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SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
DIVISION DE NUEVAS CREACIONES

E. S. D.

Ref.: Expediente No. 07-033.225
Solicitud de Patente a nombre de
Ethicon, Inc.

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



No. 07-033225- -00001-0000

Fecha: 2007-05-08 16:48:15 Dep. 2020 NUECREACIONES
Tra. 2 PATENTES Eve: 1 REGDEPOSITO
Act. 329 CTOINFORMACION Folios: 186

Yo, JIMENA ESCOBAR URIBE, identificada como aparece al pie de mi firma, domiciliada en la Carrera 11 A No. 94-76, of. 305, obrando como apoderada de la sociedad **Ethicon, Inc.**, domiciliada en Somerville, New Jersey, Estados Unidos de América, solicitante de la patente de la referencia, atentamente me permito presentar copias certificadas de la solicitudes de patente números: **11/554,849** presentada en Estados Unidos de América el día 31 de octubre de 2006 y **11/395,604** presentada en Estados Unidos de América el día 31 de marzo de 2006, con las debidas traducciones de lo pertinente.

Señor Superintendente,


JIMENA ESCOBAR URIBE
C.C.39.779.452 de Usaquén
T.P. 68228
Cód. 5376

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ESTADOS UNIDOS DE AMERICA
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28 de marzo de 2007

La presente es para certificar que el anexo es una copia fiel de los registros de la Oficina de Patentes y Marcas de los Estados Unidos, de los documentos de la solicitud de patente identificada más adelante, que cumplieron con los requerimientos para concederse una fecha de presentación de acuerdo con 35 USC 111.

Número de Solicitud: 11/554,849

Fecha de Presentación: 31 de octubre de 2006

EL CÓDIGO DEL PAÍS Y EL NÚMERO DE SU SOLICITUD DE PRIORIDAD, PARA SER USADA EN LA PRESENTACIÓN EXTRANJERA BAJO EL CONVENIO DE PARÍS ES US11/554,849.

Por la autoridad de
Bajo el Secretario de Comercio para la Propiedad Intelectual y el Director de la
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APPLICATION THAT MET THE REQUIREMENTS TO BE GRANTED A
FILING DATE UNDER 35 USC 111.**

APPLICATION NUMBER: 11/554,849

FILING DATE: October 31, 2006

**THE COUNTRY CODE AND NUMBER OF YOUR PRIORITY
APPLICATION, TO BE USED FOR FILING ABROAD UNDER THE PARIS
CONVENTION, IS US11/554,849**

**By Authority of the
Under Secretary of Commerce for Intellectual Property
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**P. SWAIN
Certifying Officer**

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UTILITY PATENT APPLICATION TRANSMITTAL (only for new nonprovisional applications under 37 CFR 1.53(b))		Attorney Docket No. ASP-5042USCIP First Inventor Charles G. Roberts Title A METHOD AND SYSTEM FOR PRION INACTIVATION
APPLICATION ELEMENTS See MPEP Chapter 600 concerning utility patent application contents.		ADDRESS TO: Commissioner for Patents Box Patent Application Washington, DC 20231
1. ☒ Fee Transmittal Form (e.g., PTO/SB/17) (submit an original and a duplicate for fee processing) 2. ☐ Applicant claims small entity status. 3. ☒ Specification [Total Pages 49] (Preferred arrangement set forth below) - Descriptive Title of the Invention - Cross Reference to Related Applications - Statement Regarding Fed sponsored R&D - Reference to sequence listing, a table, or a computer program listing appendix - Background of the Invention - Brief Summary of the Invention - Brief Description of the Drawings (if filed) - Detailed Description - Claim(s) - Abstract of the Disclosure 4. ☒ Drawing(s) (35 USC 113) [Total Sheets 25] 5. Oath or Declaration [Total Pages] a. ☐ Newly executed (original or copy) b. ☐ Copy from a prior application (37 CFR 1.63(d)) (for continuation/divisional with Box 18 completed) i. ☐ DELETION OF INVENTOR(S) Signed statement attached deleting inventor(s) named in the prior application, see 37 CFR 1.63(d)(2) and 1.33(b). 6. ☐ Application Data Sheet. See 37 CFR 1.76		7. ☐ CD-ROM or CD-R in duplicate, large table or Computer Program (Appendix) 8. Nucleotide and/or Amino Acid Sequence Submission (if applicable, all necessary) a. ☐ Computer Readable Form (CRF) b. ☐ Specification Sequence Listing on: i. ☐ CD-ROM or CD-R (2 copies); or ii. ☐ paper c. ☐ Statement verifying identity of above copies ACCOMPANYING APPLICATION PARTS 9. ☐ Assignment Papers (cover sheet & document(s)) 10. ☐ 37 CFR 3.73(b) Statement ☐ Power of Attorney (when there is an assignee) 11. ☐ English Translation Document (if applicable) 12. ☐ Information Disclosure Statement (IDS)/PTO-1449 ☐ Copies of IDS Citations 13. ☐ Preliminary Amendment 14. ☐ Return Receipt Postcard (MPEP 503) (Should be specifically itemized) 15. ☐ Certified Copy of Priority Document(s) (if foreign priority is claimed) 16. ☐ Request and Certifications under 35 U.S.C. 122 (b)(2)(B)(i). Applicant must attach form PTO/SB/35 or its equivalent. 17. ☐ Other
18. ☐ If a CONTINUING APPLICATION, check appropriate box and supply the requisite information below and in a preliminary amendment, or in an Application Data Sheet under 37 CFR 1.76: ☐ Continuation ☐ Divisional ☒ Continuation-in-Part (CIP) of prior application No.: 11/395,604, filed March 31, 2006. Prior application information: Examiner Unassigned Group Art Unit: Unassigned For CONTINUATION or DIVISIONAL APPS only: The entire disclosure of the prior application, from which an oath or declaration is supplied under Box 5b, is considered a part of the disclosure of the accompanying continuation or divisional application and is hereby incorporated by reference. The incorporation <u>can only</u> be relied upon when a portion has been inadvertently omitted from the submitted application parts.		
19. CORRESPONDENCE ADDRESS ☒ Customer Number or Bar Code Label 000027777 or ☐ Correspondence Address below Name: Philip S. Johnson, Esq. Address: Johnson & Johnson One Johnson & Johnson Plaza New Brunswick, NJ 08933-7003 USA		
20. TELEPHONE CONTACT Please direct all telephone calls or telefaxes to Andrew C. Farmer at: Telephone: (732) 524-2825 Fax: (732) 524-2808		
21. SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT REQUIRED		
NAME	Andrew C. Farmer Reg. No. 35,868	
SIGNATURE	/Andrew C. Farmer/	
DATE	October 31, 2006	

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FEE TRANSMITTAL	<i>Complete if Known</i>	
	Application Number	New Application
	Filing Date	Herewith
	First Named Inventor	Charles G. Roberts
	Group Art Unit	N/A
	Examiner Name	N/A
	Attorney Docket Number	ASP-5042USCIP

FEE CALCULATION

CLAIMS AS FILED

(1)	(2)	(3)	(4)	(5)
FOR:	NUMBER FILED	NUMBER EXTRA	RATE	BASIC FEE \$300.00
TOTAL CLAIMS	53 - 20 =	33	x 50.00	\$1,650.00
INDEPENDENT CLAIMS	2 - 3 =	0	x 200.00	\$ 0.00
SEARCH FEE	NA	NA	NA	\$ 500.00
EXAMINATION FEE	NA	NA	NA	\$ 200.00
APPLICATION SIZE FEE If the specification and drawings exceed 100 sheets of paper, the application size fee due is \$250 (\$125 for small entity) for each additional 50 sheets or fraction thereof. See 25 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).	74 - 100 =	/50	x 250.00 (If the specification and drawings exceed 100 sheets of paper, for each additional 50 sheets or fraction thereof)	\$
MULTIPLE DEPENDENT CLAIMS	☐	N/A	\$360.00	

METHOD OF PAYMENT

- ☒ Please charge Deposit Account No. 10-0750/ASP5042USCIP/ACF in the amount of \$1950.00.
- ☒ The Commissioner is hereby authorized to charge any additional fees which may be required in connection with the filing of this communication, or credit any overpayment, to Account No. 10-0750/ASP5042USCIP/ACF.

SUBMITTED BY:			<i>Complete (if applicable)</i>
Typed or Printed Name	Andrew C. Farmer		Reg. No. 35,868
Signature	/Andrew C. Farmer/	Date: 10/31/06	Deposit Account No. 10-0750

Electronic Acknowledgement Receipt

EFS ID:	1284284
Application Number:	11554849
International Application Number:	
Confirmation Number:	6043
Title of Invention:	A METHOD AND SYSTEM FOR PRION INACTIVATION
First Named Inventor/Applicant Name:	Charles G. Roberts
Customer Number:	27777
Filer:	Ruby T. Hope/Amy Mahaffey
Filer Authorized By:	Ruby T. Hope
Attorney Docket Number:	ASP-5042USCIP
Receipt Date:	31-OCT-2006
Filing Date:	
Time Stamp:	14:48:36
Application Type:	Utility

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Payment was successfully received in RAM	\$2080
RAM confirmation Number	42
Deposit Account	100750
The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows: Charge any Additional Fees required under 37 C.F.R. Section 1.16 and 1.17	

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)	Multi Part /.zip	Pages (if appl.)
1	Drawings	aspdwgs.PDF	316986	no	25

Warnings:

Information:

2	Specification	ASP5042USCIPspec.pdf	362323	no	49
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Warnings:

Information:

3		ASP5042USCIPTransmittal.pdf	331308	yes	2
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Multipart Description/PDF files in .zip description

Document Description	Start	End
Transmittal letter	1	1
Fee Worksheet (PTO-875)	2	2

Warnings:

Information:

4	Fee Worksheet (PTO-875)	fee-info.pdf	8411	no	2
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Information:

Total Files Size (in bytes): 1019028

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

A METHOD AND SYSTEM FOR PRION INACTIVATION

This application is a continuation-in-part of U.S. Application Serial No. 11/395,604 filed March 31, 2006, the entire contents of which are hereby incorporated by reference.

FIELD OF THE INVENTION

The invention relates to treatment of articles, and more particularly to treatment of articles to inactivate prions thereon.

BACKGROUND OF THE INVENTION

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Most medical instruments are sterilized prior to use. Most are sterilized and sold in protective packaging to maintain their sterile state until the package is opened and the instrument is used in a medical procedure. Some instruments are re-used and must be sterilized prior to such re-use. Common methods of sterilization include high temperature steam, irradiation, and chemical vapors such as ethylene oxide and hydrogen peroxide.

Prions are proteinacious infectious agents which cause similar fatal brain diseases, known as transmissible spongiform encephalopathies (TSEs). These diseases include Creutzfeldt-Jakob disease (CJD) in humans, Bovine Spongiform Encephalopathy (BSE) in cattle, also known as "mad cow" disease, Scrapie in sheep, and Wasting disease in elk and deer. Creutzfeldt-Jakob variant disease (CJDv)

in humans is believed to be caused by the same proteins which cause BSE in cattle. The prions are believed to be an abnormal form of a protein commonly found in the host. However, unlike the normal form of the protein, the
5 abnormal proteins accumulate, particularly in neural tissue, eventually causing neural cell death.

Common sterilization methods have not been successful in rendering prions non-infectious. Given that prions
10 contain no DNA or RNA they are typically not considered alive and cannot be killed in the conventional sense in which one thinks of sterilization of articles by killing infections microorganisms thereon. Rather, the goal is to inactivate the prion in some manner, such as by breaking
15 one or more of its chemical bonds, to leave it unable to cause prion disease such as CJD or CJDv in a host.

The generally accepted methodology for inactivating prions involves treatment with solutions having extremely
20 high pH and temperature in an effort to denature the prion. The manner in which a prion is folded tends to make denaturing the prion using typical protein denaturing agents ineffective. The elevated temperature and pH of the accepted methodology is often quite damaging to the
25 instruments.

It had been thought that sterilization systems which employ hydrogen peroxide vapor and or hydrogen peroxide vapor coupled with plasma would be unable to inactivate
30 prions. Tests were run on a typical system in which a 59% solution of hydrogen peroxide is admitted into a sterilization chamber under vacuum conditions to create an effective sterilizing vapor of hydrogen peroxide and in which the vapor is at one point excited into the plasma

stage. This methodology failed to sufficiently inactivate prions on the instruments to render them non-infectious.

Surprisingly, the present inventors have found that application of hydrogen peroxide vapor of higher concentrations and/or higher plasma density is effective in inactivating prions and rendering an article so treated non-infections for prion diseases.

SUMMARY OF THE INVENTION

A method of inactivating prions according to the present invention comprises the steps of: placing an article having a quantity of prions thereon into a sterilization chamber; lowering pressure in the sterilization chamber to a pressure below the vapor pressure of hydrogen peroxide; admitting a solution comprising hydrogen peroxide into the sterilization chamber and contacting the article with hydrogen peroxide vapor; and inactivating prions in the chamber through contact between the prions and the hydrogen peroxide vapor.

Preferably, the concentration of the hydrogen peroxide in the solution admitted into the chamber exceeds 70 percent, more preferably 75 percent, more preferably 80 percent, more preferably 85 percent, and most preferably exceeds 90 percent.

Preferably, the temperature of the article during the step of contacting the article with hydrogen peroxide vapor exceeds 30 degrees Celsius, more preferably 35

degrees Celsius, more preferably 40 degrees Celsius, and most preferably exceeds 45 degrees Celsius.

In one aspect of the invention, the method further
5 comprises exciting the hydrogen peroxide vapor into the plasma phase and contacting the prions with the hydrogen peroxide in the plasma phase. Preferably, the plasma density is at least 10 milliwatts/cm³, more preferably 20 milliwatts/cm³, more preferably 30 watts/cm³, more
10 preferably 40 watts/cm³, and most preferably at least 50 milliwatts/cm³.

Preferably, the plasma is in contact with the prions for at least 2 minutes, more preferably 3 minutes, and
15 most preferably at least 4 minutes.

Preferably, the plasma is generated between an anode and a cathode and wherein a gap therebetween is less than 0.6 inches, perhaps less than 0.5 inches. A gap of about
20 0.5 inches is also preferred. Preferably, a minimum distance between the prions and the closer of the anode and electrode is 1.5 inches, more preferably one inch. The minimum distance between the prions and the anode may be one inch or less.

25

Preferably, the hydrogen peroxide also effects sterilization of the article.

The concentration of at least a portion of the
30 hydrogen peroxide can be increased prior to contacting the prions therewith, preferably by selectively removing water from the solution and exhausting that water through the sterilization chamber.

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Gases surrounding the prions can be excited into the plasma phase and then contacted with the prions.

The steps of steps of lowering pressure in the sterilization chamber and admitting the solution into the sterilization chamber comprise a cycle and wherein the cycle is repeated one or more times.

Preferably, the hydrogen peroxide vapor which contacts the article has a concentration of 10 mg/L or more, preferably 15 mg/L or more, preferably 20 mg/L or more, most preferably 25 mg/L or more.

Preferably, the method further includes the step of condensing a portion of the hydrogen peroxide vapor onto the article and wherein the concentration of that condensed hydrogen peroxide is at least 80% hydrogen peroxide by weight, more preferably at least 85%, more preferably at least 90% and most preferably at least 95%. Preferably at least a portion, if not all, of the hydrogen peroxide which has condensed onto the article is re-vaporized by pumping the chamber down to a lower pressure.

A method, according to the present invention, of inactivating prions comprises the steps of: placing an article having a quantity of prions thereon into a sterilization chamber; contacting the article with a plasma to effect inactivation of the prions. Preferably, the plasma is formed from a gas comprising hydrogen peroxide. Preferably, the plasma density is at least 10 milliwatts/cm³, more preferably 20 milliwatts/cm³, more preferably 30 watts/cm³, more preferably 40 watts/cm³, and most preferably at least 50 milliwatts/cm³. The plasma

density is measured between an anode and electrode when so generated.

5 BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a block diagram of a sterilization system according to the present invention;

10 FIG. 2 is a block diagram of a vaporizer and diffusion path of the sterilization system of FIG. 1;

FIG. 3 is a block diagram of an alternate embodiment of a sterilization system according to the present
15 invention;

FIG. 3A is a block diagram of an alternative embodiment of a sterilization system according to the present invention.

20 FIG. 3B is a sectional view taken along lines 3B--3B of FIG 3A;

FIG. 4 is a block diagram of an alternate embodiment of a sterilization system according to the present
25 invention;

FIG. 5 is a block diagram of an alternate embodiment of a sterilization system according to the present
invention;

30 FIG. 6 is a section view taken along lines 6--6 of FIG. 5;

FIG. 7 is a block diagram of an alternate embodiment of a sterilization system according to the present invention;

5 FIG. 8 is a section view taken along lines 8--8 of FIG. 7;

FIG. 9 is a block diagram of a sterilization system according to the present invention;

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FIG. 10 is a cut-away view of an outlet condenser/vaporizer for use in the system of FIG. 9;

FIG. 11 is a cut-away view of an inlet
15 condenser/vaporizer for use in the system of FIG. 9;

FIG. 12 is a perspective view of an alternative inlet condenser/vaporizer for use in the system of FIG. 9;

20 FIG. 13 is an exploded perspective view of the condenser/vaporizer of FIG. 12;

FIG. 14 is a section view taken along lines 14--14 of FIG. 12;

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FIG. 14A is a close-up section view of the valve assembly shown in FIG. 14;

FIG. 15 is an exploded perspective view of a
30 thermoelectric heat pump and rod assembly employed in the condenser/vaporizer of FIG. 12;

FIG. 16 is an alternative sterilization system according to the present invention;

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FIG. 17 is an alternative sterilization system according to the present invention;

5 FIG. 18 is an alternative sterilization system according to the present invention;

FIG. 19 is an alternative sterilization system according to the present invention;

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FIG. 20 is a perspective view of an alternative inlet condenser/vaporizer for use in the system of FIG. 9;

15 FIG. 21 is a valve block employed in the inlet condenser/vaporizer of FIG. 20;

FIG. 22 is a cut-away view of the valve block of FIG. 21 as employed in the inlet condenser/vaporizer of FIG. 20; and

20

FIG. 23 is a flow diagram for calculating the concentration of peroxide which condenses upon the load.

25 DETAILED DESCRIPTION

FIG. 1 shows in block diagram form a sterilization system 10 which is effective not only in killing traditional infectious microorganisms such as bacteria and viruses, but has also been shown to be effective in inactivating prions. It comprises in gross a sterilization chamber 12, a vaporizer 14, and a vacuum pump 16. The vacuum pump is capable of drawing a vacuum on the chamber, preferably as low as 0.5 torr. Between the

vacuum pump 16 and the chamber 12, is preferably located at throttle valve 18 and optionally an orifice plate 20. The throttle valve 18 preferably also has good shut-off capability. A pressure gauge 22, preferably located
5 adjacent to the throttle valve 18, shows the vacuum in the chamber 12. A vent valve 23 employing a HEPA antimicrobial filter allows clean sterile air to enter the chamber 12. The vaporizer 14 connects to the chamber 12 by means of an elongated diffusion path 24. Turning also
10 to FIG. 2, the diffusion path 24 incorporates temperature control elements 26 to control the temperature along the diffusion path 24.

Vaporizers suitable for vaporizing a liquid sterilant
15 such as hydrogen peroxide solution are known in the art. Kohler et al. U.S. Patent No. 6,106,772 and Nguyen et al. U.S. Patent Application No. 09/728,973 filed December 10, 2000, both incorporated herein by reference, illustrate vaporizers suitable for the present application. In its
20 simplest form the vaporizer can comprise a small chamber into which the liquid hydrogen peroxide solution is injected. The low pressure in the vaporizer caused by the vacuum in the chamber causes the hydrogen peroxide solution to vaporize.

25
Preferably, the vaporizer 14 itself incorporates heating elements 28 which control the temperature in the vaporizer to optimize the vaporization process. Preferably, where the vaporizer 14 connects to the
30 diffusion path 24 some form of thermal insulation 30 provided at the interface so that the high temperatures of the vaporizer 14 will not unduly affect the temperature in the diffusion path 24. The vaporizer 14 and diffusion path 24 are preferably formed of aluminum; the thermal

insulation 30 can take the form of a polyvinyl chloride (PVC) joint connecting the two together.

Further, it is preferable to include a heater 32 inside the chamber 12, preferably near a lower portion of the chamber 12 for revaporizing condensed hydrogen peroxide inside the chamber 12.

The chamber 12 preferably includes a mechanism (not shown) to create a plasma therein. Such mechanism can include a source of radio or low frequency energy as described by Jacobs et al. U.S. Patent No. 4,643,867, or by Platt, Jr. et al. in published U.S. Application Document No. 20020068012, both of which are incorporated herein by reference.

The present invention achieves its beneficial effect by allowing some of the hydrogen peroxide which is vaporized out of solution in the vaporizer 14 to condense onto the diffusion path 24. After most of the hydrogen peroxide solution has vaporized, the temperature control elements 26 raise the temperature of the diffusion path to allow the condensed hydrogen peroxide to re-vaporize. Water has a higher vapor pressure than hydrogen peroxide, thus hydrogen peroxide in the vapor condenses more easily than water. Thus, the material which condenses in the diffusion path will have a higher concentration of hydrogen peroxide than the starting concentration of the hydrogen peroxide solution in the vaporizer 14.

The temperature control elements 26 in simple form can comprise mere electric resistance heaters. In such case, the low ambient temperature of the diffusion path 24 provides the low temperature for condensing hydrogen

peroxide thereon, and the control elements 26 later heat the diffusion path 24 to re-vaporize the now more highly concentrated hydrogen peroxide from the diffusion path 24. Because the vapor pressure of hydrogen peroxide drops with lower temperatures, lower initial temperatures in the diffusion path 24 allows a lower pressure in the chamber 24 without subsequently preventing the condensation of hydrogen peroxide in the diffusion path. Lower chamber pressures promote system efficiency and thus, the temperature control elements 26 can further comprise a chilling component to lower the temperature of the diffusion path below ambient. Suitable chilling components include thermoelectric coolers or a typical mechanical refrigeration system. In such case, the diffusion path 24 would be first chilled, preferably to about 10°C, and then some time after vaporization has begun or even after it has completed, the diffusion path 24 is then heated, preferably up to 50°C or 110°C.

When vertically oriented as in FIG. 2, the diffusion path 24 can potentially cause the vaporizing sterilant to condense in cooler regions between the temperature control elements 26 and then re-vaporize as it passes the temperature control element 26.

The following example illustrates the benefits of controlling the heat in the diffusion path.

EXAMPLE 1

The efficacy tests were conducted by placing a CSR-wrapped tray (3.5"x10"x20") consisting of representative medical devices and test lumens in a 20-liter aluminum chamber (4.4"x12"x22"). A one-inch stainless steel wire

inoculated with at least 1×10^6 *Bacillus stearothermophilus* spores was placed in the center of each of the test lumens. The effects with and without temperature control of the diffusion path were investigated with both a

5 TEFLON, poly(tetrafluoroethylene) lumen having an internal diameter of 1mm and a length of 700mm, and a stainless steel lumen having an internal diameter of 1mm, and a length of 500mm. All lumens were open at both ends. Each

10 of the samples were subjected to a sterilization cycle in a 20 liter vacuum chamber, which was held at 40°C and 3 torr for 5 minutes. 1.44 ml of a 59% solution of hydrogen peroxide in water was injected at atmospheric pressure

15 into the vaporizer which was held at 60°C. The 5 minute clock then started and the chamber was pumped down to 3 torr, which took less than one minute. In one case the

20 diffusion path 24 had an initial temperature of 30°C for the first minute while the chamber was evacuated to 3 torr and was then heated to 50°C to release the condensed peroxide from the diffusion path into the chamber for the

25 remainder of the cycle while pressure was maintained at 3 torr. In the other case, the diffusion path was held at 50°C throughout the cycle. By maintaining the diffusion path at 50°C, no or little peroxide was retained in the diffusion path. Sterilization effectiveness was measured

by incubating the test samples in growth media at 55°C and checking for growth of the test organism. Table 1 shows the results of these tests.

TABLE 1

Lumen Type	ID & Length	50°C Diffusion Path Throughout Process	30°C Diffusion Path For One Minute Then increased to 50°C
Teflon	1 x 700	2/2	0/3
Stainless Steel	1 x 500	1/2	0/3

When the diffusion path temperature was maintained at high temperature throughout the process, all of the samples in the TEFLON lumen tested positive for bacteria growth, indicating failure of sterilization, and one of two samples in the stainless steel lumen tested positive. Under the same conditions, but with an initially lower temperature diffusion path which was heated starting one minute after the diffusion began, none of the samples tested positive. Condensing the peroxide in the diffusion path during the initial vaporization stage and then re-vaporizing the condensed peroxide from the diffusion path into the chamber greatly enhance the efficacy.

Additional efficiencies can be achieved by alternating cool and warm regions in the diffusion path as primarily illustrated in FIG. 2. The temperature control elements 26, in simple form heating elements, are spaced apart from one another. Also, preferably, the diffusion path 24 is vertical in this respect. As the hydrogen peroxide solution vaporizes and passes through the diffusion path 24, it is thought that it may alternately condense and re-vaporize as it passes over the heated and unheated sections of the diffusion path 24.

The diffusion path could alternatively comprise alternating heating and cooling elements.

5 The heater 32 within the chamber 12 acts similarly to the heating of the diffusion path 24. By controlling the heater 32 temperature, the peroxide can be first condensed on the heater 32 and then re-vaporized into the chamber 12 to concentrate the peroxide.

10 A preferred cycle would be a modification of a cycle described in the Wu et al. U.S. Patent No. 6,365,102, incorporated herein by reference. A series of pre-plasma energy additions with venting in-between dries moisture from the chamber 12. A vacuum is then drawn upon the
15 chamber 12 and the hydrogen peroxide solution injected into the vaporizer 14. Alternatively, the peroxide solution can also be injected at atmospheric pressure. Some of the vaporizing solution condenses upon the cool diffusion path 24. After a time sufficient for most or
20 all of the hydrogen peroxide solution to vaporize from the vaporizer 14, the diffusion path 24 is warmed by the temperature control elements 26 and the condensed hydrogen peroxide solution re-vaporizes. At about this time, the throttle valve 18 is closed and the pump 16 turned off to
25 seal the chamber 12. Much of the water fraction of the hydrogen peroxide solution has thus been drawn out of the chamber 12 by the vacuum pump 16 and the remaining hydrogen peroxide solution which re-vaporizes from the diffusion path 24, or from the heater 32 in the chamber 12
30 if present, is of a higher hydrogen peroxide concentration than the starting solution. Preferably, a computer based control system (not shown) controls the functions of the process for ease and repeatability.

The hydrogen peroxide vapor thus produced contacts an article 34 or articles 34 in the chamber 12 and effects sterilization thereof. If those articles 34 have diffusion restricted areas, such as long, narrow lumens, it may be preferable to then vent the chamber 12 and allow clean sterile air therein to drive the hydrogen peroxide vapor deeper into the diffusion restricted areas. Then the chamber 12 is again subjected to vacuum and an additional injection of hydrogen peroxide, preferably with the heating sequence on the diffusion path, is repeated. After a time period sufficient to effect sterilization of the article 34, preferably with a six-log reduction in challenge organisms such as *Bacillus stearothermophilus*, a plasma is lit within the chamber 12, thereby enhancing the sterilization and breaking down the hydrogen peroxide into water and oxygen.

Plasma is generated by inducing a voltage between an anode 35 and a cathode which in this case is the interior wall 37 of the sterilization chamber 12. The anode 35 is a sheet of perforated metal spaced apart from and electrically insulated from the interior wall 37. US Patent Application Publication No. 20040262146, published December 30, 2004, the entire contents of which are incorporated herein by reference, describes in detail a particularly efficient method for generating such a plasma. Density of the plasma is defined in the space between the anode and cathode.

The orifice plate 20 can enhance the effect of concentrating the hydrogen peroxide during its vaporization. As described in the Lin et al. U.S. Patent No. 5,851,485, incorporated herein by reference, a controlled or slow pump-down of the chamber 12 initially

draws off more water than hydrogen peroxide from solution as the water has a higher vapor pressure, thereby leaving a higher concentration hydrogen peroxide behind.

Controlling the pump-down can be difficult as vacuum pumps
5 generally do not throttle back well and throttle valves in such service are difficult to control and expensive. By placing the orifice plate 20 in the flow path to the pump 16, the amount of atmosphere from the chamber 12 exhausted by the pump 16 is limited, and by selecting a proper size
10 orifice 36 in the plate 20 can be controlled to a rate which effectively concentrates hydrogen peroxide in the chamber 12.

Turning also to FIG. 3, a system 10a, similar in most respects to the system 10 of FIGS. 1 and 2, with like part
15 numbers denoted with an "a" appended thereto, also incorporates an orifice plate 20a. However, to allow a quick pump-down of the chamber 12a, yet retain the controlled pump-down benefits of the orifice plate 20a, it incorporates two path ways from the pump 16a to the
20 chamber 12a. A first pathway 40 contains a throttle valve 42 and a second pathway 44 contains a throttle valve 46 and the orifice plate 20a. Thus, during initial pump-down the first throttle valve 42 is open leaving the pump 16a freely connected to the chamber 12a. As the chamber 12a
25 approaches the vapor pressure of water, the first throttle valve 42 is closed thereby forcing the pump 16a to evacuate through the orifice plate 20a and thus draw out of the chamber 12a at a slower, controlled rate more conducive to preferentially drawing water out of the
30 hydrogen peroxide solution and out of the chamber 12a.

Turning also to FIGS. 3A and 3B, a system 110 similar to that of FIG. 1 is shown. Here, rather than use two paths as in the system 10a of FIG. 3, a valve 112

comprises a valve body 114, a valve seat 116 and a valve element 118, such as a butterfly disc, plug or the like. An orifice 120 is provided through the valve element. Thus, when the valve 112 is open evacuation can occur quickly, and when the valve 112 is closed it can occur more slowly. Such a valve could also be employed between the vaporizer 14 and the chamber 12 to further control the preferential vaporization and removal of the water from the germicide solution.

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Turning now to FIG. 4, while highly concentration of the sterilizing vapor is helpful in achieving sterilization efficiency and efficacy, getting the vapor into contact with the items to be sterilized is also a concern. Typically, the low pressures (0.5 torr to 10.0 torr) inside of a chamber 12 promotes quick diffusion of the sterilant vapor to all areas therein.

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FIG. 4 illustrates a sterilization system 60 comprising a chamber 62 having a vaporizer 64, vacuum pump 66 and vent 68 connected thereto. Preferably, an elongated, temperature controlled diffusion path 70 as previously described connects the vaporizer 64 to the chamber 62. A throttle valve 72 and pressure gauge 74 are provided at the pump 66.

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Articles 76 to be sterilized are placed into trays or containers 78. Two types of packaging are commonly used in preparing articles 76 for sterilization. In one, the articles 76 are placed into a tray having a plurality of openings therein, and the tray is then wrapped with a material such as CSR wrap which passes sterilizing gases and blocks contaminating microorganisms. Such a tray is described in the Wu, U.S. Patent No. 6,379,631,

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incorporated herein by reference. An alternative package comprises a sealable container with several ports, preferably on top and bottom surfaces thereof, with each of the ports covered by a semi-permeable membrane which
5 passes sterilizing gases and blocks admission of contaminating microorganisms. Such a container is described in Nichols U.S. Patent No. 4,704,254, incorporated herein by reference. The first type of packaging is typically called a "tray" and the second a
10 "container." However, the term "container" as used herein is meant to refer to any container, packaging or enclosure suitable for containing articles to be sterilized in a chemical vapor environment.

15 The pump 66 connects to the chamber 62 via an exhaust manifold 80. The manifold 80 comprises one or more shelves 82 for supporting and receiving one or more containers 78 and which connect fluidly through the throttle valve 72 to the pump 66. An opening, or
20 preferably a plurality of openings 84 on the upper surfaces of the shelves 82 allow the pump 66 to draw atmosphere within the chamber 62 through the openings 84, through the manifold 80 and out through the pump 66.

25 The containers 78 preferably have openings 86 on a lower surface 88 thereon and additional openings 90 on at least one other surface. When the containers 78 are placed on the shelves 82 atmosphere being exhausted by the pump 66 is drawn in part through the openings 90 into the
30 container 78, through the container into contact with the article or articles 76 therein and then out through the openings 86 into the manifold 80 through the openings 84 therein. When the atmosphere being so exhausted contains a sterilizing gas it enhances its penetration into the

containers 78 and into contact with the articles 76 therein.

5 Sterilizing gases are so exhausted during the previously described cycle as the sterilant solution is vaporizing and immediately before the second admission of hydrogen peroxide. Such a cycle can also further provide a pump-down after some period of diffusion. After admitting the sterilant vapor the chamber 62 pressure
10 rises slightly due to the presence of additional gas therein, typically from about 0.5 torr to about 10 torr. Higher pressures are as efficient with higher load and chamber temperatures.

15 Turning also to FIGS. 5 and 6, an alternative design (in which like part numbers to those of the design of FIG. 4 are designated with a "b" appended thereto) replaces the manifold 80 of the design of FIG. 4 with a simple port 92. The port 92 is covered by a support 94 for the container
20 78, the support 94 having a plurality of openings 96 therethrough so that the chamber 62b is in fluid communication with the pump 66b through the container 78, the support 94 and the port 92. The support 94 can be removable.

25 Turning also to FIGS. 7 and 8 (in which like part numbers to those of the designs of FIGS. 4 to 6 are designated with a "c" appended thereto) shows a support 100 resting on a surface 102 in the chamber 62c through
30 which penetrates the port 92c. The support 100 surrounds the port 92c. Thus, most or all of the atmosphere being exhausted by the pump 66c passes through the container 78 into a space 104 formed between the container 78, the

support 100 and the surface 102 and then onto the pump 66c through the port 92c.

FIG. 9 discloses an alternative system in which, similar to the system of FIG. 1, a portion of the vaporized germicide solution can be condensed and the solvent, typically water, which has not condensed as quickly is removed from the atmosphere to further concentrate the germicide. The germicide is then revaporized to produce a more concentrated germicidal vapor for more efficient sterilization. The system comprises a sterilization chamber 200 containing a load 202 of items to be sterilized. A source 204 of liquid germicide solution provides the solution through a valve 206 to a first vaporizer/condenser 208 where it is vaporized and then supplied to the chamber 200. A valve 210 can be provided to isolate the vaporizer/condenser 208 from the chamber 200. The chamber 200 is also provided with a valved vent 212.

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A vacuum pump 214 provides for lowering the chamber pressure as described in reference to the previous embodiments. Between the pump 214 and the chamber 200 a second vaporizer/condenser 216 is provided for condensing the vaporized solution. Preferably valves 218 and 220 isolate the second vaporizer/condenser 216 from the pump 214 and chamber 200 respectively.

Turning also to FIG. 10 a simple version of the second vaporizer/condenser 216 preferably comprises walls 222 defining an enclosure 224 having an inlet 226 connected to the chamber 200 and an outlet 228 connected to the pump 214. A plurality of baffles 230 provides a torturous flow path 232 through the vaporizer/condenser

216. The walls 222, and potentially the baffles 230, are temperature controllable to enhance condensation of and re-vaporization of the solution.

5 A similar structure with an inlet can be employed on the first vaporizer/condenser 208 as well. Turning also to FIG. 11, a simple version of the first condenser/vaporizer 208 is illustrated. It comprises an enclosure 240 having an inlet 242 connected to the source
10 of solution 204 (not shown in FIG. 11) and an outlet 244 connected to the chamber 200 (not shown in FIG. 11). A plurality of baffles 246 provides a tortuous flow path through the first vaporizer/condenser 208. The enclosure 240 and potentially the baffles 246 are temperature
15 controllable to enhance condensation and revaporization of the solution.

 In a simple cycle, a liquid germicide solution, such as hydrogen peroxide and water is admitted into the first
20 vaporizer/condenser 208 where it is vaporized and then flows into the chamber 200 which is at a low pressure, all as described in reference to previous embodiments herein. During vaporization and for sometime thereafter pump 214 continues to exhaust atmosphere from the chamber 200. By
25 controlling temperature and pressure this preferentially vaporizes water from the solution over the hydrogen peroxide and the water vapor is extracted from the system via the pump 214 to concentrate the hydrogen peroxide solution during the vaporization phase. Additionally,
30 hydrogen peroxide, having the lower vapor pressure, will tend to condense more quickly than the water vapor in the first vaporizer/condenser 208. As the pump 214 continues to exhaust atmosphere from the chamber 200 the vaporized hydrogen peroxide solution flows out of the chamber and

into the second vaporizer/condenser 216 where a portion thereof will condense. Due to the preferential condensation of hydrogen peroxide over the water more of the water vapor will pass through the condenser 216

5 uncondensed and be exhausted via the pump 214 thus allowing further concentration of the hydrogen peroxide solution. At some point, the pump is turned off and the valve 218 closed. The condensed hydrogen peroxide within the vaporizer/condenser 216 is then re-vaporized
10 preferably by heating the condenser 216. This hydrogen peroxide will have a higher concentration for more efficient sterilization of the load 202.

Turning also to FIGS. 12 through 15, a more elaborate condenser/vaporizer 250 is illustrated. In gross, it
15 comprises an inlet manifold 252 which connects to the source of sterliant solution 204 and which provides initial vaporization, a condensing/revaporization section 254, an outlet manifold 256 and a control valve 258 via which the vaporizer/condenser 250 connects to the chamber
20 200. A resistance heater 260 affixes to the inlet manifold 252 and to the outlet manifold 256 to provide heat to assist in the initial vaporization within the inlet manifold 252 and to prevent condensation in the outlet manifold 256. Preferably, the inlet manifold 252
25 and outlet manifold 256 are formed of aluminum. Further, an insulator 262 is provided between the inlet manifold 252 and the vaporizer/revaporizer section 254.

The vaporizer/revaporizer section 254 comprises a
30 housing 264, preferably formed of aluminum, open on a first side 266 and second side 268. A first thermo-electric device 270 and second thermo-electric device 272 affix to the first side 266 and second side 268, respectively. The thermoelectric devices 270 and 272

preferably operate under the Peltier effect, although other classes of thermoelectric devices could be substituted therefor. More conventional heat pumps, such as freon or ammonia based systems can also be employed
5 with somewhat greater complexity.

A first rod assembly 274, comprising a plate 276 and a plurality of rods 278 extending normally therefrom affixes to the first thermo-electric device 270 with the
10 rods 278 extending laterally into the housing 264. A second rod assembly 280 similarly attaches to the second thermo-electric device 272 with its rods 278 extending laterally into the housing 264 in facing relationship to the first rod assembly 274. The rod assemblies 274 and 280
15 are preferably formed of aluminum.

Preferably, the rods 278 extend almost to, without touching, the opposing plate 276. Also, the rods 278 from the two rod assemblies 274 and 280 lie in a generally
20 parallel relationship with each other with a spacing therebetween designed to, along with the volume within the vaporizer/revaporizer section 254, provide a preferred flow rate of the vaporized sterliant therethrough to provide efficient condensation on to the rods 278.
25 Preferably, a flow rate is in the range of 0.1 ft/sec to 5 ft/sec, and more preferably a flow rate of 0.24 ft/sec is provided.

In a small condenser with a vapor path length of 3
30 inches, the residence time would be 1 second at a preferred velocity of 0.24 ft/sec. This residence time would be sufficient for the vaporized sterlant to interact with the cooler condenser surfaces and to condense. For a typical injection volume of 2 ml of

sterilant solution, the surface area of the
condensing/revaporization section 254 would be about 90
square inches to permit mass transfer for condensation.
High temperature at low pressure in the initial vaporizer
5 (inlet manifold 252) maintains the water and hydrogen
peroxide in the vapor phase for delivery to the
condensing/revaporization section 254. For example, a
vaporizer temperature of 70 degrees C or greater at a
pressure of 125 torr or lower ensures that a 59 wt%
10 solution of hydrogen peroxide and water will be in the
vapor phase.

As vapor enters the condensing/revaporization section
254, which has a lower temperature, the hydrogen peroxide
15 condenses on the cooler surface forming a concentrated
solution. The temperature and pressure therein determine
the concentration of the condensed solution. For example,
at 50 degrees C and 13 torr in the
condensing/revaporization section 254, the condensed
20 hydrogen peroxide concentration would be 94 wt%. At 30
degrees C and 3.8 torr, the condensed hydrogen peroxide
concentration also would be 94 wt%. As the pressure in
the condensing/revaporization section 254 is lowered, the
temperature must also be lowered to maintain the same
25 concentration of solution.

The orifice 308 offers the advantage of a more
concentrated solution by restricting the flow from the
condensing/revaporization section 254 to provide a more
30 controlled vaporization. Variations in pressure in the
condensing/revaporization section 254 and in the vaporizer
due to vacuum pump pressure fluctuations are dampened out
by the orifice 308 to prevent surges of water vapor from
carrying hydrogen peroxide droplets from the

condensing/revaporization section 254. Another advantage of flow restriction by the orifice 308 is achieving a low pressure (less than 1 torr) in the sterilization chamber 200 to improve the diffusion coefficient in lumens while maintaining a greater pressure in the vaporizer/condenser 250 to operate at a greater temperature in the condensing/revaporization section 254. Without an orifice 308, sterilization chamber 200 and vaporizer/condenser 250 pressures must both be reduced to the same low pressure together, and the condenser must be operated at a very low temperature to maintain equilibrium of the solution. A lower condenser temperature is more difficult to control and may produce ice or condensate, which requires a more expensive design to protect electrical equipment.

An O-ring 282 seals the plates 276 on the thermo-electric devices 270 and 272 against the housing 264. An aperture 284 through the housing 264 aligns with an aperture 286 through the insulator 262 to place a chamber 288 defined by the housing 264 into fluid communication with the inlet manifold 252. An outlet passage 290 in the housing 264 connects to an upper portion of the chamber 288 and to a second aperture 292 through the insulator 262 which in turn aligns with the outlet manifold 256 to place the chamber 288 in fluid communication with the outlet manifold 256. A safety thermostat 294 atop the housing 264 is wired outside of the control system to shut down heating of the vaporizer/condenser 250 above a predetermined temperature. Temperature sensors 295 and 297 measure temperature in the inlet manifold 252 and condensing/revaporization section 254 respectively. A pressure sensor 296 interfaces with the outlet manifold 256. Heat sinks 298 having fan housings attach to each of the thermo-electric devices 270 and 272.

The outlet manifold connects to a valve manifold 300 which provides three possible flow paths between the vaporizer/condenser 250 outlet manifold 256 and a valve manifold outlet 302 from the valve manifold 300. The valve manifold outlet 302 communicates with the main chamber 200. A main flow passage 304 is controlled by a valve 306 which can open to allow flow through the main passage 304 to the valve manifold outlet 302 or close to block such flow. The second passage is through an orifice 308 in an orifice plate 310 which provides a flow restriction to enhance the ability to preferentially draw water vapor from the vaporizer/condenser 250. A third potential passage is through a rupture disk 312 which is designed to rupture in case of a catastrophic overpressure within the housing chamber 288, such as in the unlikely event that an oxidizable sterliant such as hydrogen peroxide combusts therein. The orifice 308 could be moved to a position within the shut-off valve 306, similar to that described in reference to the valve element 118 in FIGS. 3A and 3B.

In operation, the main chamber is first evacuated to a low pressure sufficient to induce vaporization, such as 0.4 torr and the valve 306 is closed placing the vaporizer/condenser 250 into fluid communication with the chamber 200 solely through the orifice 308. The inlet manifold 252 is heated with the heater 260 and a quantity of sterliant solution such as a 59% hydrogen peroxide/water solution is injected into the inlet manifold 252 where it vaporizes and diffuses into the housing 264 through the apertures 286 and 284. The thermo-electric devices 270 and 272 at this time are drawing energy out of the rods 278 and dissipating it

through the heat sinks 298 thus allowing the vaporized sterilant to recondense on the rods 278.

5 The temperature of the inlet manifold 252 can be controlled to slowly vaporize the sterilant thus allowing the water to more quickly vaporize and flow through the vaporizer 250 and out through the orifice 308 to concentrate the remaining sterilant. The condenser/revaporization section 254 quite effectively
10 concentrates the sterilant such that to speed up the process a fast vaporization in the inlet manifold can be employed while still achieving a high degree of concentration.

15 The condensate on the rods 278 tends to be more highly concentrated in the sterilant. After a time, when the initial charge of sterilant solution has been vaporized and a portion thereof condensed on to the rods 278, the thermo-electric devices 270 and 272 are reversed
20 to apply heat to the rods 278 and revaporize the sterilant. At this time, the heat sink 298 will still contain heat which had been extracted during the prior step and that heat can be used by the thermo-electric devices 270 and 272 to very efficiently heat the rods 278
25 and revaporize the sterilant. This added efficiency improves the energy efficiency of the device and allows a smaller and more compact vaporize condenser 250 to provide adequate heating and cooling. After the sterilant has been revaporized, the valve 306 is opened to allow
30 efficient diffusion of the sterilant vapor into the main chamber 200.

If a second vaporizer/condenser 216 is employed, its structure preferably mimics that of the

vaporizer/condenser 250 without the inlet manifold 252. In such a system, after initial diffusion into the main chamber 200, rods within the second condenser 216 would be chilled and the pump 214 turned on to preferably extract
5 water vapor from the condensing sterilant. After a period of time when sterilant has condensed, the rods would be heated to revaporize the sterilant and the pump 214 turned off. This revaporized sterilant would have somewhat higher concentration and would then re-diffuse into the
10 chamber 200 to further enhance the sterilization process.

Other system arrangements are possible. FIG. 16 illustrates an alternative embodiment which can enhance efficiency in conserving and concentrating the germicide
15 solution. In this system, a chamber 314 containing a load 316 has a first condenser/vaporizer 318 connected to a source 320 of germicide solution and a second condenser/vaporizer 322. The first condenser vaporizer 318 is isolated from the source 320 by a valve 323 and
20 from the chamber 314 by a valve 324. It also connects to an exhaust pump 325 and is isolated therefrom via a valve 326. The second condenser vaporizer 322 is isolated from the chamber 314 by a valve 327 and connects to the pump 325 and is isolated therefrom via a valve 328. A vent 329
25 is also provided.

FIG. 17 illustrates a similar system 330 employing a single condenser/vaporizer 332 (of structure similar to the condenser/vaporizer 250 with an additional outlet)
30 connected to a sterilization chamber 334 adapted to receive a load 336 of instruments to be sterilized. A vacuum pump 338 connects to the chamber 334 via a valve 340 and to the condenser/vaporizer 332 via a valve 342. A three-way valve may substitute for valves 340 and 342. A

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source of germicidal solution 344 connects to the condenser/vaporizer 332 and the chamber 334 has a vent 346. During initial vaporization and concentration of germicide from the source 344, valve 342 is closed. After
5 the vapor is diffused into the chamber 334, valve 340 can be closed and the pump 338 used to draw vapor out of the chamber through the condenser/vaporizer 332 in its condensing mode to further concentrate the germicide. The concentrated germicide is then revaporized and diffused
10 back into the chamber 334.

The second condenser/vaporizer 216 of FIG. 9 can be used to maximize germicide utilization when running a sterilization process with two full cycles of vacuum,
15 inject, diffuse and vent. Prior to venting during the first cycle, the pump 214 is run with the condenser/vaporizer 216 being chilled to condense the germicide therein. The valves 220 and 218 are closed during the venting process. During the subsequent pump
20 down, the condenser/vaporizer is kept chilled to keep the germicide from unduly vaporizing and being carried out of the system.

The systems of FIGS. 16 and 17 allow even more of the germicide to be retained between cycles in a two cycle
25 process. Prior to venting in the first cycle germicide is condensed into the condenser/vaporizer 332. However, during the subsequent pump down it can be isolated from the pump via the valve 342 thus minimizing the tendency of
30 the pump 338 to pump the saved germicide out of the system during pump down.

In each of this type of system the steps of condensing and concentrating the vaporized germicide and

then revaporizing it can be repeated as needed to further concentrate the germicide.

FIG. 18 illustrates a system 350 plumbed in an alternative fashion. In this system 350 a condenser/vaporizer 352 connects through a valve 354 to a sterilization chamber 356 adapted to receive a load 358 and having a vent 360. A vacuum pump 362 connects to the condenser/vaporizer 352 through a valve 364, but has no separate connection to the chamber 356. A source 366 of germicide connects to the condenser/vaporizer 352.

FIG. 19 illustrates a system 370 plumbed as in FIG. 17, having a condenser/vaporizer 372 which connects through a valve 374 to a sterilization chamber 376 adapted to receive a load 378 and having a vent 380. A vacuum pump 382 connects to the condenser/vaporizer 372 through a valve 384, but has no separate connection to the chamber 356. Rather than an inlet for germicide through the condenser/vaporizer 382, a source 386 of germicide solution is provided within the chamber 376. The source can be simple such as a well containing a quantity of liquid germicide solution. Preferably, it is covered with a semi-permeable membrane or filter so that liquid germicide can not be accidentally spilled therefrom yet as the germicide vaporizes under low chamber pressures the vapors thus generated can pass through the membrane into the chamber. In both systems the condenser/vaporizer 352 or 372 concentrates the germicide via condensation and revaporization of germicide vapor as described above.

FIG. 20 illustrates a further embodiment of an inlet condenser/vaporizer 400. It is similar in most respects to that illustrated in FIG. 12. However, as shown

primarily in FIGS. 21 and 22, it features an orifice control valve 402. A valve block 404 receives an outlet control valve 406, a rupture disk 408 and the orifice control valve 404.

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FIG. 21 shows the valve block 404 in isolation and illustrates three manifold passages which connect the valve block 404 to the rest of the condenser/vaporizer 400: a large pressure relief manifold passage 410 which leads to the rupture disk 408, a smaller upper manifold passage 412 which leads to the outlet control valve 406 and a smaller lateral manifold passage 414 which leads to an orifice 416 and the orifice control valve 402.

FIG. 22 best illustrates the orifice control valve 402. A valve seat 418 on the valve block 404 surrounds the orifice 416. A valve member 420 on the orifice control valve 402 can extend toward to valve seat 418 to seal against it and block fluid communication through the orifice 416. A cleaning pin 422 penetrates the orifice 416 when the orifice control valve 402 is closed to clean the orifice 416 and keep it clear of foreign matter. An annular guide 424 connected to the valve member 420 slides within a bore 426 within the valve block 404 to properly align the cleaning pin 422 with the orifice 416. This view also illustrates a valve seat 428 for the outlet control valve 406 and a valve block outlet passage 430 which leads to the sterilization chamber (not shown in FIGS. 20 to 22).

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Operation of a sterilization cycle proceeds nearly the same as afore-described regarding the system shown in FIGS. 12 to 15. However, after the initial vaporization of the sterilant in the inlet manifold 252 (see FIG. 14)

the orifice control valve 402 is closed thereby isolating the condenser/vaporizer 400 from the sterilization chamber (not shown in FIGS. 20 to 22). This condition can be monitored most easily by monitoring the pressure within the vaporizer/condenser 400 and assuming that when a particular pressure has been reached that essentially all of the sterilant has been vaporized. Pressure in the sterilization chamber is then reduced, preferably to approximately 0.5 Torr. The outlet control valve 406 is then opened and the rods 278 (see FIG. 14) are heated to vaporize condensed sterilant and pass it through the outlet control valve 406 and outlet passage 430 to the sterilization chamber.

By lowering the pressure in the sterilization chamber prior to admitting the bulk of the sterilant it has been found that overall cycle times may be reduced. Closing the orifice control valve 402 and reducing pressure in the sterilization chamber takes additional time. However, the lower pressure provides a more favorable condition for diffusion of the sterilant into diffusion restricted areas, such as lumens, of instruments to be sterilized. It has been found that the time saved through the increased diffusion efficiency can more than offset the time lost in lowering the pressure in the sterilization chamber. Sterilization cycle speed is an important factor for sterilizer users.

Water vapor in the sterilization chamber can affect the time required to lower the pressure therein. Such water vapor typically arises from a load of instruments that have not been properly dried. If undue time is required to remove the water vapor it can be indicated to the user so that they can be reminded to be more vigilant

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in drying the load for future cycles. There may exists loads of water vapor for which it may take too long to withdraw or to withdraw effectively. In such case the cycle should be cancelled and the user informed as to why.

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Table 2 shows control points for three different cycles - a flash or very quick cycle having no lumens, a short cycle having only lumens which present a mild challenge and a long cycle for sterilizing devices with more challenging long and narrow lumens. During an initial pump-down to remove air from the sterilization chamber and vaporizer/condenser 400 the outlet control valve 406 is left open. As the pressure reaches P1 the outlet control valve 406 is closed but the orifice control valve 402 is left open; this starts the vaporization and concentration of the sterilant. Upon reaching pressure P2 within the vaporizer/condenser 400 the pressure Pc within the chamber is checked. If it is above the value listed in Table 2 then the orifice control valve 402 is closed and pump-down continues until Pc is reached and then the outlet control valve 406 is opened to transfer the sterilant into the sterilization chamber. Otherwise, the outlet control valve 406 is opened right away. If the chamber pressure exceeds Pc-cancel at the time that the vaporizer/condenser pressure reaches P2 it is assumed that the sterilization chamber contains too much water and the cycle is cancelled.

Table 2
Examples of temperature and pressure set points

	Flash	Short	Long
Load condition	Surface	1mmx150mm SS 1mmx350mm Plastic	1mmx500mm SS 1mmx1000mm Plastic
Vaporizer temperature	70°C	70°C	70°C
Condenser temperature	58°C	52°C	43°C
P1 Vaporizer/condenser pressure to remove air	140 torr	140 torr	140 torr
P2 Vaporizer/condenser pressure to concentrate sterilant	22 torr	16 torr	10 torr
Pc Chamber pressure to select transfer, additional vacuum or cancellation	1.5 torr	0.6 torr	0.3 torr
Pc-cancel Chamber pressure to cancel cycle	8 torr	6 torr	4 torr
Condenser temperature to transfer concentrated sterilant	68°C	68°C	68°C

5 The vapor concentration of the process can also be measured in mg/L. It is preferably 6 mg/L to 25 mg/L or even higher, with values of about 20 to 25 mg/L being most preferred.

10 At these concentrations a portion of the injected hydrogen peroxide will condense upon the items to be sterilized. The subsequent pump down of the chamber re-vaporizes this condensed hydrogen peroxide thus further enhancing the concentration of hydrogen peroxide by weight

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percent. Figure 23 provides a flow chart for calculating the concentration of the condensed hydrogen peroxide and relies upon the following equations 1 to 10.

5 (1) $p = a + bw + cw^2 + dw^3$ (where p is density & w is wt% H_2O_2)

(2) $a = J_a + K_at + L_at^2 + M_at^3$

10 (3) $b = J_b + K_bt + L_bt^2 + M_bt^3$ (where t is solution temperature in degree Celsius)

(4) $c = J_c + K_ct + L_ct^2 + M_ct^3$

15 (5) $d = J_d + K_dt + L_dt^2 + M_dt^3$

The coefficients for equations 1 to 5 are shown in Table 3.

Table 3

	J	$K \cdot 10^3$	$L \cdot 10^5$	$M \cdot 10^7$
a	0.99957	0.07603	-0.8603	0.51204
b	0.39763	-2.8732	3.2488	-1.6363
c	0.02206	3.5357	-6.0947	3.6165
d	0.05187	-1.9414	3.9061	-2.5500

20 (6) $\log p_{ho} \text{ (torr)} = 44.5760 - 4025.3 (1/T) - 12.996 (\log(T)) + 0.0046055 (T)$

(where p_{ho} is vapor pressure of H_2O_2 in torr & T is temperature in degree Kelvin)

25 (7) $\log p_{wo} \text{ (torr)} = 30.75050 + 3120.5 (1/T) + 7.921 (\log(T)) + 0.0023172 (T)$

30 (where p_{wo} is vapor pressure of H_2O in torr & T is temperature in degree Kelvin)

(8) $P = p_{wo}x_wr_w + p_{ho}(1-x_w)r_h$

35 (where P is the total vapor pressure in torr
 x_w is the wt% of water concentration
 r_w is the activity coefficient of water
 r_h is the activity coefficient of hydrogen peroxide)

40

$$(9) \quad r_w = \exp(((1-x_w)^2)/RT) (B_0 + B_1(1-4x_w) + B_2(1-2x_w)(1-6x_w))$$

(Where R is the universal gas constant [62.36
torr*liter/mole*⁰K]

$$B_0 = -752 + 0.97t = -1017 + 0.97T \text{ (where } t \text{ is } ^\circ\text{C} \text{ and } T \text{ is } ^\circ\text{K})$$

$$B_1 = 85$$

$$B_2 = 13)$$

$$(10) \quad r_h = \exp(((x_w)^2)/RT) (B_0 + B_1(3-4x_w) + B_2(1-2x_w)(5-6x_w))$$

In addition to the effectiveness of such systems in killing infectious microorganisms they are also effective in inactivating prions. Experiments were conducted comparing known methodologies to the highly concentrated hydrogen peroxide vapor of the present disclosure.

20

Steel Wire Preparation

Soft stainless steel wire (1.4301; diameter, 0.25 mm; Forestadent, Pforzheim, Germany) was placed in the Sterrad 100S GMP sterilizer, a hydrogen peroxide gas plasma sterilizer. The steel wire was then aseptically cut into fragments of 30 mm in length.

The wires were contaminated by immersion into freshly, prepared 10% brain homogenates from hamsters with scrapie in phosphate-buffered saline (PBS) for 16 hours at room temperature; spiked wires were then air dried for at least 1 hour before further treatment.

Cleaning was performed in a custom-made test washing machines, a closed two-container system. The lower container served as an open reservoir; a working volume of 10 L was pumped into the upper container and then drawn out freely back into the lower container through an

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opening on the bottom of the upper container. A circular rack with wires fixed in the edge was placed within the upper container and the lid of the upper container was tightly closed during the washing process.

5

After each treatment, wires were rinsed once with 1 x PBS followed by washing three times with double distilled water.

10

Wire Implantation

The processed wired were then implanted into hamster thalami with the assistance of a stereotaxic apparatus for small animals (coordinates: bregma, -2.0 mm; mediolateral, 2.0 mm; and dorsoventral, 6.0 mm). The same location was chosen for the intracerebral injection of scrapie brain homogenates into the hamster brain by a syringe and for the controls.

15

Animals were deeply anesthetized with 10% ketamine (SANofi-CEVA GmbH, Dusseldorf, Germany) during the operation.

20

Animal Surveillance

Hamsters implanted with the wires were kept three to four per cage in a biological safety level-3 facility, with free access to standard diet and water. Test animals were initially observed twice a week, and daily after 60 days postimplantation. Hamsters with definite signs of scrapie were designated as terminally sick and euthanized.

25

Treatment Regiments Compared

Samples of the prion prepared wires were processed with the following treatments to assess their effectiveness in inactivating the prions on the wires.

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Twelve animals were used for each treatment, and five animals were used as control.:

1. Neodisher V 4009/1; 1%; 55°C for 10 minutes (control)
- 5 2. Neodisher V 4009/1; 1%; 55°C for 10 minutes and exposure to STERRAD NX - Advanced Cycle (38 min)
3. Neodisher V 4009/1; 1%; 55°C for 10 minutes and exposure to STERRAD 100 S - Long Cycle
4. Alka One; 1%; 55°C for 10 minutes (control)
- 10 5. Alka One; 1%; 55°C for 10 minutes and exposure to STERRAD NX - Advanced Cycle (38 min)
6. Alka One; 1%; 55°C for 10 minutes and exposure to STERRAD 100 S - Long Cycle
7. Exposure to STERRAD NX - Advanced Cycle (38 min)
- 15 only; no washing
8. Exposure to STERRAD NX - Double Advanced Cycle (38 min) only; no washing
9. Exposure to STERRAD 100 S - Long Cycle only; no washing
- 20 10. Exposure to STERRAD 100 S - Double Long Cycle only; no washing

Neodisher V 4009/1 is an alkaline cleaning solution available from Chemische Fabrik Dr. Weigert GmbH & Co, Hamburg, Germany. Alka One is an alkaline cleaning solution available from Borer Chemie AG, Zuchwil, Switzerland. The STERRAD 100 S is available from Advanced Sterilization Products division of Ethicon, Inc. (ASP), Irvine, CA. Its long cycle comprises a 15-minute pre-exposure plasma with about 9.5 mWatts/cc power density and two 100S half cycles and its double long cycle comprises two long cycles. Each 100S half cycle comprises a 6-minute injection of 59% peroxide, a 10-minute diffusion, and a 2-minute plasma with about 9.5 mwatts/cc plasma

power density. The chamber temperature is maintained around 45°C throughout the process.

The STERRAD NX is also available from ASP. Its
5 advanced cycle comprises two NX half cycles and its double
advanced cycle comprises two advanced cycles. Each NX
half cycle comprises a concentration process, which
concentrates the injected 59% peroxide to about 90%, a 7-
minute transfer stage to transfer the concentrated into
10 sterilizer, a 30-second diffusion, and a 4-minute plasma
with about 50 mWatts/cc plasma power density. The chamber
is maintained around 50°C throughout the process. Due to
the higher chamber temperature, higher peroxide liquid
concentration, higher plasma power density, and longer
15 plasma time, the load in the STERRAD NX Sterilizer is
actually exposed to more effective and energetic
sterilization environment than the STERRAD 100S
Sterilizer. The results of these trials are shown in
Table 4 which shows the lifespan in days of the hamsters
20 (as of the compilation of the data) after implementation
with the treated wires. Figures in bold indicate a
deceased animal and figures indicated with an asterisk
indicate an animal deceased due to conflict with another
animal.

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146

Table 4
Comparison of Treatments to Inactivate Prions

	(1) 1% V4009/1 55°C 10min	(2) AlkaOne 55°C 10min	(3) No wash NX 38min double	(4) No wash NX 38min	(5) 1% V4009/1 55°C 10min/NX 38min	(6) AlkaOne 55°C 10min/NX 38min
Implantation	9/21/2005	9/22/2005	10/6/2005	10/7/2005	10/11/2005	10/13/2005
Hamster 1	168	167	153	152	148	146
Hamster 2	168	167	153	152	148	146
Hamster 3	168	134*	153	152	148	146
Hamster 4	168	167	153	152	148	146
Hamster 5	168	167	153	152	148	146
Hamster 6	99*	167	153	115*	148	146
Hamster 7	168	167	153	152	85*	146
Hamster 8	168	167	153	130*	148	146
Hamster 9	168	167	153	152	148	146
Hamster 10	168	167	153	152	148	146
Hamster 11	168	167	90*	152	148	146
Hamster 12	168	167	153	152	85*	146

	(7) AlkaOne 55°C 10min/100S long	(8) 1% V4009/1 55°C 10min/100S long	(9) No wash 100S long double	(10) No wash 100S long	Positive control wires
Implantation	11/8/2005	11/8/2005	11/9/2005	11/9/2005	7/6/2005
Hamster 1	120	120	107	93	75
Hamster 2	120	120	103	103	85
Hamster 3	120	120	97	107	85
Hamster 4	120	120	93	93	85
Hamster 5	120	120	119	97	85
Hamster 6	120	120	107	103	
Hamster 7	120	120	103	93	
Hamster 8	120	120	107	93	
Hamster 9	120	120	107	107	
Hamster 10	120	120	93	107	
Hamster 11	120	120	107	93	
Hamster 12	120	120	103	93	

5 The results show the high concentration hydrogen peroxide vapor treatment of the STERRAD NX to be as effective as alkaline wash treatment in inactivating prions.

The invention has been described with reference to the preferred embodiments. Obviously, modifications and alterations will occur to others upon reading and understanding the preceding detailed description. It is
5 intended that the invention be construed as including all such modifications and alterations insofar as they come within the scope of the appended claims or the equivalents thereof.

WHAT IS CLAIMED IS:

1. A method of inactivating prions comprising the steps of:

5 placing an article having a quantity of prions thereon into a sterilization chamber;

lowering pressure in the sterilization chamber to a pressure below the vapor pressure of hydrogen peroxide;

admitting a solution comprising hydrogen peroxide
10 into the sterilization chamber and contacting the article with hydrogen peroxide vapor; and

inactivating prions in the chamber through contact between the prions and the hydrogen peroxide vapor.

15 2. A method according to claim 1 wherein the concentration of the hydrogen peroxide in the solution admitted into the chamber exceeds 70 percent.

3. A method according to claim 2 wherein the
20 concentration of the hydrogen peroxide in the solution admitted into the chamber exceeds 75 percent.

4. A method according to claim 3 wherein the
25 concentration of the hydrogen peroxide in the solution admitted into the chamber exceeds 80 percent.

5. A method according to claim 4 wherein the
concentration of the hydrogen peroxide in the solution admitted into the chamber exceeds 85 percent.

30 6. A method according to claim 5 wherein the concentration of the hydrogen peroxide in the solution admitted into the chamber exceeds 90 percent.

7. A method according to claim 1 and wherein the temperature of the article during the step of contacting the article with hydrogen peroxide vapor exceeds 30 degrees Celsius.

5

8. A method according to claim 7 and wherein the temperature of the article during the step of contacting the article with hydrogen peroxide vapor exceeds 35 degrees Celsius.

10

9. A method according to claim 8 and wherein the temperature of the article during the step of contacting the article with hydrogen peroxide vapor exceeds 40 degrees Celsius.

15

10. A method according to claim 9 and wherein the temperature of the article during the step of contacting the article with hydrogen peroxide vapor exceeds 45 degrees Celsius.

20

11. A method according to claim 1 and further comprising exciting the hydrogen peroxide vapor into the plasma phase and contacting the prions with the hydrogen peroxide in the plasma phase.

25

12. A method according to claim 11 wherein the plasma density is at least 10 milliwatts/cm³.

13. A method according to claim 12 wherein the plasma density is at least 20 milliwatts/cm³.

30

14. A method according to claim 13 wherein the plasma density is at least 30 milliwatts/cm³.

15. A method according to claim 14 wherein the plasma density is at least 40 milliwatts/cm³.

16. A method according to claim 15 wherein the
5 plasma density is at least 50 milliwatts/cm³.

17. A method according to claim 11 wherein the plasma is in contact with the prions for at least 2 minutes.

10

18. A method according to claim 17 wherein the plasma time is in contact with the prions for at least 3 minutes.

15

19. A method according to claim 18 wherein the plasma time is in contact with the prions for at least 4 minutes.

20

20. A method according to claim 11 and wherein the plasma is generated between an anode and a cathode and wherein a gap therebetween is less than 0.6 inches.

21. A method according to claim 20 wherein the gap is 0.5 inches or less.

25

22. A method according to claim 20 wherein the gap is about 0.5 inches.

30

23. A method according to claim 11 and wherein the plasma is generated between an anode and a cathode and wherein a minimum distance between the prions and the closer of the anode and electrode is 1.5 inches.

24. A method according to claim 23 wherein the distance is one inch or less.

25. A method according to claim 24 wherein the
5 distance between the prions and the anode is one inch or less.

26. A method according to claim 1 in which the
10 hydrogen peroxide effects sterilization of the article.

27. A method according to claim 1 and further
comprising increasing concentration of at least a portion
of the hydrogen peroxide prior to contacting the prions
therewith.
15

28. A method according to claim 27 wherein the step
of increasing concentration of the hydrogen peroxide is
performed by selectively removing water from the solution
and exhausting that water through the sterilization
20 chamber.

29. A method according to claim 1 and further
comprising exciting gases surrounding the prions into the
plasma phase and contacting the prions with the gases in
25 the plasma phase.

30. A method according to claim 1 wherein the steps
of steps of lowering pressure in the sterilization chamber
and admitting the solution into the sterilization chamber
30 comprise a cycle and wherein the cycle is repeated.

31. A method according to claim 30 wherein the cycle
is repeated more than once.

32. A method according to claim 1 wherein during the step of contacting the article with hydrogen peroxide vapor, the vapor has a concentration of 10 mg/L or more.

5 33. A method according to claim 32 wherein during the step of contacting the article with hydrogen peroxide vapor, the vapor has a concentration of 15 mg/L or more.

10 34. A method according to claim 33 wherein during the step of contacting the article with hydrogen peroxide vapor, the vapor has a concentration of 20 mg/L or more.

15 35. A method according to claim 34 wherein during the step of contacting the article with hydrogen peroxide vapor, the vapor has a concentration of 25 mg/L or more.

20 36. A method according to claim 1 and further comprising the step of condensing a portion of the hydrogen peroxide vapor onto the article and wherein the concentration of that condensed hydrogen peroxide is at least 80% hydrogen peroxide by weight.

25 37. A method according to claim 36 wherein the concentration of that condensed hydrogen peroxide is at least 85% hydrogen peroxide by weight.

30 38. A method according to claim 37 wherein the concentration of that condensed hydrogen peroxide is at least 90% hydrogen peroxide by weight.

39. A method according to claim 38 wherein the concentration of the condensed hydrogen peroxide is at least 95% hydrogen peroxide by weight.

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40. A method according to claim 36 and further comprising the step of evaporating at least a portion of that condensed hydrogen peroxide by pumping the sterilization chamber to a lower pressure.

5

41. A method of inactivating prions comprising the steps of:

placing an article having a quantity of prions thereon into a sterilization chamber;

10

contacting the article with a plasma to effect inactivation of the prions.

42. A method according to claim 41 wherein the plasma is formed from a gas comprising hydrogen peroxide.

15

43. A method according to claim 41 wherein the plasma density is at least 10 milliwatts/cm³.

44. A method according to claim 43 wherein the plasma density is at least 20 milliwatts/cm³.

20

45. A method according to claim 44 wherein the plasma density is at least 30 milliwatts/cm³.

46. A method according to claim 45 wherein the plasma density is at least 40 milliwatts/cm³.

25

47. A method according to claim 46 wherein the plasma density is at least 50 milliwatts/cm³.

30

48. A method according to claim 41 wherein the plasma is generated between an anode and a cathode and wherein a gap therebetween is less than 0.6 inches.

NOVEDAD DE LA INVENCION

REIVINDICACIONES

5 1.- Un método para la inactivación de priones que comprende los
pasos de: colocar un artículo que tiene una cantidad de priones sobre éste
dentro de una cámara de esterilización; disminuir la presión en la cámara de
esterilización a una presión por debajo de la presión de vapor del peróxido de
hidrógeno; permitir la entrada una solución que comprende peróxido de
10 hidrógeno dentro de la cámara de esterilización y poner en contacto del
artículo con el vapor de peróxido de hidrógeno; e inactivar los priones en la
cámara a través del contacto entre los priones y el vapor de peróxido de
hidrógeno.

 2.- El método de conformidad con la reivindicación 1,
15 caracterizado además porque la concentración del peróxido de hidrógeno en
la solución que ingresa dentro de la cámara excede el 70%.

 3.- El método de conformidad con la reivindicación 2,
caracterizado además porque la concentración del peróxido de hidrógeno en
la solución que ingresa dentro de la cámara excede el 75%.

20 4.- El método de conformidad con la reivindicación 3,
caracterizado además porque la concentración del peróxido de hidrógeno en
la solución que ingresa dentro de la cámara excede el 80%.

5.- El método de conformidad con la reivindicación 4, caracterizado además porque la concentración del peróxido de hidrógeno en la solución que ingresa dentro de la cámara excede el 85%.

5 6.- El método de conformidad con la reivindicación 5, caracterizado además porque la concentración del peróxido de hidrógeno en la solución que ingresa dentro de la cámara excede el 90%.

7.- El método de conformidad con la reivindicación 1, caracterizado además porque la temperatura del artículo durante el paso de poner en contacto el artículo con el vapor de peróxido de hidrógeno excede
10 los 30 grados Celsius.

8.- El método de conformidad con la reivindicación 7, caracterizado además porque la temperatura del artículo durante el paso de poner en contacto el artículo con el vapor de peróxido de hidrógeno excede los 35 grados Celsius.

15 9.- El método de conformidad con la reivindicación 8, caracterizado además porque la temperatura del artículo durante el paso de poner en contacto el artículo con el vapor de peróxido de hidrógeno excede los 40 grados Celsius.

10.- El método de conformidad con la reivindicación 9, caracterizado además porque la temperatura del artículo durante el paso de poner en contacto el artículo con el vapor de peróxido de hidrógeno excede
20 los 45 grados Celsius.

11.- El método de conformidad con la reivindicación 1, caracterizado además porque comprende adicionalmente excitando el vapor de peróxido de hidrógeno hacia la fase de plasma y poner en contacto los priones con el peróxido de hidrógeno en la fase de plasma.

5 12.- El método de conformidad con la reivindicación 11, caracterizado además porque la densidad del plasma es de al menos 10 miliwatts/cm³.

10 13.- El método de conformidad con la reivindicación 12, caracterizado además porque la densidad del plasma es de al menos 20 miliwatts/cm³.

14.- El método de conformidad con la reivindicación 13, caracterizado además porque la densidad del plasma es de al menos 30 miliwatts/cm³.

15 15.- El método de conformidad con la reivindicación 14, caracterizado además porque la densidad del plasma es de al menos 40 miliwatts/cm³.

16.- El método de conformidad con la reivindicación 15, caracterizado además porque la densidad del plasma es de al menos 50 miliwatts/cm³.

20 17.- El método de conformidad con la reivindicación 11, caracterizado además porque el plasma se pone en contacto con los priones por al menos 2 minutos.

18.- El método de conformidad con la reivindicación 17, caracterizado además porque el plasma se pone en contacto con los priones por al menos 3 minutos.

5 19.- El método de conformidad con la reivindicación 18, caracterizado además porque el plasma se pone en contacto con los priones por al menos 4 minutos.

20.- El método de conformidad con la reivindicación 11, caracterizado además porque el plasma se genera entre un ánodo y un cátodo y en donde un espacio entre éstos es menor de 1.5 centímetros.

10 21.- El método de conformidad con la reivindicación 20, caracterizado además porque el espacio es de aproximadamente 1.27 centímetros o menos.

22.- El método de conformidad con la reivindicación 20, caracterizado además porque el espacio es de aproximadamente 1.27
15 centímetros.

23.- El método de conformidad con la reivindicación 11, caracterizado además porque el plasma se genera entre un ánodo y un cátodo y en donde una distancia mínima entre los priones y la parte más cercana del ánodo y electrodo es de 3.6 centímetros.

20 24.- El método de conformidad con la reivindicación 23, caracterizado además porque la distancia es de 2.5 centímetros o menos.

25.- El método de conformidad con la reivindicación 24, caracterizado además porque la distancia entre los priones y el ánodo es de 2.5 centímetros o menos.

5 26.- El método de conformidad con la reivindicación 1, caracterizado además porque el peróxido de hidrógeno produce la esterilización del artículo.

27.- El método de conformidad con la reivindicación 1, caracterizado además porque comprende adicionalmente incrementar la concentración de al menos una porción del peróxido de hidrógeno antes de
10 poner en contacto los priones con éste.

28.- El método de conformidad con la reivindicación 27, caracterizado además porque el paso de incrementar la concentración del peróxido de hidrógeno se lleva a cabo mediante la remoción selectiva de agua a partir de la solución y agotando esa agua a través de la cámara de
15 esterilización.

29.- El método de conformidad con la reivindicación 1, caracterizado además porque comprende adicionalmente excitando los gases que rodean a los priones en la fase de plasma y poner en contacto los priones con los gases en la fase de plasma.

20 30.- El método de conformidad con la reivindicación 1, caracterizado además porque los pasos de disminuir la presión en la cámara de esterilización y permitiendo la entrada de la solución en la cámara de esterilización comprende un ciclo y en donde el ciclo se repite.

31.- El método de conformidad con la reivindicación 30, caracterizado además porque el ciclo se repite más de una vez.

32.- El método de conformidad con la reivindicación 1, caracterizado además porque durante el paso de poner en contacto el artículo
5 con el vapor de peróxido de hidrógeno, el vapor tiene una concentración de 10 mg/Lo más.

33.- El método de conformidad con la reivindicación 32, caracterizado además porque durante el paso de poner en contacto el artículo con el vapor de peróxido de hidrógeno, el vapor tiene una concentración de 15
10 mg/Lo más.

34.- El método de conformidad con la reivindicación 33, caracterizado además porque durante el paso de poner en contacto el artículo con el vapor de peróxido de hidrógeno, el vapor tiene una concentración de 20 mg/Lo más.

15 35.- El método de conformidad con la reivindicación 34, caracterizado además porque durante el paso de poner en contacto el artículo con el vapor de peróxido de hidrógeno, el vapor tiene una concentración de 25 mg/Lo más.

20 36.- El método de conformidad con la reivindicación 1, caracterizado además porque comprende adicionalmente el paso de condensar una porción del vapor de peróxido de hidrógeno sobre el artículo y en donde la concentración de ese peróxido de hidrógeno condensado es de al menos 80% de peróxido de hidrógeno en peso.

37.- El método de conformidad con la reivindicación 36, caracterizado además porque la concentración de ese peróxido de oxígeno condensado es de al menos 85% de peróxido de hidrógeno en peso.

5 38.- El método de conformidad con la reivindicación 37, caracterizado además porque la concentración de ese peróxido de oxígeno condensado es de al menos 90% de peróxido de hidrógeno en peso.

39.- El método de conformidad con la reivindicación 38, caracterizado además porque la concentración del peróxido de oxígeno condensado es de al menos 95% de peróxido de hidrógeno en peso.

10 40.- El método de conformidad con la reivindicación 36, caracterizado además porque comprende adicionalmente el paso de evaporar al menos una porción de ese peróxido de hidrógeno condensado mediante el bombeo de la cámara de esterilización a una presión menor.

15 41.- Un método para inactivar priones que comprende los pasos de: colocar un artículo que tiene una cantidad de priones sobre éste dentro de una cámara de esterilización; poner en contacto del artículo con un plasma para producir la inactivación de los priones.

20 42.- El método de conformidad con la reivindicación 41, caracterizado además porque el plasma se forma a partir de un gas que comprende peróxido de hidrógeno.

43.- El método de conformidad con la reivindicación 41, caracterizado además porque la densidad del plasma es de al menos 10 miliwatts/cm³.

44.- El método de conformidad con la reivindicación 43, caracterizado además porque la densidad del plasma es de al menos 20 miliwatts/cm³.

5 45.- El método de conformidad con la reivindicación 44, caracterizado además porque la densidad del plasma es de al menos 30 miliwatts/cm³.

46.- El método de conformidad con la reivindicación 45, caracterizado además porque la densidad del plasma es de al menos 40 miliwatts/cm³.

10 47.- El método de conformidad con la reivindicación 46, caracterizado además porque la densidad del plasma es de al menos 50 miliwatts/cm³.

48.- El método de conformidad con la reivindicación 41, caracterizado además porque el plasma se genera entre un ánodo y un cátodo y en donde un espacio entre éstos es menor de 1.5 centímetros.

49.- El método de conformidad con la reivindicación 48, caracterizado además porque el espacio es de 1.5 centímetros o menos.

50.- El método de conformidad con la reivindicación 48, caracterizado además porque el espacio es de aproximadamente 1.5 centímetros.

51.- El método de conformidad con la reivindicación 41, caracterizado además porque el plasma se genera entre un ánodo y un

cátodo y en donde una distancia mínima entre los priones y la parte más cercana del ánodo y del cátodo es de 3.6 centímetros.

52.- El método de conformidad con la reivindicación 51, caracterizado además porque la distancia es de 2.5 centímetros o menos.

5 53.- El método de conformidad con la reivindicación 52, caracterizado además porque la distancia entre los priones y el ánodo es de 2.5 centímetros o menos.

49. A method according to claim 48 wherein the gap is 0.5 inches or less.

50. A method according to claim 48 wherein the gap
5 is about 0.5 inches.

51. A method according to claim 41 and wherein the plasma is generated between an anode and a cathode and wherein a minimum distance between the prions and the
10 closer of the anode and cathode is 1.5 inches.

52. A method according to claim 51 wherein the distance is one inch or less.

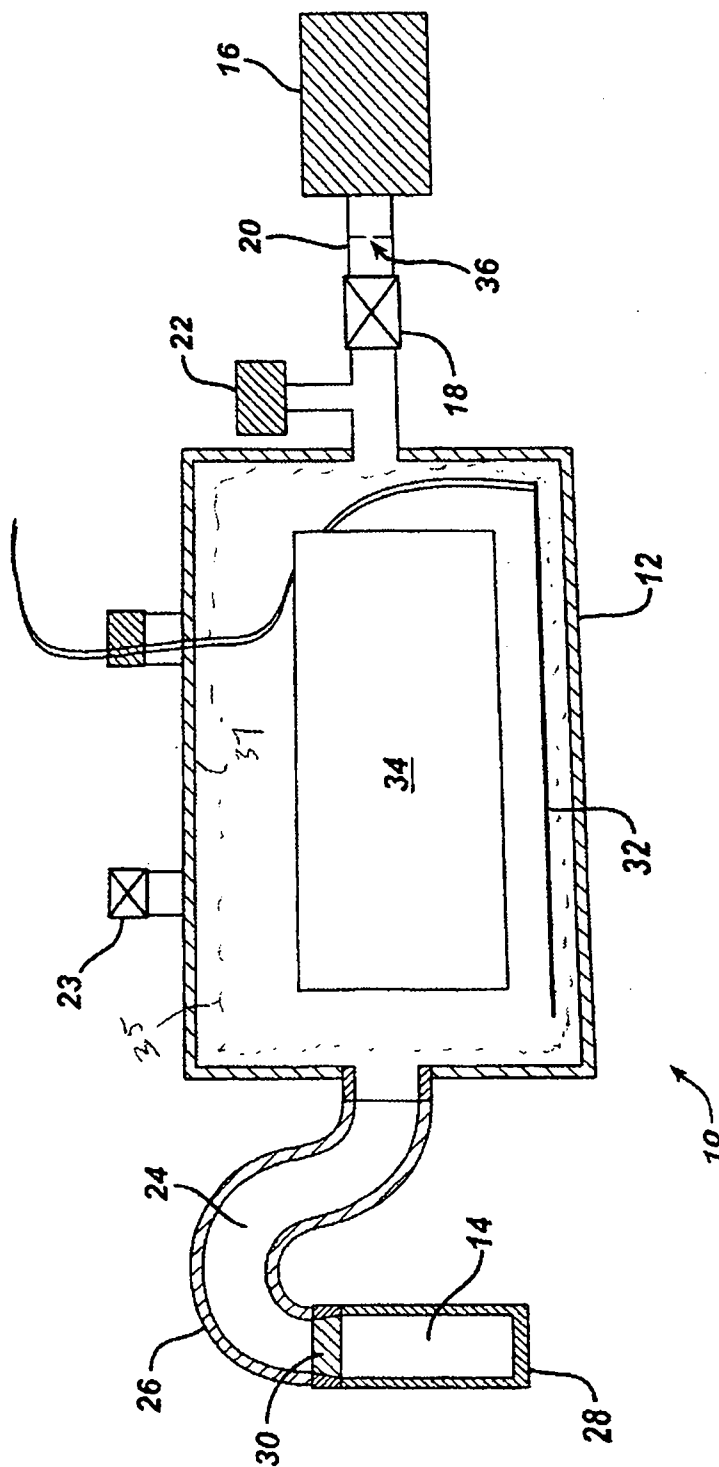
15 53. A method according to claim 52 wherein the distance between the prions and the anode is one inch or less.

20

ABSTRACT

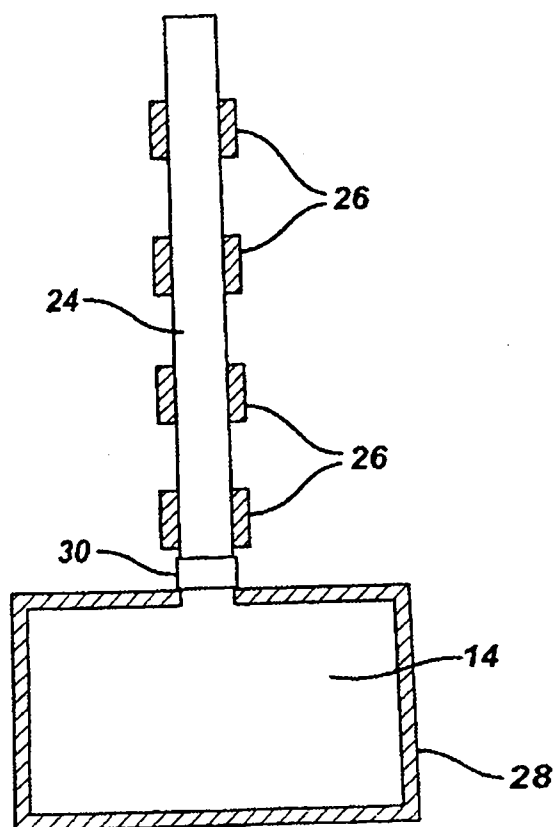
A method is provided for inactivating prions and is particularly effective in inactivating prions on
5 medical devices. An article having a quantity of prions thereon is placed into a sterilization chamber. Pressure in the sterilization chamber is lowered to a pressure below the vapor pressure of hydrogen peroxide and a solution of hydrogen peroxide is admitted into the
10 sterilization chamber and placed into contact with the article to inactivate prions on the article.

FIG. 1



67
165

FIG. 2



68
16b

FIG. 3

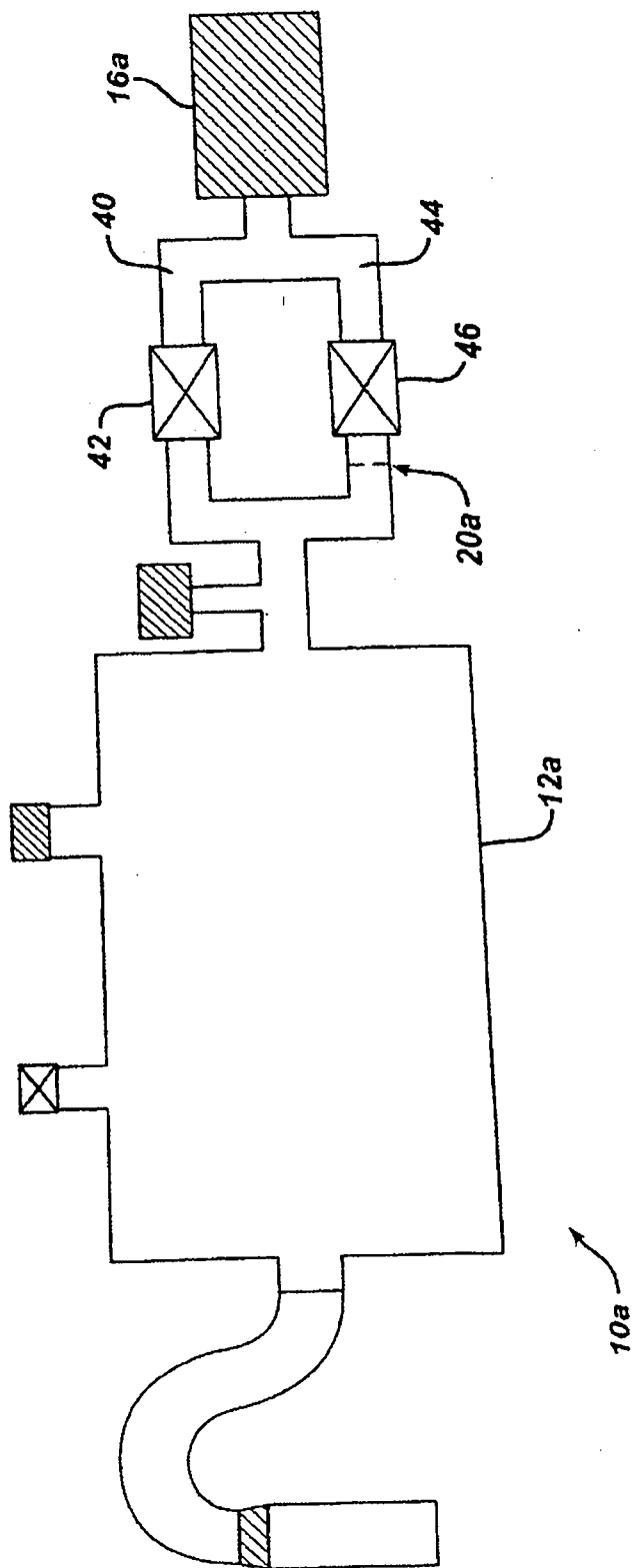
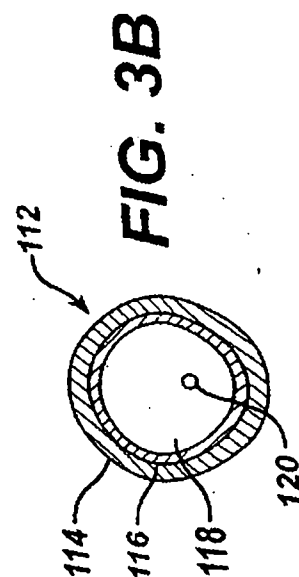
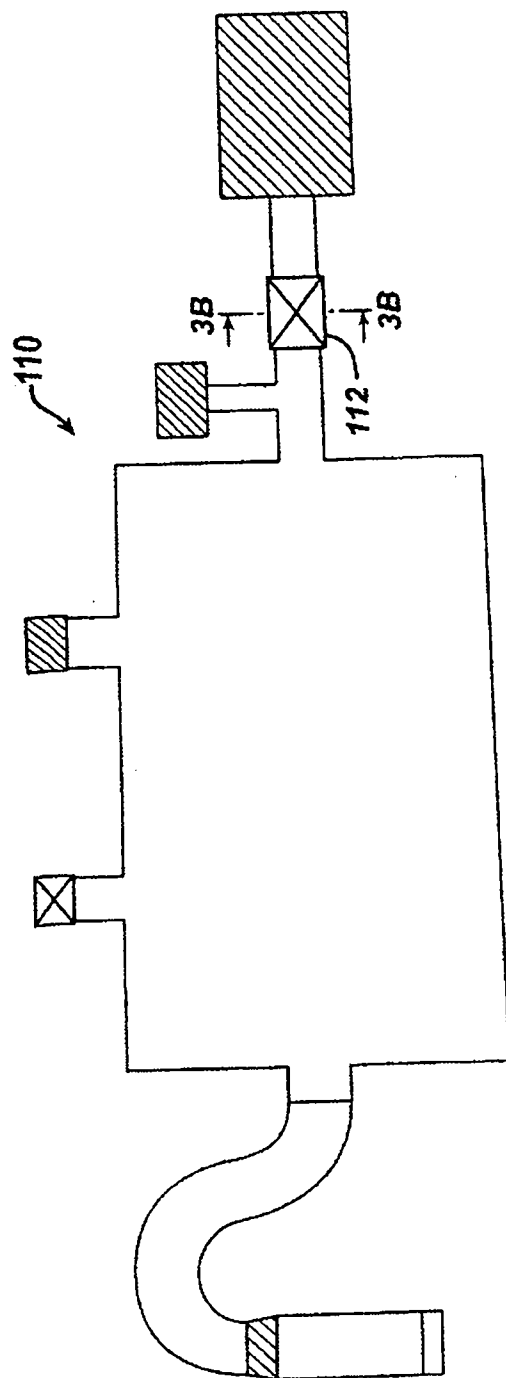


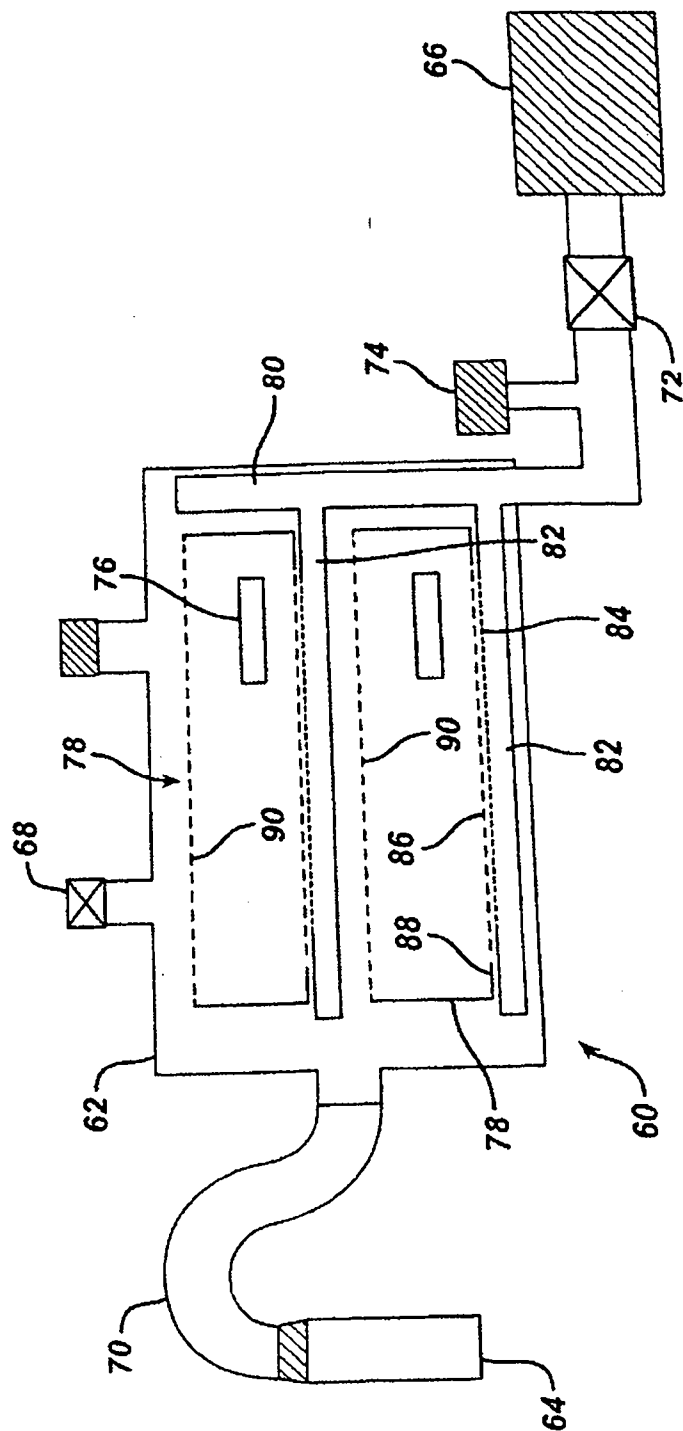
FIG. 3A



69
167

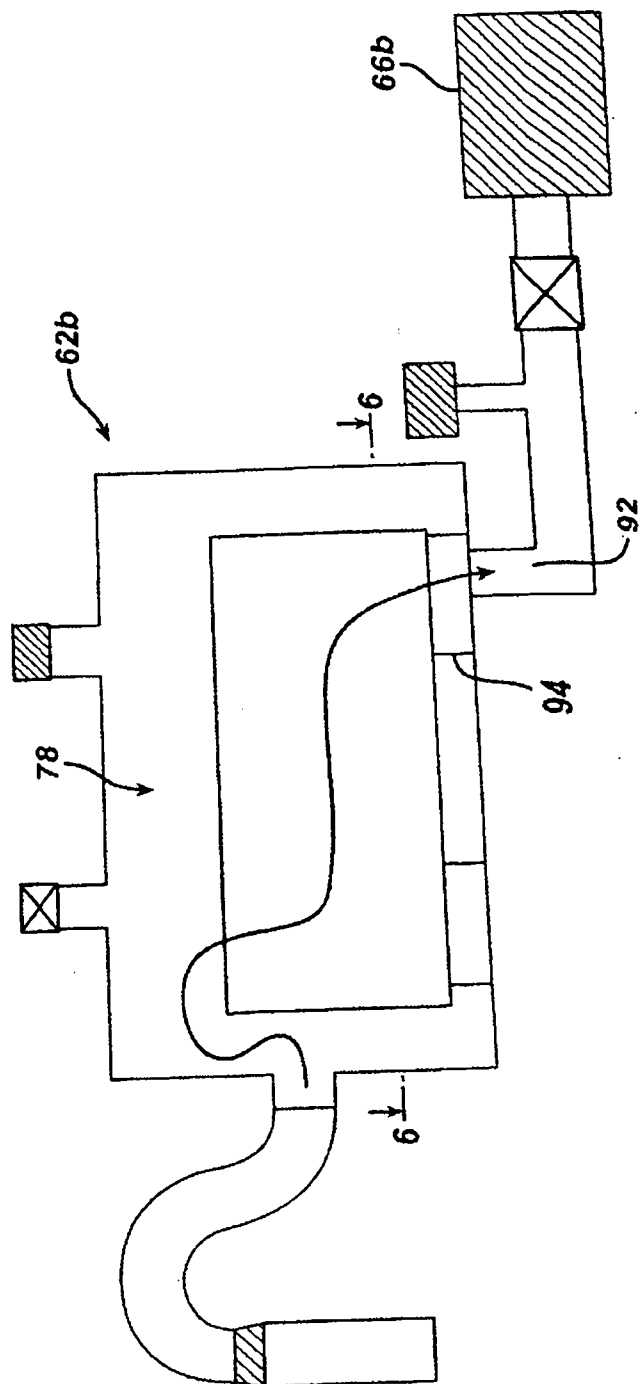
20
768

FIG. 4



269

FIG. 5



72
120

FIG. 6

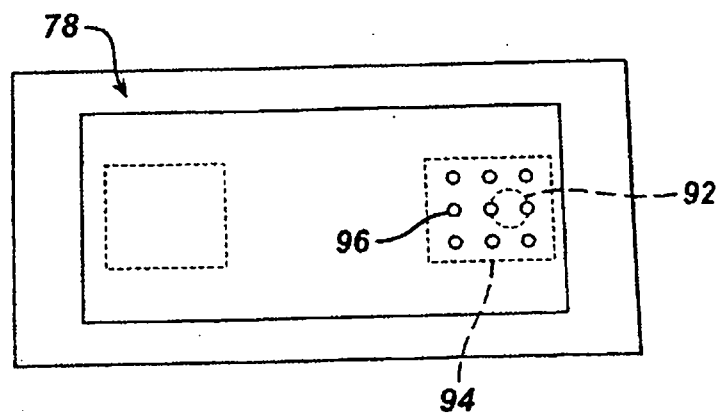
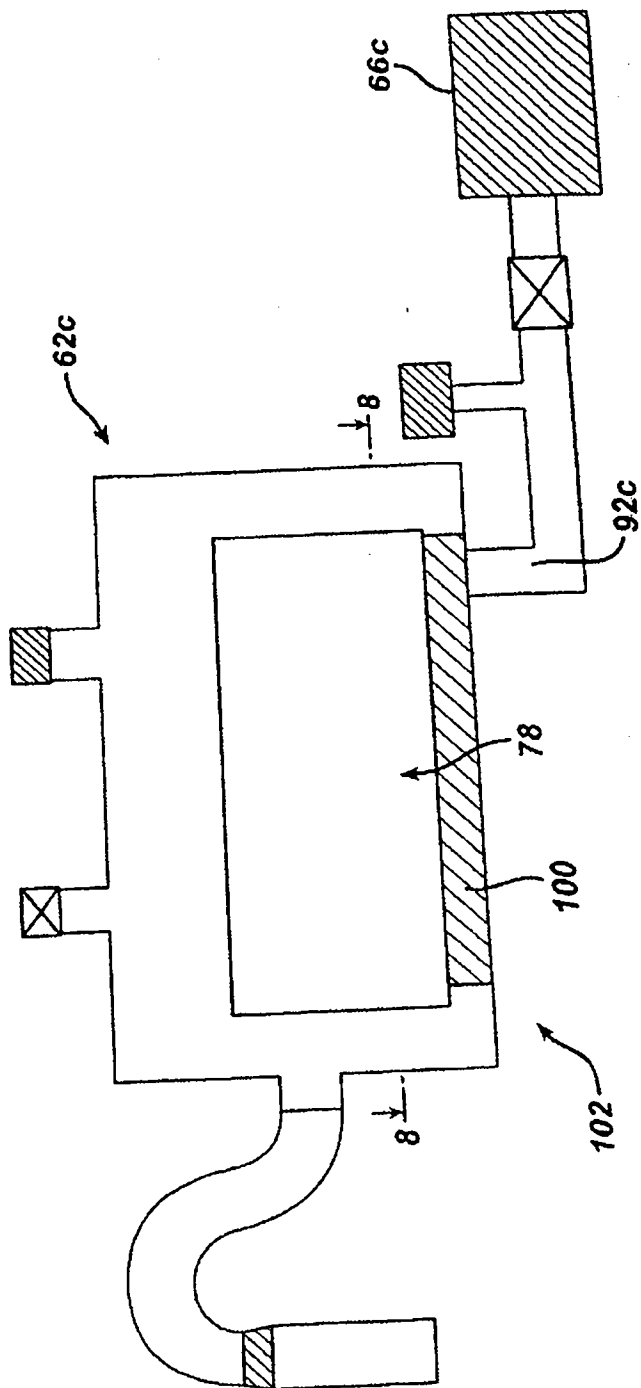


FIG. 7



74
FR

FIG. 8

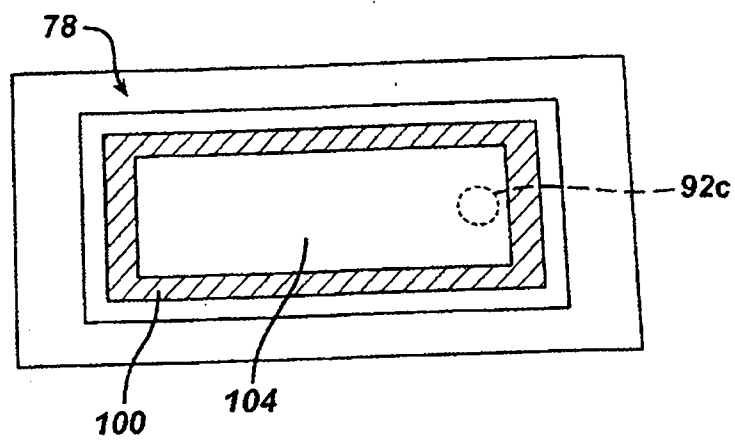
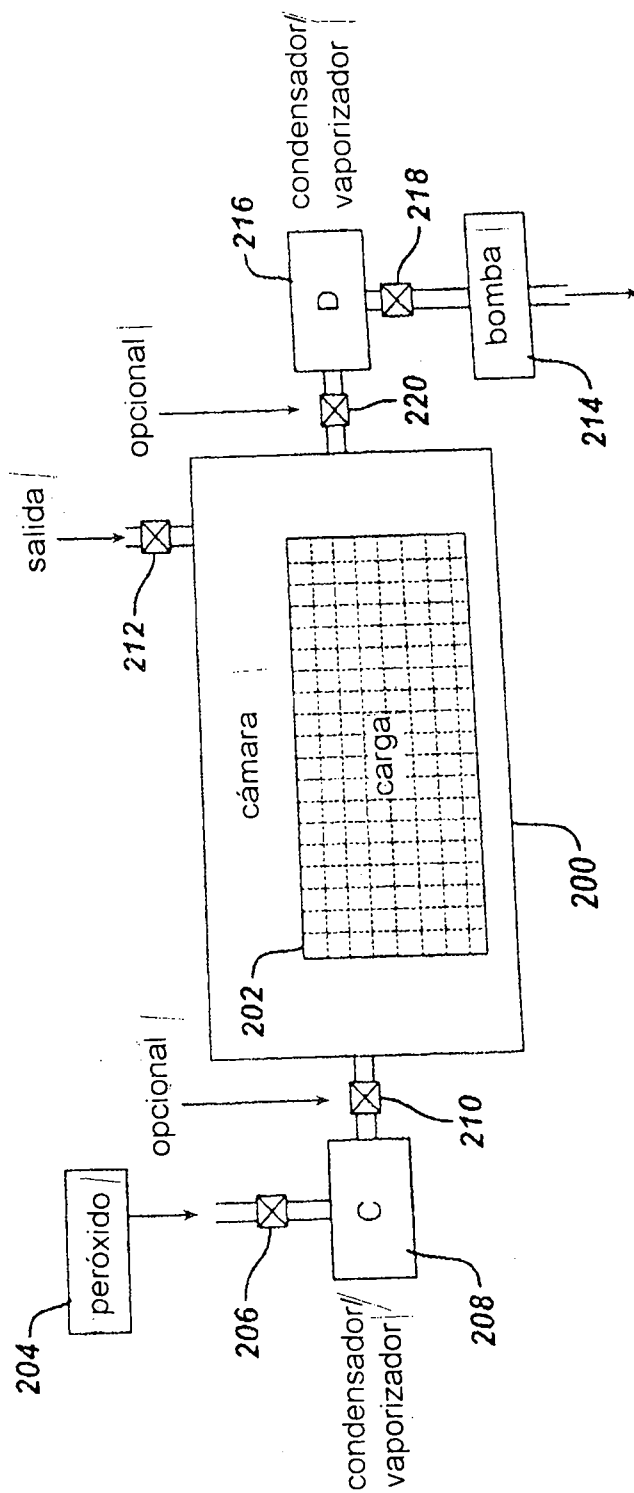
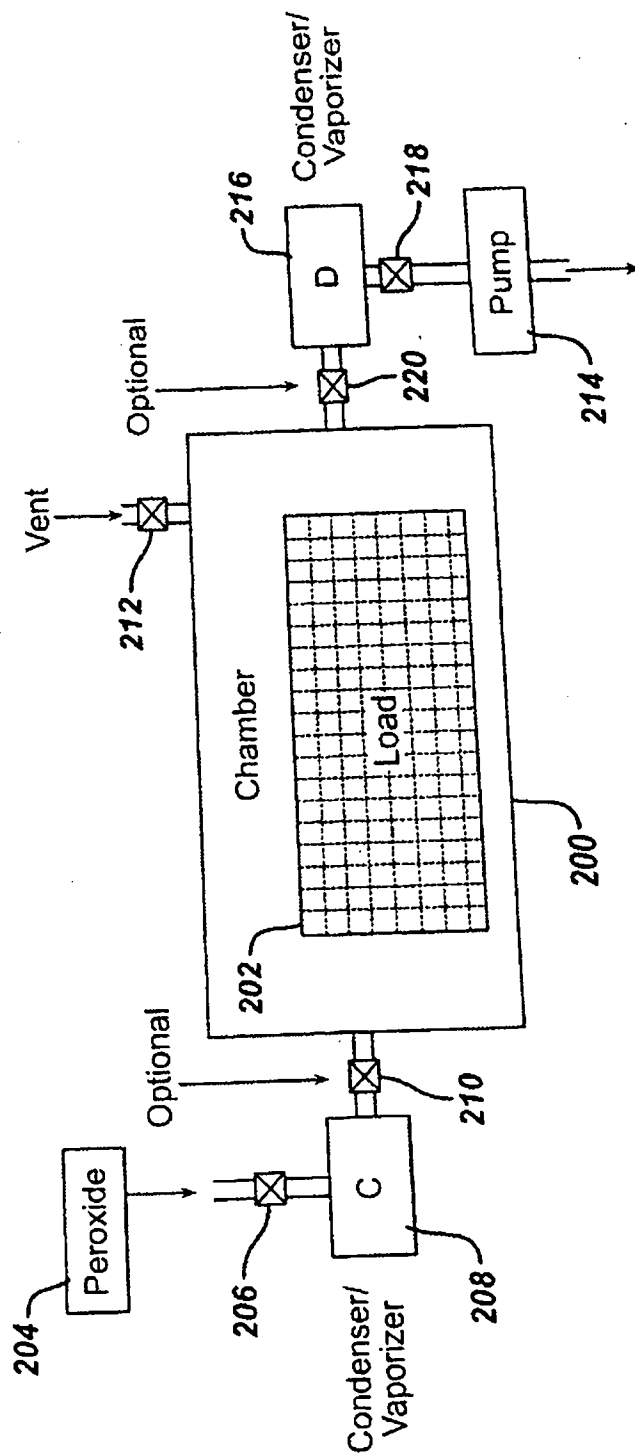


FIG. 9



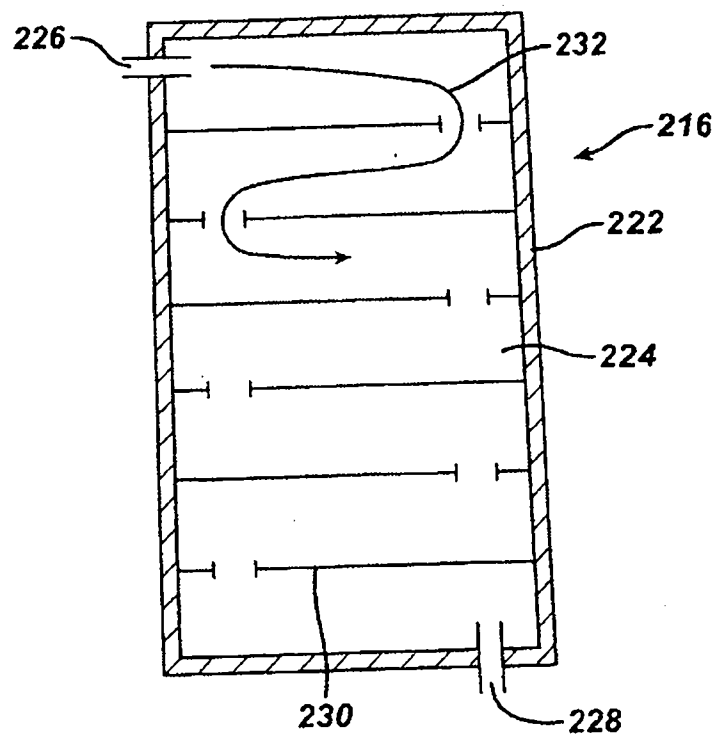
38
173

FIG. 9



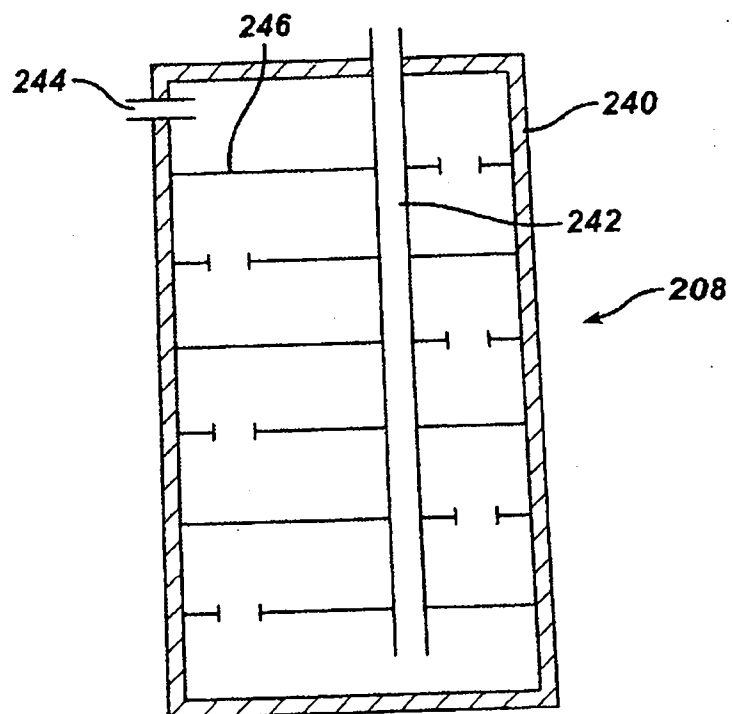
775

FIG. 10



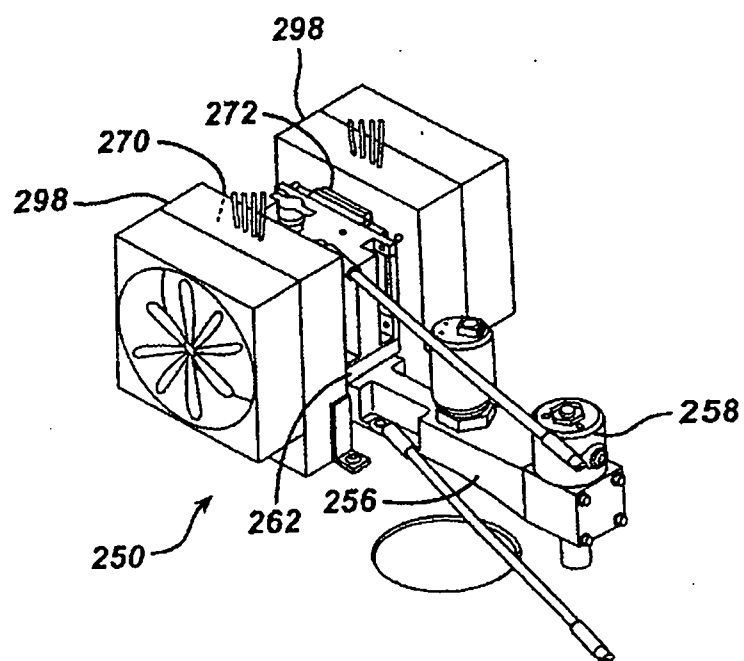
78
776

FIG. 11



309
177

FIG. 12



178

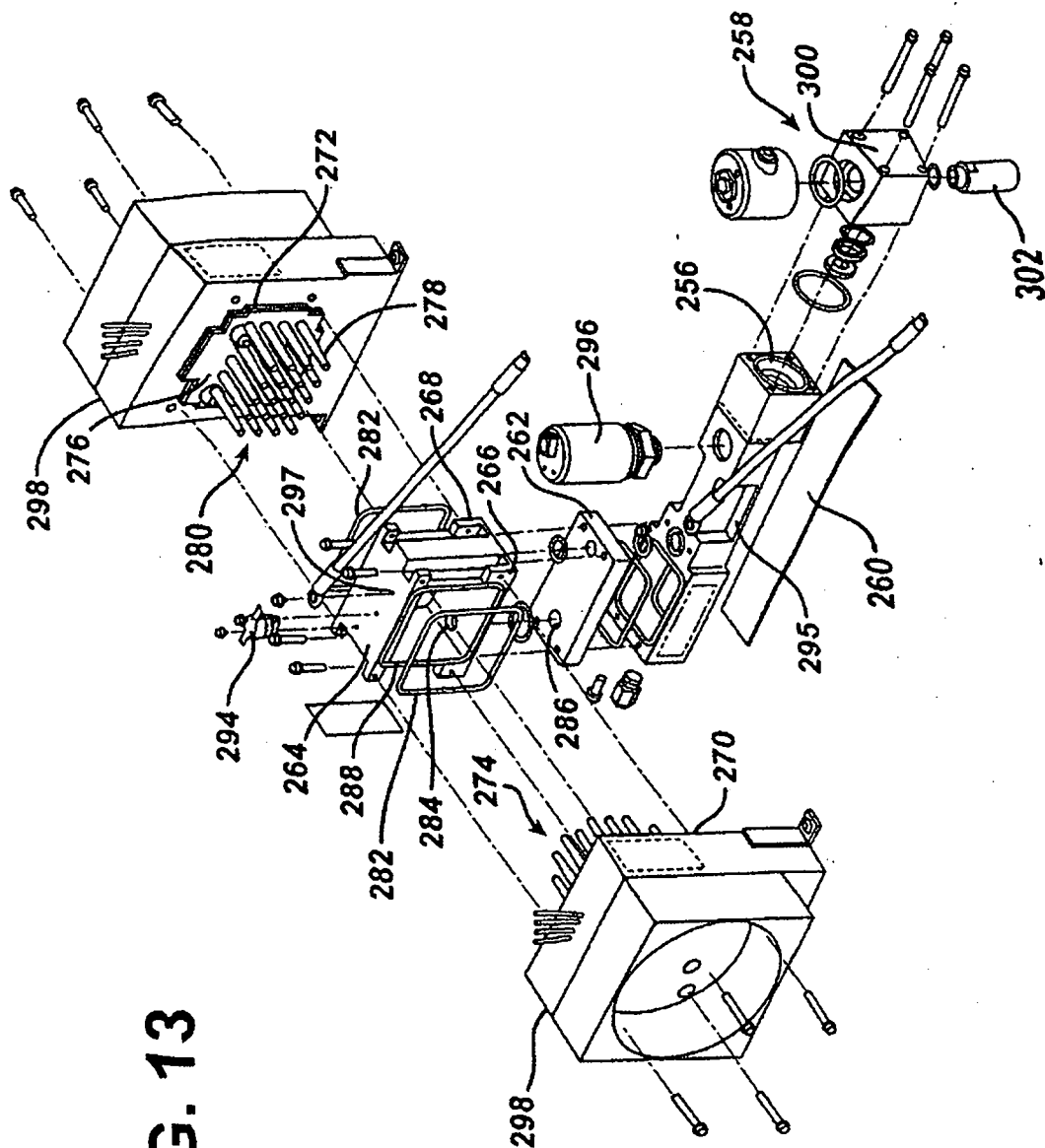


FIG. 13

FIG. 14

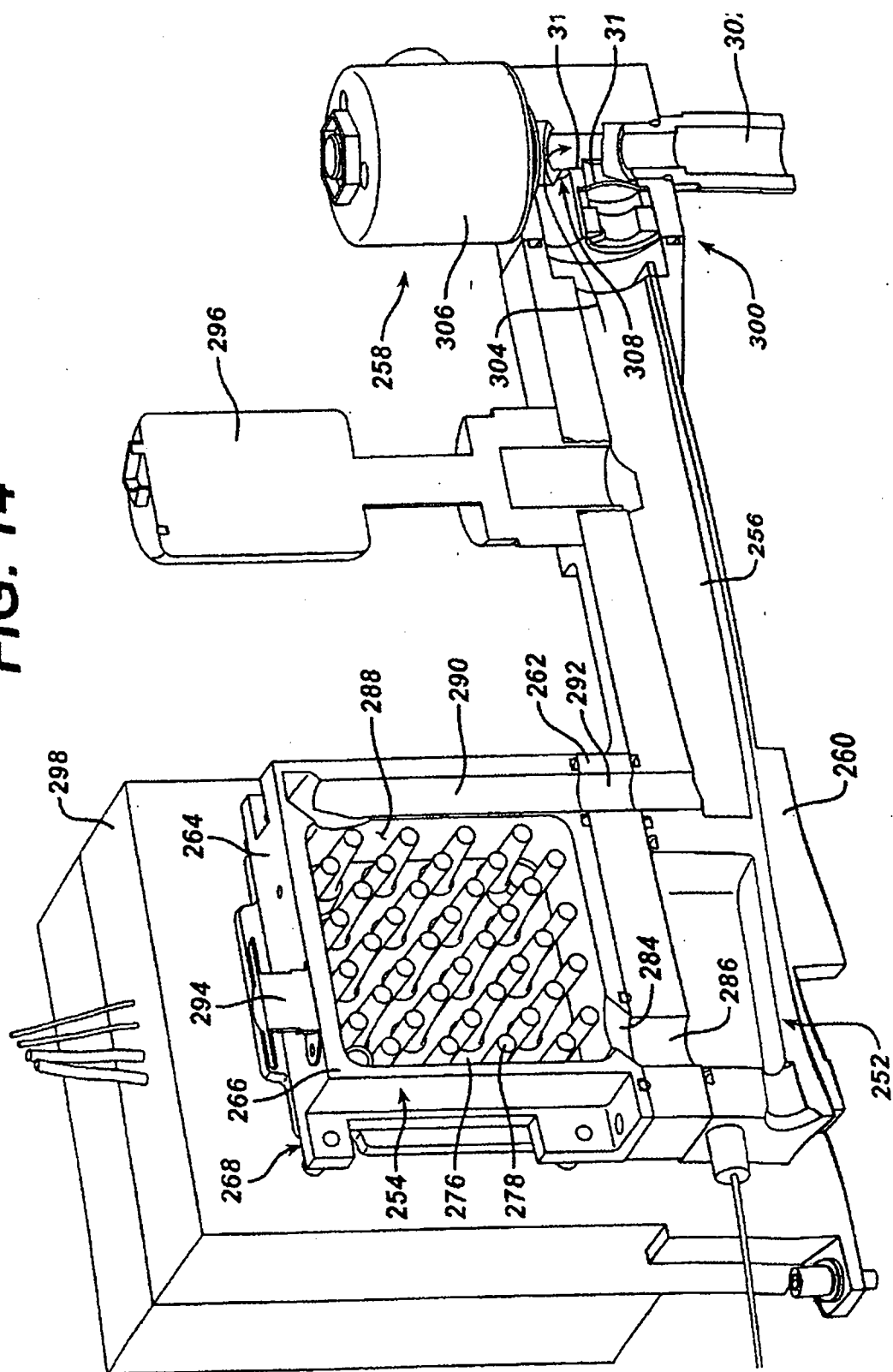


FIG. 14A

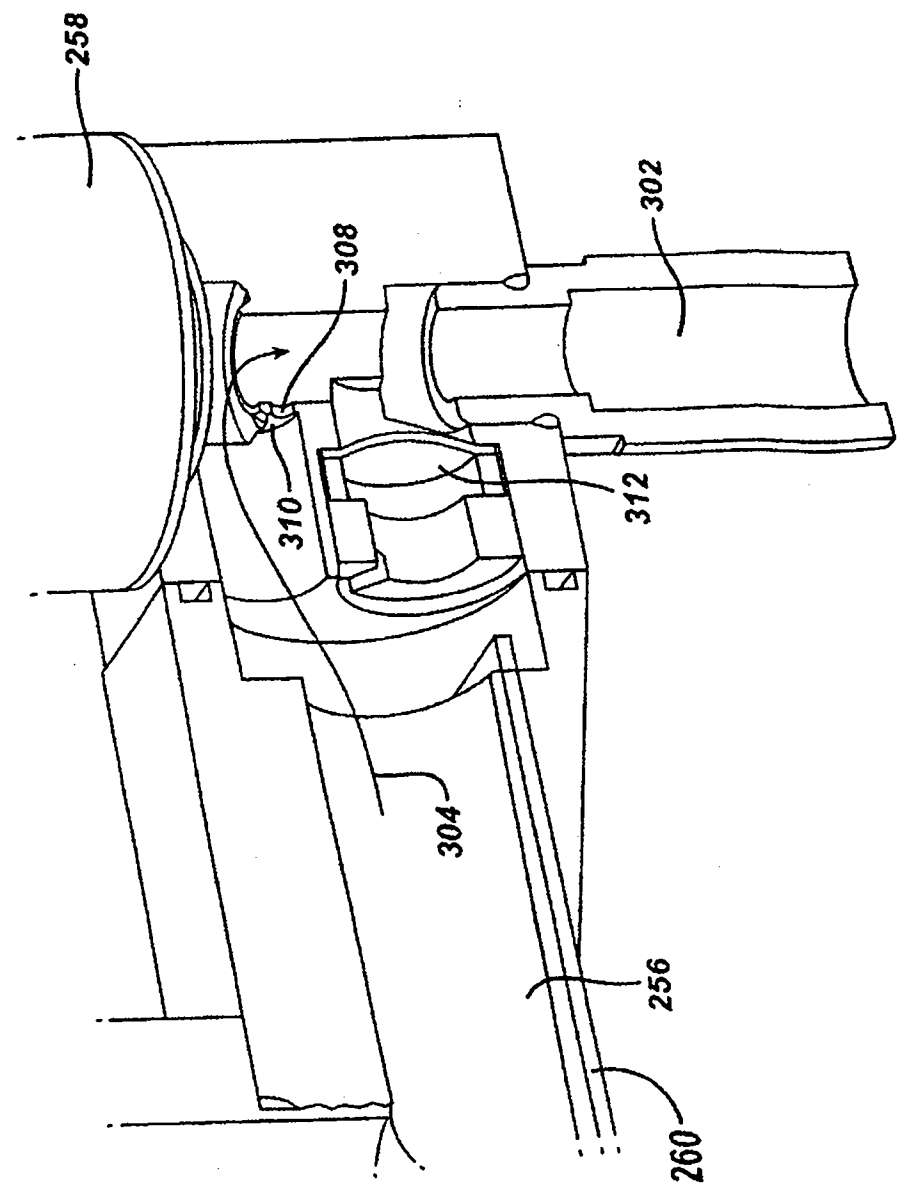


FIG. 15

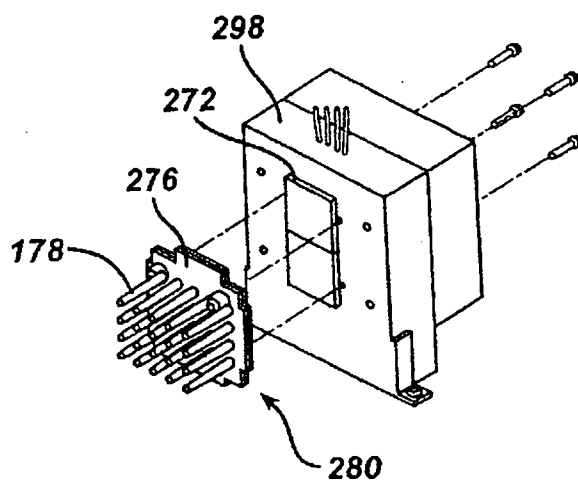
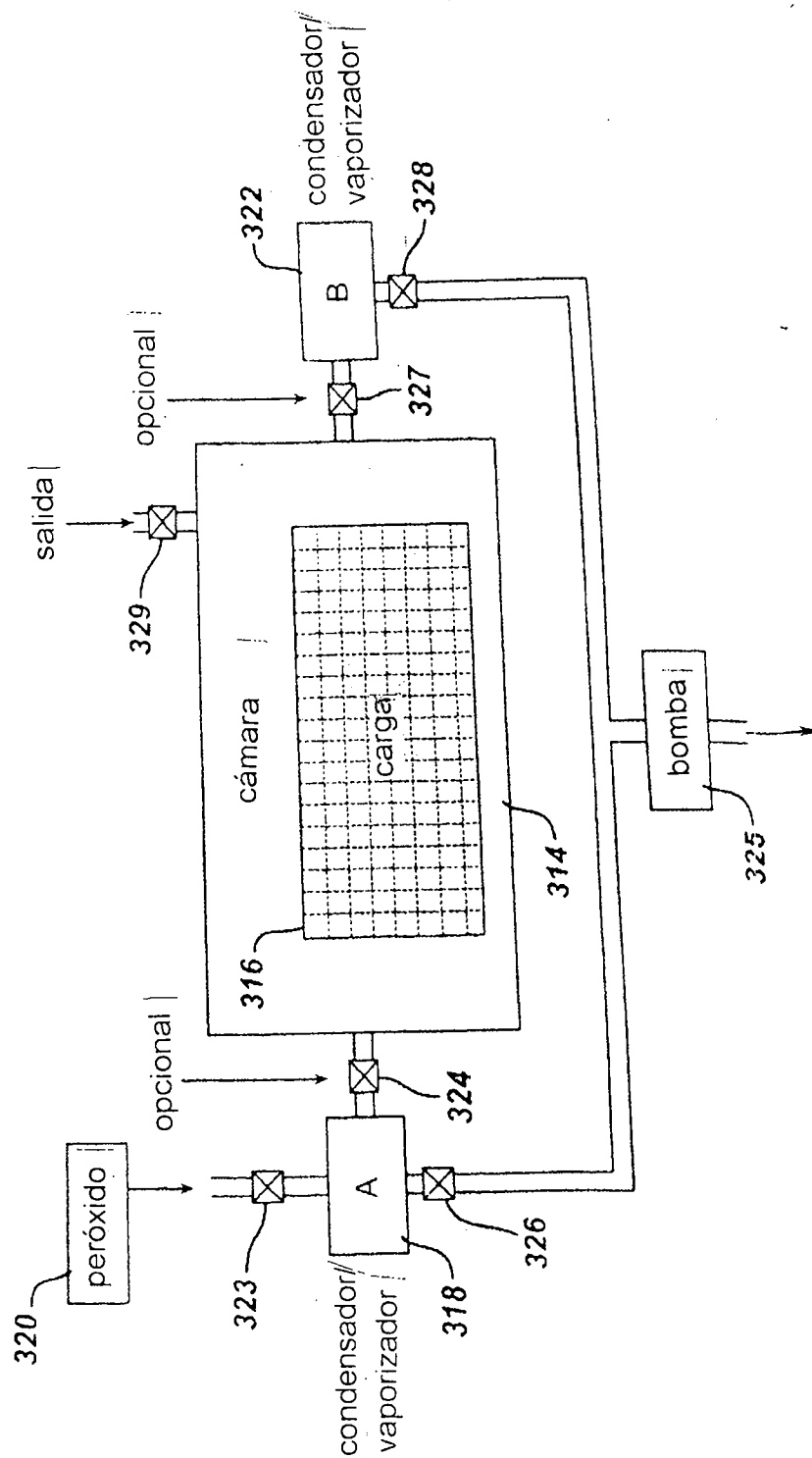
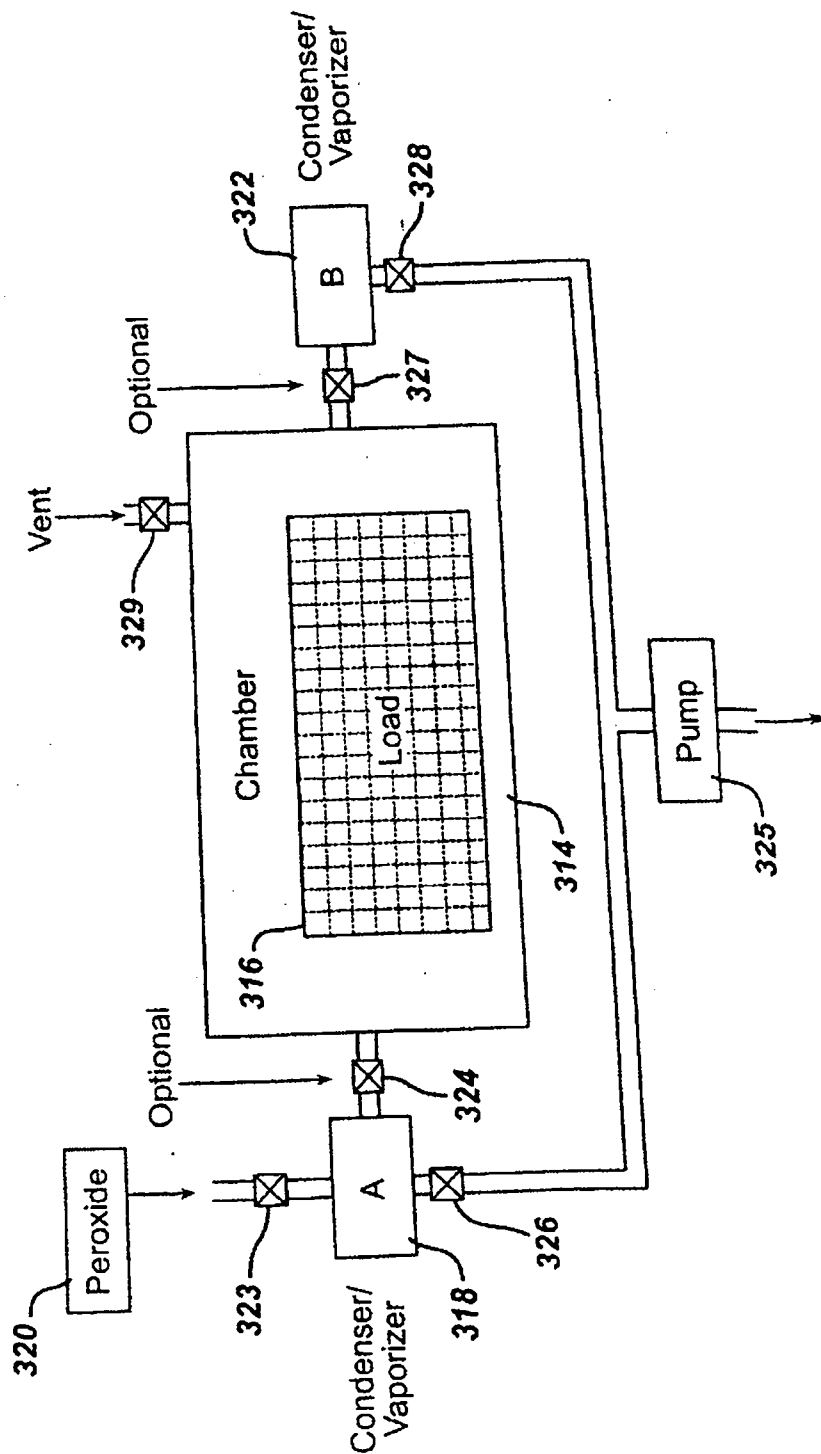


FIG. 16



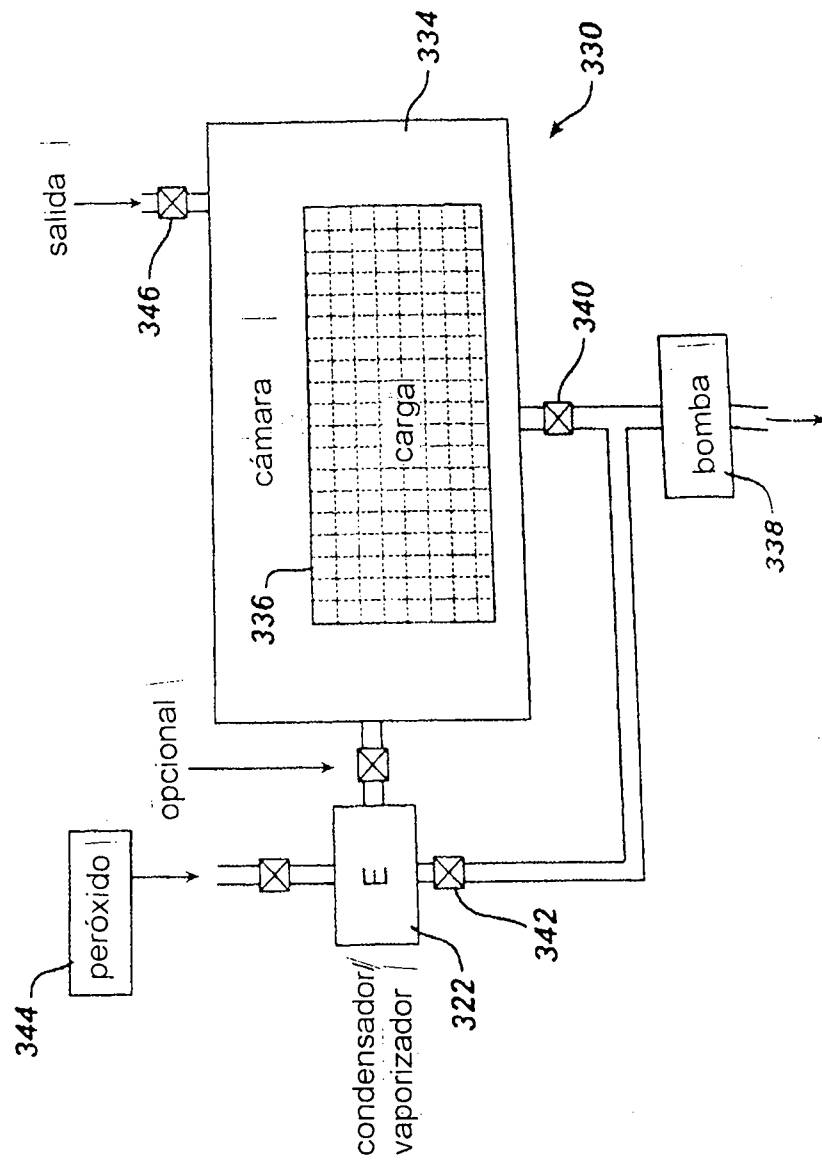
84
182

FIG. 16



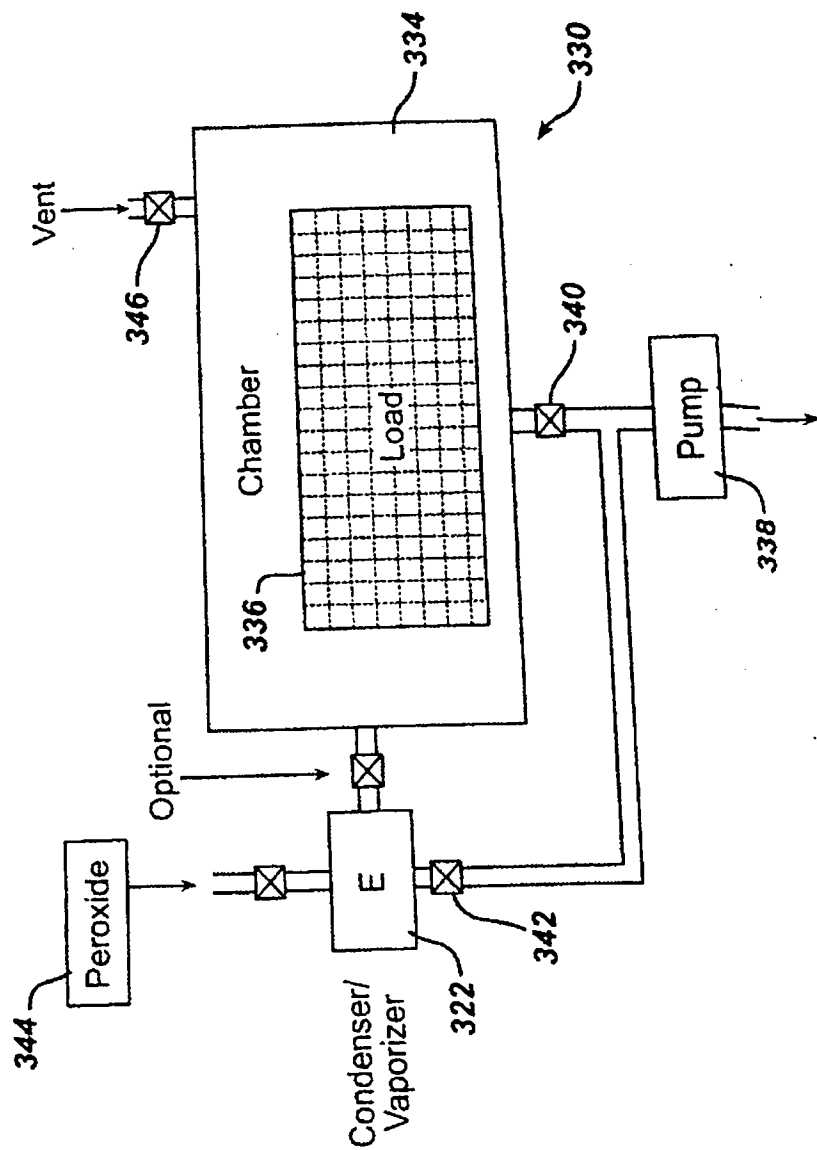
85
183

FIG. 17



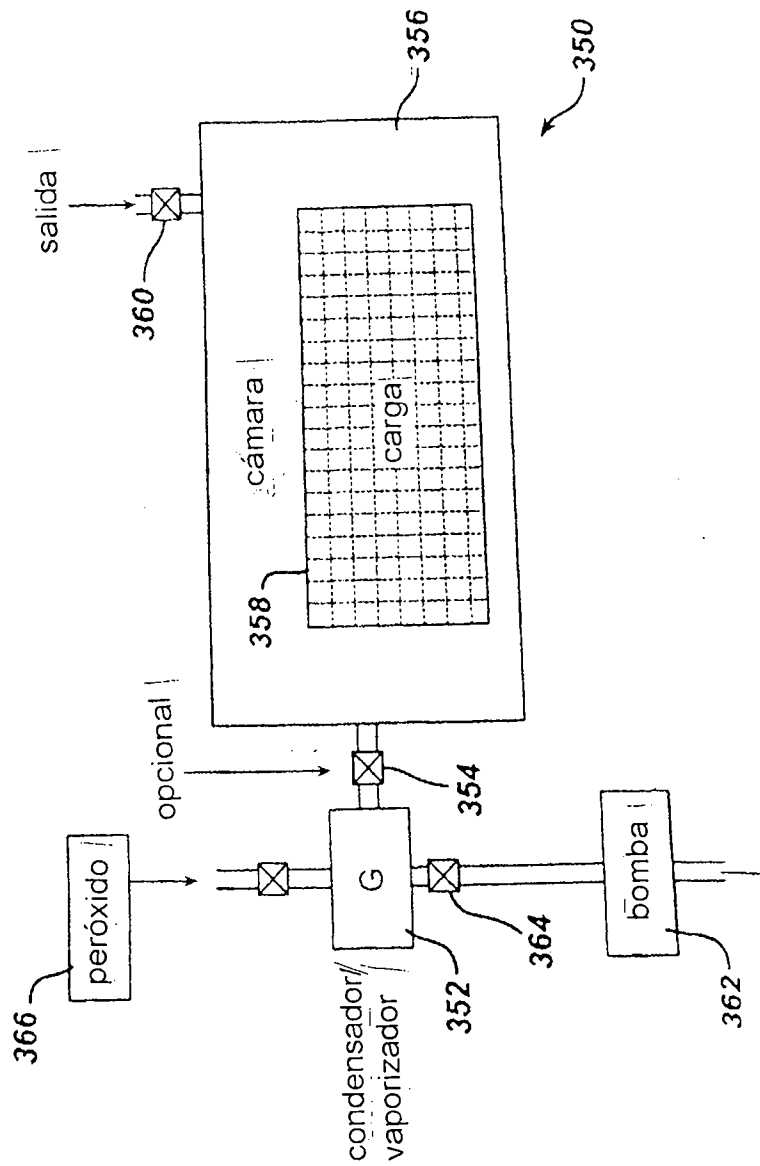
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FIG. 17



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FIG. 18



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FIG. 18

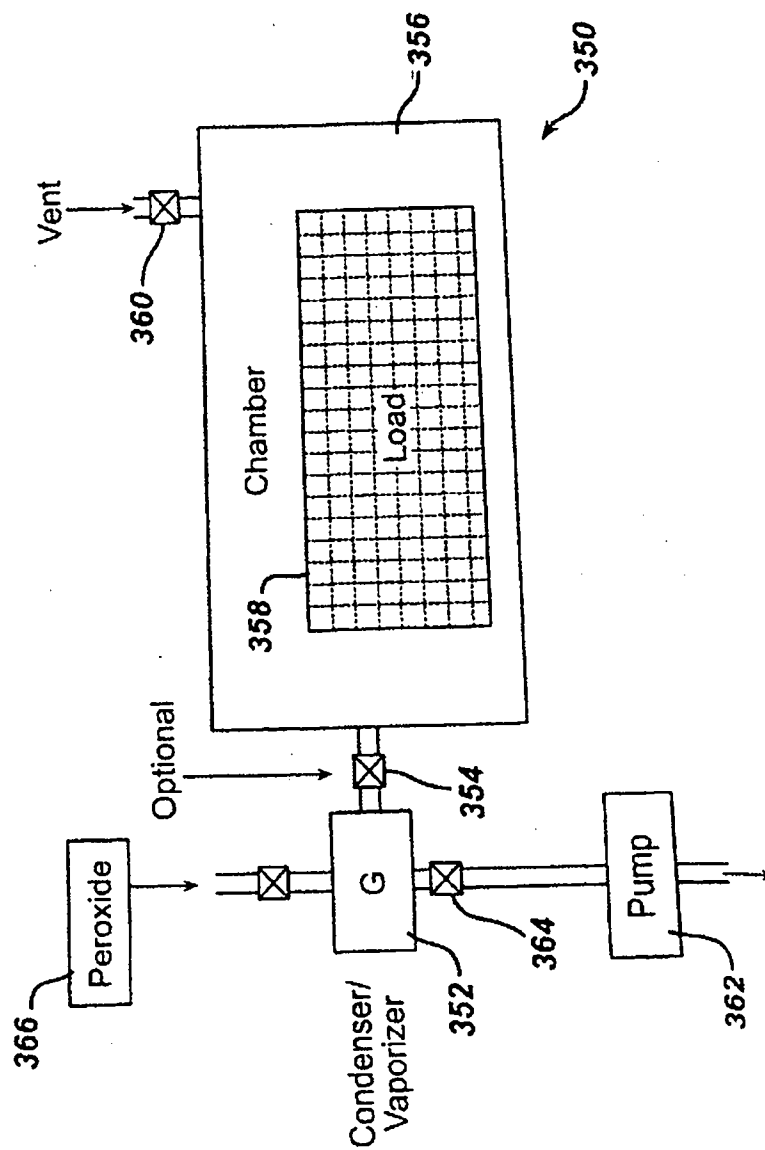
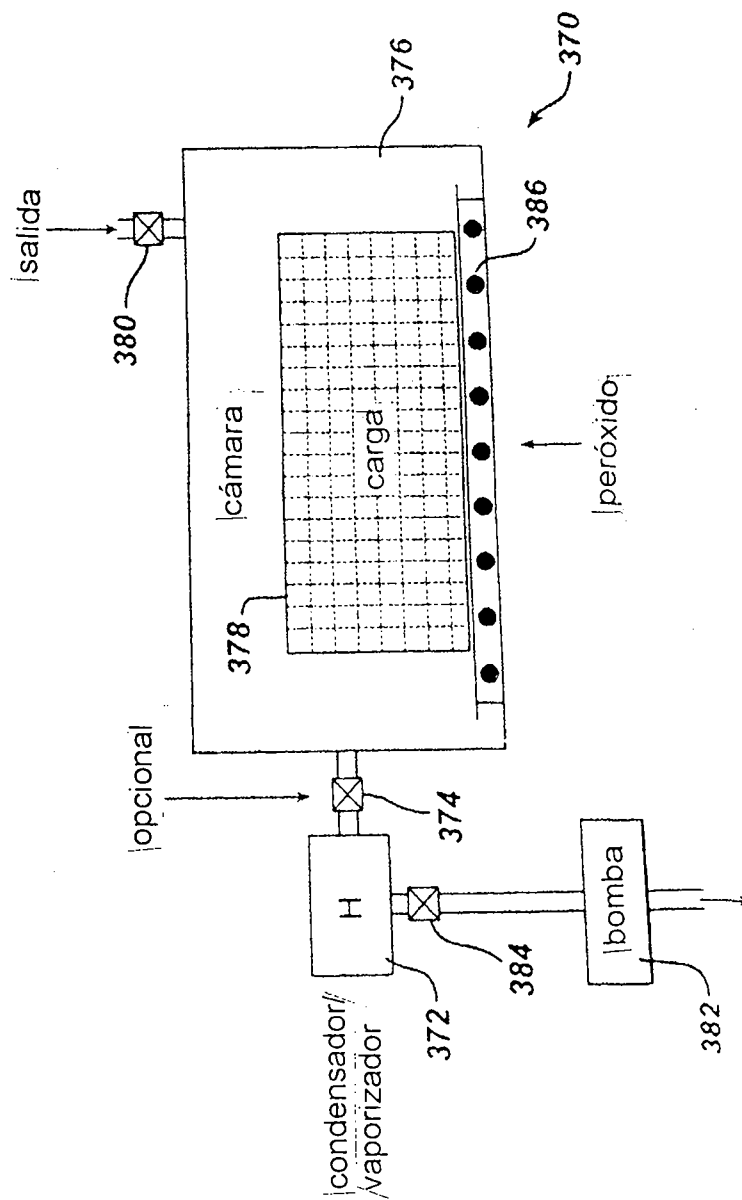


FIG. 19



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FIG. 19

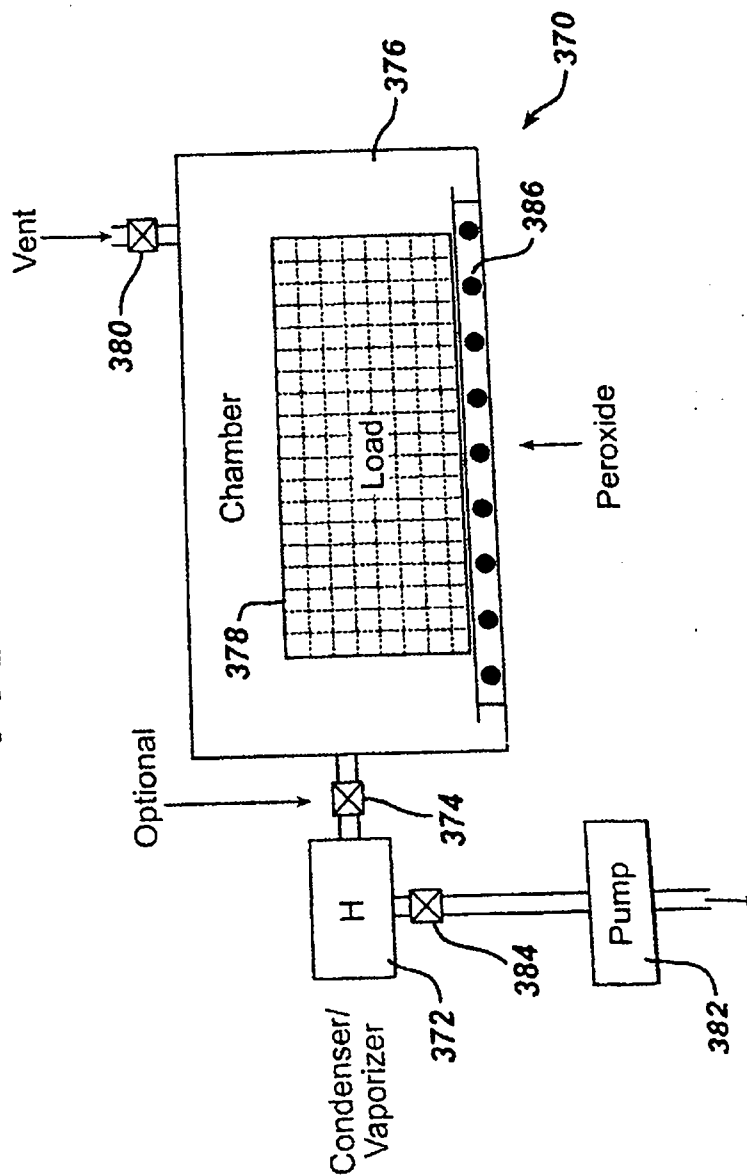
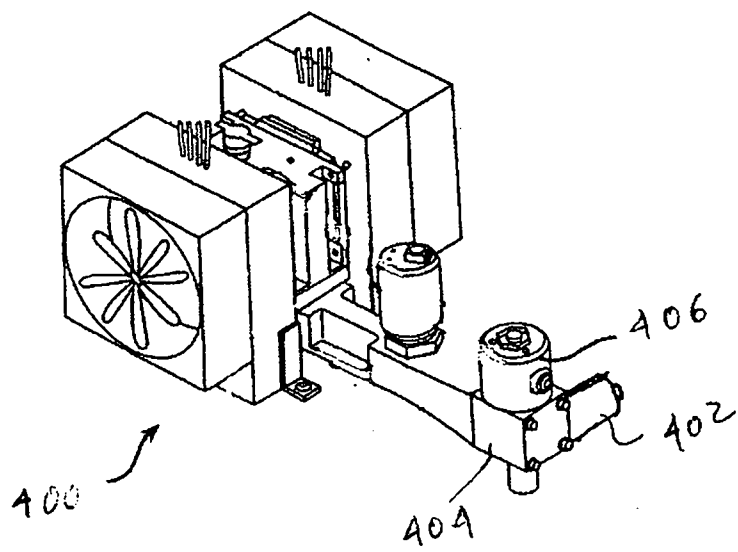


FIG. 20



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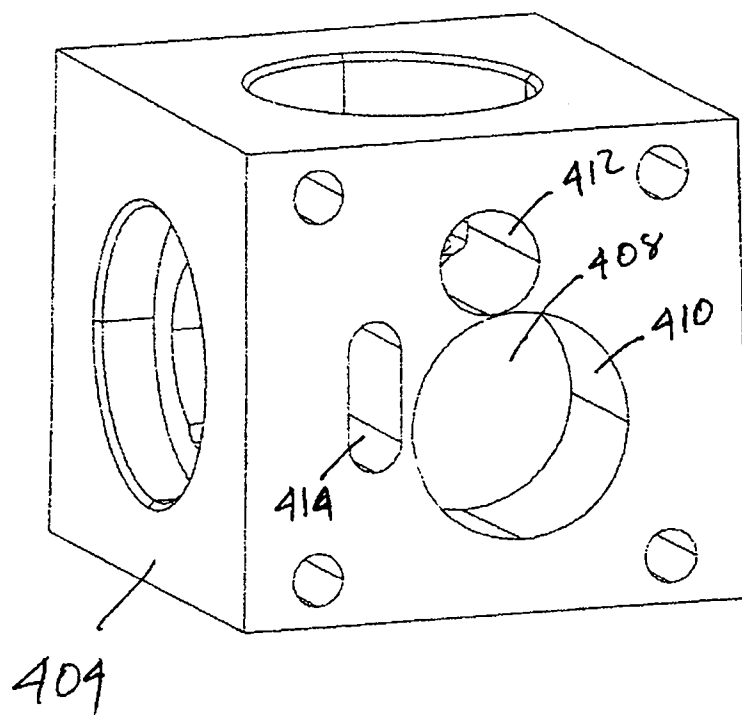


FIG. 21

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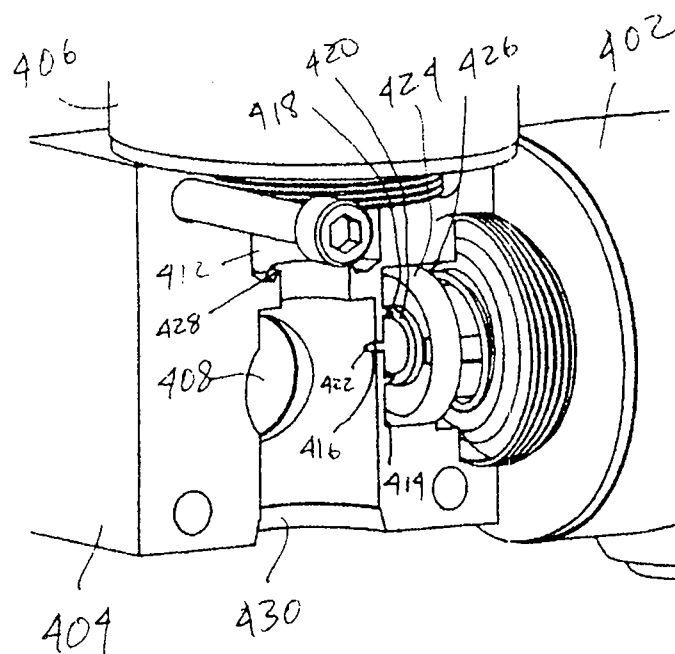
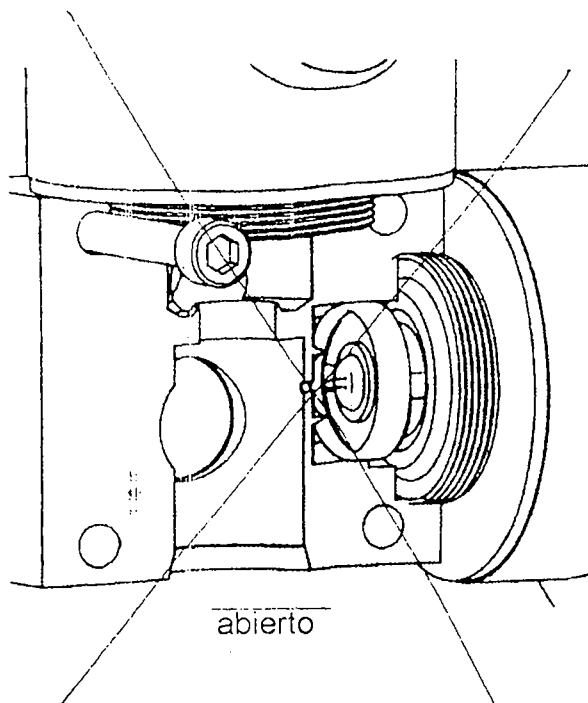


FIG. 22

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143

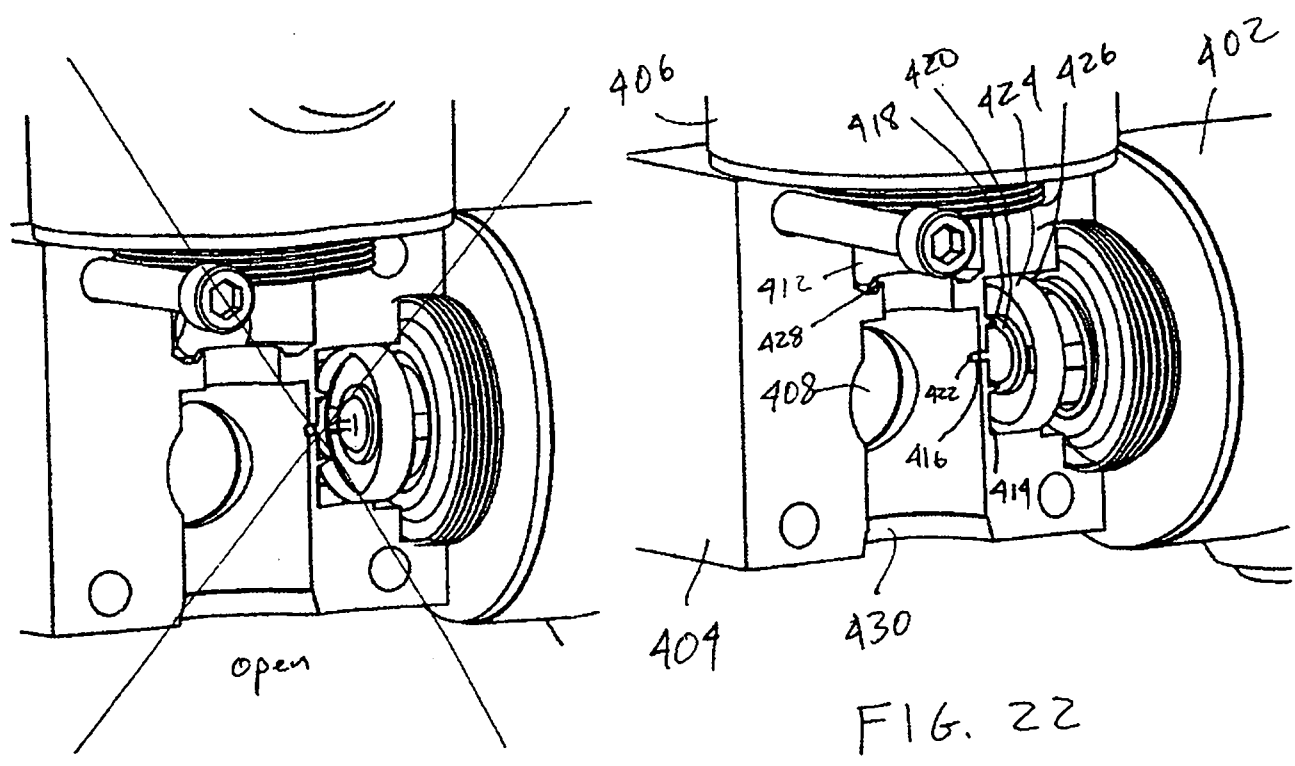
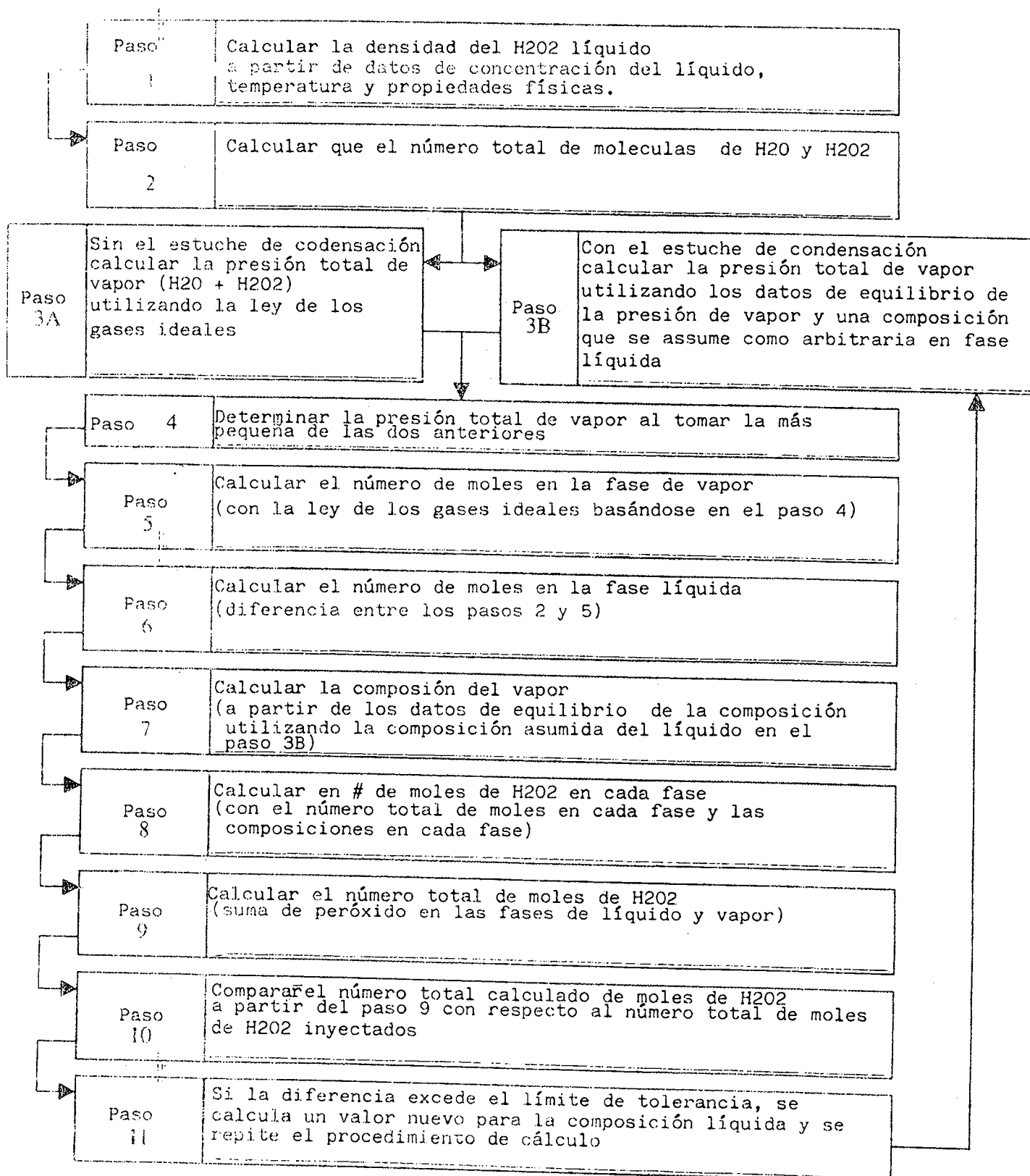


FIG. 23

Diagrama de flujo para calcular la concentración del peróxido condensado

Parámetros conocidos: Temperatura y tamaño de la cámara,
Concentración de peróxido líquido y volumen de inyección

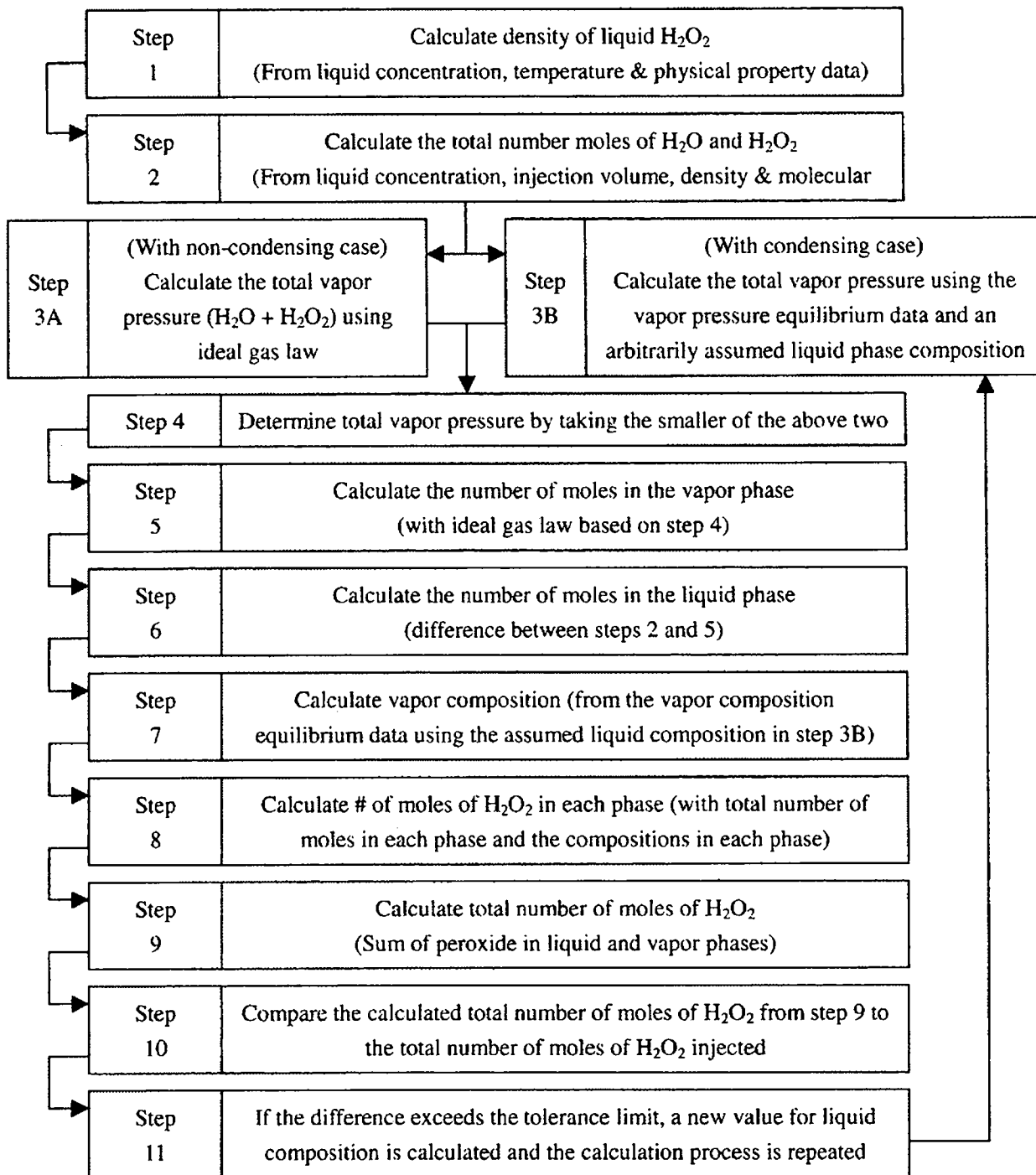


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FIG. 23

Flow chart for calculating concentration of condensed peroxide

Known parameters: Chamber temperature & size,
Peroxide liquid concentration & injection volume



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ESTADOS UNIDOS DE AMERICA
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DEPARTAMENTO DE COMERCIO DE LOS ESTADOS UNIDOS
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28 de marzo de 2007

La presente es para certificar que el anexo es una copia fiel de los registros de la Oficina de Patentes y Marcas de los Estados Unidos, de los documentos de la solicitud de patente identificada más adelante, que cumplieron con los requerimientos para concederse una fecha de presentación de acuerdo con 35 USC 111.

Número de Solicitud: 11/395,604

Fecha de Presentación: 31 de marzo de 2006

EL CÓDIGO DEL PAÍS Y EL NÚMERO DE SU SOLICITUD DE PRIORIDAD, PARA SER USADA EN LA PRESENTACIÓN EXTRANJERA BAJO EL CONVENIO DE PARÍS ES US11/395,604.

Por la autoridad de
Bajo el Secretario de Comercio para la Propiedad Intelectual y el Director de la Oficina de Patentes y Marcas de los Estados Unidos de América

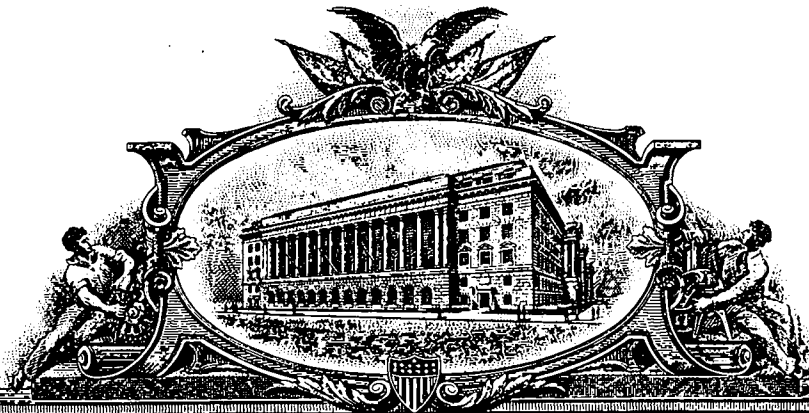
(fdo) M. K. CARTER

Oficial Certificador

Sello oficial de la Oficina de Patentes y Marcas de los Estados Unidos de América

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PA 1592020



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March 28, 2007

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APPLICATION NUMBER: 11/395,604

FILING DATE: March 31, 2006

THE COUNTRY CODE AND NUMBER OF YOUR PRIORITY APPLICATION, TO BE USED FOR FILING ABROAD UNDER THE PARIS CONVENTION, IS US11/395,604

**By Authority of the
Under Secretary of Commerce for Intellectual Property
and Director of the United States Patent and Trademark Office**




M. K. CARTER
Certifying Officer

033106

033106

UTILITY PATENT APPLICATION TRANSMITTAL		Attorney Docket No.	ASP-5042USNP
PTO 15866 U (only for new nonprovisional applications under 37 CFR 1.53(b))		Inventor	Charles G. Roberts, Martin Favero
		Title	A METHOD AND SYSTEM FOR PRION INACTIVATION
		Express Mail Label No.	EL961542132
APPLICATION ELEMENTS See MPEP Chapter 600 concerning utility patent application contents.		ADDRESS TO: Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450	
1. ☒ Fee Transmittal Form (e.g., PTO/SB/17) (submit an original and a duplicate for fee processing) 2. ☐ Applicant claims small entity status. 3. ☒ Specification [Total Pages 45] (Preferred arrangement set forth below) - Descriptive Title of the Invention - Cross Reference to Related Applications - Statement Regarding Fed sponsored R&D - Reference to sequence listing, a table, or a computer program listing appendix - Background of the Invention - Brief Summary of the Invention - Brief Description of the Drawings (if filed) - Detailed Description - Claim(s) - Abstract of the Disclosure 4. ☒ Drawing(s) (35 USC 113) [Total Sheets 24] 5. Oath or Declaration [Total Pages 3] a. ☒ unexecuted b. ☐ Copy from a prior application (37 CFR 1.63(d)) (for continuation/divisional with Box 18 completed) i. ☐ DELETION OF INVENTOR(S) Signed statement attached deleting inventor(s) named in the prior application, see 37 CFR 1.63(d)(2) and 1.33(b). 6. ☐ Application Data Sheet. See 37 CFR 1.76		7. ☐ CD-ROM or CD-R in duplicate, large table or Computer Program (Appendix) 8. Nucleotide and/or Amino Acid Sequence Submission (if applicable, all necessary) a. ☐ Computer Readable Form (CRF) b. ☐ Specification Sequence Listing on: i. ☐ CD-ROM or CD-R (2 copies); or ii. ☐ paper c. ☐ Statement verifying identity of above copies ACCOMPANYING APPLICATION PARTS 9. ☐ Assignment Papers (cover sheet & document(s)) 10. ☐ 37 CFR 3.73(b) Statement ☐ Power of Attorney (when there is an assignee) 11. ☐ English Translation Document (if applicable) 12. ☐ Information Disclosure Statement (IDS)/PTO-1449 ☐ Copies of IDS Citations 13. ☐ Preliminary Amendment 14. ☒ Return Receipt Postcard (MPEP 503) (Should be specifically itemized) 15. ☐ Certified Copy of Priority Document(s) (if foreign priority is claimed) 16. ☐ Request and Certifications under 35 U.S.C. 122 (b)(2)(B)(i). Applicant must attach form PTO/SB/35 or its equivalent. 17. ☐ Other	
18. ☐ If a CONTINUING APPLICATION, check appropriate box and supply the requisite information below and in a preliminary amendment, or in an Application Data Sheet under 37 CFR 1.76: ☐ Continuation ☐ Divisional ☐ Continuation-in-Part (CIP) of prior application No.: , filed . Prior application information: Examiner Group Art Unit: For CONTINUATION or DIVISIONAL APPS only: The entire disclosure of the prior application, from which an oath or declaration is supplied under Box 5b, is considered a part of the disclosure of the accompanying continuation or divisional application and is hereby incorporated by reference. The incorporation <u>can only</u> be relied upon when a portion has been inadvertently omitted from the submitted application parts.			
19. CORRESPONDENCE ADDRESS ☒ Customer Number or Bar Code Label 000027777 or ☐ Correspondence Address below Name: Philip S. Johnson, Esq. Address: Johnson & Johnson One Johnson & Johnson Plaza New Brunswick, NJ 08933-7003 USA			
20. TELEPHONE CONTACT Please direct all telephone calls or telefaxes to Andrew C. Farmer at: Telephone: (732) 524-2825 Fax: (732) 524-2808			
21. SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT REQUIRED			
NAME	Andrew C. Farmer		Reg. No. 35868
SIGNATURE	/Andrew C. Farmer/		
DATE	March 31, 2006		

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FEE TRANSMITTAL	<i>Complete if Known</i>	
	Application Number	
	Filing Date	March 31, 2006
	Inventor	Charles G. Roberts, Martin Favero
	Group Art Unit	
	Examiner Name	
	Attorney Docket Number	ASP-5042USNP

FEE CALCULATION

CLAIMS AS FILED

(1)	(2)	(3)	(4)	(5)
FOR:	NUMBER FILED	NUMBER EXTRA	RATE	BASIC FEE \$300.00
TOTAL CLAIMS	32 - 20 =	12	x 50.00	\$ 600.00
INDEPENDENT CLAIMS	2 - 3 =	0	x 200.00	\$ 0.00
SEARCH FEE	NA	NA	NA	\$ 500.00
EXAMINATION FEE	NA	NA	NA	\$ 200.00
APPLICATION SIZE FEE If the specification and drawings exceed 100 sheets of paper, the application size fee due is \$250 (\$125 for small entity) for each additional 50 sheets or fraction thereof. See 25 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).	0 - 100 =	/50	x 250.00 (If the specification and drawings exceed 100 sheets of paper, for each additional 50 sheets or fraction thereof)	\$
MULTIPLE DEPENDENT CLAIMS	☒	N/A	\$360.00	
			TOTAL FEES	\$ 1600.00

METHOD OF PAYMENT

- ☒ Please charge Deposit Account No. 10-0750/ASP-5042USNP/ACF in the amount of \$1,600.00. Three copies of this sheet are enclosed.
- ☒ The Commissioner is hereby authorized to charge any additional fees which may be required in connection with the filing of this communication, or credit any overpayment, to Account No. 10-0750/ASP-5042USNP/ACF. Three copies of this sheet are enclosed.

SUBMITTED BY:		<i>Complete (if applicable)</i>
Typed or Printed Name	Andrew C. Farmer	Reg. No. 35,868
Signature	/Andrew C. Farmer/	Date: March 31, 2006
		Deposit Account No. 10-0750

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DOCKET NO. ASP-5042USNP

IN THE UNITED STATES
PATENT AND TRADEMARK OFFICE

Applicant: Charles G. Roberts et al.

For : A METHOD AND SYSTEM FOR PRION INACTIVATION

Express Mail Certificate

"Express Mail" mailing number: EL961542132US

Date of Deposit: March 31, 2006

I hereby certify that this complete application, including specification pages, claims, drawings and an unexecuted Declaration and Power of Attorney, is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Laurie Phillips

(Typed or printed name of person mailing paper or fee)

/Laurie Phillips/

(Signature of person mailing paper or fee)

A METHOD AND SYSTEM FOR PRION INACTIVATION

FIELD OF THE INVENTION

The invention relates to treatment of articles, and more particularly to treatment of articles to inactivate prions thereon.

5

BACKGROUND OF THE INVENTION

Most medical instruments are sterilized prior to use.
10 Most are sterilized and sold in protective packaging to maintain their sterile state until the package is opened and the instrument is used in a medical procedure. Some instruments are re-used and must be sterilized prior to such re-use. Common methods of sterilization include high
15 temperature steam, irradiation, and chemical vapors such as ethylene oxide and hydrogen peroxide.

Prions are proteinacious infectious agents which cause similar fatal brain diseases, known as transmissible
20 spongiform encephalopathies (TSEs). These diseases include Creutzfeldt-Jakob disease (CJD) in humans, Bovine Spongiform Encephalopathy (BSE) in cattle, also known as "mad cow" disease, Scrapie in sheep, and Wasting disease in elk and deer. Creutzfeldt-Jakob variant disease (CJDv)
25 in humans is believed to be caused by the same proteins which cause BSE in cattle. The prions are believed to be an abnormal form of a protein commonly found in the host. However, unlike the normal form of the protein, the abnormal proteins accumulate, particularly in neural
30 tissue, eventually causing neural cell death.

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Common sterilization methods have not been successful in rendering prions non-infectious. Given that prions contain no DNA or RNA they are typically not considered
5 alive and cannot be killed in the conventional sense in which one thinks of sterilization of articles by killing infections microorganisms thereon. Rather, the goal is to inactivate the prion in some manner, such as by breaking one or more of its chemical bonds, to leave it unable to
10 cause prion disease such as CJD or CJDv in a host.

The generally accepted methodology for inactivating prions involves treatment with solutions having extremely high pH and temperature in an effort to denature the
15 prion. The manner in which a prion is folded tends to make denaturing the prion using typical protein denaturing agents ineffective. The elevated temperature and pH of the accepted methodology is often quite damaging to the instruments.

20

It had been thought that sterilization systems which employ hydrogen peroxide vapor and or hydrogen peroxide vapor coupled with plasma would be unable to inactivate prions. Tests were run on a typical system in which a 59%
25 solution of hydrogen peroxide is admitted into a sterilization chamber under vacuum conditions to create an effective sterilizing vapor of hydrogen peroxide and in which the vapor is at one point excited into the plasma stage. This methodology failed to sufficiently inactivate
30 prions on the instruments to render them non-infectious.

Surprisingly, the present inventors have found that application of hydrogen peroxide vapor of higher concentrations and/or higher plasma density is effective

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in inactivating prions and rendering an article so treated non-infections for prion diseases.

5 SUMMARY OF THE INVENTION

A method of inactivating prions according to the present invention comprises the steps of: placing an article having a quantity of prions thereon into a sterilization chamber; lowering pressure in the
10 sterilization chamber to a pressure below the vapor pressure of hydrogen peroxide; admitting a solution comprising hydrogen peroxide into the sterilization chamber and contacting the article with hydrogen peroxide
15 vapor; and inactivating prions in the chamber through contact between the prions and the hydrogen peroxide vapor.

Preferably, the concentration of the hydrogen
20 peroxide in the solution admitted into the chamber exceeds 70 percent, more preferably 75 percent, more preferably 80 percent, more preferably 85 percent, and most preferably exceeds 90 percent.

25 Preferably, the temperature of the article during the step of contacting the article with hydrogen peroxide vapor exceeds 30 degrees Celsius, more preferably 35 degrees Celsius, more preferably 40 degrees Celsius, and most preferably exceeds 45 degrees Celsius.

30

In one aspect of the invention, the method further comprises exciting the hydrogen peroxide vapor into the plasma phase and contacting the prions with the hydrogen peroxide in the plasma phase. Preferably, the plasma

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density is at least 10 milliwatts/cm³, more preferably 20 milliwatts/cm³, more preferably 30 watts/cm³, more preferably 40 watts/cm³, and most preferably at least 50 milliwatts/cm³.

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Preferably, the plasma is in contact with the prions for at least 2 minutes, more preferably 3 minutes, and most preferably at least 4 minutes.

10 Preferably, the hydrogen peroxide also effects sterilization of the article.

The concentration of at least a portion of the hydrogen peroxide can be increased prior to contacting the prions therewith, preferably by selectively removing water from the solution and exhausting that water through the sterilization chamber.

15 Gases surrounding the prions can be excited into the plasma phase and then contacted with the prions.

The steps of steps of lowering pressure in the sterilization chamber and admitting the solution into the sterilization chamber comprise a cycle and wherein the cycle is repeated one or more times.

25 A method, according to the present invention, of inactivating prions comprises the steps of: placing an article having a quantity of prions thereon into a sterilization chamber; contacting the article with a plasma to effect inactivation of the prions. Preferably, the plasma is formed from a gas comprising hydrogen peroxide. Preferably, the plasma density is at least 10 milliwatts/cm³, more preferably 20 milliwatts/cm³, more

preferably 30 watts/cm³, more preferably 40 watts/cm³, and most preferably at least 50 milliwatts/cm³.

5 BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a block diagram of a sterilization system according to the present invention;

10 FIG. 2 is a block diagram of a vaporizer and diffusion path of the sterilization system of FIG. 1;

FIG. 3 is a block diagram of an alternate embodiment of a sterilization system according to the present
15 invention;

FIG. 3A is a block diagram of an alternative embodiment of a sterilization system according to the present invention.

20 FIG. 3B is a sectional view taken along lines 3B--3B of FIG 3A;

FIG. 4 is a block diagram of an alternate embodiment of a sterilization system according to the present
25 invention;

FIG. 5 is a block diagram of an alternate embodiment of a sterilization system according to the present
invention;

30 FIG. 6 is a section view taken along lines 6--6 of FIG. 5;

FIG. 7 is a block diagram of an alternate embodiment of a sterilization system according to the present invention;

5 FIG. 8 is a section view taken along lines 8--8 of FIG. 7;

FIG. 9 is a block diagram of a sterilization system according to the present invention;

10

FIG. 10 is a cut-away view of an outlet condenser/vaporizer for use in the system of FIG. 9;

FIG. 11 is a cut-away view of an inlet
15 condenser/vaporizer for use in the system of FIG. 9;

FIG. 12 is a perspective view of an alternative inlet condenser/vaporizer for use in the system of FIG. 9;

20 FIG. 13 is an exploded perspective view of the condenser/vaporizer of FIG. 12;

FIG. 14 is a section view taken along lines 14--14 of FIG. 12;

25

FIG. 14A is a close-up section view of the valve assembly shown in FIG. 14;

FIG. 15 is an exploded perspective view of a
30 thermoelectric heat pump and rod assembly employed in the condenser/vaporizer of FIG. 12;

FIG. 16 is an alternative sterilization system according to the present invention;

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FIG. 17 is an alternative sterilization system according to the present invention;

5 FIG. 18 is an alternative sterilization system according to the present invention;

FIG. 19 is an alternative sterilization system according to the present invention;

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FIG. 20 is a perspective view of an alternative inlet condenser/vaporizer for use in the system of FIG. 9;

15 FIG. 21 is a valve block employed in the inlet condenser/vaporizer of FIG. 20; and

FIG. 22 is a cut-away view of the valve block of FIG. 21 as employed in the inlet condenser/vaporizer of FIG. 20.

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DETAILED DESCRIPTION

FIG. 1 shows in block diagram form a sterilization system 10 which is effective not only in killing traditional infectious microorganisms such as bacteria and viruses, but has also been shown to be effective in inactivating prions. It comprises in gross a sterilization chamber 12, a vaporizer 14, and a vacuum pump 16. The vacuum pump is capable of drawing a vacuum on the chamber, preferably as low as 0.5 torr. Between the vacuum pump 16 and the chamber 12, is preferably located a throttle valve 18 and optionally an orifice plate 20. The throttle valve 18 preferably also has good shut-off

capability. A pressure gauge 22, preferably located adjacent to the throttle valve 18, shows the vacuum in the chamber 12. A vent valve 23 employing a HEPA antimicrobial filter allows clean sterile air to enter the chamber 12. The vaporizer 14 connects to the chamber 12 by means of an elongated diffusion path 24. Turning also to FIG. 2, the diffusion path 24 incorporates temperature control elements 26 to control the temperature along the diffusion path 24.

10

Vaporizers suitable for vaporizing a liquid sterilant such as hydrogen peroxide solution are known in the art. Kohler et al. U.S. Patent No. 6,106,772 and Nguyen et al. U.S. Patent Application No. 09/728,973 filed December 10, 2000, both incorporated herein by reference, illustrate vaporizers suitable for the present application. In its simplest form the vaporizer can comprise a small chamber into which the liquid hydrogen peroxide solution is injected. The low pressure in the vaporizer caused by the vacuum in the chamber causes the hydrogen peroxide solution to vaporize.

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Preferably, the vaporizer 14 itself incorporates heating elements 28 which control the temperature in the vaporizer to optimize the vaporization process. Preferably, where the vaporizer 14 connects to the diffusion path 24 some form of thermal insulation 30 is provided at the interface so that the high temperatures of the vaporizer 14 will not unduly affect the temperature in the diffusion path 24. The vaporizer 14 and diffusion path 24 are preferably formed of aluminum; the thermal insulation 30 can take the form of a polyvinyl chloride (PVC) joint connecting the two together.

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Further, it is preferable to include a heater 32 inside the chamber 12, preferably near a lower portion of the chamber 12 for revaporizing condensed hydrogen peroxide inside the chamber 12.

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The chamber 12 preferably includes a mechanism (not shown) to create a plasma therein. Such mechanism can include a source of radio or low frequency energy as described by Jacobs et al. U.S. Patent No. 4,643,867, or by
10 Platt, Jr. et al. in published U.S. Application Document No. 20020068012, both of which are incorporated herein by reference.

The present invention achieves its beneficial effect
15 by allowing some of the hydrogen peroxide which is vaporized out of solution in the vaporizer 14 to condense onto the diffusion path 24. After most of the hydrogen peroxide solution has vaporized, the temperature control elements 26 raise the temperature of the diffusion path to
20 allow the condensed hydrogen peroxide to re-vaporize. Water has a higher vapor pressure than hydrogen peroxide, thus hydrogen peroxide in the vapor condenses more easily than water. Thus, the material which condenses in the diffusion path will have a higher concentration of
25 hydrogen peroxide than the starting concentration of the hydrogen peroxide solution in the vaporizer 14.

The temperature control elements 26 in simple form can comprise mere electric resistance heaters. In such
30 case, the low ambient temperature of the diffusion path 24 provides the low temperature for condensing hydrogen peroxide thereon, and the control elements 26 later heat the diffusion path 24 to re-vaporize the now more highly concentrated hydrogen peroxide from the diffusion path 24.

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Because the vapor pressure of hydrogen peroxide drops with lower temperatures, lower initial temperatures in the diffusion path 24 allows a lower pressure in the chamber 24 without subsequently preventing the condensation of hydrogen peroxide in the diffusion path. Lower chamber pressures promote system efficiency and thus, the temperature control elements 26 can further comprise a chilling component to lower the temperature of the diffusion path below ambient. Suitable chilling components include thermoelectric coolers or a typical mechanical refrigeration system. In such case, the diffusion path 24 would be first chilled, preferably to about 10°C, and then some time after vaporization has begun or even after it has completed, the diffusion path 24 is then heated, preferably up to 50°C or 110°C.

When vertically oriented as in FIG. 2, the diffusion path 24 can potentially cause the vaporizing sterilant to condense in cooler regions between the temperature control elements 26 and then re-vaporize as it passes the temperature control element 26.

The following example illustrates the benefits of controlling the heat in the diffusion path.

EXAMPLE 1

The efficacy tests were conducted by placing a CSR-wrapped tray (3.5"x10"x20") consisting of representative medical devices and test lumens in a 20-liter aluminum chamber (4.4"x12"x22"). A one-inch stainless steel wire inoculated with at least 1×10^6 *Bacillus stearothermophilus* spores was placed in the center of each of the test lumens. The effects with and without temperature control

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of the diffusion path were investigated with both a TEFLON, poly(tetrafluoroethylene) lumen having an internal diameter of 1mm and a length of 700mm, and a stainless steel lumen having an internal diameter of 1mm, and a length of 500mm. All lumens were open at both ends. Each of the samples were subjected to a sterilization cycle in a 20 liter vacuum chamber, which was held at 40°C and 3 torr for 5 minutes. 1.44 ml of a 59% solution of hydrogen peroxide in water was injected at atmospheric pressure into the vaporizer which was held at 60°C. The 5 minute clock then started and the chamber was pumped down to 3 torr, which took less than one minute. In one case the diffusion path 24 had an initial temperature of 30°C for the first minute while the chamber was evacuated to 3 torr and was then heated to 50°C to release the condensed peroxide from the diffusion path into the chamber for the remainder of the cycle while pressure was maintained at 3 torr. In the other case, the diffusion path was held at 50°C throughout the cycle. By maintaining the diffusion path at 50°C, no or little peroxide was retained in the diffusion path. Sterilization effectiveness was measured by incubating the test samples in growth media at 55°C and checking for growth of the test organism. Table 1 shows the results of these tests.

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TABLE 1

Lumen Type	ID & Length	50°C Diffusion Path Throughout Process	30°C Diffusion Path For One Minute Then increased to 50°C
Teflon	1 x 700	2/2	0/3
Stainless Steel	1 x 500	1/2	0/3

When the diffusion path temperature was maintained at high temperature throughout the process, all of the samples in the TEFLON lumen tested positive for bacteria growth, indicating failure of sterilization, and one of two samples in the stainless steel lumen tested positive. Under the same conditions, but with an initially lower temperature diffusion path which was heated starting one minute after the diffusion began, none of the samples tested positive. Condensing the peroxide in the diffusion path during the initial vaporization stage and then re-vaporizing the condensed peroxide from the diffusion path into the chamber greatly enhance the efficacy.

Additional efficiencies can be achieved by alternating cool and warm regions in the diffusion path as primarily illustrated in FIG. 2. The temperature control elements 26, in simple form heating elements, are spaced apart from one another. Also, preferably, the diffusion path 24 is vertical in this respect. As the hydrogen peroxide solution vaporizes and passes through the diffusion path 24, it is thought that it may alternately condense and re-vaporize as it passes over the heated and unheated sections of the diffusion path 24.

The diffusion path could alternatively comprise alternating heating and cooling elements.

5 The heater 32 within the chamber 12 acts similarly to the heating of the diffusion path 24. By controlling the heater 32 temperature, the peroxide can be first condensed on the heater 32 and then re-vaporized into the chamber 12 to concentrate the peroxide.

10 A preferred cycle would be a modification of a cycle described in the Wu et al. U.S. Patent No. 6,365,102, incorporated herein by reference. A series of pre-plasma energy additions with venting in-between dries moisture from the chamber 12. A vacuum is then drawn upon the
15 chamber 12 and the hydrogen peroxide solution injected into the vaporizer 14. Alternatively, the peroxide solution can also be injected at atmospheric pressure. Some of the vaporizing solution condenses upon the cool diffusion path 24. After a time sufficient for most or
20 all of the hydrogen peroxide solution to vaporize from the vaporizer 14, the diffusion path 24 is warmed by the temperature control elements 26 and the condensed hydrogen peroxide solution re-vaporizes. At about this time, the throttle valve 18 is closed and the pump 16 turned off to
25 seal the chamber 12. Much of the water fraction of the hydrogen peroxide solution has thus been drawn out of the chamber 12 by the vacuum pump 16 and the remaining hydrogen peroxide solution which re-vaporizes from the diffusion path 24, or from the heater 32 in the chamber 12
30 if present, is of a higher hydrogen peroxide concentration than the starting solution. Preferably, a computer based control system (not shown) controls the functions of the process for ease and repeatability.

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The hydrogen peroxide vapor thus produced contacts an article 34 or articles 34 in the chamber 12 and effects sterilization thereof. If those articles 34 have diffusion restricted areas, such as long, narrow lumens, it may be preferable to then vent the chamber 12 and allow clean sterile air therein to drive the hydrogen peroxide vapor deeper into the diffusion restricted areas. Then the chamber 12 is again subjected to vacuum and an additional injection of hydrogen peroxide, preferably with the heating sequence on the diffusion path, is repeated. After a time period sufficient to effect sterilization of the article 34, preferably with a six-log reduction in challenge organisms such as *Bacillus stearothermophilus*, a plasma is lit within the chamber 12, thereby enhancing the sterilization and breaking down the hydrogen peroxide into water and oxygen.

The orifice plate 20 can enhance the effect of concentrating the hydrogen peroxide during its vaporization. As described in the Lin et al. U.S. Patent No. 5,851,485, incorporated herein by reference, a controlled or slow pump-down of the chamber 12 initially draws off more water than hydrogen peroxide from solution as the water has a higher vapor pressure, thereby leaving a higher concentration hydrogen peroxide behind. Controlling the pump-down can be difficult as vacuum pumps generally do not throttle back well and throttle valves in such service are difficult to control and expensive. By placing the orifice plate 20 in the flow path to the pump 16, the amount of atmosphere from the chamber 12 exhausted by the pump 16 is limited, and by selecting a proper size orifice 36 in the plate 20 can be controlled to a rate which effectively concentrates hydrogen peroxide in the chamber 12.

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Turning also to FIG. 3, a system 10a, similar in most respects to the system 10 of FIGS. 1 and 2, with like part numbers denoted with an "a" appended thereto, also incorporates an orifice plate 20a. However, to allow a quick pump-down of the chamber 12a, yet retain the controlled pump-down benefits of the orifice plate 20a, it incorporates two path ways from the pump 16a to the chamber 12a. A first pathway 40 contains a throttle valve 42 and a second pathway 44 contains a throttle valve 46 and the orifice plate 20a. Thus, during initial pump-down the first throttle valve 42 is open leaving the pump 16a freely connected to the chamber 12a. As the chamber 12a approaches the vapor pressure of water, the first throttle valve 42 is closed thereby forcing the pump 16a to evacuate through the orifice plate 20a and thus draw out of the chamber 12a at a slower, controlled rate more conducive to preferentially drawing water out of the hydrogen peroxide solution and out of the chamber 12a.

Turning also to FIGS. 3A and 3B, a system 110 similar to that of FIG. 1 is shown. Here, rather than use two paths as in the system 10a of FIG. 3, a valve 112 comprises a valve body 114, a valve seat 116 and a valve element 118, such as a butterfly disc, plug or the like. An orifice 120 is provided through the valve element. Thus, when the valve 112 is open evacuation can occur quickly, and when the valve 112 is closed it can occur more slowly. Such a valve could also be employed between the vaporizer 14 and the chamber 12 to further control the preferential vaporization and removal of the water from the germicide solution.

Turning now to FIG. 4, while highly concentration of the sterilizing vapor is helpful in achieving

sterilization efficiency and efficacy, getting the vapor into contact with the items to be sterilized is also a concern. Typically, the low pressures (0.5 torr to 10.0 torr) inside of a chamber 12 promotes quick diffusion of the sterilant vapor to all areas therein.

FIG. 4 illustrates a sterilization system 60 comprising a chamber 62 having a vaporizer 64, vacuum pump 66 and vent 68 connected thereto. Preferably, an elongated, temperature controlled diffusion path 70 as previously described connects the vaporizer 64 to the chamber 62. A throttle valve 72 and pressure gauge 74 are provided at the pump 66.

Articles 76 to be sterilized are placed into trays or containers 78. Two types of packaging are commonly used in preparing articles 76 for sterilization. In one, the articles 76 are placed into a tray having a plurality of openings therein, and the tray is then wrapped with a material such as CSR wrap which passes sterilizing gases and blocks contaminating microorganisms. Such a tray is described in the Wu, U.S. Patent No. 6,379,631, incorporated herein by reference. An alternative package comprises a sealable container with several ports, preferably on top and bottom surfaces thereof, with each of the ports covered by a semi-permeable membrane which passes sterilizing gases and blocks admission of contaminating microorganisms. Such a container is described in Nichols U.S. Patent No. 4,704,254, incorporated herein by reference. The first type of packaging is typically called a "tray" and the second a "container." However, the term "container" as used herein is meant to refer to any container, packaging or enclosure

suitable for containing articles to be sterilized in a chemical vapor environment.

The pump 66 connects to the chamber 62 via an exhaust manifold 80. The manifold 80 comprises one or more shelves 82 for supporting and receiving one or more containers 78 and which connect fluidly through the throttle valve 72 to the pump 66. An opening, or preferably a plurality of openings 84 on the upper surfaces of the shelves 82 allow the pump 66 to draw atmosphere within the chamber 62 through the openings 84, through the manifold 80 and out through the pump 66.

The containers 78 preferably have openings 86 on a lower surface 88 thereon and additional openings 90 on at least one other surface. When the containers 78 are placed on the shelves 82 atmosphere being exhausted by the pump 66 is drawn in part through the openings 90 into the container 78, through the container into contact with the article or articles 76 therein and then out through the openings 86 into the manifold 80 through the openings 84 therein. When the atmosphere being so exhausted contains a sterilizing gas it enhances its penetration into the containers 78 and into contact with the articles 76 therein.

Sterilizing gases are so exhausted during the previously described cycle as the sterilant solution is vaporizing and immediately before the second admission of hydrogen peroxide. Such a cycle can also further provide a pump-down after some period of diffusion. After admitting the sterilant vapor the chamber 62 pressure rises slightly due to the presence of additional gas therein, typically from about 0.5 torr to about 10 torr.

Higher pressures are as efficient with higher load and chamber temperatures.

Turning also to FIGS. 5 and 6, an alternative design (in which like part numbers to those of the design of FIG. 4 are designated with a "b" appended thereto) replaces the manifold 80 of the design of FIG. 4 with a simple port 92. The port 92 is covered by a support 94 for the container 78, the support 94 having a plurality of openings 96 therethrough so that the chamber 62b is in fluid communication with the pump 66b through the container 78, the support 94 and the port 92. The support 94 can be removable.

Turning also to FIGS. 7 and 8 (in which like part numbers to those of the designs of FIGS. 4 to 6 are designated with a "c" appended thereto) shows a support 100 resting on a surface 102 in the chamber 62c through which penetrates the port 92c. The support 100 surrounds the port 92c. Thus, most or all of the atmosphere being exhausted by the pump 66c passes through the container 78 into a space 104 formed between the container 78, the support 100 and the surface 102 and then onto the pump 66c through the port 92c.

FIG. 9 discloses an alternative system in which, similar to the system of FIG. 1, a portion of the vaporized germicide solution can be condensed and the solvent, typically water, which has not condensed as quickly is removed from the atmosphere to further concentrate the germicide. The germicide is then revaporized to produce a more concentrated germicidal vapor for more efficient sterilization. The system comprises a sterilization chamber 200 containing a load

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202 of items to be sterilized. A source 204 of liquid germicide solution provides the solution through a valve 206 to a first vaporizer/condenser 208 where it is vaporized and then supplied to the chamber 200. A valve
5 210 can be provided to isolate the vaporizer/condenser 208 from the chamber 200. The chamber 200 is also provided with a valved vent 212.

A vacuum pump 214 provides for lowering the chamber
10 pressure as described in reference to the previous embodiments. Between the pump 214 and the chamber 200 a second vaporizer/condenser 216 is provided for condensing the vaporized solution. Preferably valves 218 and 220 isolate the second vaporizer/condenser 216 from the pump
15 214 and chamber 200 respectively.

Turning also to FIG. 10 a simple version of the second vaporizer/condenser 216 preferably comprises walls 222 defining an enclosure 224 having an inlet 226
20 connected to the chamber 200 and an outlet 228 connected to the pump 214. A plurality of baffles 230 provides a torturous flow path 232 through the vaporizer/condenser 216. The walls 222, and potentially the baffles 230, are temperature controllable to enhance condensation of and
25 re-vaporization of the solution.

A similar structure with an inlet can be employed on the first vaporizer/condenser 208 as well. Turning also to FIG. 11, a simple version of the first
30 condenser/vaporizer 208 is illustrated. It comprises an enclosure 240 having an inlet 242 connected to the source of solution 204 (not shown in FIG. 11) and an outlet 244 connected to the chamber 200 (not shown in FIG. 11). A plurality of baffles 246 provides a tortuous flow path

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through the first vaporizer/condenser 208. The enclosure 240 and potentially the baffles 246 are temperature controllable to enhance condensation and revaporization of the solution.

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In a simple cycle, a liquid germicide solution, such as hydrogen peroxide and water is admitted into the first vaporizer/condenser 208 where it is vaporized and then flows into the chamber 200 which is at a low pressure, all as described in reference to previous embodiments herein. During vaporization and for sometime thereafter pump 214 continues to exhaust atmosphere from the chamber 200. By controlling temperature and pressure this preferentially vaporizes water from the solution over the hydrogen peroxide and the water vapor is extracted from the system via the pump 214 to concentrate the hydrogen peroxide solution during the vaporization phase. Additionally, hydrogen peroxide, having the lower vapor pressure, will tend to condense more quickly than the water vapor in the first vaporizer/condenser 208. As the pump 214 continues to exhaust atmosphere from the chamber 200 the vaporized hydrogen peroxide solution flows out of the chamber and into the second vaporizer/condenser 216 where a portion thereof will condense. Due to the preferential condensation of hydrogen peroxide over the water more of the water vapor will pass through the condenser 216 uncondensed and be exhausted via the pump 214 thus allowing further concentration of the hydrogen peroxide solution. At some point, the pump is turned off and the valve 218 closed. The condensed hydrogen peroxide within the vaporizer/condenser 216 is then re-vaporized preferably by heating the condenser 216. This hydrogen peroxide will have a higher concentration for more efficient sterilization of the load 202.

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Turning also to FIGS. 12 through 15, a more elaborate condenser/vaporizer 250 is illustrated. In gross, it comprises an inlet manifold 252 which connects to the source of sterliant solution 204 and which provides
5 initial vaporization, a condensing/revaporization section 254, an outlet manifold 256 and a control valve 258 via which the vaporizer/condenser 250 connects to the chamber 200. A resistance heater 260 affixes to the inlet manifold 252 and to the outlet manifold 256 to provide
10 heat to assist in the initial vaporization within the inlet manifold 252 and to prevent condensation in the outlet manifold 256. Preferably, the inlet manifold 252 and outlet manifold 256 are formed of aluminum. Further, an insulator 262 is provided between the inlet manifold
15 252 and the vaporizer/revaporizer section 254.

The vaporizer/revaporizer section 254 comprises a housing 264, preferably formed of aluminum, open on a first side 266 and second side 268. A first thermo-
20 electric device 270 and second thermo-electric device 272 affix to the first side 266 and second side 268, respectively. The thermoelectric devices 270 and 272 preferably operate under the Peltier effect, although other classes of thermoelectric devices could be
25 substituted therefor. More conventional heat pumps, such as freon or ammonia based systems can also be employed with somewhat greater complexity.

A first rod assembly 274, comprising a plate 276 and
30 a plurality of rods 278 extending normally therefrom affixes to the first thermo-electric device 270 with the rods 278 extending laterally into the housing 264. A second rod assembly 280 similarly attaches to the second thermo-electric device 272 with its rods 278 extending

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laterally into the housing 264 in facing relationship to the first rod assembly 274. The rod assemblies 274 and 280 are preferably formed of aluminum.

5 Preferably, the rods 278 extend almost to, without touching, the opposing plate 276. Also, the rods 278 from the two rod assemblies 274 and 280 lie in a generally parallel relationship with each other with a spacing therebetween designed to, along with the volume within the
10 vaporizer/revaporizer section 254, provide a preferred flow rate of the vaporized sterilant therethrough to provide efficient condensation on to the rods 278. Preferably, a flow rate is in the range of 0.1 ft/sec to 5 ft/sec, and more preferably a flow rate of 0.24 ft/sec is
15 provided.

 In a small condenser with a vapor path length of 3 inches, the residence time would be 1 second at a preferred velocity of 0.24 ft/sec. This residence time
20 would be sufficient for the vaporized sterilant to interact with the cooler condenser surfaces and to condense. For a typical injection volume of 2 ml of sterilant solution, the surface area of the condensing/revaporization section 254 would be about 90
25 square inches to permit mass transfer for condensation. High temperature at low pressure in the initial vaporizer (inlet manifold 252) maintains the water and hydrogen peroxide in the vapor phase for delivery to the
30 condensing/revaporization section 254. For example, a vaporizer temperature of 70 degrees C or greater at a pressure of 125 torr or lower ensures that a 59 wt% solution of hydrogen peroxide and water will be in the vapor phase.

As vapor enters the condensing/revaporization section 254, which has a lower temperature, the hydrogen peroxide condenses on the cooler surface forming a concentrated solution. The temperature and pressure therein determine the concentration of the condensed solution. For example, at 50 degrees C and 13 torr in the condensing/revaporization section 254, the condensed hydrogen peroxide concentration would be 94 wt%. At 30 degrees C and 3.8 torr, the condensed hydrogen peroxide concentration also would be 94 wt%. As the pressure in the condensing/revaporization section 254 is lowered, the temperature must also be lowered to maintain the same concentration of solution.

The orifice 308 offers the advantage of a more concentrated solution by restricting the flow from the condensing/revaporization section 254 to provide a more controlled vaporization. Variations in pressure in the condensing/revaporization section 254 and in the vaporizer due to vacuum pump pressure fluctuations are dampened out by the orifice 308 to prevent surges of water vapor from carrying hydrogen peroxide droplets from the condensing/revaporization section 254. Another advantage of flow restriction by the orifice 308 is achieving a low pressure (less than 1 torr) in the sterilization chamber 200 to improve the diffusion coefficient in lumens while maintaining a greater pressure in the vaporizer/condenser 250 to operate at a greater temperature in the condensing/revaporization section 254. Without an orifice 308, sterilization chamber 200 and vaporizer/condenser 250 pressures must both be reduced to the same low pressure together, and the condenser must be operated at a very low temperature to maintain equilibrium of the solution. A lower condenser temperature is more difficult to control

and may produce ice or condensate, which requires a more expensive design to protect electrical equipment.

An O-ring 282 seals the plates 276 on the thermo-
5 electric devices 270 and 272 against the housing 264. An
aperture 284 through the housing 264 aligns with an
aperture 286 through the insulator 262 to place a chamber
288 defined by the housing 264 into fluid communication
10 with the inlet manifold 252. An outlet passage 290 in the
housing 264 connects to an upper portion of the chamber
288 and to a second aperture 292 through the insulator 262
which in turn aligns with the outlet manifold 256 to place
the chamber 288 in fluid communication with the outlet
15 manifold 256. A safety thermostat 294 atop the housing
264 is wired outside of the control system to shut down
heating of the vaporizer/condenser 250 above a
predetermined temperature. Temperature sensors 295 and
297 measure temperature in the inlet manifold 252 and
condensing/revaporization section 254 respectively. A
20 pressure sensor 296 interfaces with the outlet manifold
256. Heat sinks 298 having fan housings attach to each of
the thermo-electric devices 270 and 272.

The outlet manifold connects to a valve manifold 300
25 which provides three possible flow paths between the
vaporizer/condenser 250 outlet manifold 256 and a valve
manifold outlet 302 from the valve manifold 300. The
valve manifold outlet 302 communicates with the main
chamber 200. A main flow passage 304 is controlled by a
30 valve 306 which can open to allow flow through the main
passage 304 to the valve manifold outlet 302 or close to
block such flow. The second passage is through an orifice
308 in an orifice plate 310 which provides a flow
restriction to enhance the ability to preferentially draw

water vapor from the vaporizer/condenser 250. A third potential passage is through a rupture disk 312 which is designed to rupture in case of a catastrophic overpressure within the housing chamber 288, such as in the unlikely event that an oxidizable sterliant such as hydrogen peroxide combusts therein. The orifice 308 could be moved to a position within the shut-off valve 306, similar to that described in reference to the valve element 118 in FIGS. 3A and 3B.

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In operation, the main chamber is first evacuated to a low pressure sufficient to induce vaporization, such as 0.4 torr and the valve 306 is closed placing the vaporizer/condenser 250 into fluid communication with the chamber 200 solely through the orifice 308. The inlet manifold 252 is heated with the heater 260 and a quantity of sterliant solution such as a 59% hydrogen peroxide/water solution is injected into the inlet manifold 252 where it vaporizes and diffuses into the housing 264 through the apertures 286 and 284. The thermo-electric devices 270 and 272 at this time are drawing energy out of the rods 278 and dissipating it through the heat sinks 298 thus allowing the vaporized sterliant to recondense on the rods 278.

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The temperature of the inlet manifold 252 can be controlled to slowly vaporize the sterilant thus allowing the water to more quickly vaporize and flow through the vaporizer 250 and out through the orifice 308 to concentrate the remaining sterilant. The condenser/revaporization section 254 quite effectively concentrates the sterilant such that to speed up the process a fast vaporization in the inlet manifold can be

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employed while still achieving a high degree of concentration.

The condensate on the rods 278 tends to be more
5 highly concentrated in the sterilant. After a time, when
the initial charge of sterilant solution has been
vaporized and a portion thereof condensed on to the rods
278, the thermo-electric devices 270 and 272 are reversed
to apply heat to the rods 278 and revaporize the
10 sterilant. At this time, the heat sink 298 will still
contain heat which had been extracted during the prior
step and that heat can be used by the thermo-electric
devices 270 and 272 to very efficiently heat the rods 278
and revaporize the sterilant. This added efficiency
15 improves the energy efficiency of the device and allows a
smaller and more compact vaporize condenser 250 to provide
adequate heating and cooling. After the sterilant has
been revaporized, the valve 306 is opened to allow
efficient diffusion of the sterilant vapor into the main
20 chamber 200.

If a second vaporizer/condenser 216 is employed, its
structure preferably mimics that of the
vaporizer/condenser 250 without the inlet manifold 252.
25 In such a system, after initial diffusion into the main
chamber 200, rods within the second condenser 216 would be
chilled and the pump 214 turned on to preferably extract
water vapor from the condensing sterilant. After a period
of time when sterilant has condensed, the rods would be
30 heated to revaporize the sterilant and the pump 214 turned
off. This revaporized sterilant would have somewhat
higher concentration and would then re-diffuse into the
chamber 200 to further enhance the sterilization process.

Other system arrangements are possible. FIG. 16 illustrates an alternative embodiment which can enhance efficiency in conserving and concentrating the germicide solution. In this system, a chamber 314 containing a load 5 316 has a first condenser/vaporizer 318 connected to a source 320 of germicide solution and a second condenser/vaporizer 322. The first condenser vaporizer 318 is isolated from the source 320 by a valve 323 and from the chamber 314 by a valve 324. It also connects to 10 an exhaust pump 325 and is isolated therefrom via a valve 326. The second condenser vaporizer 322 is isolated from the chamber 314 by a valve 327 and connects to the pump 325 and is isolated therefrom via a valve 328. A vent 329 is also provided.

FIG. 17 illustrates a similar system 330 employing a single condenser/vaporizer 332 (of structure similar to the condenser/vaporizer 250 with an additional outlet) connected to a sterilization chamber 334 adapted to 20 receive a load 336 of instruments to be sterilized. A vacuum pump 338 connects to the chamber 334 via a valve 340 and to the condenser/vaporizer 332 via a valve 342. A three-way valve may substitute for valves 340 and 342. A source of germicidal solution 344 connects to the 25 condenser/vaporizer 332 and the chamber 334 has a vent 346. During initial vaporization and concentration of germicide from the source 344, valve 342 is closed. After the vapor is diffused into the chamber 334, valve 340 can be closed and the pump 338 used to draw vapor out of the 30 chamber through the condenser/vaporizer 332 in its condensing mode to further concentrate the germicide. The concentrated germicide is then revaporized and diffused back into the chamber 334.

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The second condenser/vaporizer 216 of FIG. 9 can be used to maximize germicide utilization when running a sterilization process with two full cycles of vacuum, inject, diffuse and vent. Prior to venting during the first cycle, the pump 214 is run with the condenser/vaporizer 216 being chilled to condense the germicide therein. The valves 220 and 218 are closed during the venting process. During the subsequent pump down, the condenser/vaporizer is kept chilled to keep the germicide from unduly vaporizing and being carried out of the system.

The systems of FIGS. 16 and 17 allow even more of the germicide to be retained between cycles in a two cycle process. Prior to venting in the first cycle germicide is condensed into the condenser/vaporizer 332. However, during the subsequent pump down it can be isolated from the pump via the valve 342 thus minimizing the tendency of the pump 338 to pump the saved germicide out of the system during pump down.

In each of this type of system the steps of condensing and concentrating the vaporized germicide and then revaporizing it can be repeated as needed to further concentrate the germicide.

FIG. 18 illustrates a system 350 plumbed in an alternative fashion. In this system 350 a condenser/vaporizer 352 connects through a valve 354 to a sterilization chamber 356 adapted to receive a load 358 and having a vent 360. A vacuum pump 362 connects to the condenser/vaporizer 352 through a valve 364, but has no separate connection to the chamber 356. A source 366 of germicide connects to the condenser/vaporizer 352.

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FIG. 19 illustrates a system 370 plumbed as in FIG. 17, having a condenser/vaporizer 372 which connects through a valve 374 to a sterilization chamber 376 adapted to receive a load 378 and having a vent 380. A vacuum pump 382 connects to the condenser/vaporizer 372 through a valve 384, but has no separate connection to the chamber 356. Rather than an inlet for germicide through the condenser/vaporizer 382, a source 386 of germicide solution is provided within the chamber 376. The source can be simple such as a well containing a quantity of liquid germicide solution. Preferably, it is covered with a semi-permeable membrane or filter so that liquid germicide can not be accidentally spilled therefrom yet as the germicide vaporizes under low chamber pressures the vapors thus generated can pass through the membrane into the chamber. In both systems the condenser/vaporizer 352 or 372 concentrates the germicide via condensation and revaporization of germicide vapor as described above.

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FIG. 20 illustrates a further embodiment of an inlet condenser/vaporizer 400. It is similar in most respects to that illustrated in FIG. 12. However, as shown primarily in FIGS. 21 and 22, it features an orifice control valve 402. A valve block 404 receives an outlet control valve 406, a rupture disk 408 and the orifice control valve 404.

FIG. 21 shows the valve block 404 in isolation and illustrates three manifold passages which connect the valve block 404 to the rest of the condenser/vaporizer 400: a large pressure relief manifold passage 410 which leads to the rupture disk 408, a smaller upper manifold passage 412 which leads to the outlet control valve 406

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and a smaller lateral manifold passage 414 which leads to an orifice 416 and the orifice control valve 402.

FIG. 22 best illustrates the orifice control valve 402. A valve seat 418 on the valve block 404 surrounds the orifice 416. A valve member 420 on the orifice control valve 402 can extend toward to valve seat 418 to seal against it and block fluid communication through the orifice 416. A cleaning pin 422 penetrates the orifice 416 when the orifice control valve 402 is closed to clean the orifice 416 and keep it clear of foreign matter. An annular guide 424 connected to the valve member 420 slides within a bore 426 within the valve block 404 to properly align the cleaning pin 422 with the orifice 416. This view also illustrates a valve seat 428 for the outlet control valve 406 and a valve block outlet passage 430 which leads to the sterilization chamber (not shown in FIGS. 20 to 22).

Operation of a sterilization cycle proceeds nearly the same as afore-described regarding the system shown in FIGS. 12 to 15. However, after the initial vaporization of the sterilant in the inlet manifold 252 (see FIG. 14) the orifice control valve 402 is closed thereby isolating the condenser/vaporizer 400 from the sterilization chamber (not shown in FIGS. 20 to 22). This condition can be monitored most easily by monitoring the pressure within the vaporizer/condenser 400 and assuming that when a particular pressure has been reached that essentially all of the sterilant has been vaporized. Pressure in the sterilization chamber is then reduced, preferably to approximately 0.5 Torr. The outlet control valve 406 is then opened and the rods 278 (see FIG. 14) are heated to vaporize condensed sterilant and pass it through the

outlet control valve 406 and outlet passage 430 to the sterilization chamber.

By lowering the pressure in the sterilization chamber
5 prior to admitting the bulk of the sterilant it has been
found that overall cycle times may be reduced. Closing
the orifice control valve 402 and reducing pressure in the
sterilization chamber takes additional time. However, the
lower pressure provides a more favorable condition for
10 diffusion of the sterilant into diffusion restricted
areas, such as lumens, of instruments to be sterilized.
It has been found that the time saved through the
increased diffusion efficiency can more than offset the
time lost in lowering the pressure in the sterilization
15 chamber. Sterilization cycle speed is an important factor
for sterilizer users.

Water vapor in the sterilization chamber can affect
the time required to lower the pressure therein. Such
20 water vapor typically arises from a load of instruments
that have not been properly dried. If undue time is
required to remove the water vapor it can be indicated to
the user so that they can be reminded to be more vigilant
in drying the load for future cycles. There may exists
25 loads of water vapor for which it may take too long to
withdraw or to withdraw effectively. In such case the
cycle should be cancelled and the user informed as to why.

Table 2 shows control points for three different
30 cycles - a flash or very quick cycle having no lumens, a
short cycle having only lumens which present a mild
challenge and a long cycle for sterilizing devices with
more challenging long and narrow lumens. During an
initial pump-down to remove air from the sterilization

chamber and vaporizer/condenser 400 the outlet control valve 406 is left open. As the pressure reaches P1 the outlet control valve 406 is closed but the orifice control valve 402 is left open; this starts the vaporization and concentration of the sterilant. Upon reaching pressure P2 within the vaporizer/condenser 400 the pressure Pc within the chamber is checked. If it is above the value listed in Table 2 then the orifice control valve 402 is closed and pump-down continues until Pc is reached and then the outlet control valve 406 is opened to transfer the sterilant into the sterilization chamber. Otherwise, the outlet control valve 406 is opened right away. If the chamber pressure exceeds Pc-cancel at the time that the vaporizer/condenser pressure reaches P2 it is assumed that the sterilization chamber contains too much water and the cycle is cancelled.

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Table 2

Examples of temperature and pressure set points

	Flash	Short	Long
Load condition	Surface	1mmx150mm SS 1mmx350mm Plastic	1mmx500mm SS 1mmx1000mm Plastic
Vaporizer temperature	70°C	70°C	70°C
Condenser temperature	58°C	52°C	43°C
P1 Vaporizer/condenser pressure to remove air	140 torr	140 torr	140 torr
P2 Vaporizer/condenser pressure to concentrate sterilant	22 torr	16 torr	10 torr
Pc Chamber pressure to select transfer, additional vacuum or cancellation	1.5 torr	0.6 torr	0.3 torr
Pc-cancel Chamber pressure to cancel cycle	8 torr	6 torr	4 torr
Condenser temperature to transfer concentrated sterilant	68°C	68°C	68°C

5 In addition to the effectiveness of such systems in killing infectious microorganisms they are also effective in inactivating prions. Experiments were conducted comparing known methodologies to the highly concentrated hydrogen peroxide vapor of the present disclosure.

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Steel Wire Preparation

Soft stainless steel wire (1.4301; diameter, 0.25 mm; Forestadent, Pforzheim, Germany) was placed in the Sterrad 100S GMP sterilizer, a hydrogen peroxide gas plasma

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sterilizer. The steel wire was then aseptically cut into fragments of 30 mm in length.

5 The wires were contaminated by immersion into freshly, prepared 10% brain homogenates from hamsters with scrapie in phosphate-buffered saline (PBS) for 16 hours at room temperature; spiked wires were then air dried for at least 1 hour before further treatment.

10 Cleaning was performed in a custom-made test washing machines, a closed two-container system. The lower container served as an open reservoir; a working volume of 10 L was pumped into the upper container and then drawn out freely back into the lower container through an
15 opening on the bottom of the upper container. A circular rack with wires fixed in the edge was placed within the upper container and the lid of the upper container was tightly closed during the washing process.

20 After each treatment, wires were rinsed once with 1 x PBS followed by washing three times with double distilled water.

Wire Implantation

25 The processed wired were then implanted into hamster thalami with the assistance of a stereotaxic apparatus for small animals (coordinates: bregma, -2.0 mm; mediolateral, 2.0 mm; and dorsoventral, 6.0 mm). The same location was chosen for the intracerebral injection of
30 scrapie brain homogenates into the hamster brain by a syringe and for the controls.

Animals were deeply anesthetized with 10% ketamine (SANOfi-CEVA GmbH, Dusseldorf, Germany) during the operation.

5 Animal Surveillance

Hamsters implanted with the wires were kept three to four per cage in a biological safety level-3 facility, with free access to standard diet and water. Test animals were initially observed twice a week, and daily after 60
10 days postimplantation. Hamsters with definite signs of scrapie were designated as terminally sick and euthanized.

Treatment Regiments Compared

Samples of the prion prepared wires were processed
15 with the following treatments to assess their effectiveness in inactivating the prions on the wires. Twelve animals were used for each treatment, and five animals were used as control.:

1. Neodisher V 4009/1; 1%; 55°C for 10 minutes
20 (control)
2. Neodisher V 4009/1; 1%; 55°C for 10 minutes and exposure to STERRAD NX - Advanced Cycle (38 min)
3. Neodisher V 4009/1; 1%; 55°C for 10 minutes and exposure to STERRAD 100 S - Long Cycle
- 25 4. Alka One; 1%; 55°C for 10 minutes (control)
5. Alka One; 1%; 55°C for 10 minutes and exposure to STERRAD NX - Advanced Cycle (38 min)
6. Alka One; 1%; 55°C for 10 minutes and exposure to STERRAD 100 S - Long Cycle
- 30 7. Exposure to STERRAD NX - Advanced Cycle (38 min) only; no washing
8. Exposure to STERRAD NX - Double Advanced Cycle (38 min) only; no washing

9. Exposure to STERRAD 100 S - Long Cycle only; no washing

10. Exposure to STERRAD 100 S - Double Long Cycle only; no washing

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Neodisher V 4009/1 is an alkaline cleaning solution available from Chemische Fabrik Dr. Weigert GmbH & Co, Hamburg, Germany. Alka One is an alkaline cleaning solution available from Borer Chemie AG, Zuchwil, Switzerland. The STERRAD 100 S is available from Advanced Sterilization Products division of Ethicon, Inc. (ASP), Irvine, CA. Its long cycle comprises a 15-minute pre-exposure plasma with about 9.5 mWatts/cc power density and two 100S half cycles and its double long cycle comprises two long cycles. Each 100S half cycle comprises a 6-minute injection of 59% peroxide, a 10-minute diffusion, and a 2-minute plasma with about 9.5 mwatts/cc plasma power density. The chamber temperature is maintained around 45°C throughout the process.

20

The STERRAD NX is also available from ASP. Its advanced cycle comprises two NX half cycles and its double advanced cycle comprises two advanced cycles. Each NX half cycle comprises a concentration process, which concentrates the injected 59% peroxide to about 90%, a 7-minute transfer stage to transfer the concentrated into sterilizer, a 30-second diffusion, and a 4-minute plasma with about 50 mWatts/cc plasma power density. The chamber is maintained around 50°C throughout the process. Due to the higher chamber temperature, higher peroxide liquid concentration, higher plasma power density, and longer plasma time, the load in the STERRAD NX Sterilizer is actually exposed to more effective and energetic sterilization environment than the STERRAD 100S

Sterilizer. The results of these trials are shown in Table 3 which shows the lifespan in days of the hamsters (as of the compilation of the data) after implementation with the treated wires. Figures in bold indicate a
5 deceased animal and figures indicated with an asterisk indicate an animal deceased due to conflict with another animal.

240
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Table 3
Comparison of Treatments to Inactivate Prions

	(1) 1% V4009/1 55°C 10min	(2) AlkaOne 55°C 10min	(3) No wash NX 38min double	(4) No wash NX 38min	(5) 1% V4009/1 55°C 10min/NX 38min	(6) AlkaOne 55°C 10min/NX 38min
Implantation	9/21/2005	9/22/2005	10/6/2005	10/7/2005	10/11/2005	10/13/2005
Hamster 1	168	167	153	152	148	146
Hamster 2	168	167	153	152	148	146
Hamster 3	168	134*	153	152	148	146
Hamster 4	168	167	153	152	148	146
Hamster 5	168	167	153	152	148	146
Hamster 6	99*	167	153	115*	148	146
Hamster 7	168	167	153	152	85*	146
Hamster 8	168	167	153	130*	148	146
Hamster 9	168	167	153	152	148	146
Hamster 10	168	167	153	152	148	146
Hamster 11	168	167	90*	152	148	146
Hamster 12	168	167	153	152	85*	146

	(7) AlkaOne 55°C 10min/100S long	(8) 1% V4009/1 55°C 10min/100S long	(9) No wash 100S long double	(10) No wash 100S long	Positive control wires
Implantation	11/8/2005	11/8/2005	11/9/2005	11/9/2005	7/6/2005
Hamster 1	120	120	107	93	75
Hamster 2	120	120	103	103	85
Hamster 3	120	120	97	107	85
Hamster 4	120	120	93	93	85
Hamster 5	120	120	119	97	85
Hamster 6	120	120	107	103	
Hamster 7	120	120	103	93	
Hamster 8	120	120	107	93	
Hamster 9	120	120	107	107	
Hamster 10	120	120	93	107	
Hamster 11	120	120	107	93	
Hamster 12	120	120	103	93	

The results show the high concentration hydrogen peroxide vapor treatment of the STERRAD NX to be as effective as alkaline wash treatment in inactivating prions.

The invention has been described with reference to the preferred embodiments. Obviously, modifications and alterations will occur to others upon reading and understanding the preceding detailed description. It is
5 intended that the invention be construed as including all such modifications and alterations insofar as they come within the scope of the appended claims or the equivalents thereof.

REIVINDICACIONES.

1. Un método de inactivación de priones que comprende las etapas de:
Colocar un artículo que tenga una cantidad de priones en él en una cámara de esterilización;
Disminuir la presión en la cámara de esterilización a una presión por debajo de la presión de vapor del peróxido de hidrógeno;
Agregar a la cámara de esterilización una solución que comprende peróxido de hidrógeno y poner en contacto el artículo con vapor de peróxido de hidrógeno; e
Inactivar los priones en la cámara a través del contacto entre los priones y el vapor de peróxido de hidrógeno.
2. Un método de acuerdo con la reivindicación 1, donde la concentración de peróxido de hidrógeno en la solución agregada a la cámara, excede el 70 por ciento.
3. Un método de acuerdo con la reivindicación 2, donde la concentración de peróxido de hidrógeno en la solución agregada a la cámara, excede el 75 por ciento.

4. Un método de acuerdo con la reivindicación 3, donde la concentración de peróxido de hidrógeno en la solución agregada a la cámara, excede el 80 por ciento.
5. Un método de acuerdo con la reivindicación 4, donde la concentración de peróxido de hidrógeno en la solución agregada a la cámara, excede el 85 por ciento.
6. Un método de acuerdo con la reivindicación 5, donde la concentración de peróxido de hidrógeno en la solución agregada a la cámara, excede el 90 por ciento.
7. Un método de acuerdo con la reivindicación 1, donde la temperatura del artículo durante la etapa de poner en contacto el artículo con vapor de peróxido de hidrógeno excede 30 grados Celsius
8. Un método de acuerdo con la reivindicación 7, donde la temperatura del artículo durante la etapa de poner en contacto el artículo con vapor de peróxido de hidrógeno excede 35 grados Celsius.

9. Un método de acuerdo con la reivindicación 8, donde la temperatura del artículo durante la etapa de poner en contacto el artículo con vapor de peróxido de hidrógeno excede 40 grados Celsius.
10. Un método de acuerdo con la reivindicación 9, donde la temperatura del artículo durante la etapa de poner en contacto el artículo con vapor de peróxido de hidrógeno excede 45 grados Celsius.
11. Un método de acuerdo con la reivindicación 1, que además comprende excitación del vapor de peróxido de hidrógeno en la fase de plasma y poner en contacto los priones con el peróxido de hidrógeno en la fase de plasma.
12. Un método de acuerdo con la reivindicación 11, donde la densidad del plasma es por lo menos 10 milivatios/ cc.
13. Un método de acuerdo con la reivindicación 12, donde la densidad del plasma es por lo menos 20 milivatios/ cc.
14. Un método de acuerdo con la reivindicación 13, donde la densidad del plasma es por lo menos 30 milivatios/ cc.

15. Un método de acuerdo con la reivindicación 14, donde la densidad del plasma es por lo menos 40 milivatios/ cc.
16. Un método de acuerdo con la reivindicación 15, donde la densidad del plasma es por lo menos 50 milivatios/ cc.
17. Un método de acuerdo con la reivindicación 11, donde el plasma esta en contacto con los priones por lo menos 2 minutos.
18. Un método de acuerdo con la reivindicación 17, donde el tiempo de plasma en contacto con los priones es por lo menos 3 minutos.
19. Un método de acuerdo con la reivindicación 18, donde el tiempo de plasma en contacto con los priones es por lo menos 4 minutos.
20. Un método de acuerdo con la reivindicación 1, en el cual el peróxido de hidrógeno efectúa la esterilización del artículo.
21. Un método de acuerdo con la reivindicación 1, que además comprende aumentar la concentración de por lo menos una porción del peróxido de hidrógeno antes de poner en contacto los priones con él.

22. Un método de acuerdo con la reivindicación 21, donde la etapa de aumentar la concentración de peróxido de hidrógeno se realiza por remoción selectiva de agua de la solución y extraer esa agua a través de la cámara de esterilización.

23. Un método de acuerdo con la reivindicación 1, que además comprende excitar gases alrededor de los priones en la fase de plasma y poner en contacto los priones con los gases en la fase de plasma.

24. Un método de acuerdo con la reivindicación 1, donde los pasos de las etapas de disminución de presión en la cámara de esterilización y de adición de la solución a la cámara de esterilización comprenden un ciclo y donde el ciclo se repite.

25. Un método de acuerdo con la reivindicación 24, donde el ciclo se repite más de una vez.

26. Un método de inactivación de priones que comprende las etapas de:

Colocar un artículo que tenga una cantidad de priones en él en una cámara de esterilización;

Poner en contacto el artículo con un plasma para inactivar los priones.

27. Un método de acuerdo con la reivindicación 26, donde el plasma esta formado por un gas que contiene peróxido de hidrógeno.
28. Un método de acuerdo con la reivindicación 26, donde la densidad de plasma es por lo menos 10 milivatios/cc.
29. Un método de acuerdo con la reivindicación 28, donde la densidad de plasma es por lo menos 20 milivatios/cc.
30. Un método de acuerdo con la reivindicación 29, donde la densidad de plasma es por lo menos 30 milivatios/cc.
31. Un método de acuerdo con la reivindicación 30, donde la densidad de plasma es por lo menos 40 milivatios/cc.
32. Un método de acuerdo con la reivindicación 31, donde la densidad de plasma es por lo menos 50 milivatios/cc.

WHAT IS CLAIMED IS:

1. A method of inactivating prions comprising the steps of:

5 placing an article having a quantity of prions thereon into a sterilization chamber;

lowering pressure in the sterilization chamber to a pressure below the vapor pressure of hydrogen peroxide;

10 admitting a solution comprising hydrogen peroxide into the sterilization chamber and contacting the article with hydrogen peroxide vapor; and

inactivating prions in the chamber through contact between the prions and the hydrogen peroxide vapor.

15 2 A method according to claim 1 wherein the concentration of the hydrogen peroxide in the solution admitted into the chamber exceeds 70 percent.

20 3. A method according to claim 2 wherein the concentration of the hydrogen peroxide in the solution admitted into the chamber exceeds 75 percent.

25 4. A method according to claim 3 wherein the concentration of the hydrogen peroxide in the solution admitted into the chamber exceeds 80 percent.

30 5. A method according to claim 4 wherein the concentration of the hydrogen peroxide in the solution admitted into the chamber exceeds 85 percent.

6. A method according to claim 5 wherein the concentration of the hydrogen peroxide in the solution admitted into the chamber exceeds 90 percent.

7. A method according to claim 1 and wherein the temperature of the article during the step of contacting the article with hydrogen peroxide vapor exceeds 30 degrees Celsius.

5

8. A method according to claim 7 and wherein the temperature of the article during the step of contacting the article with hydrogen peroxide vapor exceeds 35 degrees Celsius.

10

9. A method according to claim 8 and wherein the temperature of the article during the step of contacting the article with hydrogen peroxide vapor exceeds 40 degrees Celsius.

15

10. A method according to claim 9 and wherein the temperature of the article during the step of contacting the article with hydrogen peroxide vapor exceeds 45 degrees Celsius.

20

11. A method according to claim 1 and further comprising exciting the hydrogen peroxide vapor into the plasma phase and contacting the prions with the hydrogen peroxide in the plasma phase.

25

12. A method according to claim 11 wherein the plasma density is at least 10 milliwatts/cm³.

13. A method according to claim 12 wherein the plasma density is at least 20 watts/cm³.

30

14. A method according to claim 13 wherein the plasma density is at least 30 milliwatts/cm³.

15. A method according to claim 14 wherein the plasma density is at least 40 milliwatts/cm³.

16. A method according to claim 15 wherein the
5 plasma density is at least 50 milliwatts/cm³.

17. A method according to claim 11 wherein the plasma is in contact with the prions for at least 2 minutes.

10

18. A method according to claim 17 wherein the plasma time is in contact with the prions for at least 3 minutes.

15 19. A method according to claim 18 wherein the plasma time is in contact with the prions for at least 4 minutes.

20 20. A method according to claim 1 in which the hydrogen peroxide effects sterilization of the article.

21. A method according to claim 1 and further comprising increasing concentration of at least a portion of the hydrogen peroxide prior to contacting the prions
25 therewith.

22. A method according to claim 21 wherein the step of increasing concentration of the hydrogen peroxide is performed by selectively removing water from the solution
30 and exhausting that water through the sterilization chamber.

23. A method according to claim 1 and further comprising exciting gases surrounding the prions into the

plasma phase and contacting the prions with the gases in the plasma phase.

24. A method according to claim 1 wherein the steps
5 of steps of lowering pressure in the sterilization chamber and admitting the solution into the sterilization chamber comprise a cycle and wherein the cycle is repeated.

25. A method according to claim 24 wherein the cycle
10 is repeated more than once.

26. A method of inactivating prions comprising the steps of:

placing an article having a quantity of prions
15 thereon into a sterilization chamber;

contacting the article with a plasma to effect inactivation of the prions.

27. A method according to claim 26 wherein the
20 plasma is formed from a gas comprising hydrogen peroxide.

28. A method according to claim 26 wherein the plasma density is at least 10 milliwatts/cm³.

25 29. A method according to claim 28 wherein the plasma density is at least milli20 watts/cm³.

30 30. A method according to claim 29 wherein the plasma density is at least 30 milliwatts/cm³.

31. A method according to claim 30 wherein the plasma density is at least 40 milliwatts/cm³.

32. A method according to claim 31 wherein the plasma density is at least 50 milliwatts/cm³.

ABSTRACT

A method is provided for inactivating prions and is particularly effective in inactivating prions on
5 medical devices. An article having a quantity of prions thereon is placed into a sterilization chamber. Pressure in the sterilization chamber is lowered to a pressure below the vapor pressure of hydrogen peroxide and a
10 sterilization chamber and placed into contact with the article to inactivate prions on the article.

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DECLARATION AND POWER OF ATTORNEY FOR UTILITY OR DESIGN PATENT APPLICATION (37 CFR 1.63)	Attorney Docket Number	ASP-5042USNP	
	First Named Inventor	Charles G. Roberts	
	<i>COMPLETE IF KNOWN</i>		
	Application Number		
	Filing Date	March 31, 2005	
	Group Art Unit		
☒ Declaration Submitted with Initial Filing ☐ Declaration Submitted after Initial Filing (Surcharge (37 CFR 1.16(e)) required)		Examiner Name	
As a below named inventor, I hereby declare that: My residence, mailing address, and citizenship are as stated below next to my name. I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:			
A METHOD AND SYSTEM FOR PRION INACTIVATION <i>(Title of the Invention)</i>			
the specification of which ☒ is attached hereto OR ☐ was filed on (MM/DD/YYYY) as United States Application Number or PCT International Application Number and was amended on (MM/DD/YYYY)			
I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment specifically referred to above.			
I acknowledge the duty to disclose information which is material to patentability as defined in 37 CFR 1.56, including for continuation-in-part applications, material information which became available between the filing date of the prior application and the national or PCT international filing date of the continuation-in-part application.			
I hereby claim foreign priority benefits under 35 U.S.C. 119(a)-(d) or 365(b) of any foreign application(s) for patent or inventor's certificate, or 365(a) of any PCT international application which designated at least one country other than the United States of America, listed below and have also identified below, by checking the box, any foreign application for patent or inventor's certificate, or any PCT international application having a filing date before that of the application on which priority is claimed.			
Prior Foreign Application Number(s)	Country	Foreign Filing Date (MM/DD/YYYY)	Priority Not Claimed
			☐ ☐ ☐ ☐
			☐ ☐ ☐ ☐
☐ Additional foreign application numbers are listed on a supplemental priority data sheet PTO/SB/02B attached hereto:			

DECLARATION - Utility or Design Patent Application

I hereby claim the benefit under 35 U.S.C. 119(e) of any United States provisional application(s) listed below.

Application Number(s)	Filing Date (MM/DD/YYYY)	
		☐ Additional provisional application numbers are listed on a supplemental priority data sheet PTO/SB/02B attached hereto.

I hereby claim the benefit under Title 35, United States Code, § 120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, § 112, I acknowledge the duty to disclose material information as defined in Title 37, Code of Federal Regulations, § 1.56(a) which occurred between the filing date of the prior application and the national or PCT international filing date of this application:

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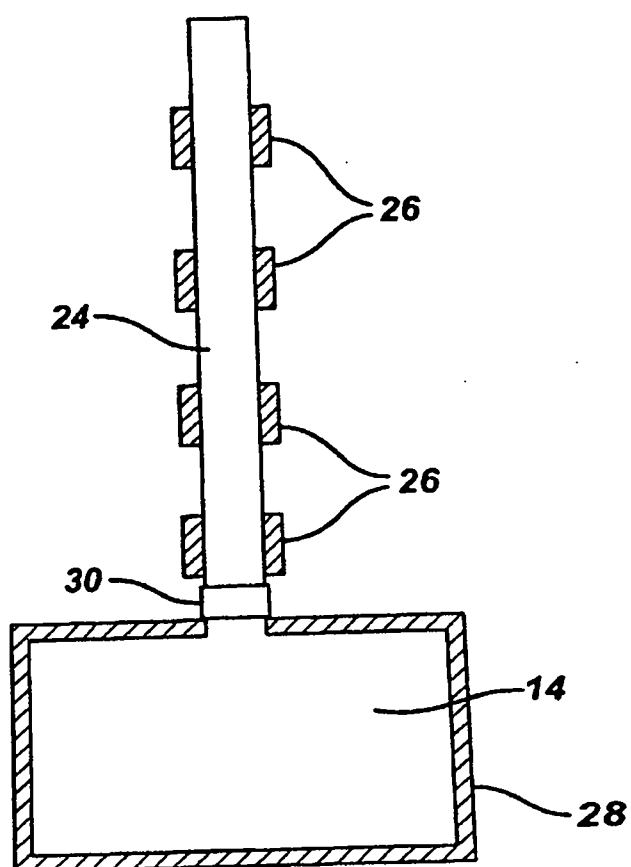
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NAME OF SOLE OR FIRST INVENTOR:		☐ A petition has been filed for this unsigned inventor	
Given Name (first and middle (if any)) Charles G.		Family Name or Surname Roberts	
Inventor's Signature		Date	
Residence: City Long Beach	State CA	Country USA	Citizenship USA
Mailing Address 2221 Senasac Ave			
City Long Beach	State CA	ZIP 90815	Country USA
I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. 1001 and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.			
NAME OF SECOND INVENTOR:		☐ A petition has been filed for this unsigned inventor	
Given Name (first and middle (if any)) Martin		Family Name or Surname Favero	
Inventor's Signature		Date	
Residence: City San Clemente	State CA	Country USA	Citizenship USA
Mailing Address 2339 Via Zafiro			
City San Clemente	State CA	ZIP 92673	Country USA
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NAME OF THIRD INVENTOR:		☐ A petition has been filed for this unsigned inventor	
Given Name (first and middle (if any))		Family Name or Surname	
Inventor's Signature		Date	
Residence: City	State	Country	Citizenship
Mailing Address			
City	State	ZIP	Country

FIG. 1



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FIG. 2



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257

FIG. 3

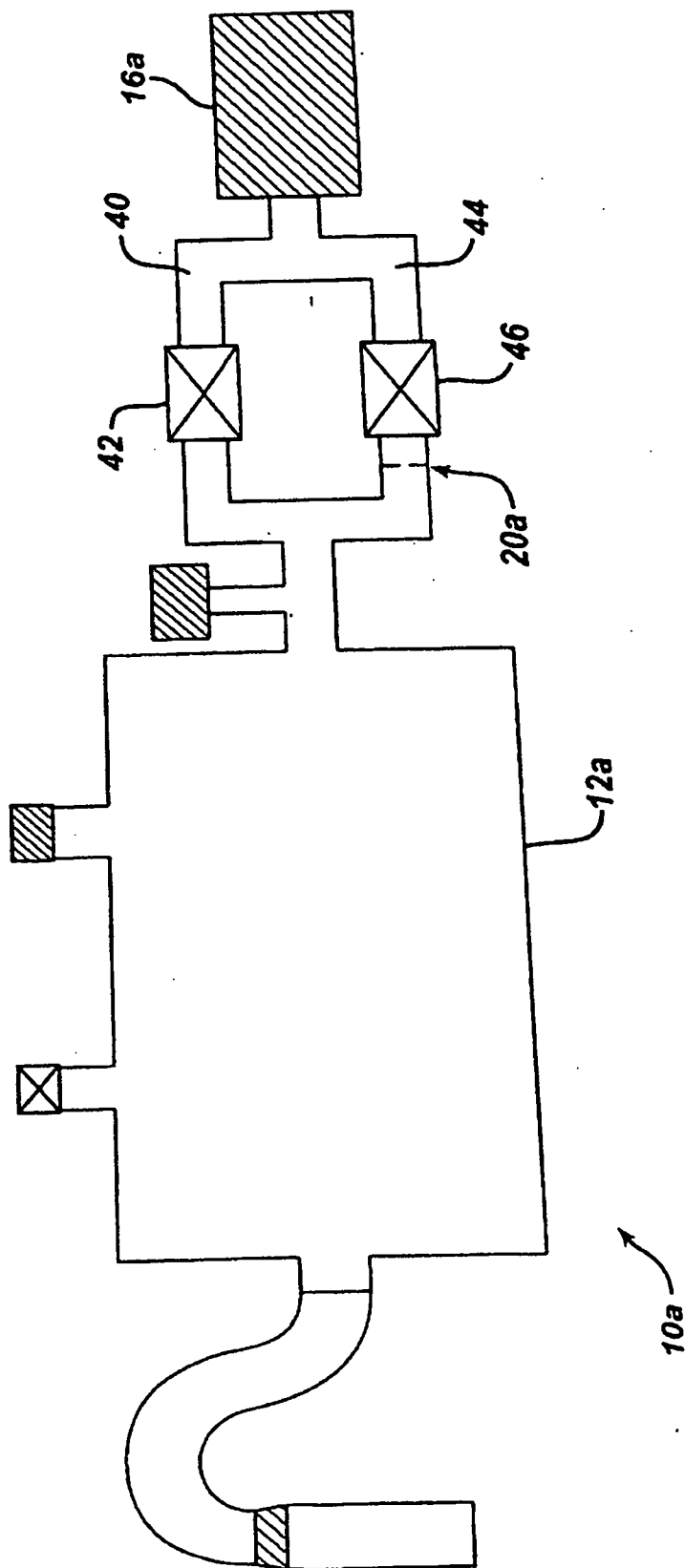
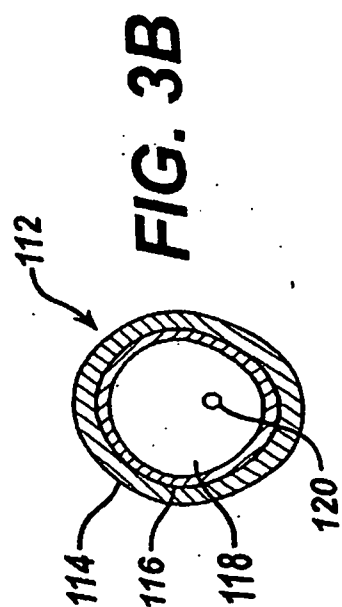
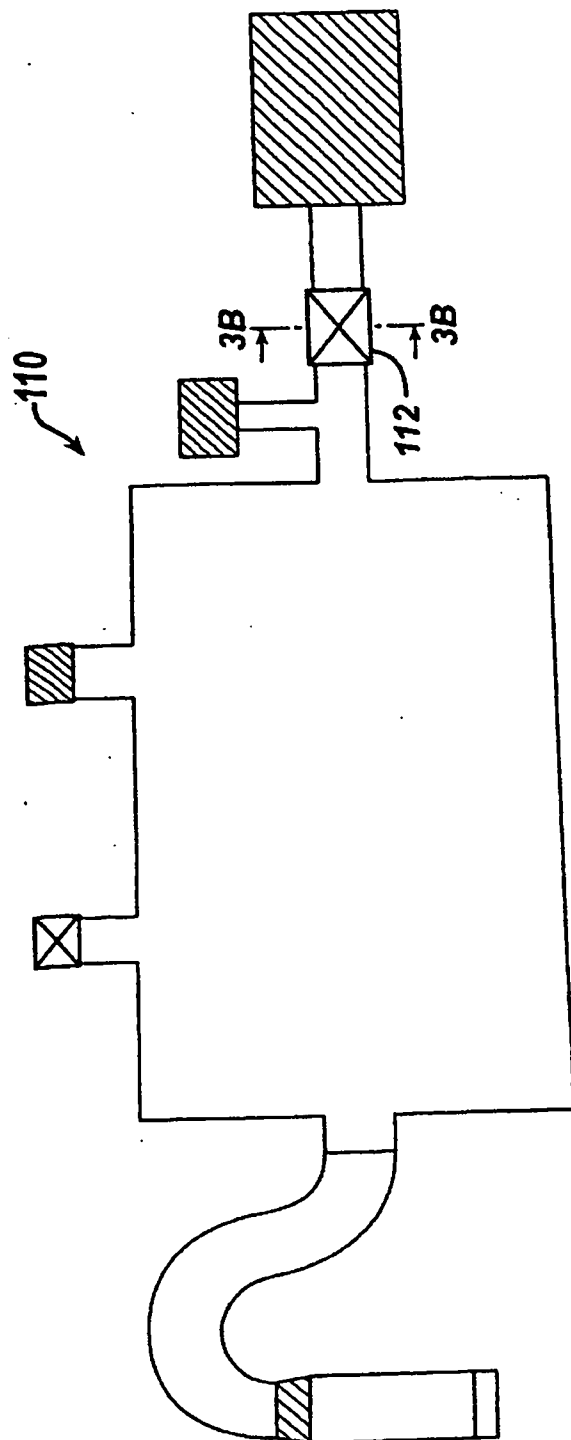


FIG. 3A



161
259

FIG. 4

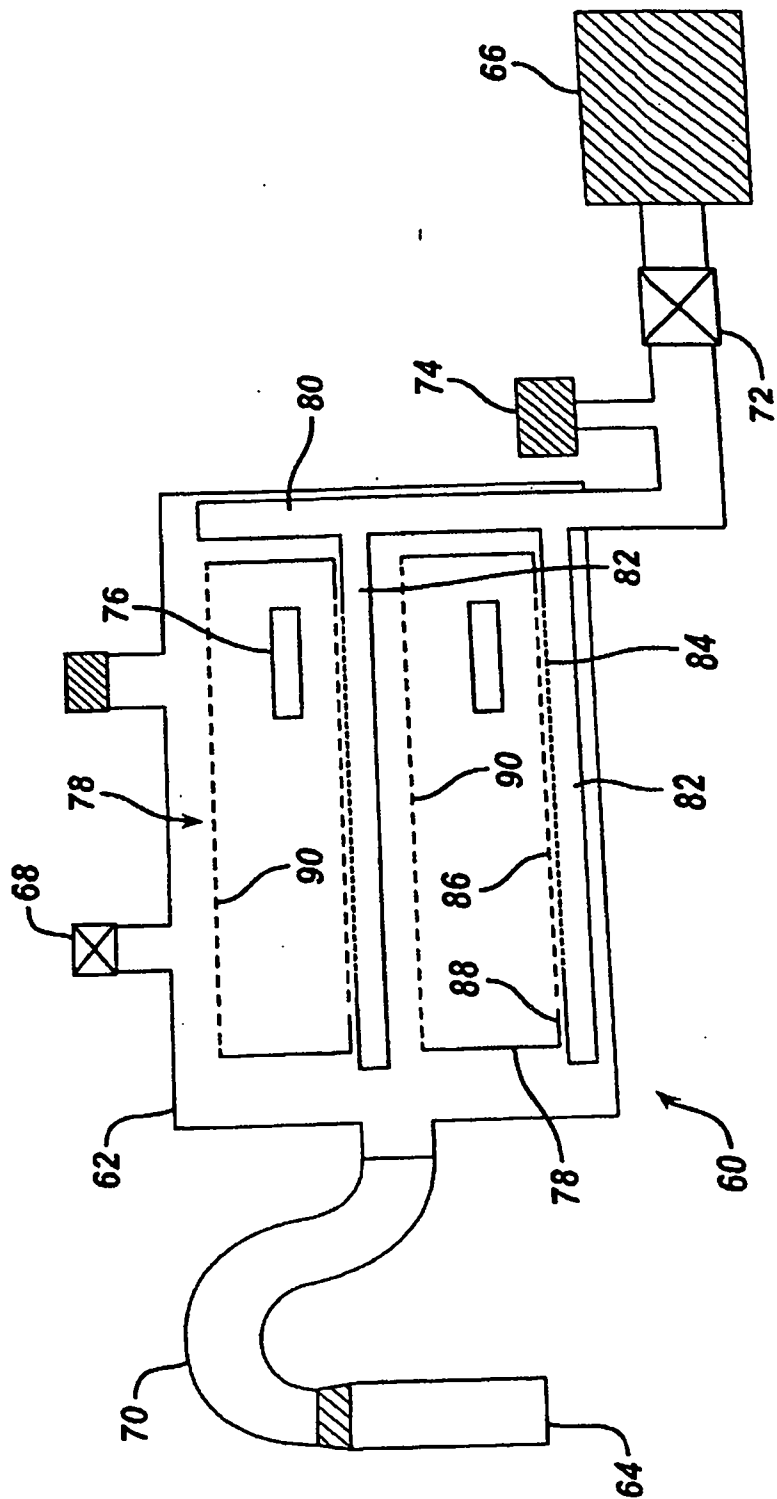
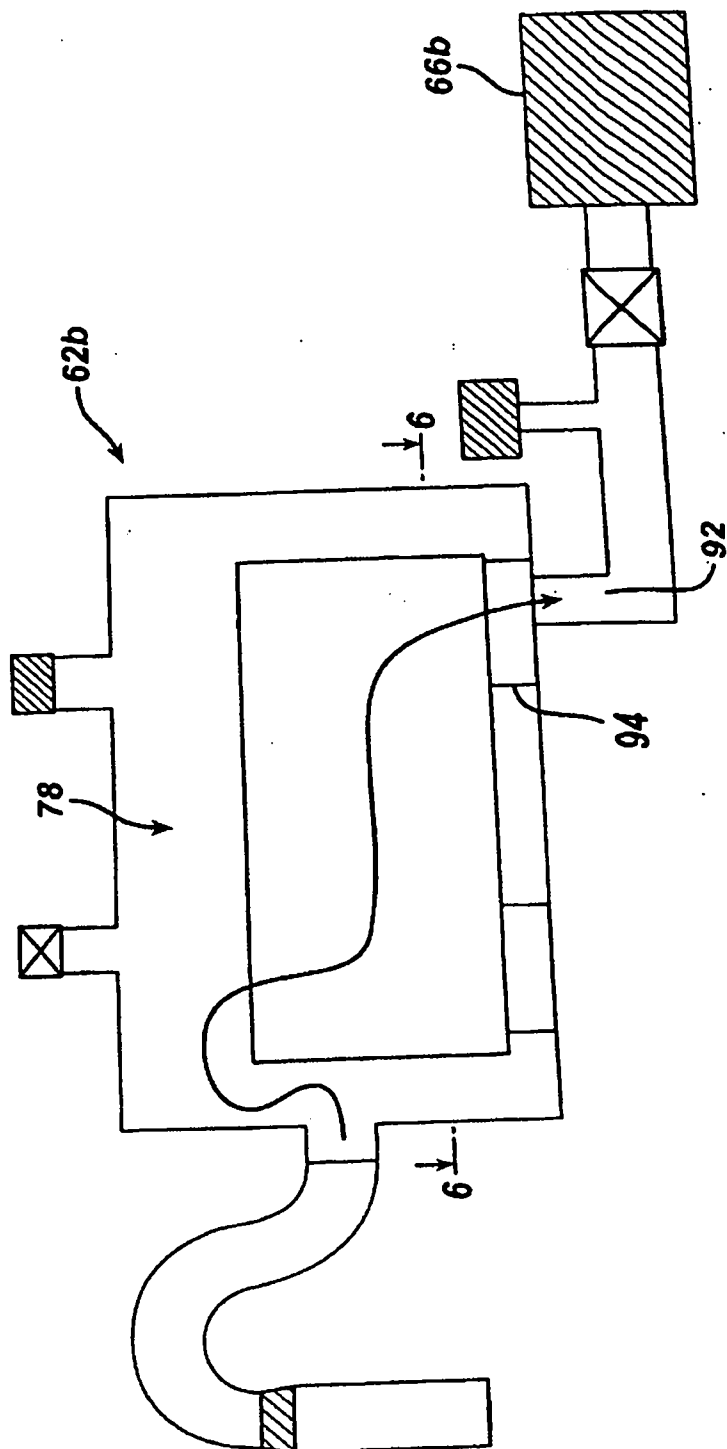


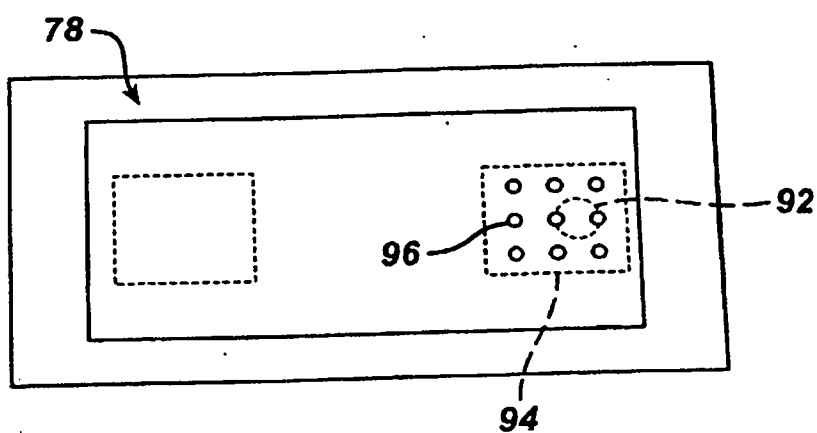
FIG. 5



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FIG. 6



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963

FIG. 8

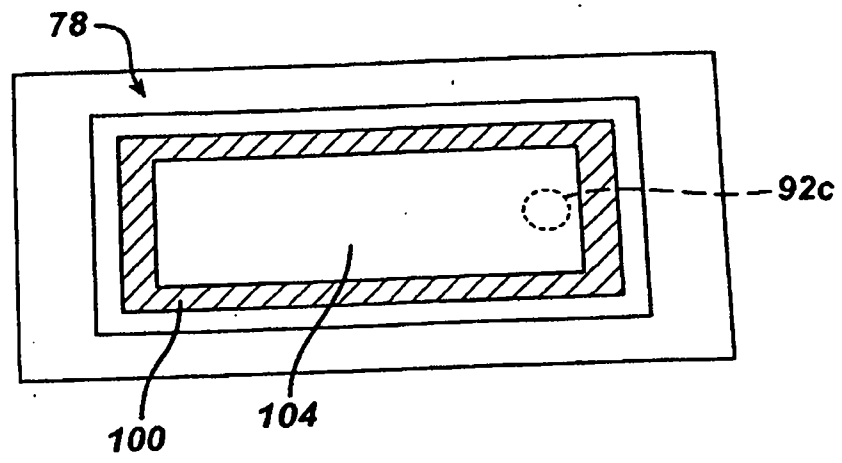
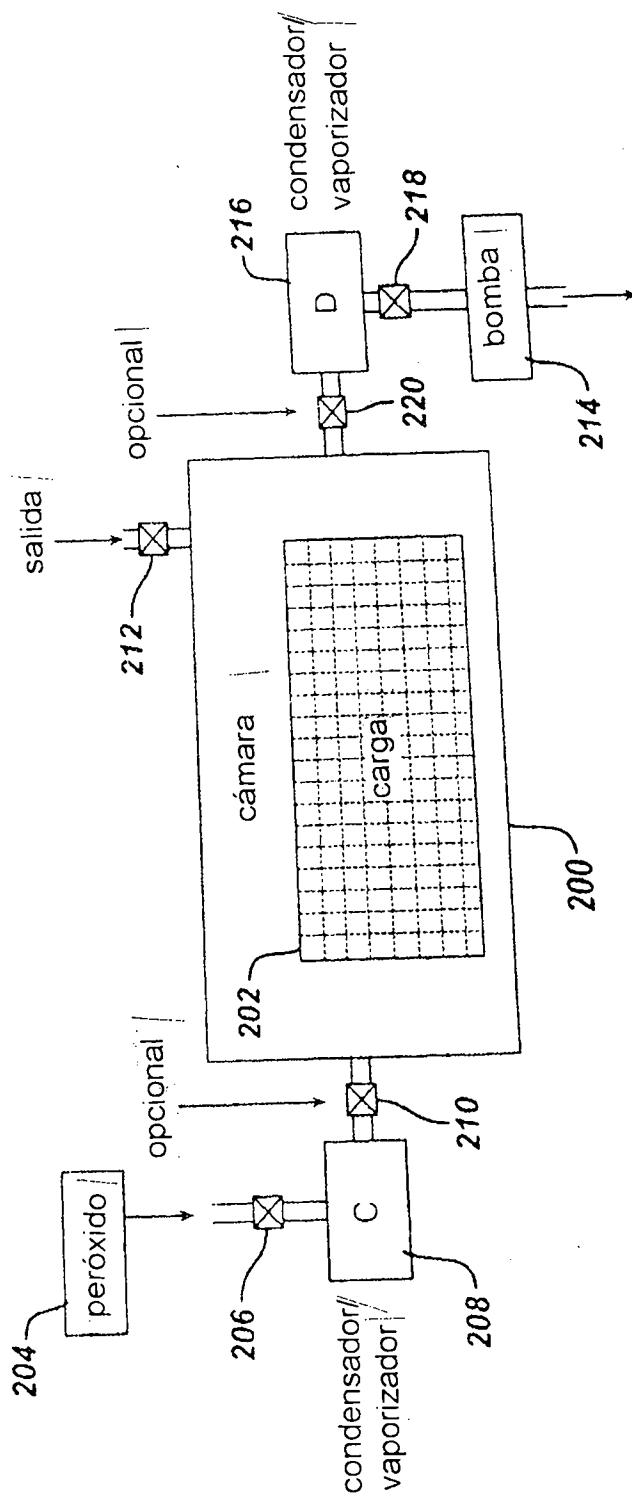
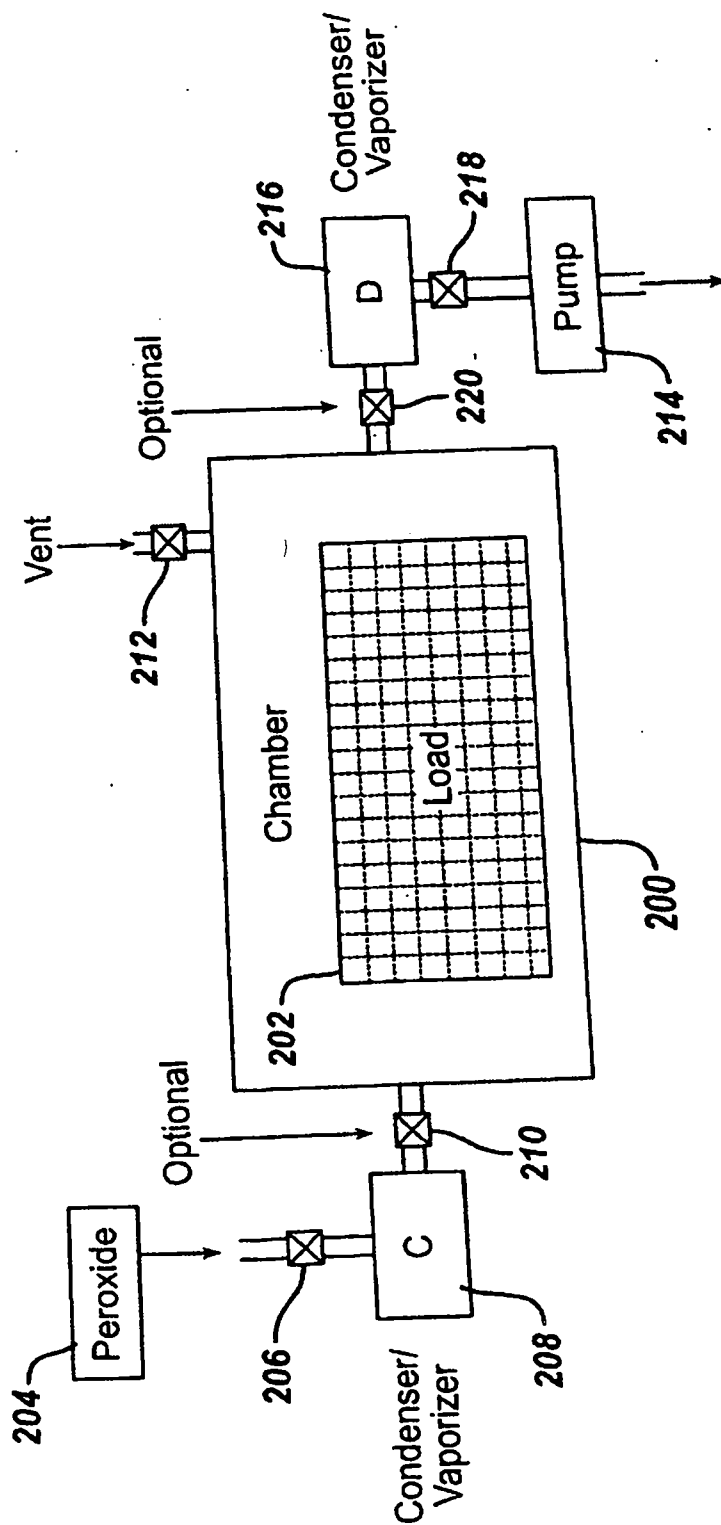


FIG. 9



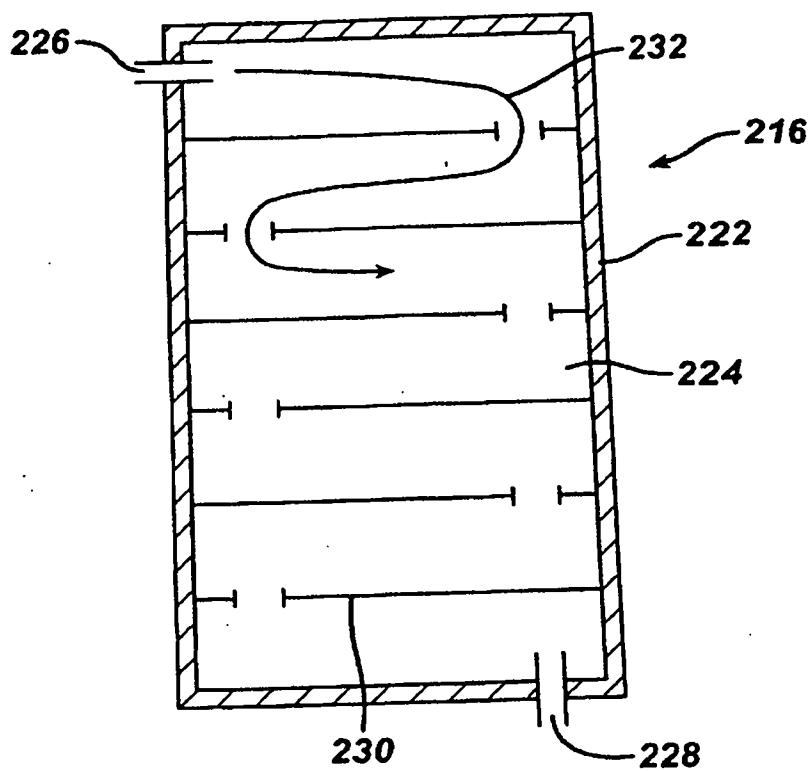
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FIG. 9



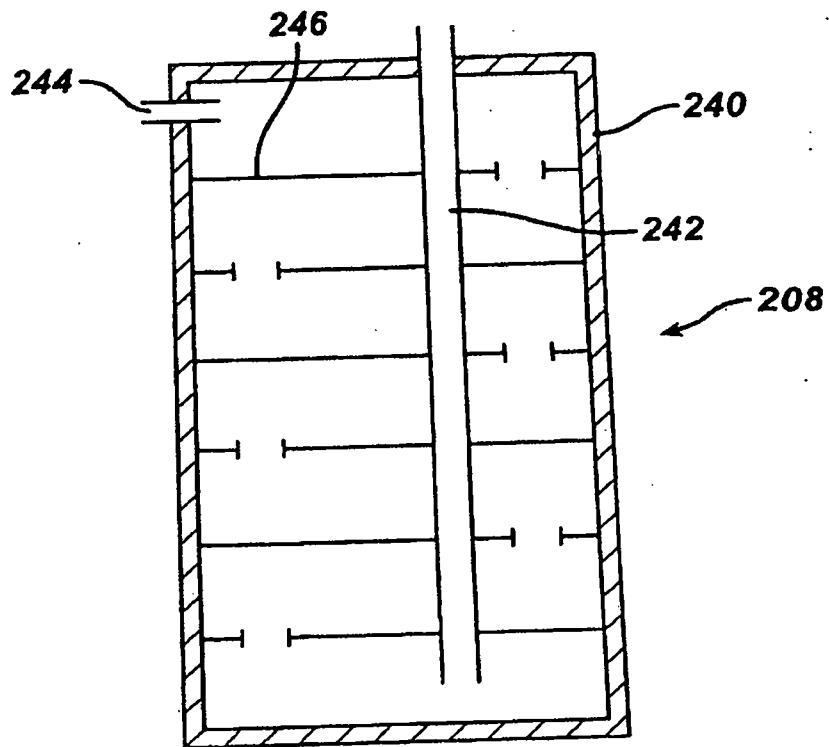
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FIG. 10



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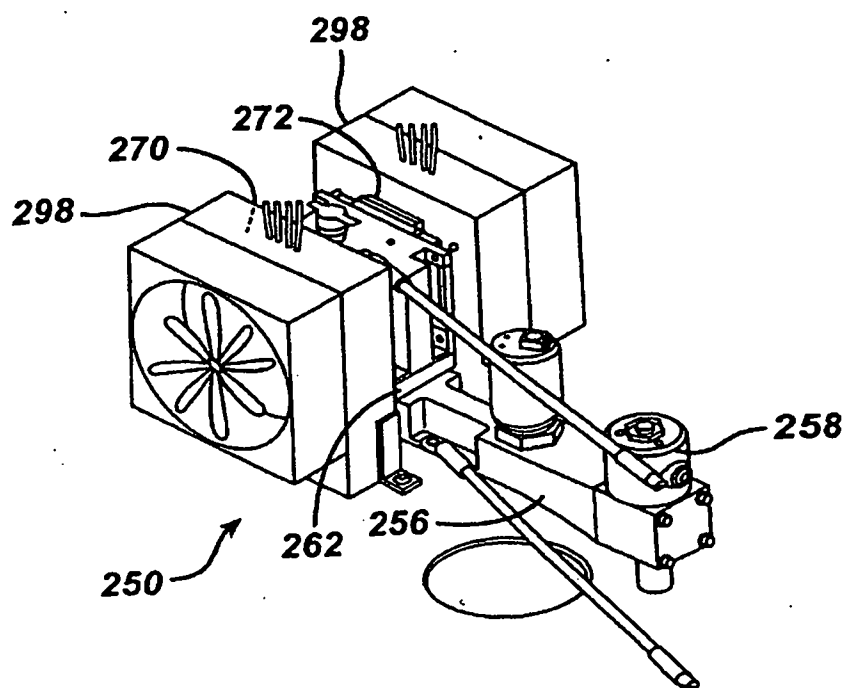
FIG. 11



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FIG. 12



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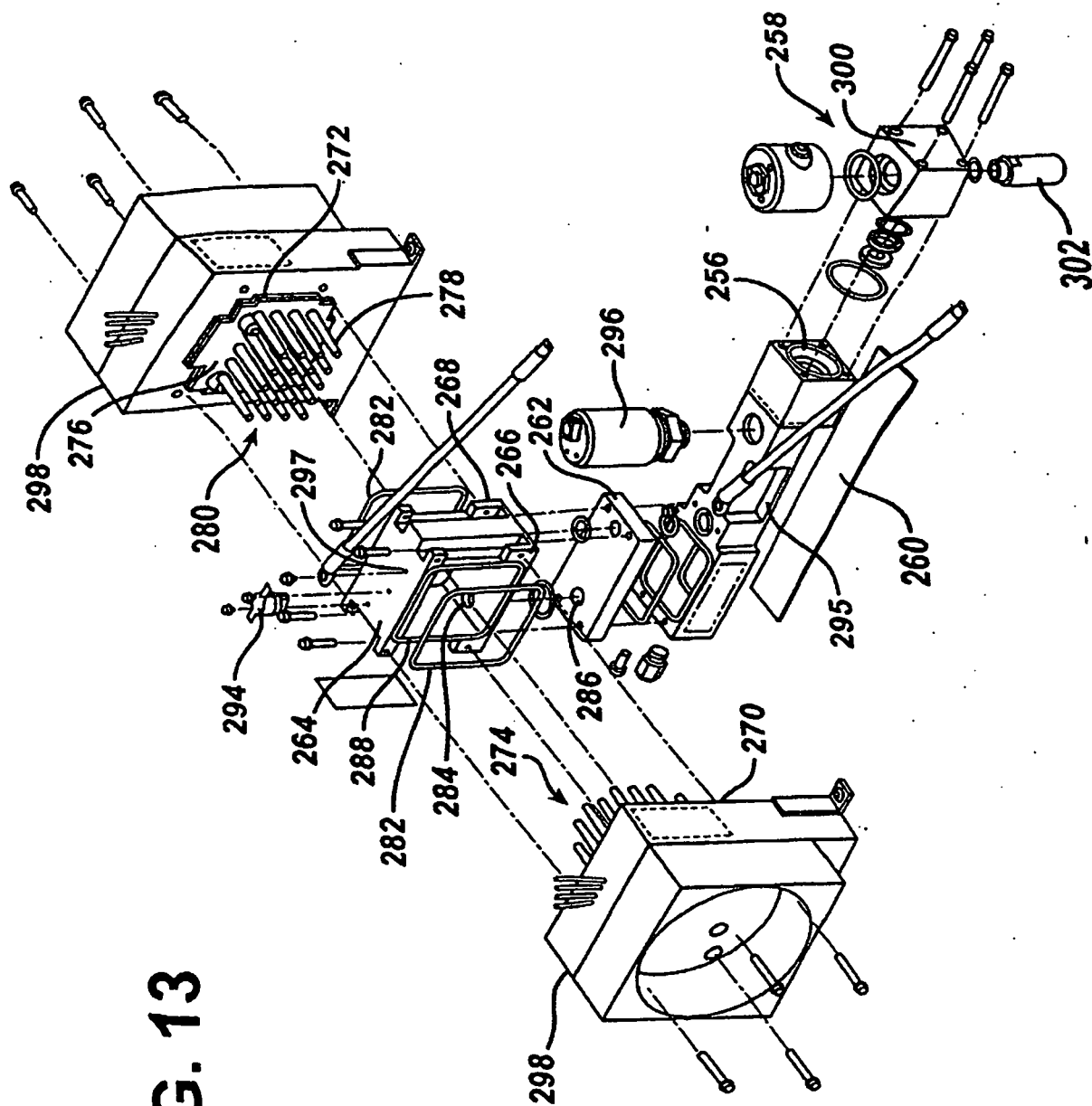
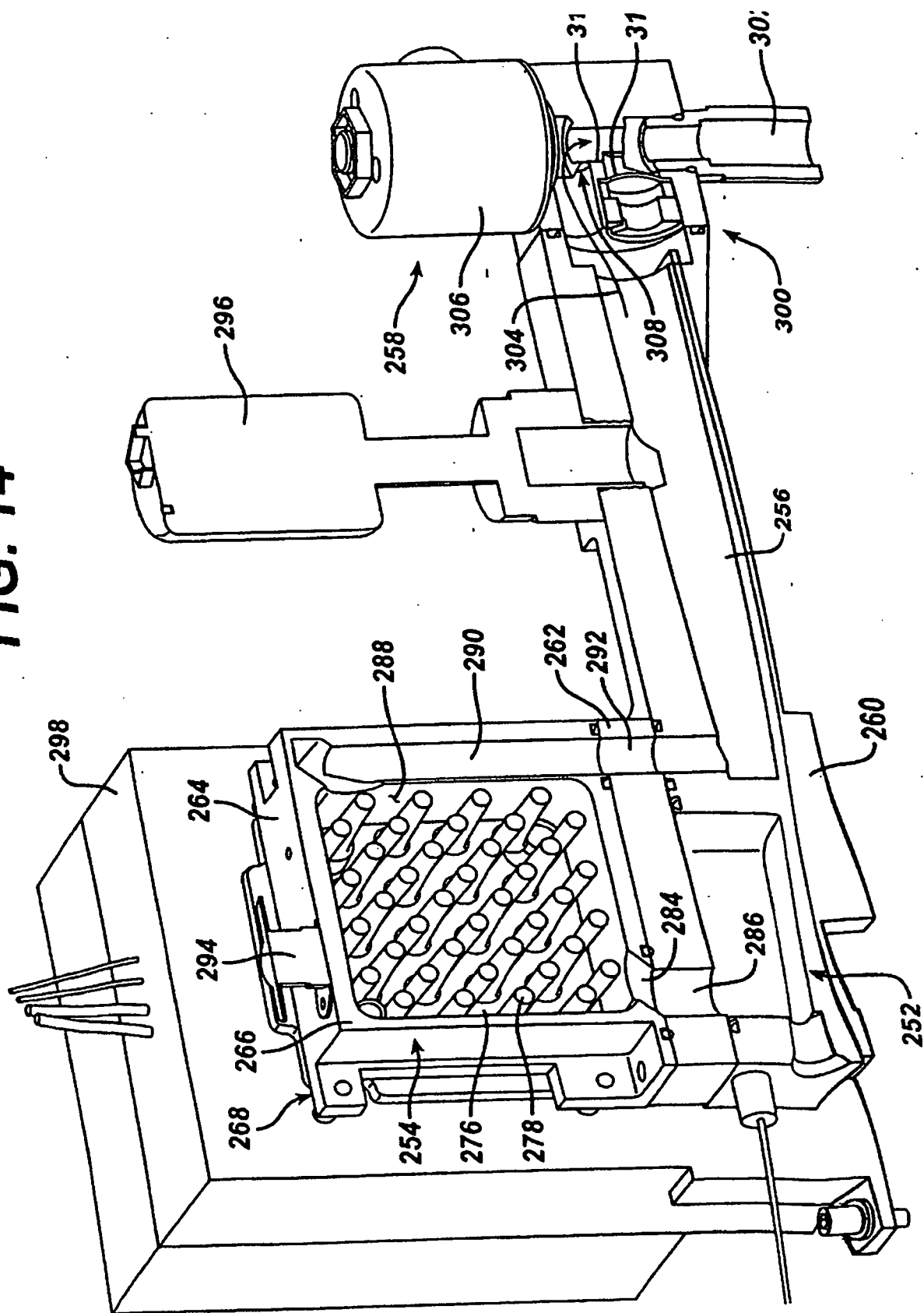


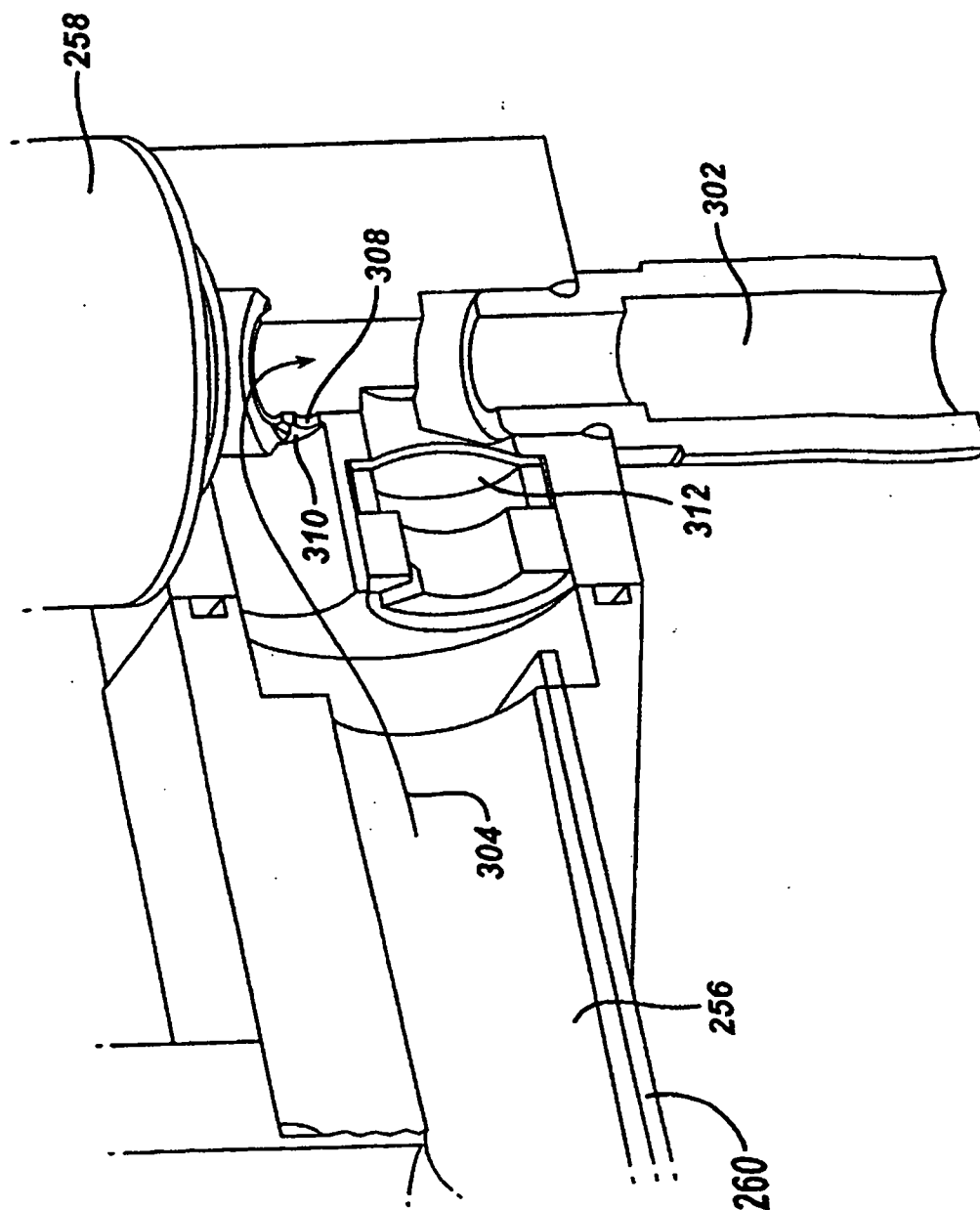
FIG. 13

FIG. 14



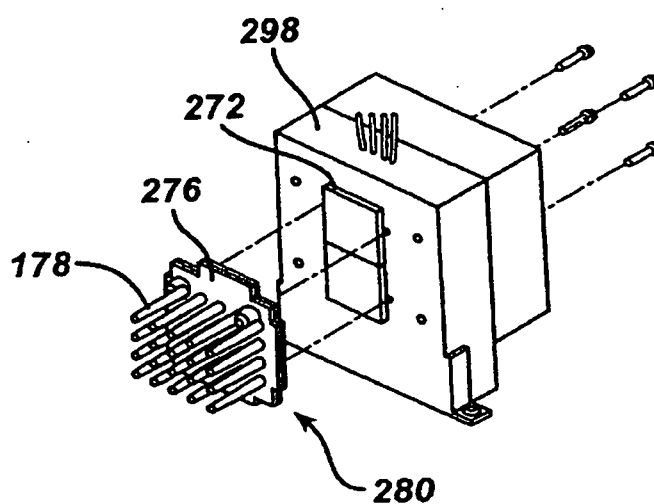
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FIG. 14A



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FIG. 15



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FIG. 16

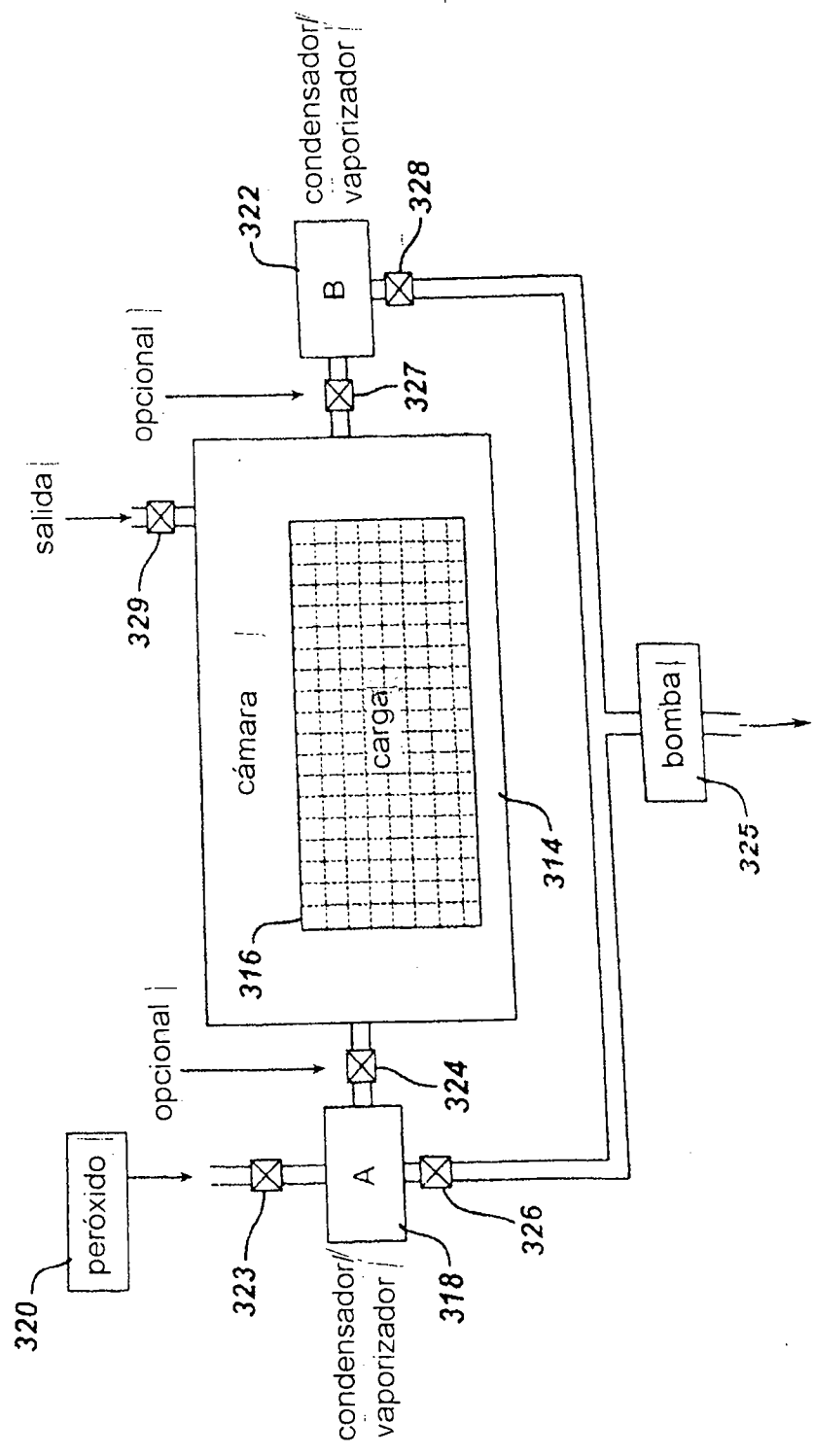
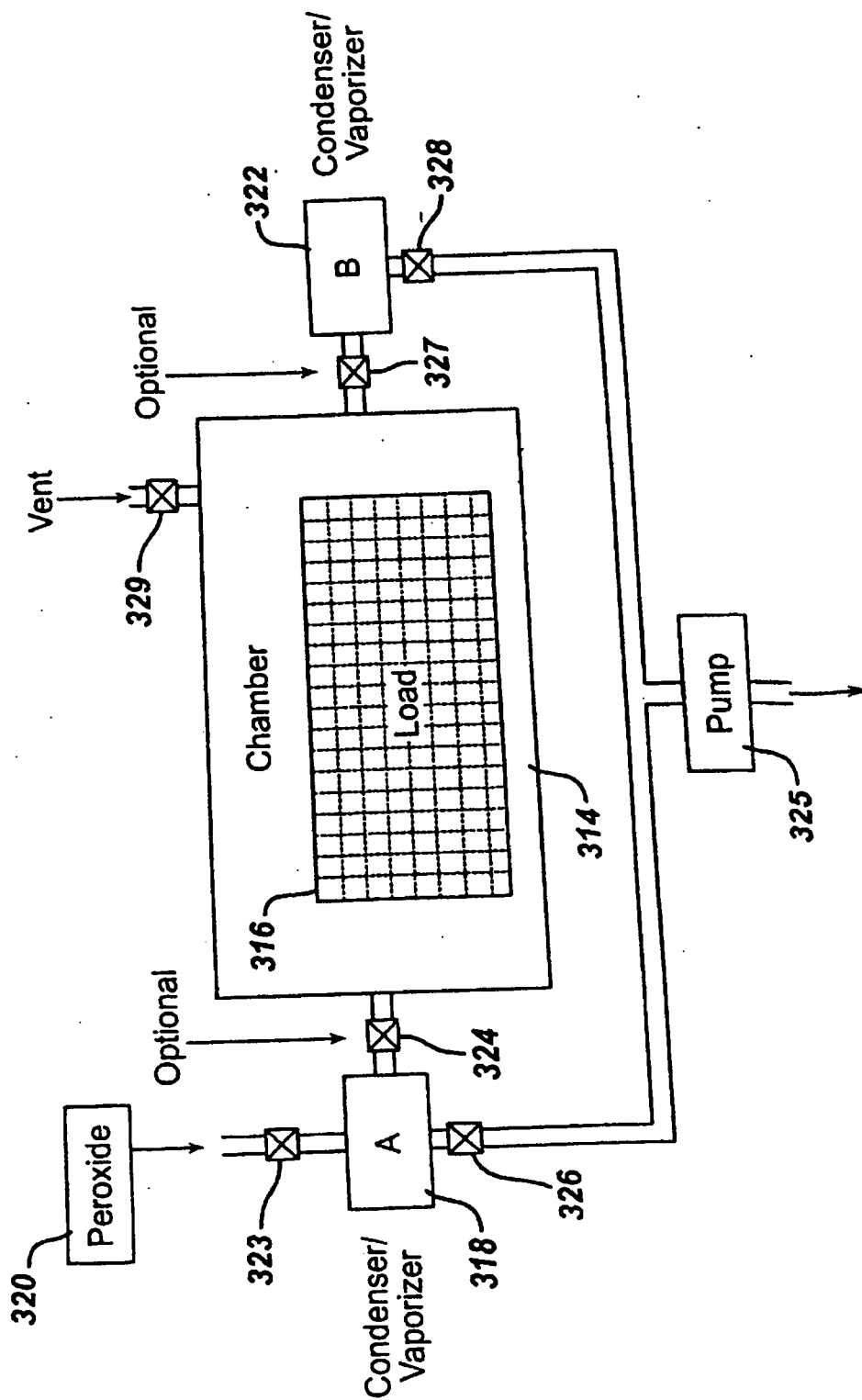
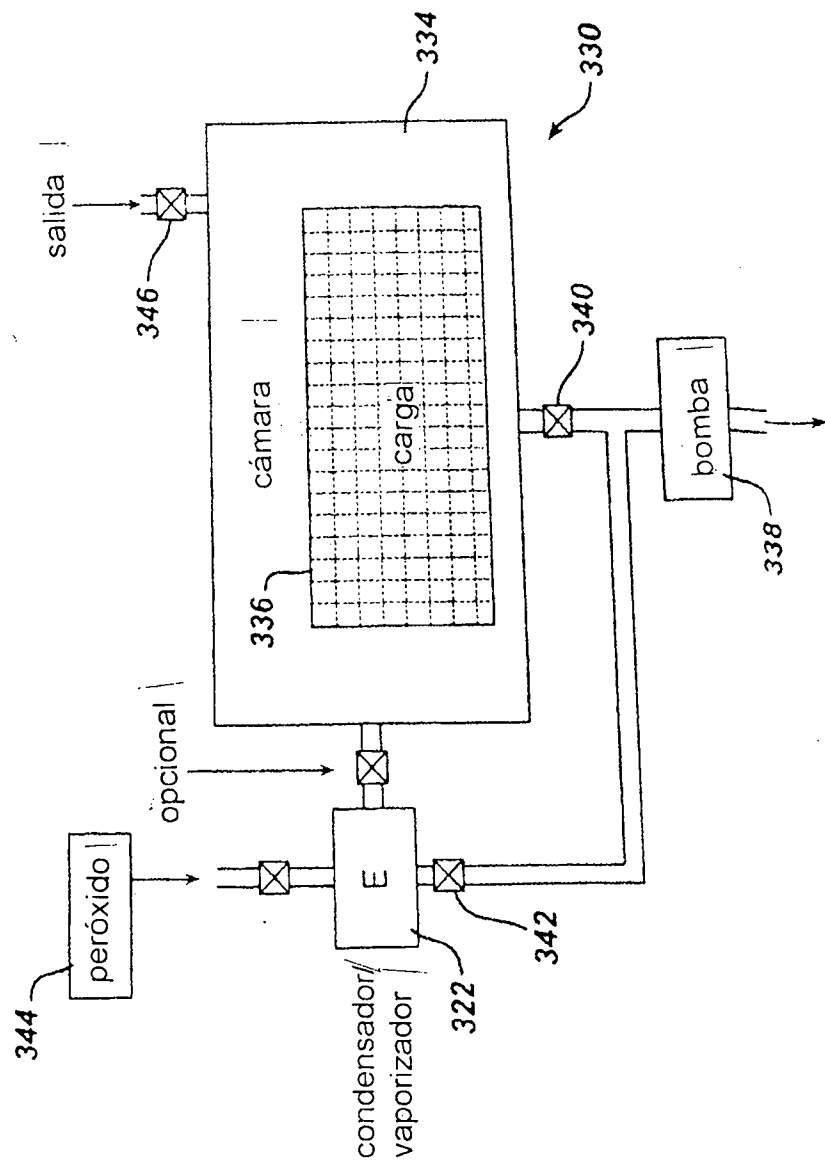


FIG. 16



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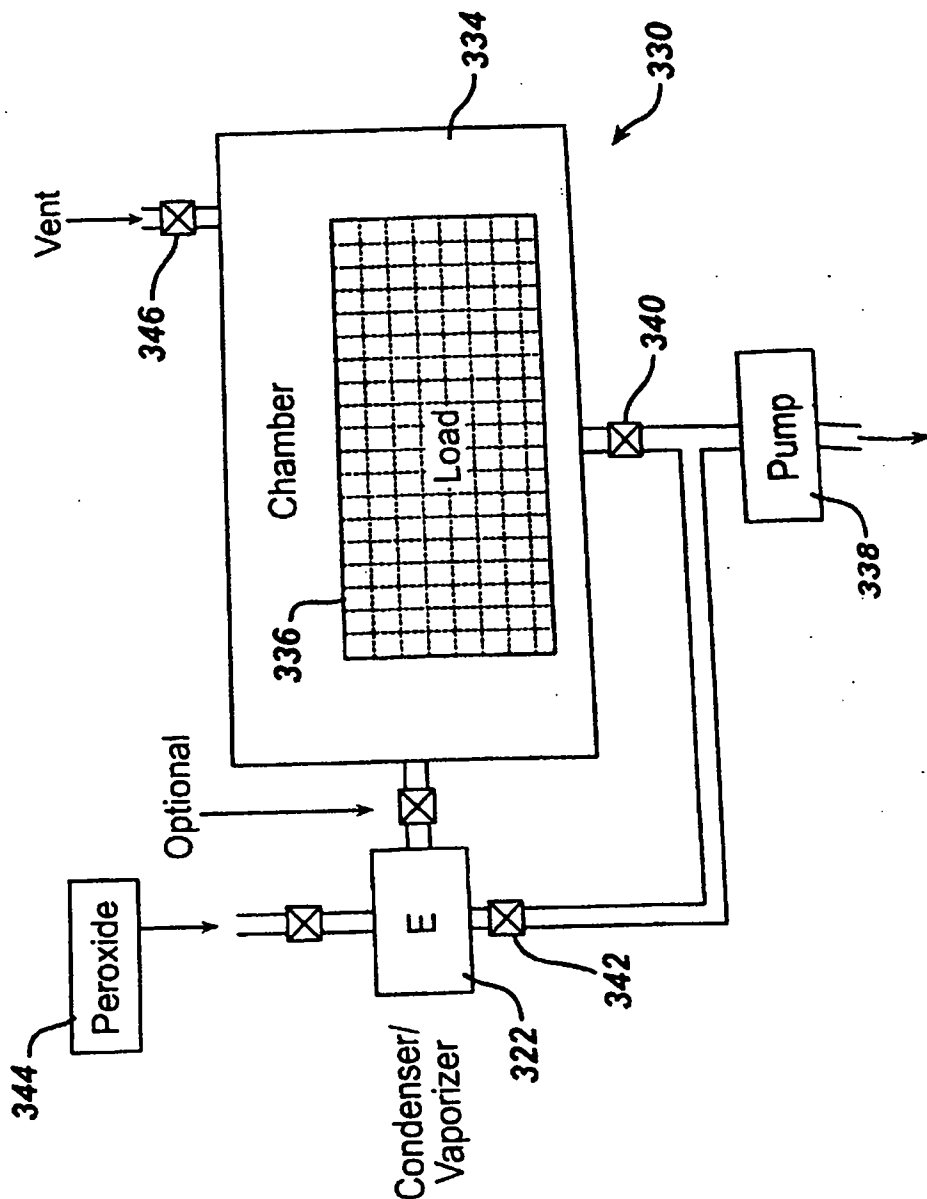
FIG. 17



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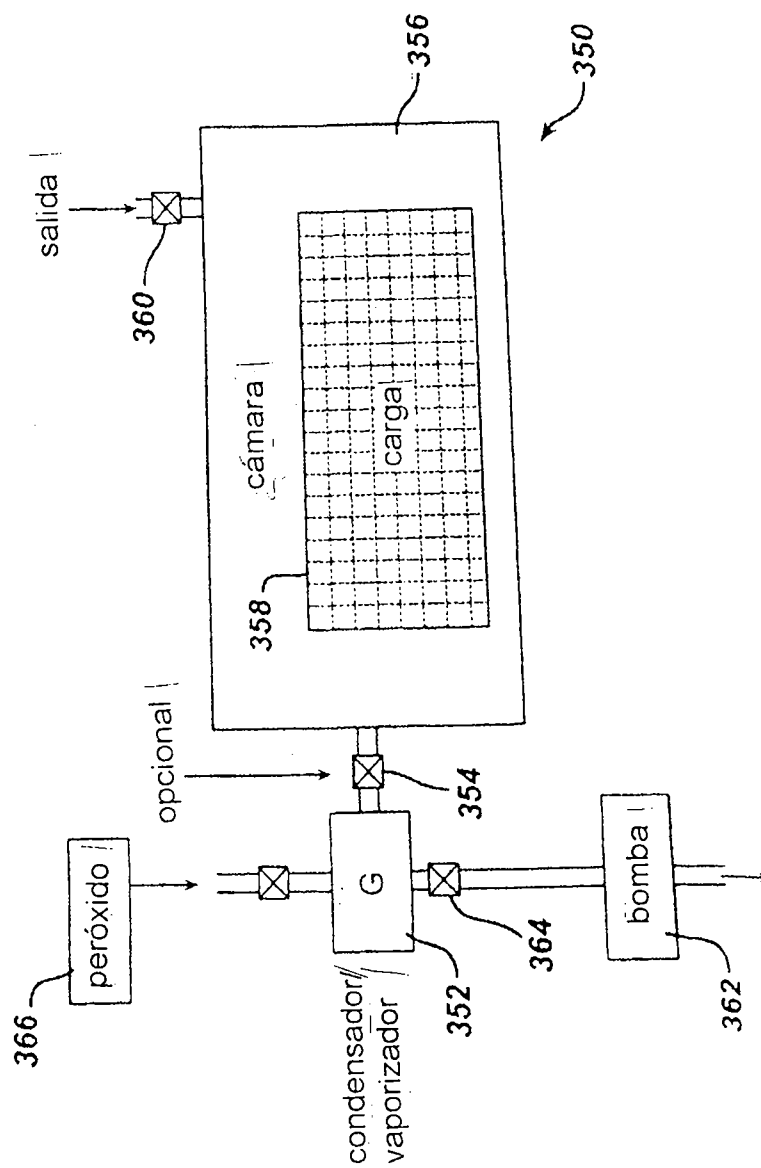
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FIG. 17



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FIG. 18



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FIG. 18

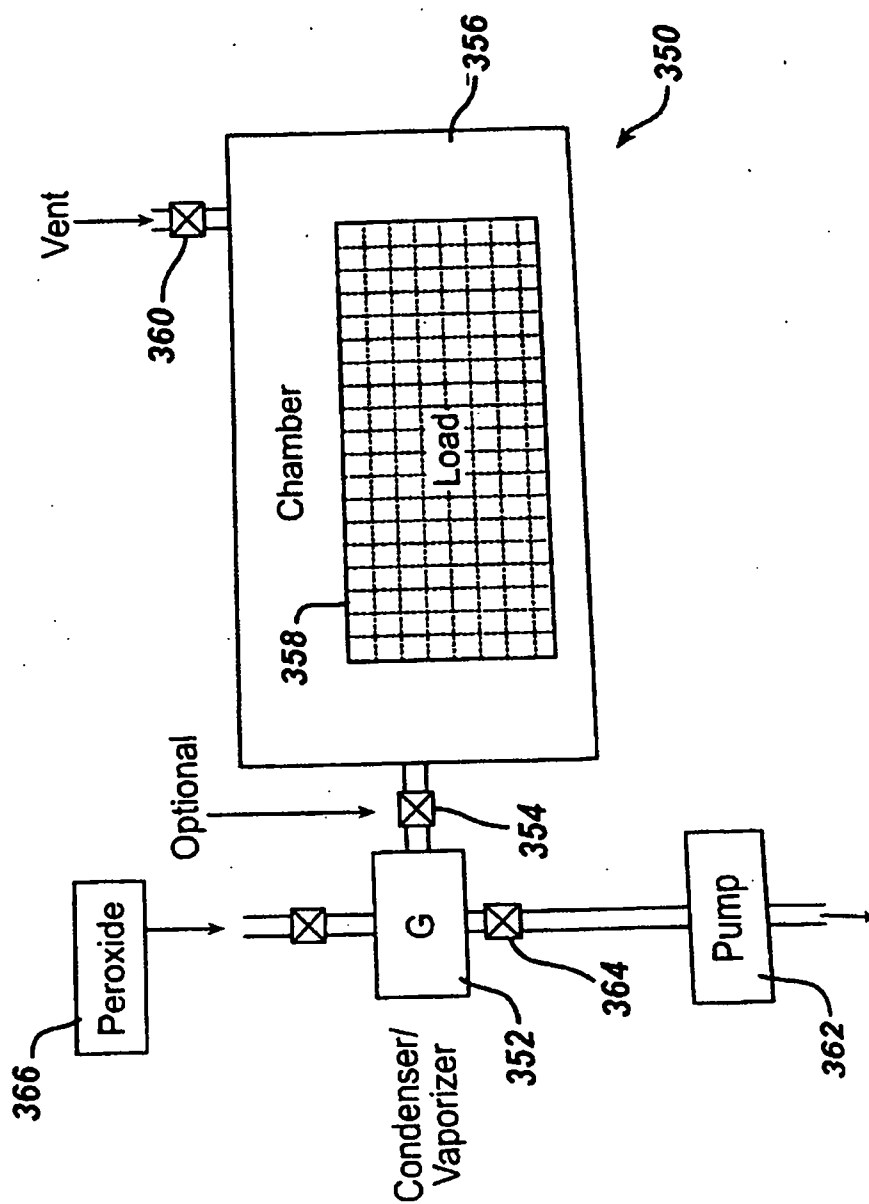
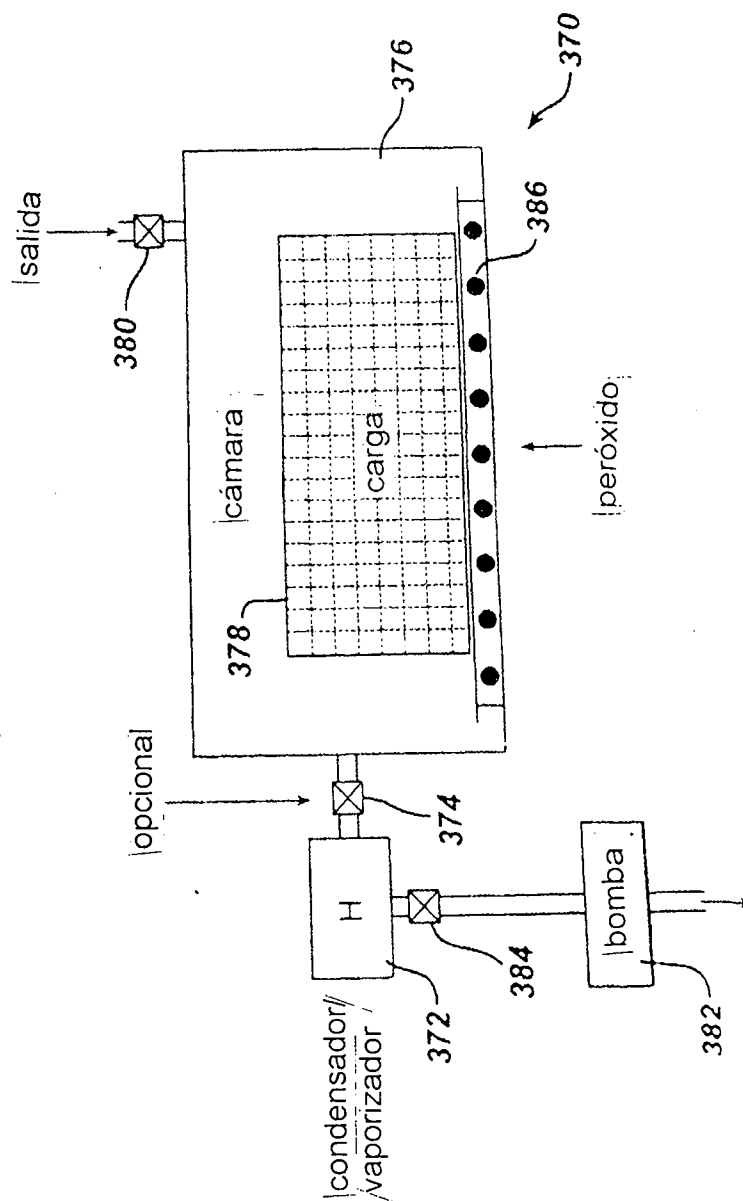


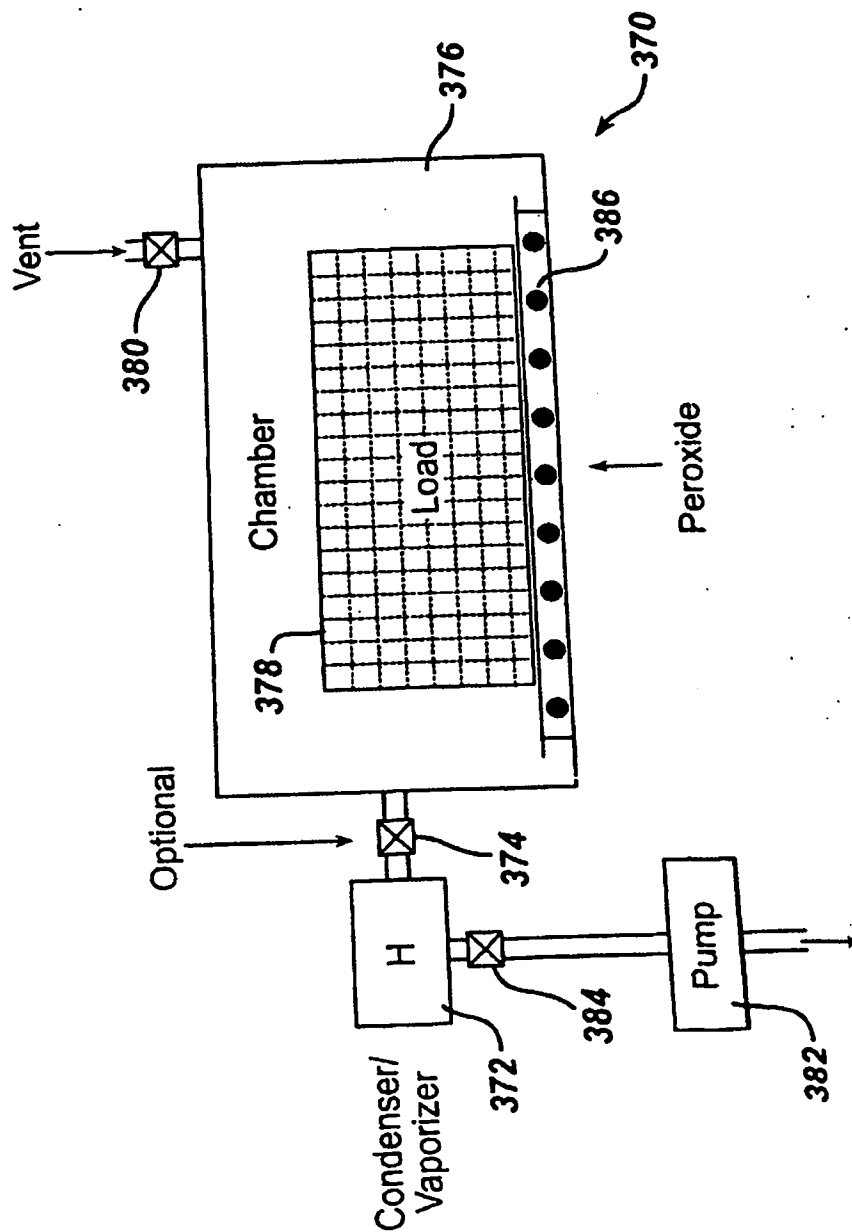
FIG. 19



279

181

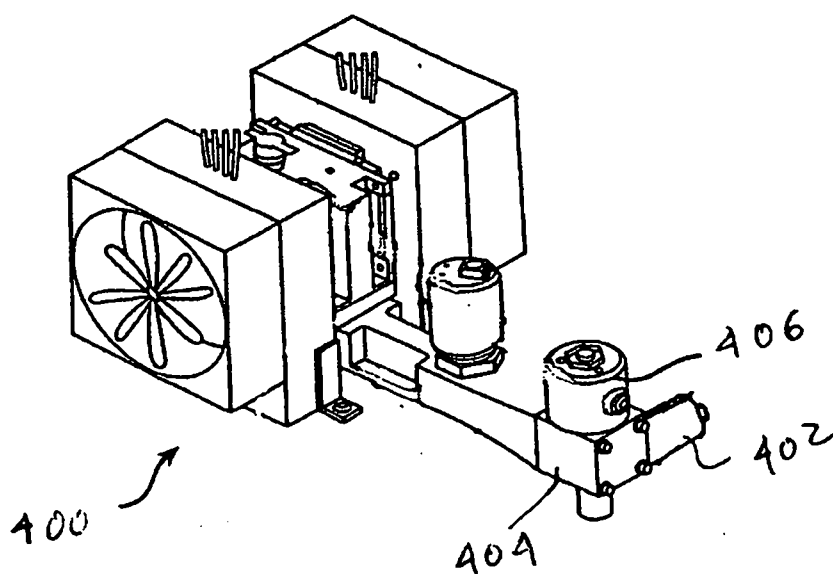
FIG. 19



188

281

FIG. 20



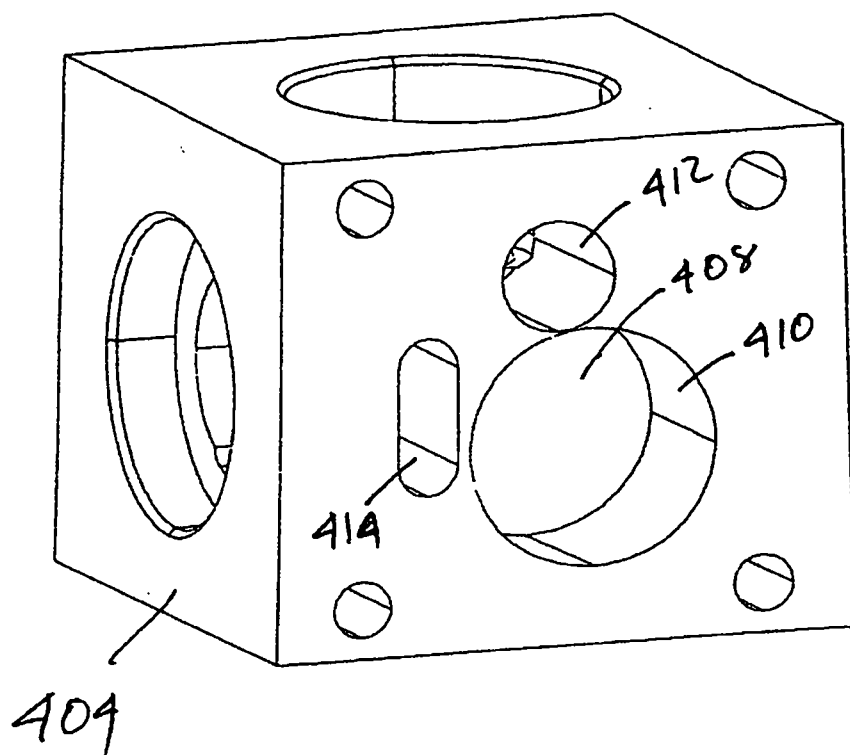


FIG. 21

185
283

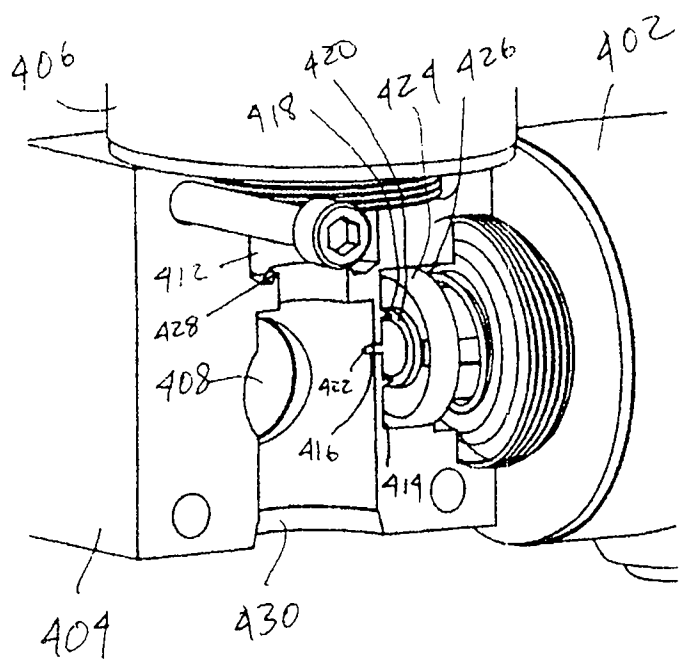
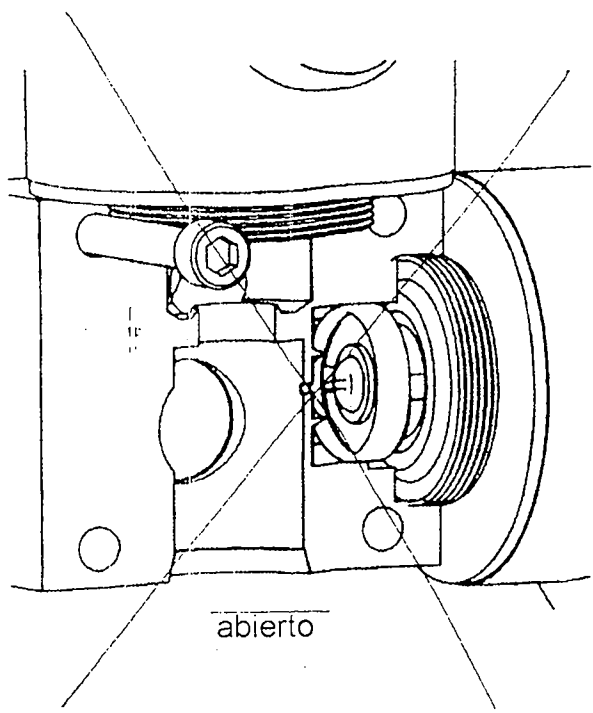


FIG. 22

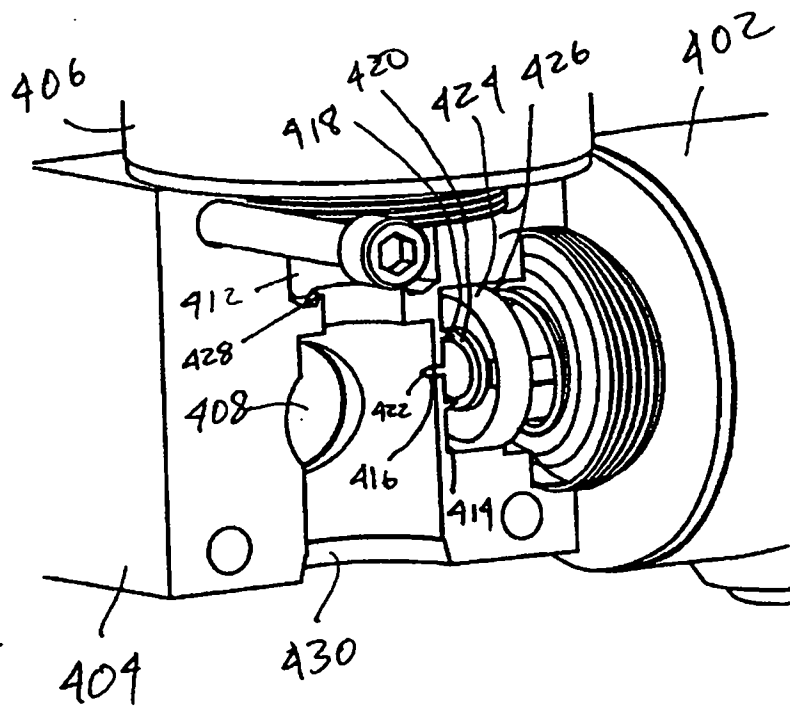
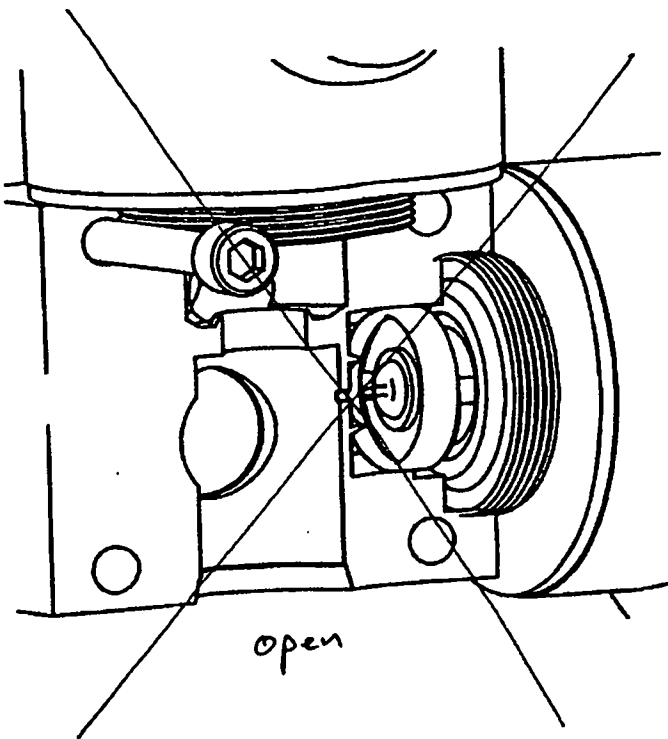


FIG. 22