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Controllable Additives Used in Plastic Pharmaceutical Packaging Materials and Application Guidance

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Foreword

This standard is drafted in accordance with the rules listed in GB/T 1.1-2020 Directives for standardization- Part 1: Rules for the structure and drafting of standardizing documents.

Please be aware that some contents in this standard may be patentable. China National Pharmaceutical Packaging Association shall not be held responsibility for identifying patent rights.

This standard was proposed by and is under the jurisdiction of China National Pharmaceutical Packaging Association.

Units participating in the drafting of the standards:

Main drafters of the standard:

Introduction

Plastic additives are chemical substances that are intentionally added to plastic materials to achieve a physical or chemical effect during processing of the plastic or in the final material or container. They may consist of a single chemical substance, a polymeric substance or a defined mixture of different. The types and amounts of plastic additives directly affect the medicine's quality and the patient's safety. Annex 4 of the State Food and Drug Administration [2012] No. 267 Technical Guideline for Research on Compatibility of Chemical Injection and Plastic Packaging Materials(Trial) lists the commonly used additives in injection packaging for polyethylene and polypropylene plastics and the additives permitted content in plastics. China National Standard GB 9685-2016 National Food Safety Standard: Standard for the Use of Additives in Food Contact Materials and Articles and the related announcements list the allowable additives with their use requirements that can be used in food contact plastic materials and their products. At present, there is no complete list and use requirements of additives for plastic pharmaceutical packaging materials in China.

European Pharmacopoeia (EP) series general chapter 3.1 materials used for the manufacture of containers list 48 additives and their maximum permitted content used in 7 plastic materials, 27 of which are European Pharmacopoeia Plastic Additives as described in general chapter 3.1.13. EP General Chapters require that unless otherwise justified and authorized, additives are chosen from the list, and meet the limit requirement specified for each substance. United States Pharmacopoeia (USP) General Chapter <661.1> Plastic Additives for Plastic Component Materials lists 27 additives and limit requirements for 9 plastic materials. These additives information are important references for appendix A of this standard.

This standard introduces the commonly used additives for plastic pharmaceutical packaging materials, summarizes the additives and usage limitation for plastic pharmaceutical packaging materials recorded in domestic and foreign pharmacopoeias, and partially adopts food contact materials and product additives for oral preparations. The additives listed in this standard are consistent with the CDE "Technical Guideline for Research on Compatibility of Chemical Injection and Plastic Packaging Materials(Trial)", and a more complete additives and use requirements for plastic pharmaceutical packaging materials is listed with the reference of domestic food standards and domestic and foreign

pharmacopoeia standards. This standard provides guidance for the application of additives for plastic pharmaceutical packaging materials.

Safety is the primary condition for selecting additives for plastic pharmaceutical packaging materials. The assessment is described in the further application considerations of additives for plastic pharmaceutical packaging materials in Chapter 6 of this standard. This standard is used to guide packaging material manufacturers to select the types and use contents of additives for plastic pharmaceutical packaging materials. The maximum permitted content is the maximum allowable use content. If a compatibility study is required, the maximum permitted content cannot replace the compatibility study.

This standard may not cover all additives used in plastic pharmaceutical packaging materials, and with the continuous development of science and technology, additives not included in the list may will be used, and the relevant content of this standard will also be adjusted appropriately. This standard doesn't include the administrative matter of registration and approval, so it must not be referred as a regulation and should be used on the premise of relevant regulations.

Controllable Additives Used in Plastic Pharmaceutical Packaging Materials and Application Guidance

1. Scope

This standard provides the basic information, controllable list and use requirements of additives used in plastic pharmaceutical packaging materials.

The controllable list of the additives included in this standard is a summary of the additives used in plastics, which are specified in the main regulatory documents at home and abroad.

This standard provides use method of additives used in pharmaceutical packaging materials for pharmaceutical packaging materials manufacturing enterprises. The plastic materials include polyethylene (PE), polypropylene (PP), polyethylene terephthalate (PET), polycarbonate (PC), cyclic olefins (COC, COP, etc.), polyvinyl chloride (PVC), polyvinylidene chloride (PVDC), poly (ethylene - vinyl acetate) (EVA), polyamide (nylon PA), etc., and the composite materials formed by compounding of the materials. This standard is a reference for preparation enterprises.

2. Normative references

The following documents are essential for the application of this standard. For reference documents with reference dates, only the version of the reference date applies to this standard. The latest version (including all amendments) of any reference document with no dates also applies to this standard.

GB 9685-2016 National Standards for Food Safety: Standard for the Use of Additives in Food Contact Materials and Articles

NMPA-I-[2012] No. 267 Technical Guideline for Research on Compatibility of Chemical Injection and Plastic Packaging Materials(Trial)

3. Terminology

The following terms and definitions are applicable to this document.

3.1 Plastic additives

Chemical substances that are intentionally added to plastic materials to achieve a physical or chemical effect during processing of the plastic or in the final material or container. They may consist of a single chemical substance, a polymeric substance or a defined mixture of different.(EP 11 general chapter 3.1.13)

3.2 Maximum permitted content

The maximum permitted quantity of a certain additive or a certain class of additives added during the production of a plastic pharmaceutical packaging materials, expressed as a mass fraction (%).

4. Classification of additives used in plastic pharmaceutical packaging materials

Depending on the intended use of a material, they may contain additives to optimize their processing or their chemical, physical and mechanical properties. Substances present that have not been added intentionally are considered to be impurities and include reaction and degradation products, which may be limited by a suitable specification.

Types of additives commonly used in plastic pharmaceutical packaging materials mainly include antioxidants, light stabilizers, heat stabilizers, plasticizers, antistatic agents, colorants, process aids and others (such as nucleating agents, impact modifiers) etc.

Antioxidants and light stabilizers: plastic aids that are added to plastic materials to effectively inhibit or reduce the thermal oxidation and light oxidation reaction rate of plastic macromolecules, significantly improve the heat resistance and light resistance of plastic materials, delay the degradation and aging process of plastic materials, and prolong the service life of plastic products.

Heat stabilizers: aids added to prevent plastics from degrading due to heat during high-temperature processing, which is mainly used in PVC.

Plasticizers: a class of fine chemical products that can increase the plasticity of a polymer system. It's the most important additive used during processing of polymer materials, especially of PVC plastics, to enhance the flexibility and facilitate processing.

Antistatic agents: chemicals that reduce the surface resistance of plastic objects and evacuate the surface charge of objects. With high surface resistivity and low permittivity, the plastic surface is inclined to have charge accumulated and therefore antistatic agents are needed to solve the problem caused by static electricity.

Colorants: additives that can change the color of plastics into various colors such as white, yellow, green, blue, red, black, etc. Colorants can be classified into two categories according to the different physical properties: pigments that are insoluble in the medium used and dyes that are soluble in the medium used.

Processing aids: usually refer to additives used to improve the processing performance of plastics. They mainly take effect when the polymer substrate is molten, including compounds that reduce the

viscosity of the molten object without increasing the quantity of the plasticizer (viscosity inhibitors), compounds that offer additional stability by increasing the internal adhesion of the heterogeneous system or emulsion (emulsifiers/surfactants), or an aid that offers lubrication during processing(slip agents), etc.

5. List and application of controllable additives for plastic pharmaceutical packaging materials

5.1 General rules for controllable additives list of plastic pharmaceutical packaging materials

1) The list of additives in this standard refers to the Technical Guideline for Research on Compatibility of Chemical Injection and Plastic Packaging Materials(Trial), relevant general rules of pharmacopoeias at home and abroad and relevant standards in domestic food field. For detailed information, please refer to Appendix A, Controllable Additives Used in Plastic Pharmaceutical Packaging Materials and Application Requirements, including controllable additives for plastic pharmaceutical packaging materials, maximum permitted content and applied plastic materials, examples of general application scenarios, etc. The general application scenarios of additives are not all described in the referenced additive documents, see Appendix A.6 of this standard for details.

2) Appendix A is a summary of priori knowledge, which provides reference for pharmaceutical packaging materials manufacturing enterprises to choose the types and use contents of additives. Choosing suitable additives for plastic pharmaceutical packaging materials and meeting the requirements of dosages provide a reasonable basis for selecting materials when designing packaging systems and minimizes the risk of systematic inapplicability caused by material additives.

3) The additives listed in Appendix A are widely used in the industry. With the development of science and the application of new additives, the content of Appendix A can be adjusted appropriately.

5.2 Basic principles for the use of controllable additives for plastic pharmaceutical packaging materials

Plastic pharmaceutical packaging materials contain additives to achieve certain processing, physical, chemical and mechanical effects. However, due to the particularity of drugs and the diversity of dosage forms and formulations, the use of additives of plastic pharmaceutical packaging materials should at least follow the following basic principles:

1) When plastic pharmaceutical packaging materials contact with drugs under the recommended conditions of use, the levels of additives and impurities migrated to drugs should not endanger human health.

2) The content of additives in plastic pharmaceutical packaging materials should be reduced as much

as possible under the expected effect, while the stability and quality of the final materials and containers should be ensured.

3) Additives to be used should conform to the corresponding quality specifications, the acceptable criteria for identification, physical and chemical properties, impurities and assay should be specified.

4) When the substances listed in Appendix A are allowed to be used as additives for plastic pharmaceutical packaging materials, they should not produce technical functions for the drugs themselves.

5.3 Regulations on the use of controllable additives for plastic pharmaceutical packaging materials

1) The use of additives for plastic pharmaceutical packaging materials should comply with the provisions of Appendix A

2) Unless there is a reasonable explanation or regulatory approval, the additives listed in Appendix A should be preferred for plastic materials, and the corresponding use requirements should be met.

3) The limit in Appendix A refers to the maximum permitted content of one or a class of additives contained in plastic pharmaceutical packaging materials, which provides reference for the selection of additives. In Appendix A, no more than 3 kinds of antioxidants should be added to each plastic resin, and the total amount should not exceed 0.3%.

4) Using the additives in Appendix A and meeting the maximum permitted content requirements does not necessarily mean safety. It should be based on the risk level of the packaged drugs, and further evaluation of additives may be required according to the principles in Chapter 6. If a compatibility study is required, the maximum permitted content cannot replace the compatibility study.

6. Further application consideration of additives for plastic pharmaceutical packaging materials

In addition to meeting the requirements of 5.2 and 5.3 of this standard, the selection of additives for plastic packaging materials should also evaluate the safety risks, such as the type of additives, the maximum use content, monomer residues, etc.

Safety is the primary condition for selecting additives for plastic pharmaceutical packaging materials. The safety evaluation of additives for plastic pharmaceutical packaging materials refers to the following risk assessment model.

1) The collection of relevant information is essential for the use of additives, which provided by suppliers or obtained from experiments which material itself contains and/or be added during processing.

2) And then, it should be considered whether the additive is in the list and whether the amount meets the maximum permitted content.

3) Conducting the safety assessment based on the risk level of the packaged drugs.

a) For plastic pharmaceutical packaging additives used in non-high-risk preparations, such as oral preparations, it's suggested to refer to the requirements of relevant food packaging materials in various

countries, such as GB 9685《Standard for the Use of Additives in Food Contact Materials and Articles》and related announcements, and the feasibility of referring standards for additives used in food in other countries.

b) For plastic pharmaceutical packaging additives for high-risk preparations, such as pharmaceutical packaging materials for inhalation preparations, injections, and ophthalmic preparations. It is not necessarily safe that additives in packaging materials are listed in Appendix A and meet the dosage requirements. The packaging materials may have been suffered different processing and sterilization treatment, so that an additive may undergo different chemical changes when applied to different products, such as oxidation and degradation. Extractable/leachable studies and corresponding toxicological risk assessments may be required.

Appendix A
(Normative)
Controllable Additives Used in Plastic Pharmaceutical Packaging Materials and Application Requirements

A.1: This appendix provides a tabular summary of the allowable additives for plastics listed in the CDE guidelines, the United States Pharmacopoeia and the European Pharmacopoeia. Additives should comply with all requirements in the columns of the table.

A.2: The additives in Table A.1 are sorted by CAS number. The additives which have no CAS number are listed at the end of Table A.1 and sorted by the characters, digits, English letters, and the first letter of the Chinese phonetic alphabet.

A.3: The additives in Table A.2 are sorted according to the characters, digits, English letters, and the first letter of the Chinese phonetic alphabet.

A.4: For the maximum permitted content of additives listed in the column *CDE/USP/EP Maximum permitted content* of Table A.1 and Table A.2, summarize the maximum amount of a particular or class of additives that specified in *Technical Guideline for Research on Compatibility of Chemical Injection and Plastic Packaging Materials(Trial)* (NMPA-I-[2012] No. 267) , USP <661.1> ①and EP General Chapters 3.1.3②、3.1.5③、3.1.6④、3.1.7⑤、3.1.10⑥、3.1.11⑦、3.1.13⑧or 3.1.14⑨.

A.5: The types of plastic resins to which additives can be applied were listed in the column *Types of Plastics* (①CDE Guidelines, ②USP, ③EP) of Table A.1 and Table A.2 and denoted by resin abbreviations. The resin abbreviation marks①②③ respectively represent the resins listed by ①*Technical Guideline for Research on Compatibility of Chemical Injection and Plastic Packaging Materials(Trial)*(NMPA-I-[2012] No. 267), ②USP general chapter <661.1> and ③EP material related general chapters.

A.6：The chapter number and specified application scenarios of additives in USP and EP were listed in the column Examples of General Application Scenarios. USP: 661.1(Unrestricted) refers to the application scenarios of plastic additives not restricted by USP 661.1, EP: 3.1.13 (Unrestricted Plastic additives) refers to the plastic materials and application scenarios not restricted by EP 3.1.13, EP 3.1.3 (unrestricted polyolefin) refers to the application scenarios in polyolefin not restricted by EP 3.1.3, and other application scenarios are described in Table A.1 and Table A.2. The plastic additives included in CDE *Technical Guideline for Research on Compatibility of Chemical Injection and Plastic Packaging Materials(Trial)(NMPA-I-[2012] No. 267)*are applicable to polyethylene and polypropylene plastics, so it's not listed in the table duplicately.

A.7: The names of additives in Tables A.1 and A.2 comply with the United States Pharmacopoeia and/or the European Pharmacopoeia. Some additives that may contain different designations, the CAS number shall prevail.

A.8: Some additives may have more than one CAS number due to isomers or different proportions of ingredients. Additives with multiple Chinese names are distinguished according to CAS number, which without CAS number are distinguished according to Chinese name.

A.9：Each resin may contain at most 3 antioxidants, and the total of antioxidant additives does not exceed 0.3 percent.

Note:

①USP 661.1 Plastic Materials of Construction

②EP 3.1.3 Polyolefin

③EP 3.1.5 Polyethylene with Additives for Containers for Parenteral Preparations and for Ophthalmic Preparations

④EP 3.1.6 Polypropylene for Containers and Closures for Parenteral Preparations and Ophthalmic Preparations

⑤EP 3.1.7 Poly(ethylene - vinyl acetate) for containers and tubing for total parenteral nutrition preparations

⑥EP 3.1.10 Materials Based on Non-plasticised Poly(vinyl chloride) for Containers for Non-injectable Aqueous Solutions

⑦EP 3.1.11. Materials Based on Non-plasticised Poly(vinyl chloride) for Containers for Solid Dosage Forms for Oral Administration

⑧EP 3.1.13 Plastic Additives

⑨EP 3.1.14 Materials Based on Plasticised Poly(vinyl chloride) for Containers for Aqueous Solutions for Intravenous Infusion

Table A.1 Controllable Additives Used in Plastic Pharmaceutical Packaging Materials and Application Requirements Sorted by CAS Number

Additives NO.	CAS No.	Name	CDE/USP/EP Maximum Permitted Content	Types of Plastics (CDE guidelines, USP, EP)	Examples of General Application Scenarios
1	[50-70-4]	Sorbitol	USP/EP: Not more than 1.5%	Non-plasticised PVC②③	USP: 661.1 (Unrestricted), EP: 3.1.10 (Materials based on non-plasticised poly(vinyl chloride) for containers for non-injectable, aqueous solutions) 3.1.11 (Materials based on non-plasticised poly(vinyl chloride) for containers for solid dosage forms for oral administration)
2	[57-11-4]	Stearic Acid	CDE/USP/EP: Not more than 0.5%	PE①③,PP①③, COC②, Polyolefin③, EVA③	USP: 661.1 (Unrestricted) EP: 3.1.13 (Plastic additives are not restricted) 3.1.3 (Polyolefins are not restricted) 3.1.5 (Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations) 3.1.6 (Polypropylene for containers and closures for parenteral preparations and ophthalmic preparations) 3.1.7 (Poly(ethylene-vinyl acetate) for containers and tubing for total parenteral nutrition preparations)
3	[112-84-5]	Erucamide	CDE/USP/EP: Not more than 0.5%; USP: Not more than 0.2% for EVA	PE①②③,PP①②③, EVA②③, COC②,Polyolefin③	USP: 661.1 (Unrestricted) EP: 3.1.13 (Plastic additives are not restricted) 3.1.3 (Polyolefins are not restricted) 3.1.5 (Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations) 3.1.6 (Polypropylene for containers and

Additives NO.	CAS No.	Name	CDE/USP/EP Maximum Permitted Content	Types of Plastics (CDE guidelines, USP, EP)	Examples of General Application Scenarios
					closures for parenteral preparations and ophthalmic preparations) 3.1.7 (Poly(ethylene-vinyl acetate) for containers and tubing for total parenteral nutrition preparations)
4	[117-81-7]	Di(2-ethylhexyl) phthalate	USP/EP: Not more than 40%	Plasticised PVC②③	USP: 661.1 (Unrestricted) EP: 3.1.13 (Plastic additives are not restricted) 3.1.14 (Materials based on plasticised poly(vinyl chloride) for containers for aqueous solutions for intravenous infusion)
5	[123-28-4]	Didodecyl 3,3′-thiodipropionate	CDE/USP/EP: Not more than 0.3%	PP①②③,PE①③,COC②,Polyolefin③	USP: 661.1 (Unrestricted) EP: 3.1.13 (Plastic additives are not restricted) 3.1.3 (Polyolefins are not restricted) 3.1.5 (Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations) 3.1.6 (Polypropylene for containers and closures for parenteral preparations and ophthalmic preparations)
6	[128-37-0]	2,6-di-tert-butyl-4-methylphenol	CDE/USP/EP: Not more than 0.125%	PE①②③,PP①②③,EVA②③,COC②,Polyolefin③	USP: 661.1 (Unrestricted) EP: 3.1.13 (Plastic additives are not restricted) 3.1.3 (Polyolefins are not restricted) 3.1.5 (Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations) 3.1.6 (Polypropylene for containers and closures for parenteral preparations and ophthalmic preparations)

Additives NO.	CAS No.	Name	CDE/USP/EP Maximum Permitted Content	Types of Plastics (CDE guidelines, USP, EP)	Examples of General Application Scenarios
					3.1.7 (Poly(ethylene-vinyl acetate) for containers and tubing for total parenteral nutrition preparations)
7	[136-53-8]	Zinc Octanoate	EP: Not more than 1%	Plasticised PVC③	EP: 3.1.13 (Plastic additives are not restricted) 3.1.14 (Materials based on plasticised poly(vinyl chloride) for containers for aqueous solutions for intravenous infusion)
8	[301-02-0]	Oleamide	CDE/USP/EP: Not more than 0.5%; USP: Not more than 0.2% for EVA	PE①②③,PP①②③, EVA②③, COC②,Polyolefin③	USP: 661.1 (Unrestricted) EP: 3.1.13 (Plastic additives are not restricted) 3.1.3 (Polyolefins are not restricted) 3.1.5 (Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations) 3.1.6 (Polypropylene for containers and closures for parenteral preparations and ophthalmic preparations) 3.1.7 (Poly(ethylene-vinyl acetate) for containers and tubing for total parenteral nutrition preparations)
9	[471-34-1] or [1310-58-3]	Calcium Carbonate or Potassium Hydroxide	EP: Not more than 0.5%, Calcium carbonate is not more than 1% when used in non-plasticised PVC; USP: Calcium carbonate is not more than 1%	Non-plasticised PVC②③, EVA③	USP: 661.1 (Unrestricted) EP: 3.1.7 (Poly(ethylene-vinyl acetate) for containers and tubing for total parenteral nutrition preparations) 3.1.11 (Materials based on non-plasticised poly(vinyl chloride) for containers for solid dosage forms for oral administration)

Additives NO.	CAS No.	Name	CDE/USP/EP Maximum Permitted Content	Types of Plastics (CDE guidelines, USP, EP)	Examples of General Application Scenarios
10	[532-32-1]	Sodium Benzoate	CDE/EP: Not more than 0.5%	PE①③,PP①③ ,Polyolefin③	EP: 3.1.3 (Polyolefins are not restricted) 3.1.5 (Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations) 3.1.6 (Polypropylene for containers and closures for parenteral preparations and ophthalmic preparations)
11	[693-36-7]	Dioctadecyl 3,3′-thiodipropionate	CDE/USP/EP: Not more than 0.3%	PP①②③,PE①③,COC②,Polyolefin③	USP: 661.1 (Unrestricted) EP: 3.1.13 (Plastic additives are not restricted) 3.1.3 (Polyolefins are not restricted) 3.1.5 (Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations) 3.1.6 (Polypropylene for containers and closures for parenteral preparations and ophthalmic preparations)
12	[1309-48-4]	Magnesium Oxide	CDE/EP: Not more than 0.2%	PE①③,PP①③ ,Polyolefin③	EP:3.1.3 (Polyolefins are not restricted) 3.1.5 (Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations) 3.1.6 (Polypropylene for containers and closures for parenteral preparations and ophthalmic preparations)

Additives NO.	CAS No.	Name	CDE/USP/EP Maximum Permitted Content	Types of Plastics (CDE guidelines, USP, EP)	Examples of General Application Scenarios
13	[1314-13-2]	Zinc Oxide	CDE/EP: Not more than 0.5%	PE①③,PP①③ ,Polyolefin③	EP:3.1.3 (Polyolefins are not restricted) 3.1.5 (Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations) 3.1.6 (Polypropylene for containers and closures for parenteral preparations and ophthalmic preparations)
14	[1344-00-9]	Sodium Silico-Aluminate	CDE/EP: Not more than 0.5%	PE①③,PP①③ ,Polyolefin③	EP:3.1.3 (Polyolefins are not restricted) 3.1.5 (Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations) 3.1.6 (Polypropylene for containers and closures for parenteral preparations and ophthalmic preparations)
15	[1592-23-0]或 [557-05-1]	Calcium Stearate or Zinc Stearate or a mixture of both	EP: Not more than 0.5%; Not more than 1% for plasticised PVC	Polyolefin③,PE③,PP③,EVA③,Plasticised PVC③	EP:3.1.3 (Polyolefins are not restricted) 3.1.5 (Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations) 3.1.6 (Polypropylene for containers and closures for parenteral preparations and ophthalmic preparations) 3.1.7 (Poly(ethylene-vinyl acetate) for containers and tubing for total parenteral nutrition preparations)

Additives NO.	CAS No.	Name	CDE/USP/EP Maximum Permitted Content	Types of Plastics (CDE guidelines, USP, EP)	Examples of General Application Scenarios
					3.1.14 (Materials based on plasticised poly(vinyl chloride) for containers for aqueous solutions for intravenous infusion)
16	[1709-70-2]	1,3,5-trimethyl-2,4,6-tris(3,5-di-tert-butyl-4-hydroxybenzyl)benzene	CDE/USP/EP: Not more than 0.3%; USP/EP: Not more than 0.2% for EVA	PE①②③,PP①②③, EVA②③, COC②,Polyolefin③	USP: 661.1 (Unrestricted) EP: 3.1.13 (Plastic additives are not restricted) 3.1.3 (Polyolefins are not restricted) 3.1.5 (Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations) 3.1.6 (Polypropylene for containers and closures for parenteral preparations and ophthalmic preparations) 3.1.7 (Poly(ethylene-vinyl acetate) for containers and tubing for total parenteral nutrition preparations)
17	[2082-79-3]	Octadecyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate	CDE/USP/EP: Not more than 0.3%; USP/EP: Not more than 0.2% for EVA	PE①②③,PP①②③, EVA②③, COC②,Polyolefin③	USP: 661.1 (Unrestricted) EP: 3.1.13 (Plastic additives are not restricted) 3.1.3 (Polyolefins are not restricted) 3.1.5 (Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations) 3.1.6 (Polypropylene for containers and closures for parenteral preparations and ophthalmic preparations) 3.1.7 (Poly(ethylene-vinyl acetate) for containers and tubing for total parenteral

Additives NO.	CAS No.	Name	CDE/USP/EP Maximum Permitted Content	Types of Plastics (CDE guidelines, USP, EP)	Examples of General Application Scenarios
					nutrition preparations)
18	[2500-88-1]	Dioctadecyl Disulfide	CDE/USP/EP: Not more than 0.3%	PP①②③,PE①③,COC②,Polyolefin③	USP: 661.1 (Unrestricted) EP: 3.1.13 (Plastic additives are not restricted) 3.1.3 (Polyolefins are not restricted) 3.1.5 (Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations) 3.1.6 (Polypropylene for containers and closures for parenteral preparations and ophthalmic preparations)
19	[3319-31-1]	Tris(2-ethylhexyl) trimellitate	EP: Not more than 45%	Plasticised PVC（for human blood or blood components）③	EP: 3.1.13 (Plastic additives are not restricted)
20	[3806-34-6]	2,2′-bis(octadecyloxy)-5,5′-spirobi[1,3,2-dioxaphosphinane]	CDE/EP: Not more than 0.3%	PO,PE,PP, PE①③,PP①③,Polyolefin③	EP: 3.1.13 (Plastic additives are not restricted) 3.1.3 (Polyolefins are not restricted) 3.1.5 (Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations) 3.1.6 (Polypropylene for containers and closures for parenteral preparations and ophthalmic preparations)

Additives NO.	CAS No.	Name	CDE/USP/EP Maximum Permitted Content	Types of Plastics (CDE guidelines, USP, EP)	Examples of General Application Scenarios
21	[5518-18-3]/ [110-30-5]	N,N′-diacylethylenediamines(acyl means in particular palmitoyl and stearoyl)	CDE: Not more than 0.5% USP/EP: Not more than 1%	PE①,PP①,Plasticised PVC②③	USP: 661.1 (Unrestricted) EP: 3.1.13 (Plastic additives are not restricted) 3.1.14 (Materials based on plasticised poly(vinyl chloride) for containers for aqueous solutions for intravenous infusion)
22	[6422-86-2]	Bis(2-ethylhexyl) terephthalate	EP: Not more than 45%	Plasticised PVC（for human blood or blood components）③	EP: 3.1.13 (Plastic additives are not restricted)
23	[6683-19-8]	Pentaerythrityl tetrakis[3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate]	CDE/USP/EP: Not more than 0.3% USP/EP: Not more than 0.2% for EVA	PE①②③,PP①②③, EVA②③, COC②,Polyolefin③	USP: 661.1 (Unrestricted) EP: 3.1.13 (Plastic additives are not restricted) 3.1.3 (Polyolefins are not restricted) 3.1.5 (Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations) 3.1.6 (Polypropylene for containers and closures for parenteral preparations and ophthalmic preparations) 3.1.7 (Poly(ethylene-vinyl acetate) for containers and tubing for total parenteral nutrition preparations)
24	[7601-54-9]	Trisodium Phosphate	CDE/EP: Not more than 0.5%	PE①③,PP①③ ,Polyolefin③	EP: 3.1.3 (Polyolefins are not restricted) 3.1.5 (Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations) 3.1.6 (Polypropylene for containers and closures for parenteral preparations and ophthalmic preparations)

Additives NO.	CAS No.	Name	CDE/USP/EP Maximum Permitted Content	Types of Plastics (CDE guidelines, USP, EP)	Examples of General Application Scenarios
25	[7631-86-9]	Silica	CDE/USP/EP: Not more than 0.5%, EP: Not more than 1% for non-plasticised PVC	PE①③,PP①③,Non-plasticised PVC②③,Polyolefin③	USP: 661.1 (Unrestricted) EP: 3.1.3 (Polyolefins are not restricted) 3.1.5 (Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations) 3.1.6 (Polypropylene for containers and closures for parenteral preparations and ophthalmic preparations) 3.1.11 (Materials based on non-plasticised poly(vinyl chloride) for containers for solid dosage forms for oral administration)
26	[8013-07-8]	Epoxidised Soya Oil	USP/EP: Not more than 10% or the total amount of both should be no more than 10%	Plasticized PVC②③	USP: 661.1 (Unrestricted) EP: 3.1.13 (Plastic additives are not restricted) 3.1.14 (Materials based on plasticised poly (vinyl chloride) for containers for aqueous solutions for intravenous infusion)
27	[8016-11-3]	Epoxidised Linseed Oil			

Additives NO.	CAS No.	Name	CDE/USP/EP Maximum Permitted Content	Types of Plastics (CDE guidelines, USP, EP)	Examples of General Application Scenarios
28	[8020-83-5]	Liquid Paraffin	CDE/USP/EP: Not more than 0.5% EP: Not more than 1.5% for non-plasticized PVC	PE①③, PP①③, Non-Plasticized PVC②③, Polyolefin③	USP: 661.1 (Unrestricted) EP: 3.1.3 (Polyolefins are not restricted) 3.1.5 (Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations) 3.1.6 (Polypropylene for containers and closures for parenteral preparations and ophthalmic preparations) 3.1.10 (Materials based on non-plasticised poly (vinyl chloride) for containers for non-injectable, aqueous solutions) 3.1.11 (Materials based on non-plasticised poly(vinyl chloride) for containers for solid dosage forms for oral administration)
29	[12304-65-3]	Hydrotalcite	CDE/EP: Not more than 0.5%	PE①③, PP①③, Polyolefin③	EP: 3.1.3 (Polyolefins are not restricted) 3.1.5 (Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations) 3.1.6 (Polypropylene for containers and closures for parenteral preparations and ophthalmic preparations)
30	[13463-67-7]	Titanium Dioxide	EP: Not more than 4%	Polyolefin③, PE③, PP③	EP: 3.1.3 (Polyolefins are not restricted) 3.1.5 (Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations) 3.1.6 (Polypropylene for containers and closures for parenteral preparations and ophthalmic preparations)

Additives NO.	CAS No.	Name	CDE/USP/EP Maximum Permitted Content	Types of Plastics (CDE guidelines, USP, EP)	Examples of General Application Scenarios
31	[14807-96-6]	Talc	CDE/EP: Not more than 0.5%	PP[①③], PE[①], Polyolefin[③]	EP: 3.1.3 (Polyolefins are not restricted) 3.1.6 (Polypropylene for containers and closures for parenteral preparations and ophthalmic preparations)
32	I [26401-97-8] II [26401-86-5]	I: di(isooctyl) 2,2'–[(dioctylstannylene)bis(thio)] diacetate II: tri(isooctyl) 2,2',2''-[(monooctylstannylidyne)tris(thio)] triacetate	USP/EP: The tin content should be not more than 0.25%	Non-Plasticized PVC[②③]	USP: 661.1 (unrestricted) EP: 3.1.13 (Plastic additives are not restricted) 3.1.10 (Materials based on non-plasticised poly (vinyl chloride) for containers for non-injectable, aqueous solutions) 3.1.11 (Materials based on non-plasticised poly(vinyl chloride) for containers for solid dosage forms for oral administration)
33	[27676-62-6]	1, 3, 5-tris-(3,5-di-tert-butyl-4-hydroxybenzyl)-s-triazine-2, 4, 6-(1H, 3H, 5H)-trione	CDE/USP/EP: Not more than 0.3%	PP[①②③], PE[①③], COC[②], Polyolefin[③]	USP: 661.1 (unrestricted) EP: 3.1.13 (Unrestricted plastic additives) 3.1.3 (Polyolefins are not restricted) 3.1.5 (Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations) 3.1.6 (Polypropylene for containers and closures for parenteral preparations and ophthalmic preparations)
34	[31570-04-4]	Tris (2, 4-di-tert-butylphenyl) phosphite	CDE/USP/EP: Not more than 0.3%; USP/EP: Used for EVA no more than 0.2%	PE[①②③], PP[①②③], EVA[②③], COC[②], Polyolefin[③]	USP: 661.1 (unrestricted) EP: 3.1.13 (Plastic additives are not restricted) 3.1.3 (Polyolefins are not restricted) 3.1.5 (Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations) 3.1.6 (Polypropylene for containers and closures for parenteral preparations and ophthalmic preparations)

Additives NO.	CAS No.	Name	CDE/USP/EP Maximum Permitted Content	Types of Plastics (CDE guidelines, USP, EP)	Examples of General Application Scenarios
					3.1.7 (Poly (ethylene - vinyl acetate) for containers and tubing for total parenteral nutrition preparations)
35	[32509-66-3]	ethylene bis [3, 3-bis [3-(1, 1-dimethylethyl)-4-hydroxyphenyl] butanoate]	CDE/USP/EP: Not more than 0.3%	PE①②③, PP①②③, COC②, Polyolefin③	USP: 661.1 (Unrestricted) EP: 3.1.13 (Plastic additives are not restricted) 3.1.3 (Polyolefins are not restricted) 3.1.5 (Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations) 3.1.6 (Polypropylene for containers and closures for parenteral preparations and ophthalmic preparations)
36	[57455-37-5] (TSCA)/ [101357-30-6] (EINECS)/Pigment blue 29 (CI 77007)	Ultramarine Blue	EP: When colouring materials are added, ultramarine blue is used. Other colouring materials may be added, provided that the safety of the material is demonstrated	Plasticized PVC③	EP: 3.1.13 (Plastic additives are not restricted) 3.1.14 (Materials based on plasticised poly (vinyl chloride) for containers for aqueous solutions for intravenous infusion)
37	[58446-52-9] or [52047-59-3] or [36265-41-5]	1-phenyleicosane-1, 3-dione(benzoylstearoylmethane) or 2-(4-dodecylphenyl) indole or didodecyl1, 4-dihydropyridine-2, 6-dimethyl-3, 5-dicarboxylate	EP: Not more than 1% or the total amount of both should be no more than 1%. When used in oral solid formulations, benzoyl stearyl methane should be not more than 1%. USP: benzoyl stearyl methane should be not more than 1% .	Non-Plasticized PVC②③	USP: 661.1 (Unrestricted), EP: 3.1.10 (Materials based on non-plasticised poly (vinyl chloride) for containers for non-injectable, aqueous solutions) 3.1.11 (Materials based on non-plasticised poly(vinyl chloride) for containers for solid dosage forms for oral administration)

Additives NO.	CAS No.	Name	CDE/USP/EP Maximum Permitted Content	Types of Plastics (CDE guidelines, USP, EP)	Examples of General Application Scenarios
38	[64033-89-2] or [763042-48-4] or [26523-78-4]	2, 4-dinonylphenyl phosphite or di(4-nonylphenyl) phosphite or tris(nonylphenyl) phosphite	EP/USP: Not more than 1%	Non-Plasticized PVC②③	USP: 661.1 (Unrestricted) EP: 3.1.10 (Materials based on non-plasticised poly (vinyl chloride) for containers for non-injectable, aqueous solutions) 3.1.11 (Materials based on non-plasticised poly(vinyl chloride) for containers for solid dosage forms for oral administration)
39	[65447-77-0]	Copolymer of dimethyl succinate and (4-hydroxy-2, 2, 6, 6-tetramethylpiperidin-1-yl) ethanol	CDE/USP/EP: Not more than 0.3%	PE①, PP①, COC②, Polyolefin③	USP: 661.1 (Unrestricted) EP: 3.1.13 (Plastic additives are not restricted) 3.1.3 (Polyolefins are not restricted)
40	[82469-79-2]	Butyryl tri-n-hexyl citrate	EP: Not more than 45%	Plasticized PVC (for human blood or blood components)③	EP: 3.1.13 (Plastic additives are not restricted)
41	[119345-01-6]	Mixture of 7 products corresponding to reaction product of di-*tert*-butyl phosphonite with phosphorous trichloride, reaction products with 1,1’-biphenyl and 2, 4-di-tert-butylphnol	CDE/EP: Not more than 0.1%	PE①, PP①, Polyolefin③	EP: 3.1.13 (Plastic additives are not restricted) 3.1.3 (Polyolefins are not restricted)

Additives NO.	CAS No.	Name	CDE/USP/EP Maximum Permitted Content	Types of Plastics (CDE guidelines, USP, EP)	Examples of General Application Scenarios
42	[166412-78-8]	Cyclohexane 1, 2-dicarboxylic acid, diisononyl ester	EP: Not more than 45%	Plasticized PVC (for human blood or blood components)③	EP: 3.1.13 (Plastic additives are not restricted)
43	/	Calcium, Magnesium or Zinc salts of Aliphatic Fatty Acids with more than 7 carbon atoms	USP/EP: Not more than 1.5% or total amount no more than 1.5%	Non-Plasticized PVC②③	USP: 661.1 (Unrestricted), EP: 3.1.10 (Materials based on non-plasticised poly (vinyl chloride) for containers for non-injectable, aqueous solutions) 3.1.11 (Materials based on non-plasticised poly(vinyl chloride) for containers for solid dosage forms for oral administration)
44	/	Waxes	USP/EP: Not more than 4% EP: For non-injection aqueous solutions no more than 1.5%	Non-Plasticized PVC②③	USP: 661.1 (Unrestricted) EP: 3.1.10 (Materials based on non-plasticised poly (vinyl chloride) for containers for non-injectable, aqueous solutions) 3.1.11 (Materials based on non-plasticised poly(vinyl chloride) for containers for solid dosage forms for oral administration)
45	/	Macrogol Esters	USP/EP: Not more than 1.5%	Non-Plasticized PVC②③	USP: 661.1 (Unrestricted) EP: 3.1.10 (Materials based on non-plasticised poly (vinyl chloride) for containers for non-injectable, aqueous solutions) 3.1.11 (Materials based on non-plasticised poly(vinyl chloride) for containers for solid dosage forms for oral administration)
46	/	Colloidal Silica	EP: Not more than 0.2%	EVA③	EP: 3.1.7 Poly (ethylene - vinyl acetate) for containers and tubing for total parenteral nutrition preparations

Additives NO.	CAS No.	Name	CDE/USP/EP Maximum Permitted Content	Types of Plastics (CDE guidelines, USP, EP)	Examples of General Application Scenarios
47	/	Hydrogenated Oils or Esters of Aliphatic Fatty Acids	USP/EP: Not more than 2%	Non-Plasticized PVC②③	USP: 661.1 (Unrestricted) EP: 3.1.10 (Materials based on non-plasticised poly (vinyl chloride) for containers for non-injectable, aqueous solutions) 3.1.11 (Materials based on non-plasticised poly(vinyl chloride) for containers for solid dosage forms for oral administration)
48	/	Fatty Acid Esters or Salts	CDE/EP: Not more than 0.5%	PP①③, PE①③, Polyolefin③	EP: 3.1.3 (Plastic additives are not restricted) 3.1.5 (Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations) 3.1.6 (Polypropylene for containers and closures for parenteral preparations and ophthalmic preparations)
49	/	GB 9685-2016 Appendix A Table A.1 Admissible Additives for Plastic Materials and Products in Food Contact*	Refer to Table A.1 in Appendix A of GB 9685-2016 standard for maximum usage, and also refer to the given migration amount**	See Table A.1 Scope of Use	Oral solid preparations

*Appropriately cite additives recognized by regulations in the food industry for safety evaluation of oral solid and liquid formulations (refer to the FDA industry guidance for container sealing systems for packaging of human drugs and biological products).

**Oral solid formulations can refer to the migration amount requirements provided in Table A.1 of Appendix A of GB 9685-2016

Table A.2 Controllable Additives Used in Plastic Pharmaceutical Packaging Materials and Application Requirements Sorted by Chinese Name

Additives NO.	Name	CAS No.	CDE/USP/EP Maximum Permitted Content	Types of Plastics (CDE guidelines, USP, EP)	Examples of General Application Scenarios
1	1, 3, 5-tris-(3,5-di-tert-butyl-4-hydroxybenzyl)-s-triazine-2, 4, 6-(1H, 3H, 5H)-trione	[27676-62-6]	CDE/USP/EP: Not more than 0.3%	PP①②③, PE①③, COC②, Polyolefin③	USP: 661.1 (unrestricted) EP: 3.1.13 (Unrestricted plastic additives) 3.1.3 (Polyolefins are not restricted) 3.1.5 (Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations) 3.1.6 (Polypropylene for containers and closures for parenteral preparations and ophthalmic preparations)
2	1,3,5-trimethyl-2,4,6-tris(3,5-di-tert-butyl-4-hydroxybenzyl)benzene	[1709-70-2]	CDE/USP/EP: Not more than 0.3%; USP/EP: Not more than 0.2% for EVA	PE①②③,PP①②③, EVA②③, COC②,Polyolefin③	USP: 661.1 (Unrestricted) EP: 3.1.13 (Plastic additives are not restricted) 3.1.3 (Polyolefins are not restricted) 3.1.5 (Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations) 3.1.6 (Polypropylene for containers and closures for parenteral preparations and ophthalmic preparations) 3.1.7 (Poly(ethylene-vinyl acetate) for containers and tubing for total parenteral nutrition preparations)
3	1-phenyleicosane-1, 3-dione(benzoylstearoylmethane) or 2-(4-dodecylphenyl) indole or	[58446-52-9] or [52047-59-3] or [36265-41-5]	EP: Not more than 1% or the total amount of both should be no more than 1%. When used in oral solid formulations, benzoyl stearyl methane should be no more than 1%. USP:	Non-Plasticized PVC②③	USP: 661.1 (Unrestricted), EP: 3.1.10 (Materials based on non-plasticised poly (vinyl chloride) for containers for non-injectable, aqueous solutions) 3.1.11 (Materials based on non-plasticised poly(vinyl chloride) for containers for solid

Additives NO.	Name	CAS No.	CDE/USP/EP Maximum Permitted Content	Types of Plastics (CDE guidelines, USP, EP)	Examples of General Application Scenarios
	didodecyl1, 4-dihydropyridine-2, 6-dimethyl-3, 5-dicarboxylate		benzoyl stearyl methane should be not more than 1% .		dosage forms for oral administration)
4	2,2′-bis(octadecyloxy)-5,5′-spirobi[1,3,2-dioxaphosphinane]	[3806-34-6]	CDE/EP: Not more than 0.3%	PO,PE,PP,PE①③, PP①③,Polyolefin③	EP: 3.1.13 (Plastic additives are not restricted) 3.1.3 (Polyolefins are not restricted) 3.1.5 (Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations) 3.1.6 (Polypropylene for containers and closures for parenteral preparations and ophthalmic preparations)
5	2, 4-dinonylphenyl phosphite or di(4-nonylphenyl) phosphite or tris(nonylphenyl) phosphite	[64033-89-2] or [763042-48-4] or [26523-78-4]	EP/USP: Not more than 1%	Non-Plasticized PVC②③	USP: 661.1 (Unrestricted) EP: 3.1.10 (Materials based on non-plasticised poly (vinyl chloride) for containers for non-injectable, aqueous solutions) 3.1.11 (Materials based on non-plasticised poly(vinyl chloride) for containers for solid dosage forms for oral administration)
6	2,6-di-tert-butyl-4-methylphenol	[128-37-0]	CDE/USP/EP: Not more than 0.125%	PE①②③,PP①②③, EVA②③,COC②,Polyolefin③	USP: 661.1 (Unrestricted) EP: 3.1.13 (Plastic additives are not restricted) 3.1.3 (Polyolefins are not restricted) 3.1.5 (Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations) 3.1.6 (Polypropylene for containers and closures for parenteral preparations and

Additives NO.	Name	CAS No.	CDE/USP/EP Maximum Permitted Content	Types of Plastics (CDE guidelines, USP, EP)	Examples of General Application Scenarios
					ophthalmic preparations) 3.1.7 (Poly(ethylene-vinyl acetate) for containers and tubing for total parenteral nutrition preparations)
7	Zinc Octanoate	[136-53-8]	EP: Not more than 1%	Plasticised PVC③	EP: 3.1.13 (Plastic additives are not restricted) 3.1.14 (Materials based on plasticised poly(vinyl chloride) for containers for aqueous solutions for intravenous infusion)
8	Didodecyl 3,3′-thiodipropionate	[123-28-4]	CDE/USP/EP: Not more than 0.3%	PP①②③,PE①③,COC②,Polyolefin③	USP: 661.1 (Unrestricted) EP: 3.1.13 (Plastic additives are not restricted) 3.1.3 (Polyolefins are not restricted) 3.1.5 (Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations) 3.1.6 (Polypropylene for containers and closures for parenteral preparations and ophthalmic preparations)
9	Octadecyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate	[2082-79-3]	CDE/USP/EP: Not more than 0.3%; USP/EP: Not more than 0.2% for EVA	PE①②③,PP①②③,EVA②③,COC②,Polyolefin③	USP: 661.1 (Unrestricted) EP: 3.1.13 (Plastic additives are not restricted) 3.1.3 (Polyolefins are not restricted) 3.1.5 (Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations) 3.1.6 (Polypropylene for containers and closures for parenteral preparations and ophthalmic preparations) 3.1.7 (Poly(ethylene-vinyl acetate) for

Additives NO.	Name	CAS No.	CDE/USP/EP Maximum Permitted Content	Types of Plastics (CDE guidelines, USP, EP)	Examples of General Application Scenarios
					containers and tubing for total parenteral nutrition preparations)
10	Dioctadecyl 3,3′-thiodipropionate	[693-36-7]	CDE/USP/EP: Not more than 0.3%	PP①②③,PE①③,COC②,Polyolefin③	USP: 661.1 (Unrestricted) EP: 3.1.13 (Plastic additives are not restricted) 3.1.3 (Polyolefins are not restricted) 3.1.5 (Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations) 3.1.6 (Polypropylene for containers and closures for parenteral preparations and ophthalmic preparations)
11	I: di(isooctyl) 2,2'–[(dioctylstannylene)bis(thio)] diacetate II: tri(isooctyl) 2,2',2''-[(monooctylstannylidyne)tris(thio)] triacetate	I [26401-97-8] II [26401-86-5]	USP/EP: The tin content should be not more than 0.25%	Non-Plasticized PVC②③	USP: 661.1 (unrestricted) EP: 3.1.13 (Plastic additives are not restricted) 3.1.10 (Materials based on non-plasticised poly (vinyl chloride) for containers for non-injectable, aqueous solutions) 3.1.11 (Materials based on non-plasticised poly(vinyl chloride) for containers for solid dosage forms for oral administration)
12	N,N′-diacylethylenediamines(acyl means in particular palmitoyl and stearoyl)	[5518-18-3]/[110-30-5]	CDE: Not more than 0.5% USP/EP: Not more than 1%	PE①,PP①Plasticised PVC②③	USP: 661.1 (Unrestricted) EP: 3.1.13 (Plastic additives are not restricted) 3.1.14 (Materials based on plasticised poly(vinyl chloride) for containers for aqueous solutions for intravenous infusion)

Additives NO.	Name	CAS No.	CDE/USP/EP Maximum Permitted Content	Types of Plastics (CDE guidelines, USP, EP)	Examples of General Application Scenarios
13	Copolymer of dimethyl succinate and (4-hydroxy-2, 2, 6, 6-tetramethylpiperidin-1-yl) ethanol	[65447-77-0]	CDE/USP/EP: Not more than 0.3%	PE①, PP①, COC②, Polyolefin③	USP: 661.1 (Unrestricted) EP: 3.1.13 (Plastic additives are not restricted) 3.1.3 (Polyolefins are not restricted)
14	Butyryl tri-n-hexyl citrate	[82469-79-2]	EP: Not more than 45%	Plasticized PVC (for human blood or blood components)③	EP: 3.1.13 (Plastic additives are not restricted)
15	Tris (2, 4-di-tert-butylphenyl) phosphite	[31570-04-4]	CDE/USP/EP: Not more than 0.3%; USP/EP: Used for EVA no more than 0.2%	PE①②③, PP①②③, EVA②③, COC②, Polyolefin③	USP: 661.1 (unrestricted) EP: 3.1.13 (Plastic additives are not restricted) 3.1.3 (Polyolefins are not restricted) 3.1.5 (Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations) 3.1.6 (Polypropylene for containers and closures for parenteral preparations and ophthalmic preparations) 3.1.7 (Poly (ethylene - vinyl acetate) for containers and tubing for total parenteral nutrition preparations)
16	Dioctadecyl Disulfide	[2500-88-1]	CDE/USP/EP: Not more than 0.3%	PP①②③,PE①③,COC②,Polyolefin③	USP: 661.1 (Unrestricted) EP: 3.1.13 (Plastic additives are not restricted) 3.1.3 (Polyolefins are not restricted) 3.1.5 (Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations) 3.1.6 (Polypropylene for containers and

Additives NO.	Name	CAS No.	CDE/USP/EP Maximum Permitted Content	Types of Plastics (CDE guidelines, USP, EP)	Examples of General Application Scenarios
					closures for parenteral preparations and ophthalmic preparations)
17	ethylene bis [3, 3-bis [3-(1, 1-dimethylethyl)-4-hydroxyphenyl] butanoate]	[32509-66-3]	CDE/USP/EP: Not more than 0.3%	PE①②③, PP①②③, COC②, Polyolefin③	USP: 661.1 (Unrestricted) EP: 3.1.13 (Plastic additives are not restricted) 3.1.3 (Polyolefins are not restricted) 3.1.5 (Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations) 3.1.6 (Polypropylene for containers and closures for parenteral preparations and ophthalmic preparations)
18	Silica	[7631-86-9]	CDE/USP/EP: Not more than 0.5%, EP: Not more than 1% for non-plasticised PVC	PE①③,PP①③, Non-plasticised PVC②③,Polyolefin③	USP: 661.1 (Unrestricted) EP: 3.1.3 (Polyolefins are not restricted) 3.1.5 (Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations) 3.1.6 (Polypropylene for containers and closures for parenteral preparations and ophthalmic preparations) 3.1.11 (Materials based on non-plasticised poly(vinyl chloride) for containers for solid dosage forms for oral administration)
19	Titanium Dioxide	[13463-67-7]	EP: Not more than 4%	Polyolefin③, PE①③, PP①③	EP: 3.1.3 (Polyolefins are not restricted) 3.1.5 (Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations) 3.1.6 (Polypropylene for containers and closures

Additives NO.	Name	CAS No.	CDE/USP/EP Maximum Permitted Content	Types of Plastics (CDE guidelines, USP, EP)	Examples of General Application Scenarios
					for parenteral preparations and ophthalmic preparations)
20	Tris(2-ethylhexyl) trimellitate	[3319-31-1]	EP: Not more than 45%	Plasticised PVC（for human blood or blood components）③	EP: 3.1.13 (Plastic additives are not restricted)
21	Calcium, Magnesium or Zinc salts of Aliphatic Fatty Acids with more than 7 carbon atoms	/	USP/EP: Not more than 1.5% or total amount no more than 1.5%	Non-Plasticized PVC②③	USP: 661.1 (Unrestricted), EP: 3.1.10 (Materials based on non-plasticised poly (vinyl chloride) for containers for non-injectable, aqueous solutions) 3.1.11 (Materials based on non-plasticised poly(vinyl chloride) for containers for solid dosage forms for oral administration)
22	Mixture of 7 products corresponding to reaction product of di-*tert*-butyl phosphonite with phosphorous trichloride, reaction products with 1,1’-biphenyl and 2, 4-di-tert-butylphnol	[119345-01-6]	CDE/EP: Not more than 0.1%	PE①, PP①, Polyolefin③	EP: 3.1.13 (Plastic additives are not restricted) 3.1.3 (Polyolefins are not restricted)

Additives NO.	Name	CAS No.	CDE/USP/EP Maximum Permitted Content	Types of Plastics (CDE guidelines, USP, EP)	Examples of General Application Scenarios
23	Pentaerythrityl tetrakis[3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate]	[6683-19-8]	CDE/USP/EP: Not more than 0.3% USP/EP: Not more than 0.2% for EVA	PE①②③,PP①②③, EVA②③, COC②,Polyolefin③	USP: 661.1 (Unrestricted) EP: 3.1.13 (Plastic additives are not restricted) 3.1.3 (Polyolefins are not restricted) 3.1.5 (Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations) 3.1.6 (Polypropylene for containers and closures for parenteral preparations and ophthalmic preparations) 3.1.7 (Poly(ethylene-vinyl acetate) for containers and tubing for total parenteral nutrition preparations)
24	Bis(2-ethylhexyl) terephthalate	[6422-86-2]	EP: Not more than 45%	Plasticised PVC（for human blood or blood components）③	EP: 3.1.13 (Plastic additives are not restricted)
25	Sorbitol	[50-70-4]	USP/EP: Not more than 1.5%	Non-plasticised PVC②③	USP: 661.1 (Unrestricted), EP: 3.1.10 (Materials based on non-plasticised poly(vinyl chloride) for containers for non-injectable, aqueous solutions) 3.1.11 (Materials based on non-plasticised poly(vinyl chloride) for containers for solid dosage forms for oral administration)
26	Zinc Oxide	[1314-13-2]	CDE/EP: Not more than 0.5%	PE①③,PP①③ ,Polyolefin③	EP:3.1.3 (Polyolefins are not restricted) 3.1.5 (Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations) 3.1.6 (Polypropylene for containers and

Additives NO.	Name	CAS No.	CDE/USP/EP Maximum Permitted Content	Types of Plastics (CDE guidelines, USP, EP)	Examples of General Application Scenarios
					closures for parenteral preparations and ophthalmic preparations)
27	Magnesium Oxide	[1309-48-4]	CDE/EP: Not more than 0.2%	PE①③,PP①③ ,Polyolefin③	EP:3.1.3 (Polyolefins are not restricted) 3.1.5 (Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations) 3.1.6 (Polypropylene for containers and closures for parenteral preparations and ophthalmic preparations)
28	Oleamide	[301-02-0]	CDE/USP/EP: Not more than 0.5%； USP: Not more than 0.2% for EVA	PE①②③,PP①②③, EVA②③, COC②,Polyolefin③	USP: 661.1 (Unrestricted) EP: 3.1.13 (Plastic additives are not restricted) 3.1.3 (Polyolefins are not restricted) 3.1.5 (Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations) 3.1.6 (Polypropylene for containers and closures for parenteral preparations and ophthalmic preparations) 3.1.7 (Poly(ethylene-vinyl acetate) for containers and tubing for total parenteral nutrition preparations)

Additives NO.	Name	CAS No.	CDE/USP/EP Maximum Permitted Content	Types of Plastics (CDE guidelines, USP, EP)	Examples of General Application Scenarios
29	Liquid Paraffin	[8020-83-5]	CDE/USP/EP: Not more than 0.5% EP: Not more than 1.5% for non-plasticized PVC	PE[①③], PP[①③], Non-Plasticized PVC[②③], Polyolefin[③]	USP: 661.1 (Unrestricted) EP: 3.1.3 (Polyolefins are not restricted) 3.1.5 (Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations) 3.1.6 (Polypropylene for containers and closures for parenteral preparations and ophthalmic preparations) 3.1.10 (Materials based on non-plasticised poly (vinyl chloride) for containers for non-injectable, aqueous solutions) 3.1.11 (Materials based on non-plasticised poly(vinyl chloride) for containers for solid dosage forms for oral administration)
30	Talc	[14807-96-6]	CDE/EP: Not more than 0.5%	PP[①③], PE[①], Polyolefin[③]	EP: 3.1.3 (Polyolefins are not restricted) 3.1.6 (Polypropylene for containers and closures for parenteral preparations and ophthalmic preparations)
31	Cyclohexane 1, 2-dicarboxylic acid, diisononyl ester	[166412-78-8]	EP: Not more than 45%	Plasticized PVC (for human blood or blood components)[③]	EP: 3.1.13 (Plastic additives are not restricted)
32	Epoxidised Linseed Oil	[8016-11-3]	USP/EP: Not more than 10% or the total amount of both should be no more than 10%	Plasticized PVC[②③]	USP: 661.1 (Unrestricted) EP: 3.1.13 (Plastic additives are not restricted) 3.1.14 (Materials based on plasticised poly (vinyl chloride) for containers for aqueous solutions for intravenous infusion)

Additives NO.	Name	CAS No.	CDE/USP/EP Maximum Permitted Content	Types of Plastics (CDE guidelines, USP, EP)	Examples of General Application Scenarios
33	Epoxidised Soya Oil	[8013-07-8]			
34	Waxes	/	USP/EP: Not more than 4% EP: For non-injection aqueous solutions no more than 1.5%	Non-Plasticized PVC②③	USP: 661.1 (Unrestricted) EP: 3.1.10 (Materials based on non-plasticised poly (vinyl chloride) for containers for non-injectable, aqueous solutions) 3.1.11 (Materials based on non-plasticised poly(vinyl chloride) for containers for solid dosage forms for oral administration)
35	Sodium Silico-Aluminate	[1344-00-9]	CDE/EP: Not more than 0.5%	PE①③,PP①③ ,Polyolefin③	EP:3.1.3 (Polyolefins are not restricted) 3.1.5 (Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations) 3.1.6 (Polypropylene for containers and closures for parenteral preparations and ophthalmic preparations)
36	Stearic Acid	[57-11-4]	CDE/USP/EP: Not more than 0.5%	PE①③,PP①③, COC②, Polyolefin③, EVA③	USP: 661.1 (Unrestricted) EP: 3.1.13 (Plastic additives are not restricted) 3.1.3 (Polyolefins are not restricted) 3.1.5 (Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations) 3.1.6 (Polypropylene for containers and closures for parenteral preparations and ophthalmic preparations) 3.1.7 (Poly(ethylene-vinyl acetate) for

Additives NO.	Name	CAS No.	CDE/USP/EP Maximum Permitted Content	Types of Plastics (CDE guidelines, USP, EP)	Examples of General Application Scenarios
					containers and tubing for total parenteral nutrition preparations)
37	Calcium Stearate or Zinc Stearate or a mixture of both	[1592-23-0] 或 [557-05-1]	EP: Not more than 0.5%; Not more than 1% for plasticised PVC	Polyolefin③,PE③,PP③,EVA③,Plasticised PVC③	EP:3.1.3 (Polyolefins are not restricted) 3.1.5 (Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations) 3.1.6 (Polypropylene for containers and closures for parenteral preparations and ophthalmic preparations) 3.1.7 (Poly(ethylene-vinyl acetate) for containers and tubing for total parenteral nutrition preparations) 3.1.14 (Materials based on plasticised poly(vinyl chloride) for containers for aqueous solutions for intravenous infusion)
38	Hydrotalcite	[12304-65-3]	CDE/EP: Not more than 0.5%	PE①③, PP①③, Polyolefin③	EP: 3.1.3 (Polyolefins are not restricted) 3.1.5 (Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations) 3.1.6 (Polypropylene for containers and closures for parenteral preparations and ophthalmic preparations)
39	Calcium Carbonate or Potassium Hydroxide	[471-34-1] or [1310-58-3]	EP: Not more than 0.5%, Calcium carbonate is not more than 1% when used in non-plasticised PVC; USP: Calcium carbonate is	Non-plasticised PVC②③, EVA③	USP: 661.1 (Unrestricted) EP: 3.1.7 (Poly(ethylene-vinyl acetate) for containers and tubing for total parenteral nutrition preparations) 3.1.11 (Materials based on non-plasticised

Additives NO.	Name	CAS No.	CDE/USP/EP Maximum Permitted Content	Types of Plastics (CDE guidelines, USP, EP)	Examples of General Application Scenarios
			not more than 1%		poly(vinyl chloride) for containers for solid dosage forms for oral administration)
40	Trisodium Phosphate	[7601-54-9]	CDE/EP: Not more than 0.5%	PE①③,PP①③ ,Polyolefin③	EP: 3.1.3 (Polyolefins are not restricted) 3.1.5 (Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations) 3.1.6 (Polypropylene for containers and closures for parenteral preparations and ophthalmic preparations)
41	Ultramarine Blue	[57455-37-5] (TSCA)/ [101357-30-6] (EINECS)/Pigment blue 29 (CI 77007)	EP: When colouring materials are added, ultramarine blue is used. Other colouring materials may be added, provided that the safety of the material is demonstrated	Plasticized PVC③	EP: 3.1.13 (Plastic additives are not restricted) 3.1.14 (Materials based on plasticised poly (vinyl chloride) for containers for aqueous solutions for intravenous infusion)
42	Macrogol Ester	/	USP/EP: Not more than 1.5%	Non-Plasticized PVC②③	USP: 661.1 (Unrestricted) EP: 3.1.10 (Materials based on non-plasticised poly (vinyl chloride) for containers for non-injectable, aqueous solutions) 3.1.11 (Materials based on non-plasticised poly(vinyl chloride) for containers for solid dosage forms for oral administration)

Additives NO.	Name	CAS No.	CDE/USP/EP Maximum Permitted Content	Types of Plastics (CDE guidelines, USP, EP)	Examples of General Application Scenarios
43	Colloidal Silica	/	EP: Not more than 0.2%	EVA③	EP: 3.1.7 Poly (ethylene - vinyl acetate) for containers and tubing for total parenteral nutrition preparations
44	Hydrogenated Oils or Esters of Aliphatic Fatty Acids	/	USP/EP: Not more than 2%	Non-Plasticized PVC②③	USP: 661.1 (Unrestricted) EP: 3.1.10 (Materials based on non-plasticised poly (vinyl chloride) for containers for non-injectable, aqueous solutions) 3.1.11 (Materials based on non-plasticised poly(vinyl chloride) for containers for solid dosage forms for oral administration)
45	Fatty Acid Esters or Salts	/	CDE/EP: Not more than 0.5%	PP①③, PE①③, Polyolefin③	EP: 3.1.3 (Plastic additives are not restricted) 3.1.5 (Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations) 3.1.6 (Polypropylene for containers and closures for parenteral preparations and ophthalmic preparations)
46	Erucamide	[112-84-5]	CDE/USP/EP: Not more than 0.5%; USP: Not more than 0.2% for EVA	PE①②③,PP①②③, EVA②③, COC②,Polyolefin③	USP: 661.1 (Unrestricted) EP: 3.1.13 (Plastic additives are not restricted) 3.1.3 (Polyolefins are not restricted) 3.1.5 (Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations) 3.1.6 (Polypropylene for containers and closures for parenteral preparations and ophthalmic preparations) 3.1.7 (Poly(ethylene-vinyl acetate) for containers and tubing for total parenteral

Additives NO.	Name	CAS No.	CDE/USP/EP Maximum Permitted Content	Types of Plastics (CDE guidelines, USP, EP)	Examples of General Application Scenarios
					nutrition preparations)
47	Sodium Benzoate	[532-32-1]	CDE/EP: Not more than 0.5%	PE①③,PP①③ ,Polyolefin③	EP: 3.1.3 (Polyolefins are not restricted) 3.1.5 (Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations) 3.1.6 (Polypropylene for containers and closures for parenteral preparations and ophthalmic preparations)
48	Di(2-ethylhexyl) phthalate	[117-81-7]	USP/EP: Not more than 40%	Plasticised PVC②③	USP: 661.1 (Unrestricted) EP: 3.1.13 (Plastic additives are not restricted) 3.1.14 (Materials based on plasticised poly(vinyl chloride) for containers for aqueous solutions for intravenous infusion)
49	GB 9685-2016 Appendix A Table A.1 Admissible Additives for Plastic Materials and Products in Food Contact*	/	Refer to Table A.1 in Appendix A of GB 9685-2016 standard for maximum usage, and also refer to the given migration amount**	See Table A.1 Scope of Use	Oral solid preparations

*Appropriately cite additives recognized by regulations in the food industry for safety evaluation of oral solid and liquid formulations (refer to the FDA industry guidance for container sealing systems for packaging of human drugs and biological products).

**Oral solid formulations can refer to the migration amount requirements provided in Table A.1 of Appendix A of GB 9685-2016

reference

[1] United States Pharmacopoeia 2023 edition

[2] European Pharmacopoeia 11.1

[3] Chinese pharmacopoeia 2020 edition

[4] China Food and Drug Administration Note [2012]267 Technical guidelines for research on compatibility of chemical injection and plastic packaging materials (trial)

[5] GB 9685-2016 National food safety standard -- Standard for uses of additives in food contact materials and their products

[6] Plastic additives and formulation technology (4th edition, Wang Xingwei)

[7] Introduction to Fine Chemical Industry (Third edition, Xiang Jie)

[8] Handbook of Plastic Additives (5th Edition, Hansz Weifel)

[9] Handbook for the Chemical Analysis of Plastic and Polymer Additives 2007

[10] FDA Guidance for Industry Container Closure Systems for Packaging Human Drugs and Biologics, May 1999.