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 NO2- to NH4+ 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

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Study contact

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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