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STUDY TITLE

Report

DHDPS

Modified extended one-generation reproduction toxicity study
in Sprague-Dawley rats
Oral Administration (Gavage)

LABORATORY PROJECT IDENTIFICATION

Project No.: 90R0066/05R034

PART III OF III
(SUPPLEMENT)

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(Mean values and Individual values)****Clinical observations (including mortality)**

- Males
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- Males
- Females

Body weight (g)

- Males
- Females

Body weight change (g)

- Males
- Females

THIS REPORT CONSISTS OF PART I, II AND III

1. Analyses of the test substance

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Competence Center Analytics

Final Report**Characterization of "4,4'-dihydroxydiphenylsulfone"**
Study No. 16L00571 (confidential)

Page 1 of 10

Test item	"4,4'-dihydroxydiphenylsulfone"
Chemical identity	4,4'-dihydroxydiphenylsulfone (DHDPS)
Batch identification	03508136W0
Date of production (test item)	Nov 23, 2016
Origin of test item	[REDACTED]
PSN	05/0066-8
CAS no.	80-09-1
Sponsor	[REDACTED]
Date of receipt of order	Nov 29, 2016
Date of receipt of test item	Dec 01, 2016
Testing facility	Competence Center Analytics, BASF SE, D-67056 Ludwigshafen
Study director	[REDACTED]
Storage cond. test item	ambient temperature
Test period	Dec 13 – Jan 10, 2017
Storage of records	GLP archives, Competence Center Analytics
Storage of sample of test item	Archives, Competence Center Analytics

Competence Center Analytics

Final Report
Characterization of "4,4'-dihydroxydiphenylsulfone"
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Summary of results

Appearance and homogeneity	The test item are white powderlike crystals. It is obviously homogeneous.
Identity via ¹ H-NMR spectroscopy	The ¹ H-NMR spectrum shows the expected signals for the given structure.
Identity via ¹³ C-NMR spectroscopy	The ¹³ C-NMR spectrum shows the expected signals for the given structure.
Content of identified main component and by-products	w(C ₁₂ H ₁₀ O ₄ S) = 99.9 g/100 g via ¹ H-NMR spectroscopy By-products were not observed.

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Final Report
Characterization of "4,4'-dihydroxydiphenylsulfone"
 Study No. 16L00571 (confidential)

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1 Appearance and homogeneity

Method	Visual inspection at room temperature.
Result	The test item are white powderlike crystals. It is obviously homogeneous.
Date of test	Dec 13, 2016
Head of laboratory	██████████; I-██████████

2 Identity by ¹H-NMR spectroscopy

Method	¹ H-NMR spectroscopy
Apparatus	Bruker AV3-500p
Reagents	solvent: [D6]-DMSO (Euriso-top) reference: Tetramethylsilane (TMS) (Cambridge Isotope Lab)
Sample preparation	In a suitable vial, the test item was dissolved in [D6]-DMSO containing TMS. The resulting solution was transferred into a 5 mm NMR tube for measurement.
Test parameters	Measuring frequency = 500 MHz, measuring temperature = 298 K; further parameters see at ¹ H-NMR spectrum displayed in figure on page 7.
Result	The ¹ H-NMR spectrum shows the expected signals for the given test item. For assignments see spectrum on page 7.
Date of test	Jan 10, 2015
Head of laboratory	██████████; I-██████████


3 Identity of by ¹³C-NMR spectroscopy

Method	¹³ C-NMR spectroscopy
Apparatus	Bruker AV3-500p (PG/01992)
Reagents	solvent: [D6]-DMSO (Euriso-top, ord. no. D010-H) reference: Tetramethylsilane (TMS) (Cambridge Isotope Lab))
Sample preparation	In a suitable vial, the test item was dissolved in [D6]-DMSO containing TMS. The resulting solution was transferred into a 5 mm NMR tube for measurement.
Test parameters	Measuring frequency = 126 MHz, measuring temperature = 298 K; further parameters see at ¹³ C-NMR spectrum displayed in figure on page 8.

Competence Center Analytics

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Characterization of "4,4'-dihydroxydiphenylsulfone"
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Result	The ¹³ C-NMR spectrum shows the expected signals for the given test item. For assignments see spectrum
Date of test	Jan 10, 2017
Head of laboratory	

4 Content of identified main and by-products

Method	Quantitative ¹ H-NMR spectroscopy
Apparatus	Bruker AV3-500p
Reagents	solvent [D6]-DMSO (Euriso-top) reference: Tetramethylsilane (TMS) (Cambridge Isotope Lab))
Internal Standard	1,3,5-Trimethoxy benzene (Sigma Aldrich)
	Molecular Weight: 168.19 g/mol Purity: 99.9 g/100 g (for calc.)
Sample preparation	Test item and internal standard were weighed into a suitable vial and dissolved in [D6]-DMSO containing TMS. The resulting solution was transferred into a 5 mm NMR tube.
Test parameters	Measuring frequency = 500 MHz, measuring temperature 298 K; further parameters see at ¹ H-NMR spectrum displayed in figure on page 9.
Evaluation	The content of test item was calculated by using the following equation:

$$w = \frac{E_{St} \cdot I_K \cdot M_K \cdot A_{St} \cdot R_{St}}{E_P \cdot I_{St} \cdot M_{St} \cdot A_K}$$

w = mass fraction [g/100 g]
 I_K = peak intensity test item
 I_{St} = peak intensity standard
 E_P = weighed test item
 E_{St} = weighed standard

A_K = protons/molecule of test item
 A_{St} = protons/molecule of standard
 M_K = molecular weight test item
 M_{St} = molecular weight standard
 R_{St} = purity standard

Competence Center Analytics

Final Report
Characterization of "4,4'-dihydroxydiphenylsulfone"

Study No. 16L00571 (confidential)

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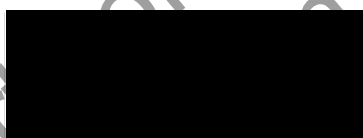
Result

For quantitation triplicate determinations were carried out. Evaluation was performed by using 3 protons/molecule of the internal standard (at ~ 6.1 ppm) and 8 selected protons/molecule of the analyte (at ~ 6.9 and 7.7 ppm). An exemplary spectrum is displayed in figure on page 9):

Det.	test item		internal standard		resulting mass fraction w(C ₁₂ H ₁₀ O ₄ S) [g/100 g]
	weight [mg]	peak intensity [area units]	weight [mg]	peak intensity [area units]	
1	41.69	3581.78	20.84	1000.00	99.8
2	38.87	2547.93	27.40	1000.00	100.1
3	27.73	1919.10	25.90	1000.00	99.9
mean					99.9 ± 0.2

Date of test Jan 10, 2017

Head of laboratory Dr. Weiß, RAA/AR – B 9


Feb 07, 2017
Date

Competence Center Analytics



We create chemistry

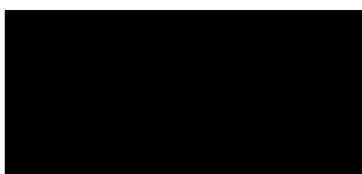
Final Report**Characterization of "4,4'-dihydroxydiphenylsulfone"**

Study No. 16L00571 (confidential)

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GLP Compliance Statement

This study was conducted in accordance with the OECD Principles of Good Laboratory Practice and the GLP Principles of the German "Chemikaliengesetz" (Chemicals Act).



Feb 07, 2017

Date

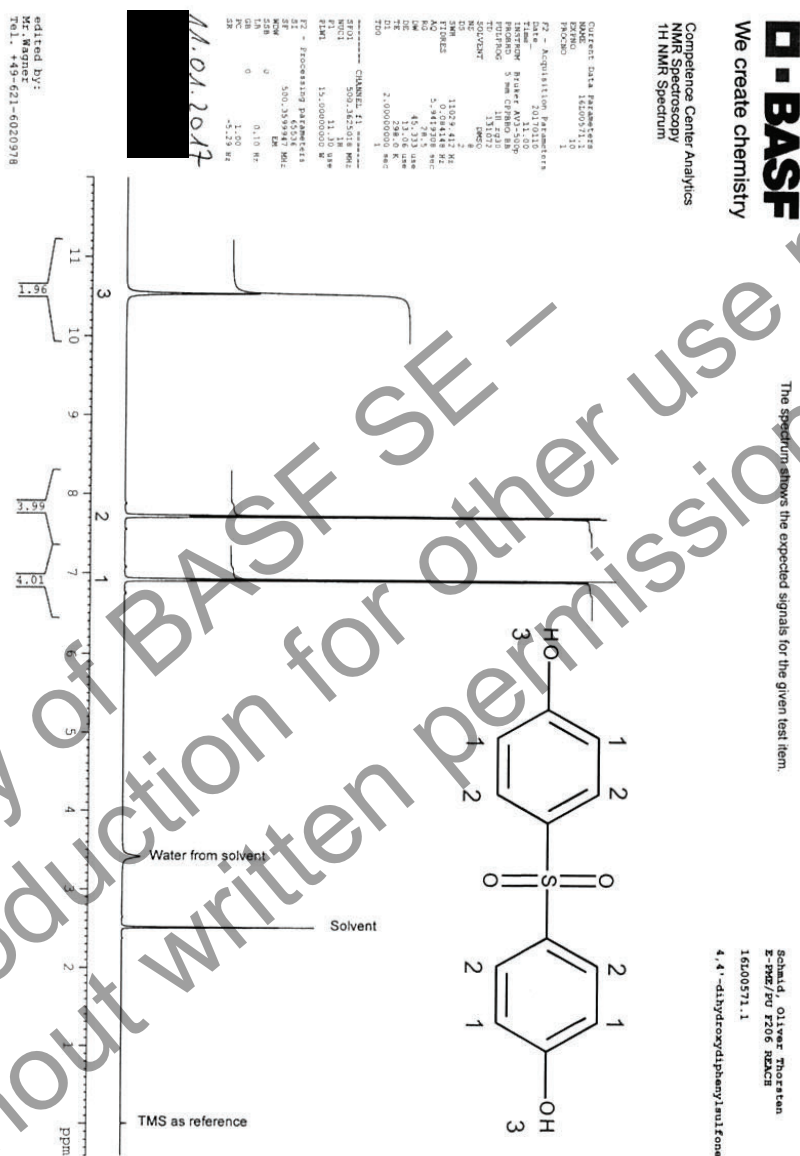
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Final Report

Characterization of "4,4'-dihydroxydiphenylsulfone"

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¹H-NMR-spectrum

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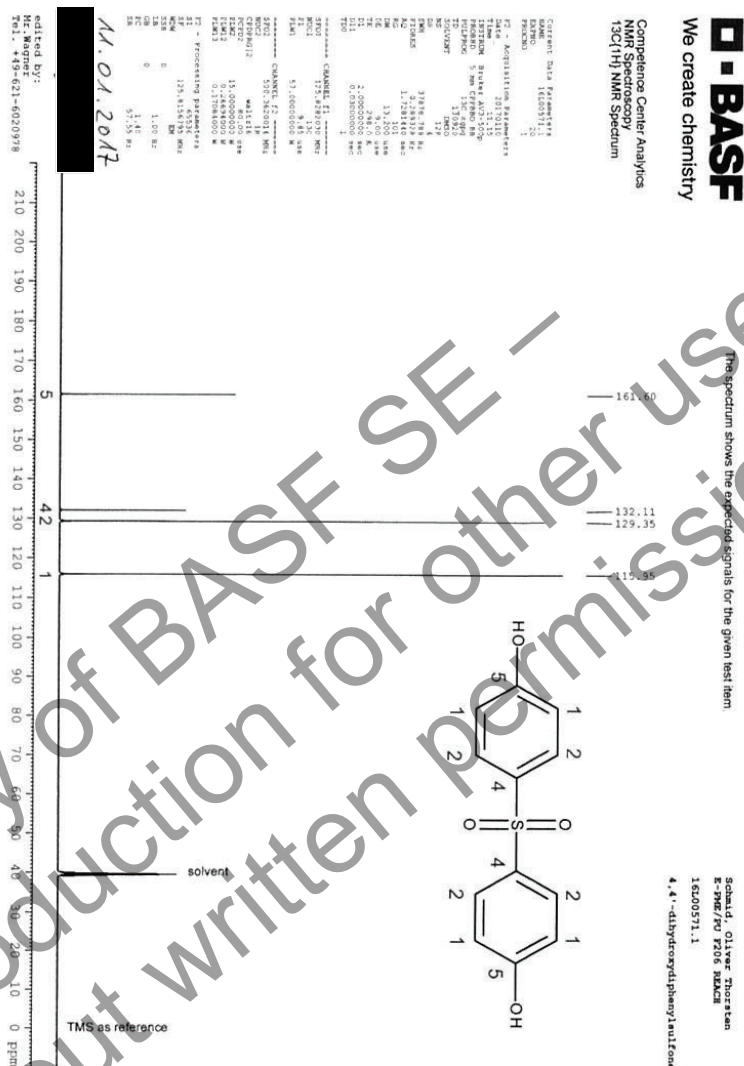
Final Report

Characterization of "4,4'-dihydroxydiphenylsulfone"

Study No. 16L00571 (confidential)

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¹³C-NMR spectrum

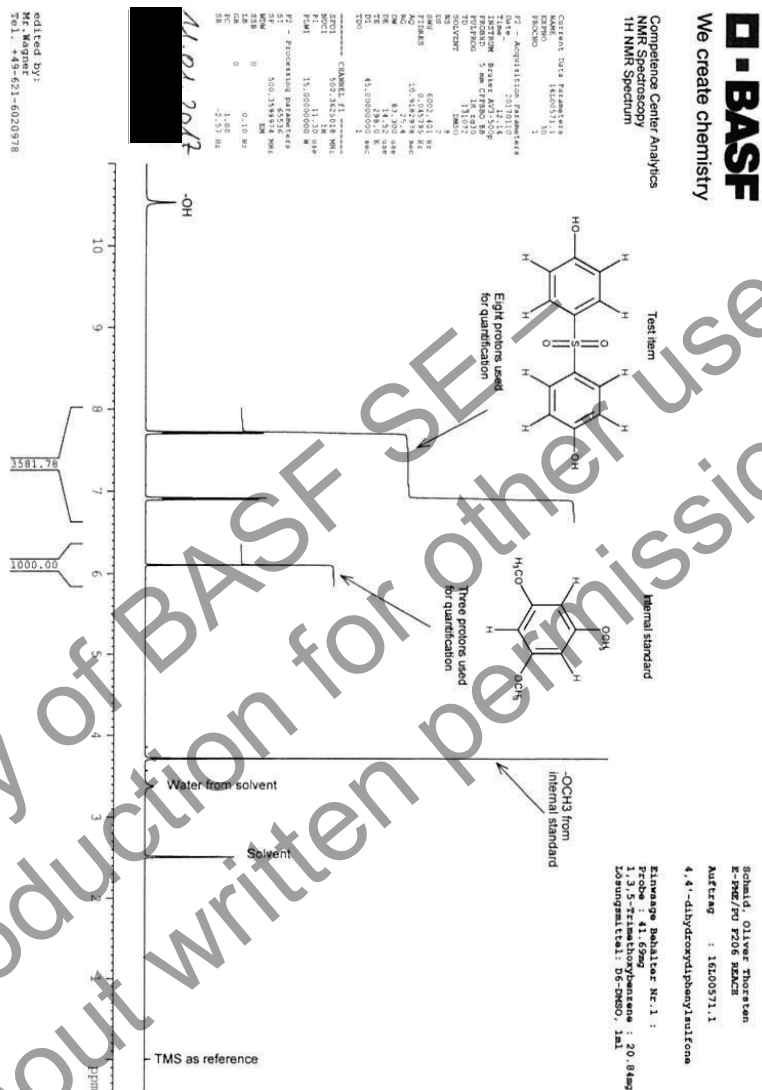


Competence Center Analytics

Final Report
Characterization of "4,4'-dihydroxydiphenylsulfone"
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Quant. ¹H NMR spectrum



Competence Center Analytics

Final Report
Characterization of "4,4'-dihydroxydiphenylsulfone"
 Study No. 16L00571 (confidential)

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Statement of the Quality Assurance Unit

The Quality Assurance Unit inspects all studies in accordance with the OECD Principles of Good Laboratory Practice and the GLP Principles of the German "Chemikaliengesetz" (Chemicals Act). The particular items inspected in this study are listed below.

The study-based inspections in terms of the Competence Center Analytics include "study-based inspections" and "process-based inspections" as defined in the Consensus Document "Quality Assurance and GLP" of the OECD.

Additionally the Quality Assurance Unit inspects the laboratories of the department Competence Center Analytics in regular intervals (equates to "facility-based inspections").

Findings are reported to study director and to management.

Verification of study plan Dec 12, 2016

Inspection of	Date of inspection	Reported to study director and management
Raw data:	Jan 23, 2017 Feb 07, 2017	Feb 07, 2017
Final report:	Jan 23, 2017 Feb 07, 2017	Feb 07, 2017

The final report reflects the raw data.

Ludwigshafen



Feb 07, 2017
 Date

PSN: 0510012-10 * evg-7.9 1/7 PR

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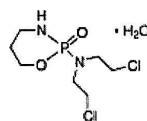
Email USA: techserv@sial.com

Outside USA: eurtechserv@sial.com

Certificate of Analysis

Product Name:
Cyclophosphamide monohydrate – bulk package

Product Number: C0768
Batch Number: MKBX1822V
Brand: SIGMA
CAS Number: 6055-19-2
MDL Number: MFCD00149395
Formula: C₇H₁₅Cl₂N₂O₂P · H₂O
Formula Weight: 279.10 g/mol
Storage Temperature: Store at 2 - 8 °C
Quality Release Date: 13 JAN 2016
Recommended Retest Date: DEC 2018



Test	Specification	Result
Appearance (Color)	White to Off-White	White
Appearance (Form)	Powder	Powder
Solubility (Color)	Colorless	Colorless
Solubility (Turbidity)	Clear	Clear
100 mg/ml in H ₂ O		
Water (by Karl Fischer)	4.7 - 7.8 %	6.0 %
Proton NMR Spectrum	Conforms to Structure	Conforms
Purity (HPLC)	97.0 - 103.0 %	100.0 %
Recommended Retest Period		
3 Years		

Quality Control
Milwaukee, WI US

Sigma-Aldrich warrants, that at the time of the quality release or subsequent retest date this product conformed to the information contained in this publication. The current Specification sheet may be available at Sigma-Aldrich.com. For further inquiries, please contact Technical Service. Purchaser must determine the suitability of the product for its particular use. See reverse side of invoice or packing slip for additional terms and conditions of sale.

Version Number: 1

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2. Analyses of the test substance preparations

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STUDY TITLE

ANALYTICAL REPORT

DHDPS

Stability Analysis in

1% Carboxymethylcellulose in Drinking Water

AUTHOR(S)**STUDY COMPLETION DATE**

29 August 2013

TEST FACILITYBASF SE
Experimental Toxicology and Ecology
67056 Ludwigshafen, Germany**TEST FACILITY PROJECT IDENTIFICATION**

Project No.: 01Y0066/05Y009

SPONSORBASF SE
67056 Ludwigshafen, Germany

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GLP COMPLIANCE STATEMENT

This study was conducted in accordance with the OECD Principles of Good Laboratory Practice and the GLP Principles of the German "Chemikaliengesetz" (Chemicals Act) which meet the United States Environmental Protection Agency Good Laboratory Practice Standards [40 CFR Part 160 (FIFRA) and Part 792 (TSCA)], with the exception that recognized differences exist between the GLP Principles/Standards of OECD and the Principles/Standards of FIFRA and TSCA.

Study Director

Typed name of Study Director:

Typed name of Laboratory:

BASF SE
Experimental Toxicology and Ecology
67056 Ludwigshafen
Germany

Date:

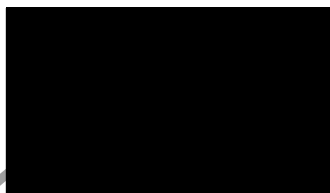
29 Aug. 2013

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SIGNATURE PAGE

Study Director:



29. Aug. 2013

Management:



27. Aug. 2013

STATEMENT OF THE QUALITY ASSURANCE UNIT

The Quality Assurance Unit (QAU) inspected the study and reported any inspection results to the Study Director and to Management.

The final report reflects the raw data.

Phase of study	Date of inspection (mm-dd-yyyy)	Reported to Study Director and to Management (mm-dd-yyyy)
Study Plan:	10-09-2012	10-09-2012
Conduct of study:	10-12-2012	10-12-2012
Report:	08-08-2013	08-08-2013

Ludwigshafen, 29 August 2013

GLP CERTIFICATE (FROM THE COMPETENT AUTHORITY)

Rheinland-Pfalz

Gute Laborpraxis / Good Laboratory Practice

GLP-Bescheinigung / Statement of GLP Compliance

(gem. / according to § 19 Abs. 1 Chemikaliengesetz)



Eine GLP-Inspektion zur Überwachung und der Einhaltung der GLP-Grundsätze gemäß Chemikaliengesetz bzw. Richtlinie 2004/9/EG wurde durchgeführt in:

Assessment of conformity with GLP according to Chemikaliengesetz and Directive 2004/9/EC at:

Prüfeinrichtung / Test facility

BASF SE
Experimentelle Toxikologie und Ökologie
67056 Ludwigshafen

BASF SE
Experimental Toxicology and Ecology
67056 Ludwigshafen, Germany

Prüfung nach Kategorien / Areas of Expertise
(gem. / according ChemVwV-GLP Nr. 53/OECD guidance)

1,2,3,4,5,8,9

Kat. 9 – Biochemische und pathologische Untersuchungen zu Wirkmechanismen /
Biochemical and pathological examinations concerning mode of action

Datum der Inspektion / Date of Inspection

(Tag/Monat/Jahr / day.month/year)

19.05.2009 & 06. bis 08.07.2009

Die genannte Prüfeinrichtung befindet sich im nationalen GLP-Überwachungsverfahren und wird regelmäßig auf Einhaltung der GLP-Grundsätze überwacht.

The above mentioned test facility is included in the national GLP Compliance Programme and is inspected on a regular basis.

Auf der Grundlage des Inspektionsberichtes wird hiermit bestätigt, dass in dieser Prüfeinrichtung die oben genannten Prüfungen unter Einhaltung der GLP-Grundsätze durchgeführt werden können.

Eine erneute behördliche Überprüfung der Einhaltung der GLP-Grundsätze durch die Prüfeinrichtung ist so rechtzeitig zu beantragen, dass die Folgeinspektion spätestens vier Jahre nach dem Beginn der o.g. Inspektion stattfinden kann. Ohne diesen Antrag wird die Prüfeinrichtung nach Ablauf der Frist aus dem deutschen GLP-Überwachungsprogramm genommen und diese GLP-Bescheinigung verliert ihre Gültigkeit.

Based on the inspection report it can be confirmed, that the test facility is able to conduct the aforementioned studies in compliance with the Principles of GLP.

Verification of the compliance of the test facility with the Principles of the GLP has to be applied for in time to allow for a follow-up inspection to take place within four years after commencing the above mentioned inspection. Elapsing this term, the test facility will be taken out of the German GLP-Monitoring Programme and this GLP Certificate becomes invalid.

Unterschrift, Datum / Signature, Date

Dr. Pia Hirsch 22.10.2009

Dr. Pia Hirsch - stellv. Präsidentin -

(Name und Funktion der verantwortlichen Person / name and function of responsible person)



Landesamt für Umwelt, Wasserwirtschaft und Gewerbeaufsicht
Kaiser-Friedrich-Straße 7
55116 Mainz

(Name und Adresse der GLP-Überwachungsbehörde / Name and address of the GLP Monitoring Authority)

Landesamt für
Umwelt, Wasserwirtschaft
und Gewerbeaufsicht



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GLP COMPLIANCE STATEMENT

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STATEMENT OF THE QUALITY ASSURANCE UNIT

GLP CERTIFICATE (FROM THE COMPETENT AUTHORITY)

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1. INTRODUCTION

In the context of toxicological studies the stability of the test substance DHDPs in the vehicle 1% carboxymethylcellulose in drinking water has to be verified. The results of these analyses are reported and discussed.

2. RETENTION OF RECORDS

GLP-relevant records and materials are stored at BASF SE for at least the period of time specified in the GLP principles. Details concerning responsibilities or locations of archiving can be seen from the respective SOPs and from the raw data.

3. TIME SCHEDULE

Study initiation date:	09 October 2012
Experimental starting date:	12 October 2012
Experimental completion date:	19 October 2012

4. MATERIAL AND METHODS

4.1. TEST ITEM

The analyses of the test item (= test substance) were carried out at the Competence Center Analytics of BASF SE, Ludwigshafen, Germany.

Name of test substance:	DHDPS
Test substance No.:	05/0066-4
Batch identification:	69611767J0
CAS No.:	80-09-1
Purity:	(1) 99.3 and 99.5 %, (HPLC) (2) 99.4 g/100 g, (1H-NMR) (according to the project number 12L00002)
Homogeneity:	Given
Storage stability:	stable until: 28 May 2013 The stability of the test substance under storage conditions over the test period was guaranteed by the sponsor, and the sponsor holds this responsibility.
Additional Test Substance Information	
Date of production:	28 Nov 2011
Physical state/ Appearance:	Solid / white
Storage conditions	Room temperature

4.2. SAMPLE DATA

Sponsor: [REDACTED]
Vehicle: 1% carboxymethylcellulose in drinking water
Target concentration: 0.05 g/100 mL
Duration of the stability test period: 7 days
Storage conditions of the samples during the stability period: Refrigerator

4.3. TEST SUBSTANCE PREPARATION

51.2 mg of the test substance were dissolved in 5 mL acetone. 0.5 mL of this solution were transferred into 100 mL volumetric flasks. After acetone evaporation at room temperature, 10 mL 1% carboxymethylcellulose in drinking water were added. For each time point a sample was prepared. The final nominal concentration was 0.0512 g / 100 mL.

4.4. SAMPLE PREPARATION AND ANALYSIS

The sample preparation and analysis of the test substance was carried out according to the valid control procedure 05/0066_01-01.

A detailed description of the control procedure is given in the appendix of this report.

4.5. LIST OF DEVIATIONS

4.5.1. LIST OF DEVIATIONS FROM THE CONTROL PROCEDURE

There were no deviations from the described control procedure 05/0066_01-01.

5. RESULTS AND DISCUSSION

5.1. ANALYSIS OF STABILITY

The results obtained for the stability of the test substance in 1% carboxymethylcellulose in drinking water are summarized in the following table.

All calculated values in the table are rounded. Calculations were performed with a full set of decimal places.

Nominal concentration [g/100 mL]	Time after starting	Concentration found [g/100 mL]	Nominal concentration (%)
0.0512	0h	0.055	107.3
0.0512	4h	0.053	104.9
0.0512	4d	0.055	108.5

The stability samples from 0 hours until 4 days were stored at room temperature

Nominal concentration [g/100 mL]	Time after starting	Concentration found [g/100 mL]	Nominal concentration (%)
0.0512	7d	0.054	106.6

The stability sample for the duration of 7 days was stored in the refrigerator.

5.2. DISCUSSION

Based on the analytical results it is concluded, that DHDPS is stable in 1% carboxymethylcellulose in drinking water over a period of 4 days at room temperature and 7 days in the refrigerator.

All determined concentrations were in the range of 90 % - 110 % of the nominal concentration.

FIGURES

Figure 1: Chromatogram of matrix solution (measured on 19 Oct 2012)

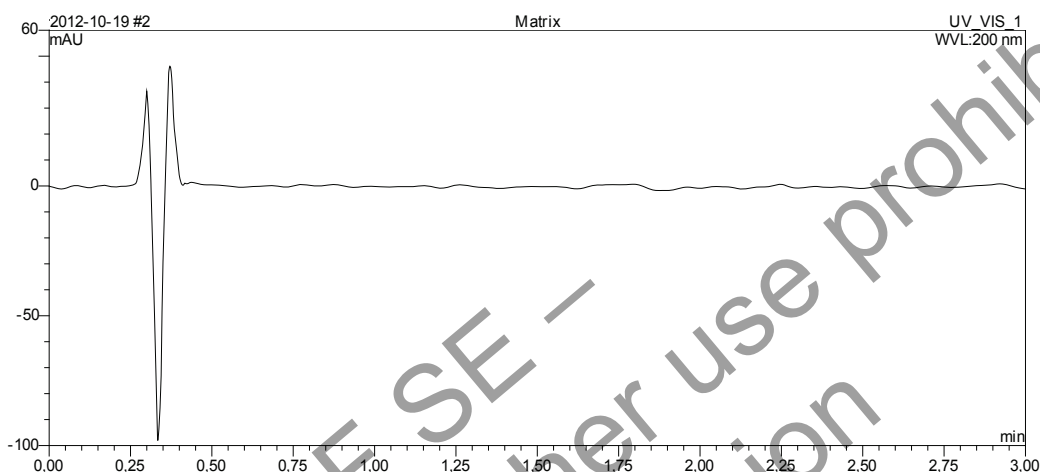


Figure 2: Chromatogram of calibration solution 1 (2.044 mg/100 mL, measured on 19 Oct 2012)

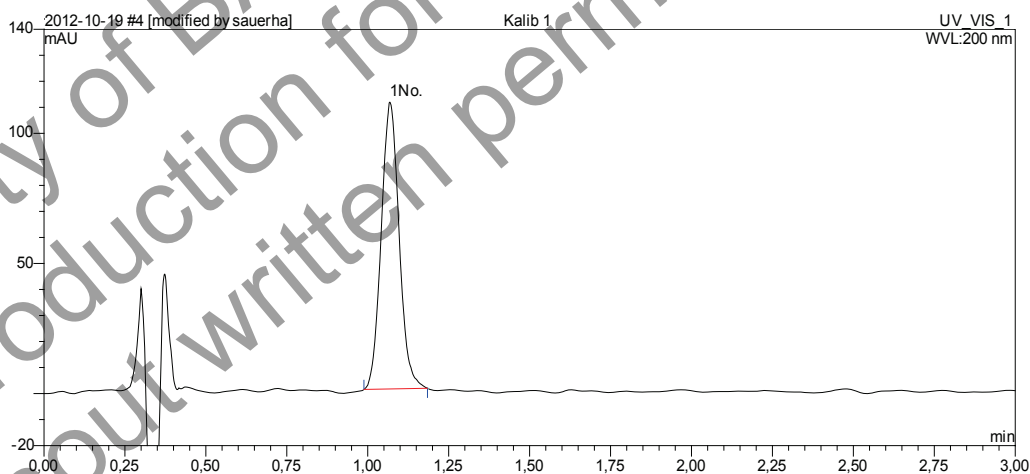


Figure 3: Chromatogram sample solution day 7 (measured on 19 Oct 2012)

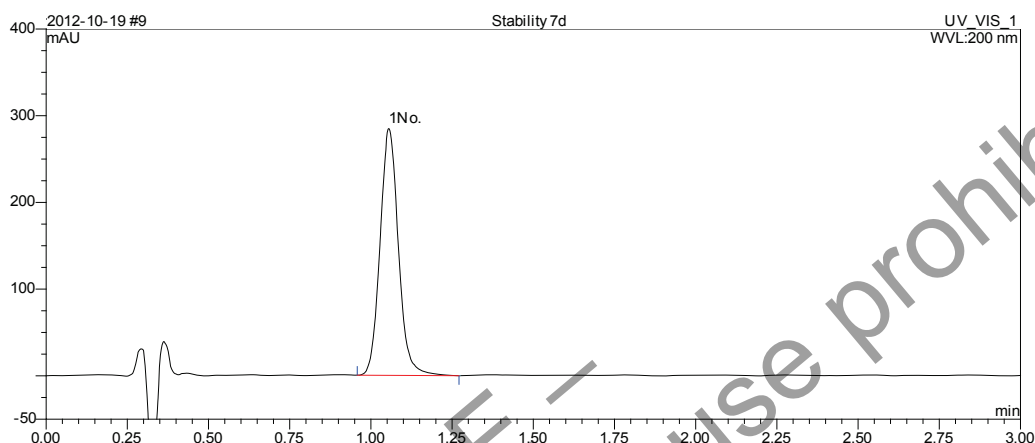
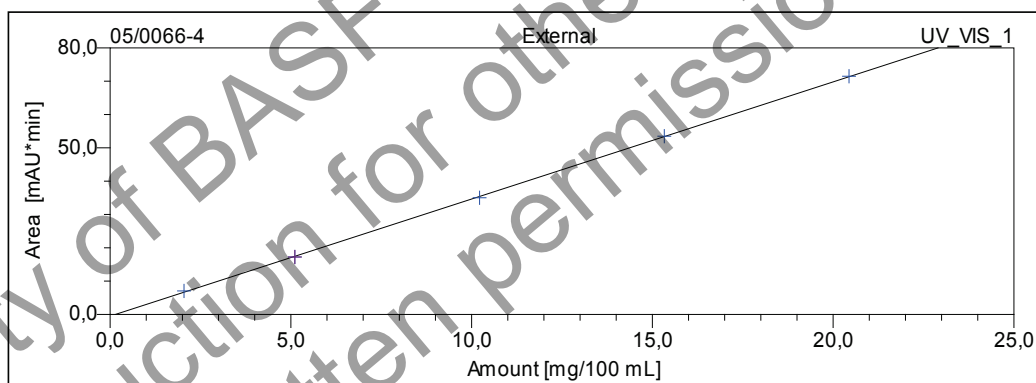


Figure 4: Calibration curve (19 Oct 2012, Concentration range 2.044 – 20.44 mg/100 mL)



6. APPENDIX

6.1. CONTROL PROCEDURE 05/0066_01-01

BASF SE
Test Facility
Experimental Toxicology and Ecology / Analytical Chemistry


The Chemical Company

CONTROL TEST

Test substance number: 05/0066	No.: 05/0066_01-01
Name of test substance: DHDPs	Effective from: 09 Oct 2012
Control procedure: Content (LC) / Carboxymethylcellulose(CMC) in drinking water	Page 1 of 5

Technique	HPLC
System:	Waters alliance 2487 with auto sampler, Dionex Chromeleon-Software (Dionex), or equivalent system
Column:	Length: 100 mm Inner diameter: 4.6 mm
Stationary Phase:	Chromolith Performance RP 18e, Merck or equivalent
Mobile Phase A:	1000 mL acetonitrile are mixed with 1 mL formic acid (HCOOH)
Mobile Phase B:	1000 mL water are mixed with 1 mL formic acid (HCOOH)
Isocratic:	
Mobile Phase A 20 %	Mobile Phase B 80 %
Injection volume:	10 µL
Flow rate:	5 mL/min
Detection:	200 nm
Column temperature:	Ambient
Run time:	Approx. 3 min

BASF SE
Test Facility
Experimental Toxicology and Ecology / Analytical Chemistry


The Chemical Company

CONTROL TEST

Test substance number: 05/0066	No.: 05/0066_01-01
Name of test substance: DHDPs	Effective from: 09 Oct 2012
Control procedure: Content (LC) / Carboxymethylcellulose(CMC) in drinking water	Page 2 of 5

Sample solution: Samples are diluted completely with methanol using appropriate volumetric flasks to obtain sample solutions with test substance concentrations that match the calibration range.
If required, all dilutions are sonicated for 5 minutes to ensure a complete dissolution of the test substance.

The samples are filtered (cellulose filter, 0.2 µm) prior HPLC analysis.

Annotation: If the amount of test substance in the sample solution is outside the calibration range (calibration solutions 1 – 5), an adequate dilution step with matrix solution has to be performed to match the described concentration range.

Matrix solution: The preparation of the matrix solution has to be performed according to the procedure described for sample solution preparation

Stock solution: Approx. 50 mg test substance are dissolved to a final volume of 100 mL with methanol (50 mg/100 mL)

Calibration solution 1: 1.0 mL stock solution are diluted with matrix solution to 25 mL (2 mg/100 mL)

Calibration solution 2: 1.0 mL stock solution are diluted with matrix solution to 10 mL (5 mg/100 mL)

Calibration solution 3: 1.0 mL stock solution are diluted with matrix solution to 5 mL (10 mg/100 mL)

Calibration solution 4: 1.5 mL stock solution are diluted with matrix solution to 5 mL (15 mg/100 mL)

Calibration solution 5: 2.0 mL stock solution are diluted with matrix solution to 5 mL (20 mg/100 mL)

System-suitability solution: System-suitability solution is prepared with a second independent weighing according to calibration solution 3 (10 mg/100 mL)

Procedure After conditioning the HPLC system, sample solutions, matrix solution, calibration solutions and system-suitability solution are injected according to the sequence described in the raw data. All solutions are injected at least once.

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Experimental Toxicology and Ecology / Analytical Chemistry


The Chemical Company

CONTROL TEST

Test substance number: 05/0066	No.: 05/0066_01-01
Name of test substance: DHDPs	Effective from: 09 Oct 2012
Control procedure: Content (LC) / Carboxymethylcellulose(CMC) in drinking water	Page 3 of 5

Retention time:

Test substance : 4,4'-Dihydroxydiphenylsulfon:
Approx. 1 min

System suitability:

The calculated content of the system-suitability solution has to be in the range from 95 % to 105 %.

The coefficient of determination (R^2) has to be ≥ 0.990 . If the correlation coefficient (R) is used, this value has to be ≥ 0.995 .

Calculation:

The concentration control measurements are based on external calibration (calibration solutions 1 – 5).

The calculation of the content is performed electronically. (e.g. Dionex Chromeleon – Software, Microsoft Excel). Basic formulas for calculations are described below (e.g. Dionex Chromeleon – Software)

Formulas:

Calibration curve

$$Y = a \cdot x + b$$

a = slope of calibration curve
b = intercept

Analysed concentration (C_A)

$$C_A = \frac{(Y-b) \cdot V \cdot d}{a \cdot w}$$

or

$$C_A = \frac{(Y-b)}{a} \cdot \frac{V \cdot d}{v}$$

w = weight sample
V = final sample volume
d = dilution factor

v = volume sample
V = final sample volume
d = dilution factor

Analysed concentration (C_A)

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CONTROL TEST

Test substance number: 05/0066

No.: 05/0066_01-01

Name of test substance: DHDPs

Effective from: 09 Oct 2012

Control procedure: Content (LC) / Carboxymethylcellulose(CMC) in drinking water

Page 4 of 5

Figure 1.1: Example chromatogram matrix solution (08 Oct 2012, Project no.: 01Y0066/05Y009) for illustration

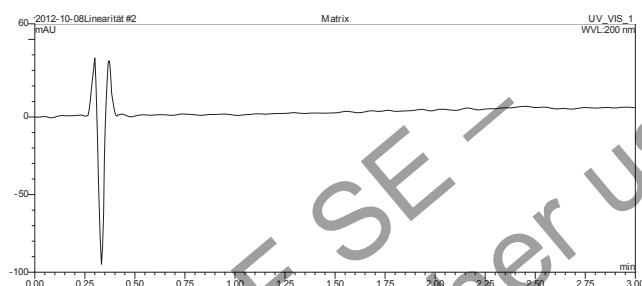
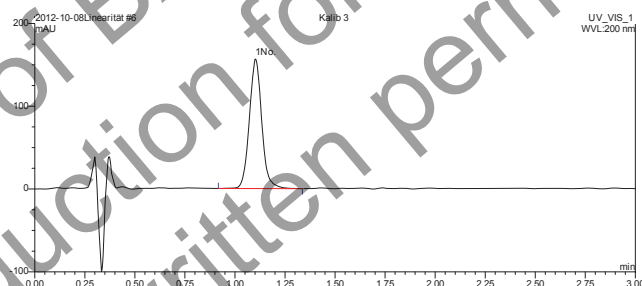


Figure 1.2: Example chromatogram calibration solution (08 Oct 2012, Project no.: 01Y0066/05Y009) for illustration



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The Chemical Company

CONTROL TEST

Test substance number: 05/0066

No.: 05/0066_01-01

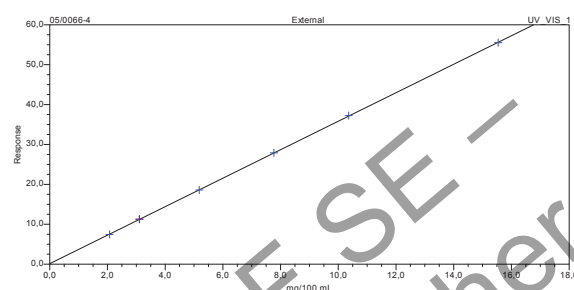
Name of test substance: DHDPs

Effective from: 09 Oct 2012

Control procedure: Content (LC) / Carboxymethylcellulose(CMC) in drinking water

Page 5 of 5

Figure 1.3 Example calibration curve (08 Oct 2012, Project no.: 01Y0066/05Y009) for illustration



STUDY TITLE

ANALYTICAL REPORT

Cyclophosphamide Monohydrate

Stability Analysis in

drinking water

AUTHOR**STUDY COMPLETED ON**

26 March 2010

Test Facility

Experimental Toxicology and Ecology
BASF SE
67056 Ludwigshafen, Germany

TEST FACILITY PROJECT IDENTIFICATION

Project No.: 01Y0012/058064

SPONSOR

BASF SE
67056 Ludwigshafen, Germany

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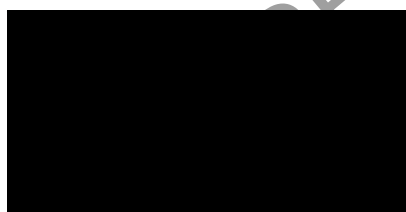


The Chemical Company

Report; Project No.: 01Y0012/058064

GLP COMPLIANCE STATEMENT

This study was conducted in accordance with the OECD Principles of Good Laboratory Practice and the GLP Principles of the German "Chemikaliengesetz" (Chemicals Act), which meet the United States Environmental Protection Agency Good Laboratory Practice Standards [40 CFR Part 160 (FIFRA) and Part 792 (TSCA)], with the exception that recognized differences exist between the GLP Principles/Standards of OECD and the Principles/Standards of FIFRA and TSCA.



26 March 2010

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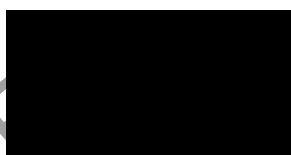


The Chemical Company

Report; Project No.: 01Y0012/058064

SIGNATURES

Study Director:



26 March 2010

Management:



24 March 2010

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STATEMENT OF THE QUALITY ASSURANCE UNIT

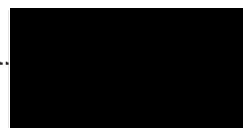
The Quality Assurance Unit (QAU) inspected the study and reported any inspection results to the Study Director and to Management.

The final report reflects the raw data.

Phase of study	Date of inspection (mm-dd-yyyy)	Reported to Study Director and to Management (mm-dd-yyyy)
Study Plan:	11-27-2009	11-27-2009
Conduct of study:	01-28-2010	01-28-2010
Report:	03-23-2010	03-23-2010

Ludwigshafen,

25 March 2010



STATEMENT OF GLP COMPLIANCE (FROM THE COMPETENT AUTHORITY)

Rheinland-Pfalz

Gute Laborpraxis / Good Laboratory Practice

GLP-Bescheinigung / Statement of GLP Compliance
(gem. / according to § 19 Abs. 1 Chemikaliengesetz)

Eine GLP-Inspektion zur Überwachung und der Einhaltung der GLP-Grundsätze gemäß Chemikaliengesetz bzw. Richtlinie 2004/9/EG wurde durchgeführt in:

Assessment of conformity with GLP according to Chemikaliengesetz and Directive 2004/9/EC at::

Prüfeinrichtung / Test facility

BASF SE
Experimentelle Toxikologie und Ökologie
67056 Ludwigshafen

BASF SE
Experimental Toxicology and Ecology
67056 Ludwigshafen, Germany

Prüfung nach Kategorien / Areas of Expertise
(gem. / according ChemVwV-GLP Nr. 5.3/OECD guidance)
1,2,3,4,5,8,9

Kat. 9 – Biochemische und pathologische Untersuchungen zu Wirkmechanismen /
Biochemical and pathological examinations concerning mode of action

Datum der Inspektion / Date of Inspection
(Tag/Monat/Jahr / day.month/year)
19.05.2009 & 06. bis 08.07.2009

Die genannte Prüfeinrichtung befindet sich im nationalen GLP-Überwachungsverfahren und wird regelmäßig auf Einhaltung der GLP-Grundsätze überwacht.

The above mentioned test facility is included in the national GLP Compliance Programme and is inspected on a regular basis.

Auf der Grundlage des Inspektionsberichtes wird hiermit bestätigt, dass in dieser Prüfeinrichtung die oben genannten Prüfungen unter Einhaltung der GLP-Grundsätze durchgeführt werden können. Eine erneute behördliche Überprüfung der Einhaltung der GLP-Grundsätze durch die Prüfeinrichtung ist so rechtzeitig zu beantragen, dass die Folgeinspektion spätestens vier Jahre nach dem Beginn der o.g. Inspektion stattfinden kann. Ohne diesen Antrag wird die Prüfeinrichtung nach Ablauf der Frist aus dem deutschen GLP-Überwachungsprogramm genommen und diese GLP-Bescheinigung verliert ihre Gültigkeit.

Based on the inspection report it can be confirmed, that the test facility is able to conduct the aforementioned studies in compliance with the Principles of GLP.

Verifikation der Compliance der Prüfeinrichtung mit den Prinzipien der GLP hat so zu beauftragt in time to allow for a follow-up inspection to take place within four years after commencing the above mentioned inspection. Elapsing this term, the test facility will be taken out of the German GLP-Monitoring Programme and this GLP Certificate becomes invalid.

Unterschrift, Datum / Signature, Date

Dr. Pia Hirsch 22.10.2009

Dr. Pia Hirsch - stellv. Präsidentin -
(Name und Funktion der verantwortlichen Person / name and function of responsible person)

Landesamt für Umwelt, Wasserwirtschaft und Gewerbeaufsicht
Kaiser-Friedrich-Straße 7
55116 Mainz

(Name und Adresse der GLP-Überwachungsbehörde /
Name and address of the GLP Monitoring Authority)



Landesamt für
Umwelt, Wasserwirtschaft
und Gewerbeaufsicht

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4.2. SAMPLE DATA

4.3. SAMPLE PREPARATION FOR ANALYSIS

4.4. ANALYTICAL METHOD

5. RESULTS AND DISCUSSION

5.1. ANALYSIS OF STABILITY

FIGURES

1. INTRODUCTION

In the context of toxicological studies the stability of the test item (= test substance) Cyclophosphamide Monohydrate in the vehicle drinking water has to be verified. The results of these analyses are reported and discussed.

2. RETENTION OF RECORDS

GLP-relevant records and materials are stored at BASF SE for at least the period of time specified in the GLP principles. Details concerning responsibilities or locations of archiving can be seen from the respective SOPs and from the raw data.

3. TIME SCHEDULE

Study initiation date:	26 November 2009
Experimental starting date:	28 January 2010
Experimental completion date:	01 March 2010

4. MATERIAL AND METHODS

4.1. TEST ITEM

The test item (=test substance) will be used with the given specifications of the producer (Sigma-Aldrich, Taufkirchen, Germany). No further analyses will be conducted.

Name of the test substance:	Cyclophosphamide Monohydrate
Test substance No.:	05/0012-4
Batch No.:	1362353
CAS No.:	6055-19-2
Purity/Composition:	100 %
Homogeneity:	homogeneous

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Stability:

Stable until: 08 October 2010

The stability of the test substance under storage conditions over the test period was guaranteed by the sponsor, and the sponsor holds this responsibility.

Additional Test Substance Information

Date of production: unknown
Physical state / appearance: Solid / white
Storage conditions: Refrigerator/ under N₂

4.2. SAMPLE DATA

Sender: [REDACTED]
Project No. in sender's laboratory: unknown
Vehicle: drinking water
Nominal concentration: 0.045 g/100 mL
Duration of the stability test period: 7 days at ambient temperature and 32 days in freezer
Storage conditions of the samples during the stability period: ambient and in the freezer

4.3. SAMPLE PREPARATION FOR ANALYSIS

The test substance is soluble in the vehicle.
Approximately 45 mg of the test substance were weighed into 100 mL measuring flasks which was filled up with drinking water to the calibration mark. To the given time points an aliquot of 1 mL was diluted with acetonitrile/ highly deionized water 1/1 (v/v) at a ratio of 1 to 20 (v/v). Aliquots of the dilutions were used for HPLC/MS – analyses.

4.4. ANALYTICAL METHOD

HPLC/MS with external calibration

Column: Synergi 4 μ Polar RP, 150 x 3 mm

Eluent: Eluent A: acetonitrile + HCOOH (1 mL/L)

Eluent B: highly deionized water + HCOOH (1 mL/L)

Gradient:

Time [min]	% B
0 – 8	75
8 – 9	75 - 25
9 – 15	25
15 – 16	25 - 75
16 – 25	75

Flow rate: 0.5 mL/min

Injection volume: 10 μ L

Column temperature : Ambient

Detection parameters: Ionization mode: ES +
LC-MS Mass 261.0 Dwell 0.5 Cone 34

Stock solution concentration: 10.8 mg/100 mL (prepared on 28 January 2010)
12.2 mg/100 mL (prepared on 04 February 2010)
12.9 mg/100 mL (prepared on 01 March 2010)

Storage of the stock solution: Prepared freshly

Stock standard diluent: Acetonitrile/ highly deionized water 1/1 v/v

Chromatographic Standards: For quantification, three standard solutions (Kalib 1 - 3) were prepared by diluting the stock solutions with stock standard diluent.

External calibration: Under the described chromatographic conditions, aliquots (10 μ L) of the standards were analyzed by HPLC. Record peak response was recorded as area under the curve. Each sample was analyzed twice. Means were used for quantification. Linearity between concentration and area under the curve was given in the range of the analysis. One calibration curve is shown Figure 1.

Limit of quantification: 0.645 mg/100 mL (lowest concentration in calibration)

Figures of the calibration curve and examples of chromatograms will follow within this report.

5. RESULTS AND DISCUSSION

5.1. ANALYSIS OF STABILITY

The results obtained for the stability of Cyclophosphamide Monohydrate in drinking water are summarized in the following table:

Initial concentration [g/100 mL]	Time after starting, storage	Analytical value [g/100 mL]			% of initial value
		Sample I	Sample II	Mean	
0.0433	0 h	0.0424	0.0442	0.0433	100.0
0.0433	4 h, stored ambient	0.0434	0.0435	0.0435	100.5
0.0433	7 d, stored ambient	0.0466	0.0460	0.0463	106.9
0.0433	32 d, stored in the freezer	0.0398	0.0402	0.0400	92.4

Based on the results obtained for the analysis of the stability it is concluded, that Cyclophosphamide Monohydrate is stable in drinking water over a period of 7 days stored at ambient temperature and over a period of 32 days stored in the freezer.

FIGURES

Figure 1 Standard calibration curve (measured on 04 February 2010)

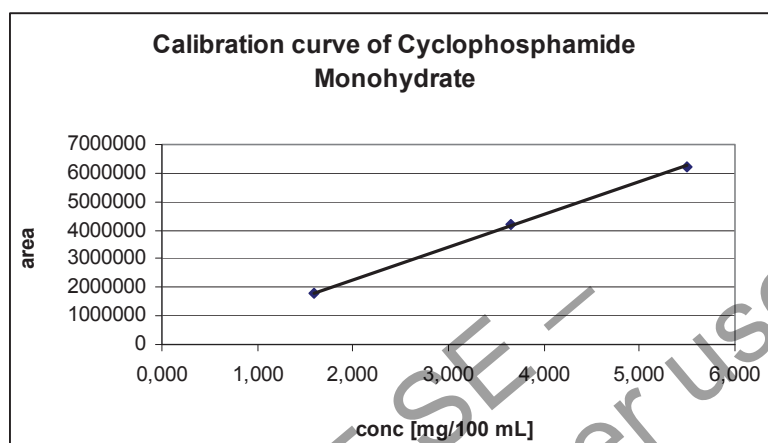


Figure 2 Chromatogram of a blank sample

Name: 01Y0012-058064-005, Vial: 3, Date: 28-Jan-2010, Time: 11:23:49, Description: Blindwert

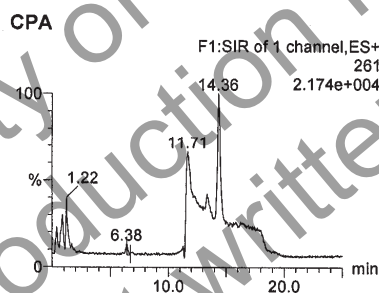


Figure 3 Chromatogram of the standard solution with the lowest substance concentration (lowest concentration in calibration)

Name: 01Y0012-058064-058, Vial: 28, Date: 01-Mar-2010, Time: 14:04:29, Description: Kalib.1

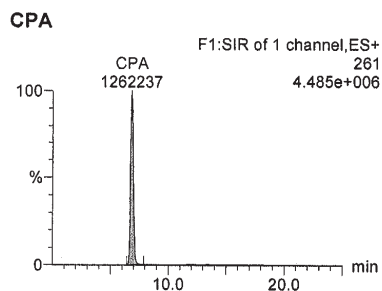


Figure 4 Chromatogram of the sample containing an initial value of 0.0433 g/100 mL test substance, analyzed immediately after sample preparation

Name: 01Y0012-058064-002, Vial: 2, Date: 28-Jan-2010, Time: 10:04:40, Description: 0h-Wert

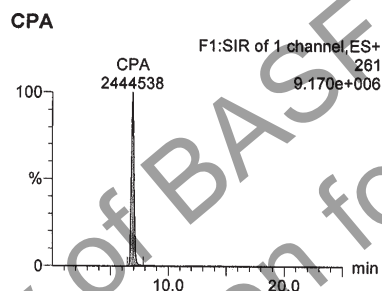


Figure 5 Chromatogram of the sample containing an initial value of 0.0433 g/100 mL, analyzed approximately 7 days (stored at room temperature) after sample preparation

Name: 01Y0012-058064-024, Vial: 75, Date: 04-Feb-2010, Time: 10:39:57, Description: 7d-Wert

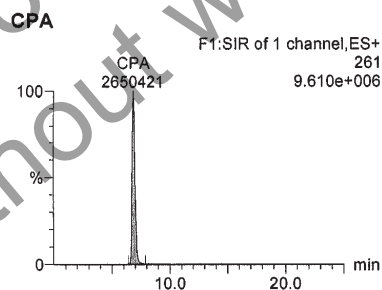
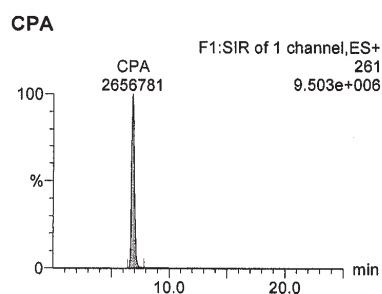


Figure 6 Chromatogram of the sample containing an initial value of 0.0433 g/100 mL, analyzed approximately 32 days (storage freezer) after sample preparation

Name: 01Y0012-058064-055, Vial: 27, Date: 01-Mar-2010, Time: 12:45:03, Description: 32d-Wert



Concentration Control Analysis of DHDPS in 0.5 % Sodium carboxymethyl cellulose in drinking water

1. PROJECT AND TEST SUBSTANCE INFORMATION

Project No.: 90R0066/05R034
Test item (= test substance): DHDPS
Batch No.: 03508136W0

2. SAMPLE DATA

2.1. CONCENTRATION CONTROL ANALYSIS

Vehicle: 0.5 % Sodium carboxymethyl cellulose in drinking water

Storage conditions of the
samples until analysis: Freezer

3. MATERIAL AND METHODS

3.1. SAMPLE PREPARATION AND ANALYSIS

The sample preparation and analysis of the test substance was carried out according to the valid control procedure 05/0066_01-05.

A detailed description of the control procedure is given in the appendix of this report.

3.2. LIST OF DEVIATIONS

3.2.1. List of deviations from the control procedure

There was one deviation from the described control procedure 05/0066_01-05.

On 15.09.2017 (samples from beginning of the study) the calibration solutions had the following approximate concentrations: 1, 2, 3, 4, 5 and 10 mg/100 mL and not 1, 2, 4, 6, 8 and 10 as described in the control procedure. This had no adverse effect on the results obtained because the linear range remained consistent.

4. RESULTS AND DISCUSSION

4.1. CONCENTRATION CONTROL ANALYSIS

The results obtained for the concentration control analysis of DHDPS in 0.5 % Sodium carboxymethyl cellulose in drinking water are summarized in the following tables:

All calculated values in the table are rounded. Calculations were performed with non-rounded values.

Date of sample preparation:	10 Aug 2017
Date of sampling:	10 Aug 2017
Date of receipt sample:	10 Aug 2017
Starting date of analytical determination:	15 Sep 2017

Name	Amount	Nominal Conc	Nominal Conc	Mean	RSD
	g/100 mL	g/100 mL	%	%	%
Sample 03	0.195	0.200	97.3%		
Sample 04	0.190	0.200	94.9%		
Sample 05	0.196	0.200	98.0%	96.7%	1.7%
Sample 06	0.597	0.600	99.4%		
Sample 07	1.748	1.800	97.1%		
Sample 08	1.699	1.800	94.4%		
Sample 09	1.763	1.800	97.9%	96.5%	1.9%

Date of sample preparation:	10 Apr 2018
Date of sampling:	10 Apr 2018
Date of receipt sample:	10 Apr 2018
Starting date of analytical determination:	15 May 2018

Name	Amount	Nominal Conc	Nominal Conc
	g/100mL	g/100mL	%
Sample 17	0.190	0.200	94.9%
Sample 18	0.566	0.600	94.3%
Sample 19	1.734	1.800	96.3%

No test substance could be detected in the vehicle control samples (samples 02 and 16) with a concentration of ≥ 30 % of the lowest calibration solution.

Considering the low relative standard deviation in the homogeneity analysis, it can be concluded that DHDPS was distributed homogeneously in 0.5 % Sodium carboxymethyl cellulose in drinking water.

The mean values (samples 03 – 05 and 07 – 09) and single values (samples 06, 17, 18 and 19) of DHDPS in 0.5 % Sodium carboxymethyl cellulose in drinking water were found to be in the range of 90 % – 110 % of the nominal concentrations.

These results demonstrated the correctness of the concentrations of DHDPS in 0.5 % Sodium carboxymethyl cellulose in drinking water.

Figures of the calibration curve and examples of chromatograms will follow within this report.

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Figure 1: Chromatogram of matrix solution, vehicle control sample (measured on 15 May 2018)

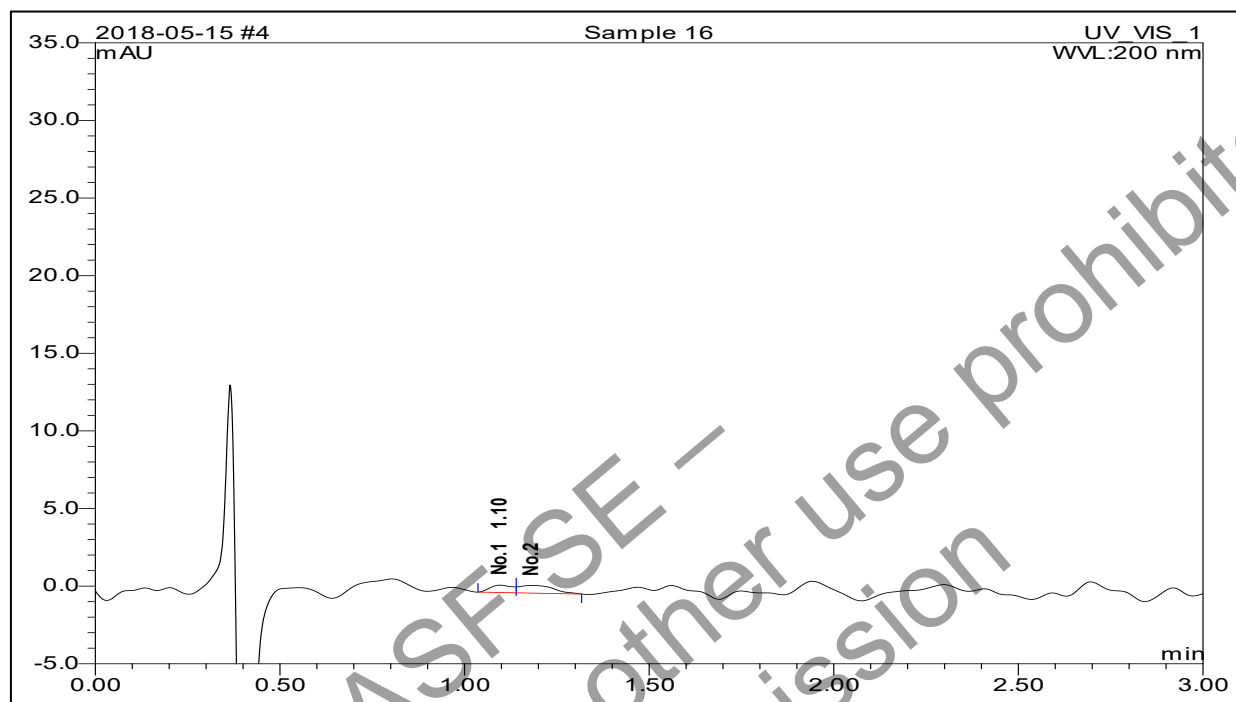


Figure 2: Chromatogram of calibration solution 1 (1 mg/100 mL, measured on 15 May 2018)

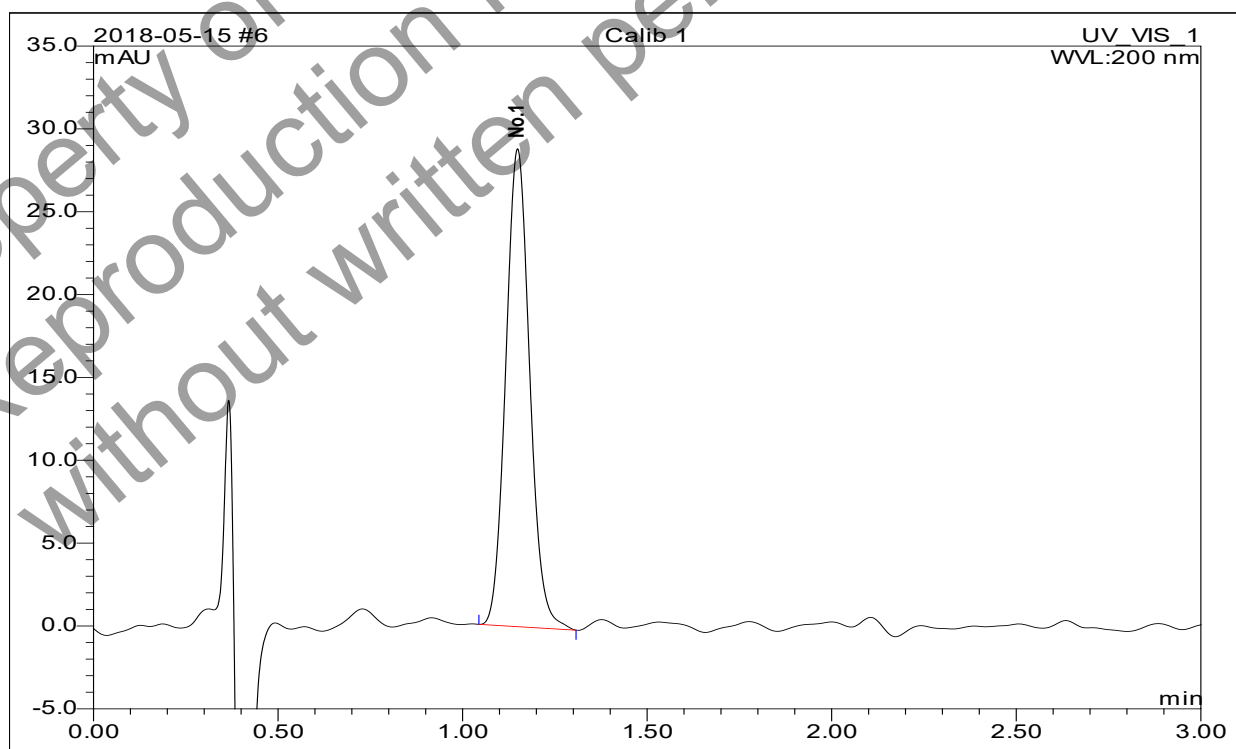


Figure 3: Chromatogram of sample 18 (measured on 15 May 2018)

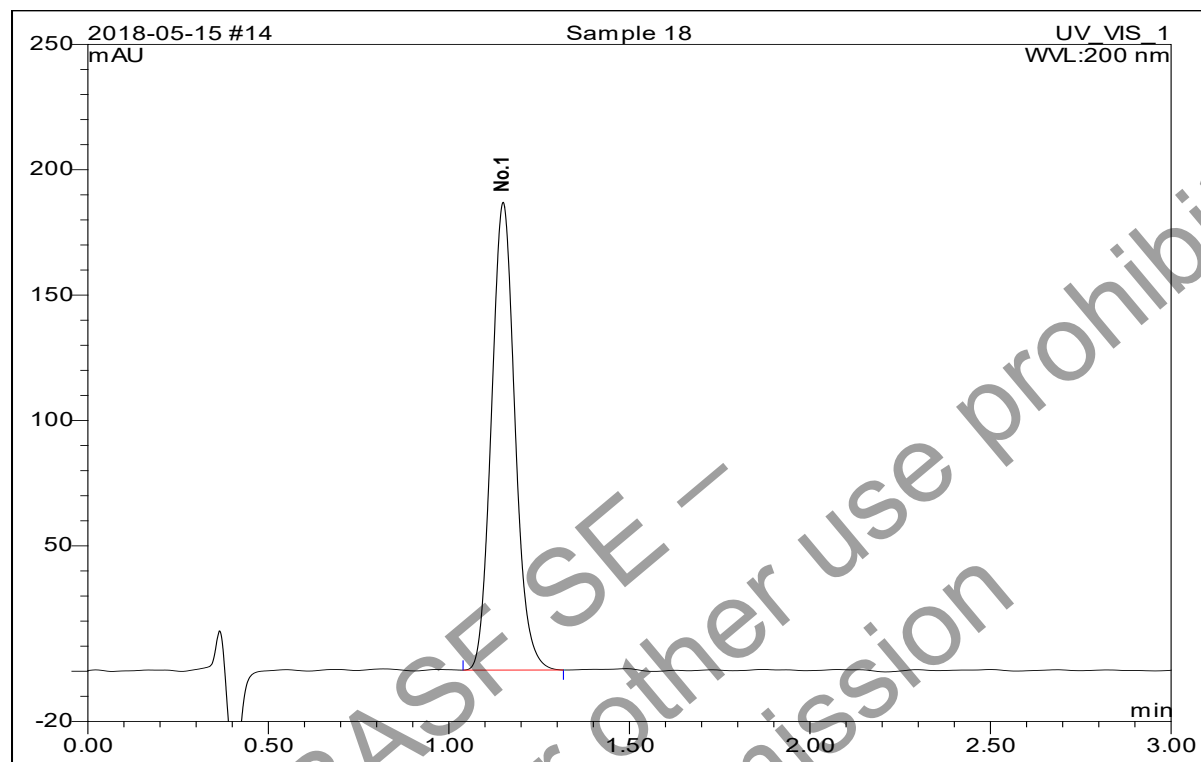
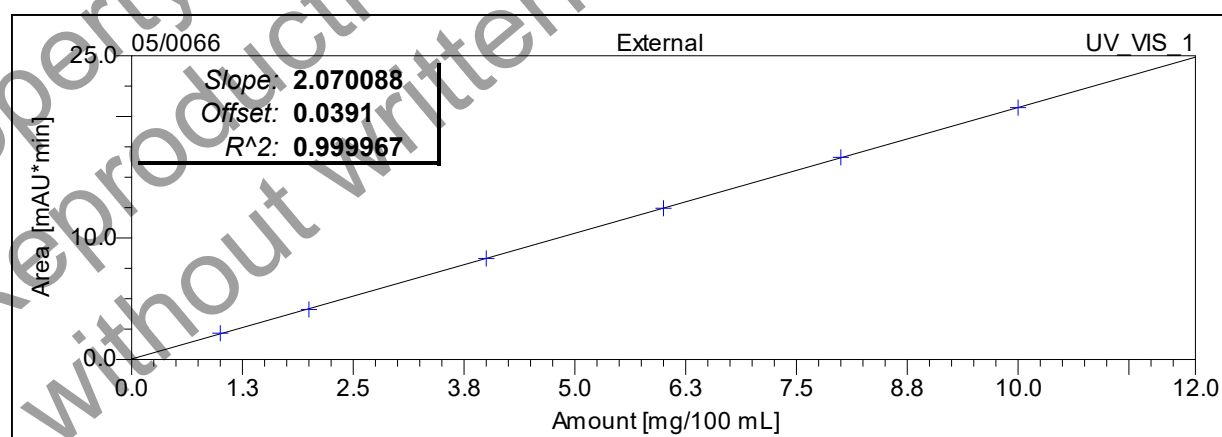


Figure 4: Calibration curve (measured on 15 May 2018, Concentration range 1 - 10 mg/100 mL)



5. APPENDIX**5.1. CONTROL PROCEDURE 05/0066_01-05**

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**CONTROL TEST**

Test substance number: 05/0066

No.: 05/0066_01-05

Name of test substance: DHDPS

Effective from: 15 Sep 2017

Control procedure: Content (LC) / aqueous carboxymethylcellulose

Page 1 of 9

Technique	HPLC
System:	Agilent 1100 with autosampler, DAD, Dionex Chromeleon – Software (Dionex), or equivalent system
Column:	Length: 100 mm Inner diameter: 4.6 mm
Stationary Phase:	Chromolith Performance RP 18e, Merck or equivalent
Mobile Phase A:	950 mL acetonitrile mixed with 50 mL water and 1 mL formic acid
Mobile Phase B:	950 mL water mixed with 50 mL acetonitrile and 1 mL formic acid
Isocratic:	
Mobile Phase A 20 %	Mobile Phase B 80 %
Injection volume:	5 µL
Flow rate:	4.0 mL/min
Detection:	200 nm
Column temperature:	25°C or room temperature
Run time:	Approximately 3 min

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**CONTROL TEST**

Test substance number: 05/0066

No.: 05/0066_01-05

Name of test substance: DHDPS

Effective from: 15 Sep 2017

Control procedure: Content (LC) / aqueous carboxymethylcellulose

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Sample solution: The samples are transferred into appropriate volumetric flasks with approximately 10 mL water and filled up to the mark with acetonitrile to obtain sample solutions with test substance concentrations that fall within the calibration range.
If required, all dilutions are sonicated for five minutes to ensure complete dissolution of the test substance.

The samples have to be diluted at least 1 + 39 (sample + solvents).

The samples are filtered (cellulose filter, 0.2 µm) prior HPLC analysis.

NOTE: If the amount of test substance in the sample solution is outside the calibration range (calibration solutions 1 – 6), an adequate dilution step with matrix solution has to be performed to reach the described concentration range.

Matrix solution: The preparation of the matrix solution has to be performed according to the procedure described for sample solution preparation.
The matrix solution should represent the sample with the lowest test substance concentration.

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CONTROL TEST

Test substance number: 05/0066

No.: 05/0066_01-05

Name of test substance: DHDPS

Effective from: 15 Sep 2017

Control procedure: Content (LC) / aqueous carboxymethylcellulose

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Stock solution ①: Approximately 50 mg (+/- 10 %) test substance is dissolved to a final volume of 100 mL with acetonitrile (50 mg/100 mL).

Calibration solution 1: 0.2 mL stock solution ① is diluted with matrix solution to 10 mL (1.0 mg/100 mL).

Calibration solution 2: 0.4 mL stock solution ① is diluted with matrix solution to 10 mL (2.0 mg/100 mL).

Calibration solution 3: 0.8 mL stock solution ① is diluted with matrix solution to 10 mL (4.0 mg/100 mL).

Calibration solution 4: 1.2 mL stock solution ① is diluted with matrix solution to 10 mL (6.0 mg/100 mL).

Calibration solution 5: 1.6 mL stock solution ① is diluted with matrix solution to 10 mL (8.0 mg/100 mL).

Calibration solution 6: 2.0 mL stock solution ① is diluted with matrix solution to 10 mL (10.0 mg/100 mL).

The concentrations of the solutions above are absolute, the used volumes can be changed.

System-suitability solution:

System-suitability solution is prepared with a second independent weighing according to calibration solution 3 (4.0 mg/100 mL)

Procedure

After conditioning the LC system, sample solutions, matrix solution, calibration solutions and system-suitability solution are injected according to the sequence described in the raw data. All solutions are injected at least once.

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**CONTROL TEST**

Test substance number: 05/0066

No.: 05/0066_01-05

Name of test substance: DHDPS

Effective from: 15 Sep 2017

Control procedure: Content (LC) / aqueous carboxymethylcellulose

Page 4 of 9

Retention time:

Test substance: DHDPS:
Approximately 1 min

System suitability:

The calculated content of the system-suitability solution has to be in the range from 95 % to 105 %.

The coefficient of determination (R^2) has to be ≥ 0.990 . If the correlation coefficient (R) is used, this value has to be ≥ 0.995 .

Calculation:

The concentration control measurements are based on external calibration (calibration solutions 1 – 6).

Content calculation is performed electronically. (e.g. Dionex Chromeleon – Software, Microsoft Excel). Basic formulas for calculations are described below (e.g. Dionex Chromeleon – Software)

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Experimental Toxicology and Ecology / Analytical Chemistry

**CONTROL TEST**

Test substance number: 05/0066

No.: 05/0066_01-05

Name of test substance: DHDPS

Effective from: 15 Sep 2017

Control procedure: Content (LC) / aqueous carboxymethylcellulose

Page 5 of 9

Formulas:

Calibration curve

$$Y = a \cdot x + b$$

a = slope of calibration curve

b = intercept

x = concentration

Analysed concentration (C_A)

$$C_A = \frac{(Y - b)}{a} \cdot \frac{V \cdot d}{w} \quad \text{or}$$

$$C_A = \frac{(Y - b)}{a} \cdot \frac{V \cdot d}{v}$$

w = weight sample

V = final sample volume

d = dilution factor

v = volume sample

V = final sample volume

d = dilution factor

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Test Facility
Experimental Toxicology and Ecology / Analytical Chemistry

**CONTROL TEST**

Test substance number: 05/0066

No.: 05/0066_01-05

Name of test substance: DHDPS

Effective from: 15 Sep 2017

Control procedure: Content (LC) / aqueous carboxymethylcellulose

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Control chart Basic Validation:

Selectivity	Linearity	Accuracy	LoQ	Stability	Carry over
Passed	Passed	Passed	50 mg/100 mL	-	No carry over

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CONTROL TEST

Test substance number: 05/0066

No.: 05/0066_01-05

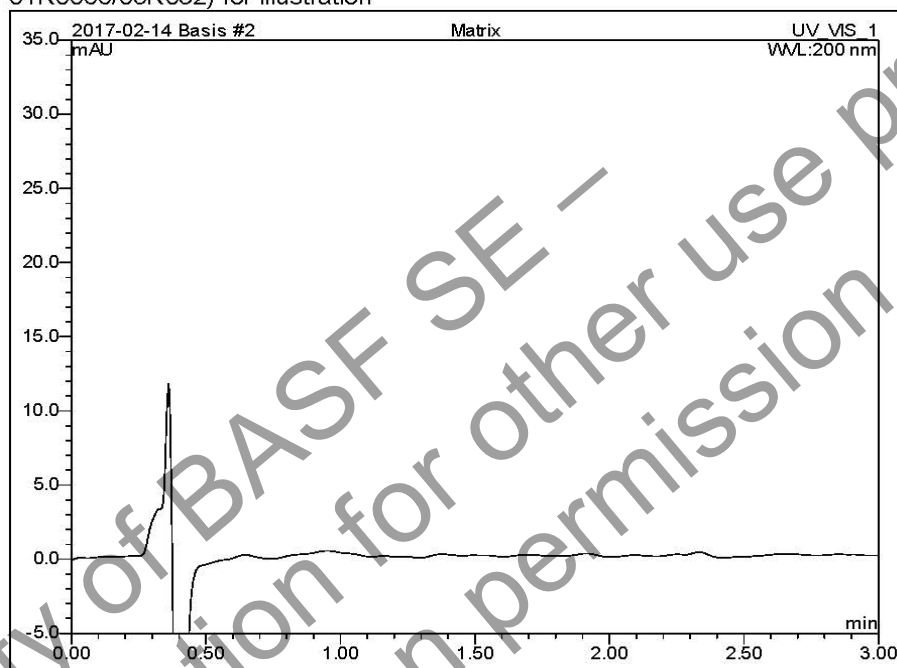
Name of test substance: DHGPS

Effective from: 15 Sep 2017

Control procedure: Content (LC) / aqueous carboxymethylcellulose

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Figure 1.1: Example chromatogram matrix solution (08 Feb 2017, Project no.: 01R0066/05R032) for illustration



BASF SE
Test Facility
Experimental Toxicology and Ecology / Analytical Chemistry

BASF
The Chemical Company

CONTROL TEST

Test substance number: 05/0066

No.: 05/0066_01-05

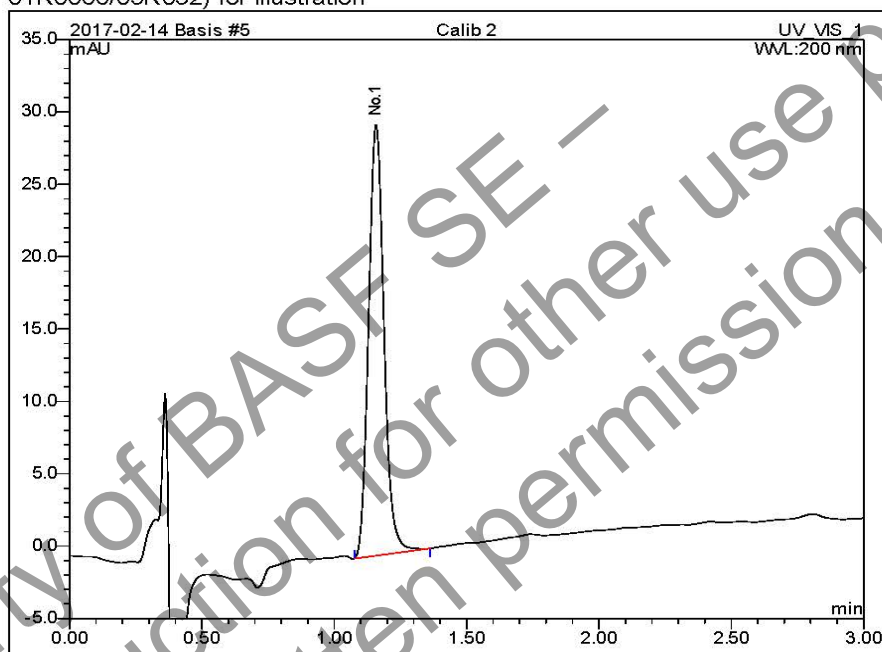
Name of test substance: DHDPS

Effective from: 15 Sep 2017

Control procedure: Content (LC) / aqueous carboxymethylcellulose

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Figure 1.2: Example chromatogram calibration solution (14 Feb 2017, Project no.: 01R0066/05R032) for illustration



BASF SE
Test Facility
Experimental Toxicology and Ecology / Analytical Chemistry


The Chemical Company

CONTROL TEST

Test substance number: 05/0066

No.: 05/0066_01-05

Name of test substance: DHDPS

Effective from: 15 Sep 2017

Control procedure: Content (LC) / aqueous carboxymethylcellulose

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Figure 1.3: Example chromatogram LoQ (Sample 01, 14 Feb 2017, Project no.: 01R0066/05R032) for illustration

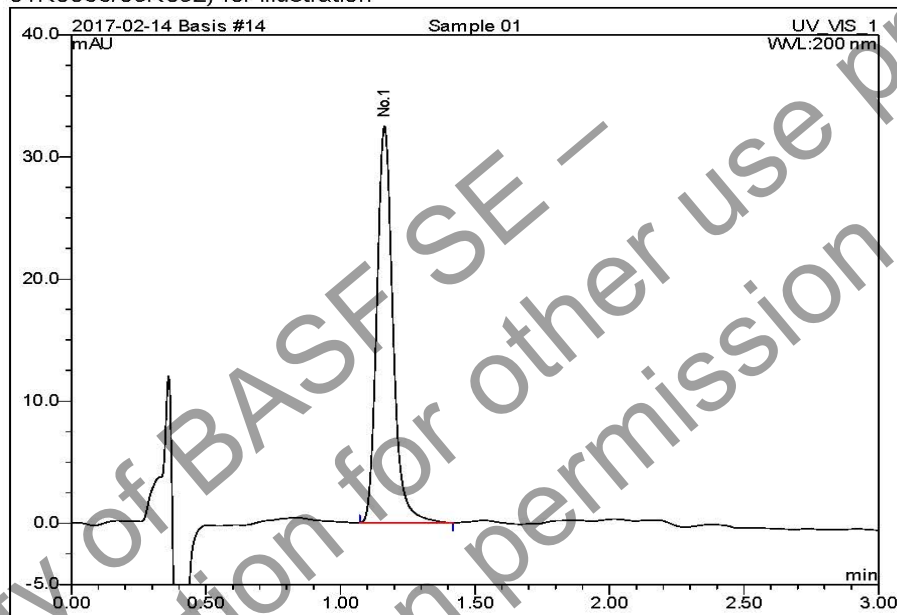
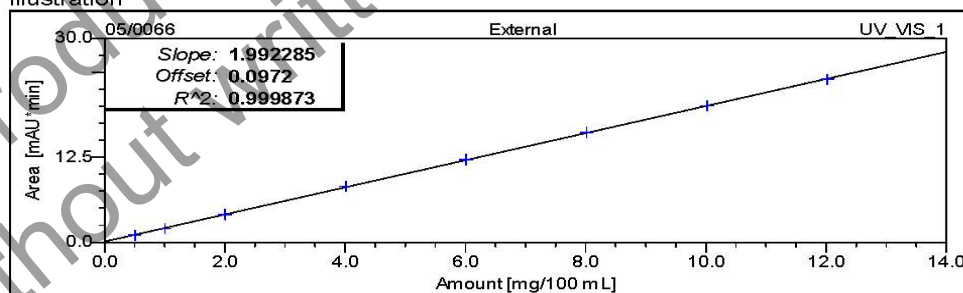


Figure 1.4 Example calibration curve (14 Feb 2017, Project no.: 01R0066/05R032) for illustration



3. Nipple/areola anlagen
(in order of delivery per group)

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Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034

Group: 00

F1-Generation

Dam No.	Pup No. ♂	Nipple count
104	1	6
	2	6
	3	4
	4	4
	5	4
124	1	4
	2	3
	3	4
	4	4
	5	4

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034

Group: 00

F1-Generation

Dam No.	Pup No. ♂	Nipple count
102	1	0
	2	4
	3	2
	4	6
	5	2
103	1	4
	2	0
	3	2
	4	4
	5	4
108	1	2
	2	0
	3	6
	4	4
	5	4
109	1	0
	2	2
	3	0
	4	0
	5	0
110	1	6
	2	0
	3	2
	4	2
	5	0

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034

Group: 00

F1-Generation

Dam No.	Pup No. ♂	Nipple count
111	1	2
	2	2
	3	0
	4	0
	5	0
	6	0
114	1	0
	2	0
	3	2
	4	0
	5	4
119	1	2
	2	2
	3	4
	4	2
	5	6

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034

Group: 00

F1-Generation

Dam No.	Pup No. ♂	Nipple count
113	1	4
	2	0
	3	2
	4	4
	5	0
115	1	0
	2	0
	3	0
	4	0
	5	0
117	1	2
	2	2
	3	0
	4	1
	5	4
118	1	0
	2	0
	3	2
	4	0
	5	1
	6	0

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034

Group: 00

F1-Generation

Dam No.	Pup No. ♂	Nipple count
121	1	2
	2	4
	3	2
	4	0
	5	4
122	1	2
	2	0
	3	2
	4	1
	5	2

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034

Group: 00

F1-Generation

Dam No.	Pup No. ♂	Nipple count
101	1	2
	2	4
	3	2
	4	1
	5	3
106	1	0
	2	0
	3	2
	4	0
	5	0
107	1	1
	2	2
	3	6
	4	2
112	1	1
	2	3
	3	1
	4	0
	5	0

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034

Group: 00

F1-Generation

Dam No.	Pup No. ♂	Nipple count
116	1	0
	2	0
	3	1
	4	2
	5	2

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Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034

Group: 00

F1-Generation

Dam No.	Pup No. ♂	Nipple count
120	1	2
	2	1
	3	0
	4	2
	5	4
123	1	4
	2	4
	3	2
	4	4
	5	6

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034

Group: 01

F1-Generation

Dam No.	Pup No. ♂	Nipple count
125	1	4
	2	4
	3	1
	4	2
	5	0
128	1	4
	2	4
	3	2
	4	4
	5	5
134	1	4
	2	4
	3	4
	4	4
	5	6
139	1	0
	2	0
	3	2
	4	0
	5	2
142	1	2
	2	2
	3	0
	4	4
	5	4

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034

Group: 01

F1-Generation

Dam No.	Pup No. ♂	Nipple count
143	1	2
	2	2
	3	4
	4	2
	5	4
146	1	1
	2	4
	3	1
	4	0
	5	0

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034

Group: 01

F1-Generation

Dam No.	Pup No. ♂	Nipple count
131	1	4
	2	2
	3	4
	4	2
	5	2
	6	0
133	1	1
	2	0
	3	0
	4	0
	5	0
	6	0
135	1	2
	2	4
	3	2
	4	4
	5	2
138	1	0
	2	0
	3	1
	4	2
	5	2

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034

Group: 01

F1-Generation

Dam No.	Pup No. ♂	Nipple count
147	1	4
	2	2
	3	1
	4	4
	5	0
148	1	0
	2	0

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Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034

Group: 01

F1-Generation

Dam No.	Pup No. ♂	Nipple count
126	1	0
	2	1
	3	0
	4	2
	5	3
129	1	0
	2	0
	3	0
	4	2
	5	0
130	1	2
	2	1
	3	2
	4	4
	5	1
132	1	0
	2	1
	3	0
	4	0
	5	4

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034

Group: 01

F1-Generation

Dam No.	Pup No. ♂	Nipple count
136	1	2
	2	4
	3	2
	4	2
137	1	1
	2	2
	3	4
	4	1
	5	2

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034

Group: 01

F1-Generation

Dam No.	Pup No. ♂	Nipple count
140	1	0
	2	3
	3	4
	4	2
	5	4
144	1	4

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Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034

Group: 02

F1-Generation

Dam No.	Pup No. ♂	Nipple count
154	1	1
	2	2
155	1	2
	2	4
	3	4
	4	4
	5	4
156	1	0
	2	3
	3	0
	4	2
	5	1
158	1	2
	2	2
164	1	2
	2	2
	3	0
	4	2
	5	2

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034

Group: 02

F1-Generation

Dam No.	Pup No. ♂	Nipple count
166	1	4
	2	0
	3	4
	5	2
	6	0
172	1	0
	2	0
	3	1
	4	0
	5	0

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034

Group: 02

F1-Generation

Dam No.	Pup No. ♂	Nipple count
149	1	2
	2	2
	3	2
	4	2
	5	6
151	1	0
	2	1
	3	0
	4	0
	5	1
153	1	0
	2	2
	3	0
	4	4
	5	0
161	1	2
	2	0
	3	1
	4	1
	5	2

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034

Group: 02

F1-Generation

Dam No.	Pup No. ♂	Nipple count
162	1	2
	2	2
	3	4
	4	2
	5	2
169	1	4
	2	2
	3	0
	4	0
	5	2
	6	2
170	1	2
	2	1
	3	4
	4	2
	5	3
171	1	2
	2	2
	3	2
	4	2
	5	2

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034

Group: 02

F1-Generation

Dam No.	Pup No. ♂	Nipple count
152	1	0
	2	4
	3	0
	4	2
	5	0
157	1	0
	2	2
	3	3
	4	2
	5	1
159	1	0
163	1	1
	2	2
	3	0
	4	1
	5	2

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034

Group: 02

F1-Generation

Dam No.	Pup No. ♂	Nipple count
167	1	0
	2	0
	3	0
	4	0
	5	0
168	1	2
	2	0
	3	2
	4	0
	5	2

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034

Group: 02

F1-Generation

Dam No.	Pup No. ♂	Nipple count
150	1	0
	2	2
	3	0
	4	1
	5	0
160	1	4
	2	2
	3	4
	4	4
	5	2
165	1	0
	2	2
	3	4
	4	2
	5	2

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034

Group: 03

F1-Generation

Dam No.	Pup No. ♂	Nipple count
196	1	4
	2	4
	3	6
	4	6
	5	4

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Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034

Group: 03

F1-Generation

Dam No.	Pup No. ♂	Nipple count
174	1	2
	2	0
	3	0
	4	1
	5	2
176	1	1
	2	0
179	1	2
	2	1
	3	2
185	1	0
	2	2
	3	1
	4	2
	5	2
	6	2
192	1	2
	2	4
	3	4
	4	3
	5	4

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034

Group: 03

F1-Generation

Dam No.	Pup No. ♂	Nipple count
173	1	0
	2	1
	3	4
	4	0
	5	2
175	1	0
	2	4
	3	4
	4	2
	5	2
177	1	4
	2	2
	3	0
	4	0
	5	0
178	1	0
	2	0
	3	1
	4	0
	5	0

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034

Group: 03

F1-Generation

Dam No.	Pup No. ♂	Nipple count
181	1	0
	2	0
	3	0
	4	0
	5	1
182	1	2
	2	0
	3	0
	4	2
184	1	2
	2	4
190	1	0
	2	3
	3	2
	4	2
	5	0

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034

Group: 03

F1-Generation

Dam No.	Pup No. ♂	Nipple count
187	1	3
	2	2
	3	2
	4	0
	5	0
189	1	0
	2	0
	3	0
	4	2
	5	1
191	1	1
	2	1
	3	2
	4	2
	5	4
193	1	0
	2	4
	3	1
	4	1
	5	2
	6	3

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034

Group: 03

F1-Generation

Dam No.	Pup No. ♂	Nipple count
194	1	4
	2	2
	3	4
	4	0
	5	0
195	1	0
	2	0
	3	0
	4	0
	5	1
	6	0
	7	0

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034

Group: 03

F1-Generation

Dam No.	Pup No. ♂	Nipple count
180	1	0
	2	1
	3	0
	4	4
	5	2
186	1	1
	2	0
	3	2
	4	2
188	1	2
	2	1
	3	4
	4	2
	5	1

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 10

F2-Generation

Dam No.	Pup No. ♂	Nipple count
507	1	4
	2	4
	3	4
	4	4
	5	2
517	1	2
	2	1
	3	0
	4	2
	5	0
522	1	2
	2	0
	3	1
	4	1
	5	0

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 10

F2-Generation

Dam No.	Pup No. ♂	Nipple count
505	1	2
	2	0
	3	2
	4	0
	5	0
	6	2
506	1	4
	2	4
	3	2
	4	4
	5	2
519	1	2
	2	0
	3	0
	4	1
	5	0
520	1	1
	2	0
	3	1
	4	2
	5	2

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 10

F2-Generation

Dam No.	Pup No. ♂	Nipple count
521	1	2
	2	4
	3	1
	4	0
	5	2
524	1	2
	2	4
	3	1
	4	2
	5	2

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 10

F2-Generation

Dam No.	Pup No. ♂	Nipple count
501	1	0
	2	1
	3	0
	4	1
	5	0
502	1	4
	2	4
	3	2
	4	2
	5	4
	6	4
510	1	4
	2	2
	3	2
	4	2
	5	4

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 10

F2-Generation

Dam No.	Pup No. ♂	Nipple count
516	1	2
	2	1
	3	1
	4	0
	5	4
523	1	2
	2	4
	3	4
	4	4
	5	2

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 10

F2-Generation

Dam No.	Pup No. ♂	Nipple count
503	1	4
	2	4
	3	0
	4	3
	5	1
504	1	2
	2	1
	3	0
	4	4
	5	1
508	1	1
	2	2
	3	1
	4	4
509	1	3
	2	2
	3	0
	4	4
	5	2
	6	1
	7	0
	8	0
512	1	2
	2	4
	3	2
	4	2
	5	2

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 10

F2-Generation

Dam No.	Pup No. ♂	Nipple count
513	1	1
	2	0
	3	2
	4	0
	5	2
514	1	4
	2	2
	3	2
	4	4
	5	3
515	1	2
	2	2
	3	0
	4	2
	5	0
518	1	0
	2	4
	3	2
	4	2

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 10

F2-Generation

Dam No.	Pup No. ♂	Nipple count
511	1	4
	2	4
	3	3
	4	3

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Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 11

F2-Generation

Dam No.	Pup No. ♂	Nipple count
525	1	4
	2	4
	3	4
	4	6
	5	4
543	1	4
	2	6
	3	4
	4	4
	5	2

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 11

F2-Generation

Dam No.	Pup No. ♂	Nipple count
526	1	2
	2	0
	3	2
533	1	0
	2	1
	3	0
	5	4
535	1	4
	2	2
	3	4
	4	2
538	1	4
	2	4
	3	2
	4	2
	5	4

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 11

F2-Generation

Dam No.	Pup No. ♂	Nipple count
529	1	0
	2	2
	3	0
	4	2
	5	2
530	1	0
	2	0
	3	1
	4	2
	5	1
532	1	0
	2	0
	3	0
	4	0
	5	0
534	1	2
	2	0
	3	3
	4	2
	5	0
537	1	2
	2	4
	3	2
	4	2
	5	2

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 11

F2-Generation

Dam No.	Pup No. ♂	Nipple count
539	1	0
	2	2
	3	2
	4	2
	5	4
541	1	1
	2	1
	3	0
	4	0
	5	1
542	1	0
	2	2
	3	1
	4	0
	5	0
	6	1
548	1	4
	2	0
	3	2
	4	4
	5	0

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 11

F2-Generation

Dam No.	Pup No. ♂	Nipple count
544	1	1
	2	0
	3	2
	4	0
	5	0
545	1	0
	2	2
	3	2
	4	2
	5	4

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 11

F2-Generation

Dam No.	Pup No. ♂	Nipple count
527	1	0
	2	1
	3	2
	4	0
528	1	4
	2	4
	3	4
	4	6
	5	4
531	1	2
	2	1
	3	2
	4	2
	5	1
536	1	2
	2	1
	3	2
	4	1
	5	3

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 11

F2-Generation

Dam No.	Pup No. ♂	Nipple count
540	1	2
	2	2
	3	2
	4	2
	5	4
546	1	2
	2	4
	3	2
	4	4
	5	2
547	1	2
	2	2
	3	3
	4	4
	5	2

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 12

F2-Generation

Dam No.	Pup No. ♂	Nipple count
564	1	4
	2	4
	3	2
	4	2
	5	4

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Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 12

F2-Generation

Dam No.	Pup No. ♂	Nipple count
555	1	1
	2	0
	4	0
	5	0
567	1	4
	2	1
	3	1
	4	1
	5	0
570	1	0
	2	2
	3	1
571	1	2
	2	2
	3	4
	4	2
	5	4

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 12

F2-Generation

Dam No.	Pup No. ♂	Nipple count
549	1	2
	2	0
	3	1
	4	1
	5	2
558	1	0
	2	0
	3	1
	4	2
	5	1
560	1	4
	2	4
	3	2
	4	4
	5	1
561	1	4
	2	0
	3	1
	4	4
	5	4

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 12

F2-Generation

Dam No.	Pup No. ♂	Nipple count
563	2	2
	3	2
	4	0
	5	0
	6	2
	7	4
	8	4

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 12

F2-Generation

Dam No.	Pup No. ♂	Nipple count
551	1	0
	2	1
	3	0
	4	0
554	1	0
	2	2
	3	1
	4	1
	5	0
556	1	6
	2	2
	3	4
	4	2
	5	2
	6	4

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 12

F2-Generation

Dam No.	Pup No. ♂	Nipple count
562	1	0
	2	3
	3	3
	4	2
	5	2
569	1	2
	2	0
	3	0
	4	2
	5	2

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 12

F2-Generation

Dam No.	Pup No. ♂	Nipple count
552	1	2
	2	0
	3	4
	4	4
557	1	0
	2	3
	3	2
	4	4
	5	1
559	1	2
	2	4
	3	0
	4	0
	5	2
565	1	6
	2	4

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 12

F2-Generation

Dam No.	Pup No. ♂	Nipple count
566	1	2
	2	2
	3	4
	4	2
	5	4
568	1	2
	2	2
	3	4
	4	1
	5	2

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 13

F2-Generation

Dam No.	Pup No. ♂	Nipple count
576	1	4
	2	5
	3	4
	4	2
	5	6
578	1	1
	2	4
	3	2
	4	0
	5	0
582	1	0
	2	2
	3	0
584	1	0
	2	1
	3	0
594	1	1
	2	1
	3	2
	5	0

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 13

F2-Generation

Dam No.	Pup No. ♂	Nipple count
580	1	0
	2	0
591	1	2
	2	2
	3	0
	4	0
	5	0
	6	0

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 13

F2-Generation

Dam No.	Pup No. ♂	Nipple count
574	1	0
	2	0
	3	2
	4	0
	5	0
	6	0
	7	0
577	1	0
	2	0
	3	0
579	1	2
	2	1
	3	2
	4	2
	5	0
583	1	1
	2	1
	3	4
	4	4
	5	4
587	1	0
	2	0
589	1	0
	2	3
	3	2

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 13

F2-Generation

Dam No.	Pup No. ♂	Nipple count
590	1	0
592	1	4
	2	1
	3	2
	4	4
	5	4
596	1	2
	2	2
	3	3
	4	4
	5	2

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 13

F2-Generation

Dam No.	Pup No. ♂	Nipple count
573	1	2
	2	6
	3	4
585	1	2
	2	2
	3	4
	4	2
	5	2
586	1	2
	2	1
	3	4
595	1	1
	2	4
	3	4
	4	2
	5	2

Nipple/Areola - Anlagen PND 13

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 13

F2-Generation

Dam No.	Pup No. ♂	Nipple count
588	1	0
	2	2
	3	2
	4	2
	5	0

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Nipple/Areola - Anlagen PND 20

Projekt-Nr. 90R0066/05R034

Group: 00

F1-Generation

Dam No.	Pup No. ♂	Nipple count
104	1	0
	2	0
	3	0
	4	0
	5	0
124	1	0
	2	0
	3	0
	4	0
	5	0

Nipple/Areola - Anlagen PND 20

Projekt-Nr. 90R0066/05R034

Group: 00

F1-Generation

Dam No.	Pup No. ♂	Nipple count
102	1	0
	2	0
	3	0
	4	0
	5	0
103	1	0
	2	0
	3	0
	4	0
	5	0
108	1	0
	2	0
	3	0
	4	0
	5	0
109	1	0
	2	0
	3	0
	4	0
	5	0
	6	0
110	1	0
	2	0
	3	0
	4	0

Nipple/Areola - Anlagen PND 20

Projekt-Nr. 90R0066/05R034

Group: 00

F1-Generation

Dam No.	Pup No. ♂	Nipple count
111	1	0
	2	0
	3	0
	4	0
	5	0
	6	0
114	1	0
	2	0
	3	0
	4	0
	5	0
119	1	0
	2	0
	3	0
	4	0
	5	0

Nipple/Areola - Anlagen PND 20

Projekt-Nr. 90R0066/05R034

Group: 00

F1-Generation

Dam No.	Pup No. ♂	Nipple count
113	1	0
	2	0
	3	0
	4	0
	5	0
115	1	0
	2	0
	3	0
	4	0
	5	0
117	1	0
	2	0
	3	0
	4	0
	5	0
118	1	0
	2	0
	3	0
	4	0
	5	0
	6	0

Nipple/Areola - Anlagen PND 20

Projekt-Nr. 90R0066/05R034

Group: 00

F1-Generation

Dam No.	Pup No. ♂	Nipple count
121	1	0
	2	0
	3	0
	4	0
	5	0
122	1	0
	2	0
	3	0
	4	0
	5	0

Nipple/Areola - Anlagen PND 20

Projekt-Nr. 90R0066/05R034

Group: 00

F1-Generation

Dam No.	Pup No. ♂	Nipple count
101	1	0
	2	0
	3	0
	4	0
	5	0
106	1	0
	2	0
	3	0
	4	0
	5	0
107	1	0
	2	0
	3	0
	4	0
112	1	0
	2	0
	3	0
	4	0
	5	0

Nipple/Areola - Anlagen PND 20

Projekt-Nr. 90R0066/05R034

Group: 00

F1-Generation

Dam No.	Pup No. ♂	Nipple count
116	1	0
	2	0
	3	0
	4	0
	5	0

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Nipple/Areola - Anlagen PND 20

Projekt-Nr. 90R0066/05R034

Group: 00

F1-Generation

Dam No.	Pup No. ♂	Nipple count
120	1	0
	2	0
	3	0
	4	0
	5	0
123	1	0
	2	0
	3	0
	4	0
	5	0

Nipple/Areola - Anlagen PND 20

Projekt-Nr. 90R0066/05R034

Group: 01

F1-Generation

Dam No.	Pup No. ♂	Nipple count
125	1	0
	2	0
	3	0
	4	0
	5	0
128	1	0
	2	0
	3	0
	4	0
	5	0
134	1	0
	2	0
	3	0
	4	0
	5	0
139	1	0
	2	0
	3	0
	4	0
	5	0
142	1	0
	2	0
	3	0
	4	0
	5	0

Nipple/Areola - Anlagen PND 20

Projekt-Nr. 90R0066/05R034

Group: 01

F1-Generation

Dam No.	Pup No. ♂	Nipple count
143	1	0
	2	0
	3	0
	4	0
	5	0
146	1	0
	2	0
	3	0
	4	0
	5	0

Nipple/Areola - Anlagen PND 20

Projekt-Nr. 90R0066/05R034

Group: 01

F1-Generation

Dam No.	Pup No. ♂	Nipple count
131	1	0
	2	0
	3	0
	4	0
	5	0
	6	0
133	1	0
	2	0
	3	0
	4	0
	5	0
	6	0
135	1	0
	2	0
	3	0
	4	0
	5	0
138	1	0
	2	0
	3	0
	4	0
	5	0

Nipple/Areola - Anlagen PND 20

Projekt-Nr. 90R0066/05R034

Group: 01

F1-Generation

Dam No.	Pup No. ♂	Nipple count
147	1	0
	2	0
	3	0
	4	0
	5	0
148	1	0
	2	0

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Nipple/Areola - Anlagen PND 20

Projekt-Nr. 90R0066/05R034

Group: 01

F1-Generation

Dam No.	Pup No. ♂	Nipple count
126	1	0
	2	0
	3	0
	4	0
	5	0
129	1	0
	2	0
	3	0
	4	0
	5	0
130	1	0
	2	0
	3	0
	4	0
	5	0
132	1	0
	2	0
	3	0
	4	0
	5	0

Nipple/Areola - Anlagen PND 20

Projekt-Nr. 90R0066/05R034

Group: 01

F1-Generation

Dam No.	Pup No. ♂	Nipple count
136	1	0
	2	0
	3	0
	4	0
137	1	0
	2	0
	3	0
	4	0
	5	0

Nipple/Areola - Anlagen PND 20

Projekt-Nr. 90R0066/05R034

Group: 01

F1-Generation

Dam No.	Pup No. ♂	Nipple count
140	1	0
	2	0
	3	0
	4	0
	5	0
144	1	0

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Nipple/Areola - Anlagen PND 20

Projekt-Nr. 90R0066/05R034

Group: 02

F1-Generation

Dam No.	Pup No. ♂	Nipple count
154	1	0
	2	0
155	1	0
	2	0
	3	0
	4	0
	5	0
156	1	0
	2	0
	3	0
	4	0
	5	0
158	1	0
	2	0
164	1	0
	2	0
	3	0
	4	0
	5	0

Nipple/Areola - Anlagen PND 20

Projekt-Nr. 90R0066/05R034

Group: 02

F1-Generation

Dam No.	Pup No. ♂	Nipple count
166	1	0
	2	0
	3	0
	5	0
	6	0
172	1	0
	2	0
	3	0
	4	0
	5	0

Nipple/Areola - Anlagen PND 20

Projekt-Nr. 90R0066/05R034

Group: 02

F1-Generation

Dam No.	Pup No. ♂	Nipple count
149	1	0
	2	0
	3	0
	4	0
	5	0
151	1	0
	2	0
	3	0
	4	0
	5	0
153	1	0
	2	0
	3	0
	4	0
	5	0
161	1	0
	2	0
	3	0
	4	0
	5	0

Nipple/Areola - Anlagen PND 20

Projekt-Nr. 90R0066/05R034

Group: 02

F1-Generation

Dam No.	Pup No. ♂	Nipple count
162	1	0
	2	0
	3	0
	4	0
	5	0
169	1	0
	2	0
	3	0
	4	0
	5	0
	6	0
170	1	0
	2	0
	3	0
	4	0
	5	0
171	1	0
	2	0
	3	0
	4	0
	5	0

Nipple/Areola - Anlagen PND 20

Projekt-Nr. 90R0066/05R034

Group: 02

F1-Generation

Dam No.	Pup No. ♂	Nipple count
152	1	0
	2	0
	3	0
	4	0
	5	0
157	1	0
	2	0
	3	0
	4	0
	5	0
159	1	0
163	1	0
	2	0
	3	0
	4	0
	5	0

Nipple/Areola - Anlagen PND 20

Projekt-Nr. 90R0066/05R034

Group: 02

F1-Generation

Dam No.	Pup No. ♂	Nipple count
167	1	0
	2	0
	3	0
	4	0
	5	0
168	1	0
	2	0
	3	0
	4	0
	5	0

Nipple/Areola - Anlagen PND 20

Projekt-Nr. 90R0066/05R034

Group: 02

F1-Generation

Dam No.	Pup No. ♂	Nipple count
150	1	0
	2	0
	3	0
	4	0
	5	0
160	1	0
	2	0
	3	0
	4	0
	5	0
165	1	0
	2	0
	4	0
	5	0

Nipple/Areola - Anlagen PND 20

Projekt-Nr. 90R0066/05R034

Group: 03

F1-Generation

Dam No.	Pup No. ♂	Nipple count
196	1	0
	2	0
	3	0
	4	0
	5	0

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Nipple/Areola - Anlagen PND 20

Projekt-Nr. 90R0066/05R034

Group: 03

F1-Generation

Dam No.	Pup No. ♂	Nipple count
174	1	0
	2	0
	3	0
	4	0
	5	0
176	1	0
179	1	0
	2	0
	3	0
185	1	0
	2	0
	3	0
	4	0
	5	0
	6	0
192	1	0
	2	0
	3	0
	4	0
	5	0

Nipple/Areola - Anlagen PND 20

Projekt-Nr. 90R0066/05R034

Group: 03

F1-Generation

Dam No.	Pup No. ♂	Nipple count
173	1	0
	2	0
	3	0
	4	0
	5	0
175	1	0
	2	0
	3	0
	4	0
	5	0
177	1	0
	2	0
	3	0
	4	0
	5	0
178	1	0
	2	0
	3	0
	4	0
	5	0

Nipple/Areola - Anlagen PND 20

Projekt-Nr. 90R0066/05R034

Group: 03

F1-Generation

Dam No.	Pup No. ♂	Nipple count
181	1	0
	2	0
	3	0
	4	0
	5	0
182	1	0
	2	0
	3	0
	4	0
184	1	0
	2	0
190	1	0
	2	0
	3	0
	4	0
	5	0

Nipple/Areola - Anlagen PND 20

Projekt-Nr. 90R0066/05R034

Group: 03

F1-Generation

Dam No.	Pup No. ♂	Nipple count
187	1	0
	2	0
	3	0
	4	0
	5	0
189	1	0
	2	0
	3	0
	4	0
	5	0
191	1	0
	2	0
	3	0
	4	0
	5	0
193	1	0
	2	0
	3	0
	4	0
	5	0
	6	0

Nipple/Areola - Anlagen PND 20

Projekt-Nr. 90R0066/05R034

Group: 03

F1-Generation

Dam No.	Pup No. ♂	Nipple count
194	1	0
	2	0
	3	0
	4	0
	5	0
195	1	0
	2	0
	3	0
	4	0
	5	0
	6	0
	7	0

Nipple/Areola - Anlagen PND 20

Projekt-Nr. 90R0066/05R034

Group: 03

F1-Generation

Dam No.	Pup No. ♂	Nipple count
180	1	0
	2	0
	3	0
	4	0
	5	0
186	1	0
	2	0
	3	0
	4	0
188	1	0
	2	0
	3	0
	4	0
	5	0

Nipple/Areola - Anlagen PND 21

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 10

F2-Generation

Dam No.	Pup No. ♂	Nipple count
507	1	0
	2	0
	3	0
	4	0
	5	0
517	1	0
	2	0
	3	0
	4	0
	5	0
522	1	0
	2	0
	3	0
	4	0
	5	0

Nipple/Areola - Anlagen PND 21

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 10

F2-Generation

Dam No.	Pup No. ♂	Nipple count
505	1	0
	2	0
	3	0
	4	0
	5	0
	6	0
506	1	0
	2	0
	3	0
	4	0
	5	0
519	1	0
	2	0
	3	0
	4	0
	5	0
520	1	0
	2	0
	3	0
	4	0
	5	0

Nipple/Areola - Anlagen PND 21

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 10

F2-Generation

Dam No.	Pup No. ♂	Nipple count
521	1	0
	2	0
	3	0
	4	0
	5	0
524	1	0
	2	0
	3	0
	4	0
	5	0

Nipple/Areola - Anlagen PND 21

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 10

F2-Generation

Dam No.	Pup No. ♂	Nipple count
501	1	0
	2	0
	3	0
	4	0
	5	0
502	1	0
	2	0
	3	0
	4	0
	5	0
	6	0
510	1	0
	2	0
	3	0
	4	0
	5	0

Nipple/Areola - Anlagen PND 21

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 10

F2-Generation

Dam No.	Pup No. ♂	Nipple count
516	1	0
	2	0
	3	0
	4	0
	5	0
523	1	0
	2	0
	3	0
	4	0
	5	0

Nipple/Areola - Anlagen PND 21

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 10

F2-Generation

Dam No.	Pup No. ♂	Nipple count
503	1	0
	2	0
	3	0
	4	0
	5	0
504	1	0
	2	0
	3	0
	4	0
	5	0
508	1	0
	2	0
	3	0
	4	0
509	1	0
	2	0
	3	0
	4	0
	5	0
	6	0
	7	0
	8	0
512	1	0
	2	0
	3	0
	4	0
	5	0

Nipple/Areola - Anlagen PND 21

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 10

F2-Generation

Dam No.	Pup No. ♂	Nipple count
513	1	0
	2	0
	3	0
	4	0
	5	0
514	1	0
	2	0
	3	0
	4	0
	5	0
515	1	0
	2	0
	3	0
	4	0
	5	0
518	1	0
	2	0
	3	0
	4	0

Nipple/Areola - Anlagen PND 21

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 10

F2-Generation

Dam No.	Pup No. ♂	Nipple count
511	1	0
	2	0
	3	0
	4	0

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Nipple/Areola - Anlagen PND 21

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 11

F2-Generation

Dam No.	Pup No. ♂	Nipple count
525	1	0
	2	0
	3	0
	4	0
	5	0
543	1	0
	2	0
	3	0
	4	0
	5	0

Nipple/Areola - Anlagen PND 21

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 11

F2-Generation

Dam No.	Pup No. ♂	Nipple count
526	1	0
	2	0
	3	0
533	1	0
	2	0
	3	0
	5	0
535	1	0
	2	0
	3	0
	4	0
538	1	0
	2	0
	3	0
	4	0
	5	0

Nipple/Areola - Anlagen PND 21

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 11

F2-Generation

Dam No.	Pup No. ♂	Nipple count
529	1	0
	2	0
	3	0
	4	0
	5	0
530	1	0
	2	0
	3	0
	4	0
	5	0
532	1	0
	2	0
	3	0
	4	0
	5	0
534	1	0
	2	0
	3	0
	4	0
	5	0
537	1	0
	2	0
	3	0
	4	0
	5	0

Nipple/Areola - Anlagen PND 21

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 11

F2-Generation

Dam No.	Pup No. ♂	Nipple count
539	1	0
	2	0
	3	0
	4	0
	5	0
541	1	0
	2	0
	3	0
	4	0
	5	0
542	1	0
	2	0
	3	0
	4	0
	5	0
	6	0
548	1	0
	2	0
	3	0
	4	0
	5	0

Nipple/Areola - Anlagen PND 21

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 11

F2-Generation

Dam No.	Pup No. ♂	Nipple count
544	1	0
	2	0
	3	0
	4	0
	5	0
545	1	0
	2	0
	3	0
	4	0
	5	0

Nipple/Areola - Anlagen PND 21

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 11

F2-Generation

Dam No.	Pup No. ♂	Nipple count
527	1	0
	2	0
	3	0
	4	0
528	1	0
	2	0
	3	0
	4	0
	5	0
531	1	0
	2	0
	3	0
	4	0
	5	0
536	1	0
	2	0
	3	0
	4	0
	5	0

Nipple/Areola - Anlagen PND 21

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 11

F2-Generation

Dam No.	Pup No. ♂	Nipple count
540	1	0
	2	0
	3	0
	4	0
	5	0
546	1	0
	2	0
	3	0
	4	0
	5	0
547	1	0
	2	0
	3	0
	4	0
	5	0

Nipple/Areola - Anlagen PND 21

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 12

F2-Generation

Dam No.	Pup No. ♂	Nipple count
564	1	0
	2	0
	3	0
	4	0
	5	0

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Nipple/Areola - Anlagen PND 21

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 12

F2-Generation

Dam No.	Pup No. ♂	Nipple count
555	1	0
	2	0
	4	0
	5	0
567	1	0
	2	0
	3	0
	4	0
	5	0
570	1	0
	2	0
	3	0
571	1	0
	2	0
	3	0
	4	0
	5	0

Nipple/Areola - Anlagen PND 21

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 12

F2-Generation

Dam No.	Pup No. ♂	Nipple count
549	1	0
	2	0
	3	0
	4	0
	5	0
558	1	0
	2	0
	3	0
	4	0
	5	0
560	1	0
	2	0
	3	0
	4	0
	5	0
561	1	0
	2	0
	3	0
	4	0
	5	0

Nipple/Areola - Anlagen PND 21

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 12

F2-Generation

Dam No.	Pup No. ♂	Nipple count
563	2	0
	3	0
	4	0
	5	0
	6	0
	7	0
	8	0

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Nipple/Areola - Anlagen PND 21

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 12

F2-Generation

Dam No.	Pup No. ♂	Nipple count
551	1	0
	2	0
	3	0
	4	0
554	1	0
	2	0
	3	0
	4	0
	5	0
556	1	0
	2	0
	3	0
	4	0
	5	0
	6	0

Nipple/Areola - Anlagen PND 21

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 12

F2-Generation

Dam No.	Pup No. ♂	Nipple count
562	1	0
	2	0
	3	0
	4	0
	5	0
569	1	0
	2	0
	3	0
	4	0
	5	0

Nipple/Areola - Anlagen PND 21

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 12

F2-Generation

Dam No.	Pup No. ♂	Nipple count
552	1	0
	2	0
	3	0
	4	0
557	1	0
	2	0
	3	0
	4	0
	5	0
559	1	0
	2	0
	3	0
	4	0
	5	0
565	1	0
	2	0

Nipple/Areola - Anlagen PND 21

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 12

F2-Generation

Dam No.	Pup No. ♂	Nipple count
566	1	0
	2	0
	3	0
	4	0
	5	0
568	1	0
	2	0
	3	0
	4	0
	5	0

Nipple/Areola - Anlagen PND 21

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 13

F2-Generation

Dam No.	Pup No. ♂	Nipple count
576	1	0
	2	0
	3	0
	4	0
	5	0
578	1	0
	2	0
	3	0
	4	0
	5	0
582	1	0
	2	0
	3	0
584	1	0
	2	0
	3	0
594	1	0
	2	0
	3	0
	5	0

Nipple/Areola - Anlagen PND 21

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 13

F2-Generation

Dam No.	Pup No. ♂	Nipple count
580	1	0
	2	0
591	1	0
	2	0
	3	0
	4	0
	5	0
	6	0

Nipple/Areola - Anlagen PND 21

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 13

F2-Generation

Dam No.	Pup No. ♂	Nipple count
574	1	0
	2	0
	3	0
	4	0
	5	0
	6	0
	7	0
577	1	0
	2	0
	3	0
579	1	0
	2	0
	3	0
	4	0
	5	0
583	1	0
	2	0
	3	0
	4	0
	5	0
587	1	0
	2	0
589	1	0
	2	0
	3	0

Nipple/Areola - Anlagen PND 21

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 13

F2-Generation

Dam No.	Pup No. ♂	Nipple count
590	1	0
592	1	0
	2	0
	3	0
	4	0
	5	0
596	1	0
	2	0
	3	0
	4	0
	5	0

Nipple/Areola - Anlagen PND 21

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 13

F2-Generation

Dam No.	Pup No. ♂	Nipple count
573	1	0
	2	0
	3	0
585	1	0
	2	0
	3	0
	4	0
	5	0
586	1	0
	2	0
	3	0
595	1	0
	2	0
	3	0
	4	0
	5	0

Nipple/Areola - Anlagen PND 21

Projekt-Nr. 90R0066/05R034 (Cohort 1B)

Group: 13

F2-Generation

Dam No.	Pup No. ♂	Nipple count
588	1	0
	2	0
	3	0
	4	0
	5	0

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4. Additional individual estrous cycle data

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Study 90R0066/05R034

Individual Estrous Cycles Report

Sex: Female - Phase: In-life

Dose Group	Animal Number	Day
	101	121 M
	102	D
	103	M
	104	D
	105	/P
	106	D
	107	D
	108	D
	109	D
	110	/E
	111	D
Test Group 00/F 0 mg/kg bw/d	112	/P
	113	/E
	114	M
	115	/E
	116	D
	117	/E
	118	M
	119	D
	120	D
	121	D
	122	D
	123	M
	124	D

/ = Start of Cycle; M = Metestrus; D = Diestrus; P = Proestrus; E = Estrus

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Study 90R0066/05R034

Individual Estrous Cycles Report

Sex: Female - Phase: In-life

Dose Group	Animal Number	Day
	125	122 M
	126	/E
	128	/E
	129	M
	130	/E
	131	D
	132	D
	133	D
	134	M
	135	/E
	136	/P
	137	/P
	138	/E
	139	D
	140	D
	141	/P
	142	M
	143	M
	144	D
	145	/E
	146	D
	147	/E
	148	/E

Test Group 01/F
20 mg/kg bw/d

/ = Start of Cycle; M = Metestrus; E = Estrus; D = Diestrus; P = Proestrus

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Study 90R0066/05R034

Individual Estrous Cycles Report

Sex: Female - Phase: In-life

Dose Group	Animal Number	Day
	149	121
	150	122
	151	/E
	152	/E
	153	M
	154	D
	155	M
	156	M
	157	D
	158	M
	159	D
	160	D
	161	D
	162	D
	163	M
	164	/E
	165	/E
	166	D
	167	/P
	168	M
	169	/E
	170	/E
	171	/E
	172	D

Test Group 02/F
60 mg/kg bw/d

/ = Start of Cycle; E = Estrous; D = Diestrous; M = Metestrous; P = Proestrous

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Study 90R0066/05R034

Individual Estrous Cycles Report

Sex: Female - Phase: In-life

Dose Group	Animal Number	Day
	173	122 M
	174	D
	175	M
	176	M
	177	M
	178	/E
	179	M
	180	D
	181	D
	182	/E
	183	/E
	184	/E
	185	/P
	186	M
	187	M
	188	D
	189	/P
	190	/E
	191	D
	192	/E
	193	M
	194	D
	195	D
	196	D

Test Group 03/F
180 mg/kg bw/d

/ = Start of Cycle; M = Metestrus; D = Diestrus; E = Estrus; P = Proestrus

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Individual Estrous Cycles Report

Sex: Female - Phase: In-life

Dose Group	Animal Number	Day	62	63	64	65
Test Group 10/F 0 mg/kg bw/d	301				D	NS
	302				M	NS
	303				/E	NS
	304				D	NS
	305				/E	NS
	306					M
	307					D
	308					/E
	309					D
	310					M
	311		D	NS	NS	NS
	312	/E	NS	NS	NS	NS
	313	M	NS	NS	NS	NS
	314	/E	NS	NS	NS	NS
	315	D	NS	NS	NS	NS
	316			D	NS	NS
	317			/P	NS	NS
	318			M	NS	NS
	319			D	NS	NS
	320			D	NS	NS

/ = Start of Cycle; D = Diestrous; M = Metestrus; E = Estrus; P = Proestrus
NS = No More Scheduled

Study 90R0066/05R034_1A

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Individual Estrous Cycles Report

Sex: Female - Phase: In-life

Dose Group	Animal Number	Day	62	63	64	65
Test Group 11/F 20 mg/kg bw/d	321				/E	NS
	322				D	NS
	323				M	NS
	324				/P	NS
	325				/P	NS
	326					M
	327					M
	328					/E
	329					D
	330					D
	331		D	NS	NS	NS
	332		M	NS	NS	NS
	333		/E	NS	NS	NS
	334		/E	NS	NS	NS
	335		/E	NS	NS	NS
	336			/E	NS	NS
	337			D	NS	NS
	338			/E	NS	NS
	339			D	NS	NS
	340			M	NS	NS

/ = Start of Cycle; E = Estrous; D = Diestrous; M = Metestrous; P = Proestrous
NS = No More Scheduled

Study 90R0066/05R034_1A

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Individual Estrous Cycles Report

Sex: Female - Phase: In-life

Dose Group	Animal Number	Day	62	63	64	65
Test Group 12/F 60 mg/kg bw/d	341				M	NS
	342				M	NS
	343				D	NS
	344				M	NS
	345				/E	NS
	346					M
	347					/P
	348					D
	349					D
	350					/P
	351		M	NS	NS	NS
	352		M	NS	NS	NS
	353		D	NS	NS	NS
	354		D	NS	NS	NS
	355		D	NS	NS	NS
	356			/P	NS	NS
	357			M	NS	NS
	358			M	NS	NS
	359			/E	NS	NS
	360			M	NS	NS

/ = Start of Cycle; M = Metestrus; D = Diestrus; E = Estrus; P = Proestrus
NS = No More Scheduled

Study 90R0066/05R034_1A

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Individual Estrous Cycles Report

Sex: Female - Phase: In-life

Dose Group	Animal Number	Day	62	63	64	65
Test Group 13/F 180 mg/kg bw/d	361				M	NS
	362	NS	NS	NS		NS
	363			M		NS
	364			/E	/E	NS
	365			/E		NS
	366			D		NS
	367					M
	368					/E
	369					M
	370					D
	371					/E
	372	D	NS	NS		NS
	373	D	NS	NS		NS
	374	D	NS	NS		NS
	375	/E	NS	NS		NS
	376	/E	NS	NS		NS
	377		/E	NS	NS	NS
	378		D	NS		NS
	379		M	NS		NS
	380		/P	NS		NS

/ = Start of Cycle; M = Metestrus; E = Estrus; D = Diestrus; P = Proestrus
NS = No More Scheduled

Study 90R0066/05R034_F1

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Individual Estrous Cycles Report

Sex: Female - Phase: In-life

Dose Group	Animal Number	Day
	501	128 D
	502	D
	503	D
	504	/E
	505	D
	506	M
	507	M
	508	D
	509	D
	510	D
	511	M
Test Group 10/F 0 mg/kg bw/d	512	D
	513	D
	514	/E
	515	D
	516	D
	517	/P
	518	D
	519	D
	520	D
	521	M
	522	D
	523	/E
	524	/E

/ = Start of Cycle; D = Diestrous; E = Estrous; M = Metestrous; P = Proestrous

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Study 90R0066/05R034_F1

Individual Estrous Cycles Report

Sex: Female - Phase: In-life

Dose Group	Animal Number	Day
	525	128 D
	526	D
	527	D
	528	D
	529	/E
	530	/E
	531	/E
	532	M
	533	D
	534	M
	535	/E
	536	M
	537	/P
	538	D
	539	D
	540	D
	541	D
	542	D
	543	M
	544	D
	545	/E
	546	D
	547	D
	548	/E

Test Group 11/F
20 mg/kg bw/d

/ = Start of Cycle; D = Diestrous; E = Estrous; M = Metestrous; P = Proestrous

Study 90R0066/05R034_F1

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Individual Estrous Cycles Report

Sex: Female - Phase: In-life

Dose Group	Animal Number	Day
	549	128 /E
	550	NS
	551	M
	552	D
	553	D
	554	D
	555	M
	556	D
	557	/E
	558	M
	559	D
	560	M
Test Group 12/F 60 mg/kg bw/d	561	/E
	562	D
	563	M
	564	D
	565	M
	566	D
	567	D
	568	/E
	569	M
	570	D
	571	D
	572	/E

/ = Start of Cycle; E = Estrous; M = Metestrous; D = Diestrous
NS = No More Scheduled

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Ascentos™ 1.3

Study 90R0066/05R034_F1

Individual Estrous Cycles Report

Sex: Female - Phase: In-life

Dose Group	Animal Number	Day
	573	128 D
	574	/E
	575	M
	576	D
	577	/P
	578	M
	579	/E
	580	/E
	581	D
	582	D
	583	D
	584	D
Test Group 13/F 180 mg/kg bw/d	585	D
	586	/E
	587	D
	588	/E
	589	M
	590	D
	591	D
	592	/E
	593	D
	594	D
	595	/E
	596	M

/ = Start of Cycle; D = Diestrous; E = Estrous; M = Metestrous; P = Proestrous

05R0341A

PROJ. NO. 90R0066/05R034, MODIFIED EXTENDED ONE-GENERATION REPRODUCTION TOXICITY STUDY IN SPRAGUE-DAWLEY RATS

ORAL ADMINISTRATION (GAVAGE) / F1A FEMALES

INDIVIDUAL ESTROUS STAGES ON THE DAY VAGINAL OPENING

TEST GROUP 10 (0 MG/KG BW/D)	DEC 11	DEC 12	DEC 13	DEC 14	DEC 15	DEC 16	DEC 17	DEC 18	DEC 19	DEC 20
FEMALE #										
2017										
301	-	-	-	-	-	-	METESTROUS	METESTROUS	DIESTROUS	PROESTROUS
302	-	-	-	-	-	ESTROUS				
303	-	-	-	-	-	ESTROUS				
304	-	-	-	-	-	-	-	-	DIESTROUS	ESTROUS
305	-	-	-	ESTROUS						
306	-	-	-		ESTROUS					
307	-	-	-	-	-	-	-	-	-	-
308	-	-	-	-	-	ESTROUS		ESTROUS		
309	-	-	-	-	-	-				
310	-	-	-	-	ESTROUS			ESTROUS		
311	-	-	-	-	-					
312	-	-	-	-	-	ESTROUS				
313	-	-	-	-	-	ESTROUS				
314	-	-	-	-	-		ESTROUS			
315	-	-	-	-	-	-		ESTROUS		
316	-	-	-	-	-	-	METESTROUS	METESTROUS	METESTROUS	PROESTROUS
317	-	-	-	-	-	-	METESTROUS	METESTROUS	DIESTROUS	DIESTROUS
318	-	-	-	-	ESTROUS					
319	-	-	-	-	-	-	-	-	ESTROUS	
320	-	-	-	-	-	ESTROUS				

05R0341A

PROJ. NO. 90R0066/05R034 - MODIFIED EXTENDED ONE-GENERATION REPRODUCTION TOXICITY STUDY IN SPRAGUE-DAWLEY RATS
ORAL ADMINISTRATION (GAVAGE) / F1A FEMALES
INDIVIDUAL ESTROUS STAGES ON THE DAY VAGINAL OPENING

TEST GROUP 10 (0 MG/KG BW/D)	
FEMALE #	DEC 21
2017	DEC 22
301	ESTROUS
302	
303	
304	
305	
306	
307	ESTROUS
308	
309	
310	
311	
312	
313	
314	
315	
316	ESTROUS
317	PROESTROUS
318	ESTROUS
319	
320	

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PROJ. NO. 90R0066/05R034, MODIFIED EXTENDED ONE-GENERATION REPRODUCTION TOXICITY STUDY IN SPRAGUE-DAWLEY RATS
ORAL ADMINISTRATION (GAVAGE) / F1A FEMALES
INDIVIDUAL ESTROUS STAGES ON THE DAY VAGINAL OPENING

TEST GROUP 11 (20 MG/KG BW/D)	DEC 11	DEC 12	DEC 13	DEC 14	DEC 15	DEC 16	DEC 17	DEC 18	DEC 19	DEC 20
FEMALE #										
2017										
321	-	-	-	-	ESTROUS	METESTROUS	METESTROUS	DIESTROUS	DIESTROUS	PROESTROUS
322	-	-	-	-	-	-	-	-	METESTROUS	METESTROUS
323	-	-	-	-	-	-	-	METESTROUS	DIESTROUS	ESTROUS
324	-	-	-	-	-	ESTROUS	-	-	-	-
325	-	-	-	-	-	ESTROUS	-	-	-	-
326	-	-	-	-	-	-	ESTROUS	-	-	-
327	-	-	-	-	-	-	-	-	-	-
328	-	-	-	-	-	-	-	-	-	-
329	-	-	-	-	-	-	-	-	ESTROUS	-
330	-	-	-	-	-	ESTROUS	-	-	ESTROUS	-
331	-	-	-	-	-	ESTROUS	-	-	-	-
332	-	-	-	-	-	ESTROUS	-	-	-	-
333	-	-	-	-	-	ESTROUS	-	-	-	-
334	-	-	-	-	-	-	ESTROUS	-	-	-
335	-	-	-	-	-	-	-	-	-	-
336	-	-	-	-	-	-	-	METESTROUS	DIESTROUS	-
337	-	-	-	-	-	-	-	-	-	DIESTROUS
338	-	-	-	-	-	-	-	-	-	-
339	-	-	-	-	-	-	-	-	-	METESTROUS
340	-	-	-	-	-	-	-	-	-	-

05R0341A

PROJ. NO. 90R0066/05R034 - MODIFIED EXTENDED ONE-GENERATION REPRODUCTION TOXICITY STUDY IN SPRAGUE-DAWLEY RATS
ORAL ADMINISTRATION (GAVAGE) / F1A FEMALES
INDIVIDUAL ESTROUS STAGES ON THE DAY VAGINAL OPENING

TEST GROUP 11 (20 MG/KG BW/D)	
FEMALE #	
2017	DEC 21 DEC 22 DEC 23 DEC 24 DEC 25 DEC 26
321	
322	ESTROUS
323	METESTROUS
324	METESTROUS
325	ESTROUS
326	
327	
328	
329	
330	
331	
332	
333	
334	
335	METESTROUS
336	ESTROUS
337	
338	METESTROUS
339	METESTROUS
340	METESTROUS

DIESTROUS DIESTROUS DIESTROUS PROESTROUS ESTROUS
ESTROUS - - - ESTROUS
METESTROUS METESTROUS PROESTROUS ESTROUS
METESTROUS DIESTROUS PROESTROUS
METESTROUS DIESTROUS PROESTROUS

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PROJ. NO. 90R0066/05R034, MODIFIED EXTENDED ONE-GENERATION REPRODUCTION TOXICITY STUDY IN SPRAGUE-DAWLEY RATS
ORAL ADMINISTRATION (GAVAGE) / F1A FEMALES
INDIVIDUAL ESTROUS STAGES ON THE DAY VAGINAL OPENING

TEST GROUP 12 (60 MG/KG BW/D)		DEC 11	DEC 12	DEC 13	DEC 14	DEC 15	DEC 16	DEC 17	DEC 18	DEC 19	DEC 20
FEMALE #											
2017											
341		-	-	-	-	-	-	-	ESTROUS	-	-
342		-	-	-	-	ESTROUS	-	-	-	-	-
343		-	-	-	-	PROESTROUS	ESTROUS	-	-	-	-
344		-	-	-	-	ESTROUS	-	-	-	-	-
345		-	-	-	-	-	ESTROUS	-	-	-	-
346		-	-	-	-	-	ESTROUS	-	-	-	-
347		-	-	-	-	-	-	ESTROUS	-	-	-
348		-	-	-	-	-	-	-	-	-	ESTROUS
349		-	-	-	-	-	-	ESTROUS	-	-	-
350		-	-	-	-	-	-	-	-	-	-
351		-	-	-	-	-	-	-	-	METESTROUS	METESTROUS
352		-	-	-	-	ESTROUS	-	-	PROESTROUS	ESTROUS	-
353		-	-	-	-	-	-	-	ESTROUS	-	-
354		-	-	-	-	-	-	-	-	-	-
355		-	-	-	-	-	-	ESTROUS	-	-	-
356		-	-	-	-	-	-	-	-	-	-
357		-	-	-	-	-	-	-	-	-	ESTROUS
358		-	-	-	-	ESTROUS	-	-	-	-	-
359		-	-	-	-	-	-	-	ESTROUS	-	-
360		-	-	-	-	-	-	-	-	-	-

05R0341A

PROJ. NO. 90R0066/05R034; MODIFIED EXTENDED ONE-GENERATION REPRODUCTION TOXICITY STUDY IN SPRAGUE-DAWLEY RATS
ORAL ADMINISTRATION (GAVAGE) / F1A FEMALES
INDIVIDUAL ESTROUS STAGES ON THE DAY VAGINAL OPENING

TEST GROUP 12 (60 MG/KG BW/D)

FEMALE #	DEC 21	DEC 22	DEC 23
2017			
341			
342			
343			
344			
345			
346			
347			
348			
349			
350	METESTROUS	METESTROUS	ESTROUS
351			
352			
353			
354			
355			
356	PROESTROUS	ESTROUS	
357			
358			
359			
360	ESTROUS		

05R0341A

PROJ. NO. 90R0066/05R034, MODIFIED EXTENDED ONE-GENERATION REPRODUCTION TOXICITY STUDY IN SPRAGUE-DAWLEY RATS
ORAL ADMINISTRATION (GAVAGE) / F1A FEMALES
INDIVIDUAL ESTROUS STAGES ON THE DAY VAGINAL OPENING

TEST GROUP 13 (180 MG/KG BW/D)										
FEMALE #	DEC 11	DEC 12	DEC 13	DEC 14	DEC 15	DEC 16	DEC 17	DEC 18	DEC 19	DEC 20
2017	-	-	-	-	ESTROUS	-	-	ESTROUS	-	-
361	-	-	-	-	ESTROUS	-	-	ESTROUS	-	-
363	-	-	-	-	-	ESTROUS	-	-	-	-
364	-	-	-	-	ESTROUS	-	-	-	-	-
365	-	-	-	-	ESTROUS	-	-	-	-	-
366	-	-	-	-	ESTROUS	-	-	-	-	-
367	-	-	-	-	DIESTROUS	-	-	-	-	-
368	-	-	-	-	-	ESTROUS	-	-	-	-
369	-	-	-	-	-	-	-	METESTROUS	DIESTROUS	DIESTROUS
370	-	-	-	-	-	-	-	METESTROUS	DIESTROUS	ESTROUS
371	-	-	-	-	-	ESTROUS	-	-	-	-
372	-	-	DIESTROUS	ESTROUS	-	-	-	-	-	-
373	-	-	-	-	-	-	ESTROUS	-	METESTROUS	METESTROUS
374	-	-	-	-	-	-	-	METESTROUS	DIESTROUS	DIESTROUS
375	-	-	-	-	-	-	-	-	-	-
376	-	-	-	-	-	-	-	-	-	-
377	-	-	-	-	-	-	ESTROUS	-	-	-
378	-	-	-	-	-	ESTROUS	-	-	DIESTROUS	DIESTROUS
379	-	-	-	-	-	-	-	METESTROUS	ESTROUS	-
380	-	-	-	-	-	-	-	-	-	-

05R0341A

PROJ. NO. 90R0066/05R034, MODIFIED EXTENDED ONE-GENERATION REPRODUCTION TOXICITY STUDY IN SPRAGUE-DAWLEY RATS
ORAL ADMINISTRATION (GAVAGE) / F1A FEMALES
INDIVIDUAL ESTROUS STAGES ON THE DAY VAGINAL OPENING

TEST GROUP 13 (180 MG/KG BW/D)

FEMALE #	DEC 21	DEC 22	DEC 23	DEC 24	DEC 25	DEC 26
2017						
361						
363						
364						
365						
366						
367						
368						
369	DIESTROUS	ESTROUS				
370						
371						
372						
373						
374	ESTROUS	ESTROUS				
375	PROESTROUS	METESTROUS				
376	-	METESTROUS	METESTROUS	DIESTROUS	PROESTROUS	ESTROUS
377						
378						
379	DIESTROUS	ESTROUS				
380						

5. Selection of animals

Property of BASF SE —
Reproduction for other use prohibited
without written permission

Selection for F1 rearing animals (Cohort 1A)

Project-No.: 90R0066/05R034

Group: 00

Dam No.	Pup No. allotted ♂	Animal No. for breeding	Pup No. allotted ♀	Animal No. for breeding
102	3	201	14	301
103	1	202	13	302
108	2	203	9	303
109	1	204	11	304
110	4	205	5	305
111	3	206	12	306
114	1	207	12	307
119	4	208	8	308
113	2	209	11	309
115	5	210	13	310
117	2	211	14	311
118	4	212	11	312
121	5	213	10	313
122	3	214	11	314
101	1	215	11	315
106	4	216	13	316
112	4	217	9	317
116	3	218	10	318
120	2	219	15	319
123	1	220	16	320

Selection for F1 rearing animals (Cohort 1A)

Project-No.: 90R0066/05R034

Group: 01

Dam No.	Pup No. allotted ♂	Animal No. for breeding	Pup No. allotted ♀	Animal No. for breeding
125	1	221	13	321
128	4	222	7	322
134	-	-	11	323
139	1	224	12	324
142	5	225	7	325
146	2	226	14	326
131	2	227	12	327
133	3	228	11	328
135	1	229	12	329
138	5	230	14	330
147	4	231	10	331
148	1	232	5	332
126	1	233	15	333
129	1, 5	223, 234	9	334
130	3	235	8	335
132	3	236	9	336
136	2	237	7	337
137	4	238	13	338
140	2	239	10	339
144	1	240	2	340

Selection for F1 rearing animals (Cohort 1A)

Project-No.: 90R0066/05R034

Group: 02

Dam No.	Pup No. allotted ♂	Animal No. for breeding	Pup No. allotted ♀	Animal No. for breeding
155	2	241	10	341
164	4	242	9	342
166	-	-	8	343
172	1	244	7	344
149	4	245	15	345
151	3	246	9	346
153	1	247	8	347
161	2	248	9	348
162	5	249	11	349
169	5	250	8	350
170	2	251	10	351
171	3	252	12	352
152	2, 3	253, 243	10	353
157	5	254	6	354
159	1	255	4	355
163	4	256	10	356
167	1	257	7	357
168	2	258	10	358
150	5	259	11	359
160	3	260	13	360

Selection for F1 rearing animals (Cohort 1A)

Project-No.: 90R0066/05R034

Group: 03

Dam No.	Pup No. allotted ♂	Animal No. for breeding	Pup No. allotted ♀	Animal No. for breeding
174	2	261	6	361
176	1	262	4	362
185	5	263	10	363
192	4	264	8	364
173	5	265	9	365
175	3	266	10	366
177	5	267	8	367
178	3	268	12	368
181	1	269	7	369
182	3	270	8	370
184	2	271	3	371
190	2	272	10	372
187	4	273	11	373
189	2	274	9	374
191	1	275	10	375
193	6	276	9	376
194	2	277	7	377
195	6	278	8	378
180	4	279	11	379
188	2	280	7	380

Selection for F1 rearing animals (Cohort 1B)

Project-No.: 90R0066/05R034

Group: 00

Dam No.	Pup No. allotted ♂	Animal No. for breeding	Pup No. allotted ♀	Animal No. for breeding
104	2, 5	401, 402	10	501
124	3	403	8, 10	502, 503
102	4	404	15	504
103	2	405	10	505
108	1	406	7	506
109	3	407	12	507
110	2	408	6	508
111	5	409	11	509
114	4	410	15	510
119	5	411	9	511
113	1	412	13	512
115	2	413	10	513
117	3	414	13	514
118	6	415	10	515
121	2	416	8	516
122	4	417	12	517
101	5	418	9	518
106	1	419	11	519
107	3	420	5	520
112	2	421	7	521
116	4	422	14	522
120	3	423	11	523
123	3	424	15	524

Selection for F1 rearing animals (Cohort 1B)

Project-No.: 90R0066/05R034

Group: 01

Dam No.	Pup No. allotted ♂	Animal No. for breeding	Pup No. allotted ♀	Animal No. for breeding
125	5	425	11	525
128	1	426	8, 10	526, 527
134	3	427	9	528
139	5	428	10	529
142	1, 4	429, 430	8	530
143	3	431	13	531
146	1	432	13	532
131	3, 5	433, 434	11	533
133	6	435	12	534
135	4	436	11, 14	535, 536
138	1	437	12	537
147	2, 5	438, 439	9	538
126	3	440	12, 14	539, 540
129	2, 4	441, 442	13	541
130	4	443	9, 12	542, 543
132	2	444	8	544
136	1	445	5	545
137	2, 3	446, 447	11	546
140	4	448	6, 9	547, 548

Selection for F1 rearing animals (Cohort 1B)

Project-No.: 90R0066/05R034

Group: 02

Dam No.	Pup No. allotted ♂	Animal No. for breeding	Pup No. allotted ♀	Animal No. for breeding
154	1	449	3	549
155	5	450	9	550
156	3	451	11	551
158	2	452	7	552
164	1	453	10	553
166	5	454	9	554
172	2	455	10	555
149	5	456	13	556
151	2	457	8	557
153	5	458	6	558
161	4	459	11	559
162	2	460	12	560
169	3	461	7	561
170	4	462	11	562
171	1	463	8	563
152	1	464	9	564
157	2	465	8	565
163	3	466	8	566
167	4	467	10	567
168	5	468	9	568
150	1, 3	469, 470	12	569
160	4	471	10	570
165	2	472	12, 14	571, 572

Selection for F1 rearing animals (Cohort 1B)

Project-No.: 90R0066/05R034

Group: 03

Dam No.	Pup No. allotted ♂	Animal No. for breeding	Pup No. allotted ♀	Animal No. for breeding
196	1, 4	473, 474	9	573
174	4	475	7	574
176	-	-	6	575
179	1	476	4	576
185	1, 3	477, 478	11	577
192	3	479	12	578
173	2	480	11	579
175	5	481	9	580
177	3	482	10	581
178	5	483	8	582
181	4	484	10	583
182	2	485	5	584
190	5	486	13	585
187	2	487	12	586
189	5	488	8	587
191	4	489	11	588
193	1	490	10	589
194	3	491	8	590
195	1	492	9	591
180	2	493	8, 10	592, 593
186	4	494	7, 8	594, 595
188	3, 5	495, 496	9	596

Selection for F1 rearing animals (Cohort 2A)

Project-No.: 90R0066/05R034

Group: 00

Dam No.	Pup No. allotted ♂	Animal No. for breeding	Pup No. allotted ♀	Animal No. for breeding
102	2	601	-	-
108	4	602	-	-
119	3	603	-	-
113	3	604	-	-
117	5	605	-	-
122	1	606	-	-
101	4	607	-	-
107	1	608	-	-
116	2	609	-	-
123	5	610	-	-
103	-	-	11	701
109	-	-	13	702
110	-	-	7	703
114	-	-	14	704
115	-	-	11	705
118	-	-	12	706
121	-	-	7	707
106	-	-	9	708
112	-	-	8	709
120	-	-	14	710

Selection for F1 rearing animals (Cohort 2A)

Project-No.: 90R0066/05R034

Group: 01

Dam No.	Pup No. allotted ♂	Animal No. for breeding	Pup No. allotted ♀	Animal No. for breeding
125	2	611	-	-
142	2	612	-	-
143	1	613	-	-
146	4	614	-	-
135	3	615	-	-
147	3	616	-	-
148	2	617	-	-
126	4	618	-	-
130	1	619	-	-
132	4	620	-	-
128	-	-	9	711
134	-	-	7	712
139	-	-	13	713
131	-	-	14	714
133	-	-	9	715
138	-	-	11	716
129	-	-	10	717
136	-	-	6	718
137	-	-	12	719
140	-	-	7	720

Selection for F1 rearing animals (Cohort 2A)

Project-No.: 90R0066/05R034

Group: 02

Dam No.	Pup No. allotted ♂	Animal No. for breeding	Pup No. allotted ♀	Animal No. for breeding
155	4	621	-	-
164	2	622	-	-
172	4	623	-	-
151	4	624	-	-
162	3	625	-	-
169	6	626	-	-
163	5	627	-	-
167	3	628	-	-
168	1	629	-	-
150	2	630	-	-
156	-	-	10	721
166	-	-	7	722
153	-	-	10	723
161	-	-	12	724
171	-	-	11	725
152	-	-	7	726
157	-	-	9	727
159	-	-	2	728
160	-	-	14	729
165	-	-	10	730

Selection for F1 rearing animals (Cohort 2A)

Project-No.: 90R0066/05R034

Group: 03

Dam No.	Pup No. allotted ♂	Animal No. for breeding	Pup No. allotted ♀	Animal No. for breeding
179	3	631	-	-
192	5	632	-	-
173	1	633	-	-
181	2	634	-	-
182	4	635	-	-
187	1	636	-	-
191	3	637	-	-
195	4	638	-	-
180	5	639	-	-
186	2	640	-	-
174	-	-	8	731
176	-	-	9	732
185	-	-	9	733
175	-	-	13	734
177	-	-	11	735
178	-	-	10	736
189	-	-	7	737
193	-	-	8	738
194	-	-	11	739
188	-	-	6	740

Selection for F1 rearing animals (Cohort 2B)

Project-No.: 90R0066/05R034

Group: 00

Dam No.	Pup No. allotted ♂	Animal No. for breeding	Pup No. allotted ♀	Animal No. for breeding
103	3	801	-	-
109	5	802	-	-
111	6	803	-	-
114	2	804	-	-
115	4	805	-	-
118	1	806	-	-
121	3	807	-	-
106	2	808	-	-
112	1	809	-	-
120	1	810	-	-
102	-	-	12	901
108	-	-	6	902
119	-	-	11	903
113	-	-	10	904
117	-	-	16	905
122	-	-	9	906
101	-	-	13	907
107	-	-	7	908
116	-	-	13	909
123	-	-	14	910

Selection for F1 rearing animals (Cohort 2B)

Project-No.: 90R0066/05R034

Group: 01

Dam No.	Pup No. allotted ♂	Animal No. for breeding	Pup No. allotted ♀	Animal No. for breeding
128	5	811	-	-
134	2	812	-	-
139	4	813	-	-
131	6	814	-	-
133	1	815	-	-
138	4	816	-	-
129	3	817	-	-
136	4	818	-	-
137	5	819	-	-
140	3	820	-	-
125	-	-	12	911
142	-	-	10	912
143	-	-	15	913
146	-	-	12	914
135	-	-	10	915
147	-	-	8	916
148	-	-	6	917
126	-	-	10	918
130	-	-	11	919
132	-	-	10	920

Selection for F1 rearing animals (Cohort 2B)

Project-No.: 90R0066/05R034

Group: 02

Dam No.	Pup No. allotted ♂	Animal No. for breeding	Pup No. allotted ♀	Animal No. for breeding
164	5	821	-	-
166	2	822	-	-
149	1	823	-	-
153	2	824	-	-
171	4	825	-	-
152	5	826	-	-
157	4	827	-	-
163	1	828	-	-
160	1	829	-	-
165	4	830	-	-
154	-	-	6	921
155	-	-	12	922
158	-	-	3	923
151	-	-	11	924
162	-	-	8	925
170	-	-	9	926
159	-	-	5	927
167	-	-	8	928
168	-	-	13	929
150	-	-	10	930

Selection for F1 rearing animals (Cohort 2B)

Project-No.: 90R0066/05R034

Group: 03

Dam No.	Pup No. allotted ♂	Animal No. for breeding	Pup No. allotted ♀	Animal No. for breeding
174	3	831	-	-
185	6	832	-	-
192	2	833	-	-
175	4	834	-	-
177	1	835	-	-
178	2	836	-	-
189	1	837	-	-
193	4	838	-	-
195	3	839	-	-
188	4	840	-	-
176	-	-	5	931
179	-	-	8	932
181	-	-	9	933
182	-	-	7	934
190	-	-	12	935
187	-	-	13	936
191	-	-	9	937
194	-	-	10	938
180	-	-	9	939
186	-	-	5	940

Selecton for F1 rearing animals (Cohort 3)

Project-No.: 90R0066/05R034

Group: 00

Dam No.	Pup No. allotted ♂	Animal No. for breeding	Pup No. allotted ♀	Animal No. for breeding
102	1	1001	-	-
108	5	1002	-	-
114	3	1003	-	-
115	1	1004	-	-
117	4	1005	-	-
118	5	1006	-	-
106	3	1007	-	-
112	3	1008	-	-
116	1	1009	-	-
123	2	1010	-	-
103	-	-	12	1101
110	-	-	8	1102
111	-	-	9	1103
119	-	-	12	1104
113	-	-	14	1105
121	-	-	6	1106
122	-	-	10	1107
101	-	-	10	1108
107	-	-	8	1109
120	-	-	13	1110

Selecton for F1 rearing animals (Cohort 3)

Project-No.: 90R0066/05R034

Group: 01

Dam No.	Pup No. allotted ♂	Animal No. for breeding	Pup No. allotted ♀	Animal No. for breeding
125	3	1011	-	-
128	2	1012	-	-
139	2	1013	-	-
131	1	1014	-	-
133	4	1015	-	-
135	2	1016	-	-
126	5	1017	-	-
130	2	1018	-	-
132	5	1019	-	-
140	1	1020	-	-
134	-	-	8	1111
142	-	-	9	1112
143	-	-	12	1113
146	-	-	15	1114
138	-	-	13	1115
147	-	-	11	1116
148	-	-	4	1117
129	-	-	12	1118
136	-	-	9	1119
137	-	-	14	1120

Selecton for F1 rearing animals (Cohort 3)

Project-No.: 90R0066/05R034

Group: 02

Dam No.	Pup No. allotted ♂	Animal No. for breeding	Pup No. allotted ♀	Animal No. for breeding
156	1	1021	-	-
166	3	1022	-	-
172	5	1023	-	-
149	3	1024	-	-
153	4	1025	-	-
161	1	1026	-	-
157	3	1027	-	-
167	5	1028	-	-
168	4	1029	-	-
165	1	1030	-	-
154	-	-	8	1121
158	-	-	5	1122
162	-	-	10	1123
170	-	-	8	1124
171	-	-	9	1125
152	-	-	11	1126
159	-	-	3	1127
163	-	-	11	1128
150	-	-	8	1129
160	-	-	12	1130

Selecton for F1 rearing animals (Cohort 3)

Project-No.: 90R0066/05R034

Group: 03

Dam No.	Pup No. allotted ♂	Animal No. for breeding	Pup No. allotted ♀	Animal No. for breeding
174	5	1031	-	-
185	2	1032	-	-
177	2	1033	-	-
181	3	1034	-	-
190	1	1035	-	-
193	2	1036	-	-
194	5	1037	-	-
195	2	1038	-	-
180	3	1039	-	-
186	1	1040	-	-
176	-	-	7	1131
179	-	-	6	1132
192	-	-	9	1133
173	-	-	8	1134
175	-	-	12	1135
178	-	-	9	1136
187	-	-	9	1137
189	-	-	10	1138
191	-	-	8	1139
188	-	-	10	1140

**Selection for PND 22
(thyroid hormones and pathology)**

Project-No.: 90R0066/05R034

Group: 00

Dam No.	Pup No. allotted ♂	Animal No. for breeding	Pup No. allotted ♀	Animal No. for breeding
104	4	1601	-	-
124	1	1602	-	-
102	5	1603	-	-
103	4	1604	-	-
109	6	1605	-	-
110	3	1606	-	-
111	4	1607	-	-
113	4	1608	-	-
101	2	1609	-	-
116	5	1610	-	-
108	-	-	10	1701
114	-	-	11	1702
119	-	-	10	1703
115	-	-	12	1704
117	-	-	15	1705
106	-	-	10	1706
107	-	-	6	1707
112	-	-	11	1708
120	-	-	12	1709
123	-	-	13	1710

**Selection for PND 22
(thyroid hormones and pathology)**

Project-No.: 90R0066/05R034

Group: 01

Dam No.	Pup No. allotted ♂	Animal No. for breeding	Pup No. allotted ♀	Animal No. for breeding
128	3	1611	-	-
134	1	1612	-	-
143	4	1613	-	-
146	5	1614	-	-
133	2	1615	-	-
135	5	1616	-	-
138	3	1617	-	-
130	5	1618	-	-
136	3	1619	-	-
140	5	1620	-	-
125	-	-	14	1711
139	-	-	11	1712
142	-	-	6	1713
131	-	-	13	1714
147	-	-	12	1715
126	-	-	13	1716
129	-	-	11	1717
132	-	-	12	1718
137	-	-	10	1719
144	-	-	3	1720

**Selection for PND 22
(thyroid hormones and pathology)**

Project-No.: 90R0066/05R034

Group: 02

Dam No.	Pup No. allotted ♂	Animal No. for breeding	Pup No. allotted ♀	Animal No. for breeding
155	3	1621	-	-
166	1	1622	-	-
161	5	1623	-	-
162	1	1624	-	-
169	4	1625	-	-
152	4	1626	-	-
163	2	1627	-	-
167	2	1628	-	-
168	3	1629	-	-
150	4	1630	-	-
154	-	-	5	1721
156	-	-	12	1722
158	-	-	8	1723
164	-	-	12	1724
172	-	-	8	1725
149	-	-	16	1726
151	-	-	7	1727
157	-	-	7	1728
160	-	-	11	1729
165	-	-	13	1730

**Selection for PND 22
(thyroid hormones and pathology)**

Project-No.: 90R0066/05R034

Group: 03

Dam No.	Pup No. allotted ♂	Animal No. for breeding	Pup No. allotted ♀	Animal No. for breeding
196	2	1631	-	-
185	4	1632	-	-
192	1	1633	-	-
173	4	1634	-	-
175	1	1635	-	-
178	4	1636	-	-
187	5	1637	-	-
189	3	1638	-	-
195	7	1639	-	-
180	1	1640	-	-
174	-	-	10	1731
176	-	-	3	1732
179	-	-	7	1733
177	-	-	9	1734
181	-	-	11	1735
191	-	-	12	1736
193	-	-	11	1737
194	-	-	9	1738
186	-	-	10	1739
188	-	-	8	1740

Selection for F1 rearing animals (positive control)

Project-No.: 90R0066/05R034

Group: 00

Dam No.	Pup No. allotted ♂	Animal No. for breeding	Pup No. allotted ♀	Animal No. for breeding
103	5	1041	-	-
109	2	1042	-	-
111	1	1043	-	-
119	2	1044	-	-
113	5	1045	-	-
118	2	1046	-	-
101	3	1047	-	-
107	4	1048	-	-
120	5	1049	-	-
123	4	1050	-	-
102	-	-	16	1141
108	-	-	8	1142
110	-	-	10	1143
114	-	-	13	1144
115	-	-	14	1145
117	-	-	12	1146
121	-	-	9	1147
122	-	-	8	1148
106	-	-	12	1149
116	-	-	11	1150

6. Historical control data

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HISTORICAL CONTROL DATA OF CLINICAL PATHOLOGY TESTING 1)

Species: Rat
Sex: Male
Strain: CrI:Wi(Han)
Study period: about 3 months
Administration route: Oral
Fasting before blood sampling: 16 hours
Anaesthesia: Isoflurane
Data print out at: 15-Nov-18

Study No.	Generation	Animals examined	Sampling time	motility %
03S007	F0	10	Apr 13	85
07S047	F0	10	Apr 13	88
04I036	F0	10	Jul 13	86
13S013	F0	10	Aug 13	86
11R220	F0	25	Okt 13	83
01R025	F0	25	Okt 13	85
13C020	F0	10	Nov 13	84
01R025	F1	20	Dec 13	87
05S025	F0	10	Dec 13	87
11R220	F1	25	Feb 14	87
08S031	F0	10	Feb 14	89
10R167	F0	25	Apr 14	89
12R120	F0	5	Mai 14	93
11S244	F0	10	Jun 14	90
11R238	F0	25	Jul 14	90
10R167	F1	25	Aug 14	89
11R238	F1	25	Nov 14	88
14R078	F0	25	Mrz 15	83
14I060	F0	12	Apr 15	88
14R068	F0	25	Apr 15	83
14R078	F1	25	Mai 15	87
14R090	F0	25	Aug 15	82
11C205	F0	10	Aug 15	83
14R092	F0	25	Sep 15	88
11S166	F0	10	Sep 15	*56
13R117	F0	25	Oct 15	86
14R092	F1	25	Nov 15	85
13R117	F1	25	Dec 15	88
11S254	F0	10	Feb 16	82
15R036	F0	10	Feb 16	84
02I041	F0	10	Apr 16	79
10S064	F0	10	Apr 16	85
13S141	F0	10	Apr 16	81
06R018	F0	25	May 16	87
10C098	F0	10	May 16	80
15R063	F0	10	Jul 16	88
08S034	F0	10	Aug 16	88
14R059	F0	25	Jun 16	86
14R059	F1	25	Aug 16	90
02R044	F0	25	Jan 17	89
16R046	F0	25	Feb 17	84
02R044	F1	25	Mar 17	88
10S185	F0	10	Mar 17	87
16R046	F1	25	Apr 17	83
12S151	F0	10	May 17	88
09R138	F0	25	Jun 17	86
09R138	F1	25	Aug 17	79
11R272	F0	10	Sep 17	85

N (wo. outliers) 41
Mean 86
25. Percentile (Q25) 84
75. Percentile (Q75) 88
Q25-1.5x(Q75-Q25) 77
Q75+1.5x(Q75-Q25) 94
Minimum (wo. outliers) 79
Maximum (wo.outliers) 93

*Outliers: < Q25-1.5x(Q75-Q25) or > Q75+1.5x(Q75-Q25)

1) Source: All data were collected at the test facility Experimental Toxicology and Ecology, BASF SE, 67056 Ludwigshafen, Germany, in accordance with the OECD principles of Good Laboratory Practice (GLP) and the GLP principles of the German "Chemikaliengesetz" (Chemicals Act)

7. Functional Observation Battery

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Functional Observational Battery (FOB):
Detailed description of examinations, ranking and documentation procedures

The following describes in detail the scope of examinations and the ranking of the findings.

HOME CAGE OBSERVATIONS

1. Posture

The posture of the animals is examined for any abnormal findings.

- 0 animal is sitting or lying
- 1 animal is standing and moving
- 2 squatting posture
- 3 abdominal position
- 4 abdominal position with splayed limbs
- 5 lateral position
- 6 oblique head posture
- 7 opisthotonus

2. Tremors

Any tremors are documented.

- 0 no tremors
- 1 slight tremors
- 2 moderate tremors
- 3 severe tremors

3. Convulsions

If convulsions are seen, the severeness will be assessed. If possible, also the type of convulsions, i.e. clonic (alternate muscular contraction and relaxation in rapid succession) or tonic (characterized by continuous tension), is documented.

- 0 no convulsions
- 1 slight convulsions
- 2 moderate convulsions
- 3 severe convulsions

4. Abnormal movements

Any abnormal movement or bizarre behaviour is documented.

- 0 no abnormalities
- 1 manege movements
- 2 head shaking
- 3 excessive cleaning
- 4 frequent chewing

5. Gait

If any impairment of gait is observed, the type and severeness is documented. Different types of gait impairment are ataxia (irregularity of muscular action), paralysis (loss of motor function) and paresis (slight or incomplete paralysis). If possible, also the affected limbs (forelimbs, hindlimbs) are documented.

- 0 animal is not walking during observation
- 1 no impairment of gait
- 2 stiff gait
- 3 slight impairment of coordination, unsteady gait
- 4 moderate impairment of coordination, shuffling gait
- 5 severe impairment of coordination, dragging of the hindlimbs
- 6 severe impairment of coordination, with splayed limbs
- 7 animal is unable to walk (abdominal or lateral position)

6. Other findings

- 0 no other findings
- * If findings appear which are not included in this grading system, they will be described in detail.

OPEN FIELD OBSERVATIONS

1. Behavior on removal from the cage

The animal is removal from the home cage, and the reaction is documented.

- 0 animal is tense, but it shows no resistance against handling
- 1 animal shows a slight resistance against the handling
- 2 animal shows no resistance against the handling but appears indifferent
- 3 animal is difficult to handle, it shows aggressiveness
- 4 animal is very difficult to handle, it shows severe aggressiveness

2. Fur

The fur of the animals is examined for any abnormal signs.

- 0 nothing abnormal detected
- 1 discolored fur
- 2 urine staining of anogenital region
- 3 piloerection
- 4 alopecia
- 5 reduced care on fur

3. Skin

The visible parts of the skin (e.g. nose) are examined for any abnormal signs.

- 0 nothing abnormal detected
- 1 discolored skin
- 2 reddening
- 3 paleness
- 4 dehydration (exsiccosis)
- 5 hypothermia (skin feels cold during handling)
- 6 lesion(s)
- 7 crust(s)

4. Salivation

The area around the mouth is examined for signs of discharge; if possible, also the color of discharge is documented.

- 0 no salivation
- 1 slight salivation (area around the mouth is moist)
- 2 moderate salivation (wet mouth)
- 3 severe salivation (mouth very wet, wet paws)

5. Nasal discharge

Any discharge is documented.

- 0 no discharge, dry nose
- 1 clear discharge
- 2 reddish discharge

6. Lacrimation

Any lacrimation or secretion of pigmented tears is documented. If possible, the color of the tears is also assessed.

- 0 no lacrimation
- 1 slight lacrimation
- 2 moderate lacrimation
- 3 severe lacrimation

7. Eyes/Pupil size

- 0 nothing abnormal detected, pupils contracted at room light
- 1 chromodacryorrhea
- 2 exophthalmus
- 3 pupils dilated
- 4 abnormal shape of pupils
- 5 oblique eye posture
- 6 opacity
- 7 cataract

8. Posture

The posture of the animals is examined for any abnormal findings.

- 0 animal is sitting or lying
- 1 animal is standing and moving
- 2 squatting posture
- 3 abdominal position
- 4 abdominal position with splayed limbs
- 5 lateral position
- 6 oblique head posture
- 7 opisthotonus

9. Palpebral closure

The level of eyelid closure is examined. Usually, the eyelids of rats are completely opened (except when blinking).

- 0 nothing abnormal detected
- 1 eyelid(s) slight closure
- 2 eyelid(s) half closure
- 3 eyelid(s) permanent closure

10. Respiration

The respiration is examined for any abnormalities.

- 0 nothing abnormal detected
- 1 respiration labored
- 2 gasping/respiratory sounds
- 3 respiration accelerated
- 4 respiration irregular

11. Tremors

Any tremors are documented.

- 0 no tremors
- 1 slight tremors
- 2 moderate tremors
- 3 severe tremors

12. Convulsions

If convulsions are seen, the severeness will be assessed. If possible, also the type of convulsions, i.e. clonic (alternate muscular contraction and relaxation in rapid succession) or tonic (characterized by continuous tension), is documented.

- 0 no convulsions
- 1 slight convulsions
- 2 moderate convulsions
- 3 severe convulsions

13. Abnormal movements/ stereotypes

Any abnormal movements or bizarre behavior are documented

- 0 no abnormalities
- 1 manege movements
- 2 head shaking
- 3 excessive cleaning
- 4 frequent chewing

14. Gait

If any impairment of gait is observed, the type and severeness will be documented. Different types of gait impairment are ataxia (irregularity of muscular action), paralysis (loss of motor function) and paresis (slight or incomplete paralysis). If possible, also the affected limbs (forelimbs, hindlimbs) are documented.

- 0 animal is not walking during observation
- 1 no impairment of gait
- 2 stiff gait
- 3 slight impairment of coordination, unsteady gait
- 4 moderate impairment of coordination, shuffling gait
- 5 severe impairment of coordination, dragging of the hindlimbs
- 6 severe impairment of coordination, with splayed limbs
- 7 animal is unable to walk (abdominal or lateral position)

15. Activity/ arousal level

The activity of the animals in the open field and the arousal level is examined for any deviation from normal.

- 0 normal exploration of the area
- 1 reduced exploration of the area
- 2 severe reduced exploration of the area, animal apathetic
- 3 increased exploration of the area, sudden or jerky movements
- 4 hyperactivity

16. Feces excreted within 2 minutes

The appearance and consistency of the feces are described.

- 0 no defecation during observation period
- 1 feces without abnormalities
- 2 discolored feces
- 3 crumbly feces
- 4 soft feces
- 5 muicid feces
- 6 diarrhea

17. Urine excreted within 2 minutes

The amount and the color of the urine are described.

- 0 no urination during observation period
- 1 urine without abnormalities (some wet areas on the filter paper)
- 2 discoloration of urine
- 3 polyuria (great wet areas on the filter paper)

18. Rearing within 2 minutes

In the open field, the animals usually rear several times in order to explore the new environment. A rear is counted, if both forelimbs are removed from the floor. The number of rearings is counted within a 2 minute observation period.

Documentation:
- (number)

19. Other findings

- 0 no other findings
- * If findings appear which are not included in this grading system, they will be described in detail.

SENSORY-MOTORIC TEST/REFLEXES**1. Reaction to an object being moved towards the face (Approach response)**

A stick is approached slowly to the head of the animal. Normal reaction of the animal is to approach to the object or to ignore the object.

- 0 no reaction
- 1 approaching to object
- 2 escape reaction
- 3 aggressive reaction and attacking of object

2. Touch sensitivity (Touch Response)

The animal is touched with a stick along the flank. Normal reaction is to orientate to the stimulus or to ignore the stimulus.

- 0 no reaction
- 1 orientation to the stimulus
- 2 escape after touch
- 3 aggressive reaction and attacking of object
- 4 reaction to the stimulus but no ability to localize (e.g. turning to wrong side)

3. Vision (Visual placing response)

The animal is held on the tail and moved slowly towards the wire cover of a cage. Normal reaction of the animal is to stretch the forelimbs in order to grasp the object.

- 0 nothing abnormal detected (grasping with forelimbs)
- 1 no grasping

4. Pupillary reflex

The capacity of the pupils to adapt to darkness and to light is examined. The animals are put into a dark box for about 10 seconds and the pupils are examined using an electric torch. Normally, the pupil dilates in the dark and contracts immediately in the light.

- 0 nothing abnormal detected, physiological adaptation of the pupil to light
- 1 retarded adaptation of the pupil to light
- 2 no adaptation of the pupil to light, pupils permanently contracted
- 3 no adaptation of the pupil to light, pupils permanently dilated

5. Pinna reflex

The pinna of the animal is touched with a small bristle. Normally, the animal jerks the pinna or head immediately after the stimulus.

- 0 immediate response to the stimulus
- 1 no response to the stimulus

6. Audition (startle response)

The animal is exposed to a sharp, electrically produced noise and the reaction to the sound is tested. Normally the animal shows a startle response (e.g. moving the ears, jerking, jumping backwards).

- 0 nothing abnormal detected, immediate normal response to the stimulus
- 1 no response
- 2 increased response
- 3 hyperreaction

7. Coordination of movements (Righting response)

The animal is turned into dorsal position and released. Normal reaction is that the animal immediately turns to an upright position.

- 0 nothing abnormal detected, immediate righting response
- 1 retarded righting response
- 2 fails to turn into upright position, animal stays in lateral position
- 3 no righting response, animal stays in dorsal position

8. Behavior during handling

- 0 normal behavior, easy to handle, animal is tense, but it shows no resistance against handling
- 1 very easy to handle, animal hangs limply in the hand
- 2 slightly difficult to handle, animal shows a slight resistance against handling
- 3 difficult to handle, animal shows a severe resistance against handling

9. Vocalization

- 0 no or only sporadic vocalizations when touched
- 1 very frequent vocalizations when touched
- 2 vocalizations always when touched
- 3 vocalization without touching

10. Pain perception (Tail pinch)

The tip of the tail is squeezed with a forceps. Normally the animal responds to the stimulus, e.g. it moves away.

- 0 nothing abnormal detected, immediate response to the stimulus
- 1 weak or retarded reaction to the stimulus
- 2 no response to the stimulus
- 3 hyperreaction to the stimulus

11. Other findings

- 0 no other findings
- * If findings appear which are not included in this grading system, they will be described in detail

12. Grip strength of forelimbs and hindlimbs

Measurement of grip strength is performed according to the method described by Meyer et al. 1979 (Neurobehavioral Toxicology, 1, 233-236):

The animal is brought into a position that forelimbs/hindlimbs are able to grip the metal bar of a newtonmeter. Then the animal is pulled gently backwards until it releases the grid. The average of two measurements is taken for each hindlimbs and forelimbs.

Documentation:

- (number)

13. Landing foot-splay test

The animal is held about 30 cm above and dropped onto a flat area covered with putty. This results in clearly visible footprints. The distance between the fourth digits of the left and right hindlimb is measured. The average of two measurements is taken for each rat.

Documentation:

- (number)

GENERAL REMARK:

Details of localization or color, or detailed descriptions of findings (e.g. tonic or clonic convulsions) have to be described using abbreviations (letter or a combination of letters), if they are not already given in the SOP.

8. Positive Control (Cyclophosphamide monohydrate)
(Mean values and Individual values)

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Study 90R0066/05R034_PP

Summary - Clinical Observation

Sex: Male - Phase: In-life

Test Group 14/M 4.5 mg/kg bw/d		
Animals examined	N	10
dead		
sacrificed scheduled	N	10
normal		
NAD	N	10

day 0 [00:00 - 24:00] -> day 33 [00:00 - 24:00]

14-Dec-2018 17:22
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Study 90R0066/05R034_PP

Summary - Clinical Observation

Sex: Female - Phase: In-life

Test Group 14/F 4.5 mg/kg bw/d			
Animals examined		N	10
dead			
sacrificed scheduled		N	10
normal			
NAD		N	10

day 0 [00:00 - 24:00] -> day 33 [00:00 - 24:00]

14-Dec-2018 17:55
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Study 90R0066/05R034_PP

Summary Food Consumption Per Animal And Day

Sex: **Male** - Phase: **In-life**

	Test Group 14/M 4.5 mg/kg bw/d		
d 0 -> 5	Mean [g]	16.6	
	S.d.	0.8	
	N	5	
d 5 -> 12	Mean [g]	21.1	
	S.d.	0.9	
	N	5	
d 12 -> 19	Mean [g]	22.8	
	S.d.	1.0	
	N	5	
d 19 -> 26	Mean [g]	25.9	
	S.d.	1.1	
	N	5	
d 0 -> 26	Mean [g]	22.0	
	S.d.	0.9	
	N	5	
Total	Total [g]	108.4	
	Mean [g]	21.7	

d = day

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Study 90R0066/05R034_PP

Summary Food Consumption Per Animal And Day

Sex: Female - Phase: In-life

	Test Group 14/F 4.5 mg/kg bw/d		
d 0 -> 5	Mean [g]	14.0	
	S.d.	0.8	
	N	5	
d 5 -> 12	Mean [g]	15.9	
	S.d.	1.5	
	N	5	
d 12 -> 19	Mean [g]	17.0	
	S.d.	2.2	
	N	5	
d 19 -> 26	Mean [g]	18.3	
	S.d.	3.9	
	N	5	
d 0 -> 26	Mean [g]	16.5	
	S.d.	2.1	
	N	5	
Total	Total [g]	81.7	
	Mean [g]	16.3	

d = day

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Study 90R0066/05R034_PP

Summary Body Weights - BW / Body Weights [g]

Sex: **Male** - Phase: **In-life**

	Test Group 14/M 4.5 mg/kg bw/d		
day 0	Mean	112.3	
	S.d.	9.0	
	N	10	
day 5	Mean	152.0	
	S.d.	13.3	
	N	10	
day 12	Mean	210.4	
	S.d.	22.5	
	N	10	
day 19	Mean	262.4	
	S.d.	28.7	
	N	10	
day 26	Mean	315.6	
	S.d.	30.3	
	N	10	

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Study 90R0066/05R034_PP

Summary Body Weights - BW / Body Weights [g]

Sex: Female - Phase: In-life

	Test Group 14/F 4.5 mg/kg bw/d		
day 0	Mean		100.7
	S.d.		5.6
	N		6
day 5	Mean		128.4
	S.d.		8.0
	N		10
day 12	Mean		159.2
	S.d.		13.2
	N		10
day 19	Mean		182.6
	S.d.		14.2
	N		10
day 26	Mean		199.8
	S.d.		14.8
	N		10

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Summary Changes Body Weights - BW / Body Weights [g]

Sex: **Male** - Phase: **In-life**

	Test Group 14/M 4.5 mg/kg bw/d		
d 0 -> 5	Mean	39.7	
	S.d.	5.3	
	N	10	
d 5 -> 12	Mean	58.4	
	S.d.	9.5	
	N	10	
d 12 -> 19	Mean	52.0	
	S.d.	8.0	
	N	10	
d 19 -> 26	Mean	53.2	
	S.d.	5.7	
	N	10	
d 0 -> 26	Mean	203.3	
	S.d.	23.6	
	N	10	

d = day

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Study 90R0066/05R034_PP

Summary Changes Body Weights - BW / Body Weights [g]

Sex: Female - Phase: In-life

	Test Group 14/F 4.5 mg/kg bw/d		
d 0 -> 5	Mean	S.d.	N
	30.4	4.2	6
d 5 -> 12	Mean	S.d.	N
	30.8	7.1	10
d 12 -> 19	Mean	S.d.	N
	23.5	3.5	10
d 19 -> 26	Mean	S.d.	N
	17.1	4.6	10
d 0 -> 26	Mean	S.d.	N
	100.8	9.7	6

d = day

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Study 90R0066/05R034_PP

Individual Signs - Clinical Observation

Sex: Male - Phase: In-life

Dose Group	Animal Number	Sign Type	Sign	Modifier	Remark	First Last Duration	
						Day	Day [Days]
Test Group 14/M 4.5 mg/kg bw/d	1041	normal	NAD			0	33
		dead	sacrificed scheduled			33	33
	1042	normal	NAD			0	33
		dead	sacrificed scheduled			33	33
	1043	normal	NAD			0	33
		dead	sacrificed scheduled			33	33
	1044	normal	NAD			0	33
		dead	sacrificed scheduled			33	33
	1045	normal	NAD			0	33
		dead	sacrificed scheduled			33	33
Test Group 14/M 4.5 mg/kg bw/d	1046	normal	NAD			0	33
		dead	sacrificed scheduled			33	33
	1047	normal	NAD			0	33
		dead	sacrificed scheduled			33	33
	1048	normal	NAD			0	33
		dead	sacrificed scheduled			33	33
	1049	normal	NAD			0	33
		dead	sacrificed scheduled			33	33
	1050	normal	NAD			0	33
		dead	sacrificed scheduled			33	33

Study 90R0066/05R034_PP

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Individual Signs - Clinical Observation

Sex: Female - Phase: In-life

Dose Group	Animal Number	Sign Type	Sign	Modifier	Remark	First Last Duration	
						Day	Day [Days]
Test Group 14/F 4.5 mg/kg bw/d	1141	normal	NAD			0	33
		dead	sacrificed scheduled			33	33
	1142	normal	NAD			0	33
		dead	sacrificed scheduled			33	33
	1143	normal	NAD			0	33
		dead	sacrificed scheduled			33	33
	1144	normal	NAD			0	33
		dead	sacrificed scheduled			33	33
	1145	normal	NAD			0	33
		dead	sacrificed scheduled			33	33
	1146	normal	NAD			0	33
		dead	sacrificed scheduled			33	33
	1147	normal	NAD			1	33
		dead	sacrificed scheduled			33	33
	1148	normal	NAD			1	33
		dead	sacrificed scheduled			33	33
	1149	normal	NAD			1	33
		dead	sacrificed scheduled			33	33
	1150	normal	NAD			1	33
		dead	sacrificed scheduled			33	33

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Study 90R0066/05R034_PP

Individual Food Consumption Per Animal And Day [g/Day]

Sex: Male - Phase: In-life

Group	Cage	Animals	d 0 -> 5	d 5 -> 12	d 12 -> 19	d 19 -> 26
Test Group 14/M 4.5 mg/kg bw/d	CNo-1021	1041, 1042	15.5	20.4	21.8	25.8
	CNo-1022	1043, 1044	16.8	21.2	23.6	25.8
	CNo-1023	1045, 1046	16.6	20.4	22.4	24.7
	CNo-1024	1047, 1048	17.7	22.6	24.1	27.8
	CNo-1025	1049, 1050	16.5	20.7	22.0	25.5

d = day

14-Dec-2018 17:51

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Study 90R0066/05R034_PP

Individual Food Consumption Per Animal And Day [g/Day]

Sex: Female - Phase: In-life

Group	Cage	Animals	d 0 -> 5	d 5 -> 12	d 12 -> 19	d 19 -> 26
Test Group 14/F 4.5 mg/kg bw/d	CNo-1121	1141, 1142	13.1	14.9	16.5	15.9
	CNo-1122	1143, 1144	15.2	18.3	20.8	24.9
	CNo-1123	1145, 1146	14.3	15.2	15.5	17.0
	CNo-1124	1147, 1148	13.4	14.8	15.4	15.5
	CNo-1125	1149, 1150	14.1	16.5	16.7	18.1

d = day

Study 90R0066/05R034_PP

14-Dec-2018 18:06
Ascentos™ 1.3

Individual Body Weights - BW / Body Weights [g]

Sex: Male - Phase: In-life

Dose Group	Animal Number	day 0	day 5	day 12	day 19	day 26
Test Group 14/M 4.5 mg/kg bw/d	1041	93.5	128.3	175.1	225.6	285.7
	1042	113.7	160.4	226.6	286.8	348.8
	1043	120.0	159.2	219.8	271.1	329.9
	1044	112.6	151.4	212.3	262.1	312.2
	1045	115.1	157.1	217.3	276.1	320.4
	1046	110.0	146.7	199.3	248.5	298.2
	1047	110.9	151.6	207.8	264.4	315.8
	1048	120.4	164.6	228.2	284.7	337.4
	1049	123.9	169.0	243.8	298.8	353.8
	1050	102.6	131.6	173.7	205.8	253.9

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Ascentos™ 1.3

Study 90R0066/05R034_PP

Individual Body Weights - BW / Body Weights [g]

Sex: Female - Phase: In-life

Dose Group	Animal Number	day 0	day 5	day 12	day 19	day 26
Test Group 14/F 4.5 mg/kg bw/d	1141	102.4	127.5	146.8	175.9	197.5
	1142	98.0	128.1	152.4	173.7	191.5
	1143	99.9	135.0	168.0	189.0	204.0
	1144	102.1	137.9	179.9	204.0	221.2
	1145	92.3	120.1	148.3	166.6	187.9
	1146	109.3	137.8	170.3	194.9	206.7
	1147	NM	116.8	140.2	164.7	183.0
	1148	NM	128.6	167.1	190.7	204.0
	1149	NM	117.7	149.3	169.2	179.5
	1150	NM	134.3	169.5	197.8	222.5

NM = Not measured

14-Dec-2018 18:09

Ascentos™ 1.3

Study 90R0066/05R034_PP

Individual Changes Body Weights - BW / Body Weights [g]

Sex: Male - Phase: In-life

Dose Group	Animal Number	d 0 -> 5	d 5 -> 12	d 12 -> 19	d 19 -> 26	d 0 -> 26
Test Group 14/M 4.5 mg/kg bw/d	1041	34.8	46.8	50.5	60.1	192.2
	1042	46.7	66.2	60.2	62.0	235.1
	1043	39.2	60.6	51.3	58.8	209.9
	1044	38.8	60.9	49.8	50.1	199.6
	1045	42.0	60.2	58.8	44.3	205.3
	1046	36.7	52.6	49.2	49.7	188.2
	1047	40.7	56.2	56.6	51.4	204.9
	1048	44.2	63.6	56.5	52.7	217.0
	1049	45.1	74.8	55.0	55.0	229.9
	1050	29.0	42.1	32.1	48.1	151.3

d = day

14-Dec-2018 18:10

Ascentos™ 1.3

Study 90R0066/05R034_PP

Individual Changes Body Weights - BW / Body Weights [g]

Sex: Female - Phase: In-life

Dose Group	Animal Number	d 0 -> 5	d 5 -> 12	d 12 -> 19	d 19 -> 26	d 0 -> 26
Test Group 14/F 4.5 mg/kg bw/d	1141	25.1	19.3	29.1	21.6	95.1
	1142	30.1	24.3	21.3	17.8	93.5
	1143	35.1	33.0	21.0	15.0	104.1
	1144	35.8	42.0	24.1	17.2	119.1
	1145	27.8	28.2	18.3	21.3	95.6
	1146	28.5	32.5	24.6	11.8	97.4
	1147		23.4	24.5	18.3	
	1148		38.5	23.6	13.3	
	1149		31.6	19.9	10.3	
	1150		35.2	28.3	24.7	

d = day