Innovative Dermatological Assessments For Early Drug Development

Our dermatology studies provide results that are more than skin deep. Because the skin is the largest and most easily accessible organ, our dermatology research also facilitates drug development in other areas, including immunology and endocrinology. In addition, we are engaged in studying ways to improve wound healing.

Highlights

- CHDR conducts clinical trials in dermatology in order to study targeted drug delivery and treatment of a wide range of dermatological conditions, including psoriasis, eczema, and premalignant lesions.
- Most of our dermatology trials use Trial@home, CHDR's unique approach to outpatient research.
- Topical application of the study compound can take place transdermally, intradermally, or subcutaneously, and we can study both local pharmacokinetics and the compound's effects on the skin.
- Our customised, user-friendly apps for smartphones and tablets ensure patient compliance and help researchers monitor the lesion and the patient's daily activities.

Summary

In the field of dermatology, CHDR has developed a unique approach to early-stage drug development by combining outpatient trials with innovative new measurement techniques. Although patients come to our facility for selection and follow-up visits, the trial itself takes place off-site, with the patients at home, going about their daily activities.

We are committed to helping meet the needs of dermatology patients everywhere. At CHDR, we conduct clinical phase I/IIa trials for pharmaceuticals, medical devices, cosmetics, food supplements and consumer products. We are able to offer a range of techniques depending on study requirements, including:

- Psoriasis plaque test
- Vasoconstriction test / blanching
- UV erythema model
- Histamine challenge
- Barrier function assessment including lipid profiling
- Systemic absorption and pharmacokinetics
- Dermal tolerability and sensitisation potential of transdermals
- Circulating and ex vivo stimulated biomarkers

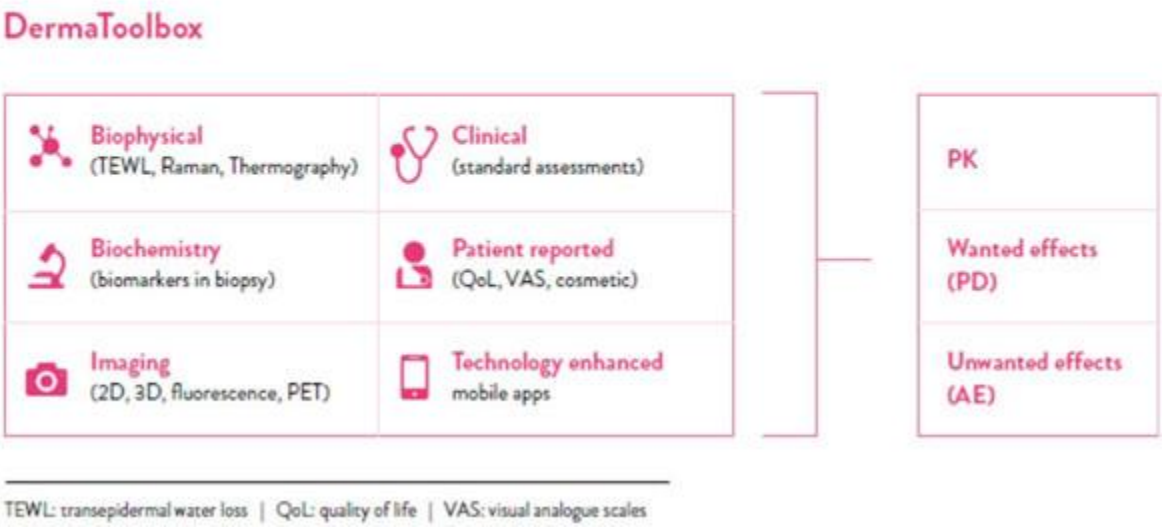
Objective measurement of skin lesions using DermaToolbox

In addition to measuring the patient's subjective experience (e.g. pain, discomfort, and ease of application), objective measurements also play a key role in assessing the effects of a new dermatological treatment. Therefore, we combined several robust techniques commonly used for dermatology research to create DermaToolbox, a comprehensive set of objective measurements and instruments used to systematically quantify subjective symptoms.

In addition to conventional clinical photography, DermaToolbox uses high-definition 3D photography to measure the lesion's dimensions, properties, and surface features. This powerful method – which was originally developed for use in the cosmetics industry – has quickly become an extremely valuable tool for

studying dermatological conditions. DermaToolbox also includes a wide variety of methods for objectively measuring the compound's effects on the skin, including transepidermal water loss, lipid profiling, colourimetry, and laser Doppler imaging. In addition, our Biomarker group can develop biomarkers to address specific research questions.

DermaToolbox at a glance



TEWL: transepidermal water loss | QoL: quality of life | VAS: visual analogue scales

Pharmacological challenges in skin research

Challenge	Condition induced/mimicked	Application
Capsaicin	Erythema, hyperemia	Pain assessment
Histamine	Dose-dependent 'wheal and flare' reaction	Assess the potency and duration histamine receptor antagonists or anti-inflammatory drugs
Mechanical (tape strip/shaving)	Removal of the stratum corneum and hair	Induce local inflammation, increase drug delivery
UVB irradiation	Erythema	Pain assessment, skin sensitisation
TLR7 agonist (e.g. imiquimod)	Local inflammation	Assess the effect of anti-inflammatory compounds
PAC1 receptor agonist (e.g. maxadilan)	Local inflammation	Assess the effect of PAC1 receptor antagonists
LPS/SEB challenge	Local TLR challenge	Inflammatory response/inflammasome activation

LPS, lipopolysaccharide; PAC1 receptor, pituitary adenylate cyclase-activating polypeptide type I receptor; TLR, toll like receptor; SEB, Staphylococcus aureus enterotoxin- B; UVB, ultraviolet B

Table 2: Pharmacological challenges in skin research

Practical answers to important research questions

Does our compound treat the targeted skin condition?

Early in drug development, CHDR can collect a wealth of data regarding the compound's intended and/or unintended effects, even in healthy subjects. This data-intensive approach facilitates rational decision-making regarding the course of drug development. In dermatology, we derive robust predictors of clinical efficiency through the use of 3D photography, total body mapping of skin lesions, objective lesion quantification and other innovative measurements.

How well is the compound absorbed, and how is it eliminated?

Pharmacokinetics is one of our main areas of expertise, and CHDR researchers study systemic absorption in the initial clinical phases of drug development. This proactive approach allows researchers to minimise the risk of adverse systemic effects in subsequent trials, which is particularly important when patients apply the compound at home.

Does our compound have anti-inflammatory properties?

In recent years, CHDR has selected and validated a comprehensive panel of biomarkers for measuring inflammation ex vivo. In addition, we have developed several pharmacological and mechanical challenge models to study inflammation. Using these approaches, we can measure the effects of both systemic and topical drugs for allergy and/or inflammation in healthy volunteers.