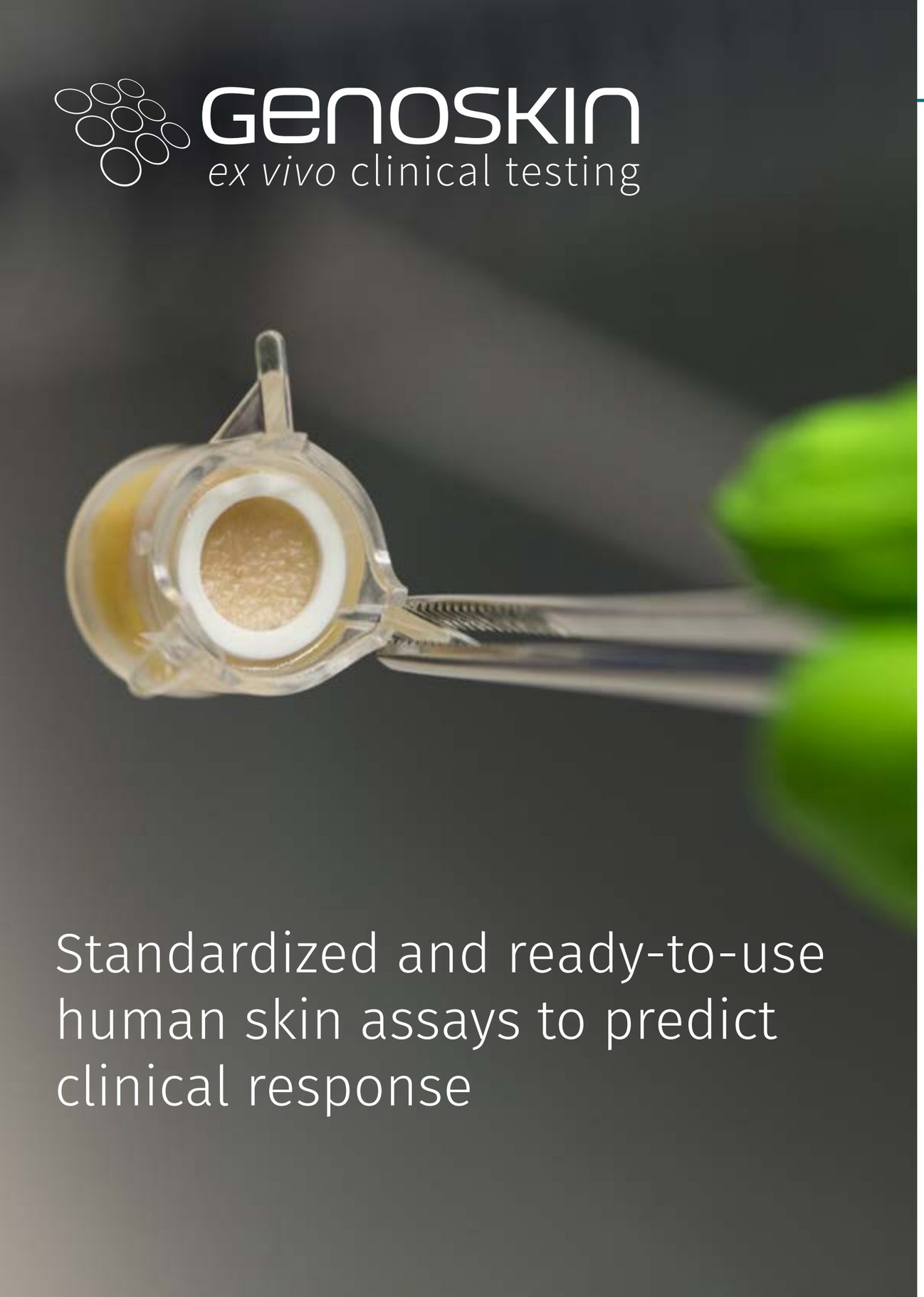
GENOSKIN

ex vivo clinical testing

NativeSkin®
NativeSkin® Access

User manual

Live and standardized
human skin assays



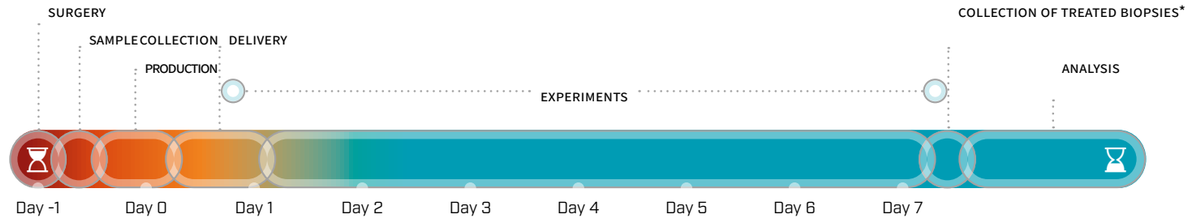
Product description

USING HUMAN SKIN TO BETTER PREDICT SKIN RESPONSE TO TREATMENT

Genoskin works in close collaboration with hospitals and clinics in France and in the United States to efficiently collect human skin samples from healthy donors, immediately after plastic surgery. Our unique, patented and standardized technology maintains donated human skin biopsies alive for up to seven days to enable efficacy and safety testing of your products on real, live human skin.
Skin samples are obtained with the donors' informed consent and are in full compliance with the Declaration of Helsinki and all other applicable regulations. For each skin sample collected, the serum of the donor is tested for the absence of HIV-1 and -2, and Hepatitis B and C. Genoskin is ISO 9001:2015 certified.

TYPICAL WORKFLOW

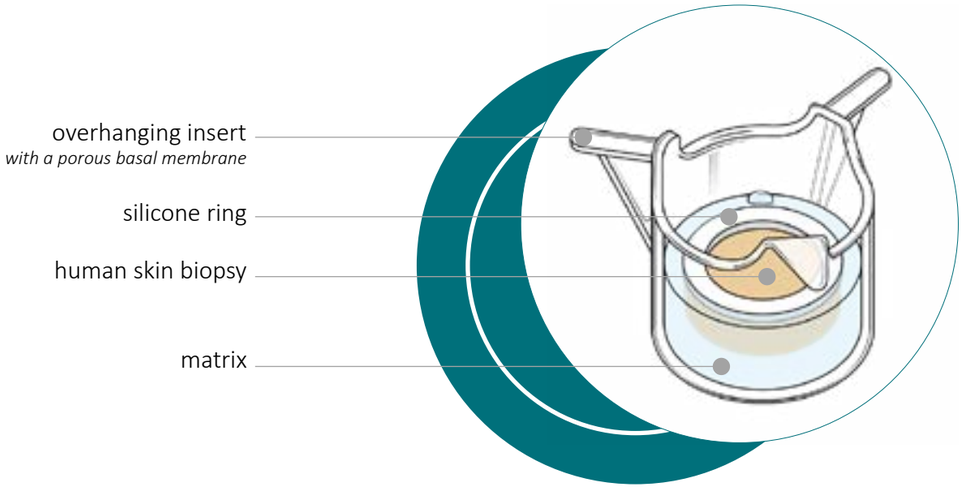
Genoskin collects the samples required for production just after surgery.
All the samples needed are stored at room temperature until production starts (less than 24 hours after surgery).
As soon as production is completed, Genoskin kits are shipped to the customer. Orders are usually delivered Wednesdays to Fridays.



** Biopsies might be collected at any time point within the 7 days of culture.*

NativeSkin®

Live and immunocompetent human skin



REAL HUMAN SKIN STRUCTURE

NativeSkin® testing kits contain round skin biopsies prepared from surgical residue from volunteering adult donors.

NativeSkin® models exhibit normal skin barrier function and a mature stratum corneum. They hold all cell types and skin appendages that are naturally present in *in vivo* human skin.

LIVE HUMAN SKIN RESPONSE

To allow for repeated applications, the skin biopsies are embedded in a proprietary, solid matrix that nourishes the skin and keeps it alive for *ex vivo* culture.

After several days of culture, NativeSkin® models still maintain the normal histological structure of *in vivo* human skin.

READY. EASY. STANDARDIZED.

NativeSkin® is designed as a ready-to-use kit to simplify your testing procedures. The models allow for fast, reliable studies and assays with reproducible results.

NativeSkin® models are easy to manipulate using forceps. The matrix firmly maintains the skin biopsy into the cell culture insert. Genoskin produces NativeSkin® models according to a very strict manufacturing process that is entirely standardized.

ADAPTED TO YOUR NEEDS

To mimic topical or systemic applications, you can choose to apply your compound either on the skin surface or in the culture medium.

A silicone ring is firmly fixed onto the biopsy to prevent topically applied formulations from leaking into the culture medium.

NativeSkin® comes in different sizes and formats to answer all your study and assay requirements.

NativeSkin® - NSA11

NATIVESKIN® ACCESS

REFERENCE	DESCRIPTION	WORKING SURFACE	Ø	RECOMMENDED TOPICAL VOLUME	*EX VIVO* CULTURE DURATION	PLATE FORMAT	REQUIRED VOLUME OF MEDIUM / DAY	MINIMUM ORDER
NSA08	NativeSkin® Access (no silicone ring)	-	8 mm	-	7 days	12 wells	1 mL	n.a.
NSA11	NativeSkin® Access	0.5 cm^2	11 mm	5-20 µL	7 days	12 wells	1 mL	n.a.

NATIVESKIN® CUSTOM

REFERENCE	DESCRIPTION	WORKING SURFACE	Ø	RECOMMENDEDTOPI-CAL VOLUME	*EX VIVO* CULTURE DURATION	PLATE FORMAT	REQUIRED VOLUME OF MEDIUM / DAY	MINIMUM ORDER
NS004	NativeSkin® Medium	1.13 cm^2	15 mm	25-45 µL	7 days	6 wells	2 mL	12 wells
NS005	NativeSkin® Large	1.76 cm^2	20 mm	50-70 µL	7 days	6 wells	2 mL	12 wells
NS006	NativeSkin® XL	2.54 cm^2	23 mm	100-200 µL	5 days	6 wells	3 mL	12 wells

Get started

KIT CONTENT

Genoskin models are supplied as ready-to-use kits. They are packed in a specifically designed box that can be shipped by express airfreight.

Every kit contains:

- The required amount of models, which are presented in individual inserts for a 6 or 12-well plate. The inserts are loaded in a transport plate covered by a lid. Every skin biopsy is firmly maintained in our proprietary matrix within the insert.
- The required volume of culture medium to maintain the biopsies alive (storage 4°C).
- A QA/QC lot release certificate with donor information (age, gender, skin type).

Should you encounter any abnormalities on receipt, please call us or send an email to: contact@genoskin.com.

OTHER MATERIALS REQUIRED*

For the culture and systemic administration:

- Class II biological safety cabinet
- Incubator (37 °C, 5 % CO_2, 95 % humidity)
- Water bath (37 °C)
- Micro-Pipettor (sterile)
- Pipette tips (sterile)

For topical administration:

- Pair of forceps (sterile)
- Positive displacement pipette for semisolid materials
- Mortar with pestle for solid materials
- Sharp spoon for solid materials

** Not provided by Genoskin.*

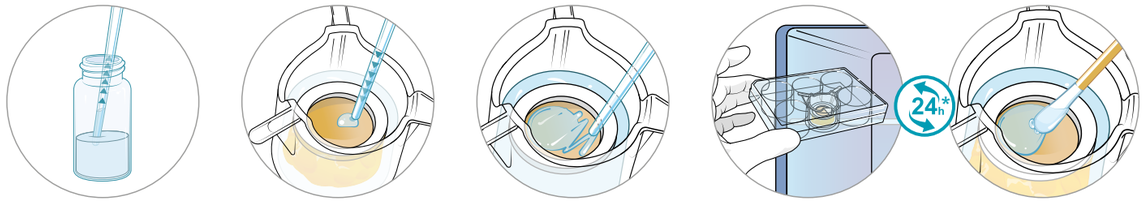
PREPARATION ON RECEIPT

Always check the kit for completeness and potential transport damages immediately upon receipt.
Before handling the skin biopsies, please follow the instructions below:

1. Take the transport plate containing the models to a sterile room. Under sterile conditions, remove the plastic film from the NativeSkin® transport plate and open the culture dish.
2. Use a pipette to add the required volume of culture medium (at room temperature) to each well according to the volume indicated in the table on p. 5 for NativeSkin®
3. Check that no bubbles are present beneath the porous membrane of the insert when the culture medium is added.
4. Incubate the culture dish for at least 1 hour at 37 °C, 5 % CO_2, and 95 % relative humidity before performing the first experiment. It is also possible to incubate overnight, in which case, the culture medium needs to be changed before administrating any compounds, products, or formulas.
5. Follow the procedure:
   - for topical administration: p. 7 A
   - for systemic administration: p. 7 B
6. Cultivate the skin models in an incubator (37 °C, 5 % CO_2, 95 % humidity) for up to 7 days by renewing the medium every day.
7. Change the culture medium daily, by aspirating the medium and replacing it by new culture medium (at room temperature) for each well.

How to administrate your compound

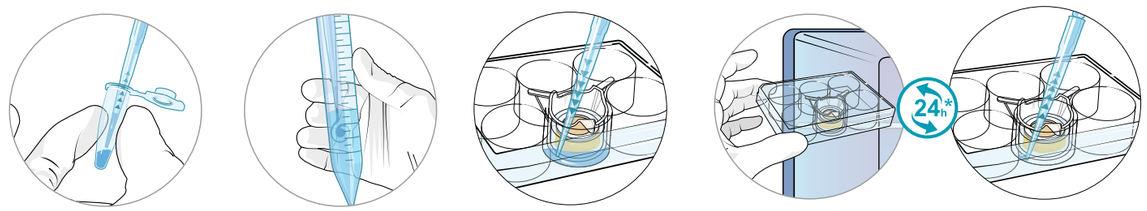
A TOPICAL ADMINISTRATION



1. Collect the desired volume of formulation.
2. Apply the formulation directly on the skin surface.
3. Spread the formulation homogeneously with the tip.
4. Put the plate in the CO_2 incubator at 37°C.
5. After incubation remove any excess formulation.

** Time is dependent on the experiment.*

B SYSTEMIC ADMINISTRATION



1. Collect the desired volume of compound.
2. Dilute your compound in the required volume of medium.
3. Dispense this solution in the well.
4. Put the plate in the CO_2 incubator at 37°C.
5. After incubation remove the medium.

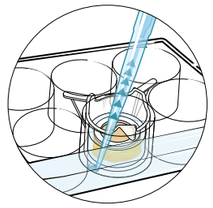
RELEVANT APPLICATIONS FOR NATIVESKIN®

Skin explant culture has a long tradition in investigative dermatology. It is used to conduct *in vitro* studies on the physiology and pathophysiology of human skin and its epidermal appendages.

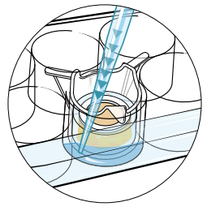
NativeSkin® is relevant for the following applications:

- Efficacy testing
- Topical applications
- Dermal studies
- Epidermal studies
- Percutaneous absorption
- Metabolism
- Repeated dose assay
- Langerhans cells studies
- Skin resident T cells studies
- Immune response
- Melanogenesis
- Melanocyte studies

How to cultivate



1 Remove the culture medium from the well.

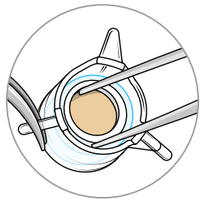


2 Add fresh culture medium into the well.

3 Put the plate in the CO_2 incubator at 37°C.

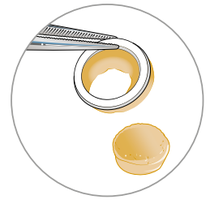
Skin models can be cultivated for up to 7 days.

How to collect NativeSkin®



1 Use forceps to grip the edge of the skin biopsy while you hold the insert with another pair of forceps.

2 Remove the skin biopsy from the transparent jellified matrix. If the matrix adheres to the skin biopsy, use forceps to gently detach it from the tissue.



3 Use a skin puncher of 8 mm in diameter to punch out the part of the skin biopsy inside the silicone ring. NativeSkin® that do not have silicone rings do not require this step.

4 Use forceps to grip the skin biopsy and cut the skin tissue in two parts using scissors. Process the two samples as required, e.g. fix one part in formalin and snap freeze the other part.

We recommend not to include the part of the skin that is covered by the silicone ring in your analysis.

APPROVED PROTOCOLS FOR NATIVESKIN® ANALYSIS

To analyze the effects of your compound on NativeSkin® models, Genoskin has designed and approved several protocols:

- MTT-based cell viability assay
- Formaldehyde fixation for paraffin embedding
- Epidermal separation with Dispase
- Immunofluorescence
- ELISA
- RNA extraction
- Protein extraction

References

De Wever B., Kurdykowski S., and Descargues P., Human Skin Models for Research Applications in Pharmacology and Toxicology: Introducing NativeSkin, the “Missing Link” Bridging Cell Culture and/or Reconstructed Skin Models and Human Clinical Testing. Applied *in vitro* Toxicology. 1 : 26-32, (2015).

Duracher L.,Visdal-Johnsen L., Kurdykowski S., Descargues P. and Mavon A., A Novel Explant Model for Skin Delivery Assessment, Cosmetics & Toileteries. 130: 30-40, (2015).

Norsgaard H, Kurdykowski S, Descargues P, Gonzalez T, Marstrand T, Dünstl G, Røpke M. Calcipotriol counteracts betamethasone-induced decrease in extracellular matrix components related to skin atrophy. Arch Dermatol Res. 306: 719-29 (2014).

A wide range of human skin models

NativeSkin® *Ex vivo* human skin biopsies (epidermis & dermis) in a ready-to-use format.

HypoSkin® *Ex vivo* human skin biopsies with adipose tissue for subcutaneous injection, topical and systemic administration.

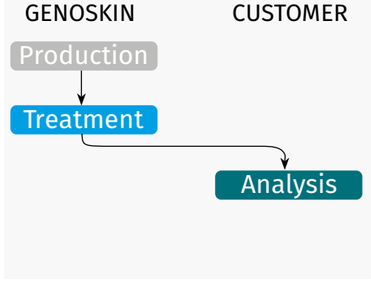
HairSkin® *Ex vivo* human skin biopsies from normal human scalp.
This model is avaibale only as an in-house service.

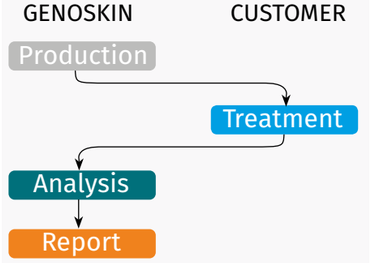
InflammaSkin® *Ex vivo* human skin biopsies with an induced Th17/Th1 psoriasis-like phenotype.
This model is avaibale only as an in-house service.

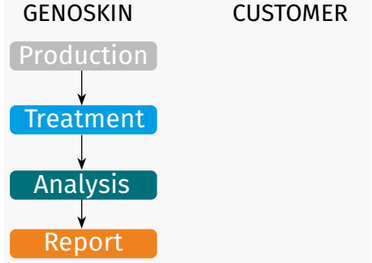
WoundSkin® Ex vivo human skin biopsies with a wound, suited to assess the efficacy of wound-healing formulations.

Services that fit your needs

Genoskin provides custom preclinical R&D services that fit your needs:



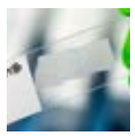




Please contact our expert team if you wish to develop a new model or have a custom need.

Suited tools for various studies

FrozenSkin® Frozen sheets of human skin for absorption studies with Franz cell diffusion chambers.



HistoSkin® Formalin-fixed paraffin-embedded human skin sections for histological analysis through staining, immuno-staining and immunofluorescence.

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