new drugs. These are divided into Cyclic Olefin Copolymers (COC) and Cyclic Olefin Polymers (COP).

COC are transparent amorphous copolymers based on cyclic and linear olefins. They exhibit a unique combination of properties, including high transparency, low density, excellent moisture barrier capabilities, and resistance to aqueous and polar organic media.

COP, is distinguished by:

- **High transparency:** Light transmission comparable to glass, essential for visualising the solution inside the primary packaging. This makes it preferable to polypropylene, which has lower light transmittance.
- **High break resistance:** Compared to glass, the breaking point is higher, and the failure mode is different (glass shatters into multiple pieces), making it safer for users.
- **Greater resistance to low temperatures:** Compared to PP, it resists temperatures as low as -194°C, allowing for low-temperature storage.
- **Low impurity levels.**
- **Low residual metal levels:** Lower than PP and other plastics, and lower tungsten levels than glass, improving performance with protein-based drugs.
- **Absence of delamination:** Avoiding the critical phenomenon of microscopic flakes detaching from the internal surface.
- **Sterilisation compatibility:** Compatible with Gamma radiation, steam, EtO, and E-beam.
- **High moisture barrier.**
- **Low levels of protein absorption and aggregation:** Preventing the compromise of drug efficacy and stability.

In conclusion, plastic syringes are significantly increasing due to characteristics that allow for wide use in the pre-filled syringe field, providing notable advantages in clinical and home settings. Therefore, the choice of the appropriate plastic type is decisive in meeting needs related to both cost and performance regarding drug interactions, as well as the ability to keep characteristics unchanged from the filling process to final use.

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What the Injectables Surge Is Really Asking of Pharmaceutical Packaging

The scale of the GLP-1 market is well understood by anyone working in pharmaceutical manufacturing. Semaglutide and tirzepatide, at least in the context of weight loss, have moved from a clinical curiosity to global phenomenon in a remarkably short period. The pipeline behind them, including further obesity treatments, next-generation autoinjectors, and expanded indications, shows no sign of slowing. For packaging professionals, the interesting question is not whether this growth will continue, but what that growth is actually demanding in practical terms from secondary packaging design, production infrastructure and patient communication.

The answer, on close examination, is rather a lot, and much of it is genuinely new. This is not because injectables are new, but because the combination of speed-to-market pressure, mass consumer adoption of self-administration, and tightening regulatory expectations around security and sustainability, has created a set of simultaneous demands that packaging has not previously had to meet all at once.

The market context reveals the stakes. The global biopharmaceutical market is projected to reach $856 billion by 2030 according to Precedence Research, expanding at a CAGR of 12.5%, and prefilled syringes represent one of the fastest-growing delivery segments within that. The figures illustrate a mainstream shift in how medicines are delivered, and one that places packaging at the centre of a very large commercial and clinical equation.

Speed to Market as the Primary Pressure

The pace at which GLP-1 therapies have reached market has been extraordinary. Commercial timelines have compressed what would previously have taken years of packaging development and line qualification into months. That compression has had real consequences: pharmaceutical manufacturers have had to adapt packaging lines rapidly, often before ideal specifications have been fully locked down, and in some cases before packaging suppliers have had adequate time to test and validate components against machine performance.

This is where the relationship between manufacturer and packaging partner becomes extremely consequential. A supplier that can test carton designs directly on machine suppliers' own infrastructure, validate performance at commercial speeds before launch, and iterate formats quickly in response to line feedback, is going beyond a commodity service. It is providing a development partnership that has direct bearing on when a product reaches patients. For the GLP-1 market specifically, where demand has consistently outpaced supply at various points, every week matters. Packaging that delays qualification or causes line stoppages is not acceptable.

The speed pressure is unlikely to ease. As competition intensifies and manufacturers race to establish solid market position for follow-on treatments, the expectation that packaging can be specified, validated and scaled quickly, will only increase.

Designing for Patients Who Are Not Patients in the Traditional Sense

GLP-1 therapies have introduced a population of self-injecting patients who are largely new to the experience.

Unlike patients managing chronic conditions such as diabetes or rheumatoid arthritis, who typically receive structured clinical training before self-administration begins, many GLP-1 users are initiating treatment with limited hands-on guidance and a high expectation of intuitive usability. The packaging is, in many cases, the primary interface between the product and the patient at the moment of first use.

This changes the overall design brief in a very meaningful way. Secondary packaging for autoinjectors must provide immediate, unambiguous access to the device and any required auxiliary components. Top-opening carton designs have become increasingly important here: a pack that enables a patient to lift a flap and see all components clearly positioned, in the correct sequence, with the device oriented for immediate use, reduces the cognitive burden at a moment when errors carry clinical risk. The physical interaction with the pack is part of the treatment experience, and poor design has consequences for adherence.

Protection during transport is equally important. Autoinjectors that activate within the packaging, whether due to compression, impact, or thermal stress in transit, represent a product integrity failure with direct patient safety implications. Carton engineering must account for the specific activation force thresholds of each device, and packaging must be validated against realistic distribution conditions, rather just static testing. As more GLP-1 treatments move into direct-to-patient delivery models, the range of transit environments that secondary packaging must survive is widening considerably.

Instructions for Use: The Case for Going Beyond the Leaflet

Self-administration places a heavier burden on instructions for use (IFU) than clinic-administered treatments. The patient leaflet remains a regulatory requirement, but its limitations for a population of first-time self-injectors are real. Print instructions, however clearly written, cannot demonstrate injection technique, cannot update in response to revised guidance, and cannot confirm whether a patient has actually read and understood them.

This is where NFC-enabled (Near-Field Communication) secondary packaging offers a practical alternative. A tag embedded in a carton or label could deliver, for example, a video demonstration of injection techniques, step-by-step digital IFUs in the patient's language, dosing reminders, or direct links to support resources, all via a standard smartphone with no app required. For patients with visual impairments or low health literacy, audio-guided instructions delivered this way can be the difference between successful self-administration and a medication error.

The case for digital IFU integration is not purely patient-facing. As regulators in several markets move toward accepting or encouraging digital alternatives to printed leaflets, the ability to update guidance without a packaging change provides manufacturers with major flexibility. For products with

evolving usage guidance, that flexibility has real commercial and compliance value.

Security Demands for High-Value, High-Visibility Products

The commercial profile of GLP-1 therapies makes them a prime target for counterfeiters. High price points, strong consumer demand, and widespread media coverage have created exactly the conditions that attract counterfeit activity, and there is already evidence of falsified GLP-1 products entering markets where legitimate supply has been constrained. The World Health Organization estimates that around 10% of medical products in low- and middle-income countries are substandard or falsified, and high-demand branded injectables are disproportionately represented in that figure.

Effective product security for injectable packaging requires layered thinking. A single tamper-evident seal is a minimum standard, not a deterrent. The more robust approach combines, or better still layers, security features. This includes visual indicators such as tamper-evidence and holographic elements, semi-visible security printing and microtext that require specialist capability to reproduce, and covert features including serialised data matrix codes, RFID tags and encrypted NFC, which enable verification at any point in the supply chain. Each layer addresses a different attacker capability; the combination creates a defence substantially harder to replicate in its entirety than any individual feature.

Serialisation, mandated under the EU Falsified Medicines Directive and the US Drug Supply Chain Security Act, provides the foundational digital layer. Compliance with these frameworks should be understood as baseline for market entry, not the ceiling. For products with the risk profile of high-demand GLP-1 injectables, the business and patient safety case for going further is very strong.

Multi-Dose Formats and the Coming Returns Question

As GLP-1 therapies develop, multi-dose formats are becoming more prevalent. Weekly injection regimens delivered via multi-use pens require packaging that accommodates reclosure between doses, maintains product integrity across multiple openings, and remains patient-friendly throughout a treatment period that may span months.

Packaging that needs to repeatedly open and close securely, is a more challenging

specification than single-dose formats, and one that rewards close collaboration between the packaging design team and the device manufacturer.

Looking further ahead, the global sustainability agenda is raising questions about end-of-life responsibility for autoinjector devices and their packaging. Several European markets are moving toward requirements for device disassembly and component recycling, which will have implications for how secondary packaging supports the returns and disposal process. Packaging that supports correct separation of device components, or that incorporates return instructions and mechanisms as part of its design, is likely to become a regulatory expectation rather than a voluntary commitment within the current decade. Manufacturers specifying packaging now for products with long commercial lives would be wise to consider how those packs will perform against future sustainability obligations.

The Sum of the Demands

Taken individually, none of the requirements explored here is without precedent. Speed-to-market pressure, patient-centric design, digital IFUs, product security and sustainability have all been on the pharmaceutical packaging agenda for years. What the GLP-1 wave has done is collapse them into a single, simultaneous specification challenge, at a scale and pace the industry has not previously encountered.

Meeting that challenge requires packaging partners who can engage across all of these dimensions without treating any of them as secondary. A carton that protects the device, guides the patient, deters the counterfeiter, carries digital content and accommodates a future returns process is not a simple deliverable, but the result of genuine technical investment across multiple disciplines, tested against real production and distribution conditions, and developed in close collaboration with the manufacturer.

The GLP-1 market has been, in many respects, a stress test for pharmaceutical packaging. The industry has largely passed it, but the question now is whether the lessons learned at pace, and under pressure, will be applied more systematically as the next wave of high-demand self-injectable therapies follows.

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