

Apparatus for Producing Container Products from Plastic Material

The invention relates to an apparatus for producing at least one container product from plastic material, which is molded by a molding device, provided with a predeterminable container contents by means of a filling device, and sealed by means of a sealing device.

Methods and apparatuses for the production of container products made of plastic are known in the prior art. For the production of the respective container product(s), a tube of plasticized plastic material is extruded into a mold, the one end of the tube already has been or is sealed by welding, and the tube is expanded by generating a pneumatic pressure gradient acting on it, and, for the production of the container, it is brought into contact with the shaping walls of the molding device, consisting of two opposed individual molded parts. During the execution of the bottelpack® process, which is known in this technical field, the respective filling material is then aseptically filled, via a corresponding filling mandrel and into the respective container product, which is closed on one side, which is then, after the filling mandrel is pulled away, hermetically sealed by means of a sealing device to form a definable head geometry, wherein, in order to create the actual plastic container, in which the fluid or filling material will subsequently be stored, two individual molding parts, for example in the form of molding jaws of the molding device, are movable, for example by means of hydraulic or servo-electric drive means, toward each other for reaching a closed position and in opposite directions, away from each other, into an open position thereof.

In order to reach very high discharge rates of container products in such a BFS (blow fill seal) process, as shown by way of example in US 8 137 096 B2, several adjacent containers are molded at the same time in the molding device in order to form a container chain with several adjacent containers, for example, eight or ten containers, wherein this process takes less than 4 to 5 seconds in non-synchronized machines.

For synchronized machines, as shown by way of example in EP 1 626 903 B1, the production process may take significantly longer, for example, 10 to 11 seconds. With these known production machines, several stations are arranged successively in the direction of production, in a type of carousel arrangement, wherein the respective tube

of plasticized plastic material can be introduced into the mold apparatus in a first station. In a second station, which is subsequent in turning direction, this tube is blow-moldable for creating the container, wherein, in turn, in a third station, subsequent in the turning direction, the blow molded containers are filled in a sterile manner and can be closed at the head end by means of a sealing device, and in fourth station, again subsequent in said turning direction, the mold separation of the respective blow molded, filled, and sterilely sealed container product takes place.

These *per se* very advantageous preparation methods all represent more or less high-temperature methods since, with the advantageously used plastic materials, such as a polypropylene material, the homogenization of the molten polymer mass, the distribution in the tube head, and the molding, and especially the tight welding of the container, necessitate relatively high temperatures. Due to the high temperature levels in the molding phase, the *per se* advantageous BFS methods are very poorly suited for temperature-sensitive filling material. For containers in ampule form, formulations of biotechnologically manufactured drugs and diagnostic agents are often used as filling material. The group of such substances include therapeutic enzymes, clotting factors, numerous hormones, such as insulin, epoetin or growth hormones, monoclonal antibodies, as well as biotechnologically manufactured vaccines. Due to the temperature-related problems, such substances are usually not sold on the market in BFS containers, but in conventional glass bottles.

This problem is known among experts and is the subject of ongoing scientific discussions. In this respect, reference should be made to a publication by Wei Liu, Philippe Lam, et al., which was published in Bio Pharm International, July 2011, Pages 22 to 29. The authors propose to prevent the degradation of the filling material by supplying their pharmaceutical formulation in a very cold state. For processes to be executed quickly for high output rates, this is difficult to implement because a decrease in temperature results in an increase in viscosity of the filling material, which would require increased filling pressures to achieve the same filling time, which in turn may adversely affect the stability of the filling material due to the shear sensitivity of most proteins. A disadvantage of a cooled supply of the filling material at temperatures of less than 15 °C is the fact that this may result in condensation of air humidity in the BFS machine and, in particular, on the filling tube. This causes condensed water to be brushed off on the container opening, which in turn results in leakage during welding of the container. If, as would be obvious, low mold temperatures of less than 15 °C are applied, condensation effects also result, which in turn would require complex and expensive dry air conditioning of the mold surfaces and would result in temperatures of

the head region and head jaw of the mold that would no longer ensure tight welding. Lowering of the container wall thickness is also not a reasonable and efficient control value to minimize the available amount of heat acting on the filling material since the container wall thicknesses are determined by defined parameters, such as the allowable permeation (water loss by permeation over the storage period) and the mechanical specifications (mechanical stability, opening behavior, deformability for emptying, etc.).

With regard to this problem, the object of the invention is to provide an apparatus that allows for providing containers that are filled with temperature-sensitive, biopharmaceutical filling material in the BFS method and that, on one hand, are well molded and tight and, on the other hand, ensure the stability of the filling material as well as that ensured by traditional glass packaging.

According to the invention, this problem is solved by an apparatus having the features of claim 1 in its entirety. A substantial feature of the invention, accordingly, is that each finished created container product, with its filling material, is supplied to a post-treatment zone outside the molding device in which the respective container product, and/or the respective container contents in the form of filling material, can be subjected to a temperature-influencing effect.

Surprisingly, it has been found that the stability of the different biopharmaceutical formulations, which make up the filling material, is not greatly affected by the average temperatures during the BFS process or by the maximum temperatures of a portion of the filling material during filling, but is affected to a far greater extent by the progression over time of the temperature at the boundary layer between filling material/container product after sealing the container product, which can be influenced in the desired manner by the post-treatment zone provided in accordance with the invention. Through controlled temperature influence during a post-treatment phase in the post-treatment zone, it is possible to maintain the stability, and in particular the biological activity, of the filling material and, at the same time, produce well-molded and tight BFS containers.

In a preferred embodiment of the apparatus according to the invention, the proposed post-treatment zone allows convective cooling of the container product, preferably of at least 20 seconds duration, during which the same orientation is preferably maintained for the container product as during filling of the container. It has been found that a particularly high pharmaceutical stability for the filling material (container content) can be achieved if a cooling effect is applied to the respective container product, while it has at least approximately the same orientation over the duration of the post-treatment in the

post-treatment zone as it has had from the filling of the container, which in practice typically means a continuous vertical orientation. If the post-treatment zone in terms of its possible effect on the respective container product is designed to be long enough in terms of space and/or time, and the movement with stable orientation is ensured as explained, said free convection cooling for a time period of 20 to 30 seconds can already be sufficient to fill some thermally unstable filling materials safely and free from adverse effects.

The advantage resulting from the consistent orientation is probably based on the fact that, with consistent orientation, no boundary layer displacement at the contents/container boundary takes place and thus a favorable progression over time of the boundary temperature profile is given.

In a particularly preferred embodiment of the apparatus according to the invention, however, it is provided that, in the post-treatment zone, at least one tempering device is provided as a post-treatment device, in particular in the form of a cooling device. With a certain complexity in terms of the apparatus, post-cooling of container products can be achieved with certainty after the molding.

In the container products in ampule form, with fill volumes up to 10 ml, that are considered for thermosensitive filling, a filling time that is as short as possible is provided for each filling operation, with a dwell time of the container-forming polymer in the sealed manufactured state of less than 7 seconds.

In a particularly advantageous manner, the post-treatment device may include an apparatus for generating a cooling air flow for at least acting upon the respective container product. Herein, a flow guide device may be provided for producing a flat air flow of cooled, compressed air that is blown out, which generates a directed air flow of compressed cooling air. In this regard, a commercial device "LINEBLOW", which is available from Karger GmbH, Paul-Ehrlich Str. 10a, D-63128 Dietzenbach, may be provided together with a cold air generator "COLDER." This allows for a generation of flat airflows of, for example, up to 600 mm base length with cold air temperatures of -25 °C that coat the respective container products for post-treatment.

Alternatively or additionally, the post-treatment device may include a type of the cooling tunnel with a passage for the passage of the container chain and with tunnel walls at least partially defining the passage, which may be cooled by means of a cooling medium flowing through the walls.

As another possibility or in addition to generating a cooling air flow and/or to the cooling tunnel, the post-treatment device may include a freezing or freezer device, for example in the form of a flowing liquid nitrogen bath, such as in the form of a CRYOLINE® immersion bath freezer, through which the container chain is passed.

Alternatively, or in addition to said temperature influencing devices, the post-treatment device may also include a feeding of the respective container product, also in the form of a conveyor device, creating a container chain having conveying elements acting on the container product or the container chain, wherein the conveying elements can be cooled by means of a coolant flow flowing through them. The post-treatment device thus forms both a cooling device and a conveying device for the respective container product.

Another object of the invention is a method for producing blow-molded and filled container products from plastic material, having the features of claim 11.

Further embodiments of the method are listed in the dependent claims 12 to 14.

The invention is explained in detail below, based on the exemplary embodiments depicted in the drawings.

In the figures:

- Fig. 1 is a highly simplified representation of an exemplary embodiment of the apparatus according to the invention;
- Fig. 2 is a perspective oblique view and an enlarged view of individual blowing strips of the post-treatment device of the exemplary embodiment of Fig. 1;
- Fig. 3 is a depiction, similar to Fig. 1, of a second exemplary embodiment of the apparatus according to the invention, without an associated demolding device and
- Fig. 4 is a perspective oblique view of an individual depiction of a post-treatment device in the form of a combined cooling and conveying apparatus for a third exemplary embodiment of the apparatus according to the invention.

Fig. 1 shows an exemplary embodiment of the apparatus according to the invention as part of a non-synchronized rotational molding machine (not shown), in which the actual molding device 1 is provided with a demolding device 3, which supports the demolding process of the containers molded in the molding device 1. The molding device 1 is a

device for performing a blow-molding process according to the known bottelpack® system, namely, in one embodiment, in which, as shown in U.S. Patent 8 137 096 B2, various molding portions are performed at different stations along a production line 5. In a type of carrousel or paternoster arrangement, individual molded parts 7, of which only a few are numbered in Fig. 1, are moved toward each other in pairs on an imaginary circular arc path in order to form a closed manufacturing mold and are moved apart again to open the mold. Since devices according to the bottelpack® method are known *per se*, a more thorough explanation of the details of the molding device 1 of Fig. 1 is unnecessary.

As can be seen from this figure, the formed container chain 9 exits along the production line 5 from the demolding device 3 as a container chain 9 at the exit point indicated with 2. As is usual with such devices, the container chain 9 has a large-area shape, wherein a plurality of individual containers, in the present case of ampule-like shape, are adjacent in the container chain 9. For example, the container chain 9 can have eight adjacent ampules. In order to support the separation of the containers from the walls of the individual mold parts 7 moving away from each other after the molding process, the demolding device 3 applies a deflection movement to the container chain 9, as indicated with the double arrow 13 in Fig. 1. For this purpose, the demolding device 3 has a tappet assembly 15, which generates the deflection movement of the container chain 9, in operational connection with an electric drive motor 17, in order to safely separate the containers from the mold wall parts.

The tappet assembly 15, together with a frame part 19, forms fixed wall parts of a passage channel for the container chain 9, which ends at the exit point 2. The frame part 19 of the tappet assembly 15 is guided on guideways 27 for deflection movements, extending as indicated by the double arrow 13, which, like the motor 17, are mounted on a device part 29. This is in turn mounted pivotably about a pivot axis 33 on an apparatus frame 31 of the demolding device 3. At a distance from this pivotable mounting, a linear actuator 35 is hinged on the support part 29 in the form of a hydraulic or pneumatic working cylinder 28, which in turn is supported on a hinge point 37 on the apparatus frame 31 at a distance from the pivot bearing 33.

Due to the pivotal mounting of the support part 29 of the demolding device 3 on the apparatus frame 31, the demolding device 3 can be folded from the working position shown in Fig. 1 to a rest position, in which the tappet assembly 15 is outside the area of the production line 5, for adjustment and maintenance, as well as preparation for start-up, by retracting the linear actuator 35. For the movement of the tappet assembly 15,

the motor 17 includes an output gear 39, having an eccentric tappet device 41, converting the rotational movement into a reciprocating motion, which is coupled to the frame part 19 by means of adjustable push rods 43. With this gear assembly, a reciprocating vibrating movement can be applied to the frame part 19, and thus the container chain 9 positioned between the tappet assembly 15, through which safe separation of the molded containers from the mold walls is ensured at the front exit point 23 even if difficult to demold materials, particularly polypropylene materials, are used for which high processing temperatures are present.

To avoid damage to temperature-sensitive filling material caused by high processing temperatures, the apparatus according to the invention has a post-treatment device, designated as a whole with 4. It is disposed along the production line 5 along the container chain 9 after its discharge at the exit point 2 of the demolding device 3. In the exemplary embodiment of Fig. 1, the post-treatment device 4 has a device for post-cooling the discharged container chain 9 by means of flat air streams of cooled, blown compressed air. In order to generate cold flat air streams 9 that coat the container chain on both flat sides, two blowing strips 6 are provided in the example of Fig. 1, which are arranged opposite each other on one and the other long side next to the container chain 9 and of which one is shown separately in Fig. 2. The blowing strips 6 are typical devices of the type "LINEBLOW" in the form of strip bodies with a base length that is adapted to the width of the container chain 9. As Fig. 2 shows most clearly, each blowing strip 6 has a base body 10 having a front-end compressed air connection 12, which opens out on the planar top surface of the base body 10. A cover plate 14 is screwed to the flat upper surface of the base 10, which tapers and ends at a short distance in front of the edge of the base body 10, which is positioned on the left side in Fig. 2. Between the pointed end of the cover plate 14 and the base body 10, a fine air outlet gap 16 is formed for the cold air supplied via the connection 12, wherein the outlet gap 16 has a width of 50 μm ; A curvature 18, extending to the lateral edge, is adjacent to the gap 16 at the top side. In this configuration, the blower strip 6, by taking advantage of the Coanda effect, generates a layered air flow 22 along the smooth curve on the curvature 18 from the compressed air blown out at the gap 16 and draws along ambient air 20, so that an air curtain is produced in which about 25 to 30 times as much air is delivered as the compressed air volume supplied via the connection 12. For the operation, compressed air can be supplied through the connection 12 at a temperature of $-25\text{ }^{\circ}\text{C}$, produced for example by means of a cold air generator of the type "COLDER."

Fig. 3 shows a further exemplary embodiment of the apparatus according to the

invention as part of a non-synchronized rotational molding machine (not shown), in which a forming device 1 is provided without a corresponding demolding device. Again, as in the example of Fig. 1, a post-treatment device 4 is provided after the exit point 2, at which the container chain 9 exits the molding device 1. In this exemplary embodiment, the post-treatment device 4 includes a cooling tunnel 51, which is directly adjacent to the exit point 2 of the mold 1 and forms a passage 52 for the passage of the container chain 9. It is limited on both sides of the container chain 9 by tunnel walls, which are each formed by the inner surface of a cooling plate 53, which are opposite each other and extend on one side and the other side of the container chain 9 in the longitudinal direction of the production line 5. The cooling plates 53 extend over a longitudinal section of the container chain 9, corresponding to the length of several ampules and selected to have a length so that a dwell time or cooling time for post-cooling of about 40 to 60 seconds duration results. The cooling plates 53, which extend over the entire width of the multi-row container chain 9, have inner fluid guides for a cooling fluid circulating in the cooling plates 53 through connections 54, which are connected to a cooling circuit. Depending on the desired cooling capacity, different refrigerants come into consideration, such as water-glycol cooling liquids, cold air, liquid or gaseous nitrogen, or compressed refrigerants, wherein the cooling plates 53 can form evaporators.

Fig. 4 shows, for a further exemplary embodiment of the apparatus according to the invention, a post-treatment device 4 in the form of a combined conveying and cooling device, as they could be easily used even with synchronized molding machines. It includes a base plate 61 of rectangular-shaped outline, having a centrally located passage 63 for the container chain 9, extending parallel to the long sides of the rectangular shape, which is not shown in Fig. 4, showing the post-treatment device 4 in an individual representation. Strips 65 are provided as cooling and conveying elements, having an identical form and each of which extends along a long side of the passage 63 on both sides of the container chain 9 lying therebetween. Each strip 65 is composed of an outer cooling plate 67, which are also formed identically and each of which have a structure corresponding to that of the cooling plates 53 of the cooling tunnel 51 of Fig. 3. As with those cooling plates 53, the cooling plates 67 also have front-side connections 69 for connecting to a cooling circuit. Similarly, a cooling medium can flow through the cooling plates 67, again similarly to the cooling tunnel 51 of Fig. 3. Tappet bodies 71 are mounted on the insides of the cooling plates 67, forming the actual conveyance elements, in which recessed ampule receivers 73 are formed. The strips 65, which are shown in a separated position in Fig. 4, are guided movably toward and away from each other on the base plate 61, as indicated by the double arrows 65. For these movements,

each strip 65 is connected with a linear actuator 77, having connections 81 for actuation by means of a pressure medium, but electro-mechanically operable linear actuators 77 may also be provided. For the combined conveying and cooling function, the strips 65, along with the cooling plates 67 and the ampule receivers 73, are moved against each other, so that the containers are received in the ampule receivers 73 and a cooling process takes place. The base plate 61, with the strips 65 moved together, is then moved in the conveying direction of the container chain 9 along the production line 5 by means of a lifting drive, not shown, which in turn may again be operated by a pressure medium electro-mechanically, over a time period corresponding to the desired post-cooling time. The strips 65 are then moved apart, and the base plate 61, along with the strips 65, is then moved upward to the starting position for a subsequent cooling and conveying step for which the strips 65 are again moved back towards each other.

As can be seen, the post-treatment in the post-treatment devices 4 shown is preferably carried out each time with the containers located in unchanged position, i.e., in the filling position with the head region of the containers at the top. The boundary layer structure of the filling material/container wall thus remains undisturbed during the post-treatment. As already indicated above, the types of post-treatment devices 4 shown may be provided individually or in combination with one another in any order. Preferably a post-treatment device 4 is disposed immediately downstream of the exit point 2 of the molding device 1.

In examples given below, the results achievable by the post-treatment according to the invention are indicated.

In the examples, a BFS system is used along with post-cooling/post-conditioning, immediately subsequent to the discharge from the BFS machine, which substantially maintains the orientation of the containers (e.g., container head upwards) as during filling. The post-cooling took about 10-60 s and was implemented with flat air flows of cooled, blown compressed air. A commercial device "LINEBLOW" (with 60 mm blowing length, manufactured by Karger GmbH, Paul-Ehrlich Str. 60a, D-63128 Dietzenbach, was used together with two "COLDER" cold air generators (cold air temperature -25 °C). Comparable results were achieved with a cooling tunnel, in which the containers are transported in a cold air flow between two cooled plates having an equivalent cooling capacity.

Examples with known temperature-sensitive, liquid pharmaceuticals:

Formulations:

-a- Adalimumab

Machine bottelpack type 460 (non-synchronized) by Rommelag

Material: low density polyethylene, LDPE Lyondell Basell 3020 D LDPE

Filling volume 0.8 ml; 1.5 ml BFS ampule

Parameters:

Polymer temperature at tube exit °C	180
Filling temperature filling material °C	15
Filling time s	1
Time tube free to tube in mold s	5.5
Time tube in mold s	5.5
Mold temperature °C	20
Time between molding and filling s	0.6
Time discharge from BFS to post-conditioning s	30
Post-conditioning type	flat stream of compressed air, orientation stable,
Post-conditioning duration s	30
Cold air flow rate liters per min	150

Formulation: Adalimumab (Humira®) 40µg in phosphate/citrate buffered, aqueous solution, containing the following stabilizers: mannitol, NaCl and polysorbate 80.

After filling and 1 to 3 and 12 months of storage at 2 °C to 8 °C, there was no significant difference in the biological activity/stability (agglomerates, pH, discoloration, precipitation, etc.) compared to a commercially available packaging configuration in glass vials.

If, prior to or in the post-treatment zone, the containers are not moved with stable orientation, i.e., the container is rotated, turned, or tilted, the biological activity is significantly reduced even after 30 days, compared to transportation with a stable orientation, while similar movements in the glass vial packaging or containers manufactured with stable orientation according to the invention showed no significant activity changes.

-b- Epoetin alfa

Machine bottelpack type 460 (non-synchronized) by Rommelag

Material: LDPE Lyondell Basell 1840 H

Filling volume 1 ml in 2 ml BFS ampule

Parameters:

Polymer temperature at tube exit °C	170
Filling temperature filling material °C	17
Filling time s	1.2
Time tube free to tube in mold s	6
Time tube in mold s	6
Mold temperature °C	17
Time between molding and filling s	0.6
Time discharge from BFS to post-conditioning s	25
Post-conditioning type	flat stream of compressed air
Post-conditioning duration s	50
Cold air flow rate liters per min	200

Formulation: Epoetin alfa: 10,000 IU/ml in phosphate buffered, aqueous solution, containing the following stabilizers: aminoacetic acid, NaCl, and polysorbate 80.

After filling and 1 to 3 and 12 months of storage at 2 °C to 8 °C, there was no significant difference in the biological activity/stability compared to a packaging configuration in glass vials.

-c- interferon beta-1a

Machine bottelpack type 321 (synchronized) by Rommelag

Material: LDPE Lyondell Basell 1840 H

Filling volume 0.5 ml in 1 ml BFS ampule

Parameters:

Polymer temperature at tube exit °C	172
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Filling temperature filling material °C	20
Filling time s	1
Time tube free to tube in mold s	5.5
Time tube in mold s	5.5
Mold temperature °C	20
Time between molding and filling s	0.5
Time discharge from BFS to post-conditioning s	30
Post-conditioning type	flat stream of compressed air
Post-conditioning duration s	30
Cold air flow rate liters per min	40

Formulation: 33 µg/ml Interferon beta-1a in acetate buffered aqueous solution (pH 4), containing the following additional ingredients: poloxamer 188, L-methionine, benzyl alcohol.

After filling and 1 to 3 and 12 months of storage at 2 °C to 8 °C, there was no significant difference in the biological activity/stability compared to a packaging configuration in prefilled syringes.

If the containers are not moved in stable orientation prior to or in the post-treatment zone, the biological activity compared to the orientation stable transport was significantly reduced. Similar movements of the container procuded with stable orientation after completion of post-conditioning showed no significant changes in product stability.

-d- Trastuzumab

Machine bottelpack type 321 (synchronized) by Rommelag

Material: LDPE Lyondell Basell 3020 D

Filling volume 7 ml in 10 ml BFS ampule

Parameters:

Polymer temperature at tube exit °C	180
Filling temperature filling material °C	15
Filling time s	1.2

Time tube free to tube in mold s	6
Time tube in mold s	6
Mold temperature °C	20
Time between molding and filling s	0.6
Time discharge from BFS to post-conditioning s	15
Post-conditioning type	flat stream of compressed air
Post-conditioning duration s	50
Cold air flow rate liters per min	400

Formulation: 21 ug/ml Trastuzumab in aqueous solution (pH 6) containing the following additional ingredients: L-histidine, L-histidine α , α -trehalose dihydrate, polysorbate 20.

After filling and 1 to 3 and 12 months of storage at 2 °C to 8 °C, there was no significant difference in the biological activity/stability compared to a packaging configuration in glass ampules.

-e- Filgrastim

Machine bottelpack type 321 (synchronized) by Rommelag

Material: Borealis LE 6601-PH Polyolefin

Filling volume 1.6 ml in 2.5 ml BFS ampule

Parameters:

Polymer temperature at tube exit °C	170
Filling temperature filling material °C	20
Filling time s	1
Time tube free to tube in mold s	4.5
Time tube in mold s	4.5
Mold temperature	15
Time between molding and filling s	0.6
Time discharge from BFS to post-conditioning s	20
Post-conditioning type	flat stream of compressed air

Post-conditioning duration s	60
Cold air flow rate liters per min	100

Formulation: 480 μ g Filgrastim aqueous solution, containing the following additional ingredients: sodium acetate, sorbitol, and polysorbate 80 (Tween 80).

After filling and 1 to 3 and 12 months of storage at 2 °C to 8 °C, there was no significant difference in the biological activity/stability compared to a packaging configuration in prefilled glass syringes.

-f- rotavirus vaccine

Machine bottelpack type 312 (synchronized) by Rommelag

Material: Polypropylene PP Lyondell Basell Purell SM170G

Filling volume 1 ml in 2.5 ml BFS drinking ampule

Parameters:

Polymer temperature at tube exit °C	192
Filling temperature filling material °C	18
Filling time s	1.1
Time tube free to tube in mold s	6.5
Time tube in mold s	6.5
Mold temperature °C	18
Time between molding and filling s	0.5
Time discharge from BFS to post-conditioning s	35
Post-conditioning type	flat stream of compressed air
Post-conditioning duration s	65
Cold air flow rate liters per min	150

Formulation: Human rotavirus (live, attenuated) at least 106.0, CCID50 in aqueous solution, inter alia, with the other auxiliaries, additives: sucrose, dextran, sorbitol, calcium carbonate, as well as xanthan gum.

After filling and 1 to 3 and 12 months of storage at 2 °C to 8 °C, there was no significant difference in the biological activity/stability compared to a packaging configuration in a polyethylene tube.

-g- Octreotide acetate

Machine bottlpack type 312 (synchronized) by Rommelag

Material: Polypropylene PP Lyondell Basell Purell SM170G

Filling volume 5 ml in 7.5 ml BFS ampule

Parameters:

Polymer temperature at tube exit °C	175
Filling temperature filling material °C	1
Filling time s	1.2
Time tube free to tube in mold s	6
Time tube in mold s	6
Mold temperature	20
Time between molding and filling s	0.6
Time discharge from BFS to post-conditioning s	25
Post-conditioning type	flat stream of compressed air
Post-conditioning duration s	50
Cold air flow rate liters per min	300

Formulation: 4.4 mg/ml octreotide acetate in aqueous solution, *inter alia*, with the further auxiliaries, additives: mannitol, sodium carboxymethyl cellulose.

After filling and 1 to 3 and 12 months of storage at 2 °C to 8 °C, there was no significant difference in the biological activity/stability compared to a packaging configuration in a polyethylene tube.

In a preferred embodiment of the device according to the invention, not shown in further detail, a post-treatment device, such as a cooling device, can be omitted entirely for some filling materials that are not too thermally unstable. For example, it may be sufficient to provide a post-treatment zone after the exit point of the respective container product that allows for convective cooling of the container for at least 20 seconds, preferably for a duration from 20 to 30 seconds, wherein it has further proved to be advantageous, as already explained, that the respective container product has an orientation in the post-treatment zone, which is approximately equal to the orientation of the container product during container filling.

Instead of individual container products which can also be connected in an arrangement beside each other via a carton composite (not shown), the configuration of the container composite is also possible by means of the container chain 9 arranged one on top of the other, as described above. However, the post-treatment zone discussed, as well as any post-treatment devices, can also be used in devices, in which only individual container products are molded, filled, and sealed and delivered to the exit of a molding device. Regardless, a temperature treatment, particularly in the form of cooling, should only be applied to the container product after it is sealed; previous cooling could otherwise adversely affect the head-end sealing process of the container product because correspondingly sufficiently high mold temperatures must be present in the plastic material for the respective molding process.

The post-treatment zone, which is aimed at convective ambient cooling of the containers, is not shown directly in the figures. If the cooling device 53 shown for example in Fig. 3 was completely omitted, the convective air flow could directly reach the containers of the container line 9 without further hindrance as soon as they exit the molding device 1. In order to be able to achieve a sufficient cooling effect, it is then advantageous to increase the length of the convective post-treatment zone by at least four times, but preferably five times, the preset length within the mold production line. The mold production line in this case is substantially determined by the length of the molding device 1, which is required after closing the upper pairs of mold halves 7 for container production, until, at the bottom end of the molding device 1, the corresponding mold pairs 7 move apart again and release the container products of the container chain 9. The respective mold production line must then be extended by a factor of 4 to 5 or more, starting from the release of the container product at the bottom end of the molding device 1, specifically, according to the illustration in Fig. 3, preferably in the vertical direction in order not to change the relative position between the container wall and the received container contents. After crossing the thus extended post-treatment zone (not shown), preferably

by a factor of 4 to 5 of the production line, cooling then takes place in such a manner that the deflection of the container chain 9 to the left for further processing, as shown by way of example in Fig. 3, can be easily accomplished.

C l a i m s

1. An apparatus for producing at least one container product from plastic material, which is molded by a molding device (1), provided with a predeterminable container content by means of a filling device, and sealed by a sealing device, characterized in that the respective finished manufactured container product is supplied to a post-treatment zone in which a temperature-influencing effect is exerted to the respective container product and/or the respective container contents.
2. The apparatus according to claim 1, characterized in that the post-treatment zone allows convective cooling of the container product, preferably of at least 20 seconds duration, during which at least approximately the same orientation is maintained for the container product as during filling of the container.

3. The apparatus according to claim 1 or 2, characterized in that, in the post-treatment zone, at least one tempering device is provided as a post-treatment device (4), in particular in the form of a cooling device.
4. The apparatus according to claim 1 or 2, characterized in that the dwell time for the container product in the sealed production state is set to be less than 7 seconds.
5. The apparatus according to one of the preceding claims, characterized in that the post-treatment device (4) includes an apparatus (6) for generating a cooling air flow for at least acting upon the respective container product.
6. The apparatus according to claim 4, characterized in that the post-treatment device includes a flow guide device for generating a directed air flow (20, 22) of compressed cooling air.
7. The apparatus according to one of the preceding claims, characterized in that the post-treatment device (4) includes a type of cooling tunnel (51) having a passage (52) for the passage of the respective container product and having tunnel walls (53) at least partially defining the passage (52), which may be cooled by means of a cooling medium flowing through the walls (53).

8. The apparatus according to one of the preceding claims, characterized in that the post-treatment device (4) includes a freezer device, for example in the form of a basin with flowing liquid nitrogen or liquid air.
9. The apparatus according to one of the preceding claims, characterized in that the post-treatment device (4) has a conveyor device (61) effecting the advancing of the container products, having conveyor elements (65, 67, 71, 73) acting on the container products, wherein the conveying elements (65, 67, 71, 73) can be cooled by means of a coolant flow flowing through them.
10. The apparatus according to one of the preceding claims, characterized in that the post-treatment device (4) exerts a cooling effect on the container products, which have at least approximately the same orientation over the duration of the post-treatment.
11. A method for producing blow-molded and filled container products made of plastic material by means of a molding device (1), having individual molding parts (7), which can be moved toward and away from one another in pairs to close or open a manufacturing mold in which the respective container product is molded, provided with a container content, and sealed, characterized in that, after an exit point (2) of the respective container product from the molding device (1), it is supplied to a post-treatment zone in which the respective container product and/or on the respective container contents are subjected to a temperature-influencing effect.
12. The method according to claim 11, characterized in that, in the post-treatment zone, convective cooling of the container product of preferably at least 20 seconds duration is carried out during which at least approximately the same orientation is maintained for the container product as during filling of the container.
13. The method according to claim 11 or 12, characterized in that, in the post-treatment zone, at least one tempering device is provided as a post-treatment device (4), in particular in the form of a cooling device.
14. The method according to one of the claims 11 to 13, characterized in that the dwell time in the sealed manufacturing state for the container product is set to be less than 7 seconds.