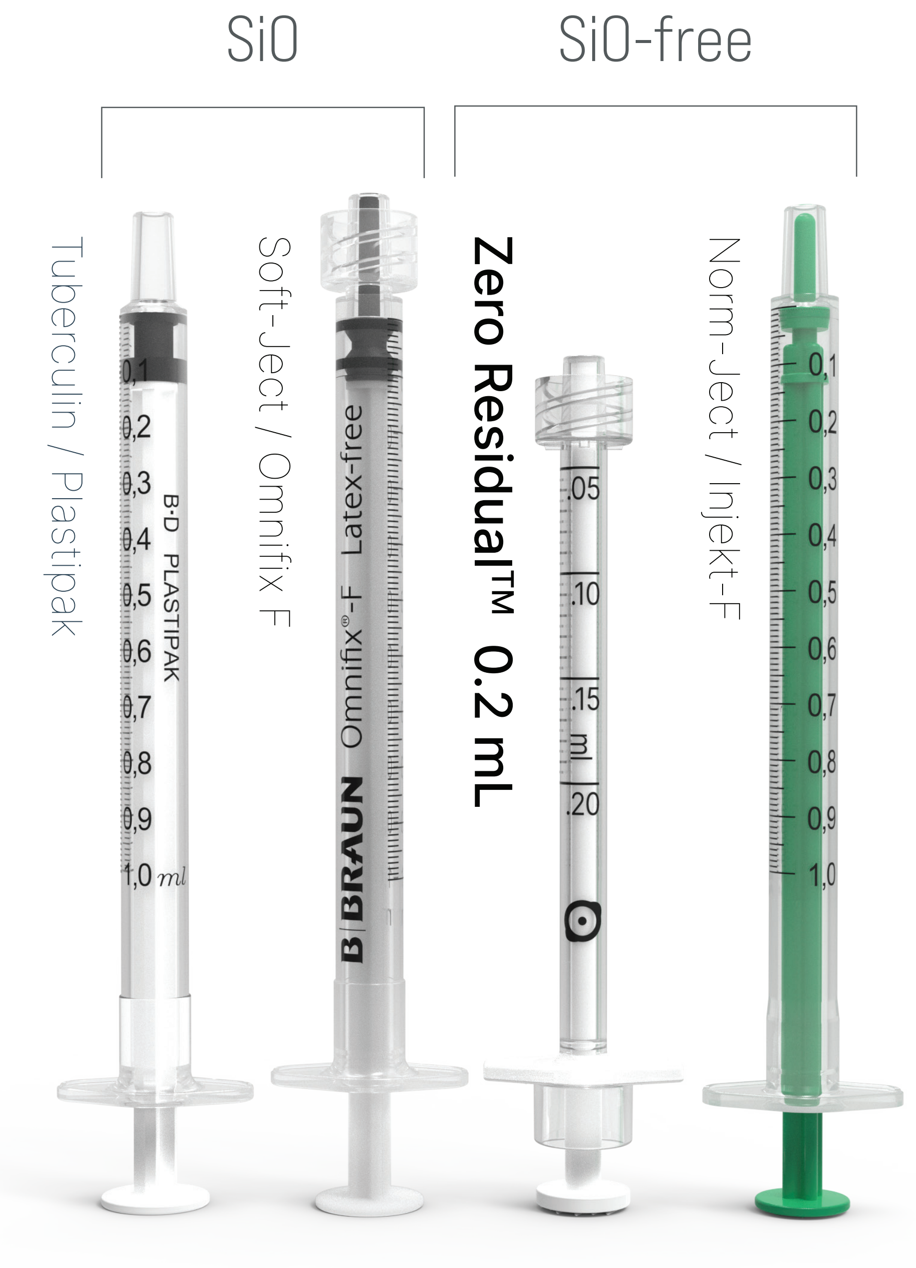
SJJ Solutions

Comprehensive Syringe Selection

1 Syringe comparison

While intravitreal injections (IVIs) are routinely administered by Ophthalmologists, it is crucial to note that these injections have historically utilized syringes not specifically designed for ocular applications. Given that the majority of IVIs involve antibody-based biologics and often necessitate long-term, repetitive treatments, there is an increased risk of injection related adverse events, such as vision-threatening non-infectious endophthalmitis and spikes in intraocular pressure. Hence, careful consideration of syringe selection is paramount for ensuring patient safety, maintaining product integrity, and enhancing the practicality of IVI administration. The following provides an evidence-based, comprehensive comparison of the most frequently used IVI syringes.



There are many commercially available syringes in the market that are currently being used for compounding of protein therapeutics for Intravitreal Injection.

Some of the most commonly used for IVI are in the table below:

Syringe type	Manufacturer	Needle attachment
Zero Residual™ 0.2 mL SiO-free	SJJ	Luer Lock
Tuberculin / Plastipak 1 mL	BD	Slip Tip
Soft-Ject / Omnifix F 1 mL	HSW / B. Braun	Slip Tip or Luer Lock
Norm-Ject / Injekt-F 1 mL	HSW / B. Braun	Slip Tip

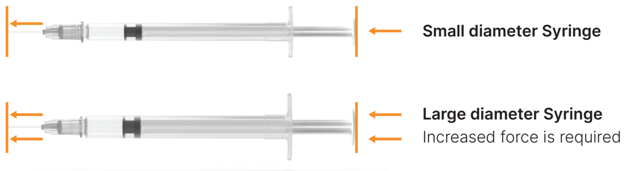
Injection Force

To provide the maximum amount of therapeutic protein in the limited intravitreal injection volume (approx. 50 pl), formulations are increasingly trending towards higher protein concentrations. This has led to formulations with viscosity as high as 120 cP (20 - 120 centipoise (CP)). If protein therapeutics are not allowed to reach room temperature after removal from cold storage, then viscosity levels are even higher. The syringeability (injection force) of these highly viscous formulations can be partly mitigated by syringe and needle choices. Optimal syringe and needle combinations can minimize the necessary injection force for the administration of biologics.

Reducing Injection Force

Syringe Barrel Diameter

Reducing the syringe barrel diameter decreases injection force.



Needle Inner Radius

As the size in the hole of the needle increases the injection force decreases.

Increasing needle gauge results in smaller inner radius where 30 gauge needle has lower injection force than a 33 gauge needle.

Decreasing needle wall thickness also leads to lower injection force.

Volumetric flow rate

Using a syringe with a narrower barrel, while keeping the needle constant, helps to reduce the pressure differential during use. This lower differential allows for a more consistent volumetric flow throughout the syringe, making it easier to control the injection force. As a result, the user can more accurately dose the amount of liquid being dispensed, improving precision and control during application.

3 Dose accuracy

Dose accuracy is influenced by various facets of syringe design, encompassing both the inherent precision of the syringe itself and potential inaccuracies stemming from human error, often attributable to less effective syringe design.

Intrinsic Accuracy

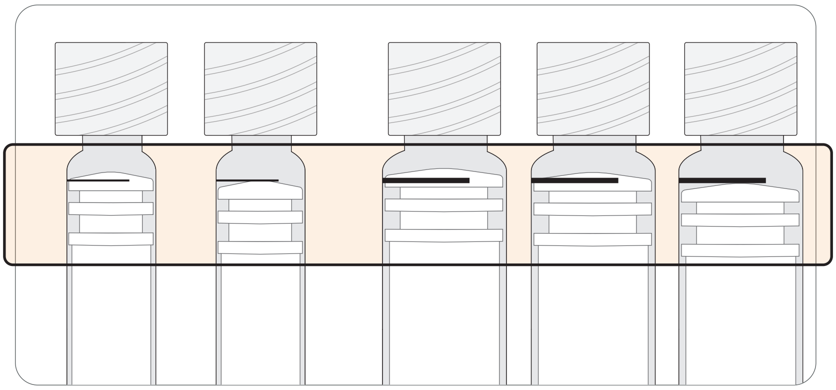
Total Syringe Volume

A smaller total syringe volume can enhance dosing precision compared to larger syringe volumes. For example, a 0.2 mL syringe tends to offer greater accuracy than a 1 mL syringe.

Design Features That Increase User Error

Dose Markings

Thick dose markings can lead to misalignment errors with the plunger, while thinner dose markings contribute to increased accuracy.



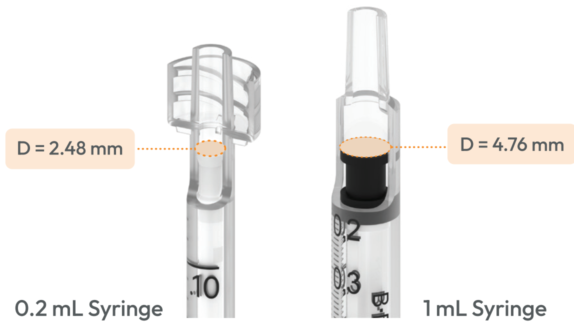
Small misalignments in the plunger can lead to possible overdosing.

Patient Safety

Increased syringe accuracy can reduce overdosing-related spikes in IOP which, after repeated injections, has been associated with reductions in retinal nerve fiber layer (Agra etl at., 2023).

Barrel Diameter

Studies have demonstrated that a larger inner barrel diameter can result in even minor misalignments translating into significant dosing errors (Gallagher et al., 2021). Additionally, a larger diameter contributes to higher injection forces (Lee et al., 2022). Therefore, a smaller inner barrel diameter is generally preferred to enhance dosing accuracy and reduce the potential for injection-related issues.

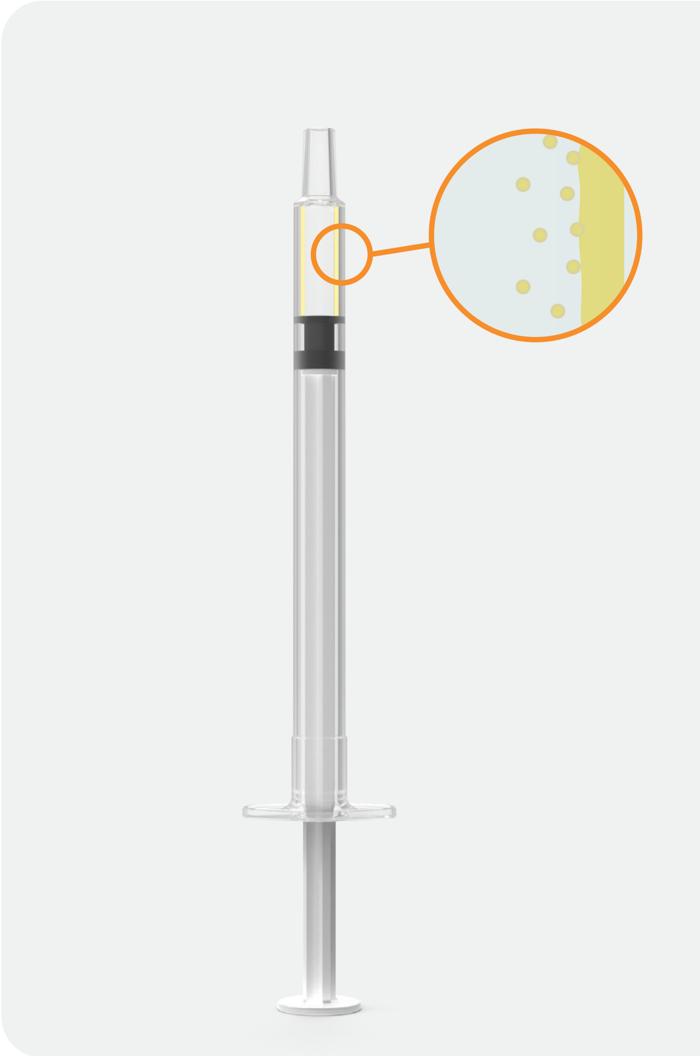


Plunger Shape

The shape of the plunger is a crucial consideration. A domed plunger shape can present challenges in aligning the dome with the dose marker, potentially leading to significant volumetric discrepancies between injections. In contrast, the flat plunger design of the SJJ or BD syringe greatly simplifies this task, ensuring more consistent and accurate dosing.

4 Silicone Oil

While Silicone Oil (SiO) is commonly used in syringes to ensure smooth plunger movement, it is essential to be aware that SiO has been demonstrated to have several adverse effects. These include an increase in protein aggregation (Thirumangalathu et al., 2009), potential stimulation of immune reactions (Chisholm et al., 2016; da Cruz et al., 2022), and, over multiple treatments, the accumulation of SiO in the vitreous of patients, leading to SiO floaters. In severe cases, this may necessitate removal through vitrectomy (Avery et al., 2019; Bakri & Ekdawi, 2008; Khurana et al., 2017; Yu et al., 2018). SiO-free syringes are preferred.



Patient Safety

SiO has been associated with immune reaction and SiO floaters.

Product Integrity

SiO has shown to increase protein aggregation (Jones et al., 2005; Thirumangalathu., 2009)

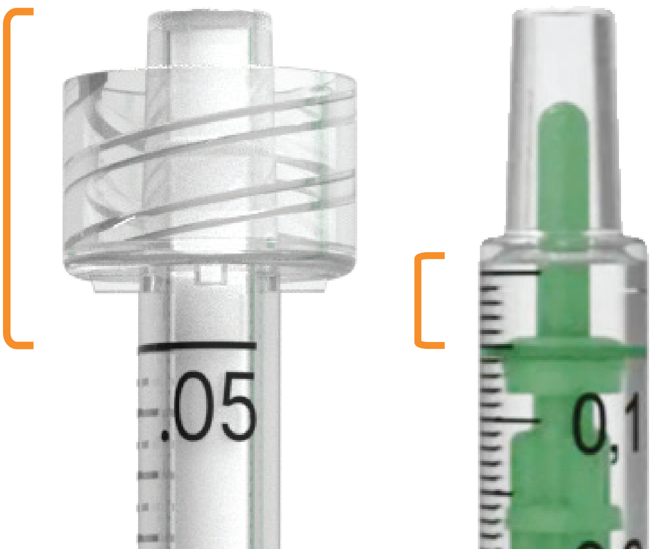
5 Injection Speed

When IVI is administered, syringe design can affect the ability of prescribers to inject at a controlled rate. Stroke length is closely tied to the potential to induce spikes in patient intraocular pressure (IOP).

Patient Safety

Longer stroke length can reduce spikes in IOP which, after repeated injections, has been associated with reductions in retinal nerve fiber layer (de Vries et al., 2020).

Stroke Length



6 In-Use Practicality

Secure Needle Attachment

When viscous medications are required, Luer Lock syringes provide a more secure needle attachment than slip tip syringes preventing possible leakage or needle pop-off that could occur due to higher plunger forces.

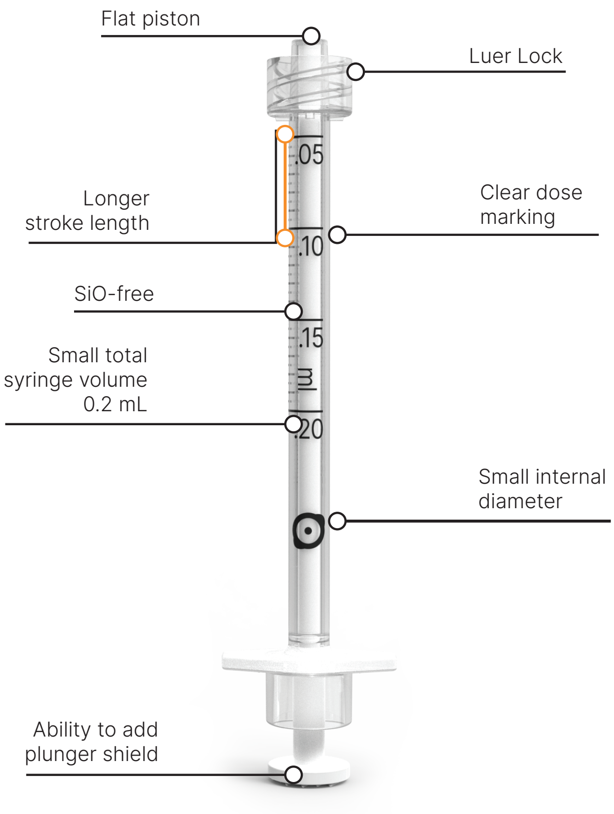
Smooth Injection

Though some syringes are Silicone Oil-free, the quality may vary. Many of them lack the smoothness on injection that would be required for a sensitive procedure such as an intravitreal injection.

Comfortable Size

Shorter, more comfortable syringes are easier to handle for many ophthalmologists, offering improved ergonomics that enhance ease of use, making them a preferred option.

Anatomy of Ideal Syringe for Intravitreal Injection



Critical IVI Syringe Selection Factors	Ideal Features	Soft-Ject / Omnifix F	Norm-Ject / Injekt-F	BD Tuberculin	Zero Residual™ 0.2 mL SiO-free
Accuracy	Flat Plunger			✓	✓
	Clear Dose Marking				✓
	Small Inner Barrel Diameter				✓
	Small Total Syringe Volume (less than 0.3 mL)				✓
Particle amount	USP 789 Compliant	N/A	N/A	N/A	✓
SiO Content	SiO-Free		✓		✓
Injection Speed	Longer Stroke Length for Controlled Injection				✓
In-Use Practicality	Secure Needle Attachment (Luer Lock)	✓			✓
	Smooth Injection	✓		✓	✓
	Comfortable Size				✓

Zero Residual™ 0.2mL SiO-free

Zero Residual Volume = Zero Waste

The Zero Residual™ 0.2mL SiO-free syringe provides a syringe that checks all of the boxes related to Patient Safety, Product Integrity, and In-Use Practicality for Ophthalmologists. Specifically designed for the small IVI volumes, the 0.2mL syringes addresses unique ophthalmic needs currently unmet by conventional 1 mL syringes.

Improved Patient Safety

Accuracy - avoids IOP spikes associated with conventional syringe overdosing

Increased stroke length - enables controlled delivery, reducing IOP spikes

SiO Free - negative impacts of SiO avoided

Luer Lock - secure needle connection

In-Use Practicality

Reduced total length

Smooth injection

Increased stroke length

Low injection force

Overall improved syringe control and comfort

More controlled injection speed

Product Integrity Maintained

- ✓ Low particulate contamination
- ✓ Low protein aggregation
- ✓ Protein stability maintained (Gjølberg et al., 2022 & Jorstad et al., 2023)

Safety and Regulatory

Until now, commercially available syringes have not been optimized for intravitreal injection and safety issues have prompted syringe manufacturers to reiterate that the use of their syringes in IVI is off-label. The Zero Residual™ 0.2mL SiO-free syringe is the first CE-approved syringe that is specifically tailored and optimized for intravitreal injections.

Recommendations and Considerations

Given their heightened product stability, enhanced patient safety profile, user-friendliness for Ophthalmologists, increased comfort for patients, and improved dosing accuracy, syringes like the Zero Residual™ 0.2mL SiO-free should be preferred. Additionally, syringes without an attached or staked-on needle are also preferred, as they minimize potential complications and ensure a smoother injection process. In cases where therapeutic solutions have a higher viscosity, luer lock syringes are recommended over slip tip syringes for added security and precision during administration.

Conclusion

Following a thorough evaluation of the scientific literature, rigorous testing by independent third-party laboratories, and meticulous in-house assessments, it has been determined that the Zero Residual™ 0.2mL SiO-free syringes from SJJ Solutions stands out as the optimal choice for intravitreal injections. Demonstrating superior safety and efficacy, with no wastage of costly sight-saving medication.

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