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Guideline for evaluating the cosmetic defects of pharmaceutical glass containers

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PREFACE

This document is drafted in accordance with the provisions of GB/T 1.1 2020 "Guidelines for Standardization Work: Structure and Drafting Rules of Standardization Documents".

Please note that some content of this document may involving patents. The release agency of this document does not assume any responsibility for identifying patents.

This document is proposed and under the jurisdiction of the China National Pharmaceutical Packaging Association.

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FORWARD

The pharmaceutical glass containers referred to this document include glass components and containers used in pharmaceutical glass packaging systems. The cosmetic defect of pharmaceutical glass containers refers to the cosmetic defects that cause the drug packaging to not meet the expected requirements for protection, compatibility, safety, functionality, and other usage requirements.

This document is a method for evaluating the cosmetic defects and its risks of pharmaceutical glass containers, used to guide the quality control of pharmaceutical glass container manufacturers and incoming inspection of pharmaceutical manufacturers. Pharmaceutical glass container manufacturers and pharmaceutical manufacturers should evaluate the relevant defects that need to be controlled based on the potential impact of cosmetic defects of pharmaceutical glass containers on drug packaging quality.



GUIDELINE FOR EVALUATING THE COSMETIC DEFECTS OF PHARMACEUTICAL GLASS CONTAINERS

1 Scope

This document provides guide information on the classification, identification, and evaluation of cosmetic defects in pharmaceutical glass containers.

This document is applicable to molded and tubular glass containers that come into direct contact with drugs. The main types include glass infusion bottles, glass injection vials, glass ampoules, glass drug bottles, glass barrels for pen-injectors and glass barrels for prefilled syringes.

2 Normative References

The content in the following documents constitutes an essential clause of this document through normative references in this guideline. In them, for dated references, only the version corresponding to that date is applicable to this document; for undated references, the latest version (including all modifications) applies to this document.

GB/T 9987-2011 Terminology for the Manufacturing of Glass Bottles and Cans

3 Definitions and Terminology

The following terms and definitions apply to this document.

3.1

Defect

Nonconformity related to the intended or specified use.

4 Defect Classification

Pharmaceutical glass containers should have performance that is suitable for the quality requirements of drugs. According to the impact of the cosmetic defects on the intended use, cosmetic defects of pharmaceutical glass containers can be classified into three types:

Critical defects: Defects that may seriously affect the intended use of pharmaceutical glass containers, leading to personal injury or potential danger to patients, including any defects that damage the sealing integrity of the container and lead to a microbial contamination risk of sterile preparations.

Major defects: Defects that may affect the part of intended use of pharmaceutical glass containers, make the packaging unusable, or reduce production efficiency.

Minor defects: Defects that may cause slight impact on the intended use of pharmaceutical glass containers.

5 Defect Identification

The cosmetic defects of different pharmaceutical glass containers have common and unique characteristics in terms of cause and morphological characterization. Therefore, this document identifies and classifies common and unique defects in cosmetic, as detailed in Tables 1 ~ 6. The names of cosmetic defects in both Chinese and English can be found in Appendix A, and some schematic images of defects can be found in Appendix B.

Table 1 Common cosmetic defects of pharmaceutical glass containers

Defect Nr.	Defect Name	Defect position	Defect description	Potential defect risk	Defect classification
1.01	Split, crack	Any position	Cracks penetrating the glass in depth or completely penetrating the wall	Impact CCI	Critical Defect
1.02	Broken	Any position	Part of the glass is broken or damaged due to impact or crack expansion	Impact CCI	Critical Defect
1.03	Wavy ring *	Sealing surface of bottle mouth	obvious protrusions, depressions, waves, and other phenomena on the sealing surface	Impact CCI	Critical defect: affect CCI; Minor defect: do not affect CCI or the aesthetics of the product
1.04	Check	Any position	Non penetrating crack, a small crack caused by contact between the surface of cold and hot glass, usually small but relatively deep	Affect the mechanical resistance and thermal shock of the product	Major Defect
1.05	Severely deformed	Any position	Incomplete or irregular forming of bottle mouth, neck, shoulder, body, bottom, and other parts during processing	Affect the filling efficiency of drug	Major Defect
1.06	Rocker bottom *	Bottom	The center of the bottom protrudes from the outer edge of the bottom, causing the container to be unstable on a horizontal plane	Affect the filling efficiency of drug	Major Defect
1.07	Non-removable contamination	Any position	Deposited, adhered, or embedded pollution on the interior or exterior surface of the container that cannot be removed	Affect drug quality and the aesthetics of the product	Cartridge, glass barrel for prefilled syringe: Critical defect: internal surface contaminants that cannot be removed $\geq 0.3\text{mm}^2$; Major defect: contaminants that cannot be removed from the outer surface $\geq 0.3\text{mm}^2$ Tubular injection vial, tubular medical bottle, and ampoule: Critical defect: with contaminants on the inner surface that cannot be removed $\geq 0.3\text{mm}^2$; Major defect : contaminants that cannot be removed from the outer surface $\geq 0.5\text{mm}^2$

					<p>Molded bottle: Critical defect: with contaminants on the inner surface that cannot be removed $\geq 0.3\text{mm}^2$; Minor defect: contaminants that cannot be removed from the outer surface $\geq 1.7\text{mm}^2$</p>
1.08	Glass particles	Interior of container	Glass particles and fragments attached to the interior of the container	Affect drug quality	Critical defect: attachment of $\geq 0.5\text{mm}$ inside the container that cannot be removed
1.09	Stone	Any position	Opaque inclusions in glass, impurities, particles from furnaces or raw materials	Affect the aesthetics, mechanical resistance, and thermal shock of the product	Cartridge, glass barrel for pre-filled syringe: Major Defect: protruding stones inside; Minor defect: if the stone is on the outside and $>1\text{mm}$
					Tubular injection vial, tubular medical bottle: Major Defect: affect use; Minor defect: if it does not affect the use, but the stone is greater than 1mm
					Stone in the ampoule stem area is the Major Defect; If the stone on the bottle body is greater than 1mm , it is a minor defect
					Moulded bottle: Minor defect: stone $>1.6\text{mm}$
1.10	Knot	Any position	Nodular glassy inclusions, usually with slender tails	Affect the aesthetics, mechanical resistance, and thermal shock of the product	Cartridge, glass barrel of pre-filled syringe: Critical defect: sealing is damaged; Major defect: if the movement of the plunger is limited; Minor defect: if the nodule is external and $>1\text{mm}$
					Tubular injection vial, tubular medical bottle: Minor defect: knot $>1\text{mm}$
					Knot in the ampoule stem area is the Major Defect; other position is greater than 1mm , it is a minor defect
					Moulded bottle: Minor defect: knot $>1.6\text{mm}$

1.11	Cord	Any position	Clear and visible thick lines that differ from the main body of glass due to uneven chemical or physical composition, sometimes protruding from the surface of the product	Affect the aesthetics of the product	Minor Defect
1.12	Bubble	Any position	Glass filled, partially filled with gas, or in a vacuum cavity	Affect the aesthetics of the product	Cartridge, glass barrel of pre-filled syringe: Minor defect: body, bubble>0.5mm
					Tubular injection vial, tubular medical bottle: Minor defect: signal bubble>0.5mm
					Bubble in the ampoule stem area is the Major Defect; body part is greater than 0.5mm, it is a minor defect
					Moulded bottle, minor defect or non-defect needs to be classified by limit samples
1.13	Air line	Any position	Small elongated bubbles in the cross-section of glass	Affect the aesthetics, mechanical resistance and thermal shock of the product	Tubular injection vial, tubular medical bottle, ampule, cartridge and glass barrel for pre-filled syringe: Minor defect: length exceeds the bottle body, and the width is $\geq 0.25\text{mm}$
1.14	Bump check	Exterior surface	Crescent or dot shaped marks on the surface of containers caused by mechanical impact or contact between glass	Affects the mechanical resistance and thermal shock of container	Tubular injection vial, ampoule, cartridge and glass barrel for pre-filled syringe: Major defect: $>0.5\text{mm}$; Minor defect: $\leq 0.5\text{mm}$
					Moulded bottle: Major defect: $>2.5\text{mm}$
Note: Glass barrel for pen-injectors is also known as Cartridge					
*: The wavy ring defect is not applicable to prefilled products; The rocker bottom defect is not applicable to containers that run through both ends, such as glass barrels.					

Table2 Unique cosmetic defects of Pharmaceutical glass infusion bottles, Pharmaceutical moulded glass injection vial, pharmaceutical moulded glass medicinal bottles

Defect Nr.	Defect Name	Defect position	Defect description	Potential defect risk	Defect classification
2.01	Bird cage	Interior of container	glass fibers attached to the internal wall of the bottle, or glass fibers that overlap on the opposite side of the container	Affect drug quality	Critical Defect
2.02	Flanged finish	Sealing surface of bottle mouth	protruding circular flying wings at the bottle mouth mostly occur on the internal edge of the bottle mouth	Impact CCI	Critical defect: affect CCI; Minor defect: not affect the CCI, but affect the aesthetics of the product
2.03	Glass thread	Exterior surface	During the product forming process, the uneven force on the glass during extension causes filamentous glass on the external surface of the container	Affect the aesthetics of the product	Major Defect: length \geq 10mm; Minor defect: length $<$ 10mm
2.04	Shear mark	Any position	Feather shaped glass surfaces caused by improper cutting operations, although not common, may occur in any part of the container, mainly at the bottom and neck of the bottle	Impact CCI	Major Defect: penetrating the sealing surface of the bottle mouth
				Affect the aesthetics of the product	Minor defect: $>$ 5mm
2.05	Dim design	Body, bottom	Unclear markings due to mold wear or poor contact between glass and mold	Affect the product information and causing confusion	Major Defect
2.06	Prominent joint	Any position	The protrusion on the exterior surface of the container caused by incorrect closure of mold components that affects its use	Affect the aesthetics of the product	Minor defect: The seam line of the bottle mouth sealing surface protrudes \geq 0.3mm
2.07	Soft blister	Any position	Glass filled, partially filled with gas, or in a vacuum cavity	Affect drug quality	Critical defect: interior, \geq 0.8mm; Minor defect: exterior, \geq 0.8mm

Table 3 Unique cosmetic defects of Pharmaceutical tubular glass injection vials, Pharmaceutical tubular glass medicinal bottles

Defect Nr.	Defect Name	Defect position	Defect description	Potential defect risk	Defect classification
3.01	Uneven shoulder	Shoulder	Bottle shoulder is high on one side and low on the other	Affect the filling efficiency of drug	Major Defect
				Affect the aesthetics of the product	Minor Defect
3.02	Tailed, heel sticker	Bottom	protruding glass objects resembling tails or small braids on the outside of the bottle bottom	Affect the filling efficiency of drug	Major Defect



Table 4 Unique cosmetic defects of Glass ampoules

Defect Nr.	Defect Name	Defect position	Defect description	Potential defect risk	Defect classification
4.01	Color error	Neck, stem	Color break band /identification band/color spot - color error	Affect the product information identification and Causing confusion	Critical Defect
4.02	Misprint	Body	Incorrect use of printing colors, image, text, and other information	Affect the product information identification and Causing confusion	Critical Defect
4.03	Badness printing	Body	Some printed patterns, text, and other information may be blurry, missing, scratched, worn out, blurred, or ink may fall off	Affect the product information identification and Causing confusion	Critical defect: info mistake; Major defect: Incomplete information caused by ink detachment
4.04	Badness score	Neck	Double scores or missing score at the neck of the ampoule	Affect the functionality of ampoule	Critical Defect
4.05	Incomplete color band	Neck	Color break band is incomplete or less than 360 degrees around construction	Affect the functionality of ampoule	Critical defect: gap > 1mm; Major defect: gap ≤1mm
4.06	Unflat opening section	Neck	Sharp protrusions, notches, and cracks exceeding the length of the shoulder after manual breaking	Affect the functionality of ampoule	Major Defect
4.07	Color spot missed	Bulb	Missing color spot	Affect the functionality of the product	Major Defect
4.08	Improper glaze	Flared end	The bottle mouth has not been glazed and has a rough surface	Affect the filling efficiency of drug	Major Defect
4.09	Partially closed funnel	Flared end	The bottle mouth is closed inward and covers more than 1/4	Affect the filling efficiency of drug	Major Defect

Table 5 Unique cosmetic defects of Glass barrels for pen-injectors

Defect Nr.	Defect Name	Defect position	Defect description	Potential defect risk	Defect classification
5.01	By-pass missing	Body	Cartridge by-pass missing	Affect the functionality of the product	Critical Defect
5.02	By-pass deformed	Body	By-pass deformed on the body	Affect the functionality of the product	Major defect: affect the movement of the plunger or liquid flow; Minor defect: others
5.03	Unglazed	Flared end	The bottle mouth has not been glazed and has a rough surface	Affect the aesthetics and functionality of the product	Major Defect
5.04	Flared	Flared end	Over flared of the bottom flame leads to the accumulation of bottom glass material	Affect the aesthetics and functionality of the product	Major defect: OD of bottom is greater than OD of body; Minor defect: others
5.05	Toenail	Bottom	Due to poor cutting, there is some protrusion at the bottom end	Affect the aesthetics and functionality of the product	Major defect: toenail>1mm
5.06	Uneven shoulder	Shoulder	Bottle shoulder is high on one side and low on the other	Affect the aesthetics and functionality of the product	Major defect: affect use; Minor defect: not affect use
Note: The glass barrel for pen-injectors includes the glass barrel for medical pen-injectors and the glass barrel for disposable dental anesthesia cartridges.					

Table 6 Unique cosmetic defects of Glass barrels for prefilled syringes

Defect Nr.	Defect Name	Defect position	Defect description	Potential defect risk	Defect classification
6.01	Contamination	Interior, Exterior surface	Contaminants present on the inner and outer surfaces of containers	Affect drug quality	Critical defect: Contaminations on the interior surface of RTU products
				Affect the aesthetics of the product	Major defect: Contaminations $\geq 0.5\text{mm}^2$ on the exterior surface of RTU products
6.02	Bad printing	Body	Phenomena such as blurring, missing, and ghosting of units, scales, or numbers when printing scales	Affect the product information identification	Critical defect: info mistake; Major defect: Incomplete information caused by ink detachment; Minor defect: no info mistake;
6.03	Scratch	Body	Appears on the surface of the barrel body, shallow and concave, but does not penetrate the wall, and its function is not damaged	Affect the aesthetics of the product	Major defect: Width $> 0.2\text{mm}$ or length $> 10\text{mm}$; Minor defect: Width $\leq 0.2\text{mm}$ and $\leq 10\text{mm}$
6.04	Through hole blockage	Cone	The internal hole of the cone is blocked and not unobstructed	Affect the functionality of the product	Major Defect
6.05	Incomplete cone forming	Cone	Incompleteness caused by forming	Affect the aesthetics and functionality of the product	Minor Defect
6.06	Finger grip deformed	Flange	Incompleteness of finger grip	Affect the functionality of the product	Major Defect

6 Cosmetic Defects Evaluation

The manufacturers and users of pharmaceutical glass containers should aim to ensure controllable drug quality, meet clinical needs, and ensure safe use. Based on the actual production and use situation, appropriate quality requirements including but not limited to the provisions of this document should be selected to develop enterprise standards or quality agreements.

When evaluating cosmetic defects, greater attention should be paid to cosmetic defects that may cause container protection, compatibility, safety, and functional failure.

According to the risk management requirements of production and use, inspection rules can be developed. A more statistically significant sampling plan can be used to evaluate the batches quality of pharmaceutical packaging materials. A sampling plan can be designed according to the "Guidance of Pharmaceutical Packaging Material Inspection Rules". Critical defects are inspected according to "Class A Non-Conforming", Major defects are inspected according to "Class B Non-Conforming", and Minor defects are inspected according to "Class C Non-Conforming".

When the conditions are met, reliable and validated online real-time inspection data can be used as the basis for parametric release during the product release process.



APPENDIX A
(INFORMATIVE)

The names of cosmetic defects in both Chinese and English are shown in Table A.1





Table A.1 Defect names in both Chinese and English





Defect Nr.	CN	EN	Defect Nr.	CN	EN
1.01	开裂, 破裂	Split, crack	3.02	拖尾	tailed, heel sticker
1.02	破损	broken	4.01	易折环/识别环/ 色点颜色错误	color error
1.03	口面不平整	wavy ring	4.02	印刷错误	misprint
1.04	表面裂纹	check	4.03	印刷不良	badness printing
1.05	畸形	severely deformed	4.04	刻痕不良	badness score
1.06	凸底	rocker bottom	4.05	易折色环不良	incomplete color band
1.07	无法清除的污染	non-removable contamination	4.06	折断面不平整	unflat opening section
1.08	玻璃碎片/屑	glass particles	4.07	色点缺失	color spot missed
1.09	结石	stone	4.08	未圆口	improper glaze
1.10	节瘤	knot	4.09	包口	partially closed funnel
1.11	条纹	cord	5.01	旁通缺失	by-pass missing
1.12	气泡	bubble	5.02	旁通变形	by-pass deformed
1.13	气线	air line	5.03	底端未抛光	unglazed
1.14	撞伤	bump check	5.04	底端抛光过度	flared
2.01	瓶内搭丝	bird cage	5.05	底端不平整	toenail
2.02	瓶口飞边	flanged finish	5.06	高低肩	uneven shoulder
2.03	玻璃丝	glass thread	6.01	污染	contamination
2.04	剪刀印	shear mark	6.02	印刷不良	bad printing
2.05	标记模糊	dim design	6.03	管身划痕	scratch
2.06	合缝缺陷	prominent joint	6.04	锥孔堵塞	through hole blockage
2.07	薄气泡	soft blister	6.05	锥头不完整	incomplete cone forming
3.01	高低肩	uneven shoulder	6.06	卷边变形	finger grip deformed

**APPENDIX B
(INFORMATIVE)**





SOME EXAMPLES OF DEFECTS





Some examples of defects (* ones are provided by enterprises)




1.01 split, crack			
			
Pic 1.01	Pic 1.01 - 1	Pic 1.01 - 3	Pic 1.01 - 4

1.02 broken			
			
Pic 1.02 - 1	*Pic 1.02 - 2	*Pic 1.02 - 3	*Pic 1.02 - 4





1.03 wavy ring	1.04 check
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Pic 1.03 - 1	*Pic 1.03 - 2	Pic 1.04 - 1	Pic 1.04 - 2





1.04 check		1.05 severely deformed	
			
*Pic 1.04 - 3	Pic 1.04-4 (Partial enlarged view of 1.04-3)	Pic 1.05 - 1	*Pic 1.05 - 2





1.05 severely deformed			
			
Pic 1.05 - 3	*Pic 1.05 - 4	Pic 1.05 - 5	*Pic 1.05 - 6

1.06 rocker bottom





			
*Pic 1.06 - 1	*Pic 1.06 - 2	Pic 1.06 - 3	Pic 1.06 - 4





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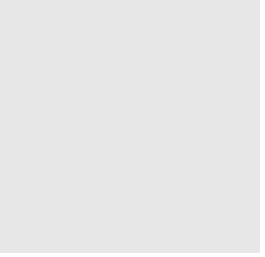
1.07 non-removable contamination			
			
Pic 1.07 - 1	Pic 1.07 - 2	Pic 1.07 - 3	Pic 1.07 - 4

1.08 glass particles	1.09 stone	1.10 knot	
			
Pic 1.08 - 1	Pic 1.08 - 2	*Pic 1.09 - 1	*Pic 1.10 - 1





1.12 bubble





			
Pic 1. 12 - 1	Pic 1. 12 - 2	Pic 1. 12 - 3	Pic 1. 12 - 4





1.13 air line			
			
Pic 1. 13 - 1	Pic 1. 13 - 2	Pic 1. 13 - 3	Pic 1. 13 - 4

1.14 bump check			
			
*Pic 1. 14 - 1	Pic 1. 14-2 (Partial enlarged view of 1. 14- 1)	Pic 1. 14 - 3	Pic 1. 14-4 (Partial enlarged view of 1. 14-3)





2.04 shear mark	2.05 dim design
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Pic 2.04 - 1	Pic 2.04-2 (Partial enlarged view of 2.04- 1)	Pic 2.05 - 1	Pic 2.05-2 (Partial enlarged view of 2.05- 1)





2.06 prominent joint	2.07 soft blister	3.01 uneven shoulder	
			
Pic 2.06 - 1	*Pic 2.07 - 1	Pic 3.01 - 1	Pic 3.01 - 2

3.02 tailed, heel sticker		4.03 badness printing	
			
Pic 3.02 - 1	Pic 3.02-2 (Partial enlarged view of 3.02- 1)	Pic 4.03 - 1	*Pic 4.03 - 2





4.04 badness score	4.05 incomplete color band
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Pic 4.04 - 1	Pic 4.04 - 2	Pic 4.05 - 1	Pic 4.05 - 2





4.07 color spot missed		4.08 improper glaze	
			
Pic 4.07 - 1	Pic 4.07-2 (Partial enlarged view of 4.07- 1)	Pic 4.08 - 1	Pic 4.08-2 (Partial enlarged view of 4.08- 1)

4.09 partially closed funnel	5.01 by-pass missing	5.02 by-pass deformed
		
Pic 4.09 - 1	*Pic 4.09 - 2	*Pic 5.01 - 1
		
		*Pic 5.02 - 1

5.02 by-pass deformed	5.03 unglazed	5.05 toenail	5.06 uneven shoulder
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*Pic 5.02 - 2	*Pic 5.03 - 1	Pic 5.05- 1	*Pic 5.06 - 1

6.01 contamination	6.02 bad printing	6.03 scratch	
			
Pic 6.01 - 1	Pic 6.02- 1	Pic 6.03 - 1	Pic 6.03 - 2

6.04 through hole blockage		6.05 incomplete cone forming	6.06 finger grip deformed
			
Pic 6.04 - 1	Pic 6.04 - 2	Pic 6.05 - 1	Pic 6.06 - 1