



P910068

# Memorandum

Date **SEP 30 1997**

From Director, Office of Device Evaluation (HFZ-400)  
Center for Devices and Radiological Health (CDRH)

Subject Premarket Approval of Vitrophage, Inc.'s VITREON®  
(Perfluoroperhydrophenanthrene) Intraocular Fluid - ACTION

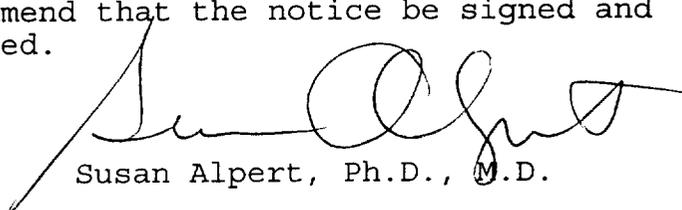
To The Director, CDRH  
ORA \_\_\_\_\_

ISSUE. Publication of a notice announcing approval of the subject PMA.

FACTS. Tab A contains a FEDERAL REGISTER notice announcing:

- (1) a premarket approval order for the above referenced medical device (Tab B); and
- (2) the availability of a summary of safety and effectiveness data for the device (Tab C).

RECOMMENDATION. I recommend that the notice be signed and published.



Susan Alpert, Ph.D., M.D.

Attachments  
Tab A - Notice  
Tab B - Order  
Tab C - S & E Summary

DECISION

Approved \_\_\_\_\_ Disapproved \_\_\_\_\_ Date \_\_\_\_\_

Prepared by EMFelton, CDRH, HFZ-460, September 18, 1997, 594-1744.

## DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

**DRAFT**

[DOCKET NO. \_\_\_\_\_]

Vitrophage, Inc.; Premarket Approval of VITREON®

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing its approval of the application submitted by Vitrophage, Inc., Lyons, IL, for premarket approval, under the Federal Food, Drug, and Cosmetic Act (the act), of VITREON®. After reviewing the recommendation of the Ophthalmic Devices Panel, FDA's Center for Devices and Radiological Health (CDRH) notified the applicant, by letter of September 30, 1997, of the approval of the application.

DATES: Petitions for administrative review by (insert date 30 days after date of publication in the FEDERAL REGISTER).

ADDRESSES: Written requests for copies of the summary of safety and effectiveness data and petitions for administrative review to the Dockets Management Branch (HFA-305), Food and Drug Administration, 12420 Parklawn Dr., rm. 1-23, Rockville, MD 20857.

## FOR FURTHER INFORMATION CONTACT:

James F. Saviola,  
Center for Devices and Radiological Health (HFZ-460),  
Food and Drug Administration,  
9200 Corporate Blvd.,  
Rockville, MD 20850,  
301-594-1744.

SUPPLEMENTARY INFORMATION: On December 6, 1991, VitroPhage, Inc., Lyons, IL 60534, submitted to CDRH an application for premarket approval of VITREON®. The device is a purified perfluorocarbon liquid and is indicated for use as an intraoperative surgical aid during vitreoretinal surgery in patients with primary and recurrent complicated retinal detachments. Complicated cases include giant retinal tear or retinal dialysis, proliferative vitreoretinopathy, proliferative diabetic retinopathy, tractional retinal detachments, and blunt or penetrating ocular trauma.

On October 19, 1995, the Ophthalmic Devices Panel of the Medical Devices Advisory Committee, an FDA advisory committee, reviewed and recommended approval of the application.

On September 30, 1997, CDRH approved the application by a letter to the applicant from the Director of the Office of Device Evaluation, CDRH.

A summary of the safety and effectiveness data on which CDRH based its approval is on file in the Dockets Management Branch (address above) and is available from that office upon written request. Requests should be identified with the name of the device and the docket number found in brackets in the heading of this document.

#### Opportunity for Administrative Review

Section 515(d)(3) of the act, (21 U.S.C. 360e(d)(3)) authorizes any interested person to petition, under section 515(g) of the act, for administrative review of CDRH's decision to approve this application. A petitioner may request either a

formal hearing under 21 CFR part 12 of FDA's administrative practices and procedures regulations or a review of the application and CDRH's action by an independent advisory committee of experts. A petition is to be in the form of a petition for reconsideration under 21 CFR 10.33(b). A petitioner shall identify the form of review requested (hearing or independent advisory committee) and shall submit with the petition supporting data and information showing that there is a genuine and substantial issue of material fact for resolution through administrative review. After reviewing the petition, FDA will decide whether to grant or deny the petition and will publish a notice of its decision in the FEDERAL REGISTER. If FDA grants the petition, the notice will state the issue to be reviewed, the form of the review to be used, the persons who may participate in the review, the time and place where the review will occur, and other details.

Petitioners may, at any time on or before (insert date 30 days after date of publication in the FEDERAL REGISTER), file with the Dockets Management Branch (address above) two copies of each petition and supporting data and information, identified with the name of the device and the docket number found in brackets in the heading of this document. Received petitions may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

This notice is issued under the Federal Food, Drug, and Cosmetic Act (secs. 515(d), 520(h) (21 U.S.C. 360e(d), 360j(h))) and under authority delegated to the Commissioner of Food and Drugs (21 CFR 5.10) and redelegated to the Director, Center for Devices and Radiological Health (21 CFR 5.53).

Dated: \_\_\_\_\_.

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Food and Drug Administration  
9200 Corporate Boulevard  
Rockville MD 20850

Mr. Frederick A. Stearns  
Counsel for Vitrophage, Inc.  
c/o Keller and Heckman LLP  
1001 G Street, N.W.  
Suite 500 West  
Washington, DC 20001

SEP 30 1997

Re: P910068  
VITREON® (Perfluoroperhydrophenanthrene) Intraocular Fluid  
Filed: December 6, 1991  
Amended: December 19, 1991; March 31, October 7, November 23, 1992; April 2, 13, and 29, June 22 and 25, July 2 and 23, August 20, September 13, October 15, and November 1, 1993; January 7, March 30, April 15, 19 and 20, and June 15, 1994; January 12 and 25, March 14, May 9 and 26, August 30, September 1 and 25, 1995; January 29, March 20, May 9, June 19, July 30 and 31, and November 18, 1996; and January 23, July 14, and September 17 and 25, 1997

Dear Mr. Stearns:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of the premarket approval application (PMA) that you submitted on behalf of your client, Vitrophage, Inc. for VITREON® (Perfluorophenanthrene) Intraocular Fluid. This device is indicated for use as an intraoperative surgical aid during vitreoretinal surgery in patients with primary and recurrent complicated retinal detachments. Complicated cases include giant retinal tear or retinal dialysis, proliferative vitreoretinopathy, proliferative diabetic retinopathy, tractional retinal detachments, and blunt or penetrating ocular trauma. We are pleased to inform you that the PMA is approved for a single batch (Batch # 672-45-0001) of the finished product packaged in sterile 6 mL vials. This approval is subject to the conditions described below and in the "Conditions of Approval" (enclosed). You may begin commercial distribution of the device upon receipt of this letter.

You have informed FDA in a meeting on February 6, 1996, that you will be changing the raw material supplier. Your approval is limited to batch # 672-45-0001, therefore, if you wish to market other batches using a new raw material supplier, you must submit and receive FDA approval for a PMA supplement which supports the change in the raw material supplier.

The sale, distribution, and use of this device are restricted to prescription use in accordance with 21 CFR 801.109 within the meaning of section 520(e) of the Federal Food, Drug, and Cosmetic Act (the act) under the authority of section 515(d)(1)(B)(ii) of the act. FDA has also determined that to ensure the safe and effective use of the device that the device is further restricted within the meaning of section 520(e) under the authority of section 515(d)(1)(B)(ii) insofar as the sale, distribution, and use must not violate sections 502(q) and (r) of the act.

Expiration dating for this device has been established and approved at 2 years for the 6 mL vials. This is to advise you that the protocol you used to establish this expiration dating is considered an approved protocol for the purpose of extending the expiration dating as provided by 21 CFR 814.39(a)(8).

CDRH will publish a notice of its decision to approve your PMA in the FEDERAL REGISTER. The notice will state that a summary of the safety and effectiveness data upon which the approval is based is available to the public upon request. Within 30 days of publication of the notice of approval in the FEDERAL REGISTER, any interested person may seek review of this decision by requesting an opportunity for administrative review, either through a hearing or review by an independent advisory committee, under section 515(g) of the Federal Food, Drug, and Cosmetic Act (the act).

Failure to comply with the conditions of approval invalidates this approval order. Commercial distribution of a device that is not in compliance with these conditions is a violation of the act.

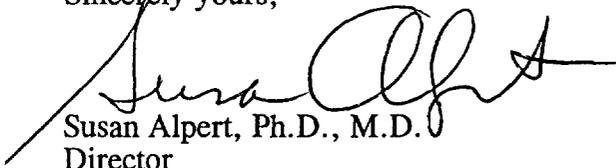
You are reminded that, as soon as possible and before commercial distribution of your device, you must submit an amendment to this PMA submission with copies of all approved labeling in final printed form.

All required documents should be submitted in triplicate, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing.

PMA Document Mail Center (HFZ-401)  
Center for Devices and Radiological Health  
Food and Drug Administration  
9200 Corporate Blvd.  
Rockville, Maryland 20850

If you have any questions concerning this approval order, please contact Ms. Eleanor M. Felton or James F. Saviola, O.D., at (301) 594-1744.

Sincerely yours,



Susan Alpert, Ph.D., M.D.  
Director  
Office of Device Evaluation  
Center for Devices and  
Radiological Health

Enclosure

CONDITIONS OF APPROVAL

APPROVED LABELING. As soon as possible, and before commercial distribution of your device, submit three copies of an amendment to this PMA submission with copies of all approved labeling in final printed form to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration (FDA), 9200 Corporate Blvd., Rockville, Maryland 20850.

ADVERTISEMENT. No advertisement or other descriptive printed material issued by the applicant or private label distributor with respect to this device shall recommend or imply that the device may be used for any use that is not included in the FDA approved labeling for the device. If the FDA approval order has restricted the sale, distribution and use of the device to prescription use in accordance with 21 CFR 801.109 and specified that this restriction is being imposed in accordance with the provisions of section 520(e) of the act under the authority of section 515(d)(1)(B)(ii) of the act, all advertisements and other descriptive printed material issued by the applicant or distributor with respect to the device shall include a brief statement of the intended uses of the device and relevant warnings, precautions, side effects and contraindications.

PREMARKET APPROVAL APPLICATION (PMA) SUPPLEMENT. Before making any change affecting the safety or effectiveness of the device, submit a PMA supplement for review and approval by FDA unless the change is of a type for which a "Special PMA Supplement-Changes Being Effectuated" is permitted under 21 CFR 814.39(d) or an alternate submission is permitted in accordance with 21 CFR 814.39(e). A PMA supplement or alternate submission shall comply with applicable requirements under 21 CFR 814.39 of the final rule for Premarket Approval of Medical Devices.

All situations which require a PMA supplement cannot be briefly summarized, please consult the PMA regulation for further guidance. The guidance provided below is only for several key instances.

A PMA supplement must be submitted when unanticipated adverse effects, increases in the incidence of anticipated adverse effects, or device failures necessitate a labeling, manufacturing, or device modification.

A PMA supplement must be submitted if the device is to be modified and the modified device should be subjected to animal or laboratory or clinical testing designed to determine if the modified device remains safe and effective.

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A "Special PMA Supplement - Changes Being Effectuated" is limited to the labeling, quality control and manufacturing process changes specified under 21 CFR 814.39(d)(2). It allows for the addition of, but not the replacement of previously approved, quality control specifications and test methods. These changes may be implemented before FDA approval upon acknowledgment by FDA that the submission is being processed as a "Special PMA Supplement - Changes Being Effectuated." This acknowledgment is in addition to that issued by the PMA Document Mail Center for all PMA supplements submitted. This procedure is not applicable to changes in device design, composition, specifications, circuitry, software or energy source.

Alternate submissions permitted under 21 CFR 814.39(e) apply to changes that otherwise require approval of a PMA supplement before implementation of the change and include the use of a 30-day PMA supplement or annual postapproval report. FDA must have previously indicated in an advisory opinion to the affected industry or in correspondence with the applicant that the alternate submission is permitted for the change. Before such can occur, FDA and the PMA applicant(s) involved must agree upon any needed testing protocol, test results, reporting format, information to be reported, and the alternate submission to be used.

POSTAPPROVAL REPORTS. Continued approval of this PMA is contingent upon the submission of postapproval reports required under 21 CFR 814.84 at intervals of 1 year from the date of approval of the original PMA. Postapproval reports for supplements approved under the original PMA, if applicable, are to be included in the next and subsequent annual reports for the original PMA unless specified otherwise in the approval order for the PMA supplement. Two copies identified as "Annual Report" and bearing the applicable PMA reference number are to be submitted to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration, 9200 Corporate Blvd., Rockville, Maryland 20850. The postapproval report shall indicate the beginning and ending date of the period covered by the report and shall include the following information required by 21 CFR 814.84:

- (1) Identification of changes described in 21 CFR 814.39(a) and changes required to be reported to FDA under 21 CFR 814.39(b).
- (2) Bibliography and summary of the following information not previously submitted as part of the PMA and that is known to or reasonably should be known to the applicant:
  - (a) unpublished reports of data from any clinical investigations or nonclinical laboratory studies involving the device or related devices ("related" devices include devices which are the same or substantially similar to the applicant's device); and

- (b) reports in the scientific literature concerning the device.

If, after reviewing the bibliography and summary, FDA concludes that agency review of one or more of the above reports is required, the applicant shall submit two copies of each identified report when so notified by FDA.

ADVERSE REACTION AND DEVICE DEFECT REPORTING. As provided by 21 CFR 814.82(a)(9), FDA has determined that in order to provide continued reasonable assurance of the safety and effectiveness of the device, the applicant shall submit 3 copies of a written report identified, as applicable, as an "Adverse Reaction Report" or "Device Defect Report" to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration, 9200 Corporate Blvd., Rockville, Maryland 20850 within 10 days after the applicant receives or has knowledge of information concerning:

- (1) A mixup of the device or its labeling with another article.
- (2) Any adverse reaction, side effect, injury, toxicity, or sensitivity reaction that is attributable to the device and
  - (a) has not been addressed by the device's labeling or
  - (b) has been addressed by the device's labeling, but is occurring with unexpected severity or frequency.
- (3) Any significant chemical, physical or other change or deterioration in the device or any failure of the device to meet the specifications established in the approved PMA that could not cause or contribute to death or serious injury but are not correctable by adjustments or other maintenance procedures described in the approved labeling. The report shall include a discussion of the applicant's assessment of the change, deterioration or failure and any proposed or implemented corrective action by the applicant. When such events are correctable by adjustments or other maintenance procedures described in the approved labeling, all such events known to the applicant shall be included in the Annual Report described under "Postapproval Reports" above unless specified otherwise in the conditions of approval to this PMA. This postapproval report shall appropriately categorize these events and include the number of reported and otherwise known instances of each category during the reporting period. Additional information regarding the events discussed above shall be submitted by the applicant when determined by FDA to be necessary to provide continued reasonable assurance of the safety and effectiveness of the device for its intended use.

REPORTING UNDER THE MEDICAL DEVICE REPORTING (MDR) REGULATION. The Medical Device Reporting (MDR) Regulation became effective on December 13, 1984, and requires that all manufacturers and importers of medical devices, including in vitro diagnostic devices, report to FDA whenever they receive or otherwise became aware of information that reasonably suggests that one of its marketed devices

- (1) may have caused or contributed to a death or serious injury or
- (2) has malfunctioned and that the device or any other device marketed by the manufacturer or importer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

The same events subject to reporting under the MDR Regulation may also be subject to the above "Adverse Reaction and Device Defect Reporting" requirements in the "Conditions of Approval" for this PMA. FDA has determined that such duplicative reporting is unnecessary. Whenever an event involving a device is subject to reporting under both the MDR Regulation and the "Conditions of Approval" for this PMA, you shall submit the appropriate reports required by the MDR Regulation and identified with the PMA reference number to the following office:

Division of Surveillance Systems (HFZ-531)  
Center for Devices and Radiological Health  
Food and Drug Administration  
1350 Piccard Drive, Room 240  
Rockville, Maryland 20850  
Telephone (301) 594-2735

Events included in periodic reports to the PMA that have also been reported under the MDR Regulation must be so identified in the periodic report to the PMA to prevent duplicative entry into FDA information systems.

Copies of the MDR Regulation and an FDA publication entitled, "An Overview of the Medical Device Reporting Regulation," are available by written request to the address below or by telephoning 1-800-638-2041.

Division of Small Manufacturers Assistance (HFZ-220)  
Center for Devices and Radiological Health  
Food and Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20857

## SUMMARY OF SAFETY AND EFFECTIVENESS DATA

### I. GENERAL INFORMATION

- A. Device Generic Name: Perfluorocarbon Liquid (ProCode 86 LWL - Intraocular Fluid)
- B. Trade Name of Device: VITREON®
- C. Applicant's Name and Address: Vitrophage, Inc.  
8643 W. Ogden Avenue  
Lyons, IL 60534
- D. Investigational Device Exemption (IDE) Number: G900050
- E. Date of Panel Recommendation: October 19, 1995
- F. Premarket Approval Application (PMA) Number: P910068  
Date Filed: December 6, 1991
- G. GMP Inspection: August 22, 1997
- H. Date of Notice of Approval to Applicant: September 30, 1997

### II. INDICATION

VITREON® is indicated for use as an intraoperative surgical aid during vitreoretinal surgery in patients with primary and recurrent complicated retinal detachments. Complicated cases include giant retinal tear or retinal dialysis proliferative vitreoretinopathy, proliferative diabetic retinopathy, tractional retinal detachments, and blunt or penetrating ocular trauma.

### III. CONTRAINDICATIONS

#### Contraindications

VITREON® is contraindicated as a vitreous replacement.

### IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the VITREON® labeling (Attachment 1).

## V. DEVICE DESCRIPTION

VITREON® sterile intraocular fluid is a purified perfluorocarbon liquid comprised of perfluoroperhydrophenanthrene (PFPHP) (C<sub>14</sub>F<sub>24</sub>) with perfluoro-n-butyldecalin and related perfluorinated isomers. PFP is a liquid fluorocarbon, the chemical structure of which is shown in the package insert (Attachment).

VITREON® is optically clear, immiscible with water, and has a much higher specific gravity than water.

The chemical and physical properties of VITREON® are listed below:

Molecular Weight	624.12
Boiling Point (°C)	215
Specific Gravity	2.03
Surface Tension (dynes/cm @25°C)	23.9
Refractive Index	1.33
Vapor Pressure (torr @ 37°C)	0.35
Viscosity (centistoke @ 25°C)	7.80

VITREON® has the following chemical and physical specifications:

ORGANIC HYDROGEN (PPM, W/W)	≤ 10
Residual Fluoride (ppm)	≤ 1 ppm
Non-volatile Residue (%)	≤ 0.015
Heavy Metals (ppm)	≤ 10
Particulates	Not more than 50 particles/mL ≥ 10 μm Not more than 5 particles/mL ≥ 25 μm

VITREON® contains no preservatives or other ingredients.

VITREON® is supplied sterile in 6 mL single-dose vials capped with a rubber stopper. Each single-dose vial is packaged in an individual carton.

## **VI. ALTERNATIVE PRACTICES AND PROCEDURES**

The management of complicated retinal detachment associated with giant retinal tears has stimulated the development of many approaches to unfold the flap of the tear and maintain its position against the retinal pigment epithelium. The use of intraocular gases may necessitate turning the patient intraoperatively into the prone position to help unroll the flap of the tear. Surgical tables have been designed for this purpose.

Silicone oil techniques involve direct bimanual manipulation of the retina under the silicone oil interface until the flap is correctly positioned. A posterior retinotomy is occasionally necessary to evacuate residual subretinal fluid after the tear is closed.

Methods have also been developed to fixate the flap of the tear intraoperatively, such as retinal incarceration or microincarceration retinal suturing or retinal tacks.

Various liquid devices with a higher specific gravity than water have also been used to unfold the flap of a giant retinal tear, and to flatten the retina against the choroidal surface. The use of hyaluronate sodium or silicone oil has been previously reported. Also, there is one other PMA approved for a perfluorocarbon liquid with the same indications for use.

## **VII. DOSAGE AND ADMINISTRATION**

The dosage and administration can be found in the VITREON® labeling, directions for use (attachment 1). That section addresses general steps as well as specific steps for GRT, PVR and ocular trauma.

## **VIII. MARKETING HISTORY**

VITREON® has not been marketed in the United States as an intraocular fluid.

## **IX. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH**

### **A. Adverse Reactions and Complications**

Data were divided into two segments and were analyzed separately. The “cohort” group consisted of 389 patients evaluated for safety and effectiveness parameters. The “non-cohort” group included data on 1241 additional patients evaluated for safety parameters only. In the following discussion, occurrence rates are reported by the specific group in which the complication occurred.

Adverse effects reported during the clinical studies of VITREON® include melanoma (1 patient), diabetic complications (3 patients), cancer (5 patients), heart failure (2 patients), suicide (1 patient), no reason provided (4 patients). None were considered to be associated with the use of VITREON®.

The following adverse reactions related to the use of VITREON® were observed during the clinical studies:

	Cohort	Overall
Intraoperative subretinal VITREON® migration	0.9%	--
Postoperative residual VITREON®	9.0%	6.5%

Other complications reported by the investigators are general complications of complicated vitreoretinal surgery, and may not be associated with the use of VITREON®:

	Cohort %	Overall %
• Corneal disorders	17.9	13.7
• Corneal edema	12.4	7.5
• Anterior chamber abnormalities	18.2	8.3
• Elevated IOP	0.7	2.2
• Hypotony	25.9	17.5
• Iris abnormalities	8.5	5.0
• Cataract formation in phakic eyes	3.0	Not Reported
• Intraoperative retinal slippage	7.7	Not Reported
• Progression to NLP (No Light Perception)	6.1	4.9

## X. SUMMARY OF PRE-CLINICAL STUDIES

### A. Safety and Toxicity Studies

A series of non-clinical studies were undertaken to demonstrate that VITREON® used intraoperatively in retinal detachment surgery and removed immediately after surgery, could reasonably be expected to be non-toxic and raise no safety concerns. A complete list of all non-clinical testing on this material is presented below.

## IN VITRO TESTS

<u>TEST</u>	<u>RESULTS</u>
<u>Cytotoxicity</u> : material extracted in MEM elution exposed to monolayer of mouse fibroblast cells for up to 72 hours at 1:4 dilution	non-toxic
<u>Cell Growth</u> : retinoblastoma cells grown in culture exposed to perfluorophenanthrene and fluorosilicone with growth media as the control <sup>1</sup>	growth slower in test group than control
<u>Ames Mutagenicity</u> : Standard Ames test	negative

## IN VIVO TESTS

<u>Rabbit Eye Vitrectomy</u> : 34 rabbit eyes vitrectomized, 22 filled with VITREON® and 12 used balanced salt solution examined by light and electron microscopes, followed for up to 6 weeks then performed histopathology and light adapted electroretinography <sup>1</sup>	non-toxic
<u>Monkey Eye Vitrectomy</u> : 6 African green monkeys had vitrectomy and vitreous replacement with VITREON® in 3 eyes and VITREON® plus silicone oil in 3 eyes as a control examined after 45 days, enucleating at day 162 <sup>2</sup>	non-toxic
<u>Rabbit Intravenous</u> : 35 day subacute intravenous study VITREON® appeared to be phagocytized by histiocytes accumulated primarily in the spleen and liver.	no direct toxic effect or inflammatory reaction
<u>Dog Intravenous</u> : same as Rabbit Intravenous above	
<u>Guinea Pig Dermal Sensitivity</u> : 10 guinea pigs with historical control	negative
<u>Oral Irritation Rats</u> : 5 male and 5 female Sprague Dawley rats with direct administration of VITREON® into the stomach by gavage; 14 days observation and necropsy	no macroscopic abnormalities
<u>Inhalation Toxicity</u> : 5 male and 5 female Sprague Dawley rats, 2 groups of 5 control and 5 test. Exposed to test material vapor for 4	no exposure related abnormal pharmacokinetic



<u>Intravenous Toxicity</u> : 4 Swiss mice administered 100 mL/kg clear liquid test sample	appeared normal no macroscopic abnormalities at necropsy after 14 days
45 Swiss mice with varying doses of amber liquid test sample, 14 day observation then necropsy	LD <sub>50</sub> = 51.78 confirmed
<u>Acute Oral Toxicity</u> : rats given a dose of 10 ml PFP/kg 14 days necropsy	LD <sub>50</sub> for PFP > 5 g/kg
<u>LC<sub>50</sub> in rats</u> : rats exposed to atomized PFP at a rate of 1.5 mg/L	non-toxic
<u>Corneal Toxicity</u> : 6 rabbit eyes injected with VITREON® into the anterior chamber	endothelial cell loss toxic to cornea
<u>Eye Irritation Test</u> : Draize test on 3 albino rabbit eyes observed at 1 hour and 1 day	no corneal opacity or iritis noted at 1 day
<u>Final Package Closure and Stopper Material Testing:</u>	
Full UV spectrum (200-350 nm)	no effect on extractives
IR spectrum (2900 wave numbers - 3200)	
In Vitro cytotoxicity	
Ocular irritation testing	
Sterilization and coating of stopper with medical grade silicone	negative
Safety evaluation of stopper material USP testing criteria	negative

## B. Shelf-Life Dating

Shelf-life testing results support a 2 year shelf-life. A shelf-life and stability protocol is approved.

# XI. SUMMARY OF CLINICAL STUDIES

## A. Objective and Study Design

The data upon which the claims of safety and effectiveness for VITREON® are based were derived from a multi-center clinical trial conducted at 32 centers in the United States. The purpose of the clinical trial was to evaluate the safety and effectiveness of VITREON® for use as an intraoperative surgical aid in complicated retinal detachments. The original protocol called for VITREON® to be left in the eyes of a group of subjects for up to 29 days to evaluate the presence

of VITREON® in the eye during the postoperative period. Due to the lack of recruitment of subjects and the desire to have the indicated use of VITREON® for intraoperative purposes only, the study design was revised. The revised study design required that the VITREON® be removed at the completion of surgery. Subjects initially enrolled in the study to be included in the subgroup with VITREON® left in at the completion of surgery, in addition to subjects in whom it was left in after the protocol revision, were analyzed separately and categorized as protocol violations.

Eight centers were selected to comprise a "cohort" of subjects upon which both safety and effectiveness were to be evaluated. The remaining centers comprised a subgroup of the centers referred to as the "non-cohort" where the focus of evaluation was on safety. At the time the eight centers were selected it was believed that 80% of the subjects would have follow-up to at least the 78-180 day time period and had consecutive evaluations up to this time. After the selection of the cohort centers, the desired time for minimum follow up was increased to 120-180 days or 4-6 months. A subsequent analysis has demonstrated that the subjects in the cohort group were representative of all the subjects in the clinical trial.

## **B. Subject Selection and Exclusion Criteria**

### **Inclusion Criteria**

To be included in the investigation, subjects had to meet all of the following inclusion criteria:

Subject must have complicated retinal detachment to include proliferative vitreoretinopathy; giant retinal tears and dialysis; tractional retinal detachments; blunt or penetrating retinal trauma; subjects with dislocated intraocular lenses without retinal involvement; choroidal detachments; and other diagnosis without retinal detachments.

### **Exclusion Criteria**

Subject with uncomplicated cases of retinal detachment were to be excluded from the study.

## **C. Demographics**

Of the 481 subjects enrolled into the cohort group, 13 subjects did not participate in the current study and 76 subjects had VITREON® left in the eye, leaving 392 subjects in the primary analysis. Of these 392 subjects, 343 had retinal detachments and accounted for subjects for which efficacy data was provided. An additional 49 subjects did not have retinal detachments but did use the subject device for other disorders.

Of the 1347 subjects enrolled into the non-cohort group, 4 subjects had unknown preoperative diagnosis and 30 subjects had VITREON® left in the eye, leaving 1313 subjects in the primary analysis. Of these 1313 subjects 1183 had retinal detachments and accounted for subjects for which safety data was provided.

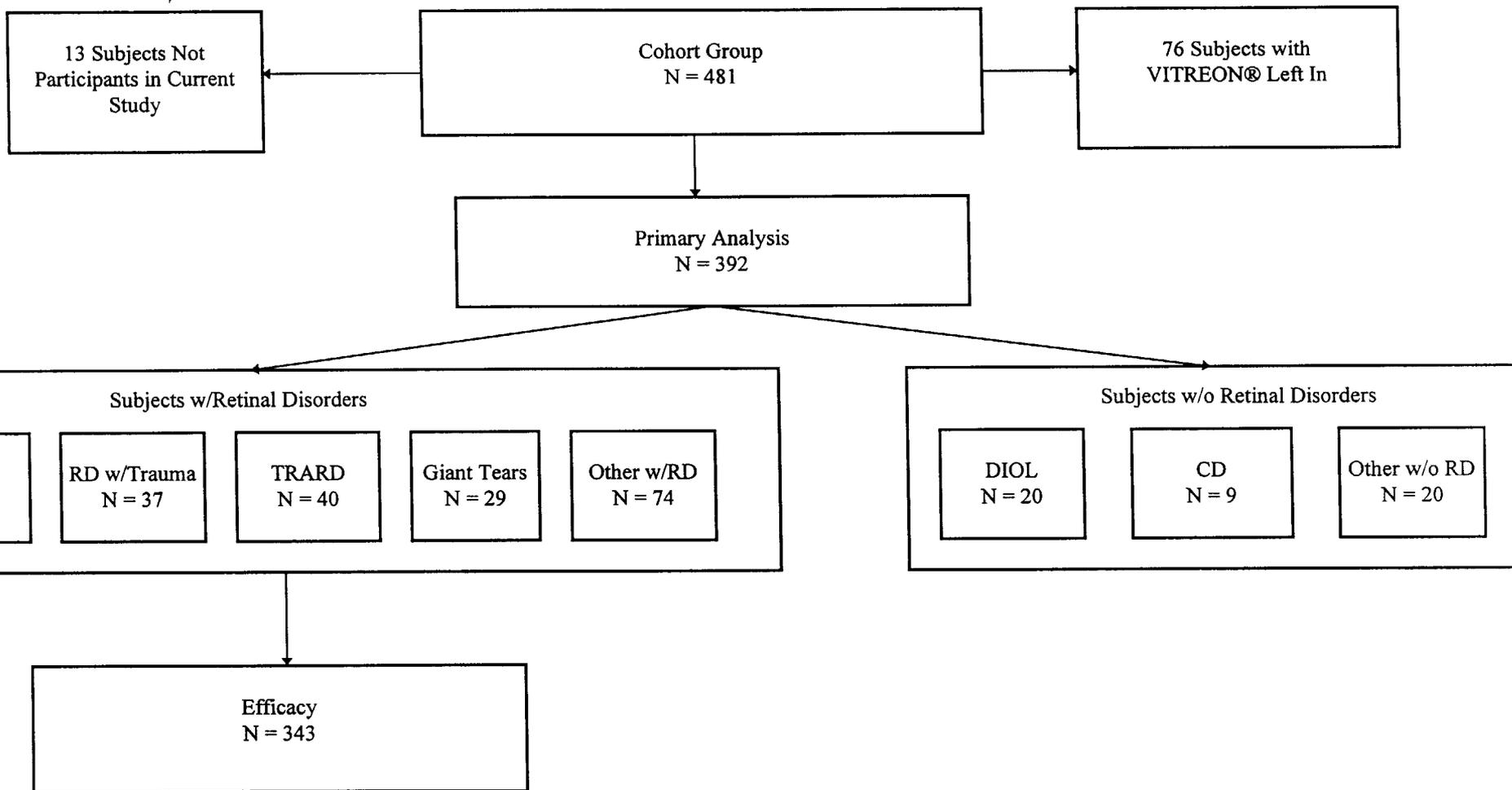
NUMBER OF PATIENTS PER CENTER - COHORT	
NAME OF CENTER	# PTS.
LSU EYE CENTER	140
MARY POTTER PHYS. PAV.	106
HOLMES REG. HOSP.	30
ST. JOSEPH O'DEA	29
U. OF MISS.	28
CALIFORNIA RET. ASSOC.	24
RETINAL ASSOC - LITTLE ROCK	20
RETINAL ASSOC - MUSKEGON	15
TOTAL	392

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NUMBER OF PATIENTS PER CENTER - NON-COHORT	
NAME OF CENTER	# PTS.
WILLS EYE CENTER	620
ASSOC'D RET. CONSULT.	206
JOHNS HOPKINS HOSPITAL	146
U. OF MIAMI	91
N. FLA. REGIONAL MED. CTR.	46
MERCY HEALTHCARE WAREHOUSE	40
U. OF MISSOURI	34
RETINA CONSULTANTS	29
LSU MEDICAL CENTER	17
VANDERBILT U. MED. CTR.	13
COLORADO RETINA CENTER	12
M.L. KING/DREW L.A.	12
RETINA ASSOC. BOSTON	11
ROCKY MOUNTAIN EYE CENTER	8
TEXAS RETINA ASSOCIATION	7
VITREO RETINAL CONSULTANTS	6
RET. ASSOC. CLEVE.	4
OUR LADY OF LAKE	2
ALBANY MEDICAL CENTER	2
FRANKLIN SQUARE HOSPITAL	2
SIBLEY MEMORIAL HOSPITAL	2
USCD MEDICAL CENTER	1
RICHMOND RETINAL ASSOC.	1
U. OF UTAH MEDICAL CENTER	1
TOTAL	1313

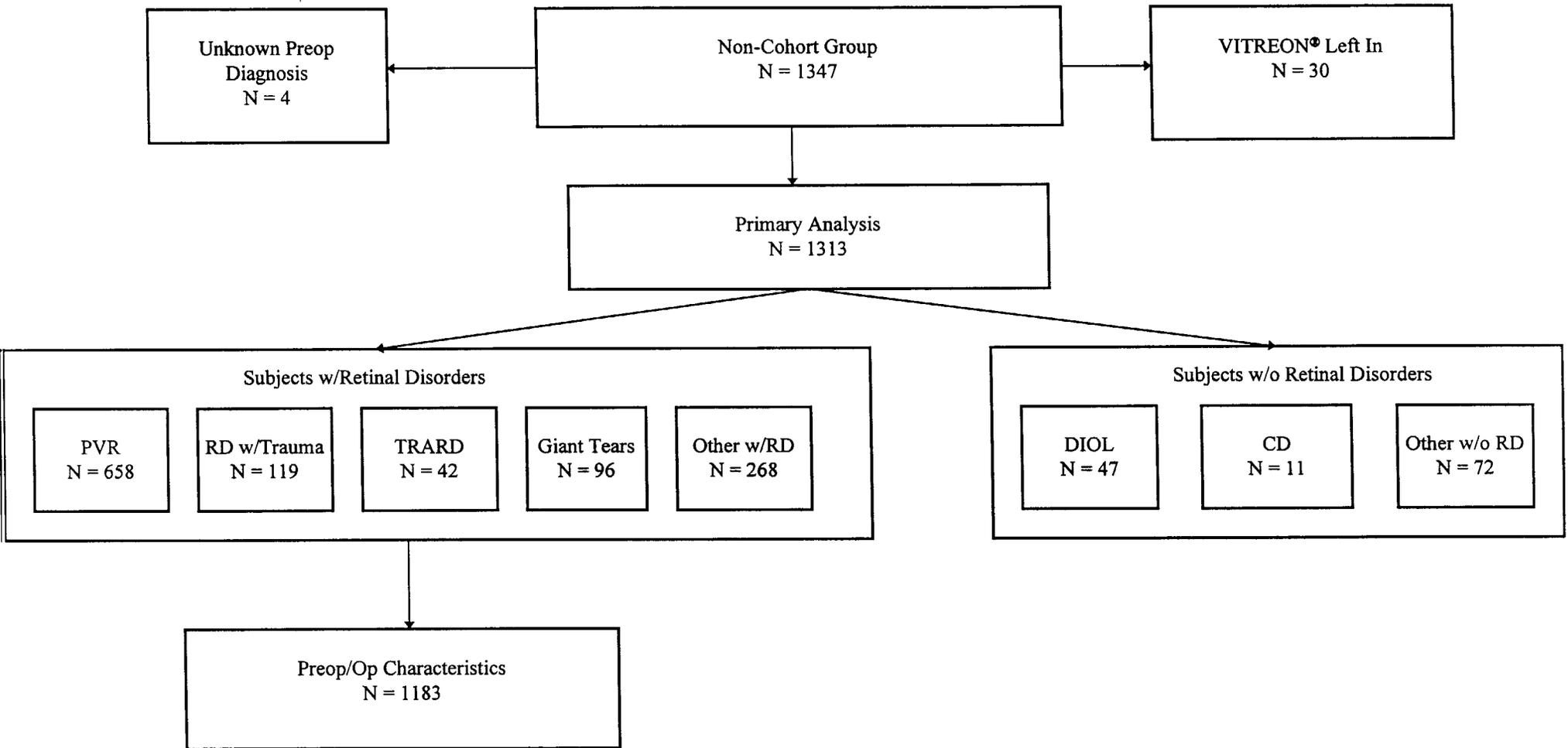
The subjects were categorized by preoperative diagnosis; proliferative vitreoretinopathy (PVR), retinal detachment associated with trauma (RD w/Trauma), tractional retinal detachment (TRARD), giant retinal tears (GRT), all other retinal detachments (Other w/RD).

**Cohort Demographics**



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### Non-Cohort Demographics



#### D. Efficacy and Safety Endpoints

Efficacy was measured both by anatomic success, defined as:

1. the ability of VITREON® to flatten the retina
2. successful retinal reattachment at initial surgery
3. number of posterior drainage retinotomies
4. number of membrane dissections
5. number of relaxing retinotomies; and

by visual acuity success, defined as:

1. the percent of eyes with preservation (no loss) of visual acuity; and
2. the percent of eyes with minimum functional vision.

For the purposes of data analysis, visual acuities were graded in eight steps. The steps were:

- 20/20 - 99
- 20/100 - 199
- 20/200 - 299
- 20/300 - 399
- 20/400 - CF (count fingers)
- HM (hand motion)
- LP (light perception)
- NLP (no light perception)

Preservation of visual acuity was defined to be a postoperative visual acuity in the same or higher group than the preoperative visual acuity. Minimum functional vision was defined to be a visual acuity of 20/399 or better.

Safety variables were characterized by complications, including hypotony and elevated IOP, and corneal abnormalities. Normal IOP was defined to be in the range 6-25 mm Hg. Hypotony was defined to be  $IOP \leq 5$  mm Hg, and elevated IOP was defined to be  $IOP \geq 25$  mm Hg.

#### E. Pre-operative (Baseline) Data

In the cohort group, initial clinical presentation included 163 PVR's, 29 GRT's, 37 RD w/Trauma's, 40 TRARD's, and 74 Other w/RD's. In the non-cohort group, initial clinical presentation included 658 PVR's, 119 GRT's, 42 RD w/Trauma's, 96 TRARD's, and 268 Other w/RD's. The most common presentation in both groups was PVR (41.6% cohort and 50.1% non-cohort). The preoperative diagnosis for these groups were as follows:

CLINICAL PRESENTATION	COHORT			NON-COHORT		
	#	PTS	%	#	PTS	%
PVR	163		41.6	658		50.1
RD w/TRAUMA	37		9.4	42		3.2
TRARD	40		10.2	96		7.3
GRT	29		7.4	119		9.1
OTHER w/RD	74		18.9	268		20.4
DIOL	20		5.1	47		3.6
CD	9		2.3	11		0.8
OTHER w/o RD	20		5.1	72		5.5
Total	392		100	1313		100

Forty nine subjects were evaluable for safety and had one of the following preoperative diagnoses; choroidal detachments (CD), dislocated intraocular lenses (DIOL), and other without retinal detachment (Other w/o RD).

### Gender Analysis

Males accounted for 200/343 (58.3%) of the subjects in the cohort group and 765/1183 (64.7%) of the subjects in the non-cohort group. Although the potential exists for minor differences in physiological response by gender for the study population, the minimal number of clinically significant findings does not indicate gender differences to be of clinical importance for this device.

PRESENTATION BY GENDER - COHORT					
PRESENTATION	# MALES %		# FEMALES %		
	PVR	92	46	71	
RD w/Trauma	30	15	7	4.9	
TRARD	20	10	20	14	
GRT	19	9.5	10	7	
OTHER w/RD	39	19.5	35	24.5	
TOTAL	200	100	143	100.1	

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PRESENTATION BY GENDER - NON-COHORT				
PRESENTATION	# MALES %		# FEMALES %	
PVR	413	54	245	58.6
RD w/Trauma	98	12.8	21	5.0
TRARD	23	3.0	19	4.5
GRT	75	9.8	21	5.0
OTHER w/RD	156	20.4	112	26.8
TOTAL	765	100	418	99.9

### G. Age Analysis

Patient age at the time of detachment varied according to clinical presentation. In both the cohort and the non-cohort groups, patients presenting PVR tended to be older than those with other presentations. Ages in both the cohort and non-cohort groups ranged from less than 18 years to greater than 75 years.

The mean age was 52.2 years for the cohort group and 50.3 years for the non-cohort group.

PRESENTATION BY AGE - COHORT							
	< 18	18-35	36-50	51-65	66-75	> 75	NR
PVR	6	26	24	37	42	17	11
RD w/Trauma	7	14	6	2	2	0	6
TRARD	3	5	11	9	1	5	6
GRT	2	4	9	8	4	2	0
OTHER w/RD	3	5	9	19	18	13	7
TOTAL	21	54	59	75	67	37	30

PRESENTATION BY AGE - NON-COHORT						
	< 18	18-35	36-50	51-65	66-75	> 75
PVR	78	78	85	139	135	82
RD w/Trauma	18	41	20	11	9	7
TRARD	3	7	8	11	4	0
GRT	13	12	25	23	6	7
OTHER w/RD	16	39	36	53	52	53
TOTAL	128	177	174	237	206	149

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## H. Ocular History

### 1. Prior Surgery

The majority of subjects in both groups had ocular surgery prior to entering the study.

HISTORY OF PRIOR OCULAR SURGERY				
Presentation	# Cohort	%	# Non-cohort*	%
PVR	300	62.0	1201	101.9
RD w/Trauma	40	8.3	124	10.5
TRARD	52	10.7	48	4.1
GRT	25	5.2	52	4.4
Other w/RD	67	13.8	365	30.9
Total	484	100	1183	151.8

\*multiple surgeries reported

### 2. Prior Retinal Detachment

In the cohort group 101/343 (29.4%) subjects had a history of prior retinal detachment and 71/343 (20.7%) of treated eyes were previously vitrectomized. In the non-cohort group 288/1183 (24.3%) subjects had a history of prior retinal detachment and 316/1183 (26.7%) of treated eyes were previously vitrectomized.

HISTORY OF PRIOR RETINAL DETACHMENT				
Presentation	# Cohort	%	# Non-cohort	%
PVR	66	65.3	215	74.7
RD w/Trauma	2	2.0	8	2.8
TRARD	6	5.9	10	3.5
GRT	3	3.0	3	1.0
Other w/RD	24	23.8	52	18.1
TOTAL -	101	100	288	100.1

HISTORY OF PRIOR VITRECTOMY				
Presentation	# Cohort	%	# Non-cohort	%
PVR	40	56.3	224	70.9
RD w/Trauma	4	5.6	17	5.4
TRARD	5	7.0	11	3.5
GRT	5	7.0	4	1.3
Other w/RD	17	23.9	60	19.0
TOTAL	71	99.8	316	100.1

### 3. Intraocular Pressure

In the cohort group 70.6% of the eyes (242/343) had intraocular pressures (IOP's) between 6 mmHg and 25 mmHg prior to their procedures. In the non-cohort group 58.0% of the eyes (686/1183) had IOP between 6 mmHg and 25 mmHg prior to their procedures. The majority of abnormal IOP's in both groups were below normal (hypotony) at a range of  $\leq 5$  mmHg. In the cohort group the incidence of hypotony was 39/343 (11.4%) and in the non-cohort group it occurred in 136/1183 (11.5%) of the subjects. Hypotony was operationally defined as any value below 5 mmHg.

PRESENTATION OF IOP (PRE-OP) - COHORT							
IOP	PVR	RD w/Trauma	TRARD	GRT	OTHER w/RD	# PTS	% PTS
$\leq 5$	26	5	2	2	4	39	11.4
6-15	81	16	18	16	47	178	51.9
16-25	29	6	12	7	10	64	18.7
26-40	5	4	2	0	3	14	4.1
> 40	1	0	0	0	0	1	0.3
NR	21	6	6	4	10	47	13.7
TOTAL	163	37	40	29	74	343	100.1

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PRESENTATION OF IOP (PRE-OP) - NON-COHORT							
IOP	PVR	RD w/Trauma	TRARD	GRT	OTHER w/RD	# PTS	% PTS
≤ 5	78	18	4	10	26	136	11.5
6-15	279	47	17	43	102	488	41.3
16-25	97	12	6	20	63	198	16.7
26-40	11	2	1	1	8	23	1.9
> 40	0	2	0	1	1	4	0.3
NR	193	38	14	21	68	334	28.2
TOTAL	658	119	42	96	268	1183	99.9

#### 4. Lens Characteristics

In the cohort group 38.2% (131/343) eyes and in the non-cohort group 27.9% (330/1183) eyes were phakic. The prevalence of pseudophakic eyes, aphakic eyes, and others differed by clinical presentation.

PRESENTATION OF LENS CHARACTERISTICS (PRE-OP) - COHORT							
	PVR	RD w/Trauma	TRARD	GRT	OTHER w/RD	# PTS	% PTS
Opacity	9	1	1	2	5	18	5.2
Aphakic	27	9	3	5	10	54	15.7
PCIOL	1	0	1	0	0	2	0.6
Phakic	54	19	25	11	22	131	38.2
PSEPH	6	1	1	1	1	10	2.9
Psephaciol	11	1	0	0	2	14	4.1
Psephpciol	35	1	4	6	20	66	19.2
DIOL	0	0	0	0	2	2	0.6
Other	0	0	1	0	1	2	0.6
NR	20	5	4	4	11	44	12.8
TOTAL	163	37	40	29	74	343	99.9

PRESENTATION OF LENS CHARACTERISTICS (PRE-OP) - NON-COHORT							
	PVR	RD w/ Trauma	TRARD	GRT	OTHER w/RD	# PTS	% PTS
Opacity	31	6	3	3	2	45	3.8
Aphakic	137	29	5	7	36	214	18.1
PCIOL	3	0	0	0	1	4	0.3
Phakic	156	31	18	29	76	310	26.2
PSEPH	154	7	5	14	57	237	20.0
Psephaciol	28	1	0	8	13	50	4.2
psephpciol	29	1	0	1	8	39	3.3
DIOL	2	2	0	0	1	5	0.4
Other	1	1	2	1	4	9	0.8
NR	117	41	9	33	70	270	22.8
TOTAL	658	119	42	96	268	1183	99.9

#### 5. Pre-Operative Visual Acuity

Approximately 14.9% cohort eyes and 14.2% non-cohort eyes had minimum functional vision prior to this procedure. Minimum functional vision is defined as visual acuity equal to 20/399 or better.

PRESENTATION OF VISUAL ACUITY (PRE-OP) - COHORT							
VA	PVR	RD w/Trauma	TRARD	GRT	OTHER w/RD	# PTS	% PTS
20/20-99	7	2	0	8	9	26	7.6
20/100-199	5	1	2	1	1	10	2.9
20/200-299	10	0	0	1	3	14	4.1
20/300-399	1	0	0	0	1	2	0.6
20/400-CF	34	5	12	7	22	80	23.3
HM	59	13	11	8	17	108	31.5
LP	39	16	12	4	16	87	25.4
NR	8	0	3	0	5	16	4.7
TOTAL	163	37	40	29	74	343	100.1

*JR*

PRESENTATION OF VISUAL ACUITY (PRE-OP) - NON-COHORT							
VA	PVR	RD w/Trauma	TRARD	GRT	OTHER w/RD	# PTS	% PTS
20/20-99	25	8	2	18	30	83	7.0
20/100-199	3	1	0	4	9	17	1.4
20/200-299	27	1	5	9	17	59	5.0
20/300-399	4	0	0	1	4	9	0.8
20/400-CF	142	11	12	22	66	253	21.4
HM	221	31	12	19	69	352	29.8
LP	182	59	4	14	56	315	26.6
NLP	0	1	0	0	2	3	0.3
NR	54	7	7	9	15	92	7.8
TOTAL	658	119	42	96	268	1183	100.1

#### 6. Retinal Characteristics

For subjects in the Cohort analysis, Partial detachment (PD) and total detachment (TD) represented 26.2% and 16.9% respectively. Subjects with a retinal detachment associated with PVR accounted for 30.6% of the study population.

Pre-operative retinal characteristics for the subjects in the Non-cohort group included partial detachment noted for 22.7%. Retinal characteristics of total detachment and PVR, (TD,PVR) was noted for 19.7% of this study population.

PRESENTATION OF RETINAL CHARACTERISTICS (PRE-OP) - COHORT							
	PVR	RD w/Trauma	TRARD	GRT	OTHER w/RD	# PTS	% PTS
Partial Detachment	21	12	8	3	46	90	26.2
Total Detachment	15	8	16	3	16	58	16.9
FLAT	0	1	0	0	1	2	0.6
Giant Tear	10	6	0	21	0	37	10.8
PD,PVR	34	0	0	0	0	34	9.9
PD,PDR	0	0	12	0	1	13	3.8
TD,PVR	70	1	0	0	0	71	20.7
RD	1	1	0	2	2	6	1.7
OTHER	4	2	1	0	0	7	2.0
NR	8	6	3	0	8	25	7.3
TOTAL	163	37	40	29	74	343	99.9

PRESENTATION OF RETINAL CHARACTERISTICS (PRE-OP) - NON COHORT							
	PVR	RD w/Trauma	TRARD	GRT	OTHER w/RD	# PTS	%PTS
PD	64	35	9	28	133	269	22.7
TD	71	28	13	10	69	191	16.1
FLAT	2	2	0	0	7	11	0.9
GT	55	21	0	50	5	131	11.1
PD, PVR	184	1	0	0	4	189	16.0
PD, PDR	1	0	8	0	4	13	1.1
TD, PVR	231	0	0	0	2	233	19.7
RD	8	5	2	0	4	19	1.6
OTHER	41	27	9	8	40	125	10.6
NR	1	0	1	0	0	2	0.2
TOTAL	658	119	42	96	268	1183	100

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## I. Post-Operative Efficacy Data

### 1. Flat Retina Post-Op (at any time) - Cohort

The data which have been reviewed above demonstrates that VITREON® successfully flattened most of the retinas. The rate of intraoperative flattening of the retina as determined by review of the operative notes was highest in the subjects with traumatic retinal detachment and other with retinal detachment. All partially detached and completely detached retinas in subjects with traumatic retinal detachment were flattened after VITREON® injection. It was lower in the subjects with PVR where 128/158 (81%) of subjects had the retina successfully flattened after the use of VITREON®.

FLAT RETINA POST-OP COHORT		
Presentation	Cohort #	Cohort %
PVR	128/158	81.0
RD w/ Trauma	33/36	91.7
TRARD	34/39	87.2
GRT	21/27	77.8
Other w/RD	60/67	89.6
Total	276/327	84.4

### 2. Successful Retinal Attachment at Initial Surgery

Retinal reattachment was successful in 154/163 (94.5%) of subjects in the PVR group. The final reattachment rate at the completion of the operative procedure was 332/343 (96.8%). All subjects in the tractional retinal detachment, giant tear and other with retinal detachment diagnostic groups had their retinas successfully reattached. The surgical procedure failed in 11 of 343 eyes.

SUCCESSFUL RETINAL REATTACHMENT AT INITIAL SURGERY		
Presentation	Cohort #	Cohort %
PVR	154/163	94.5
RD w/Trauma	35/37	94.6
TRARD	40/40	100
GRT	29/29	100
Other w/RD	74/74	100
Total	332/343	96.8

### 3. Retinal Redetachments

A total of 133 (40.3%) retinal redetachments were reported for the cohort group and 377 (34.4%) for the non-cohort group. The rate of retinal redetachment varied by preoperative diagnosis. Overall 40% of subjects had a post operative

redetachment. The rate of redetachment in subjects with PVR was 40.9% during the postoperative period.

PREVALENCE OF RETINAL REDETACHMENT				
Presentation	# Cohort	%	# Non-cohort	%
PVR	63/154	40.9	225/598	37.6
RD w/Trauma	16/34	47.1	38/110	34.5
TRARD	12/40	30.0	12/39	30.8
GRT	14/29	48.3	22/93	23.7
Other w/RD	28/73	38.4	80/255	31.4
Total	133/330	40.3	377/1095	34.4

#### 4. Posterior Drainage Retinotomies

The rate of posterior drainage retinotomy in subjects with a retinal detachment in this study was 12/327 (3.7%). A low rate of this surgical manipulation avoids the possible complications of posterior retinotomy. No subjects with tractional retinal detachment and only 6/157 (3.8%) of subjects with PVR underwent a drainage retinotomy. Since the posterior retina cannot be flattened without drainage of subretinal fluid, the low incidence of retinotomy indicates that VITREON® was successful in displacing the subretinal fluid anteriorly so that it could egress from peripheral retinal breaks without further compromise of the posterior retina. The highest incidence of posterior retinotomies occurred in subjects 3/36 (8.3%) with traumatic retinal detachments.

POSTERIOR DRAINAGE RETINOTOMIES		
Presentation	Cohort #	Cohort %
PVR	6/157	3.8
RD w/Trauma	3/36	8.3
TRARD	0/39	0
GRT	1/27	3.7
Other w/RD	2/68	2.9
Total	12/327	3.7

5. Membrane Dissection and Relaxing Retinotomies

Since the instillation of VITREON® can highlight tractional components of a complicated retinal detachment, the dissection of membranes following VITREON® instillation was evaluated. Ten of 39 (25.6%) of subjects with tractional retinal detachments had membrane dissection performed under VITREON® indicating that the use of VITREON® aided in identifying membranes and traction and hence allowing dissection to relieve the traction. Similarly 33/158 (20.9%) of PVR subjects had membrane dissections performed following instillation of VITREON®.

The number of relaxing retinotomies performed was also analyzed. In the PVR group, 4.5% of the subjects received a relaxing retinotomy for the first time after the instillation of VITREON®.

MEMBRANE DISSECTION - COHORT		
Presentation	Cohort #	Cohort %
PVR	33/158	20.9
RD w/ Trauma	2/36	5.6
TRARD	10/39	25.6
GRT	0/27	0
Other w/RD	3/68	4.1
Total	48/328	14.6

RELAXING RETINOTOMIES - COHORT		
Presentation	Cohort #	Cohort %
PVR	7/157	4.5
RD w/ Trauma	1/36	2.8
TRARD	4/39	10.3
GRT	0/27	0
Other w/RD	0/68	0
Total	12/327	3.7

6. Post-Operative Visual Acuity

Postoperatively, visual acuity was reported at each follow-up visit. In both the cohort and non-cohort groups visual acuity for subjects with 0-30 days follow-up and 181-360 days follow-up visual acuity was reported as follows:

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POST-OP VISUAL ACUITY - COHORT (0-30 Days)							
	PVR	RD w/Trauma	TRARD	GRT	Other w/RD	# PTS	% PTS
20/20-99	3	1	0	0	1	5	1.7
20/100-199	0	1	0	0	1	2	0.7
20/200-299	0	2	0	2	1	5	1.7
20/300-399	1	0	0	0	0	1	0.3
20/400-CF	18	2	5	6	17	48	16.2
HM	58	14	14	14	23	123	41.6
LP	55	12	13	6	21	107	36.1
NLP	0	2	2	0	1	5	1.7
TOTAL	135	34	34	28	65	296	100

POST-OP VISUAL ACUITY - NON-COHORT (0-30 Days)							
	PVR	RD w/TRAUMA	TRARD	GRT	Other w/RD	# PTS	% PTS
20/20-99	6	3	0	3	6	18	3.6
20/100-199	1	1	0	2	1	5	1.0
20/200-299	11	0	0	3	5	19	3.8
20/300-399	2	0	0	0	1	3	0.6
20/400-CF	77	15	0	11	51	154	30.6
HM	113	25	5	17	45	205	40.8
LP	52	8	6	8	20	94	18.7
NLP	1	1	0	0	3	5	1.0
TOTAL	263	53	11	44	132	503	100.1

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POST-OP VISUAL ACUITY - COHORT (181-360 Days)							
	PVR	RD w/TRAUMA	TRARD	GRT	Other w/RD	# PTS	% PTS
20/20-99	8	1	0	4	4	17	10.4
20/100-199	3	1	0	4	2	10	6.1
20/200-299	7	0	2	1	1	11	6.7
20/300-399	0	1	0	1	1	3	1.8
20/400-CF	17	3	3	6	10	39	23.8
HM	24	5	7	3	3	42	25.6
LP	18	3	5	0	6	32	19.5
NLP	6	0	0	0	4	10	6.1
TOTAL	83	14	17	19	31	164	100

POST-OP VISUAL ACUITY -NON-COHORT (181-360 Days)							
	PVR	RD w/TRAUMA	TRARD	GRT	Other w/RD	# PTS	% PTS
20/20-99	20	7	0	8	5	40	17.8
20/100-199	5	0	0	0	2	7	3.1
20/200-299	15	5	0	2	10	32	14.2
20/300-399	3	1	0	1	0	5	2.2
20/400-CF	62	6	2	4	14	88	39.1
HM	21	1	1	1	5	29	12.9
LP	8	3	0	1	3	15	6.7
NLP	6	1	0	0	2	9	4.0
TOTAL	140	24	3	17	41	225	100

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Minimum functional vision was reported as maintained by 13/296 cohort subjects (4.4%) and 45/503 non-cohort subjects (8.9%) at 0-30 days follow-up. At 181-360 days follow-up minimum functional vision was reported as maintained by 41/164 cohort subjects (25.0%) and 84/225 non-cohort subjects (37.3%).

MAINTENANCE OF MINIMUM FUNCTIONAL VISION (20/399 or Better) 0-30 Days		
Presentation	Cohort	Non-cohort
PVR	4/135	20/263
RD w/Trauma	4/34	4/53
TRARD	0/34	0/11
GRT	2/28	8/44
Other w/RD	3/65	13/132
Total	13/296	45/503

MAINTENANCE OF MINIMUM FUNCTIONAL VISION (20/399 or Better) 181-360 Days		
Presentation	Cohort	Non-cohort
PVR	18/83	43/140
RD w/Trauma	3/14	13/24
TRARD	2/17	0/3
GRT	10/19	11/17
Other w/RD	8/31	17/41
Total	41/164	84/225

## J. Post Operative Safety Data

### 1. Intraocular Pressure

In the cohort group 77.0% of the subjects (224/291) had IOP's between 6 mmHg and 25 mmHg zero to 30 days following their procedures. In the non-cohort group 79.0% of the subjects (469/594) had IOP between 6 mmHg and 25 mmHg 0 - 30 days following their procedures. There were 9/291 (3.1%) cohort

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subjects and 38/594 (6.4%) non-cohort subjects with hypotony. The rate of hypotony decreased within 30 days of surgery.

POST-OP IOP - COHORT (0 - 30 Days)							
	PVR	RD w/Trauma	TRARD	GRT	Other w/RD	# PTS	% PTS
≤ 5	6	1	0	0	2	9	3.1
6 - 15	63	13	12	9	21	118	40.5
16 - 25	45	11	13	9	28	106	36.4
26 - 40	21	5	7	7	7	47	16.2
> 40	4	1	3	0	3	11	3.8
TOTAL	139	31	35	25	61	291	100

POST-OP IOP - NON-COHORT (0 - 30 Days)							
	PVR	RD w/Trauma	TRARD	GRT	Other w/RD	# PTS	% PTS
≤ 5	16	7	1	5	9	38	6.4
6 - 15	140	19	7	14	51	231	38.9
16 - 25	127	22	5	26	58	238	40.1
26 - 40	39	9	2	8	19	77	13.0
> 40	6	1	1	0	2	10	1.7
TOTAL	328	58	16	53	139	594	100.1

## 2. Postoperative Complications

No episodes of severe intraocular inflammation were reported although more than 60% of subjects had preoperative anterior chamber inflammatory responses. None of the subjects developed endophthalmitis during the postoperative period. The incidence of postoperative fibrin in the anterior chamber at any time during the postoperative follow up was 5.6%.

The most common complication in subjects in whom VITREON® was removed was PVR (20.3%). This is unlikely to be a VITREON® related complication since over half of these subjects had PVR prior to surgery and PVR is a common complication of repair retinal detachment related to giant retinal tear or traumatic retinal detachment.

POSTOPERATIVE COMPLICATIONS						
	Cohort			Non-Cohort		
	#	Patients	%	#	Patients	%
PVR	69/340		20.3	133/1117		11.9
Hyphema	43/340		12.6	36/1117		3.2
Fibrin in AC	19/340		5.6	23/1117		2.1
Corneal Disorders	61/340		17.9	139/1117		12.4
Corneal Edema	42/340		12.4	67/1117		6.0
Iris Disorders	29/340		8.5	44/1117		3.9
Subretinal Fluid or Blood	22/340		6.5	69/1117		6.2
Total	285/340		83.8	511/1117		45.7

## XII. CONCLUSIONS DRAWN FROM THE CLINICAL STUDIES

### A. Discussion of Valid Scientific Evidence

In accordance with 21 C.F.R. §860.7 the validity of the evidence presented in the Premarket Approval Application (PMA) was based upon an objective trial with a matched control. The study comprised a prospective, multi-center, non-randomized, open label clinical trial. Clinical results were compared to a non-cohort group derived from patient at 24 of the 32 participating centers.

The non-clinical and clinical data presented in the PMA provides reasonable assurance of safety and effectiveness of the device for its intended use when accompanied by appropriate labeling.

### B. Benefits of VITREON®

1. **Mechanical tool during vitreoretinal surgery.** VITREON® acts as a mechanical tool, providing hydrokinetic manipulation, flattening, smoothing, and/or unrolling of the detached retinal membrane starting from the posterior aspect, and/or creating gentle traction on epiretinal membranes, thus facilitating their visualization.
2. **Anterior displacement of subretinal fluids.** VITREON® facilitates the anterior displacement of subretinal fluids and reduces the incidence of posterior drainage retinotomies during the repair of rhegmatogenous retinal detachments.
3. **Intraoperative tamponade.** VITREON® provides temporary mechanical fixation of the retina against the choroid to allow application of thermal adhesive modalities.

### C. Risks of VITREON®

1. **General Health.** There have been no reports of intraocular VITREON® causing any adverse event as related to the general health of the patient.
2. **Ocular complications.** The clinical studies with VITREON® established that additional risks added to the surgical procedure were minor. The two VITREON® associated risks, intraoperative subretinal VITREON® Migration (0.9%) and postoperative Residual VITREON® (9.0%) do not add major risks to the surgery. Removal of the subretinal VITREON® can be achieved by aspiration through an existing retinal break or by creation of a posterior retinotomy. Comparing cases of residual VITREON® with no residual, there were no significant differences with respect to retinal redetachment, elevated IOP, hypotony, newly acquired cataracts, or last reported ocular status in terms of anterior chamber abnormalities or corneal abnormalities.

There was no evidence from the clinical trial that known postoperative complications of complicated retinal detachment surgery were higher when VITREON® was used. Based on acutely successful cohort group patients, there was no significant difference between cohort and non-cohort subjects with respect to: NLP eyes, anterior chamber abnormalities, cataract formation, elevated IOP, hypotony, or iris abnormalities.

### D. Conclusion

In conclusion, the relative benefit/risk ratio for VITREON® was weighed based on the following:

1. an acceptable chance for restoration or maintenance of ambulatory vision;
2. fewer posterior retinotomies and low rates of retinal redetachment associated with VITREON®; and,
3. a higher proportion of procedures in which minimum functional vision was maintained.

Therefore, it is reasonable to conclude that the benefits of use of the device for the target population outweigh the risk of illness or injury when used as indicated in accordance with the directions for use.

### **XIII. PANEL RECOMMENDATION**

On May 20, 1994, this PMA was reviewed by the Ophthalmic Devices Panel at the request of the applicant, to solicit the panel's advice on a clinical study design. The applicant responded to this panel discussion with a proposal to reevaluate the existing data. The results of this reevaluation and restructuring were presented to FDA and reviewed at the October 19, 1995, panel meeting. At this panel meeting the Ophthalmic Devices Panel recommended that Vitrophage's PMA for VITREON® be approved without conditions.

### **XIV. CDRH DECISION**

CDRH concurred with the Ophthalmic Devices Panel's recommendation of October 19, 1995, and issued a letter to Vitrophage, on November 14, 1995, advising that its PMA was approvable subject to Vitrophage's submission of additional microbiological, toxicology, chemistry information, revised labeling and FDA inspection to determine compliance with applicable device Good Manufacturing Practice regulations (GMP). Vitrophage submitted multiple amendments to the PMA to provide the data to adequately address CDRH's preclinical concerns. Upon determining that the data and the labeling were acceptable, FDA issued an approval order on September 30, 1997.

The manufacturing facility used to package the finished product was inspected on August 22, 1997, and was found to be in compliance with the device GMP regulations. The manufacturing facility used to produce the medical grade of raw material has ceased production; therefore, this approval is limited to a single batch (batch #672-45-0001) of the finished product packaged in 6 mL vials. In order to market other batches using a new raw material supplier, a PMA supplement will be required.

### **XV. APPROVAL SPECIFICATIONS**

A copy of the package insert is attached. In addition to the standard "Conditions of Approval" included with the approval order, the sale, distribution, and use of this device are restricted to prescription use in accordance with 21 CFR 801.109 within the meaning of section 520(e) of the Federal Food, Drug, and Cosmetic Act (the act) under the authority of section 515(d)(1)(B)(ii) of the act. FDA has also determined that to ensure the safe and effective use of the device that the device is further restricted within the meaning of section 520(e) under the authority of section 515(d)(1)(B)(ii) insofar as the sale, distribution, and use must not violate sections 502(q) and (r) of the act.

Directions for Use - See the attached labeling.

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

Postapproval Requirements and Restrictions: See approval order.

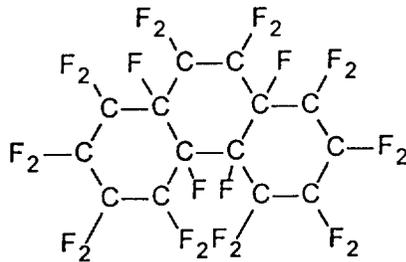
## **XVI. REFERENCES**

1. Nabih, M et al (1989). Experimental Evaluation of Perfluorophenanthrene as a High Specific gravity Vitreous Substitute: A Preliminary Report. *Ophthal Surg* 20: 286-93.
2. Peyman, GA et al (1991). Long-Term Vitreous Replacement in Primates with Intravitreal Vitreon® or Vitreon® Plus Silicone. *Ophthal Surg* 22: 657-64.

**VITREON®** R  
**(perfluoroperhydrophenanthrene)**

**DESCRIPTION**

VITREON® sterile intraocular fluid is a purified perfluorocarbon liquid comprised of perfluoroperhydrophenanthrene (PFPHP) (C<sub>14</sub>F<sub>24</sub>), with perfluoro-n-butyldecalin and related perfluorinated isomers. PFPHP has the following chemical structure:



VITREON has the following chemical and physical properties:

- Optically clear
- Immiscible with water
- Easily injectable
- Molecular Weight 624.12
- Specific Gravity 2.03
- Surface Tension 23.9  
(dynes/cm, 25°C)
- Refractive Index 1.3340
- Vapor Pressure (torr @ 37°C) 0.35
- Viscosity (centistoke @ 25°C) 7.80
- Boiling Point (°C) 215

VITREON contains no preservatives.

VITREON is supplied in 6-ml single-dose glass vials capped with a rubber stopper. Each single-dose vial is packaged in an individual carton.

The finished product testing for each batch of VITREON includes tests and specifications to limit potential impurities. Each batch of VITREON is also tested for particulate matter and bacterial endotoxins with strict limits appropriate for injectable ophthalmic products.

**INDICATIONS FOR USE**

VITREON is indicated for use as an intraoperative surgical aid during vitreoretinal surgery in patients with primary and recurrent complicated retinal detachments. Complicated cases include giant retinal tear or retinal dialysis, proliferative vitreoretinopathy, proliferative diabetic retinopathy, tractional retinal detachments, and blunt or penetrating ocular trauma.

**CONTRAINDICATIONS**

- VITREON is contraindicated as a vitreous replacement.

## WARNINGS

- VITREON should not be injected directly into the anterior chamber, or be removed from the vitreous cavity through the anterior chamber, as corneal endothelial cell damage may occur. VITREON cannot be removed completely via the anterior chamber.
- At the conclusion of the surgical procedure, VITREON must be removed completely from the vitreous chamber, via the pars plana, and replaced with an appropriate vitreous substitute.

## PRECAUTIONS

- Directions for Use of VITREON should be followed closely.
- Animal tests indicate that VITREON may be physically irritating to the cornea when there is direct contact. Corneal endothelial cell damage can occur in as few as three days after direct contact. Any VITREON in the anterior chamber must be removed. A conscientious effort should be made to remove all VITREON at the conclusion of surgery in accordance with the Directions for Use. If a small amount (0.5 DD area) of VITREON remains in the vitreous chamber at the conclusion of surgery, the patient must be carefully monitored until any residual VITREON has completely dissipated to prevent entry into the anterior chamber in aphakic eyes.
- Posterior retinal slippage occurred in 7.7% of patients with giant retinal tears in the cohort group (See Directions for Use). To help prevent slippage, gradually remove the VITREON under air-VITREON exchange or silicone-VITREON exchange.
- The use of VITREON intraoperatively in patients with complicated retinal detachments in conjunction with large posterior breaks associated with residual traction may allow migration of VITREON into the subretinal space. While such migration occurred infrequently in the clinical studies, VITREON should be removed via these retinal breaks if it enters the subretinal space. (See Directions for Use)
- As with any invasive procedure, there is the possibility of infection. Aseptic techniques must be strictly adhered to.

- VITREON is supplied in a sterile vial intended for single use only for a single patient.
- VITREON should not be re-sterilized and unused portions should be discarded.
- Do not mix VITREON with any other substances prior to injection.
- VITREON should be discarded following the expiration date.
- The safety and effectiveness of long-term use of VITREON postoperatively have not been established.
- Rate of retinal redetachment:  
Overall, 40.3% of the cohort subjects had a redetachment during the postoperative period. The rate of retinal redetachment in the non-cohort group was 34.4%. Although more of the subjects were followed for a greater length of time in the cohort group, the majority of redetachments observed occurred prior to four months postoperatively in both groups.
- Proliferative Vitreoretinopathy (PVR):  
PVR was present preoperatively in 41.6% of the cohort group and 50.1% of the non-cohort. PVR occurred in 20.3% of the cohort (11.9% of the non-cohort) subjects from whom VITREON was removed.

## ADVERSE REACTIONS AND COMPLICATIONS

The data supporting the rates of occurrence of complications were derived from a U.S.-based multicenter clinical trial. Data were divided into two segments and were analyzed separately. The "cohort" group consisted of 343 patients evaluated for safety and effectiveness parameters. The "non-cohort" group included data on 1241 additional patients evaluated for safety parameters only. In the following discussion, occurrence rates are reported by the specific group in which the complication occurred.

The following adverse reactions related to the use of VITREON were observed:

### COHORT GROUP

- Intraoperative subretinal VITREON migration (preoperative diagnosis of retinal detachment) 0.9%
- Postoperative residual VITREON 9.0%

*OVERALL GROUP*

- Postoperative residual VITREON 6.5%

The following complications reported by the investigators are general complications that are observed in complex vitreoretinal surgery, and were not associated specifically with the use of VITREON:

*COHORT GROUP*

- Corneal disorders (including bands and keratopathy) 17.9%
- Corneal edema 12.4%
- Anterior chamber abnormalities (fibrin in AC, hyphema) 18.2%
- Elevated IOP (181-360 days follow up) 0.7%
- Elevated IOP > 25 mmHg was observed in 19.9% of subjects in the first month, decreasing to 1.9% in the 4 to 6 month follow up.
- Hypotony (181-360 days follow up) 25.9%
- Iris abnormalities 8.5%

- Cataract formation in phakic eyes 3.0%
- Intraoperative retinal slippage 7.7%
- Progression to "no light perception" (NLP) (181 - 360 days follow up) 6.1%

*OVERALL GROUP*

- Corneal disorders (including bands and keratopathy) 13.7%
- Corneal edema 7.5%
- Anterior chamber abnormalities (fibrin in AC, hyphema) 8.3%
- Elevated IOP (181 - 360 days follow up) 2.2%
- Hypotony (181-360 days follow up) 17.5%
- Iris abnormalities 5.0%
- Progression to "no light perception" (NLP) (181 - 360 days follow up) 4.9%
- Other:  
In addition to the complications

above, other less commonly occurring reactions reported in the combined cohort and non-cohort groups (1630 subjects), in more than 2% of patients and ranked by frequency of occurrence, included: hyphema; various membrane related conditions (pucker, epiretinal membrane, retinal fibrosis, gliosis, fibrosis, subretinal fibrosis, epimacular membrane, maculopathy) subretinal fluid or blood; corneal epithelial defects; vitreous hemorrhage; lens-related problems; choroidal detachment; retinal folds. The following complications occurred at rates of less than 2% in the patients in the combined cohort and non-cohort groups: retinal hemorrhage; macular/retinal edema; macular folds; choroidal folds; choroidal hemorrhage; giant tear; retinal striae/ macular striae; age-related macular degeneration (AMD); pupil disorders; extra-ocular problems.

## DIRECTIONS FOR USE

**Caution:** The outer surfaces of the container are not sterile. Carefully follow directions below for loading VITREON. Remove the VITREON vial from the carton, flip off cap to remove top of crimp seal and expose target surface of the stopper, disinfect exposed stopper surface, and load the VITREON

into a Luer-Lok screw syringe. Avoid introduction of air bubbles into the VITREON by careful withdrawal or decanting of the fluid into the syringe. Place the syringe on a sterile tray.

The surgical procedure consists of a standard 20-gauge three-port pars plana vitrectomy. Once partial or total vitrectomy is completed, inject 0.5-4 ml VITREON through a blunt 20- to 27-gauge needle over the optic disc. In the case of a giant tear, injection must be over the retina, or under the retinal flap if it is in a folded position. A partial air-fluid exchange may be necessary during the injection process in order to tamponade the peripheral retina.

Upon completion of VITREON injection, additional procedures such as endolaser photocoagulation, internal or external cryopexy, and membranectomy may be performed.

### **Do Not Resterilize VITREON**

#### *Post-Procedure*

**VITREON must be removed at the conclusion of the operative procedure.**

VITREON can be removed by "passive" flow through a flute needle or active suction while the vitreous cavity is filled with air or infusion fluid. The surface of VITREON is easiest to see

during air-VITREON replacement which ensures a more complete removal of VITREON. Remove VITREON only through the pars plana. Do not remove through anterior chamber. Upon removal, multiple fluid washings must be performed to maximize complete evacuation. It may then be replaced by an approved vitreous substitute. Any VITREON in the anterior chamber must be removed immediately using standard techniques. (See Precautions)

The patient should be monitored closely by the physician for the development of routine postoperative complications and be scheduled for follow up at regular intervals.

## The Use of VITREON

### *Properties*

VITREON contains inherent physical properties necessary for a desirable denser-than-water temporary vitreous substitute. It is immiscible with water, optically clear, radiopaque, easily injected and removed through a small-bore (20- to 25-gauge) needle. Its low vapor pressure permits air travel without the danger of gas formation in case a small amount of residual VITREON remains in the eye. VITREON has a high surface tension (23.9 dynes/cm @ 25°C) and a high viscosity (7.80 cs), two important characteristics to reduce bubble formation and migration through

small retinal holes. Intraoperative sub-retinal migration has been seen in only 0.9% of retinal detachment cases in the cohort group.

### *Toxicity and Metabolism*

VITREON is a biologically inert substance. There are no known biological enzymes which metabolize the carbon-fluoride bonds in perfluorocarbons.

VITREON is non-pyrogenic, non-mutagenic and non-irritating in the posterior chamber.

Experimental studies demonstrated that VITREON has no toxic effect on tissue culture-grown cells. *In vivo* studies in rabbits have shown no acute toxic or inflammatory reactions for up to 6 weeks. *In vivo* studies in primates have shown that VITREON has no toxic effects up to 162 days, although emulsification started at approximately 72 days.

Animal tests indicate that VITREON may be physically irritating to the cornea when there is direct contact. Corneal damage can occur in as few as three days after direct contact. Any VITREON in the anterior chamber must be removed. A conscientious effort should be made to remove all VITREON at the conclusion of surgery in accordance with the Directions for Use. Small amounts of residual

VITREON (0.5 DD) in the vitreous cavity were observed in the clinical studies but were not associated with any complications or adverse reaction. (See Precautions)

### *General Use*

VITREON should be injected through a 20-gauge needle over the optic disc, forcing the subretinal fluid anteriorly, where it escapes through an anteriorly located retinal hole.

VITREON is then removed using a flute needle or active aspiration through a 20-gauge blunt cannula. The tip of the cannula is brought over the surface of the retina. Intermittent air and fluid exchanges are performed to maximize removal of all the VITREON.

Removal of VITREON from the subretinal space can be done through existing retinal breaks or a posterior retinotomy. Infusion of irrigating solution through the infusion cannula is performed simultaneously with removal of the VITREON through an extrusion needle inserted through the break or retinotomy, until complete removal of the VITREON is achieved. After removal, the break or retinotomy is coagulated with endolaser. The retina can then be tamponaded with appropriate vitreous substitutes.<sup>1</sup>

Intermittent air and fluid exchanges are performed to remove all VITREON. If small amounts (< 0.5 DD) of residual VITREON are left in the vitreous cavity they should be monitored and their time of complete dissipation noted. Larger amounts should be removed. In aphakic eyes in which there is no barrier (capsule) to the anterior chamber, any residual VITREON must be removed to protect against migration to the anterior chamber.<sup>1</sup>

### **In GIANT RETINAL TEARS<sup>2</sup>**

VITREON facilitates repair of a giant tear (to hydrokinetically manipulate the retina back into position) with the patient in a supine position.

After vitrectomy and adequate removal of retinal traction, VITREON is injected with a blunt 20-gauge to 27-gauge needle over the optic disc. The subretinal fluid is pushed in a posterior-to-anterior direction and out to the edge of the giant retinal tear.

The clinical studies have shown that retinal slippage occurred in 7.7% of patients (cohort group) with giant retinal tears. When slippage of the retina occurs, the mechanical action of the reinjected VITREON elevates the retina into proper apposition with the retinal pigment epithelium (RPE) and unfolds the retinal flap of the giant tear.

When the retina is completely flat, endolaser photocoagulation, cryopexy, or a combination of these procedures is performed. At this point, a decision is made to replace the VITREON intraoperatively with either sulfur hexafluoride ( $\text{SF}_6$ ) (15% to 20%), perfluoropropane ( $\text{C}_3\text{F}_8$ ) (10% to 15%), or silicone oil for a longer tamponading effect.

To remove the VITREON from the eye, an air-VITREON exchange is followed by three or four partial fluid-VITREON exchanges to remove any residual VITREON. A silicone-air exchange is then performed, or the air-filled eyes are flushed with 25 cc 20%  $\text{SF}_6$  or  $\text{C}_3\text{F}_8$ . An encircling scleral buckle can be placed.

### In PROLIFERATIVE VITREO-RETINOPATHY (PVR)<sup>3</sup>

The use of VITREON permits initial membrane dissection and intraoperative retinal stabilization of posterior PVR.

A three-port pars plana technique is used. Using a pick, an attempt is made to create an edge in the membrane close to the optic nerve head. After initial dissection, a small amount of VITREON is injected over the optic nerve, which flattens the adjacent retina. The membrane dissection continues from the posterior to the anterior direction.

VITREON stabilizes the posterior retina by forcing subretinal fluid out of anteriorly located retinal breaks. It facilitates dissection of posterior PVR. Anterior PVR can then be dissected and removed subsequently while the posterior retina is attached and kept in place by the weight of the VITREON.<sup>1,3</sup>

After reattachment of the retina, the VITREON can be exchanged either with gas or silicone oil to provide a longer term tamponading effect.<sup>1,3</sup>

### In OCULAR TRAUMA<sup>4</sup>

Traumatic eye injuries are often accompanied by vitreous hemorrhage and retinal detachment caused by peripheral tears. These injuries may include cases of giant retinal tears, large areas of missing retina and/or where there is the need to perform extensive retinotomy in the presence of extensive traction or retinal scarring. After the diagnosis is established by the use of ultrasound, the surgeon must decide when to intervene surgically.

As soon as the surgeon cuts the detached posterior hyaloid, the vitrectomy instrument is removed and a 20-gauge blunt needle connected to a syringe with 5 ml VITREON is inserted in the vitreous cavity. The tip of the needle is passed through the opening in the posterior hyaloid membrane in the

retrohyaloid space. VITREON is injected gradually into the space between the posterior hyaloid membrane and the detached retina. The height of the infusion bottle is lowered as the vitreous cavity gradually fills with VITREON. As the VITREON fills the posterior part of the vitreous cavity and flattens the posterior retina, the subretinal fluid is pressed out from the anteriorly located retinal hole or tears. During this procedure, the entire vitreous containing the hemorrhage is pushed forward toward the anterior part of the vitreous cavity. At this stage, the vitrectomy instrument is reinserted into the vitreous cavity and vitrectomy is performed until the majority of the vitreous opacities are removed.

Endolaser or cryotherapy is applied to the retinal hole. VITREON can be removed by air-VITREON or VITREON-silicone exchange. The operation concludes with further endolaser application to the peripheral retina, and suturing of an encircling band to the sclera to support the anterior retina.<sup>1</sup>

## HOW SUPPLIED

VITREON is supplied in 6-ml single-dose vials capped with a rubber stopper. Each single-dose vial is packaged in an individual carton.

For intraocular use only.

## STORAGE

The product should be stored at room temperature (20°C - 25°C).

## REFERENCES

1. Peyman GA, Schulman JA: *Intravitreal Surgery: Principles and Practice*. Norwalk, CT: Appleton & Lange, 1994.
2. Millsap CM, Peyman GA, Mehta NJ, Greve MDJ, Lee KJ, Ma PE, Dunlap WA: Perfluoroperhydrophenanthrene (Vitreon®) in the management of giant retinal tears: results of a collaborative study. *Ophthalmic Surg* 24:759-763, 1993.
3. Carroll BF, Peyman GA, Mehta NJ: Repair of retinal detachment associated with proliferative vitreoretinopathy using perfluoroperhydrophenanthrene (Vitreon®). *Can J Ophthalmol* 29:66-69, 1994.
4. Desai UR, Peyman GA, Harper CA III: Perfluorocarbon liquid in traumatic vitreous hemorrhage and retinal detachment. *Ophthalmic Surg* 24:537-541, 1993.

VITREON is a registered trademark of Vitrophage, Inc.

VITREON is manufactured for Vitrophage, Inc., 8643 W. Ogden Avenue, Lyons, IL 60534

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