CLNICAL EVALUATION REPORT

Sterile PLLA(Poly-L-Lactic Acid) Suture with Needle

Approval of the Clinical evaluation report is performed in accordance with the responsibility of the following functional area representatives

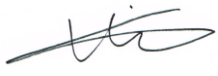
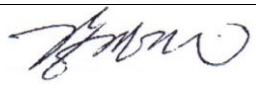
The following product applies ClassⅢ according to Council Directive 93/42/EEC amended by 2007/47/EEC AnnexⅨ Rule8.

Product name	Sterile PLLA(Poly-L-Lactic Acid) Suture with Needle
Brand name	Re:Jur
Model codes	total 57 models including 'YRN-PL25-01'

Revision history

Rev. No	Rev. Date	Modified contents	Remark
0	Jan. 15, 2016	Firstly prepared	-
1	Jun. 10, 2016	Addition of literature related with absorbing of raw material (PLLA suture)	
2	Apr. 25, 2017	Modification of model and brand name	

Functional area representatives

Division	Department	Name	Date	Signature
Authored by	Quality assurance team	Lee Min Woo	Apr. 25, 2017	
Reviewed by	President	Yahng Hae June	Apr. 25, 2017	
Approved by	Medical Doctor of clinical evaluation	Kang Kyoung Jin	Apr. 25, 2017	

Kang Kyoung Jin CV
- MD & PhD
- Ex-Professor of Catholic University of Daegu, Medical School, South Korea
- Founder & 1st president of Korean College of Cosmetic Surgery

1. INSTURCTION

The objectives of this clinical evaluations are :

- To verify that, normal conditions of use, the characteristic and the performance of the below device to those referred to in Section 1 and 3 of Annex Ⅰ of Council Directive 93/42/EEC amended by MDD 2007/47/EEC of the European Parliament and of the Council of 5 September 2007 concerning medical devices, and
- To determine any undesirable side-effects, under normal conditions of use, and assess whether they constitute risks when weighed against the intended performance of the device.

2. SCOPE

The following product was applied.

Product name	Sterile PLLA(Poly-L-Lactic Acid) Suture with Needle
Brand name	Re:Jur
Model	total 57 models including 'YRN-PL25-01'

3. REFERENCE STANDARDS

3.1 Directive 2007/47/EC of the European Parliament and of the Council of 5 September 2007
3.2 EN ISO14971:2012 Medical devices - Application of risk management to medical devices (ISO 14971:2007, Corrected version 2007-10-01)
3.3 Evaluation of clinical data: A guide for manufacturers and notified bodies (MEDDEV.2.7.1)

4. TERMS AND DEFINITIONS

4.1 Medical device

Any instrument, apparatus, appliance, material or other article, whether used alone or in combination, including the software necessary for its proper application, intended by the manufacturer to be used on human beings for the purpose of:

- Diagnosis, prevention, monitoring, treatment or alleviation of disease;
- Diagnosis, monitoring, treatment, alleviation or compensation for an injury or handicap;
- Evaluation, replacement or modification of the anatomy or of a physiological process;
- Control of conception

And which does not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its function by such means.

4.2 Device; device intended for clinical evaluation

Any MEDICAL DEVICE intended for use by an appropriately qualified practitioner when conducting CLINICAL EVALUATIONS in an adequate clinical environment.

4.3 Clinical evaluation

Any systematic study in human SUBJECTS, undertaken to verify the safety and PERFORMANCE of a specific MEDICAL DEVICE, under normal conditions of use

4.4 Clinical evaluation plan; protocol

A document which includes detailed information on the rationale, aims and objectives, design and proposed analyses, methodology, and conduct of the CLINICAL EVALUATION.

4.5 Clinical investigator

The investigator responsible for the conduct of a CLINICAL EVALUATION and who takes the clinical responsibility for the well-being of the SUBJECTS involved.

4.6 Performance of the device

The action of a specific MEDICAL DEVICE with reference to its intended use when correctly applied to applied to appropriate SUBJECTS.

4.7 Ethics committee, research ethics committee, institutional review board and properly constituted body of medical professionals and non-medical members, appointed in accordance with current practice, whose responsibility is to ensure that the safety, well-being and human right of the SUBJECTS participating in a particular CLINICAL EVALUATION are protected.

4.8 Final report of clinical evaluation
A comprehensive description of the CLINICAL EVALUATION on completion.

4.9 Sponsor; promoter
An individual or an organization which takes responsibility for the initiation and/or implementation of a CLINICAL EVALUATION.

4.10 Subject
A human being, either a patient or a non-patient volunteer, participating in a CLINICAL EVALUATION.

4.11 Informed consent; consent
The voluntary confirmation and documentation of a SUBJECT's willingness (or his legal guardian or representative's permission) to participate in a particular evaluation, after information has been given to the SUBJECT on the nature of the CLINICAL EVALUATION.

4.12 Monitor
A person appointed by the SPONSOR and responsible to him for monitoring and reporting on the progress of the CLINICAL EVALUATION.

4.13 Adverse event
Any undesirable clinical occurrence in a SUBJECT whether it is considered to be DEVICE related or not.

4.14 Adverse device effect; undesirable side effect
A DEVICE related ADVERSE EVENT.

4.15 Multicentre evaluation
A CLINICAL EVALUATION, conducted according to a single CLINICAL EVALUATION PLAN, which takes place at different evaluational sites.

4.16 Principal clinical investigator
A CLINICAL EVALUATION INVESTIGATOR appointed by the SPONSOR to coordinate the work in a MULTICENTRE CLINICAL EVALUATION or that of several CLINICAL EVALUATION INVESTIGATORS at one site.

4.17 Case report form
A set of documents, designed for complete recording of all relevant patient- and device-related data, as required by the CLINICAL EVALUATION PLAN,

4.18 Clinical evaluation investigator's brochure
A collection of relevant information known prior to the onset of a CLINICAL EVALUATION.

5. DESCRIPTION OF THE DEVICE

5.1 Overview

'Sterile PLLA(Poly-L-Lactic Acid) Suture with Needle' consists of needle, needle cap, hub, sponge, PLLA(Poly-L-Lactic Acid) Suture and is sterilized by EO gas. The safety and effectiveness of PLLA(Poly-L-Lactic Acid) is acceptable because PLLA(Poly-L-Lactic Acid) to be used to this device is absorb suture that has already used to sew the wound at normal hospital and needle also has been used in hospital. Materials to use to this device have been used to many medical device as syringe and disposable medical devices

5.2 Device Name: Sterile PLLA(Poly-L-Lactic Acid) Suture with Needle

Brand name : Re:Jur

5.3 Model code : total 57 models including 'YRN-PL25-01'

5.3.1 GENERAL NEEDLE

A. TRADITIONAL GENERAL NEEDLE

1) General PLLA suture with general needle (45 models)

(1) Normal (18 models)

YRN-PL25-01	YRN-PL26-01	YRN-PL27-01	YRN-PL29-01	YRN-PL30-01
YRN-PL25-02	YRN-PL26-02	YRN-PL27-02	YRN-PL29-02	YRN-PL30-02
YRN-PL25-03	YRN-PL26-03	YRN-PL27-03	YRN-PL29-03	
YRN-PL25-05	YRN-PL26-05	YRN-PL27-05	YRN-PL29-04	

(2) Pair Spiral (8 models)

YRT-PL25-01	YRT-PL26-01
YRT-PL25-02	YRT-PL26-02
YRT-PL25-03	YRT-PL26-03
YRT-PL25-05	YRT-PL26-05

(3) Normal Spiral (12 models)

YRS-PL25-03	YRS-PL26-01	YRS-PL27-01	YRS-PL29-02	YRS-PL30-02
	YRS-PL26-02	YRS-PL27-02	YRS-PL29-03	
	YRS-PL26-03	YRS-PL27-03	YRS-PL29-04	
		YRS-PL27-05		

(4) Duo Normal Spiral (7models)

YRDS-PL25-01	YRDS-PL26-01
YRDS-PL25-02	YRDS-PL26-02
YRDS-PL25-03	YRDS-PL26-03
	YRDS-PL26-05

2) Cog PLLA suture with general needle (4 models)

(1) CA type (2 models)

YRPN-PL21-40	YRPN-PL23-40

(2) FE type (2 models)

YRPN-PL21-80	YRPN-PL23-80

5.3.2 BLUNT NEEDLE

A.GENERAL "W"BLUNT NEEDLE

1) Cog PLLA suture with general "W" blunt needle (4 models)

(1) CA type (2 models)

YRPN-PL21-40-W	YRPN-PL23-40-W

(2) FE type (2 models)

YRPN-PL21-80-W	YRPN-PL23-80-W

B. GENERAL "L"BLUNT NEEDLE

1) Cog PLLA suture with general "L" blunt needle (4 models)

(1) CA type (2 models)

YRPN-PL21-40-L	YRPN-PL23-40-L

(2) FE type (2 models)

YRPN-PL21-80-L	YRPN-PL23-80-L

5.4 Intended use :

This device is intended to fixate sub dermal tissue in an elevated position in plastic and reconstructive surgery. PLLA(Poly-L-Lactic Acid) Suture provides wound support for longer period as compared to other synthetic absorbable suture. It also prolongs the stimulation time that increases the treatment effect on the body.

5.5 Classification applied

1) 'Sterile PLLA(Poly-L-Lactic Acid) Suture with Needle' has been classified as **ClassⅢ** According to MDD93/42/EEC amended by 2007/47/EEC AnnexⅨ, Rule8.
2) GMDN Code : 16584 (Suture)
3) Categorization according to EN ISO 10993-1:2009
   - Category : Implant, absorbable
   - Contact : Tissue / Bone
   - Contact duration : C(＞30days)

5.6. Characteristic

1) Ethylene oxide gas be sterilized by Yurim Medical Co., Ltd.
   - Sterilization parameter
   ① Sterilizing agent : 20 : 80(E.O : CO_2)
   ② Sterilization assurance level[SAL] : 10^{-6}
2) Packing method & material
   ① Blister heat sealing
   ② Polyethylene Terephthalate (PET)+Linear low density polyethylene
3) This device should be used for Single-use.
4) Shelf-life : 2years

5.7 Usage method

5.7.1 Preparation before use

1) Confirm the model codes in accordance with dimensions
2) Check the validity period and packaging damaged.
3) Know how to use the product.

5.7.2 How to operate and how to use

1) Determine the length of the needle in accordance with the position to operate
2) Sterilize the affected part to operate
3) Push the needle in until the end of the suture is inserted into the cortex of the affected part completely
4) Pull the needle out and paste the band on the affected part

5.7.3 How to store and manage after use.
1) Keep it in normal temperature
2) Avoid direct sunlight and where to be high temperature and humidity.
3) Discard the product if it is opened once even if it does not used
4) Don't reuse because of single use product.

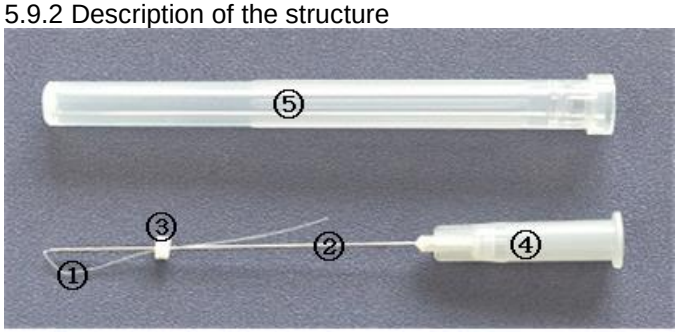
5.8 Attention

1) Do not use the product that the validity period is passed.
2) Do not use the product that the package is damaged.
3) Do not use this product for other purpose besides the intended use.
4) This product should be used only by professional medical personnel.
5) Do not use if there is inflammation or concerned about infection in the position to operate

5.9 APPEARANCE & STRUCTURE

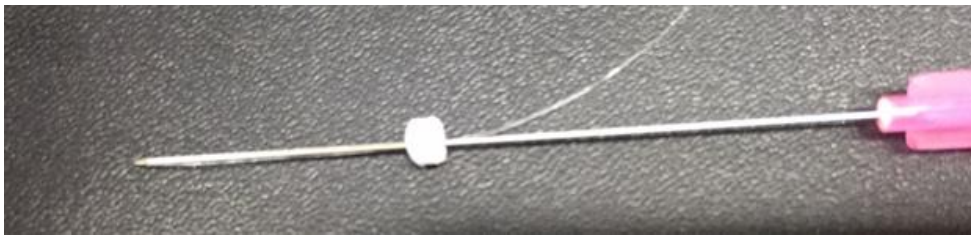
5.9.1 Photographs

5.9.2 Description of the structure



NO.	Part name	Function
1	Suture	Absorbable sutures to insert in the skin
2	Sponge	To fix cannula and suture
3	Cannula	Needle to insert absorbable PLLA(Poly-L-Lactic Acid) Suture into the skin
4	Hub	Giving help to adhere the needle easily and grip role when giving medical treatment
5	Protect cap	Protect cover to keep suture and the blade tip of needle

(1) Normal

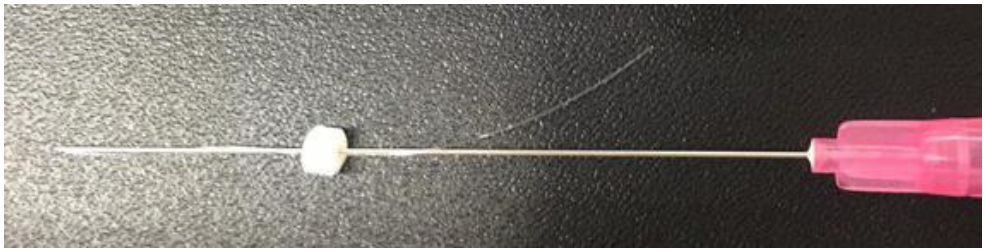


(2) Pair Spiral

(3) Normal Spiral

(5) Duo Normal Spiral

(6) Normal Coil

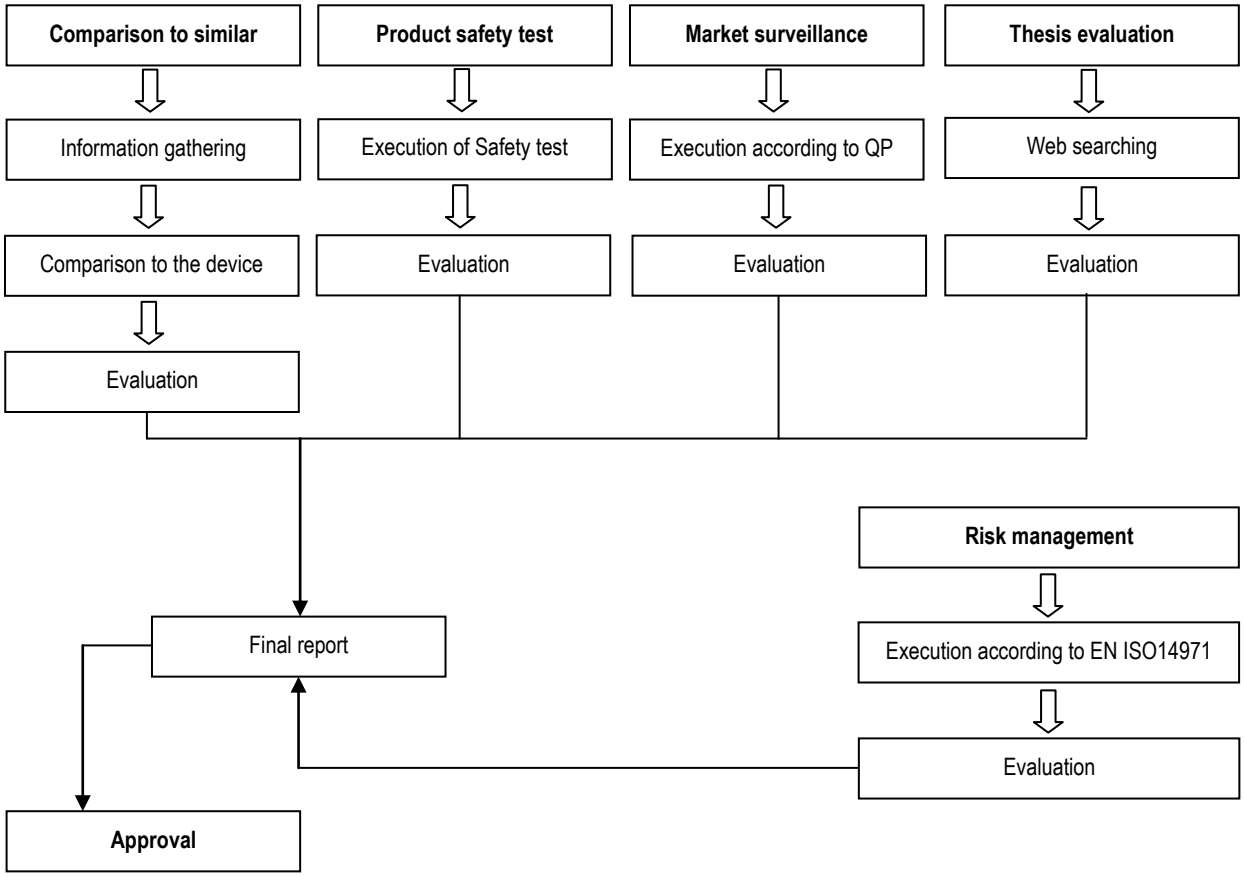


6. RAW MATERIAL OF THE DEVICE

No	Part name	Material	Standard	Cas no.	Supplier	Remark
1	Suture	Poly-L-LACTIC ACID(Poly[oxy(1-methyl-2-oxoethylene)	- Appearance : White Pellet - Melting point: 180~198℃	Cas 33135-50-1	.Dexlevo Inc.	Contact (tissue)
2	sponge	Polyethylene	-Appearance: white -Odor: Essentially odorless pellet. -PH: Not applicable -Solubility: (In water)Insoluble (Other solvent): soluble in toluene, xylene, trichloroethane etc. -Melt point: 126~ 136℃ -Specific gravity(H20=1): 0.940~0.970 -Molecular weight:>10.000	Cas 9002-88-4	.KS sponge Co.	Non-contact
3	cannula	Stainless Steel(STS 304)	KS D3698 (STS 304)	Cas7439-89-6	Ace medical industry Co.,Ltd.	Contact (tissue)
4	HUB	Polypropylene	- Appearance: white solid - Smell: odorless - Melting point / freezing point: <165 ℃ - Solubility in water: insoluble - Relative density (water = 1): 0.9 - Spontaneous ignition temperature: 375 ~ 400 ℃ - Molecular weight:> 40,000	Cas 9003-07-0		Non-contact
5	protect cap	Polypropylene	- Appearance: white solid - Smell: odorless - Melting point / freezing point: <165 ℃ - Solubility in water: insoluble - Relative density (water = 1): 0.9 - Spontaneous ignition temperature: 375 ~ 400 ℃ - Molecular weight:> 40,000	Cas 9003-07-0		Non-contact

7. OVERVIEW OF THE CLINICAL EVALUATION

8.1 Process flow for the clinical evaluation performance



8. RESPONSIBILITY AND AUTHORITY

8.1 Responsibility and authority

No	Step	Authored by	Reviewed by	Approved by
1	Comparison to similar	Lee Min Woo	Lee Min Woo	Yahng Hae June
2	Product safety test			
3	Market surveillance			
4	Thesis searching			
5	Final report			
6	Risk management	According to the risk management procedure		
7	Human part	Kang Kyoung Jin (Medical doctor)		

8.2 Qualification of the person who intervene on Clinical evaluation

1) Lee Min Woo

2013	11	28	Quality management leader of Yurim Medical Co., Ltd.

2) Yahng Hae June

No	Period	Education or Career
1	2013. 01 ~	President of Yurim Medical Co., Ltd.

3) Kang Kyoung Jin (Medical doctor)

- MD & PhD
- Ex-Professor of Catholic University of Daegu, Medical School, South Korea
- Founder & 1st president of Korean College of Cosmetic Surgery

9. EVALUATION_PRODUCT SAFETY TEST

9.1 Contamination test results in manufacture process

No	Testing item	Standard	TEST LAB	ISSUE DATE	Test result
1	Airborne particle counting report	ISO14644 Series	MENG Co.	Dec. 28, 2015	Pass
2	Airborne microorganism measurement report	ISO14644 Series	MENG Co.	Dec. 28, 2015	Pass
3	Falling microorganism measurement report	ISO14644 Series	MENG Co.	Dec. 28, 2015	Pass
4	Surface microorganism on work table report	ISO14644 Series	MENG Co.	Dec. 28, 2015	Pass
5	Microorganism on worker's hand report	ISO14644 Series	MENG Co.	Dec. 28, 2015	Pass

9.2 Product test

Ⅰ. Needle

1. PRODUCT TEST RESULTS

All our products were performed by laboratories acquired ISO17025. Test samples to be used in this test

were from manufacture line.

1.1 Biocompatibility test

- Test Client : **Ace Medical Industry Co., Ltd.**
- Test Laboratory : KCL
- The date of issue : Aug.19,2013

No	Test item	Test method / Test criteria	Test result	TEST LAB	ISSUE DATE	REP NO
1	Test for in vitro cytotoxicity	EN ISO 10993-5(2009) Biological evaluation of medical devices - Part 5: Tests for in vitro cytotoxicity Non-cytotoxic	Qualitative result (Grade) of test on extracts was 0.0. (Pass)	KCL	Aug.19, 2013	MT13-00158-A1
2	Acute systemic toxicity test	EN ISO 10993-11(2009) Biological evaluation of medical devices - Part 11: Tests for systemic toxicity Non-toxic	None of animals on study were observed with abnormal clinical signs (Pass)	KCL	Aug.19, 2013	
	Pyrogen Test	Korea Pharmacopoeia 9th General testing method <9>-Test for pyrogen ISO (material mediated) Rabbit Pyrogens Test - *in vivo* Non-pyrogenic	the test substance extract was judged as non-pyrogenic (Pass)	KCL	Aug.19, 2013	
4	Intracutaneous reactivity test	EN ISO 10993-10(2013) Biological evaluation of medical devices - Part 10: Tests for irritation and skin sensitization if the final test sample score is 1.0 or less.	The test substance meets the ISO requirement (Pass)	KCL	Aug.19, 2013	
5	Skin sensitization test	EN ISO 10993-10(2013) Biological evaluation of medical devices - Part 10: Tests for irritation and skin sensitization No- skin hypersensitivity reactions.	extraction solution for the test sample was not considered to be Skin hypersensitivity reactions. (pass)	KCL	Aug.19, 2013	
6	Hemolysis test	EN ISO10993-4(2009) Biological evaluation of medical devices - Part 4: Selection of tests for interactions with blood Non-hemolytic	The test sample extraction solution was nonhemolytic. (Pass)	KCL	Aug.19, 2013	

1.2 Chemical test

- Test Client : Ace Medical Industry Co., Ltd.
- Test Laboratory : KCL
- The date of issue : Aug.19,2013

No	Test item		Test method		
			Test criteria	Test result	Test record
1	Extraction Test	PH	Korea Pharmacopoeia 9th General testing method <56>-Extract testing Extract testing for plastic container of medicinal drug [Difference of PH]		
			Difference of PH ≤ 1.0	0.56 (Pass)	MT13-00158-A1
		Potassium permanganate reducing substances	Korea Pharmacopoeia 9th General testing method <56>-Extract testing Extract testing for plastic container of medicinal drug [KMnO4 Consumption]		
			Difference in titres ≤ 2.0ml	0.8 (Pass)	MT13-00158-A1

		Residue after evaporation	Korea Pharmacopoeia 9th General testing method <56>-Extract testing Extract testing for plastic container of medicinal drug [Evaporation residue]		
			Difference in extractales ≤ 1.0mg	0.2 (Pass)	MT13-00158-A1
		Heavy metals	Korea Pharmacopoeia 9th General testing method <53>-Heavy metal test [Atomic absorption spectrophotometry]		
			Not greater than a comined total of the Sn, Pb, Zn and Fe Shall be less than 0.1mg/L of Cd	Conform (Pass)	MT13-00158-A1

1.3 Performance test
- Test Client : Ace Medical Industry Co., Ltd.
- Test Laboratory : KCL
- The date of issue : Aug.19,2013

No	Test item	Test method		
		Test criteria	Test result	
1	Inner/ Outside and Structure	ISO7864:1993 Sterile hypodermic needles for single use –Section 4.5		
		See the test report	Pass	MT13-00158-A1
2	Dimension	ISO9626: 1991/Amd1:2001 Stainless steel needle tubing for the manufacture of medical devices–Section 8		
		See the test report	Pass	MT13-00158-A1
3	Draw Test	ISO7864:1993 Sterile hypodermic needles for single use –Section 13.1		
		See the test report	Pass	MT13-00158-A1
4	Elasticity Test	ISO7864:1993 Sterile hypodermic needles for single use –Section 4.5		
		See the test report	Pass	*MT13-00158-A1*
5	Flexual Rigidity	ISO7864:1993 Sterile hypodermic needles for single use –Section 4.5		
		See the test report	Pass	*MT13-00158-A1*

Ⅱ. PLLA Suture

1. PRODUC TEST RESULTS

1.1 Biocompatibility test

- Test Client : Yurim Medical Co., Ltd.
- Test Laboratory : KTC
- The date of issue : Jun. 10, 2016

No	Test item	Test method / Test criteria	Test result	TEST LAB	ISSUE DATE	REP NO
1	Cytotoxicity test	ISO 10993-5(2009) Biological evaluation of medical devices - Part 5: Tests for in vitro cytotoxicity 8.2 Test on extracts The test article met the requirements of the test if the biological response was less than or equal to grade 2(mild)	The 1x MEN test article extract showed evidence of causing (0-6)% cell lysis or toxicity (evaluation grade : 1) (pass)	KTC	Jun. 10, 2016	MD 2016-00430
2	Guinea pig maximization	ISO 10993-10(2010) Biological evaluation of medical devices - Part 10: Tests for irritation and skin	The test article extracts showed no evidence of causing delayed dermal	KTC	Jun. 10, 2016	MD 2016-00430

		sensitization, 7.5 Guinea pig maximization test Negative	contact sensitization in the guinea pig (pass)			
3	Intracutaneous reactivity test	ISO 10993-10(2010) Biological evaluation of medical devices - Part 10: Tests for irritation and skin sensitization, 6.4 Animal intracutaneous (intradermal) reactivity test The final test sample score is 1.0 or less	There are no evidence of significant irritation from SC extract and CO extract injected intracutaneously into rabbits. (Pass)	KTC	Jun. 10, 2016	MD 2016-00430
4	Acute systemic toxicity test	ISO 10993-11(2006) Biological evaluation of medical devices - Part 11: Tests for systemic toxicity, 5 Acute systemic toxicity. Non-toxicity	There was no mortality or evidence of acute systemic toxicity from the extract. (Pass)	KTC	Jun. 10, 2016	MD 2016-00430
5	Pyrogen Test	ISO 10993-11 (2006) Biological evaluation of medical devices Part 11: Tests for systemic toxicity, Annex F information on material-mediated pyrogens Non-pyrogenic	The test rise of rabbit temperatures during the 3 hour observation period was within acceptable limits. The test extract was judged as non-pyrogenic (Pass)	KTC	Jun. 10, 2016	MD 2016-00430
6	Bacterical Endotoxin test –Limulus Amebocyte Lysale Test (kinetic-chromogenic)	USP <85>, Bacterial Endotoxin Test The endotoxin recovery, calculated from the concentration found in solution B after subtracting the endotoxin concentration found in Solution A is within (50-200)%	The sample Endotoxin concentration was 0.026 EU/device. The Endotoxin Recovery is 121% (pass)	KTC	Jun. 10, 2016	MD 2016-00430
7	Genotoxicity test (Bacterial Reverse Mutation test)	ISO 10993-3(2014) Biological evaluation of medical devices - Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity, 4.Genotoxicity tests Negative	The test article exracted was not mutagenic for any tester strain, either with or whithout S9 metabolic activation (pass)	KTC	Jun. 10, 2016	MD 2016-00430
8	Genotoxicity test (Mammalian Erythrocyte Micronucleus test)	ISO 10993-3(2014) Biological evaluation of medical devices - Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity, 4.Genotoxicity tests Negative	The test article showed no evidence of causing micronucleus in the immature erythrocytes of the test animals. (pass)	KTC	Jun. 10, 2016	MD 2016-00430
9	Subchronic systemic toxicity test (Implantation Test)	ISO 10993-11(2006) Biological evaluation of medical devices - Part 11: Tests for systemic toxicity, 6 Repeated exposure systemic toxicity (subacute systemic toxicity) Non-toxic (Non-irritant)	In the microscopical observation, mean score difference between the test article and the negative control article was0.0 (non-irritact (pass)	KTC	Jun. 10, 2016	MD 2016-00430
10	Subchronic systemic toxicity test (90days subchronic toxicity test)	ISO 10993-6(2007) Biological evaluation of medical devices - Part 6: Tests for local effects after implantation, Annex C Test methods for implantation in muscle. Non-toxic (Non-irritant)	There were no evidence of systemic toxicity from the test article following implantation in the rat (pass)	KTC	Jun. 10, 2016	MD 2016-00430

1.2 Safety test

- Test Client : Yurim Medical Co., Ltd.
- Test Laboratory : KTC
- The date of issue : Jun. 10, 2016

No	Test item	Test method / Test criteria	Test result	TEST LAB	ISSUE DATE	REP NO
1	Extractable color	USP 37, absorbable surgical suture, extractable color Weigh a quantity of suture, equivalent to not less than 250mg, and place in a conical flask containing 1.0ml of water for each 10mg of the sample. Close the flask, and allow it to stand at (37±0.5)℃ for 24 hours. Cool, decant the water from the suture, and compare it with the matching solution : any color present is not more intense than that of the appropriate matching solution	Pass	KTC	Jun. 10, 2016	MD 2016-00430

Ⅲ. Suture with needle

1) Shelf life and packaging qualification

- Test Client : Yurim Medical Co.,Ltd.
- Test Laboratory : MENG Co.
- The date of issue : Jul. 1, 2015

No	Test item	Test method		
		Test criteria	Test result	Test record
1	Shelf life test 2years	ASTM F1980:2002 Standard Guide for Accelerated Aging of Sterile medical device packages		
		See the attached shelf life test	Pass	YR-SL15001

2) E.O gas sterilization validation

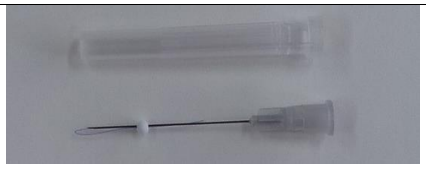
- Test Client : Yurim Medical Co.,Ltd.
- Test Laboratory : MENG Co..
- The date of issue : Apr. 08, 2016

No	Test item	Test method		
		Test criteria	Test result	Test record
1	Ethylene Oxide Sterilization Validation Test	EN ISO 11135(2014) Sterilization of health-care products -- Ethylene oxide -- Requirements for the development, validation and routine control of a sterilization process for medical devices		
		See the attached Ethylene Oxide Sterilization Validation Test	Pass	YR-SVR-1601

9.3. Evaluation : we confirmed that our device has no problems about performance and biocompatibility.

10. EVALUATION_COMPARISON TO SIMILAR DEVICE

10.1 Needle part

No	Division	Yurim Medical Co., Ltd.	Dongwon Medical Co.,Ltd.	Substantial Equivalence Discussion
1	Shape			similar

2	Needle Diameter	(1.020-1.100), (0.800-0.830), (0.600~0.673) (0.500~0.530), (0.440~0.470), (0.400~0.420) (0.324~0.351), (0.298~0.320)mm	19G(1.030~1.100), 20G(0.860~0.920) 21G(0.800~0.830), 22G(0.698~0.730) 23G(0.600~0.673), 24G(0.550~0.580) 25G(0.500~0.530),26G(0.440~0.470), 27G(0.400~0.420), 28G(0.349~0.370) 29G(0.324~0.351), 30G(0.298~0.320) (mm)	similar
3	Needle Length	25,38,50,60,70,90 100mm	25, 30, 32, 38, 50, 55, 60, 70, 80, 90, 100, 120 mm	similar
4	Lubricant	Silicon	Silicon	Identical
5	Needle gauge	19G, 21G, 23G, 25G, 26G, 27G, 29G, 30G	19G, 20G, 21G, 22G, 23G, 24G, 25G, 26G, 27G, 28G, 29G, 30G	similar
6	Sterilization method	EO Gas	EO Gas	Identical
7	Needle point shape	Bevel Sharp	Bevel Sharp	Identical

10.2 Suture

No	Division	Yurim Medical Co.,Ltd.	Feeltech Co.,Ltd.	Substantial Equivalence Discussion
1	Product name	Sterile PLLA(Poly-L-Lactic Acid) Suture with Needle	Sterile PLLA(Poly-L-Lactic Acid) Suture with Needle	
2	Intended for use	This device is intended to fixate sub dermal tissue in an elevated position in plastic and reconstructive surgery. PLLA(Poly-L-Lactic Acid) Suture provides wound support for longer period as compared to other synthetic absorbable suture. It also prolongs the stimulation time that increases the treatment effect on the body.	This device is intended to fixate sub dermal tissue in an elevated position in plastic and reconstructive surgery. PLLA(Poly-L-Lactic Acid) Suture provides wound support for longer period as compared to other synthetic absorbable suture. It also prolongs the stimulation time that increases the treatment effect on the body.	Identical
3	Device description	'Sterile PLLA(Poly-L-Lactic Acid) Suture with Needle' consists of needle, needle cap, hub, sponge, PLLA(Poly-L-Lactic Acid) Suture and is sterilized by EO gas. The safety and effectiveness of PLLA(Poly-L-Lactic Acid) is acceptable because PLLA(Poly-L-Lactic Acid) to be used to this device is absorb suture that has already used to sew the wound at normal hospital and needle also has been used in hospital. Materials to use to this device have been used to many medical device as syringe and disposable medical devices	'Sterile PLLA(Poly-L-Lactic Acid) Suture with Needle' consists of needle, needle cap, hub, sponge, PLLA(Poly-L-Lactic Acid) Suture and is sterilized by EO gas. The safety and effectiveness of PLLA(Poly-L-Lactic Acid) is acceptable because PLLA(Poly-L-Lactic Acid) to be used to this device is absorb suture that has already used to sew the wound at normal hospital and needle also has been used in hospital. Materials to use to this device have been used to many medical device as syringe and disposable medical devices	Identical
4	Augmentation	Continue until the 8th week and will last for 2 years after the procedure.	Continue until the 8th week and will last for 2 years after the procedure.	Identical

Technical equivalence				
5	Material	1) PLLA (Poly-L-lactic acid)	100% PLLA (Poly-L-lactic acid)	Identical
Biological equivalence				
6	Biocompatibility test	1) Subchronic Toxicity test (ISO 90 Dats, Subcutaneous) 2) Cytotoxicity test (Agar diffusion test) 3) Intracutaneous (intradermal) Reactivity Test 4) Skin sensitization test 5) Acute Systemic Toxicity Test 6) Genotoxicity test (Bacteria Reverse Mutation test) 7) Genotoxicity test (Micronucleus test) 8) Pyrogen Test	1) Cytotoxicity test 2) Acute systemic toxicity 3) Pyrogen Test 4) Intracutaneous 5) Bacterial reverse mutation test 6) Chromosome aberration test 7) Skin sensitization test 8) Subchronic Toxicity test (ISO 90 Days, Intramuscular)	Identical

10.3 Evaluation

When our device is compared to similar device, we confirmed that the structure, material, intended use, usage method, sterilization method of our device are equal similar device. Therefore, our device is not new development medical device.

11. EVALUATION_MARKET SURVEILLANCE

1) Sales record

Sales Period	Quantity (EA)	Remark
2015-11 ~ 2015-12.	100	Korea,

2) Customer complaints

No major complaints have been occurred since the first distribution.

No.	Items of side-effects	No. of incident	Complaints received	Corrective action
1.	Harm of patient/user	0	0	0
2.	Damage packaging	0	0	0
3.	Others	0	0	0
Total		0	0	0

3) Evaluation

As above data, this product is not new device. And this device has no complaint from customers and biological safety and no critical performance nonconformity reported.

12. EVALUATION_RISK MANAGEMENT

12.1 Risk evaluation

1) Severity

The severity of harm consists of five stages;

level	Common terms	Possible description
5	Catastrophic	Results in patient death
4	Critical	Results in permanent impairment or life-threatening injury
3	Serious	Results in injury or impairment requiring professional medical intervention
2	Minor	Results in temporary injury or impairment not requiring professional medical intervention
1	Negligible	Inconvenience or temporary discomfort

2) Frequency

The frequency of harm consists of five stages;

level	Common terms	Examples of probability range
5	Frequent	$\geq 10^{-3}$
4	Probable	$< 10^{-3}$ and $\geq 10^{-4}$
3	Occasional	$< 10^{-4}$ and $\geq 10^{-5}$
2	Remote	$<10^{-5}$ and $\geq 10^{-6}$
1	Improbable	$< 10^{-6}$

3) Acceptability of risk

Frequent (5)					
Probable(4)					
Occasional(3)					
Remote(2)					
Improbable(1)					
	Negligible(1)	Mimor(2)	Serious(3)	Critical(4)	Catastrophic(5)

	Unacceptable risk
	Invastigation further risk reduction
	Insignificant risk

(S : Severity, F: Frequency)

Identification of Possible hazards	Examples of hazards	Possible Situation	S	F	Result	ID No.
Biological	Bacteria	If the device is non-sterile It will cause patient's infection	4	2	Non-accept	ID-1
		If the device is damaged packaging It will cause patient's infection	4	2	Non-accept	ID-2
	Viruses	If the device is non-sterile It will cause patient's infection	4	2	Non-accept	ID-3
		If the device is damaged packaging It will cause patient's infection	4	2	Non-accept	ID-4
		If the product that the expiration date is	3	2	accept	ID-5

		ended is used, it will cause patient's infection				
	Re-or cross-infection	If the device is re-used It will cause patient's infection	3	2	accept	ID-6
Chemical	Residues	If there is residues, it will cause the problem of immune system.	3	2	accept	ID-7
	Degradation products	If there is degradation products, it will cause the problem of immune system.	3	2	accept	ID-8
Bio compatibility	Toxicity of chemical constituents, e.g.	If the device is use of inappropriate materials, It will cause the problem of immune system.	3	2	accept	ID-9
	allergenicity / irritancy	If the device is cleanliness problem, It will cause patient's infection	3	2	accept	ID-10
	Pyrogenicity	If the device is cleanliness problem, It will cause patient's infection	3	2	accept	ID-11
		If the device is damaged packaging, It will cause patient's infection	3	2	accept	ID-12
		If the device is re-sterilized, It will cause patient's infection	3	2	accept	ID-13
Function	Loss or deterioration of function	Due to loss or deterioration of function, It will cause dysfunction of device	3	2	accept	ID-14
		If there is loss or deterioration of tensile strength of suture, It will cause dysfunction of device	2	2	accept	ID-15
Use error	Attention failure	If this device is not used only by doctor, this device can be used incorrectly without paying attention. Then It will cause patient's infection	3	2	accept	ID-16
		If there is using beyond intended use, It will cause hazard.	4	2	Non-accept	ID-17
	Rule-based failure	If this device is used in inflammation treatment site without rule-base, It will cause contaminate	2	3	accept	ID-18
Labeling	Incomplete instructions for use	If instruction for use is described incomplete in labelling, It will cause patient's infection	2	3	accept	ID-19
	Inadequate description of performance characteristics	If performance characteristics is described inadequately in labelling, It will cause patient's infection	2	3	accept	ID-20
	Inadequate specification of intended use	If specification of intended use is described inadequately in labelling, It will cause patient's infection	2	3	accept	ID-21
	Inadequate disclosure of limitations	If disclosure of limitations is described inadequately in labelling, It will cause patient's infection	2	3	accept	ID-22
Operating Instructions	Inadequate specification of accessories to be used with the medical device	If specification of accessories to be used with the medical device is described inadequately in IFU, It will cause patient's infection	2	2	accept	ID-23
	Inadequate specification of pres-use checks	If specification of pre-use checks is described inadequately in IFU, It will cause patient's infection	2	3	accept	ID-24

Warnings	Of side effects	If side effects is described inadequately in IFU, It will cause patient's infection	2	3	accept	ID-25
	Of hazards likely with re-use of single-use medical devices	If hazards likely with re-use of single-use medical devices is described inadequately in IFU It will cause patient's infection.	2	3	accept	ID-26
Design	Design development	If design development has defect, It will cause dysfunction of device	3	2	accept	ID-27
Production	Production process	If production process is inappropriate, It will cause dysfunction of device	3	2	accept	ID-28
	Component analysis	If there is wrong component analysis, It will cause problem to function of device	3	2	accept	ID-29
Monitoring and Measuring Equipment	Control of monitoring and measuring equipment	If measuring instrument has error, It will cause dysfunction of device	3	2	accept	ID-30
Second usage	Re-use	If there is re-use for device, It will cause infection to patient	4	2	Non-accept	ID-31

4) Evaluation result of identification of possible hazards.

Frequent (5)					
Probable(4)					
Occasional(3)		8 cases			
Remote(2)		2 case	15 cases	6 cases	
Improbable(1)					
	Negligible (1)	Mimor(2)	Serious(3)	Critical(4)	Catastrophic(5)

12.2 Risk Control

From Identification of Possible hazards, to reduce hazards until acceptable level, risk control is performed by modified design, precaution in process and information of safety.
Risk control should be evaluated by the Residual risk. Related data is as following

Identification of Possible hazards	Examples of hazards	Risk Control & Perform	Residual risk			Result	Risk/ Benefit	Other generated hazards	Completion of control	ID No.
			S	F	Risk					
Biological	Bacteria	1)Sterilization validation 2)B.I monitoring and recording 3)warning against non-sterilization and of the adverse consequence that could arise from any such non-sterilization (Make sure there are no problems with the sterile packaging and check whether or not attached and sterile)	4	1	4	accept	Blocking infection from bacteria	No	Yes	ID-1
		1)Packaging process validation 2) final inspection for packaging 3)warning against damaged packaging and of the adverse consequence that could arise from	4	1	4	accept	Blocking infection from bacteria	No	Yes	ID-2

		any such damaged packaging (Do not use the product that packaging is damaged)								
	Viruses	1)Sterilization validation 2)B.I monitoring and recording 3)warning against non-sterilization and of the adverse consequence that could arise from any such non-sterilization (Use sterilization-packed products.)	4	1	4	accept	Blocking infection from viruses	No	Yes	ID-3
		1)packaging process validation 2)final inspection for packaging 3)warning against damaged packaging and of the adverse consequence that could arise from any such damaged packaging (Do not use the product that packaging is damaged)	4	1	4	accept	Blocking infection from viruses	No	Yes	ID-4
		1)shelf life and packaging qualification test report 2)final inspection for expiration date 3)warning against use that the product expiration date is over and of the adverse consequence that could arise from any such product that expiration date is over (Do not use the product that the expiration period is ended)	3	1	3	accept	Safe using within expiration date	No	Yes	ID-5
	Re-or cross-infection	1)packaging process validation 2)self-destruction after use 3)warning against re-use and of the adverse consequence that could arise from any such re-use (Discard the product that is once opened.)	3	1	3	accept	Blocking infection by no reuse	No	Yes	ID-6
Chemical	Residues	1)chemical testing 2)incoming inspection for raw material 3)warning against other raw material and of the adverse consequence that could arise from any such other raw material (Confirm it there is transformations, flaws or cracks of the item)	3	1	3	accept	Protection of immune system by using passed raw material	No	Yes	ID-7
	Degradation products	1)clinical evaluation report 2)incoming inspection for raw material 3)warning against other raw material and of the adverse consequence that could arise from any such other raw material (Confirm it there is transformations, flaws or cracks of the item)	3	1	3	accept	Protection of disfunction by using passed raw material	No	Yes	ID-8
Bio compatibility	Toxicity of chemical constituents, e.g.	1) biocompatibility testing 2)incoming inspection for raw material 3)warning against toxicity of chemical constituents, e.g. and of the adverse consequence that could arise from any such toxicity of chemical constituents, e.g (If your medical history contains foreign body reaction, subcutaneous swelling (papules) etc, get an advice with a doctor)	3	1	3	accept	Protection of toxicity exposure by using passed raw material	No	Yes	ID-9
	allergenicity / irritancy	1) cleanroom validation testing 2)promoting use of personal hygienic equipment and cleanroom	3	1	3	accept	Prevention of allergenicity/irritancy by cleanroom control	No	Yes	ID-10

		circumstance when handling product 3) warning against allergenicity / irritancy and of the adverse consequence that could arise from any such allergenicity / irritancy (This product should not be used in the case of acute or chronic skin disease (infection or inflammation near the area to be treated)					and using passed raw material			
	Pyrogenicity	1) cleanroom validation testing 2)cleanroom monitoring and recording 3) warning against pyrogenicity and of the adverse consequence that could arise from any such pyrogenicity (If there is inflammation treatment site, or other infections is concerned, it shall not be used).	3	1	3	accept	Prevention of pyrogenicity by cleanroom environment	No	Yes	ID-11
		1)packaging validation 2)final inspection for packaging 3)warning against damaged packaging and of the adverse consequence that could arise from any such damaged packaging (Do not use the product that packaging is damaged.)	3	1	3	accept	Prevention of pyrogenicity by packing control	No	Yes	ID-12
		1)sterilization validation 2)final inspection and monitoring 3)warning against re-sterilization and of the adverse consequence that could arise from any such re-sterilization (Do not re-sterilize or reuse)	3	1	3	accept	Prevention of pyrogenicity by re-sterilization	No	Yes	ID-13
Function	Loss or deterioration of function	1)shelf life and packaging qualification test 2) in-process inspection and final inspection for product function 3)warning on labelling for user (Check the validity period)	3	1	3	accept	Using without Loss or deterioration of function by using within expiration date	No	Yes	ID-14
		1)vacuum drying validation 2)dehumidication of suture below 500ppm 3)warning on labelling for using within expiration date (Check the validity period.)	2	1	2	accept	Using without dysfunction by tensile strength control	No	Yes	ID-15
Use error	Attention failure	1)IFU design report 2)labelling in indivisual packaging and in-box 3)warning against using of anyone except doctor and of the adverse consequence that could arise from any such using of anyone except doctor (This product should be used only by medical professional, doctor.)	3	1	3	accept	Prevention of infection with 'preparation before use' on packing labeling	No	Yes	ID-16
		1)Design development file 2)labelling on packaging and box 3)warning against using beyond intended use and of the adverse consequence that could arise from any such using beyond intended use (see intended use on IFU, This product is not used for else purposes except the intended use.)	4	1	4	accept	Prevention for using beyond intended use	No	Yes	ID-17
	Rule-based failure	1)IFU design report 2)labelling in indivisual packaging and in-box	2	2	4	accept	Prevention of infection by rule based manual	No	Yes	ID-18

		3)warning against using in inflammation treatment site without rule-base and of the adverse consequence that could arise from any such rule-base failure (Use after reading the manuals/ Before using, user should be aware of how to use completely)									
Labeling	Incomplete instructions for use	1)IFU design report 2)final inspection for labelling 3)warning against incomplete instruction for use and of the adverse consequence that could arise from any such incomplete instruction for use (Before using, user should be aware of how to use completely)	2	2	4	accept	Prevention of infection by complete instruction on packing labeling	No	Yes	ID-19
	Inadequate description of performance characteristics	1)essential requirement report 2) final inspection for labelling 3)warning against inadequate description of performance characteristics and of the adverse consequence that could arise from any such inadequate description of performance characteristics (read device charateristecs on IFU)	2	2	4	accept	Prevention of infection by adequate description on packing labeling	No	Yes	ID-20
	Inadequate specification of intended use	1)clinical evaluation report 2)final inspection for labelling 3)warning against inadequate specification of intended use and of the adverse consequence that could arise from any such Inadequate specification of intended use (read intended use on IFU)	2	2	4	accept	Prevention of infection by adequate specification on packing labeling	No	Yes	ID-21
	Inadequate disclosure of limitations	1)label and packaging design 2)final inspection for labelling 3)warning against Inadequate disclosure of limitations and of the adverse consequence that could arise from any such Inadequate disclosure of limitations (Avoid direct sunlight and where to be high temperature and humidity.)	2	2	4	accept	Prevention of infection by adequate disclosure on packing labeling	No	Yes	ID-22
Operating Instructions	Inadequate specification of accessories to be used with the medical device	1)product description 2) final inspection for labelling 3)warning against Inadequate specification of accessories to be used with the medical device and of the adverse consequence that could arise from any such Inadequate specification of accessories to be used with the medical device (Confirm the content and packaging of the product.)	2	2	4	accept	Using device without dysfunction by adequate specification on packing labeling	No	Yes	ID-23
	Inadequate specification Of pre-use checks	1) label and packaging design 2)final inspection for labelling 3)warning against Inadequate specification of pre-use checks and of the adverse consequence that could arise from any such Inadequate specification of pre-use checks (read preparations before use)	2	2	4	accept	Using device without dysfunction by side effect on packing labeling	No	Yes	ID-24
Warnings	Of side effects	1)clinical evaluation report 2)final inspection for labelling 3)warning against side effects and of the adverse consequence that could arise from any such side effects	2	2	4	accept	Prevention of infection by adequate disclosure on packing labeling	No	Yes	ID-25

		(Inflammation and foreign body reaction)								
	Of hazards likely with re-use of single-use medical devices	1) label and packaging design 2) final inspection for labelling 3)warning against hazards likely with re-use of single-use medical devices and of the adverse consequence that could arise from any such hazards likely with re-use of single-use medical devices (Because this product is a single use product, it must not be reused)	2	2	4	accept	Prevention of infection by Indication of hazards likely with re-use on packing labeling	No	Yes	ID-26
Design	Design development	1)design development file 2)verification and validation for design output 3)report against inappropriate output and of the adverse consequence that could arise from inappropriate output (Design development report : YRF-702-01,02,03,04)	3	1	3	accept	Prevention and modification for wrong output	No	Yes	ID-27
Production	Production process	1)process control procedure 2)process inspection and monitoring 3)process inspection certificate against inappropriate production process and of the adverse consequence that could arise from inappropriate production process (Process control : YRF-706-02)	3	1	3	accept	Prevention and modification for inappropriate production process	No	Yes	ID-28
	Component analysis	1)Inspection measurement and testing equipment control procedure 2)periodic inspection for measuring instrument 3)calibration certificate against incorrect measuring instrument and of the adverse consequence that could arise from using of incorrect measuring instrument (calibration control : YRF-709-04)	3	1	3	accept	Prevention and modification for incorrect measuring instrument	No	Yes	ID-29
Monitoring and Measuring Equipment	Control of monitoring and measuring equipment	1) inspection and testing procedure 2)incoming inspection for raw material 3)certificate of analysis against wrong component analysis and of the adverse consequence that could arise from wrong component analysis (Incoming inspection : YRF-803-01)	3	1	3	accept	Prevention and modification for wrong component analysis	No	Yes	ID-30
Second usage	Re-use	1)shelf life and packaging qualification report 2)labelling on packaging and box 3)warning against re-using of device and of the adverse consequence that could arise from re-use of device (Do not re-use) (because this product is a single use product, it must not be reused)	4	1	4	accept	Prevention for re-use of device	No	Yes	ID-31

1) Risk control result of identification of possible hazards.

Frequent (5)					
Probable(4)					
Occasional(3)					
Remote(2)		9 case			
Improbable(1)		1case	15 cases	6 cases	
	Negligible (1)	Mimor(2)	Serious(3)	Critical(4)	Catastrophic(5)

2) Risk/benefit Analysis

The residual risk has been reduced or removed through the control of residual risk.

The result of risk management has accepted the Risk /benefit analysis. We could find there were benefits of the device overweigh the risks of the product

12.3 Risk re-control

Risk control should be controlled again to decrease to AFAP. Related data is as following

Identification of Possible hazards	Examples of hazards	Risk Control & Perform	Residual risk			Result	Risk/ Benefit	Other generated hazards	Completion of control	ID No.
			S	F	Risk					
Biological	Bacteria	1)Sterilization validation 2)B.I monitoring and recording 3)warning against non-sterilization and of the adverse consequence that could arise from any such non-sterilization (Make sure there are no problems with the sterile packaging and check whether or not attached and sterile)	4	1	4	accept	Blocking infection from bacteria	No	Yes	ID-1
		1)Packaging process validation 2) final inspection for packaging 3)warning against damaged packaging and of the adverse consequence that could arise from any such damaged packaging (Do not use the product that packaging is damaged)	4	1	4	accept	Blocking infection from bacteria	No	Yes	ID-2
	Viruses	1)Sterilization validation 2)B.I monitoring and recording 3)warning against non-sterilization and of the adverse consequence that could arise from any such non-sterilization (Use sterilization-packed products.)	4	1	4	accept	Blocking infection from viruses	No	Yes	ID-3
		1)packaging process validation 2)final inspection for packaging 3)warning against damaged packaging and of the adverse consequence that could arise from any such damaged packaging (Do not use the product that packaging is damaged)	4	1	4	accept	Blocking infection from viruses	No	Yes	ID-4
		1)shelf life and packaging qualification test report 2)final inspection for expiration date 3)warning against use that the product expiration date is over and of the adverse consequence that could arise from any such product that expiration date is over (Do not use the product that the expiration period is ended)	3	1	3	accept	Safe using within expiration date	No	Yes	ID-5
	Re-or cross-infection	1)packaging process validation 2)self-destruction after use 3)warning against re-use and of the adverse consequence that could arise from any such re-use	3	1	3	accept	Blocking infection by no reuse	No	Yes	ID-6

		(Discard the product that is once opened.)								
Chemical	Residues	1)chemical testing 2)incoming inspection for raw material 3)warning against other raw material and of the adverse consequence that could arise from any such other raw material (Confirm it there is transformations, flaws or cracks of the item)	3	1	3	accept	Protection of immune system by using passed raw material	No	Yes	ID-7
	Degradation products	1)clinical evaluation report 2)incoming inspection for raw material 3)warning against other raw material and of the adverse consequence that could arise from any such other raw material (Confirm it there is transformations, flaws or cracks of the item)	3	1	3	accept	Protection of disfunction by using passed raw material	No	Yes	ID-8
Bio compatibility	Toxicity of chemical constituents, e.g.	1) biocompatibility testing 2)incoming inspection for raw material 3)warning against toxicity of chemical constituents, e.g. and of the adverse consequence that could arise from any such toxicity of chemical constituents, e.g (If your medical history contains foreign body reaction, subcutaneous swelling (papules) etc, get an advice with a doctor.)	3	1	3	accept	Protection of toxicity exposure by using passed raw material	No	Yes	ID-9
	allergenicity / irritancy	1) cleanroom validation testing 2)promoting use of personal hygienic equipment and cleanroom circumstance when handling product 3) warning against allergenicity / irritancy and of the adverse consequence that could arise from any such allergenicity / irritancy (This product should not be used in the case of acute or chronic skin disease (infection or inflammation near the area to be treated)	3	1	3	accept	Prevention of allergenicity/irritancy by cleanroom control and using passed raw material	No	Yes	ID-10
	Pyrogenicity	1) cleanroom validation testing 2)cleanroom monitoring and recording 3) warning against pyrogenicity and of the adverse consequence that could arise from any such pyrogenicity (If there is inflammation treatment site, or other infections is concerned, it shall not be used).	3	1	3	accept	Prevention of pyrogenicity by cleanroom environment	No	Yes	ID-11
		1)packaging validation 2)final inspection for packaging 3)warning against damaged packaging and of the adverse consequence that could arise from any such damaged packaging (Do not use the product that packaging is damaged.)	3	1	3	accept	Prevention of pyrogenicity by packing control	No	Yes	ID-12
		1)sterilization validation 2)final inspection and monitoring 3)warning against re-sterilization and of the adverse consequence that could arise from any such re-sterilization (Do not re-sterilize or reuse)	3	1	3	accept	Prevention of pyrogenicity by re-sterilization	No	Yes	ID-13
Function	Loss or deterioration of function	1)shelf life and packaging qualification test 2) in-process inspection and final inspection for product function 3)warning on labelling for user (Check the validity period)	3	1	3	accept	Using without Loss or deterioration of function by using within expiration date	No	Yes	ID-14
		1)vacuum drying validation 2)dehumidication of suture below 500ppm 3)warning on labelling for using within expiration date (Check the validity period.)	2	1	2	accept	Using without dysfunction by tensile strength control	No	Yes	ID-15
Use error	Attention failure	1)IFU design report 2)labelling in indivisual packaging and in-box	3	1	3	accept	Prevention of infection with	No	Yes	ID-16

		3)warning against using of anyone except doctor and of the adverse consequence that could arise from any such using of anyone except doctor (This product should be used only by medical professional, doctor.)					'preparation before use' on packing labeling			
		1)Design development file 2)labelling on packaging and box 3)warning against using beyond intended use and of the adverse consequence that could arise from any such using beyond intended use (see intended use on IFU, This product is not used for else purposes except the intended use.)	4	1	4	accept	Prevention for using beyond intended use	No	Yes	ID-17
	Rule-based failure	1)IFU design report 2)labelling in indivisual packaging and in-box 3)warning against using in inflammation treatment site without rule-base and of the adverse consequence that could arise from any such rule-base failure (Use after reading the manuals / Before using, user should be aware of how to use completely)	2	1	2	accept	Prevention of infection by rule based manual	No	Yes	ID-18
Labeling	Incomplete instructions for use	1)IFU design report 2)final inspection for labelling 3)warning against incomplete instruction for use and of the adverse consequence that could arise from any such incomplete instruction for use (Before using, user should be aware of how to use completely)	2	1	2	accept	Prevention of infection by complete instruction on packing labeling	No	Yes	ID-19
	Inadequate description of performance characteristics	1)essential requirement report 2) final inspection for labelling 3)warning against inadequate description of performance characteristics and of the adverse consequence that could arise from any such inadequate description of performance characteristics (read device charateristecs on IFU)	2	1	2	accept	Prevention of infection by adequate description on packing labeling	No	Yes	ID-20
	Inadequate specification of intended use	1)clinical evaluation report 2)final inspection for labelling 3)warning against inadequate specification of intended use and of the adverse consequence that could arise from any such Inadequate specification of intended use (read intended use on IFU)	2	1	2	accept	Prevention of infection by adequate specification on packing labeling	No	Yes	ID-21
	Inadequate disclosure of limitations	1)label and packaging design 2)final inspection for labelling 3)warning against Inadequate disclosure of limitations and of the adverse consequence that could arise from any such Inadequate disclosure of limitations (Avoid direct sunlight and where to be high temperature and humidity.)	2	1	2	accept	Prevention of infection by adequate disclosure on packing labeling	No	Yes	ID-22
Operating Instructions	Inadequate specification of accessories to be used with the medical device	1)product description 2) final inspection for labelling 3)warning against Inadequate specification of accessories to be used with the medical device and of the adverse consequence that could arise from any such Inadequate specification of accessories to be used with the medical device (Confirm the content and packaging of the product.)	2	1	2	accept	Using device without dysfunction by adequate specification on packing labeling	No	Yes	ID-23
	Inadequate specification Of pre-use checks	1) label and packaging design 2)final inspection for labelling 3)warning against Inadequate specification of pre-use checks and of the adverse consequence that could arise from any such Inadequate	2	1	2	accept	Using device without dysfunction by side effect on packing labeling	No	Yes	ID-24

		specification of pre-use checks (read preparations before use)									
Warnings	Of side effects	1)clinical evaluation report 2)final inspection for labelling 3)warning against side effects and of the adverse consequence that could arise from any such side effects (Inflammation and foreign body reaction)	2	1	2	accept	Prevention of infection by adequate disclosure on packing labeling	No	Yes	ID-25
	Of hazards likely with re-use of single-use medical devices	1) label and packaging design 2) final inspection for labelling 3)warning against hazards likely with re-use of single-use medical devices and of the adverse consequence that could arise from any such hazards likely with re-use of single-use medical devices (Because this product is a single use product, it must not be reused)	2	1	2	accept	Prevention of infection by Indication of hazards likely with re-use on packing labeling	No	Yes	ID-26
Design	Design development	1)design development file 2)verification and validation for design output 3)report against inappropriate output and of the adverse consequence that could arise from inappropriate output (Design development report : YRF-702-01,02,03,04)	3	1	3	accept	Prevention and modification for wrong output	No	Yes	ID-27
Production	Production process	1)process control procedure 2)process inspection and monitoring 3)process inspection certificate against inappropriate production process and of the adverse consequence that could arise from inappropriate production process (Process control : YRF-706-02)	3	1	3	accept	Prevention and modification for inappropriate production process	No	Yes	ID-28
	Component analysis	1)Inspection measurement and testing equipment control procedure 2)periodic inspection for measuring instrument 3)calibration certificate against incorrect measuring instrument and of the adverse consequence that could arise from using of incorrect measuring instrument (calibration control : YRF-709-04)	3	1	3	accept	Prevention and modification for incorrect measuring instrument	No	Yes	ID-29
Monitoring and Measuring Equipment	Control of monitoring and measuring equipment	1) inspection and testing procedure 2)incoming inspection for raw material 3)certificate of analysis against wrong component analysis and of the adverse consequence that could arise from wrong component analysis (Incoming inspection : YRF-803-01)	3	1	3	accept	Prevention and modification for wrong component analysis	No	Yes	ID-30
Second usage	Re-use	1)shelf life and packaging qualification report 2)labelling on packaging and box 3)warning against re-using of device and of the adverse consequence that could arise from re-use of device (Do not re-use) (because this product is a single use product, it must not be reused)	4	1	4	accept	Prevention for re-use of device	No	Yes	ID-31

1) Risk control result of identification of possible hazards.

Frequent (5)					
Probable(4)					
Occasional(3)					

Remote(2)					
Improbable(1)		10case	15 cases	6 cases	
	Negligible (1)	Mimor(2)	Serious(3)	Critical(4)	Catastrophic(5)

14. ANALYSIS AND EVALUATION FOR POST-LITERATURE SEARCHING

14.1 Objective

- The objective of this literature searching is to verify that the product can be able to sell safely and to search other side effects.

14.2 Methodology

1) A protocol is developed to identify, select and collate relevant publications to address these questions. This should be developed and executed by persons with expertise in information retrieval, having due regard to the scope of the clinical evaluation set out by Yurim Medical Co., Ltd.

2) The literature search protocol should include.
   - The sources of data that will be used and a justification for their choice;
   - The extent of any searches of scientific literature databases (the database search strategy);
   - The selection/criteria to be applied to published literature and justification for their choice; and
   - Strategies for addressing the potential for duplication of data across multiple publications;

3) Once the literature search has been executed, a report should be compiled to present the results of the search.
   A copy of the protocol should be included and any deviations noted. A possible format for the literature search report is located at the literature search protocol.

4) The following documentation should be used in the clinical evaluation by the clinical evaluator
   - The literature search protocol;
   - The literature search report; and
   - Published articles and other references identified as being relevant to the device in question and suitable for evaluation.

14.3 Literature search protocol

1) This should be developed and executed by persons with expertise in information retrieval

- Lee Min Woo : QA manager

No	Period	Career
1	2012. 03 ~	Quality management leader of Yurim Medical Co., Ltd.

■ Academic ability
- University graduation
- Major : Chemical / industrial engineering

■ Main task
- The development of 'Sterile PLLA(Poly-L-Lactic Acid) Suture with Needle'
- Material analysis / Information searching / statistical analysis

2) The sources of data that will be used and a justification for their choice

- EMBASE- Excerpta Medica published by Elsevier
- CENTRAL- The Cochrane Central Register of Controlled Trials
- IRIS- The TGA"s medical device Incident Report Investigation Scheme
- MAUDE- US FDA"s Manufacturer And User Facility Device Experience database
- MEDION- Database that indexes literature on diagnostic tests
- MEDLINE- Published by US National Library of Medicine-
- ScicenceDirect

3) The extent of any searches of scientific literature databases

- Scientific databases – bibliographic
- Specialized databases
- Systematic review databases
- **C**linical trial registers
- Adverse event report databases
- Reference texts

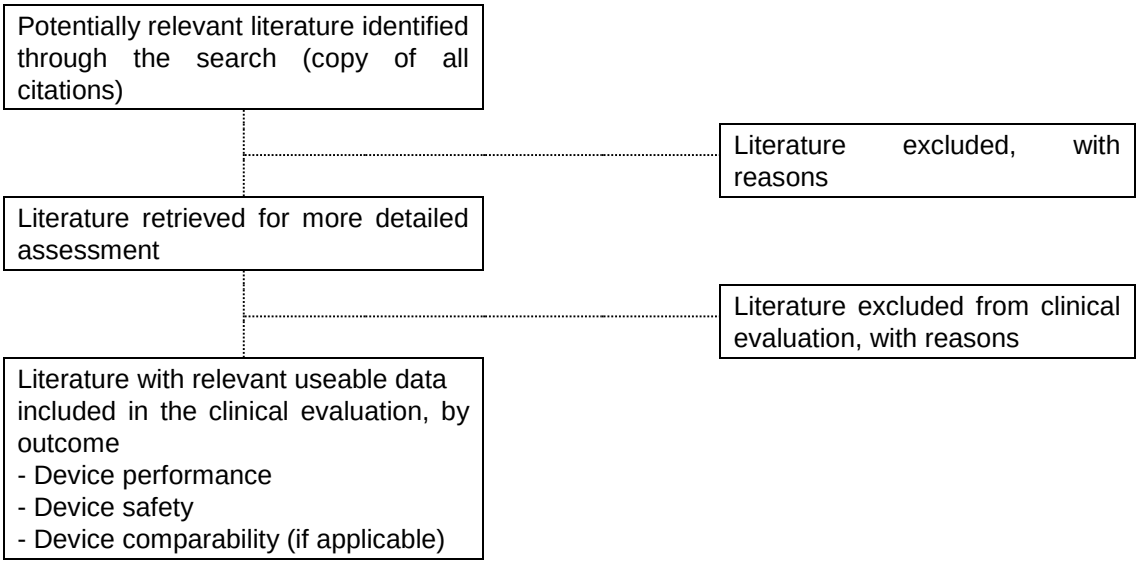
4) Literature search index

(1) The words used to search the literature must be selected with consideration of our products and the searching must be done by using the words as follows.

- poly-L-lactic acid
- poly-L-lactic acid performance
- poly-L-lactic acid safety
- poly-L-lactic acid biocompatibility

(2) Criteria of useful literature
- The most recent thesis published to be selected
- The thesis with conclusions both on 'clinical safety' and 'performance' to be selected
- The thesis with conclusions either on 'clinical safety' or 'performance' to be selected
- Period covered by search : 2000 ~ 2015

5) **Possible methodology for documenting the screening and selection of literature within a literature search report**



6) Common criteria of literature selection

(1) The common criteria for selecting literatures are as follows :

* Literatures that have to be included
  - poly-L-lactic acid
  - poly-L-lactic acid + biocompatibility / safety / performance
  - poly-L-lactic acid + effect / effectiveness / efficacy

* Literatures that are not included
  - Literatures about beauty,cosmetic

(2) Firstly, titles were investigated to select proper literatures

(3) Secondly, abstracts were examined to select proper literatures

(4) Lastly, the full contents of literatures selected from the second step were examined in terms of their number of samples, test protocols and results in order to select suitable literatures.

7) Methodology of literature selection

For the literatures, the weighing is assigned by grading and the category is as followings.

a. 9~12 points : Sufficient for scientific literature databases

b. 13~16 points : Not enough for scientific literature databases, but available for clinical databases

c. 17~22 points : Inappropriate for clinical evaluation

Suitability Criteria	Description	Grading	Weight (point)
Appropriate device	Were the data generated from the device in question?	D1	1
		D2	2
		D3	3
Appropriate device application	Was the device used for the same intended use (e.g.,methods of deployment, application. etc.)?	A1	1
		A2	2

		A3	3
Appropriate patient group	Where the data generated from a patient group that is representative of the intended treatment population (e.g.,age,sex,etc.) and clinical condition(i.e.,disease, including state and severity)?	P1	1
		P2	2
		P3	3
Acceptable report/data collation	Do the reports or collations of data contain sufficient information to be able to undertake a rational and objective assessment?	R1	1
		R2	2
		R3	3

[D1. Appraisal criteria for suitability]

Contribution Criteria	Description	Grading	Weight (point)
Data source type	Was the design of the study appropriate?	T1	1
		T2	2
Outcome measures	Do the outcome measures reported reflect the intended performance of the device?	O1	1
		O2	2
Follow up	Is the duration of follow-up long enough to assess whether duration of treatment effects and identify complications?	F1	1
		F2	2
Statistical significance	Has a statistical analysis of the data been provided and is it appropriate?	S1	1
		S2	2
Clinical significance	Was the magnitude of the treatment effect observed clinically significant?	C1	1
		C2	2

[D2. Appraisal criteria for data contribution]

14.4 Criteria for review

1) Sample Appraisal Criteria for Suitability

Suitability Criteria	Description	Grading system	
Appropriate device	Were the data generated from the device in question ?	D1	Actual device
		D2	Equivalent device
		D3	Other device
Appropriate device application	Was the device used for the same intended use (e.g.,methods of deployment, application. etc.)?	A1	Same use
		A2	Minor deviation
		A3	Major deviation
Appropriate patient group	Where the data generated from a patient group that is representative of the intended treatment Population(e.g.,age,sex,etc.) and clinical condition (i.e.,disease, including state and severity)?	P1	Applicable
		P2	Limited
		P3	Different population
Acceptable report/data collation	Do the reports or collations of data contain sufficient information to be able	R1	High quality
		R2	Minor deficiencies

	to undertake a rational and objective assessment?	R3	Major deficiencies

2) Sample Appraisal Criteria for Data Contribution

Suitability Criteria	Description	Grading system	
Data source type	Was the design of the study appropriate?	T1	Yes
		T2	No
Outcome measures	Do the outcome measures reported reflect the intended performance of the device?	O1	Yes
		O2	No
Follow up	Is the duration of follow-up long enough to assess whether duration of treatment effects and identify complications?	F1	Yes
		F2	No
Statistical significance	Has a statistical analysis of the data been provided and is it appropriate?	S1	Yes
		S2	No
Clinical significance	Was the magnitude of the treatment effect observed clinically significant?	C1	Yes
		C2	No

☞) The more level 1 grades, the greater the weight of evidence provided by that particular data set in comparison to other datasets

14.5 Possible methodology for documenting the screening and selection of literature within a literature search report

(1) Potentially relevant literature identified through the search (copy of all citations)

No.	Title	Choose
1	Neuropathic Pain Following Poly-L-Lactic Acid (Sculptra) Injection.	selected
2	Poly-L-lactic acid for the aesthetic correction of facial volume loss.	excluded
3	A randomized study of the efficacy and safety of injectable poly-L-lactic acid versus human-based collagen implant in the treatment of nasolabial fold wrinkles	selected
4	The Effect of Surface Modification of Aligned Poly-L-Lactic Acid Electrospun Fibers on Fiber Degradation and Neurite Extension.	selected
5	Comparison of acute recoil between bioabsorbable poly-L-lactic acid XINSORB stent and metallic stent in porcine model.	selected
6	Facial volumetric correction with injectable poly-L-lactic acid.	excluded
7	Correction of Chest Wall Deformity After Implant-Based Breast Reconstruction Using poly-l-Lactic Acid (Sculptra)	selected
8	Development and Testing of X-Ray Imaging-Enhanced Poly-L-Lactide Bone Screws.	selected
9	The safety and efficacy of poly-L-lactic acid on sunken cheeks in Asians.	selected
10	Dispelling the myth : appropriate use of poly-L-lactic acid and clinical considerations	selected
11	A new dermal filler made of cross-linked and auto-cross-linked hyaluronic acid in the correction of facial aging defects.	selected

12	Three-dimensional digital surface imaging measurement of the volumizing effect of injectable poly-L-lactic acid for nasolabial folds.	excluded
13	Evaluation of a new hyaluronic acid dermal filler for volume restoration.	selected
14	Facial enhancement and the European experience with Sculptra (Poly-L-Lactic Acid)	selected
15	Clinical experience with complications of hand rejuvenation.	excluded
16	Biomechanical analysis of poly-L-lactic acid and titanium plates fixated for mandibular symphyseal fracture with a conservatively treated unilateral condylar fracture using the three-dimensional finite element method.	excluded
17	Injectable Poly-L-Lactic Acid (Sculptra) : Technical considerations in Soft-tissue contouring	selected
18	Objective Analysis of Poly-L-Lactic Acid Injection Efficacy in Different Settings.	selected
19	Short-term safety and effects of a novel fully bioabsorable poly-L-lactic acid sirolimus-eluting stents in porcine coronary arteries.	selected
20	Treatment of atrophic scars with fractionated CO2 laser facilitating delivery of topically applied poly-L-lactic acid.	selected
21	Femtosecond laser induced periodic surface structure on poly-L-lactic acid.	excluded
22	Long-term safety and efficacy of poly-L-lactic acid in the treatment of HIV-related facial lipoatrophy	selected
23	Efficacy and safety of injection with poly-L-lactic acid compared with hyaluronic acid for correction of nasolabial fold: a randomized, evaluator-blinded, comparative study.	selected
24	Nano-composite of poly(L-lactide) and halloysite nanotubes surface-grafted with L-lactide oligomer under microwave irradiation.	selected
25	Subject global evaluation and subject satisfaction using injectable poly-L-lactic acid versus human collagen for the correction of nasolabial fold wrinkles	selected
26	Modified Poly-L-Lactic Acid injection technique	selected
27	Simple surface coating of electrospun poly-L-lactic acid scaffolds to induce angiogenesis.	excluded
28	Effects of VEGF loading on scaffold-confined vascularization.	excluded
29	Safety of poly-L-lactic acid (New-Fill®) in the treatment of facial lipoatrophy: a large observational study among HIV-positive patients.	selected
30	Structure, morphology and cell affinity of poly(L-lactide) films surface-functionalized with chitosan nanofibers via a solid-liquid phase separation technique.	selected
31	A Canadian study of the use of poly-L-lactic acid dermal implant for the treatment of hill and valley acne scarring.	selected
32	Influence of poly-L-lactic acid scaffold's pore size on the proliferation and differentiation of dental pulp stem cells.	excluded
33	Sculptra : the New three-Dimensional Filler	selected
34	Human histology and persistence of various injectable filler substances for soft tissue augmentation.	selected
35	Coaxially electrospun core/shell structured poly(L-lactide) acid/chitosan nanofibers for potential drug carrier in tissue engineering.	selected

36	A longitudinal evaluation of the impact of a polylactic acid injection therapy on health related quality of life amongst HIV patients treated with anti-retroviral agents under real conditions of use.	selected
37	Soft Tissue Augmentation Using Sculptra	selected
38	Characterization of ion-irradiated poly-L-lactic acid using nano-cutting.	excluded
39	Treatment of facial asymmetry with poly-L-lactic Acid: a case study.	selected
40	Preparation of Porous Core-Shell Poly L-Lactic Acid/Polyethylene Glycol Superfine Fibres Containing Drug.	selected
41	In vitro and in vivo degradability and cytocompatibility of poly(L-lactic acid) scaffold fabricated by a gelatin particle leaching method	selected
42	In vitro and in vivo degradation studies for development of a biodegradable patchbased on poly(3-hydroxybutyrate)	selected
43	In vitro degradation of porous PLLA/pearl powder composite scaffolds	selected
44	In tivo degradation and biocompaGbility study of in vitro pre-degraded as-polymerized polylactide particles	selected
45	In vitro and in vivo degradability and cytocompatibility of poly(L-lactic acid) scaffold fabricated by a gelatin particle leaching method	selected
46	In vitro and in vivo degradation studies for development of a biodegradable patchbased on poly(3-hydroxybutyrate)	selected
47	In vitro degradation of porous PLLA/pearl powder composite scaffolds	selected
48	In tivo degradation and biocompaGbility study of in vitro pre-degraded as-polymerized polylactide particles	selected

(2) Literature retrieved for more detailed assessment

- Literature excluded, with reasons : Literature less than those associated with our product were excluded.

No.	Title	Selected or excluded
1	Neuropathic Pain Following Poly-L-Lactic Acid (Sculptra) Injection.	excluded
2	A randomized study of the efficacy and safety of injectable poly-L-lactic acid versus human-based collagen implant in the treatment of nasolabial fold wrinkles	selected
3	Comparison of acute recoil between bioabsorbable poly-L-lactic acid XINSORB stent and metallic stent in porcine model.	selected
4	The safety and efficacy of poly-L-lactic acid on sunken cheeks in Asians.	selected
5	Correction of Chest Wall Deformity After Implant-Based Breast Reconstruction Using poly-l-Lactic Acid (Sculptra)	selected
6	The Effect of Surface Modification of Aligned Poly-L-Lactic Acid Electrospun Fibers on Fiber Degradation and Neurite Extension.	excluded
7	Dispelling the myth : appropriate use of poly-L-lactic acid and clinical considerations	selected

8	Short-term safety and effects of a novel fully bioabsorable poly-L-lactic acid sirolimus-eluting stents in porcine coronary arteries.	selected
9	Treatment of atrophic scars with fractionated CO2 laser facilitating delivery of topically applied poly-L-lactic acid.	selected
10	Facial enhancement and the European experience with Sculptra (Poly-L-Lactic Acid)	selected
11	Development and Testing of X-Ray Imaging-Enhanced Poly-L-Lactide Bone Screws.	excluded
12	Injectable Poly-L-Lactic Acid (Sculptra) : Technical considerations in Soft-tissue contouring	selected
13	A new dermal filler made of cross-linked and auto-cross-linked hyaluronic acid in the correction of facial aging defects.	excluded
14	Efficacy and safety of injection with poly-L-lactic acid compared with hyaluronic acid for correction of nasolabial fold: a randomized, evaluator-blinded, comparative study.	selected
15	Long-term safety and efficacy of poly-L-lactic acid in the treatment of HIV-related facial lipoatrophy	selected
16	Evaluation of a new hyaluronic acid dermal filler for volume restoration.	excluded
17	Subject global evaluation and subject satisfaction using injectable poly-L-lactic acid versus human collagen for the correction of nasolabial fold wrinkles	selected
18	Objective Analysis of Poly-L-Lactic Acid Injection Efficacy in Different Settings.	excluded
19	Modified Poly-L-Lactic Acid injection technique	selected
20	A Canadian study of the use of poly-L-lactic acid dermal implant for the treatment of hill and valley acne scarring.	selected
21	Nano-composite of poly(L-lactide) and halloysite nanotubes surface-grafted with L-lactide oligomer under microwave irradiation.	excluded
22	Safety of poly-L-lactic acid (New-Fill®) in the treatment of facial lipoatrophy: a large observational study among HIV-positive patients.	selected
23	Human histology and persistence of various injectable filler substances for soft tissue augmentation.	selected
24	Structure, morphology and cell affinity of poly(L-lactide) films surface-functionalized with chitosan nanofibers via a solid-liquid phase separation technique.	excluded
25	A longitudinal evaluation of the impact of a polylactic acid injection therapy on health related quality of life amongst HIV patients treated with anti-retroviral agents under real conditions of use.	selected
26	Coaxially electrospun core/shell structured poly(L-lactide) acid/chitosan nanofibers for potential drug carrier in tissue engineering.	excluded
27	Sculptra : the New three-Dimensional Filler	selected
28	Treatment of facial asymmetry with poly-L-lactic Acid: a case study.	selected
29	Soft Tissue Augmentation Using Sculptra	selected
30	Preparation of Porous Core-Shell Poly L-Lactic Acid/Polyethylene Glycol Superfine Fibres Containing Drug.	excluded

31	In vitro and in vivo degradability and cytocompatibility of poly(L-lactic acid) scaffold fabricated by a gelatin particle leaching method	selected
32	In vitro and in vivo degradation studies for development of a biodegradable patchbased on poly(3-hydroxybutyrate)	selected
33	In vitro degradation of porous PLLA/pearl powder composite scaffolds	selected
34	In tivo degradation and biocompaGbility study of in vitro pre-degraded as-polymerized polylactide particles	selected
35	In vitro and in vivo degradability and cytocompatibility of poly(L-lactic acid) scaffold fabricated by a gelatin particle leaching method	selected
36	In vitro and in vivo degradation studies for development of a biodegradable patchbased on poly(3-hydroxybutyrate)	selected
37	In vitro degradation of porous PLLA/pearl powder composite scaffolds	selected
38	In tivo degradation and biocompaGbility study of in vitro pre-degraded as-polymerized polylactide particles	selected

(3) Final selection and exclusion

- Literature excluded from clinical evaluation, with reasons

The literature that is less directly related to performance and safety of our products the content is excluded.

No.	Title	Selected or excluded	Excluded reason
1	Comparison of acute recoil between bioabsorbable poly-L-lactic acid XINSORB stent and metallic stent in porcine model.	Excluded	not best
2	A randomized study of the efficacy and safety of injectable poly-L-lactic acid versus human-based collagen implant in the treatment of nasolabial fold wrinkles	Selected	It is suitable
3	The safety and efficacy of poly-L-lactic acid on sunken cheeks in Asians.	Excluded	not best
4	Short-term safety and effects of a novel fully bioabsorable poly-L-lactic acid sirolimus-eluting stents in porcine coronary arteries.	Excluded	not best
5	Correction of Chest Wall Deformity After Implant-Based Breast Reconstruction Using poly-l-Lactic Acid (Sculptra)	Excluded	not best
6	Treatment of atrophic scars with fractionated CO2 laser facilitating delivery of topically applied poly-L-lactic acid.	Excluded	not best
7	Efficacy and safety of injection with poly-L-lactic acid compared with hyaluronic acid for correction of nasolabial fold: a randomized, evaluator-blinded, comparative study.	Excluded	not best
8	Dispelling the myth : appropriate use of poly-L-lactic acid and clinical considerations	Selected	It is suitable

9	Facial enhancement and the European experience with Sculptra (Poly-L-Lactic Acid)	Excluded	not best
10	Subject global evaluation and subject satisfaction using injectable poly-L-lactic acid versus human collagen for the correction of nasolabial fold wrinkles.	Excluded	not best
11	Injectable Poly-L-Lactic Acid (Sculptra) : Technical considerations in Soft-tissue contouring	Selected	It is suitable
12	A Canadian study of the use of poly-L-lactic acid dermal implant for the treatment of hill and valley acne scarring.	Excluded	not best
13	Long-term safety and efficacy of poly-L-lactic acid in the treatment of HIV-related facial lipoatrophy	Selected	It is suitable
14	Modified Poly-L-Lactic Acid injection technique	Excluded	not best
15	Human histology and persistence of various injectable filler substances for soft tissue augmentation.	Excluded	not best
16	Safety of poly-L-lactic acid (New-Fill®) in the treatment of facial lipoatrophy: a large observational study among HIV-positive patients.	Selected	It is suitable
17	A longitudinal evaluation of the impact of a polylactic acid injection therapy on health related quality of life amongst HIV patients treated with anti-retroviral agents under real conditions of use.	Excluded	not best
18	Sculptra : the New three-Dimensional Filler	Excluded	not best
19	Soft Tissue Augmentation Using Sculptra	Excluded	not best
20	Treatment of facial asymmetry with poly-L-lactic Acid: a case study.	Excluded	not best
21	In vitro and in vivo degradability and cytocompatibility of poly(L-lactic acid) scaffold fabricated by a gelatin particle leaching method	Selected	It is suitable
22	In vitro and in vivo degradation studies for development of a biodegradable patchbased on poly(3-hydroxybutyrate)	Selected	It is suitable
23	In vitro degradation of porous PLLA/pearl powder composite scaffolds	Selected	It is suitable
24	In tivo degradation and biocompaGbility study of in vitro pre-degraded as-polymerized polylactide particles	Selected	It is suitable
25	In vitro and in vivo degradability and cytocompatibility of poly(L-lactic acid) scaffold fabricated by a gelatin particle leaching method	Selected	It is suitable
26	In vitro and in vivo degradation studies for development of a biodegradable patchbased on poly(3-hydroxybutyrate)	Excluded	not best
27	In vitro degradation of porous PLLA/pearl powder composite scaffolds	Selected	It is suitable
28	In tivo degradation and biocompaGbility study of in vitro pre-degraded as-polymerized polylactide particles	Selected	It is suitable

14.6 Data analysis

☞ Data analysis for the literature search was performed in accordance with literature search protocol.

14.4.1 Selected literature list

No.	Title
1	A randomized study of the efficacy and safety of injectable poly-L-lactic acid versus human-based collagen implant in the treatment of nasolabial fold wrinkles
2	Dispelling the myth : appropriate use of poly-L-lactic acid and clinical considerations
3	Injectable Poly-L-Lactic Acid (Sculptra) : Technical considerations in Soft-tissue contouring
4	Long-term safety and efficacy of poly-L-lactic acid in the treatment of HIV-related facial lipoatrophy
5	Safety of poly-L-lactic acid (New-Fill®) in the treatment of facial lipoatrophy: a large observational study among HIV-positive patients.
6	In vitro and in vivo degradability and cytocompatibility of poly(L-lactic acid) scaffold fabricated by a gelatin particle leaching method
7	In vitro degradation of porous PLLA/pearl powder composite scaffolds
8	In tivo degradation and biocompaGbility study of in vitro pre-degraded as-polymerized polylactide particles

1) Literature(1st)

(1) Literature analysis

Literature title	Description	Grading system	
A randomized study of the efficacy and safety of injectable poly-L-lactic acid versus human-based collagen implant in the treatment of nasolabial fold wrinkles.	Were the data generated from the device in question?	D1	Actual device
		D2	**Equivalent device**
		D3	Other device
	Was the device used for the same intended use (e.g.,methods of deployment, application. etc.)?	**A1**	**Same use**
		A2	Minor deviation
		A3	Major deviation
	Where the data generated from a patient group that is Representative of the intended treatment population ? (e.g.,age,sex,etc.) and clinical condition (i.e.,disease, including state and severity)	**P1**	**Applicable**
		P2	Limited
		P3	Different population
Author	Do the reports or collations of data contain sufficient information to be able to undertake a rational and objective assessment?	**R1**	**High quality**
Narins RS[1], Baumann L, Brandt FS, Fagien S, Glazer S, Lowe NJ, Monheit GD, Rendon MI, Rohrich RJ, Werschler WP.		R2	Minor deficiencies
		R3	Major deficiencies
	Was the design of the study appropriate?	**T1**	**Yes**
Issued date		T2	No
J Am Acad Dermatol. 2010 Mar	Do the outcome measures reported reflect the intended performance of the device?	**O1**	**Yes**
		O2	No

	Is the duration of follow-up long enough to assess whether duration of treatment effects and identify complications?	F1	Yes
Application/Non-application		**F2**	**No**
Application	Has a statistical analysis of the data been provided and is it appropriate?	**S1**	**Yes**
		S2	No
Literature search report No.	Was the magnitude of the treatment effect observed clinically significant?	**C1**	**Yes**
YRM-PLLA-LSR-01		C2	No

(2) Literature summary report (YRM –PLLA-LSR-01)

Item	Contents
Source	US National Library of Medicine National Institutes of Health (http://www.ncbi.nlm.nih.gov)
Title	A randomized study of the efficacy and safety of injectable poly-L-lactic acid versus human-based collagen implant in the treatment of nasolabial fold wrinkles.
Summary	**Abstract** **BACKGROUND:** Injectable poly-L-lactic acid (PLLA) is a synthetic, biodegradable, biocompatible polymer device. **OBJECTIVE:** We sought to compare the efficacy and safety of injectable PLLA with human-derived collagen in treating nasolabial fold wrinkles. **METHODS:** In this randomized, evaluator-blinded, parallel-group, multicenter study, subjects received injectable PLLA (n = 116) or collagen (n = 117) injections (1-4 visits, 3-week intervals). Wrinkle Assessment Scale scores were calculated at screening; posttreatment week 3; months 3, 6, 9, and 13 (injectable PLLA or collagen groups); and months 19 and 25 (injectable PLLA group). Safety data were obtained from subject interviews and case report forms. **RESULTS:** Injectable PLLA significantly improved mean Wrinkle Assessment Scale scores (all time points, P < .001). Improvements (up to 25 months after last treatment) were significantly greater (P < .001) than with collagen for posttreatment months 3 to 13. **LIMITATIONS:** Mostly white women and subjects with Fitzpatrick skin types II and III were included.
Conclusion	Injectable PLLA provides well-tolerated, effective, and long-lasting (up to 25 months) nasolabial fold wrinkle correction.

(3) Evaluation for literature

① **Clinical aspect**

This literature states that In this randomized, evaluator-blinded, parallel-group, multicenter study, subjects received injectable PLLA (n = 116) or collagen (n = 117) injections (1-4 visits, 3-week intervals). Wrinkle Assessment Scale scores were calculated at screening; posttreatment week 3; months 3, 6, 9, and 13 (injectable PLLA or collagen groups); and months 19 and 25 (injectable PLLA group). Safety data were obtained from subject interviews and case report forms.

② **Biological aspect**

The literature states that Injectable PLLA significantly improved mean Wrinkle Assessment Scale scores (all time points, P\.001). Improvements (up to 25 months after last treatment) were significantly greater (P\.001) than with collagen for posttreatment months 3 to 13.

And Injectable PLLA provides well-tolerated, effective, and long-lasting (up to 25 months) nasolabial fold wrinkle correction.

- Therefore, the results of this study demonstrate that injectable PLLA is safe and effective for the cosmetic correction of NLFW in an immunocompetent population, and that the improvement is gradual and longlasting, maintained for up to 25 months after last treatment. The efficacy of injectable PLLA will provide subjects and physicians with a new treatment option for the correction of NLFW.

③ **Technical aspect**

The literature states that on Table II. Change from baseline in Wrinkle Assessment Scale score (intent-to-treat population), *Based on median of 3 evaluators' scores, where each score is average of left and right nasolabial folds Wrinkle Assessment Scale scores.

Difference in mean change is difference in raw mean change (or LS mean change) from baseline values between treatments.

Based on treatment comparison using analysis of covariance model with main effects for treatment and site and covariates for baseline median wrinkle score and age group.

④ Side-effect aspect

- There were no reports of granulomas during the entire 25-month study period.
- On Table IV. Adverse events from physician case report forms experienced by $2% of subjects*(all-treated population, through month 13), there are pain, swelling etc.

⑤ Intended use of item aspect

- The literature states that Injectable PLLA was demonstrated to be a safe and effective treatment for NLFW. In the 13-month comparative phase with human collagen, injectable PLLA treatment resulted in consistent and significant improvements over baseline for the efficacy variable (WAS scores) beginning 3 weeks after last treatment and continuing through 13 months of follow-up (P \.001). The safety profile for the injectable PLLA treatment group was similar to that for the human-collagen treatment group, with a higher incidence of overall AEs observed for the human-collagen treatment. Commonly occurring short-term injection siteerelated reactions were reported in both treatment groups. Product-related nodule and papule events in the injectable PLLA treatment group were 6.9% and 8.6%, respectively.

- during the 25-month posttreatment long-term surveillance phase, the injectable PLLA group continued to demonstrate significant improvements over baseline WAS scores (P\.001).

2) Literature (2nd)

(1) Literature analysis

Literature title	Description	Grading system	
Dispelling the myth: appropriate use of poly-L-lactic acid and clinical considerations.	Were the data generated from the device in question?	D1	Actual device
		D2	**Equivalent device**
		D3	Other device
	Was the device used for the same intended use (e.g.,methods of deployment, application. etc.)?	**A1**	**Same use**
		A2	Minor deviation
		A3	Major deviation
	Where the data generated from a patient group that is representative of the intended treatment population ? e.g.,age,sex,etc.) and clinical condition (i.e.,disease, including state and severity)	**P1**	**Applicable**
		P2	Limited
		P3	Different population
Author	Do the reports or collations of data contain sufficient information to be able to undertake a rational and objective assessment?	**R1**	**High quality**
Lowe NJ[1].		R2	Minor deficiencies
		R3	Major deficiencies
	Was the design of the study appropriate?	**T1**	**Yes**
Issued date		T2	No
J Eur Acad Dermatol Venereol. 2006 May	Do the outcome measures reported reflect the intended performance of the device?	**O1**	**Yes**
		O2	No
Application/Non-application	Is the duration of follow-up long enough to assess whether duration of treatment effects and identify complications?	**F1**	**Yes**
		F2	No
Application	Has a statistical analysis of the data been provided and is it appropriate?	**S1**	**Yes**
		S2	No
Literature search report No.	Was the magnitude of the treatment effect observed clinically significant?	**C1**	**Yes**
YRM –PLLA-LSR-02		C2	No

(2) Literature summary report (YRM –PLLA-LSR-02)

Item	Contents
Source	US National Library of Medicine National Institutes of Health (http://www.ncbi.nlm.nih.gov)
Title	Dispelling the myth: appropriate use of poly-L-lactic acid and clinical considerations.
Summary	**Abstract** **OBJECTIVES:** Injectable poly-L-lactic acid (PLLA; Sculptra) is widely used throughout Europe and the USA to restore volume in depressed areas of the face by stimulating neocollagenesis. Injectable PLLA was previously marketed as New-Fill, which was often injected incorrectly and at too high a concentration, resulting in some physicians losing confidence in this product. Today, Sculptra is still regarded with a degree of scepticism by some physicians, due to direct or indirect

	experience with New-Fill. Sculptra, both in formulation and use, is vastly superior to New-Fill and clinical experience with this product dispels the myths associated with the earlier types of injectable PLLA. **RESULTS:** PLLA is a very safe, biodegradable compound that has been used in a wide range of medical devices for the last 30 years. In injectable form a good safety profile has been proven; however, when the device is overconcentrated, localized overstimulation of the fibroblasts can result in the formation of small lumps (subcutaneous papules), which are non-pathological but nevertheless palpable by the patient. Physicians must also be trained in the injection of this device, as incorrect injection technique can cause device-related adverse events.
Conclusion	New product guidelines have ensured that problems with PLLA concentration have been countered, and tried and tested injection techniques have been shown to ameliorate device-related adverse events, both of which are dispelling the myths associated with modern injectable PLLA.

(3) Evaluation for literature

① **Clinical aspect**

This literature states that Following 3 years of clinical experience with PLLA, 130 patients have been treated, either with PLLA alone or with it as part of combination therapy. This experience has given insights into the correct technique that should be used to administer PLLA and the most appropriate treatment areas.

- Cases 1 and 2: correction of the nasolabial folds : Results obtained from using PLLA in clinical practice suggest the nasolabial folds, the cheeks and the lateral face are the optimal treatment areas for this device.

- correction of acne scars
- **correction of an atrophic scar**

② **Biological aspect**

The literature states that Injectable poly-L -lactic acid (PLLA; Sculptra ®) is widely used throughout Europe and the USA to restore volume in depressed areas of the face by stimulating neocollagenesis. Injectable PLLA was previously marketed as New-Fill™, which was often injected incorrectly and at too high a concentration, resulting in some physicians losing confidence in this product. Today, Sculptra ® is still regarded with a degree of scepticism by some physicians, due to direct or indirect experience with New-Fill. Sculptra ® , both in formulation and use, is vastly superior to New-Fill and clinical experience with this product dispels the myths associated with the earlier types of injectable PLLA.

PLLA is a very safe, biodegradable compound that has been used in a wide range of medical devices for the last 30 years. In injectable form a good safety profile has been proven;

③ **Technical aspect**

The literature states that Poly-L - lactic acid should always be injected into the low dermal layer or the upper subcutaneous layer. It is important for the patient to massage the treated area for 4–5 days.

④ Side-effect aspect

- The mid-forehead is a potential site for treatment, but it must be injected with caution due to the possibility of vascular occlusion in this region.
- when the device is over concentrated, localized overstimulation of the fibroblasts can result in the formation of small lumps (subcutaneous papules), which are non-pathological but nevertheless palpable by

the patient. Physicians must also be trained in the injection of this device, as incorrect injection technique can cause device-related adverse events.

- During this time PLLA was shown to be safe, with the most common device-related adverse event being the manifestation of subcutaneous papules, which occurred in 5% of treated patients
- These small < 5 mm lumps were non-visible, but could be felt by the patient. More than 90% of patients treated with PLLA reported high levels of satisfaction with their treatment.
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⑤ Intended use of item aspect

- The literature states that poly-L -lactic acid (PLLA; Sculptra ®) is widely used throughout Europe and the USA to restore volume in depressed areas of the face by stimulating neocollagenesis.
- The volumizing effects of this device were shown to last for at least 3 years.

3) Literature (3rd)
(1) Literature analysis

Literature title	Description	Grading system	
Injectable poly-L-lactic acid (Sculptra): technical considerations in soft-tissue contouring.	Were the data generated from the device in question?	D1	Actual device
		D2	**Equivalent device**
		D3	Other device
	Was the device used for the same intended use (e.g.,methods of deployment, application. etc.)?	**A1**	**Same use**
		A2	Minor deviation
		A3	Major deviation
	Where the data generated from a patient group that is Representative of the intended treatment population ? (e.g.,age,sex,etc.) and clinical condition (i.e.,disease, including state and severity)	**P1**	**Applicable**
		P2	Limited
		P3	Different population
Author	Do the reports or collations of data contain sufficient information to be able to undertake a rational and objective assessment?	**R1**	**High quality**
Lam SM[1], Azizzadeh B, Graivier M.		R2	Minor deficiencies
		R3	Major deficiencies
	Was the design of the study appropriate?	**T1**	**Yes**
Issued date		T2	No
Plast Reconstr Surg. 2006 Sep	Do the outcome measures reported reflect the intended performance of the device?	**O1**	**Yes**
		O2	No
	Is the duration of follow-up long enough to assess whether duration of treatment effects and identify complications?	F1	Yes
Application/Non-application		**F2**	**No**
Application	Has a statistical analysis of the data been provided and is it appropriate?	**S1**	**Yes**
		S2	No

Literature search report No.	Was the magnitude of the treatment effect observed clinically significant?	C1	Yes
YRM –PLLA-LSR-03		C2	No

(2) Literature summary report (YRM –PLLA-LSR-03)

Item	Contents
Source	US National Library of Medicine National Institutes of Health (http://www.ncbi.nlm.nih.gov)
Title	Injectable poly-L-lactic acid (Sculptra): technical considerations in soft-tissue contouring.
Summary	**Abstract** **BACKGROUND:** Poly-L-lactic acid gained U.S. Food and Drug Administration approval for use in human immunodeficiency virus-related facial lipoatrophy in August of 2004. Since that time, it has become available for use in the United States for human immunodeficiency virus facial lipoatrophy patients and for off-label uses in other areas for soft-tissue contouring. This article is intended to enumerate reconstitution, injection techniques, management, and avoidance of complications. **METHODS:** The authors have pooled their experiences to arrive at a consensus opinion for recommendations on treatment protocols for injectable poly-L-lactic acid use. **RESULTS:** This article prescribes techniques to achieve safer, consistent results while minimizing risks of complications with injectable poly-L-lactic acid. Although the product has been used widely in Europe since 1999, physicians in the United States have only recently begun to explore the uses of Sculptra as a volumizing agent in the face and the body. U.S. physicians have benefited from the European experience with this product, including early problems secondary to overaggressive use, low-volume reconstitution, higher volume injection of product at one session, and inadequate time between injection sessions.
Conclusion	The authors therefore have opted for a more conservative approach in their treatment recommendations. Higher volume dilution (8 to 12 cc), fewer vials used at each session, injections placed in the subcutaneous plane without any product being placed in the dermis, adequate time between injection sessions (at least 6 weeks), and postinjection patient massage should decrease the risks and avoid the potential complications associated with poly-L-lactic acid soft-tissue augmentation.

(3) Evaluation for literature

① **Clinical aspect**

This literature states that two major clinical studies have been conducted into injectable poly-L-lactic acid in Europe: the VEGA study and the Chelsea and Westminster study. The VEGA study was a prospective, openlabel, single-center evaluation that included 47 patients with human immunodeficiency virus–related facial lipoatrophy who were studied over a period of 2 years and who attended up to six injection sessions, with one vial per cheek per session. Injection sessions were undertaken every 2 weeks, with the majority of patients (86 percent) completing four to five injections. Ultrasound measurements of mean skin thickness demonstrated a statistically significant three-fold increase in skin thickness, with results that were sustained over the 2-year evaluation.2 Treatment-related adverse events that occurred included subcutaneous papules that arose on average 7 months (range, 0.3 to 25 months) after treatment initiation, with spontaneous resolution in 24 percent during the study.

② **Biological aspect**

The literature states that this article prescribes techniques to achieve safer, consistent results while minimizing risks of complications with injectable poly-L-lactic acid. Although the product has been used widely in Europe since 1999, physicians in the United States have only recently begun to explore the uses of Sculptra as a volumizing agent in the face and the body. U.S. physicians have benefited from the European experience with this product, including early problems secondary to overaggressive use, low-volume reconstitution, higher volume injection of product at one session, and inadequate time between injection sessions.

③ **Technical aspect**

The literature states that the authors therefore have opted for a more conservative approach in their treatment recommendations. Higher volume dilution (8 to 12 cc), fewer vials used at each session, injections placed in the subcutaneous plane without any product being placed in the dermis, adequate time between injection sessions (at least 6 weeks), and postinjection patient massage should decrease the risks and avoid the potential complications associated with poly-L-lactic acid soft-tissue augmentation

④ Side-effect aspect

- The mid-forehead is we will focus on the techniques (i.e., reconstitution, injection, and postoperative care) that may reduce the occurrence of adverse events, such as subcutaneous papules, and management of complications associated with poly-L-lactic acid.

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⑤ Intended use of item aspect

- The literature states that all patients underwent three treatment sessions with one vial of poly-L-lactic acid per cheek. One arm of the study received treatment at 0, 2, and 4 weeks; the other arm, at 12, 14, and 16 weeks. In the immediate treatment group, significant changes in skin thickness were observed at week 12 when compared with the delayed treatment group, which had not been treated at that point.

4) Literature (4th)

(1) Literature analysis

Literature title	Description	Grading system	
Long-term safety and efficacy of poly-L-lactic acid in the treatment of HIV-related facial lipoatrophy.	Were the data generated from the device in question?	D1	Actual device
		D2	**Equivalent device**
		D3	Other device
	Was the device used for the same intended use (e.g.,methods of deployment, application. etc.)?	**A1**	**Same use**
		A2	Minor deviation
		A3	Major deviation
	Where the data generated from a patient group that is Representative of the intended treatment population ? (e.g.,age,sex,etc.) and clinical condition (i.e.,disease, including state and severity)	**P1**	**Applicable**
		P2	Limited
		P3	Different population

Author	Do the reports or collations of data contain sufficient information to be able to undertake a rational and objective assessment?	**R1**	**High quality**
Moyle GJ[1], Brown S, Lysakova L, Barton SE.		R2	Minor deficiencies
		R3	Major deficiencies
	Was the design of the study appropriate?	**T1**	**Yes**
Issued date		T2	No
HIV Med. 2006 Apr	Do the outcome measures reported reflect the intended performance of the device?	**O1**	**Yes**
		O2	No
	Is the duration of follow-up long enough to assess whether duration of treatment effects and identify complications?	F1	Yes
Application/Non-application		**F2**	**No**
Application	Has a statistical analysis of the data been provided and is it appropriate?	**S1**	**Yes**
		S2	No
Literature search report No.	Was the magnitude of the treatment effect observed clinically significant?	**C1**	**Yes**
YRM –PLLA-LSR-04		C2	No

(2) Literature summary report (YRM –PLLA-LSR-04)

Item	Contents
Source	US National Library of Medicine National Institutes of Health (http://www.ncbi.nlm.nih.gov)
Title	Long-term safety and efficacy of poly-L-lactic acid in the treatment of HIV-related facial lipoatrophy.
Summary	**Abstract** **OBJECTIVE:** We evaluated the long-term safety and efficacy of injectable poly-L-lactic acid (PLLA) for the correction of facial lipoatrophy. **METHODS:** This was a randomized, open-label, comparative, single-centre study of injected PLLA in patients with HIV-related facial lipoatrophy. Thirty subjects were randomized to immediate or delayed PLLA treatments, administered as three sets of bilateral injections, 2 weeks apart, into the deep dermis above the buccal fat pad. Week 24 results have been published previously (Moyle et al, HIV Medicine 2004, Vol. 5, pp. 82-87). Long-term efficacy was assessed at a recall visit using visual analogue scales (VASs) to record patient satisfaction, and by the Hospital Anxiety and Depression Scale (HADS). Patients also reported any adverse events (AEs) during the treatment period and at the recall visit. **RESULTS:** Twenty-seven patients returned for the recall visit, a minimum of 18 months post final study treatment. Fourteen of these patients were excluded from the recall visit because of additional treatment with PLLA. Improvements in VAS scores for facial appearance were sustained from baseline to the recall visit in both randomization groups ($P<0.05$ and $P<0.001$). Trends in improvement in HADS scores were also noted, with patients in the delayed group experiencing significant improvements in depressive symptoms ($P<0.05$). One case of injection-site induration and nine cases of injection-site nodules were noted at the recall visit, none of which was described as serious or severe.
Conclusion	Physical and psychological benefits of PLLA are sustained over at least 18 months. Delayed AEs include mild nodularity at the treatment site.

(3) Evaluation for literature

① **Clinical aspect**

This literature states that Twenty-seven patients returned for the recall visit, a minimum of 18 months post final study treatment. Fourteen of these patients were excluded from the recall visit because of additional treatment with PLLA. Improvements in VAS scores for facial appearance were sustained from baseline to the recall visit in both randomization groups (Po0.05 and Po0.001). Trends in improvement in HADS scores were also noted, with patients in the delayed group experiencing significant improvements in depressive symptoms (Po0.05). One case of injection-site induration and nine cases of injection-site nodules were noted at the recall visit, none of which was described as serious or severe.

② **Biological aspect**

The literature states that The lumps were not associated with clinically evident inflammation [12–14], and no further investigation was clinically warranted or requested by the patients

③ **Technical aspect**

The literature states that This was a randomized, open-label, comparative, singlecentre study of injected PLLA in patients with HIV-related facial lipoatrophy. Patients who were HIV positive, and with physician and patient-assessed moderate-to-severe nasolabial fat pad loss, were enrolled in the study. The degree of facial lipoatrophy was classified as normal, mild, moderate and severe. Eligible patients had received no previous treatment for the correction of their HIVassociated lipoatrophy. As part of the original study design, eligible individuals (n530) were randomized in a 1 : 1 fashion to receive immediate (n515) or delayed (n515) treatment. All patients received three sessions, separated by fortnightly intervals, of bilateral injections of PLLA into the deep dermis overlying the buccal fat pads. For each treatment session, 0.15 g of PLLA was reconstituted by the addition of 2mL of sterile water for injection and 1mL of 2% lidocaine to give a total volume of 3 mL. Up to 3mL of reconstituted PLLA was injected into the treatment area. Patients in the delayed group commenced treatment 12 weeks after those in the immediate group. Injection techniques, and details of assessments undertaken at time-points other than the recall visit, are reported elsewhere [8].

④ Side-effect aspect

The literature states that Furthermore, because only two of nine patients reported that the lumps were visible, it may be more accurate to describe these events as subcutaneous papules (o5 mm);

- The literature states that patients also reported any adverse events (AEs) during the treatment period and at the recall visit.
- Over 2 years, no serious or severe side effects were reported.
- The one case of infection was a self-limiting superficial local cellulitis, which did not require antibiotic therapy (n51) and was not cultured [8].

⑤ Intended use of item aspect

- The literature states that Long-term efficacy was assessed at a recall visit using visual analogue scales (VASs) to record patient satisfaction, and by the Hospital Anxiety and Depression Scale (HADS).
- Physical and psychological benefits of PLLA are sustained over at least 18 months. Delayed AEs

include mild nodularity at the treatment site.

- The safety data presented here suggest that PLLA has a favourable long-term safety and efficacy profile. Over 2 years, no serious or severe side effects were reported. As indicated by the significant improvement in VAS scores from baseline, and the trend for improvements in HADS scores, the positive results achieved with PLLA noted at 24 weeks [8] persisted to the recall visit, up to 2 years post treatment initiation.

5) Literature (5th)

(1) Literature analysis

Literature title	Description	Grading system	
Safety of poly-L-lactic acid (New-Fill®) in the treatment of facial lipoatrophy: a large observational study among HIV-positive patients.	Were the data generated from the device in question ?	D1	Actual device
		D2	**Equivalent device**
		D3	Other device
	Was the device used for the same intended use (e.g.,methods of deployment, application. etc.)?	**A1**	**Same use**
		A2	Minor deviation
		A3	Major deviation
	Where the data generated from a patient group that is Representative of the intended treatment population ? (e.g.,age,sex,etc.) and clinical condition (i.e.,disease, including state and severity)	**P1**	**Applicable**
		P2	Limited
		P3	Different population
Author	Do the reports or collations of data contain sufficient information to be able to undertake a rational and objective assessment?	**R1**	**High quality**
Duracinsky M[1], Leclercq P, Herrmann S, Christen MO, Dolivo M, Goujard C, Chassany O.		R2	Minor deficiencies
		R3	Major deficiencies
Issued date	Was the design of the study appropriate?	**T1**	**Yes**
		T2	No
BMC Infect Dis. 2014 Sep	Do the outcome measures reported reflect the intended performance of the device?	**O1**	**Yes**
		O2	No
Application/Non-application	Is the duration of follow-up long enough to assess whether duration of treatment effects and identify complications?	F1	Yes
		F2	**No**
Application	Has a statistical analysis of the data been provided and is it appropriate?	**S1**	**Yes**
		S2	No
Literature search report No.	Was the magnitude of the treatment effect observed clinically significant?	**C1**	**Yes**
YRM –PLLA-LSR-05		C2	No

(2) Literature summary report (YRM –PLLA-LSR-05)

Item	Contents
Source	US National Library of Medicine National Institutes of Health (http://www.ncbi.nlm.nih.gov)
Title	Safety of poly-L-lactic acid (New-Fill®) in the treatment of facial lipoatrophy: a large observational study among HIV-positive patients
Summary	**Abstract** **BACKGROUND:** Facial lipoatrophy is a frequently reported condition associated with use of antiretroviral (ARV) drugs. Poly-L-lactic acid (PLLA) acid has been used to correct facial lipoatrophy in people with HIV since 2004 both in Europe and the United States. The objective of this study was to establish, in real life conditions and in a large sample, the safety of PLLA (New Fill®, Valeant US, Sinclair Pharma Paris, France) to correct facial lipoatrophy among HIV-positive patients. **METHODS:** A longitudinal study was conducted between 2005 and 2008 in France. Data from 4,112 treatment courses (n = 4,112 patients) and 15,665 injections sessions (1 to 5 injection sessions per treatment course) were gathered by 200 physicians trained in the use of PLLA. **RESULTS:** The average age of patients (88.3% males) treated for lipoatrophy was 47.1 ± 8.1 years (Mean ± SD); 91.2% of patients had been receiving ARV treatment for 10.9 (±4.2) years; CD4 T-cell count was 535 ± 266 cells/mm3. The duration of facial lipoatrophy was 5 ± 2.8 years and the severity was such that 47.3% of patients required five injection sessions of PLLA and 81.9% of the sessions required two vials of the preparation. The final visit, scheduled two months after the last injection session, was attended by 66.0% of patients (n = 2,713). 48 treatment courses (2.8%) were discontinued due to adverse events (AEs). The overall incidence of AEs per course was 18.8%. Immediate AEs, bleeding (3.4%), bruising (2.3%), pain (2.0%), redness at injection site (1.6%), and swelling of the face (0.7%), occurred in 15.4% of courses and 7.0% of sessions (usually during the first session). Non-immediate AEs, mainly nodules (5.7%), inflammation (0.7%), granuloma (0.3%), discolouration (0.2%), and skin hypertrophy (0.1%), occurred in 6.7% of courses. Non-immediate AEs occurred within a time ranging from 21 days (inflammation) to 101 days (granuloma) and all but three of the 13 cases of granuloma resolved. Product efficacy was rated satisfactory by 95% of the patients and physicians.
Conclusion	This study demonstrated, in real-life conditions and on a large sample, that PLLA injections were feasible, efficient, and safe when performed by trained physicians.

(3) Evaluation for literature

① **Clinical aspect**

This literature states that facial lipoatrophy is a frequently reported condition associated with use of antiretroviral (ARV) drugs. Poly-L-lactic acid (PLLA) acid has been used to correct facial lipoatrophy in people with HIV since 2004 both in Europe and the United States. The objective of this study was to establish, in real life conditions and in a large sample, the safety of PLLA (New Fill®, Valeant US, Sinclair Pharma Paris, France) to correct facial lipoatrophy among HIV-positive patients.

② **Biological aspect**

The literature states that this study demonstrated, in real-life conditions and on a large sample, that PLLA injections were feasible, efficient, and safe when performed by trained physicians.

③ **Technical aspect**

The literature states that a longitudinal study was conducted between 2005 and 2008 in France. Data from 4,112 treatment courses (n = 4,112 patients) and 15,665 injections sessions (1 to 5 injection sessions per treatment course) were gathered by 200 physicians trained in the use of PLLA

④ Side-effect aspect

- The mid-forehead is immediate AEs, bleeding (3.4%), bruising (2.3%), pain (2.0%), redness at injection site (1.6%), and swelling of the face (0.7%), occurred in 15.4% of courses and 7.0% of sessions (usually during the first session). Non-immediate AEs, mainly nodules (5.7%), inflammation (0.7%), granuloma (0.3%), discolouration (0.2%), and skin hypertrophy (0.1%), occurred in 6.7% of courses. Non-immediate AEs occurred within a time ranging from 21 days (inflammation) to 101 days (granuloma) and all but three of the 13 cases of granuloma resolved.

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⑤ Intended use of item aspect

- The literature states that the subjective efficacy of the treatment was reported as satisfied or very satisfied by most patients and physicians.

6) Literature (6th)

(1) Literature analysis

Literature title	Description	Grading system	
In vitro and in vivo degradability and cytocompatibility of poly(L-lactic acid) scaffold fabricated by a gelatin particle leaching method	Were the data generated from the device in question ?	D1	Actual device
		D2	**Equivalent device**
		D3	Other device
	Was the device used for the same intended use (e.g.,methods of deployment, application. etc.)?	**A1**	**Same use**
		A2	Minor deviation
		A3	Major deviation
	Where the data generated from a patient group that is Representative of the intended treatment population ? (e.g.,age,sex,etc.) and clinical condition (i.e.,disease, including state and severity)	**P1**	**Applicable**
		P2	Limited
		P3	Different population
Author	Do the reports or collations of data contain sufficient information to be able to undertake a rational and objective assessment?	**R1**	**High quality**
Gong Y[1], Zhou Q, Gao C, Shen J.		R2	Minor deficiencies
		R3	Major deficiencies
	Was the design of the study appropriate?	**T1**	**Yes**
Issued date		T2	No
Acta Biomater. 2007 Jul;3(4):531-40. Epub 2007 Mar 9.	Do the outcome measures reported reflect the intended performance of the device?	**O1**	**Yes**
		O2	No
	Is the duration of follow-up long enough to	F1	Yes

Application/Non-application	assess whether duration of treatment effects and identify complications?	**F2**	**No**
Application	Has a statistical analysis of the data been provided and is it appropriate?	**S1**	**Yes**
		S2	No
Literature search report No.	Was the magnitude of the treatment effect observed clinically significant?	**C1**	**Yes**
YRM –PLLA-LSR-6		C2	No

(2) Literature summary report (YRM –PLLA-LSR-6)

Item	Contents
Source	US National Library of Medicine National Institutes of Health (http://www.ncbi.nlm.nih.gov)
Title	In vitro and in vivo degradability and cytocompatibility of poly(L-lactic acid) scaffold fabricated by a gelatin particle leaching method
Summary	**Abstract** Porous poly(l-lactic acid) (PLLA) scaffolds fabricated by a gelatin particle-leaching technique have good mechanical property and cytocompatibility, as demonstrated by a previous in vitro study. Here we investigate further the in vitro degradation of the scaffolds in terms of weight loss, water uptake, weight-average molecular weight, thermal behavior and morphology during a 39 week period in phosphate-buffered saline. The water uptake decreased dramatically during the initial stage due to release of the remaining gelatin, and then increased slightly with degradation time. The weight-average molecular weight decreased linearly as a function of time, while the crystallinity steadily increased with slightly decreased melting temperature. After degradation, many defects and big holes were seen in the scaffolds by scanning electron microscopy. Cartilage regeneration and scaffold disappearance in vivo were compared by implanting the construct into nude mice for 30-120 days. While the scaffolds maintained their intact pore structure after 23 weeks of degradation in vitro, they almost disappeared in vivo at the same time, implying a faster degradation rate in vivo. By 120 days after implantation, the scaffolds were hardly seen in the newly formed cartilage-like tissue. The regenerated cartilages could not maintain their predesigned shape after a long period of in vivo culture due to the weakening of the mechanical strength of the constructs as a result of PLLA degradation. The regions occupied initially by PLLA scaffold were filled later by collagen type II secreted by the chondrocytes, but with no evident basophilic proteoglycan.

(3) Evaluation for literature

① **Clinical aspect**

This literature states that Compared with the degradation in vitro, the degradation rate of the PLLA scaffolds in vivo was much faster. While most parts of the scaffold existed and maintained intact pore structure even after 23 weeks of degradation in vitro (Fig. 4b), it is hard to find the scaffold in the sectioned sample after in vivo implantation for 120 days (17 weeks)

Histological examination of the constructs implanted for 30–120 days was performed to assess the degradation of the scaffold and the response of the cultured cells (Fig. 6). The traces of polymer scaffold (P) in the section of the implant after 30 days of culture suggest the existence of a large amount of PLLA. However, after 120 days of culture in vivo, most of the polymer scaffold (P) had disappeared.

Some regions with no chondrocytes but only collagen (C) could be clearly identified (Fig. 6b–d), as indicated by the arrows.

② **Biological aspect**

The literature states that the weight-average molecular weight decreased linearly as a function of time, while the crystallinity steadily increased with slightly decreased melting temperature. After degradation, many defects and big holes were seen in the scaffolds by scanning electron microscopy. Cartilage regeneration and scaffold disappearance in vivo were compared by implanting the construct into nude mice for 30–120 days. While the scaffolds maintained their intact pore structure after 23 weeks of degradation in vitro, they almost disappeared in vivo at the same time, implying a faster degradation rate in vivo. By 120 days after implantation, the scaffolds were hardly seen in the newly formed cartilage-like tissue. The regenerated cartilages could not maintain their predesigned shape after a long period of in vivo culture due to the weakening of the mechanical strength of the constructs as a result of PLLA degradation. The regions occupied initially by PLLA scaffold were filled later by collagen type II secreted by the chondrocytes, but with no evident basophilic proteoglycan

- The porous PLLA scaffolds degrade in PBS (pH 7.4) at 37 C in vitro at a relatively slow rate.

Different from the exponential degradation of bulk material, we find here that the molecular weight decreases linearly as a function of degradation time.

The highly porous structure with interconnected pores ensures sufficient wetting of the scaffold

by the buffer solution, and greatly reduces the accumulation of generated acids within the pore walls.

This will surely eliminate the autocatalytic effect brought about by the acids, which would mean that the "burst" disappearance of the bulk PLLA material may not happen for the porous scaffold, or at least would not be so severe. Nonetheless, due to the poorer exchanging ability of the scaffold interior, bigger defects are formed there.

③ **Technical aspect**

The literature states that The PLLA (Mn = 99,000, Mw = 212,000) was synthesized using the method described previously [30]. Gelatin and 1,4-dioxane were obtained from Shanghai Chemical Industries Co. Ltd. A 10% (w/v) PLLA/1,4-dioxane solution was prepared for further use.

- The porous PLLA scaffolds degrade in PBS (pH 7.4) at 37 C in vitro at a relatively slow rate. Different from the exponential degradation of bulk material, we find here that the molecular weight decreases linearly as a function of degradation time. The highly porous structure with interconnected pores ensures sufficient wetting of the scaffold by the buffer solution, and greatly reduces the accumulation of generated acids within the pore walls.

④ Side-effect aspect

The literature states that the environment in vivo, including the ease of substance diffusion and the existence of enzymes, is usually regarded as accelerating the degradation of the polymer scaffold.

- Although the tissue engineering approach is a potential alternative for cartilage reconstruction, there are still many unresolved issues. The loss of the precise shape of the tissue-engineered constructs

is a common problem that has been recognized by other researchers

⑤ Intended use of item aspect

- The literature states that The degradation rate is accelerated in vivo. After 120 days of culture subcutaneously in nude mice, most of the scaffold has disappeared. The regions initially occupied by the polymer scaffold are filled with collagen type II, with no evident basophilic proteoglycan. The scaffold is also unable to maintain its predesigned shape after a long period of implantation, due to the weakening of the mechanical strength of the construct. In order to regenerate cartilage with ideal properties, we suggest that a scaffold is needed which maintains enough mechanical strength throughout most of the tissue regeneration process. Moreover, the in vivo study of a scaffold seeded with targeted cells will draw more accurate conclusions in terms of scaffold degradation.

7) Literature (7th)

(1) Literature analysis

Literature title	Description	Grading system	
In vitro degradation of porous PLLA/pearl powder composite scaffolds	Were the data generated from the device in question ?	D1	Actual device
		D2	**Equivalent device**
		D3	Other device
	Was the device used for the same intended use (e.g.,methods of deployment, application. etc.)?	**A1**	**Same use**
		A2	Minor deviation
		A3	Major deviation
	Where the data generated from a patient group that is Representative of the intended treatment population ? (e.g.,age,sex,etc.) and clinical condition (i.e.,disease, including state and severity)	**P1**	**Applicable**
		P2	Limited
		P3	Different population
Author	Do the reports or collations of data contain sufficient information to be able to undertake a rational and objective assessment?	**R1**	**High quality**
Liu YS[1], Huang QL[1], Kienzle A[2], Müller WE[2], Feng QL[3].		R2	Minor deficiencies
		R3	Major deficiencies
	Was the design of the study appropriate?	**T1**	**Yes**
Issued date		T2	No
Mater Sci Eng C Mater Biol Appl. 2014 May 1;38:227-34. doi: 10.1016/j.msec.2014.02.007. Epub 2014 Feb 12.	Do the outcome measures reported reflect the intended performance of the device?	**O1**	**Yes**
		O2	No
	Is the duration of follow-up long enough to assess whether duration of treatment effects and identify complications?	F1	Yes
Application/Non-application		**F2**	**No**
Application	Has a statistical analysis of the data been provided and is it appropriate?	**S1**	**Yes**
		S2	No
Literature search report No.	Was the magnitude of the treatment effect observed clinically significant?	**C1**	**Yes**
YRM –PLLA-LSR-7		C2	No

(2) Literature summary report (YRM –PLLA-LSR-7)

Item	Contents
Source	US National Library of Medicine National Institutes of Health (http://www.ncbi.nlm.nih.gov)
Title	In vitro degradation of porous PLLA/pearl powder composite scaffolds
Summary	**Abstract** The in vitro degradation behavior of poly-L-lactide (PLLA), PLLA/aragonite pearl powder and PLLA/vaterite pearl powder scaffolds was investigated. The scaffolds were soaked in phosphate buffer solution (PBS) up to 200 days. Scanning electron microscopy (SEM), gel permeation chromatography (GPC), and differential scanning calorimetry (DSC) were used to observe any degradation of the scaffolds. Degradation behaviors such as changes in pH, porosity, bulk density, water absorption, weight loss and mechanical properties were discussed. The results show that a gradual increase of the pH in composite scaffolds can decrease the rate of hydrolysis of PLLA. PLLA/vaterite and PLLA/aragonite scaffolds have a similar degradation behavior but a slower rate of degradation than PLLA.

(3) Evaluation for literature

① **Clinical aspect**

This literature states that different degradation behaviors of PLLA, PLLA/vaterite and PLLA/aragonite scaffolds in PBS have been studied. The gradual increase of pH in composite scaffolds can decrease the hydrolysis rate of PLLA. Moreover, composite scaffolds show a greater ability to release Ca2+ than pearl powders in PBS. During the degradation, PLLA cooperating with pearl powders displays changes such as mechanical properties, weight loss, bulk density and porosity. Alkalinity products released from composite scaffolds can provide a relatively steady environment for slowing down the degradation rate of PLLA and prolonging the degradation time of composite scaffolds. PLLA/vaterite and PLLA/ aragonite scaffolds showsimilar degradation behaviors. Further investigation could be performed on biological properties including degradation behavior in vivo and biocompatibility in order to promote the novel material in clinical applications.

② **Biological aspect**

The literature states that the in vitro degradation behavior of poly-L-lactide (PLLA), PLLA/aragonite pearl powder and PLLA/vaterite pearl powder scaffolds was investigated. The scaffolds were soaked in phosphate buffer solution (PBS) up to 200 days. Scanning electron microscopy (SEM), gel permeation chromatography (GPC), and differential scanning calorimetry (DSC) were used to observe any degradation of the scaffolds. Degradation behaviors such as changes in pH, porosity, bulk density,water absorption, weight loss and mechanical properties were discussed. The results show that a gradual increase of the pH in composite scaffolds can decrease the rate of hydrolysis of PLLA. PLLA/vaterite and PLLA/aragonite scaffolds have a similar degradation behavior but a slower rate of degradation than PLLA.

③ **Technical aspect**

The literature states that PLLA (Mw=17.9 × 104 Da) was purchased from Shandong Medical Device Company. The 1,4-dioxane was purchased from Beijing Modern Eastern Fine Chemical Co., Ltd. 99.7% ethanol was purchased from Beijing Chemical Works. All the reagents were of analytical grade.

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④ Side-effect aspect

The literature states that The weight loss of the composite scaffolds is relatively faster compared to the PLLA scaffold. During 1 to 4 weeks the composite scaffolds show a higher weight loss, slowly increasing after 4 weeks. Considering the fast decrease in the mechanical properties of composite scaffolds (Fig. 6) and gradual increase of pH in PBS (Fig. 1), the dissolution of CaCO3 from pearl powders is the main factor for the weight loss of the composite scaffolds in the first 4 weeks. After 4 weeks there is a complex process of degradation because at the same time PLLA possibly degrades and pearl powder dissolves

⑤ Intended use of item aspect

- The literature states that The composite scaffolds display a gradual decrease of the compressive strength and compressive modulus. After 200 days, the compressive strength is still higher than that of the PLLA scaffold before degradation. The compressive modulus is slightly less than that of the PLLA scaffold before degradation. During the 200 days of degradation, the dissolution of pearl powdersmay be themain factor for a decreasing compressive strength and compressive modulus. At the same time, the dissolution of pearl powders and the hydrolysis of PLLA increasing defects will result in losing the order of whole porous structure and decreasing the mechanical properties of the scaffolds.

8) Literature (8th)

(1) Literature analysis

Literature title	Description	Grading system	
In tivo degradation and biocompaGbility study of in vitro pre-degraded as-polymerized polylactide particles	Were the data generated from the device in question ?	D1	Actual device
		D2	**Equivalent device**
		D3	Other device
	Was the device used for the same intended use (e.g.,methods of deployment, application. etc.)?	**A1**	**Same use**
		A2	Minor deviation
		A3	Major deviation
	Where the data generated from a patient group that is Representative of the intended treatment population ? (e.g.,age,sex,etc.) and clinical condition (i.e.,disease, including state and severity)	**P1**	**Applicable**
		P2	Limited
		P3	Different population
Author	Do the reports or collations of data contain sufficient information to be able to undertake a rational and objective assessment?	**R1**	**High quality**
J.E. Bergsma*, F.R. Rozema*, R.R.M. Bos*, G. Boer@*,		R2	Minor deficiencies
		R3	Major deficiencies
	Was the design of the study appropriate?	**T1**	**Yes**

Issued date		T2	No
Biomaterials (1995) 16 (4), 267-274	Do the outcome measures reported reflect the intended performance of the device?	**O1**	**Yes**
		O2	No
	Is the duration of follow-up long enough to assess whether duration of treatment effects and identify complications?	F1	Yes
Application/Non-application		**F2**	**No**
Application	Has a statistical analysis of the data been provided and is it appropriate?	**S1**	**Yes**
		S2	No
Literature search report No.	Was the magnitude of the treatment effect observed clinically significant?	**C1**	**Yes**
YRM –PLLA-LSR-8		C2	No

(2) Literature summary report (YRM –PLLA-LSR-8)

Item	Contents
Source	US National Library of Medicine National Institutes of Health (http://www.ncbi.nlm.nih.gov)
Title	In tivo degradation and biocompaGbility study of in vitro pre-degraded as-polymerized polylactide particles
Summary	**Abstract** The degradation of high molecular weight as-polymerized poly(L-lactide) (PLLA) is very slow; it takes more than 5.6 yr for total resorption. Moreover, the degradation products of as-polymerized PLLA bone plates, consisting of numerous stable particles of high crystallinity, are related with a subcutaneous swelling in patients 3yr postoperatively. In order to avoid these complications, polymers were developed that are anticipated to have comparable mechanical properties but a higher degradation rate and do not degrade into highly stable particles that can induce a subcutaneous swelling. On chemical grounds it can be expected that copolymerization of PLLA with 4% o-lactide (PLA96) or by modifying PLLA through cross-linking (CL-PLLA) will lead to less stable particles and a higher degradation rate. To evaluate the long-term suitability of these as-polymerized polymers, the biocompatibility of the degradation products should be studied. Considering the very slow degradation rate of as-polymerized PLLA, *in vitro* pre-degradation at elevated temperatures was used to shorten the in viva follow-up periods. In this study, the biocompatibility and degradation of as-polymerized PLLA, PLA96 and CL-PLLA were investigated by implanting pre-degraded particulate materials subcutaneously in rats. Animals were killed after a postoperative period varying from 3 to 80wk. Light and electron microscopical analysis and quantitative measurements were performed. The histological response of all three pre-degraded materials showed a good similarity with *in viva* implanted material. Pre-degraded PLLA induced a mild foreign body reaction and showed a slow degradation rate. PLA96 and CL-PLLA had a substantially lower crystallinity, a smaller mean particle size and an enhanced degradation rate compared to PLLA. Based on the chemical and quantitative analysis, the degradation of PLA96 and CL-PLLA was much more enhanced and thus more favourable than the degradation of PLLA.

(3) Evaluation for literature

① **Clinical aspect**

This literature states that the biocompatibility and degradation of as-polymerized PLLA,

PLA96 and CL-PLLA were investigated by implanting pre-degraded particulate materials subcutaneously in rats. Animals were killed after a postoperative period varying from 3 to 80wk. Light and electron microscopical analysis and quantitative measurements were performed. The histological response of all three pre-degraded materials showed a good similarity with in viva implanted material.

② **Biological aspect**

The literature states that Pre-degraded PLLA induced a mild foreign body reaction and showed a slow degradation rate. PLA96 and CL-PLLA had a substantially lower crystallinity, a smaller mean particle size and an enhanced degradation rate compared to PLLA. Based on the chemical and quantitative analysis, the degradation of PLA96 and CL-PLLA was much more enhanced and thus more favourable than the degradation of PLLA.

③ **Technical aspect**

The literature states that after 50wk, the mean particle size and polymer fraction of CL-PLLA has decreased. Both intracellular (in macrophages) and extracellular CL-PLLA particles were observed (P). Toluidine blue, original magnification x150.

- Transmission electron microscopic photograph of fields of needle-like CL-PLLA particles (P), which are mostly located in membrane-bound vacuoles that can be described as phagosomes (arrows). Bar = 1 pm.

④ Side-effect aspect

In order to avoid these complications, polymers were developed that are anticipated to have comparable mechanical properties but a higher degradation rate and do not degrade into highly stable particles that can induce a subcutaneous swelling.

- they might induce a detectable foreign body reaction, as seen with PLLA plates used in patients. However, the moment of clinical manifestation, the intensity and duration of such a possible foreign body reaction are factors that are directly dependent on the chemical structure of the implant, since the rate of degradation and the intensity of the histological reaction vary among the three implants.
- Moreover, the degradation products of as-polymerized PLLA bone plates, consisting of numerous stable particles of high crystallinity, are related with a subcutaneous swelling in patients 3yr postoperatively. In order to avoid these complications, polymers were developed that are anticipated to have comparable mechanical properties but a higher degradation rate and do not degrade into highly stable particles that can induce a subcutaneous swelling

⑤ Intended use of item aspect

Considering the very slow degradation rate of as-polymerized PLLA, in vitro pre-degradation at elevated temperatures was used to shorten the in viva follow-up periods. In this study, the biocompatibility and degradation of as-polymerized PLLA, PLA96 and CL-PLLA were investigated by implanting pre-degraded particulate materials subcutaneously in rats. Animals were killed after a postoperative period varying from 3 to 80wk. Light and electron microscopical analysis and quantitative measurements were performed. The histological response of all three pre-degraded materials showed a good similarity with in viva implanted

material. Pre-degraded PLLA induced a mild foreign body reaction and showed a slow degradation rate.

15. CONCLUSTION

Clinical evidence is demonstrated by way of

- Comparison chart of predicate device
- Market experience
- Experience from previous use
- Testing reports, analysis
- New material is not applied
- Evaluation risk management
- Evaluation for literature searching

From the above clinical evidence, we can conclude that

1) The 'Sterile PLLA(Poly-L-Lactic Acid) Suture with Needle' is substantially equivalent to the marketed predicate device, and do not raise any new issues of safety or effectiveness

2) Our device is similar to product of the investigated thesis and our device is not new development medical device and using it on the field is safe.

3) All details regarding the essential requirements mentioned corresponds clinical evidence has been verified in performance and safety as it originally intended. Therefore, it is confirmed that there is no problem using this device.

Reviewer

Reviewer:

Medical Doctor of clinical evaluation Kang Kyoung Jin

- MD & PhD
- Ex-Professor of Catholic University of Daegu, Medical School, South Korea
- Founder & 1st president of Korean College of Cosmetic Surgery