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# Development of skin inflammation model in healthy volunteers

| Submission date | Recruitment status | [_] Prospectively registered |
|---|---|---|
| 23/10/2020 | No longer recruiting | [_] Protocol |
| **Registration date** | **Overall study status** | [_] Statistical analysis plan |
| 16/11/2020 | Completed | [X] Results |
| **Last Edited** | **Condition category** | [_] Individual participant data |
| 18/08/2021 | Other | |

## Plain English summary of protocol

Background and study aims
Inflammation is a process by which your body's white blood cells and the things they make protect you from infection from outside invaders, such as bacteria and viruses.
New anti-inflammatory drugs are hard to evaluate in healthy volunteers, as healthy volunteers do not have ongoing inflammation. We want to induce a local inflammatory reaction in healthy volunteers and study this reaction so that the induced inflammatory reaction can be used in future clinical trials with new anti-inflammatory drugs.

Who can participate?
Healthy non-smoking male volunteers age 18 - 45

What does the study involve?
The study involves the administration of LPS (purified lipopolysaccharide) which is part of a bacteria. The administration is done with a needle into the skin of the forearms. Subjects also receive an injection with a salt solution which acts as placebo. The response to the LPS and salt solution are monitored for 48 hours. In order to study the response, suction blisters are raised and skin punch biopsies are taken, next to that several cameras will be used that can measure heat, redness and blood flow in the skin.

What are the possible benefits and risks of participating?
There are no benefits for the volunteers. Risks include a small scar from the biopsy and a pigmentated spot on the skin from the suction blister.

Where is the study run from?
Centre for Human Drug Research, Leiden (The Netherlands)

When is the study starting and how long is it expected to run for?
September 2017 to November 2018

Who is funding the study?
1. Centre for Human Drug Research (The Netherlands)
2. Cutanea Life Sciences (The Netherlands)

Who is the main contact?
Matthijs Moerland, mmoerland@chdr.nl

# Contact information

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Public

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# Additional identifiers

### EudraCT/CTIS number
Nil known

### IRAS number

### ClinicalTrials.gov number
Nil known

### Secondary identifying numbers
CHDR1752

# Study information

## Scientific Title
Development of a dermal TLR4 challenge in healthy volunteers

## Study objectives
The aim of this study is to characterize the inflammatory response upon intradermal LPS injection in healthy volunteers. By doing so we create a challenge model that temporarily induces skin inflammation via a specific pathway which enables future application as proof-of-pharmacology or drug profiling in drug developmental programs.

## Ethics approval required
Old ethics approval format

## Ethics approval(s)
Approved 16/05/2018, Stichting Beoordeling Ethiek Biomedisch Onderzoek (Dr. Nassaulaan 10, 9401HK Assen, Netherlands; +31 (0)592 405871; info@stbebo.nl), ref: NL65297.056.18

## Study design
Interventional non-randomized controlled trial

## Primary study design
Interventional

## Secondary study design
Non randomised study

## Study setting(s)
Other

## Study type(s)
Other

## Participant information sheet
Not available in web format, please use contact details to request a participant information sheet

## Health condition(s) or problem(s) studied
The aim of this study is to characterize the inflammatory response upon intradermal LPS injection in healthy volunteers

## Interventions
LPS, purified lipopolysaccharide prepared from Escherichia Coli: 113: H10:K negative (U.S. Standard
Reference Endotoxin) will be used. This LPS batch is manufactured in the US by List Biological Laboratories. Subjects will receive in total two or four intradermal doses of LPS on the lower forearms on day 0 . The dose per injection is 10 ng. An intradermal saline (NaCl 0.9%) injection will act as placebo.

Subjects 1 – 6 received one saline injection and two LPS injections, subjects 7 – 18 received one saline injection and four LPS injections.

### Intervention Type
Other

### Primary outcome measure
1. Non-invasive measures:
1.1. Skin Perfusion was measured by Laser speckle contrast imaging (LSCI) pre LPS/saline administration and at 3h 6h, 10h, 24h and 48h after administration
1.2. Erythema was measured by Antera 3D camera pre LPS/saline administration and at 3h 6h, 10h, 24h and 48h after administration
1.3. Erythema was scored by a physician (erythema grading scale) pre LPS/saline administration and at 3h 6h, 10h, 24h and 48h after administration
1.4. Temperature was measured by thermography pre LPS/saline administration and at 3h 6h, 10h, 24h and 48h after administration
2. Invasive measures:
Skin punch biopsies were taken pre LPS/saline administration and at 3h 6h, 10h, 24h and 48h after administration and analyzed for the following:
2.1. Immunochemistry: Neutrophils, Monocytes/macrophages, CD4+ lymphocytes, CD8+ lymphocytes, CD1a+ dendritic cells
CD19+ B cells
2.2. mRNA analysis by qPCR: IFN-gamma, IL10, IL1-beta, IL6, IL8, TNF, MXA
3. Suction blisters were raised pre LPS/saline administration and at 3h 6h, 10h, 24h and 48h after administration and analyzed for the following:
3.1. Flowcytometry: Neutrophils, classical monocytes, non-classical monocytes, intermediate monocytes, dendritic cells, NK cells, CD4 T cells, CD8 T cells, B cells.
MSD (protein): IFN-gamma, IL10, IL1-beta, IL6, IL8, TNF

### Secondary outcome measures
1. Adverse events were monitored throughout the study
2. Blood pressure, heart rate and temperature were measured pre LPS/saline administration and at 3h 6h, 10h, 24h and 48h after administration
3. Local tolerance was measured pre LPS/saline administration and at 3h 6h, 10h, 24h and 48h after administration by using Numeric Rating Scale (NRS) for pruritus and pain for the injection site
4. Circulating cytokines and leukocytes were measured pre LPS/saline administration and at 3h 6h, 10h, 24h and 48h after administration

### Overall study start date
27/09/2017

### Completion date
12/11/2018

## Eligibility

### Key inclusion criteria
1. Healthy male subjects, 18 to 45 years of age, inclusive. Healthy status is defined by absence of evidence of any active or chronic disease following a detailed medical and surgical history, a complete physical examination including vital signs, 12-lead ECG, hematology, blood chemistry, blood serology and urinalysis
2. Body mass index (BMI) between 18 and 30 kg/m$^2$, inclusive, and with a minimum weight of 50 kg

3. Fitzpatrick skin type I-III (Caucasian)
4. Able and willing to give written informed consent and to comply with the study restrictions

### Participant type(s)
Healthy volunteer

### Age group
Adult

### Lower age limit
18 Years

### Sex
Male

### Target number of participants
18

### Total final enrolment
18

### Key exclusion criteria
1. Any disease associated with immune system impairment, including auto-immune diseases, HIV and transplantation patients
2. Any vaccination within the last 3 months
3. Family history of psoriasis
4. History of pathological scar formation (keloid, hypertrophic scar)
5. Have any current and / or recurrent pathologically, clinical significant skin condition at the treatment area (i.e. atopic dermatitis)
6. Hypersensitivity for dermatological marker at screening
7. Requirement of immunosuppressive or immunomodulatory medication within 30 days prior to enrollment or planned to use during the course of the study
8. Tanning due to sunbathing, excessive sun exposure or a tanning booth within 3 weeks of enrollment
9. Participation in an investigational drug or device study within 3 months prior to screening or more than 4 times a year
10. Loss or donation of blood over 500 mL within three months prior to screening. Or the donation of plasma within 14 days prior to screening
11. Current smoker and/or regular user of other nicotine-containing products (e.g., patches)
12. History of or current drug or substance abuse considered significant by the PI (or medically qualified designee), including a positive urine drug screen

### Date of first enrolment
17/05/2018

### Date of final enrolment
04/09/2018

## Locations

**Countries of recruitment**
Netherlands

**Study participating centre**
**Centre for Human Drug Research**
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# Sponsor information

**Organisation**
Centre for Human Drug Research

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**Sponsor type**
Research organisation

**Website**
http://www.chdr.nl/

**ROR**
https://ror.org/044hshx49

# Funder(s)

**Funder type**
Industry

**Funder Name**
Cutanea Life Sciences

# Results and Publications

## Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal.

## Intention to publish date
01/02/2021

## Individual participant data (IPD) sharing plan
All data generated or analysed during this study will be included in the subsequent results publication.

## IPD sharing plan summary
Other

## Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Results article | | 22/07/2021 | 18/08/2021 | Yes | No |