

Final Report – CORRIGENDUM

**Acute Nose-Only Inhalation Toxicity Study in Wistar Rats
with the Synthetic Amorphous Silica Aerosil® R 812**

(Conduct according to OECD Guideline 436)

Fraunhofer ITEM Study No. 02 G 21 009

SASFORREACH Consortium
c/o knoell Germany GmbH

Marie Curie Strasse 11
51377 Leverkusen, Germany

Sponsor's Study Monitors

Evonik Operations GmbH
RE-ES-PS-HRA / 713-303
Rodenbacher Chaussee 4
63457 Hanau-Wolfgang, Germany
Phone: [REDACTED]
[REDACTED]

Grace Europe Holding GmbH

In der Hollerhecke 1
67547 Worms, Germany
Phone: [REDACTED]
[REDACTED]

Test Facility

**Fraunhofer Institute for Toxicology
and Experimental Medicine (ITEM)**

Nikolai Fuchs Strasse 1
30625 Hannover, Germany

Study Director: [REDACTED]

Phone: [REDACTED]

Fax: [REDACTED]

Test Facility Management: [REDACTED]

Original 1 of 4 originals

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This final report corrigendum consists of 4 pages.

Page 22:

6 Results

6.1 Clinical Observations

In-life Observations Including Inhalation and Post-inhalation Period

The first male was found dead after 2¾ hours of exposure, five minutes after showing a reduced respiratory rate, followed by one animal from each sex three hours after exposure start, that prior to death revealed signs of anemia and reduced respiratory rate. Because of these mortalities, the exposure was stopped after 3¼ hours for animal welfare reasons and the remaining male and two females were transferred to their cages. Approx. one hour later oxygen and heart rate measurements were performed on the remaining animals, followed by rectal temperature measurements. Shortly thereafter, one additional animal per sex with respiratory distress died in the cage while being transferred to the sacrifice laboratory for sacrifice due to animal welfare reasons. The last animal was sacrificed for concurrent moribund conditions and respiratory distress after measuring heart rate and oxygen. For more details see Table 6.

Table 6 Timepoints of deaths/sacrifices for all animals

7.30 am: Start of exposure	
10.15 am	1102 found dead
10.35 am	1103 and 1202 found dead
10.40 am	Exposure ended after 3 ¼ hrs for the remaining 3 rats (1101, 1201 and 1203); transfer of these rats into cage
11.40 am	1101 and 1201 died in the cage 1203 was killed in moribund condition
all animals were necropsied approx. 10 min after death	

Rectal temperatures were measured in all rats before exposure and in two rats approx. 1 hour after exposure stopped, see Table 7.

Table 7 Rectal temperatures

Animal no.	Nominal day 0
	Temperature [°C]
1101	25.6
1102	Dead
1103	Dead
1201	27.2
1202	Dead
1203	killed in moribund condition

Nominal day 0 = day of exposure

Page 24:**6.4 Oxygen Measurement in Blood**

On day of exposure heart rate and oxygen measurements could only be performed in remaining two moribund animals approx. 1 hr after exposure stopped, see Table 11. The measurement in animal 1101 did not work, because it was already in a very poor condition. Animal 1201 died shortly after while animal 1203 was killed in moribund condition due animal welfare reasons. Because of the small group size the measurements are inconclusive.

Table 11 Oxygen Saturation [%SpO₂] at the rats tail

Animal no.	Nominal Day 0*	
	%SpO ₂	Heart rate bpm
1101	n.a.	n.a.
1102	dead	dead
1103	dead	dead
1201	75	356
1202	dead	dead
1203	124	124

Nominal day 0 = day of exposure, n.a. = not applicable – here: measurement did not work, see above
measured with cuff on the tail in moribund condition

* measured approx. 1 hour after exposure stopped in moribund animals

07.02.2023

Date

Signature

Fraunhofer Institute for Toxicology and Experimental Medicine
(Fraunhofer ITEM)

Study Director: [REDACTED]

Page 26:

7 Abbreviations

bpm	beats per minute
EDX	Energy Dispersive X-Ray Analysis
F	Female(s)
GLP	Good laboratory praxis
GSD	Geometric standard deviation
HE	Haematoxylin and eosin staining
hr	Hour
LALN	Lung-associated lymph nodes
M	Male(s)
MMAD	Mass median aerodynamic diameter
NALT	Nasopharynx-associated lymphoid tissues
NBF	Neutral-buffered-formalin
OECD	Organization for Economic Cooperation and Development
PI	Principal investigator
QA/QAU	Quality Assurance Unit
RAC	Risk Assessment Committee
RS	Responsible scientist
SAS	Synthetic amorphous dioxide
SEM	Scanning electron microscope
SD	Study director