



The Universe of Pre-filled Syringes & Injection Devices

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The Development Story of Rotaject®

A Novel Autoinjector for High Volume, High Viscosity, and Outstanding Usability

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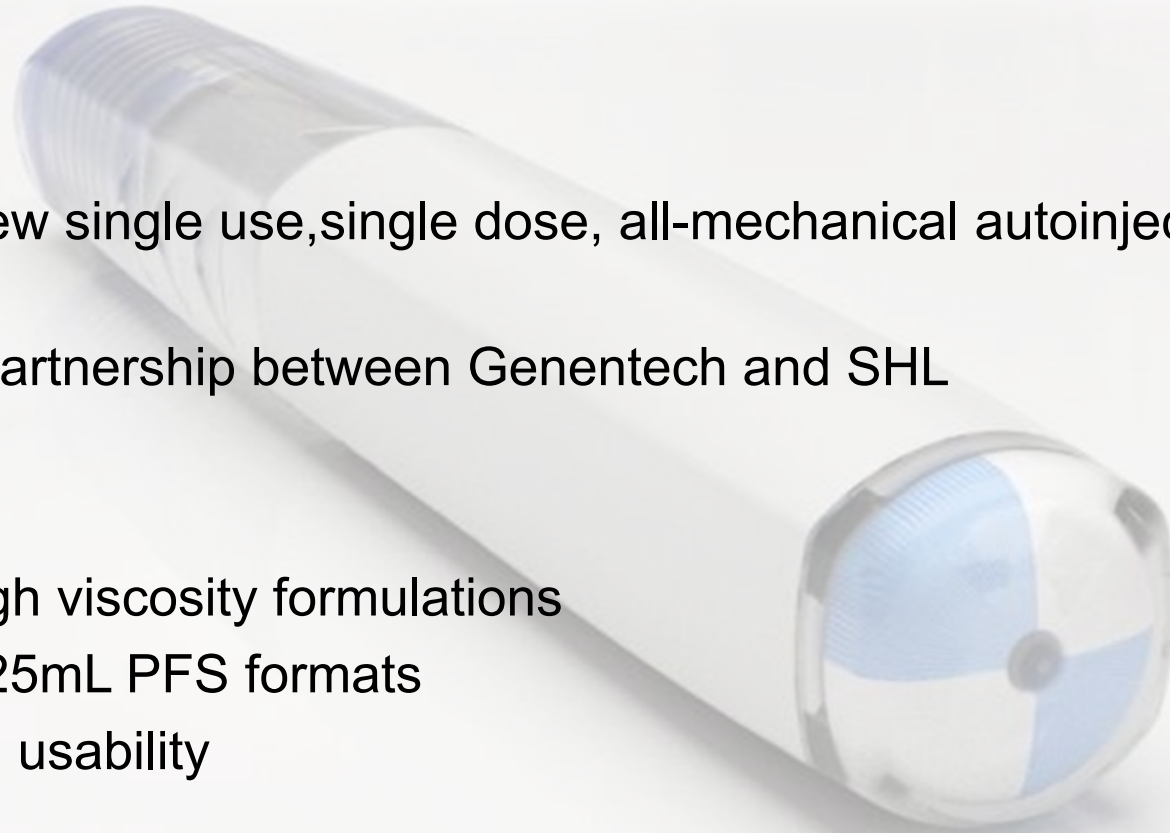
What is Rotaject?

Rotaject is a new single use, single dose, all-mechanical autoinjector

Developed in partnership between Genentech and SHL

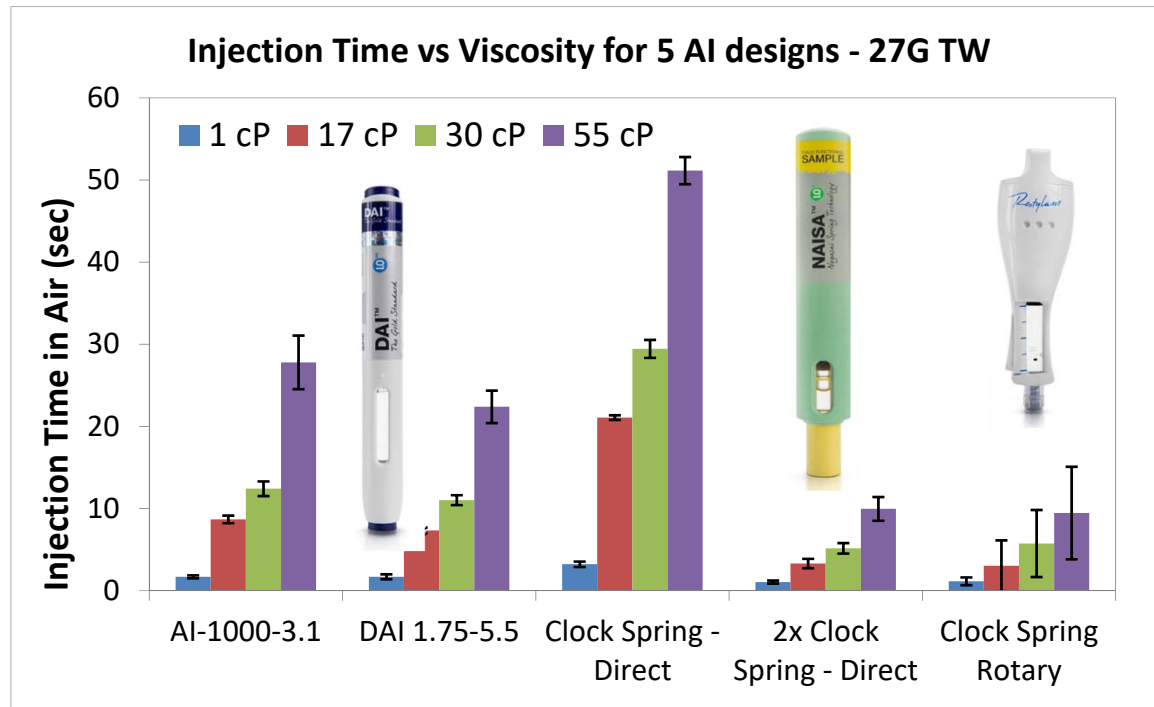
Designed for:

- Low and High viscosity formulations
- 1mL and 2.25mL PFS formats
- Outstanding usability



Why develop a new autoinjector?

- Genentech had a need for AI with high viscosity and 2mL capability
 - We believe that long injection times and/or large ID needles are not the answer
- SHL technologies had the most promise. A feasibility study was executed



SHL's clock spring technologies demonstrated the highest viscosity capability



Advantages of rotary drive clock spring technology (Rotaject)

High viscosity/volume capability

- Enables short injection times
- Enables smaller needles
- Better for patient comfort and compliance

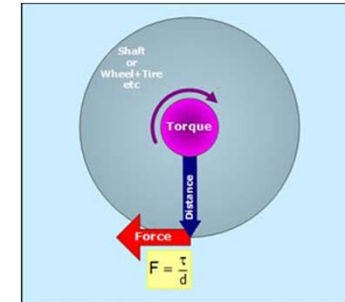


High injection force with low “release” force

- Does not require high activation force
- Does not have high “creep” forces
- Allows for independent needle insertion spring

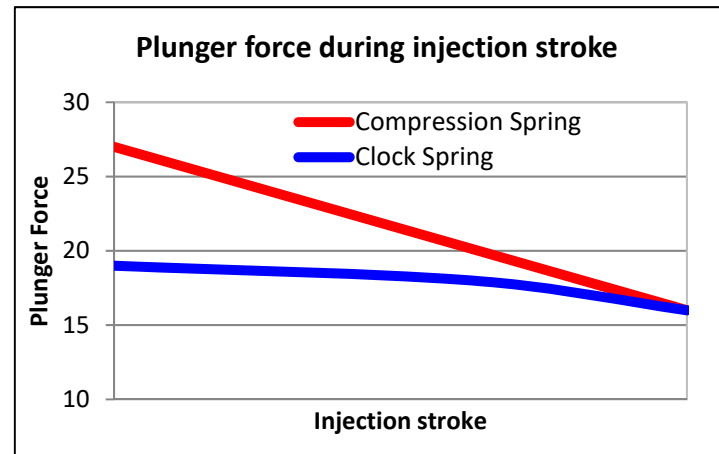
Most customizable injection force

- Clock spring length, width, thickness
- Spring pre-load
- Lead screw pitch



Flatter force profile

- Lower impact at activation
 - Reduced risk of glass break
 - Less “startle” for patients
- Consistent injection rate



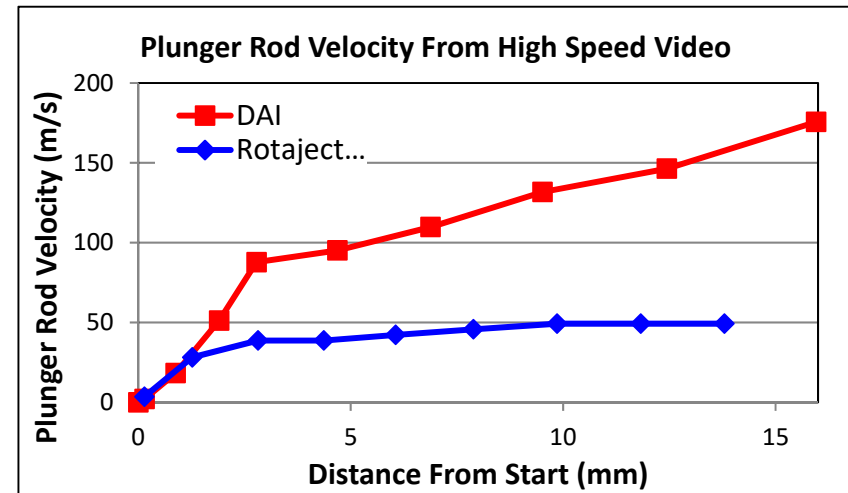
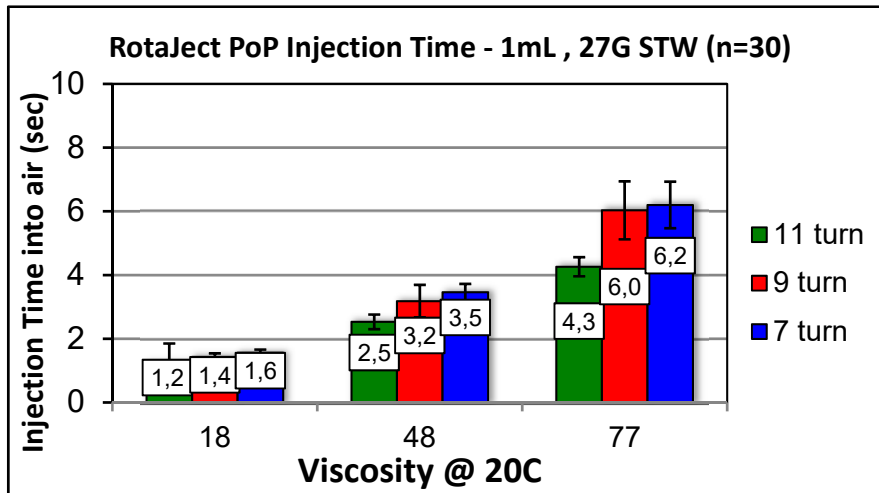
Base technology has been commercialized





SHL designed and manufacture fully functional Proof-of-Principle prototypes

- The PoP prototypes (~3,000) were tested extensively for performance and manufacturability, including:
 - Injection Time vs clock spring torque, viscosity, and volume
 - Activation Force vs clock spring torque
 - ISO tests (e.g. dose accuracy, NC override, drop tests, etc)
 - Accelerated aging and “Edge of Failure” testing



PoP devices gave confidence to embark on final design and opportunity to identify design flaws

Usability and Human Factors assessments

What is the safest and most intuitive activation mode?

Study Materials

Functional prototypes w/ 4 activation modes:

- Needle cover activated (NCA)
- Persistent lock + NCA
- Button w/ NC interlock (sequence dependent)
- Button w/ NC interlock (sequence independent)

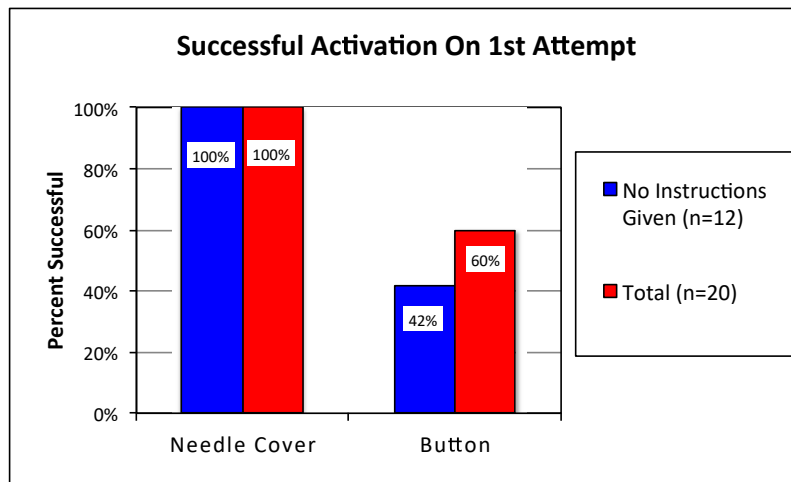


20 Study Participants:

- 6 HV, 5 MS, 5 RA, 2 Cancer, 2 Diabetes
- Mix of AI naive and AI experienced

Study Design

- 12/20 were given no instruction
- 5/20 verbal description, no demo
- 3/20 verbal description w/ demo



Results

- Needle cover activation was most intuitive and most preferred
 - 100% success rate, even with no instructions

- Needle cover activation mode was selected for Rotaject
- Simplifies training, reduces use errors, and reduces complaints

Usability and Human Factors assessments

How can we improve injection feedback?

Study Materials

POP devices w/ 3 feedback modes:

- Spinning Top as in-process feedback
- Proportional spinner as “fuel gauge”
- End-of-Dose feedback via pop-up and click

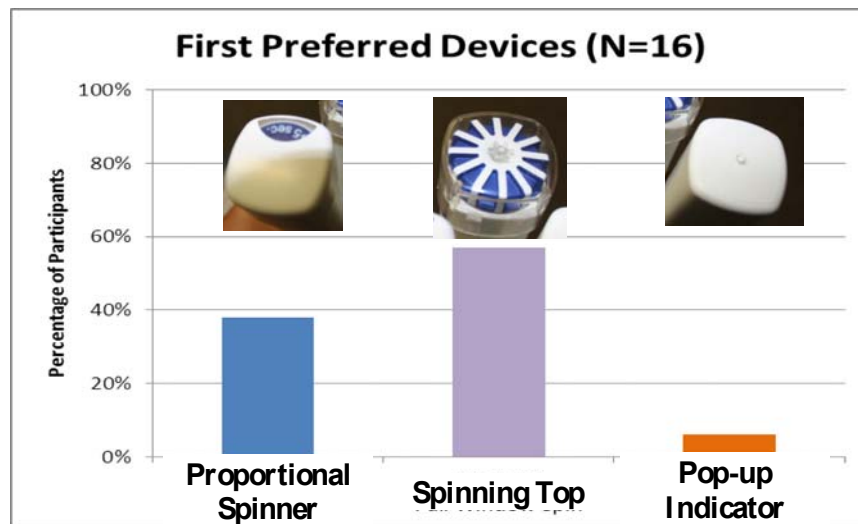


20 Study Participants:

- 6 HV, 8 MS, 2 RA, 2 Lupus, 2 Diabetes
- Mix of AI naive and AI experienced

Study Design

- 12/20 were given no instruction
- 5/20 verbal description, no demo
- 3/20 verbal description w/ demo



Results

- The Spinning Top was most intuitive due to its ability to clearly communicate the start and stop of the injection.

The Spinning Top was selected to provide reduce use errors due to early withdrawal

Usability and Human Factors assessments Activation force & stroke, and hold force

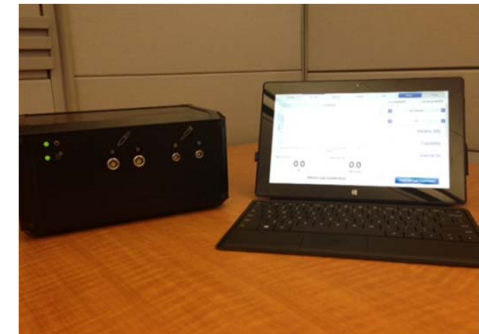
Activation Stroke/Force

- Mechanical models were fabricated in which compression force and stroke could be varied
- 30 healthy volunteers evaluated trade-off between comfort and perceived safety



Activation and Holding Force

- Anthropometric study with 30 healthy volunteers
- Instrumented Rotaject device to measure the user's applied force
- 3 injection sites:
 - Thigh, Abdomen, Back of Arm (caregiver)

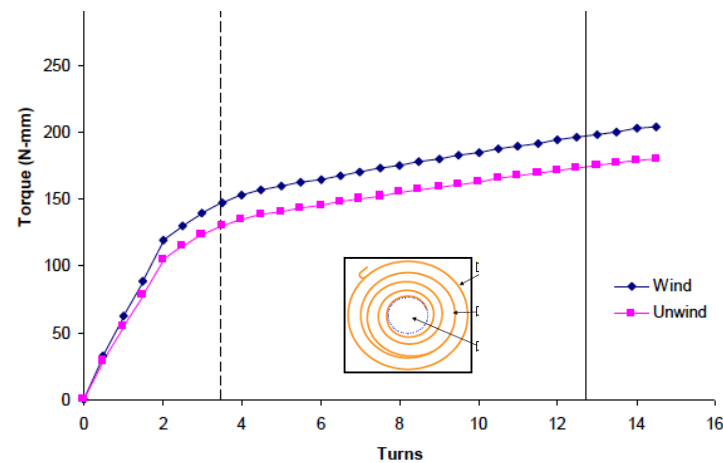


Study results provided rationale for Activation Force, Activation Stroke, and Hold Force requirements based on on user comfort and use-safety



Final design optimized through comprehensive tolerance analysis, mathematical modeling, and testing

- Applied principles of robust design and design for manufacture
- Analyzed all tolerance loops relevant to functionality and assembly
 - CAD drawing for each tolerance loop - 374 tolerance loops analyzed!
 - Determined “criticality” based on impact of failure
 - Determined “weight” of each dimension in the loop
 - Identified critical dimensions based on the criticality and weight
- Optimized drive mechanism (clock spring / lead screw) for mass and plunger force
- Optimized materials for performance, improved frictional pairings, aesthetics





Final Rotaject design is a flexible platform with high viscosity capability and outstanding usability

Easy Cap Removal

- Large easy-to-grip cap
- Pull-off or twist-off

Large Viewing Window

- Easy to inspect
- In-Process feedback

Intuitive and safe “Push on Skin” Activation Mode

Automatic Needle Insertion

Customizable Injection Force

- Enables short injection time
- Enables small needles

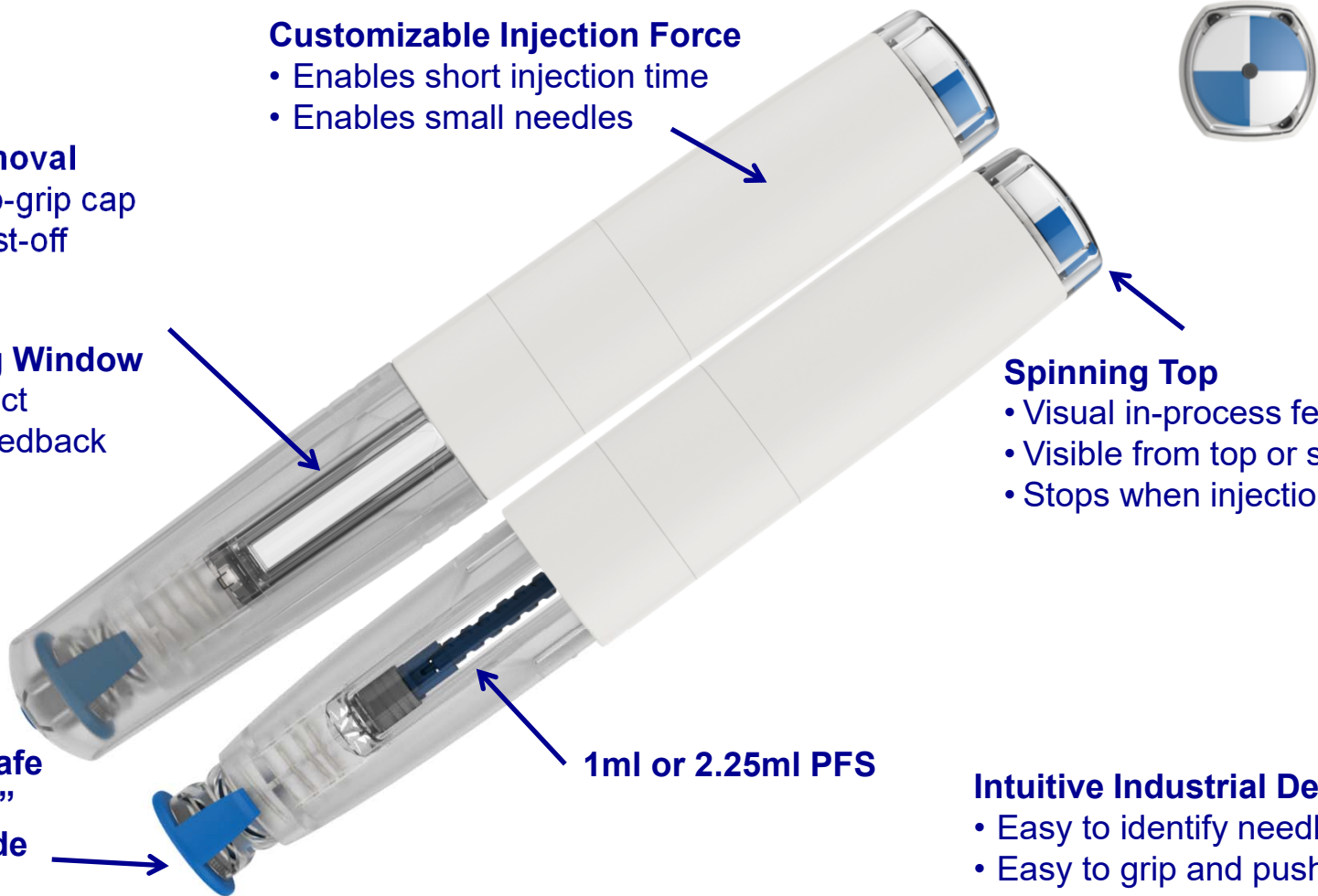
1ml or 2.25ml PFS

Spinning Top

- Visual in-process feedback
- Visible from top or side
- Stops when injection stops

Intuitive Industrial Design

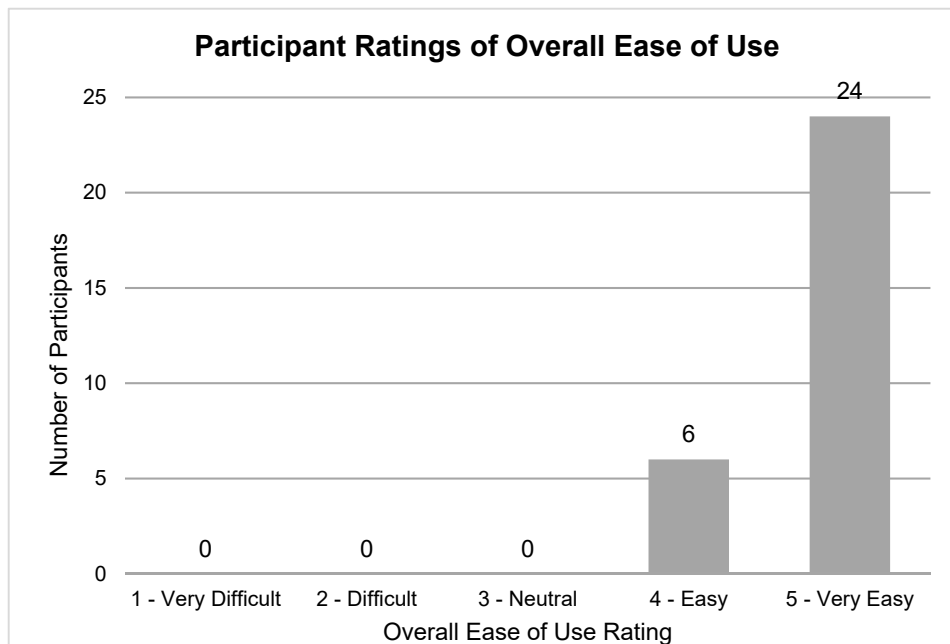
- Easy to identify needle end
- Easy to grip and push down





Excellent usability was demonstrated in actual use human factors study

- 30 healthy subjects at two clinical study sites
- Study site mimicked home use setting
- Subjects self-administered RotaJect into thigh or abdomen



Results:

- Participants found Rotaject to be easy to use
- No pattern of use errors
- In-process feedback was effective and well-received



In Summary...

- RotaJect was developed through a rigorous process and in close collaboration between Genentech and SHL
- Rotaject is for low and high volume...
 - 1mL and 2.25mL PFS formats (only 3 different component)
 - No change in plunger rod for different volume
- ...low and high viscosity...
 - Customizable spring – no other component changes
 - Design verification with up to 60cP in <10 seconds (27G TW needle)
- ...outstanding usability to enable safe and effective use
 - Easy cap removal
 - Intuitive and safe activation
 - Multiple signals for in-process feedback
- ...and is clinically proven



Acknowledgements

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