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(54) Title: LAMINATED BAG FOR PHARMACEUTICALS

(57) Abstract: The present invention relates to a laminated bag containing an active pharmaceutical ingredient, a method for pack-  
aging an active pharmaceutical ingredient and the use of a laminated bag for packaging an active pharmaceutical ingredient.



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## LAMINATED BAG FOR PHARMACEUTICALS

### Field of the invention

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The present invention relates to a laminated bag containing an active pharmaceutical ingredient, a method for packaging an active pharmaceutical ingredient and the use of a laminated bag for packaging an active pharmaceutical ingredient.

10

### Background of the invention

Various laminated packaging materials have been developed which protect the packaged materials from moisture, light and air and in some cases maintain the moisture content of the contents of the package. US 1,538,277 describes a package for food and commodities from a laminated sheet. The sheet comprises an inner layer of metal foil, such as tin foil, attached with a layer of paraffin wax to a middle wax impregnated sheet of paper and an outer paper wrapper coated with a waxy material. Said package hermetically seals the contents of the package. US 2,400,390 describes a vacuum packaging sheet material formed by adhesively laminating aluminum or tin foil to a chlorinated rubber film. The edges of the chlorinated rubber film are heat sealed under vacuum to form a moisture, light and air resistant package. In US 3,560,223 a food product cooked in situ in a multilayer casing is described. The tubular casing is formed by laminating layers of thermoplastic film to both sides of a metal foil. The sealed tube formed therefrom is relatively impervious to moisture and oxygen transmission. US 4,096,309 describes a self-sealing packaging laminate of high strength and capacity. The laminate is composed of an outer sheet of non-woven spun-bonded polymeric filament such as polyethylene or polyester, a second layer of flexible metal foil, preferably aluminum, and an inner layer of heat sealable polyolefin. A face ply of smooth non-porous material such as Kraft paper is bonded to the outer spun-bonded polymeric filament layer. In US 4,364,989 a multilayer packaging material for snack food is described. The material comprises an outer layer of polypropylene, a low density polyethylene laminator and an inner layer which is a co-extrusion. The inner co-

extruded layer comprises a first layer of high density polyethylene, a second layer of polypropylene and a third layer of ethylene methyl acrylate. The ethylene methyl acrylate surface is coated with an emulsion of polyvinylidene chloride, which seals the inner layers together upon application of heat. In US 2013/0213827 there is described  
5 a flexible container for storing food having a pad of liquid absorbing material disposed proximate the open end for absorbing liquid while the flexible container is evacuated prior to heat sealing the open end.

The laminated bags described above are designed for packaging foods and commodities. Innovative concepts for packaging pharmaceuticals are focused at  
10 formulated products such as tablets, such as for example the biodegradable films for blister packages as described in WO 2013/076734.

Conventional packaging for bulk pharmaceutical use generally comprise a box-type non-flexible body. Active pharmaceutical ingredients (API) are stored and shipped in HDPE drums or corrugated boxes. One problem associated with such packaging is  
15 that these consume a significant amount of plastic and paper which have adverse impact on the environment, with millions of sea birds and mammals dying each year due to plastic ingestion or entanglement. Moreover, with increased consumption of plastic and paper it is becoming difficult to dispose of non-biodegradable waste. In addition, the prior art box-type non-flexible containers have another major disadvantage  
20 in that the amount of space occupied by the filled container is much higher than the space occupied by the pharmaceutical product itself. This is a problem in transport and storage where occupancy of minimal space is key. However, the conventional packaging containers such as boxes and drums are usually well-equipped to withstand external moisture from reaching the often sensitive pharmaceutical products and are  
25 also resilient to mechanical damage.

Hence, there is a need for innovative packaging which can significantly minimize the consumption of plastic and paper. The technical aim of the present invention is to produce a packaging structure for pharmaceutical use that overcomes the aforesaid technical problems, *i.e.* bringing flexible packaging economics whilst having sufficient  
30 resilience to penetration of moisture and mechanical damage.

### **Detailed description of the invention**

The present invention describes laminate bags filled with active pharmaceutical ingredients. Laminate bags are known for packaging of plastic granules. However, plastic granules are highly stable compounds requiring no particular temperature, moisture or other controls and precisely the contrary is required in the field of the present invention, namely bulk active pharmaceutical ingredients. We have found that bags comprising four layers of polyester, metal (such as tin or aluminum), nylon and polyethylene give protection to active pharmaceutical ingredient from external moisture during storing and transportation. Quality and stability surprisingly was found to be equal or even better when compared to existing packaging.

In the context of the present invention, the term “bag” refers to a non-rigid container. The term “laminated” refers to the result of lamination which is the technique of manufacturing a material in multiple layers, so that the composite material achieves improved strength, stability, sound insulation, appearance or other properties from the use of differing materials. A laminate is usually permanently assembled by heat, pressure, welding, or adhesives. The term “amoxicillin” refers to the compound (2*S*,5*R*,6*R*)-6-[[*(2R)*-amino(4-hydroxyphenyl)acetyl]amino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid and is also meant to include salts and hydrates thereof, notably the sodium salt and the trihydrate. The term “ampicillin” refers to the compound (2*S*,5*R*,6*R*)-6-[[*(2R)*-aminophenylacetyl]amino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid and is also meant to include salts and hydrates thereof, notably the sodium salt, the monohydrate, trihydrate and sesquihydrate. The term “atorvastatin” refers to the compound ( $\beta$ *R*, $\delta$ *R*)-2-(4-fluorophenyl)- $\beta$ , $\delta$ -dihydroxy-5-(1-methylethyl)-3-phenyl-4-[(phenylamino)carbonyl]-1*H*-pyrrole-1-heptanoic acid and lactones, hydrates and salts thereof, notably the calcium salt, the calcium salt trihydrate, the lactone and the sodium salt. The term “cefaclor” refers to the compound (6*R*,7*R*)-7-[[*(2R)*-aminophenylacetyl]amino]-3-chloro-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid and is also meant to include salts and hydrates thereof, notably the monohydrate. The term “cefadroxil” refers to the compound (6*R*,7*R*)-7-[[*(2R)*-amino-(4-hydroxyphenyl)acetyl]amino]-3-methyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid and salts and hydrates thereof, notably the monohydrate. The term “cephalexin” refers to the compound (6*R*,7*R*)-7-

[[*(2R)*-aminophenylacetyl]amino]-3-methyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid and salts and hydrates thereof, notably the monohydrate, the monohydrochloride monohydrate and the sodium salt. The term "cephradine" refers to the compound (*6R,7R*)-7-[[*(2R)*-amino-1,4-cyclohexadien-1-ylacetyl]amino]-3-methyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid and is also meant to include salts and hydrates thereof, notably the dihydrate and the monohydrate. The term "cloxacillin" refers to the compound (*2S,5R,6R*)-6-[[[3-(2-chlorophenyl)-5-methyl-4-isoxazolyl]carbonyl]amino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid and salts and hydrates thereof, notably the benzathine salt, the sodium salt and the sodium salt monohydrate. The term "dicloxacillin" refers to the compound (*2S,5R,6R*)-6-[[[3-(2,6-dichlorophenyl)-5-methyl-4-isoxazolyl]carbonyl]amino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid and salts and hydrates thereof, notably the sodium salt monohydrate. The term "flucloxacillin" refers to the compound (*2S,5R,6R*)-6-[[[3-(2-chloro-6-fluorophenyl)-5-methyl-4-isoxazolyl]carbonyl]amino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid and salts and hydrates thereof, notably the sodium salt monohydrate. The term "oxacillin" refers to the compound (*2S,5R,6R*)-3,3-dimethyl-6-[[[5-methyl-3-phenyl-4-isoxazolyl]carbonyl]amino]-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid and salts and hydrates thereof, notably the sodium salt monohydrate. The term "rosuvastatin" refers to the compound (*3R,5S,6E*)-7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl-(methylsulfonyl)amino]-5-pyrimidinyl]-3,5-dihydroxy-6-heptenoic acid and lactones, hydrates and salts thereof, notably the calcium salt.

In a first aspect, the present invention provides a laminated bag containing an active pharmaceutical ingredient characterized in that said laminated bag comprises an inner polyethylene layer completely embracing said active pharmaceutical ingredient and a metal layer completely embracing said inner polyethylene layer. The metal may be aluminum or tin.

In a first embodiment the laminated bag further comprises a layer of an aliphatic polyamide such as nylon like nylon-6,6; nylon-6; nylon-6,9; nylon-6,10; nylon-6,12; nylon-11; nylon-12 and nylon-4,6. Preferably said layer of aliphatic polyamide completely embraces the inner polyethylene layer. Most preferably the nylon layer is positioned between said polyethylene layer and said aluminum layer. In another

preferred embodiment the laminated bag further comprises a layer of polyester completely embracing said inner polyethylene layer. Preferred examples of suitable polyesters are polybutylene succinate (PBS), polybutylene terephthalate (PBT), polycaprolactone (PCL), polyethylene adipate (PEA), polyethylene naphthalate (PEN),  
5 polyethylene terephthalate (PET), polyglycolic acid (PGA), polyhydroxyalkanoate (PHA), polyhydroxybutyrate (PHB), poly(3-hydroxybutyrate-co-3-hydroxyvalerate) (PHBV), polylactic acid (PLA) and polytrimethylene terephthalate (PTT). Most preferably the polyester is PET. In a most preferred embodiment the laminated bag comprises an inner polyethylene layer, a nylon layer completely embracing said inner polyethylene  
10 layer, an aluminum layer completely embracing said nylon layer and a polyester layer completely embracing said aluminum layer.

In a second embodiment the thickness of the layers is from 3 to 3000  $\mu\text{m}$ , preferably from 5 to 2000  $\mu\text{m}$ , more preferably from 10 to 1000  $\mu\text{m}$ , most preferably from 12 to 750  $\mu\text{m}$ . Preferably the thickness of the polyethylene layer is from 50 to  
15 300  $\mu\text{m}$ , more preferably from 100 to 200  $\mu\text{m}$ . Preferably the thickness of the nylon layer is from 10 to 50  $\mu\text{m}$ , more preferably from 12 to 25  $\mu\text{m}$ . Preferably the thickness of the metal layer is from 300 to 1000  $\mu\text{m}$ , more preferably from 500 to 750  $\mu\text{m}$ . Preferably the thickness of the polyester layer is from 10 to 50  $\mu\text{m}$ , more preferably from 10 to 25  $\mu\text{m}$ .

20 In a third embodiment the layers of the laminated bag comprise an adhesive in between two layers. Suitable adhesives are those known to the skilled person such as, for example, double component polyurethane adhesives.

In a fourth embodiment of the invention, a one way valve is connected to the laminated bag. One way valves are used to create a unidirectional flow in a device such  
25 as the laminated bag of the present invention. A one way valve may be an elastomeric sealing element that allows forward flow and prevent backward flow of gases. In the laminated bag of the present invention the one way valve is connected such that gas can flow from the inside of the laminated bag to the outside. There are various designs available that are suitable for application in the present invention. In case a low opening  
30 pressure and ease of assembly is required a preferred one way valve is a duckbill valve. In case a certain cracking pressure or a low-pressure drop at higher flows is needed, an umbrella valve is preferred. The skilled person is aware of the existing and function of the various types of one way valves that are applicable in the present

invention such as Belleville valves, cross-slit valves, dome valves, duckbill valves, mini valve balls and umbrella valves. The valves mentioned above are commercially available and can be made from various materials, usually but not necessarily polymers. Assembly of the valves mentioned above to the laminated bag of the present invention can be done according to procedures known to the skilled person.

In a fifth embodiment of the invention the active pharmaceutical ingredient is an antibiotic chosen from the list consisting of amoxicillin, ampicillin, cefaclor, cefadroxil, cefprozil, cephalexin, cephradine, cloxacillin, dicloxacillin, flucloxacillin and oxacillin or a statin chosen from the list consisting of atorvastatin, lovastatin, nystatin, pitavastatin, pravastatin, rosuvastatin and simvastatin. Preferably the antibiotic is amoxicillin, most preferably in the form of amoxicillin trihydrate.

In a sixth embodiment the active pharmaceutical ingredient is packaged in one or two separate bags prior to packaging in the laminated bag of the present invention. Preferably the active pharmaceutical ingredient is packaged in a polyethylene bag. More preferably the resulting active pharmaceutical ingredient packaged in a polyethylene bag is packaged in a second bag. Said second bag may be polyethylene or metal film, depending on specific needs as usually dictated by customers. Suitable metal films are aluminum and tin, preferably aluminum.

In a second aspect, the present invention provides a method for packaging an active pharmaceutical ingredient comprising bringing said active pharmaceutical ingredient into a laminated bag as described in the first aspect of the invention. Insertion of the active pharmaceutical ingredient may be done using automated bag-filling equipment as known to the skilled person.

In a third aspect, the present invention provides the use of a laminated bag as described in the first aspect of the invention for packaging active pharmaceutical ingredients such as amoxicillin, ampicillin, atorvastatin, cefaclor, cefadroxil, cefprozil, cephalexin, cephradine, cloxacillin, dicloxacillin, flucloxacillin, lovastatin, nystatin, oxacillin, pitavastatin, pravastatin, rosuvastatin and simvastatin.

Use of the laminated bags of the present invention by a large antibiotic production facility is estimated to result in an annual reduction of 1,500 mt CO<sub>2</sub> by reducing the use of close to 400 mt of plastic and paper. Further estimated advantages

for a large antibiotics production facility are conservation of nonrenewable fossil fuels (and thus electricity), over 500,000 l crude oil savings (1.75 l crude oil produces 1 kg HDPE), or 24,000 GJ in energy savings (1 l crude oil is needed for  $\sim 100 \text{ MJ.kg}^{-1}$  plastic). In addition the reduction in required storage and transportation space amounts up to 80% (leading to energy savings for electricity consumption and cooling processes in warehouses and fuel for transports).

### **Legend to the Figures**

Figure 1 a schematic representation of a one way valve (top, A): A1 represents the exterior wherein gas flow cannot pass the one way valve and A2 represent the interior from where the gas flow can pass the one way valve. The positioning in the laminated bag of the present invention and the functioning of the one way valve is depicted thereof in B (bottom). Upon application of pressure (B1) on the laminated bag, gas flows from the interior (B2) to the exterior (B3). Upon release of pressure there is no return gas flow.



**EXAMPLES****Example 1****Properties of laminated bag**

5 Physical properties of a laminated bag comprising an inner polyethylene (linear low-density polyethylene, LLDPE) layer having a thickness of 135  $\mu\text{m}$ , followed by a nylon (oriented polyamide, OPA) layer having a thickness of 15  $\mu\text{m}$ , followed by an aluminum layer having a thickness of 635  $\mu\text{m}$  and finally a polyester (PET) layer having a thickness of 12  $\mu\text{m}$  were determined. Adhesive was present in between two layers: 3  $\mu\text{m}$  of adhesive between  
 10 polyethylene and nylon, 3  $\mu\text{m}$  of adhesive between nylon and aluminum and 4  $\mu\text{m}$  of adhesive between aluminum and polyester.

Weight per surface unit:

	• Inner polyethylene layer:	120 $\text{g.m}^{-2}$
	• Adhesive layer between polyethylene and nylon:	3 $\text{g.m}^{-2}$
15	• Nylon (oriented polyamide, OPA) layer:	17 $\text{g.m}^{-2}$
	• Adhesive layer between nylon and aluminum:	3 $\text{g.m}^{-2}$
	• Aluminum layer:	17 $\text{g.m}^{-2}$
	• Adhesive layer between aluminum and polyester:	4 $\text{g.m}^{-2}$
	• Polyester layer:	17 $\text{g.m}^{-2}$
20	• Total of laminated bag:	183 $\text{g.m}^{-2}$

Tensile strength:

	• Tensile strength MD:	83 N.15 $\text{mm}^{-1}$
	• Tensile strength TD:	125 N.15 $\text{mm}^{-1}$
	• Elongation MD:	66%
25	• Elongation TD:	102%

Puncture resistance:

## Out/in:

	• Max force:	49 N
	• Deformation:	0.72 cm
30	• Max energy:	14.0 N.cm

## In/out:

	• Max force:	60 N
	• Deformation:	0.79 cm

- Max energy: 20.0 N.cm

Seal strength (P: 230 kPa, t: 1.5 s):

- Seal strength: 94 N.15 mm<sup>-1</sup>
- Temperature: 200°C

5 Barrier properties:

- Oxygen permeability (23°C and 0% rel. humidity): < 0.1 cc.m<sup>-2</sup>/24 h
- Moisture permeability (38°C and 90% rel. humidity): < 0.1 g.m<sup>-2</sup>/24 h

Slipperiness:

- COF static: > 0.6
- 10 • COF dynamic: > 0.5

Tearing resistance:

- MD: > 10,000 mN
- TD: > 15,000 mN

15

**Example 2****Stability of amoxicillin trihydrate packaged in laminated bag**

Batches of amoxicillin trihydrate were stored for 6 months at 40±2°C and a relative humidity (RH) of 75±5%. Samples were analyzed after 0, 1, 2, 3 and 6 months. Batches A1 and A2 represent existing packaging (25 kg batches of amoxicillin in a primary bag of polyethylene, a secondary bag of aluminum or polyethylene and a tertiary bag which is a corrugated box or HDPE drum) and batches B1 and B2 represent packaging according to the present invention (25 kg batches of amoxicillin in a primary bag of polyethylene, a secondary bag of polyethylene and a tertiary bag which is a laminated bag as described in Example 1). The laminate bag was further equipped with a one way valve. Storage and analysis was according to ICH and EU Guidelines on stability studies. Specification of amoxicillin trihydrate are as follows:

Assay:	95-102%
Water:	11.5-14.5%
30 Appearance of solution:	To conform
pH:	3.5-5.5
Specific rotation:	+290 to 315°
Related substances:	Individual known impurities (NMT 1.0%)

Stability data of the four tested batches are as follows:

Table 1 Stability data of batches A1 and A2 (25 kg batches of amoxicillin trihydrate packaged in a primary bag of polyethylene, a secondary bag of aluminum or polyethylene and a tertiary bag which is a corrugated box or HDPE drum).

Time (months)	HPLC Assay (%)		Water (%)		pH		Specific optical rotation (°)	
	A1	A2	A1	A2	A1	A2	A1	A2
0	99.4	99.4	13.1	13.1	4.8	4.9	304	304
1	98.7	98.8	13.0	13.0	4.8	4.8	301	301
2	98.6	98.7	13.1	13.1	4.8	4.8	299	300
3	98.4	98.4	13.1	13.1	4.9	4.9	298	298
6	98.3	98.4	13.4	13.3	4.9	4.9	298	298

Table 2 Stability data of batches B1 and B2 (25 kg batches of amoxicillin trihydrate packaged in a primary bag of polyethylene, a secondary bag of polyethylene and a tertiary bag which is a laminated bag as described in Example 1).

Time (months)	HPLC Assay (%)		Water (%)		pH		Specific optical rotation (°)	
	B1	B2	B1	B2	B1	B2	B1	B2
0	99.8	99.7	13.1	13.1	5.0	5.0	304	304
1	99.5	99.5	13.0	13.0	5.0	5.0	303	304
2	99.4	99.4	13.2	13.0	5.0	5.0	303	303
3	99.3	99.3	13.0	13.1	5.0	4.9	303	303
6	99.1	99.1	13.1	13.0	4.9	4.9	302	303

Upon comparing the results as depicted in Tables 1 and 2 it became clear that packaging amoxicillin trihydrate in the laminated bags according to the present invention lead to equal or improved stability results as was the case when amoxicillin trihydrate was packaged and stored in a traditional fashion.

**CLAIMS**

1. A laminated bag containing an active pharmaceutical ingredient characterized in that said laminated bag comprises an inner polyethylene layer completely embracing said active pharmaceutical ingredient and an aluminum layer completely embracing said inner polyethylene layer.  
5
2. Laminated bag according to claim 1 further comprising a nylon layer completely embracing said inner polyethylene layer and/or a polyester layer completely embracing said inner polyethylene layer.  
10
3. Laminated bag according to claim 2 wherein said nylon layer is positioned between said polyethylene layer and said aluminum layer and wherein said polyester layer completely embraces said aluminum layer.  
15
4. Laminated bag according to claim 3 comprising an inner polyethylene layer, a nylon layer completely embracing said inner polyethylene layer, an aluminum layer completely embracing said nylon layer and a polyester layer completely embracing said aluminum layer.  
20
5. Laminated bag according to any one of claims 1 to 4 wherein the thickness of said layer is from 10 to 1000  $\mu\text{m}$ .
6. Laminated bag according to any one of claims 3 to 5 wherein the thickness of said polyethylene layer is from 50 to 300  $\mu\text{m}$ , the thickness of said nylon layer is from 10 to 50  $\mu\text{m}$ , the thickness of said aluminum layer is from 300 to 1000  $\mu\text{m}$  and the thickness of said polyester layer is from 10 to 50  $\mu\text{m}$ .  
25
7. Laminated bag according to any one of claims 1 to 6 wherein an adhesive is present between two layers.  
30
8. Laminated bag according to any one of claims 1 to 7 further comprising a one way valve positioned such that gas can pass from the interior of said laminated bag to the exterior.

- 5 9. Laminated bag according to any one of claims 1 to 8 wherein said active pharmaceutical ingredient is an antibiotic chosen from the list consisting of amoxicillin, ampicillin, cefaclor, cefadroxil, cefprozil, cephalixin, cephradine, cloxacillin, dicloxacillin, flucloxacillin and oxacillin or a statin chosen from the list consisting of atorvastatin, lovastatin, nystatin, pitavastatin, pravastatin, rosuvastatin and simvastatin.
- 10 10. Laminated bag according to claim 9 wherein said active pharmaceutical ingredient is amoxicillin trihydrate.
11. Laminated bag according to any one of claims 1 to 10 wherein said active pharmaceutical ingredient is packaged in a polyethylene bag.
- 15 12. Laminated bag according to claim 11 wherein said active pharmaceutical ingredient packaged in a polyethylene bag is packaged in a second bag which is polyethylene or aluminum.
- 20 13. Method for packaging an active pharmaceutical ingredient comprising bringing said active pharmaceutical ingredient into a laminated bag comprising an inner polyethylene layer and an aluminum layer completely embracing said inner polyethylene layer.
- 25 14. Use of a laminated bag comprising an inner polyethylene layer and an aluminum layer completely embracing said inner polyethylene layer for packaging active pharmaceutical ingredients.
15. Use according to claim 14 wherein said laminated bag further comprises a nylon layer completely embracing said inner polyethylene layer and/or a polyester layer completely embracing said inner polyethylene layer.

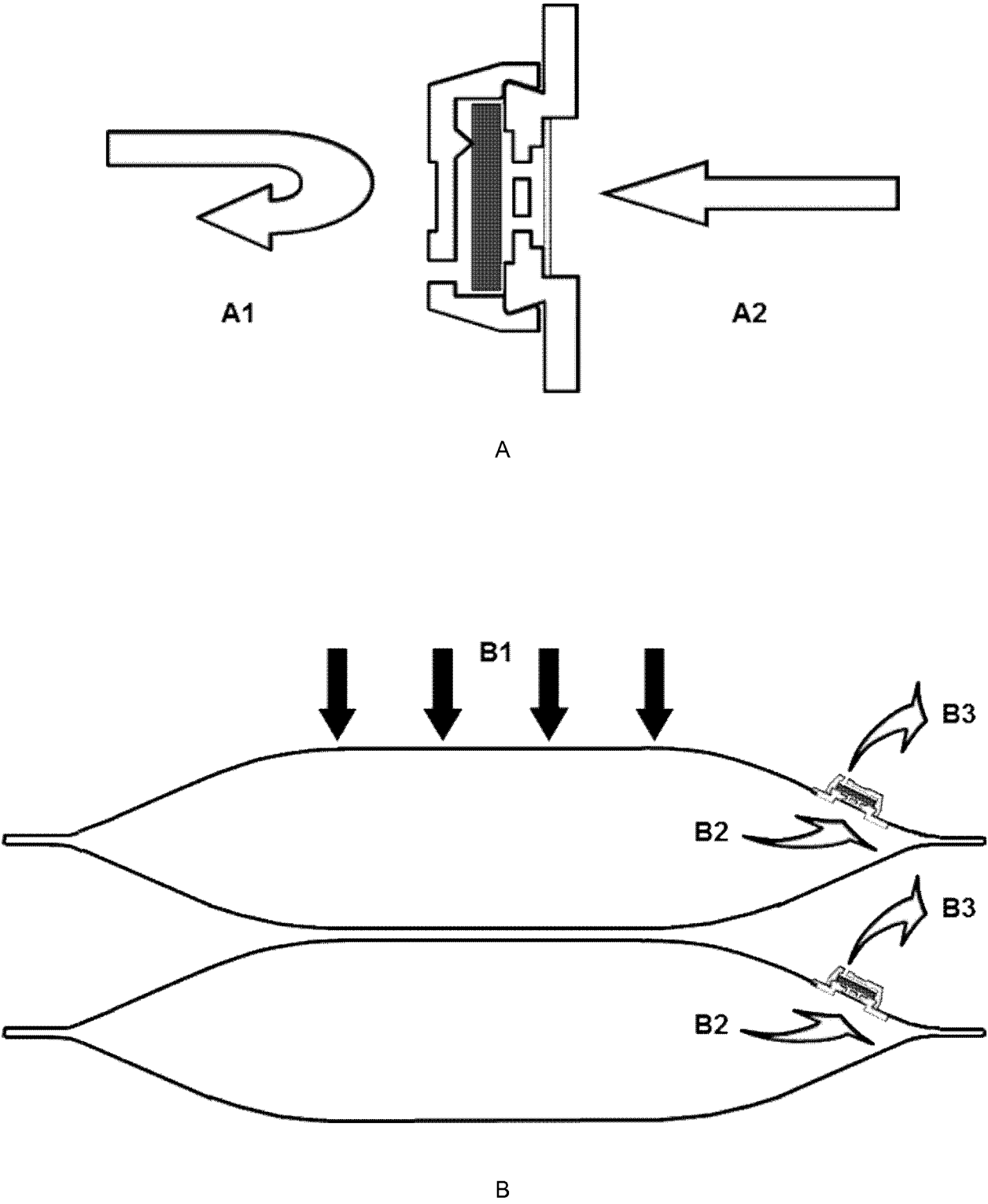


Fig. 1

# INTERNATIONAL SEARCH REPORT

International application No  
PCT/EP2015/050392

<b>A. CLASSIFICATION OF SUBJECT MATTER</b> INV. B32B15/08 A61J1/10 B32B15/085 B32B15/088 B32B15/09 B32B15/20 B32B1/02 B65D65/00 ADD. According to International Patent Classification (IPC) or to both national classification and IPC																				
<b>B. FIELDS SEARCHED</b> Minimum documentation searched (classification system followed by classification symbols) B32B A61J B65D Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) EPO-Internal, WPI Data, COMPENDEX																				
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b> <table border="1"> <thead> <tr> <th>Category*</th> <th>Citation of document, with indication, where appropriate, of the relevant passages</th> <th>Relevant to claim No.</th> </tr> </thead> <tbody> <tr> <td>X</td> <td>US 2006/222792 A1 (BRAVERMAN OLEG [IL] ET AL) 5 October 2006 (2006-10-05)</td> <td>1-15</td> </tr> <tr> <td>Y</td> <td>claims 1,8-14</td> <td>2,3,15</td> </tr> <tr> <td>X</td> <td>EP 0 201 880 A2 (ANTIBIOTICI CRISTALLIZZATI STE [IT]) 20 November 1986 (1986-11-20)</td> <td>1-15</td> </tr> <tr> <td>Y</td> <td>claim 1 page 1, line 1 - line 10</td> <td>2,3,15</td> </tr> <tr> <td>Y</td> <td>DATABASE WPI Week 201381 Thomson Scientific, London, GB; AN 2013-P06427 XP002737587, &amp; CN 103 010 577 A (ZHANGJIAGANG BAISHENG PACKAGING MATERIALS CO LTD) 3 April 2013 (2013-04-03) abstract</td> <td>2,3,15</td> </tr> </tbody> </table>			Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	X	US 2006/222792 A1 (BRAVERMAN OLEG [IL] ET AL) 5 October 2006 (2006-10-05)	1-15	Y	claims 1,8-14	2,3,15	X	EP 0 201 880 A2 (ANTIBIOTICI CRISTALLIZZATI STE [IT]) 20 November 1986 (1986-11-20)	1-15	Y	claim 1 page 1, line 1 - line 10	2,3,15	Y	DATABASE WPI Week 201381 Thomson Scientific, London, GB; AN 2013-P06427 XP002737587, & CN 103 010 577 A (ZHANGJIAGANG BAISHENG PACKAGING MATERIALS CO LTD) 3 April 2013 (2013-04-03) abstract	2,3,15
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<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input checked="" type="checkbox"/> See patent family annex.																				
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Date of the actual completion of the international search  20 March 2015		Date of mailing of the international search report  30/03/2015																		
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016		Authorized officer  Hillebrand, Gerhard																		

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2015/050392

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2006222792	A1	05-10-2006	CA 2585406 A1 21-10-2007
			DE 102007018552 A1 25-10-2007
			FR 2900134 A1 26-10-2007
			US 2006222792 A1 05-10-2006
EP 0201880	A2	20-11-1986	CA 1260883 A1 26-09-1989
			DE 3675809 D1 10-01-1991
			EP 0201880 A2 20-11-1986
			IT 1183613 B 22-10-1987
			JP H0533631 B2 20-05-1993
			JP S6264751 A 23-03-1987
			US 4700838 A 20-10-1987
CN 103010577	A	03-04-2013	NONE