

# Change in markers of immune function associated with Bacillus subtilis CU1 intervention in different age groups

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Primary objective: Explore, quantify and interpret the effect of 4-week intervention with 2 x 10<sup>9</sup> spores of BSCU1 on fecal sIgA, in healthy adults, elderly and 3-6 year old children. Secondary objectives: Explore, quantify and interpret the effect of...

<b>Ethical review</b>	Approved WMO
<b>Status</b>	Recruitment stopped
<b>Health condition type</b>	Other condition
<b>Study type</b>	Interventional

## Summary

### ID

NL-OMON51589

### Source

ToetsingOnline

### Brief title

BSCU1 and immune function

### Condition

- Other condition

### Synonym

immune system

### Health condition

normal immune response

### Research involving

Human

## Sponsors and support

**Primary sponsor:** Gnosis by Lesaffre

**Source(s) of monetary or material Support:** Funding by Gnosis by Lesaffre

## Intervention

**Keyword:** immune function, mechanism of action, probiotic

## Outcome measures

### Primary outcome

- Change in fecal sIgA concentration after 4 weeks intervention, compared to baseline

### Secondary outcome

- Change in fecal sIgA concentration after 2 weeks intervention, compared to baseline

- Change in the following markers of immune function, after 4 weeks intervention, compared to baseline, in healthy adults and older subjects:

\* Serum cytokine levels (in elderly only)

\* Ex vivo cytokines concentration in (LPS-) stimulated and unstimulated whole blood

\* Ex vivo phagocytosis in whole blood (using flow cytometry), expressed as % of positive monocytes, % positive granulocytes, mean fluorescence intensity monocytes, and mean fluorescence intensity granulocytes

## Study description

### Background summary

Limited data from clinical studies indicate that the probiotic strain *Bacillus*

subtilis CU1 may be effective in reducing common infections. To further support a beneficial effect of BSCU1 on immune function and resistance to infections, additional clinical studies are required. However, relatively little is known as yet with regard to the mechanism of action. More insight into such mechanisms will help to select the most appropriate study design, target population and outcomes in future controlled intervention studies. Therefore, the current study aims to explore a range of possible pathways by which BSCU1 could beneficially modulate the immune system, in three target populations representing the general population.

## **Study objective**

Primary objective: Explore, quantify and interpret the effect of 4-week intervention with  $2 \times 10^9$  spores of BSCU1 on fecal sIgA, in healthy adults, elderly and 3-6 year old children.

Secondary objectives:

Explore, quantify and interpret the effect of 2-week intervention with  $2 \times 10^9$  spores of BSCU1 on fecal sIgA, in healthy adults, elderly and 3-6 year old children.

Explore, quantify and interpret the change in the following markers of immune function, after 4 weeks intervention with  $2 \times 10^9$  spores of BSCU1, in healthy adults and older subjects:

- \* Serum cytokine levels (in elderly only)
- \* Ex vivo production of cytokines by (LPS-) stimulated whole blood
- \* Ex vivo phagocytosis in whole blood

## **Study design**

Single-arm study with repeated measures, involving three different populations, in which each subject serves as its own control

## **Intervention**

All subjects will receive (the content of) one capsule of BSCU1 (containing  $2 \times 10^9$  spores) once daily, for 4 weeks.

## **Study burden and risks**

Parents of the participating children will be invited for 1 screening and 3 site visits, the children will be asked to come to the screening visit for assessment of height and weight and to the final visit. Parents will collect fecal samples from their child at 3 timepoints, bring these to the clinical site, and answer questions on fecal consistency, study product intake and wellbeing. No invasive measures will be performed. The study product is on the market in the EU and in the US, and has been approved for children in this age

category. To obtain insight in the immune stimulatory effect in this specific age group, data need to be collected in this age group and compared with data from other age categories.

Adults/elderly will attend 1 screening visit and 3 site visits. Fasting blood samples will be collected at 1 timepoint during 2 site visits. The total amount of blood collected is 45 ml per visit. Fecal samples will be collected at 3 timepoints and brought to the clinical site. Participants will answer questions on fecal consistency, study product intake and wellbeing at each site visit.

## Contacts

### Public

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### Scientific

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## Trial sites

### Listed location countries

Netherlands

## Eligibility criteria

### Age

Adults (18-64 years)

Children (2-11 years)

Elderly (65 years and older)

### Inclusion criteria

Adults:

4 - Change in markers of immune function associated with Bacillus subtilis CU1 inter ... 23-06-2025

#### Substantial

- 30 ≤ age ≤ 49 years
- BMI ≥ 18.5 and ≤ 25 kg/m<sup>2</sup>
- In good health as assessed during screening (by questionnaire), and the medical investigator's professional judgment
- Non-smoking

#### Elderly:

##### Substantial

- 65 ≤ age ≤ 79 years
- BMI 22.0 - 28.0 kg/m<sup>2</sup>
- Generally healthy as assessed during screening (by questionnaire), and the medical investigator's professional judgment
- Non-smoking

#### Procedural (both for adults and elderly):

- Ability to follow Dutch verbal and written instructions
- Signed informed consent
- Willingness to give up blood donation during the entire study

#### Children:

##### Substantial

- 3 ≤ age ≤ 6 years
- Healthy BMI, cut-off points will be used as indicated by JGZ (BMI jongens en meisjes | Voedingscentrum)
- Generally healthy as assessed during screening (by parental anamnesis), and the study physician's professional judgment

#### Procedural:

- Parents/caretakers having the ability to follow Dutch verbal and written instructions
- Signed informed consent

## Exclusion criteria

#### Adults and elderly

##### Substantial

- Chronic illness (e.g., diabetes mellitus, cardiac insufficiency, respiratory insufficiency, cancer, chronic kidney or liver disease),
- Acute infection in the past month
- Gastrointestinal disorders (e.g., inflammatory bowel disease),
- Acute gastroenteritis in the past 2 months
- Any vaccination in the past month
- Treatment with antibiotics within 2 months of the start of the study,
- Regular use of laxative agents

- Immunodeficiency disorder
- Use of immunosuppressive drugs (e.g.cyclosporine, azathioprine, systemic corticosteroids, antibodies)
- Unexplained weight loss or weight gain of > 3 kg in the 3 months prior to pre-study screening
- Regular consumption of probiotics within 1 month before start of the study
- Evidence of current excessive alcohol consumption (>4 consumptions/day or >20 consumptions/week) or drug (ab)use
- Mental status that is incompatible with the proper conduct of the study

#### Procedural:

- Not having a general practitioner, not allowing disclosure of participation to the general practitioner or not allow to inform the general practitioner about abnormal results. Participation in any clinical trial including blood sampling and/or administration of substances starting 1 month prior to study start and during the entire study.
- Personnel of NIZO or Gnosis by Lesaffre, their partner and their first and second degree relatives.

#### Children

##### Substantial

- Acute respiratory or gastrointestinal or chronic infections
- Chronic systemic or metabolic diseases
- Gastrointestinal disorders (e.g., inflammatory bowel disease),
- Acute gastroenteritis in the past 2 months
- Any vaccination in the past month
- Treatment with antibiotics within 2 months of the start of the study,
- Immunodeficiency disorder
- Use of anti-inflammatory or immunosuppressive drugs (e.g.cyclosporine, azathioprine, systemic corticosteroids, antibodies)
- Regular use of laxative agents
- Regular consumption of probiotic supplements within 1 month before start of the study

#### Procedural:

- Parents or caretakers not having a general practitioner, not allowing disclosure of participation to the general practitioner or not allowing to inform the general practitioner about abnormal results.
- Participation in any clinical trial starting 1 month prior to study start and during the entire study.
- Parents who are personnel of NIZO or Gnosis by Lesaffre, their partner and their first and second degree relatives.

## Study design

### Design

**Study type:** Interventional

Masking: Open (masking not used)

Control: Uncontrolled

Primary purpose: Other

### Recruitment

NL

Recruitment status: Recruitment stopped

Start date (anticipated): 23-05-2022

Enrollment: 90

Type: Actual

## Ethics review

Approved WMO

Date: 08-04-2022

Application type: First submission

Review commission: CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

## Study registrations

### Followed up by the following (possibly more current) registration

No registrations found.

### Other (possibly less up-to-date) registrations in this register

No registrations found.

**In other registers**

Register	ID
CCMO	NL79890.000.21