United States Patent

[11] **3,574,950**

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[54] **LYOPHILIZING APPARATUS**
12 Claims, 10 Drawing Figs.

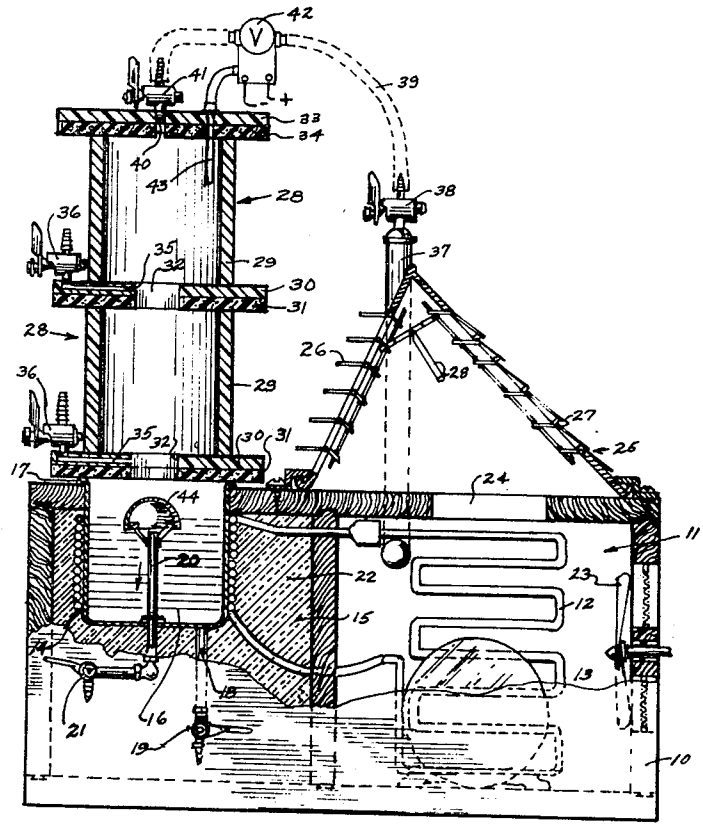
[52] **U.S. Cl.** **34/92,**
34/5, 62/55.5, 62/324
[51] **Int. Cl.** **F26b 13/30**
[50] **Field of Search** 34/5, 92

[56] **References Cited**
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ABSTRACT: A lyophilizing apparatus having a refrigeration system including an evaporator section and a condenser section, the evaporator section refrigerating a well-shaped cold trap over which one or more chambers for containing the material to be freeze-dried can be stacked, a source of vacuum in the cold trap subjecting all of the stacked chambers to a low pressure to cause sublimation of the moisture in the material in the chambers and condensation thereof in the cold trap and a means to direct heat given off by the refrigeration condenser against the exterior surface of the chambers and into the same to enhance the sublimation process.



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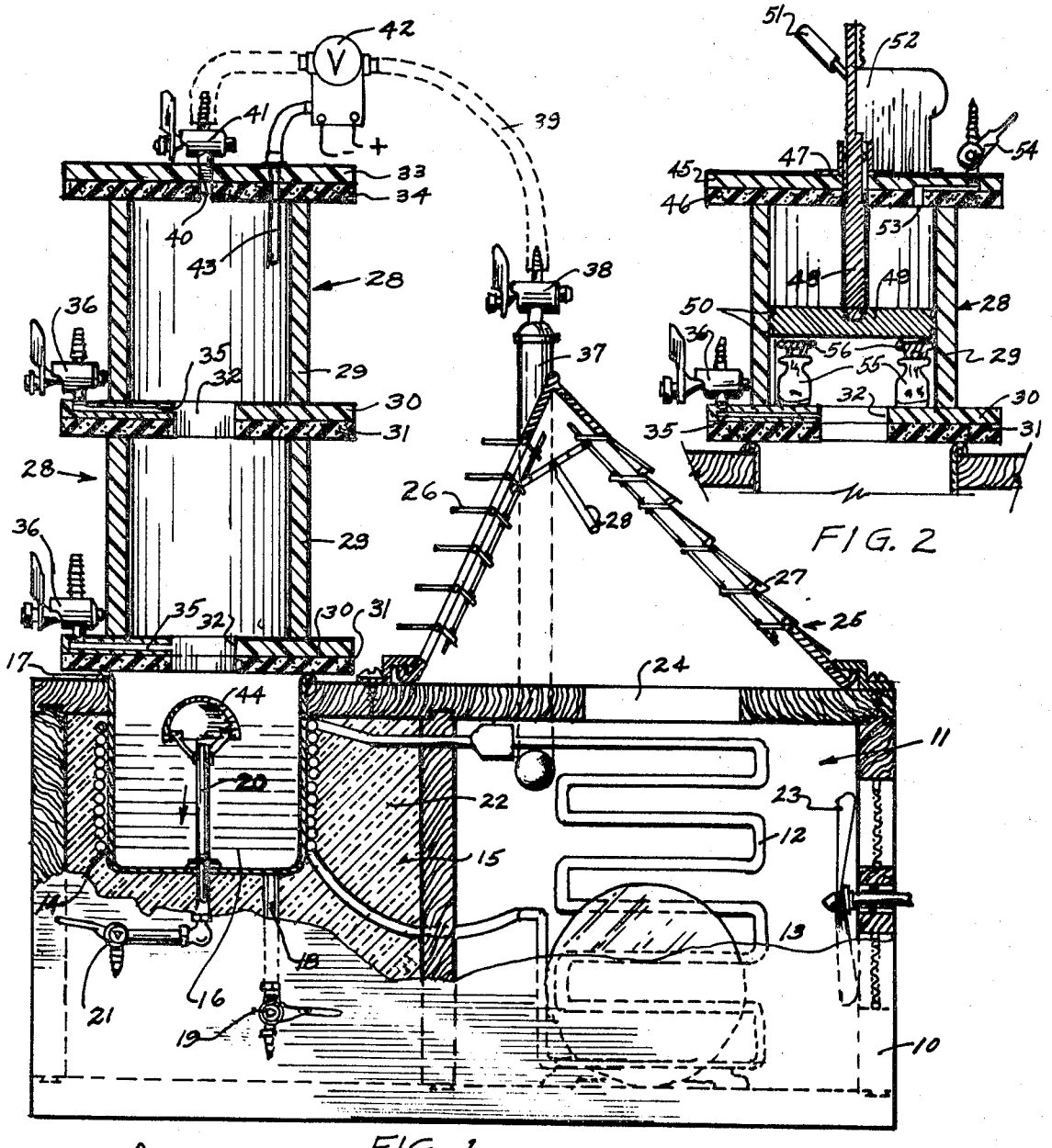


FIG. 1

FIG. 2

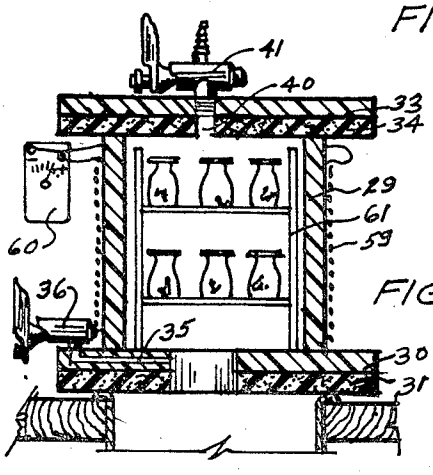


FIG. 3

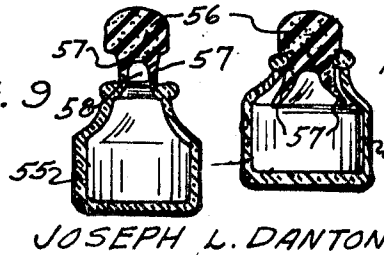


FIG. 9

FIG. 10

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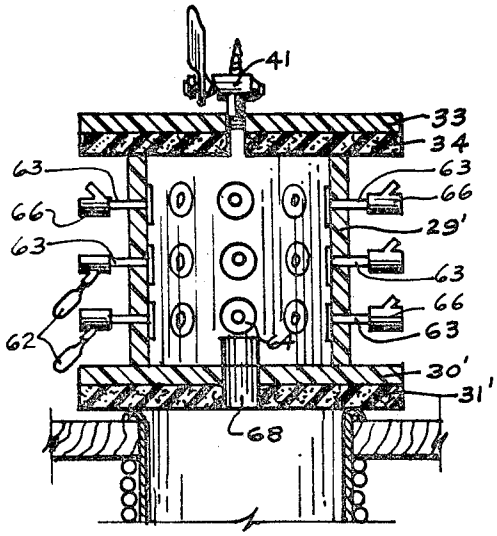


FIG. 4

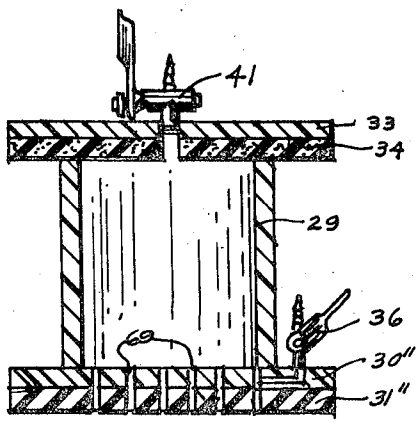


FIG. 7

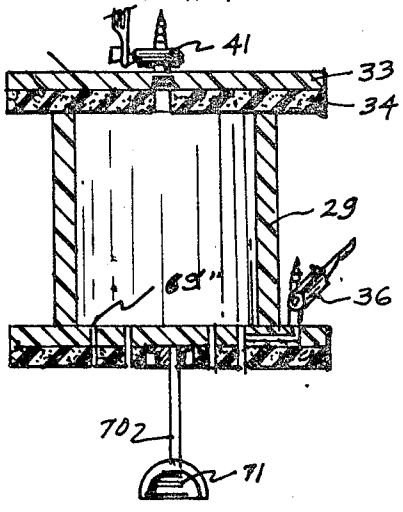


FIG. 8

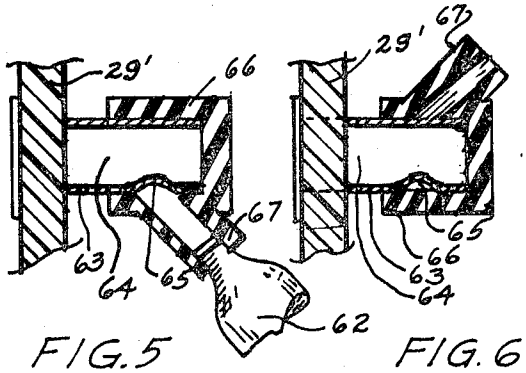


FIG. 5

FIG. 6

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LYOPHILIZING APPARATUS

This invention relates to lyophilization or freeze-drying apparatus and more particularly to such apparatus which can accommodate both bulk material and material in containers separately or simultaneously.

In conventional methods of lyophilization, material is placed in containers and fast frozen at very low temperatures. The frozen material is transferred to a vacuum apparatus and moisture is removed by sublimation. Very often heat is applied to the material by use of steam, infrared, or thermal electric devices. Usually the water vapor is condensed in a cold trap. When the freeze-drying process is complete, the vacuum is broken and the dried material is removed.

Most of the equipment used for lyophilization in the prior art is bulky, complicated, and expensive. Use is frequently made of special types of containers and material must be transferred to several pieces of apparatus to accomplish the freeze-drying process. Each transfer of material increases the risk of contamination and very often the process becomes lengthy. A number of different apparatuses are required, making lyophilization apparatus very expensive.

It is among the objects of this invention to provide an apparatus in which substantially the entire freeze-drying process may be accomplished with a minimum of handling and transferring to minimize the possibility of contamination.

It is another object to provide an apparatus in which material in containers may be freeze-dried and sealed or stoppered in a vacuum, in air or in an atmosphere of inert gas.

It is still another object to provide such an apparatus which the heat of the refrigeration machinery may be conveniently utilized to speed the drying process.

It is a further object to provide an apparatus of this character in which several chambers with material to be freeze-dried may be stacked in communication with each other so that all may be processed at once and all use the same cold trap and source of vacuum.

The above objects are realized in applicant's device by providing a number of chambers each with sidewalls, preferably of transparent material, such as a plastic "Lucite," a bottom also preferably of plastic sealed to the lower edges of the sidewalls, and a sealing ring of relatively thick rubberlike material fixedly sealed to the bottom wall. The bottom of each chamber has one or more openings therein to afford communication with the interior of the chamber. Any number of such chambers, within limits, may thus be stacked one upon the other with the sealing ring of each resting in sealing engagement with the upper sidewall edges of the chamber below and the lowermost chamber resting on the upper edge of the cold trap wall into which a vacuum line extends. A top plate member with a sealing ring attached is then used to close the top of the uppermost chamber. All the chambers are thus connected in "series" and are subject to the conditions of vacuum created in the cold well and the moisture evaporated from materials in each of the chambers will be conducted to the cold well and there condensed. Various valved ports for introduction of inert gases, air, etc., may be provided for the chambers through the bases thereof and through the top plate as hereinafter more fully explained.

The objects outlined above and other objects and advantages will become more apparent as this description proceeds and reference is had to the accompanying drawing forming a part of this specification and in which:

FIG. 1 is a side view mostly in section of a freeze-drying apparatus incorporating my invention;

FIG. 2 is a sectional view of one chamber provided with a top with means thereon for closing or stoppering bottles contained therein;

FIG. 3 is a sectional view of a chamber equipped with an external electric heater;

FIG. 4 is a sectional view of a chamber equipped with a number of valves for attaching vessels, vials and the like to be processed;

FIGS. 5 and 6 are views partly in section showing details of the valves used in FIG. 4;

FIG. 7 is a sectional view of a chamber with a slightly modified bottom;

FIG. 8 is a sectional view of chamber with a further modified bottom equipped with a depending deflector for the vacuum pipe;

FIGS. 9 and 10 are sectional views of a form of bottle and stopper such as may be used to contain material to be treated shown in open and closed condition respectively.

Referring to the drawing in greater detail and for the present to FIG. 1 thereof, 10 represents a cabinet which encloses a refrigeration plant or system generally indicated at 11 with the usual condenser portion 12 located in one portion 13 of the cabinet and the evaporator or cooling portion 14 located in a second portion 15 of the cabinet. The cooling portion 14 is in the form of a coil wound around the exterior or interior of a well-like receptacle or cooling trap 16 which is open through the top of the cabinet and is there provided with a slightly raised turned over rim 17 the purpose of which will become apparent as this description proceeds.

The cold trap 16 is provided with a drain 18 and cutoff valve 19 and a second pipe 20 extends upwardly through the bottom thereof which, when the device is in use, is connected to a source of vacuum, not shown. The pipe 20 is suitably valved at 21.

The well-like cold trap 16 with its surrounding cooling coil 14 is enclosed in insulating material 22 in the portion 15 of the cabinet to isolate these parts from the outside temperature.

The condenser portion of the refrigeration system is located in the cabinet portion 13 adjacent the insulated evaporator section thereof. The condenser, as is well known, gives off heat and to dissipate this heat a fan 23 is mounted in the side of the cabinet to force air into the cabinet portion 13 and out through the top opening 24 thereof.

A hood, generally indicated by 25, is located on the cabinet above the opening 24 and is provided with inclined louvered panels 26 and 27, the louvers of which may be opened or closed by means of a lever 28 and they may be so controlled that when the louvers of one panel are closed those on the other panel are open so that the heated exhaust air from the refrigeration condenser may be directed in either of two directions. The purpose of this construction will be more clearly understood from the description that follows.

Chamber members generally indicated 28 are provided for receiving the materials to be subjected to the freeze-drying process. Each chamber consists of a sidewall portion 29 preferably of transparent plastic such as "Lucite" with a bottom wall 30 also of plastic such as "Bakelite" sealed to the bottom edges of the sidewalls and a relatively thick resilient gasket 31 fixed and sealed to the lower surface of the bottom wall. An opening 32 of fair size through the bottom wall and gasket affords communication therethrough.

As may be seen from FIG. 1 a chamber may be placed directly on the rim 17 of the cold trap and one or more chambers may be placed or "stacked" one above the other on the first chamber, the lowermost in sealing engagement with the rim 17 of the cold trap and all the other chambers in sealing engagement with the one below.

The uppermost chamber is closed at its top with a closure plate 33 having a sealing gasket 34 attached to its under surface similar to the gaskets 31 on the bottoms of the chambers.

Each chamber is provided with a port 35 extending outwardly through the bottom thereof from the opening 32 to the outside and is there provided with a stop cock 36 to which a hose may be attached. While these chambers and other parts are preferably constructed of plastic, any suitable material may be used.

As previously stated, the condenser section of the refrigeration system is located adjacent the evaporator section and cold trap. This places the hood 25 with its inclined louvers 26 facing the chamber or chambers 28 positioned over the cold trap whereby the heat from the condenser section may either be exhausted through the louvers 26 and directed

against the chambers to assist in the evaporation and sublimation of the moisture contained in the materials in the chambers and it may also be regulated by the lever **28** to exhaust through the louvers **27** or through both sets of louvers to regulate the amount of heat thus supplied to the chambers. In addition the amount of heat thus supplied to the chambers through regulation of the louvers may be accomplished automatically by thermostatic control if desired.

Provision is also made to supply heated air directly to the interior of the chambers through the pipe **37** leading from the interior of the condenser section of the cabinet through a control valve **38** and hose **39** to the port **40** in the top plate **33** closing the uppermost chamber. For convenience in closing off the port **40** when interior heating is not used a valve **41** may be used.

Flow of heated air into the chambers may be automatically regulated, if desired, by providing a thermostatic valve **42** in the line **39** controlled from a sensing device **43** inserted into the chamber through the top plate **33**.

The operation of the apparatus shown in FIG. **1** is as follows: With the refrigeration machinery in operation one or several of the chambers **28** containing the prefrozen materials to be lyophilized are placed over the cold trap in stacked relation and a cover plate **33** is placed over the uppermost chamber. The pipe **20** through its valve **21** is then connected to a source of vacuum. This will subject the interiors of the chambers to a very low pressure and will cause the frozen materials to begin losing moisture by sublimation. The moisture will be drawn into the cold trap and there condensed and frozen on the low temperature walls of the cold trap. This process will continue until all the moisture has been extracted from the materials being processed, after which the source of vacuum may be cut off and the dried materials removed from the chambers.

It may be desirable under certain circumstances to heat the chambers during the drying process to speed evaporation. With the instant device this may be accomplished by opening the louvers **26** to direct the heated air from the refrigeration condenser toward and against the chambers or heated air may be introduced directly into the chambers through the pipes **37** and **39** by opening the valves **38** and **41**. The sensor **43** acting on thermostatic valve **42** may then be used to control the amount of heat to suit the particular conditions.

In addition the freeze-drying process may be effected in an atmosphere of inert gas such as nitrogen or sterile air by connecting a source of supply of such gases through the valved ports **35** and **36** in the chambers.

It should be noted that the vacuum pipe **20** is provided with a deflector or hood **44** for the purpose of preventing entry into the vacuum pipe of moisture and ice crystals and thus avoid clogging and damage to the vacuum system.

After completion of the freeze-drying run the refrigeration system is, of course, shutdown and the frozen moisture in the cold well allowed to melt whereupon it may be drained off through pipe **18** by opening the valve **19**.

The device shown in FIG. **2** is one means whereby a number of bottles containing material to be lyophilized may be stoppered while still under vacuum and enclosed in a chamber. A special top plate **45** adapted to fit any of the chambers **28** is employed. This top plate is provided with a sealing gasket **46** on its lower surface and a central opening **47** through which a reciprocatory rod **48** extends. A piston **49** is mounted on the lower end of the rod and is slidable on the inner surface of the chamber and is sealed against leakage by means of O-rings or the like **50**. The upper end of the rod **48** extends above the top plate and a suitable lever **51** and ratchet arrangement **52** mounted on the top plate may be employed to propel the rod and piston downwardly. As an alternative means for moving the piston, the top plate is provided with a port **53** and stop cock **54** for attachment to a source of pressure to force the piston downwardly.

In using the device shown in FIG. **2** bottles **55** containing the material to be freeze-dried are employed. These bottles are equipped with stoppers **56** which have depending leg portions **57** leaving open side ports **58** when the stoppers are not pressed fully down as shown in detail in FIG. **9** but which fully seal the bottles when pressed down. The bottles and contents with their stoppers in the position shown in FIG. **9** are placed in the chamber for processing, the open side ports **58** enabling the contents to be subjected to conditions within the chamber. After completion of the drying process the stoppers are pressed to closed position by the piston **49**. These chambers may in many instances carry an inert gas such as nitrogen which may be introduced through the valve **36**.

FIG. **3** shows a modified form of chamber which, for all intents and purposes, is substantially similar to those shown in FIG. **1** except that an external electric heating element **59** surrounds the sidewall **29** which may be used in lieu of or in combination with the above-mentioned heating means to enhance the evaporation process. This heater may be controlled by a suitable thermostatic switch **60** if desired.

FIG. **3** also shows a rack or shelf device **61** for holding several rows of bottles or containers which may be used in any of the chambers shown.

FIG. **4** shows a chamber with sidewalls **29'** equipped with a plurality of outlets to which bottles or vials **62** may be attached for processing the contents thereof. Each outlet (see FIGS. **5** and **6** for details) consists of a nipple **63** sealed in the sidewall **29'** and having an axial passage **64** therein in communication with the interior of the chamber, and a lateral port **65** near the end thereof communicating with the axial passage. A cap member **66** of rubber or resilient plasticlike material is fitted rotatably on the end of the nipple and is provided with a diagonally positioned hollow branch **67** which in one position of rotation will register with the port **65** to open the valve, and in another position be out of registry with the port to close the valve. The bottles or vials to be processed may be directly connected to the branches **67** as seen in FIG. **5**.

The top **33, 34** utilized with the chamber shown in FIG. **4** is duplicate of that shown in FIGS. **1** and **4**, while the bottom **30', 31'** is similar to that shown in FIGS. **1** and **4** except that the opening in the center is provided with an inserted thimble **68** which projects upwardly somewhat from the interior bottom surface and forms a flange about the openings, and the port **35** and valve **36** shown in FIGS. **1** and **4** are not provided.

FIG. **7** is a modified form of chamber in which the bottom wall **30''** and gasket **31''** are provided with a plurality of small openings **69** in lieu of a single large opening as shown in FIGS. **1** and **4**. The sidewalls **29** and top plate **33, 34** are identical to those in FIGS. **1** and **4**.

FIG. **8** is also a modification but is very similar to that of FIG. **7** except that it is equipped centrally of its bottom with a removable depending stem **70** which carries at its lower extremity a deflector **71** which may be used in place of the deflector **44** previously described. Small openings **69'** are used in this form similar to the small openings **69** in the form shown in FIG. **7**.

It is to be understood that the forms of chambers shown in FIGS. **2, 3** and **4** are shown in position directly over the cold trap, they may also be used in stacked arrangement over other chambers if desired.

I claim:

1. A lyophilizing apparatus comprising:
   a. a refrigeration apparatus having an evaporator section and a condenser section, the evaporator section refrigerating a moisture condensing cold trap, and the condenser section having a heat dissipating means;
   b. a source of vacuum in said cold trap;
   c. at least one enclosed chamber member adapted to contain the material to be freeze-dried positioned over said cold trap with its interior in communication therewith and with the source of vacuum therein whereby the interior of said chamber with its contained material is subjected to the low pressure of said vacuum source to cause sublimation of the moisture contained in said

material and conduction thereof to said cold trap to be condensed therein; and

d. means to direct the heat dissipated by said condenser section against said chamber to enhance the sublimation process.

2. The structure defined in claim 1 in which a plurality of chambers are stacked one upon the other in sealing engagement with each other and interiorly communicating with each other whereby all of the chambers are subjected to the low pressure in said cold trap.

3. The structure defined in claim 1 in which the means to direct the heat dissipated from said condenser section comprises a hood disposed over said condenser section, said hood having an inclined panel with louvers facing the chamber and a means to force the air from said condenser section through said louvers and against the outer surface of said chamber to heat the same.

4. The structure defined in claim 1 in which the means to direct the heat dissipated from said condenser section comprises a duct in communication with said condenser section said duct connected to and in communication with the interior of said chamber and means to force the air from said condenser section through said duct and into the chamber to heat the same.

5. The structure defined in claim 3 in which the hood is provided with a second inclined panel with louvers facing in a direction opposite said first panel and away from said chamber, the louvers of both panels provided with means to open and close the same whereby the amount of air emitted through the louvers of both panels may be controlled.

6. The structure defined in claim 1 in which the chamber comprises sidewalls, a bottom wall sealed to the bottom edges of said sidewalls, said bottom wall having at least one opening therethrough, a sealing means adhered to said bottom wall for sealing engagement with said cold trap and a top plate having a sealing means on its under surface for sealingly engaging the upper edges of said sidewalls.

7. The structure defined in claim 6 in which the bottom wall has a port extending from the interior of said chamber to the exterior thereof and a valve in said port.

8. The structure defined in claim 6 in which an electric heating element surrounds said sidewalls.

9. The structure defined in claim 6 in which said top plate is provided with a piston rod extending therethrough, a piston on the lower end of the piston rod adapted to slidably engage the interior surface of said sidewalls and means to propel said piston downwardly in said chamber.

10. The structure defined in claim 6 in which the sidewalls of the chamber are provided with a plurality of radially extending hollow nipples communicating with the interior of said chamber, each said nipple having a lateral port near the outer end thereof, a cap of resilient material rotatably mounted on each nipple and having a tube extending laterally therefrom which by rotation of the cap may be brought into registry with said lateral port or out of registry therewith, said lateral tube adapted to receive and hold a bottle.

11. A lyophilizing apparatus comprising:

a. a refrigeration apparatus having an evaporator section and a condenser section, the evaporator section refrigerating a moisture condensing cold trap, and the condenser section having a heat dissipating means;

b. a source of vacuum in said cold trap;

c. at least one enclosed chamber member positioned over said cold trap with its interior in communication therewith and with the source of vacuum therein whereby the interior of said chamber is subjected to the low pressure of said vacuum source, at least one container in said chamber containing the material to be freeze-dried whereby said container with its contained material will be subjected to the low pressure of said vacuum source to cause sublimation of the moisture contained therein; and

d. means for supplying a predetermined amount of heat from the condenser section to the material to be freeze-dried while the said chamber is subjected to low pressure.

12. A structure defined in claim 11 with means to introduce into said chamber while the chamber is subjected to the low pressure vacuum and means for sealing the material in said container prior to releasing the said vacuum in said chamber.