# Gastrointestinal benefit of dairy ingredients to prevent symptoms of gut infection in healthy adult subjects

No registrations found.

| | |
|---|---|
| **Ethical review** | Positive opinion |
| **Status** | Recruiting |
| **Health condition type** | - |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON22648

**Source**
NTR

**Brief title**
GIGA

**Health condition**

Enterotoxigenic E. coli
Gut infections
Diarrhea
Dairy ingredients

Enterotoxische E. coli
Darm infecties
Diarree
Zuivel ingredienten

### Sponsors and support

**Primary sponsor:** FrieslandCampina Nederland BV
**Source(s) of monetary or material Support:** - Sponsor<br>
- Operational Program Eastern Netherlands, a joint program of the provinces of Overijssel and Gelderland, the city networks Zwolle, Kampen, Apeldoorn, Deventer, Zutphen, and Arnhem-Nijmegen, and the regional networks in Twente and The Valley. The program covers activities

that are co-financed by the European Regional Development Fund.

## Intervention

## Outcome measures

### Primary outcome

Main study parameters:

-Stool frequency: number of stools per
day, recorded in online diary

- Diarrhea complaints as measured by GSRS questionnaire (Gastro-intestinal Symptom Rating Scale, domain diarrhea), recorded in online diary

### Secondary outcome

Secondary parameter:

- Stool consistency as measured by Bristol Stool Score (BSS, scale 1-7, recorded in online diary)

# Study description

### Background summary

Rationale: Diarrhea is an important cause of morbidity and mortality in all regions of the world and among all ages. The annual number of enterotoxigenic Escherichia coli (ETEC) cases in the developing world is estimated at 840 million, with another 50 million asymptomatic carriers in children aged <5 years. Food-borne infections are also frequently encountered by travelers to tropical countries, with incidences up to 80%. Antibiotics can be a form of treatment, but the growing resistance of pathogens against antibiotics is a drawback.

The sponsor would like to develop dairy based products and/or ingredients that are able to improve the protective response of babies/children against infection and thereby diminishing the severity of the infectious diarrhea. Based on results of its investigations, the sponsor has identified dairy derived products/ingredients that might be able to protect
against infection. In this proof-of-concept study, the sponsor would like to further substantiate the support of the protective response of these products/ingredients. The product of interest is a
minimally processed milk product of the sponsor.

Objective: To investigate whether minimally processed milk product, can decrease the diarrheagenic E. coli-induced changes in reported stool frequency and gastrointestinal complaints.

Study design: The GIGA study is a double-blind parallel 4-weeks intervention study. Subjects will be randomly assigned to one of three treatment groups: Placebo, minimally processed milk product high dose, or minimally processed milk product low dose (n=40 per group). Subjects will be instructed to maintain their usual pattern of physical activity and their habitual food intake, but to standardize their dietary calcium intake (mainly dairy). Before and after a 2-week run-in period, a 24h fecal sample and blood sample will be collected. At study day 14, after a standardized evening meal and an overnight fast, subjects will be orally infected with a live, but attenuated, diarrheagenic E. coli (strain E1392/75-2A; collection NIZO; dose 1E10 CFU). At various time points before and after diarrheagenic E. coli challenge, an online diary will be kept to record information on stool consistency, frequency and severity of symptoms.

Main study parameters/endpoints:

- Stool frequency at day 16 (2 days after infection) compared to day 15 (1 day after infection): number of stools per day (recorded in online diary);

- Diarrhea complaints at day 16 compared to day 15 as measured by GSRS questionnaire (Gastro-intestinal Symptom Rating Scale, domain diarrhea), recorded in online diary.

### Study objective

Minimally processed milk product, decreases the diarrheagenic E. coli-induced changes in reported stool frequency and gastrointestinal complaints.

### Study design

day 16 (2 days after infection) compared to day 15 (1 day after infection)

### Intervention

During 4 weeks, subjects will receive either placebo (control protein product, 23 g/dose twice daily), high dose minimally processed milk product (23 g/dose twice daily) or low dose minimally processed milk product (11 g/dose twice daily)

## Contacts

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# Eligibility criteria

## Inclusion criteria

1. Male

2. Age between 18 and 55 years.

3. BMI ≥18.5 and ≤30.0 kg/m2.

4. Healthy as assessed by the NIZO food research medical questionnaire.

## Exclusion criteria

1. Acute gastroenteritis in the 2 months prior to inclusion.

2. Any confirmed or suspected immunosuppressive or immunodeficient condition including human
immunodeficiency virus infection (HIV).

3. Disease of the GI tract, liver, bile bladder, kidney, thyroid gland (self-reported), except for appendicitis.

4. History of microbiologically confirmed ETEC or cholera infection within 3 years prior to inclusion.

5. Symptoms consistent with Travelers' Diarrhea concurrent with travel to countries where ETEC infection is
endemic (most of the developing world) within 3 years prior to inclusion, OR planned travel to endemic
countries during the length of the study.

6. Vaccination for, or ingestion of cholera within 3 years prior to inclusion, including studies at NIZO.

7. Occupation involving handling of ETEC or Vibrio cholerae currently, or within 3 years prior to inclusion.

8. Vaccination for, or ingestion of ETEC or E coli heat labile toxin, including E. coli challenge studies at NIZO.
9. Evidence of current excessive alcohol consumption (>4 consumptions/day or >20 consumptions/week) or
drug (ab)use, and not willing/able to stop this during the study.

10. Known allergy to the following antibiotics: ciprofloxacin, trimethoprim, sulfamethoxazole, and penicillins.

11. Reported average stool frequency of >3 per day or <1 per 2 days.

12. Use of antibiotics (up till 6 months prior to inclusion), norit, laxatives, cholestyramine, antacids H2 receptor
antagonists or proton pump inhibitors (during 3 months prior to inclusion).

13. Use of immunosuppressive drugs (e.g. cyclosporine, azathioprine, systemic corticosteroids, antibodies).

14. Vegans.

15. Mental status that is incompatible with the proper conduct of the study.
16. A self-reported milk allergy, lactose intolerance or sensitivity to dairy ingredients.

# Study design

## Design

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|---|---|
| Study type: | Interventional |
| Intervention model: | Parallel |
| Allocation: | Randomized controlled trial |
| Masking: | Double blinded (masking used) |
| Control: | Placebo |

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruiting |
| Start date (anticipated): | 27-02-2019 |

| | |
|---|---|
| Enrollment: | 120 |
| Type: | Anticipated |

### IPD sharing statement

**Plan to share IPD:** Undecided

## Ethics review

Positive opinion

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|---|---|
| Date: | 09-11-2018 |
| Application type: | First submission |

## Study registrations

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

ID: 48558
Bron: ToetsingOnline
Titel:

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

No registrations found.

### In other registers

| Register | ID |
|---|---|
| NTR-new | NL7348 |
| NTR-old | NTR7613 |
| CCMO | NL66645.028.18 |
| OMON | NL-OMON48558 |

## Study results

**Summary results**
- Ten Bruggencate SJ, Frederiksen PD, Pedersen SM, Floris-Vollenbroek EG, Lucas-van de Bos E, van Hoffen E, Wejse PL. Dietary Milk-Fat-Globule Membrane Affects Resistance to

Diarrheagenic Escherichia coli in Healthy Adults in a Randomized, Placebo-Controlled, Double-Blind Study. J Nutr 2016;146:249-55<br><br>

- Ten Bruggencate SJ, Girard SA, Floris-Vollenbroek EG, Bhardwaj R, Tompkins TA. The effect of a multi-strain probiotic on the resistance toward Escherichia coli challenge in a randomized, placebo-controlled, double-blind intervention study. Eur J Clin Nutr 2015;69:385-91.
<br><br>
- Ouwehand AC, ten Bruggencate SJ, Schonewille AJ, Alhoniemi E, Forssten SD, Bovee-Oudenhoven IM. Lactobacillus acidophilus supplementation in human subjects and their resistance to enterotoxigenic Escherichia coli infection. Br J Nutr. 2014;111(3):465-73.
<br><br>
- Bovee-Oudenhoven IM, Lettink-Wissink ML, Van Doesburg W, Witteman BJ, Van Der Meer R. Diarrhea caused by enterotoxigenic Escherichia coli infection of humans is inhibited by dietary calcium. Gastroenterology 2003;125: 469–76.