A partnership worth more than the sum of its parts

Device component suppliers fulfil syringe and system performance requirements in Pharma combination product development

Aptar pharma

gerresheimer
innovating for a better life

Background

Prefilled syringes are complex medical devices. Comprehensive data on essential performance requirements (EPRs) and primary functions (PF) needs to be collected and evaluated.

Suppliers of prefilled syringe components can proactively test and qualify their components with regard to ISO 11040-8.

Component suppliers can carry out drug-agnostic platform design verification and validation in joint projects to collect relevant data.

Such supplier data reduces R&D efforts, minimizes risk at Pharma and can accelerate time to market. Gerresheimer, Aptar Pharma and autoinjector companies address unmet needs of Pharma companies regarding syringe system performance.

This poster addresses break-loose & gliding forces of different syringe systems, latest improvements in needle shield pull-off force, and shows data for integration of syringes into autoinjectors.

Challenges for Suppliers

Generally, suppliers have limited insight into drug formulation, user requirements and intended use. A complete drug related risk evaluation acc. ISO 14971 is impossible. Device and component suppliers can

- suggest best fit „platform device" to best knowledge prior to stability, clinical testing, human factor testing
- anticipate final requirements of performance requirements, do a basic device risk management
- perform molecule agnostic testing, supported by model liquids w/o API
- provide design verification and design validation of „platform devices"

What tests can be done by Pharma Device Suppliers?

A series of drug-agnostic testings can be made at suppliers, drug-related testing can also be performed on customer request

Examples for important test data from supplier testing

1. Break-loose and Gliding force tests with model liquids
2. Needle shield pull-off force
3. Autoinjector fit – dimensions, forces

By following some basic platform assumptions:

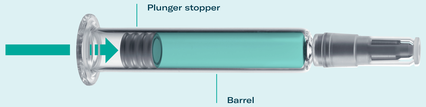
- Subcutaneous injection
- Volume between 0.5 ml up to 3 ml
- Viscosity 1 CP to >20 CP
- Storage between +2° C to +8° C

Risk assessment at Supplier – example

System performance	Essential performance requirements	Risk of failure – supplier assessment	Which part of the system contributes			Risk of failure	Risk mitigation strategies through suppliers collaboration
			Components	Syringe	Autoinjector		
Break–loose and Gliding force	Forces enable manual injection or AI integration	Mostly Predictable based on solution properties	√	√	(√)	Low to moderate	Generate platform datasets to predict real case results. Spring force of AI can be adapted f or compatibility with gliding and break loose forces
Finger flange and cone break	PFS resistance higher than spring force	Drug independent		√	√	Low	Comparison of PFS and AI specifications. Resistance tests
Needle shield and cap removal force	Cap gripping force higher than RNS pull–off	Drug independent	√	√	√	Low	Determination of RNS pull of force, and comparison with AI specification
Dimensional fit into AI	Compatibility of key dimensions	Drug independent		√	√	Low	Comparison of key dimensional requirements and tolerances
Administration time	Acceptable time for sub cutaneous injection	Mostly Predictable based on solution properties	√	√	√	Low to moderate	Integration of multiple parameters to anticipate results (BL, GL, needle length, needle diameter, drug viscosity…)

Interface of syringe barrel and elastomer components 1

1. Break loose and Gliding Forces



2.25 ml Gx Elite syringe with Aptar Premium Coat plunger stopper for autoinjector use

Gx® Elite syringes: Break loose and Gliding force (BLGF) for Aptar Pharma PremiumCoat® plungers

Syringe barrel Gx Elite ID 10.85 mm	Barrel material	Silicon-ization	Cannula	Filled with	Plunger stopper	Stoppe-ring	Storage time	Test speed (mm/min)
1 ml short	Glass	0.5 mg	25G ⅝" Standard wall	WFI 1 cp	Aptar Premium Coat®	Vent tube	3 months acc. aging 40° C	270
2.25 ml	COP	0.8 mg	27 G ½" thin wall	WFI 1 cP	Aptar Premium Coat®	Vent tube	3 months acc. aging 40° C	270
2.25 ml	Glass	0.8 mg	w/o	WFI 1 cP	Aptar Premium Coat®	Vent tube	3 months ambient	300

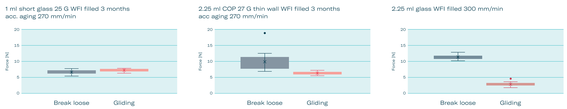
A wide variety of syringe features is possible. Available platform test data helps to define the best device according to the intended use and application.

Drug dependent feature
Physical Functionality Bracketing (Platform) assessment made with WFI filled syringes, depending on

a. Barrel material and ID, length
b. Needle length and ID
c. Viscosity
d. Elastomer type and design
e. Siliconization type and amount
f. Stoppering method
g. Storage time an conditions
h. Speed parameters

→ **Performance test and best choice of components can be facilitated through supplier cooperation**

Example BLGF curves from Gerresheimer and Aptar Pharma test labs



Example data gives guidance for early development steps. Direct comparison not useful, Tests do not replace evaluating the final system: Many parameters influence BLGF.

Typical BLGF curve, test acc. ISO 11040-4.

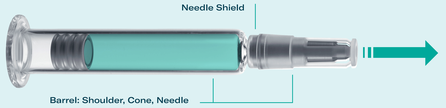
$$F = \frac{8 * Q * \eta * L}{\pi * R^4 * A}$$

Hagen–Poiseuille equation –
giving a very first indication but does not replace realistic test conditions

Formula valid for Newtonian fluids with
F – frictionless travel force; Q – volumetric flow rate; η – fluid viscosity; L – needle length; R – needle inner diameter; A – cross sectional area of syringe plunger

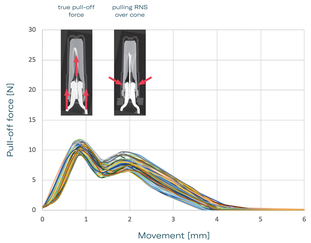
Interface of syringe barrel and elastomer components 2

2. RNS Pull-off Force



2.25 ml Gx Elite syringe with Aptar Pharma RNS for autoinjector use

Gx® Elite syringes: Pull-off force of Aptar RNS*



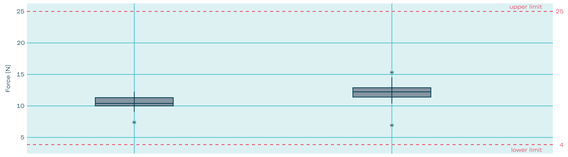
Drug agnostic feature
Physical Functionality Bracketing (Platform) assessment made with platform syringes depending on

a. Cone dimensions and design
b. RNS dimensions and design
c. Elastomer type
d. Siliconization
e. Needle dimensions
f. Sterilization
g. Storage time an conditions

→ **Performance test and best choice of components can be facilitated through supplier cooperation**

*RNS: Rigid needle shield

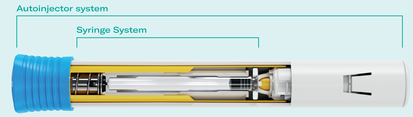
Typical rigid needle shield pull-off force (example). 1st and 2nd peak caused by friction of cap on cone



Box plots of RNS pull-off force (PoF) for optimized Cone and RNS interface, room temperature vs. cold storage 5°C (worst case). Lab testing and optimization of customized needs possible

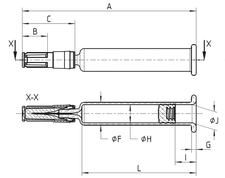
Interface of syringe and autoinjector

3. Device integration: Dimensions and Functionality



Picture by courtesy of SHL

Basic and Critical Dimensions for a 2.25 ml Syringe, to be mounted into an Autoinjector



Dimension	Gx 2.25 ml glass syringe dimensions incl. RNS	Autoinjector device dimensions
A	√	√
B	√	–
C	√	√
F	√	√
G	√	–
H	√	–
I	n/a	√
J	√	√
L	√	√
N	√	√
O	√	√

All the functionality tests need to follow ISO 11608-1, ISO 11608-5. Other dimensional aspects may be considered for specific AI designs

Drug dependent features

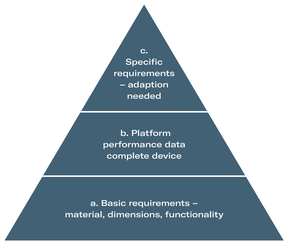
Pharma performance assessment depends on

a. basic material requirements (ISO 11040-4)
- basic dimensions: e.g. barrel dimensions and tolerances
- syringe functionality

b. variables suppliers know – platform data
- critical dimensions (2): basic tolerance stacking of barrel + cap + autoinjector

c. unknown to suppliers – adaption needed
- critical dimensions (1) acc. ISO 11040-8: exact fill volume and plunger position (e.g. 2.25ml)
- intended use
- drug viscosity
- user/patient group

→ **Test and best choice of components can be made by supplier and customer cooperation**



Conclusion

Device component manufacturer strengths:

1. Recommend best fit materials and components
2. Support with existing platform data
3. Adapt final device on top of platform

- Gerresheimer, Aptar Pharma and autoinjector companies jointly collect functionality data
- Various syringe system configurations and platform devices are available, match with various needs (intended use)
- Drug-agnostic platform test data packages are available

Design verification and design validation help to

- **minimize risk** of failure in stability studies and in fill & finish
- **reduce development** cost and regulatory efforts
- **accelerate time** in clinical trials and to commercial application

References

- ISO 11040-8: 2016: Requirements and test methods for finished prefilled syringes
- ISO 11608-1:2022: Needle-based injection systems for medical use
- PDA 2015: Technical Report No. 73: Prefilled Syringe User Requirements for Biotechnology Applications
- US FDA 2019: Draft Guidance for Industry Bridging for Drug-Device and Biologic-Device Combination Products
- US FDA 1999: Guidance for Industry: Container Closure Systems for Packaging Human Drugs and Biologics

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