

# Claim support for products containing CBD

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# Agenda

- Introduction
- Legal and regulatory issues
- Working mechanism
- Suitable targets and study designs to investigate CBD products
- Summary
- Questions & Answers



# Introduction

Cannabis-based ingredients, such as hemp oil and other cannabis extracts like cannabidiol (CBD), are becoming increasingly common ingredients in cosmetics.

Studies have demonstrated the potential use of cannabidiol to treat dermatological conditions, such as

- acne,
- psoriasis,
- pruritus,
- and inflammatory skin diseases.

CBD has antioxidant, anti-sebum, skin protection and skin care properties



# Definitions/Terminology

- Cannabis: any plant of the genus cannabis, e.g. *Cannabis sativa* or *indica*
- Hemp: commonly used for specific varieties of cannabis that typically have lower content of THC and are grown for industrial purposes
- Cannabinoids: compounds found in cannabis
- Cannabidiol (CBD): is the second most abundant cannabinoid present in *Cannabis sativa* without psychotropic activity
- Tetrahydrocannabinol (THC): is a cannabinoids with psychoactive properties and is said to be responsible for the main part of the intoxicating effect



# CBD Legal



# CPR: COMMISSION REGULATION (EU) No 1223/2009

22.12.2009

EN

Official Journal of the European Union

L 342/59

REGULATION (EC) No 1223/2009 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL  
of 30 November 2009  
on cosmetic products  
(recast)  
(Text with EEA relevance)

THE EUROPEAN PARLIAMENT AND THE COUNCIL OF THE EUROPEAN UNION,

Having regard to the Treaty establishing the European Community, and in particular Article 95 thereof,

Having regard to the proposal from the Commission,

Having regard to the opinion of the European Economic and Social Committee <sup>(1)</sup>,

Acting in accordance with the procedure laid down in Article 251 of the Treaty <sup>(2)</sup>,

(5) The environmental concerns that substances used in cosmetic products may raise are considered through the application of Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) and establishing a European Chemicals Agency <sup>(4)</sup>, which enables the assessment of environmental safety in a cross-sectoral manner.

(6) This Regulation relates only to cosmetic products and not to medicinal products, medical devices or biocidal products. The delimitation follows in particular from the detailed definition of cosmetic products, which refers both to their areas of application and to the purposes of their use.

## Chapter 1, Article 2 (1a) - Definition of a cosmetic product

A cosmetic product is a substance intended to be applied to the external parts of the human body:

- epidermis
- hair system
- nails
- lips
- external genital organs
- teeth
- mucous membrane of the oral cavity

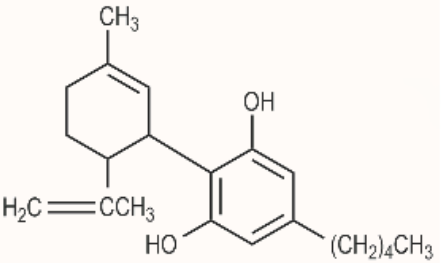

And its main purpose is to:

- clean
- perfume
- change appearance
- correct body odor
- protect
- keep in good condition



# CBD - EU

Ingredient : CANNABIDIOL - DERIVED FROM EXTRACT OR TINCTURE OR RESIN OF CANNABIS 🚫

INCI Name	CANNABIDIOL - DERIVED FROM EXTRACT OR TINCTURE OR RESIN OF CANNABIS
Description	 <chem>CC1=CC(=C(C=C1)C(=O)C2=CC(=C(C=C2)O)C(C)C</chem>
CAS #	13956-29-1
EC #	
Cosmetics Regulation provisions 	
Functions	<ul style="list-style-type: none"><li>• <a href="#">ANTI-SEBUM</a></li><li>• <a href="#">ANTIOXIDANT</a></li><li>• <a href="#">SKIN CONDITIONING</a></li><li>• <a href="#">SKIN PROTECTING</a></li></ul>
SCCS opinions	

- In February 2021 whole-plant hemp extracts were legalized for use in the EU
- THC levels need to be  $\leq 0.2\%$
- Before only synthetically derived CBD was legal
- [CosIng](#) (Cosmetic Ingredient Database by the European Commission) was updated
- CBD products can be legally marketed with the following properties:  
**antioxidant, anti-sebum, skin protection and skin conditioning**

Source: CosIng Database (23-JAN 2022)



# CBD – US (Federal Food, Drug and Cosmetic Act (FD&C Act))

- cosmetic products and ingredients are not subject to premarket approval by FDA
- cannabis or cannabis-derived ingredients such as CBD are not restricted
- cannot be used in a cosmetic if it causes the product to be adulterated or misbranded in any way
- *“A cosmetic generally is adulterated if it bears or contains any poisonous or deleterious substance which may render it injurious to users under the conditions of use prescribed in the labeling, or under such conditions of use as are customary or usual “*
- *“If a product is intended to affect the structure or function of the body, or to diagnose, cure, mitigate, treat or prevent disease, it is a drug, or possibly both a cosmetic and a drug, even if it affects the appearance.”*

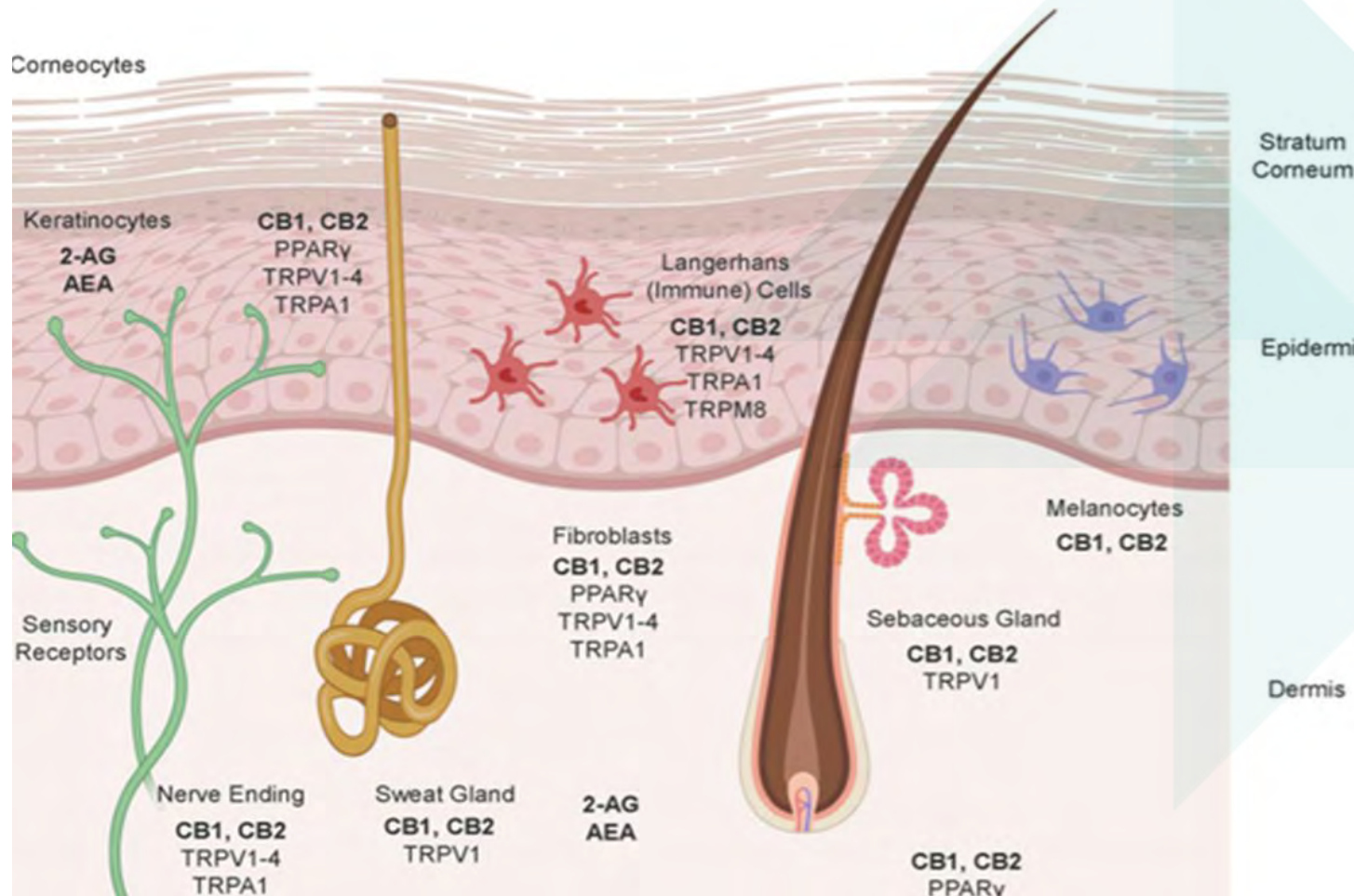




# CBD Working Mechanism



# Endocannabinoid System (ECS) of the Skin



- Endocannabinoids bind to Cannabinoid 1 (CB1) and 2 (CB2) Receptor
- Also to Transient Receptor Potential (TRP) receptors and to Peroxisome Proliferator-Activated Receptors (PPAR)
- Those are involved in different functions: the skin barrier, cell growth, cell differentiation, immunological and inflammatory processes and analgesic actions



# Cannabidiol (CBD) Penetration



# Challenges in CBD Delivery

CBD has a reasonable molecular weight (314.46 Da)

High log P value (lipid/water partitioning) of  $\sim 6.3$ , poses unique challenges to its transdermal delivery (lipophilic)

Therefore difficult to get into the epidermis to the receptors



Identify suitable "carrier systems"



# Confocal Raman Microspectroscopy

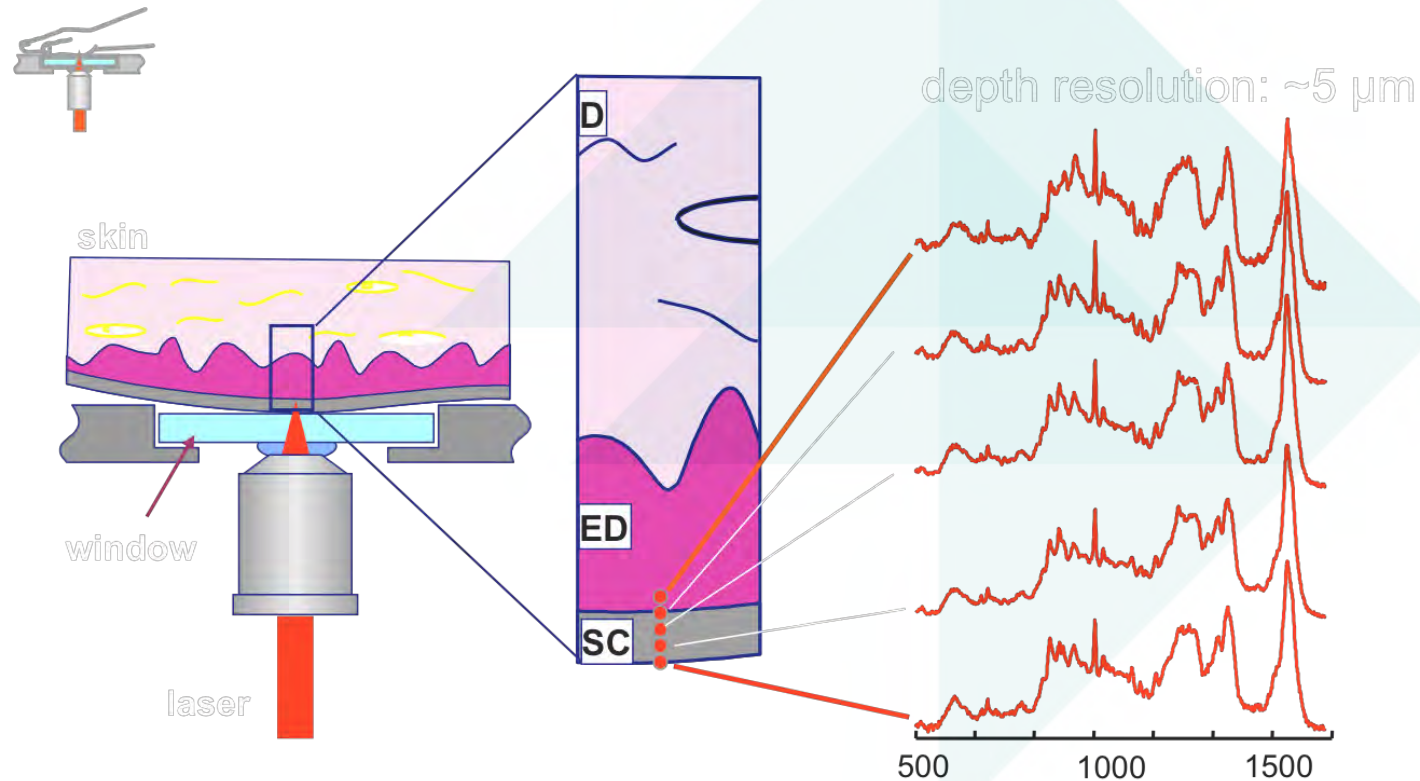


Raman spectroscopy enables **non-invasive in vivo** analysis of the molecular composition of the skin

- Water concentration profiles from skin surface to dermis in minutes
  - Determination of Natural Moisturizing Factors concentration or other molecules in the stratum corneum and below
  - Studies of the penetration of topically applied materials
- Gen2\_SCA Raman



# Confocal Raman MicroSpectroscopy

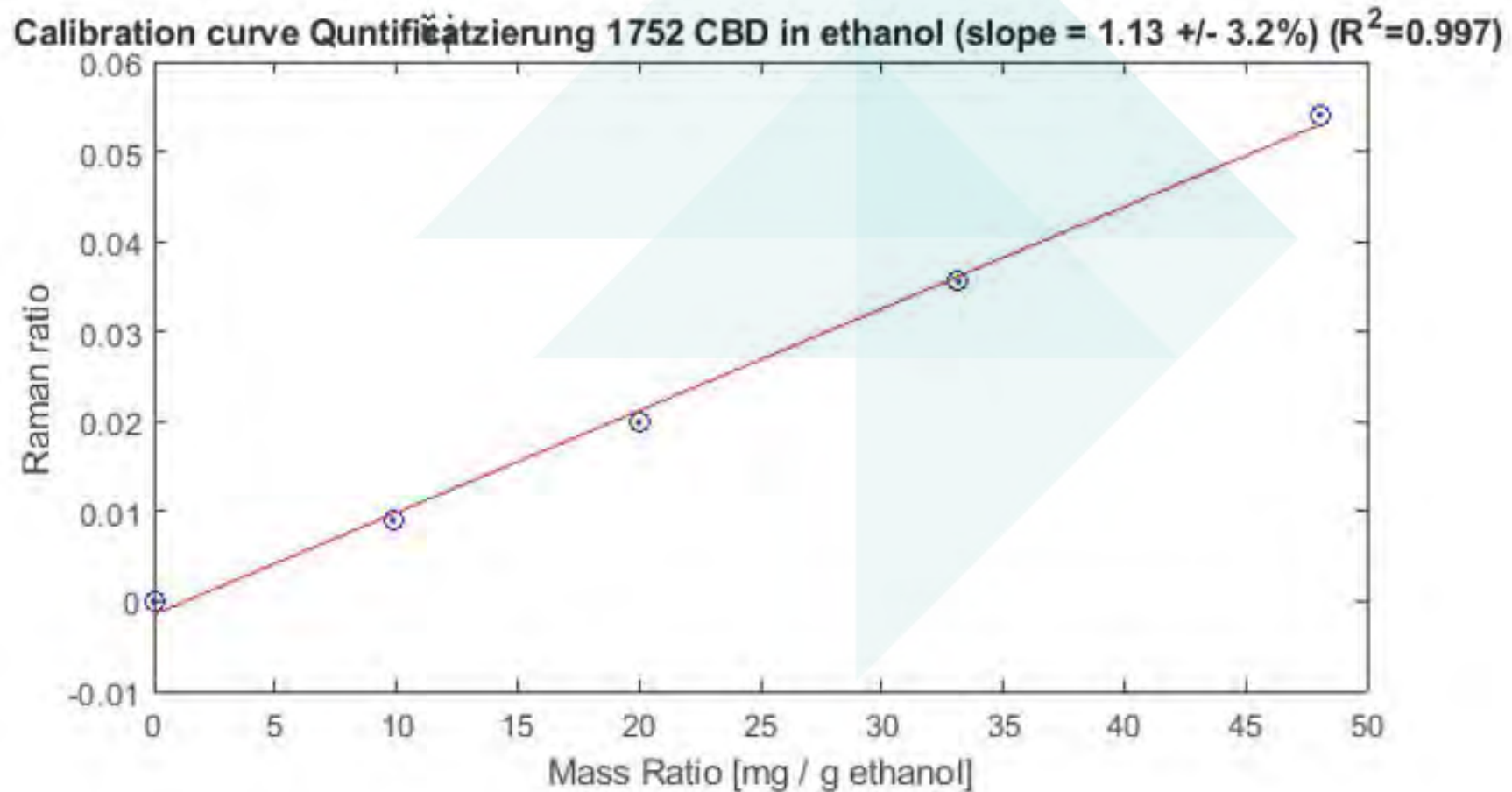


Up to 200 μm in depth  
Best depth resolution: ~3 μm



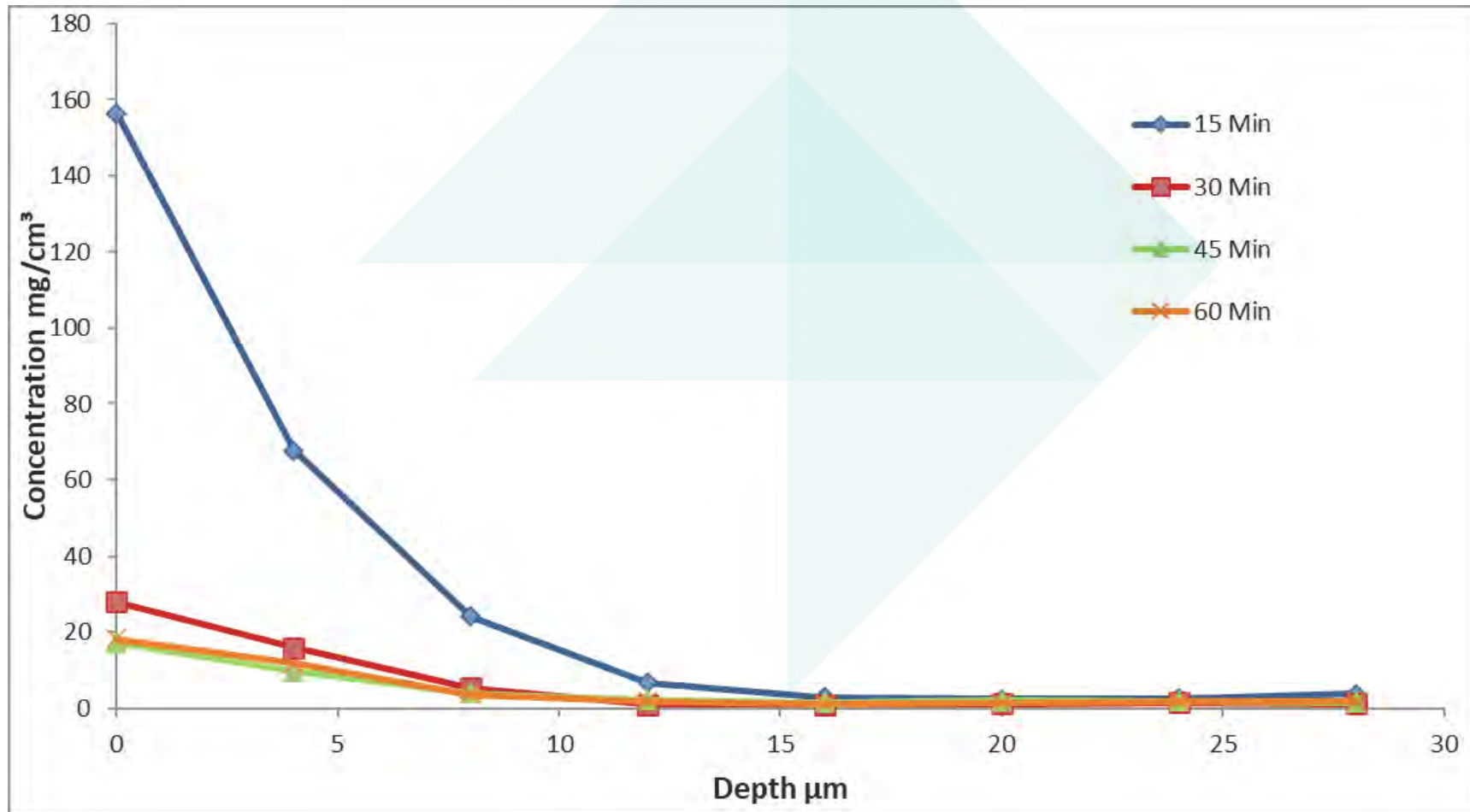
# Quantification of Skin Penetration

## CBD: Calibration Curve with Different Concentrations in Ethanol





# Penetration of CBD after Finite Dosing







# CBD in Topical Applications



# CBD Potential in Topical Applications

- Skin Protection / Barrier Function
- Skin Inflammation/Soothing and Moisturizing ←
- Pruritus or Itching ←
- Pain Sensation and Muscle Relief
- Aging ←
- Wound Healing ←
- Alopecia and Hair Growths Disorders ←
- Skin or Hair Pigmentation
- Antibacterial
- Oral Care ←
- Skin Disorders
  - Atopic Dermatitis ←
  - Allergic Contact Dermatitis
  - Acne / Seborrhea ←
  - Psoriasis ←
  - Cutaneous lupus erythematosus



# CBD in Skin Inflammation and Soothing

## Possible Claims:

“Soothing”

“Soothing after Shaving”

“For stressed/irritated skin after hair removal”

“Non-irritative”

“Suitable for irritated skin”



# Soothing Efficacy after UV-Erythema and optional Pain Induction by Heat

- Subjects:** 35 (30 finishing) healthy volunteers
- Duration:** 4 days
- Exposure:** Irradiation with 1,25 MED followed by application of occluded or semi-occluded patch; 2 applications for 4 and 20h
- Test Products:** Active, vehicle, positive control (untreated irradiated control), negative control (untreated not irradiated control)
- Evaluations after 4 and 24h:** Erythema, Temperature-induced pain (HPT)

# Example Study: soothing properties after shaving irritation

- Subjects:** 28 healthy volunteers
- Duration:** 4 days
- Area:** volar forearm, 4 areas
- Test Product:** 3 products, 1 untreated but shaved control area
- Evaluations:** Days 1-4, Burning, Itching, Tension, Erythema and Skin redness





# Soothing Properties after Irritation

Ranking evaluation of erythema on the last day of the study





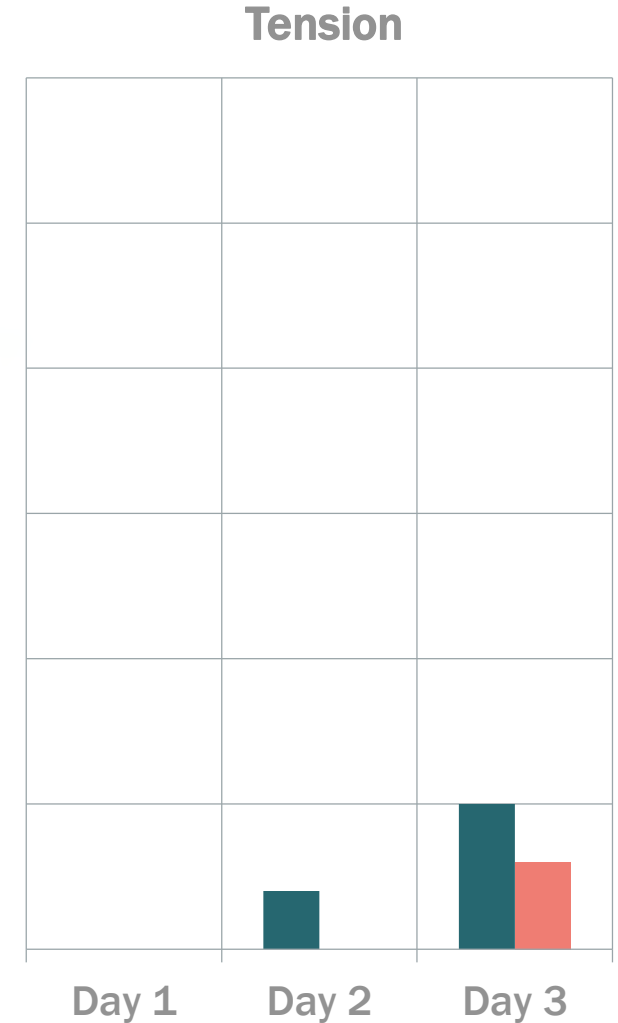
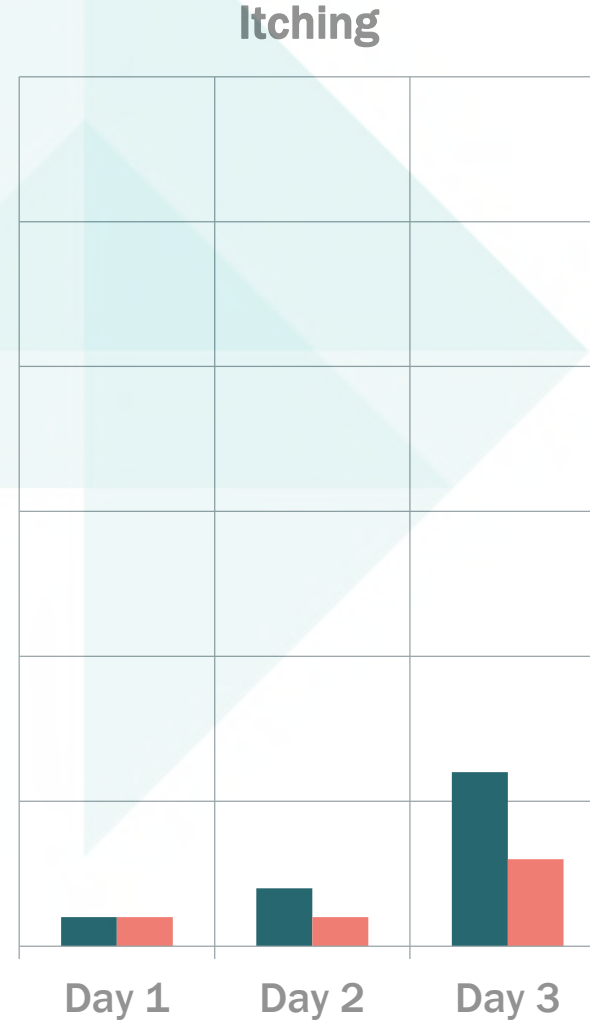
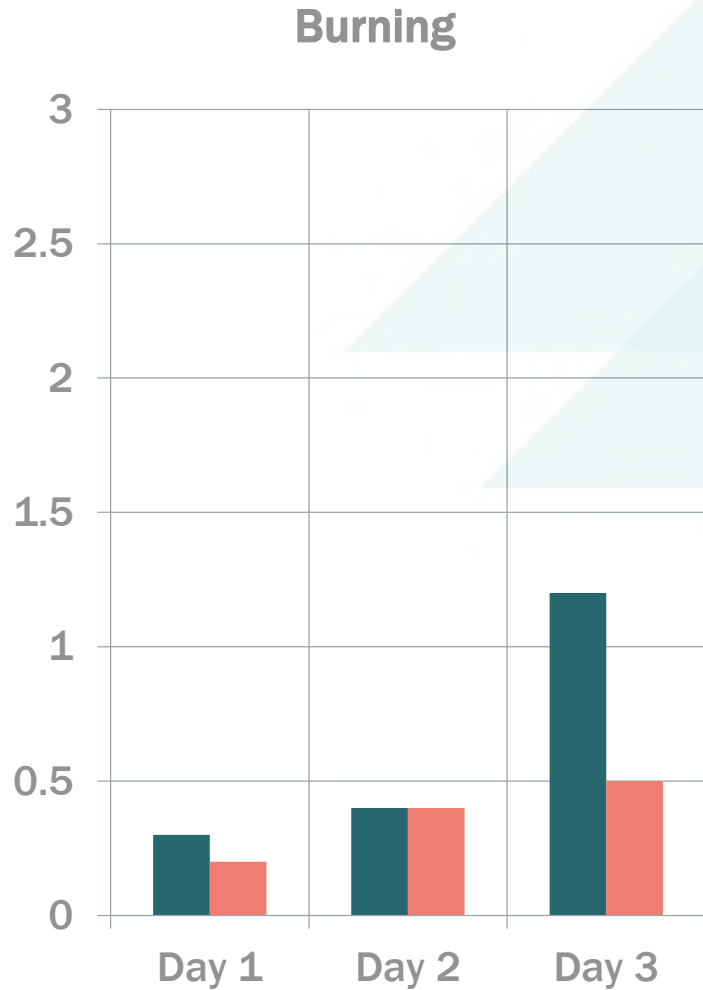
# Soothing – Study Design *Soothing after Irritation*

Subjective Evaluation, Mean Scores, n=32

Score:  
0 = none  
0.5 = very slight  
1 = slight  
2 = moderate  
3 = strong

■ Untreated irritated

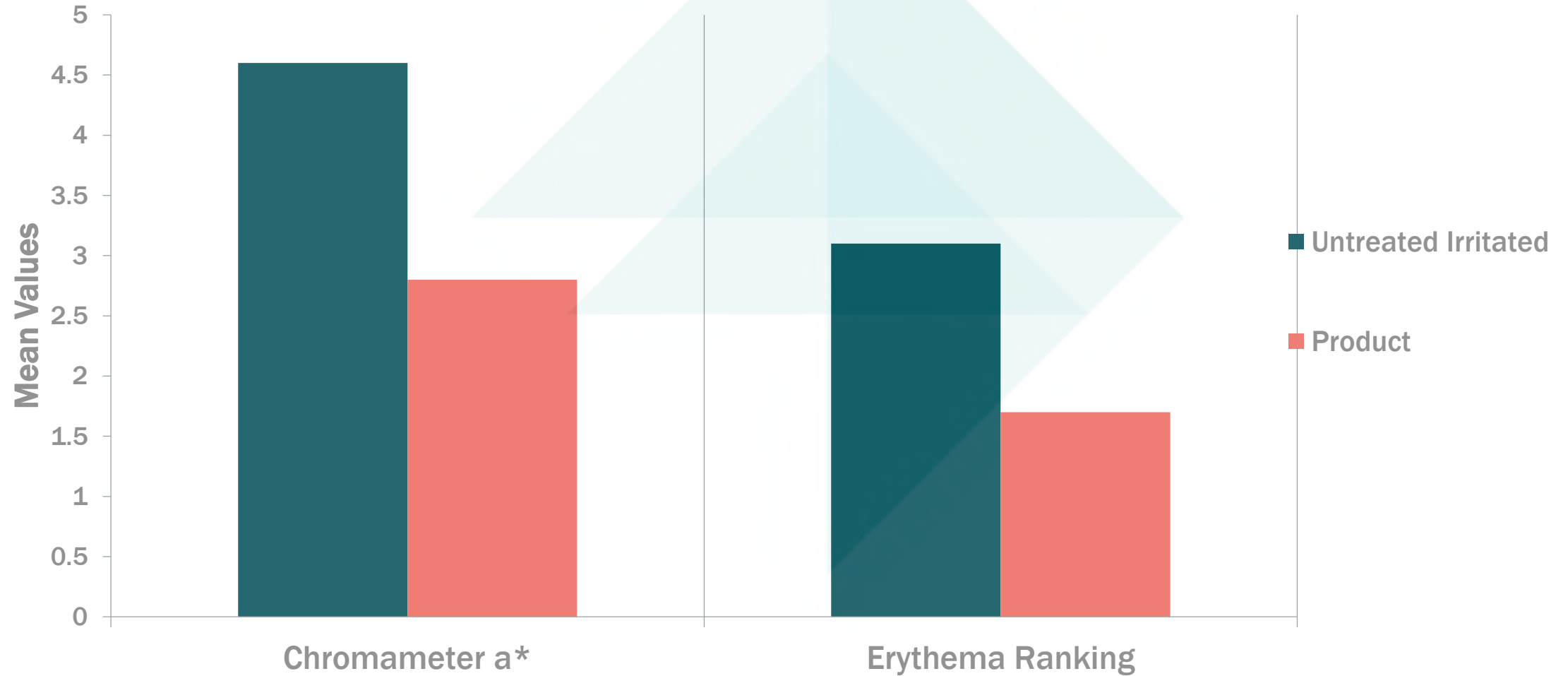
■ Product





# Soothing – Study Design *Soothing after Irritation*

Objective Evaluation and Measurements, Mean Scores, n=32







## CBD in Pruritus or Itching

### Possible Claims:

- “Reduces itching sensation”
- “Calms itchy skin”
- “Suitable for itchy skin”
- “Soothes itchy, dry skin”

# Anti-itch – Study Design



## Study Parameters

Panel	<p>32 female or male (or larger panels)</p> <p>Regular itching sensation due to DRY SKIN, atopic dermatitis, psoriasis, or itching after sport, sweating, eating, bathing</p>
Visits	<p>Day 1, day 18</p>
Assessments and Times	<p>Itching evaluation (intensity, frequency)</p> <ul style="list-style-type: none"><li>- Starts between day 1-3</li><li>- 24 hours evaluation period after 1st application</li><li>- Day 18</li></ul>
Application	<p>Starts when subject perceives a clear itching sensation</p> <p>Over 2 weeks, twice daily at home</p>

# Anti-itch – Itching Intensity

Mean Values, n=64

During 24 hours after 1<sup>st</sup> application

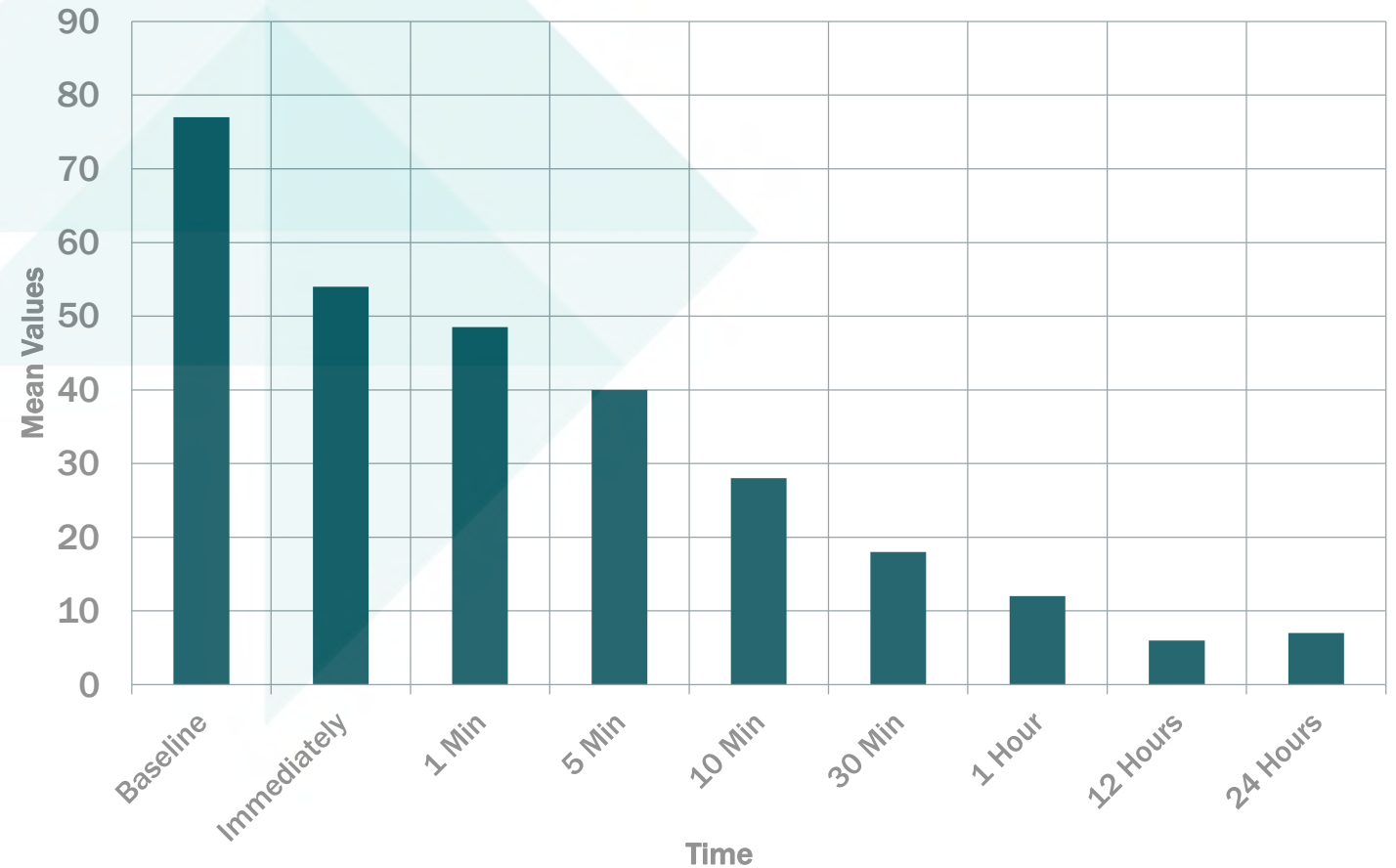
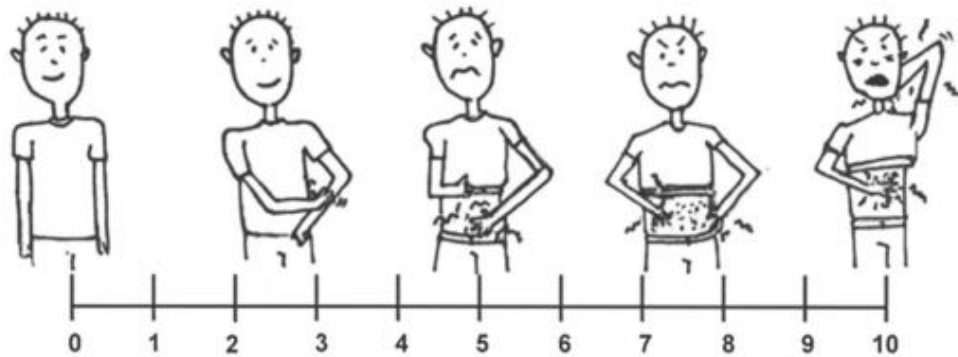
Itching intensity

On a VAS scale, ranging from

0 (no itching)

Continuously to

100 (extreme itching)





# Anti-itch – Questionnaire

Frequency in %, n=32

After application

Agreement Scale

-2 /-1: fully disagree/ disagree

1 / 2: agree/ fully agree

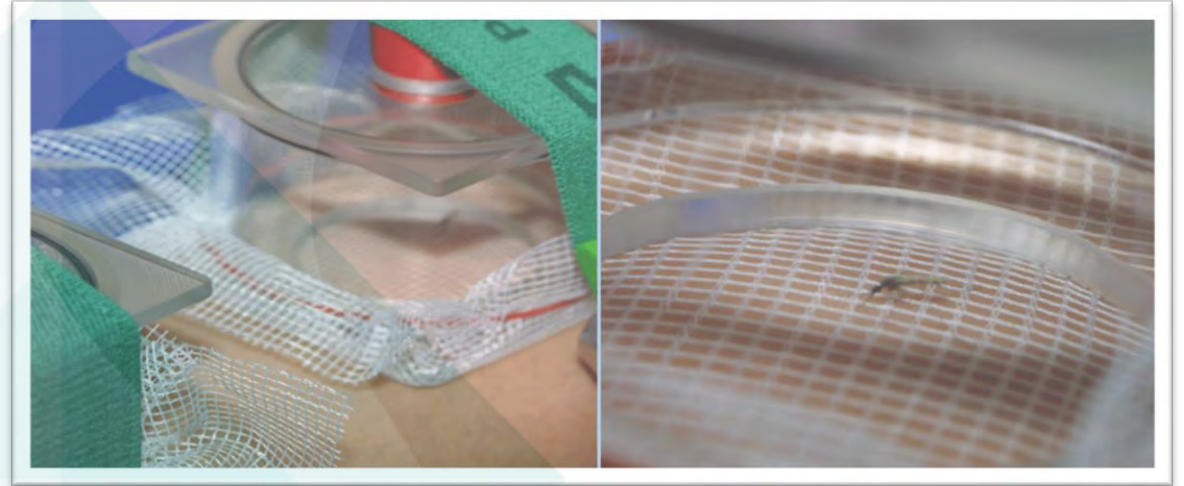
- Q01. In an acute phase of itching I long for **immediate soothing**.
- Q02. Immediately after application the **intensity of itching decreases**.
- Q03. After continued application previously itchy body sites feel **soothed**.
- Q04. When applying the product it leaves a **pleasant feeling**.
- Q05. When applying the product my skin doesn't feel greasy.
- Q06. I find this test product a sensible **addition for acute phases**.
- Q07. The test product is better than my usually used care product
- Q08. After product application **no burning** occurs.
- Q09. After product application **no redness** occurs.
- Q10. I would buy / recommend the test product.





# Other Itch Models

- Histamine-induced itch
- Mosquito Itch
- Cowhage spicules
- UV- induced itch
- Electrically Evoked Itch
- Exaggerated – Eczema Surfactant



Histamine iontophoresis

Mosquito Itch



## CBD in Aging

### Possible Claims:

- Helps prevent signs of aging
- Refresh your looks
- Reduces fine lines slows the signs of premature aging
- Reduces the signs of aging
- Minimizes fine lines
- helps prevent (reduce, slow) the signs (appearance) of ageing (age lines, premature ageing)
- smooths wrinkles



# Example Study: Epidermal effects

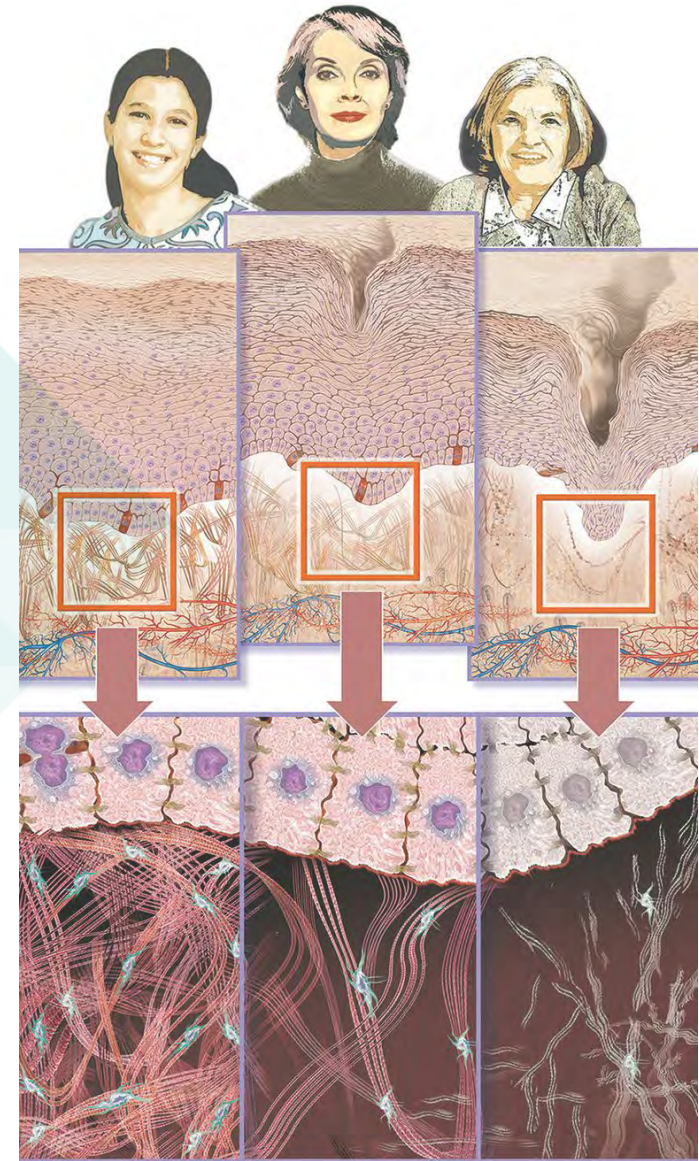
**Subjects:** 35 (30 finishing) healthy volunteers, aged between 35 and 70 years

**Duration:** 29 days

**Area:** Face, Split-design

**Test Products:** Active, vehicle or untreated

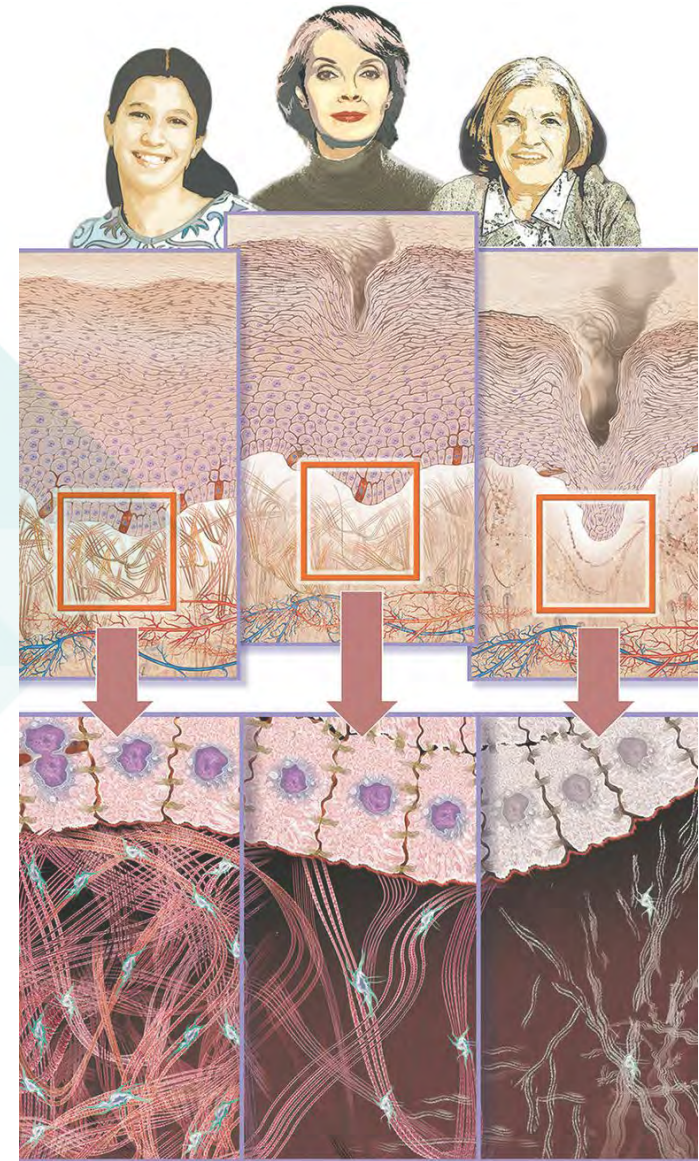
**Evaluations:** Baseline, 28 days  
Wrinkles, Hydration, Skin Elasticity, Images





# Example Study: Dermal effects

- Subjects:** 35 (30 finishing) healthy volunteers, aged between 35 and 70 years
- Duration:** 85 days
- Area:** Face, Split-design
- Test Products:** Active, vehicle or untreated
- Evaluations:** Baseline, 85 days  
Collagen, Biomarkers, Skin Firmness, Images

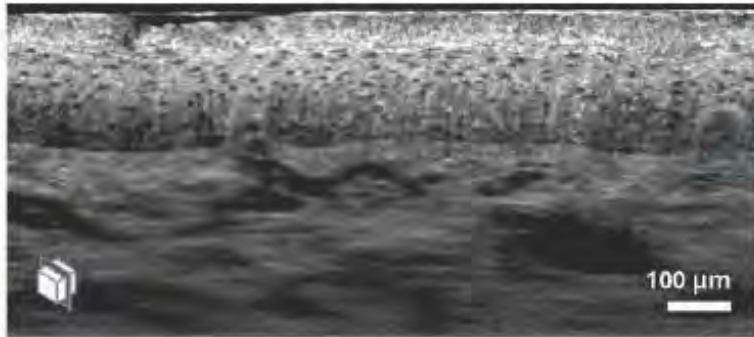




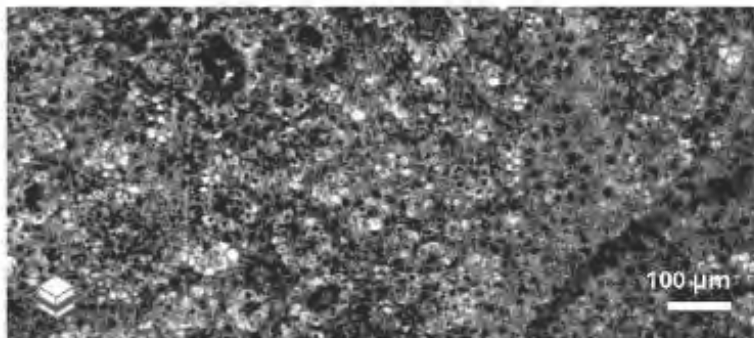


# LC-OCT (line-field confocal optical coherence tomography)

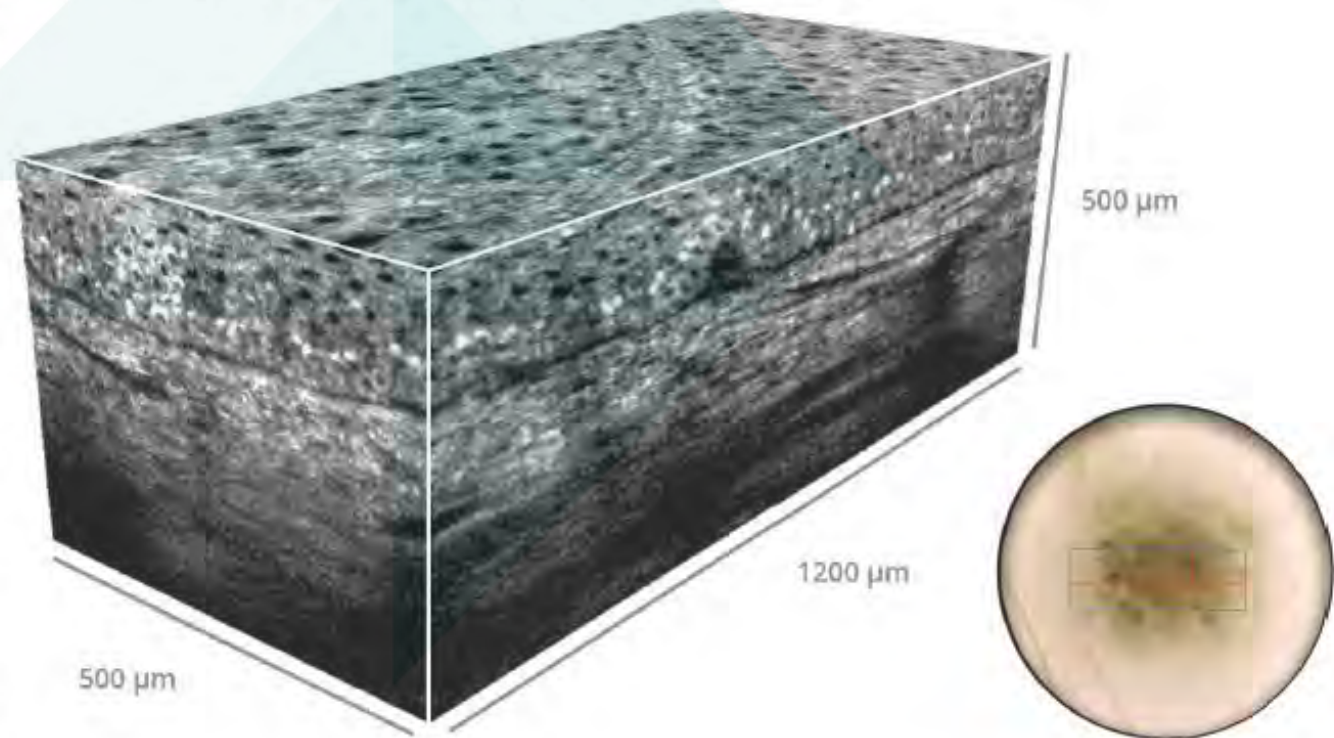
Vertical live mode



Horizontal live mode



3D stack with isotropic cellular resolution



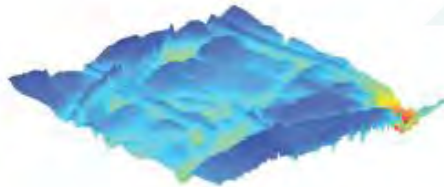


# What can be measured?

## SKIN LAYERS & DEJ

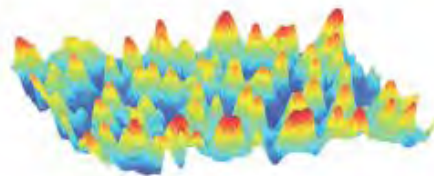
### SKIN LAYERS

*Thickness of  
Stratum Corneum,  
Stratum Spinosum,  
Superficial Dermis*



### DERMO-EPIDERMAL JUNCTION (DEJ)

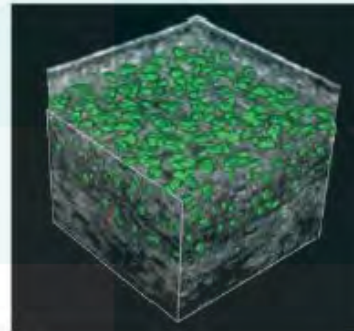
*DEJ & papillae  
morphology,  
size and distribution*



## CELLULAR

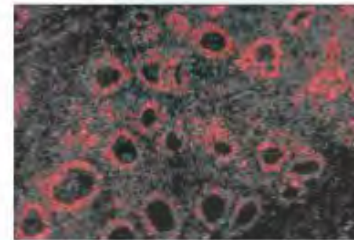
### KERATINOCYTES

*3D quantification  
of keratinocyte nuclei  
size and density*



### MELANIN

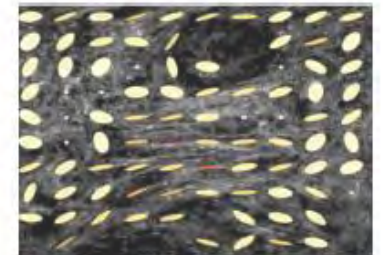
*3D quantification  
of melanin density  
and distribution*



## TISSULAR

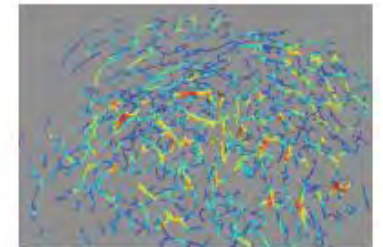
### COLLAGEN

*Collagen density  
Fiber orientation*



### BLOOD VESSELS

*Size of the vessels  
Vascularization  
organization*





# CBD in Wound Healing



# Current Models

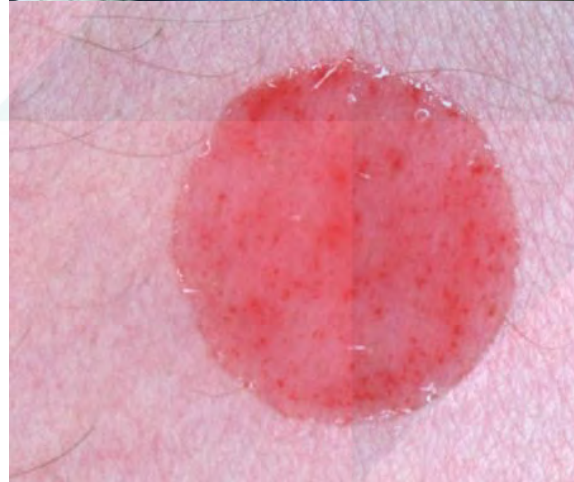
- Tape Stripping
- Scratches
- Razor Burn
- **Suction Blisters**
- **Abrasive Model**
- 1st Degree Burn
- Mini Incisions (bleeding time)
- Punch biopsies
- **CO2 Laser**



# Suction Blister, Abrasive and Laser Wounds



Suction Blister Induction



Abrasive Wound Induction



Laser Wound Induction

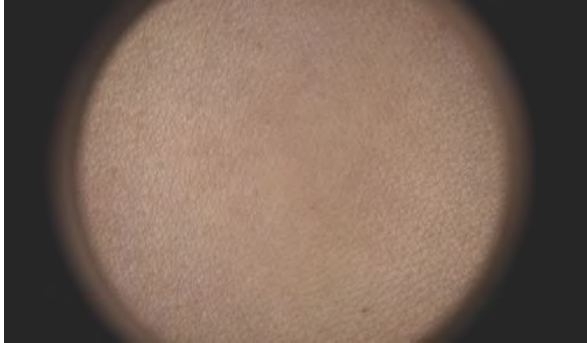


## Example Study

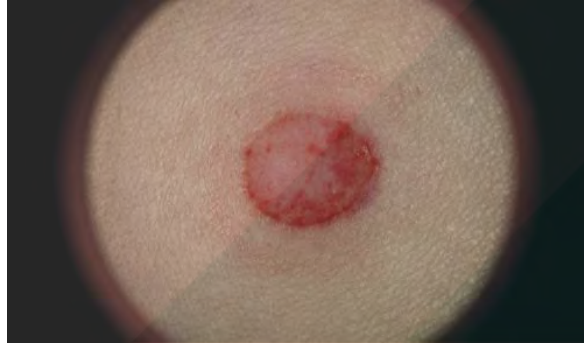
Subjects:	30 healthy volunteers, aged between 18 and 55 years
Duration:	22-29 days
Area:	volar forearm, 4 areas
Test Products:	Active, vehicle or untreated
Evaluations:	Days 1-6, 8, 10, 12, 15, 18, 22, (29) Wound area (determination on images), Skin barrier damage by TEWL, Pain, cosmetic outcome



# Suction Blister



Before



Day 1



Day 2



Day 4



Day 6



Day 8



Day 10



Day 14



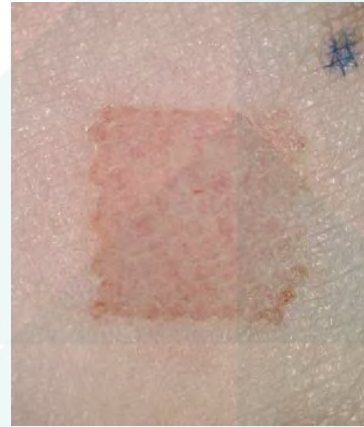
# Laser Model – Healing Process



Day 1 - Before Laser



Day 1 - After Laser



Day 2



Day 3



Day 4



Day 5



Day 6



Day 8



Day 10



Day 12





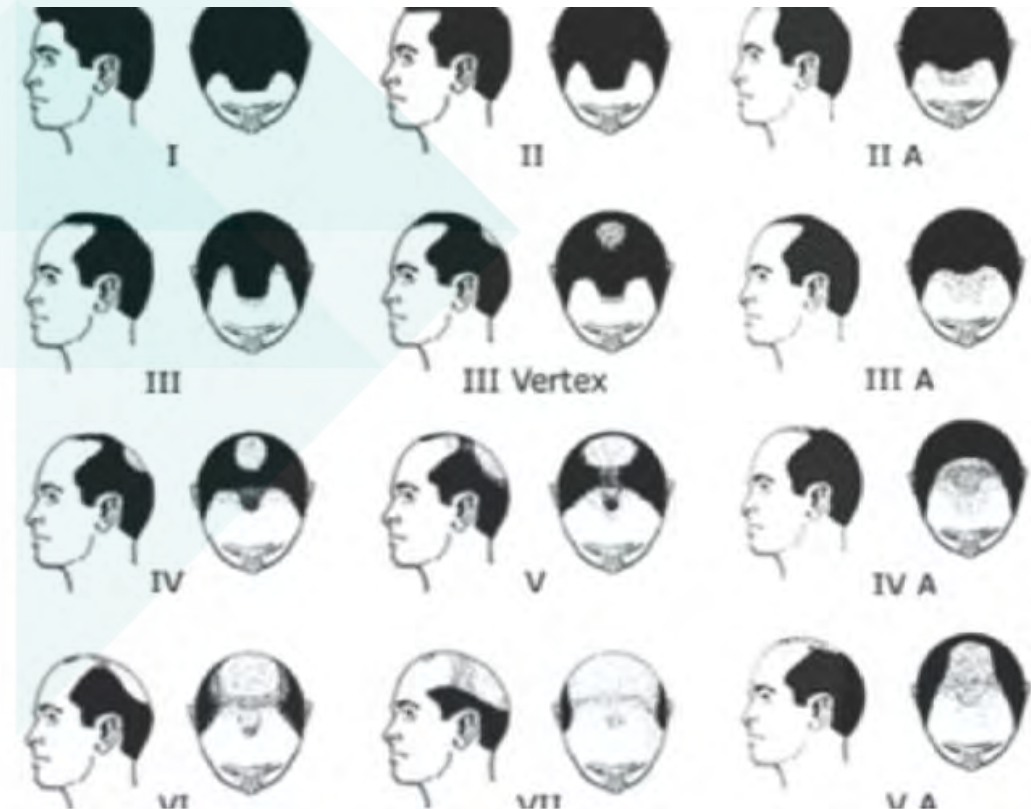
# CBD in Alopecia and Hair Growth Disorders

# Alopecia— Study Design



Inclusion according to norwood Hamilton Score (male) or Savin Score (female), Pull-test or according to self-estimation (weaker)

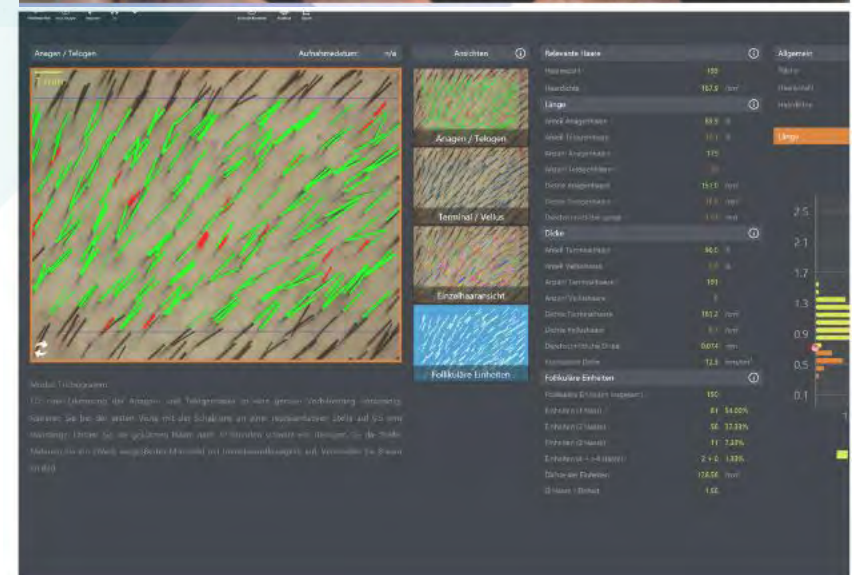
Evaluation over 4, better 6 months



# Phototrichogram method



Androgenetic alopecia and the use of the PTG-method in the proderm clinical research unit: image generation, hair clipping and a screenshot of a trichogram investigation



# Alopecia— Study Design



Inclusion according to norwood Hamilton Score (male) or Savin Score (female), Pull-test or according to self-estimation (weaker)

Evaluation over 4, better 6 months

Phototrichogram

Vertex images and subsequent rating by lay raters

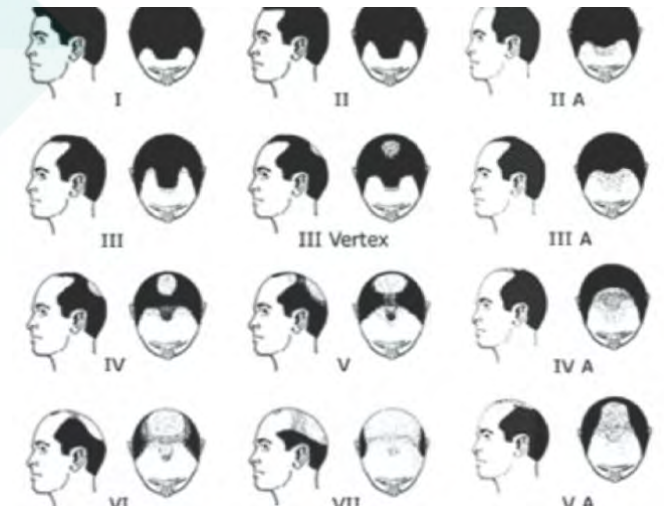
Combing, counting of combed-out hairs

Hair dresser's evaluation

Panelists' questionnaire

Biomarkers

QoL





## CBD in Oral Care

### Possible Claims:

- Reduces inflammation that can lead to gum diseases
- Attacks bacteria associated with tooth decay
- It helps fight bad breath
- Sensitivity relief
- Reduces risk of cavities
- Encourages tooth remineralizing
- Restores pH balance



# Example Study: Plaque

- Subjects:** 60 healthy volunteers, with moderate plaque
- Duration:** 29 days
- Area:** Mouth and Teeth, parallel groups
- Test Products:** Oral Care product, placebo
- Evaluations:** Days 1 and 29  
Plaque Index  
Gingival index  
Bacterial analysis of pathogenic strains  
option Microbiome





# CBD in Skin Disorders

- Atopic Dermatitis
- Allergic Contact Dermatitis
- Acne / Seborrhea
- Psoriasis
- Cutaneous lupus erythematosus



# Atopic Dermatitis

Example Study: Prone to Atopic Dermatitis

- Subjects:** 30 volunteers, with history of atopy (mild to moderate) with/without acute lesions
- Duration:** 29 days
- Area:** Lesional area
- Test Products:** Product, placebo
- Evaluations:** Days 1 and 29  
Hydration, Skin Barrier, (local) SCORAD, Images  
Option lipid composition (Lipbarvis, Raman, others), Single strains or Microbiome



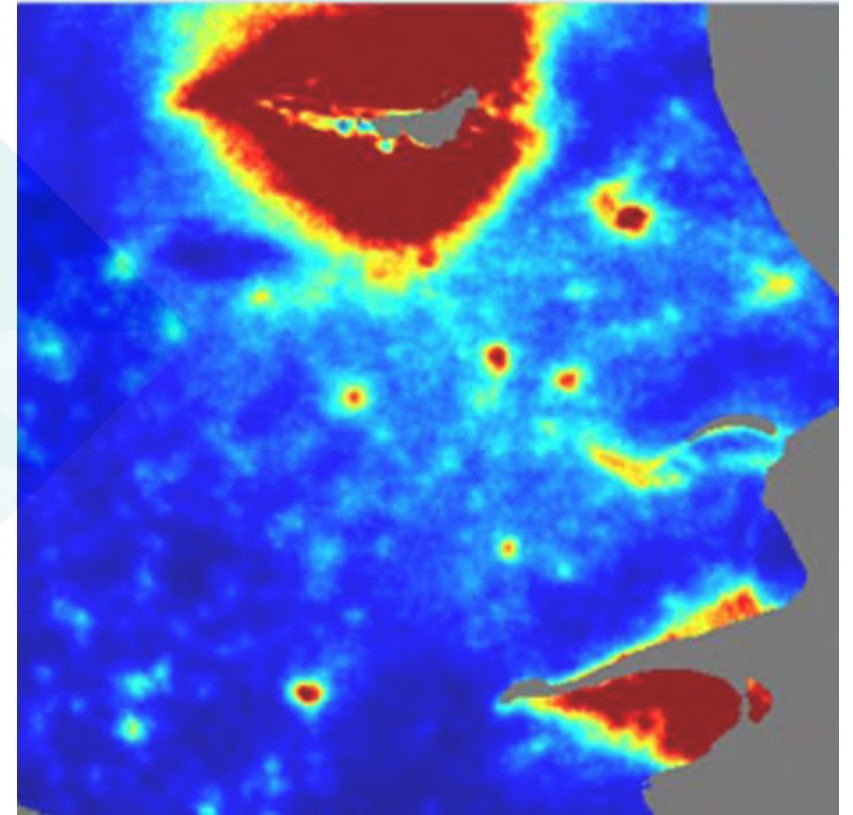




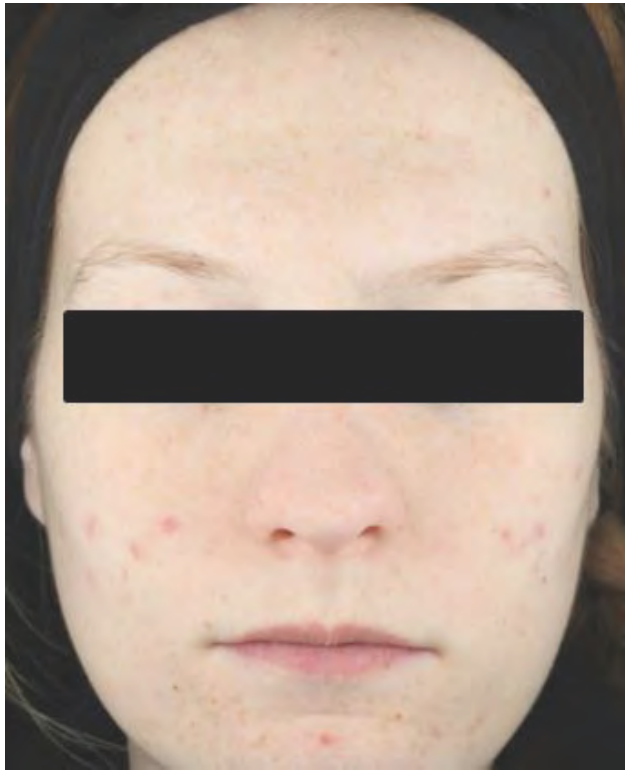
# Acne

Example Study: Prone to Acne

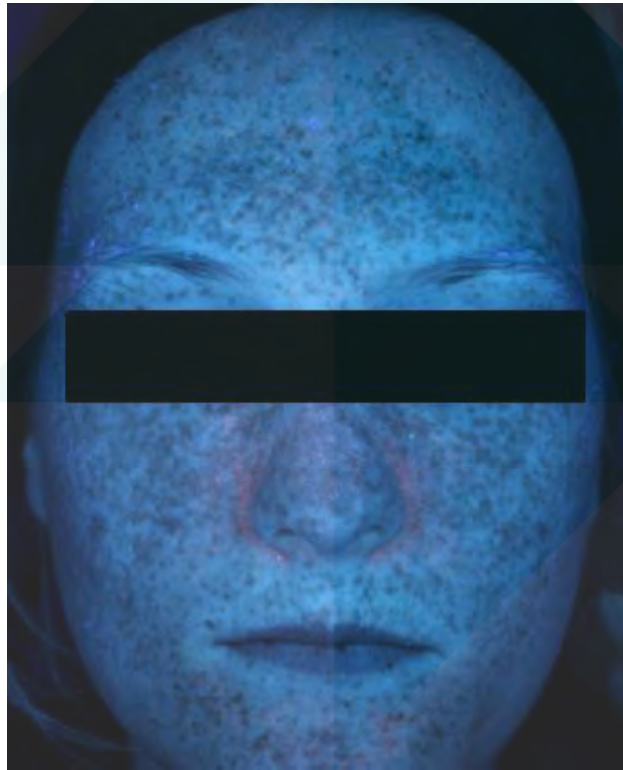
- Subjects:** 30 volunteers, with with minimum 3-4 inflammatory lesions per area
- Duration:** 57 days
- Area:** Split Face
- Test Products:** Product, placebo
- Evaluations:** Days 1 and 57  
Lesion Count, Tolerability, Questionnaire, Images  
Option Microbiome or single strains such as *C. acnes*, Skin temperature and skin blood flow, demodex, sebum levels and porphyrine



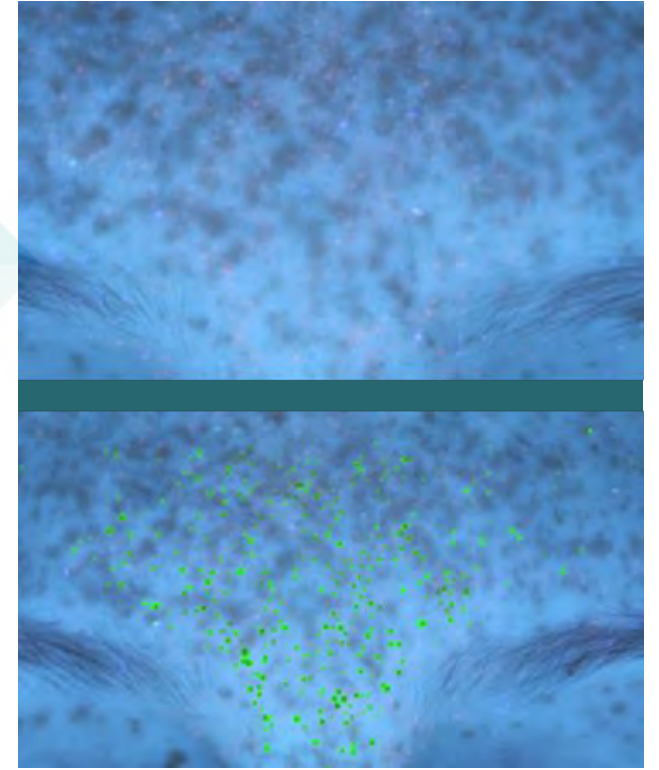
# Porphyria



Visia – standard image



Visia – UV image



Detailed magnification and detected spots by image analysis



# Psoriasis Use Test

## Example Study

**Subjects:** 30 volunteers, with a local PASI of at least 4

**Duration:** 29 days

**Area:** Lesional and non-lesional area

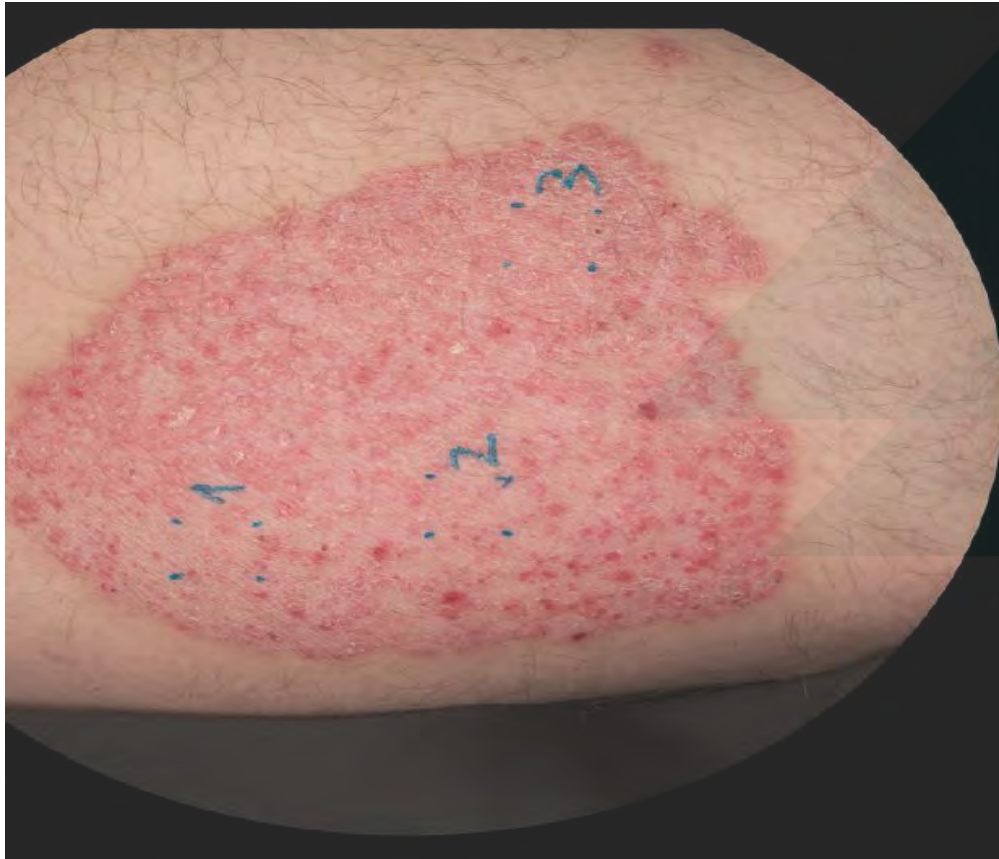
**Test Products:** Product, placebo

**Evaluations:** Days 1 and 57  
(local) PASI, Tolerability,  
Questionnaire, Images  
Option Redness, Skin Thickness (for  
infiltrate thickness)

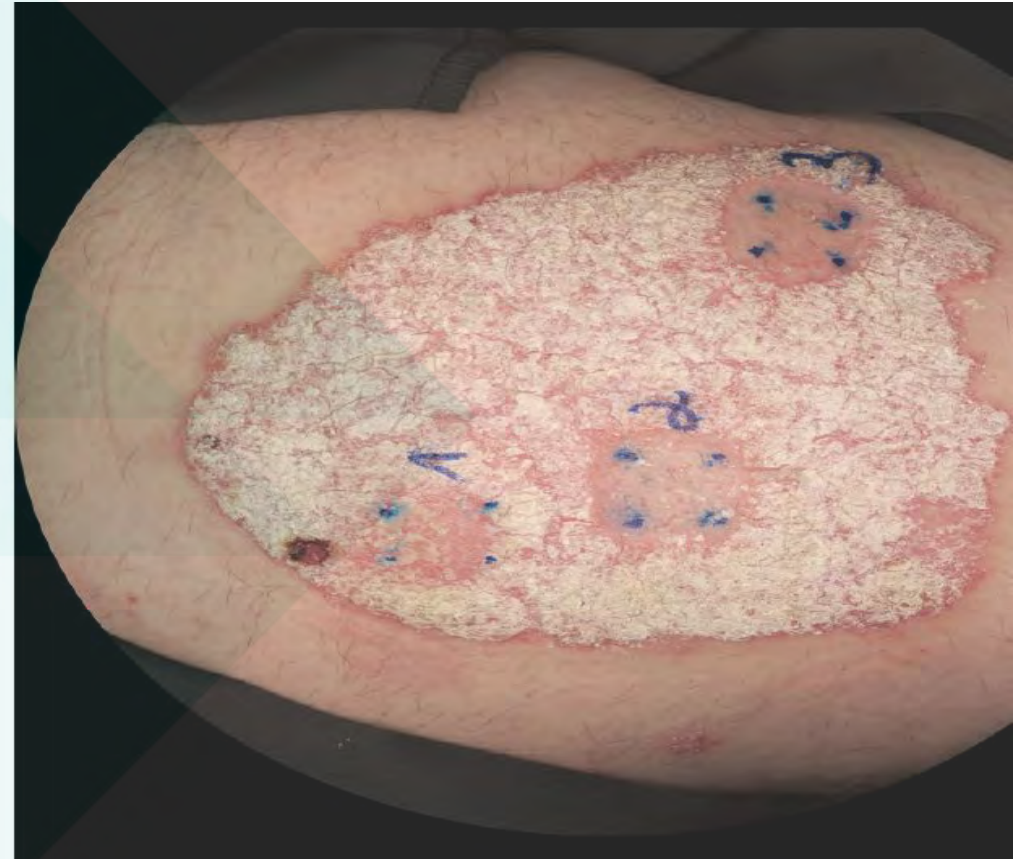




# Psoriasis Plaque Test



Day 1



Day 29



# Summary/Conclusion

- In EU and US it is legal to use CBD in cosmetics, if it comes from hemp or is synthetically derived
- THC content not higher than 0.2% of dry weight of the plant
- CBD has an influence on almost every cell type in the epidermis, which makes it so very interesting for topical applications:

## CBD Potential in Topical Applications

- Skin Protection / Barrier Function
  - Skin Inflammation/Soothing and Moisturizing
  - Pruritus or Itching
  - Pain Sensation and Muscle Relief
  - Aging
  - Wound Healing
  - Alopecia and Hair Growths Disorders
  - Skin or Hair Pigmentation
  - Antibacterial
  - Oral Care
  - Skin Disorders
    - Atopic Dermatitis
    - Allergic Contact Dermatitis
    - Acne / Seborrhea
    - Psoriasis
    - Cutaneous lupus erythematosus
- 
- More scientific studies are needed to prove the efficacy of CBD
  - But the cosmetic market is already growing

Thank you for your attention!

proderm 

Web: <https://www.proderm.de/en/>  
LinkedIn: <https://www.linkedin.com/company/proderm/>  
Contact: [gspringmann@proderm.de](mailto:gspringmann@proderm.de)  
[ksebald@proderm.de](mailto:ksebald@proderm.de)