Nov. 11, 1969 M. BROWN ET AL 3,477,192

CONTAINER FILLING PROCESS

Filed March 2, 1967 2 Sheets-Sheet 1

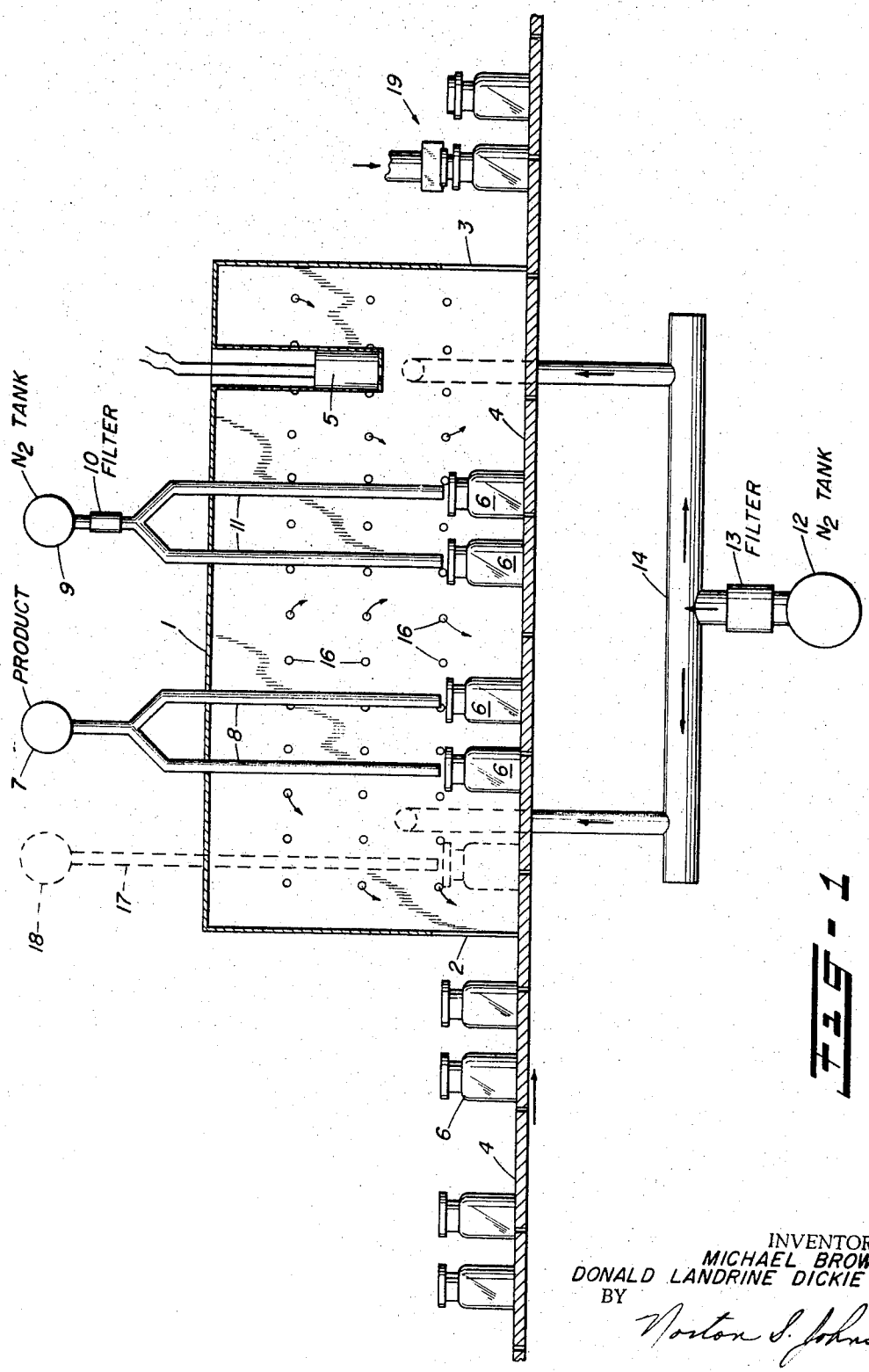

FIG. 1

INVENTORS
MICHAEL BROWN
DONALD LANDRINE DICKIE
BY
Norton S. Johnson
ATTORNEY

CONTAINER FILLING PROCESS

Filed March 2, 1967 2 Sheets-Sheet 2

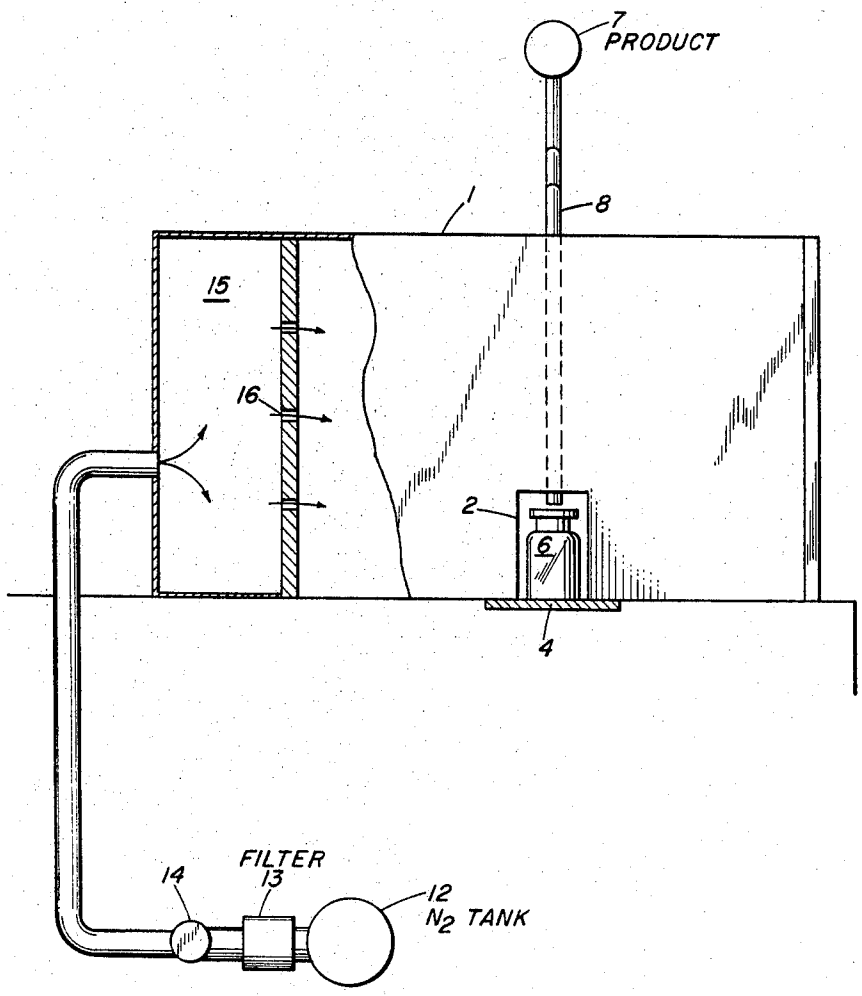

FIG-2

INVENTORS.
MICHAEL BROWN
DONALD LANDRINE DICKIE
BY
Norton S. Johnson
ATTORNEY

United States Patent Office

3,477,192

Patented Nov. 11, 1969

1

3,477,192
CONTAINER FILLING PROCESS

Michael Brown, Spring Valley, N.Y., and Donald Landrine Dickie, Upper Saddle River, N.J., assignors to American Cyanamid Company, Stamford, Conn., a corporation of Maine

Filed Mar. 2, 1967, Ser. No. 620,003
Int. Cl. B65b *31/02;* B67c *7/00*
U.S. Cl. 53—22 3 Claims

ABSTRACT OF THE DISCLOSURE

Machine for progressive automated filling of vials or other containers with materials which are sensitive to air, foaming, or to other factors, such as contamination, is designed with a hood over the conventional table or track along which vials or containers are moved. The hood is connected to a source of protective inert gas, such as nitrogen, and means are provided, such as a baffle with small openings, to introduce the nitrogen under slight positive pressure into the hood without excessive turbulence.

The ends of the hood are closed with walls provided with entrance and exit gates for openings respectively through which the vials can move in and, after filling, move out. As the vials move along thier predetermined track, they come under filling needles or tubes in the conventional manner. Through these tubes a definite amount of material, such as a liquid or powdered pharmaceutical, is filled into each vial. The vials are then brought into alignment with other tubes or needles which introduce a protective gas, such as nittrogen, into the top of each vial, filling the head space above the contents with the protective or inert gas. The vials are then capped or plugged at a station of conventional design, which may if desired be also under the same hood or under a second hood in which the protective atmosphere is maintained.

Sensitive materials, such as pharmaceuticals, are protected against oxidation from air, which otherwise is in the head space above the filling material. Also, foaming is reduced by layering the protective gas in the head space and hood during filling, as has been described. If desired, the vials before entering the hood may be filled with protective or inert gas, or after they enter the hood they may first be subjected to needles or tubes which fill them with the protective gas in the hood itself.

A number of protective gases are available, such as particularly nitrogen in the case of oxygen sensitive materials, carbon dioxide, and where the reduction of foaming is the only function desired and the material is not sensitive to oxidation, the gas introduced may even be air.

The introduction of a protecting gas into the hood is baffled and this prevents undue turbulence and hence contamination by dust and other materials in the case of pharmaceuticals which are in critical need of filling without any contamination.

BACKGROUND OF THE INVENTION

Automatic filling of vials or other containers from needles or tubes under which the vials are periodically stopped is a very old procedure. In can be automated, vials being moved in pairs or in multiple lines under the tubes or needles at the filling stations. In some cases the filling heads are moved from vial to vial instead of the reverse.

Problems are presented where the material filled is sensitive to oxidation, tends to foam, or both. In the case of materials which are sensitive to oxidation, the oxygen which is present in the head space of the vial above the material filled in is retained there after capping or otherwise plugging and can cause deterioration of the materials on standing. Even when antioxidants are added, these may become exhausted, and in many cases a sufficient amount of antioxidant to permit indefinite storage is objectionable because of its effect when the pharmaceutical is used.

2

It has been proposed in the past to sparge out air with nitrogen or similar material, but this has not been entirely satisfactory because, even though temporarily in some cases the content of oxygen in the head spaces in the vials has been reduced, it does not remain reduced but becomes again contaminated with more oxygen. Sparging if at all violent also caused undesirable turbulence, which can introduce contaminations by dust or other undesired material. This is not to say that sparging with nitrogen is without any effect, as it does reduce to some extent the oxygen content in the head spaces and so is of some slight benefit, which in the case of certain materials which are not oxidation sensitive to any high degree may be sufficient. The sparging, of course, does nothing to reduce the foaming problem and may in some cases actually make it more serious.

SUMMARY OF THE INVENTION

The present invention provides a hood over the filling stations of the automatic vial filling machine and, if necessary, over a plugging or capping station. Protective atmosphere is introduced into the hood without excessive turbulence, for example, nitrogen under positive pressure introduced through perforated baffles at the side of the hood, and an atmosphere high in protective gas content is maintained in the hood. End walls are provided with restricted openings or doors through which the vials move into the hood to reduce leakage from the atmosphere.

The ordinary type of filling by means of needles or tubes connected to a reservoir which portions out predetermined amounts of material occurs also in the present invention, the vials of course being stationary underneath the needles or tubes for the requisite time. This portion of the apparatus of the present invention does not differ from standard designs, and in fact it is an advantage that standard filling equipment may be used with the invention.

After the vials have been filled in the normal manner, they pass under further needles or tubes through which the protective gas, such as nitrogen, flows, displacing the atmosphere in the head space in each vial so that its oxygen content is very greatly reduced. This produces a layer of nitrogen, but as the hood itself is full or nitrogen there is little or no tendency for diffusion out of the layer, which would be the case if the hood were full of air or other gas which is heavier than nitrogen. Of course in the case of other protective gases, such as, for example, carbon dioxide, which is heavier than air, the problem of diffusion upward is not so serious. After layering, the vials move out through an exit door or slit, which is also kept small in dimension to prevent leakage in of air into the hood. The small positive pressure of nitrogen maintains a slow outward flow of nitrogen and any oxygen which is displaced, tends to be swept out through the entrance and exit openings, which are of course at the low point in the hood.

The plugging or capping mechanism for the vials is normally right behind the filling mechanism and so there is no long travel to the capping station. The slow outflow of nitrogen from the exit opening thus creates a curtain and continues to protect the head space of the vials from contamination until they are finally capped. The invention also contemplates having the capping or plugging stations under the same hood as the filling and the layering stations or under a separate hood maintained with a protective atmosphere.

Another very important and rather surprising result is that where liquids which tend to foam badly are filled into the vials, foaming is drastically reduced and in many cases eliminated. The mechanism for this additional function has not been completely determined and, therefore, the invention is not intended to be limited to any theory of why this result takes place. This makes it possible also to use layering of other gases, such as air, where materials are completely unaffected by oxygen but where the foaming problem is serious. This is an additional field in which the present invention can be used; however, in most cases it is desirable to prevent oxidation, and so the modification using nitrogen is the preferred modification of the present invention.

The vials before entering the hood may be filled with nitrogen or other protective gas, although this is not necessary because even if they are filled with air this is displaced as the vials are filled and the remaining air in the head space is then displaced or its oxygen content very drastically reduced by the layering which has been described. If desired, the vials may pass under tubes or needles before they are filled and nitrogen can flow down through these, sweeping out any air in the vials. In this case the nitrogen pressure or velocity may be somewhat greater than in the layering station where it is undesirable to have a large flow of gas in the filled vial.

While the present invention is very applicable to automated filling machines, and in this aspect may be considered as an improved filling machine, it also constitutes a process; and regardless of the particular mechanical design of the vial filling and layering mechanisms, the desirable effects may be obtained by introducing the protective atmosphere by any suitable means. This phase of the invention is, of course, pure process; and it is included and constitutes an advantage of the present invention that the improved results are not tied in with any particular design of equipment.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a side section of the hood with vials passing therethrough, and

FIG. 2 is an end elevation, partly in section, of one end wall of the hood.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

The filling machine shown in the drawings is provided with the conventional track or floor **4** along which vials **6** are moved in through an entrance opening **2** and out through an exit opening **3**. The intermitent movement of the vial is by conventional means, which are therefore not shown as they are in no way changed by the present invention. Over the filling zones there is a hood **1** into which nitrogen in introduced from a side chamber **15** through small openings **16**. The nitrogen supply is from **12** through a filter **13** into a manifold **14**. The small openings result in a mechanical barrier or baffle so that turbulence is decreased and contamination by dust or other undesirable material is minimized or completely eliminated.

As the vials **6** move along, a pair comes under two filling needles or tubes **8** into which are introduced predetermined charges of material from a product supply **7**. The introduction of predetermined charges is by conventional mechanism, the details of which are not shown as they are not changed by the invention. After the vials have been filled to the requisite height, they then move on under two tubes **11** which are fed with nitrogen which displaces any oxygen in the head space in the vials with a layer of nitrogen. Once the position of the tubes **11** has been set for vials of a given size they are preferably held stationary to minimize gas leakage. The introduction is sufficiently gradual so that they is no danger of blowing out particulate solids in a vial or of unduly agitating liquids.

The oxygen content, or rather its lack, is monitored continuously by an oxygen monitor **5** of conventional design, and the atmosphere in the hood is maintained with a negligible oxygen content. The inflow of nitrogen through the openings **16** of course causes any oxygen which is introduced with the vials or in the vials to be swept out through entrance and exit openings **2** and **3**.

If it is desired, the empty vials may be purged of air by a third set of tubes **17** which are connected to a source of nitrogen **18**. As this is an alternative or rather an additional provision, only a single tube is shown and the whole mechanism is in dashed lines.

As there is a steady flow of nitrogen out through the exit **3**, this in effect acts as a curtain over the vials protecting them for some distance beyond the hood so that when the vials are capped or plugged by the conventional plugging equipment, which is shown as a block **19**, contamination of the head space with oxygen from the atmosphere is avoided. of course, if desired, the plugging operation could be under the same hood that provides filling and layering.

The preferred embodiment which has been described uses separate tubes or needles for filling and layering. This can also be effected by single tubes which first fill and then introduce the nitrogen.

The invention will be illustrated further in connection with the following example:

As a test material, vitamin B_{12} was chosen as it is extremely sensitive. 1.1 ml. dose of liquid vitamin B_{12} was introduced into vials in three different operations. The first involved the standard nitrogen sparging technique, which has been referred to above as part of the prior art; the second with no sparging, and the third using the procedure of the present invention. The first two were tested by storing at 42° C. with assaying at rather short periods, whereas the third was assayed at much longer periods.

The control, second operation, which had no protection showed some loss of potency even immediately after filling and capping the vial. An examination of the head space in the vial showed, of course, a normal oxygen content of about 21% by weight, which is present in air. Sparging with nitrogen lowered this to about 13%, while the present invention permitted lowering the oxygen content to 2.5%. In the case of the present invention, the atmosphere in the hood contained 0.5% oxygen. The results of the tests by microbiological assay are shown for the standard nitrogen sparging technique and the control in the following table:

TABLE I.—MICROBIOLOGICAL ASSAY FOR VITAMIN B_{12} IN A LIQUID FORMULA USING CURRENT STANDARD N_2 PROCEDURES AND CONTROL WITHOUT NITROGEN

Days at 42°:	Std. N_2 Technique, Percent Label Claim	Control Without Nitrogen, Percent Label Claim
0.1	103	88
13	86	38
22	65	31

The following table shows the results when the present invention is used:

TABLE II.—MICROBIOLOGICAL ASSAY FOR VITAMIN B_{12} IN A LIQUID FORMULA USING THIS INVENTION

Days at 42°	Percent Label Claim
0	115
6	111
13	116
19	117
31	110

It will be noted that after a little over 2 hours the standard nitrogen technique showed a somewhat greater potency than the control at the start, whereas the latter had lost 12%. After 22 days the standard technique

showed a drop to 65% and without any nitrogen to 31%. On the other hand, in the present invention even after 31 days the potency was still greater than the original right after filling where no nitrogen was used at all. The variations in the last percentage digit in all cases are within the normal range of experimental error for the microbiological assay. The vitamin B_{12} in all of the three tests described above had no antioxidant, and the tests are of course accelerated by reason of the fairly high temperature on storage.

What is claimed is:

1. A process for filling containers with oxygen sensitive material which comprises,

(a) displacing the atmosphere in empty containers with a nonoxidizing, inert gas,

(b) moving the containers to a filling station under an atmosphere of the inert gas free from substantial amounts of oxygen,

(c) filling the containers to a predetermined height, leaving a head space thereover, subjecting the head space to a substantially non-turbulent layer of the inert gas to produce an inert gas in the head space

having an oxygen content which does not significantly exceed 2.5%, and

(d) capping the container under a protective gas atmosphere which does not substantially introduce any further significant amounts of oxygen to the head space during capping.

2. A process according to claim 1 in which the inert gas is nitrogen.

3. A process according to claim 2 in which the oxygen content of the protective gas is not substantially in excess of 0.5%.

References Cited

UNITED STATES PATENTS

2,439,773	4/1948	Hohl et al.	53—112
2,514,027	7/1950	Clifcorn et al.	53—11 X
2,759,307	8/1956	Eolkin	53—11
2,763,107	9/1956	Day et al.	53—110 X

TRAVIS S. McGEHEE, Primary Examiner

U.S. Cl. X.R.

53—7