Genentech
A Member of the Roche Group

REINTRODUCTION OF THE PORT DELIVERY SYSTEM WITH RANIBIZUMAB:

DEVICE UPDATES

This is a medical resource for scientific information and is intended for healthcare providers practicing in the United States.
Current as of July 2024

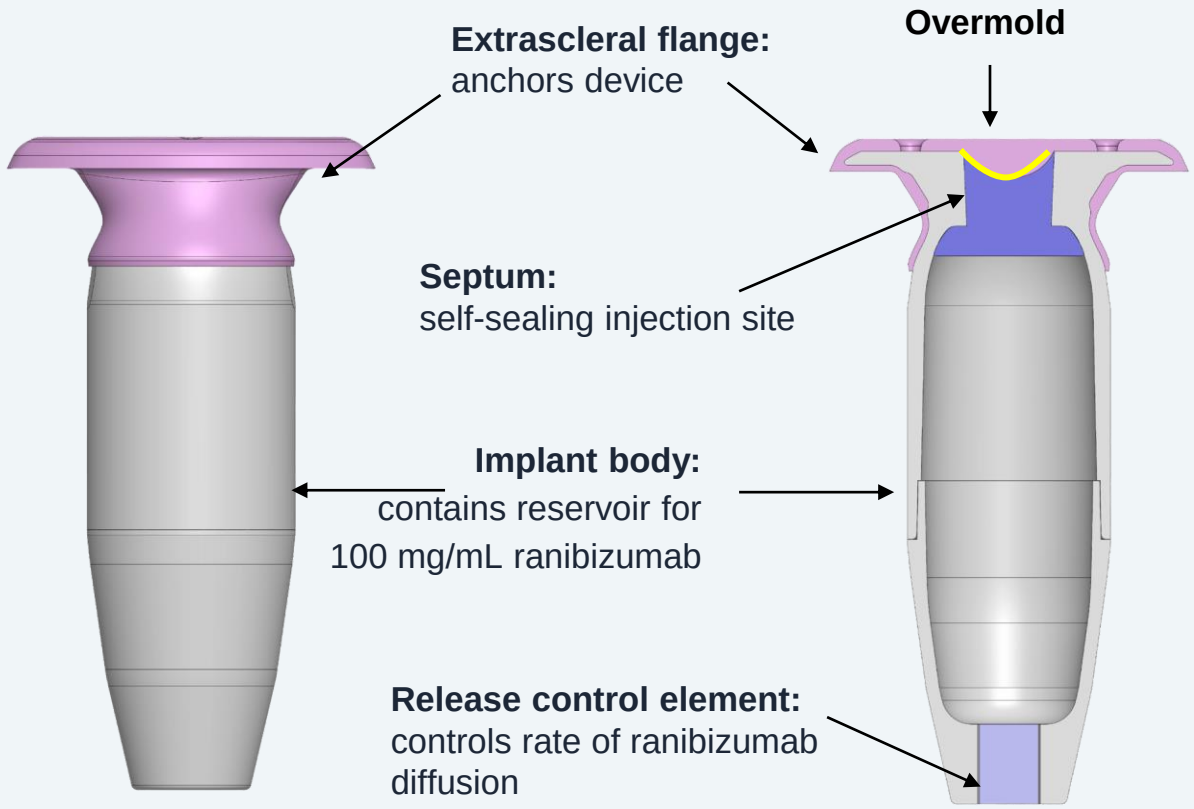
DISCLAIMER

Please Note: The information we provide may include references to a Genentech product or use of a Genentech product that the FDA has not approved; because the FDA has not approved such product(s) or use, no conclusions regarding safety or efficacy may be made. Providing this information should not be construed as recommendation for use of a Genentech product for unapproved uses. For FDA approved products please consult the product's full prescribing information for a complete discussion of risks and benefits of the product(s) for its approved indication(s).

The information we provide may additionally include relevant references to non-Genentech product information derived from publicly available sources.

Genentech
A Member of the Roche Group

CONTINUOUS DELIVERY VIA THE PORT DELIVERY SYSTEM WITH RANIBIZUMAB (PDS)



Innovative Drug Delivery System

Refillable ocular implant for **continuous delivery** of a customized formulation of ranibizumab 100 mg/mL

Implanted surgically at the pars plana with in-clinic refill-exchange procedures 1 or 2 times a year

PDS, Port Delivery System with ranibizumab. Pieramici D et al. Presented at: Angiogenesis; February 3, 2024; Online. Data on File [image on right].

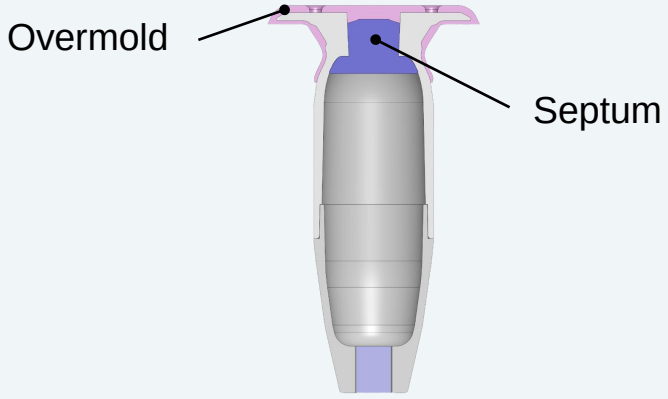
GENENTECH VOLUNTARILY RECALLED* PDS AFTER IDENTIFYING SOME IMPLANTS DID NOT MEET PRESPECIFIED PERFORMANCE SPECIFICATIONS

Root Cause of Septum Dislodgement

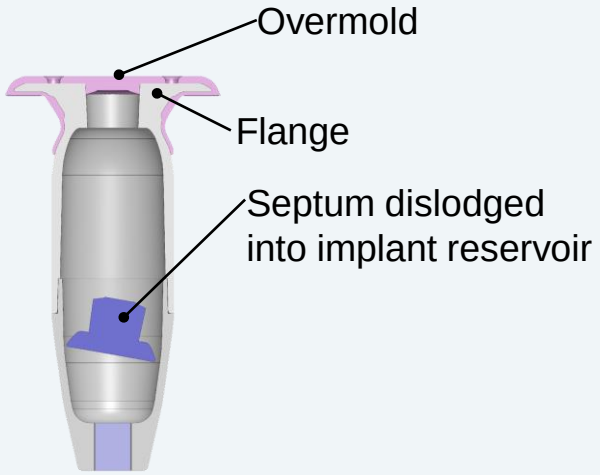
The root cause investigation revealed the following as the leading factors contributing to septum dislodgement:

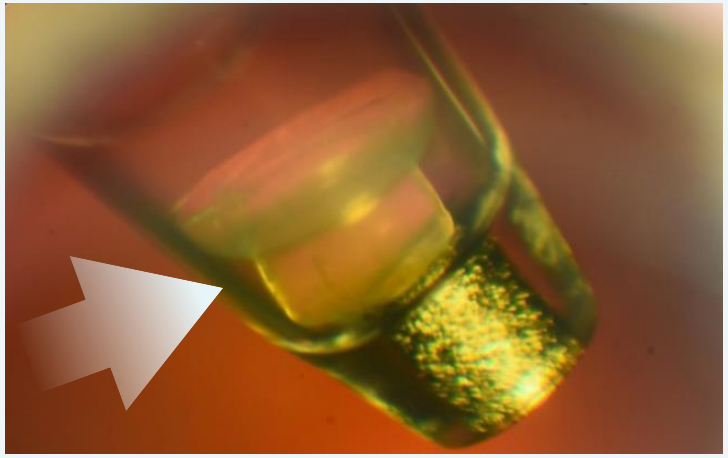
- **Insufficient bonding** between the septum and overmold
- **Excessive insertion force** from the refill needle

Normal Position of the Septum



Septum Dislodgement[a]





***The voluntary recall of the Susvimo Ocular Implant and Insertion Tool Assembly also included Susvimo (ranibizumab) drug vial and initial fill needle (lot numbers 3499188 and 3523071) which are sold together. This recall was lifted in April 2024.**

[a] Septum dislodgement is a known risk associated with the PDS and is included in the FDA-approved Prescribing Information and clinical trial protocols. Images used with permission. FDA, US Food and Drug Administration; PDS, Port Delivery System with ranibizumab. Pieramici D et al. Presented at: Angiogenesis; February 3, 2024; Online.

REPORTED CASES OF SEPTUM DISLODGEMENT IN PDS CLINICAL TRIALS

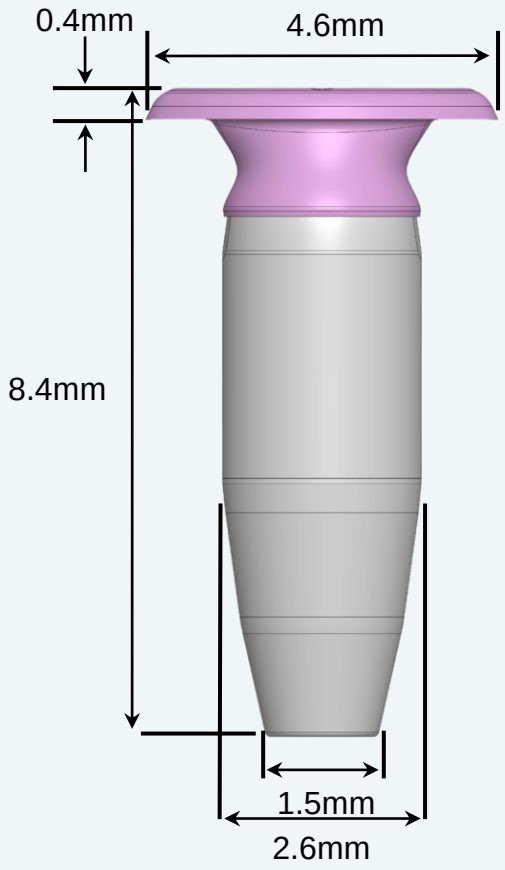
All Implants: 78 Cases of Septum Dislodgement (SD)[a]	
Number of patients implanted:	1466
SD rate per 100 implants:	**5.3%**

	Phase 3	Phase 2	Commercial
Number of SD	**78[b]**	**0[c]**	**0[c]**
Patients implanted (n)	1082	195	189
SD rate per 100 implants	**7.2%**	**0%**	**0%**

Septum dislodgement is listed in the Susvimo prescribing information under Warnings & Precautions

Data as of October 31, 2023, unless specified. [a] Includes patients implanted with phase 2, phase 3, and commercial implants. [b] Includes reimplantations. [c] There were 0 septum dislodgements out of ~195 implanted patients with phase 2 implants and 0 septum dislodgements out of ~189 patients that were implanted with commercial implants in clinical trials. [d] Data as of September 30, 2023. PDS, Port Delivery System with ranibizumab; SD, septum dislodgement. Pieramici D et al. Presented at: Angiogenesis; February 3, 2024; Online.

COMPONENT-LEVEL CHANGES AND MANUFACTURING PROCESS IMPROVEMENTS WERE IMPLEMENTED TO STRENGTHEN THE SEPTUM–OVERMOLD BOND[1]



Extrascleral flange:
anchors device

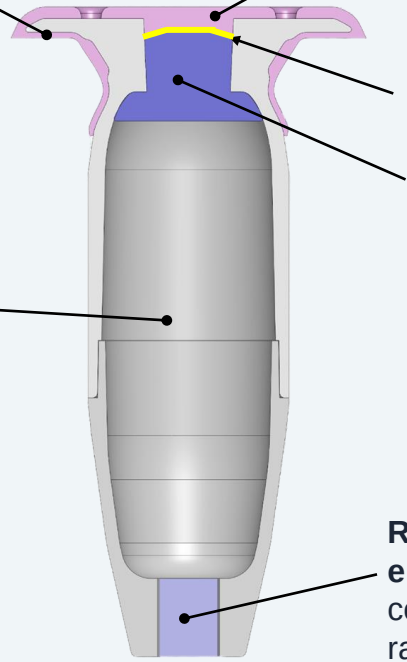
Overmold

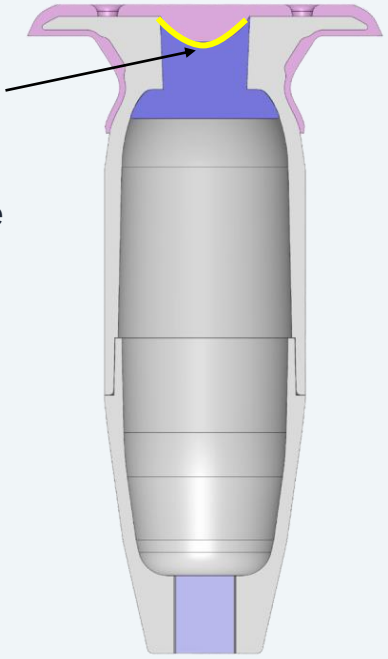
Septum–overmold interface

Septum:
self-sealing injection site

Implant body:
contains reservoir for 100 mg/mL ranibizumab

Release control element:
controls rate of ranibizumab diffusion





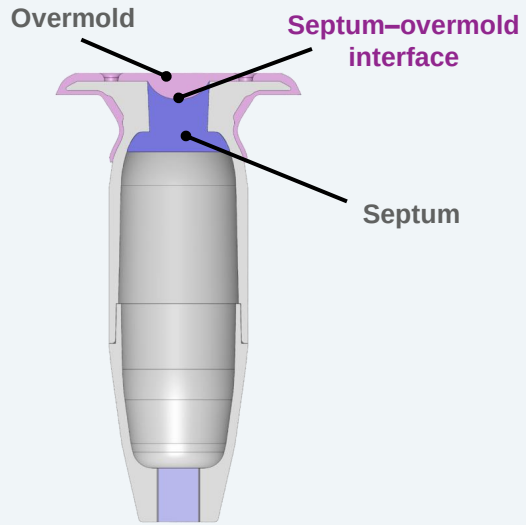
Recalled implant

Updated implant

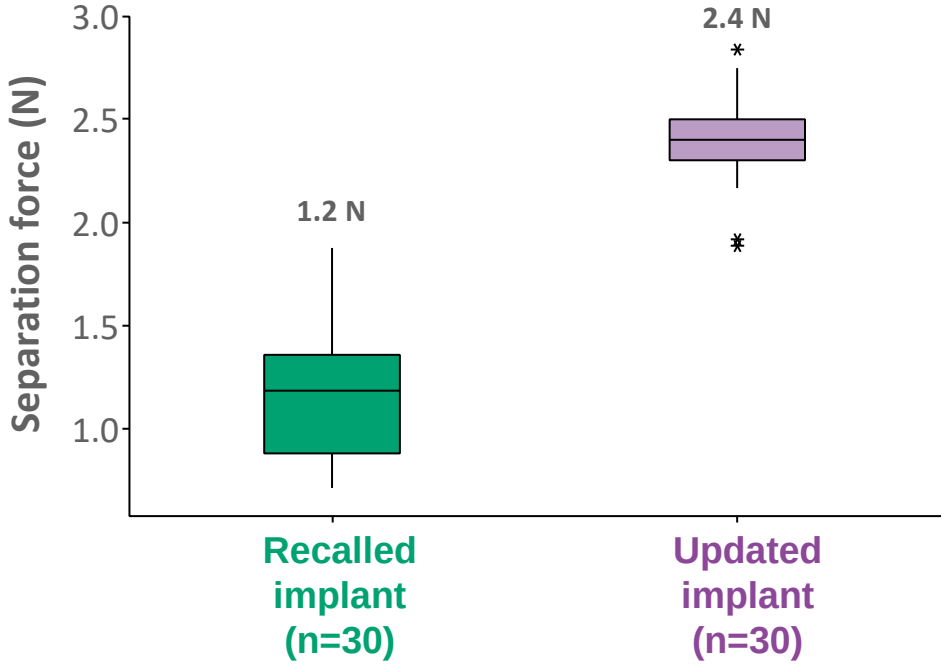
 Pieramici D et al. Presented at: Angiogenesis; February 3, 2024; Online.

UPDATES TO THE IMPLANT DOUBLE THE BOND STRENGTH BETWEEN THE SEPTUM AND OVERMOLD, PROVIDING HIGH CONFIDENCE OF LONG-TERM SEPTUM DURABILITY.[1]

Implant



Schematic



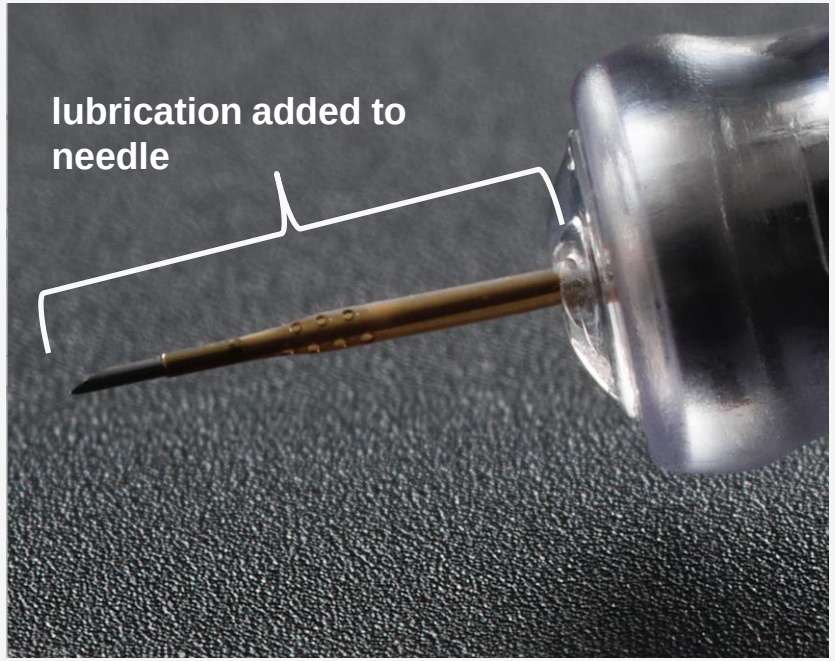
The retention force between the septum and overmold **is doubled**

Photo depicts the previous version of the implant. Images used with permission. Copyright © 2024 F. Hoffmann-La Roche Ltd. All rights reserved

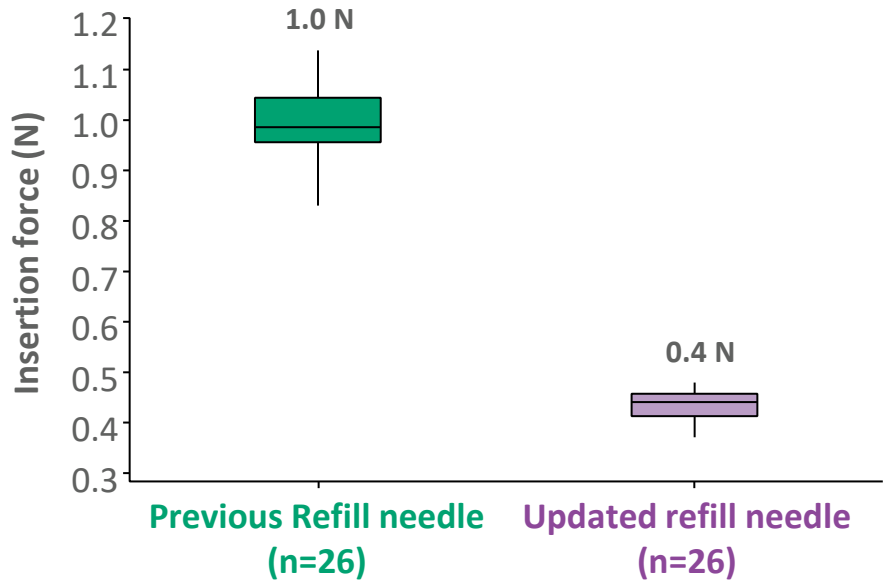
1. de Juan E, et al. Presented at Macula Society 2024

Genentech
A Member of the Roche Group

LIGHT LUBRICATION OF THE REFILL NEEDLE ALLOWS THE NEEDLE TO BE INSERTED INTO THE SEPTUM MORE SMOOTHLY, REDUCING THE INSERTION FORCE BY HALF[1]



Refill needle



Updated refill-exchange needle reduces the insertion force by more than 50%

Data were collected with the recalled commercial implant. Photo depicts the previous version of the refill needle. Image used with permission.

1. de Juan E, et al. Presented at Macula Society 2024

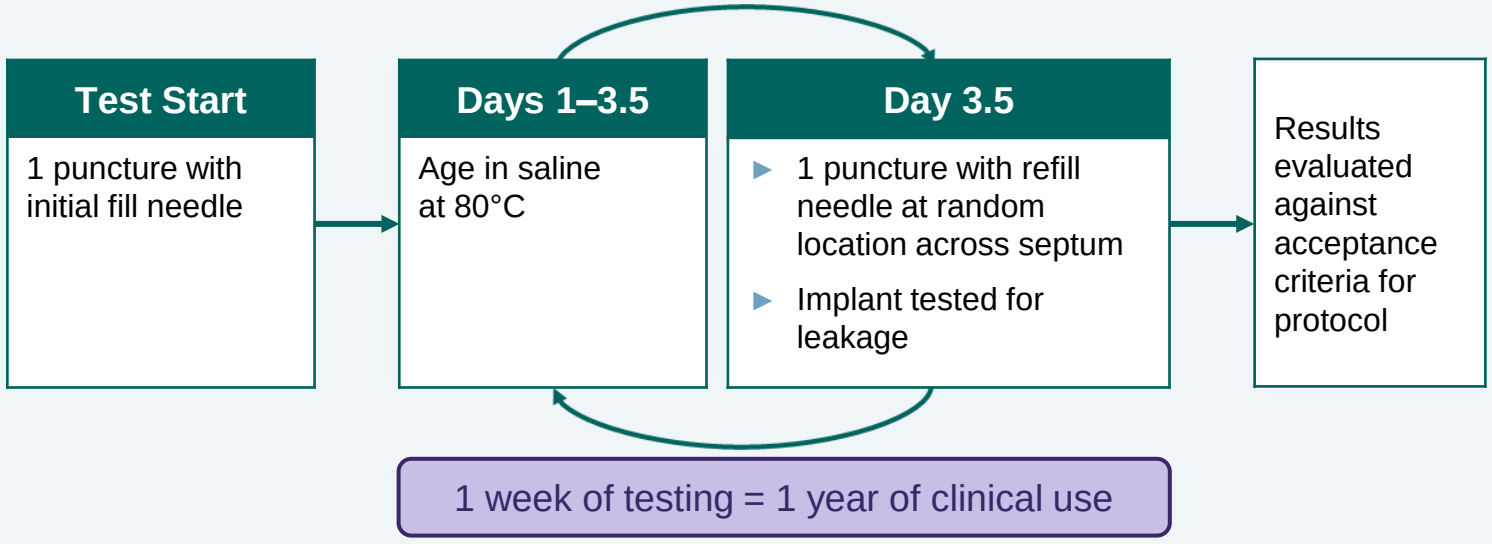
Genentech
A Member of the Roche Group

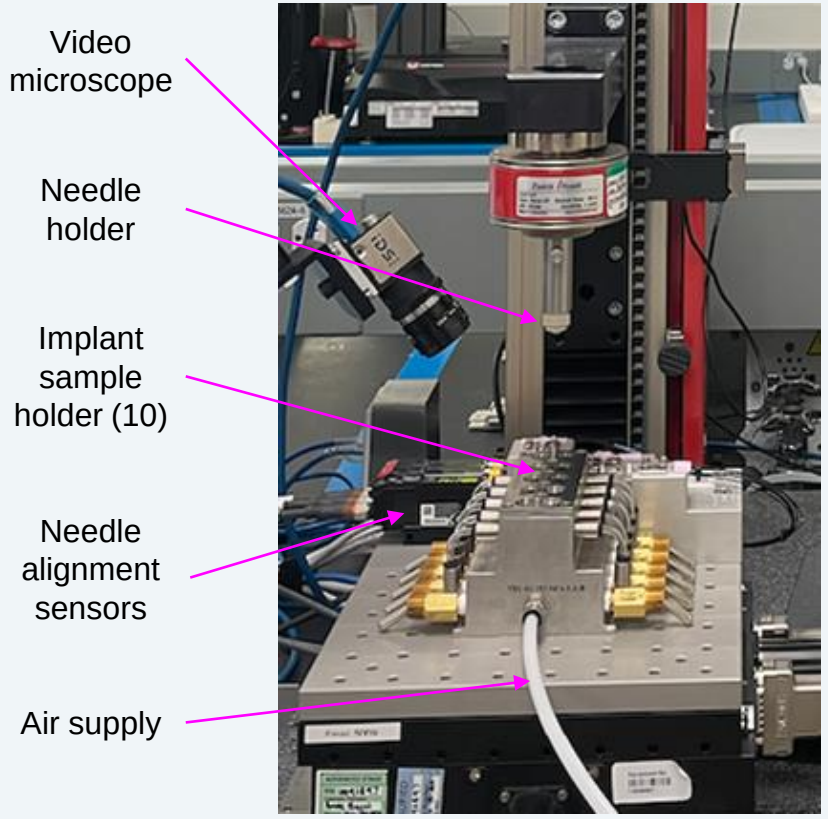
SEPTUM PERFORMANCE TEST METHOD

Clinical use is simulated by accelerated aging and puncturing of the implant septum by refill needle

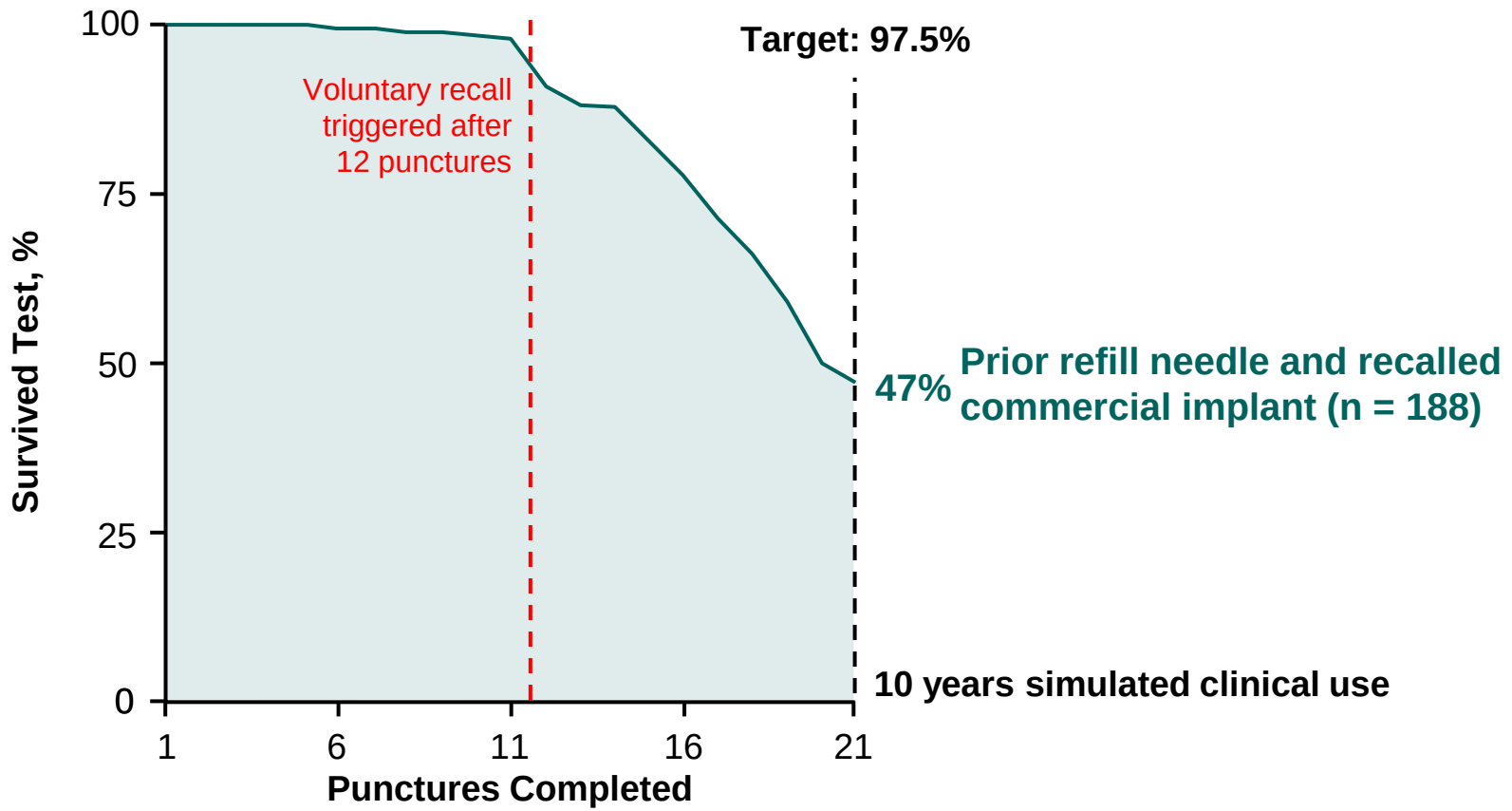
Test objectives:

- Evaluate the ability of the implant septum to seal after refill needle puncture
- Tests for needle track leakage and septum dislodgement

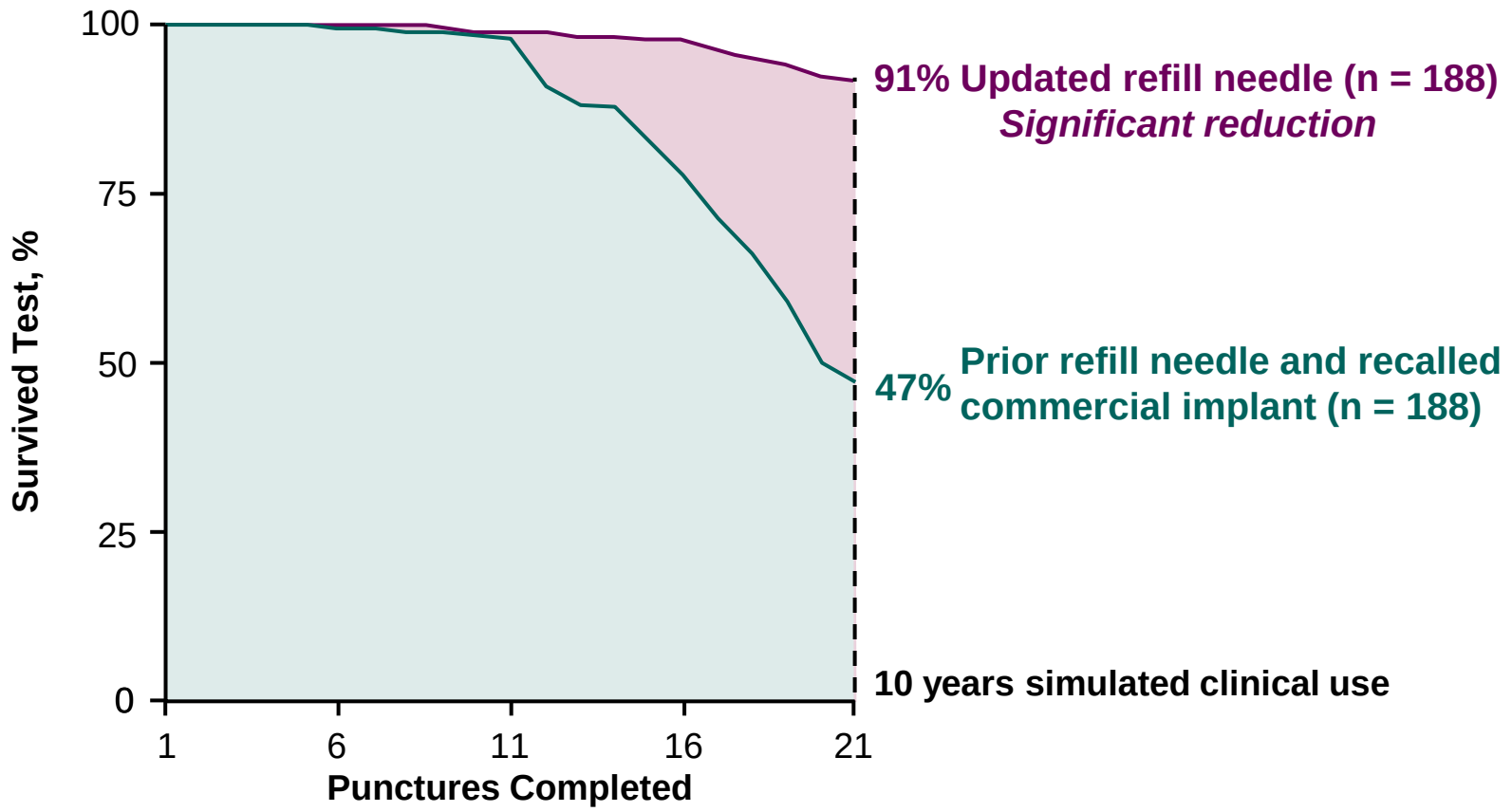




PERFORMANCE TESTING DEMONSTRATED RECALLED COMMERCIAL IMPLANTS DID NOT MEET PRE-SPECIFIED REQUIREMENTS, LEADING TO 2022 VOLUNTARY RECALL

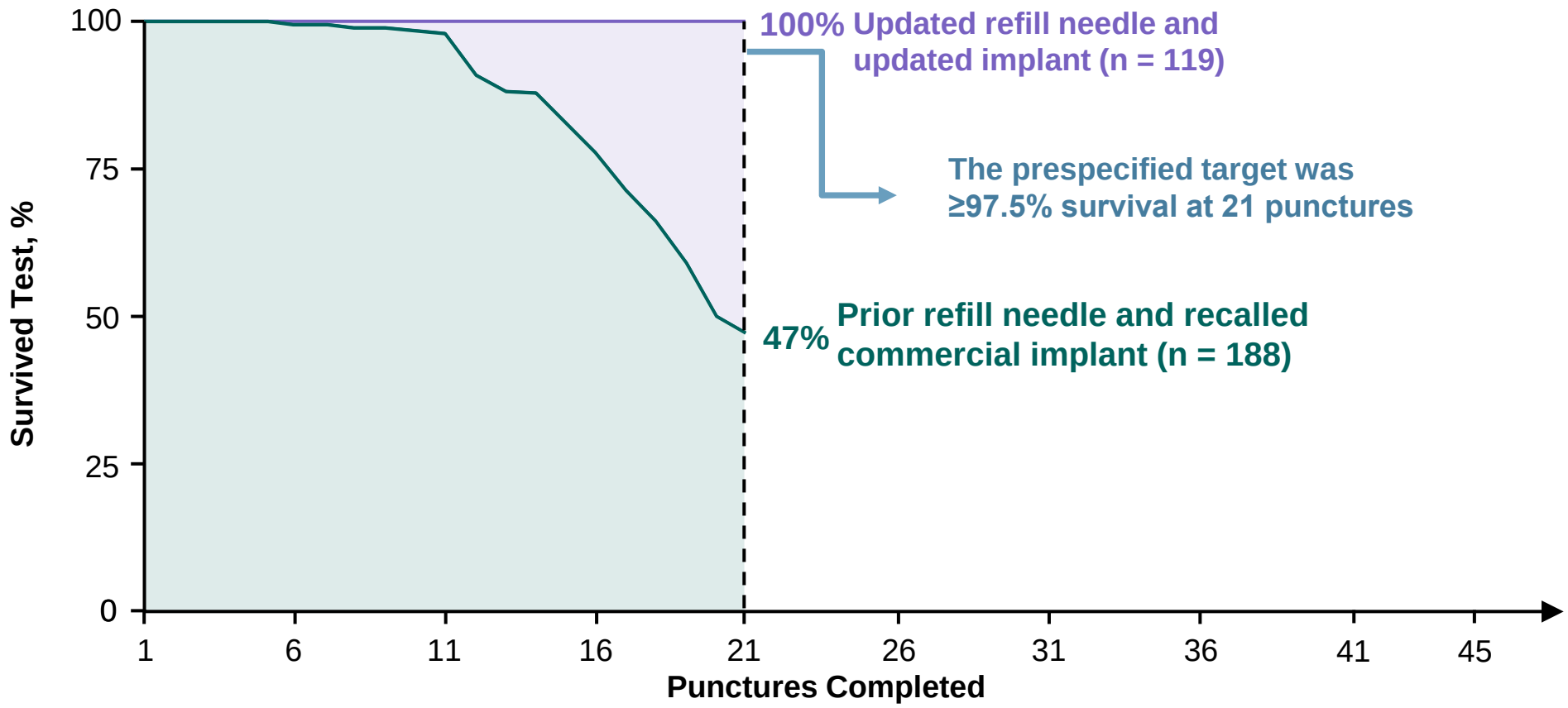


UPDATED REFILL NEEDLE TESTED WITH RECALLED COMMERCIAL IMPLANT SIGNIFICANTLY IMPROVES SURVIVAL RATE OF SEPTUM



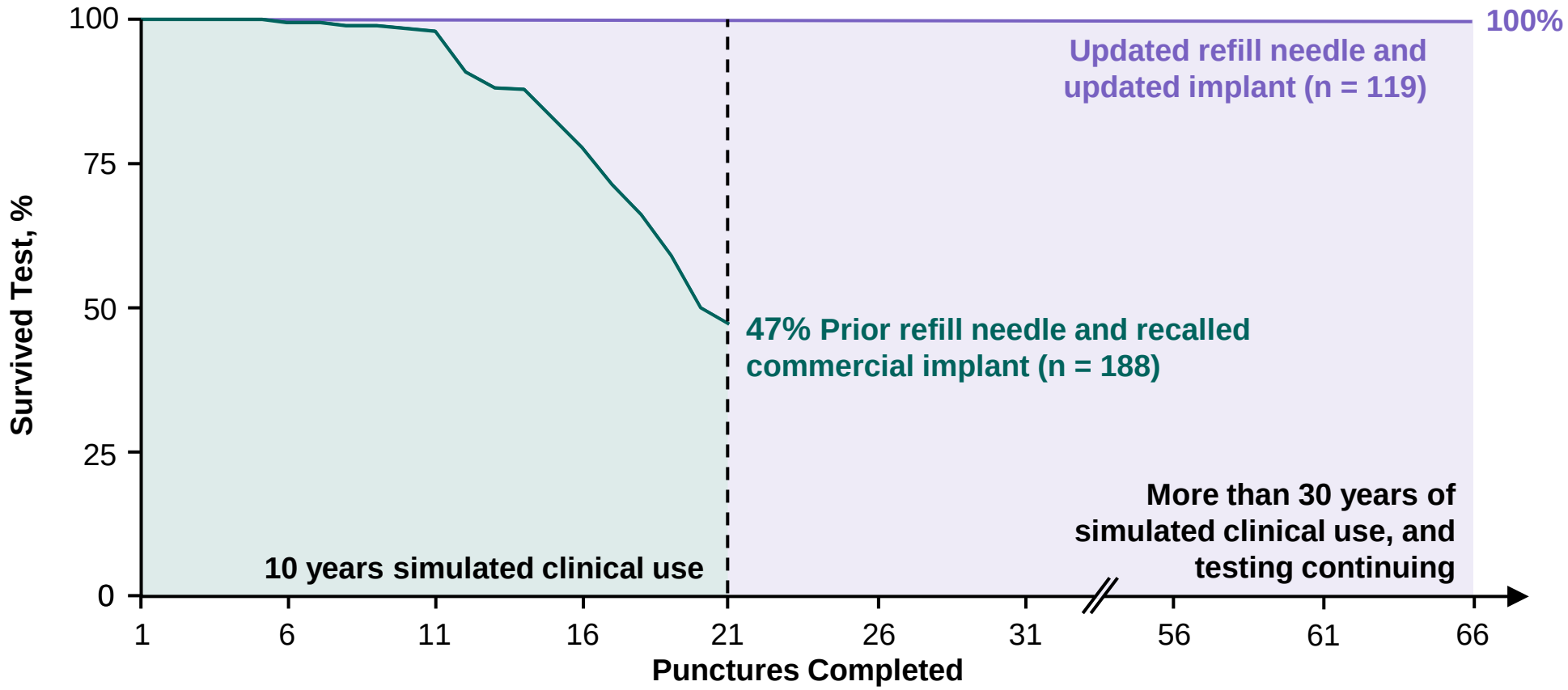
Septum puncture testing shows a significant difference in survival rate between the prior refill needle and updated refill needle with recalled commercial implant at 10 years of simulated use.

ACCELERATED SEPTUM PUNCTURE TESTING WITH THE UPDATED IMPLANT EXCEEDS ALL PERFORMANCE SPECIFICATIONS, MITIGATING RISK OF SEPTUM DISLODGEMENT



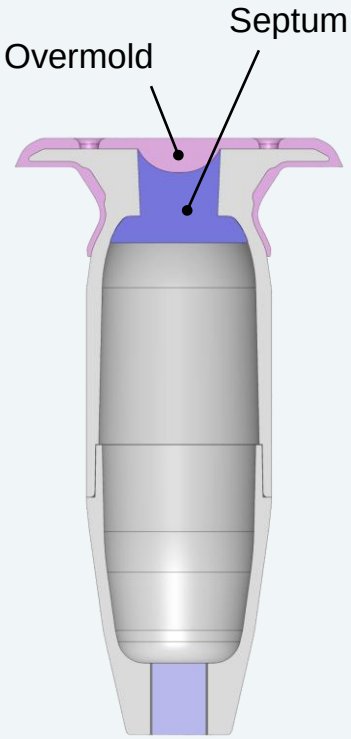
ACCELERATED SEPTUM PUNCTURE TESTING WITH THE UPDATED IMPLANT EXCEEDS ALL PERFORMANCE SPECIFICATIONS, MITIGATING RISK OF SEPTUM DISLODGEMENT

No septum dislodgements observed across more than 30 years of simulated clinical use with the updated implant–refill needle combination



THE UPDATED IMPLANT AND UPDATED REFILL NEEDLE ARE FDA APPROVED AND REINTRODUCED FOR PATIENT USE

Implant



Schematic

Refill Needle

- **Accelerated septum puncture testing** confirms that the updated implant and updated refill needle exceeded prespecified requirements
- The updates to the implant and refill needle provide high confidence of long-term septum durability
  - Component-level changes implemented, along with manufacturing process improvements and additional quality controls
  - **Septum–overmold bond strength is doubled**
  - Light lubrication of refill needle **reduces the insertion force by more than 50%**

Pieramici D et al. Presented at: Angiogenesis; February 3, 2024; Online.