

# Endogenous formation of nitrosamines from drug substance (GITox)

**First published:** 26/09/2022

**Last updated:** 14/03/2024

Study

Planned

## Administrative details

### EU PAS number

EUPAS49089

---

### Study ID

49090

---

### DARWIN EU® study

No

---

### Study countries

 Germany

---

### Study description

Endogenous formation of N-nitrosamines from drug substance. the aim of the study is to investigate the impact of physiological conditions on the formation of nitrosamines from secondary amines adjacent to various alkyl or aromatic

moieties. Main topics: 1) Cultivate relevant APIs with representative microbiomal strains like *Helicobacter pylori*, *E. coli* and artificial intestinal flora under primarily anaerobic conditions to mimic conditions in the large and small intestine. 2) Investigate the impact of nitrite/nitrate concentrations and the pH-value on NA formation. 3) Investigate kinetics of NA-formation for those APIs that show biotransformation. 4) Investigate the potential of selected microbiome strains to reduce  $\text{NO}_2^-$  to  $\text{NH}_4^+$  and thus contribute to detoxification process.

---

### Study status

Planned

## Research institutions and networks

### Institutions

[Fraunhofer Institute for Toxicology and Experimental Medicine \(ITEM\)](#)

**First published:** 01/02/2024

**Last updated:** 01/02/2024

Institution

[Federal Institute for Drugs and Medical Devices \(BfArM\)](#)



Germany

**First published:** 01/02/2024

**Last updated:** 30/04/2024

**Institution**

**Regulatory Authority**

**BfArM Berlin, University of Bonn Bonn**

## Contact details

### Study institution contact

Sylvia Escher [sylvia.escher@item.fraunhofer.de](mailto:sylvia.escher@item.fraunhofer.de)

**Study contact**

[sylvia.escher@item.fraunhofer.de](mailto:sylvia.escher@item.fraunhofer.de)

### Primary lead investigator

Sylvia Escher

**Primary lead investigator**

## Study timelines

### Date when funding contract was signed

Planned: 08/12/2021

---

### Study start date

Planned: 01/01/2022

---

**Data analysis start date**

Planned: 01/09/2022

---

**Date of interim report, if expected**

Planned: 31/03/2023

---

**Date of final study report**

Planned: 30/06/2023

## Sources of funding

- Other

## More details on funding

BfArM, ITEM/Uni Bonn

## Study protocol

[220916 Study plan D2\\_revision for upload.pdf](#) (1.72 MB)

## Regulatory

**Was the study required by a regulatory body?**

Yes

---

**Is the study required by a Risk Management Plan (RMP)?**

Not applicable

# Other study registration identification numbers and links

SPECIFIC CONTRACT No. 03 implementing framework contract No. EMA/2020/46/L1.02

## Methodological aspects

### Study type

#### Study type list

**Study type:**

Non-interventional study

---

**Scope of the study:**

Other

**If 'other', further details on the scope of the study**

Formation of impurities in drugs

**Main study objective:**

Investigate the impact of physiological conditions on the formation of nitrosamines from secondary amines adjacent to various alkyl or aromatic moieties.

### Study Design

## **Non-interventional study design**

Other

---

## **Non-interventional study design, other**

Research study testing in vitro assays

## Study drug and medical condition

### **Anatomical Therapeutic Chemical (ATC) code**

(B03BB) Folic acid and derivatives

Folic acid and derivatives

## Population studied

### **Age groups**

- Adolescents (12 to < 18 years)
  - Adults (18 to < 46 years)
  - Adults (46 to < 65 years)
  - Adults (65 to < 75 years)
  - Adults (75 to < 85 years)
  - Adults (85 years and over)
- 

### **Estimated number of subjects**

0

## Study design details

## Outcomes

Define the conditions under which N-nitrosamines can be formed in the gastrointestinal tract and derive structure-activity relationships.

---

## Data analysis plan

Kinetics of NA formation from selected agents simulating realistic conditions in the GIT

# Data management

## ENCePP Seal

The use of the ENCePP Seal has been discontinued since February 2025. The ENCePP Seal fields are retained in the display mode for transparency but are no longer maintained.

## Data sources

### Data sources (types)

[Other](#)

---

### Data sources (types), other

The study will generate experimental data, which will be published in terms of a peer-reviewed publications.

## Use of a Common Data Model (CDM)

## **CDM mapping**

No

## Data quality specifications

### **Check conformance**

Unknown

---

### **Check completeness**

Unknown

---

### **Check stability**

Unknown

---

### **Check logical consistency**

Unknown

## Data characterisation

### **Data characterisation conducted**

No