SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Intraocular Gas

Device Trade Name: UNIPURE SF_6 Ophthalmic Gas in the UNIFEYE Gas Delivery System
UNIPURE SF_6 Ophthalmic Gas in the UNIPEXY Gas Delivery System

Device Procode: LPO

Applicant's Name and Address: Alcon Research, LLC
20511 Lake Forest Drive,
Lake Forest, CA 92630, USA

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P230012

Date of FDA Notice of Approval: 08/26/2024

II. INDICATIONS FOR USE

The UNIPURE SF_6 Ophthalmic Gas in the UNIFEYE Gas Delivery System is indicated for intraocular injection into the eye for the treatment of uncomplicated retinal detachments. Associated measures used include vitrectomy, fluid/air exchange, transconjunctival and transscleral cryotherapy, laser photocoagulation, and air/gas exchange.

The UNIPURE SF_6 Ophthalmic Gas in the UNIPEXY Gas Delivery System is indicated for intraocular injection into the eye for the treatment of uncomplicated retinal detachments. Associated measures used include vitrectomy, fluid/air exchange, transconjunctival and transscleral cryotherapy, and laser photocoagulation.

III. CONTRAINDICATIONS

Proliferative vitreoretinopathy (PVR) greater than Stage C, the mental or physical inability to maintain the therapeutic position for 5 postoperative days, severe glaucoma with more than a minimum of vision field loss and a cup to disc ratio equal to or greater than 0.6; uveitis; severe peripheral retinal degeneration; congenital malformations (such as coloboma), and any other condition that may facilitate the migration of the gas bubble out of the vitreous chamber; and high-altitude travel, including but not limited to airline travel.

- Air travel is contraindicated until the gas/air bubble has completely dissipated. Normal cabin pressure changes will cause a severe enlargement of the gas/air bubble with a resultant potential blinding, due to an increase in intraocular pressure (IOP)[1-7].
- Patients should not travel through high elevations and over mountain ranges until the mixed gas/air bubble has dissipated[8].

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the UNIPURE SF_6 Ophthalmic Gas in the UNIFEYE Gas Delivery System and in the UNIPURE SF_6 Ophthalmic Gas in the UNIPEXY Gas Delivery System labeling.

V. DEVICE DESCRIPTION

The integrated UNIPURE SF_6 Ophthalmic Gas pico-cylinder in the UNIFEYE Gas Delivery System contains undiluted, non-sterile, liquefied sulfur hexafluoride (SF_6) gas under pressure. The gas is non-toxic, inert, non-flammable, odorless, and colorless. The UNIFEYE Gas Delivery System is used to mix filtered UNIPURE SF_6 Ophthalmic Gas with filtered air and inject the gas/air mix into the vitreous cavity of the eye. The prepared gas/air mixture for injection is sterile via the 0.2-micron filtration of the gas and air.

Figure 1. UNIPURE SF_6 Ophthalmic Gas in the UNIFEYE Gas Delivery System

The integrated UNIPURE SF_6 Ophthalmic Gas pico-cylinder in the UNIPEXY Gas Delivery System contains undiluted, non-sterile, liquefied sulfur hexafluoride (SF_6) gas under pressure. The gas is non-toxic, inert, non-flammable, odorless, and colorless. The UNIPEXY Gas Delivery System is used to inject filtered UNIPURE SF_6 Ophthalmic Gas directly into the vitreous cavity to form a gas/air bubble. The prepared gas for injection is sterile via the 0.2-micron filtration of the gas.

Figure 2. UNIPURE SF_6 Ophthalmic Gas in the UNIPEXY Gas Delivery System

The physical properties for the UNIPURE SF_6 Ophthalmic Gas in the UNIFEYE Gas Delivery System and the UNIPURE SF_6 Ophthalmic Gas in the UNIPEXY Gas Delivery System are presented in Table 1.

Table 1: Summary of Physical Properties

Property	Description
Physical Attributes	colorless, odorless, non-toxic, and non-flammable gas at room temperature and atmospheric pressure
Molecular Formula	SF_6
Molecular Weight	146.06 g/mol
CAS Registry Number	2551-62-4
Sublimation Point	-63.9°C
Melting Point	-50.8°C
Vapor Pressure at 20°C	350 psia
Density at 20°C	1.620 g/cc
Viscosity at 25°C	4.619 millipoise

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the correction of uncomplicated retinal detachments.

The primary alternative practice to use of UNIPURE SF_6 Ophthalmic Gas is the use of other sources of the same type of gas, other types of gases or air to form an ocular endotamponade. Currently, both perfluoropropane (C_3F_8) and sulfur hexafluoride (SF_6) gases are approved, for commercial sale as gas ocular endotamponades in the U.S. No other gas ocular endotamponades have been approved for commercial sale in the U.S. These two ocular endotamponades are sold separately from accessory devices that would

be needed to prepare them for use in intraocular surgery. Air-only ocular endotamponades are also used.

An alternative to using a gas ocular endotamponade with or without vitrectomy is vitrectomy with a silicone oil endotamponade. This is usually for patients who are not capable of or who wish to avoid postoperative positioning regimens, and for patients wishing to have uninterrupted vision while the endotamponade is in the eye.

Another alternative is a scleral buckling procedure, which is frequently chosen for younger, more active patients who wish to avoid postoperative positioning regimen, or to avoid the risk of cataract due to iatrogenic damage to the lens and who are open to spectacle use (due to distortion of the eye by the buckle). In many cases, scleral buckling procedures are combined with vitrectomy either with or without gas ocular endotamponades.

Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

The UNIPURE SF_6 Ophthalmic Gas in the UNIFEYE Gas Delivery System and the UNIPURE SF_6 Ophthalmic Gas in the UNIPEXY Gas Delivery System have not been marketed in the United States or any foreign country.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (e.g., complications) associated with the use of the device.

Operative complications associated with the use of gas/air ocular endotamponades in eyes with or without vitrectomy may include:

- Central retinal artery occlusion
- Subconjunctival gas
- Subretinal hemorrhage
- Small subretinal gas bubble
- Hypotony
- Choroidal hemorrhage
- Choroidal detachment
- Crystalline lens touch by needle
- Hyphema
- Escape of mixed gas/air through the surgical incisions
- Vitreous or iris incarceration at the wound
- Elevated IOP, which may require additional medical or surgical intervention to reduce pressure

Postoperative complications associated with surgical procedures using gas/air ocular endotamponades in eyes with or without vitrectomy may include:

- Elevated IOP, which may require additional medical or surgical intervention to reduce pressure
- Severe elevated IOP that has been known to result in vision decrease or blindness if N_2O is administered during a subsequent surgical or dental procedure with a gas bubble present in the eye
- Central retinal artery occlusion
- Malignant glaucoma
- Changes to the crystalline lens
- Cataract
- New, missed, or recurrent retinal detachment or retinal breaks
- Subconjunctival gas
- Subconjunctival hemorrhage
- Vitreous hemorrhage
- Subretinal fluid
- Subretinal hemorrhage
- Subretinal gas
- Macular hole
- Macular pucker/epiretinal membrane
- Proliferative vitreoretinopathy
- Choroidal hemorrhage
- Choroidal detachment
- Uveitis
- Cystoid macular edema/macular edema
- Hyphema
- Extrafoveal subretinal pigment migration
- Vitreal opacification (known as “floaters” or “tobacco dust”)
- Endophthalmitis
- Refractive changes
- Escape of mixed gas/air through the surgical incisions
- Vitreous or iris incarceration at the wound

For the specific adverse events that occurred in the clinical studies reported in literature, please see Section X below.

IX. SUMMARY OF NON-CLINICAL STUDIES

A. Laboratory Studies

Table 2: Physical and Chemical Characterization Summary

Test	Acceptance Criteria	Results	Analysis Type
Characterization Study	Comparison of quantities of the targeted and unknown impurities (control [marketed] and test [proposed] gases).	N/A	There is no pass/fail criteria for this study. Test results from the characterization study demonstrated the impurity profile of the as-delivered UNIPURE SF_6 Ophthalmic Gas and the SF_6 control gas is equivalent. No targeted impurities were detected above specification limits and no unknown impurities were detected in the test UNIPURE SF_6 Ophthalmic Gas.
Extractable and Leachable	Performed in compliance with ISO 10993- 18:2020.	Pass	UNIPEXY Gas Delivery System components were successfully characterized for extractables per ISO 10993-18:2020.
Gas Analytical Test	Acceptance criteria in accordance with product specification.	Pass	Gas analytical tests met acceptance criteria for the raw gas, pico-cylinder and as- delivered gas delivery systems per product specification.

A toxicological risk assessment was performed on the as-delivered UNIPURE SF_6 Ophthalmic Gas per ISO 10993-17.

B. Animal Studies

1. Intraocular Implantation Test – UNIPURE SF_6 Ophthalmic Gas

The UNIPURE SF_6 Ophthalmic Gas is categorized per ISO 10993-1:2018, *Biological evaluation of medical devices – Part 1: Evaluation and testing within a risk management process*, as an implant medical device with long-term contact duration (greater than 30 days) with tissue. Intraocular implantation in New Zealand White (NZW) rabbit eyes with histopathology was conducted according to Annex A of ISO 16672:2020 to determine the ocular toxicity of sulfur hexafluoride (SF_6). The contralateral eyes served as control and received either the commercially available and unmodified ISPAN sulfur hexafluoride (SF_6) gas (P900067) or air.
The ophthalmic tissue responses in the eyes implanted with the UNIPURE SF_6 Ophthalmic Gas as delivered by the UNIFEYE and UNIPEXY Gas Delivery Systems were compared to tissue responses of the control eyes. The rabbit intraocular implantation study (Table 3) showed that the tissue responses in eyes implanted with UNIPURE SF_6 Ophthalmic Gas and the commercially available ISPAN SF_6 gas are comparable, and the UNIPURE SF_6 Ophthalmic Gas does not lead to toxicity and inflammation in the animal model. The animal implantation study was conducted in accordance with FDA Title 21, CFR Part 58: Good Laboratory Practice for Non-Clinical Laboratory Studies.

Table 3: UNIPURE SF_6 Ophthalmic Gas Animal Study Results

Endpoint	Test	Animal model	Results
Implantation	Ocular Implantation (Eight-Weeks; Rabbit) in accordance with ISO 16672:2020	NZW rabbit	Non-toxic; Non-Inflammatory

2. Biocompatibility Test - Pico-cylinder, UNIFEYE and UNIPEXY Gas Delivery Systems

The UNIFEYE Gas Delivery System and pico-cylinder components have indirect tissue contact via the UNIPURE SF_6 Ophthalmic Gas.

The UNIPEXY Gas Delivery System is intended to provide the surgeon with a filled syringe of undiluted UNIPURE SF_6 Ophthalmic Gas for delivery to the eye via an included syringe needle. Except for the syringe needle and hub that have direct limited ($\leq$ 24 h) tissue contact, all the components of the UNIPEXY Gas

Delivery System have indirect tissue contact via the UNIPURE SF_6 Ophthalmic Gas.

Biocompatibility assessment of the pico-cylinder and the UNIFEYE and UNIPEXY Gas Delivery System was conducted in accordance with ISO 10993-1:2018 . The biocompatibility tests were conducted in accordance with 21 CFR Part 58. The biocompatibility test results are summarized in Table 4.

Table 4: UNIFEYE, UNIPEXY, Pico-cylinder Biocompatibility Results

Endpoint	Test	Results
Cytotoxicity	MEM Elution Assay using L-929 Fibroblasts Cells (ISO 10993-5:2009)	No evidence of cell lysis or cell toxicity
Irritation	Intraocular Irritation (ISO 10993-10:2013)	Not irritating to intraocular tissues
Sensitization	Guinea Pig Maximization Test (ISO 10993-10:2013)	No evidence of delayed dermal contact sensitization

C. Additional Studies

Table 5: Summary of Additional Studies

Test	Acceptance Criteria	Results	Analysis Type
Sterilization			
Sterilization	Acceptance criteria in accordance with ISO 11135:2014 and EN 556-1:2001.	Pass	Sterility assurance level of 10^{-6} was demonstrated for EO sterilization process through microbiological testing of control microorganisms.
EO/ECH Residual	Acceptance criteria in accordance with ISO 10993-7:2008.	Pass	Results for EO and ECH residual levels met permanent intraocular device acceptance criteria per the limits in EN ISO 10993-7:2008.
Endotoxin	Acceptance criteria in accordance with ANSI/AAMI ST72 and 2015 FDA Guidance, Endotoxin Testing Recommendations for Single-Use Intraocular Ophthalmic Devices	Pass	Endotoxin test results conform to the intraocular device limit of ≤0.2 Endotoxin Units (EU)/device
Shelf Life			
Stability	Acceptance criteria in accordance with ASTM F1980-16 and ASTM D4169-16.	Pass	Results indicated that product is stable at elevated temperature and transportation conditioning at 22-month shelf-life.
Package Integrity	Acceptance criteria in accordance with ISO 11607-1:2019+LC2020, ISO 11607-2:2019, ASTM F1929-12,	Pass	Results of dye penetration, bubble leak test, and seal strength testing met respective ASTM test method acceptance

	ASTM F2096-11, and ASTM F88/F88M-15		criteria, and conform to ISO 11607-1 and ISO 11607-2 requirements.
Functional and Performance			
Functional and Performance Tests <u>UNIFEYE Gas Delivery System</u> – Latch Mechanical Hold – Ratchet Mechanism Break Force – Plunger Draw Force – Force to Expel Mixed Gas – User Selection – Gas Release – Automatic Plunger Movement – Unmixed Gas Volume Indicators – Air Draw – 50 mL Stop – Ratchet Mechanism Engagement – Expelling Mixed Gas – Lever Packaging Securement – Purge Air – Visual Inspection of Piston and O-ring Assembly – Destructive Testing – Helium Leak Testing	Acceptance criteria in accordance with product specification.	Pass	The device met all functional and performance acceptance criteria per product specification throughout the product shelf life.

– Gap and Height Inspection – Pre- to Post-Weight Check – Semi-Automatic Weight Assessment of Microcylinders (SWAMY) Leak Check – Batch Testing for Purity			
Functional and Performance Tests <u>UNIPEXY Gas Delivery System</u> – Latch Break Test – Package Protection – Device Activation – Plunger Stop – Gas Vent – Latch Open and Fill Volume – Expel Gas – Needle Pull Test – Visual Inspection of Piston and O-ring Assembly – Destructive Testing – Helium Leak Testing – Gap and Height Inspection – Pre- to Post-Weight Check – SWAMY Leak Check – Batch Testing for Purity – Pad Printing Inspection	Acceptance criteria in accordance with product specification.	Pass	The device met all functional and performance acceptance criteria per product specification throughout the product shelf life.

– Body Bleed Filter and Flow Restrictor Leak Testing – Component Cleaning Water Conductivity Testing			
Mix Ratio Accuracy Test	Upper and lower tolerance limits within the ±1.5% per product specification.	Pass	Test results demonstrated that the UNIFEYE Gas Delivery System upper and lower tolerance limits are within the ±1.5% specification for each gas/air mix ratio throughout product shelf life.
Filter Integrity Tests	Acceptance criteria in accordance with ASTM F1929-12.	Pass	Gas filter integrity was maintained throughout the product shelf life and met acceptance criteria per ASTM F1929-12.
Particulate Test (Gas)	Acceptance criteria in accordance with USP <788>:2012 and USP <789>:2012.	Pass	Test results provided evidence that the test articles meet the acceptance criteria per USP <788>:2012 and <789>:2012, respectively.
Canister Burst Test	Withstand at least 1300 psi of internal pressure without catastrophic failure.	Pass	Test results demonstrated that the pico-cylinder could withstand at least 1300 psi of

			internal pressure without catastrophic failure.
Gas Weight Verification	At least 200 mg through product shelf-life.	Pass	Test results for the pico-cylinder were within the acceptance criteria throughout product shelf-life.
Usability and Human Factors			
Summative Human Factors Testing and DFU Comprehension Studies	All critical tasks were evaluated based on defined successful task performance	Two (2) user groups performed all critical tasks, use problems were captured and assessed for root cause analysis, residual risks and effectiveness of risk control measures were evaluated to demonstrate use-related risks were reduced to acceptable levels	The subject device and its accessories are safe and effective for the intended users, uses, and use environments in alignment with FDA's 2016 Guidance - Applying Human Factors and Usability Engineering to Medical Devices, and in adherence to IEC 62366-1:2015 and ANSI/AAMI HE75:2018.

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a systematic clinical literature review to establish a reasonable assurance of safety and effectiveness of the UNIPURE SF_6 Ophthalmic Gas in the UNIFEYE and UNIPEXY Gas Delivery Systems for the treatment of uncomplicated retinal detachment. Data from this clinical literature review were the basis for the PMA approval decision. A summary of the clinical literature review is presented below.

A. Study Design

Data was evaluated from published literature to generate clinical evidence that supports the safety and effectiveness of the UNIPURE SF_6 Ophthalmic Gas in the UNIFEYE and UNIPEXY Gas Delivery Systems. Online literature databases, including Medline, Embase, Cochrane, Clinicaltrials.gov, and WHO International Clinical Trial Registry Platform, were searched for a period spanning January 1, 1980 to July 1, 2022. The range of databases searched aimed to provide adequate coverage of treatments in use worldwide and identified relevant publications of user experience for the indication of treatment of uncomplicated retinal detachments. The output from the search results were then reviewed for inclusion in the clinical literature review using the PICO (patient characteristics, type of intervention, control, and outcome of interest) review method. The first review was performed by title/abstract and articles remaining were then reviewed as full text according to the following criterion.

1. Clinical Inclusion and Exclusion Criteria

   For an article to be recommended for inclusion in the safety and effectiveness analysis, it must have met at least one of the following criteria:

   a. Clinical studies and/or studies in animals evaluating the safety and/or effectiveness of the evaluated device or equivalent device; or
   b. Isolated case reports that describe new risk(s).

   Articles were excluded based on the following criteria:

   a. Articles not related to the device of interest or equivalent device.
   b. Articles that did not provide data on the safety and/or effectiveness of the device of interest or equivalent device in humans or in animals.
   c. Articles with date of publication outside the reporting period.
   d. Letters to the editor, opinions, editorials, surveys, manufacturer's advertisements, and press releases.
   e. Laboratory research, such as in vitro or ex vivo studies, post-mortem studies, biomechanical studies, simulation studies.
   f. Non-peer reviewed articles.
   g. Abstracts or conference proceedings.
   h. Review articles.
   i. Isolated case reports, unless new risks are described.
   j. Duplicate articles or duplicate publications of the same study data.
   k. Articles using the device of interest in ways unrelated to the indicated use.
   l. Articles using the device of interest with associated procedures that are not

included in the indicated use.

m. Articles from registries without final results.

2. Clinical Endpoints

With regards to safety, the primary safety endpoint was the Rate of Elevated Intraocular Pressure (IOP): Report of elevated IOP >25 mm Hg in literature.

Target Rate: Elevated IOP (defined as >25 mm Hg) reported in literature will be no more than 34% reported 1 to 7 days postoperatively.

With regards to effectiveness, the primary effectiveness endpoint was the Anatomical Success Rate: Primary retinal reattachment rate.

Target Rate: The primary operational success rate reported in literature will be at least 72% reported at least 3 months postoperatively.

3. Statistical Methods

Primary safety and effectiveness endpoint data were analyzed using a logistic regression model fit with a random effect to account for study heterogeneity. Data were reported with the 95% confidence intervals of the primary endpoints and forest plots and comparisons were made between the point estimate and the proposed primary endpoint target rates.

B. Accountability of PMA Cohort

N/A

C. Study Population Demographics and Baseline Parameters

The demographics of the literature review population are shown in Table 6 and are typical for uncomplicated retinal detachment treatments in the US. The mean age for SF_6-treated participants was 58.6 years with an age range of 12 to 93 years. The SF_6-treated participants were 63.5% of the 2051 SF6-treated participants were male and 36.5% of the 2051 SF6-treated participants were female.

Table 6 Demographics of Literature Review Population

Total Study Participants* N=5669			Participants Treated With SF_6 N=2051		
Mean Age, year	**Age Range, year**	**Male,**	**Mean Age, year**	**Age Range, year**	**Male,**
Weighted mean = 58.9	Range = 12-94	64.9%	Weighted mean = 58.6	Range = 12-93	63.5%

*Treatments including SF_6 and other tamponade agents and procedures

D. Safety and Effectiveness Results

The literature review included 61 studies that reported safety and effectiveness of the use of SF_6 gas for the treatment of uncomplicated retinal detachments. Of these, 23 studies reported rates of elevated IOP and 48 studies reported primary retinal reattachment rates. Studies with data eligible for quantitative analyses included 5 for safety outcomes and 32 for effectiveness outcomes.

1. Safety Results

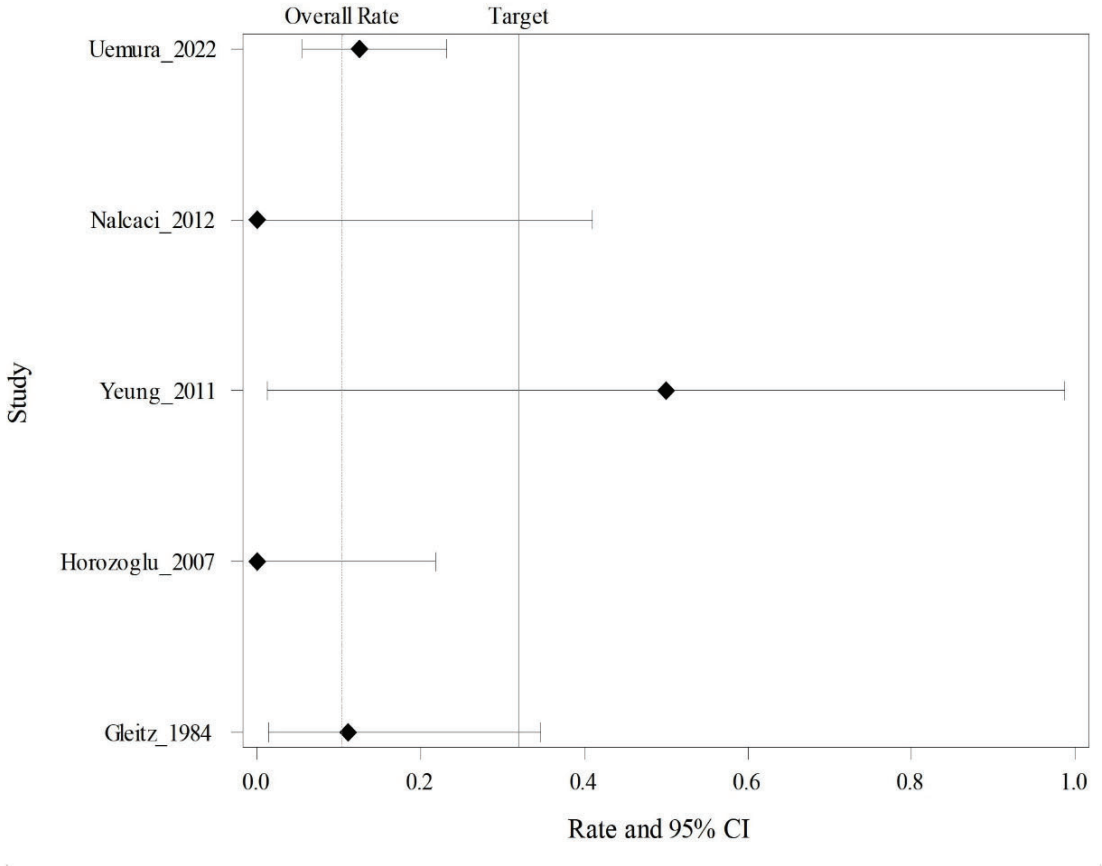
   The analysis of safety was based on the quantitative cohort of 106 eyes reported with rates of elevated IOP > 25 mmHg at 1- to-7-day postoperative visits. The overall rate of elevated IOP >25 mmHg reported 1 to 7 days postoperatively in the analyzed studies was 10.4%, (95% CI: 6.8%, 15.6%), which is less than the prespecified threshold of 34%. The key safety outcomes for this study are presented below in Table 7 and Figure 3. Adverse effects are reported in Tables 8 and 9.

Table 7 Safety – Elevated IOP Rate, All Studies and Subgrouped by Study Type

Study type	Number of studies (n)	Mean	95% CI
All studies	**5**	**0.1038**	**(0.0679, 0.1555)**
C	2	0.0606	(0.0166, 0.1979)
E	3	0.1233	(0.0956, 0.1577)

Level A studies collected pivotal data via a prospective, randomized clinical trial. Level C studies collected data via a prospective, non-randomized study without a control. Level E studies collected data via a retrospective, non-randomized study without a control.

Figure 3
Forest Plot: Safety – Elevated IOP Rate-All Studies



Adverse events (AEs) and complications were reported in the literature review in 49 of 60 included articles involving human participants. All events were tabulated, including events that were not likely device-related. Forty-one articles reported AEs specifically in eyes treated with SF_6 gas only, while eight reported on other tamponades or treatments (mixed). AEs reported without specification of the agent/treatment (mixed) were tabulated separately.

AEs were categorized by treatment (SF_6 or mixed treatment), time of occurrence and by anterior segment/posterior segment/surgical complication/vision/other AEs. Tables 8 and 9 show the reported intraoperative adverse events for SF_6 and mixed studies.

Table 8 - Intraoperative Adverse Events of SF_6 Reported in Included Studies

Category	Intraoperative AEs	Intraoperative			
		S#*	n	N	%
Anterior segment	Increased intraocular pressure (IOP)	2	8	29	27.6
	Intraocular lens (IOL) posterior luxation	1	1	75	1.3
	Subconjunctival gas	1	1	12	8.3
Posterior segment	Central retinal artery (CRA) occlusion	2	8	29	27.6
	Iatrogenic creation of breaks	1	9	75	12.0
	New breaks	1	22	75	29.3
	Subretinal fluid (SRF)	1	89	100	89.0
	Vitreous extruded	1	3	12	25.0

* Number of studies

Table 9 Intraoperative Adverse Events of SF_6 with Mixed Agent or Procedure Reported in Included Studies

Category	Reported AE	Intraoperative			
		S#*	n	N	%
Anterior segment	Hyphema	1	1	65	1.5
	Subconjunctival gas	1	3	100	3.0
Posterior segment	Vitreous hemorrhage	2	2	120	1.7
	Vitreous strand incarcerated in the paracentesis site	1	1	100	1.0
Surgery and complications	Detached pars plana epithelium	1	1	100	1.0

* Number of studies

Tables 10 and **11** show the reported postoperative adverse events for SF_6 and mixed studies.

Table 10: Postoperative Adverse Events of SF_6 Reported in Included Studies

Category	Reported AE	Timeframe Reported										
		Day 1 to ≤ Month 1			> Month 1 to < Month 6			≥ Month 6			Unspecified		
		S#*	n / N	%	S#*	n / N	%	S#*	n / N	%	S#*	n / N	%
Anterior segment	Anterior chamber collapse	1	4 / 36	11.1	-	-	-	-	-	-	-	-	-
	Anterior chamber inflammation	-	-	-	-	-	-	-	-	-	1	1 /16	6.3
	Cataract	1	4 / 16	25.0	-	-	-	2	18 / 188	9.6	5	25 / 331	7.6
	Choroidal detachment / infarct	1	1 / 219	0.5	-	-	-	-	-	-	2	2 / 97	2.1
	Endophthalmitis	1	1 / 39	2.6	-	-	-	-	-	-	1	1 / 88	1.1
	Fibrin reaction	1	27 / 142	19.0	-	-	-	-	-	-	1	3 /23	13.0
	Hyphema	-	-	-	-	-	-	-	-	-	1	2 /23	8.7
	Hypotony	1	3 / 100	3.0	-	-	-	-	-	-	1	8 / 100	8.0
	Increased IOP	4	29 / 169	17.2	-	-	-	-	-	-	4	43 / 281	15.3
	Inflammation	-	-	-	-	-	-	-	-	-	1	1 / 8	12.5
	IOL capture	-	-	-	-	-	-	-	-	-	2	8 / 165	4.8
	Pupillary block	-	-	-	-	-	-	-	-	-	1	1 /75	1.3
	Subconjunctival gas	1	4 / 20	20.0	-	-	-	-	-	-	-	-	-
	Traction of the iris	-	-	-	-	-	-	-	-	-	1	1 / 12	8.3
	Uveitis	1	2 / 219	0.9	-	-	-	-	-	-	1	1 / 24	4.2
Posterior segment	Cystoid macular edema	1	2 / 13	15.4	-	-	-	-	-	-	2	8 / 103	7.8
	Epiretinal membrane / macular pucker	-	-	-	-	-	-	1	5 / 100	5.0	11	67 / 1163	5.8
	Macular edema	-	-	-	-	-	-	-	-	-	1	15 / 62	24.2
	Macular hole	-	-	-	-	-	-	-	-	-	1	1 / 142	0.7

	Mild transient vitreous opacity	-	-	-	-	-	-	-	-	-	1	2 / 9	22.2
	New retinal breaks	-	-	-	1	9 / 71	12.7	-	-	-	2	13 / 253	5.1
	New retinal detachment	-	-	-	-	-	-	-	-	-	1	3 / 219	1.4
	New retinal detachment in fellow eye	-	-	-	-	-	-	-	-	-	1	1 / 219	0.5
	Persistent subretinal fluid	1	25 / 219	11.4	-	-	-	-	-	-	-	-	-
	Proliferative vitreoretinopathy	-	-	-	-	-	-	-	-	-	4	10 / 455	2.2
	SRF	-	-	-	-	-	-	-	-	-	1	2 / 62	3.2
	Subretinal pigment migration	-	-	-	-	-	-	-	-	-	1	1 / 24	4.2
	Vitreous floaters	-	-	-	-	-	-	-	-	-	1	4 / 24	16.7
	Vitreous hemorrhage	-	-	-	-	-	-	-	-	-	1	1 / 85	1.2
Surgery and complications	Secondary surgical intervention	7	26 / 197	13.2	2	14 / 93	15.1	1	2 / 88	2.3	22	114 / 1050	10.9
Vision	Duane retraction syndrome (eye movements affected)	-	-	-	-	-	-	-	-	-	1	1 / 24	4.2
	Visual acuity deterioration	-	-	-	-	-	-	2	8 / 124	6.5	7	13 / 134	9.7
	Visual disturbance (blurred vision, diplopia, metamorphopsia)	-	-	-	-	-	-	1	48 / 66	72.7	1	11 / 10**	100
	Visual field defect	1	1 / 7	14.3	-	-	-	1	1 / 23	4.3	-	-	-
Other ocular AE	Intermediate or strong ocular pain	-	-	-	-	-	-	-	-	-	1	2 / 20	10.0
Non-ocular AE	Death	-	-	-	-	-	-	-	-	-	1	1 / 88	1.1
	Discomfort in prone position	-	-	-	-	-	-	-	-	-	1	18 / 20	90.0
	Headache	-	-	-	-	-	-	-	-	-	1	1 / 9	11.1
	Nausea	-	-	-	-	-	-	-	-	-	1	3 / 9	33.3

* Number of studies

** Ten subjects reported 11 visual disturbances (various types of visual disturbances)

Table 11: Postoperative Adverse Events of SF_6 with Mixed Agent or Procedure Reported in Included Studies

Category	Reported AE	Timeframe Reported											
		Day 1 to ≤ Month 1			> Month 1 to < Month 6			≥ Month 6			Unspecified		
		S#*	n / N	%	S#*	n / N	%	S#*	n / N	%	S#*	n / N	%
Anterior segment	Cataract	-	-	-	-	-	-	1	1 / 43	2.3	2	52 / 154	33.8
	Choroidal detachment	1	1 / 43	2.3	-	-	-	-	-	-	-	-	-
	Choroidal hemorrhage	-	-	-	-	-	-	-	-	-	1	1 / 43	2.3
	Glaucoma	-	-	-	-	-	-	-	-	-	1	6 / 82	7.3
	Hypotony	-	-	-	-	-	-	-	-	-	2	2 / 208	1.0
	Increased IOP	-	-	-	-	-	-	-	-	-	4	45 / 221	20.4
	Pupillary block	-	-	-	-	-	-	-	-	-	1	1 / 126	0.8
	Subconjunctival gas	-	-	-	-	-	-	-	-	-	1	2 / 20	10.0
	Subconjunctival hemorrhage	-	-	-	-	-	-	-	-	-	1	12 / 20	60.0
	Uveitis	-	-	-	-	-	-	-	-	-	2	2 / 120	1.7
Posterior segment	Cystoid macular edema	-	-	-	-	-	-	-	-	-	3	13 / 296	4.4
	CRA closure	-	-	-	-	-	-	-	-	-	3	5 / 20	25.0
	Epiretinal membrane / macular pucker	-	-	-	-	-	-	-	-	-	5	12 / 520	2.3
	New retinal breaks / tears	-	-	-	-	-	-	-	-	-	4	12 / 323	3.7
	Proliferative vitreoretinopathy	-	-	-	-	-	-	-	-	-	3	8 / 303	2.6
	Retinal displacement	-	-	-	1	12 / 21	57.1	-	-	-	-	-	-
	Retinal re-detachment	-	-	-	-	-	-	-	-	-	2	5 / 138	3.6

	SRF	1	15 / 32	46.9	-	-	-	-	-	-	1	1 / 65	1.5
	Subretinal hemorrhage	-	-	-	-	-	-	-	-	-	1	6 / 56	10.7
	Subretinal pigment	-	-	-	-	-	-	-	-	-	2	2 / 120	1.7
	Subretinal residual perfluorocarbon	-	-	-	-	-	-	-	-	-	1	2 / 147	1.4
	Tear enlargement	-	-	-	-	-	-	-	-	-	1	1 / 56	1.8
	Vitreous hemorrhage	-	-	-	-	-	-	-	-	-	1	2 / 56	3.6
	Vitreous floaters / opacities	1	1 / 43	2.3	-	-	-	-	-	-	3	19 / 140	13.6
Surgery and complications	Secondary surgical intervention	1	1 / 126	0.8	-	-	-	1	4 / 88	4.5	6	50 / 846	5.9
Vision	Visual acuity deterioration	-	-	-	-	-	-	-	-	-	1	5 / 100	5.0
	Visual disturbance (diplopia, metamorphopsia)	-	-	-	-	-	-	1	59 / 60	98.3	-	-	-
Other ocular AE	Intravitreal dexamethasone injection	-	-	-	-	-	-	1	27 / 88	30.7	-	-	-
Non-ocular AE	Headache	-	-	-	-	-	-	-	-	-	1	1 / 20	5.0
	Nausea	-	-	-	-	-	-	-	-	-	1	1 / 20	5.0
	Neck pain	-	-	-	-	-	-	-	-	-	1	2 / 20	10.0

* Number of studies

The most commonly reported possible device-related intraoperative AEs were retinal artery occlusion (27.6% of eyes in 2 studies) and subconjunctival gas (8.3% of eyes in 1 study). Other reported intraoperative AEs were likely associated with the surgical procedure.

The most commonly reported possible SF_6 device-related postoperative AEs were increased IOP (16.0% of eyes in 8 studies), secondary surgical intervention (10.9% of eyes in 32 studies), cataract (8.8% of eyes in 8 studies), and subconjunctival gas (20.0% of eyes in 1 study). Other postoperative AEs were likely associated with the surgical procedure or not related to either the device or procedure.

AEs reported in the mixed agent/procedure studies were similar in events and frequency.

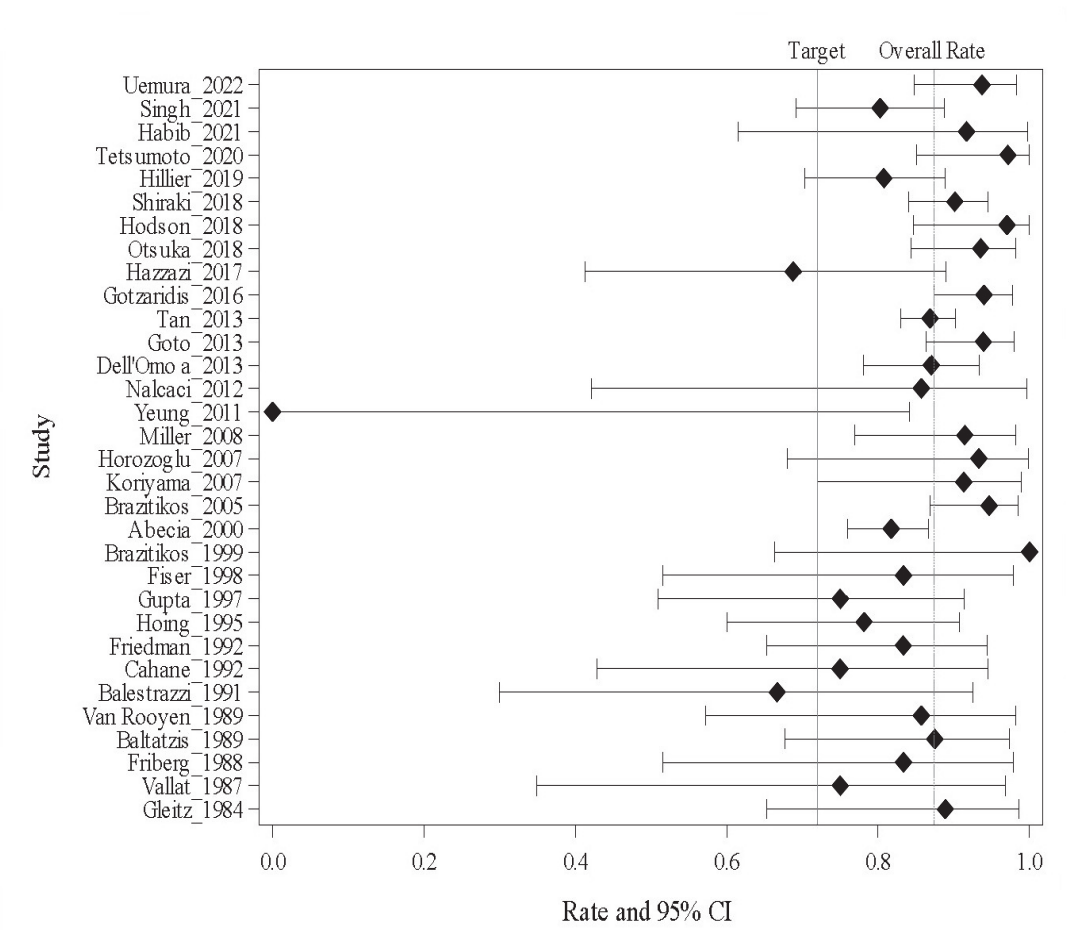
2. Effectiveness Results

The analysis of effectiveness was based on the quantitative cohort of 1723 eyes reported with rates of primary retinal reattachment at ≥3-months postoperatively. The overall primary retinal reattachment rate reported ≥3-months postoperatively in the analyzed studies was 87.4% (95% CI: 84.8%, 89.5%), which exceeds the prespecified threshold of 72%. The key effectiveness outcomes for this study are presented below in Table 12 and Figure 4.

Table 12 Effectiveness: Primary Retinal Reattachment Rate, All Studies and Subgrouped by Study Type

Study Type	Number of Studies (n)	Mean	95% CI
All Studies	**32**	**0.8735**	**(0.8483, 0.8950)**
A	3	0.8807	(0.7677, 0.9428)
C	12	0.8729	(0.8217, 0.9110)
E	17	0.8726	(0.8428, 0.8974)

Figure 4
Forest Plot: Effectiveness – Primary Retinal Reattachment Rate –All Studies



3. Subgroup Analyses

Subgroup analyses were conducted on the most recent literature published from January 1, 2012 to July 1, 2022. All recent literature were included in the above results from the original search starting January 1, 1980. The focus of these subgroup analyses were to identify changes in outcomes or treatments in the last 10 years. The search resulted in an observed trend of more publications reported using SF_6 during vitrectomy surgery rather than pneumatic retinopexy and fewer publications reported elevated IOP rates. Regarding effectiveness, the overall primary retinal reattachment rate in the analyzed vitrectomy surgery studies (n=16) was 89.8% (95% CI: 87.0.%, 92.1%) and the overall primary retinal reattachment rate in the analyzed pneumatic retinopexy studies (n=16) was 81.1% (81.1% (95% CI: 79.3%, 82.8%). The rate of elevated IOP in the analyzed vitrectomy surgery studies (n=2) was 10.1% (95% CI: 5.9%, 16.8%) and the rate

of elevated IOP in the analyzed pneumatic retinopexy studies (n=3) was 11.1% (95% CI: 5.3%, 21.9%).

No analyses were performed for sex, gender, age, race, ethnicity, or other subgroups.

4. Pediatric Extrapolation
   In this premarket application, existing clinical data was not leveraged to support approval of a pediatric patient population.

XI. FINANCIAL DISCLOSURE

N/A

XII. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

N/A

XIII. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

In accordance with the provisions of section 515(c)(3) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Ophthalmic Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIV. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The overall primary retinal reattachment rate reported ≥3-months postoperatively in the quantitative effectiveness analysis was 87.4% (95% CI: 84.8%, 89.5%), which exceeds the prespecified threshold of 72%. Therefore, the success criteria for the primary effectiveness outcome is met and the objective clinical evidence supports the effectiveness of the subject device due to the comparable SF_6 gas chemical profiles to the marketed/studied SF_6 gas.

B. Safety Conclusions

The risks of the device are based on nonclinical laboratory and animal studies (as summarized in Section IX above) as well as data collected in a clinical literature review conducted to support PMA approval as described above. Literature reported a tolerable side-effect profile, specifically in terms of adverse event rates, which were within acceptable postoperative safety limits. The overall rate of elevated IOP >25

mmHg reported 1 to 7 days postoperatively in the quantitative safety analysis was 10.4% (95% CI: 6.8%, 15.6%), which is less than the prespecified threshold of 34%. Therefore, the success criteria for the primary safety outcome is met and the objective clinical evidence supports the safety of the subject device.

C. Benefit-Risk Determination

The probable benefits of the device are also based on data reported in clinical literature published since 1980 to support PMA approval as described above. The literature shows that this device is one of several options for treating uncomplicated retinal detachment and is considered the standard of care. This device allows patients to be treated for uncomplicated retinal detachment with primary success rates of reattachment of over 80% and acceptable safety profiles of elevated IOP known to occur in ocular surgeries.

The probable risks of the device are also based on data reported in clinical literature published since 1980 to support PMA approval as described above. Risks reported were in the form of adverse events and complications reported in literature for the surgical procedure of uncomplicated retinal detachment repair. Literature reported a tolerable side-effect profile, specifically in terms of adverse event rates, which were within acceptable postoperative safety limits. Possible adverse events could include, but are not limited to, elevated intraocular pressure, retinal redetachment, subretinal migration of gas, escape of gas through surgical incisions, cataract, retinal artery occlusion, and macular hole.

1. Patient Perspective

   This submission either did not include specific information on patient perspectives or the information did not serve as part of the basis of the decision to approve or deny the PMA for this device.

In conclusion, given the available information above, the data support that for the use of UNIPURE SF_6 Ophthalmic Gas in the UNIFEYE and UNIPEXY Gas Delivery Systems in the treatment of uncomplicated retinal detachments the probable benefits outweigh the probable risks.

D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. The literature search reports did not introduce any new risks and conclude that the benefits of the device outweigh the risks when used as intended.

XV. CDRH DECISION

CDRH issued an approval order on 08/26/2024.

The applicant's manufacturing facilities have been inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XVI. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See approval order.

XVII. REFERENCES

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