BIODERMA

LABORATOIRE DERMATOLOGIQUE

UPDATES ON DERMATOLOGY

SENSITIVE SKIN

STÉPHANE FAUVERGHE
NAOS Medical Director

Edito

Dear All,

I am very pleased to present to you a new **BIODERMA Updates** dedicated to the latest advancements in Dermatology.

BIODERMA has regularly organised international events focused on Dermatology, aimed at dermatologists and all healthcare professionals interested in the field, always presented by renowned experts.

As part of our commitment to promoting the development of knowledge in Dermatology, we are pleased to offer you this new publication, which summarises the **BIODERMA Symposium** held during the European Academy of Dermatology and Venereology in Amsterdam in September 2024. The symposium was about **Sensitive Skin** and featured Brigitte Dréno from France, Joachim Fluhr from Germany, Laurent Misery from France and myself as speaker.

During the symposium:

- Laurent Misery presented on the **Impact of Sensitive Skin on Quality of Life** and the BoSS questionnaire.
- Joachim Fluhr provided an update on **Sensitive Skin and the Exposome**.
- Brigitte Dréno, our chair, delivered a lecture on **The Skin Microbiome: An Actor in Sensitive Skin**.
- Finally, I presented the **Positive Impact of SENSIBIO on Sensitive Skin**, showcasing the results of an international study.

I wish you all an enjoyable, enriching, and insightful read.

SCIENTIFIC PROGRAMME

SPEAKERS
SHORT BIOGRAPHIES

JOACHIM FLUHR
GERMANY

Update on sensitive skin and exposome

Joachim Fluhr is Professor of Dermatology, Head of the Institute of Allergology at the Charité Hospital from the University of Berlin, and Professor at the Fraunhofer Institute for Translational Medicine and Pharmacology Allergology.

Very involved in research, he is author of numerous publications.

LAURENT MISERY
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Impact on quality of life of sensitive skin: the BoSS questionnaire

Laurent Misery is Professor of Dermatology and Head of the Department of Dermatology at the University Hospital of Brest and of the French Expert Centre on Pruritus.

He founded and is the lead of the Laboratory on Interactions Neurons-Keratinocytes at the University of Brest and is President Elect of the European Society for Dermatology and Psychiatry (ESDaP).

Author of numerous peer-reviewed articles, he received the Herman Musaph Award in 2017.

Impact of sensitive skin on the quality of life: the BoSS questionnaire

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INTRODUCTION

The concept of sensitive skin has not been universally accepted when it was proposed for the first time, and has evolved over time.[1]
One of the first mentions of sensitive skin in a scientific publication dates back to 1947, in a study examining the role of soap as an irritant to sensitive skin[2]. More recently, a seminal paper by Maibach and co-authors established the existence of sensitive skin with a tendency to irritation, as assessed with biological methods.[3]

A widely accepted definition of skin sensitivity was developed in an expert position paper from the Special Interest Group on Sensitive Skin of the International Forum for the Study of Itch[4]: "***A syndrome defined by the occurrence of unpleasant sensations (stinging, burning, pain, pruritus, and tingling sensations) in response to stimuli that normally should not provoke such sensations. These unpleasant sensations cannot be explained by lesions attributable to any skin disease. The skin can appear normal or be accompanied by erythema. Sensitive skin can affect all body locations, especially the face***".

From a pathophysiological point of view, sensitive skin cannot be considered as an immunological disorder but rather a disorder of the nervous system at skin level, frequently associated to (but not determined by) abnormalities of the skin barrier.[5]

A specific tool to assess the burden of sensitive skin, the BoSS (Burden of Sensitive Skin) questionnaire, has been developed using a well-defined, rigorous methodology that includes the assessment of correlations with the severity of sensitive skin and the quality of life in 6,474 patients.[6] The validation phase involved the assessment of external validity in 4,614 patients with skin sensitivity ranging from slight to moderate, to very sensitive. The final validated version of the questionnaire contains 14 items (Figure 1) with 5 degrees (from never to always) and addresses three dimensions: personal care, daily life and appearance. The total BoSS score ranges from 0 to 56.

A cross-sectional study conducted in France evaluated the correlation between the BoSS score and the Sensitive Scale-10 (SS-10) score that is used to evaluate the severity of face skin sensitivity.[7] Severity of

the disorder can be considered as a continuum from non-sensitive skin to very sensitive skin; the French study aimed to define the optimal cut-off to diagnose sensitive skin with the SS-10. One hundred and sixty women aged from 18 to 65 years were recruited on a volunteer basis, and were asked to respond to a question regarding the severity of their sensitive symptoms on the face, and to fill in both the SS-10 and BoSS questionnaires. The receiver operating characteristic (ROC) curve revealed that a SS-10 cut-off value of 12.7 has good diagnostic ability to identify self-reported sensitive skin (sensitivity 72.4%, specificity 90.3%). In addition, **a positive correlation was observed between the BoSS score and the SS-10 score (0.567, *p*<0.0001)**, as is shown in Figure 2.[7]

Another study evaluated the BoSS score according to the self-reported facial skin sensitivity of 100 subjects.[8]

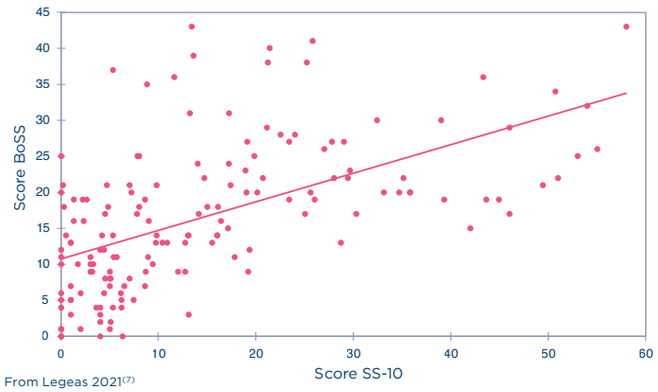
In this study, the average BoSS score was significantly higher in the self-reported sensitive skin group compared with the non-sensitive skin group (mean 25.61 *vs.* 14.05; $p< 0.001$). The authors also showed that the BoSS score was significantly higher in non-smokers than in smokers (mean 23.00 *vs.* 18.37; $p<0.05$), confirming the deleterious role of smoking in sensitive skin.

In the same study, the BoSS score was compared to a method that has been tentatively used for the objective diagnosis of sensitive skin: the assessment of current perception threshold (CPT).[8] To assess the CPT, varying electric stimuli are applied to the subject's skin using a Neurometer® (Neurotron Ltd, Baltimore, USA). Electric stimuli activate different types of nerve fibres, according to frequency: 5 Hz frequency activates the nerve fibre C, of which the main function is perception of pain and warmth; a 250 Hz stimulus activates the Aδ fibres, for perception of pain and cold; 2000 Hz frequency affects the Aβ fibres, which are responsible for touch. Measurement of the CPT is used for the detection of the affected type. **In a test conducted on both sides of the subjects' faces (n=200), CPT did not allow the detection of the presence or the absence of self-reported sensitive skin, while the BoSS score did. In addition, the CPT values were higher among smokers than non-smokers.[8]**

Figure 1. THE BoSS QUESTIONNAIRE for the evaluation of the burden of sensitive skin

	NEVER	RARELY	SOMETIMES	OFTEN	ALWAYS
I have to consider my sensitive skin when I buy my clothes and underwear					
I have to consider my sensitive skin when I buy cosmetics					
Having sensitive skin stops me from eating certain foods					
I have given up hobbias, outings and holidays because of my sensitive skin					
I find it hard to tolerate air conditioning because of my sensitive skin					
I find it hard to cope with urban pollution because of my sensitive skin					
Blushing for no reason or after I become emotional embarrasses me when I am with other people					
My face often looks very red in photographs so I avoid appearing in them					
It is impossible for me to wear jewellery (bracelets, neck chains or chain bracelets) that is not made of gold					
My face turns red when I exercise, walk quickly or climb stairs					
Wearing woollen clothes close to my skin is unbearable					
I have to consider my sensitive skin when I choose my clothes in the morning					
I have to choose my own washing powder because some washing powders can cause a skin reaction					
When I sleep away from home, I take my own soap and toiletries with me because I cannot use other people's					

Figure 2. Correlation between Sensitivity Scale 10 (SS-10) and Burden of Sensitive Skin questionnaire (BoSS) scores (n = 160)



From Legeas 2021[7]

IN CONCLUSION, the BoSS questionnaire, designed according to a rigorous methodology, is a useful tool to measure the burden of sensitive skin and performs better than a technique of objective detection (CPT). The BoSS score is significantly associated with the severity of sensitive skin, and ongoing studies will ascertain if it can be used as a diagnostic tool.

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Sensitive skin and exposome

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INTRODUCTION

Skin sensitivity has been described as "A syndrome defined by the occurrence of unpleasant sensations (stinging, burning, pain, pruritus, and tingling sensations) in response to stimuli that should not normally provoke such sensations. These unpleasant sensations cannot be explained by the lesions attributable to any skin disease. The skin can appear to be normal or can be accompanied by erythema. Sensitive skin can affect all body locations, especially the face". This widely accepted definition was developed using a 5-round Delphi process by the International Forum for the Study of Itch, and is reported in an expert position paper.[1]

The exposome can be defined as the totality of an individual's lifetime environmental and lifestyle exposures, both voluntary and involuntary, including pollutants, diet, stress, lifestyle, chemicals and encompasses all non-genetic influences. A comprehensive assessment of the exposome can complement genomic data to understand disease aetiology more fully, taking advantage of the methods of molecular epidemiology.[2] The scientific interest in studying the exposome in relation to the skin is demonstrated by the increasing number of papers retrieved from the PubMed database from 2011 to 2024, using the simple search string "skin AND exposome" (total n=129).

— Pathophysiology and risk factors —

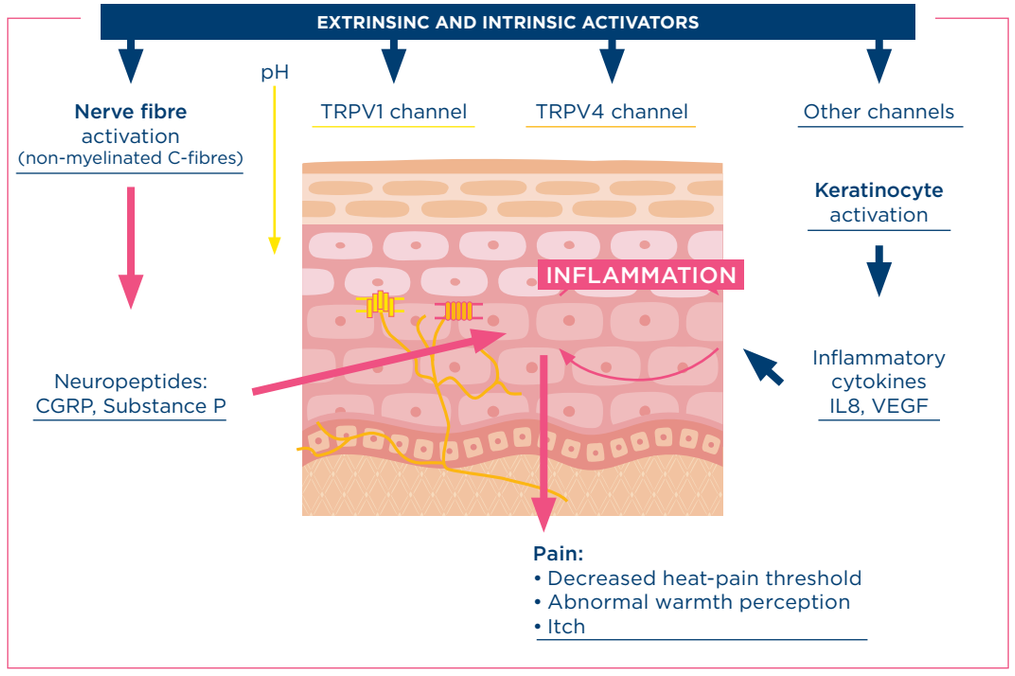
From a pathophysiological point of view, intolerant skin generally has a compromised skin barrier function that facilitates the penetration of potentially irritating molecules. When irritated, the skin reacts with keratinocyte inflammation, releasing pro-inflammatory mediators such as IL-8 or VEGF. In the case of sensitive skin, the irritating stimulus abnormally excites the skin's nerve fibres *via* activation of TRPV1 receptors, triggering both a nerve message of pain/discomfort and the release of specific neuromediators (CGRP, substance P). These neuromediators in turn act on the keratinocytes, creating a chronic inflammatory loop.[1, 3] **Extrinsic factors that may affect skin sensitivity include UV/IR light, climatic and seasonal factors, irritants and cosmetics, while intrinsic factors include impaired epidermal barrier function, small-fibre neuropathy, hormones, gender, psychological factors and possibly the presence of innate immune disorders.[4]** Both extrinsic and intrinsic factors activate TRPV1 and TRPV4 channels by a pH-dependent mechanism, causing nerve fibres to release inflammatory neuropeptides (CGRP, Substance P), ultimately leading to keratinocyte inflammation, as shown in Figure 1.[4]

— The skin barrier may also be involved —

In some patients, dysregulation of the epidermal barrier function and disruption of the crosstalk between cutaneous microbiota and immunity may lead to the development of skin disorders, such as dry, flaky or sensitive skin.[5] It has been shown that the amount of ceramides may be lower in sensitive than in non-sensitive skin (statistically significant), particularly in the most exposed areas of the body, such as the face and forearm.[6]

The triggering factors for sensitive skin were the subject of a systematic literature review and a meta-analysis, which included several studies from around the world.[7] The highest meta-odds ratio (mOR) was found for cosmetics, based on 6 studies (7.12, 95% CI 3.98 to 12.72).

Figure 1. Pathophysiology of sensitive skin: induction of inflammation and abnormal perceptions by nerve fibre and keratinocyte activation - from Misery *et al.* 2022[4]



As shown in Table 1, **several climatic factors showed statistically significant Odd Ratios (OR) ranging from 1.81 to 3.83: wet air, air conditioning, temperature variation, heat, water, pollution, dry air, cold, wind and sun. Finally, one personal factor, emotion, emerged as a statistically significant trigger for sensitive skin (OR 1.77).**

Recently, a Chinese study evaluated the association between airborne exposure and changes in body composition in 76 healthy adults aged 60 to 69 years, using a combined exposome-lipidome approach.[8] Exposures were measured by both questionnaire and personal detectors for a wide range of abiotic airborne exposures (particulate matter pollutants and chemicals, n=632), while outcomes included indicators of body composition and serum lipidomics. The study identified key pollutants, body composition indicators and lipid intermediators.

Table 1. Odds Ratios (OR) for triggering factors in sensitive skin - from Brenaut *et al.* 2020 [7]

Factor	OR	CI95	Number of studies	Number of subjects
Cosmetics	7.12	3.98-12.72	6	6969
Wet air	3.83	2.48-5.91	3	3533
Air conditioning	3.60	2.11-6.14	4	4500
Temperature variation	3.53	2.69-4.63	5	4931
Heat	3.50	2.56-4.77	5	4964
Water	3.46	2.82-4.25	4	4500
Pollution	3.18	2.37-4.27	4	4500
Dry Air	3.04	2.22-4.16	5	5539
Cold	2.73	1.94-3.84	5	4470
Wind	2.33	1.69-3.22	5	5539
Sun	1.81	1.61-2.04	5	8482
Emotion	1.77	1.44-2.17	5	8437

— Built Environment —

Several factors can affect sensitive skin in the built environment. They can be categorised into 5 classes[9]:

- **Demographic and socio-economic characteristics** (age, gender, and race);
- **Physiological and biological characteristics** (emotional changes, skin types, sleep disorders, and menstrual cycles);
- **Behavioural factors** (diet, cosmetic use, alcohol, and physical exercise);
- **Natural environmental features** (climate conditions and air pollution);
- **Built environmental features** (population density, availability of green space, density of road network, and access to public transport).

Key examples of built environment features that may affect sensitive skin include building characteristics, transport infrastructures, public spaces, utilities/services and land-use patterns.

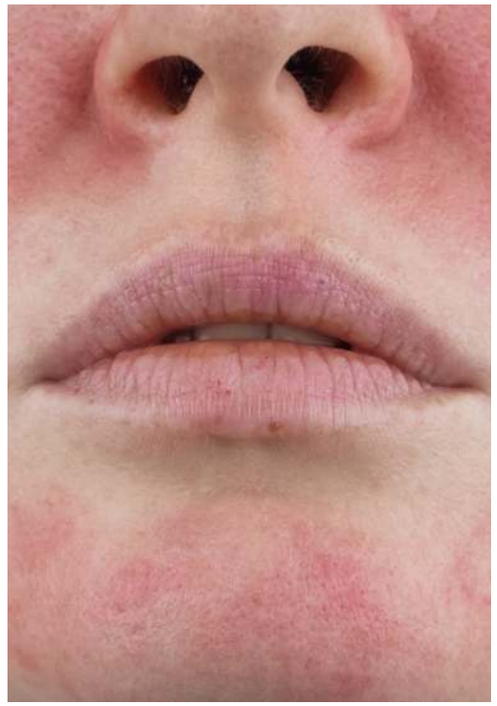
Sensitive skin can be seen as the result of interactions between individual characteristics and environmental factors. For example, population density may influence sensitive skin in several interrelated ways: high population density may lead to an increased risk of anxiety, which in turn is associated with a higher likelihood of developing sensitive skin.[9] High population density is often associated with exposure to PM 2.5, which can activate the skin inflammatory process *via* TNF-a and IL-1, trigger skin nerve fibre sensitivity and impede barrier repair. Finally, air pollution alone can cause anxiety and, consequently, sensitive skin.

In our department, we have an experimental chamber that allows us to study the effects of standardised double exposure to pollen and ozone. In a recent study, allergic patients were double exposed to grass pollen and ozone.[10] Nasal symptoms worsened when the second exposure was added to the first, with longer exposure having worse effects. The importance of the duration of double exposure was confirmed in another experiment where skin erythema increased in allergic patients but not in non-allergic individuals, especially after longer double exposure (p=0.04). Transepidermal water loss (TEWL), which is influenced by the lipid barrier, was increased after double exposure in allergic patients, but not in non-allergic individuals.[10]

In another study, we collected particulate matter (two different concentrations) from a busy street in Benin.[11] Pollutant extracts were administered to cultured reconstructed human epidermis (Episkin™, Lyon, France) and the supernatants were applied to a culture of sensory neurons. Viability of the nerve cells was not affected, indicating no direct toxicity. However, axonal growth was reduced and inflammatory neuromodulators, such as substance P, were released. In this study, air pollutants negatively affected both keratinocytes and sensory nerve endings, acting as inflammatory stimuli.

— Clinical implications —

Sensitive skin is frequently associated with other dermatological conditions such as acne, contact allergy, atopic dermatitis and



rosacea.[12,13] Influencing factors include food, cosmetics, pollen and drugs. Mites can also be involved: rosacea, for example, can be exacerbated by certain Demodex populations, in addition to blood flow and skin hydration.[14]

In a study assessing skin irritation thresholds, impaired epidermal barrier function was particularly pronounced in "stingers", *i.e.* in individuals with sensitive skin.[15]

Two recent studies have looked at mask-wearing as a provoking factor in rosacea with erythema and sensitive skin. In these studies, a specific cream (M89PF) was able to increase skin hydration and reduce sensitivity, erythema and TEWL, while usual skin care did not.[16]

There is an analogy in the aetiology of different skin diseases and conditions: **several intrinsic and extrinsic exposome factors that trigger sensitive skin are similar to drivers of squamous cell carcinoma, atopic dermatitis and skin ageing.**[17]

IN CONCLUSION, some practical advice can be provided to people with sensitive skin:

Firstly, it is advisable to avoid the vicious circle of sensitive skin as shown in Figure 1: minimise exposure to exposome stimuli that lead to toxic and irritating substances penetrating the skin barrier and triggering inflammatory and immune reactions.

Rehydration and restoration of a healthy skin barrier is recommended.

Secondly, to prevent irritation of sensitive skin, it is advisable to avoid exogenous skin damage from the sun and pollution, and to reduce psychological stress. Long, hot baths and standard soaps should also be avoided, while gentle, specific skin care is recommended.

Finally, the use of dermocosmetics that down-regulate the nervous system (especially the PAR-2 system) and soothe inflammation is very important.

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Positive impact of SENSIBIO on sensitive skin

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INTRODUCTION

BIODERMA has been developing unique expertise in sensitive skin for three decades, and continuously shared their knowledge with the scientific community. BIODERMA uses research results to develop specific skincare and cleansing products for sensitive skin, such as the products in the SENSIBIO line.

For each sensitive skin assessment of these products, the Burden of Sensitive Skin (BoSS) questionnaire published in 2018 was used.[1] The BoSS questionnaire has already been translated into 7 languages, with cross-cultural validation. Additional languages are progressively added. The goal is to be able to use this tool to assess the burden of sensitive skin in clinical trials around the world and to share this unique tool with more healthcare professionals globally.

In this spirit of knowledge sharing, BIODERMA has presented the BoSS questionnaire during many medical events over the years.

In 2021, it was introduced at the Journées Dermatologiques de Paris.[2] Clinical implications led to posters and oral presentations at the European Society for Dermatological Research Congress in Amsterdam in 2022, at the 25th World Congress of Dermatology in Singapore in 2023, and at the European Academy of Dermatology and Venereology in Amsterdam in 2024. In 2024, BIODERMA completed 8 studies on SENSIBIO products using the BoSS questionnaire in 5 European and Asian countries. These clinical trials enrolled more than 400 patients, expanding BIODERMA's expertise in sensitive skin across the globe to take account of different skin types and climates.

The environment and the entire exposome have an impact on the quality of life of people with sensitive skin.[3,4] Driven by the NAOS Ecobiology approach, BIODERMA continues to investigate these triggering factors in order to improve the design of their products.

To test the efficacy of the SENSIBIO product range on physical and chemical factors, 3 clinical studies were conducted under dermatological control, as shown in Figure 1.[5] The first study enrolled 22 women with self-reported sensitive skin, and used microcirculation imaging before and 30 minutes after stripping on the arm (to mimic abrasion and friction). In this open intra-individual study, application of SENSIBIO Cream reduced erythema by 16.2% compared to no treatment ($p<0.01$).

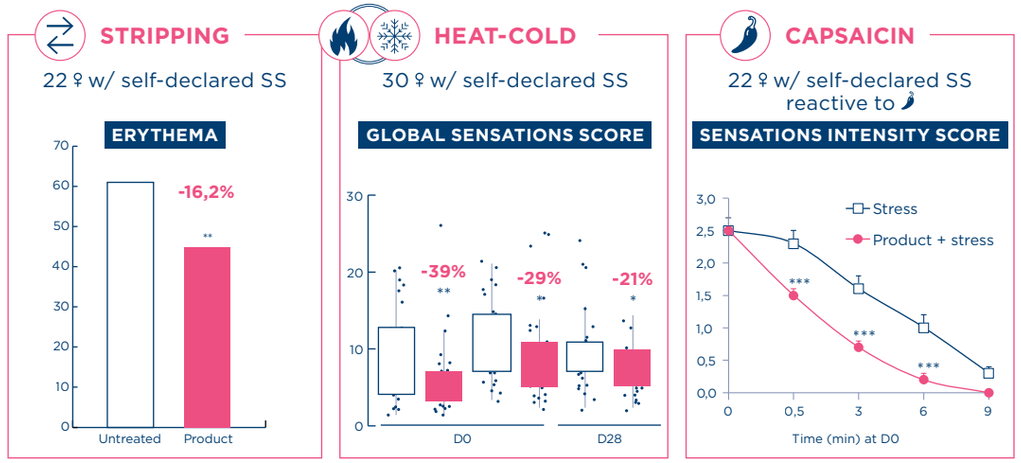
The second study was a randomised split-face study enrolling 30 women with self-reported sensitive skin. Heat/cold cycles monitored by a thermal camera mimicked thermal stress, a classic trigger for sensitive skin. Clinical evaluation was performed before and 28 days after application of SENSIBIO: the dermato-cosmetic cream showed both immediate and long-term efficacy in reducing the Global Sensation Score (statistically significant).

The third study was an open intra-individual study conducted on 22 women with self-reported sensitive skin reactive to capsaicin. Self-assessment before and after 28 days of application of SENSIBIO Cream showed a statistically significant reduction in sensation intensity and duration after capsaicin stress compared to control, from -43% at 30 seconds to -91% at 6 minutes.

All three studies demonstrated the efficacy of SENSIBIO Cream in providing significant protection against the unpleasant sensations associated with sensitive skin.

In addition, BIODERMA investigated the efficacy of the SENSIBIO product range in a global clinical analysis, beyond the triggering factors. Different populations from Poland and Thailand with different skin types from regions that differ in terms of culture, climate, ethnicity and the overall exposome were compared (Polena H *et al.*, submitted for publication).

Figure 1. Results of 3 clinical studies on sensitive skin trigger factors with SENSIBIO products[5] (Polena H *et al.*, J Cosmet Dermatol 2024)

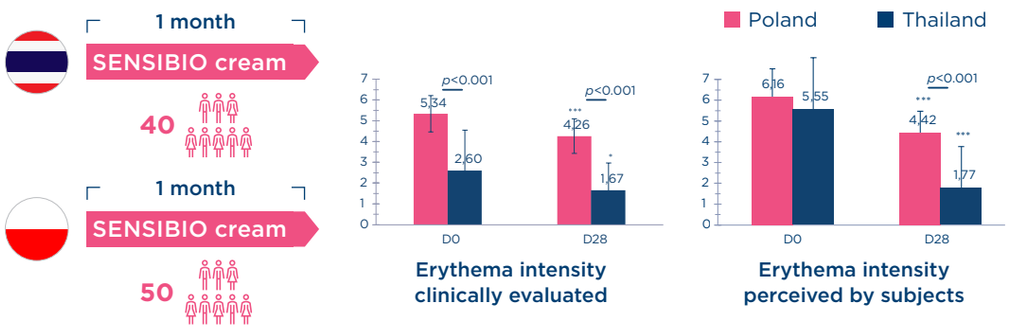


The Polish study was conducted from May 10, 2022 to January 17, 2023 by Ewa Chlebus and Monika Serafin; the Thai study was conducted from September 21, 2022 to January 18, 2023 by Waranya Boonchai, Pichanee Chaweekulrat and Silada Kanokrungsee. In both studies, subjects applied SENSIBIO Cream for 28 days and erythema intensity was assessed before and after application by both clinicians and subjects, as is shown in Figure 2. The subject-perceived erythema score was always higher than the investigator-rated redness score in both countries, and the difference was more pronounced in Thailand. At baseline, subject-perceived erythema intensity was not statistically different between Polish and Thai women, while clinician-rated erythema was twice as high in Polish women compared to Thai women. After 28 days of use of the SENSIBIO product, erythema statistically significantly improved in all subjects according to both self-assessment and clinical assessment, but remained higher in Polish than in Thai subjects (approximately +150%).

Regarding subjective sensation, Polish women had higher levels of erythema and higher BoSS scores related to visual signs than Thai women both at baseline and at 28 days (p<0.001). In addition, Thai volunteers reported higher levels of functional signs (tingling, pain and itching) and higher BoSS scores related to sensation (p<0.001). Overall, the reduction in functional signs after 28 days of SENSIBIO use ranged from 64% to 96% (statistically significant).

In the Polish arm, the efficacy of SENSIBIO was also compared to a neutral cream with a basic formulation. With SENSIBIO, the stinging sensation was reduced by 53% after 28 days of use and by 91% after 56 days, while the global BoSS score was reduced by 20% and 30%, respectively. Use of the neutral cream also resulted in slight improvements: -27% and -47% for stinging sensations and -6% and -11% in the global BoSS score after one and two months, respectively. The performance of SENSIBIO was statistically significantly better than that of the neutral cream, indicating that the benefit was not due to general cosmetic parameters such as hydration or barrier repair, but rather that the SENSIBIO product specifically addressed sensitive skin problems.

Figure 2. **Design and main results of an international clinical study comparing the efficacy of SENSIBIO cream in Polish and Thai women with sensitive skin. (Polena H *et al.*, in review)**

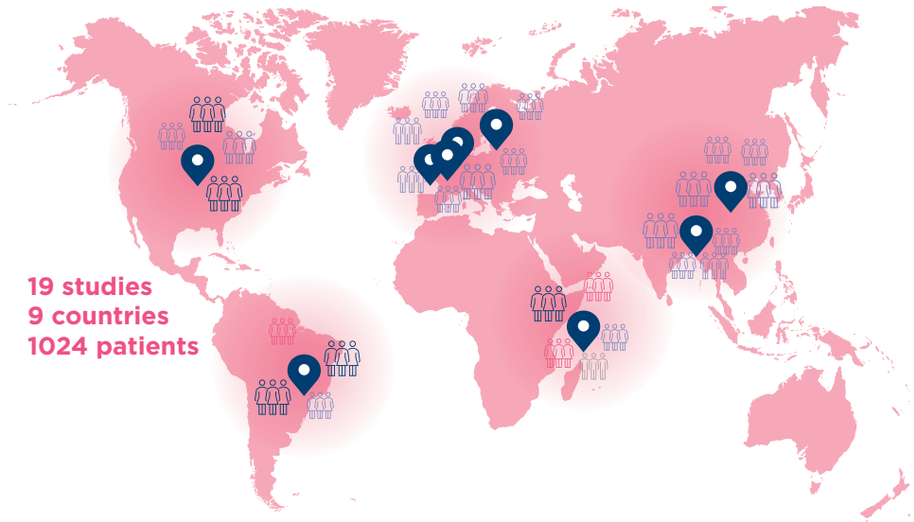


BIODERMA's journey into clinical research on sensitive skin continues. In 2025, results will be available for no less than 19 clinical studies in 9 countries on 4 continents, enrolling more than a thousand patients of all skin types and phototypes from different cultures and climates (Figure 3).

IN CONCLUSION, SENSIBIO products are tested in real life conditions with clinical expertise, in collaboration with dermatologists. The main objective of BIODERMA is to improve the quality of life of patients, not just to treat symptoms, by developing innovative products with an ecobiological approach.

Ecobiology comes from ecosystem + biology. On the ecosystem side, healthy skin and natural mechanisms are the first model. BIODERMA promotes the respect of the skin's dynamic ecosystem, made up of living cells that interact with each other and with their environment.
Moreover, BIODERMA favours biomimetic ingredients to develop effective and sustainable solutions. BIODERMA acts on natural mechanisms to help and support the skin to adapt and regain its own balance, making the root causes of problems top priority in order to provide lasting solutions before visible signs appear.

Figure 3. **BIODERMA ongoing studies on sensitive skin up to 2025**



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NAOS ECOBIOLOGY

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