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MOTION LABILE LIQUID PACKAGE

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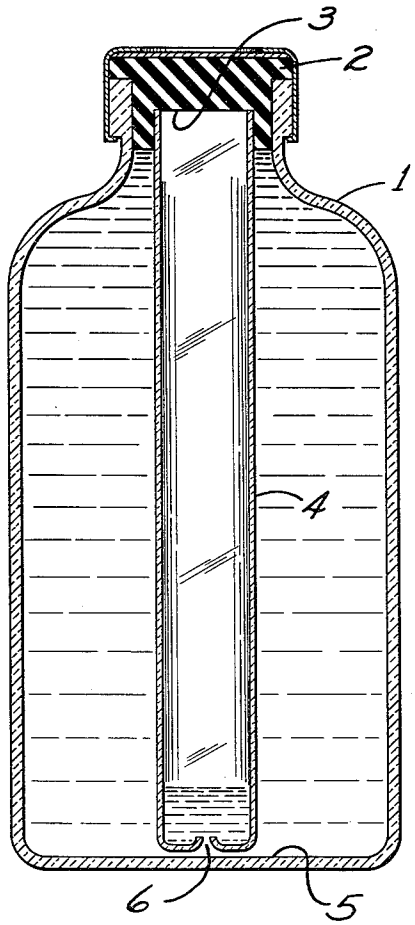


fig. 1

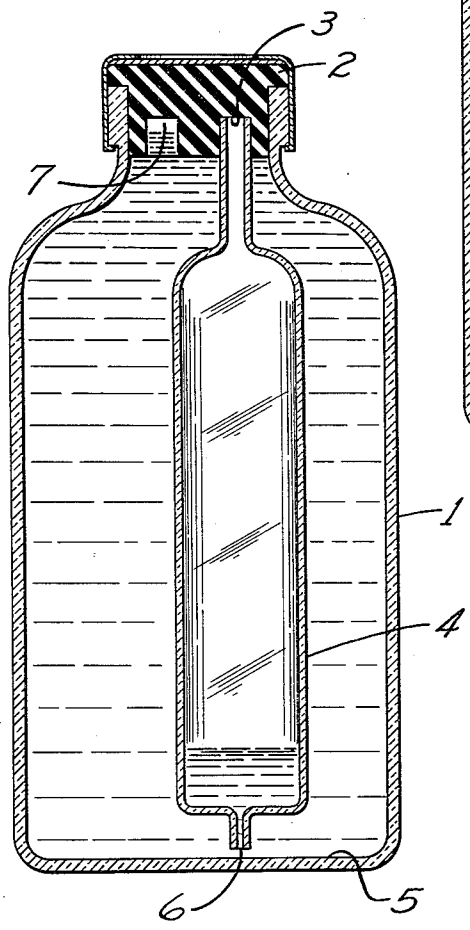


fig. 2

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MOTION LABILE LIQUID PACKAGE

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This invention relates to containers and, more particularly, to novel containers specially adapted for transporting motion labile liquids, packages containing motion labile liquids, and a method for the preparation of such packages.

The containers described herein are distinguished from those of conventional design by the provision of means for substantially limiting the surface which can be agitated in contact with a vapor space and, further, by confining the liquid-vapor space interface to a portion of the contained liquid which can be effectively segregated from the main body of liquid both in storage and in actual use. Broadly described, the present container has a closure supporting a downwardly extending expansion chamber which constitutes a submerged vapor space, the expansion chamber being closed at its upper end and terminating at its lower end approximately adjacent the bottom of the container in an orifice. The container, except for the submerged vapor space or expansion chamber, is completely filled with the liquid to be transported to constitute a package.

The transport of motion labile liquids in individual containers frequently raises problems over which the shipper has little or no control, for he can neither foresee nor avoid the rigors to which his packages may be subjected in the course of their movement in commerce. Where excessive surface movement results in physical breakdown or surface reaction of a liquid product, the material thus altered may be rendered unsuitable for its intended use. It frequently happens therefore that the shipper must sustain a relatively high returned goods ratio in products of this type.

Of particular interest is the application of novel containers as contemplated herein to the packaging and transport of pharmaceutical products, such as fat emulsions intended for injection into humans. In a broad sense, this invention serves to prevent the breakdown of fat emulsions when shaken. This breakdown is aggravated by low temperatures, such as those encountered in weather or under refrigeration, and is especially pronounced in fats having high solidification points, such as coconut oil and hydrogenated oils. For example, in order to inhibit the hydrolysis which normally occurs at ambient temperatures in coconut oil emulsions, the emulsion must be kept under refrigeration, preferably at about 4° C. But the solidification point of coconut oil is 14–22° C., substantially above the storage temperature, thereby further faciliating the destruction of the emulsion by shaking at 4° C. Under such conditions, relatively short periods of shaking are sufficient to cause coalescence, rendering the product in some instances unsuited for clinical use. Because of the necessity for transport and storage of these emulsions at reduced temperatures under conditions which produce varying degrees of surface agitation, as during transport abroad hospital ships, every effort must be exerted to minimize the surface movement of such products in their shipping containers.

Excessive shaking at low temperatures, as indicated heretofore, causes such emulsions as coconut oil emulsion to undergo a physical degradation resulting in the deposit of plainly visible fat particles ("fat rings") on the internal container surface as well as in the congregation of smaller but still objectionable fat particles seen only on microscopic examination. The development of fat rings

varies in degree between emulsions of various types but is extremely prominent with coconut oil emulsion and emulsions of other oils having solidification points above the favored storage or transport temperatures at which surface agitation may occur. With the container as adapted by this invention, reflux from the surface of the emulsion is eliminated.

In addition to the foregoing considerations, motion labile liquids intended for injection into humans must also be sterile and remain sterile until the material is actually used in the clinic. The usual practice where such containers as vials and ampoules are involved is to fill and seal the container and thereafter heat-sterilize the contents in situ. In providing for procedures of this type, it is obviously necessary that a sufficient vapor space be left in the container to accomodate the elevated pressures developed by the expanding liquid and gases within the container at sterilizing temperatures. With vials and ampoules this presents no great problem because of the small liquid volumes involved. It can readily be seen, however, that difficulties are encountered where relatively large volumes of liquid are present, as in the typical infusion bottle containing from 250 to 2000 ml. or more. In such cases a substantial vapor space volume is required to prevent undue pressure development, but the provision of such a free space over the liquid surface favors even greater surface agitation of the emulsion as the finished package is moved through the normal channels of handling and shipping.

The problems alluded to above are of such magnitude that they have resulted in primary emphasis being placed on the development of intravenous fat preparations utilizing oils which are less than ideal from the clinical standpoint but which, by virtue of their lower solidification temperatures and higher physical stability, can be safely handled and transported. The present invention now makes possible for the first time the practical consideration of certain emulsions, such as coconut oil emulsion, possessing advantageous clinical properties for intravenous fat therapy.

Referring generally to the drawings, it will be seen that FIGURE 1 represents a container which is widely applicable for the transport of motion labile liquids and in particular those which are to be sterilized within the sealed container.

FIGURE 2 represents a generally similar container but, more particularly, one suited to clinical use as an infusion bottle and containing a liquid intended for continuous intravenous infusion. Accordingly, the container of FIGURE 2 can be employed in a conventional infusion apparatus in which the container is inverted and a withdrawal tube and airway tube inserted through the closure thereof to communicate with the interior of the container in the usual manner. Again, the structure of FIGURE 2 is adapted for the storage and transport of motion labile liquids which are to be sterilized after the container has been filled and sealed.

Referring specifically to FIGURE 1, a suitable bottle or container identified by the reference character **1**, preferably made of glass, is provided with a stopper **2** of rubber or similarly resilient material disposed adjacent the neck of the container. The stopper **2** is provided with a recessed portion **3** adapted to frictionally retain an expansion tube **4** made of glass or other suitably rigid material. Alternatively, the expansion chamber can comprise a pliable bag, which can be attached to an airway tube. The expansion tube **4**, terminating at its upper end in the recess **3** of the stopper **2**, extends downwardly within the container and terminates at its lower end approximately adjacent the bottom **5** of the container. The expansion tube **4** is provided with an orifice **6** in its lower end.

In the refinement illustrated in FIGURE 2, the stopper 2 is provided with a recess 3 into which is inserted the expansion tube 4, the said expansion tube being constricted at its upper portion to a diameter less than that of the tube 4. The closure 2 is likewise provided with a recess 7, thereby affording convenient access through the closure by means of a withdrawal tube inserted from the outside.

The container can be made of any material essentially non-reactive toward the contents thereof, glass being preferred, any standard infusion bottle being acceptable. The closure can be of any type which will withstand the pressure generated within the bottle on sterilization and is advantageously made of a resilient, non-reactive material such as rubber or a plastic composition. For pharmaceutical use a preferred embodiment includes a resilient closure of the plug type, adapted for close fitting in the mouth of the container and enclosed by at metal cap as, for example, a conventional aluminum cap spun onto the bottle for increased strength. The expansion tube 4, like the container 1, can be made of any essentially non-reactive material possessing suitable strength, preferably glass. The expansion tube 4 is inserted for friction fit into the recess 3 of the closure, the said recess of the closure, the said recess preferably extending only so far into the closure as will permit firm seating of the expansion tube therein and afford positioning of the expansion tube with its base approximately adjacent the base 5 of the container 1 when the closure is driven home into the container mouth. It is not necessary that the expansion tube 4 be in actual contact with the base 5 of the container, but, particularly where the container base is convex in configuration, the tube can advantageously be in close proximity thereto in order to obtain a measure of support therefrom. The expansion tube 4 is preferably but not necessarily round and can be readily adapted from a conventional ampoule of suitable size in relation to the container. As employed in an infusion package or the like, the expansion tube serves dually as an expansion chamber and airway tube.

The size of the orifice 6 in the bottom of the expansion tube 4 is not critical, from about ½ mm. to about 3 mm. in diameter being suitable in most instances. The expansion tube can be modified to provide an extended constriction at the lower end. thereby affording greater protection against loss of vapor space from the expansion tube to the container proper on violent agitation.

Generally, it is the expansion of the liquid in the container which accounts for the major portion of the pressure increase that the closure and cap must withstand during the elevated temperatures of sterilization. The allowable pressure which can be developed therefore depends on the strength of the closure and cap, and ultimately of the container. Also important, however, is the consideration of the extent to which the liquid will contract on cooling, inasmuch as the preferred conditions for storage require relatively low temperatures. If the contraction of the liquid is excessive for the existing liquid head over the orifice, the air or artificially introduced gases comprising the vapor space will escape from the tube and establish a second vapor space in the upper portion of the container in the usual manner. Accordingly, the temperature at which the bottle is filled becomes important in determining the limitations of expansion tube diameter and liquid head height which will operably preserve the submerged vapor space under the low temperature conditions of storage as well as provide sufficient vapor space to accommodate the increased pressure on sterilization. Thus the temperature of filling determines (1) the necessary volume of the tube to prevent excessive pressure development on sterilization at elevated temperatures and (2) the minimum diameter of the tube at its lower end to prevent escape of gas from the vapor space when the liquid level is lowered due to low storage temperatures.

A critical feature of the present invention is the elimination of the conventional vapor space at the top of the container and the provision of a submerged vapor space within the expansion tube. A collateral feature of packages incorporating the present invention is found in the fact that if the liquid is subjected to freezing temperatures the closure ruptures. Where the contents are likely to be injured by freezing, this irreversible indication is a significant advantage. Observations have shown that in the infusion bottles of this invention the liquid in the expansion tube at the bottom of the container freezes first, thereby closing off the vapor space and causing any further expansion due to freezing to rupture the closure. Conventional containers normally possess adequate vapor space to accommodate this expansion on freezing, and frequently there is no indication that the contents have been frozen except by microscopic examination.

From the foregoing it follows that to be operative in maximum degree the container must be completely filled with respect to the volume outside the expansion tube. By "completely filled" is meant a container maximally filled with the liquid. In the preferred embodiment of this invention the closure is indicated as having a recess 7 extending upward from the bottom surface of the said closure to facilitate insertion of a withdrawal tube through the upper surface of the closure. It is apparent that if the closure is driven into the container when the container is filled to overflowing with liquid, a small amount of air will be trapped in the upper portion of the said recess 7. Thus the container in the strict technical sense will not be completely filled owing to the entrapment of air at this point. The presence of the small quantity of air, however, does not detract from the operation of the invention since the free surface area of the liquid extending into the recess is so small as to prevent excessive surface disturbance on agitation of the container.

In practice, then, the container is preferably filled to overflowing with the liquid to be packaged and the closure with expansion tube inserted therein is driven home to assure that with the closure in place the container is maximally filled. Since the expansion tube is deadended in the closure, the liquid will rise to a given height in the tube through the orifice, thereby establishing the vapor space and the liquid head height for the particular expansion tube being employed. It is to be noted that a high temperature fill means that the liquid is already expanded and will further expand only a relatively small amount on sterilization, while a low temperature fill means that considerable expansion will occur on sterilization. But a high temperature fill also means that the liquid will contract a greater amount at lower temperatures, this factor necessitating a tube of sufficiently small diameter to prevent excessive drop in liquid level on cooling.

Where the container is to be heated in the course of in situ processing, such as sterilization, the selection of the tube must contemplate the filling temperature, the processing temperature, the pressure developed in the tube at the higher temperature, the volume of the vapor space at the filling temperature, the total volume of liquid in the bottle and the ratio of liquid densities at the filling and processing temperatures. Thus, the relationship between the expansion tube volume (V_t) and other variables incident to the function of the tube in this invention can be expressed as follows:

$$V_t = \frac{T_1 P_2 (V_1 - V_L E + V_L)}{14.7 T_2}$$

wherein:

T_1 is the filling temperature (°A.)
T_2 is the processing temperature (°A.)
P_2 is the absolute pressure in the tube (lb./sq. in.) at processing temperature
V_1 is the volume of the vapor space in the tube at the filling temperature (cc.)
V_L is the total volume of liquid in the bottle (cc.)

E is the ratio of liquid densities at the filling and processing temperatures.

Selection of the appropriate expansion tube where unusually high or low temperatures are not anticipated is governed only by a consideration of the relatively small changes in liquid height over the orifice that will occur with normal temperature variations. Where the liquid is to be sterilized in situ but is not to be stored under refrigeration temperatures, adequate expansion volume above the liquid surface in the tube must be provided. Where, on the other hand, the liquid is to be sterilized in situ and in addition stored at low temperatures, the provisions both of adequate expansion volume and liquid head over the orifice must be considered. In the latter category are, for example, packages of injectable fat emulsions as heretofore described. All three types of packages require routine experimentation to determine the appropriate expansion tube size, and packages in the second and third categories preferably involve also the application of the gas equation to assure proper allowance for the several factors involved.

Taking as an example the determination of an appropriate expansion tube for a package to contain an injectable fat emulsion, such as a coconut oil emulsion, the following formula applies, being a rearrangement of the foregoing formula and derived from the gas equation on the assumption that the liquid is incompressible:

$$P_2=\frac{14.7V_tT_2}{T_1[V_1-(V_LE-V_L)]}$$

wherein:

P_2=absolute pressure in expansion tube (lb./sq. in.) at processing temperature
V_t=volume of tube (cc.)
T_2=processing temperature (°A.)
T_1=filling temperature (°A.)
V_1=volume of gas in expansion tube at filling temperature (cc.)
V_L=total volume of liquid (cc.)
E=ratio of liquid densities at filling and processing temperatures.

In determining the values for substitution in the foregoing equation, it is usually satisfactory to assume the appropriate values for water as representing the liquid in the container. Thus, the volume of the selected expansion tube (V_t) can be determined by direct volume measurement of water poured from the filled tube, before it is assembled with the closure, into a graduated cylinder. The total volume of liquid (V_L) can be found by filling the container to overflowing, inserting the closure and tube, removing the closure and tube and measuring the volume of water remaining in the container. The volume of gas at the filling temperature (V_1) can be ascertained by again filling the container to overflowing and inserting the closure with tube attached into the container. The container is then inverted and, by means of a syringe and an airway needle inserted through the closure directly into the container (not into the expansion tube), sufficient liquid is withdrawn to lower the liquid level below the level of the orifice. Then, the liquid contained in the expansion tube is withdrawn by syringe and measured. By subtracting the volume of liquid thus measured from the total expansion tube volume previously obtained (V_t), the volume of the vapor space above the liquid in the expansion tube can be determined. It is preferred that the temperature of the liquid be approximately at the desired filling temperature for the above operations. Applying the values thus determined and the known values for T_1, T_2 and E, an absolute pressure (P_2) is determined which represents the pressure inside the tube which must be withstood by the closure and its retaining cap. If the value thus obtained is below the allowable maximum for the particular closure means employed, the tube can be safely used at the selected filling and processing temperatures.

If desired, a family of curves can be drawn representing various tube volumes (V_t) by determining the absolute pressure (P_2) for several selected filling temperatures (T_1) at a specific processing temperature (T_2) and by then plotting filling temperature (T_1) v. pressure (P_2). In this manner, by drawing a line at the maximum allowable container pressure the minimum filling temperature which can be employed for each tube volume (V_t) to give pressures below the allowable maximum can be read directly.

There remains the necessity for determining that the selected tube, although providing ample expansion space at the processing temperature, will similarly provide sufficient liquid head over the orifice at the lowest contemplated storage temperature to prevent escape of gas from the confined vapor space to the container proper. Whether the tube is adequate for the service can readily be determined by inserting the expansion tube in the closure and driving the closure home in the neck of the container to simulate a finished package and then storing the said package at the minimum temperature likely to be encountered in transport or storage. If after a period at such lower temperatures the bottle can be agitated in any position without loss of gas from the confined vapor space, it can be safely concluded that sufficient liquid head has been provided. If, on the other hand, loss of gas to the container proper occurs, a narrower tube or at least one having a narrower base which will provide greater head height, is indicated. Alternatively, an extended constriction at the base of the tube to restrict the flow of liquid can be provided. It is desirable, both in the interests of liquid head and support of the tube, that the tube be of such length that when the closure is fully inserted into the container the tube rests immediately adjacent the bottom thereof.

Alternatively, the volume remaining at any given storage temperature when a given tube is filled at any given temperature can be determined by calculating the increase in the vapor space volume on a reduction in temperature from the filling temperature to the lower storage temperature. This figure can also be expressed as the decrease in volume of the liquid in the expansion tube occasioned by such a reduction in temperature. Accordingly, the volume of liquid remaining in the expansion tube at any reduced temperature can be obtained from the following equation:

$$V_R=V_t-V_1+V_LE-V_L$$

wherein:

V_R=volume of liquid remaining in tube at the lowest anticipated temperature (cc.)
V_t=total volume of tube (cc.)
V_1=volume of gas in expansion tube at filling temperature (cc.)
E=ratio of liquid densities at filling and lowest anticipated temperature
V_L=total volume of liquid (cc.)

From the foregoing formula the volume remaining in the expansion tube at any given lowest contemplated temperature can be determined for any given expansion tube and any given filling temperature. By solving the equation for V_R at various filling temperatures a curve can be plotted of V_R v. filling temperature. By noting the volume for the particular tube which gives the necessary or minimum liquid height above the orifice, the maximum filling temperature can be read from the curve. By then noting this maximum filling temperature on the previous graph of filling temperature v. container pressure, there is provided, in conjunction with the minimum filling temperature previously obtained and noted thereon, an indication of the permissible range of filling temperatures which will afford both sufficient vapor space to accommodate liquid expansion on sterilization and mini-

mum allowable liquid height above the orifice to prevent loss of gas on storage at low temperatures.

To illustrate the preferred embodiment of the invention described herein, the following example describes a container suitable for the transport of coconut oil emulsion which has been sterilized in situ at 120° C. This emulsion has been found to be widely applicable in the clinic, and its use as a commercial product is made practicable by the provision of a container accomplishing the objectives of the present invention. As heretofore indicated, storage of the emulsion at low temperatures, preferably at 4° C., is necessary to inhibit hydrolysis of the oil. At such low temperatures, however, relatively short periods of agitation will produce coalescence of fat particles. The following example therefore indicates the application of the present invention in providing a transport container for a motion labile liquid which is sterilized in situ.

Example 1

A standard infusion container (actual volume 685 cc.), measuring $7\frac{3}{64}$ inches in height, $3\frac{11}{32}$ inches in diameter and having a neck diameter of 43 mm., was provided with a standard rubber stopper having two recesses extending from the under surface of the stopper partially through the depth thereof. A 50-cc. glass ampoule was cut to such a height that when the stem of the ampoule was frictionally secured in the stopper and the stopper driven home into the neck of the container the ampoule rested approximately on the bottom of the container. The volume of the ampoule so cut was found to be 64 cc. A hole approximately 2 mm. in diameter was made in the bottom of the ampoule. The container was filled to overflow with water at approximately 40° C., and the stopper with the ampoule (expansion tube) frictionally secured therein was lowered into the container and the stopper driven home. The stopper and tube were then removed and volume of liquid remaining was determined to be 610 cc. After refilling the container and replacing the stopper and tube therein, the container was inverted and, by means of a syringe, water was withdrawn until the liquid level was below the level of the expansion tube orifice. With the container still inverted, the water in the expansion tube was then withdrawn in like manner. By this procedure it was found that 6.8 cc. of liquid was forced into the expansion tube from the container as the closure was driven home. (This, in effect, is a measure of the volume of the stopper displacing the liquid present in the neck of the container.) The gas equation was then applied to give P_2, the absolute pressure on the stopper, for a sterilization temperature of 120° C. at a variety of filling temperatures from 10 to 80° C., in accord with the following equation, the calculation for 40° C. filling temperature being exemplified:

$$P_2=\frac{14.7V_tT_2}{T_1[V_1-(V_LE-V_L)]}$$

wherein:

V_t=64 cc.
T_2=393° A.
T_1=313° A.
V_1=64 cc. minus 6.8 cc.=57.2 cc.
V_L=610 cc.

$$E=\frac{0.9922}{0.9434}$$

Solving the above equation, it was found that P_2=45.3 p.s.i., a figure safely below the maximum allowable pressure for the closure means employed. From the values of P_2 obtained for a variety of filling temperatures (T_1), a graph can be plotted of P_2 (abscissa) v. T_1 (ordinate) and a line drawn representing the maximum allowable pressure (P_2).

The volume of liquid remaining in the tube under the various filling temperatures resulting from storage at 4° C. was then calculated from the following formula, the calculation for a filling temperature of 40° C. being exemplified:

$$V_R=V_t-V_1+(V_LE-V_L)$$

wherein:

V_t=64 cc.
V_1=57.2 cc.
V_L=610 cc.

$$E=\frac{0.9922}{1}$$

Solving the above equation, it was found that V_R=1.8 cc.

The container equipped with the expansion tube and stopper as described and filled maximally at 40° C. with coconut oil emulsion was fitted with an aluminum cap of a type conventional for sterile pharmaceutical products and autoclaved at 120° C. to sterilize the emulsion. No deformation of the stopper or the aluminum cap was noted.

The container thus filled and sterilized was stored at 4° C. for 24 hours. No escape of gas from the vapor space was observed, there being adequate liquid head over the orifice.

A standard 685-cc. container of the type described, embodying the features of this invention and maximally filled with coconut oil emulsion which was sterilized in situ, was subjected to standard shaker tests and results compared with a similar container filled with the usual volume of 550 cc. of coconut oil emulsion but including no device of the type here described. The shaker consisted essentially of a rack in which the containers were secured, the rack moving the containers back and forth through a distance of two inches 160 times per minute. It was found that a standard container filled with 550 cc. of coconut oil emulsion tested in this manner at 4° C. for 72 hours displayed solid fat deposits on the sides of the container at the conclusion of the test. In contrast, containers which included the expansion tube of this invention exhibited no solid fat deposits whatsoever and microscopic evaluation before and after shaking indicated no physical change had occurred.

Results of an extensive testing program comparing the effects of shaking coconut oil emulsion in standard infusion bottles with and without the novel device hereof are summarized in the following table:

I	II	III	IV	V	VI
Microscopic Evaluation	Diameter of Fat Particles, Microns	Before Shaking	Shaken 3 Days, Usual Fill	Shaken 3 Days, Full Bottle	Shaken 3 Days, Bottle + Invention
		Millions of Fat Particles per cc.			
Petroff-Hauser Counter—Oil Immersion	1.5-3.0	5-10	16	6	6
		Thousands of Fat Particles per cc.			
Hemocytometer—Low power.	15	2.2-10	53	3.3-4.4	5.5-8.8
	22.5	0-1.1	8.8	0-1.1	0-1.1
	30	0-1.1	2.2	0	0-1.1
	37.5	0	2.2	0	0
	45	0	0	0	0
	52.5	0	1.1	0	0
	60	0	2.2	0	0
	67.5	0	1.1	0	0
Presence of Free Fat	----------	No	Yes	No	No

The foregoing data provide an indication of how closely containers equipped with the device of this invention approximate the ideal package, i.e., a completely full container, with reference to the prevention of coalescence of fat particles. Column III shows the approximate quantitative presence of fat particles in the diameter range of 1.5 to 3.0 microns and the distribution of fat particles of varying diameters in a volume of coconut oil emulsion

prior to the shaker test. In column IV it is seen that a standard infusion bottle containing the usual fill of the same emulsion, i.e., 550 cc. in a 685 cc. bottle, displays at the end of three days on the shaker a significant increase in the number of fat particles per cc. of nearly all the diameters for which observations were made. This shows that coalescence occurred in the course of shaking. In addition, and of primary importance as a positive observation visible to the naked eye, the infusion bottle with the usual fill was found to have fat particles deposited on the internal container surface and to display the "fat rings" heretofore described. Column V shows the results of shaking the "ideal" container, i.e., one which is completely filled so that no vapor space exists and no surface distortion or collision of surface particles with the wall of the container can occur. Column VI, on the other hand, refers to an identical container which has been equipped with the device described herein and completely filled by the method exemplified above. Comparison of the data in columns V and VI illustrates the striking proximity to the ideal which the novel package has provided. In neither the completely filled bottle of column V nor the completely filled bottle containing the expansion tube of column VI was there observed, on microscopic evaluation, any significant increase in the number of fat particles of the diameters shown. In addition, and of great importance, is the fact that in the novel package of column VI no free fat particles deposited on the internal wall of the container, an observation matched only by the ideal or completely full bottle of column V and the freshly prepared and unshaken emulsion of column III.

The package containing the 64-cc. tube can be filled at temperatures between about 5 and about 45° C. and still provide adequate vapor space volume and liquid head height over the orifice.

Substituting a 53-cc. tube for the 64-cc. tube above provides a package representing a practical minimum of submerged vapor space volume, assuming a maximum closure strength of 50 p.s.i., where the contents are to be sterilized in situ at 120° C. and stored as low as 4° C. Such a package is preferably filled at temperatures between about 40 and about 45° C.

The present invention has been exemplified in its most demanding embodiment, i.e., in its use with a motion labile liquid which is to be sterilized in situ and stored at low temperatures. It is to be understood, however, that the invention in its principal aspect is equally suited for use with liquids which are not to be stored at reduced temperatures or with liquids that are neither to be stored at reduced temperatures nor sterilized at higher than ambient temperatures. Thus, the invention as contemplated herein finds application in a broad range of industrial utilities where liquids susceptible either physically or chemically to vigorous shaking or forceful collision with container surfaces are involved.

It is to be understood therefore that the present invention is not to be limited to the exact structure or methods of use shown and described herein, as obvious modifications and equivalents will be apparent to those skilled in the art; the invention is therefore to be limited only by the scope of the appended claims.

What is claimed is:

1. A motion labile liquid package which comprises: a container having a plug-type closure, an expansion tube supported in and extending downwardly from said closure to provide a submerged vapor space, said tube being closed at its upper end and terminating at its lower end approximately adjacent the bottom of said container in an orifice, said container volume outside said tube being completely filled with said motion labile liquid.

2. A motion labile liquid package which comprises: a container having a resilient plug-type closure, an expansion tube frictionally engaged within and extending downwardly from said closure to provide a submerged vapor space, said tube being closed at its upper end by said closure and terminating at its lower end approximately adjacent the bottom of said container in an orifice, the volume of said container outside said tube being completely filled with said motion labile liquid.

3. A sterile, motion labile liquid package which comprises: a container having a resilient plug-type closure, an expansion tube frictionally engaged in and extending downwardly from said closure to provide a submerged vapor space, said tube being constricted at its upper end and terminating within said closure, said tube terminating at its lower end approximately adjacent the bottom of said container in an orifice, the volume of said container outside said tube being completely filled with said sterile, motion labile liquid, said tube being definable by the following formula:

$$V_t=\frac{T_1P_2(V_1-V_LE+V_L)}{14.7T_2}$$

wherein:

T_1 is the filling temperature (°A.)
T_2 is the sterilizing temperature (°A.)
P_2 is the absolute pressure in tube (lbs. per sq. in.) at sterilizing temperature
V_1 is the volume of vapor space in the tube at the filling temperature (cc.)
V_L is the total volume of liquid in the container (cc.)
E is the ratio of liquid densities at the filling and sterilizing temperatures.

4. A sterile, motion labile liquid package which comprises: a container having a resilient plug-type closure, said closure having two recesses extending upwardly from the lower surface thereof whereby in operation a liquid withdrawal tube can be inserted from the top into the first recess, an expansion tube extending downwardly from and frictionally engaged within the second recess of said closure to provide a submerged vapor space, said expansion tube terminating at its lower end approximately adjacent the bottom of said container in an orifice, the volume of said container outside said expansion tube being completely filled to the bottom surface of said closure with said sterile, motion labile liquid.

5. A sterile coconut oil emulsion package which comprises: a container having a resilient plug-type closure, said closure having two recesses extending upwardly from the lower surface thereof whereby in operation an emulsion withdrawal tube can be inserted from the top into the first recess and an airway needle into the second recess, an expansion tube extending downwardly from and frictionally engaged within said second recess to provide a submerged vapor space, said expansion tube terminating at its lower end approximately adjacent the bottom of said container in an extended constriction, the volume of said container outside said tube being completely filled to the bottom surface of said closure with said sterile coconut oil emulsion.

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