



PMS  
P920004

File

Memorandum

Date SEP 29 1995

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

Subject Premarket Approval of Datascope Corp.  
VasoSeal® Vascular Hemostasis Device

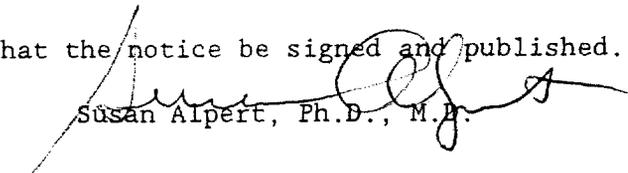
To The Director, CDRH  
Through: ORA \_\_\_\_\_

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 Christopher M. Sloan, CDRH, HFZ-450, 9/12/95, 443-8243

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**DRAFT**

DEPARTMENT OF HEALTH AND HUMAN SERVICES

FOOD AND DRUG ADMINISTRATION

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

DATASCOPE CORP.; PREMARKET APPROVAL OF THE VASOSEAL® VASCULAR HEMOSTASIS  
DEVICE

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing its approval of the application by Datascope Corp., Montvale, NJ, for premarket approval, under section 515 of the Federal Food, Drug, and Cosmetic Act (the act), of the VasoSeal® Vascular Hemostasis Device. After reviewing the recommendation of the Circulatory System Device Panel, FDA's Center for Devices and Radiological Health (CDRH) notified the applicant, by letter on September 29, 1995, of the approval of the application.

DATE: Petitions for administrative review by (insert date 30 days after date of publication in the FEDERAL REGISTER). ADDRESS: 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, Rm. 1-23, 12420 Parklawn Drive, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT:

Christopher M. Sloan  
Center for Devices and Radiological Health (HFZ-450)  
Food and Drug Administration  
9200 Corporate Boulevard  
Rockville, Maryland 20850  
301-443-8243.

SUPPLEMENTARY INFORMATION: On February 3, 1992, Datascope Corp., Montvale, NJ 07645, submitted to CDRH an application for premarket approval of the VasoSeal® Vascular Hemostasis Device. The device is a vascular hemostasis device and is indicated for use in reducing time to hemostasis at the femoral arterial puncture site in patients who have undergone diagnostic angiography or percutaneous transluminal coronary angioplasty (PTCA) procedures using an 8 French or smaller procedural sheath. The VasoSeal® VHD is also indicated for use in PTCA patients when immediate sheath removal is desired.

On May 8, 1995, the Circulatory System Devices Panel, an FDA advisory panel, reviewed and recommended approval of the application.

On September 29, 1995, 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.

B

#### 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 (21 U.S.C. 360e(g)), for administrative review of CDRH's decision to approve this application. A petitioner may request either a formal hearing under part 12 (21 CFR part 12) of FDA's administrative practices and 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 10.33(b) (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 act section 520(h), 90 Stat. 554-555, 571 (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).

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

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A handwritten mark or signature, possibly a checkmark or a stylized letter, located in the bottom right corner of the page.



Food and Drug Administration  
9200 Corporate Boulevard  
Rockville MD 20850

Ms. Susan E. Mandy  
Manager, Clinical and Regulatory Affairs  
Collagen Products Division  
Datascope Corporation  
14 Philips Parkway  
Montvale, New Jersey 07645

SEP 29 1995

Re: P920004  
VasoSeal® Vascular Hemostasis Device  
Filed: February 3, 1992  
Amended: July 1 and September 28, 1992, March 2, May 4, and  
August 26, 1993, June 27 and November 18, 1994, March 21,  
April 6, 7, and 27, May 3, 4, and 17, August 1, and  
September 19 and 29, 1995

Dear Ms. Mandy:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your premarket approval application (PMA) for the VasoSeal® Vascular Hemostasis Device (VHD). This device is indicated for use in reducing time to hemostasis at the femoral arterial puncture site in patients who have undergone diagnostic angiography or percutaneous transluminal coronary angioplasty (PTCA) procedures using an 8 French or smaller procedural sheath. The VasoSeal® VHD is also indicated for use in PTCA patients when immediate sheath removal is desired. We are pleased to inform you that the PMA is approved 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.

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), (1) insofar as the labeling specify the requirements that apply to the training of practitioners who may use the device as approved in this order and (2) insofar as the sale, distribution, and use must not violate sections 502(q) and (r) of the act.

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In addition to the postapproval requirements in the enclosure, a post-approval study protocol shall be submitted within 45 days of the date of approval of your PMA application. The purpose of this study is to examine the incidence of pseudoaneurysm associated with VasoSeal® VHD use. As recommended by the panel, follow-up ultrasound information should be analyzed by a blinded core laboratory for objective interpretation of the data.

Expiration dating for the VasoSeal® VHD has been established and approved at one year. Expiration dating for the VasoSeal® Needle Depth Indicator Kit, an accessory device, has been established and approved at two years. This is to advise you that the protocols you used to establish these expiration dates are considered approved protocols 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, that 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.

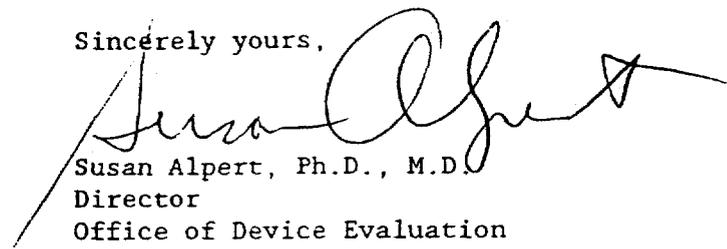
PMA Document Mail Center (HFZ-401)  
Center for Devices and Radiological Health  
Food and Drug Administration  
9200 Corporate Boulevard  
Rockville, Maryland 20850

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Page 3 - Ms. Susan E. Mandy

If you have questions concerning this approval order, please contact Christopher Sloan at (301) 443-8243.

Sincerely yours,

A handwritten signature in black ink, appearing to read "Susan Alpert", with a long horizontal stroke extending to the right.

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

Enclosure

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## SUMMARY OF SAFETY AND EFFECTIVENESS DATA

### I. General Information

Device Generic Name: Vascular Hemostasis Device

Device Trade Name: VasoSeal® Vascular Hemostasis Device

Applicant's Name and Address: Collagen Products Division  
Datascope Corp.  
14 Philips Parkway  
Montvale, NJ 07645

PMA Number: P920004

Date of Panel Recommendation: May 8, 1995

Date of Approval to the Applicant: SEP 29 1995

### II. Indications for Use

The VasoSeal® Vascular Hemostasis Device (VHD) is indicated for use in reducing time to hemostasis at the femoral arterial puncture site in patients who have undergone diagnostic angiography or percutaneous transluminal coronary angioplasty (PTCA) procedures using an 8 French or smaller procedural sheath. The VasoSeal® VHD is also indicated for use in PTCA patients when immediate sheath removal is desired.

### III. Device Description

The VasoSeal® VHD contains an 11.5F insertion sheath/tissue dilator assembly, a 45 cm (.038") guidewire, a guidewire introducer and two cartridges each containing an 80-100 mg plug of purified bovine collagen. The device permits delivery of the collagen into the tissue tract created by removal of a sheath device and onto the exterior surface of the artery. The collagen interacts with platelets in order to create a hemostatic seal directly over the puncture wound in the artery. The VasoSeal® VHD is available in seven kits which are color coded by length of the insertion sheath.

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VasoSeal® Needle Depth Indicator Kit, which is available separately, is required for the selection of the appropriate VasoSeal® VHD Kit. The Needle Depth Indicator Kit consists of a needle clamp and a measuring card.

The collagen is sterile, nonpyrogenic, and absorbable.

#### **IV. Contraindications**

VasoSeal® VHD is contraindicated in patients in whom Needle Depth Indicator measurements are outside of the range indicated on the Needle Depth Measurement Card.

#### **V. Warnings**

As with any foreign substance, use of VasoSeal® collagen in contaminated sites may potentiate infection.

#### **VI. Precautions**

##### **Special Patient Populations**

The safety and effectiveness of the VasoSeal® VHD has not been established in the following patient populations:

- \* Patients in whom procedural sheaths larger than 8 French have been used.
- \* Patients who have known allergies to beef products, collagen and/or collagen products.
- \* Patients with preexisting autoimmune diseases.
- \* Patients having a bleeding disorder, including thrombocytopenia (< 100,000 platelet count), thrombasthenia, von Willebrand's disease or anemia (Hgb < 10 mg/dl, Hct < 30).
- \* Patients who are morbidly obese.
- \* Patients with antegrade punctures.

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- \* Patients with hematomas (> 6 cm) present prior to sheath removal.
- \* Patients with elevated blood pressures (> 140/90 mmHg) which cannot be controlled with drug therapy.
- \* Patients punctured through a vascular graft.
- \* Patients younger than 18 or older than 80 years of age.
- \* Patients that are pregnant or lactating.
- \* Patients with peripheral vascular disease.

The collagen in the VasoSeal® VHD is inactivated by autoclaving and, therefore, should not be resterilized.

The VasoSeal® VHD is for single use only and should not be reused in any manner.

The VasoSeal® procedure should only be performed by physicians possessing adequate training in the use of the device, e.g., participation in a VasoSeal® physician training program or equivalent.

The VasoSeal® procedure should be performed by two people.

While the safety and effectiveness of the VasoSeal® VHD has been demonstrated in highly anticoagulated patients, hemostasis times may be longer in such patients than in ones who are not highly anticoagulated.

In the case of resistance to advancement of the tissue dilator or sheath (which may be due to scarred subcutaneous tissue) or excessive resistance during collagen deployment (which may be due to sheath kinking or tearing) discontinue the procedure and manually compress until hemostasis is achieved.

If the tissue dilator is advanced too far, it may expand the arterial puncture sufficiently to permit entry of the collagen hemostat into the artery. In the event the tissue dilator enters the artery lumen, discontinue the procedure and manually compress to achieve hemostasis.

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In the event that the proper procedure for positioning of the collagen material cannot be followed, discontinue the procedure and initiate manual compression to achieve hemostasis. Reasons for discontinuing procedure include, but are not limited to, the following situations:

- \* The Needle Depth Indicator Kit is not available.
- \* The VasoSeal® VHD sheath has been damaged.

In the event that hemostasis is not achieved following delivery of VasoSeal® collagen, apply manual compression over the puncture site in order to achieve hemostasis.

The onset of peripheral circulatory insufficiency after the procedure that was not present prior to the beginning of the procedure may indicate intra-luminal positioning of collagen. If this is suspected, appropriate evaluative and therapeutic measures should be taken.

The collagen in the VasoSeal® VHD has been shown in other applications or uses to be resorbed by the body in approximately six weeks. Should repeat femoral arterial puncture be required within this period, utilize the contra-lateral femoral artery as there is insufficient data on repuncture of a recently treated VasoSeal® site.

## **VII. Alternative Practices and Procedures**

The alternative practice to achieve hemostasis post catheterization is manual compression, including supplemental use of mechanical compression devices or pressure dressings.

## **VIII. Marketing History**

The VasoSeal® VHD is marketed in the following countries: Australia, Iceland, Canada, Italy, Holland, and Japan. The device has not been subject to adverse regulatory action in any of the above countries for any safety or effectiveness related issue.

## **IX. Adverse Effects of the Device on Health**

VasoSeal® VHD was evaluated in two independent randomized controlled clinical trials involving 626 patients [N=469 and N=157, respectively]. The studies compared VasoSeal® VHD [VasoSeal®] to manual compression [Manual]. Of the 358 patients

treated with VasoSeal®, 266 (74%) were post PTCA, 92 (26%) were post diagnostic angiography, most patients had 8F (79%) or 7F (18%) procedural sheaths, and 73% were males.

Three patients died (2 VasoSeal® and 1 Manual) within one month of the procedure. However, no deaths were considered related to use of the device.

Table 1 (on the following page) reports the adverse events as a percent of patients exposed in the two clinical investigations of VasoSeal®. The diagnostic angiography patients were all from the same study, while the PTCA patients (with the exception of the VasoSeal® [Immediate Sheath Removal] patients) were combined from two studies.

The following describes several risks which are unique to use of the VasoSeal® VHD:

- \* Use of the device may lead to entry of the tissue dilator into the artery and/or intravascular collagen insertion. Insertion of the tissue dilator into the artery may enlarge the puncture sufficiently to permit entry of the collagen into the artery. Intravascular collagen insertion may lead to obstruction of the artery.
- \* Excessive resistance encountered during advancement of the tissue dilator or sheath or during collagen deployment may result in the inability to insert the collagen plug into the tissue tract. This may result in the need to discontinue the procedure and to manually compress the site until hemostasis is achieved. Extended bleeding time and/or complications may result.
- \* The device may fail to achieve hemostasis once the collagen is inserted. This would result in the need to manually compress the site until hemostasis is achieved. Extended bleeding time and/or complications may result.

The VasoSeal® VHD is a collagen product. Therefore, the following potential adverse reactions associated with use of collagen hemostats should also be considered:

- \* allergic reaction
- \* foreign body reaction
- \* adhesion formation
- \* wound dehiscence
- \* potentiation of infection
- \* inflammation
- \* edema

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**Table 1**

**Percentage of Patients Experiencing Adverse Events**  
 (All Patients Enrolled in VasoSeal® VHD Clinical Studies; N= 626 patients)

Procedure	Diagnostic Angiography				PTCA					
	VasoSeal® (N=92)		Manual (N=75)		VasoSeal® (N=208)		VasoSeal® [Immediate Sheath Removal] (N=58)		Manual (N=193)	
	N	%	N	%	N	%	N	%	N	%
Failed to Deploy	2	2.2%			5	2.4%	3	5.2%		
Vascular Repair†	0	0%	0	0%	2	1.0%	1	1.7%	0	0%
Transfusion	1	1.1%	0	0%	5	2.4%	0	0%	3	1.6%
Infection Extending Hospitalization	0	0%	0	0%	2	1.0%	0	0%	1	0.5%
Deep Vein Thrombosis	0	0%	2	2.7%	2	1.0%	0	0%	0	0%
Hematoma > 6 cm	3	3.3%	2	2.7%	14	6.7%	4	6.9%	8	4.1%
Hematoma 2-6 cm	9	9.8%	5	6.7%	22	10.6%	5	8.6%	15	7.8%
Bleeding	4	4.3%	3	4.0%	12	5.8%	1	1.7%	12	6.2%
Any Complication	19	20.7%	13	17.3%	53	25.5%	11	19.0%	34	17.6%
No Major Complication	91	98.9%	75	100%	199	95.7%	57	98.3%	189	97.9%

† Includes intravascular collagen insertions requiring vascular repair (2 patients) and surgical removal of VasoSeal® sheath found in tissue tract at 30-day follow-up (1 patient).

**X. Summary of Non-Clinical Studies**

**A. In Vitro (Laboratory) Studies**

**1. Collagen Studies**

The collagen used in the VasoSeal® VHD is manufactured utilizing the identical textiling and chemical processes as Novacol™ Textured Collagen Hemostatic Agent [FDA approved; P850023]. The qualification and characterization test results obtained for Novacol™ as described in P850023 are incorporated by reference into this PMA for the VasoSeal® VHD.

**2. Delivery Device Studies**

The biocompatibility of each component of the VasoSeal® VHD delivery system was evaluated in accordance with the Tripartite Biocompatibility Guidance for Medical Devices. All components passed a battery of biocompatibility tests which was dependent on the degree and duration of body contact for each component.

**3. Shelf Life Studies**

Product stability testing for the VasoSeal® VHD was performed. Test results demonstrated that the functionality and sterility of the device was maintained for a minimum of 12 months. Based on these results, an expiration date of 12 months for the VasoSeal® VHD has been established. The shelf life for the VasoSeal® Needle Depth Indicator Kit has been established at 24 months.

**B. In Vivo (Animal) Studies**

**1. Collagen Studies**

A series of *in vivo* animal studies previously conducted for Novacol™ Textured Collagen Hemostatic Agent [FDA approved; P850023] are incorporated by reference into this PMA for the VasoSeal® VHD. These studies detailed the resorption and tissue reaction characteristics, antigenicity, and hemostatic effectiveness of the collagen.

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## 2. VasoSeal® VHD Animal Study

The feasibility of percutaneous delivery of collagen to the surface of an artery and subsequent promotion of hemostasis at the puncture site was evaluated in four Yorkshire albino pigs using a prototype VasoSeal® VHD. The safety and effectiveness of the VasoSeal® VHD was tested in both acute and chronic experiments. The device was able to achieve hemostasis within 5 minutes in all four animals. Examination of the puncture sites of two animals upon acute sacrifice showed patent lumens with no evidence of collagen in the artery. Two animals were sacrificed 30 days after VasoSeal® treatment to assess the chronic effects of the device. Histological analysis showed an intact lumen, normal intimal and medial layers, a fibrous adventitial cap, and no evidence of collagen remaining at the site.

## XI. Summary of Clinical Studies

Two randomized clinical studies [Study 1 (N=469) and Study 2 (N=157)] were conducted to examine the safety and effectiveness of the VasoSeal® VHD in achieving hemostasis compared to standard manual compression in both diagnostic angiography [Study 1] and percutaneous transluminal angioplasty (PTCA) patients [Studies 1 and 2]. Safety and effectiveness was assessed with regard to time to hemostasis and frequency of peripheral vascular complications.

Inclusion and exclusion criteria were chosen to avoid gender bias for both studies. The higher percentage of male patients enrolled in the studies reflected both the gender referral pattern for cardiac disease and the severity of the disease in the centers involved.<sup>1</sup> All differences between the treatment groups with respect to hemostasis time were consistent between the genders.

### Study 1: VasoSeal® VHD v. Manual Compression

**Conclusions:** In suitable diagnostic angiography and PTCA patients, use of the VasoSeal® device (V) resulted in a statistically significant shorter time to hemostasis compared to manual compression (M). This result also held in highly anticoagulated PTCA patients (ACT > 300). The risk of peripheral vascular complications was not statistically significantly increased although two (2) cases of intravascular collagen insertion were reported in the VasoSeal® group. No further clinical sequelae were

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<sup>1</sup> Mark DB, Shaw LK, DeLong ER, Califf RM, Pryor DB: Absence of sex bias in the referral of patients for cardiac catheterization. N Eng J Med 1994; 330:1101-6.

noted following removal of the collagen in these patients.

**Purpose:** The purpose of the study was to prospectively compare hemostasis time and the incidence of peripheral vascular complications for angiography and PTCA patients receiving VasoSeal® or manual compression.

**Design:** Multicenter, prospective, randomized, controlled study of angiography and PTCA patients at five U.S. sites. Inclusion criteria: patients 20-80 years of age scheduled for an angiography or PTCA procedure and standard manual compression following their procedure. Exclusion criteria: patients who were obese, had platelet disorders, had a hematoma present prior to sheath removal, were admitted for emergency angioplasty, were pregnant, had known allergies to beef or collagen products or elevated blood pressure which could not be controlled by medical therapy.

**Methods:** Patient were treated with manual compression or VasoSeal® at the time of sheath removal. Hemostasis time began at sheath removal and ended at hemostasis (defined as the absence of any signs of bleeding, e.g., oozing or spurting blood and absence of expanding or developing hematoma). First checks for hemostasis occurred at about 10-15 minutes in manual compression patients and at about 2-5 minutes in VasoSeal® patients. Subsequent checks occurred at about 5 minute intervals.

**Demography:** 469 patients were studied from September 1991 to March 1992. For PTCA patients, 140 patients were assigned to manual compression and 162 patients to VasoSeal®. For angiography patients, 75 patients were assigned to manual compression and 92 patients were assigned to VasoSeal®. The mean age was 60.4 years (PTCA) and 62.8 years (angiography). Seventy-one per cent of patients were male. Baseline and procedural characteristics were similar<sup>2</sup> between the VasoSeal® and manual compression groups.

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<sup>2</sup> No statistically significant differences, except in PTCA "% Male" category where V = 77% compared to M = 64%.

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**Results:**

**Table 2**

**Safety and Effectiveness Measures: VasoSeal® VHD v. Manual Compression  
 (Study 1; N=469)**

	OVERALL			ANGIOGRAPHY			PTCA		
EFFECTIVENESS MEASURES+ (Mean±SD)	VasoSeal	Manual	95% CI for Tmt. Diff	VasoSeal	Manual	95% CI for Tmt. Diff	VasoSeal	Manual	95% CI for Tmt. Diff
	N=251	N=215		N=92	N=75		N=159	N=140	
Hemostasis (min)	5.7±7.5	28.9±23.5	23.2±3.3‡	4.6±3.8	17.6±9.2	13.0±2.2‡	6.3±9.0	34.9±26.4	28.6±4.6‡
SAFETY MEASURES† Number (%)	N=254	N=215	95% RR*	N=92	N=75	95% RR	N=162	N=140	95% RR
Failure to Deploy	4 (2%)	--	--	2 (2%)	--	--	2 (1%)	--	--
Vascular Repair (major)	2 (.8%)	0 (0%)	na	0 (0%)	0 (0%)	n.a.	2 (1%)	0 (0%)	n.a.
Transfusion (major)	6 (2%)	3 (1%)	.4-6.7	1 (1%)	0 (0%)	n.a.	5 (3%)	3 (2%)	0.4-5.9
Infection/Hosp (major)	2 (.8%)	1 (.5%)	.2-18.5	0 (0%)	0 (0%)	n.a.	2 (1%)	1 (.7%)	0.2-18.9
Hematoma 2-6 cm	27 (11%)	19 (9%)	.7-2.1	9 (10%)	5 (7%)	0.5-4.2	18 (11%)	14 (10%)	0.5-2.2
Bleeding	16 (6%)	15 (7%)	.5-1.8	4 (4%)	3 (4%)	0.3-4.7	12 (7%)	12 (9%)	0.4-1.9
Hematoma >6 cm	16 (6%)	10 (5%)	.6-2.9	3 (3%)	2 (3%)	0.2-7.1	13 (8%)	8 (6%)	0.6-3.3
DVT	2 (.8%)	2 (.9%)	.1-6.0	0 (0%)	2 (3%)	n.a.	2 (1%)	0 (0%)	n.a.
Any Complication	66 (26%)	45 (21%)	.9-1.7	19 (21%)	13 (17%)	.6-2.3	47 (29%)	32 (23%)	.9-1.9
No Major Comps	244 (96%)	211 (98%)	.95-1.01	91 (99%)	75 (100%)	.97-1.01	153 (94%)	136 (97%)	.93-1.02

+ The number of patients listed under "Effectiveness Measures" is less than total patients studied due to missing hemostasis data for a few patients.

† No treatment difference VasoSeal to Manual, P > 0.05 by Fisher's exact test.

‡ Between treatment difference (V vs. M) statistically significant, P < 0.0001 by analysis of variance method.

\* RR = relative risk (VasoSeal/Manual)

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## Study 2: VasoSeal® VHD v. Manual Compression

**Conclusions:** In suitable PTCA patients, use of the VasoSeal® VHD at normal (4 hour) sheath removal time [V(n)] resulted in a statistically significant shorter time to hemostasis compared to manual compression [M] at the same sheath removal time. This result was also true for highly anticoagulated VasoSeal® patients who had their procedural sheaths removed immediately [V(i)]. The risk of peripheral vascular complications was not significantly increased. No intravascular collagen insertions occurred.

**Purpose:** To prospectively compare hemostasis time and incidence of peripheral vascular complications for PTCA patients receiving VasoSeal® or manual compression.

**Design:** Multicenter, prospective, randomized, controlled study of PTCA patients. The study was conducted at one U.S. and two German sites. Inclusion criteria: patients 18-80 years of age who were scheduled for a PTCA procedure followed by standard manual compression. Exclusion criteria: patients who were morbidly obese (Body Mass Index >40), had bleeding disorders, had a clinically significant hematoma (e.g., >6 cm) present prior to sheath removal, were admitted for emergency PTCA, were pregnant, had known allergies to beef or collagen products or elevated blood pressure (>140/90 mmHg) which could not be controlled by medical therapy.

**Methods:** Patients were treated with manual compression or VasoSeal® at the time of sheath removal. Hemostasis time began at sheath removal and ended at hemostasis (defined as no bleeding of any kind and no expanding hematoma). First checks for hemostasis occurred at 15 minutes in M, 5 minutes in V(n) and 10 minutes in V(i). Subsequent checks occurred at 5 minute intervals.

**Demography:** 196 patients were enrolled. After allowable withdrawals, 157 patients were studied from January-September 1994. Fifty-three patients were assigned to the manual compression group [M], 46 patients to the VasoSeal® normal sheath removal group [V(n)] and 58 patients to VasoSeal® immediate sheath removal group [V(i)]. The mean age was 61.7 years. Seventy-seven per cent of patients were male. Baseline and procedural characteristics were similar<sup>3</sup> between the V(n) or V(i) vs. M groups.

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<sup>3</sup> No statistically significant difference, except in Age for V(n) v. M, where V(n) age = 63.6 vs. M age = 60.3.

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**Results:**

**Table 3**

**Safety and Effectiveness Measures: VasoSeal® VHD v. Manual Compression  
 (Study 2; N=157)**

	VasoSeal(n)		VasoSeal(i)		Manual
<b>EFFECTIVENESS MEASURES+</b> (Mean±SD)	N=46	95% Conf. Interval V(n) v. M	N=56	95% Conf. Interval V(i) v. M	N=50
Hemostasis (min)	8.1±5.0	8.5-12.7 ‡	13.0±5.6	3.5-7.9 ‡	18.7±5.7
<b>SAFETY MEASURES</b> Number (%)	N=46	95% RR	N=58	95% RR	N=53
Failure to Deploy	3 (7%)	--	3 (5%)	--	--
Vascular Repair (major)	0 (0%)	n.a.	1 (2%)	n.a.	0 (0%)
Transfusion (major)	0 (0%)	n.a.	0 (0%)	n.a.	0 (0%)
Infection/Hosp (major)	0 (0%)	n.a.	0 (0%)	n.a.	0 (0%)
Hematoma 2-6 cm	4 (9%)	0.5 - 39.8	5 (9%)	0.6 - 37.9	1 (2%)
Hematoma >6 cm	1 (2%)	n.a.	4 (7%)	n.a.	0 (0%)
Bleeding	0 (0%)	n.a.	1 (1.7%)	n.a.	0 (0%)
Any Complication	6 (13%)	0.7 - 16.3	11 (19%)	1.2 - 21.6†*	2 (4%)
No Major Complications	46 (100%)	n.a.	57 (98%)	.95 - 1.02	53 (100%)

+ The number of patients listed under "Effectiveness Measures" is less than total patients studied due to missing hemostasis data for a few patients.

‡ Between treatment difference (V v. M) statistically significant p=0.0001 by Analysis of Variance.

† Between treatment difference (V v. M) statistically significant at ≤.05 level by Fisher's Exact Test.

\* This category includes mostly minor complications and therefore this difference is not clinically significant.

**XII. Conclusions Drawn from the Studies**

The results of the *in vivo* and *in vitro* non-clinical laboratory studies together with the clinical studies provide valid scientific evidence and reasonable assurance that the VasoSeal® VHD is safe and effective when used in accordance with its labeling.

The safety of the device has been demonstrated through the low incidence of peripheral vascular complications in patients treated with the VasoSeal® VHD compared to patients receiving standard manual compression. The risk of intravascular collagen insertion

associated with VasoSeal® VHD use was identified in the clinical studies. However, no further clinical sequelae were noted following removal of the collagen in the clinical study patients and the reported incidence of intravascular insertion of VasoSeal® collagen in the literature is quite low (15/6726; 0.22%). The effectiveness of the device has been demonstrated through the reduction of time to hemostasis in angiography and PTCA patients compared to standard manual compression. The data also demonstrate that VasoSeal® VHD facilitates immediate sheath removal in PTCA patients.

### **XIII. Panel Recommendations**

The Circulatory System Devices Advisory Panel met on May 8, 1995, and unanimously recommended approval of the VasoSeal® Vascular Hemostasis Device with the following conditions:

1. Certain changes to the Indications, Warnings, and Precautions sections of the labeling be made.
2. A postapproval study be conducted to examine the incidence of pseudoaneurysm associated with VasoSeal® use. Follow-up ultrasound information should be analyzed by a blinded core laboratory for objective interpretation of the data.

### **XIV. FDA Decision**

The FDA concurred with the recommendations of the Circulatory System Devices Panel of May 8, 1995, and issued an approvable letter on July 14, 1995. The applicant submitted amendments to the PMA as requested and FDA found the information in the amendments to be adequate. A Good Manufacturing Practice (GMP) inspection was conducted and FDA found the facility in compliance with GMP regulations (21 CFR Part 820).

### **XV. Approval Specifications**

Instructions for Use: See the labeling.

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

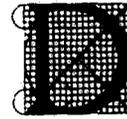
Postapproval Requirements and Restrictions: See approval order.

Color Bar Prints PMS 466C⇒

Copy Prints Black

Not to Scale

P/N: 0910-04-0006B



**VasoSeal™ Needle Depth Indicator Kit by Datascope**

**Method of Sterilization: Gamma Radiation**

Product sterile if package is undamaged or unopened.

Single use only. Do not resterilize.

Read instructions for use prior to use.

Steriles Produkt bei ungeöffnetem und unbeschädigter Verpackung. Nur für den Einmal-Gebrauch. Nicht resterilisieren. Gebrauchsanweisung beachten.

Produit stérile sauf si paquet ouvert ou endommagé. Usage unique. Ne pas restériliser. Lire les "Instructions d'utilisation" avant utilisation.

El producto está esterilizado si el empaque no está abierto o estropeado. Para un solo uso. No reesterilizar. Leer las instrucciones antes de usar el producto.

Prodotto sterile salvo apertura o danneggiamento della confezione. Per uso singolo. Non risterrilizzare. Leggere le istruzioni per l'uso prima dell'uso.

**Contents: 5 Kits**

1 ea. Needle Clamp

1 ea. Needle Depth Indicator. Card

Inhalt: 5 Kits

Je 1 Nadelkammer. Je 1 Nadeltiefe-Anzeigekarte.

Contenu: 5 trousses

1 clamp de seringue. 1 carte indicatrice de profondeur de seringue.

Contenido: 5 Kits

1 c/u clamp de aguja. 1 c/u tarjeta indicadora de profundidad de aguja

Contenuto: 5 kit

1 pinza per ago. 1 scheda indicatrice della profondità dell'ago.

**Catalog No.**

83000

**Expiration Date:**

Katalognr.

Verfalldatum:

Numéro de référence:

Date d'expiration:

No. de catálogo

Fecha de expiración:

N° di catalogo

Data di scadenza:

**Lot No.**

**Sterilization Date:**

Losnummer:

Sterilisationsdatum:

Numéro de lot:

Date de stérilisation:

Lote número:

Fecha de esterilización:

Numero di lotto:

Data di sterilizzazione:



**VasoSeal™  
Needle Depth  
Indicator Kit  
by Datascope**

Nadeltiefe-Anzeiger

Trousse indicatrice de profondeur de seringue

Kit indicator de profundidad de aguja

Kit indicatore della profondità dell'ago

Needle Depth Indicator Kit  
Carton

VasoSeal™  
Needle Depth  
Indicator Kit



Method of Sterilization: Gamma Radiation  
Product sterile if package is undamaged or unopened  
Store in a cool dry place  
Single use only Do not resterilize.  
Read instructions for use prior to use

Steriles Produkt bei ungeöffneter und unbeschädigter Verpackung  
Nur für den Einmal-Gebrauch Nicht resterilisieren  
Gebrauchsanweisung beachten

Produit stérile sauf si paquet ouvert ou endommagé Usage unique  
Ne pas restériliser Lire les "Instructions d'utilisation" avant utilisation

El producto está esterilizado si el empaque no está abierto o estropeado  
Para un solo uso No reesterilizar  
Leer las instrucciones antes de usar el producto

Prodotto sterile salvo apertura o danneggiamento della confezione. Per  
uso singolo Non risterrilizzare. Leggere le istruzioni per l'uso prima dell'uso

Contents: 1 Kit  
1 ea. Needle Clamp  
1 ea. Needle Depth Indicator Card

Inhalt: 1 Kit  
Je 1 Nadelklemme Je 1 Nadeltiefe-Anzeigekarte

Contenu: 1 trousse  
1 clamp de seringue 1 carte indicatrice de profondeur de seringue

Contenido: 1 kit  
1 c/u clamp de aguja 1 c/u tarjeta indicadora de profundidad de aguja

Contenuto: 1 kit  
1 pinza per ago 1 scheda indicatrice della profondità dell'ago

Catalog No. Expiration Date:

83000

Katalognr.	Verfalldatum:
Numero de référence:	Date d'expiration:
No. de catálogo:	Fecha de expiracion:
N° di catalogo:	Data di scadenza:
Lot No.	Sterilization Date:

Losnummer	Sterilisationsdatum:
Numéro de lot:	Date de stérilisation:
Lote numero	Fecha de esterilización:
Numero di lotto:	Data di sterilizzazione:

Novacol



VasoSeal™  
Needle Depth  
Indicator Kit  
by Datascope

Nadeltiefe-Anzeigekit  
Trousse indicatrice de profondeur de seringue  
Kit indicator de profundidad de aguja  
Kit indicatore della profondità dell'ago  
0910-03-0009A

Needle Depth Indicator Kit  
Pouch

NOT

REVISIONS			
LTR	DESCRIPTION	DATE	APPROVED

UNLESS OTHERWISE SPECIFIED  
DIMENSIONS ARE IN INCHES  
TOLERANCES ON

CONTRACT NO.

**DATASCOPE**  
580 WINTERS AVENUE PARAMOUNT, NJ

# Datascope®

Collagen Products Division

## VasoSeal® Vascular Hemostasis Device

**Sterile-Nonpyrogenic**

**Method of Sterilization: Gamma Radiation**

**Product sterile if package is undamaged or unopened.**

**Store in a cool dry place.**

**Single use only. Do not resterilize.**

---

**Contents: 1 kit**

---

1 ea. 11.5F (I.D.) Sheath/Tissue Diator Assembly

1 ea. 45cm .038" Guidewire

1 ea. Guidewire Introducer

2 ea. Collagen Cartridges (containing 80 - 100 mg. collagen each)

Catalog No.

Expiration Date:

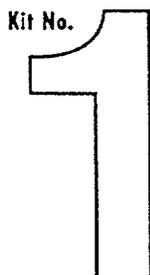
Lot No.

Sterilization Date:

**Caution: Federal law restricts this device to sale by or on the order of a physician.**

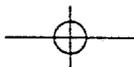


Manufactured by Bioplex Medical B.V.  
Yool, Netherlands  
A Unit of Datascope Corp.



P/N: 104.1.4005.01A

*This product may be covered by one or more of the following patents:  
US Patent 5.391.183; US Patent 5.437.631*



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# Datascope®

Collagen Products Division

## VasoSeal® Vascular Hemostasis Device

**Sterile-Nonpyrogenic**

**Method of Sterilization: Gamma Radiation**

**Product sterile if package is undamaged or unopened.**

**Store in a cool dry place.**

**Single use only. Do not resterilize.**

---

**Contents: 1 kit**

---

1 ea. 11.5F (I.D.) Sheath/Tissue Distal Assembly

1 ea. 45cm .038" Guidewire

1 ea. Guidewire Introducer

2 ea. Collagen Cartridges (containing 80 - 100 mg. collagen each)

Catalog No.

Expiration Date:

Lot No.

Sterilization Date:

**Caution: Federal law restricts this device to sale by or on the order of a physician.**



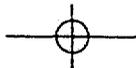
Kit No.



Manufactured by Bioplex Medical B.V.  
Yolo, Netherlands  
A Unit of Datascope Corp.

P/N: 104.1.4065.02A

*This product may be covered by one or more of the following patents:  
US Patent 5,391,183; US Patent 5,437,631*



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Datascope®

Collagen Products Division

**VasoSeal® Vascular Hemostasis Device**

**Sterile-Nonpyrogenic**  
**Method of Sterilization: Gamma Radiation**  
**Product sterile if package is undamaged or unopened.**  
**Store in a cool dry place.**  
**Single use only. Do not resterilize.**

**Contents: 1 kit**

- 1 ea. 11.5F (I.D.) Sheath/Tissue Dilator Assembly
- 1 ea. 45cm .038" Guidewire
- 1 ea. Guidewire Introducer
- 2 ea. Collagen Cartridges (containing 80 - 100 mg. collagen each)

Catalog No.

Expiration Date:

Lot No.

Sterilization Date:

**Caution: Federal law restricts this device to sale by or on the order of a physician.**



Kit No.

**3**

Manufactured by Biotex Medical B.V.  
Yook, Netherlands  
A Unit of Datascope Corp.

P/N: 104.1.4005.03A

*This product may be covered by one or more of the following patents:  
US Patent 5,391,183; US Patent 5,437,631*



*M*

Datascope®

Collagen Products Division

**VasoSeal® Vascular Hemostasis Device**

**Sterile-Nonpyrogenic**  
**Method of Sterilization: Gamma Radiation**  
**Product sterile if package is undamaged or unopened.**  
**Store in a cool dry place.**  
**Single use only. Do not resterilize.**

**Contents: 1 kit**

- 1 ea. 11.5F (I.D.) Sheath/Tissue Diator Assembly
- 1 ea. 45cm .038" Guidewire
- 1 ea. Guidewire Introducer
- 2 ea. Collagen Cartridges (containing 80 - 100 mg. collagen each)

Catalog No.

Expiration Date:

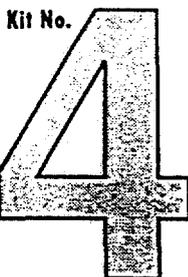
Lot No.

Sterilization Date:

**Caution: Federal law restricts this device to sale by or on the order of a physician.**



Manufactured by Bioplex Medical B.V.  
Yvoets, Netherlands  
A Unit of Datascope Corp.



P/N: 104.1.4005.04A

*This product may be covered by one or more of the following patents:*  
US Patent 5,391,183; US Patent 5,437,631



# Datascope

Collagen Products Division

## VasoSeal<sup>®</sup> Vascular Hemostasis Device

**Sterile-Nonpyrogenic**

**Method of Sterilization: Gamma Radiation**

**Product sterile if package is undamaged or unopened.**

**Store in a cool dry place.**

**Single use only. Do not resterilize.**

---

**Contents: 1 kit**

---

- 1 ea. 11.5F (I.D.) Sheath/Tissue Director Assembly
- 1 ea. 45cm .038" Guidewire
- 1 ea. Guidewire Introducer
- 2 ea. Collagen Cartridges (containing 80 - 100 mg. collagen each)

Catalog No.

Expiration Date:

Lot No.

Sterilization Date:

**Caution: Federal law restricts this device to sale by or on the order of a physician.**



Kit No.



Manufactured by Bioplex Medical B.V.  
Yvois, Netherlands  
A Unit of Datascope Corp.

P/N: 104.1.4005.05A

*This product may be covered by one or more of the following patents:  
US Patent 5.391.183; US Patent 5.437.631*



Datascope®

Collagen Products Division

**VasoSeal® Vascular Hemostasis Device**

**Sterile-Nonpyrogenic**  
**Method of Sterilization: Gamma Radiation**  
**Product sterile if package is undamaged or unopened.**  
**Store in a cool dry place.**  
**Single use only. Do not resterilize.**

**Contents: 1 kit**

- 1 ea. 11.5F (I.D.) Sheath/Tissue Distal Assembly
- 1 ea. 45cm .038" Guidewire
- 1 ea. Guidewire Introducer
- 2 ea. Collagen Cartridges (containing 80 - 100 mg. collagen each)

Catalog No.

Expiration Date:

Lot No.

Sterilization Date:

**Caution: Federal law restricts this device to sale by or on the order of a physician.**



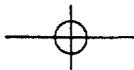
Kit No.



Manufactured by Bioplex Medical B.V.  
Voals, Netherlands  
A Unit of Datascope Corp.

P/N: 104.1.4005.06A

*This product may be covered by one or more of the following patents:*  
US Patent 5,391,183; US Patent 5,437,631



30

# Datascope

Collagen Products Division

## VasoSeal® Vascular Hemostasis Device

**Sterile-Nonpyrogenic**  
Method of Sterilization: Gamma Radiation  
Product sterile if package is undamaged or unopened.  
Store in a cool dry place.  
Single use only. Do not resterilize.

---

**Contents: 1 kit**

---

- 1 ea. 11.5F (I.D.) Sheath/Tissue Dilator Assembly
- 1 ea. 45cm .038" Guidewire
- 1 ea. Guidewire Introducer
- 2 ea. Collagen Cartridges (containing 80 - 100 mg. collagen each)

Catalog No.

Expiration Date:



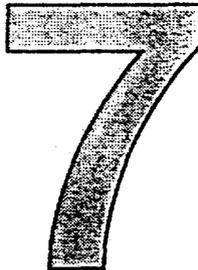
Lot No.

Sterilization Date:

**Caution: Federal law restricts this device to sale by or on the order of a physician.**



Kit No.



Manufactured by Bioplex Medical B.V.  
Yook, Netherlands  
A Unit of Datascope Corp.

P/N: 104.1.4005.07A

*This product may be covered by one or more of the following patents:  
US Patent 5,391,183; US Patent 5,437,631*



# Datascope®

*Collagen Products Division*

## **VasoSeal® Vascular Hemostasis Device**

**Sterile-Nonpyrogenic**  
**Method of Sterilization: Gamma Radiation**  
**Product sterile if package is undamaged or unopened.**  
**Store in a cool dry place.**  
**Single use only. Do not resterilize.**

---

**Contents: 5 kits**

---

- 1 ea. 11.5F (I.D.) Sheath/Tissue Dilator Assembly
- 1 ea. 45cm .038" Guidewire
- 1 ea. Guidewire Introducer
- 2 ea. Collagen Cartridges (containing 80 - 100 mg. collagen each)

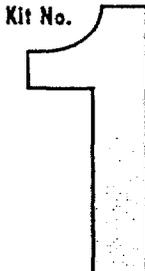
Catalog No.                      Expiration Date:

Lot. No.                              Sterilization Date:

**Caution: Federal law restricts this device  
to sale by or on the order of a physician.**



Manufactured by Bioplex Medical B.V.  
Voor, Netherlands  
A Unit of Datascope Corp.



P/N: 104.1.4005.01A

*This product may be covered by one or more of the following patents:  
US Patent 5,391,183; US Patent 5,437,631*



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Datascope®

Collagen Products Division

**VasoSeal® Vascular Hemostasis Device**

**Sterile-Nonpyrogenic**  
Method of Sterilization: Gamma Radiation  
Product sterile if package is undamaged or unopened.  
Store in a cool dry place.  
Single use only. Do not resterilize.

**Contents: 6 kits**

- 1 ea. 11.5F (I.D.) Sheath/Tissue Dilator Assembly
- 1 ea. 45cm .038" Guidewire
- 1 ea. Guidewire Introducer
- 2 ea. Collagen Cartridges (containing 80 - 100 mg. collagen each)

Catalog No.                      Expiration Date:

Lot. No.                              Sterilization Date:

**Caution: Federal law restricts this device to sale by or on the order of a physician.**



Kit No.



Manufactured by Bioplex Medical B.V.  
Yvois, Netherlands  
A Unit of Datascope Corp.

P/N: 104.1.4005.02A

*This product may be covered by one or more of the following patents:  
US Patent 5,391,183; US Patent 5,437,631*



# Datascope

Collagen Products Division

## VasoSeal<sup>®</sup> Vascular Hemostasis Device

**Sterile-Nonpyrogenic**  
Method of Sterilization: Gamma Radiation  
Product sterile if package is undamaged or unopened.  
Store in a cool dry place.  
Single use only. Do not resterilize.

---

Contents: 5 kits

---

- 1 ea. 11.5F (I.D.) Sheath/Tissue Director Assembly
- 1 ea. 45cm .038" Guidewire
- 1 ea. Guidewire Introducer
- 2 ea. Collagen Cartridges (containing 80 - 100 mg. collagen each)

Catalog No.

Expiration Date:

Lot. No.

Sterilization Date:

**Caution: Federal law restricts this device to sale by or on the order of a physician.**



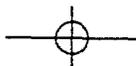
Kit No.

# 3

Manufactured by Esoplex Medical B.V.  
Voorst, Netherlands  
A Unit of Datascope Corp.

P/N: 104.1.4005.03A

*This product may be covered by one or more of the following patents:  
US Patent 5,391,183; US Patent 5,437,631*



34

Datascope®

Collagen Products Division

**VasoSeal® Vascular Hemostasis Device**

**Sterile-Nonpyrogenic**  
Method of Sterilization: Gamma Radiation  
Product sterile if package is undamaged or unopened.  
Store in a cool dry place.  
Single use only. Do not resterilize.

---

Contents: 5 kits

---

- 1 ea. 11.5F (I.D.) Sheath/Tissue Dialor Assembly
- 1 ea. 45cm .036" Guidewire
- 1 ea. Guidewire Introducer
- 2 ea. Collagen Cartridges (containing 80 - 100 mg. collagen each)

Catalog No.                      Expiration Date:

Lot. No.                              Sterilization Date:

**Caution: Federal law restricts this device to sale by or on the order of a physician.**



Manufactured by Bioplex Medical B.V.  
Voals, Netherlands  
A Unit of Datascope Corp.



P/N: 104.1.4005.04A

*This product may be covered by one or more of the following patents:  
US Patent 5,391,183; US Patent 5,437,631*



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# Datascope®

Collagen Products Division

## VasoSeal® Vascular Hemostasis Device

**Sterile-Nonpyrogenic**  
Method of Sterilization: Gamma Radiation  
Product sterile if package is undamaged or unopened.  
Store in a cool dry place.  
Single use only. Do not resterilize.

---

Contents: 5 kits

---

- 1 ea. 11.5F (I.D.) Sheath/Tissue Dilator Assembly
- 1 ea. 45cm .038" Guidewire
- 1 ea. Guidewire Introducer
- 2 ea. Collagen Cartridges (containing 80 - 100 mg. collagen each)

Catalog No.                      Expiration Date:

Lot. No.                              Sterilization Date:

**Caution: Federal law restricts this device to sale by or on the order of a physician.**



Manufactured by Bioplex Medical B.V.  
Yook, Netherlands  
A Unit of Datascope Corp.



P/N: 104.1.4005.05A

*This product may be covered by one or more of the following patents:  
US Patent 5,391,183; US Patent 5,437,631*



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Datascope®

Collagen Products Division

**VasoSeal® Vascular Hemostasis Device**

**Sterile-Nonpyrogenic**  
Method of Sterilization: Gamma Radiation  
Product sterile if package is undamaged or unopened.  
Store in a cool dry place.  
Single use only. Do not resterilize.

**Contents: 5 kits**

- 1 ea. 11.5F (I.D.) Sheath/Tissue Dialor Assembly
- 1 ea. 45cm .038" Guidewire
- 1 ea. Guidewire Introducer
- 2 ea. Collagen Cartridges (containing 80 - 100 mg. collagen each)

Catalog No.                      Expiration Date:

Lot. No.                              Sterilization Date:

**Caution: Federal law restricts this device to sale by or on the order of a physician.**



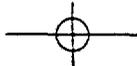
Kit No.

6

Manufactured by Bioplex Medical B.V.  
Voals, Netherlands  
A Unit of Datascope Corp.

P/N: 104.1.4005.06A

*This product may be covered by one or more of the following patents:  
US Patent 5,391,183; US Patent 5,437,631*



Datascope®

Collagen Products Division

**VasoSeal® Vascular Hemostasis Device**

**Sterile-Nonpyrogenic**  
**Method of Sterilization: Gamma Radiation**  
**Product sterile if package is undamaged or unopened.**  
**Store in a cool dry place.**  
**Single use only. Do not resterilize.**

---

**Contents: 5 kits**

---

- 1 ea. 11.5F (I.D.) Sheath/Tissue Diator Assembly
- 1 ea. 45cm .038" Guidewire
- 1 ea. Guidewire Introducer
- 2 ea. Collagen Cartridges (containing 80 - 100 mg. collagen each)

Catalog No.

Expiration Date:

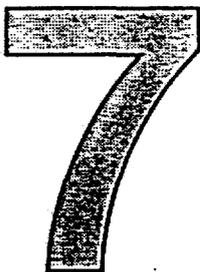
Lot. No.

Sterilization Date:

**Caution: Federal law restricts this device to sale by or on the order of a physician.**



Kit No.



Manufactured by Etoplex Medical B.V.  
Yool, Netherlands  
A Unit of Datascope Corp.

P/N: 104.1.4005.07A

*This product may be covered by one or more of the following patents:  
US Patent 5,391,183; US Patent 5,437,631*

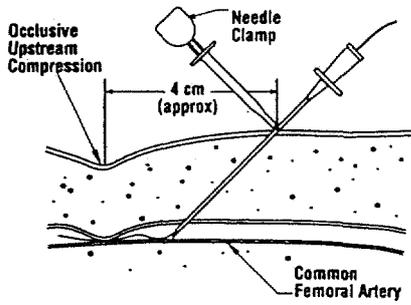


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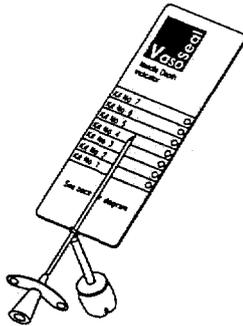
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## INSTRUCTIONS FOR USE NEEDLE DEPTH INDICATOR KIT

The Needle Depth Indicator Kit should not be used without the VasoSeal® Vascular Hemostasis Device (VHD) which is supplied separately. Please refer to the VasoSeal® VHD Instructions For Use for complete instructions on the proper use of that device.

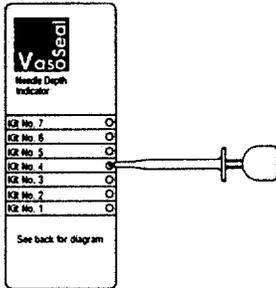


1. Prior to removing the needle from the artery, place the Needle Depth Indicator Kit clamp on the needle at the skin surface to mark the distance from the skin surface to the artery. When placing the needle clamp, occlusively compress the artery approximately 3-4 cm above the point where the needle enters the artery. Occlusive compression is defined as manual, occlusive pressure intended to be sufficient to restrict blood flow to avoid leakage from the arterial puncture site.



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2. Place the needle on the VasoSeal® color card and note the color indicated at the needle tip. If the tip of the needle falls on a black line, choose the lower numbered kit. If the tip of the needle falls outside of the range of available kits, do not use VasoSeal® VHD.



3. Attach the clip to the card at the indicated color and note the color in the patient's record. Choose the VasoSeal® kit which corresponds to the color determined by the arterial depth measurement using the Needle Depth Indicator Kit.

VasoSeal is a registered trademark of Datascope Corp.



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- Patients having a bleeding disorder, including thrombocytopenia (< 100,000 platelet count), thrombasthenia, von WilleBrand's disease or anemia (Hgb < 10 mg/dl, Hct < 30).
- Patients who are morbidly obese.
- Patients with antegrade punctures.
- Patients with hematomas (>6 cm) present prior to sheath removal.
- Patients with elevated blood pressures (>140/90 mmHg) which cannot be controlled with drug therapy.
- Patients punctured through a vascular graft.
- Patients younger than 18 or older than 80 years of age.
- Patients that are pregnant or lactating.
- Patients with peripheral vascular disease.

The collagen in the VasoSeal® VHD is inactivated by autoclaving and, therefore, should not be resterilized.

The VasoSeal® VHD is for single use only and should not be reused in any manner.

The VasoSeal® procedure should only be performed by physicians possessing adequate training in the use of the device, e.g., participation in a VasoSeal® physician training program or equivalent.

The VasoSeal® procedure should be performed by two people.

While the safety and effectiveness of the VasoSeal® VHD has been demonstrated in highly anticoagulated patients, hemostasis times may be longer in such patients than in ones who are not highly anticoagulated.

In the case of resistance to advancement of the tissue dilator or sheath (which may be due to scarred subcutaneous tissue) or excessive resistance during collagen deployment (which may be due to sheath kinking or tearing) discontinue the procedure and manually compress until hemostasis is achieved.

If the tissue dilator is advanced too far, it may expand the arterial puncture sufficiently to permit entry of the collagen hemostat into the artery. In the event the tissue dilator enters the artery lumen, discontinue the procedure and manually compress to achieve hemostasis.

In the event that the proper procedure for positioning of the collagen material cannot be followed, discontinue the procedure and initiate manual compression to achieve hemostasis. Reasons for discontinuing procedure include, but are not limited to, the following situations:

- The Needle Depth Indicator Kit is not available.
- The VasoSeal® sheath has been damaged.

In the event that hemostasis is not achieved following delivery of VasoSeal® collagen, apply manual compression over the puncture site in order to achieve hemostasis.

The onset of peripheral circulatory insufficiency after the procedure that was not present prior to the beginning of the procedure may indicate intra-luminal positioning of collagen. If this is suspected, appropriate evaluative and therapeutic measures should be taken.

The collagen in the VasoSeal® VHD has been shown in other applications or uses to be resorbed by the body in approximately six weeks. Should repeat femoral arterial puncture be required within this period, utilize the contra-lateral femoral artery as there is insufficient data on repuncture of a recently treated VasoSeal® site.

**ADVERSE EVENTS**

VasoSeal® VHD was evaluated in two independent randomized controlled clinical trials involving 626 patients [N=469 and N=157]. The studies compared VasoSeal® VHD [VasoSeal®] to manual compression [Manual]. Of the 358 patients treated with VasoSeal® VHD, 266 (74%) were post PTCA, 92 (26%) were post diagnostic angiography, most patients had 8F (79%) or 7F (18%) procedural sheaths, and 73% were males.

Three patients died (2 VasoSeal® and 1 Manual) within one month of the procedure. However, no deaths were considered related to use of the device.

The following table reports the adverse events as a percent of patients exposed in the two clinical investigations of VasoSeal® VHD. The diagnostic angiography patients were all from the same study, while the PTCA patients (with the exception of the VasoSeal® [Immediate Sheath Removal] patients) were combined from two studies.

**Percentage of Patients Experiencing Adverse Events**

(All Patients Enrolled in VasoSeal® VHD Clinical Studies; N=626 patients)

Procedure	Diagnostic Angiography				PTCA					
	VasoSeal® (N=92)		Manual (N=75)		VasoSeal® (N=208)		VasoSeal® [Immediate Sheath Removal] (N=58)		Manual (N=193)	
	N	%	N	%	N	%	N	%	N	%
Failed to Deploy	2	2.2%			5	2.4%	3	5.2%		
Vascular Repair <sup>1</sup>	0	0%	0	0%	2	1.0%	1	1.7%	0	0%
Transfusion	1	1.1%	0	0%	5	2.4%	0	0%	3	1.6%
Infection Extending Hospitalization	0	0%	0	0%	2	1.0%	0	0%	1	0.5%
Deep Vein Thrombosis	0	0%	2	2.7%	2	1.0%	0	0%	0	0%
Hematoma > 6 cm	3	3.3%	2	2.7%	14	6.7%	4	6.9%	8	4.1%
Hematoma 2-6 cm	9	9.8%	5	6.7%	22	10.6%	5	8.6%	15	7.8%
Bleeding	4	4.3%	3	4.0%	12	5.8%	1	1.7%	12	6.2%
Any Complication	19	20.7%	13	17.3%	53	25.5%	11	19.0%	34	17.6%
No Major Complication	91	98.9%	75	100%	199	95.7%	57	98.3%	189	97.9%

<sup>1</sup>Includes intravascular collagen insertions requiring vascular repair (2 patients) and surgical removal of VasoSeal® sheath found in tissue tract at 30-day follow-up (1 patient).

UB

The following describes several risks which are unique to use of the VasoSeal® VHD:

- Use of the device may lead to entry of the tissue dilator into the artery and/or intravascular collagen insertion. Insertion of the tissue dilator into the artery may enlarge the puncture sufficiently to permit entry of the collagen into the artery. Intravascular collagen insertion may lead to obstruction of the artery.
- Excessive resistance encountered during advancement of the tissue dilator or sheath or during collagen deployment may result in the inability to insert the collagen plug into the tissue tract. This may result in the need to discontinue the procedure and to manually compress the site until hemostasis is achieved. Extended bleeding time and/or complications may result.
- The device may fail to achieve hemostasis once the collagen is inserted. This would result in the need to manually compress the site until hemostasis is achieved. Extended bleeding time and/or complications may result.

The VasoSeal® VHD is a collagen product. Therefore, the following potential adverse reactions associated with use of collagen hemostats should also be considered:

- allergic reaction
- foreign body reaction
- adhesion formation
- wound dehiscence
- potentiation of infection
- inflammation
- edema

## CLINICAL TRIALS

Two independent randomized controlled clinical trials [N=469 and N=157] compared VasoSeal® VHD with manual compression regarding time to hemostasis and frequency of peripheral vascular complications in both diagnostic angiography and PTCA patients. Combined, the randomized trials were conducted at five institutions in the U.S. and two in Germany and involved a total of 626 patients.

Patients had undergone angiography or PTCA procedures. Patients' ages ranged between 31 and 85 years (mean age of PTCA = 61 and angiography = 62). Seventy-three per cent were male. Exclusion criteria included patients who were obese, had platelet disorders, experienced hematoma prior to sheath removal, were admitted for emergency angioplasty, were pregnant, had known allergies to beef or collagen products or elevated blood pressure (>140/90 mmHg) which could not be controlled by drug therapy.

For PTCA, 193 patients were assigned to manual compression and 208 patients to VasoSeal® VHD. An additional 58 PTCA patients were assigned to a group which received VasoSeal® VHD immediately following sheath removal and, as such, were highly anticoagulated (ACT > 300). For angiography, 75 patients were assigned manual compression and 92 patients were assigned VasoSeal® VHD. Of the 358 patients treated with VasoSeal® VHD, 266 (74%) were post PTCA, 92 (26%) were post diagnostic angiography, and most patients had 8F (79%) or 7F (18%) procedural sheaths. There were no clinically relevant differences in baseline or procedural characteristics between the VasoSeal® VHD and manual compression groups.

YH

In suitable diagnostic angiography and PTCA patients, use of the VasoSeal® VHD resulted in a statistically significantly shorter time to hemostasis compared to manual compression. Average time to hemostasis for VasoSeal® angiography vs. manual compression patients was 5 vs. 18 minutes, respectively. Average time to hemostasis for VasoSeal® PTCA vs. manual compression patients was 7 vs. 31 minutes, respectively. Highly anticoagulated PTCA patients who received VasoSeal® VHD had an average time to hemostasis of 13 minutes. There was no clinically relevant difference in the incidence of peripheral vascular complications among any of the VasoSeal® cohorts compared to their manual compression control groups, although 2 cases of intravascular collagen insertion were reported in VasoSeal® patients. VasoSeal® VHD, therefore, is safe and effective in patients who have undergone angiography or PTCA procedures using an 8F or smaller procedural sheath and facilitates immediate sheath removal in PTCA patients.

### CLINICAL PROCEDURE

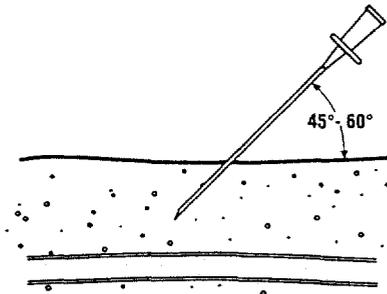
The following instructions provide technical direction but do not obviate the necessity of formal training in the use of VasoSeal® VHD.

#### General Disclaimer

Instructions and references concerning measurements used in positioning the VasoSeal® VHD are designed to give the physician guidance. Physician judgement should be exercised at all times.

#### Examination of Product

After carefully inspecting the VasoSeal® VHD package for damage to the sterile barrier, remove the device from the package.



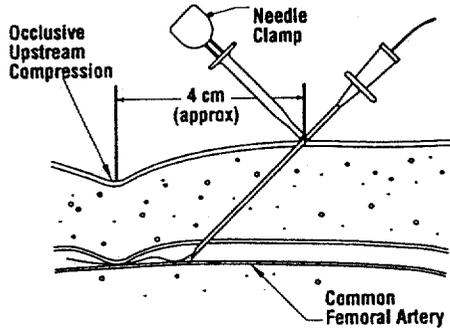
#### Arterial Puncture Consideration

In order to optimize placement of the VasoSeal® collagen, the following two points should be observed when performing the initial arterial puncture.

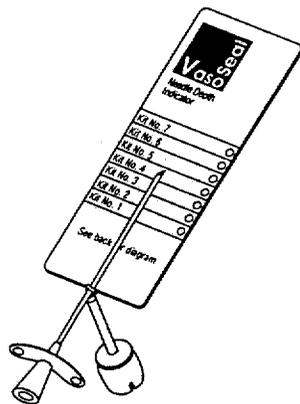
1. Puncture the femoral artery 3-4 cm below the inguinal ligament. This provides enough room between the puncture site and the inguinal ligament to allow compression of the artery and placement of the sheath without kinking. Puncture of the superficial femoral artery should be avoided.
2. Puncture the skin and artery at a 45-60 degree angle. This allows for placement of catheters and promotes proper placement of the VasoSeal® collagen on the artery.

### Arterial Depth Measurement

Use the VasoSeal® Needle Depth Indicator Kit which is supplied separately.

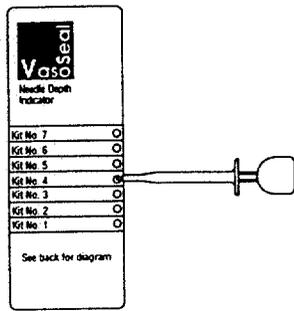


1. Prior to removing the needle from the artery, place the Needle Depth Indicator Kit clamp on the needle at the skin surface to mark the distance from the skin surface to the artery. When placing the needle clamp, occlusively compress the artery approximately 3-4 cm above the point where the needle enters the artery. Occlusive compression is defined as manual, occlusive pressure intended to be sufficient to restrict blood flow to avoid leakage from the arterial puncture site.



2. Place the needle on the VasoSeal® color card and note the color indicated at the needle tip. If the tip of the needle falls on a black line, choose the lower numbered kit. If the tip of the needle falls outside of the range of available kits, do not use VasoSeal® VHD.

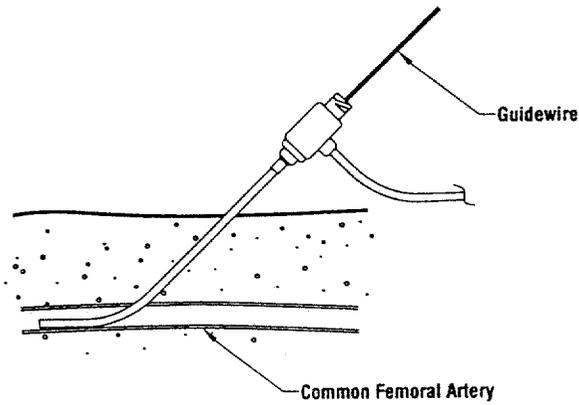
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3. Attach the clip to the card at the indicated color and note the color in the patient's record. Choose the VasoSeal® kit which corresponds to the color determined by the arterial depth measurement using the Needle Depth Indicator Kit.

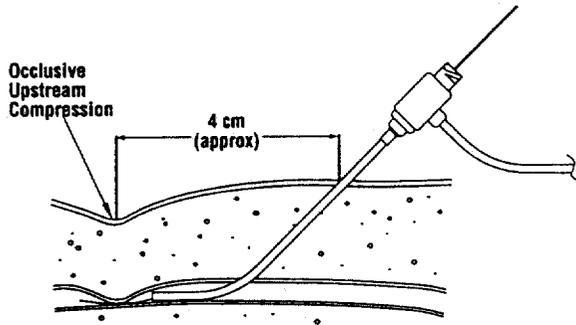
### VASOSEAL® SHEATH PLACEMENT

Assess and note peripheral circulation status prior to VasoSeal® VHD use.

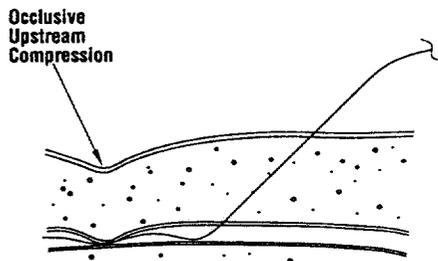


1. Before removing the procedural sheath, insert the 45 cm .038" guidewire, using the guidewire introducer (not pictured), into the sheath.

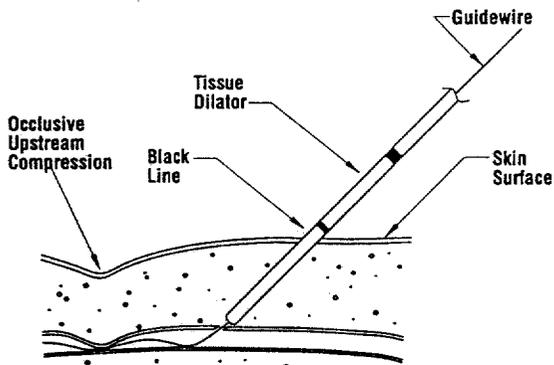
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2. Occlusively compress the artery approximately 3-4 cm above the puncture site in order to avoid kinking of the VasoSeal® sheath. Maintain occlusive compression for the remainder of the VasoSeal® insertion procedure.



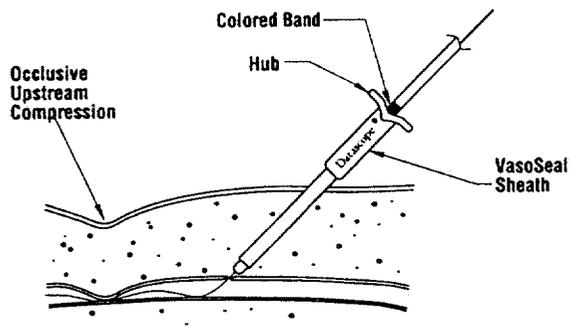
3. Remove the sheath used during the procedure and guidewire introducer, leaving the guidewire in place.



4. Insert the **blunt** tip of the tissue dilator over the guidewire as opposed to the pointed end of the dilator. Advance the tissue dilator to the point where increased resistance is felt, which should be approximately at the black line. Proceed with caution. Resistance may not always be felt. If resistance is not felt, discontinue the procedure. Do not advance the dilator beyond the black line.

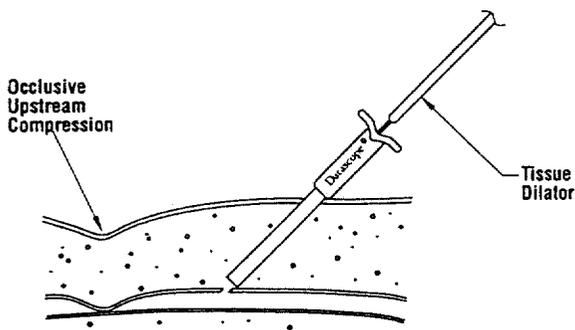
If excessive resistance is met during the insertion of the tissue dilator, discontinue the procedure, remove the dilator and guidewire and manually compress until hemostasis is achieved.

In the event the tissue dilator enters the artery lumen, discontinue the procedure and manually compress to achieve hemostasis. It is possible that the tissue dilator may expand the arterial puncture sufficiently to permit entry of the collagen hemostat.



5. Advance the VasoSeal® sheath over the tissue dilator until the proximal opening in the hub of the VasoSeal® sheath is aligned with the colored band on the tissue dilator. While advancing the sheath, maintain the position of the dilator.

If excessive resistance is met during the insertion of the VasoSeal® sheath, discontinue the procedure, remove the sheath, dilator and guidewire and manually compress until hemostasis is achieved.

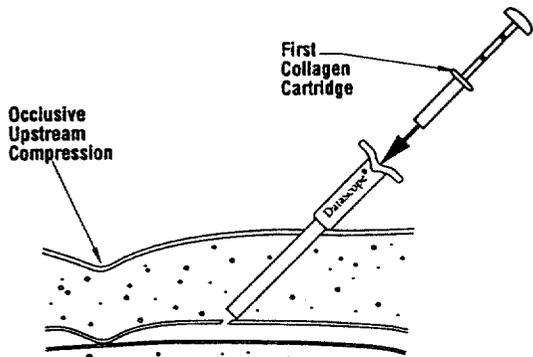


6. Remove the tissue dilator and guidewire leaving the VasoSeal® sheath in position. Carefully maintain position of the VasoSeal® sheath to ensure proper positioning of the collagen.

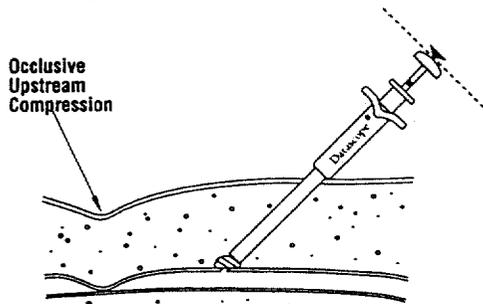
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### VASOSEAL® COLLAGEN DELIVERY

Inspect both collagen cartridges to ensure the collagen is not protruding out of the cartridge. In the event collagen is protruding from the cartridge, gently push the collagen back into the cartridge.



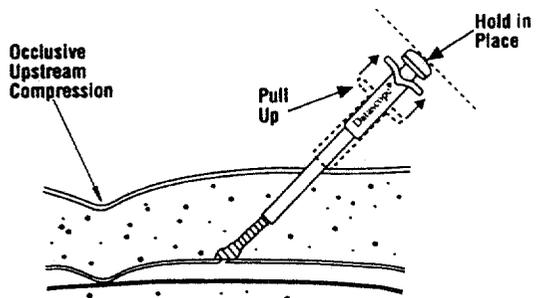
1. Insert the first collagen cartridge completely into the VasoSeal® sheath.



2. With a continuous motion and firm pressure, advance the plunger of the cartridge. At the point resistance is felt, approximately between the first and second marks on the plunger, stop for 3-5 seconds. Proceed with caution. Resistance may not always be felt. In any event, do not push beyond the second black mark.

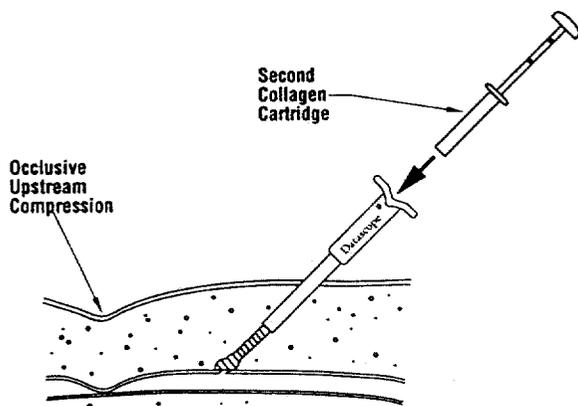
If excessive resistance is met during deployment of the collagen into the VasoSeal® sheath, discontinue the procedure and employ manual compression to achieve hemostasis.

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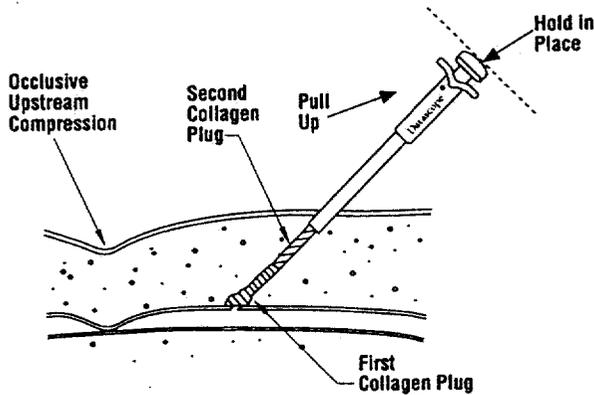


3. Maintain firm pressure on the plunger and gradually withdraw the sheath until the plunger is fully seated to complete delivery of the first plug. Remove the first collagen cartridge. Avoid lateral movement of the VasoSeal® sheath to insure proper positioning of the collagen on the arterial puncture.

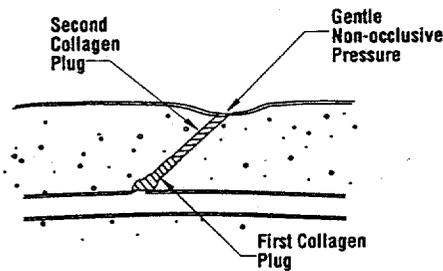
In the case of Kit #1 and Kit #2, the second collagen plug is not inserted. Proceed to step #6 of VasoSeal® Collagen Delivery Instructions.



4. Insert the second collagen cartridge completely into the VasoSeal® sheath.



5. With a continuous motion and firm pressure, advance the plunger of the second cartridge. At the point resistance is felt, approximately between the first and second black marks on the plunger, maintain firm pressure on the plunger and gradually withdraw the sheath until the plunger is fully seated to complete delivery of the second collagen plug. Remove the second collagen cartridge. Proceed with caution. Resistance may not always be felt.



6. Gently remove the VasoSeal® sheath. Apply gentle non-occlusive pressure over the puncture site until hemostasis is achieved. Do not rub or manipulate the insertion site after plug placement.

If a portion of collagen protrudes, then the portion of the collagen extending beyond the skin line must be removed. If a very small amount of collagen is protruding, tuck it under the skin being sure that the skin can close completely over the collagen. If more than a very small amount is protruding, cut it off. Cutting the collagen may be facilitated by wetting it with sterile saline. Any manipulation of the collagen must be done carefully to avoid dislodging of the collagen from the puncture site.

The onset of peripheral circulatory insufficiency after the end of the procedure that was not present prior to the beginning of the procedure, may indicate intra-luminal collagen insertion. If this is suspected, appropriate evaluative and therapeutic measures should be taken.

## POST PROCEDURE PATIENT MANAGEMENT

1. Observe that the puncture site is dry when gentle, non-occlusive pressure is released.
2. Apply an appropriate dressing to the puncture site. Use of a pressure dressing or sandbag is not recommended after the use of VasoSeal® VHD as it may displace the collagen plugs and adversely affect their positioning.
3. Assess the insertion site as per hospital procedure.

## CONTENTS:

The contents of the VasoSeal® Vascular Hemostasis Device are as follows:

- 1 11.5F Insertion Sheath/Tissue Dilator Assembly
- 1 45 cm .038" Guidewire
- 1 Guidewire Introducer
- 2 Collagen Cartridges (containing 80 - 100 mg collagen each)

Material required and available separately:

- 1 VasoSeal® Needle Depth Indicator Kit

The VasoSeal® VHD is available in seven kits which are color coded by increasing sheath length as follows:

- |                |                |
|----------------|----------------|
| Kit 1 = Yellow | Kit 5 = Purple |
| Kit 2 = Blue   | Kit 6 = Gray   |
| Kit 3 = Red    | Kit 7 = Orange |
| Kit 4 = Green  |                |

- Sterile unless package opened or damaged.
- Single use only. DO NOT re-sterilize. Autoclaving will inactivate the collagen in the device.
- Nonpyrogenic
- The device should be stored in a cool, dry place.

**Limited Warranty:**

Datascope Corp. warrants that the VasoSeal® Vascular Hemostasis Device is free from defects in workmanship and materials until the expiration date is reached. Datascope Corp. shall not be liable for any incidental, special or consequential loss, damage, or expense directly arising from the use of this product. Liability under this warranty and the buyer's exclusive remedy is limited to replacement of the product which, under normal use and services, shall have been found by the Company to have been defective in materials or workmanship. It shall be the buyer's obligation to return any such product to the Company for examination for replacement liability.

No agent, employee, or representative of Datascope Corp. has any authority to bind Datascope Corp. to any affirmation, representation, or warranty concerning its products, and any affirmation, representation, or warranty made by the agent, employee, or representative shall not be enforceable by the buyer.

**THIS WARRANTY IS EXPRESSLY IN LIEU OF ANY OTHER EXPRESSED OR IMPLIED WARRANTIES, INCLUDING ANY IMPLIED WARRANTY OF MERCHANTABILITY OR FITNESS, AND OF ANY OTHER OBLIGATION ON THE PART OF THE SELLER.**

Damage to any product or parts through misuse, neglect, accident, or by affixing any nonstandard accessory attachments or by any customer modification voids this warranty. Datascope Corp. makes no warranty of their respective manufacturers.

A condition of this warranty is that this equipment or any accessories which are claimed to be defective be returned, when authorized by Datascope, freight prepaid, to Datascope Corp., 14 Philips Parkway, Montvale, New Jersey 07645. Datascope Corp. shall not have any responsibility in the event of loss or damage in transit.

VasoSeal is a registered trademark of Datascope Corp.



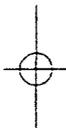
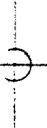
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*Collagen Products Division  
Bioplex Corp., a subsidiary of Datascope Corp.  
14 Philips Parkway,  
Montvale, NJ 07645  
P/N 104.1.4006A*

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## INSTRUCTIONS FOR USE

All Instructions Should Be  
Read Before Use



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## INSTRUCTIONS FOR USE

### VASOSEAL® Vascular Hemostasis Device

**Caution: Federal (USA) law restricts this device to sale by or on the order of a physician.**

### DEVICE DESCRIPTION

The VasoSeal® Vascular Hemostasis Device (VHD) contains an 11.5F insertion sheath/tissue dilator assembly, a 45 cm (.038") guidewire, a guidewire introducer and two cartridges each containing an 80-100 mg plug of purified bovine collagen. The device permits delivery of the collagen into the tissue tract created by removal of a sheath device and onto the exterior surface of the artery. The collagen interacts with platelets in order to create a hemostatic seal directly over the puncture wound in the artery. The VasoSeal® VHD is available in seven kits which are color coded by length of the insertion sheath.

VasoSeal® Needle Depth Indicator Kit, which is available separately, is required for the selection of the appropriate VasoSeal® Kit. The Needle Depth Indicator Kit consists of a needle clamp and a measuring card.

The collagen is sterile, nonpyrogenic, and absorbable.

### INDICATIONS

The VasoSeal® VHD is indicated for use in reducing time to hemostasis at the femoral arterial puncture site in patients who have undergone diagnostic angiography or percutaneous transluminal coronary angioplasty (PTCA) procedures using an 8 French or smaller procedural sheath. The VasoSeal® VHD is also indicated for use in PTCA patients when immediate sheath removal is desired.

### CONTRAINDICATIONS

VasoSeal® VHD is contraindicated in patients in whom Needle Depth Indicator measurements are outside of the range indicated on the Needle Depth Measurement Card.

### WARNINGS

As with any foreign substance, use of VasoSeal® collagen in contaminated sites may potentiate infection.

### PRECAUTIONS

#### Special Patient Populations

The safety and effectiveness of the VasoSeal® VHD has not been established in the following patient populations:

- Patients in whom procedural sheaths larger than 8 French have been used.
- Patients who have known allergies to beef products, collagen and/or collagen products.
- Patients with preexisting autoimmune diseases.

## INSTRUCTIONS FOR USE

### VASOSEAL® Vascular Hemostasis Device

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- Patients who have known allergies to beef products, collagen and/or collagen products.
- Patients with preexisting autoimmune diseases.

- Patients having a bleeding disorder, including thrombocytopenia (< 100,000 platelet count), thrombasthenia, von Willebrand's disease or anemia (Hgb < 10 mg/dl, Hct < 30).
- Patients who are morbidly obese.
- Patients with antegrade punctures.
- Patients with hematomas (>6 cm) present prior to sheath removal.
- Patients with elevated blood pressures (>140/90 mmHg) which cannot be controlled with drug therapy.
- Patients punctured through a vascular graft.
- Patients younger than 18 or older than 80 years of age.
- Patients that are pregnant or lactating.
- Patients with peripheral vascular disease.

The collagen in the VasoSeal® VHD is inactivated by autoclaving and, therefore, should not be resterilized.

The VasoSeal® VHD is for single use only and should not be reused in any manner.

The VasoSeal® procedure should only be performed by physicians possessing adequate training in the use of the device, e.g., participation in a VasoSeal® physician training program or equivalent.

The VasoSeal® procedure should be performed by two people.

While the safety and effectiveness of the VasoSeal® VHD has been demonstrated in highly anticoagulated patients, hemostasis times may be longer in such patients than in ones who are not highly anticoagulated.

In the case of resistance to advancement of the tissue dilator or sheath (which may be due to scarred subcutaneous tissue) or excessive resistance during collagen deployment (which may be due to sheath kinking or tearing) discontinue the procedure and manually compress until hemostasis is achieved.

If the tissue dilator is advanced too far, it may expand the arterial puncture sufficiently to permit entry of the collagen hemostat into the artery. In the event the tissue dilator enters the artery lumen, discontinue the procedure and manually compress to achieve hemostasis.

In the event that the proper procedure for positioning of the collagen material cannot be followed, discontinue the procedure and initiate manual compression to achieve hemostasis. Reasons for discontinuing procedure include, but are not limited to, the following situations:

- The Needle Depth Indicator Kit is not available.
- The VasoSeal® sheath has been damaged.

In the event that hemostasis is not achieved following delivery of VasoSeal® collagen, apply manual compression over the puncture site in order to achieve hemostasis.

The onset of peripheral circulatory insufficiency after the procedure that was not present prior to the beginning of the procedure may indicate intra-luminal positioning of collagen. If this is suspected, appropriate evaluative and therapeutic measures should be taken.