Technical Updates to Port Delivery System with Ranibizumab (PDS) and Clinical Experience With Updated Refill Exchange Needle

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Purpose

- To update on the technical data supporting PDS device updates and septum dislodgement mitigation, which provides confidence of long-term performance.

Conclusions

Updated Implant and Refill Needle FDA Approved and Re-introduced in the USA for the Treatment of nAMD

- The updated implant and updated refill needle are now FDA approved and re-introduced in the USA for the treatment of nAMD
- Updates to the implant has doubled the bond strength between the septum and overmold as compared to the voluntarily recalled implant
- Updates to the refill exchange needle allows for a smoother refill exchange, reducing the insertion force by half as compared to the prior refill exchange needle
- The combination of the updated implant and updated refill exchange has resulted in 100% septum durability observed across >46 years of simulated clinical use

Updated Implant and Refill Needles were introduced in clinical trials globally February 2024

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Introduction

- The PDS is a unique drug delivery system for continuous delivery of a customised formulation of ranibizumab into the vitreous for the treatment of nAMD, DMO and DR.
- In October 2022, Roche/Genentech voluntarily recalled the PDS ocular implant and insertion tool assembly after identifying that implants from the Phase 3 supply did not meet pre-specified performance standards.
- These implants experienced septum dislodgement, wherein the septum dislodged into the body of the implant.

Methods

- A root cause analysis explored several potential causes and ultimately determined that leading factors for septum dislodgement were insufficient bonding between the septum and the overmold and excessive insertion force from the refill needle during refill-exchange
- Component level and manufacturing process updates have been implemented to strengthen the septum-overmold bond.
- These updates include strengthening the retention force between the overmold and the septum.

Financial Disclosures

MM: None; **IP:** Consultant: AbbVie, Alimera, Apellis, Bayer, Novartis, Roche; Honoraria: Apellis, Bayer, Novartis, Roche; Travel Grants: Apellis, Bayer, Novartis, Roche; **PAC:** Grants or Contracts: Ashvattha, Mallinckrodt, Oxford Biomedica, Regenxbio, Sanofi/Genzyme; Consulting: AsclepiX, Ashvattha, Bausch + Lomb, Catawba Research, Celanese, Clearside Biomedical, Cove, Exegenesis Bio, Gyroscope, Wave Life Sciences; Payment or Honoraria: Allegro, AsclepiX, Ashvattha, Bausch + Lomb, Catawba Research, Celanese, Clearside Biomedical, Exegenesis Bio, Exonate, Genentech, Inc./Roche, Gyroscope, Perfuse, Wave Life Sciences; Stock/Stock Options: Allegro, Cove, Graybug; **MC:** Consultant: Genentech, Inc./Roche, Iveric Bio, Regenxbio; Grant/Research Support: Alexion, EyeBio, NGM Bio, Novartis, OcuTerra, Opthea; **NH:** Employee: F. Hoffmann-La Roche; **SG, CQR, NS, GW, SR, JH**: Employment and Stocks/Stock Options: Genentech, Inc.; **CDR:** Consultant: 4D Molecular Therapeutics, Adverum, Allergan, Annexon, Apellis, Aviceda, Bausch + Lomb, Clearside Biomedical, EyePoint, Genentech, Inc., Iveric Bio, Kodiak Sciences, Janssen, Lineage, Merck, NGM Bio, Notal Vision, Novartis, Ocular Therapeutix, Ocugen, Ocuphire, OcuTerra, Opthea, Ray, Regenxbio, Stealth, Takeda, Thea, Zeiss

Study and Product Disclosures

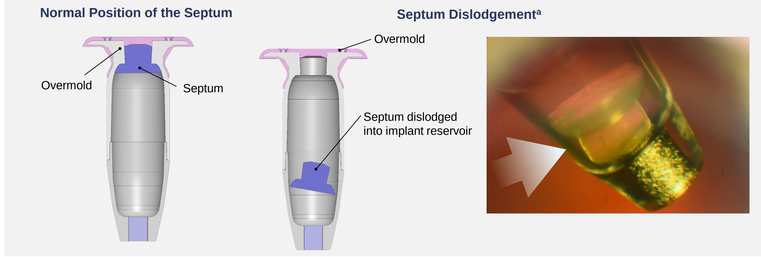
- The Port Delivery System with ranibizumab (PDS) has been approved by the US Food and Drug Administration for the treatment of nAMD in adults who have previously responded to ≥ 2 anti-VEGF injections.
- **Important note: PDS has not been approved for use outside of the United States and therefore is not approved for use in the United Kingdom or Republic of Ireland.**
- **The US Food and Drug Administration has issued a boxed warning for the PDS because it has been associated with a 3-fold higher rate of endophthalmitis compared with monthly intravitreal injections of ranibizumab[1]**
- This study includes research conducted on human subjects
- Institutional Review Board approval was obtained prior to study initiation
- Funding was provided by Genentech, Inc., a member of the Roche Group, for the study. Roche Products Ltd. provided medical writing assistance and conducted a factual accuracy check on the final article, but any decision to incorporate comments was made solely at the discretion of the authors.

References

1. Susvimo [prescribing information]. South San Francisco, CA: Genentech, Inc.; 2022.
2. Pieramici D et al. Presented at: Angiogenesis, Exudation, and Degeneration Meeting; February 3, 2024; Virtual.

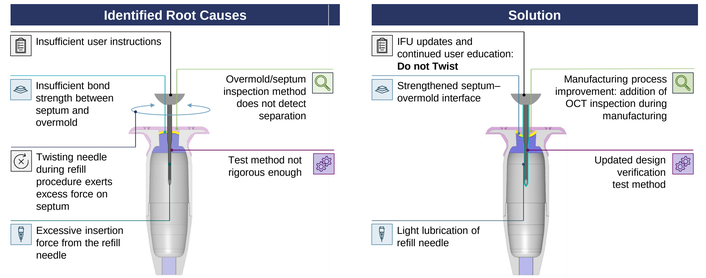
Results

Roche/Genentech, Inc. Voluntarily Recalled PDS After Identifying Some Implants Did Not Meet Prespecified Performance Requirements[2]



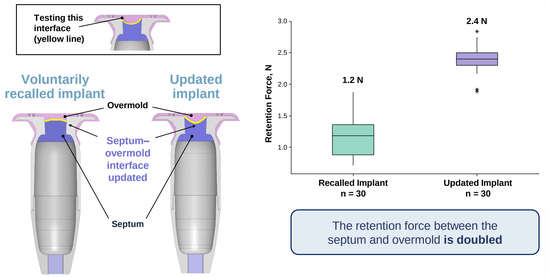
[a]Septum dislodgement is a known risk associated with the PDS and is included in the FDA-approved Prescribing Information and clinical trial protocols. Images used with permission. Photo depict the previous versions of the implant. FDA, US Food and Drug Administration; PDS, Port Delivery System with ranibizumab.

Root Cause Analysis and Related Updates

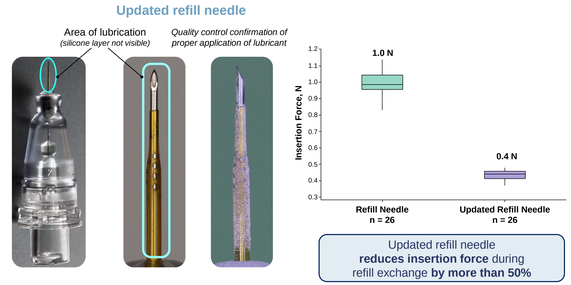


[a]IFU details for refill procedure updated to avoid twisting.
IFU, instructions for use; OCT, optical coherence tomography.

PDS Implant Updated: Component Level Changes and Manufacturing Process Improvements Double Septum–Overmold Bond Strength[2]



Light Lubrication of the Refill Needle Allows the Needle to be Inserted Into Septum More Smoothly, Reducing the Insertion Force by Half[2]



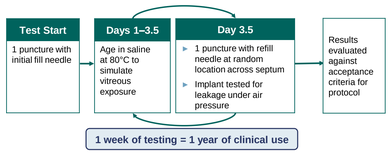
Data were collected with the recalled commercial implant. Photo on left depicts the previous version of the refill needle. Image used with permission.

Septum Performance Test Method

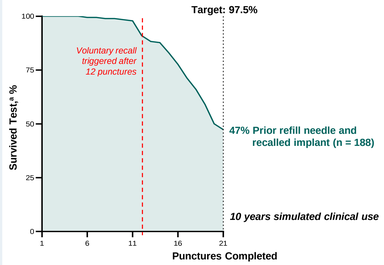
Clinical use is simulated by accelerated aging and puncturing of the implant septum by refill needle

Test objectives:

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

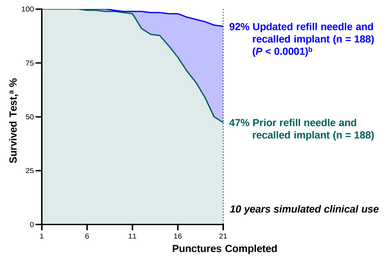


Performance Testing Demonstrated Recalled Commercial Implants Did Not Meet Prespecified Requirements, Leading to the Voluntary Recall in 2022



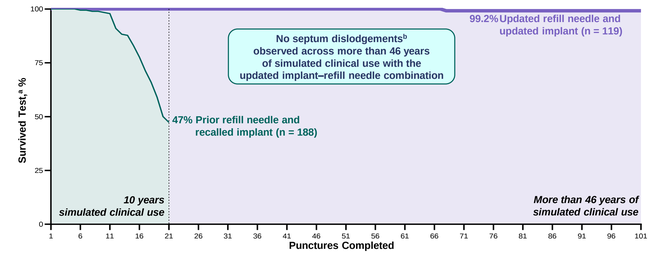
Data on file. Roche/Genentech, Inc. a Laboratory tests were conducted to determine long-term septum performance in which implants were aged at elevated temperature in saline and the septum was punctured with the refill-exchange needle every 3.5 days.

Updated Refill Needle Tested With Recalled Commercial Implant, Significantly Reduces the Risk of Septum Dislodgement



Data on file. Roche/Genentech, Inc. [a]Laboratory tests were conducted to determine long-term septum performance in which implants were aged at elevated temperature in saline and the septum was punctured with the refill-exchange needle every 3.5 days. [b]Survival percentage at 21 punctures is statistically significantly different (Pearson Chi Square).

Updated Refill Needle Tested With the Updated Implant Exceeds All Performance Specifications, Mitigating the Risk of Septum Dislodgement



Data on file. Roche/Genentech, Inc. [a]Laboratory tests were conducted to determine long-term septum performance in which implants were aged at elevated temperature in saline and the septum was punctured with the refill-exchange needle every 3.5 days. [b]One sample failed after puncture 68 by leaking when pressurized through the hole created in the septum by the refill needle; the septum did not dislodge. [c]8 physicians performing 34 uses of the updated refill needle in a clinical observation study in the US as part of the FDA reapproval process the reintroduction of the PD-P to clinical practice in the US. FDA, US Food and Drug Administration; PD-P, Port Delivery Platform.