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Selective guideline of laminated film(bag) for oral liquid dose

（Exposure Draft）

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Content

Preface

Introduction

Oral liquid dose includes oral solution, oral suspension, oral emulsion, syrup, mixture, liquor etc. The common packaging format for oral liquid dose includes glass bottle, plastic bottle, laminated sheet and laminated film.

Oral liquid dose packaging can be classified as multi dose packaging or single dose packaging due to packaging formats. Packaging selection is allowed with different structures according to the specification and requirements. It is suitable for single dose by using laminates with no more than 30ml volume.

Single dose packaging solves the problem of physical stability decrease and mildew within multi dose packaging after being opened many times. Single dose packaging gives accurate dosage without antibacterial agent in liquid formula, this can reduce the possibility of contamination to take dose as well as some conveniences such as storage, transportation, and easy open. The information of laminates with reverse printing can avoid the safety risk by using adhesive label in rigid packaging.

This guideline can be used as a reference by pharmaceutical applicants or drug marketing license holders (referred as pharmaceutical manufacturers) to research and develop new drugs, also to do package changing for commercialized drugs.

The manufacturer select laminates for oral liquid dose should meet the requirement of clinical applicability. Oral liquid dose is a low-risk product. Researches need to be implemented followed by the influence between liquid and packaging, also the possibility of interaction.

This guideline is complied with existing regulations, standards system and current cognitive level. Relevant contents will be adjusted appropriately while regulations and standards are improved continuously, also with the development of science and technology. It does not include the administration matter of registration and approval, it must not be referred as a regulation. This guideline should be used on the premise of following relevant regulations.

Selective guideline of laminated film(bag) for oral liquid dose

1 Scope

This guideline provides laminates characteristics, general structures, features as well as selection principles and requirements of oral liquid dose.

2 Terminology

2.1 Multi dose packaging

A container closure system without changing pharma's safety, dosage, quality or purity while the remain is taken out.

2.2 Single dose packaging

A closure system with opening feature to be taken once.

2.3 Laminated film(bag)

A closure system of bag format, one of common packaging forms for single dose oral liquid.

2.4 Risk source substance

This kind of substance refer to one or multiple chemical, physical or biological risk sources that have negative effects on the ecological environment. In this guideline, it specifically refers to small molecular monomers, additives, and unintentionally added substances (degradation products, reaction by-products, impurities, raw material additives, etc.) in the laminate, which may affect the effectiveness of drugs or the safety of patients when it exists in the drug.

2.5 Risk source control

When designing and producing the laminate, the manufacturer should select adhesive, ink system and dosage requirement for food and pharmaceutical products according to relevant laws and regulations, and also need to ensure the consistency of the formula of laminate (bag), the stability of production and processing technology. It should not only include the research data and evaluation report for the composition of packaging materials, adhesives, inks, production technologies, the quality standard of raw and auxiliary materials of the laminate (bag), and the effective control method for the risk source substance also should to be taken.

2.6 Risk source identification

According to the composition of the laminate and the product provided by the supplier, the drug marketing license holder should make a comprehensive analysis for the evaluation report from the laminated film(bag) supplier, preliminarily to obtain the type, usage and maximum

residue of the risk source substance, so as to judge whether they exceed the specific migration limit.

3 General structures and features of commonly used laminates

Single dose oral liquid can be packed within different composition laminate as a closure system. According to the characteristic of the preparation and the purpose of demand, the laminate with appropriate composition can be selected. The laminate with different compositions and structures have different performances, which can meet different applications for the drug marketing license holder.

General structures and features of commonly used laminates are shown in below Table 1.

Table 1 General structures and features of commonly used laminates

Serial number	**Structure of the laminate** note 1,2	**Transparency**	**Barrier function**	**Sterilization resistance** note 3
1	PET/AL/PE	Opaque	High barrier	Generally not above 115 ℃
2	PET/AL/PET/PE		High barrier	
3	PET/PE/AL/PE/PE		High barrier	
4	PET/AL/OPA/PE		High barrier	
5	PET/MPET/PE		Medium / high barrier	
6	OPP/MOPP/PE		Medium / high barrier	
7	PET/AL/CPP	Opaque	High barrier	Withstand 121 ℃

8	PET/OPA/AL/CPP		High barrier	
9	PET/AL/PET/CPP		High barrier	
10	SPET/OPA/CPP	Transparent	High barrier	Withstand 121 ℃
11	OPP/SiO_x-OPP/CPP	Transparent	High barrier	Not less than 115 ℃
	PET/Al_2O_3-PET/CPP		High barrier	

Note 1: Polyethylene terephthalate (PET) is abbreviated to PET, polypropylene is abbreviated to PP, polyethylene is abbreviated to PE, oriented polypropylene is abbreviated to OPP, oriented polyamide (nylon) is abbreviated to OPA, cast polypropylene is abbreviated to CPP, metalized polyester is abbreviated to MPET, metalized oriented polypropylene is abbreviated to MOPP, silicon oxide coated oriented polypropylene is abbreviated to SiO_x-OPP, aluminum oxide coated polyester is abbreviated to Al_2O_3-PET, aluminum layer is abbreviated to AL, silicon oxide coated polyester is abbreviated to SPET.

Note 2: Due to the difference of raw materials and production processes used in the production of the laminate by the packaging manufacturing enterprise, the performance of the finished product with the same structure are also different. The drug marketing license holder should select the laminate with appropriate composition and thickness according to the actual demand, process, equipment and other factors.

Note 3: For the laminate with the same structure, the sterilization resistance of the laminated film(bag) are different due to the different film source, supplier grade and process technology, which may not reach the temperature that listed in this table. The drug marketing license holder need to verify the parameter.

4 Selection principle

The selection of laminate for single dose oral liquid should be fully evaluated from the aspect of safety, applicability, stability, functionality, protection and convenience.

4.1 Drug applicability. The laminate for oral liquid dose can be selected according to the drug characteristic from the drug manufacturer, drug process requirement, proposed expiration date, clinical demand for the variety of the laminate with different compositions.

4.2 Production environmental requirement. The production environment from the laminate production enterprise shall meet the production environmental requirement from the drug manufacturer. Lower biological load can be achieved by controlling the production process and environment.

4.3 Protection requirement. According to the characteristic and the requirement of single dose oral liquid, the laminate with appropriate composition and structure should be selected. For example, if the liquid is required to be protected from light, the laminate should be made of aluminum or metallized material as middle layer. If the liquid needs high barrier (to prevent the loss of water and ethanol), the structure should be consist of aluminum, metalized film or aluminum oxide coating film as a barrier layer.

4.4 Sterilization resistance. If process uses hot filling or/and high temperature sterilization (disinfection), the laminate (bag) have the inner layer with different heat resistance level should be selected.

4.5 Convenience of use. If the convenience of opening is needed in clinic, different opening methods should be selected.

4.6 Safety requirement. See 5.2

5 Technical requirements

5.1 Compliance

5.1.1 The laminate manufacturer should comply with relevant requirement of quality assurance system, and the drug marketing license holder should audit them to ensure they meet the pharmaceutical requirement.

5.1.2 The laminate (bag) should meet the requirement of corresponding quality standards.

5.1.3 The stability study of the laminate (bag) should be conducted in accordance with *The Guiding Principle for the Research of the Self-stability of Plastic and Rubber Pharmaceutical Packaging Materials (exposure draft)* issued by the National Pharmacopoeia Council to determine the time limit of quality stability. The time limit for stability should be longer than the time limit requirement for the drug product stability.

5.2 Safety

5.2.1 The additive used in material of the laminate should meet the pharmaceutical requirement, and the requirement of *GB9685-2016 Food Safety Standard-The Standard for the Use of Additives for Food Contact Materials and Products* and its supplementary notices can be adopted as well. If using the material and the additive which not included in the standard, the safety assessment shall be conducted according to the new material.

5.2.2 The safety evaluation should include the recognition and identification of the risk source substance, the confirmation of their usage amount and maximum residue, and the judgment of whether the maximum migration amount of these risk source substances exceed the specific migration limit in the regulation.

5.2.3 The identification of risk source substances should refer to *GB9685-2016 National Food Safety Standard-The Standard for the Use of Additives for Food Contact Materials and Products* and its supplementary notices. The research procedure, test condition and relevant detection method can refer to ***Risk source assessment of the laminated film (bag) for oral liquid dose,*** see Appendix 2.

5.2.4 Safety studies for the laminate should be carried out according to the real situation. If the prescription contain alcohol, extraction studies should be carried out according to the prescription ingredient under enhanced conditions to determine whether risk source substances are within acceptable range. If the risk source substance is within the acceptable range, appropriate compatibility study shall be conducted as necessary after the evaluation. If the risk source substance exceeds the acceptable range, it is recommended to replace the laminate.

5.3 Applicability of production process

5.3.1 The applicability between the laminate and the process of oral liquid dose should be concerned. If oral liquid dose is sterilized, the applicability of the sterilization for the laminate should be considered.

5.3.2 Process conformity study. The suitability of equipment should be considered during filling, disinfection or sterilization (if applicable) and packaging process. The seal of the bag shall be smooth, with clear indentation or embossing, without wrinkles, burning or pressing through. The production date, batch number and identification system on the bag shall be clear and firm, and the printing (opening) position shall be consistent. The sealing strength, sealing width and loading deviation should meet the requirement of process standards.

5.3.3 Adsorption and residual effects. Full consideration should be given to the possible effects of both adsorption and residue on the accuracy of dosing.

Adsorption influence. Focus on physical adsorption, mainly adsorption by the inner layer material, such as the laminate adsorpt the liquid medicine to reduce its effective components.

Residual influence. The liquid residue is related to the design of the laminated film(bag), and also related to the structure or the shape design of the container, such as liquid residue in the flow channel during the filling process, or the design of the bag with dead corners.

5.3.4 Drying form. Using different drying forms for the residue of the volatile substance from the laminate has a direct impact. Appropriate parameter for drying form should be selected, such as, drying temperature, time and vacuum degree, etc.

5.3.5 Transportation mode. The influence of finished product transportation on the appearance of the bag shape. No risk of collision or extrusion.

5.3.6 Storage condition. The influence of temperature and air pressure in different areas on the laminate should be considered.

5.4 Functional evaluation

5.4.1 Packaging format. Stick pack is generally used. If easy opening design is involved, the size or range of tear line (if applicable), tear location and tear strength should be considered.

5.4.2 Pressure resistance. The pressure resistance can be carried out by the drop resistance test. The test can refer to the standard *GB/T 17313-2009 Bag Forming-filling-sealing Machine General Technical Conditions*.

5.4.3 Evaluation of the integrity and clarity of the inner label. The content of the inner label should meet relevant regulations and requirements of integrity and clarity. The influence of printing on the barrier of the laminate should be considered in the process of online label printing. The effect of sterilization on the articulation of printing characters should be considered. The label for the laminate shall be legible. Whether the printing can be wiped off by non-destructive ways also should be considered.

5.5 Protection

Seal integrity, heat seal strength, barrier properties, etc. The influence of vibration, temperature and air pressure on finished products during storage and transportation in different regions should be considered.

5.6 Convenience

The laminate should have convenient opening performance. The opening performance, such as opening mode, force and quality all should meet the requirement, such as, no obvious angel hair

after opening, no splash or drip during the opening process. The friendly way for elder and child to take out medicine should be considered as needed.

5.7 Quality standard suggestion

5.7.1 Item setting

The setting of quality standard test items for the laminate (bag) should reflect the change of product quality. The control item generally includes but are not limited to appearance, identification, water vapor penetration for the laminated film, water vapor penetration for the laminate bag (if applicable), solvent residue, composition of the laminate, microbial limit, abnormal toxicity, functionality, protection and convenience, the risk source substance from the laminated film(bag) (if applicable), such as, aromatic primary amine, epoxy silane coupling agent, etc.

5.7.2 The dissolved substance test for the laminate bag

The laminated film(bag) should be compatible with the formulation, relevant process and packaging specifications of the oral liquid dose. The test and inspection item of dissolved substances should include but not limited to clarity, absorbance, pH change value, readily oxidizable substance, nonvolatile substances and heavy metals. The quality standard includes testing items, analytical methods and acceptable standards. Compliance with the standard means that test result meets the acceptable standard according to the proposed analytical method. The test item of the dissolved substance for the laminated film refer to the test item for the laminate bag.

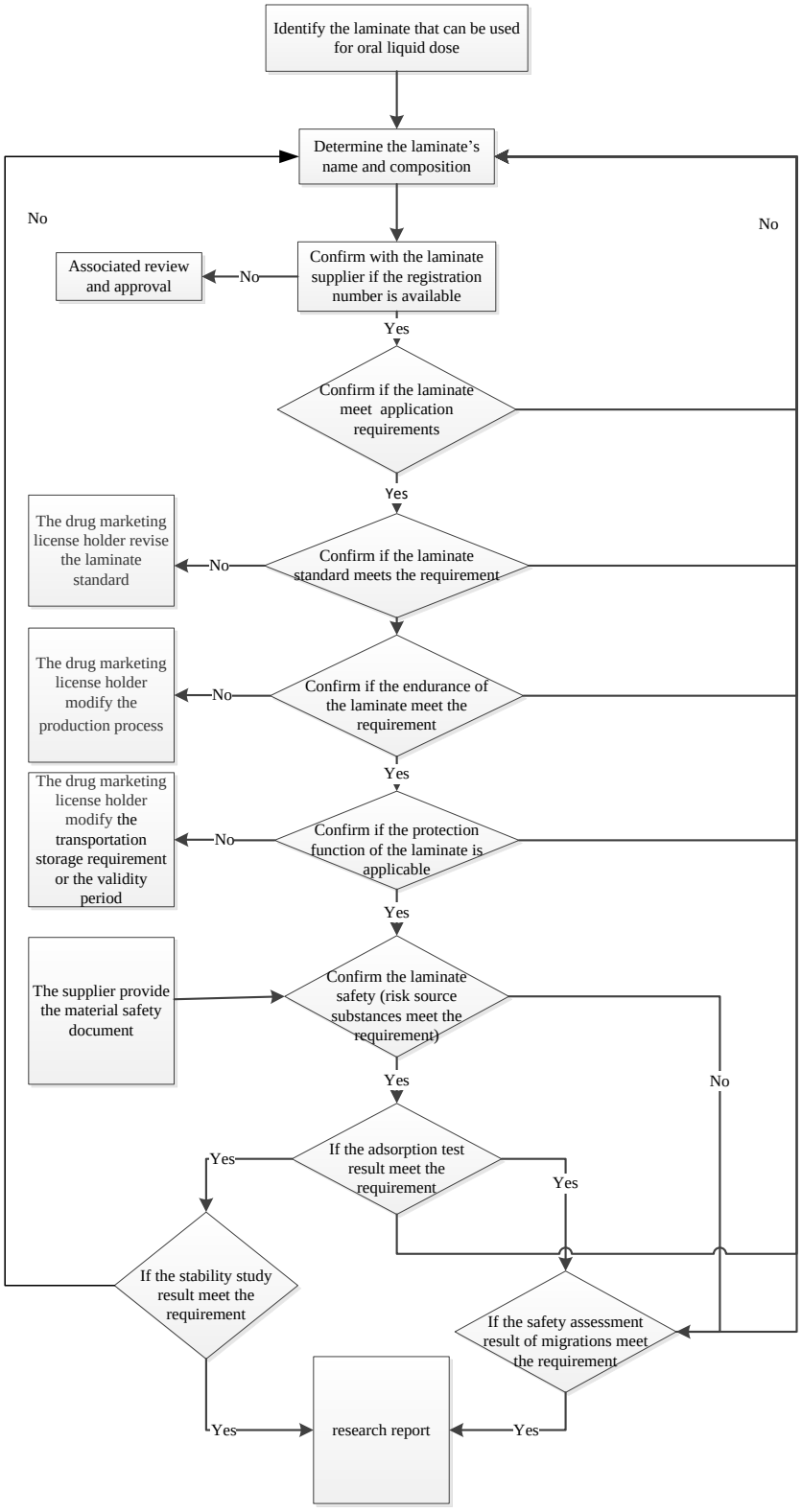
5.7.3 Stability study

The stability study is conducted in accordance with the requirement of *The Guideline for Stability Tests of API Drugs and Preparations 9001, Part IV, Chinese Pharmacopoeia 2020*, and it also can be carried out according to the technical guideline for stability studies by CDE.

The sample used for stability tests should be selected with complete packaging and it should be the same or similar to marketed or commercially produced products.

Appendix 1 Decision tree of laminate selection for oral liquid dose

Decision tree of laminate selection for oral liquid dose



Appendix 2 Risk source assessment of laminated film(bag) for oral liquid dose

1 The origin of the risk source substance

The risk source of the laminate for single dose oral liquid may come from raw materials (such as, film, adhesive and ink) of the laminate and the production processing agent. According to the example in Table 2 *The Name and The Limit of The Common Risk Source Substance*, if the material and the structure of the laminate and the production process are different, the type and quantity of the migration substance are different. Small molecular monomers, additives, agents and unintentionally added substances (such as reaction by-products, degradation products, impurities, etc.) from adhesives, inks, materials are the main risk sources. These risk sources between different materials either different laminated film(bag) supplier are different. So it's necessary to identify the risk source substance according to the origin.

The material of the laminate (bag) shall respectively comply with relevant provisions of the national food safety standards, such as GB 4806.1-2016 *National Food Safety Standard General Safety Requirements for Food Contact Materials and Products*, GB 4806.7-2016 *National Food Safety Standard Plastic Materials and Products for Food Contact*, GB 4806.9-2016 *National Food Safety Standard Metal Materials and Products for Food Contact*, etc. For the standard of the laminate, ink and adhesive, they are still the draft, please pay attention to the progress timely.

2 Sample preparation for migration test of risk source substances

Generally, for the risk source substance in products, the migration test is usually used to identify and evaluate the migration substance. For oral liquid dose which belongs to low-risk type, the method from relevant *National Food Safety Standards* can be used to identify and evaluate the migration substance. Using unified test method can ensure the test method is scientific, reasonable and unified. This way also can reduce nonstandard test methods and quantities, and the test result can be compared with each other, so as to select more suitable laminate structure, formula and supplier.

2.1 The sample are pretreated in accordance with the requirement of *GB 5009.156-2016 National Food Safety Standard-General Rules for Migration Test of Food Contact Materials and Products*, and *GB 31604.1-2015 National Food Safety Standard-General Rules for Migration Test of Food Contact Materials and Products*. If above regulations are not applicable, the pharmaceutical preparation manufacturer may determine some reasonable methods or refer to other more appropriate pretreatment procedures.

2.1.1 Sample pretreatment. The laminate (bag) should be clean and pollution-free. They usually should be consistent with production use.

2.1.2 Test sample preparation.

a. The laminated film. Take the rolling laminated film randomly, discard the first 0.5 meters, cut off the appropriate size as required, and record the contact area (S).

b. The laminate bag. The number of laminate bags needed is randomly selected, and the internal surface area (S) is calculated according to the laminate bag with a larger influence area to volume ratio that the preparation would contact.

2.1.3 Selection of extraction solution. Simulate the actual situation of drugs, such as 4% acetic acid solution, 20% ethanol solution, 50% ethanol solution, oral liquid dose carrier solution or blank preparation without drugs (if applicable) or drug solution can be used specifically.

2.1.4 Preparation of extraction solution

a. Generally, the ratio of the contact area (s) of the sample to the volume (V) of the extraction solution (S/V) is 6 dm^2:1L. The extraction solution should be as strict as possible or close to the actual situation. If it is not consistent with the actual situation, the test result should be converted to the actual S /V situation.

b. The drug marketing license holder may use the drug product of the laminate specification with high exposure impact and carry out the exposure impact calculation.

2.1.5 Filling method

a. The laminate use migration test pool method. Cut off and place appropriate size of the laminate according to the operation method of the test device, then add specified volume of the extraction solution.

b. The laminate bag use pouch-making test method. Take the bag to add specified volume of the extraction solution and take physical method to expel the air in the bag. After adding the extraction solution, the bag is sealed. Place the test sample properly to make sure the sample is in full contact with the extraction solution.

2.2 The specific migration test condition may be carried out in accordance with the *GB31604.1-2015 National Food Safety Standard-General Rules for Migration Test of Food Contact Materials and Products*.

2.2.1 The accelerated test condition for the laminate. For the oral liquid dose stored at room temperature for a long time, the test condition is generally recommended as, 60℃,10 days. For the oral liquid dose that need to be sterilized at high temperature, it is recommended to use more

stringent condition, such as, 121℃ for 0.5 hour. More suitable accelerated test conditions can also be selected according to the actual situation of the preparation.

2.2.2 The laminated film(bag) and the sample filled with the extraction solution or the stability test sample should use accelerated test conditions, such as 60 ℃ for 10 days, then let the sample cool. Or it can be conducted according to *The Guideline for Stability Tests of API Drugs and Preparations 9001, Part IV, Chinese Pharmacopoeia 2020.*

2.2.3 If the laminated film(bag) is expected to be sterilized, take the laminate bag filled with specified volume of the extraction solution, and take physical method to expel the air in the bag. Seal the bag then use the test condition, such as 121 ℃, 0.5 h, let the sample cool then use the accelerated test condition, such as 60 ℃, 10 days, let the sample cool (if use the sample filled with oral liquid dose or the stability test sample could be exempt from this step). Or it can be conducted according to the guiding principle of stability test of raw materials and preparations (*The Guideline for Stability Tests of API Drugs and Preparations 9001, Part IV, Chinese Pharmacopoeia 2020*).

3 Identification of risk source substances

According to the common risk source substance and their limits from the laminate with different compositions (Table 2), and also according to *GB9685-2016 National Food Safety Standard-Standard for the Use of Additives for Food Contact Materials and Products* and its supplementary notices, appropriate and specific detection methods should be selected.

The common test equipment includes gas chromatography-mass spectrometry (GC-MS), liquid chromatography-mass spectrometry (LC-MS), ion chromatography (IC), inductively coupled plasma atomic emission spectrometry (ICP), atomic absorption spectrometry (AAS), etc.

According to the limit requirement and combine with the daily dose of the drug, the sensitivity of the required analysis method should be selected. According to *the Analytical Method Validation Guidelines* (*9101, Part IV, Chinese Pharmacopoeia 2020*) to conduct the methodology validation for specificity, accuracy, precision, linearity, limit of detection and limit of quantification.

The migration test method related to the national food safety standard are shown in Table 3 *The Analysis Method for Risk Source Substances*, and the methodological confirmation can be conducted according to *the Guideline for Identification of Analytical Methods* (*9099, Part IV, Chinese Pharmacopoeia 2020*).

The guideline lists the name and the limit of common risk sources from the laminate for single dose oral liquid formulations, as shown in Table 2 (Note: the limit of common risk sources could refer to *GB9685-2016 National Food Safety Standard-Standard for the Use of Additives for Food Contact Materials and Products* and its supplementary notices).

4 Confirmation the limit of risk source substances

According to the information of risk source substances obtained from the specific migration test, necessary compound attribution or structure identification shall be carried out to analyze and summarize their content. Risk source substances can be analyzed using the method listed in Table 3. And according to *GB9685-2016 National Food Safety Standard-Standard for the Use of Additives for Food Contact Materials and Products* and its supplementary notices to determine if the test result of risk source substances comply with the regulation.

Table 2 The name and the limit of the common risk source substance

Material Category	**Substance Name**	**CAS No.**	**Maximum migration limit or maximum residue (mg/kg)**
Polyester film (PET)	Glycol	107-21-1	30
	Terephthalic acid	100-21-0	7.5
	Antimony trioxide	1309-64-4	0.04
	Diethylene glycol	111-46-6	30
	Triethyl phosphate	78-40-0	0.01
	Antimony glycol	29736-75-2	0.01
	Isophthalic acid	121-91-5	5
	2,2-Dimethyl-1,3-propanediol	126-30-7	0.05
Polyolefin	Octadecyl-3 - (3,5-di-tert-butyl-4-hydroxyphenyl)	2082-79-3	6

film (PE, PP)	propionate		
	1-Hexene	592-41-6	3
	1-Octene	111-66-0	15
	2,6-Di-tert-butyl-4-methylphenol	128-37-0	3
	1,3,5-Tris (3,5-di-tert-butyl-4-hydroxyphenyl) - 1,3,5-triazine-2,4,6 (1H, 2h, 3H) - trione)	27676-62-6	5
	Hexafluoropropylene	116-15-4	0.01
	Maleic anhydride	108-31-6	30
	Tris (nonylphenol) phosphite	26523-78-4	non-detectable (nonylphenol, SML, detection limit is 0.01 mg/kg)
Polyamide film (OPA)	Caprolactam	105-60-2	15
	1, 3-m-phenyldimethylamine	1477-55-0	0.05
Ink	2-Isopropylthioxanthone	5495-84-1	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	4-Isopropylthioxanthone	83846-86-0	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	Nitrosamines	——	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	Total aromatic primary amines	——	non-detectable (detection limit is 0.01 mg/kg)
	4-Aminobiphenyl	92-67-1	Not listed in the positive list of regulations,

			non-detectable (detection limit is 0.01 mg/kg)
	Benzidine	92-87-5	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	4-Chloro-o-toluidine	95-69-2	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	2-Naphthylamine	91-59-8	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	O-aminoazotoluene	97-56-3	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	2-Amino-4-nitrotoluene	99-55-8	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	Dichloroaniline	106-47-8	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	2,4-Diaminoanisole	615-05-4	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	4,4'-Methylenedianiline	101-77-9	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)

	3,3'-Dichlorobenzidine	91-94-1	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	3,3′-Dimethoxybenzidine	119-90-4	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	3,3'-Dimethyl-[1,1'-biphenyl]-4,4'-Diamine(O-Tolidine)	119-93-7	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	4,4'-diamino-3,3'-dimethyldiphenylmethane	838-88-0	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	3-Amino p-toluene methyl ether	120-71-8	Not listed in the positive list of regulations, not detected (detection limit is 0.01 mg/kg)
	4,4'- Methylene bis (2-chloroaniline)	101-14-4	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	4,4'-Oxydianiline	101-80-4	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	4,4-diaminodiphenylsulphide	139-65-1	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	O-toluidine	95-53-4	Not listed in the positive

			list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	2,4-Diaminotoluene	95-80-7	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	2,4,5-Trimethylaniline	137-17-7	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	P-aminoazobenzene	60-09-3	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	O-methoxyaniline	90-04-0	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	2,4-Dimethyl aniline	95-68-1	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	2,6-Dimethylaniline	87-62-7	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	Aniline	62-53-3	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg）
	P-phenylenediamine	106-50-3	Not listed in the positive list of regulations, non-detectable (detection

			limit is 0.01 mg/kg)
	Polycyclic aromatic compounds	——	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
Adhesive	2,2-Dimethyl-1,3-propanediol	126-30-7	0.05
	1,1,1-Trimethylolpropane	77-99-6	6
	1,2-Benzoisothiazole-3-one	2634-33-5	1.2
	1,4-Butanediol	110-63-4	5
	1,6-Hexanediol	629-11-8	0.05
	1,6-Hexamethylene diisocyanate	822-06-0	Non-detectable (detection limit is 0.01 mg/kg); 1 (isocyanate residue)
	2,2-Dimethyl-1,3-propanediol	126-30-7	0.05
	2,2-Bis-(4-glycinoxyphenyl) propane	1675-54-3	3(2,2-bis(4-hydroxyphenyl) propane: SML); 1 (ethylene oxide: QM) or non-detectable (ethylene oxide: SML, detection limit is 0.01 mg/kg)
	3-(2,3-epoxypropoxy) propyltrimethoxysilane	2530-83-8	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	3-Glycidyl ether oxypropyl triethoxysilane	2602-34-8	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	Trimethoxy [2 - (7-Oxabicyclo [4.1.0] hept-3-yl) ethyl] silane	3388-04-3	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)

	4,4'-Thiobis(6-tert-butyl-m-cresol)	96-69-5	0.48
	Hydroxyethyl acrylate	818-61-1	6
	Terephthalic acid	100-21-0	7.5
	1-isocyanato-2-[(4-isocyanatophenyl)methyl]-benzen	5873-54-1	Non-detectable (detection limit is 0.01 mg/kg); 1 (isocyanate residue)
	Diethylene glycol	111-46-6	30
	Di-n-octyltin dilaurate	3648-18-8	0.006
	Propylene oxide	75-56-9	1(residue) or non-detectable (detection limit is 0.01 mg / kg)
	Epichlorohydrin	106-89-8	Non-detectable (detection limit is 0.01 mg/kg);1(residue)
	Caprolactam	105-60-2	15
	Toluene-2,4-diisocyanate	584-84-9	Non-detectable (detection limit is 0.01 mg/kg); 1 (isocyanate residue)
	Toluene-2,6-diisocyanate	0091-08-7	Non-detectable (detection limit is 0.01 mg/kg); 1 (isocyanate residue)
	Isophthalic acid	121-91-5	5
	Octadecyl-3 - (3,5-di-tert-butyl-4-hydroxyphenyl) propionate	2082-79-3	6
	2,6-Di-tert-butyl-4-methylphenol	128-37-0	3
	Trimethylolpropane	77-99-6	6
	Bisphenol A	80-05-7	0.6
	Stannous octanoate	301-10-0	0.18
	Neopentyl glycol	126-30-7	0.05

	glycol	107-21-1	30
	Vinyl acetate	108-05-4	12
	Isophorone diisocyanate	4098-71-9	Non-detectable (detection limit is 0.01 mg/kg); 1 (isocyanate residue)
	Acrylic acid	79-10-7	6
	methacrylic acid	79-41-4	6
	Vinyl acetate	108-05-4	12
	Maleic acid	110-16-7	30
	Butyl acrylate	141-32-2	6
	1-Isocyanate-2-[(4-isocyanatophenyl) methyl] benzene	5873-54-1	Non-detectable (detection limit is 0.01 mg/kg); 1 (isocyanate residue)
	4,4'-Diphenylmethane diisocyanate	101-68-8	Non-detectable (detection limit is 0.01 mg/kg); 1 (isocyanate residue)
	Diethylene glycol	111-46-6	30
	Isophorone diisocyanate	4098-71-9	Non-detectable (detection limit is 0.01 mg/kg); 1 (isocyanate residue)
	Dibutyltin dilaurate	77-58-7	0.18
Laminate	Aromatic primary amine compounds	The list is as follows	Non-detectable (detection limit is 0.01 mg/kg)
	4-Aminobiphenyl	92-67-1	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	Benzidine	92-87-5	Not listed in the positive list of regulations, non-detectable (detection

			limit is 0.01 mg/kg)
	4-Chloro-o-toluidine	95-69-2	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	2-Naphthylamine	91-59-8	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	O-aminoazotoluene	97-56-3	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	2-Amino-4-nitrotoluene	99-55-8	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	Dichloroaniline	106-47-8	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	2,4-Diaminoanisole	615-05-4	Not listed in the positive list of regulations, non-detectable (detection limit 0.01 mg/kg)
	4,4'-Methylenedianiline	101-77-9	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	3,3'-Dichlorobenzidine	91-94-1	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)

	3,3′-Dimethoxybenzidine	119-90-4	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	3,3'-Dimethyl-[1,1'-biphenyl]-4,4'-Diamine(O-Tolidine)	119-93-7	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	4,4'-diamino-3,3'-dimethyldiphenylmethane	838-88-0	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	3-Amino p-toluene methyl ether	120-71-8	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	4,4'-Methylene bis(2-chloroaniline)	101-14-4	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	4,4'-Oxydianiline	101-80-4	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	4,4-diaminodiphenylsulphide	139-65-1	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	O-toluidine	95-53-4	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	2,4-Diaminotoluene	95-80-7	Not listed in the positive

			list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	2,4,5-Trimethylaniline	137-17-7	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	P-aminoazobenzene	60-09-3	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	O-methoxyaniline	90-04-0	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	2,4-Dimethyl aniline	95-68-1	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	2,6-Dimethylaniline	87-62-7	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	Aniline	62-53-3	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	P-phenylenediamine	106-50-3	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
Unintentional added	Phthalate esters (commonly 18 kinds)	The list is as follows	See the following remark

substances	Dimethyl phthalate (DMP)	131-11-3	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	Diethyl phthalate (DEP)	84-66-2	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	Diallyl phthalate (DAP)	131-17-9	non-detectable (detection limit is 0.01 mg/kg)
	Diisobutyl phthalate (DIBP)	84-69-5	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	Dibutyl phthalate (DBP)	84-74-2	0.3
	Di (2-methoxy) ethyl phthalate (DMEP)	117-82-8	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	Bis (4-methyl-2-pentyl) phthalate (BMPP)	146-50-9	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	Di (2-ethoxy) ethyl phthalate (DEEP)	605-54-9	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	Dipentyl phthalate (DPP)	131-18-0	Not listed in the positive list of regulations, non-detectable (detection limit is0.01 mg/kg)
	Dihexyl phthalate (DHXP)	84-75-3	Not listed in the positive list of regulations,

			non-detectable (detection limit 0.01 mg/kg)
	Butylbenzyl phthalate (BBP)	85-68-7	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	Bis (2-butoxy) ethyl phthalate (DBEP)	117-83-9	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	Dicyclohexyl phthalate (DCHP)	84-61-7	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	Di (2-ethyl) hexyl phthalate (DEHP)	117-81-7	1.5
	Diphenyl phthalate (DPHP)	84-62-8	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	Di-n-octyl phthalate (DNOP)	117-84-0	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)
	Diisoononyl phthalate (DINP)	28553-12-0	9
	Dinonyl phthalate (DNP)	84-76-4	Not listed in the positive list of regulations, non-detectable (detection limit is 0.01 mg/kg)

Table 3 The analysis method for risk source substances

Name of risk substance	Standard Name	Method Standard No
1,3-Dimethylamine	The migration test of 1,3-Dimethylamine	GB 31604.11-2016
Terephthalic acid	The migration test of terephthalic acid	GB 31604.21-2016
Di (2-ethyl) hexyl adipate	Determination of di (2-ethyl) hexyl adipate and its migration test	GB 31604.28-2016
Phthalate esters	Determination of phthalate esters and its migration test	GB 31604.30-2016
Primary aromatic amines	The migration test of aromatic primary amines	GB 31604.52-2021
Ethylene glycol and diethylene glycol	The migration test of ethylene glycol and diethylene glycol	GB 31604.44-2016
Caprolactam	Determination of caprolactam and its migration test	GB 31604.19-2016
Vinyl acetate	The migration test of vinyl acetate	GB 31604.20-2016
Epichlorohydrin	Determination of epichlorohydrin and its migration test	GB 31604.26-2016
Isocyanate	Determination of isocyanate	GB 31604.45-2016
Antimony (Sb)	Determination of As, Cd, Cr, Pb and the migration test of As, Cd, Cr, Ni, Pb, Sb, Zn	GB 31604.49-2016