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# Bovine osteopontin (a protein found in the bones and milk of cattle) for elderly immune support

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| **Submission date**<br>15/11/2023 | **Recruitment status**<br>No longer recruiting | [_] Prospectively registered<br>[X] Protocol |
| **Registration date**<br>15/03/2024 | **Overall study status**<br>Completed | [_] Statistical analysis plan<br>[_] Results |
| **Last Edited**<br>15/07/2025 | **Condition category**<br>Other | [_] Individual participant data<br>[X] Record updated in last year |

## Plain English summary of protocol

Background and study aims
Osteopontin (OPN) is a phosphorylated glycoprotein that is present in human milk and bovine milk. It has been shown to be involved in immune function. In infants, supplementation with Lacprodan® OPN-10 is well tolerated, with clinically proven immunomodulatory outcomes such as downregulation of inflammatory cytokines and increases in T-cells and monocytes. The potential beneficial effects of Lacprodan® OPN-10 in adults and elderly people have not yet been studied. The current study therefore aims to investigate the potential immune effects of Lacprodan® OPN-10 in elderly people.

Who can participate?
Healthy men and women aged at least 60 years of age.

What does the study involve?
The study is designed as a double-blind, randomized, placebo-controlled trial, with two parallel treatment arms. All subjects consumed an OPN supplement or placebo twice per day. After an 8-week intervention period, all subjects will receive a hepatitis B vaccination, at weeks 8, 10 and 12. Vaccination response will be measured at weeks 12 and 14. The intervention will be continued until the end of the study at week 14.

What are the possible benefits and risks of participating?
Benefits: The subjects will not benefit directly from participation in this study.
Risks: The risks associated with participation in this study are considered small. Potential risks could be related to a) study product, b) study procedures or c) non-investigational product (hepatitis B vaccination). Recently, the EFSA Panel on Nutrition, Novel Foods and Food Allergens (NDA) published an opinion on bovine milk OPN as a novel food, in which they conclude that the available scientific data do not raise safety concerns (EFSA NDA Panel 2022). Lacprodan® OPN-10 has a GRAS notification (Matulka 2017), based on the views of an independent Expert Panel. Standard safety evaluations have shown no indications of potential risk involved with consumption. The dose administered in this study is 3.3% of the NOAEL calculated in safety studies. The burden imposed by study procedures includes the daily intake of the study product,

the visits to the research location, the blood sampling and faecal sample collection. The collection of blood samples may produce discomfort or minor bleeding and the possibility of bruising at the site of the needle puncture. There is also a slight risk of infection at the site of the needle puncture.

Where is the study run from?
1. NIZO in Ede (Netherlands)
2. EB Medical in Almere (Denmark)

When is the study starting and how long is it expected to run for?
March 2022 to December 2023

Who is funding the study?
Arla Foods Ingredients (Denmark)

Who is the main contact?
1. Simon Bøge Riis, sirii@arlafoods.com
2. Petra Scholtens, petra.scholtens@nizo.com

# Contact information

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Public, Scientific

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# Additional identifiers

**EudraCT/CTIS number**
Nil known

**IRAS number**

**ClinicalTrials.gov number**
Nil known

**Secondary identifying numbers**
NL81499.028.22

# Study information

**Scientific Title**
Effect of bovine osteopontin on vaccination response in older individuals; a randomized, placebo-controlled clinical trial

**Acronym**
BOFEI

**Study objectives**
in a group of elderly subjects receiving Lacprodan® OPN-10 in a dose of 40 mg/kg body weight per day, the protective anti-HepB antibody titre after HepB vaccination is attained in a statistically significantly higher % of subjects compared to subjects receiving a placebo product

**Ethics approval required**
Ethics approval required

**Ethics approval(s)**
Approved 29/08/2022, Medisch Ethische Toetsingscommissie Brabant (Hasseltveste Dr Deelenlaan 9, Tilburg, 5042 AD, Netherlands; +31 132118006; info@metcbrabant.nl), ref: P2230

**Study design**
Double-blind randomized placebo-controlled multi-center trial with two treatment arms

**Primary study design**
Interventional

**Secondary study design**
Randomised controlled trial

**Study setting(s)**
Other

**Study type(s)**
Safety, Efficacy

**Participant information sheet**

Not available in web format, please use contact details to request a particpant information sheet

### Health condition(s) or problem(s) studied
Vaccination response, immune support in healthy elderly

### Interventions
Subjects will be randomly allocated to receive the active product Lacprodan® OPN-10 or a placebo product with maltodextrin. Both products are administered orally twice per day for 14 weeks. The dose of the active ingredient, osteopontin, is 40 mg/kg/day

All subjects were randomly assigned to the active product or the placebo product with an online computer program by an unblinded person who is not involved in the study team. Stratification was performed on gender and age.

### Intervention Type
Supplement

### Primary outcome measure
Percentage of responders to hepatitis B vaccination. A “responder” is defined as a subject attaining anti-hepatitis B antibody titres >10 IU/L at Visit 7 (2 weeks after the third vaccination). The Hepatitis B titer is analysed with an ELISA assessment.

### Secondary outcome measures
1. Change in serum anti-hepatitis B antibody titres from baseline (V1) to 14 days after the second vaccination (V6) and 14 days after the third vaccination (V7) determined with ELISA.
2. Change in circulating cytokines from baseline to 8 weeks intervention (V4) and to the end of the study (V7). The analyses will be performed with a multiplex assay.
3. Change in serum levels of P1NP and CTX-1 (as markers of bone formation and bone resorption) from baseline to 8 weeks intervention. Analyses will be performed by radioimmunoassay and electrochemical luminescence immunoassay respectively.
4. Change in plasma levels of hOPN and bOPN from baseline to 4 weeks and 8 weeks intervention. hOPN and bOPN will be analysed with an ELISA assay.
5. Change in serum LPS binding protein (LBP) from baseline to 8 weeks intervention. Serum LBP will be analysed with an ELISA assay.
6. Incidence of self-reported upper respiratory tract infections or lower respiratory tract infections during the trial, assessed by weekly questionnaires
7. Safety monitoring by routine assays for hematology and serum clinical chemistry throughout the study

### Overall study start date
30/03/2022

### Completion date
19/12/2023

## Eligibility

### Key inclusion criteria
1. Age ≥60 years and healthy
2. Self-reported regular Dutch eating habits as assessed by questionnaire (3 main meals per day)

3. Anti hepatitis B antibody titer ≤ 4 IU/L
4. Non-smokers (ex-smokers can participate)
5. BMI ≥22 and ≤30
6. In good health as assessed during screening, and the medical investigator's professional judgment
7. Adherence to habitual diet, no changes during study period
8. Signed informed consent
9. Ability to follow Dutch verbal and written instructions
10. Willing to accept disclosure of the financial benefit of participation in the study to the authorities concerned
11. Willing to accept use of all encoded data, including publication, and the confidential use and storage of all data for at least 15 years
12. Willing to comply with study procedures, including intake of study products and collection of stool and blood samples
13. Willingness to give up blood donation starting at screening and during the entire study

## Participant type(s)
Healthy volunteer

## Age group
Senior

## Lower age limit
60 Years

## Sex
Both

## Target number of participants
140

## Total final enrolment
129

## Key exclusion criteria
1. Prior HB vaccination or infection
2. Any vaccination in the past month or any scheduled vaccination during the study period
3. Acute infection in the past month
4. Treatment with oral antibiotics within 2 months of the start of the study,
5. Serious progressive disease or non-stabilized chronic illness (e.g., diabetes mellitus, cardiac insufficiency, respiratory insufficiency, cancer, chronic kidney or liver disease)
6. History of cancer
7. Gastrointestinal disorders (e.g., inflammatory bowel disease)
8. Immunodeficiency or autoimmune disorder
9. Use of immunosuppressive drugs (e.g. cyclosporine, azathioprine, systemic corticosteroids, antibodies)
10. Allergy or hypersensitivity to milk proteins, or lactose intolerance
11. Unexplained weight loss or weight gain of > 3 kg in the 3 months prior to pre-study screening
12. Evidence of current excessive alcohol consumption (>4 consumptions/day or >20 consumptions/week) or drug (ab)use
13. Mental status that is incompatible with the proper conduct of the study

14. 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.
15. 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.
16. Personnel of NIZO, EBMR or AFI, their partner and their first- and second-degree relatives.

### Date of first enrolment
29/08/2022

### Date of final enrolment
31/08/2023

## Locations

### Countries of recruitment
Netherlands

### Study participating centre
**EB Medical Research**
Louis Armstrongweg 88 2e
Almere
Netherlands
1311 RL

### Study participating centre
**NIZO**
Kernhemseweg 2
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## Sponsor information

### Organisation
Arla Foods (Denmark)

### Sponsor details
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**Sponsor type**
Industry

**Website**
https://www.arlafoodsingredients.com/

**ROR**
https://ror.org/01hgxez56

# Funder(s)

**Funder type**
Industry

**Funder Name**
Arla Foods Ingredients Group

**Alternative Name(s)**
Arla Foods Ingredients Group P/S

**Funding Body Type**
Private sector organisation

**Funding Body Subtype**
For-profit companies (industry)

**Location**
Denmark

# Results and Publications

**Publication and dissemination plan**
Dissemination and publication plans will be specified by the involved parties after the trial is completed

**Intention to publish date**
31/12/2027

**Individual participant data (IPD) sharing plan**
The data-sharing plans for the current study are unknown and will be made available at a later date

**IPD sharing plan summary**
Data sharing statement to be made available at a later date

## Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Protocol file | version 6.0 | 22/03/2023 | 08/01/2024 | No | No |