Perfectha®

Summary of Safety and Clinical Performance (SSCP – Switzerland only)

P.MDD.SSCP.02

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HEALTHCARE PROFESSIONAL SECTION

This Summary of Safety and Clinical Performance (SSCP) is intended to provide public access to an updated summary of the main aspects of the safety and clinical performance of Perfectha.

The SSCP is not intended to replace the Instructions for Use (IFU) which is considered to be the main document to ensure safe use of Perfectha, nor is it intended to provide diagnostic or therapeutic suggestions to intended users or patients.

The following information is intended for users/healthcare professionals. Following this information there is a summary intended for patients.

1 IDENTIFICATION DEVICE AND MANUFACTURER

1.1 Trade Name

Perfectha®

1.2 Legal Manufacturer

Sinclair France S.A.S, located at:

8 Chemin du Jubin
69570 Dardilly
France

1.3 Basic UDI-DI

Perfectha Deep: 506003304362718096140 40ND
Perfectha Derm: 506003304453627180961 40PS
Perfectha Finelines: 506003304180961406021 30J9
Perfectha Subskin: 506003304271809614091 91MV

1.4 Medical device nomenclature

GMDN 59131, Dermal tissue reconstructive material, microbe-derived

1.5 Classification

Medical Device Directive (MDD) 93/42/EEC (as amended) Annex IX, Medical Device Class III, Rule 8. Perfectha is therefore a Medical Device Class III.

1.6 CE Marking

Under Annex IX of Medical Device Directive (MDD) 93/42/EEC Perfectha Finelines, Perfectha Derm and Perfectha Deep have been CE marked since 2007, by Obvieline, now known as Sinclair France. Perfectha Subskin was CE marked in 2010. Sinclair France has been a subsidiary of Sinclair Pharma Ltd since January 2014.

1.7 Swiss Authorised Representative

Sinclair Pharma GmbH, Heidelberg (Deutschland) located at:
Zweigniederlassung Gossau SG
Industriestrasse 149, 9200 Gossau SG

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1.8 Notified Body

Szutest Uygunluk Degerlendirme A.S.
Tatlisu Mah.
Akif Inan Sk. No: 1
Ümraniye 34774 -Istanbul, Turkey

Notified Body Number: 2195

2 INTENDED USE OF THE DEVICE

2.1 Intended Purpose

Perfectha is a resorbable hyaluronic acid (HA) gel implants intended for reconstructive purposes in the treatment, for instance, of facial lipoatrophy, or morphological asymmetry associated with the aging process or other underlying conditions. Perfectha is for intradermal and subcutaneous application and is implanted in the areas of the face and hands to fill skin depressions and also for the augmentation of tissue volume.

It is supplied in a sterile, single-use syringe with cross-linked hyaluronic acid gel.

2.2 Indication

As per section 2.1, Intended Purpose.

2.2.1 Target Population

Perfectha is intended to be used in adult patients (over 18) whom are not pregnant or breast-feeding and are deemed appropriate for treatment by the healthcare professional.

2.3 Contraindications

Refer to the IFU (available on request).

3 DEVICE DESCRIPTION

3.1 Device Description

Perfectha is an implantable, resorbable, sterile cross-linked hyaluronic acid (HA) gel of non-animal origin. Each device in the Perfectha family is designed for different application areas and/ or depths, consequently the devices are provided with the needle best suited for use with each device in its intended application area.

The application areas are detailed in Table 1.

Table 1 Product Range Description

Product	Application areas
Perfectha FineLines	For intradermal injection. Filling of superficial lines and depressions, i.e., periorbital and peribuccal fine lines. For use in the tear troughs by injection into the supraperiosteal plane
Perfectha Derm	For superficial subcutaneous injection. Filling of medium lines and depressions, i.e., nasolabial folds and marionette lines, for lip enhancement and scars.
Perfectha Deep	For subcutaneous injection. Filling of deep lines and depressions, i.e., nasolabial folds and marionette lines. For moderate contouring and volumisation in areas of cheekbones, chin, jawline, temples, nose, sub-orbicularis oculi fat (SOOF) and lip augmentation.
Perfectha Subskin	For deep subcutaneous to supraperiosteal injection. For significant loss of volume in areas such as the cheekbones, chin, jawline, temples, forehead, bridge of the nose and hands.

3.2 Product History

Refer to section 1.6.

3.3 Accessories

Perfectha Finelines and Perfectha Derm are supplied with 30G needles, Perfectha Deep is supplied with 27G needles and Perfectha Subskin is supplied with 25G needles, which are purchased as CE marked devices.

3.4 Combinations

Perfectha is not required to be used in combination with any other device to meet its intended purpose. It is considered a stand-alone device.

4 RISKS and WARNINGS

4.1 Residual Risks and Undesirable Effects

The warning instructions have been applied following a comprehensive risk assessment which has been carried out in accordance with the latest and relevant international standard, ISO 14971 and no residual risks remain.

Perfectha devices have been deemed suitable for use in adults based on the safety profile of the products and their equivalents and the small numbers of adverse events (AE) associated with use. Any undesirable side-effect constitutes an acceptable risk when weighed against the performances intended.

4.1.1 Side Effects/ Adverse Events

Refer to the IFU (available on request).

4.2 Warnings and Precautions

4.2.1 Warnings

Refer to the IFU (available on request).

4.2.2 Precautions for Use

Refer to the IFU (available on request).

4.3 Field Safety Corrective Action (FSCA), Field Safety Notice (FSN)

Perfectha has not been the subject of any FSCA’s or FSN’s at this time.

5 SUMMARY OF CLINICAL EVALUATION

5.1 Summary of Clinical Data from Equivalent Devices

The data presented within the Clinical Evaluation Report (CER) is based on an analysis of available clinical literature and post market clinical data relevant to the intended use and the clinical experience of Perfectha and/ or products with equivalent design characteristics.

Equivalent devices are identified from literature and detailed within the report, and are based on their clinical equivalence, critical attributes, technical and biological equivalence. Clinical studies on the identified devices demonstrated clinical efficacy, and safety and performance of the devices are confirmed.

5.2 Summary of Clinical Data of the Device

Studies assessing the safety and performance of Perfectha provide pivotal data supporting the device range. Summary information from all studies on Perfectha is shown in Table 2.

Table 2 Perfectha clinical studies

Study (n)	Products	Duration of Effect
Kalil et al. (2011) (n=20)	Derm	Upper lip margin Nasolabial folds (12 months)
Laboratoire ObvieLine, (2006) (n=40)	Derm and Deep	Sulcus of labial commissure Lips Nasolabial folds (180 days)
Laboratoire ObvieLine, (2006a) (n=204)	Deep	Marked nasolabial folds (6 months)
Laboratoire ObvieLine, 2007 (n=54)	Derm and Deep	Nasolabial folds Sulcus of labial commissure Labial contour (Minimum 3 months)
Resende et al. (2008) (n=1,366)	Derm and Restylane	Nasolabial folds, lips, ear lobes, cheeks, other (8-12 months)
De Arruda et al. (2008) (n=33)	Derm and Deep	Nasolabial folds Lips (Minimum 3 months)
Regazzini and Fares (2008) (n=126)	Subskin	Chin Cheeks (18 months)
Ami (2009) (n=36)	Subskin	Malar Chin correction (18 months)
Pinzon et al. (2010) (n=30)	SubSkin	Moderate, severe, and extreme nasolabial folds (9 months)
Talarico et al. (2010) (n=87)	Derm	Nasolabial folds and lip correction (6 months)

MDD requires an evaluation of safety and efficacy of the devices to be certified. The CER is performed based on MDD Annex X MEDDEV-Guideline 2.7/1. “Evaluation of Clinical Data”.

Studies on the Perfectha and any equivalent devices have demonstrated effectiveness in a variety of facial conditions or hand rejuvenation with reported effectiveness ranging from 6 months to 3 years with (yearly touch-ups) at 3 years follow-up (Skeie et al. 2010).
Perfectha has an acceptable benefit/risk profile according to current knowledge/ state of the art in the medical fields concerned and according to available medical alternatives.

5.3 Post Market Clinical Follow Up (PMCF)

The adverse event rate for Perfectha is considered to be low and acceptable. The safety profile of Perfectha is well established. Further post market studies are planned.

5. THERAPEUTIC ALTERNATIVES

5.1 Age related volume loss

Dermal filler is a minimally invasive technique that offers a non-permanent alternative to more permanent fillers, laser treatments, or more involved surgical procedures. Dermal fillers, and injectable medical devices are commonly used for facial rejuvenation. Most dermal fillers are passive space filling agents and can be used in facial augmentation, whether used solely or combined (Sherman, 2009).

Since the introduction of the first dermal fillers to the USA in 1981, the practice of minimally invasive facial rejuvenation has grown exponentially. In 2010, US physicians performed more than 1 million injectable HA treatments alone (Breithaupt et al. 2012).

A systematic review on the safety and effectiveness of soft tissue fillers was conducted. The evidence indicated that soft-tissue fillers were effective and well tolerated for correcting nasolabial folds, other moderate to severe wrinkles and folds, and volume loss in cheeks (Hanke et al., 2011).

5.2 HIV Facial lipoatrophy

HIV-associated lipoatrophy affects 40-80% of patients treated with first-generation antiretroviral drugs and still affects a considerable number of HIV-infected patients. The most stigmatizing aspects of HIV-associated lipoatrophy are the cosmetically disfiguring changes affecting facial appearance and leading decreased quality of life, diminished self-esteem, and progressive social withdrawal; occasionally, these changes contribute to a reduction in patients' adherence to antiretroviral therapy, therefore seriously endangering their health. Treatment strategies for HIV-associated facial lipoatrophy include soft tissue augmentation procedures performed using autologous fat grafting or injectable dermal fillers (Becker, 2015).

Social isolation and low self-acceptance may cause depression. Decreased quality of life associated with lipodystrophy may lead to rejection of therapy by patients. HIV-associated lipodystrophy constitutes a threat to human health and life. Applying an optimal method of treatment reduces the stigma associated with facial lipodystrophy and significantly improves patients' quality of life (Szczerkowska-Dobosz et al. 2015).

A systematic review assessed the safety and effectiveness of all filler agents for aesthetic treatment of HIV facial lipoatrophy and provided evidence-based recommendations. HA had intermediate elasticity and viscosity and was able to provide high volumisation properties. Both calcium hydroxylapatite and HA only required one treatment and provided immediate visible improvement, which helped minimise health care and patient cost. HA dermal fillers were an effective and safe treatment and had the advantages of achieving immediate results. These results suggest that HA fillers are safe and effective and similar results would be expected for Perfectha (Jagdeo et al., 2015).

5.3 Atrophic Scars

The treatment of atrophic scars is difficult and dermal filler materials provide a simple alternative with immediate results (Hasson, 2010). Scar formation is an inevitable result of surgery and trauma that results in full thickness epidermal loss (Shilpa et al. 2016).

Acne scars are present in 95% of patients with acne and can cause profound psychosocial morbidity. Dermal fillers are commonly used for facial soft tissue augmentation, and there is increasing interest in their use for the treatment of acne scars, particularly for the atrophic subtype. The evidence for the use of temporary, semi-permanent and permanent fillers for acne scars have been investigated following four studies associated with the use of HA fillers in acne scarring. All studies demonstrated improvement in acne scar appearance with minimal or transient side effects (Forbat, 2017).

Kravvas and Al-Niaimi (2017) assessed the efficacy and adverse reactions of commonly used treatments against post-acne scarring, by assessing the effects of dermal fillers in five studies. All studies supported the safety and efficacy of the dermal fillers like Perfectha and indicates they would be a safe and effective option for the treatment of acne scars.

5.4 Conditions resulting in upper eyelid margin asymmetry

HA dermal fillers can be placed centrally in the subconjunctival levator-muller plane. Alternatively, the injection could be given through the skin. However, it may be more difficult to find the levator plane, because the needle cannot be visualised, and the proper plane is very thin. Care should be taken with levator injections because the globe is in close proximity in this region (Mancini et al. 2011).

6 SUGGESTED PROFILE AND TRAINING FOR USERS

Perfectha should only be used by trained healthcare trained professionals.

The IFU states that ‘This product may be administered only by a registered healthcare professional in accordance with local regulations’ and ‘This device is designed to be injected into the dermis by a healthcare professional who has been specifically trained in injection techniques for dermal filler procedures. The healthcare professional's technical competence is crucial to the success of the treatment.’

Additional training materials are available on request from Sinclair Pharmaceuticals Ltd.

7 APPLIED STANDARDS

Table 3 details the applied standards applied to the device.

Table 3 Applied Standards

Directive / Standard / Guideline Number	Name / Title
Directives/ Regulation	
Directive 93/42/EEC	European Council Directive concerning medical devices
EU Regulation No 207/2012	Commission Regulation on electronic instructions for use of medical devices
Harmonised Standards	
EN 556-1:2001/AC:2006	Sterilization of medical devices – Requirements for medical devices to be designated “STERILE”. Requirements for terminally sterilized medical devices
EN ISO 13485:2016 A11:2021	Medical Devices- Quality Management Systems – Requirements for Regulatory Purposes
EN ISO 10993-3:2014	Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity
EN ISO 10993-5:2009	Biological Evaluation of Medical Devices-Part 5: Tests for In-vitro cytotoxicity
EN ISO 10993-9:2009	Biological evaluation of medical devices – Part 9: Framework for identification and quantification of potential degradation products
EN ISO 10993-11:2018	Biological evaluation of medical devices – Part 11: Tests for systemic toxicity
EN ISO 10993-12:2012	Biological evaluation of medical devices -- Part 12: Sample preparation and reference materials
EN ISO 10993-13:2010	Biological evaluation of medical devices -- Part 13: Identification and quantification of degradation products from polymeric medical devices
EN ISO 10993-17:2009	Biological evaluation of medical devices -- Part 17: Methods for the establishment of allowable limits for leachable substances using health-based risk assessment
EN ISO 10993-18:2020	Biological Evaluation of medical devices –Part 18: Chemical characterisation of materials
EN ISO 11137-1:2015+A2:2019	Sterilization of health care products – Radiation – Requirements for development, validation and routine control of a sterilization process for medical devices
EN ISO 11137-2:2015	Sterilization of health care products – Radiation - Establishing the sterilization dose
EN ISO 17665-1:2006	Sterilization of health care products. Moist heat. Requirements for the development, validation and routine control of a sterilization process for medical devices
ISO 80369-7:2021	Small-bore connectors for liquids and gases in healthcare applications
Non Harmonised Standards	
Directive / Standard / Guideline Number	**Name / Title**
ISO 10993-1:2018*	Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process
EN ISO 10993-6:2016*	Biological evaluation of medical devices – Part 6: Tests for local effects after implantation.
EN ISO 10993-10:2013	Biological Evaluation of Medical Devices-Part 10: Tests for irritation and skin sensitisation
EN ISO 10993-16:2017*	Biological evaluation of medical devices -- Part 16: Toxicokinetic study design for degradation products and leachables
EN ISO 11135:2014+A1:2019*/ **	Sterilization of health-care products. Ethylene oxide. Requirements for the development, validation and routine control of a sterilization process for medical devices
EN ISO 11138-1:2017	Sterilization of health care products. Biological indicators. General requirements

EN ISO 11138-3:2017*	Sterilization of health care products. Biological indicators for moist heat sterilization processes
EN ISO 11138-7:2019	Sterilization of health care products. Biological indicators. Guidance for the selection, use and interpretation of results.
ISO 11040-4:2015 +A1:2020	Prefilled syringes — Part 4: Glass barrels for injectables and sterilized subassembled syringes ready for filling
EN ISO 11607-1:2020*	Packaging for terminally sterilized medical devices - Part 1: Requirements for materials and final packages
EN ISO 11607-2:2020*	Packaging for terminally sterilized medical devices - Part 2: Requirements for forming and sealing and assembly processes.
EN ISO 11737-1:2018*	Sterilization of medical devices. Microbiological methods. Determination of a population of microorganisms on products
EN ISO 14155:2020*	Clinical investigation of medical devices for human subjects. Good clinical practice
EN ISO 14630:2012*	Non active surgical implants – General requirements
EN ISO 14644-1:2015	Cleanrooms and associated controlled environments - Part 1: Classification of Air Cleanliness
EN ISO 14971:2019*	Medical Devices- Application of Risk Management to Medical Devices
ISO 15223-1:2021*	Medical devices - Symbols to be used with medical device labels, labelling and information to be supplied - General requirements
ISO 15378:2017	Primary packaging materials for medicinal products - Particular requirements for the application of ISO 9001:2015, with reference to Good Manufacturing Practice (GMP)
ISO/TS 17665-2:2009	Sterilization of health care products. Moist heat. Guidance on the application of ISO 17665-1
EN ISO 17141:2020	Cleanrooms and associated controlled environments. Biocontamination control.
EN ISO 20471:2021*	Information supplied by Manufacturers of Medical Devices
EN 62366-1:2015+A1:2020*	Medical devices. Application of usability engineering to medical devices
PD IEC/TR 62366-2: 2016	Medical devices. Guidance on the application of usability engineering to medical devices
EN ISO 7864:2016	Sterile hypodermic needles for single use. Requirements and test methods
ISO 639-1:2002	Codes for the representation of the names of languages. Alpha 2 code
Guidelines	
MEDDEV 2.1/1 April 1994	Definitions of “medical devices”, “accessory”, “manufacturer”

Directive / Standard / Guideline Number	Name / Title
Guidelines	
MEDDEV 2.4/1 Rev 9 June 2010	Classification of medical devices
MEDDEV 2.7/1 Rev.4 June 2016	Clinical Evaluation: A Guide for Manufacturers and Notified Bodies
MEDDEV 2.12/2 Rev.2 Jan 2012	Post Market Clinical Follow Up Studies: A Guide for Manufacturers and Notified Bodies
MEDDEV 2.12/1 Rev.8 Jan 2013	Guidelines on a Medical Devices Vigilance System
Additional guidance on MEDDEV 2.12/1 Rev.8 July 2019	Guidelines on a Medical Devices Vigilance System
ICH guidelines Q1A	Stability Testing of New Drug Substances and Products
GHTF SG5/N2R8 (2007)	Clinical Evaluation
MDCG 2019-5 April 2019	Registration of Legacy Devices in EUDAMED
European Pharmacopoeia (10th Edition)	
Ph.Eur 2.9.20	Particulate contamination visible particles
Ph.Eur 2.2.3	Potentiometric determination of pH
Ph.Eur 2.2.10	Viscosity - rotating viscometer method
Ph.Eur 2.6.14	Bacterial Endotoxins LAL Assay, Method D: Chromogenic Kinetic Method
Ph.Eur 2.6.1	Sterility
Ph.Eur 1472	Sodium hyaluronate - NaHA
Ph.Eur. 0193	Sodium chloride – NaCl
Ph.Eur. 0194	Sodium dihydrogen phosphate dihydrate NaH2PO4.2H2O
Ph.Eur. 0602	Disodium phosphate dihydrate Na2HPO4.2H2O
Ph.Eur. 0169	Water for injections
Ph.Eur 0008	Water, purified
Ph.Eur. 3.1.8	Silicon oil used as lubricant
Ph.Eur. 3.2.1	Glass containers for pharmaceutical use
Ph.Eur. 3.2.9	Rubber closures for containers for aqueous parenteral preparations, for powders and for freeze-dried powders
Ph.Eur 5.1.10	Guidelines for using the tests for bacterial endotoxins

8 CONCLUSION

Perfectha has an acceptable benefit/risk profile according to current knowledge/the state of the art in the medical fields concerned and according to available medical alternatives. Studies on the predecessor product range Perfectha and equivalent devices have demonstrated safety and effectiveness.

The information supplied with the device is reflective of the safe and effective use in its intended applications, the intended purpose and risk reduction measures are acceptable.

9 REFERENCES

Ami LP. (2009)' Effectiveness and safety of Perfectha Derm SubSkin in malar and chin esthetic contours'. *Unpublished*.

Becker, M.; Balague, N. (2015) 'Hyaluronic Acid Filler in HIV-Associated Facial Lipoatrophy: Evaluation of Tissue Distribution and Morpholy with MRI'. In: Dermatology, 230(4), pp: 367:74. DOI: 10.1159/000379747.

Breithaupt AD, Custis T, Beddingfield F. (2012) 'Next-Generation Dermal Fillers and Volumizers. Cosmet Dermatol' vol. 25, pp. 184-191.

De Arruda LHF, Rocha FT, Rocha A (2008) 'Studying the satisfaction of patients on the outcome of an aesthetic dermatological filler treatment'. *Journal of Cosmetic Dermatology* 7(4), pp: 246–250

Forbat, E.; Ali, F.R. (2017) 'The role of fillers in the management of acne scars'. *In: Clin Exp Dermatol.* DOI:10.1111/ced.13058.

Hasson, A; Romero, WA. (2010) 'Treatment of facial atrophic scars with Esthelis, a hyaluronic acid filler with polydense cohesive matrix CPM'. *In: Journal of Drugs in Dermatology, 9, 10.*

Hanke CW, Rohrich RJ, Busso M et al. (2011) 'Facial Soft-Tissue Fillers: Assessing the State of the Science conference-Proceedings report'. 64(4 SupPerfectha Lidocaine): S66-85.

Jagdeo J, Ho D, Lo A, Carruthers A (2015) 'A systematic review of filler agents for aesthetic treatment of HIV facial lipoatrophy (FLA)'. *J Am Acad Dermatol*. 73(6), p: 1040-54.

Kalil CLPV, Caramori APA, Balkey MD (2011) 'Evaluation of the duration of injectable hyaluronic acid in nasolabial folds and perioral rhytids'. *Surg Cosmet Dermatol* 3(2), pp:112-5.

Kravvas G, Al-Niaimi F (2017) 'A systematic review of treatments for acne scarring. Part 1: Non-energy-based techniques. Scars, Burns and Healing'. 3:2059513117695312.

Laboratoire Obvieline. (2006) 'Observational study of facial outcomes with Perfectha Derm and Perfectha Deep for the treatment of nasolabial folds, lips, sulcus of the labial commissure'. (See DC.PFD.3, Study 1).

Laboratoire Obvieline. (2006a) 'Evaluation of timeframes, ease of use and the incidence of adverse effects'. Study period between 2004 and 2006. (See DC.PFD.3, Study 2).

Laboratoire ObvieLine (2007) 'Evaluation of the efficacy, safety and duration of treatment of Perfectha Derm and Perfecth Deep'. Study period between 2006 and 2007. (See DC.PFD.3, Study 3).

Mancini R, Khadavi NM, Goldberg RA. (2011) 'Nonsurgical management of upper eyelid margin asymmetry using hyaluronic acid gel filler'. *Ophthalmic Plastic and Reconstructive Surgery* 27(1), pp: 1-3

Pinzon A, Fares J, Rivera L. (2010) 'Safety and Effectiveness of non-animal stabilized hyaluronic acid filler (Perfectha Derm Subskin) for nasolabial folds correction'. *Study period from March 2010 to December 2010*

Regazzini DV, Fares J. (2008) 'A prospective study of evaluation of the results achieved with the application of a new gel of hyaluronic acid non animal origin (Perfectha Derm sub skin) for malar and mental enhancement'. *Unpublished. Study period from October 2006 to April 2008.*

Resende VCL, Haddad A, Regazzini DV et al. (2008) 'Late evaluation of 1366 cases of dermal filler with hyaluronic acid implant in the face'. *Rev. Bras. Cir. Plas. 23* (suppl.): 34.

Shilpa, K, Sacchidanand, S, Leelavathy, B, Shilpashree, P, Divya, G, Ranjitha, R, Lakshmi, D (2016) 'Outcome of Dermal Grafting in the Management of Atrophic Facial Scars'. *Journal of Cutaneous and Aesthetic Surgery*, 9(4), p: 244–248.

Skeie L, Bugge H, Negaard A, Bergersen BM. (2010) 'Large particle hyaluronic acid for the treatment of facial lipoatrophy in HIV-positive patients: 3-year follow-up study'. *HIV Med.* 11(3), pp: 170-7.

Szczerkowska -Dobosz, A., Olszewska, B., Lemańska, M., Purzycka-Bohdan, D., & Nowicki, R. (2015). 'Acquired facial lipoatrophy: pathogenesis and therapeutic options. Advances in Dermatology and Allergology/Postępy Dermatologii I Alergologii', 32(2), pp: 127–133.

Talarico S, Hassun KM, de Oliveira Monteiro E et al. (2010) 'Safety and efficacy evaluation of a new hyaluronic acid based filler in the treatment of nasolabial folds and lips outline'. *Surg Cosmet Dermatol.* 2 (2), pp:83-6 (See DC.PFD.3, Intradermal Study 6).