Standard of China National Pharmaceutical Packaging Association

T/CNPPA 2001-2017

HDPE Non-woven Fabrics Desiccant Sachet for Oral Solid Preparation

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Foreword

Appendix A to this standard is an appendix to this standard.

This standard is centralized by China National Pharmaceutical Packaging Association.

Drafting committee of this standard: Jiangsu Sud-Chemie Performance Packaging Material Co., Ltd. and Dupont (China) Research and Development Management Co., Ltd.

Draftsman of this standard: Zhao Guangtao, Chen Yujiang, Jin Hong, Cai Rong, Wu Ping, Luo Hongyu, Zhu Bilin, Qian Jun.

This standard is the first edition.

This standard is drafted on the basis of GB/T 1.1.

Introduction

The HDPE non-woven fabrics desiccant sachet specified in this standard is composed of desiccant and HDPE non-woven fabrics sachet. It is suitable for oral solid preparation.

The desiccant refers to the material that can remove moisture in the moist material, such as silica gel and molecular sieve etc., reduce the humidity in the drug packaging container via adsorption of water vapor in the drug packaging container within the specified time, and maintain for a period of time. The variety of desiccant includes: silica gel, molecular sieve and mixed desiccant (such as silica gel: molecular sieve 4: 6）。

HDPE non-woven fabrics are made with HDPE as the main raw material via the non-woven production process. They have multilayer continuous physical structure and balanced physical properties. Antistatic agent and fluorescent whitening agent must not be used. According to different requirements, it is necessary to study and evaluate the physical and chemical properties of HDPE non-woven fabrics, material specifications (mass per unit area), material cleanliness, particulate contamination, floc falling level, waterproof permeability, particle barrier, tensile strength, tear resistance, rupture resistance and surface performance etc.

The HDPE non-woven fabrics materials specified in this standard include glue-coated materials and non-glue-coated materials, which shall not release substances sufficient to cause health risks (see GB/T 16886.1 for biological evaluation and test). Where the material is coated with glue, the continuity of the coating shall be assessed. The sachets usually shall be made via the electric heating sealing process for glue-coated materials, and shall be made via the ultrasonic sealing process for non-glue-coated materials.

HDPE non-woven fabrics desiccant sachet for oral solid preparation must be produced in the environment adaptive to the production environment of corresponding pharmaceutical, and should preferably be produced in the production environment with the relative humidity below 50%.

HDPE non-woven fabrics desiccant sachet for oral solid preparation shall be produced via the process to avoid the possible contamination of desiccant’s raw material to desiccant sachet.

HDPE Non-woven Fabrics Desiccant Sachet for Oral Solid Preparation

1 Scope

This standard stipulates the technical indicators & requirements, test methods, inspection rules and judgment rules, as well as the requirements for product packaging, marking, transportation and storage of HDPE non-woven fabrics desiccant sachet for oral solid preparation (hereinafter referred to as "desiccant sachet")

2 Normative References

The documents cited herein are indispensable to the application of this standard. For dated references, only the dated version applies. For undated references, the latest version (including all amendments) applies. The references are as follows:

Chinese Pharmacopoeia (Version 2015)

GB/T 455 Paper and Board Determination of Tearing Resistance

GB/T 2828.1 Sampling procedures for inspection by attributes - Part 1: Sampling Schemes Indexed by Acceptance Quality Limit (AQL) for Lot-by-lot Inspection

GB/T 4744 Textile Fabrics- Determination of Resistance to Water Penetration- Hydrostatic Pressure Test

GB/T 16886.1 Biological Evaluation of Medical Devices -Part 1: Evaluation and Testing within a Risk Management Process

YBB00122003-2015 Test for Welding Strength

YBB00262004-2015 Test for Infrared Spectrum of Packaging Materials

YBB00312004-2015 Test for Residual Solvent of Packaging Materials

3 Terms and Definitions

For the purpose of this document, the following terms and definitions apply.

3.1

Saturation moisture absorbed capacity Saturation moisture absorbed capacity

It refers to the ratio of the weight of vapor absorbed by the desiccant sachet after it is placed for a period of time under specific temperature and humidity conditions to the weight of desiccant.

4 Requirement

4.1 Identification

The HDPE non-woven fabrics sachet material shall be determined with the fourth method in YBB00262004-2015.

4.2 Specification and Dimension

The specification and dimension of desiccant sachet shall be in accordance with Table 1.

Table 1 Specification and Dimension

Specification and Dimension[a]	Overall Dimension[b] (mm)		Weight of Inclusions[c] (g)		Test Method
	Central Value	Tolerance Range	Central Value	Tolerance Range	
1g	22×44	±2	1	-10%/+15%	**A.1**
2g	22×57	±2	2		
3g	22×66	±2	3		

a: The specific indicators of other specifications and models may be determined by the seller and the buyer through consultation according to the filling requirements.

b: The indicator of overall dimension is only for reference.

c: The indicator of weight of inclusions is only for reference.

4.3 Appearance

The appearance defects of desiccant sachet shall comply with the provisions in Table 2.

Table 2 Appearance

Defects	Description	Inspection Level	Acceptance Quality Limit (AQL)	Test Method
Sachet breaking	Breaking of HDPE non-woven fabrics sachet for various reasons, resulting in desiccant leakage	General inspection level I	0.04	**A.2**
Empty sachet	Desiccant missing		0.04	
Dirt	The surface of desiccant sachet is contaminated, and is prone to falling off		0.65	
Printing	The pattern of desiccant sachet is not printed or incomplete, resulting in the loss of function		0.65	
	A part of the pattern on the desiccant sachet is blurred, causing the pattern to be illegible		1.0	
	A part of the pattern on the desiccant sachet is blurred, but the pattern is legible		4.0	
Printing ink	Due to printing, there are extra ink marks on the surface of the desiccant sachet which are easy to be wiped off and fall off		0.65	
	Due to printing, there are ink marks on the surface of the desiccant sachet, which are not easy to be wiped off or fall off		4.0	
Color difference	There exists color difference between different desiccant sachets due to packaging materials or production process		4.0	

4.4 Physical and chemical indicators

The physical and chemical indicators of desiccant sachet shall comply with the provisions of Table 3.

Table 3 Physical and chemical indicators

Items		Units	Indicators	Test Method
Moisture Content of Desiccant				**A.3**
Silica gel		%	≤ 4.0	
Macropore molecular sieve		%	≤ 4.0	
Mixed desiccant (such as silica gel: macropore molecular sieve=4:6)		%	≤ 4.0	
Saturation moisture absorbed capacity				**A.4**
Silica gel		%	≥30.0	
Macropore molecular sieve		%	≥19.0	
Mixed desiccant (such as silica gel : macropore molecular sieve=4:6)		%	≥24.0	
Dropping Resistance		—	The desiccant sachet shall not be broken and the desiccant shall not leak	**A.5**
Physical and Chemical Properties of HDPE Non-woven Fabrics Sachet				**A.6**
Decolorization test		—	The soaking solution shall not be darker than the blank solution	**A.6.1**
Fluorescence of HDPE Non-woven Fabrics Sachet		—	Shall comply with the provision	**A.6.2**
Residue on ignition	Including opacifying agent	%	≤ 3.0	**A.6.3**
	Excluding opacifying agent	%	≤ 0.1	

Residual solvent content	Total amount	mg/m^2	≤ 5.0	**A.6.4**
	Benzene	mg/m^2	No content shall be detected	
	Benzole	mg/m^2	No content shall be detected	
Heavy metal		—	The content shall not exceed 1 ppm	**A.6.5**
Heat-sealing strength (longitudinal sealing and transverse sealing)	Non-glue-coated	N/15mm	≥5	**A.6.6**
	Glue-coated	N/15mm	≥3	
Hydrostatic pressure		mm	≥1 000	**A.6.7**
Tearing strength		mN	≥1 000	**A.6.8**

4.5 Microbial limit

The microbial limit shall comply with the provision of Table 4.

Table 4 Microbial limit

Items	Units	Indicators	Test Methods
Total number of aerobic bacteria	cfu/ sachet	≤1 000	**A.7**
Total number of molds and yeasts	cfu/ sachet	≤100	
Escherichia coli	—	No content shall be detected	

5 Inspection Rule

5.1 Lot

A lot shall be the products which are produced continuously for a period of time under the conditions of same raw material formula, same specification & variety, same technology and same equipment or otherwise agreed in the contract.

5.2 Sampling

After the external packaging is inspected, a certain number of packages shall be randomly selected from the same lot of products according to Table 5 for sampling.

Table 5 Quantity of packages sampled

Quantity of packages sampled from each lot of products	Quantity of packages sampled
2 ~15 pieces	2
16 ~ 50 pieces	3
51 ~ 150 pieces	5
151 ~ 500 pieces	8
> 500	13

Then, the above packages shall be sampled for inspection according to Sampling Procedures for Inspection by Attributes- Part 1: Sampling Schemes Indexes by Acceptance Quality Limit (AQL) for Lot-by-lot Inspection (GB/T 2828.1).

5.3 Inspection

The dropping resistance inspection items, inspection level and acceptance quality limit (AQL) shall comply with the provisions of Table 6.

Table 6 Inspection

Inspection Items	Inspection Level	Acceptance Quality Limit
Dropping Resistance	Special Inspection Level S-3	4.0

6 Acceptance Rule

If any technical indicator cannot reach the requirement when the receiving party carries out acceptance inspection, it shall conduct the joint inspection for the defective item together with the manufacturer; the joint inspection result shall be based to judge the compliance.

7 Packaging and shelf life, marking, transportation, storage

7.1 Packaging and shelf life

The packaging form and material of desiccant sachet will directly affect the shelf life of desiccant sachet. For example: For the desiccant sachet packaged in the “polyester/aluminum/polyethylene” medicinal composite film sachet, the shelf life will 2 years as of the production date under the premise that it is unopened. For the desiccant sachet packaged in the double-layer medicinal low density polyethylene sachet, the shelf life will 1 year as of the production date under the premise that it is unopened.

For other packaging forms and materials, the shelf life shall be determined by both parties through negotiation.

According to customer needs, the humidity indicating card can be placed in the package.

7.2 Marking

The product marking shall comply with the relevant requirements of applicable national laws and regulations.

7.3 Transportation

The products shall be protected from pressure, sunshine, moisture and heat in the process of transportation. Products must not be shipped along with toxic or spoiled materials

7.4 Storage

The product must be sealed and stored in a room temperature, dark, clean, dry and ventilated warehouse.

Appendix A
(Normative)
Test Method

A.1 Specification and Dimension

A.1.1 Overall Dimension

Use the vernier caliper with accuracy of 0.01mm to measure the length.

A.1.2 Weight of Inclusions

Use the analytical balance with accuracy of 0.1mg to measure the weight.

A.2 Appearance

Take appropriate amount of this product, place in the bright place with natural light and conduct visual inspection.

A.3 Moisture Content of Desiccant

A.3.1 Silica gel

In an environment with relative humidity not more than 75%, take out the desiccant sachet quickly from the enclosed packaging bag, and take 5-7g desiccant from the desiccant sachet, put it in the weighing bottle (W1) of constant weight, weigh it (W2), place it in the oven at (180±10) ℃ (the total time from opening the packaging bag to placing the desiccant in the oven shall not exceed 5min) to constant weight, weigh precisely (W3), and calculate by the following formula:

$$\text{Moisture Content of Desiccant \%} = \frac{W2-W3}{W2-W1} \times 100 \qquad \cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots(A.1)$$

A.3.2 Macropore molecular sieve

In an environment with relative humidity not more than 75%, take out the desiccant sachet quickly from the enclosed packaging bag, and take out the desiccant from the desiccant sachet, put it in the crucible (W1) of constant weight (8-10g per crucible), weigh it precisely (W2), place it in the high temperature furnace at 950℃ (the total time from opening the packaging bag to placing the desiccant in the high temperature furnace shall not exceed 5min), dry it for 1h and take it out from the crucible, weigh precisely (W3) after cooling down and calculate by the following formula.

$$\text{Moisture Content of Desiccant \%} = \frac{W2-W3}{W2-W1} \times 100 \qquad \cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots(A.2)$$

A.3.3 Silica gel: Macropore molecular sieve(4: 6) mixture

Operate with reference to the method under the inspection item (A.3.2) of macropore molecular sieve, and calculate by the following formula.

$$\text{Moisture Content of Desiccant \%} = \frac{W2-W3}{W2-W1} \times 100 \quad -A \times 5 \qquad \cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots(A.3)$$

Where: A refers to the percentage of silica gel in the desiccant

A.4 Saturation moisture absorbed capacity

In an environment with relative humidity not more than 75%, take proper amount of the product (2 sachets for the specification below 3g, or 1 sachet for the specification of 3g and above), weigh precisely G0, place the desiccant sachet flatly on the watch glass (or other appropriate container), put it into the constant temperature humidity chamber with the temperature of (23±2) ℃ and the relative humidity of (75±5)%, take it out after 8th day, weigh G1, open the HDPE non-woven fabrics sachet, take out the desiccant which already absorbs moisture, wipe the sachet and measure the weight G2 together with the HDPE non-woven fabrics sachet. Calculate by the following formula

$$\text{Saturation moisture absorbed capacity \%} = \frac{G1-G0}{G0-G2} \times 100 \qquad \cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots(A.4)$$

A.5 Dropping Resistance

Take appropriate amount of the product, and drop onto the horizontal, rigid and smooth surface freely from the height of 1.2m.

A.6 Physical and Chemical Indicators of HDPE Non-woven Fabrics Sachet

A.6.1 Decolorization test

Take 5 sachets of the product, remove the desiccant, put them in 50ml water for soaking (60℃±2℃, 2h), and take the solvent of the same lot as the blank solution for comparison .

A.6.2 Fluorescence of HDPE Non-woven Fabrics Sachet

Take 10 sachets of the product, cut off the heat-sealed part, take out the desiccant, clean the surface of HDPE non-woven fabrics sachet, place the surface of sachet in contact with the pharmaceutical under the UV lamp with the wavelength of 365nm and 254nm for inspection; there shall be no flake fluorescent.

A.6.3 Residue on ignition

Take appropriate amount of the product, remove the desiccant, weigh 2g HDPE non-woven fabrics sachet and determine in accordance with the General Rules0841 of Part IV, Chinese Pharmacopoeia 2015.

A.6.4 Residual solvent content

(Apply to the desiccant sachet with painting) Take several HDPE non-woven fabrics sachets with desiccant removed (internal area is about 0.02m^2), and determine in accordance with the method I in YBB00312004-2015.

A.6.5 Heavy metal

A.6.5.1 Preparation of leaching solution

Take appropriate amount of the product, remove the desiccant, take 600cm2 (internal surface area) of HDPE non-woven fabrics sachet (cut into small pieces with length of 5cm and width of 0.3cm), put them in conical flask with cover, add appropriate amount of water, shake to wash the small pieces, discard the water and repeat the operations twice. Soak in (70℃±2℃) 200ml water for 24h after drying at 30℃-40℃, then take out and cool down to room temperature, supplement to the original volume with the aqueous solution for test from the same lot as the leaching solution and use the water from the same lot as the blank solution.

A.6.5.2 Detection of heavy metal

Measure out 20ml leaching solution precisely, add acetate buffer (pH3.5), and determine in accordance with the method I in General Rules 0821 of Part IV, Chinese Pharmacopoeia 2015.

A.6.6 Heat-sealing strength

Take appropriate amount of HDPE non-woven fabrics sachets with desiccant removed, and determine according to YBB00122003-2015.

A.6.7 Hydrostatic pressure

Take appropriate amount of materials for HDPE non-woven fabrics sachets, and determine according to GB/T 4744.

A.6.8 Tearing strength

Take appropriate amount of materials for HDPE non-woven fabrics sachets, and determine according to GB/T 455.

A.7 Microbial limit

Take 10 sachets of the product, put them in conical flask, add 100ml sodium chloride injection-peptone buffered solution (pH7.0), and shake out by 1min to obtain 1:10 solution for testing product. 10 solution for testing product. Determine according to the General Rules 1105 and 1106 of Part IV, Chinese Pharmacopoeia.

Standard of HDPE Non-woven Fabrics Desiccant Sachet for Oral Solid Preparation

Drafting Instruction

I. Overview

There has not been a complete standard in line with the development of modern pharmaceuticals for the desiccant manufacturers and users. Pharmacopoeia of the People's Republic of China (hereinafter referred to as “Chinese Pharmacopoeia”) stipulates some items focusing on the personal safety of from the perspective of drug use safety; although Packed Silica-gel Desiccant for Oral Solid Preparation (YBB00122005-2015) has made relatively detailed settings for desiccant inspection items, but there are many restrictions on packed desiccant in paper bags (such as easy tearing, not wear-resistant, etc.), which cannot meet the high demand of pharmaceutical manufacturers for desiccant. At present, the dominant desiccant sachets are packaged with HDPE non-woven fabrics in Europe and America. For the desiccant sachet, the part that comes into direct contact with the pharmaceutical is the HDPE non-woven fabrics sachet whose materials and characteristics will directly affect the quality of the pharmaceutical, thus causing harm to the pharmaceutical users.

As the raw material for pharmaceutical packaging material, the high density polyethylene (HDPE) has been widely applied both at home and abroad. It is non-toxic, tasteless, odorless, high in crystallinity and relatively high in density; relative molecular weight is often several hundred thousand to hundreds of thousands; the range of melt flow rate is narrow; it has relatively high rigidity and toughness, excellent mechanical strength and heat resistance, and good solvent resistance. The excellent performance of high density polyethylene provides favorable conditions for the production; for example, the melt index is moderate, the processing temperature is not high, it has the performance satisfying the pharmaceutical packaging requirement including non-toxicity, tastelessness, odorlessness, good toughness and surface hardness, tensile strength, stiffness and other mechanical strength etc., and complies with the requirement of the FDA and the European Union.

This standard is formulated for the purpose of effectively strengthening the quality control of desiccant sachet, ensuring the quality of pharmaceutical, and facilitating pharmaceutical enterprises to use desiccant sachet more confidently.

II. Description of standard project establishment and requirements

1. Name According to the preparation requirements of standard, the standards for pharmaceutical packaging materials shall be classified as per the materials, wherein one standard shall be prepared for each (variety) material and each purpose; the standard name shall follow the sequential format of administration route, pharmaceutical form, application and material. Therefore, the name of this standard is proposed as “HDPE Non-woven Fabrics Desiccant Sachet for Oral Solid Preparation”.

2. Appearance The appearance, which shall be described according to the production requirements of the product and in combination with the actual situation of the sample, can reflect the external quality of the product directly and comprehensively.

3. Moisture content of desiccant In addition to the molecular structure itself, the moisture absorption capacity of desiccant is also directly related to the water moisture of itself and the moisture contained in the packaging bag. The desiccant is also a kind of product easy to absorb moisture; thus, in order to control the moisture content absorbed by desiccant in the process of production and packaging and ensure the use effect in the future, this standard specifies “moisture content of desiccant” to control the desiccant. The HDPE non-woven fabrics sachets used in this standard are made of high density polyethylene and contain very little moisture. Meanwhile, HDPE cannot be dried for a long time at 190℃since the softening point of HDPE is relatively low, so that the method of weight reduction by desiccant heating is adopted hereby for inspection.

4. Saturation moisture absorbed capacity of desiccant sachet The saturation moisture absorbed capacity of desiccant sachet is an important indicator to investigate the moisture absorption capacity of desiccant. As compared with paper bag, the air permeability of HDPE non-woven fabrics sachets is relatively gentle. Therefore, its saturation moisture absorbed capacity is inspected by placing it along with HDPE non-woven fabrics sachets under the high-humidity condition for 8 days.

5. Dropping resistance The desiccant sachets are placed in the packaging of oral solid pharmaceutical preparations when they are used. If they drop during transportation, storage and use, the desiccant sachets without certain fastness will be damaged and the desiccant will leak out, causing contamination to the oral solid preparations. This standard specifies a "dropping resistance" item to evaluate the product endurance.

6. “Fluorescence of HDPE non-woven fabrics sachet”, “residue on ignition” and “heavy metal” In this standard, HDPE non-woven fabrics are used as the raw material for packaging bag of desiccant sachets. This

standard specifies three items, namely, “fluorescence of HDPE non-woven fabrics sachet”, “residue on ignition” and “heavy metal”, to test the performance of HDPE non-woven fabrics material.

7. “Heat-sealing strength” and “tearing strength” In order to prevent the contamination to the oral solid preparations caused by desiccant leakage, this standard specifies two items “heat-sealing strength” and “tearing strength” to test the performance of HDPE non-woven fabrics sachet materials.

8. “Hydrostatic pressure” In order to prevent the liquid water containing other substances from leaking from the desiccant sachet, thus causing contamination to the oral solid preparations. This standard specifies “hydrostatic pressure” item to test the performance of HDPE non-woven fabrics sachet materials.

9. “Residual solvent content” and “decolorization test” Considering that the wording “请勿食用” and “DO NOT EAT” are printed on the outside of the desiccant sachet, this standard specifies two items “residual solvent content” and “decolorization test” to test the performance of HDPE non-woven fabrics sachet materials.

10. Microbial limit In order to ensure that the desiccant sachet will not contaminate the oral solid preparations, this standard adopts the method specified in the Chinese Pharmacopoeia to test the microbial limit of the desiccant sachet. The total number of aerobic bacteria shall not exceed 1,000cfu/sachet; the total number of molds and yeasts shall not exceed 100cfu/sachet; no escherichia coli shall be detected in each bag.

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Secretariat of China National Pharmaceutical Packaging Association

Address: 2nd Floor, No. C23 Nanlishi Road, Xicheng District, Beijing Postal Code: 100045

Tel: 010-62267180 Fax: 010-62267098

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