Validation Guideline

Le-Flex® TPE Tubing

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1.Introduction

Single-use systems are widely used in biopharmaceutical processes, including the development and commercial production of drugs such as monoclonal antibodies, vaccines, cells and gene therapy, where product safety and reliability are extremely important. The transport and transfer of fluids between different systems is an important part of the drug development and production process. Shanghai LePure Co., Ltd. (hereinafter referred to as LePure Biologics) newly developed Le-Flex® TPE thermoplastic tube is perfectly suited for the transfer of a wide range of fluids in the biopharmaceutical process, including disposable system assembly, aseptic transfer, formulation filling, sampling, and collection. The products meet the stringent requirements of the biopharmaceutical industry, with excellent biosafety, compatibility and physical properties, and have passed quality testing and verification, providing users in biopharmaceutical companies with safe and reliable single-use systems.

This Validation Guide describes the physical and chemical properties, biosafety, key controls, quality standards, key quality parameters and other information related to the manufacturing process of Le-Flex®TPE thermoplastic tubing developed and manufactured by LePure Biologics, and provides LePure Biologics customers with basic information to evaluate and test the product before use.

This Validation Guide applies to both Le-Flex® TPE thermoplastic tubing sold as a stand-alone product and to Le-Flex® TPE thermoplastic tubing pre-assembled on Le-Pure disposable systems.

2. Supply Chain Security and Its Support

As a key consumable for fluid transfer in biopharmaceutical processes, TPE thermoplastic tubing suppliers need to provide complete solutions to ensure the safety and control of their supply chains and avoid supply chain instability due to extreme conditions.

Le-Flex® TPE thermoplastic tubing can provide stable supply chain security and safety in that:

•Localized Production

Le-Flex® TPE thermoplastic tubing is developed and produced by LePure Biologics. The main production site is located at Zhengbo Road, Lingang Free Trade Zone, Shanghai, China, and the production workshop is a Class C clean environment.

• Multi-Center Production

To avoid the risks associated with a single production site, LePure Biologics is in the process of validating a second production site overseas and will complete the layout of a second global production site by 2023 for multi-center production.

• Adequate stocking

According to the market demand, we have sufficient TPE resin particles and finished TPE thermoplastic tubes for the production of thermoplastic tubes to ensure the supply of products on schedule.

2.1Le-Flex®TPE Thermoplastic Tube Material Affirmation

Table 1 shows the declaration of key concerns for TPE materials used in Le-Flex® TPE thermoplastic

tubes, as well as the declaration of compliance with key regulations.

Table 1.Le-Flex®TPE Thermoplastic tube material affirmation

Focus on things	Affirmation
TES/BSE	No TES/BSE
Plant Origin	No Plant Origin
A Bisphenol A(BPA)	No A Bisphenol A(BPA)
Latex, Gluten and Allergens	No Latex, Gluten and Allergens
Glycerin	No Glycerin
Melamine	No Melamine
Slip Agents	No-Slip Agents
Conflict Minerals Ruled by Dodd-Frank Wall Street Reform and Consumer Protection Act	No Conflict Minerals Ruled by Dodd-Frank Wall Street Reform and Consumer Protection Act
Genetically Modified Organisms (GMO)	Genetically Modified Organisms (GMO)
Asbestos	No Asbestos
Phthalates	No Phthalates
Registration, Evaluation, Authorization and Restriction of Chemicals (REACH) and Substances of Very High Concern (SVCH)	Meet the REACH&SVCH
Restriction of Hazardous Substances (RoHS)& Coalition of Northeastern Governors (CONEG)	Meet the RoHS & CONEG

2.2 Quality System

The company has developed a quality management system by ISO 9001:2015 ISO 13485:2016 and is certified to ISO 9001:2015. The manufacturing of Le-Flex® TPE thermoplastic tubes is subject to rigorous performance testing and meets industry safety standards. Cleanroom personnel management, material management, process specifications, equipment management and validation are all performed by Good Manufacturing Practices (GMP) requirements, ensuring that standards and requirements for each step of the process are in line with regulatory compliance.

2.3 Batch Management and Traceability Management

The production of Le-Flex® TPE thermoplastic tubes establishes operating procedures for product

batches to ensure the homogeneity and consistency of product quality and characteristics of the same batch and establishes standard operating procedures for batch numbers and production dates so that each batch of products has a unique batch number.

3. Physical Performance Test

Le-Flex® TPE thermoplastic tubing was developed specifically for fluid management systems in disposable biopharmaceutical processes. It meets the fluid handling requirements for flexibility, translucency, gamma irradiation or autoclaving, aseptic heat sealing, aseptic heat welding to commercially available TPE thermoplastic tubing, and low extractable content, making it an ideal thermoplastic tubing consumable for the biopharmaceutical industry. The test data in this section demonstrates the good physical properties of Le-Flex® TPE thermoplastic tubing. These parameters are the key test parameters before the tubing leaves the factory, and are also important boundaries to guide customers in the use process.

3.1 Size and Packaging

The Le-Flex® TPE thermoplastic tubes are available in sizes between 1/8" x 1/4" (ID x OD, Figure 1) and 3/4" x 1" (ID x OD), for a total of 8 sizes, see Table 2 for specific information. each roll is packaged in a double bag, and the outer packaging is an individual carton.

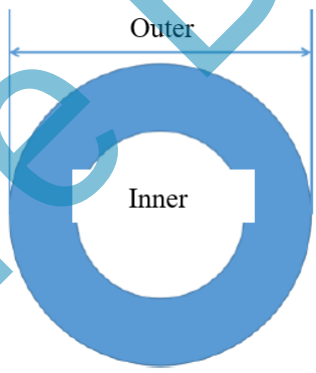

Figure 1. Schematic Diagram of Inner Diameter And Outer Diameter of The Pipeline

Table 2. Le-Flex® TPE Thermoplastic Tube Specification Parameters

Products	Dimensions (mm) (ID × OD)	Dimensions (inch) (ID × OD)	Piping length (m)
LF-0125-0250	3.2×6.4	1/8×1/4	15.0
LF-0188-0313	4.8×8.0	3/16×5/16	15.0
LF-0250-0375	6.4×9.6	1/4×3/8	15.0
LF-0250-0437	6.4×11.1	1/4×7/16	15.0

LF-0250-0500	6.4×12.7	1/4×1/2	15.0
LF-0375-0625	9.6×15.9	3/8×5/8	15.0
LF-0500-0750	12.7×19.1	1/2×3/4	15.0
LF-0750-1000	19.1×25.4	3/4×1	4.5

3.2 Physical Properties of Raw Materials for Pipelines

The physical parameters such as hardness, tensile strength and elongation at break were tested before and after 25-40 kGy gamma irradiation according to the ASTM test method, and the specific parameters are shown in Table 3.

Table 3. Basic Physical Parameters of Le-Flex® TPE Raw Materials Before And After Gamma Irradiation

Test Item	Units	Test Method	Test Result	
			After Gamma Irradiation	Before Gamma Irradiation
Hardness	Shore A	ASTM D2440	59-61	57-59
Tensile Strength	MPa	ASTM D412	14.5	12.6
Elongation At Break	%	ASTM D412	758	753
100% Constant Tensile Stress	MPa	ASTM D412	1.9	1.6
300% Constant Tensile Stress	MPa	ASTM D412	3.5	3.3
Tearing strength	KN/m	ASTM D624	30	29.8
300% tensile permanent deformation	%	ASTM D412	12	16
Compression permanent deformation "B" (22 hrs,70°C)	%	ASTM D395	61	63
Low-temperature brittle point test	°C	ASTM D746	-70	-66

3.3 FT-IR Test

The IR spectra of the Le-Flex®TPE thermoplastic tubes were compared before sterilization, after 50kGy gamma irradiation sterilization, and after autoclaving (121°C, 30min), and the results are shown in Figure 2.The results show that regardless of the sterilization method, the IR spectra of the TPE tubes

before and after sterilization have no abnormal peak addition or reduction, indicating that gamma irradiation or steam sterilization does not change the chemical properties of Le-Flex® TPE thermoplastic tubes.

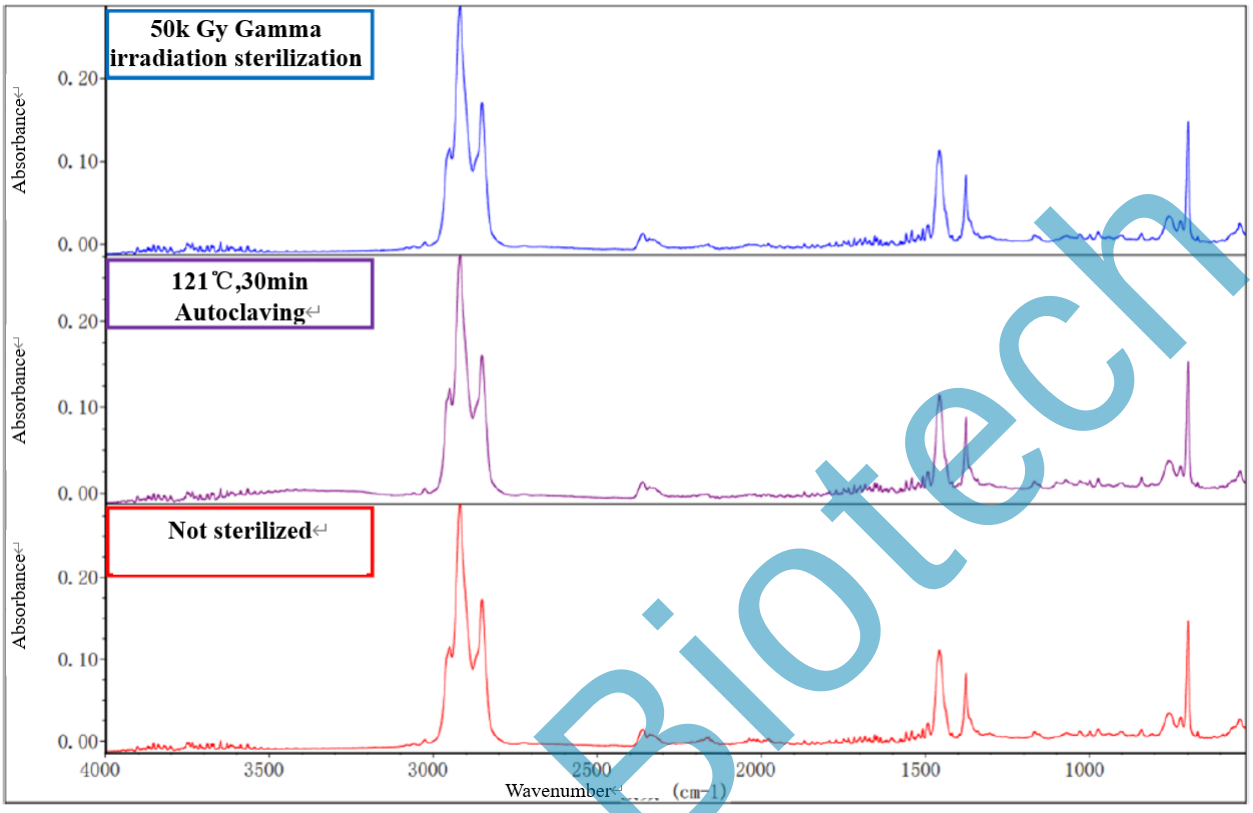

Figure 2. Comparison of infrared spectra of Le-Flex® TPE thermoplastic tubes before and after sterilization

3.4 Sterilization Compatibility Study

The Le-Flex®TPE thermoplastic tube should be compared with the yellowness index test before and after gamma irradiation, referring to the ASTMD1925 standard. The results show that after high dose 45-55kGy gamma irradiation, the yellowness index of Le-Flex® TPE thermoplastic tube increases from -7.6 to -5.8, which is within 2.0, and the yellowing phenomenon is not obvious. Some mainstream competitors in the market will increase the yellowness index by at least 3.5 after high dose irradiation, and the yellowing phenomenon will be obvious in appearance. Therefore, the degree of yellowing of Le-Flex®TPE thermoplastic tube is much lower than the mainstream competing products in the market, showing excellent resistance to gamma irradiation.

Le-Flex® TPE thermoplastic tubing is normally gamma pre-sterilized when sold pre-assembled on Le-Pure disposable reservoir bags, mixing bags, reaction bags and other related products. However, Le-Flex® TPE thermoplastic tubing is non-sterile when sold as a stand-alone product. It is recommended that Le-Flex® TPE thermoplastic tubes be sterilized by gamma (≤50kGy) or autoclave (max. 121°C for 30 min) before use. Repeated and multiple means repeated sterilization is not recommended.

4. Biocompatibility

Biocompatibility is a prerequisite for the development of Le-Flex® TPE thermoplastic tubing, and material compliance is a major factor affecting biosafety. Le-Flex®TPE thermoplastic tubing was tested after 45-55 kGy gamma irradiation by USP and ISO 10993 related standards. Table 4 summarizes the biosafety test results, and Le-Flex® TPE thermoplastic tubes passed all tests.

Table 4. Bio-safety test results for Le-Flex® TPE thermoplastic tubes

Testing Standards	Test Items	Test Result
ISO 10993-4	Hemolysis test	passed
ISO 10993-5	Cytotoxicity	passed
ISO 10993-6	Implantation test	passed
ISO 10993-10	Irritation and Sensitization tests	passed
ISO 10993-11	Acute Systemic Toxicity test	passed
USP<87>	Biological reactivity testing, in vitro	passed
USP<88>	Biological reactivity testing, in vitro, class VI	passed

5. Pharmacopeial Compliance

5.1 USP<661> Physical and Chemical Testing

Referring to USP<661>, for plastics applied in high-risk areas (inhalers, injectables, ophthalmic preparations, etc.), physical and chemical testing must be performed to ensure that no hazardous substances are precipitated.

Since Le-Flex®TPE thermoplastic tubing can be used throughout the life cycle of a drug, it was necessary to evaluate whether Le-Flex® TPE thermoplastic tubing met the criteria after irradiation at the maximum dose (45-55 kGy), as shown in Table 5.

Table 5. Physicochemical test results of Le-Flex® TPE thermoplastic tubes USP<661>

Test methods	Test Items	Judgment Criteria	Test Result	Judgment Result
USP<661>	Cushioning performance	⩽10.0ml	0.2mL	Qualified
	Heavy metal	⩽1ppm	＜1ppm	Qualified
	Non-volatile residue	⩽15mg	0.4mg	Qualified
	Scorching residue	⩽1mg	0.1mg	Qualified

5.2 USP<85> Bacterial Endotoxin Test

Referring to the requirements of CHP<1143> and USP<85>, the bacterial endotoxin test was performed at a contact area to extract ratio of 6cm2/mL, and the result was <0.125EU/mL (CHP<1143> and USP<85> standard: <0.25EU/mL, LePure Biologics internal control standard: <0.125EU/mL). It meets the requirements of Chinese Pharmacopoeia and US Pharmacopoeia as well as internal control standards of LePure Biologics.

5.3 USP<788> Insoluble Particle Test

Regarding CHP<0903> and USP<788>, the level of insoluble particles in Le-Flex® TPE thermoplastic tubes was tested at a contact area to extract a ratio of 6cm2/mL, and the results are shown in Table 6.

The internal control standards for insoluble particles of LePure Biologics are as follows.

≥10μm: ≤10 /mL

≥25μm: ≤1 /mL

After testing, Le-Flex® TPE thermoplastic tubes passed all tests.

Table 6. Le-Flex® TPE thermoplastic tubing USP<788> insoluble particles test results

Test method	Test item	Test standard	Result
USP<788>	Insoluble particles tests	≥10μm: ≤10/mL ≥25μm: ≤1/mL	≥10μm: ≤7.4 个/mL ≥25μm: ≤0 个/mL

5.4 USP<1469> Nitrosamine Impurity Test

Nitrosamine impurities are highly toxic genotoxic impurities that can be introduced into pharmaceutical products or generated as impurities through a variety of routes. The USP<1469> section follows FDA guidelines to ensure that the daily intake of nitrosamine impurities in pharmaceuticals does not exceed acceptable limits, with the FDA establishing a daily intake of 96 ng/day for NDMA and NMBA, and 26.5 ng/day for NDEA, NMPA, NIPEA, and NDIPA. The content of the six nitrosamine impurities in Le-Flex® TPE thermoplastic tubes was measured by liquid chromatography-mass spectrometry (LC-MS/MS) concerning the requirements of USP<1469>, and the results are shown in Table 7. The internal control standard for the content of nitrosamine impurities in LePure TPE is <1.0 ppb.

Table 7. Le-Flex® TPE Thermoplastic Tubing USP<1469> Nitrosamine Impurity Test Results

Test method	Test item	Test standard	Result
USP<1469>	NDMA	<1.0ppb	Qualified
	NDEA	<1.0ppb	Qualified
	NDIPA	<1.0ppb	Qualified
	NEIPA	<1.0ppb	Qualified
	NDBA	<1.0ppb	Qualified
	NMBA	<1.0ppb	Qualified

5.5 USP<381>Elastomer test

Referring to USP<661>, for plastics applied in high-risk areas, physical and chemical testing must be performed to ensure that no hazardous substances are precipitated.

Since Le-Flex®TPE thermoplastic tubing can be used throughout the life cycle of a drug, it was necessary to evaluate whether Le-Flex® TPE thermoplastic tubing met the criteria after irradiation at the maximum dose (45-55 kGy), as shown in Table 8.

Table 8. Le-Flex® TPE thermoplastic Tube USP<381>elastomer test results

Method	Test/Parameter	Specification	Result
USP<381>	Color	Sample solution is not more intensely colored than the Color standard.	Pass
	Appearance(Turbidity/Opalescenc)	N/A	Sample solution is less opalescent than Reference suspension B and Reference suspension C
	Acidity or Alkalinity	NMT 0.3 mL of 0.01 N sodium hydroxide produces a blue color or NMT 0.8 mL of 0.01 N hydrochloric acid produces a yellow color, or no titration is required.	Pass
	Absorbance	N/A	0.03
	Redycing Substances	N/A	0.1ml
	Volatile Sulfides	Any black stain on the paper produced by the test solution is not more intense than that produced by the control substance.	Pass
	Ammonium	After 5 minutes, any yellow color in the Test Solution is no darker than the Ammonium Standard Solution (no more than 2 ppm of NH4 in Solution S)	Pass

5.6 EP3.2.9 Testing

According to section 3.2.9 of the European Pharmacopoeia, the product needs to meet the specified limit requirements in order to meet the requirements of EP. The purpose of this study is to test the products according to the standard methods and restrictions described in Section 3.2.9 to see whether they meet the standards. See Table 9 for specific data.

Table 9. Le-Flex® TPE Thermoplastic Tube EP3.2.9 Test Results

Method	Test/Parameter	Specification	Result
EP 3.2.9	Appearance of solution S	N/A	Solution S is less opalescent than reference suspension II and reference suspension III
	Identification A	The spectrum obtained is identical to the spectrum obtained with the type sample.	Pass
	Absorbance	N/A	0.03
	Identification B	If A0≤5.0%， total ash is A0±0.75%; If 5.0%<A0≤10%， total ash is A0±1.0%; If A0>10%， total ash is A0±2.0%;	Pass
	Total Ash		Pass
	Total ash in type sample(A0)		Pass
	Reducing substances	N/A	0.3mL
	Residue on evaporation	N/A	0.1mg
	Acidity or alkalinity	Not more than 0.3 mL of 0.01 M sodium hydroxide or 0.8 mL of 0.01 M hydrochloric acid is required to change the colour of the indicator to blue or yellow, respectively. If after adding the indicator the solution is green, it is neutral and no titration is needed.	Pass
	Ammonium (2.4.1, MethodA)	⩽ 2 ppm	Pass
	Extractable zinc	⩽ 5 μg/mL	Pass
	Extractable heavy metals(2.4.8)	⩽ 2 ppm	Pass
	Volatile sulfides	Any black stain on the paper is not more intense than that of a standard.	Pass

6. Chemical Compatibility

There may be multiple chemical interactions between single-use systems and contact fluids, and pharmaceutical companies should fully consider the results of these interactions. Data on chemical compatibility (including from manufacturers, literature, industry experience, etc.) can be used by pharmaceutical companies to make assessments based on these chemical compatibility data if they can be directly referenced①.If data from other programs in the overall validation program portfolio can be used effectively to assess the risk of chemical compatibility, the industry will typically base its

assessment on these data as well. If a pharmaceutical company needs to test for chemical compatibility, it can also establish an appropriate approach by referring to the relevant ASTM test methods②.

Notes:① ② China Food and Drug International Exchange Center: Chapter 3.6 of the Application and Technology Guide for Single-Use Systems.

Le-Flex® TPE thermoplastic tubes filled with different solutions after 45-55 kGy gamma irradiation and then left at 30±2.5°C for 7 days were tested for appearance, cracks, and infrared, and the results are shown in Table 10. These solvent compatibility data are all based on real test results but not directly quoted.

Table 10. Le-Flex® TPE Thermoplastic Tube Compatibility List (30±2.5°C for 7 days)

No.	Solution	Test results
1.	Ethanol 95%	Compatible
2.	Ethanol 70%	Compatible
3.	Glycerol 100%	Compatible
4.	Propylene Glycol 100%	Compatible
5.	Ethyl Acetate 100%	Compatible
6.	DMSO 10%	Compatible
7.	DMSO 20%	Compatible
8.	DMF 10%	Compatible
9.	DMF 20%	Compatible
10.	DMA/DMAc 20%	Compatible
11.	N-methylpyrrolidone(NMP) 20%	Compatible
12.	Hydrochloric Acid 3%	Compatible
13.	Hydrochloric Acid 10%	Compatible
14.	Citric acid 1%	Compatible
15.	PhosphoricAcid25%	Compatible
16.	Ammonium Hydroxide(5 M)	Compatible
17.	Sodium Hydroxide1%	Compatible
18.	Sodium Hydroxide50%	Compatible

19.	HCI/KClbuffer pH3	Compatible
20.	Acetate buffer solution pH4.6	Compatible
21.	Phosphate buffer solution pH7.2	Compatible
22.	Borax sodium hydroxide pH10	Compatible
23.	Phosphate buffer solution pH12	Compatible
24.	X-100TritonX-100100%	Compatible
25.	Tween 80 100%	Compatible
26.	Olive oil 100%	Compatible
27.	Sodiumacetate27%(50mM)	Compatible
28.	Calcium Carbonate	Compatible
29.	Barium Sulfate	Compatible
30.	Sodium Bicarbonate	Compatible
31.	Sodium Chloride 5M	Compatible
32.	Hydrogen Peroxide10%	Compatible
33.	WFI	Compatible

7. Functional testing

Based on LePure Bio's in-house standard test methods, the Le-Flex® TPE thermoplastic tubes were tested for various functionalities, including mainly aseptic sealing, aseptic welding, and low-temperature performance testing.

7.1 Aseptic Disconnection

The transfer of tubing in various processes involves aseptic disconnection (aseptic sealing) and should avoid fluid leakage due to incomplete heat sealing during actual use. For untreated, 25-40 kGy gamma-irradiated, and high-pressure steam (121°C, 30 min) treated Le-Flex® TPE thermoplastic tubing, aseptic sealing was performed using Le-Pure's second-generation aseptic automatic tube sealer, as shown in Figure 3. After heat sealing, the following tests were performed to verify the aseptic sealing effect: (1) visual inspection of the sealing effect (2) gas tightness test (3) bursting pressure test.

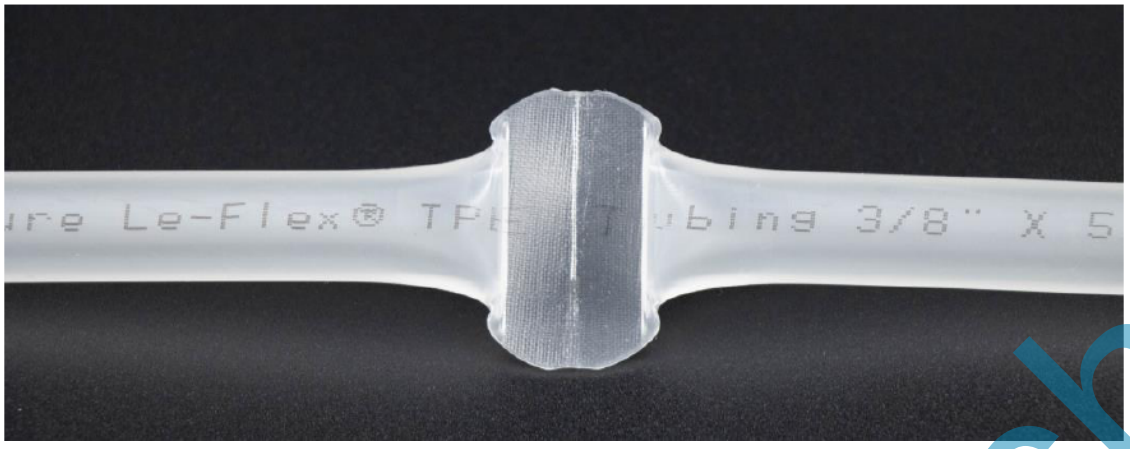

Figure 3. Effect of aseptic sealing of Le-Flex® TPE thermoplastic tube by LePure II tube sealing machine

7.1.1 Visual Inspection of Sealing Effect

The aseptic seal of Le-Flex® TPE thermoplastic tube should be smooth, flat, free of bubbles and defects, then it is considered to pass. 8 sizes of Le-Flex® TPE thermoplastic tube aseptic seal of the visual inspection results are shown in Table 9, all pass.

7.1.2 Air Tightness Test

In order to make sure that the Le-Flex® TPE thermoplastic pipe, especially the sealing place, has good airtightness, the pipe should be tested for airtightness. A pressure calibrator was used to give 0.12±0.01MPa air pressure to the pipe (length 30cm), and the pressure was stabilized for 15s, and then the pressure drop was recorded after the 30s. The results of the airtightness test are shown in Table 9, all passed.

7.1.3 Burst Pressure Test

The burst pressure test is designed to verify the pressure resistance of the piping under various conditions to avoid fluid leakage due to High-pressure in actual use. The test is a challenging test under extreme conditions and is a key verification to evaluate whether the bursting strength of the thermoplastic pipe can meet the requirements of the biopharmaceutical process for fluid handling to ensure system tightness and sterility.

The specific implementation method is: using a water pressure burst tester for bursting, the test sample length is 30cm, one side is heat sealed, the other end is filled with water, and the water pressure is raised at a rate of 0.1MPa/min until the pipeline ruptures (Figure 4), the burst pressure is greater than 0.4MPa is considered qualified. The burst pressure test results are shown in Table 11. The burst pressurerange of Le-Flex®TPE thermoplastic pipe is 0.41-0.68 Mpa, and all of them passed.

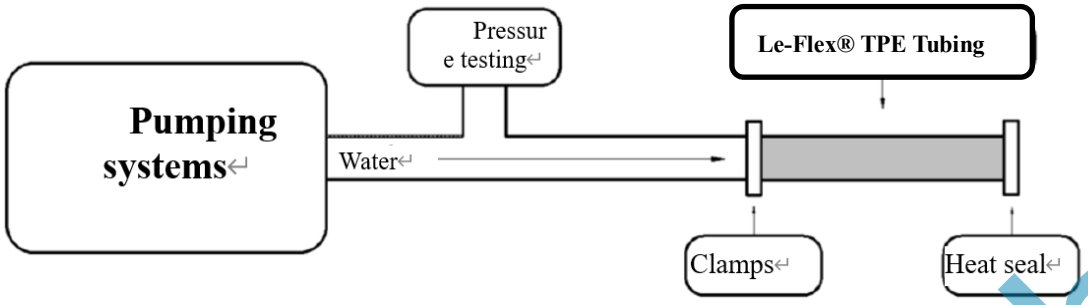

Figure 4. Diagram of Burst Pressure Test

Table 11. Le-Flex®TPE Thermoplastic Tube Aseptic Sealing Test Results

Pipe size (inch)	Sterilization conditions	Visual inspection results	Gas tightness test	Average burst pressure (MPa)
1/8×1/4	Unsterilized	Passed	Passed	0.51
	25-40 kGy Gamma irradiation sterilization	Passed	Passed	0.48
	121°C，30 min High-pressure steam	Passed	Passed	0.47
3/16×5/16	Unsterilized	Passed	Passed	0.50
	25-40 kGy Gamma irradiation sterilization	Passed	Passed	0.44
	121°C，30 min High-pressure steam	Passed	Passed	0.45
1/4×3/8	Unsterilized	Passed	Passed	0.51
	25-40 kGy Gamma irradiation sterilization	Passed	Passed	0.41
	121°C，30 min High-pressure steam	Passed	Passed	0.45
1/4×7/16	Unsterilized	Passed	Passed	0.57
	25-40 kGy Gamma irradiation sterilization	Passed	Passed	0.52
	121°C，30 min High-pressure steam	Passed	Passed	0.62
1/4×1/2	Unsterilized	Passed	Passed	0.66

	25-40 kGy Gamma irradiation sterilization	Passed	Passed	0.62
	121°C，30 min High-pressure steam	Passed	Passed	0.68
3/8×5/8	Unsterilized	Passed	Passed	0.56
	25-40 kGy Gamma irradiation sterilization	Passed	Passed	0.50
	121°C，30 min High-pressure steam	Passed	Passed	0.58
1/2×3/4	Unsterilized	Passed	Passed	0.50
	25-40 kGy Gamma irradiation sterilization	Passed	Passed	0.48
	121°C，30 min High-pressure steam	Passed	Passed	0.51
3/4×1	Unsterilized	Passed	Passed	0.49
	25-40 kGy Gamma irradiation sterilization	Passed	Passed	0.45
	121°C，30 min High-pressure steam	Passed	Passed	0.50

7.2 Aseptic Welding

The transfer of pharmaceutical processes involves the aseptic thermal welding of thermoplastic tubing to itself and to other brands of TPE thermoplastic tubing. In order to avoid possible process modifications and fluid leaks due to non-weldable or poorly welded tubing in practice, it was necessary to evaluate the thermal weldability of Le-Flex® TPE thermoplastic tubing to itself and to other brands of thermoplastic tubing. Using LePure's sterile receiver, Le-Flex® TPE thermoplastic tubes of different sizes and sterilized by different methods were thermally welded to each other, and the results are shown in Table 12.

The following tests were performed on the piping after sterile soldering

(1) Visual inspection of the sterile welding effect. If the appearance of the flange ring formed by welding is not abnormal, no bubbles or other obvious defects, it is considered qualified, as shown in Figure 5.

(2) Welded pipeline gas tightness test. Use the pressure calibrator to give the welding line (length 30cm) 0.12 ± 0.01 MPa of air pressure, steady pressure for 15s, and then record the pressure drop after 30s, the pressure drop is less than 5mbar that is considered qualified.

(3) welding pipe burst pressure test. The use of water pressure burst tester for welding pipeline bursting, test sample length of 30cm, heat welding in the middle, one end of the heat seal, the other end

of the injection of water, to 0.1 MPa/min rate of water pressure until the pipeline rupture. Burst pressure greater than 0.4 MPa is considered qualified.

Only when all the above three test items are qualified can the sterile welding test of Le Flex® TPE thermoplastic pipe pass.

Table 12. Le-Flex® TPE thermoplastic pipe aseptic welding test results

Pipe Size (inch)	Sterilization conditions	Docking pube			
		Le-Flex®	C-Flex®	TuFlux®	AdvantaFlex®
Le-Flex® 1/8×1/4	Unsterilized	Passed	Passed	Passed	Passed
	25-40 kGy Gamma irradiation sterilization	Passed	Passed	Passed	Passed
	121°C，30 min High-pressure steam	Passed	Passed	Passed	Passed
Le-Flex® 3/16×5/16	Unsterilized	Passed	Passed	N/A	N/A
	25-40 kGy Gamma irradiation sterilization	Passed	Passed	N/A	N/A
	121°C，30 min High-pressure steam	Passed	Passed	N/A	N/A
Le-Flex® 1/4×3/8	Unsterilized	Passed	Passed	N/A	N/A
	25-40 kGy Gamma irradiation sterilization	Passed	Passed	N/A	N/A
	121°C，30 min High-pressure steam	Passed	Passed	N/A	N/A
Le-Flex® 1/4×7/16	Unsterilized	Passed	Passed	Passed	Passed
	25-40 kGy Gamma irradiation sterilization	Passed	Passed	Passed	Passed
	121°C，30 min High-pressure steam	Passed	Passed	Passed	Passed
Le-Flex® 1/4×1/2	Unsterilized	Passed	N/A	N/A	N/A
	25-40 kGy Gamma irradiation sterilization	Passed	N/A	N/A	N/A
	121°C，30 min High-pressure steam	Passed	N/A	N/A	N/A
Le-Flex® 3/8×5/8	Unsterilized	Passed	Passed	Passed	Passed
	25-40 kGy Gamma irradiation sterilization	Passed	Passed	Passed	Passed

	121°C，30 min High-pressure steam	Passed	Passed	Passed	Passed
Le-Flex® 1/2×3/4	Unsterilized	Passed	Passed	Passed	Passed
	25-40 kGy Gamma irradiation sterilization	Passed	Passed	Passed	Passed
	121°C，30 min High-pressure steam	Passed	Passed	Passed	Passed
Le-Flex® 3/4×1	Unsterilized	Passed	Passed	N/A	Passed
	25-40 kGy Gamma irradiation sterilization	Passed	Passed	N/A	Passed
	121°C，30 min High-pressure steam	Passed	Passed	N/A	Passed

Note: Visual, airtightness, burst pressure, all three tests are considered to be passed;

Note: N/A means the test was not conducted.

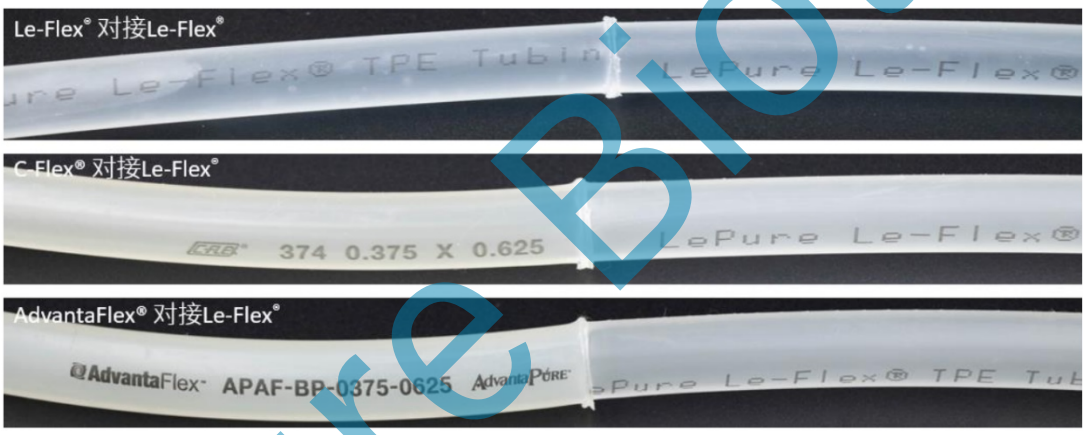

Figure 5. Thermal Weldability of Le-Flex®TPE Thermoplastic Tube with Other Brands

7.3 Low-Temperature Performance Test

In some fields of biopharmaceuticals, low-temperature storage or low-temperature fluid transfer processes (below -20°C) are used, which require good low-temperature resistance of the tubing to prevent possible brittleness or rupture of the tubing during low-temperature use, so the low-temperature resistance of Le-Flex® TPE thermoplastic tubing needs to be verified.

The 30 cm long Le-Flex® TPE thermoplastic tubing is sterilized by gamma (25-40 kGy), autoclaving (121°C, 30 min) and heat-sealed at both ends to distinguish between liquid and non-liquid Wavers. The heat-sealed tubing is placed in a -65°C environment and allowed to stand for 7 days before being removed. Immediately after removal, repeatedly fold the frozen tube to observe whether the tube wall is broken or other abnormalities. After the pipeline is placed at room temperature, repeatedly fold it again and observe whether there is damage, leakage or other abnormalities in the wall of the pipeline. If no abnormality occurs in the whole process, the pipeline is considered to be able to pass the -65°C low-temperature resistance test. The specific test results are shown in Table 13, Le-Flex®TPE

thermoplastic pipe withstands low temperature of 65°C.

Table 13.Le-Flex® TPE Thermoplastic Tube -65°C Low-Temperature Resistance Test Results

Pipe Size (inch)	-65°C Low-Temperature Tolerance			
	Gamma irradiated without liquid heat seal	Gamma irradiated without liquid heat seal	High-pressure steam without liquid heat seal	High-pressure steam with liquid heat seal
1/8×1/4	Passed	Passed	Passed	Passed
3/16×5/16	Passed	Passed	Passed	Passed
1/4×3/8	Passed	Passed	Passed	Passed
1/4×7/16	Passed	Passed	Passed	Passed
1/4×1/2	Passed	Passed	Passed	Passed
3/8×5/8	Passed	Passed	Passed	Passed
1/2×3/4	Passed	Passed	Passed	Passed
3/4×1	Passed	Passed	Passed	Passed

8. Expiration Date Verification

Accelerated aging of Le-Flex®TPE thermoplastic pipes by increasing the temperature according to ASTM F1980-2016, Simulate natural aging for 3 years. After accelerated aging, the specimens were tested for physical and chemical properties, and the product expiration dates are shown in Table 14.

Table 14: Expiration Date of "Le-Flex® TPE Thermoplastic Tubes

Product	Sample situation	Expiration date
Le-Flex® TPE thermoplastic pipe	⩽50kGy Gamma irradiate	3 years
	Unprocessed	3 years

Le-Flex® TPE thermoplastic tubing should be stored away from bright light and heat and humidity as much as possible. The recommended storage conditions are: 10-30°C / 30-60% RH.

9.Conclusion

This paper summarizes the key quality attributes in the design, development, production, inspection and validation of Le-Flex® TPE thermoplastic pipes. properties. For further requests, including but not limited to viewing raw data test reports, and for data outside of this guide, please contact For further requests, including but not limited to reviewing raw data test reports, and for data outside of this guide, please contact your LePure Bio sales representative.

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