1. ESCRIPTION AND RESPONSIBILITIES

This form is used to draw up the Summary of Safety and Clinical performance according to the Regulation (EU) 2017/745, Article 32.

This one is under the responsibility of Laboratoires Fill-Med.

The maintenance of this document is under the responsibility of the Scientific Affairs department.

2. SCOPE

Scope	☒Devices without medical purpose
	☐Cosmetics

The records are kept and archived in the technical documentation of the Regulatory Affairs department.

The form is archived in the VEEVA Vault QualityOne electronic document management database.

This form is a global form and applies to all Laboratoires FILL-MED's sites.

3. RELATED DOCUMENTS

- PG.29 –Obtaining and maintaining CE mark
- PG.22 –Post-Market Clinical Follow-up

4. HISTORY OF CHANGES

Changes are highlighted in grey.

Revision	Revision date	Change description
1	11/04/2023	Creation of the form
2	18/09/2024	Unification of the both Quality Management System (Laboratoires FILL-MED & Laboratoires FILL-MED Manufacturing S.A.) Ref: Change control CR23036 Update of the form to integrate a description of the form and a summary section dedicated to the patients/lay users
3	15/11/2024	Update of the form (Following Eurofins Nonconformity) to correct the SSCP reference number in order to remain the same throughout the lifetime of the SSCP

4	05/12/2024	Update of the form to correct the content of the scope section with the following : “Medical device” is replaced by : “device without medical purpose”

Summary of safety and clinical performance

Device name(s)

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 the device. The SSCP is not intended to replace the Instructions For Use as the main document to ensure the safe use of the device, 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.

SSCP Reference number: SSCP-NCTF-NCL

Rev	Revision date	Description of change
01	03/07/2023	Creation of the document
02	15/07/2024	Update the document: - Add a summary of the safety and clinical performance of the device, intended for patients
03	22/11/2024	Update of the document to: - Correct the SSCP reference number - Add the details of harmonized standards in section 8
04	06/12/2024	Update of the document: - Correction the content of the scope: Medical device" is replaced by: "device without medical purpose"

Written by / Date/ Signature/	Reviewed by / Date/ Signature/	Approved by/ Date/ Signature/
Marie José Moschetti, Pharm.D 06/12/2024	Frédéric GUER, Regulatory Affairs &Vigilance 06/12/2024	Ferial Fanian, MD, PhD Scientific director 06/12/2024

1. Device identification and general information

1.1 Device trade name(s)

The device trade name is **NCTF 135 HA**

TRADE NAME	CATALOGUE NUMBER	BOX COMPOSITION
NCTF 135 HA	1V401405	Box of 5 vials including 5: - 18G1½" withdrawal needle - 30G½" injection needle - 32G injection needle - 3ml Luer-Lock syringe
	1V401510	Box of 10 vials

1.2 Manufacturer's name and address

LABORATOIRES FILL-MED
38 cours Albert 1er 75008 PARIS
France

1.3 Manufacturer's single registration number (SRN)

1.4 Basic UDI-DI

GMN (Basic UDI-DI): 3664948NCTF135HADN

1.5 Medical device nomenclature

EMDN code: P900402 (Biodegradable devices, filler and reconstructive)

1.6 Class of device

Considering the Annex XVI of the European Regulation (EU) 2017/745, the product does not claim therapeutic action as it is part of list of groups of products without an intended medical purpose referred to in Article 1 (2) : "Substances, combinations of substances, or items intended to be used for facial or other dermal or mucous membrane filling by subcutaneous, submucous or intradermal injection or other introduction, excluding those for tattooing".
NCTF 135 HA is a Class III device. Considering Annex VIII of the European Regulation (EU) 2017/745 and the guidelines MDCG 2021-24, Rule 8 is applicable.(" All implantable devices and long-term surgically invasive devices are classified as class IIb unless they: … have a biological effect or are wholly or mainly absorbed, in which case they are classified as class III;")

1.7 Year when the first certificate (CE) was issued covering the device

Not applicable under Medical Device Regulation (EU) 2017/745*.
*NCTF 135 HA was first CE marked according to Directive 93/42EEC in 2007

1.8 Authorised representative if applicable, name and the SRN

Non applicable as Laboratoires FILL-MED are established in France.

1.9 NB's name (the NB that will validate the SSCP) and the NB's single identification number

Eurofins Product Testing Italy (0477)

2. Intended use of the device

2.1 Intended purpose

NCTF 135 HA are products without an intended medical purpose, they are used for aesthetic purposes. **NCTF 135 HA** are anti-ageing injectable products intended for filling of superficial wrinkles for intense revitalization and hydration of tired or dull skin, and to improve skin homogeneity and radiance. It also helps skin redensification, thickness and elasticity of mature or slack skin.

2.2 Indication(s) and target population(s)

NCTF 135 HA is indicated to be injected in the dermis of the following areas:

- Face (including periorbital area)
- Neck
- Décolleté area

NCTF 135 HA is used for aesthetic purposes, as such intended patient groups do not present any specific pathology. Aesthetic procedures are requested by patient to improve their appearance in order to look younger and increase self-esteem. According to Regulation, patients have to be older than 18 years.

2.3 Contraindications and/or limitations

NCTF 135 HA should not be injected into blood vessels and should not be used in:

- Patients with a skin alteration or disease of any kind in the treated area
- Patients with a history of autoimmune disease or under immunotherapy
- Patients with hypersensitivity or known allergy to any of the constituents
- Patients who are less than 18 years old
- Pregnant or breast-feeding women

3. Device description

3.1 Description of the device

NCTF 135 HA correspond to an injectable hyaluronic acid-based solution (5mg/ml), sterile and apyrogen presented in vials of 3 ml. 2 presentations are available, box with 5 kits (vials with needles and syringes) and box of 10 vials.

NCTF 135 HA is composed of :

- non-crosslinked Sodium Hyaluronate /Hyaluronic Acid [5 mg/ml]
- buffer solution (Final pH 6.50-7.80) for adjustment of pH
- polyrevitalising solution [9 mg/ml]

o 12 vitamins: Ascorbic acid (vit. C), Biotin (vit. B8), Pantothenic acid (vit. B5), Folic acid (vit. B9), Inositol (vit. B7), Nicotinamide/Nicotinic acid (vit. B3), Pyridoxine /Pyridoxal (vit. B6), Riboflavin (vit. B2), Thiamine (vit. B1), Tocopherol (vit. E), Retinol (vit. A), Vitamin B12
o 6 minerals: Calcium chloride, Potassium chloride, Magnesium sulfate, Sodium acetate, Sodium chloride, Sodium dihydrogenophosphate
o 5 nucleosides: Deoxyadenosine, Deoxycytidine, Deoxyguanosine, Deoxythymidine, 5-Methyl-2'-deoxycytidine
o 24 amino acids: α-Aminobutyric acid, Alanine, Arginine, Asparagine, Aspartic acid, Cystine, Glutamine, Glutamic acid, Glycine, Histidine, Hydroxyproline, Isoleucine, Leucine, Lysine, Methionine, Ornithine, Phenylalanine, Proline, Serine, Taurine, Threonine, Tryptophane, Tyrosine, Valine
o 6 coenzymes: TPP (Cocarboxylase), CoA (Coenzyme A), FAD (Flavine adenine dinucleotide), NAD (Nicotinamide adenine dinucleotide), NADP (Nicotinamide adenine dinucleotide phosphate), UTP (Uridine triphosphate)
o Other components: Glutathione, Polysorbate 80, Glucuronic acid, Glucuronic acid lactone, Glucosamine, Dextrose anhydrous

NCTF 135HA is intended to injected by a qualified practitioner using syringe and in conjunction with sterile single use withdrawal needles 18G and injection needles (30G and 32G) provided in the kit presentation. NCTF 135HA may also be used with similar syringes and needles according their manufacturer(s) intended use.

3.2 A reference to previous generation(s) or variants if such exist, and a description of the differences

Non applicable

3.3 Description of any accessories which are intended to be used in combination with the device

Non applicable. There is no accessory according to definition given in Article 2 of MDR:
'accessory for a medical device' means an article which, whilst not being itself a medical device, is intended by its manufacturer to be used together with one or several particular medical device(s) to specifically enable the medical device(s) to be used in accordance with its/their intended purpose(s) or to specifically and directly assist the medical functionality of the medical device(s) in terms of its/their intended purpose(s)

3.4 Description of any other devices and products which are intended to be used in combination with the device

NCTF 135 HA is intended to be used in conjunction with sterile and single-use syringes and standard injections devices (hypodermic needles, cannulas or other such as Nanosoft device) in accordance with their original destination (intra-dermal injections).
Those components, when they are supplied with NCTF 135 HA in a procedure pack, form following Article 22.4 of Regulation (EU) 2017/745.

4. Risks and warnings

4.1 Residual risks and undesirable effects

According to LABORATOIRES FILL-MED policy the residual risks have been identified and reduced as far as possible. These residual risks are all considered as acceptable under normal conditions of use, which

is consistent with a high level of protection for the safety and health of persons. This is in accordance with the state of science and medical knowledge.

Expected undesirable effects are:

- Redness or mild local inflammation that usually disappears within few hours to few days.
- Mild oedema and small hematomas may occur but disappear within few hours to few days.
- Minimal bleeding at the injection site that stops rapidly and spontaneously after the injection.
- Transient pain at the injection site.

As with all transcutaneous procedures, the injection of NCTF 135 HA carries a risk of infection. Standard precautions associated with injectable materials should be followed.

Based on clinical investigations and post marketing surveillance, reported undesirable effects are very rare, incidence is given for information:

Reported events	Incidence
Swelling, Erythema	0.002%
Nodule, Itching Sensation, Pain, Skin inflammation, Burning Sensation, rash	0.0005%
Hypersensitivity/Allergic reaction	0.0001%
Granuloma, Papula, Fever, Angioedema /Quincke Edema, Eczema, Fatigue, Skin Discoloration, Bruise, Local Reaction (Pruritus), Dyspnea, Local Reaction –Induration	<0.0001%

According to regulatory requirements changes (Annex XVI of MDR and Common Specifications), possible treatment of adverse events are taken into consideration and made available to users.

Adverse events	Possible treatments
Inflammatory reaction	
Erythema / Swelling /Redness Burning sensation/ Stinging/ Pain /Blister /Hematoma/ Bruise	Cold compress for 48 hours, anti-inflammatory topical creams, sun creams, antibiotics, and corticosteroids if necessary.
Rash/Local reaction /Pruritus	Same + antihistamines
Nodule/ Skin irregularities (Nodule, Papula)	Same + Hyaluronidase
Skin infection	Same + Antibiotics
Visual disturbance / Dry eye/ Red eye	Ophthalmologic intervention
Granuloma	Surgical intervention
Skin discoloration	Depigmenting agent
Allergic reaction	
Itching sensation/ Burning sensation/ Pruritus/ Urticaria	Antihistamines + Corticosteroids
Angioedema/ Quincke edema	Antihistamines + Corticosteroids + Hospitalisation if necessary
Infection	

Adverse events	Possible treatments
Abcess/ Blisters/ Skin infection - Crust	Antibiotics + Surgical intervention
Cold sores (Herpes)	Antiviral medication
Systemic Adverse events	
Malaise/ Nausea/ Chills/ Fatigue/ Dyspnea/ Fever/ Vomiting	Medical intervention by health professional
Miscellaneous	
Numbness	Medical intervention by health professional

4.2 Warnings and precautions

The following warnings are given:

- Check the expiry date on the label
- Check the integrity of the sterile barrier immediately prior to using the product.
- Do not reuse the vial & the components on other patients.
- Do not resterilize
- After use, the needles must be thrown away in a suitable safe container
- Re-use of the product involves risks (e.g. cross contamination) for the patient
- Do not use if the packaging is open or damaged
- Do not inject excessive volume, it can potentially lead to side effects.

The following precautions for use are also given

- Do not use the product if the product aspect (color, transparency...) changed
- There are no clinical data available in terms of tolerance with regard to the injection of NCTF® 135 HA in an area that has already been treated with another “permanent (non- resorbable)” filling product.
- Precaution should be taken in such cases, although NCTF® 135 HA is not injected at the same level.
- Patients receiving an anticoagulant treatment or a platelet aggregation inhibitor (for example, aspirin) must be informed of the increased risk of bruising and mild bleeding at the injection site.
- The patient should be given the recommendation not to use make-up for 12 hours following the injection and to avoid prolonged exposure to the sun, UV rays, freezing temperatures as well as use of saunas or steam rooms for at least 48 hours after the injection.
- Training in injection techniques is recommended for the use of NCTF® 135 HA. NCTF® 135 HA must not be injected at the same time as a medium or deep chemical peeling or dermabrasion.
- A local anaesthetic (patch or cream) can be applied prior to the injection. Please note that anaesthetic products can cause local redness or hypersensitivity.
- Do not inject NCTF® 135 HA into beauty spots (naevi) and in active acne lesions.

Before starting treatment, the patient must be informed of the indications of the device, its contraindications, its incompatibilities and its possible undesirable effects.

Hyaluronic acid is incompatible with quaternary ammonium compounds, such as benzalkonium chloride solutions. This is why NCTF® 135 HA must never come into contact with medical and surgical instruments treated with this type of product.

4.3 Other relevant aspects of safety, including a summary of any field safety corrective action (FSCA including FSN) if applicable

No other relevant aspects of safety are applicable.

5. Summary of clinical evaluation and post-market clinical follow-up (PMCF)

5.1 Summary of clinical data related to equivalent device, if applicable

Not applicable, all clinical data have been obtained with **NCTF 135 HA**.

5.2 Summary of clinical data from conducted investigations of the device before the CE-marking, if applicable

All clinical investigations have been conducted before CE marking according to Regulation (EU) 2017/745.

As **NCTF 135 HA** was put on the market in 2007, clinical performance and safety of NCTF 135 HA are based on Post-Marketing Clinical Follow-up (PMCF) studies considering initial CE mark according to Directive 93/42EEC. The studies are presented in chronological order.

1) An observational study (SK1946) was initiated after initial CE Mark to evaluate results obtained with NCTF 135 HA in routine conditions on 40 subjects; this open multricentric observational study was conducted in France between March and September 2008. NCTF 135 HA was found clinically efficient on the cutaneous ageing effects on the face, neck, bust-line and hands, and improvement is obtained for wrinkles and fine lines, as well as for hydration, firmness and radiance of the skin in an observational study on 40 female patients based on representative population freely selected by the practitioners (women over the age of 45 years, with no contraindications to use of NCTF 135 HA). A total of 34 patients (85%) of the population reported 94 Adverse Events. Most of them were erythema. Reported Adverse Events were from mild (69%), moderate (29%) to severe (2%). Most of them occurred after the first treatment (on D1 / N=63 (67%)) and only few of them were present all over the study (N=16 / 17%) (only 37% of Adverse Events were reported at D75).No Serious Adverse Event was reported and none of the reported A.E. justified to stop the treatment.

2) A clinical evaluation with instrumental measures of outcomes of anti-age efficacy of NCTF 135 HA (Study n° 95.10.13) conducted on 20 subjects showed a comprehensive facial rejuvenation appearing gradually. Objective criteria support improvement in skin homogeneity and brightness, smoothing of the skin with decrease in crow's feet wrinkles depth and reduction of pore size, and increase in skin density and dermis thickness. No safety assessment was done in this study.

3) A multicentric comparative randomized interventional clinical investigation (HEBE2 study) was conducted on 145 subjects divided in two groups (Randomization 3:1 for the face) with 3 months follow up. Clinical performance of NCTF 135 HA was confirmed by results reported in various standardized clinical scores and instrumental measures versus control group on decrease of wrinkles, improvement in skin radiance, skin density and skin elasticity, decrease of pore diameter. Finally, injections significantly improved the self-esteem level of the subjects based on Rosenberg Self-Esteem Scale (RSE) and difference of the satisfaction level based on GAIS scale was most particularly shown on the neck. The effect on wrinkles was detected as soon as 7 days after the third injection and the superiority of the effect persisted up to D120. Most of adverse events, whatever the concerned area reported were bruise (about 36%) or redness (23%). Intensity varied from light to severe, but most of them were of light intensity (56% / only 13 % were severe) and whose 48% last no more than 48 hours.

Most of adverse events were related to the injection procedure more than to the product.

One serious Adverse Event was reported but that was not linked to the study (a patient from the control group died due to car accident between D75 and D120).

No Adverse Event relating to the treatment that justify to stop the study was reported.

4) A prospective interventional non-comparative multicentric investigation (FEM1 study) was conducted on 99 patients (ITT) with 120 days follow-up. The objective was to demonstrate to demonstrate the efficacy and safety of a new protocol combining 2 or 3 medical devices: NCTF 135 HA with a hyaluronic acid-based dermal filler ART FILLER® Fine Lines, completed or not by ART FILLER® Universal depending on the score at baseline), through a special technique (Intradermal injection via a canula in fan technique) to improve the quality and appearance of the skin measured by Bazin Cheek folds, Scoring for the face on D30 compared to D0 before a single treatment. A significant improvement of this score was observed with regard to time and this improvement remained significant even 120 days after injections. The best results were observed on the skin radiance and satisfaction of both patients and investigators that allow to summary this efficacy of a global treatment on the face better than localized scores. Most reported reactions remained of light intensity and corresponded to usual adverse effects reported with such treatments (ecchymosis, swelling, erythema, hematoma, oedema). Slight irregularity at palpation was reported in one (1) subject at D30, no reaction were still reported at D60 nor D120 among the data collected for the N=69 (D60) or N=93 (D120) subjects concerned. No serious Adverse Event was reported. N=62 Adverse Events were reported whose N=61 were relating to adverse events that occurred on the skin of the face (One subject suffered from Zona on one arm about 2 month after injections). Most of them remained of slight intensity. These events occurred on the first 7 days following injections and last about 5 ± 1 days (from 1 to 17 days).

5) A comparative, prospective, randomized monocentric single blind investigation (HEBE3 study) aimed to determine the performance and safety of a new injection device (NanoSoft™ MICRO-NEEDLE) compared to classic needle (32G needle routinely used for skin biorevitalisation) on skin quality of face and neck. 30 days after the last injection, both injected modes allow a significant improvement of wrinkles and radiance assessed by clinical scoring. This result was confirmed by assessments performed on replicas with a significant decrease of the wrinkles volume whatever the injection but a difference of evolution that tends to be significant in favor of nanosoft needles. Nanosoft needle allowed to get a higher effect quickly (significant difference of evolution at D42+7 on the Lemperle periorbital lines, Lemperle Nasolabial and Bazin Neck wrinkles scores with a better effect for at least 1/3 of the subjects and difference that tends to be significant for the volume of the wrinkles). This benefit remain over time: benefit was still present at D120, with significant difference of evolution on the Lemperle periorbital lines, Lemperle Nasolabial and Bazin Neck wrinkles scores with a better effect for at least about 1/4 of the subjects and a difference that tends to be significant for the volume of the wrinkles versus classic needles. Finally, the pain score was significantly lower for Nanosoft® needle (at least 68% of the subjects reported a lower pain during injection with nanosoft needle than with needles, whatever the visit or the site). Most reported reactions were slight pain during injection, erythema, dyschromia, oedema or papule right after injection that mostly disappeared at D21. Pain reported during injection was lower with the Nanosoft® micro-needle than with the classic needle (about -2 on both mean and median values). A total of 7 patients (17% of the total population) reported 81 adverse event during the study, only one was not related to injection (COVID suspicion for one subject after V1 who stopped the study). Most of adverse events related to injection of NCTF 135 HA by classic needle or Nanosoft® microneedle remained of mild intensity. Most of all were erythema (21%), burning sensations (16%), irregularities to palpation (13%), ecchymosis or papules (10%). The above cited adverse events did not last more than 11 days. No serious adverse events have been reported during the study.

5.3 Summary of clinical data from other sources, if applicable

Non applicable. Although publications from sponsors other than FILL-MED are identified in the literature, none of them report clinical investigations relevant to this Summary of Safety and Clinical Performance.

5.4 An overall summary of the clinical performance and safety

Treatments with non-cross-linked hyaluronic acid (HA) is currently used for skin rejuvenation. The desired final effect is the correction of small wrinkles as well as a firm, bright, and moisturized skin, and the injection in the superficial dermis of suitable products -perfectly biocompatible and totally absorbable-can achieve these results.
Clinical performance and safety of **NCTF 135 HA** has been demonstrated through clinical studies and long marketing experience since 2007.

Reducing wrinkles with possible repeated treatments over time:	**For the correction of crow's feet wrinkles**, wrinkle volume is reduced significantly from 7 days after the last injection ($p<0.0001$). This result was maintained until 4 months ($p < 0.0001$). *(HEBE2 Study, 2019, 145 subjects)* **For the correction of nasolabial folds**, NLF clinical score is reduced significantly from 7 days after the last injection ($p<0.0001$). This result was maintained until 4 months ($p= 0.0004$). *(HEBE3 Study, 2019-2020, 40 subjects)* **For the correction of neck wrinkles**, wrinkle volume is reduced significantly from 7 days after the last injection ($p<0.0001$). This result was maintained until 4 months ($p< 0.0001$). *(proven by profilometry in HEBE2 Study, 2019, 145 subjects and by clinical scoring in HEBE3 Study, 2019-2020, 40 subjects).* **For the correction of wrinkles on the décolleté**, wrinkle volume is reduced significantly from 7 days after the last injection ($p < 0.0001$). This result was maintained until 4 months ($p<0.0001$). *(HEBE2 Study, 2019, 145 subjects).*
Hydration	**Hydration** is significantly improved from 7 days after the last injection ($p < 0.0001$). This result was maintained until 4 months ($p=0.0002$). *(HEBE2 Study, 2019, 145 subjects)*
Skin radiance	**Skin radiance** is significantly improved from 7 days after the last injection ($p < 0.0001$). This result was maintained until 4 months ($p<0.0001$). *(HEBE2 Study, 2019, 145 subjects – HEBE3 Study, 2019-2020, 40 subjects).*
Skin imaging parameters	Skin density measured by high frequency ultrasounds is improved by 42% from 7 days after the last injection. This parameter showed a progressive improvement by 54% one month after the last injection session (Day 75). This result was maintained until 4 months (Day 120 by 39%). *(HEBE2 Study, 2019, 147 subjects)*

	Sub-epidermal Low Echogenic Band (SLEB) which is a known marker for skin ageing was decreased significantly 1 month after the last injection (p = 0.04) and is maintained till 4 months (p=0.04). *(HEBE3 Study, 2019-2020, 40 subjects)*
Satisfaction level	Evaluation by GAIS demonstrates a global satisfaction by subjects and also investigators proven till 4 months.

Anti-aging treatment with **NCTF 135 HA** provides a progressive and visible improvement in the quality of the skin as to brightness, hydration, tonus and reduction in superficial wrinkles along with high levels of patient satisfaction. From the first session, the skin recovers a bright complexion. In the long term, the skin restores its elasticity and firmness. a biological, progressive treatment and its results are cumulative.

From a safety standpoint, adverse events rate, intensity and duration are within the same range as those commonly reported:

- Most common adverse events are bruise, erythema and irregularities to palpation
- No serious adverse events
- Adverse events are generally of mild or moderate intensity
- Mean duration is around a week

Anti-aging treatment with **NCTF 135 HA** is a superficial, painless aesthetic procedure presenting with very few side effects apart from risks of bruising if the injection technique is not mastered. There is no risk of overcorrection.
The clinical performance /risk ratio is acceptable as performance is achieved with limited and expected side-effects.

5.5 Ongoing or planned post-market clinical follow-up

There is no ongoing , nor planned PMCF study

6. Possible diagnostic or therapeutic alternatives

Although not being “therapeutic alternatives”, several minimally invasive cosmetic procedures such as botulinum toxin, laser resurfacing, mechanical resurfacing, dermabrasion, chemical peels and injectable products are available and decision to use one or another technique has to be taken by the healthcare professional considering the patient profile.

7. Suggested profile and training for users

These products must only be administrated by trained healthcare professionals who are qualified by education or accredited in accordance with national law and trained in injection techniques.

8. Reference to any harmonised standards and CS applied

The products are compliant with harmonized standards and common specifications applicable to **NCTF 135 HA.**
"Commission Implementing Regulation (EU) 2022/2346 of 1 December 2022 laying down common specifications for the groups of products without an intended medical purpose listed in Annex XVI to Regulation (EU) 2017/745 of the European Parliament and of the Council on medical devices" and more specifically by Annex IV laying down common specifications for substances, combinations of substances, or items intended to be used for facial or other dermal or mucous membrane filling by subcutaneous, submucous or intradermal injection or other introduction, excluding those for tattooing, as specified in Section 1 of that Annex."

Are fully applied the following harmonized standards: EN ISO 13485:2016/A11:2021, EN ISO 13485 2016, EN ISO 11737-1 2018, EN ISO 11737-1/A1 2021, EN ISO 11607-1/A1 2023, EN ISO 11607-2/A1 2023, EN ISO 14971 2019, EN ISO 14971/A11 2021, EN ISO 15223-1 2021, EN ISO 10993-9 2021, EN ISO 10993-10 2023, EN ISO 10993-12 2021, EN ISO 10993-17 2023, EN ISO 10993-18 /A1 2023, EN ISO 10993-23 2021.

9. Revision history

SSCP revision number	Date issued	Change description	Revision validated by the Notified Body
Version 1	22/09/2023	Creation	☐Yes ☒No Validation language: English
Version 2	15/07/2024	Revision	☐Yes ☒No Validation language: English
Version 3	22/011/2024	Revision	☐Yes ☒No Validation language: English
Version 4	06/12/2024	Revision	☐Yes ☒No Validation language: English

A summary of the safety and clinical performance of the device, intended for patients, is given below.

Summary of safety and clinical performance

SSCP Reference number: SSCP- NCTF- NCL

Document revision: V04

Date issued: 06/12/2024

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 the device. The information presented below is intended for patients or lay persons. A more extensive summary of its safety and clinical performance prepared for healthcare professionals is found in the first part of this document.

The SSCP is not intended to give general advice on the treatment of a medical condition. Please contact your healthcare professional in case you have questions about your medical condition or about the use of the device in your situation. This SSCP is not intended to replace an Implant card or the Instructions For Use to provide information on the safe use of the device.

1. Device identification and general information

1.1 Device trade name: NCTF 135 HA

TRADE NAME	CALOGUE NUMBER	BOX COMPOSITION
NCTF 135 HA	1V401405	Box of 5 vials including 5: - 18G1½" withdrawal needle - 30G½" injection needle - 32G injection needle - 3ml Luer-Lock syringe
	1V401510	Box of 10 vials

1.2 Manufacturer; name and address

LABORATOIRES FILL-MED
38 cours Albert 1er 75008 PARIS
France

1.3 Basic UDI-DI

GMN (Basic UDI-DI)[1]: 3664948NCTF135HADN

1.4 Year when the device was first CE-marked

Not applicable under Medical Device Regulation (EU) 2017/745*.
*NCTF 135 HA was first CE marked in 2007 according to Directive 93/42EEC (regulation applicable at that time, now replaced by Medical Device Regulation (EU) 2017/745.

2. Intended use of the device

2.1 Intended purpose

NCTF 135 HA are products without an intended medical purpose, they are used for aesthetic purposes.

NCTF 135 HA are anti-ageing injectable products intended for filling of superficial wrinkles for intense revitalization and hydration of tired or dull skin, and to improve skin homogeneity and radiance. It also helps skin redensification, thickness and elasticity of mature or slack skin.

2.2 Indications and intended patient groups

NCTF 135 HA is indicated to be injected in the dermis of the following areas:
- Face (including periorbital area)
- Neck
- Décolleté area

NCTF 135 HA is used for aesthetic purposes, as such intended patient groups do not present any specific pathology. Aesthetic procedures are requested by patient to improve their appearance in order to look younger and increase self-esteem. According to Regulation, patients have to be older than 18 years.

2.3 Contraindications

NCTF 135 HA should not be injected into blood vessels and should not be used in:

- Patients with a skin alteration or disease of any kind in the treated area
- Patients with a history of autoimmune disease[2] or under immunotherapy[3]
- Patients with hypersensitivity[4] or known allergy to any of the constituents
- Patients who are less than 18 years old
- Pregnant or breastfeeding women

[1]The Basic UDI-DI is the primary identifier of a device model. It is the device identifier assigned at the level of the device unit of use. It is the main key for records in the UDI database and is referenced in relevant certificates and EU declarations of conformity.
[2]Condition in which the body's immune system mistakes its own healthy tissues as foreign and attacks them.
[3]Prevention or treatment of disease with substances that stimulate the immune response
[4]Exaggerated response by the immune system to a drug or other substance

3. Device description

3.1 Device description and material/substances in contact with patient tissues

NCTF 135 HA correspond to an injectable hyaluronic acid-based solution (5mg/ml), sterile and apyrogen presented in vials of 3 ml. 2 presentations are available, box with 5 kits (vials with needles and syringes) and box of 10 vials.

NCTF 135 HA is composed of :

- non-crosslinked5 Sodium Hyaluronate /Hyaluronic Acid [5 mg/ml]
- buffer solution for adjustment to physiological conditions
- polyrevitalising solution [9 mg/ml]
    - 12 vitamins: Ascorbic acid (vit. C), Biotin (vit. B8), Pantothenic acid (vit. B5), Folic acid (vit. B9), Inositol (vit. B7), Nicotinamide/Nicotinic acid (vit. B3), Pyridoxine /Pyridoxal (vit. B6), Riboflavin (vit. B2), Thiamine (vit. B1), Tocopherol (vit. E), Retinol (vit. A), Vitamin B12
    - 6 minerals: Calcium chloride, Potassium chloride, Magnesium sulfate, Sodium acetate, Sodium chloride, Sodium dihydrogenophosphate
    - 5 nucleosides: Deoxyadenosine, Deoxycytidine, Deoxyguanosine, Deoxythymidine, 5-Methyl-2'-deoxycytidine
    - 24 amino acids: α-Aminobutyric acid, Alanine, Arginine, Asparagine, Aspartic acid, Cystine, Glutamine, Glutamic acid, Glycine, Histidine, Hydroxyproline, Isoleucine, Leucine, Lysine, Methionine, Ornithine, Phenylalanine, Proline, Serine, Taurine, Threonine, Tryptophane, Tyrosine, Valine
    - 6 coenzymes: TPP (Cocarboxylase), CoA (Coenzyme A), FAD (Flavine adenine dinucleotide), NAD (Nicotinamide adenine dinucleotide), NADP (Nicotinamide adenine dinucleotide phosphate), UTP (Uridine triphosphate)
    - Other components: Glutathione, Polysorbate 80, Glucuronic acid, Glucuronic acid lactone, Glucosamine, Dextrose anhydrous

NCTF 135HA is intended to injected by a qualified practitioner using syringe and in conjunction with sterile single use withdrawal needles 18G and injection needles (30G and 32G) provided in the kit presentation. NCTF 135HA may also be used with similar syringes and needles according their manufacturer(s) intended use.

[5] Also said "free". HA is not treated by crosslinking (a chemical process used to polymer in order to decrease the degradation of HA in human tissues).

3.2 Information about medicinal substances in the device, if any

NCTF 135HA does not contain any medicinal substance.

3.3 Description of how the device is achieving its intended mode of action

NCTF 135 HA acts by hydrating the skin and mechanically filling superficial wrinkles thanks to high water-binding[6] capacity and mechanical effect on the dermis of non-crosslinked hyaluronic acid while the polyrevitalising solution provides an optimal physiological environment.

NCTF 135 HA is Injected in the dermis with the needles supplied or with standard injection devices (hypodermic needles, cannulas or other such as microneedles for intra-dermal injections.

3.4 Description of accessories, if any

NCTF 135HA does not include any accessory.

4. Risks and warnings

Contact your healthcare professional if you believe that you are experiencing side effects related to the device or its use or if you are concerned about risks. This document is not intended to replace a consultation with your healthcare professional if needed.

4.1 How potential risks have been controlled or managed

According to LABORATOIRES FILL-MED policy ,the residual risks have been identified and reduced as far as possible. The actions taken by the manufacturer to mitigate any identified risks do not impact the patient safety. The main method of mitigation is the design control of the device, validation of usability of the device to the foreseeable use errors, manufacturing controls and then the information provided to the user (labelling, instruction for use, …).
The residual risks are consistent with a high level of protection for the safety and health of persons. This is in accordance with the state of science and medical knowledge.

4.2 Remaining risks and undesirable effects

Expected undesirable effects are:

Redness or mild local inflammation that usually disappears within few hours to few days.
Mild oedema and small hematomas may occur but disappear within few hours to few days.
Minimal bleeding at the injection site that stops rapidly and spontaneously after the injection.
Transient pain at the injection site.

[6] Ability to absorb water

As with all transcutaneous procedures, the injection of NCTF 135 HA carries a risk of infection. Standard precautions associated with injectable materials should be followed.

Experience show that the adverse events related to **NCTF 135HA** are very rare, minor, reversible and similar to other devices available on the market.

Reported events	Incidence
Swelling, Erythema[7]	0.002%
Nodule[8],, Itching Sensation, Pain, Skin inflammation, Burning Sensation, rash	0.0005%
Hypersensitivity/Allergic reaction	0.0001%
Granuloma[9], Papula[10], Fever, Angioedema /Quincke Edema[11], Eczema, Fatigue, Skin Discoloration, Bruise[12], Local Reaction (Pruritus), Dyspnea, Local Reaction –Induration	<0.0001%

4.3 Warnings and precautions

The following **warnings** are given:

- Check the expiry date on the label
- Check the integrity of the sterile barrier immediately prior to using the product.
- Do not reuse the vial & the components on other patients.
- Do not resterilize
- After use, the needles must be thrown away in a suitable safe container
- Re-use of the product involves risks (e.g. cross contamination) for the patient
- Do not use if the packaging is open or damaged
- Do not inject excessive volume, it can potentially lead to side effects.

The following **precautions** for use are also given

- Do not use the product if the product aspect (color, transparency...) changed
- There are no clinical data available in terms of tolerance with regard to the injection of NCTF® 135 HA in an area that has already been treated with another “permanent (non- resorbable)” filling product.
- Precaution should be taken in such cases, although NCTF® 135 HA is not injected at the same level.
- Patients receiving an anticoagulant treatment or a platelet aggregation inhibitor (for example, aspirin) must be informed of the increased risk of bruising and mild bleeding at the injection site.
- The patient should be given the recommendation not to use make-up for 12 hours following the injection and to avoid prolonged exposure to the sun, UV rays, freezing temperatures as well as use of saunas or steam rooms for at least 48 hours after the injection.
- Training in injection techniques is recommended for the use of NCTF® 135 HA. NCTF® 135 HA must not be injected at the same time as a medium or deep chemical peeling or dermabrasion.

[7] Redness
[8] Small firm lumps, usually greater than 1 cm in diameter
[9] Aggregation of cells in response to chronic inflammation
[10] Smaller raised soft tissue bumps (less than 0.5 cm)
[11] Area of swelling (edema) of the lower layer of skin and tissue just under the skin or mucous membranes
[12] Also known as a contusion, is a type of hematoma of tissue,

- A local anaesthetic (patch or cream) can be applied prior to the injection. Please note that anaesthetic products can cause local redness or hypersensitivity.
- Do not inject NCTF® 135 HA into beauty spots (naevi) and in active acne lesions.

Hyaluronic acid is incompatible with quaternary ammonium compounds, such as benzalkonium chloride solutions. This is why NCTF® 135 HA must never come into contact with medical and surgical instruments treated with this type of product.

Before starting treatment, the patient must be informed of the indications of the device, its contraindications, its incompatibilities and its possible undesirable effects.

4.4 Summary of any field safety corrective action, (FSCA including FSN) if applicable

No other relevant aspects of safety are applicable. No Field Safety corrective action (FSCA)[13], no Field Safety Notice (FSN)[14] have been implemented.

5. Summary of clinical evaluation and post-market clinical follow-up

5.1 Clinical background of the device

Skin aging is a complex biological process influenced by a combination of endogenous or intrinsic and exogenous or extrinsic factors, the consequences of this physiological process being worsened by conditions such as excessive sun exposure, smoking or environmental conditions.

Treatments with non-cross-linked hyaluronic acid (HA) is widely used for skin rejuvenation. The hydrophilic nature of HA, naturally present in all tissues of the human body, attracts and maintains water within the extracellular space, which affects dermal volume. The desired final effect is the correction of small wrinkles as well as a firm, bright, and moisturized skin, and the injection in the superficial dermis of suitable products - perfectly biocompatible with no risk of allergic reactions and totally absorbable - can achieve these results. HA may also be rapidly degraded by hyaluronidase in the event of complications.

5.2 The clinical evidence for the CE-marking

As **NCTF 135 HA** was put on the market in 2007, clinical evidence (performance and safety) of NCTF 135 HA is based on several clinical studies.

One study was conducted on 145 subjects, divided in two groups (Randomization 3:1 for the face) with 3 months follow up. Clinical performance of **NCTF 135 HA** was confirmed by results reported in various standardized clinical scores and instrumental measures versus control group on decrease of wrinkles,

[13] Action is used to reduce a risk of death or serious deterioration in the state of health associated with the use of a medical device that is already placed on the market.
[14] Means of communicating a field safety corrective action (FSCA)

improvement in skin radiance, skin density and skin elasticity, decrease of pore diameter. The effect on wrinkles was detected as soon as 7 days after the third injection and the superiority of the effect persisted up to D120. Most of adverse events reported were bruise (about 36%) or redness (23%). Intensity varied from light to severe, but most of them were of light intensity (56% / only 13 % were severe) and whose 48% last no more than 48 hours.

Another comparative study compared performance and safety of injection of NCTF 135 HA using a new injection device (NanoSoft™ MICRO-NEEDLE) compared to classic needle (32G needle routinely used for skin biorevitalisation) on skin quality of face and neck. 30 days after the last injection, both injected modes allow a significant improvement of wrinkles and radiance assessed by clinical scoring. The pain score was significantly lower for Nanosoft® needle (at least 68% of the subjects reported a lower pain during injection with nanosoft needle than with needles, whatever the visit or the site). Most reported reactions were slight pain during injection, erythema, dyschromia, oedema or papule right after injection that mostly disappeared at D21. Most of adverse events related to injection of **NCTF 135 HA** (by classic needle or Nanosoft® microneedle) remained of mild intensity. Most of all were erythema (21%), burning sensations (16%), irregularities to palpation (13%), ecchymosis or papules (10%) which did not last more than 11 days.

A third study was conducted on 99 patients (ITT) with 120 days follow-up to demonstrate the efficacy and safety of a new protocol combining 2 or 3 devices, **NCTF 135 HA** with a hyaluronic acid-based dermal filler ART FILLER® Fine Lines, completed or not by ART FILLER® Universal depending on the score at baseline), through a special technique (Intradermal injection via a canula in fan technique). A significant improvement of this score was observed with regard to time and this improvement remained significant even 120 days after injections. The best results were observed on the skin radiance and satisfaction of both patients and investigators. Most reported reactions remained of light intensity and corresponded to usual adverse effects reported with such treatments (ecchymosis, swelling, erythema, hematoma, oedema). Most of them remained of slight intensity. These events occurred on the first 7 days following injections and last about 5 ± 1 days (from 1 to 17 days).

Previous clinical data were reported from an observational study on 40 subjects in routine conditions, in which **NCTF 135 HA** was found clinically efficient on the cutaneous ageing effects with improvement on wrinkles and fine lines, as well as for hydration, firmness and radiance of the skin. Most adverse events were erythema. Most of events occurred after the first treatment (on D1 / N=63 (67%)) and only few of them were present all over the study (N=16 / 17%) (only 37% of Adverse Events were reported at D75). Finally, a clinical evaluation with instrumental measures of outcomes of anti-age efficacy of **NCTF 135 HA** conducted on 20 subjects showed a comprehensive facial rejuvenation appearing gradually. improvement in skin homogeneity and brightness, smoothing of the skin with decrease in crow's feet wrinkles depth and reduction of pore size, and increase in skin density and dermis thickness. No safety assessment was done in this study.

Anti-aging treatment with **NCTF 135 HA** provides a progressive and visible improvement in the quality of the skin as to brightness, hydration, tonus and reduction in superficial wrinkles, it is a superficial, painless aesthetic procedure presenting with limited side effects apart from risks of bruising if the injection technique is not mastered. There is no risk of overcorrection.

5.3 Safety

Undesirable side effects identified by the clinical studies on **NCTF 135 HA**, correspond to those found in the literature as well as those listed in the risk assessment. Adverse events rate, intensity and duration are within the same range as those commonly reported:

- Most common adverse events are bruise, erythema and irregularities to palpation
- No serious adverse events
- Adverse events are generally of mild or moderate intensity
- Mean duration is around a week

They are acceptable under normal conditions of use, which is consistent with a high level of protection for the safety and health of persons.

6. Possible diagnostic or therapeutic alternatives

6.1 General description of therapeutic alternatives

When considering alternative treatments, it is recommended to contact your healthcare professional who can take into account your individual situation.

Several minimally invasive cosmetic procedures such as botulinum toxin, laser resurfacing, mechanical resurfacing, dermabrasion, chemical peels and injectable products are available and decision to use one or another technique has to be taken by the healthcare professional considering your profile.

7. Suggested training for users

NCTF 135 HA is not intended to be handled directly by the subject. These products must only be administrated by trained healthcare professionals who are qualified by education or accredited in accordance with national law and trained in injection techniques.