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Persistence of gabapentin, 1H-benzotriazole, diglyme, DTPA, 1,4-dioxane, melamine and urotropin in surface water

Report

Persistence of gabapentin, 1H-benzotriazole, diglyme, DTPA, 1,4-dioxane, melamine and urotropin in surface water

Testing of chemicals according to the OECD 309 guideline

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Summary

For seven test compounds the biodegradability in surface water was measured according to the OECD 309 guideline. The goal of this study was to measure the biodegradation of a series of test substances that occur in surface water that is used as a source for drinking water, and pose a subsequent challenge for drinking water production.

The water used in the study was taken from the location “Schalterberg”, selected since it is known to contain hardly any anthropogenic compounds. Based on the results on both aniline and ATP measurements it can be concluded that the surface water showed sufficient microbial activity for biodegradation and that the test compounds weren’t toxic to the microorganisms present in the surface water.

The test compounds were spiked to bottles containing the water, and these bottles were gently shaken during the test period. At different time intervals bottles were taken and the test compound concentrations were analysed. Following the OECD 309 test requirements, all selected test compounds showed no (gabapentin, 1H-benzotriazole, diglyme, 1,4-dioxane and melamine) or only slow (DTPA, urotropin) decrease in test compound concentrations analytically determined. Therefore, abiotic and biotic degradation of the all selected test compounds is evaluated to be slow or negligible in surface water. Calculated half-lives were as follows: gabapentin >10.000 days; 1H-benzotriazole: >10.000 days; diglyme: >10.000 days; DTPA: 67.6 days; 1,4-dioxane: >10.000 days; melamine: >10.000 days; urotropin: 128 days.

According to the REACH legislation, a compound is considered persistent (P) if half-lives (DT_{50}) are larger than 40 days, and it is deemed to be very persistent (vP) if the DT_{50} in surface water exceeds 60 days. Comparing the obtained half-lives for the selected compounds in this study with vP/P-criteria, gabapentin, 1H-benzotriazole, diglyme, DTPA, 1,4-dioxane, melamine and urotropin seem to be very persistent in surface water.

Contents

1 Introduction

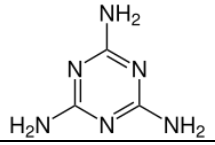
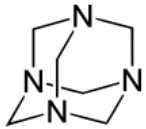
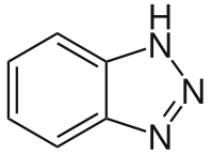
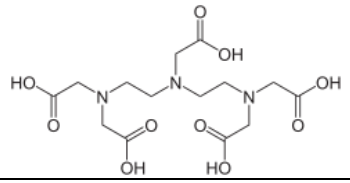
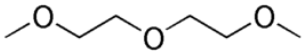
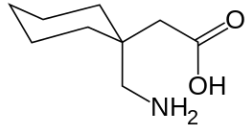
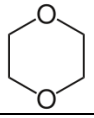
The presence of persistent compounds in sources for drinking water is a problem for the drinking water sector, as these compounds will hardly be removed during water treatment and further accumulate in the water cycle due to their resistance against biotic or abiotic degradation. This report shows the result of a study investigating the persistence of selected compounds in surface water. In total, seven compounds were tested: melamine, urotropin, 1H-benzotriazole, DTPA, 1,4-dioxane, diglyme and gabapentin (Table 1). These compounds had been chosen as they are often found in surface water that is used as a source for drinking water production, where they seem to be very persistent. Besides, it is difficult to remove these compounds in drinking water treatment. In case of gabapentin this was demonstrated among others by Henning, Kunkel et al. (2018), Herrmann, Menz et al. (2015) Ruiz-Delgado, Plaza-Bolaños et al. (2020), Bradley, Romanok et al. (2020) and by Datel and Hrabankova (2020), who also demonstrated this for 1H-benzotrizale. Other authors describe the presence of 1H-benzotriazole in surface water, e.g. Piai, Blokland et al. (2020), Albergamo, Helmus et al. (2018) and Brunsch, Langenhoff et al. (2019). Diglyme was found in surface water by e.g. Albergamo, Helmus et al. (2018) and Stepien and Püttmann (2014). Birka, Roscher et al. (2013 and 2016) report the presence of DTPA in surface water, and according to Rüdel, Körner et al. (2020) and Karges, Ott et al. (2020) 1,4-dioxane is deemed as a persistent compound. The difficult removal of urotropin from drinking water is described in a report by Bertelkamp, Hofman-Caris et al. (2017), and the presence and persistence of melamine in surface water has also been described by various authors (Minkus, Grosse et al. 2020, Piai, Blokland et al. 2020, Rauert, Kaserzon et al. 2020, Schulze, Paschke et al. 2020, Seiwert, Klöckner et al. 2020, Park and Jeon 2021).

The degradation test were performed according to OECD guideline 309 (Guideline for the testing of chemicals; aerobic mineralisation in Surface water – simulation biodegradation test) as pelagic version without the addition of suspended sediment. According to OECD 309 water from an aquatic environment that is known to have been contaminated with the test substance or its structural analogues within the previous four years should not be used for this test. As the water from the test location is frequently tested, it is known that the water that was used in the present study had not been previously contaminated.

The principal objective of the simulation test in surface water (OECD 309) is to determine the ultimate degradation (mineralisation) of the test substance at low concentrations (10-100 µg/L) in surface water. However, an optional secondary objective of the test is to obtain information on the primary degradation and the formation of major transformation products. For this purpose, however, higher concentrations of test substance (>100 µg/L and sometimes >1 mg/L) may be used for the identification and quantification of major transformation products compared to the kinetic part of the study (OECD 309). Based on the literature results shown above it was expected that the compounds tested in this study would be persistent, forming none or negligible amounts of transformation products. Therefore, the test was only conducted at low concentrations in the range from 10-100 µg/L, which makes the detection and identification difficult. Besides, analyses costs would become significantly higher if transformation products were in the focus of analytics. Therefore, it was decided not to determine any transformation products within the framework of this project. However, for compounds with an expected tendency for biodegradation, non-target analysis, aiming at detection and possible identification of transformation products is recommended.

The study on persistence of selected compounds was initiated by the Dutch drinking water sector in order to address the challenges of the drinking water utility operators with these persistent compounds within the REACH regulation of the European Union ((EG) Nr. 1907/2006). The REACH regulation is adopted to improve the protection of human health and the environment from the risks that can be posed by chemicals, while enhancing the competitiveness of the EU chemicals industry. For the assessment of persistence under REACH, commonly results from simulation degradation tests according to OECD 309 (surface water), OECD 308 (water-sediment) and OECD 306 (soil) tests are used as a base to conclude on the persistence and consequently on the environmental risks posed by these chemicals. Compounds tested in this project with appropriate physicochemical properties are shown in Table 1.

Table 1: Compounds tested in this project with appropriate physicochemical data.

Compound	**Chemical Class**	**CAS-nr.**	**Molecular structure**	**Solubility in water** (mg/L)	**pK_a**	**Henry's law constant** (atm-cu m/mol) at 25 °C	**Reference**
melamine	Industrial Chemical	108-78-1		$3.23*10^3$ at 20 °C	5.0	$1.84*10^{-14}$	PubChem
urotropin (hexamethylene tetramine)	Industrial Chemical	100-97-0		300	4.89	$3.7*10^{-10}$	Pubchem
1H-benzotriazole	Industrial Chemical	95-14-7		$1.98*10^4$ at 25 °C	8.37	$1.5*10^{-7}$	PubChem
DTPA (Di-ethylene triamine penta-acetic acid)	Industrial Chemical	67-43-6		Highly soluble	1.5 10.6	$1.49*10^{-6}$	Calculated according to note 1
diglyme	Industrial Chemical	111-96-6		miscible	-3.7	$5.23*10^{-7}$	PubChem Drugbank
gabapentin	Industrial Chemical, Pharmaceutical	60142-96-3		Freely soluble	3.68 10.70	$9.32*10^{-12}$	PubChem
1,4-dioxane	Industrial Chemical	123-91-1		$> 8*10^5$ at 25 °C	-0.27	$4.80*10^{-6}$	PubChem Drugbank

Note 1 to Table 1: Calculation and settings below based on ECHA: https://echa.europa.eu/documents/10162/13632/information_requirements_r16_en.pdf

Law constant. If the value is not available in the input data set, the required Henry's Law constant and the $K_{air-water}$ (also known as the "dimensionless" Henry's Law constant) can be estimated from the ratio of the vapour pressure to the water solubility (Equations R.16-4 and R.16-5). For water miscible compounds, direct measurement of the Henry's Law constant is recommended. For detailed information, see Appendix A.7.1-1.

$$HENRY = \frac{VP \cdot MOLW}{SOL} \qquad \textbf{(Equation R.16-4)}$$

$$K_{air-water} = \frac{HENRY}{R \cdot TEMP} \qquad \textbf{(Equation R.16-5)}$$

Explanation of symbols

VP	vapour pressure	[Pa]	data set
MOLW	molecular weight	[g·mol^{-1}]	data set
SOL	solubility	[mg·l^{-1}]	data set
R	gas constant	[Pa·m^3·mol^{-1}·k^{-1}]	8.314
TEMP	temperature at the air-water interface	[K]	285
HENRY	Henry's law constant	[Pa·m^3·mol^{-1}]	
$K_{air-water}$	air-water partitioning coefficient	[-]	

2 OECD guideline 309 for the testing of chemicals

OECD guideline 309 (OECD 309, 2004) describes a test to establish the time course of aerobic mineralisation in surface water. Its purpose is to measure the time course of biodegradation of a test substance at low concentration in aerobic natural water and to quantify the observations in the form of kinetic rate expressions. The simulation test can be performed as a laboratory shake flask batch test (biometer type system) or in a flow-through system to determine rates of aerobic biodegradation of organic substances in samples of natural surface water. Test substances are either incubated in surface water (pelagic test) or in the presence of sediment in concentrations up to 1 g/L (suspended sediment test). The present study was performed as biometer type system without the addition of sediment.

According to OECD 309 concentrations of less than 1 µg/L to 100 µg/L (preferably below 10 µg/L) should be applied, which is low enough to ensure that biodegradation kinetics obtained in the test reflect those expected in the environment. Compared to the total mass of biodegradable carbon substrates available in the natural water used for the test, the test substance present at low concentration will serve as a secondary substrate. This implies that the anticipated biodegradation kinetics should be first order and that the substance may be degraded by "co-metabolism". If first order kinetics are applicable, this implies that the rate of degradation (mg/L/day) is proportional to the concentration of substrate which declines over time. With true first order kinetics the specific degradation rate constant, *k*, is independent of time and concentration. For the present study, concentrations in the range of 1 µg/L to 100 µg/L were applied (in general 100 times the reporting limit) , as in this way the concentrations are low enough not to affect biodegradation kinetics, but high enough to ensure that 99% degradation can be analytically determined (Table 3).

According to OECD 309, the test should be carried out in surface water with low suspended solids concentrations (OECD 309, 2004). This was measured by determining the turbidity of the samples. After spiking with the test compounds, the test flasks all have been incubated in darkness at an environmentally relevant temperature (13 ^{o}C) under aerobic conditions and gentle agitation (20 rpm). All experiments should be carried out in duplicates. OECD 309 can be performed using ^{14}C-labelled substances or with unlabelled compounds, if an appropriate sensitive analytical method is available. Due to the use of highly sensitive and specialized chromatographic methods, the study was performed with unlabelled test compounds. The initial recovery of the test compounds at day 0 ranged between 70-112% based on the nominal concentration of test compounds aimed at preparing the dilutions. All tests were carried out in certified laboratories. According to the OECD 309 test guideline, degradation should be followed at appropriate time intervals by measuring the residual concentration of test substances and a minimum of five sampling points are required during the degradation phase. In this study we sampled the surface water at day 0, 7, 15, 30 and 60 after addition of the compounds.

The surface water chosen is known not to have been polluted by industrial or municipal WWTP discharge. The sampling point is very close to an intake for drinking water production, and as a result the water quality is frequently analysed. From these analyses it could be concluded that the water contains no or only very low concentrations of anthropogenic pollutants, and certainly not the ones involved in this study. Thus, it can be assumed that the microorganisms present are not used to dealing with the contaminants tested in this research, and the results will give an indication of the general biodegradability of the compounds.
All compounds studied were shown to have a Henry's law constant < 10^{-5} atm m^3/mol indicating that the substances have a low potential for volatilisation. Thus, the OECD 309 test was applicable with regard to the physicochemical properties of the selected substances in the project.

According to OECD 309, a reference substance, which is normally easily degraded under aerobic conditions, e.g. aniline, has to be tested with regard to biodegradation. The expected time interval for degradation of aniline is usually less than two weeks. By following the degradation of aniline in course of time, it can be determined whether the microbial activity of the test water is within certain limits, i.e. that the water contains an active microbial population. The activity of the microbial population in the present study was also monitored by second test determining the adenosine triphosphate (ATP) content in the surface water. ATP is an organic compound that provides energy to drive many processes in living cells. The presence of this compound in water is an indicator for the presence of microbiological activity. Besides the measurement of the activity of the microbial population, ATP determination was used to check the possible toxicity of the selected test compounds for the microorganisms present in the surface water.

As the chemical analysis were all carried out in drinking water laboratories applying certified methods for the analysis of the selected test compounds, repeatability of the analytical method wasn't checked separately, but external standards were used to follow the analytical performance during analysis. The external standards were exactly the same compounds as the ones that were tested. Furthermore, labelled internal standards are used to correct the analytical results for e.g. matrix effects. These internal standards exhibit similar behaviour to the test compounds. Performance characteristics of the methods applied are shown in Table 4 in section 3.5.

3 Experimental methods

3.1 Water sample collection

Raw water samples were taken from the site “Schalterberg”, in the Netherlands on August 7th 2020. Aerial photos of the site are shown in Figure 1. The water here originates from sub-surface springs. Water from this site is used as a source by the drinking water company Vitens, and frequently analysed for anthropogenic compounds. There is no discharge of industrial or municipal WWTP effluent upstream of the sampling point. The water was taken at a depth of 0.5 m below the water surface. After sampling the water was kept cooled at 13 °C in the darkness until August 13th 2020, when the experiments started.

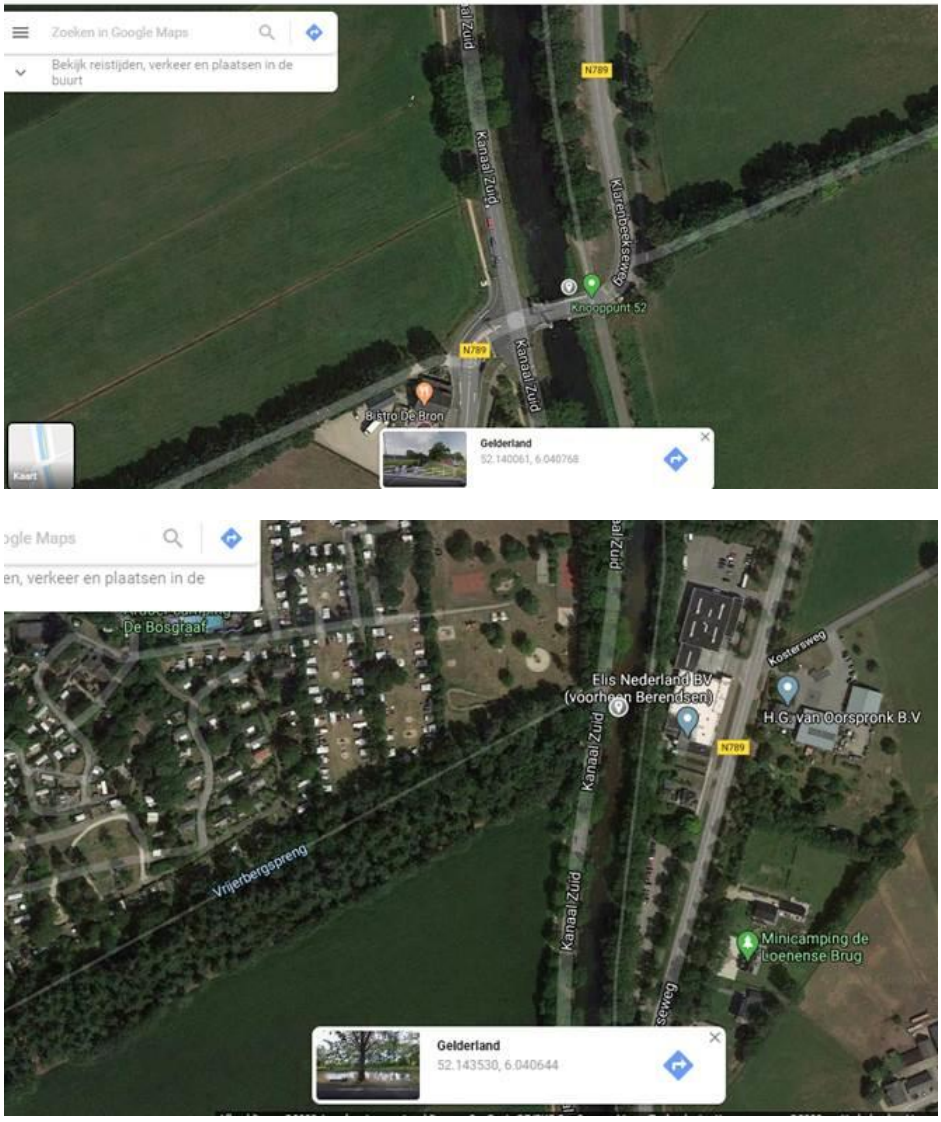


Figure 1: Sample location “Schalterberg” the Netherlands. Samples were taken at the site indicated by the grey indicator in the upper photograph. The Vitens laboratory intake is located at the grey indicator in the lower photograph, a little north of the sample location.

After sampling of the water on August 7th 2020, the water of the location "Schalterberg" was analyzed with regard to water relevant physical parameters as well as the occurrence of the selected compounds (Table 2). It was shown, that none of the selected compounds studied in this project appeared to be present in the raw water samples.

Table 2: Analysis of source water "Schalterberg" performed at August 7th 2020 (analyses carried out by Vitens laboratory). RL = reporting limit

parameter	**unit**	**value**
color	mg Pt/Co/l	5.3
Suspended substances. using a glass fiber filter	mg/l	1
phosphate-Total and phosphor	mg P/l	0.0062
phosphate-Total and phosphor	mg PO_4 / l	0.0189
Ammonium after in situ filtration (0.45 µm)	mg NH_4 / l	0.0354
Nitrite after in situ filtration (0.45 µm)	mg NO_2 / l	0.0054
Oxidative potential Redox (ORP)	mv	209
TOC	mg/l	1.353
DOC	mg/l	1.292
Biological oxygen demand (BOD)	mg O_2/l	1.46
Nitrogen Kjeldahl	mg N/l	0.3082
aniline	µg/l	< RL
gabapentin	µg/l	< RL
1H-benzotriazole	µg/l	< RL
diglyme	µg/l	< RL
DTPA	µg/l	< RL
1.4-dioxane	µg/l	< RL

3.2 General data

The following physical parameters in the water were measured during the test period:

- Electric conductivity (EC)
- pH
- temperature (T)
- nitrate concentration (NO_3-N)
- turbidity
- Oxygen

Furthermore, by measuring the mass of closed bottles the mass balance was determined. Thus it was determined that no leakage or evaporation from the bottles had occurred.

3.3 Biodegradation potential of the water

In order to determine whether or not active microorganisms were present in the sampled water, two types of tests were carried out: Degradation of reference substance aniline (CAS 62-53-3) and ATP-measurements.
For this, aniline was added to the water at a concentration of 1 µg/L (Table 3) and degradation was evaluated based on the concentration of reference substance detected in the water phase using GC-MS (Table 4). In theory, if active microorganism are present in the water, they should be able to degrade aniline within a few weeks. The aniline concentration was determined on day 0, 7, 15, 30, 45 and 60.

The concentration of ATP (adenosine triphosphate) is a measure for the activity of microorganisms. The determination method is based on the reaction of luciferin with luciferase (from fireflies) in the presence of free ATP. The amount of light produced is measured by means of a photometer reflects the concentration of free ATP. Theoretically, one photon is produced for each molecule of ATP (KWR Huisvoorschrift LMB-002). ATP was determined directly after sampling (day -6), and at day 0 before and after autoclaving. To investigate the influence of the selected compounds on the microbial activity, each of the test compounds was added separately to a water samples and concentration of ATP was monitored after 2 days of incubation. As reference, aniline was added to the water and ATP measurements were carried out accordingly.

All measurements were carried out twice. In this measurements the total ATP content, i.e. free ATP as well as ATP within cells, was measured.

3.4 Test systems and application of test compounds

Duplicate samples were prepared in 1L green bottles with Teflon lining. Each bottle contained 300 mg of water and air. Total mass of a bottle was about 695 g (Figure 2).

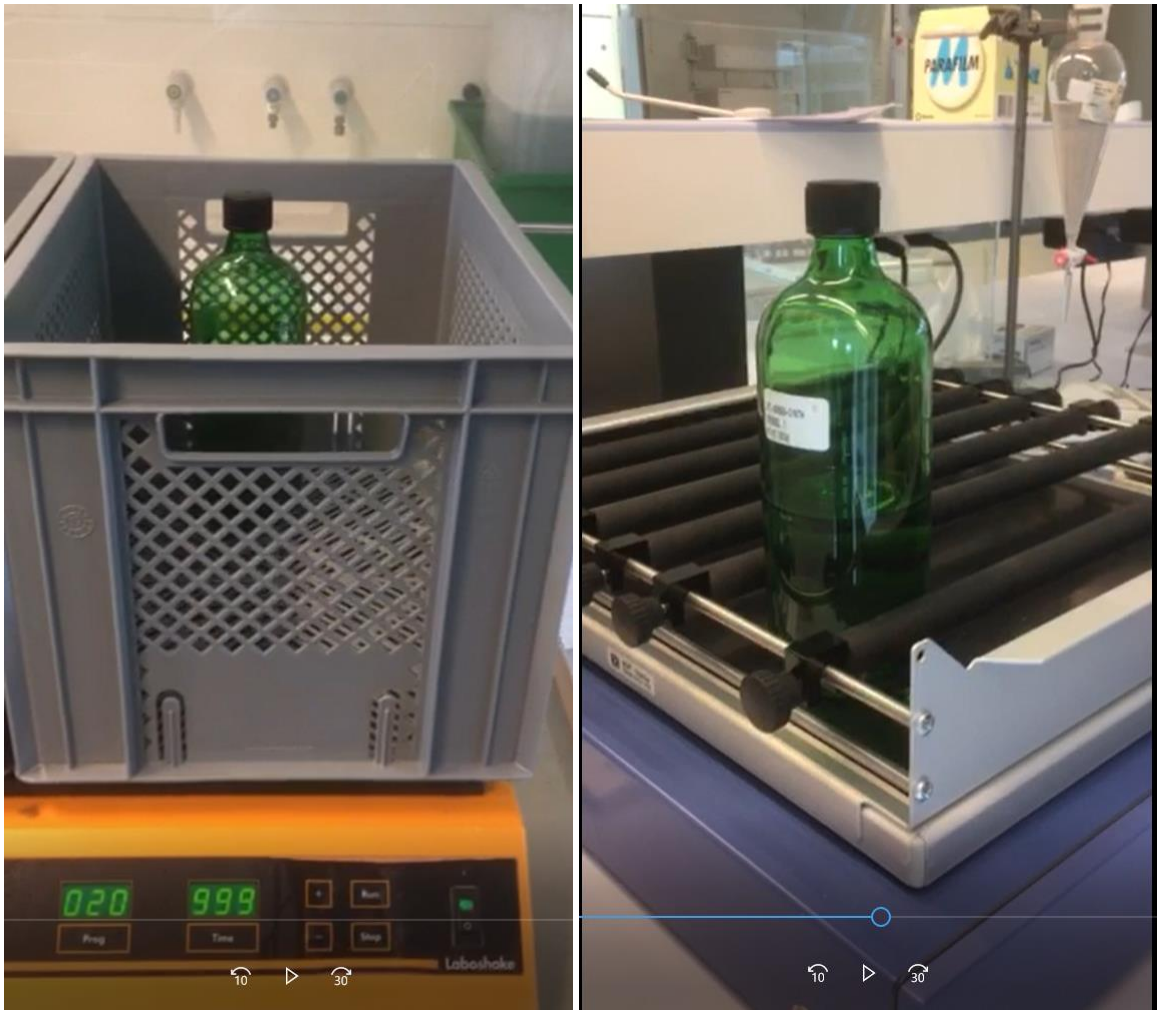


Figure 2: Experimental set-up. Two types of shaking devices have been used, but each series of compounds was placed on the same apparatus

For application of the selected test compounds to the water, stock solutions were prepared using milli-Q water (Table 3). No organic solvents have been used to prepare the solutions. All concentrations were aimed at a value 100 times higher than the reported limit of detection (LOD). Dosed concentration was 1 µg/l for reference substance aniline and ranged from 1-100 µg/l for the selected compounds.
After application of the selected test compounds, the bottles were sealed airtight. For the determination of the mass balance, separate vessels containing the selected compounds were used, which was solely analyzed at the end of the study (day 60). Besides samples containing the selected compounds, two samples were used for the analysis of physical parameters. All bottles were continuously gently homogenized (20 rpm) by means of a horizontal shaking device at a temperature of 13 ± 1 ^{o}C in darkness.

Table 3: Details on purity, stock solutions and dosed concentrations of the selected compounds. All stock solutions were prepared in Milli-Q water, no organic solvents were applied

Compound	**producer**	**Lot**	**Purity (%)**	**Shelf life**	**Amount dissolved in 1 L (mg)**	**Concentration stock solution (mg/L)**	**Limit of detection (LOD) (µg/L)**	**Dosed concentration (µg/L)**
melamine	Sigma-Aldrich	BCCC5859	99.8	Nov-22	5.208	5.2	0.05	5
urotropin	Merck	S7641512	99.2	Jul-21	5.430	5.4	0.05	5
1H-benzotriazole	TRC	4-LWJ-35-1	100.0	Nov-23	5.466	5.5	0.01	1
DTPA	Sigma-Aldrich	SLBZ4746	100.0	Apr-23	10.213	10	1.0	100
diglyme	Sigma-Aldrich	BCCB5888	99.9	Apr-22	49.257	49	0.2	20
gabapentin	TRC	2-YFD-160-1	98.0	Aug-23	5.157	5.1	0.01	1
1,4-dioxane	Sigma-Aldrich	STBH5264	100.0	Apr-23	96.300	96	1.0	100
aniline	Sigma-Aldrich	BCCB9893	99.9	Jun-21	5.187	5.2	0.01	1

3.5 Chemical Analyses

After incubation, samples with test compounds were kept cold (of 2-8 ^{o}C in the dark) until analysis. Aliquotes of 40 ml in triplicates without bubbles were sent to the Vitens laboratory for chemical analysis of gabapentin, 1,4-dioxane, 1H-benzotriazole, DTPA, diglyme and aniline within 24 hours. Chemical analysis of melamine and urotropin were done at KWR. The samples without test compounds were used to measure physical parameters at the KWR laboratory. Both laboratories have been approved as official laboratories for drinking water (see Appendix I). Analytical methods applied for the chemical analysis of the selected compounds depends on the compound as shown in Table 4. Methods used were GC-MS, LC-MS and LC-MS/MS.

Solutions were spiked using a stock solution with a known concentration of compounds (Table 3). Although the amounts of compounds for the stock solution were weighted very accurately, dilution (first dissolution in a certain volume of water for the stock solution, and subsequently spiking of the actual samples) may affect the actual sample concentration at t=0. Therefore, calculation of the recovery based on the weighted amount of material is not very accurate. It is more accurate to measure the actual concentrations in samples at t=0, and use these data as starting concentrations. However, if the concentrations measured are found to be significantly lower than the concentrations aimed at, this may be an indication that not all material was present in the solution, e.g. as a result of adsorption to the vessel wall. This wasn't observed with the compounds in this study, all concentrations measured were well within the experimental uncertainty of the dilutions.
It was decided to apply only target analysis, looking at the parent compounds and not at possibly formed transformation products. This choice was based on the following arguments:

- From literature it was expected that the test compounds in this study would be hard to degrade by micro-organisms, so concentrations of transformation products would be very low and difficult to measure.
- For some compounds certain metabolites are known to be formed in the environment, but it's not clear which transformation products may be formed by micro-organisms in surface water. As a result qualitative determination would have been very complicated at the low concentrations expected, and quantitative measurements would not have been possible.
- Non-target analysis is much more expensive than target analysis.

In this way we obtained a simple and relatively cheap method to determine how persistent compounds are in the aquatic environment.

3.6 Data analysis

Degradation kinetics for the selected compounds were modelled using the software Computer Assisted Kinetic Evaluation (CAKE, Tessella, Version 3.1). The software CAKE applies the following kinetics to calculate half-lives: SFO (Single first-order), DFOP (Double first-order in parallel), HS (Hockey-Stick) and FOMC (First-order multi-compartment). For calculation of the half-life (DT50), portions of the selected compounds in water were used. It was assumed that the remaining portions of the selected compounds, which could not be analytical monitored in case of the unlabeled test items (mineralized, volatile portions), did not contain the parent substances.

Table 4: Analytical methods applied for the selected compounds.

Compound	**Method**	**Description of method**	**Reporting Limit (µg/L)**	**Relative standard deviation (%)**	**Limit of quantification (µg/L)**	**Reproducibility** (%)	**Recovery** (%)	**Experimental uncertainty** (%)
melamine	Specials HILIC	LC-MS/MS	0.05	15	0.002	nd	107.0	14.7
urotropin	Specials HILIC	LC-MS/MS	0.05	1.6	0.005	nd	106.0	1.8
1H-benzotriazole	VL-W0OC37	LC-MS/MS	0.01	7.45	0.004	22.96	108.6	15.04
DTPA	VL-W-ME19	ICP-MS	1.0	14.77	0.69	35.21	82.1	44.41
diglyme	VL-W-OC37	LC-MS/MS	0.2	13.95	0.2112	42.99	88.8	33.28
Gabapentin*)	VL-W-OC37	LC-MS/MS	0.01	78.5	0.0674	256	111.5	557.93
1,4-dioxane	VL-W-OC07	GC-MS after online purge and trap	1.0	11.7	0.4845	33.89	89.4	23.49
aniline	VL-W-OC33	GC-MSMS after liquid/liquid extraction	0.01	5.95	0.0144	18.75	83.0	12.06

*) In 2017 the experimental uncertainty for Gabapentin analyses appeared to be 557%, which was caused by the instability of gabapentin during the analysis (it was converted into Gabapentin-lactam). However, the experimental uncertainty was based on a limited amount of data. In 2019 and 2020 more data were obtained, indicating that the experimental error in the analysis would be about 100%. However, the variation in results obtained seems to be significantly smaller.

4 Results

4.1 Physical parameters

During the testing period several physical parameters were determined (Table 5, extended data are shown in Table 11 in Appendix II).

Table 5: General parameters of the surface water measured during testing period.

parameter	unit	Average value
EC	µS/cm	*155*
pH		*7.3*
Temperature (T)	^{o}C	*13.2*
Mass balance	g	*0.0*
Nitrate concentration (NO_3-N)	mg N /L	*0.57*
Turbidity	FNE	*0.86*
Oxygen	mg O_2 /L	*7.5*

These data indicate that in general the water quality remains relatively constant throughout the whole test period. The temperature of one of the unspiked samples at day 0 and at day 30 samples seems to be a little higher than had been intended (14.3 ^{o}C), but it is not clear what may have caused the deviation.

EC, pH and turbidity on day 7 showed higher values than on the other sampling days, where these parameters seem to be constant. For nitrate (NO_3-N) a little higher concentration is observed at day 7, 30 and 60, but there is a relatively large difference between both duplicate samples measurements, indicating that it also may be related to the accuracy of the analysis. The oxygen concentration seems to have decreased a little over time, which can be explained from the activity of the microorganisms present in the water.

4.2 Microbial activity

4.2.1 Aniline measurements

Aniline was added as a very well biodegradable reference compound, to check whether there is sufficient microbial activity present in the water. The results are shown in Figure 3 in Table 12 (Appendix III).

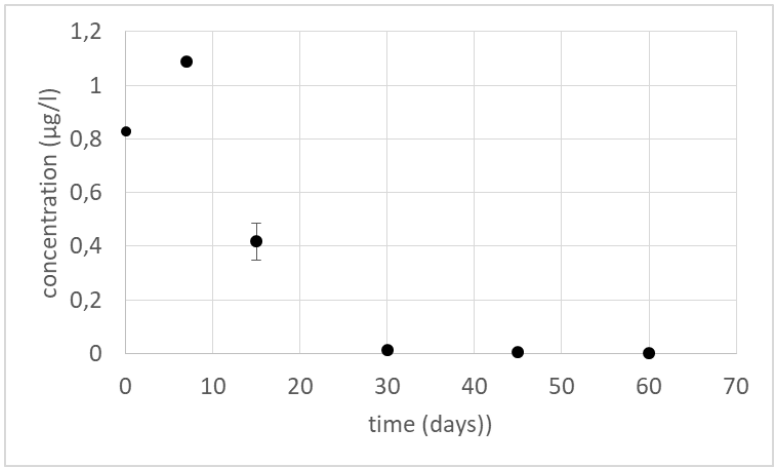


Figure 3: concentrations of aniline after 0, 7, 15, 30, 45 and 60 days of incubation

Concentrations of aniline decline in course of time. After 15 days of incubation, concentration was 0.418±0.07 µg/L. At the end of the study (day 60), no aniline could be analytically detected in the surface water. Degradation of aniline based on the concentration observed amounted 52% and >98% after 15 and 30 days of incubation. This indicates that there is sufficient microbial activity present in the water for biodegradation.

4.2.2 ATP measurements

ATP content was determined to check if 1) the surface water contained an active microbial population and 2) if the selected substances were toxic for the microorganisms in surface water. Results of ATP measurements are shown Figure 4 and in Table 13 (Appendix III).

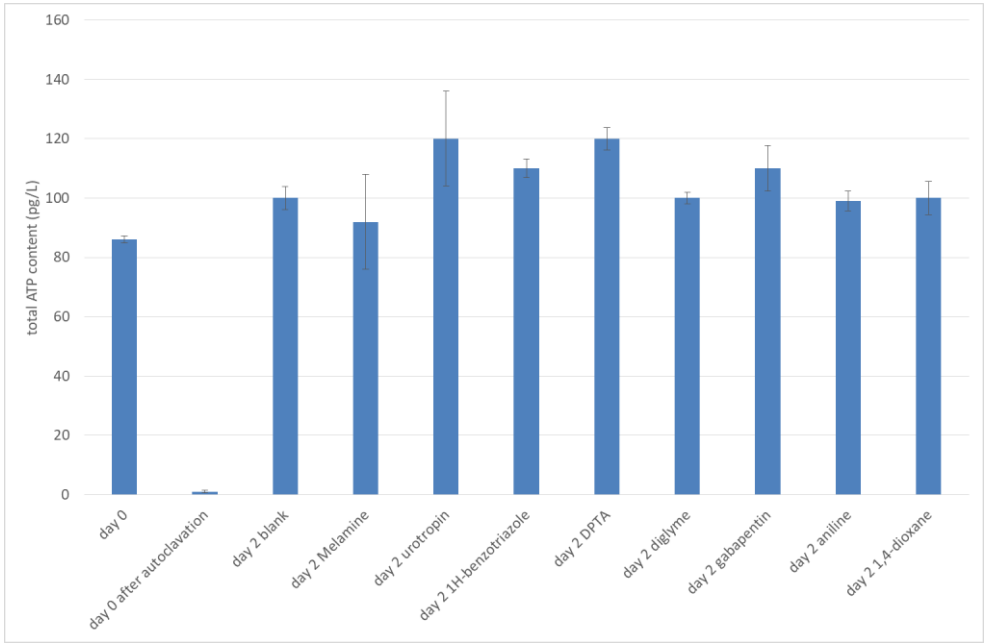


Figure 4: total ATP content at day 0 (before and after autoclavation), and at day 2, with and without addition of test compounds

The amount of ATP in the water decreased immediately after sampling (day -6, surface water) during the storage (day 0, unspiked surface water). However, on day 0 a significant concentration of ATP could be observed, indicating that active microorganisms still were present in the water. The amount of ATP in the surface water without the addition of selected compounds at day 0 was 86 ± 1.2 pg/mL. After autoclaving ATP concentration was obviously reduced (day 0, unspiked surface water after autoclavation, <1 ± 0.44 pg/mL), indicating that the ATP assay is able to reflect the microbial activity of the surface water. In the presence of the selected compounds, ATP concentration after 2 days of incubation was equal or higher to those measured in surface water without any addition (day 2, unspiked surface water), indicating that these test compounds weren't toxic to the microorganisms present in the water.

4.2.3 Conclusions on microbial activity

Based on the results on both aniline and ATP measurements it can be concluded that the surface water showed sufficient microbial activity for biodegradation to occur, and that the test compounds weren't toxic to the microorganisms present in the surface water.

4.3 Biodegradation of test compounds

4.3.1 Gabapentin

The concentrations of gabapentin measured during the test period are shown in Table 14 (Appendix III).
Recovery of the gabapentin concentration applied to this test at day 0 was 112 % and ranged between 107-122% during the study. According to OECD 309, the initial recovery should be between 70% and 110% for non-labelled substances. Nevertheless, the study is regarded as valid, taking into account that the applied concentration of the compound was determined nominally which may cause the deviation of the recovery range (section 3.5.). Gabapentin concentrations during the test period were related to the concentration analytically measured directly after addition of the gabapentin to the solution at day 0.

The gabapentin concentration remained stable in course of time, ranging between a minimum value of 1.07±0.01 µg/L at day 7 and a maximum value of 1.22±0.01 µg/L at day 60 (Figure 3). This indicates that gabapentin was not primarily degraded in surface water. As unlabelled Gabapentin was used in this study, ultimate degradation of the substance could not be determined.

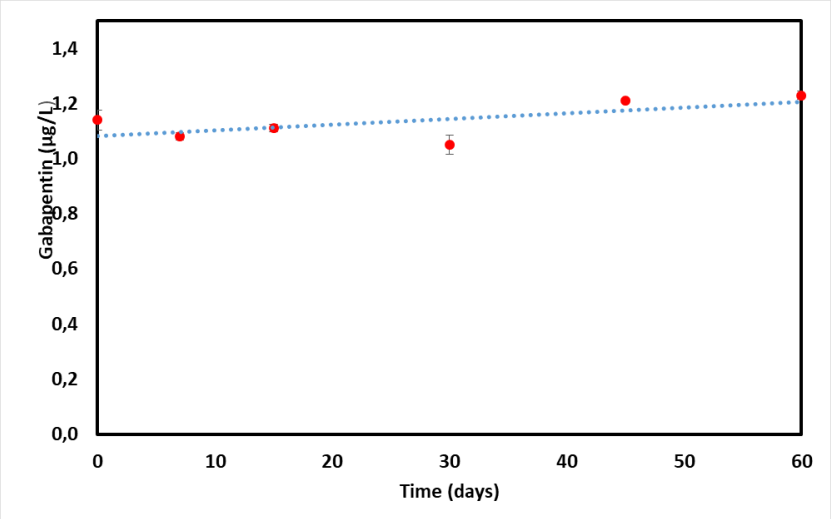


Figure 5: degradation of gabapentin during testing period displayed by the concentration (µg/L) of the compound in the test system.

Half-lives (DT_{50}) for gabapentin were calculated using the SFO (Single first-order), DFOP (Double first-order in parallel), HS (Hockey-Stick) and FOMC (First-order multi-compartment) kinetic models (Table 6). The determination of half-life of Gabapentin was calculated based on the amount of Gabapentin detected in the water phase at day 0, 7, 15, 30, 45 and 60.
According to the visual fit and obtained error, the SFO model was regarded appropriate to follow gabapentin degradation in surface water. DT_{50} (SFO) of gabapentin in surface water amounted >10,000 days.

Table 6: Kinetic calculations of half-lives (DT50) of gabapentin based on the amount of parent compound detected in the water phase.

	DT_{50} (days)	Chi2 Error	Visual fit
SFO	>10,000	4.2 %	medium
DFOP	k1 = 4.7; k2 = >10,000	5.3 %	medium
HS	k1 = >10,000; k2 = >10,000	5.3 %	medium
FOMC	>10,000	4.6 %	medium

In literature it was found that Gabapentin can show complex behavior. Transformation products, like Gabapentin-lactam, can be formed, but also show back-transformation to the parent compound (Li and McLachlan 2019).

4.3.2 1H-benzotriazole

The concentrations of 1H-benzotriazole measured during the test period are shown in Table 15 (Appendix III). Recovery of the 1H-benzotriazole concentration applied to test at day 0 was 108.6 % and ranged between 104.9-120.0%. According to OECD 309, the initial recovery should be between 70% and 110% for non-labelled substances. Thus, the study is regarded as valid.

The 1H-benzotriazole concentration remains constant in course of time and ranged between a minimum value of 1.05±0.01 µg/L at day 7 and a maximum value of 1.09±0.02 µg/L at day 45 (Figure 6). This indicates that 1H-benzotriazole was not primarily degraded in surface water. As unlabelled 1H-benzotriazole was used in this study, ultimate degradation of the substance could not be determined.

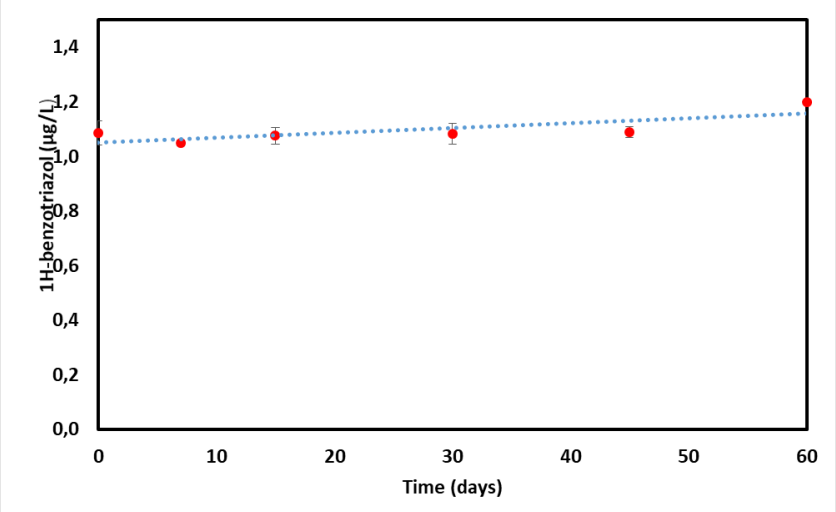


Figure 6: degradation of 1H-benzotriazole during testing period displayed by the concentration (µg/L) of the compound in the test system.

Half-lives for 1H-benzotriazole were calculated using the SFO (Single first-order), DFOP (Double first-order in parallel), HS (Hockey-Stick) and FOMC (First-order multi-compartment) kinetic models (Table 11). The determination of half-life of 1H-benzotriazole was calculated based on the amount of 1H-benzotriazole detected in the water phase at day 0, 7, 15, 30, 45 and 60.
According to the visual fit and obtained error, the SFO model was regarded appropriate to follow 1H-benzotriazole degradation in surface water. DT_{50} (SFO) of 1H-Benzotriazole in surface water amounted >10.000 days.

Table 7: Kinetic calculations of half-lives (DT_{50}) of 1H-Benzotriazol based on the amount of parent compound detected in the water phase.

	DT_{50} (days)	Chi2 Error	Visual fit
SFO	>10,000	3.4%	medium
DFOP	k1=5.6; k2=>10,000	4.3%	medium
HS	k1=>10,000; k2=>10,000	4.3%	medium
FOMC	>10,000	3.8%	medium

4.3.3 Diglyme

The concentrations of diglyme measured during the test period are shown in Table 16 (Appendix III).
Recovery of the diglyme concentration applied to test at day 0 was 88.8% and ranged between 88.5-94.8%. According to OECD 309, the initial recovery should be between 70% and 110% for non-labelled substances. Thus, the study is regarded as valid.

The diglyme concentration remained constant in course of time and ranged between a minimum value of 17.70±0.57 µg/L at day 7 and a maximum value of 18.95±0.35 µg/L at day 30 (Figure 7). This indicates that diglyme was not primarily degraded in surface water. As unlabelled diglyme was used in this study, ultimate degradation of the substance could not be determined.

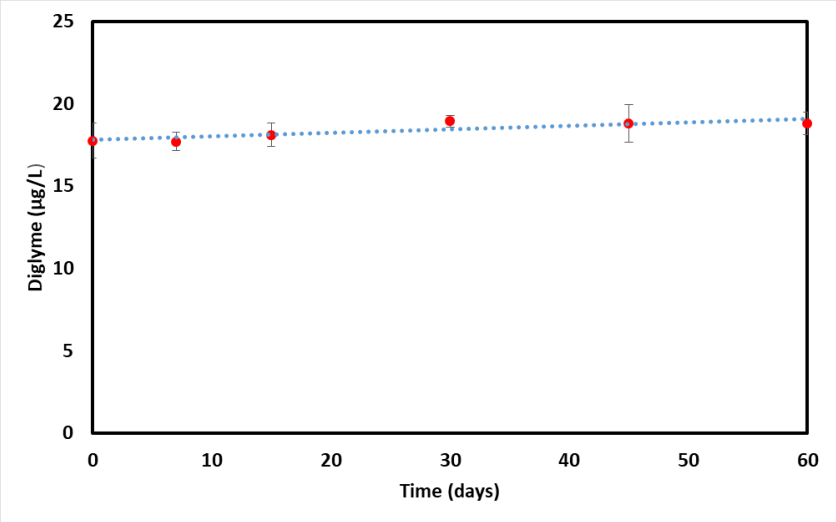


Figure 7: degradation of diglyme during testing period displayed by the concentration (µg/L) of the compound in the test system.

Half-lives (DT_{50}) for diglyme were calculated using the SFO (Single first-order), DFOP (Double first-order in parallel), HS (Hockey-Stick) and FOMC (First-order multi-compartment) kinetic models (Table 13). The determination of half-life of diglyme was calculated based on the amount of diglyme detected in the water phase at day 0, 7, 15, 30, 45 and 60.

According to the visual fit and obtained error, the SFO model was regarded appropriate to follow diglyme degradation in surface water. DT_{50} (SFO) of diglyme in surface water amounted >10.000 days.

Table 13: Kinetic calculations of half-lives (DT_{50}) of diglyme based on the amount of parent compound detected in the water phase.

	DT_{50} (days)	Chi2 Error	Visual fit
SFO	>10,000	2%	good
DFOP	k1=13.1; k2=>10,000	3%	good
HS	k1=>10.000; k2=>10,000	3%	good
FOMC	>10,000	2%	good

4.3.4 DTPA

The concentrations of DTPA measured during the test period are shown in Table 17 (Appendix III).
Recovery of the diglyme concentration applied to test at day 0 was 88.8% and ranged between 88.5-94.8%. According to OECD 309, the initial recovery should be between 70% and 110% for non-labelled substances. Thus, the study is regarded as valid.

The DTPA concentration seemed to increase until day 15 (105.6±3.7 µg/L) and then to decrease to 70.70±0.57 µg/L at day 60 (Figure 8). This indicates that DTPA was probably primarily or ultimately degraded in surface water. As unlabelled DTPA was used in this study and only the parent compound was analytically determined, primary and ultimate degradation of the substance could not be investigated.

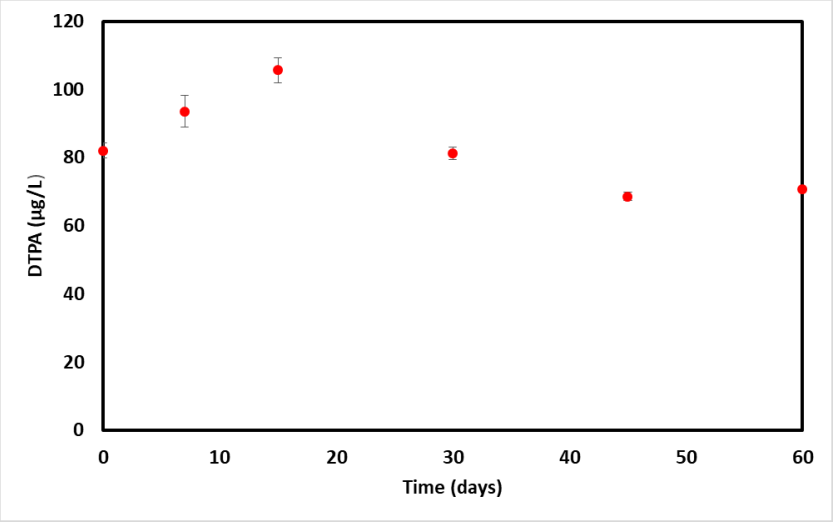


Figure 8: degradation of DTPA during testing period displayed by the concentration (µg/L) of the compound in the test system.

Half-lives (DT_{50}) for DTPA were calculated using the SFO (Single first-order), DFOP (Double first-order in parallel), HS (Hockey-Stick) and FOMC (First-order multi-compartment) kinetic models (Table 15). The determination of half-life of DTPA was calculated based on the amount of Diglyme detected in the water phase at day 15, 30, 45 and 60 as the concentration declined from day 15 onwards.
The DFOP and HS model were not applicable because no error could be obtained. According to the visual fit and obtained error, the SFO model was regarded appropriate to follow DTPA degradation in surface water.DT_{50} (SFO) of DTPA in surface water amounted 67.6 days.

Table 8: Kinetic calculations of half-lives (DT_{50}) of DTPA based on the amount of parent compound detected in the water phase.

	DT_{50} (days)	Chi2 Error	Visual fit
SFO	67.6	5.8%	good
DFOP	not applicable		
HS	not applicable		
FOMC	0.06	10.5%	bad

4.3.5 1,4-dioxane

The concentrations of 1,4-dioxane measured during the test period are shown in Table 18 (Appendix III). Recovery of the 1,4-dioxane concentration applied to test ranged at day 0 was 89.4% between 71.1-93.3%. According to OECD 309, the initial recovery should be between 70% and 110% for non-labelled substances. Thus, the study is regarded as valid.

The 1,4-dioxane concentration remained stable in course of time and ranged between a minimum value of 71.1±5.5 µg/L at day 15 and a maximum value of 93.3±0.4 µg/L at day 30 (Figure 9). At the end of the study (day 60), 85.8±3.2 µg/L 1,4-dioxane could be detected in the surface water. This indicates that 1,4-dioxane was not primarily degraded in surface water. As unlabelled 1,4-dioxane was used in this study, ultimate degradation of the substance could not be determined.

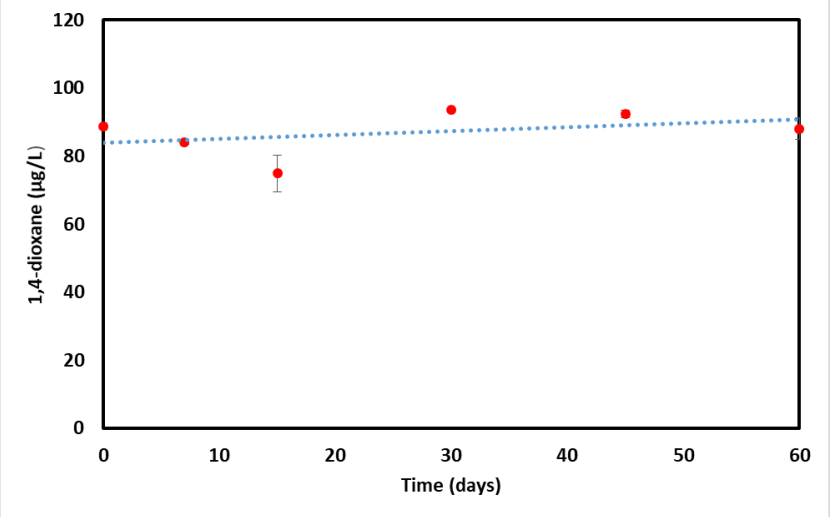


Figure 9: degradation of 1,4-dioxane during testing period displayed by the concentration (µg/L) of the compound in the test system.

Half-lives (DT_{50}) for 1,4-dioxane were calculated using the SFO (Single first-order), DFOP (Double first-order in parallel), HS (Hockey-Stick) and FOMC (First-order multi-compartment) kinetic models (Table 17). The determination of half-life of 1,4-dioxane was calculated based on the amount of 1,4-dioxane detected in the water phase at day 0, 7, 15, 30, 45 and 60.

The FOMC model was not applicable because no error could be obtained. According to the visual fit and obtained error, the SFO model was regarded appropriate to follow 1,4-dioxane degradation in surface water. DT_{50} (SFO) of 1,4-dioxane in surface water amounted >10.000 days.

Table 17: Kinetic calculations of half-lives (DT_{50}) of 1,4-dioxane based on the amount of parent detected in the water phase.

	DT_{50} (days)	Chi2 Error	Visual fit
SFO	>10,000	7%	good
DFOP	k1=0.584; k2=>10,000	9%	medium
HS	k1=86.1; k2=>10,000	9%	medium
FOMC	not applicable		

4.3.6 Melamine

The concentrations of melamine measured during the test period are shown in Table 19 (Appendix III).
Recovery of the melamine concentration applied to test at day 0 was 107.0% and ranged between 100.0-107.0%. According to OECD 309, the initial recovery should be between 70% and 110% for non-labelled substances. Thus, the study is regarded as valid.

Melamine concentration remains stable in course of time and ranged between a minimum value of 5.0±0.0 µg/L at day 45 and a maximum value of 5.35±0.07 µg/L at day 15. This indicates that Melamine was not primarily degraded in surface water. As unlabelled Melamine was used in this study, ultimate degradation of the substance could not be determined.

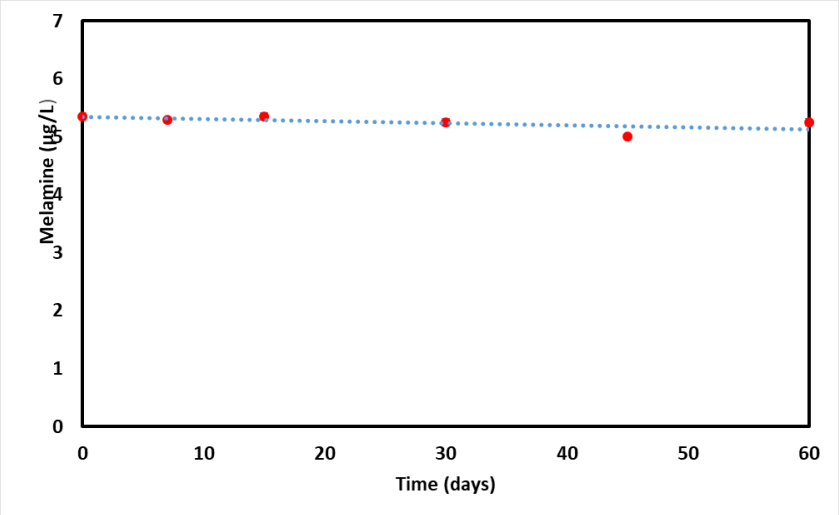


Figure 10: degradation of Melamine during testing period displayed by the concentration (µg/L) of the compound in the test system.

Half-lives (DT_{50}) for melamine were calculated using the SFO (Single first-order), DFOP (Double first-order in parallel), HS (Hockey-Stick) and FOMC (First-order multi-compartment) kinetic models (Table 9). The determination of half-life of melamine was calculated based on the amount Melamine detected in the water phase at day 0, 7, 15, 30, 45 and 60.

According to the visual fit and obtained error, the SFO model was regarded appropriate to follow melamine degradation in surface water. DT_{50} (SFO) of melamine in surface water amounted >10.000 days.

Table 9: Kinetic calculations of half-lives (DT_{50}) of melamine based on the amount of parent detected in the water phase.

	DT_{50} (days)	Chi2 Error	Visual fit
SFO	1.03E+03	1%	good
DFOP	k1=24.3; k2=>10,000	2%	good
HS	k1=874; k2=>10,000	2%	Good
FOMC	>10,000	2%	Good

4.3.7 Urotropin

The concentrations of urotropin measured during the test period are shown in Table 20.
Recovery of the urotropin concentration applied to test at day 0 was 106.0% and ranged between 80.0-108.0%. According to OECD 309, the initial recovery should be between 70% and 110% for non-labelled substances. Thus, the study is regarded as valid.

Urotropin concentration slightly decrease in course of time and ranged between a minimum value of 4.0±0.14 µg/L at day 60 and a maximum value of 5.40±0.0 µg/L at day 7. This indicates that urotropin probably primary or ultimately degraded in surface water. As unlabelled urotropin was used in this study and only the parent compound was analytically determined, primary and ultimate degradation of the substance could not be determined.

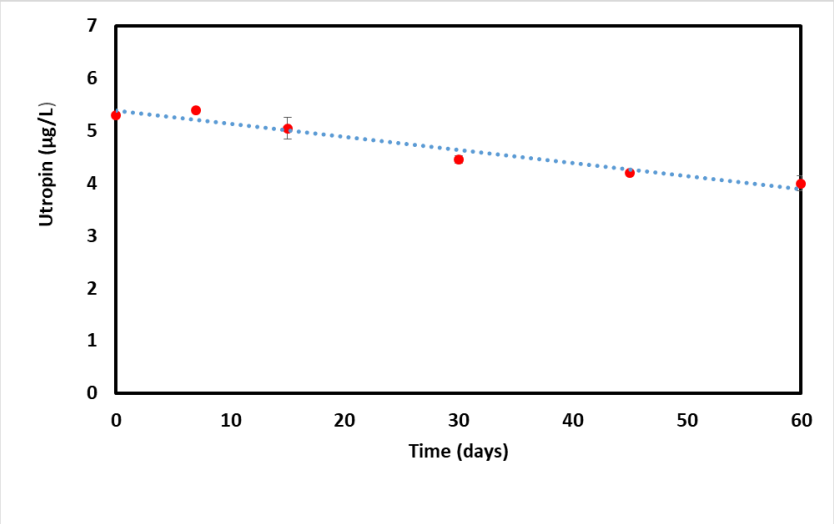


Figure 11: degradation of urotropin during testing period displayed by the concentration (µg/L) of the compound in the test system.

Half-lives for urotropin were calculated using the SFO (Single first-order), DFOP (Double first-order in parallel), HS (Hockey-Stick) and FOMC (First-order multi-compartment) kinetic models (Table 21). The determination of half-life of urotropin was calculated based on the amount urotropin detected in the water phase at day 0, 7, 15, 30, 45 and 60.
According to the visual fit and obtained error, the SFO model was regarded appropriate to follow urotropin degradation in surface water. DT_{50} (SFO) of urotropin in surface water amounted 128 days.

Table 10: Kinetic calculations of half-lives (DT_{50}) of urotropin based on the amount of parent detected in the water phase.

	DT_{50} (days)	Chi2 Error	Visual fit
SFO	128	2%	good
DFOP	k1=64; k2=>10,000	2%	good
HS	k1=113; k2=217	2%	good
FOMC	150	2%	good

4.3.8 Conclusion on biodegradation of the test compounds

All selected test compounds showed no (gabapentin, 1H-benzotriazole, diglyme, 1,4-dioxane and melamine) or only slow (DTPA, urotropin) decrease in test compound concentration analytically determined. Therefore, abiotic and biotic degradation of the all selected test compounds is evaluated to be slow or negligible in surface water. Calculated half-lives were as follows: gabapentin >10.000 days; 1H-benzotriazole: >10.000 days; diglyme: >10.000 days; DTPA: 67.6 days; 1,4-dioxane: >10.000 days; melamine: >10.000 days; urotropin: 128 days.

5 Conclusions and recommendations

The water sample taken at location “Schalterberg” didn’t contain any of the selected test compounds. Based on the results on both aniline and ATP measurements it can be concluded that the surface water showed sufficient microbial activity for biodegradation and that the test compounds weren’t toxic to the microorganisms present in the surface water.

All selected test compounds showed no (gabapentin, 1H-benzotriazole, diglyme, 1,4-dioxane and melamine) or only slow (DTPA, urotropin) decrease in test compound concentration analytically determined. Therefore, abiotic and biotic degradation of the all selected test compounds is evaluated to be slow or negligible in surface water. Calculated half-lives were as follows: gabapentin >10.000 days; 1H-benzotriazole: >10.000 days; diglyme: >10.000 days; DTPA: 67.6 days; 1,4-dioxane: >10.000 days; melamine: >10.000 days; urotropin: 128 days.

According to the REACH legislation, a compound is considered persistent (P) if half-lives (DT_{50}) are larger than 40 days, and it is deemed to be very persistent (vP) if the DT_{50} in surface water exceed 60 days. Comparing the obtained half-lives for the selected compounds in this study with vP/P-criteria, gabapentin, 1H-benzotriazole, diglyme, DTPA, 1,4-dioxane, melamine and urotropin seems to be very persistent in surface water.

As it already had been expected that the test compounds in this study would be rather persistent, only target analysis of the parent compounds was carried out. However, for compounds which are expected to be better biodegradable, it is strongly recommended to analytically determine possibly formed transformation products. The method described in this report provides a practical and relatively cheap alternative to simulation degradation tests performed with ^{14}C labelled substances to determine the persistence of contaminants with low expected degradation potential in surface water.

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I Accreditation of analytical methods

Annex to declaration of accreditation (scope of accreditation)
Normative document: EN ISO/IEC 17025:2017
Registration number: **L 043**

of **Vitens N.V.**
Vitens Laboratorium

This annex is valid from: **06-05-2020** to **01-06-2021** Replaces annex dated: **05-06-2019**

Annex to declaration of accreditation (scope of accreditation)
Normative document: EN ISO/IEC 17025:2017
Registration number: **L 479**

of **KWR Water B.V.**

This annex is valid from: **20-08-2020** to **01-09-2024** Replaces annex dated: **20-02-2019**

II Physical parameters

Table 11: detailed overview of physical parameters measured

parameter	unit	day	value
EC	µS/cm	0, without addition of OMP	*150*
			150
		0, with addition of OMP	*150*
			150
		7	*170*
			180
		15	*155*
			155
		30	*155*
			155
		45	*150*
			150
		60	*150*
			150
pH		0, without addition of OMP	*7.1*
			7.0
		0, with addition of OMP	*7.1*
			7.1
		7	*8.0*
			8.0
		15	*7.1*
			7.1
		30	*7.4*
			7.4
		45	*7.4*
			7.3
		60	*7.2*
			7.3
Temperature (T)	^{o}C	0, without addition of OMP	*13.7*
			14.4
		0, with addition of OMP	*13.2*
			12.4

		7	*13.4*
			13.6
		15	*13.1*
			12
		30	*14.3*
			14.3
		45	*12.9*
			12.9
		60	12.2
			12.2
Mass balance	g	0, without addition of OMP	*0*
			-0.1
		0, with addition of OMP	*-0.1*
			0
		7	*-0.1*
			-0.1
		15	*0.1*
			0.3
		30	*0.1*
			0.1
		45	*0.1*
			0.1
		60	0.1
			0.0
Nitrate concentration (NO_3-N)	mg N /L	0, without addition of OMP	*0.48*
			0.51
		0, with addition of OMP	*0.50*
			0.52
		7	*0.56*
			0.67
		15	*0.54*
			0.52
		30	*0.59*
			0.57
		45	*0.56*
			0.61
		60	*0.76*
			0.6

Turbidity	FNE	0, without addition of OMP	*0.85*
			0.81
		0, with addition of OMP	*0.80*
			0.91
		7	*1.2*
			1.1
		15	*0.77*
			0.78
		30	*0.84*
			0.85
		45	*0.8*
			0.76
		60	*0.79*
			0.72
Oxygen	mg O_2 /L	0, without addition of OMP	*8.3*
			7.7
		0, with addition of OMP	*7.5*
			7.8
		7	*7.2*
			7.5
		15	*7.6*
			7.9
		30	*7*
			7.1
		45	*7.6*
			7.6
		60	*7.2*
			7.1

III Concentration data

In this appendix all measured concentration data are shown.

Table 12: Aniline concentrations (in duplicate samples) (µg/L) after 0, 7, 15, 30, 45 and 60 days of incubation.

Day (after addition of aniline)	Aniline concentrations (µg/L)	
0 (before addition)	< 0.01	< 0.01
0	0.835	0.825
7	1.088	1.087
15	0.488	0.348
30	0.012	0.015
45	0.010	< 0.01
60	< 0.01	< 0.01

Table 13: Concentrations of ATP (pg/mL) and analytical error in the samples at day 0, 6 days before and 2 days after addition of the selected compounds. . Data were shown as mean value of two individual experiments with standard deviation.

Day	Sample description	ATP content (pg/ml)
-6	Surface water	200 ± 15
0	Unspiked surface water	86 ± 1.2
0	Unspiked surface water after autoclavation	< 1 ± 0.44
2	Unspiked surface water	100 ± 3.8
2	Addition of melamine	92 ± 16
2	Addition of urotropin	120±16
2	Addition of 1H-benzotriazole	110 ± 3.1
2	Addition of DTPA	120 ± 3.8
2	Addition of diglyme	100 ± 1.9
2	Addition of gabapentin	110 ± 7.7
2	Addition of aniline	99 ± 3.3
2	Addition of 1,4-dioxane	100 ± 5.6

Table 14: Concentrations of gabapentin (µg/L) in surface water. Duplicate measurements

Day	Concentration (µg/L)	
0	1.14	1.09
7	1.08	1.06
15	1.11	1.09
30	1.05	1.10
45	1.21	1.21
60	1.23	1.21

Table 15: Concentrations of 1H-benzotriazole (µg/L) in surface water. Duplicate measurements

Day	Concentration (µg/L)	
0	1.117	1.054
7	1.057	1.041
15	1.054	1.097
30	1.055	1.109
45	1.103	1.075
60	1.200	1.200

Table 16: Concentration of diglyme (µg/L) in surface water. Duplicate measurements

Day	Concentration (µg/L)	
0	18.5	17.0
7	17.3	18.1
15	17.6	18.6
30	18.7	19.2
45	19.6	18.0
60	18.3	19.3

Table 17: Concentrations of DTPA (µg/L) in surface water. Duplicate measurements

Day	Concentration (µg/L)	
0	80.50	83.60
7	96.82	90.34
15	103.01	108.27
30	79.90	82.55
45	67.76	69.41
60	71.10	70.30

Table 18: Concentrations of 1,4-dioxane (µg/L) in surface water. Duplicate measurements

Day	Concentration (µg/L)	
0	88.67	90.17
7	84.11	85.05
15	74.92	67.20
30	93.57	92.95
45	92.44	93.88
60	88.00	84.00

Table 19: Concentrations of melamine (µg/L) in surface water Duplicate measurements

Day	Concentration (µg/L)	
0	5.3	5.4
7	5.3	5.3
15	5.3	5.4
30	5.3	5.2
45	5.0	5.0
60	5.2	5.3

Table 20: Concentrations of urotropin (µg/L) in surface water. Duplicate measurements

Day	Concentration (µg/L)	
0	5.3	5.3
7	5.4	5.4
15	4.9	5.2
30	4.5	4.4
45	4.2	4.2
60	3.9	4.1

IV Kinetic modelling

Gabapentin

Data set: Experiment 1 (SFO)

Study date: Montag, 7. Dezember 2020
Report generated: Montag, 7. Dezember 2020

Model Setup:

Topology: Parent only
Optimiser: IRLS (IRLS Its. 10, IRLS Tol. 1E-05, Max. Its. 100, Tol. 1E-05)
SANN Max Iterations: 10000
Extra Solver Option: Use If Required

Initial Values of Sequence Parameters:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k_Parent	0.1	0 to (unbounded)	No

Fit step: Final

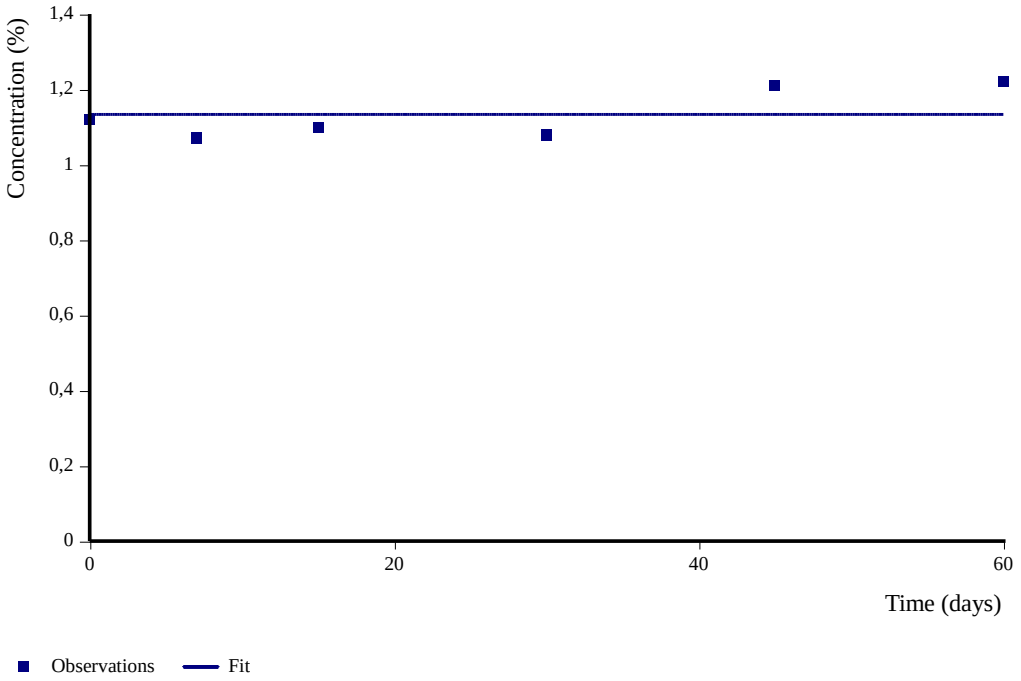
Used Extra Solver: No

Reference Table:

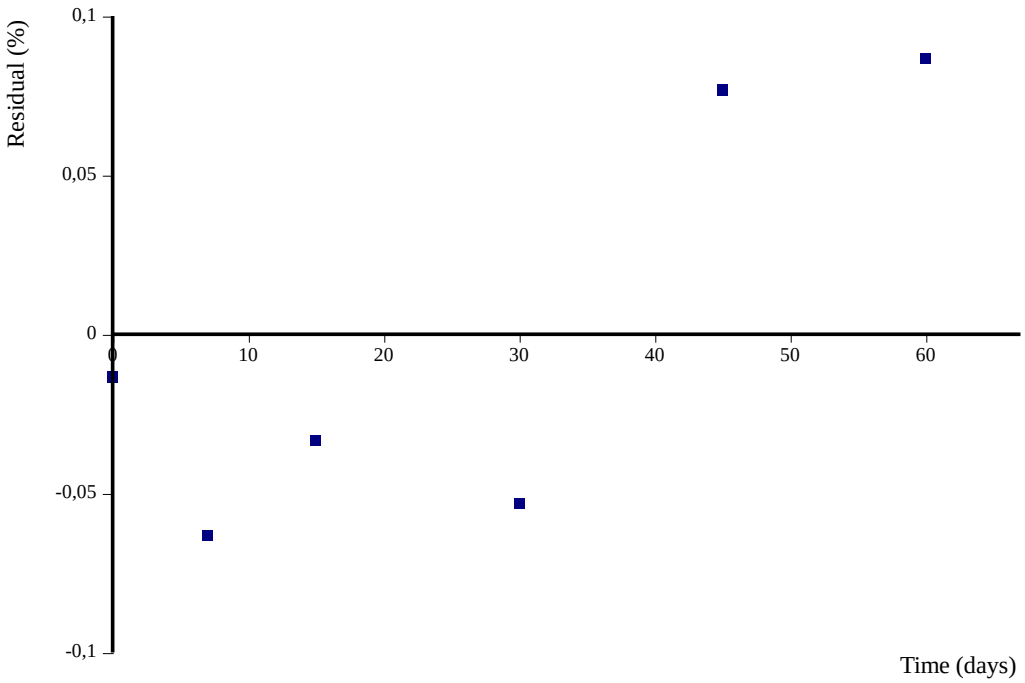
Compartment	Name
Parent	Parent

Graphical Summary:

Observations and Fitted Model:



Residuals:



Initial Values for this Step:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k_Parent	0.1	0 to (unbounded)	No

Estimated Values:

Parameter	Value	σ	Prob. > t	Lower (90%) CI	Upper (90%) CI	Lower (95%) CI	Upper (95%) CI
Parent_0	1.133	0.04761	N/A	1.032	1.235	1.001	1.266
k_Parent	1.35E-012	0.001248	0.5	-0.002661	0.002661	-0.003465	0.003

χ^2

Parameter	Error %	Degrees of Freedom
All data	4.2	4
Parent	4.2	4

Decay Times:

Compartment	DT50 (days)	DT90 (days)
Parent	>10,000	>10,000

Additional Statistics:

Parameter	r^2 (Obs v Pred)	Efficiency
All data	0.6436	6.427E-06
Parent	0.6436	6.427E-06

Parameter Correlation:

	Parent_0	k_Parent
Parent_0	1	0.7773
k_Parent	0.7773	1

Observed v. Predicted:

Compartment Parent

Time (days)	Value (%)	Predicted Value	Residual
0	1.12	1.133	-0.01333
7	1.07	1.133	-0.06333
15	1.1	1.133	-0.03333
30	1.08	1.133	-0.05333
45	1.21	1.133	0.07667
60	1.22	1.133	0.08667

Sequence Creation Information:
Fit generated by CAKE version 3.3 (Release)
running on R version 3.0.0 (2013-04-03)

Report Information:
Report generated by CAKE version 3.3 (Release)
CAKE developed by Tessella Ltd, Abingdon, Oxfordshire, UK, sponsored by Syngenta
Running on .NET version 4.0.30319.42000

Data set: Experiment 1 (DFOP)

Study date: Montag, 7. Dezember 2020
Report generated: Montag, 7. Dezember 2020

Model Setup:

Topology: Parent only
Optimiser: IRLS (IRLS Its. 10, IRLS Tol. 1E-05, Max. Its. 100, Tol. 1E-05)
SANN Max Iterations: 10000
Extra Solver Option: Use If Required

Initial Values of Sequence Parameters:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k1_Parent	0.1	0 to (unbounded)	No
k2_Parent	0.01	0 to (unbounded)	No
g_Parent	0.5	0 to 1	No

Fit step: Final

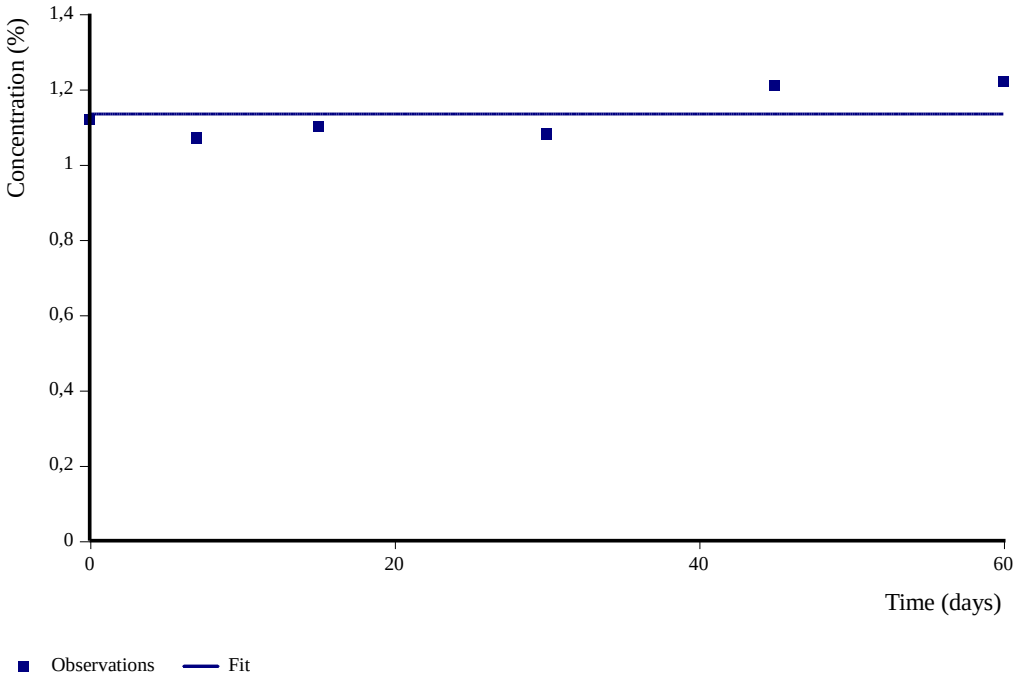
Used Extra Solver: Yes

Reference Table:

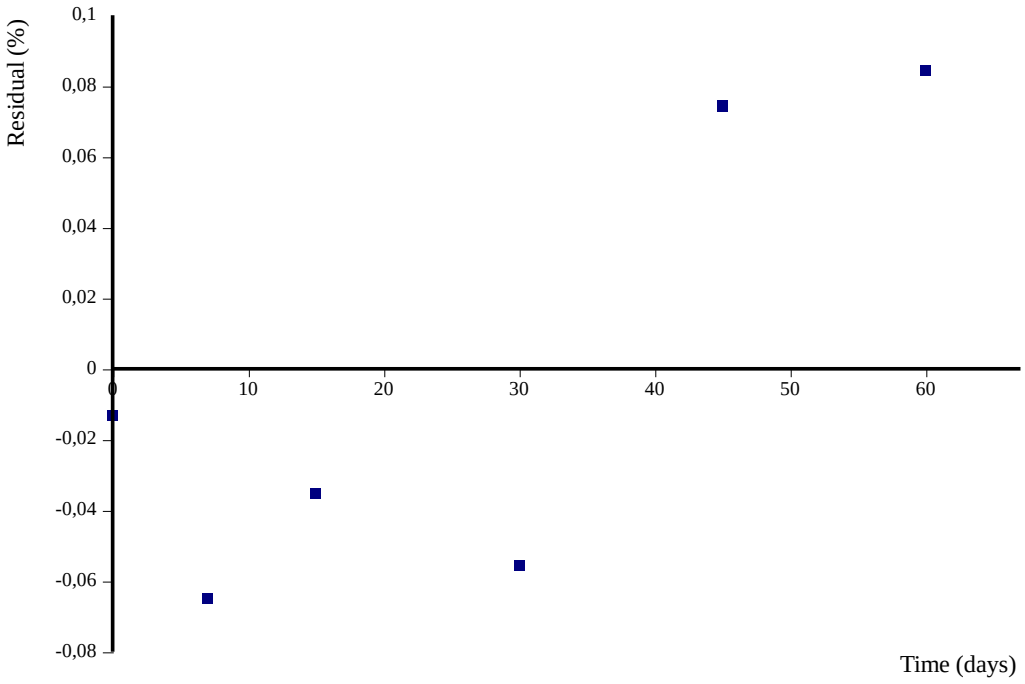
Compartment	Name
Parent	Parent

Graphical Summary:

Observations and Fitted Model:



Residuals:



Initial Values for this Step:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k1_Parent	0.1	0 to (unbounded)	No
k2_Parent	0.01	0 to (unbounded)	No
g_Parent	0.5	0 to 1	No

Estimated Values:

Parameter	Value	σ	Prob. > t	Lower (90%) CI	Upper (90%) CI	Lower (95%) CI	Upper (95%) CI
Parent_0	1.133	0.0665	N/A	0.9392	1.328	0.8472	1.419
k1_Parent	0.1476	nd	nd	nd	nd	nd	nd
k2_Parent	4.86E-011	0.001785	0.5	-0.005213	0.005213	-0.007682	0.008
g_Parent	2.91E-006	0	N/A	2.91E-006	2.91E-006	2.91E-006	0

Note: Errors and T-test values could not be calculated because the covariance matrix could not be created.

χ^2

Parameter	Error %	Degrees of Freedom
All data	5.27	2
Parent	5.27	2

Decay Times:

Compartment	DT50 (overall days)	DT90 (overall days)	k1 DT50 (days)	k2 DT50 (days)
Parent	>10,000	>10,000	4.7	>10,000

Additional Statistics:

Parameter	r^2 (Obs v Pred)	Efficiency
All data	0.09483	0.00736
Parent	0.09483	0.00736

Parameter Correlation:

	Parent_0	k1_Parent	k2_Parent	g_Parent
Parent_0	1	nd	0.7709	nd
k1_Parent	nd	1	nd	nd
k2_Parent	0.7709	nd	1	nd
g_Parent	nd	nd	nd	1

Observed v. Predicted:

Compartment Parent

Time (days)	Value (%)	Predicted Value	Residual
0	1.12	1.133	-0.01334
7	1.07	1.135	-0.0648
15	1.1	1.135	-0.03536
30	1.08	1.136	-0.05557
45	1.21	1.136	0.0744
60	1.22	1.136	0.0844

Sequence Creation Information:
Fit generated by CAKE version 3.3 (Release)
running on R version 3.0.0 (2013-04-03)

Report Information:
Report generated by CAKE version 3.3 (Release)
CAKE developed by Tessella Ltd, Abingdon, Oxfordshire, UK, sponsored by Syngenta
Running on .NET version 4.0.30319.42000

Data set: Experiment 1 (HS)

Study date: Montag, 7. Dezember 2020

Report generated: Montag, 7. Dezember 2020

Model Setup:

Topology: Parent only

Optimiser: IRLS (IRLS Its. 10, IRLS Tol. 1E-05, Max. Its. 100, Tol. 1E-05)

SANN Max Iterations: 10000

Extra Solver Option: Use If Required

Initial Values of Sequence Parameters:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k1_Parent	0.1	0 to (unbounded)	No
k2_Parent	0.01	0 to (unbounded)	No
tb_Parent	Automatic	0 to (unbounded)	No

Fit step: Final

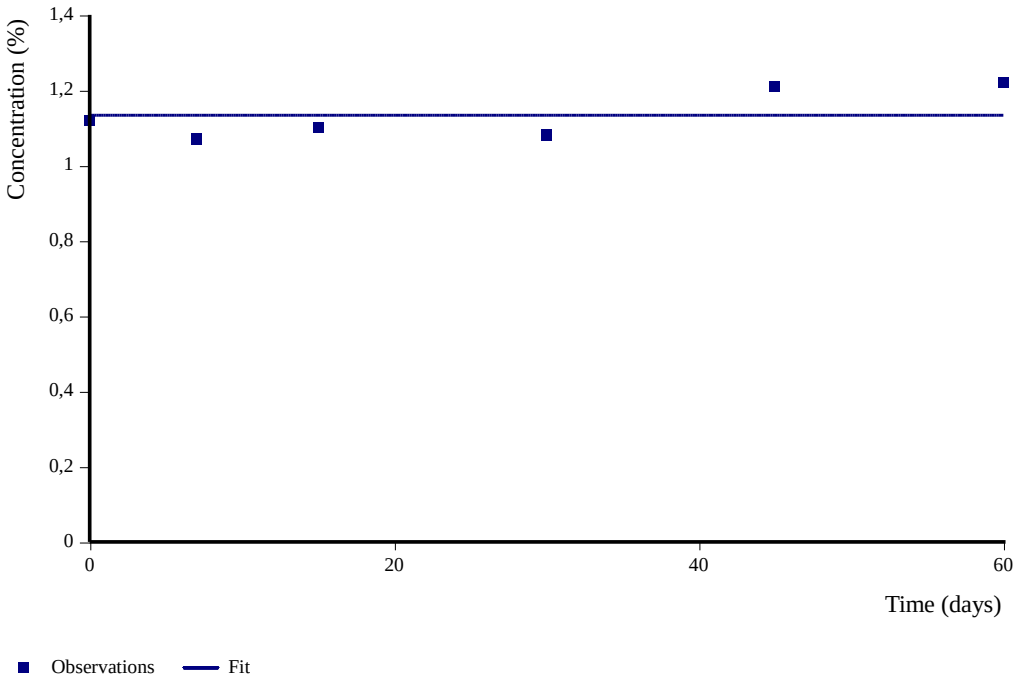
Used Extra Solver: Yes

Reference Table:

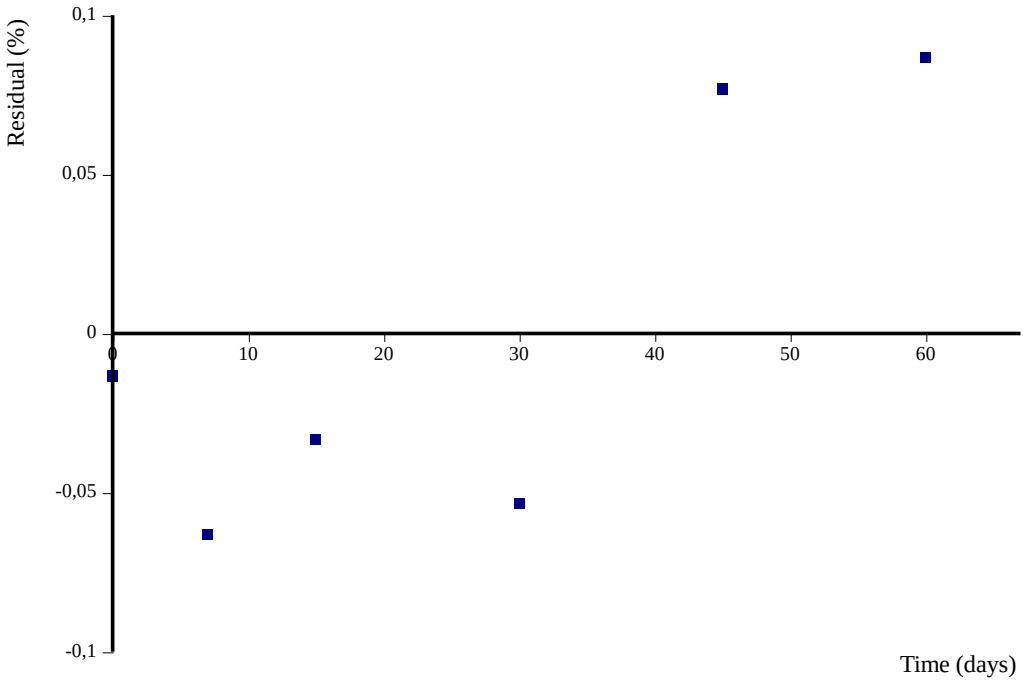
Compartment	Name
Parent	Parent

Graphical Summary:

Observations and Fitted Model:



Residuals:



Initial Values for this Step:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k1_Parent	0.1	0 to (unbounded)	No
k2_Parent	0.01	0 to (unbounded)	No
tb_Parent	30	0 to (unbounded)	No

Estimated Values:

Parameter	Value	σ	Prob. > t	Lower (90%) CI	Upper (90%) CI	Lower (95%) CI	Upper (95%) CI
Parent_0	1.133	0.07758	N/A	0.9068	1.36	0.7995	1.467
k1	3.12E-010	0.003243	0.5	-0.009469	0.009469	-0.01395	0.014
k2	5.14E-009	3.54E-004	0.5	-0.001033	0.001033	-0.001523	0.002
tb	30.3	nd	N/A	nd	nd	nd	nd

Note: Errors and T-test values could not be calculated because the covariance matrix could not be created.

χ^2

Parameter	Error %	Degrees of Freedom
All data	5.29	2
Parent	5.29	2

Decay Times:

Compartment	DT50 (overall days)	DT90 (overall days)	k1 DT50 (days)	k2 DT50 (days)
Parent	>10,000	>10,000	>10,000	>10,000

Additional Statistics:

Parameter	r^2 (Obs v Pred)	Efficiency
All data	nd	-2.154E-14
Parent	nd	-2.154E-14

Parameter Correlation:

	Parent_0	k1	k2	tb
Parent_0	1	0.8378	-0.8378	nd
k1	0.8378	1	-1	nd
k2	-0.8378	-1	1	nd
tb	nd	nd	nd	1

Observed v. Predicted:

Compartment Parent

Time (days)	Value (%)	Predicted Value	Residual
0	1.12	1.133	-0.01333
7	1.07	1.133	-0.06333
15	1.1	1.133	-0.03333
30	1.08	1.133	-0.05333
45	1.21	1.133	0.07667
60	1.22	1.133	0.08667

Sequence Creation Information:
Fit generated by CAKE version 3.3 (Release) running on R version 3.0.0 (2013-04-03)

Report Information:
Report generated by CAKE version 3.3 (Release)
CAKE developed by Tessella Ltd, Abingdon, Oxfordshire, UK, sponsored by Syngenta
Running on .NET version 4.0.30319.42000

Data set: Experiment 1 (FOMC)

Study date: Montag, 7. Dezember 2020
Report generated: Montag, 7. Dezember 2020

Model Setup:

Topology: Parent only
Optimiser: IRLS (IRLS Its. 10, IRLS Tol. 1E-05, Max. Its. 100, Tol. 1E-05)
SANN Max Iterations: 10000
Extra Solver Option: Use If Required

Initial Values of Sequence Parameters:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
alpha_Parent	0.1	0 to (unbounded)	No
beta_Parent	0.01	0 to (unbounded)	No

Fit step: Final

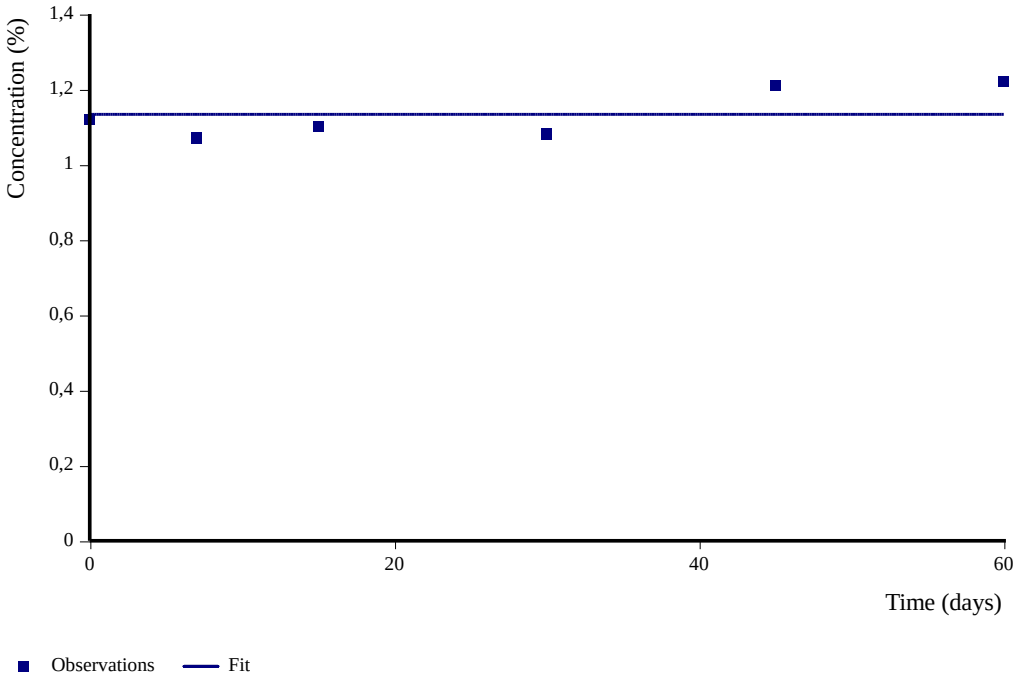
Used Extra Solver: Yes

Reference Table:

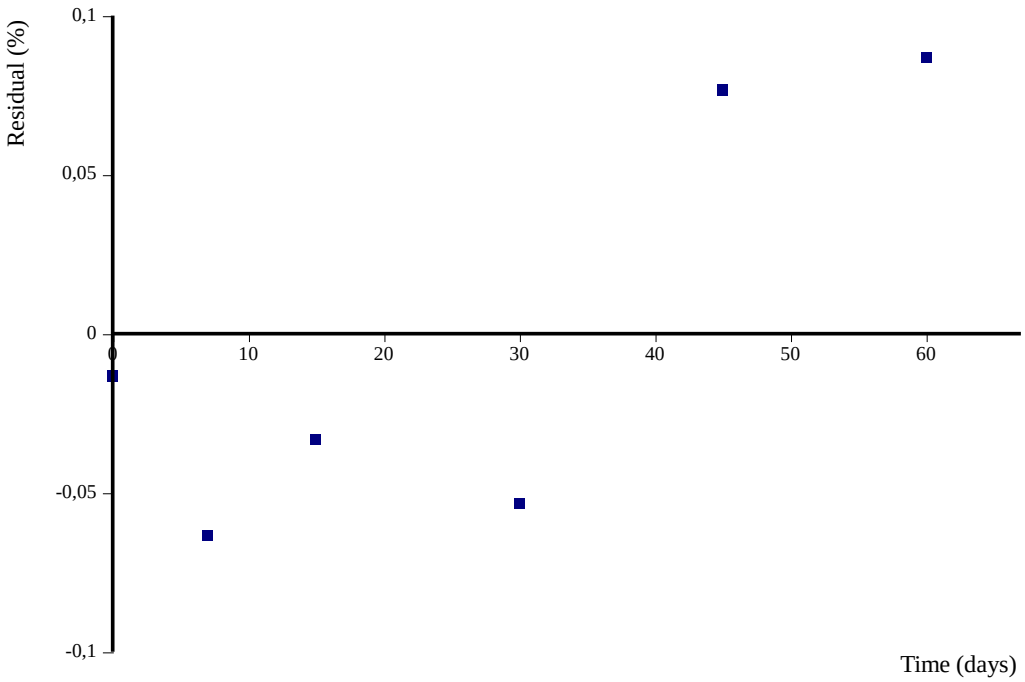
Compartment	Name
Parent	Parent

Graphical Summary:

Observations and Fitted Model:



Residuals:



Initial Values for this Step:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
alpha_Parent	0.1	0 to (unbounded)	No
beta_Parent	0.01	0 to (unbounded)	No

Estimated Values:

Parameter	Value	σ	Prob. > t	Lower (90%) CI	Upper (90%) CI	Lower (95%) CI	Upper (95%) CI
Parent_0	1.133	0.03458	N/A	1.052	1.215	1.023	1.243
alpha	1.18E-008	nd	N/A	nd	nd	nd	nd
beta	0.008543	nd	N/A	nd	nd	nd	nd

Note: Errors and T-test values could not be calculated because the covariance matrix could not be created.

χ^2

Parameter	Error %	Degrees of Freedom
All data	4.63	3
Parent	4.63	3

Decay Times:

Compartment	DT50 (days)	DT90 (days)
Parent	>10,000	>10,000

Additional Statistics:

Parameter	r^2 (Obs v Pred)	Efficiency
All data	0.1417	-2.427E-07
Parent	0.1417	-2.427E-07

Parameter Correlation:

	Parent_0	alpha	beta
Parent_0	1	nd	nd
alpha	nd	1	nd
beta	nd	nd	1

Observed v. Predicted:

Compartment Parent

Time (days)	Value (%)	Predicted Value	Residual
0	1.12	1.133	-0.01333
7	1.07	1.133	-0.06333
15	1.1	1.133	-0.03333
30	1.08	1.133	-0.05333
45	1.21	1.133	0.07667
60	1.22	1.133	0.08667

Sequence Creation Information:
Fit generated by CAKE version 3.3 (Release)
running on R version 3.0.0 (2013-04-03)

Report Information:
Report generated by CAKE version 3.3 (Release)
CAKE developed by Tessella Ltd, Abingdon, Oxfordshire, UK, sponsored by Syngenta
Running on .NET version 4.0.30319.42000

1H-Benzotriazole

Data set: Experiment 1 (SFO)

Study date: Montag, 7. Dezember 2020
Report generated: Montag, 7. Dezember 2020

Model Setup:

Topology: Parent only
Optimiser: IRLS (IRLS Its. 10, IRLS Tol. 1E-05, Max. Its. 100, Tol. 1E-05)
SANN Max Iterations: 10000
Extra Solver Option: Use If Required

Initial Values of Sequence Parameters:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k_Parent	0.1	0 to (unbounded)	No

Fit step: Final

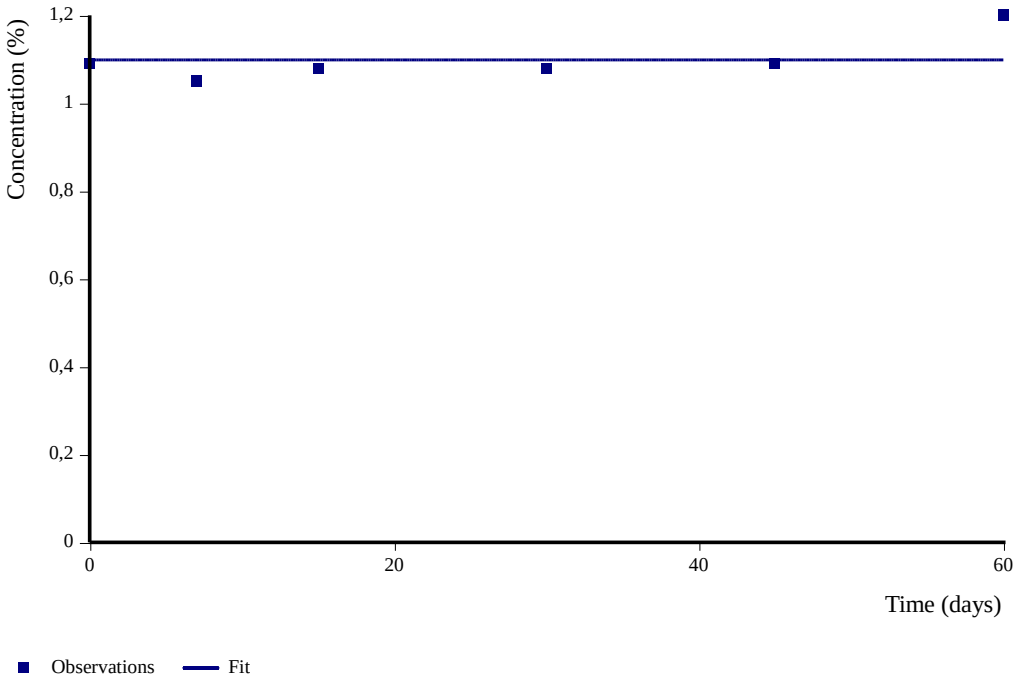
Used Extra Solver: No

Reference Table:

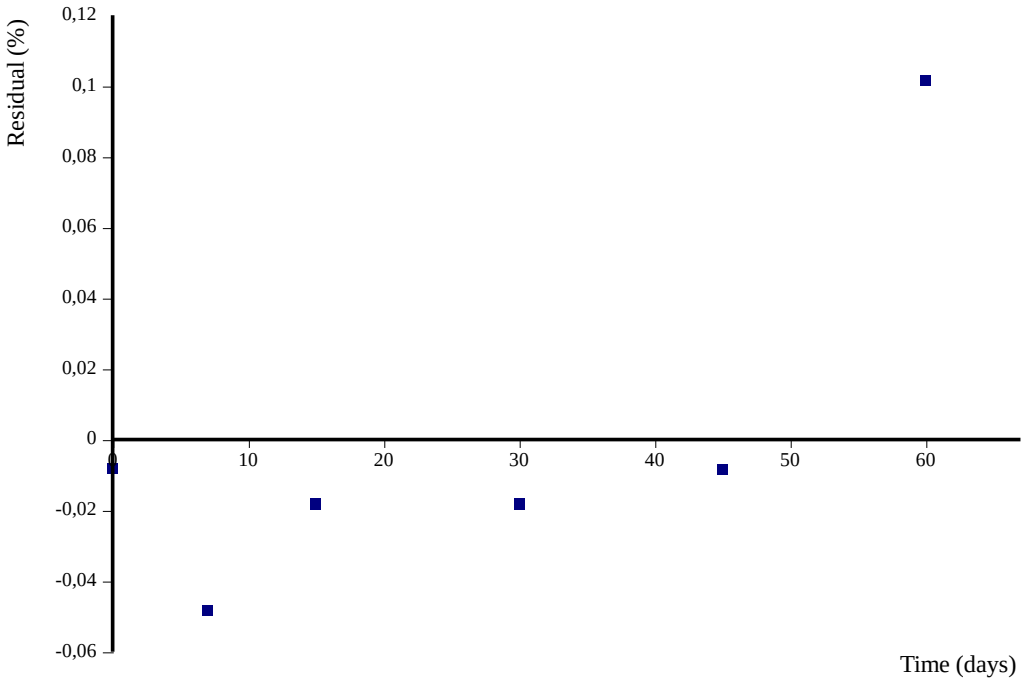
Compartment	Name
Parent	Parent

Graphical Summary:

Observations and Fitted Model:



Residuals:



Initial Values for this Step:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k_Parent	0.1	0 to (unbounded)	No

Estimated Values:

Parameter	Value	σ	Prob. > t	Lower (90%) CI	Upper (90%) CI	Lower (95%) CI	Upper (95%) CI
Parent_0	1.098	0.03768	N/A	1.018	1.179	0.9937	1.203
k_Parent	2.98E-015	0.001019	0.5	-0.002172	0.002172	-0.002829	0.003

χ^2

Parameter	Error %	Degrees of Freedom
All data	3.43	4
Parent	3.43	4

Decay Times:

Compartment	DT50 (days)	DT90 (days)
Parent	>10,000	>10,000

Additional Statistics:

Parameter	r^2 (Obs v Pred)	Efficiency
All data	0.5735	7.432E-06
Parent	0.5735	7.432E-06

Parameter Correlation:

	Parent_0	k_Parent
Parent_0	1	0.7773
k_Parent	0.7773	1

Observed v. Predicted:

Compartment Parent

Time (days)	Value (%)	Predicted Value	Residual
0	1.09	1.098	-0.008333
7	1.05	1.098	-0.04833
15	1.08	1.098	-0.01833
30	1.08	1.098	-0.01833
45	1.09	1.098	-0.008334
60	1.2	1.098	0.1017

Sequence Creation Information:
Fit generated by CAKE version 3.3 (Release)
running on R version 3.0.0 (2013-04-03)

Report Information:
Report generated by CAKE version 3.3 (Release)
CAKE developed by Tessella Ltd, Abingdon, Oxfordshire, UK, sponsored by Syngenta
Running on .NET version 4.0.30319.42000

Data set: Experiment 1 (DFOP)

Study date: Montag, 7. Dezember 2020

Report generated: Montag, 7. Dezember 2020

Model Setup:

Topology: Parent only

Optimiser: IRLS (IRLS Its. 10, IRLS Tol. 1E-05, Max. Its. 100, Tol. 1E-05)

SANN Max Iterations: 10000

Extra Solver Option: Use If Required

Initial Values of Sequence Parameters:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k1_Parent	0.1	0 to (unbounded)	No
k2_Parent	0.01	0 to (unbounded)	No
g_Parent	0.5	0 to 1	No

Fit step: Final

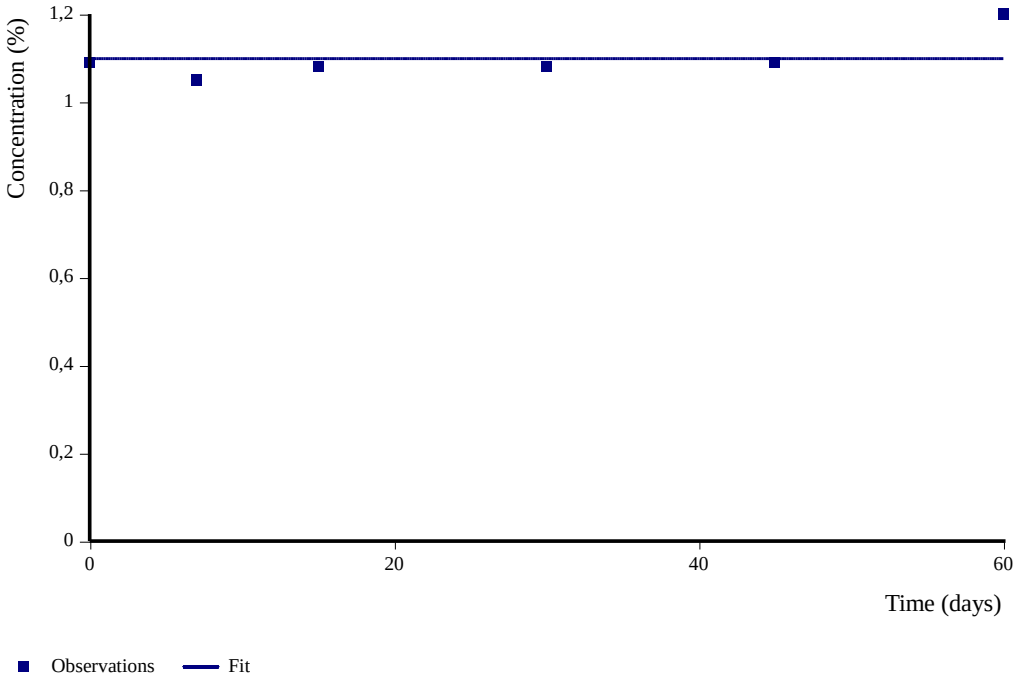
Used Extra Solver: Yes

Reference Table:

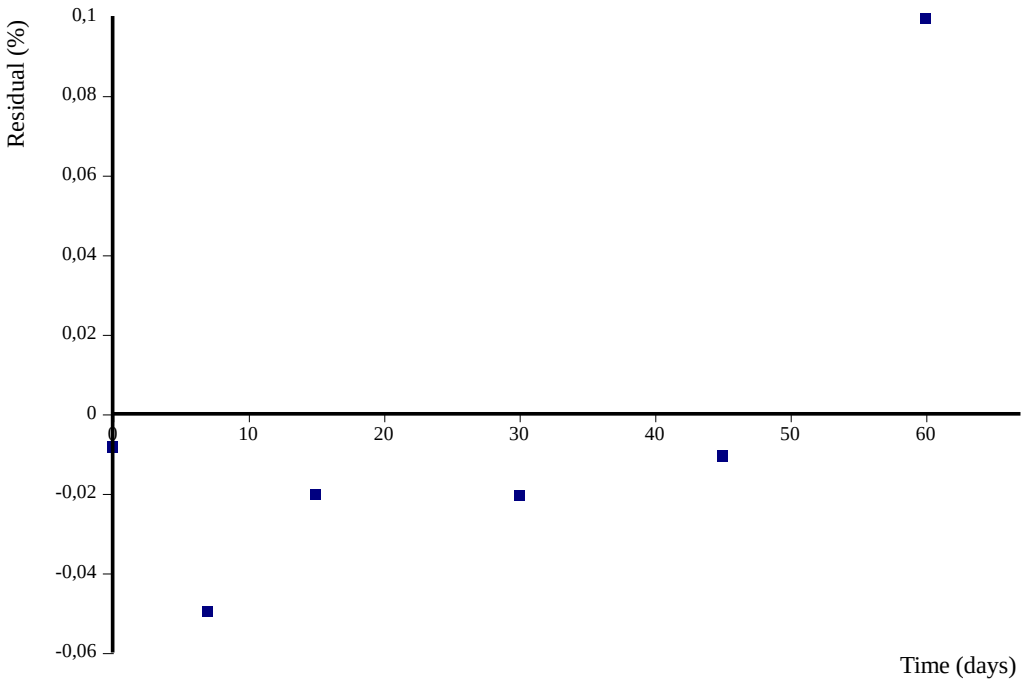
Compartment	Name
Parent	Parent

Graphical Summary:

Observations and Fitted Model:



Residuals:



Initial Values for this Step:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k1_Parent	0.1	0 to (unbounded)	No
k2_Parent	0.01	0 to (unbounded)	No
g_Parent	0.5	0 to 1	No

Estimated Values:

Parameter	Value	σ	Prob. > t	Lower (90%) CI	Upper (90%) CI	Lower (95%) CI	Upper (95%) CI
Parent_0	1.098	0.05287	N/A	0.944	1.253	0.8708	1.326
k1_Parent	0.1234	nd	nd	nd	nd	nd	nd
k2_Parent	5.56E-011	0.001458	0.5	-0.004256	0.004256	-0.006271	0.006
g_Parent	8.94E-007	0	N/A	8.94E-007	8.94E-007	8.94E-007	0

Note: Errors and T-test values could not be calculated because the covariance matrix could not be created.

χ^2

Parameter	Error %	Degrees of Freedom
All data	4.3	2
Parent	4.3	2

Decay Times:

Compartment	DT50 (overall days)	DT90 (overall days)	k1 DT50 (days)	k2 DT50 (days)
Parent	>10,000	>10,000	5.62	>10,000

Additional Statistics:

Parameter	r^2 (Obs v Pred)	Efficiency
All data	0.09705	0.008912
Parent	0.09705	0.008912

Parameter Correlation:

	Parent_0	k1_Parent	k2_Parent	g_Parent
Parent_0	1	nd	0.7733	nd
k1_Parent	nd	1	nd	nd
k2_Parent	0.7733	nd	1	nd
g_Parent	nd	nd	nd	1

Observed v. Predicted:

Compartment Parent

Time (days)	Value (%)	Predicted Value	Residual
0	1.09	1.098	-0.008334
7	1.05	1.1	-0.04961
15	1.08	1.1	-0.02019
30	1.08	1.1	-0.02048
45	1.09	1.101	-0.01052
60	1.2	1.101	0.09947

Sequence Creation Information:
Fit generated by CAKE version 3.3 (Release) running on R version 3.0.0 (2013-04-03)

Report Information:
Report generated by CAKE version 3.3 (Release)
CAKE developed by Tessella Ltd, Abingdon, Oxfordshire, UK, sponsored by Syngenta
Running on .NET version 4.0.30319.42000

CAKE Kinetic Evaluation Report

Study: New Study

Data set: Experiment 1 (HS)

Study date: Montag, 7. Dezember 2020

Report generated: Montag, 7. Dezember 2020

Model Setup:

Topology: Parent only

Optimiser: IRLS (IRLS Its. 10, IRLS Tol. 1E-05, Max. Its. 100, Tol. 1E-05)

SANN Max Iterations: 10000

Extra Solver Option: Use If Required

Initial Values of Sequence Parameters:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k1_Parent	0.1	0 to (unbounded)	No
k2_Parent	0.01	0 to (unbounded)	No
tb_Parent	Automatic	0 to (unbounded)	No

Fit step: Final

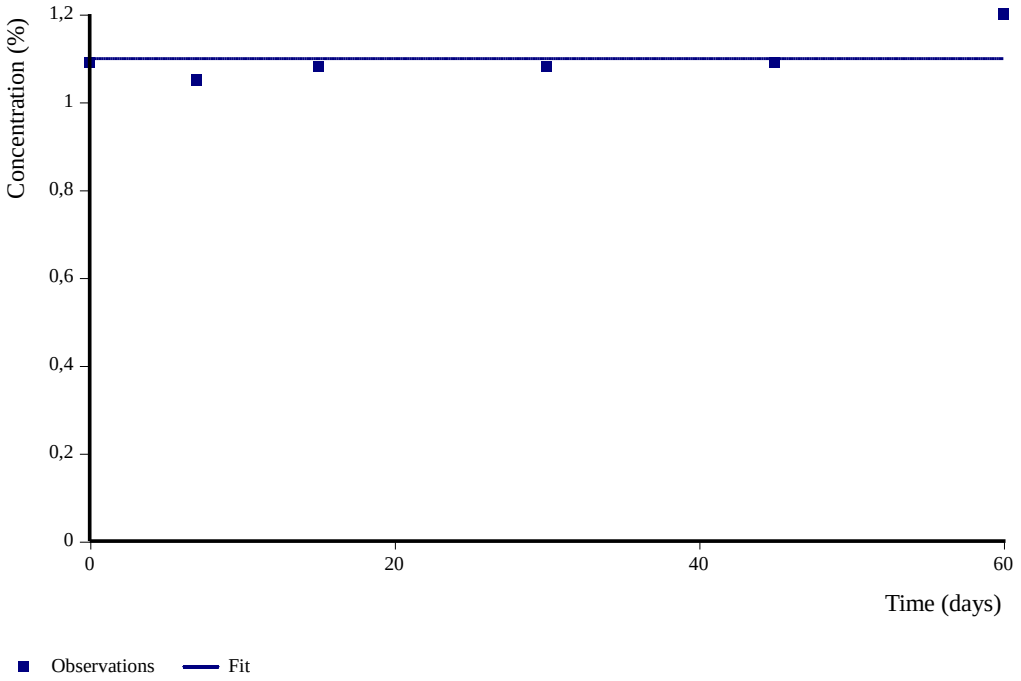
Used Extra Solver: Yes

Reference Table:

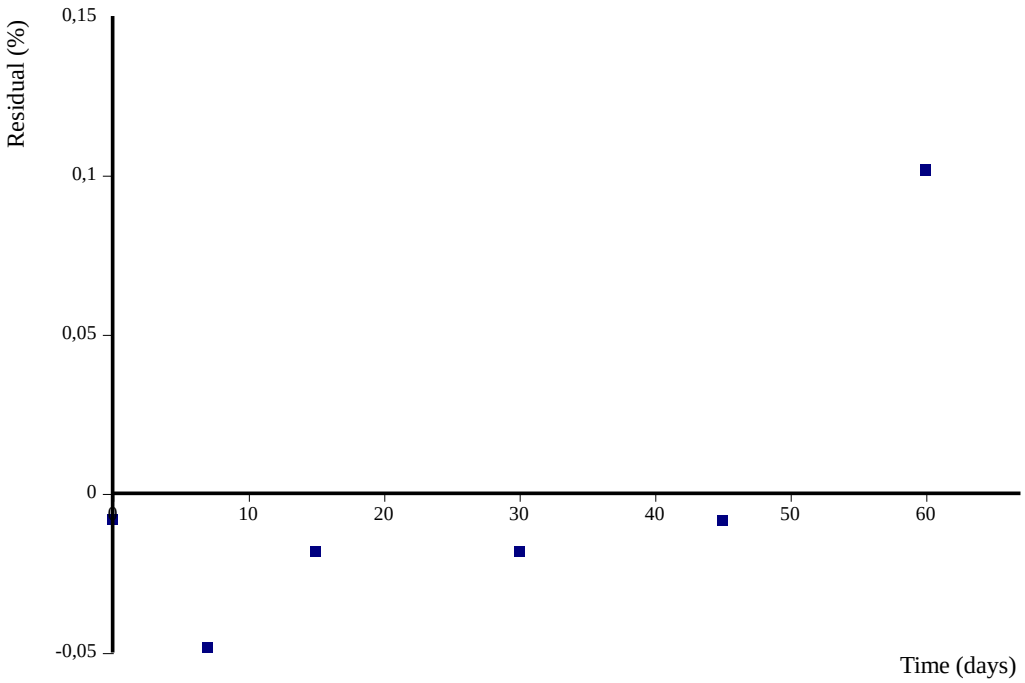
Compartment	Name
Parent	Parent

Graphical Summary:

Observations and Fitted Model:



Residuals:



Initial Values for this Step:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k1_Parent	0.1	0 to (unbounded)	No
k2_Parent	0.01	0 to (unbounded)	No
tb_Parent	30	0 to (unbounded)	No

Estimated Values:

Parameter	Value	σ	Prob. > t	Lower (90%) CI	Upper (90%) CI	Lower (95%) CI	Upper (95%) CI
Parent_0	1.098	0.05858	N/A	0.9273	1.269	0.8463	1.35
k1	1.48E-011	0.003177	0.5	-0.009278	0.009278	-0.01367	0.014
k2	3.42E-009	0.002174	0.5	-0.006348	0.006348	-0.009355	0.009
tb	30.23	nd	N/A	nd	nd	nd	nd

Note: Errors and T-test values could not be calculated because the covariance matrix could not be created.

χ^2

Parameter	Error %	Degrees of Freedom
All data	4.32	2
Parent	4.32	2

Decay Times:

Compartment	DT50 (overall days)	DT90 (overall days)	k1 DT50 (days)	k2 DT50 (days)
Parent	>10,000	>10,000	>10,000	>10,000

Additional Statistics:

Parameter	r^2 (Obs v Pred)	Efficiency
All data	nd	-5.773E-15
Parent	nd	-5.773E-15

Parameter Correlation:

	Parent_0	k1	k2	tb
Parent_0	1	0.8201	-0.8201	nd
k1	0.8201	1	-1	nd
k2	-0.8201	-1	1	nd
tb	nd	nd	nd	1

Observed v. Predicted:

Compartment Parent

Time (days)	Value (%)	Predicted Value	Residual
0	1.09	1.098	-0.008333
7	1.05	1.098	-0.04833
15	1.08	1.098	-0.01833
30	1.08	1.098	-0.01833
45	1.09	1.098	-0.008333
60	1.2	1.098	0.1017

Sequence Creation Information:
Fit generated by CAKE version 3.3 (Release) running on R version 3.0.0 (2013-04-03)

Report Information:
Report generated by CAKE version 3.3 (Release)
CAKE developed by Tessella Ltd, Abingdon, Oxfordshire, UK, sponsored by Syngenta
Running on .NET version 4.0.30319.42000

Data set: Experiment 1 (FOMC)

Study date: Montag, 7. Dezember 2020
Report generated: Montag, 7. Dezember 2020

Model Setup:

Topology: Parent only
Optimiser: IRLS (IRLS Its. 10, IRLS Tol. 1E-05, Max. Its. 100, Tol. 1E-05)
SANN Max Iterations: 10000
Extra Solver Option: Use If Required

Initial Values of Sequence Parameters:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
alpha_Parent	0.1	0 to (unbounded)	No
beta_Parent	0.01	0 to (unbounded)	No

Fit step: Final

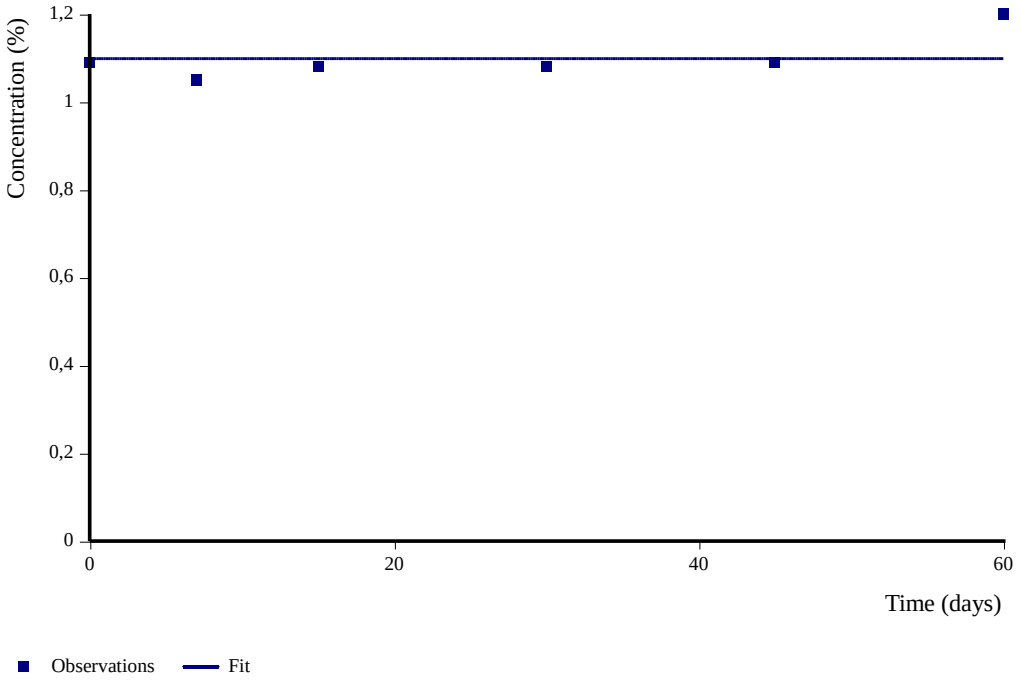
Used Extra Solver: Yes

Reference Table:

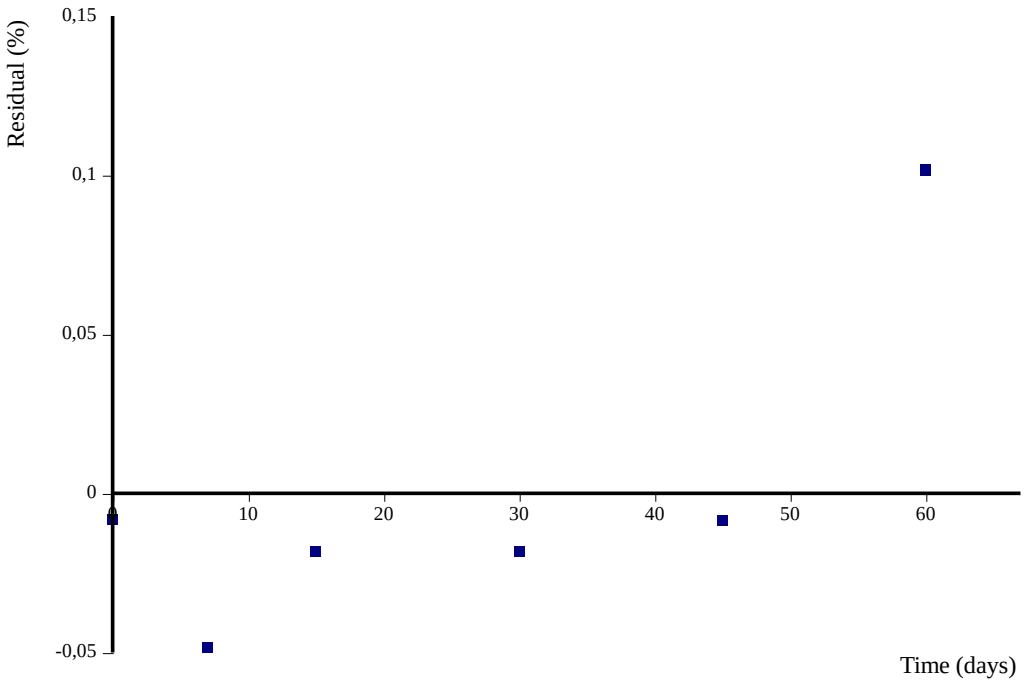
Compartment	Name
Parent	Parent

Graphical Summary:

Observations and Fitted Model:



Residuals:



Initial Values for this Step:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
alpha_Parent	0.1	0 to (unbounded)	No
beta_Parent	0.01	0 to (unbounded)	No

Estimated Values:

Parameter	Value	σ	Prob. > t	Lower (90%) CI	Upper (90%) CI	Lower (95%) CI	Upper (95%) CI
Parent_0	1.098	0.02737	N/A	1.034	1.163	1.011	1.185
alpha	1.18E-008	0	N/A	1.18E-008	1.18E-008	1.18E-008	0
beta	0.007195	nd	N/A	nd	nd	nd	nd

Note: Errors and T-test values could not be calculated because the covariance matrix could not be created.

χ^2

Parameter	Error %	Degrees of Freedom
All data	3.78	3
Parent	3.78	3

Decay Times:

Compartment	DT50 (days)	DT90 (days)
Parent	>10,000	>10,000

Additional Statistics:

Parameter	r^2 (Obs v Pred)	Efficiency
All data	nd	-3.844E-13
Parent	nd	-3.844E-13

Parameter Correlation:

	Parent_0	beta	alpha
Parent_0	1	nd	nd
alpha	nd	nd	1
beta	nd	1	nd

Observed v. Predicted:

Compartment Parent

Time (days)	Value (%)	Predicted Value	Residual
0	1.09	1.098	-0.008333
7	1.05	1.098	-0.04833
15	1.08	1.098	-0.01833
30	1.08	1.098	-0.01833
45	1.09	1.098	-0.008333
60	1.2	1.098	0.1017

Sequence Creation Information:
Fit generated by CAKE version 3.3 (Release)
running on R version 3.0.0 (2013-04-03)

Report Information:
Report generated by CAKE version 3.3 (Release)
CAKE developed by Tessella Ltd, Abingdon, Oxfordshire, UK, sponsored by Syngenta
Running on .NET version 4.0.30319.42000

Diglyme

Data set: Experiment 1 (SFO)

Study date: Montag, 19. Oktober 2020
Report generated: Montag, 19. Oktober 2020

Model Setup:

Topology: Parent only
Optimiser: IRLS (IRLS Its. 10, IRLS Tol. 1E-05, Max. Its. 100, Tol. 1E-05)
SANN Max Iterations: 10000
Extra Solver Option: Use If Required

Initial Values of Sequence Parameters:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k_Parent	0.1	0 to (unbounded)	No

Fit step: Final

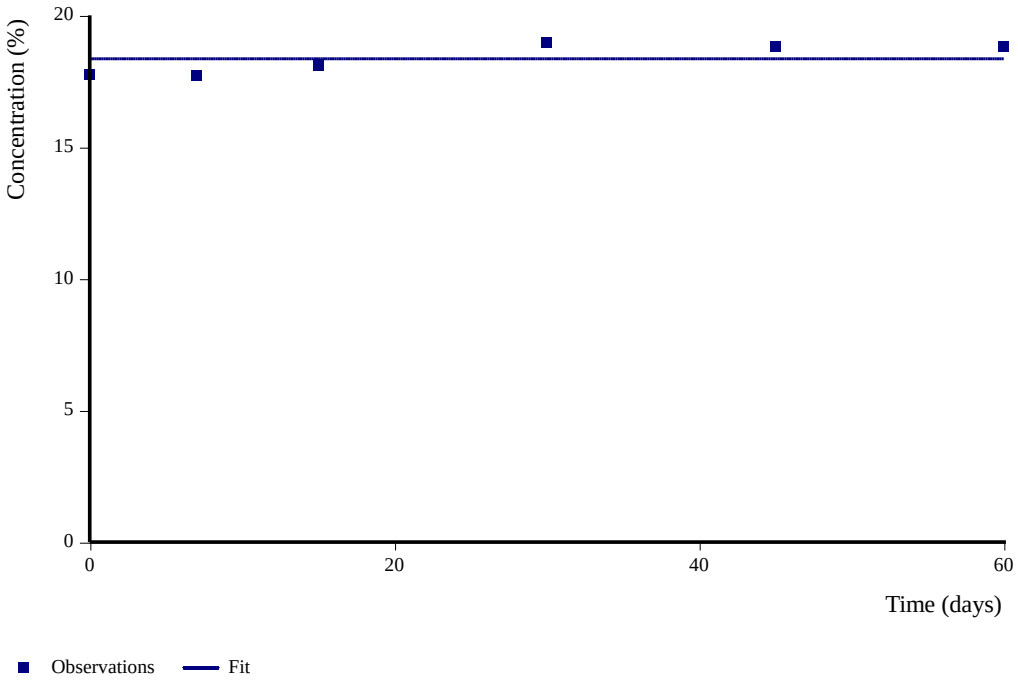
Used Extra Solver: No

Reference Table:

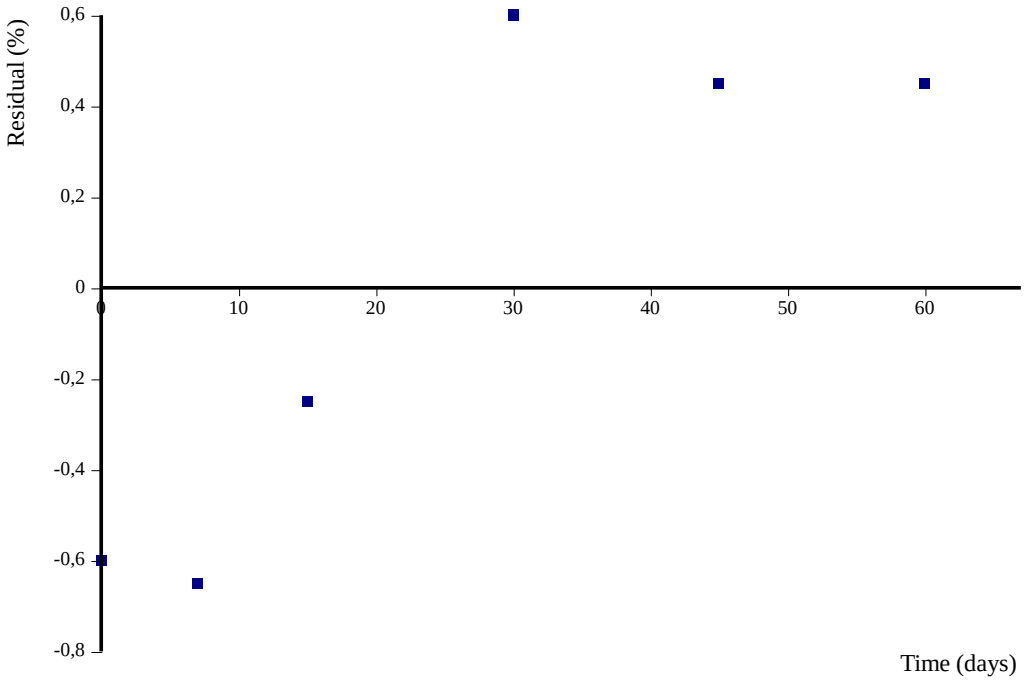
Compartment	Name
Parent	Parent

Graphical Summary:

Observations and Fitted Model:



Residuals:



Initial Values for this Step:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k_Parent	0.1	0 to (unbounded)	No

Estimated Values:

Parameter	Value	σ	Prob. > t	Lower (90%) CI	Upper (90%) CI	Lower (95%) CI	Upper (95%) CI
Parent_0	18.35	0.4117	N/A	17.47	19.23	17.21	19.49
k_Parent	2.39E-011	6.67E-004	0.5	-0.001421	0.001421	-0.001851	0.002

χ^2

Parameter	Error %	Degrees of Freedom
All data	2.25	4
Parent	2.25	4

Decay Times:

Compartment	DT50 (days)	DT90 (days)
Parent	>10,000	>10,000

Additional Statistics:

Parameter	r^2 (Obs v Pred)	Efficiency
All data	0.7486	1.295E-05
Parent	0.7486	1.295E-05

Parameter Correlation:

	Parent_0	k_Parent
Parent_0	1	0.7773
k_Parent	0.7773	1

Observed v. Predicted:

Compartment Parent

Time (days)	Value (%)	Predicted Value	Residual
0	17.75	18.35	-0.6
7	17.7	18.35	-0.65
15	18.1	18.35	-0.25
30	18.95	18.35	0.6
45	18.8	18.35	0.45
60	18.8	18.35	0.45

Sequence Creation Information:
Fit generated by CAKE version 3.3 (Release)
running on R version 3.0.0 (2013-04-03)

Report Information:
Report generated by CAKE version 3.3 (Release)
CAKE developed by Tessella Ltd, Abingdon, Oxfordshire, UK, sponsored by Syngenta
Running on .NET version 4.0.30319.42000

Data set: Experiment 1 (DFOP)

Study date: Montag, 19. Oktober 2020
Report generated: Montag, 19. Oktober 2020

Model Setup:

Topology: Parent only
Optimiser: IRLS (IRLS Its. 10, IRLS Tol. 1E-05, Max. Its. 100, Tol. 1E-05)
SANN Max Iterations: 10000
Extra Solver Option: Use If Required

Initial Values of Sequence Parameters:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k1_Parent	0.1	0 to (unbounded)	No
k2_Parent	0.01	0 to (unbounded)	No
g_Parent	0.5	0 to 1	No

Fit step: Final

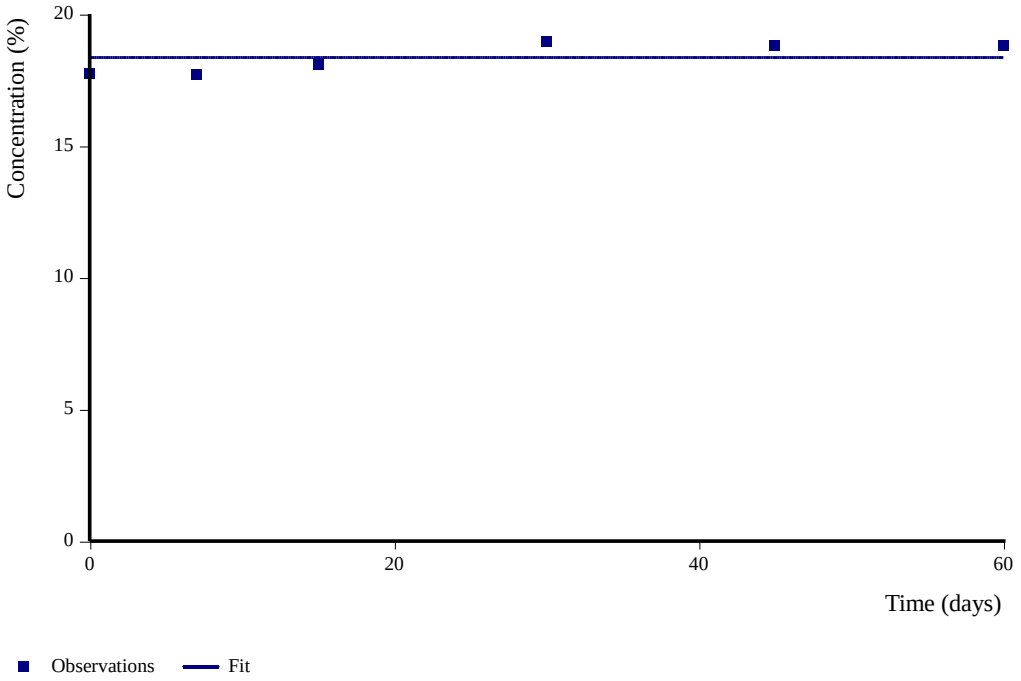
Used Extra Solver: Yes

Reference Table:

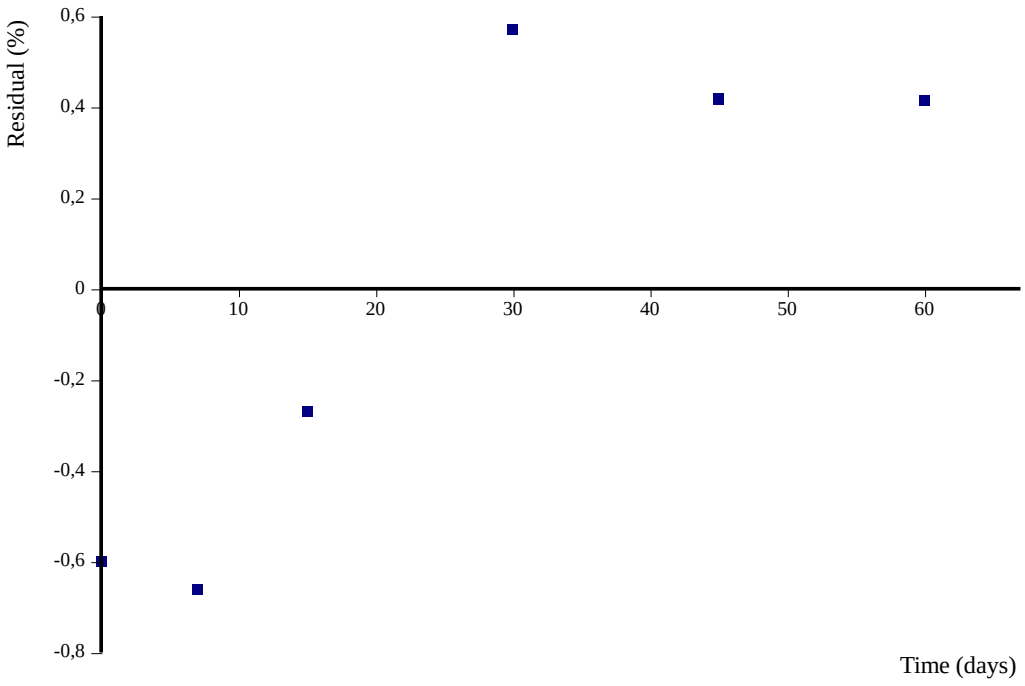
Compartment	Name
Parent	Parent

Graphical Summary:

Observations and Fitted Model:



Residuals:



Initial Values for this Step:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k1_Parent	0.1	0 to (unbounded)	No
k2_Parent	0.01	0 to (unbounded)	No
g_Parent	0.5	0 to 1	No

Estimated Values:

Parameter	Value	σ	Prob. > t	Lower (90%) CI	Upper (90%) CI	Lower (95%) CI	Upper (95%) CI
Parent_0	18.35	0.5749	N/A	16.67	20.03	15.88	20.82
k1_Parent	0.05144	nd	nd	nd	nd	nd	nd
k2_Parent	6.43E-013	9.39E-004	0.5	-0.002742	0.002742	-0.004041	0.004
g_Parent	9.44E-007	0	N/A	9.44E-007	9.44E-007	9.44E-007	0

Note: Errors and T-test values could not be calculated because the covariance matrix could not be created.

χ^2

Parameter	Error %	Degrees of Freedom
All data	2.77	2
Parent	2.77	2

Decay Times:

Compartment	DT50 (overall days)	DT90 (overall days)	k1 DT50 (days)	k2 DT50 (days)
Parent	>10,000	>10,000	13.5	>10,000

Additional Statistics:

Parameter	r^2 (Obs v Pred)	Efficiency
All data	0.8433	0.04219
Parent	0.8433	0.04219

Parameter Correlation:

	Parent_0	k1_Parent	k2_Parent	g_Parent
Parent_0	1	nd	0.7708	nd
k1_Parent	nd	1	nd	nd
k2_Parent	0.7708	nd	1	nd
g_Parent	nd	nd	nd	1

Observed v. Predicted:

Compartment Parent

Time (days)	Value (%)	Predicted Value	Residual
0	17.75	18.35	-0.6
7	17.7	18.36	-0.6611
15	18.1	18.37	-0.2697
30	18.95	18.38	0.5712
45	18.8	18.38	0.4169
60	18.8	18.39	0.415

Sequence Creation Information:
Fit generated by CAKE version 3.3 (Release) running on R version 3.0.0 (2013-04-03)

Report Information:
Report generated by CAKE version 3.3 (Release)
CAKE developed by Tessella Ltd, Abingdon, Oxfordshire, UK, sponsored by Syngenta
Running on .NET version 4.0.30319.42000

Data set: Experiment 1 (HS)

Study date: Montag, 19. Oktober 2020

Report generated: Montag, 19. Oktober 2020

Model Setup:

Topology: Parent only

Optimiser: IRLS (IRLS Its. 10, IRLS Tol. 1E-05, Max. Its. 100, Tol. 1E-05)

SANN Max Iterations: 10000

Extra Solver Option: Use If Required

Initial Values of Sequence Parameters:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k1_Parent	0.1	0 to (unbounded)	No
k2_Parent	0.01	0 to (unbounded)	No
tb_Parent	Automatic	0 to (unbounded)	No

Fit step: Final

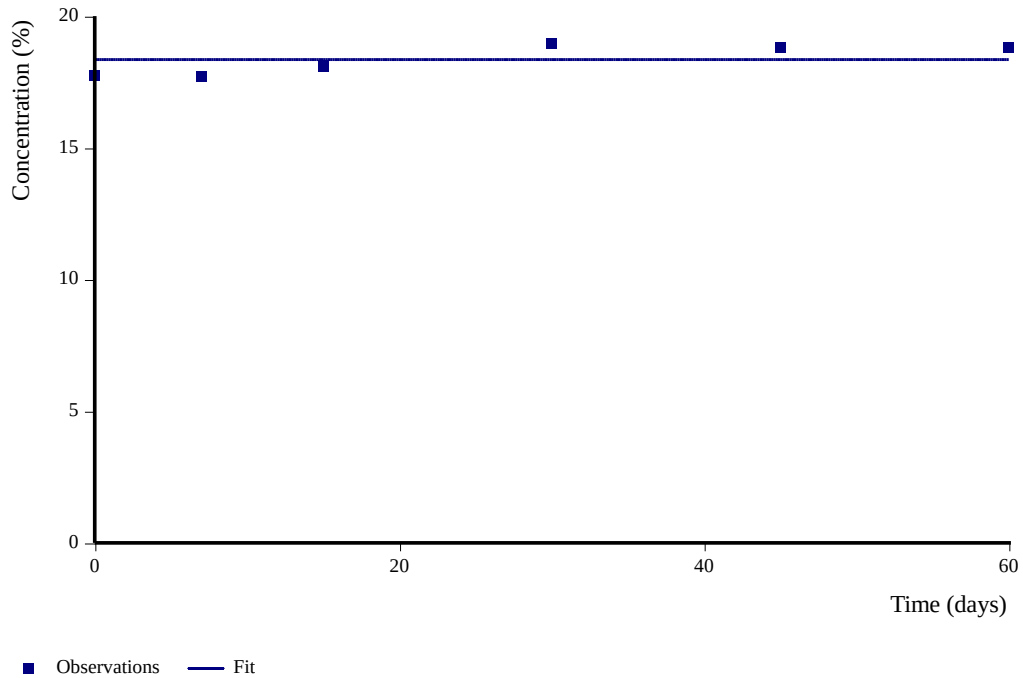
Used Extra Solver: Yes

Reference Table:

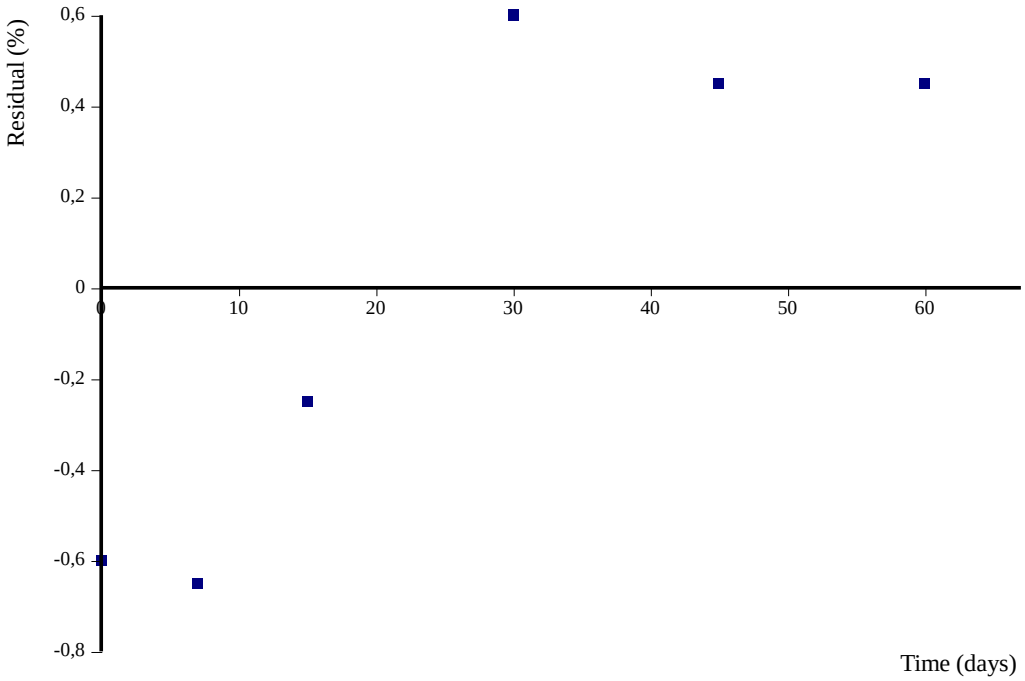
Compartment	Name
Parent	Parent

Graphical Summary:

Observations and Fitted Model:



Residuals:



Initial Values for this Step:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k1_Parent	0.1	0 to (unbounded)	No
k2_Parent	0.01	0 to (unbounded)	No
tb_Parent	36.38	0 to (unbounded)	No

Estimated Values:

Parameter	Value	σ	Prob. > t	Lower (90%) CI	Upper (90%) CI	Lower (95%) CI	Upper (95%) CI
Parent_0	18.35	0.5712	N/A	16.68	20.02	15.89	20.81
k1	3.53E-009	9.12E-004	0.5	-0.002664	0.002664	-0.003925	0.004
k2	5.17E-013	9.68E-004	0.5	-0.002827	0.002827	-0.004165	0.004
tb	27.72	nd	N/A	nd	nd	nd	nd

Note: Errors and T-test values could not be calculated because the covariance matrix could not be created.

χ^2

Parameter	Error %	Degrees of Freedom
All data	2.83	2
Parent	2.83	2

Decay Times:

Compartment	DT50 (overall days)	DT90 (overall days)	k1 DT50 (days)	k2 DT50 (days)
Parent	>10,000	>10,000	>10,000	>10,000

Additional Statistics:

Parameter	r^2 (Obs v Pred)	Efficiency
All data	nd	-2.413E-12
Parent	nd	-2.413E-12

Parameter Correlation:

	Parent_0	k1	k2	tb
Parent_0	1	0.7673	0.7673	nd
k1	0.7673	1	1	nd
k2	0.7673	1	1	nd
tb	nd	nd	nd	1

Observed v. Predicted:

Compartment Parent

Time (days)	Value (%)	Predicted Value	Residual
0	17.75	18.35	-0.6
7	17.7	18.35	-0.65
15	18.1	18.35	-0.25
30	18.95	18.35	0.6
45	18.8	18.35	0.45
60	18.8	18.35	0.45

Sequence Creation Information:
Fit generated by CAKE version 3.3 (Release)
running on R version 3.0.0 (2013-04-03)

Report Information:
Report generated by CAKE version 3.3 (Release)
CAKE developed by Tessella Ltd, Abingdon, Oxfordshire, UK, sponsored by Syngenta
Running on .NET version 4.0.30319.42000

Data set: Experiment 1 (FOMC)

Study date: Montag, 19. Oktober 2020
Report generated: Montag, 19. Oktober 2020

Model Setup:

Topology: Parent only
Optimiser: IRLS (IRLS Its. 10, IRLS Tol. 1E-05, Max. Its. 100, Tol. 1E-05)
SANN Max Iterations: 10000
Extra Solver Option: Use If Required

Initial Values of Sequence Parameters:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
alpha_Parent	0.1	0 to (unbounded)	No
beta_Parent	0.01	0 to (unbounded)	No

Fit step: Final

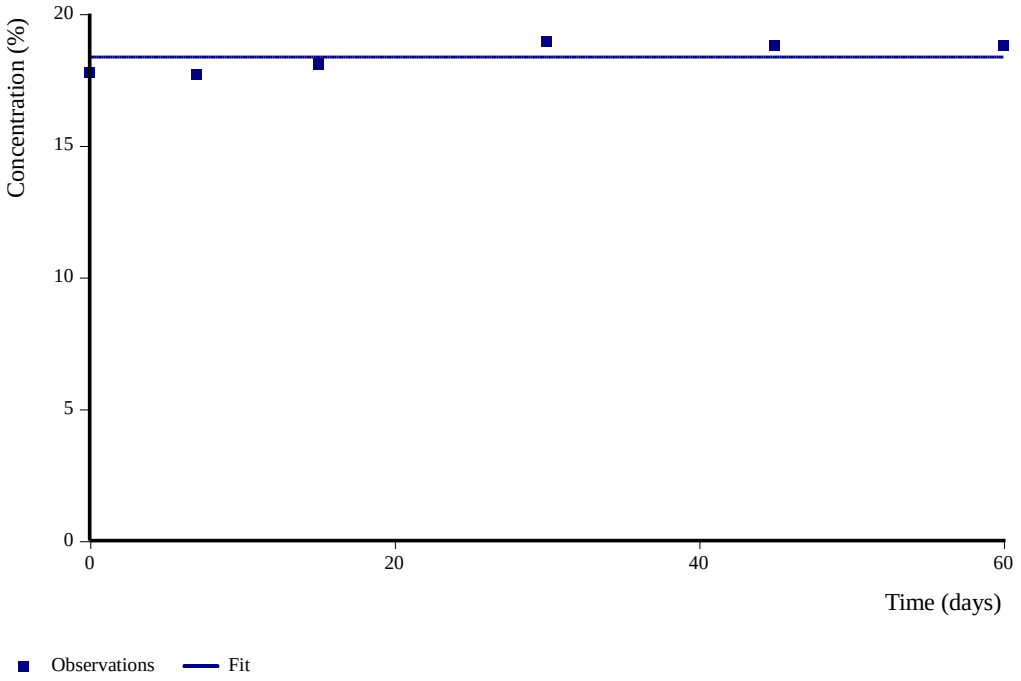
Used Extra Solver: Yes

Reference Table:

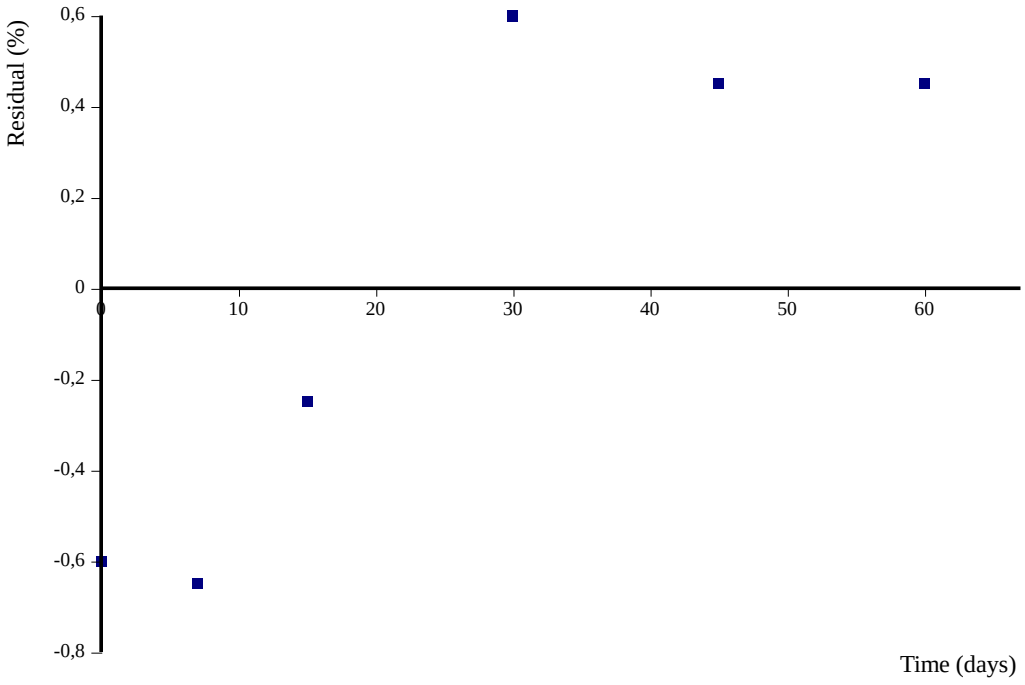
Compartment	Name
Parent	Parent

Graphical Summary:

Observations and Fitted Model:



Residuals:



Initial Values for this Step:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
alpha_Parent	0.1	0 to (unbounded)	No
beta_Parent	0.01	0 to (unbounded)	No

Estimated Values:

Parameter	Value	σ	Prob. > t	Lower (90%) CI	Upper (90%) CI	Lower (95%) CI	Upper (95%) CI
Parent_0	18.35	0.2991	N/A	17.65	19.05	17.4	19.3
alpha	3.24E-012	0	N/A	3.24E-012	3.24E-012	3.24E-012	0
beta	0.01151	nd	N/A	nd	nd	nd	nd

Note: Errors and T-test values could not be calculated because the covariance matrix could not be created.

χ^2

Parameter	Error %	Degrees of Freedom
All data	2.47	3
Parent	2.47	3

Decay Times:

Compartment	DT50 (days)	DT90 (days)
Parent	>10,000	>10,000

Additional Statistics:

Parameter	r^2 (Obs v Pred)	Efficiency
All data	nd	-7.772E-15
Parent	nd	-7.772E-15

Parameter Correlation:

	Parent_0	beta	alpha
Parent_0	1	nd	nd
alpha	nd	nd	1
beta	nd	1	nd

Observed v. Predicted:

Compartment Parent

Time (days)	Value (%)	Predicted Value	Residual
0	17.75	18.35	-0.6
7	17.7	18.35	-0.65
15	18.1	18.35	-0.25
30	18.95	18.35	0.6
45	18.8	18.35	0.45
60	18.8	18.35	0.45

Sequence Creation Information:
Fit generated by CAKE version 3.3 (Release)
running on R version 3.0.0 (2013-04-03)

Report Information:
Report generated by CAKE version 3.3 (Release)
CAKE developed by Tessella Ltd, Abingdon, Oxfordshire, UK, sponsored by Syngenta
Running on .NET version 4.0.30319.42000

DTPA

Data set: Experiment 1 (SFO)

Study date: Montag, 7. Dezember 2020
Report generated: Montag, 7. Dezember 2020

Model Setup:

Topology: Parent only
Optimiser: IRLS (IRLS Its. 10, IRLS Tol. 1E-05, Max. Its. 100, Tol. 1E-05)
SANN Max Iterations: 10000
Extra Solver Option: Use If Required

Initial Values of Sequence Parameters:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k_Parent	0.1	0 to (unbounded)	No

Fit step: Final

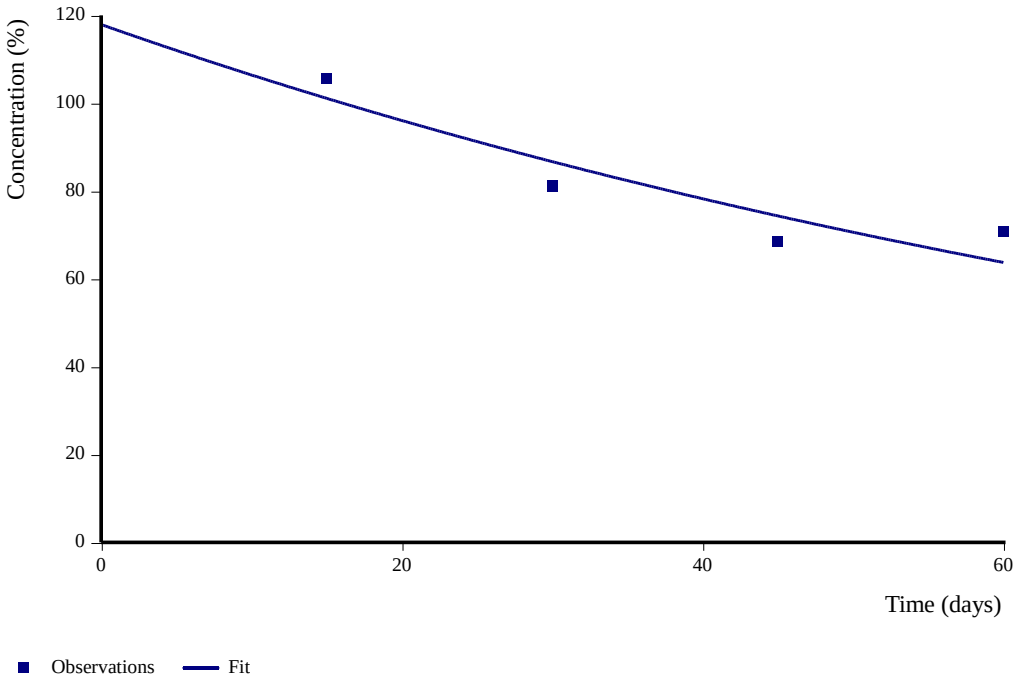
Used Extra Solver: No

Reference Table:

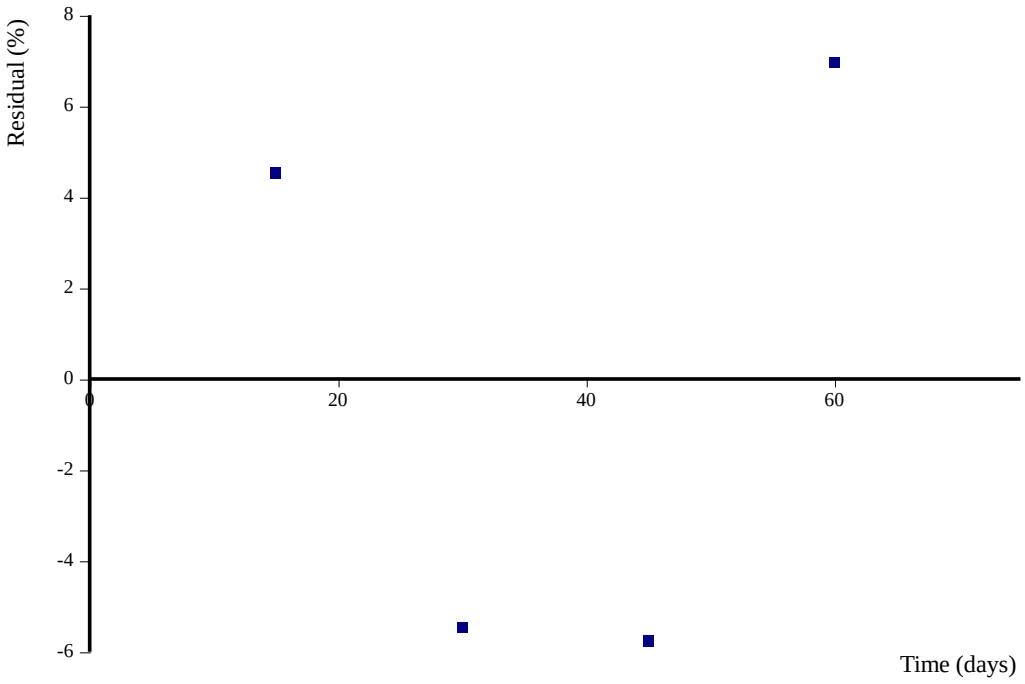
Compartment	Name
Parent	Parent

Graphical Summary:

Observations and Fitted Model:



Residuals:



Initial Values for this Step:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k_Parent	0.1	0 to (unbounded)	No

Estimated Values:

Parameter	Value	σ	Prob. > t	Lower (90%) CI	Upper (90%) CI	Lower (95%) CI	Upper (95%) CI
Parent_0	117.9	12.84	N/A	80.41	155.4	62.66	173.1
k_Parent	0.01025	0.003048	0.0391	0.00135	0.01915	-0.002865	0.023

χ^2

Parameter	Error %	Degrees of Freedom
All data	5.76	2
Parent	5.76	2

Decay Times:

Compartment	DT50 (days)	DT90 (days)
Parent	67.6	225

Additional Statistics:

Parameter	r^2 (Obs v Pred)	Efficiency
All data	0.8484	0.8476
Parent	0.8484	0.8476

Parameter Correlation:

	Parent_0	k_Parent
Parent_0	1	0.8924

k_Parent	0.8924	1

Observed v. Predicted:

Compartment Parent

Time (days)	Value (%)	Predicted Value	Residual
15	105.6	101.1	4.537
30	81.22	86.69	-5.47
45	68.58	74.34	-5.755
60	70.7	63.75	6.954

Sequence Creation Information:
Fit generated by CAKE version 3.3 (Release)
running on R version 3.0.0 (2013-04-03)

Report Information:
Report generated by CAKE version 3.3 (Release)
CAKE developed by Tessella Ltd, Abingdon, Oxfordshire, UK, sponsored by Syngenta
Running on .NET version 4.0.30319.42000

Data set: Experiment 1 (DFOP)

Study date: Montag, 7. Dezember 2020

Report generated: Montag, 7. Dezember 2020

Model Setup:

Topology: Parent only

Optimiser: IRLS (IRLS Its. 10, IRLS Tol. 1E-05, Max. Its. 100, Tol. 1E-05)

SANN Max Iterations: 10000

Extra Solver Option: Use If Required

Initial Values of Sequence Parameters:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k1_Parent	0.1	0 to (unbounded)	No
k2_Parent	0.01	0 to (unbounded)	No
g_Parent	0.5	0 to 1	No

Fit step: Final

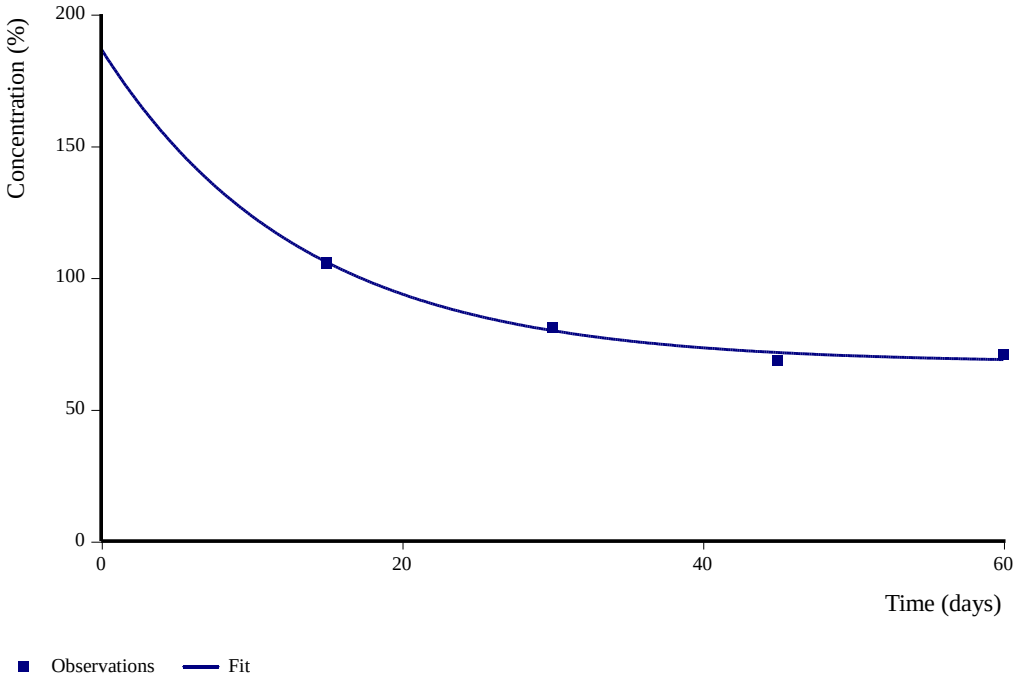
Used Extra Solver: Yes

Reference Table:

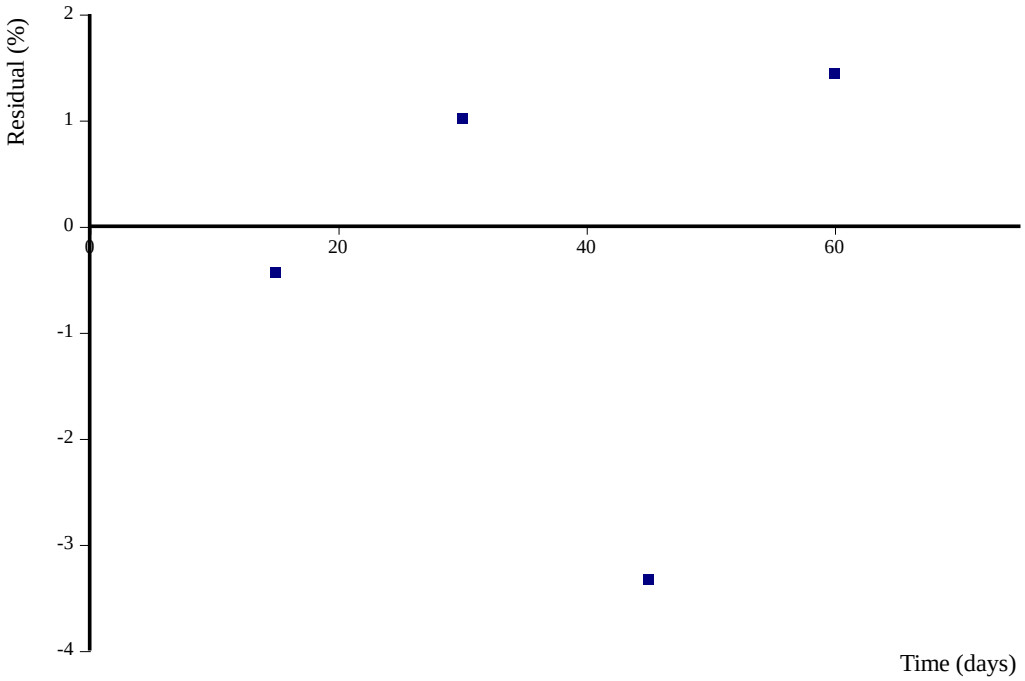
Compartment	Name
Parent	Parent

Graphical Summary:

Observations and Fitted Model:



Residuals:



Initial Values for this Step:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k1_Parent	0.1	0 to (unbounded)	No
k2_Parent	0.01	0 to (unbounded)	No
g_Parent	0.5	0 to 1	No

Estimated Values:

Parameter	Value	σ	Prob. > t
Parent_0	186.7	nd	N/A
k1_Parent	0.07583	nd	nd
k2_Parent	1.03E-012	nd	nd
g_Parent	0.6379	nd	N/A

Note: Errors and T-test values could not be calculated because the covariance matrix could not be created.

χ^2

Parameter	Error %	Degrees of Freedom
All data	nd	nd
Parent	nd	nd

Decay Times:

Compartment	DT50 (overall days)	DT90 (overall days)	k1 DT50 (days)	k2 DT50 (days)
Parent	20.2	>10,000	9.14	>10,000

Additional Statistics:

Parameter	r^2 (Obs v Pred)	Efficiency
All data	0.9839	0.9834
Parent	0.9839	0.9834

Parameter Correlation:

	Parent_0	k1_Parent	k2_Parent	g_Parent
Parent_0	1	0.9453	0.741	-0.2324
k1_Parent	0.9453	1	0.9054	-0.5249
k2_Parent	0.741	0.9054	1	-0.8202
g_Parent	-0.2324	-0.5249	-0.8202	1

Observed v. Predicted:

Compartment Parent

Time (days)	Value (%)	Predicted Value	Residual
15	105.6	106.1	-0.4398
30	81.22	80.21	1.012
45	68.58	71.92	-3.333
60	70.7	69.26	1.441

Sequence Creation Information:
Fit generated by CAKE version 3.3 (Release)
running on R version 3.0.0 (2013-04-03)

Report Information:
Report generated by CAKE version 3.3 (Release)

CAKE developed by Tessella Ltd, Abingdon, Oxfordshire, UK, sponsored by Syngenta
Running on .NET version 4.0.30319.42000

Data set: Experiment 1 (HS)

Study date: Montag, 7. Dezember 2020

Report generated: Montag, 7. Dezember 2020

Model Setup:

Topology: Parent only

Optimiser: IRLS (IRLS Its. 10, IRLS Tol. 1E-05, Max. Its. 100, Tol. 1E-05)

SANN Max Iterations: 10000

Extra Solver Option: Use If Required

Initial Values of Sequence Parameters:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k1_Parent	0.1	0 to (unbounded)	No
k2_Parent	0.01	0 to (unbounded)	No
tb_Parent	Automatic	0 to (unbounded)	No

Fit step: Final

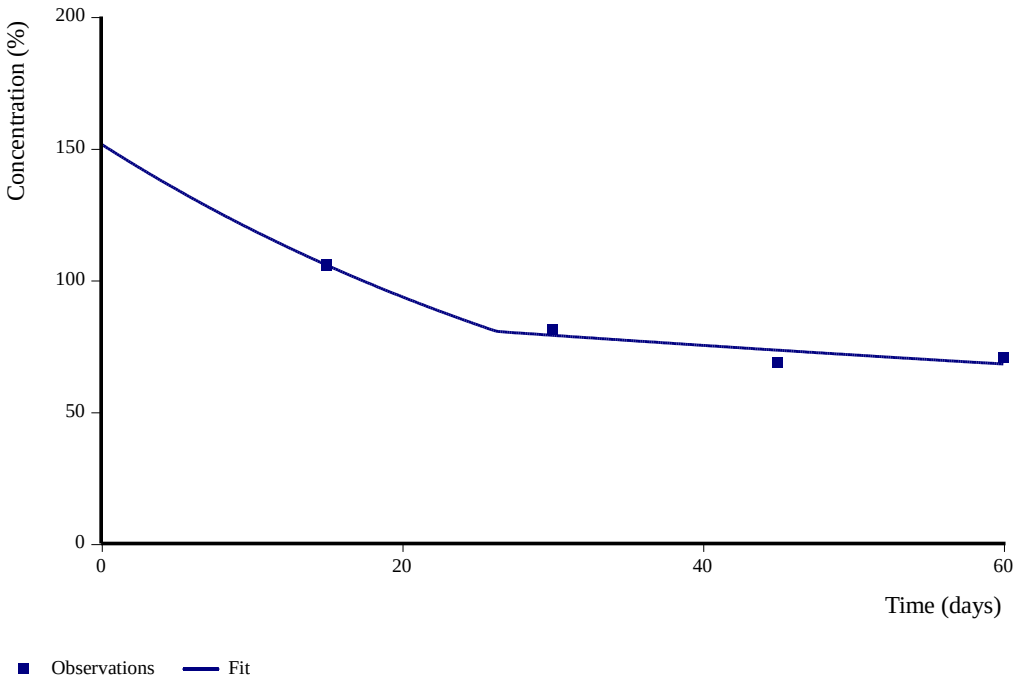
Used Extra Solver: Yes

Reference Table:

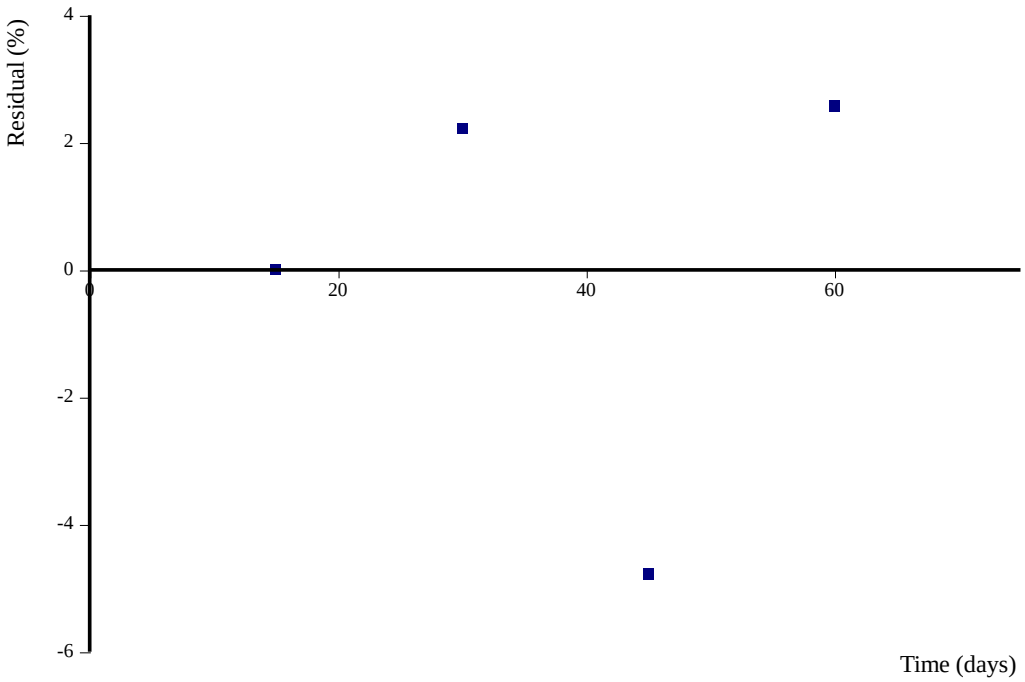
Compartment	Name
Parent	Parent

Graphical Summary:

Observations and Fitted Model:



Residuals:



Initial Values for this Step:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k1_Parent	0.1	0 to (unbounded)	No
k2_Parent	0.01	0 to (unbounded)	No
tb_Parent	30	0 to (unbounded)	No

Estimated Values:

Parameter	Value	σ	Prob. > t
Parent_0	151.6	nd	N/A
k1	0.02407	nd	nd
k2	0.004942	nd	nd
tb	26.31	nd	N/A

Note: Errors and T-test values could not be calculated because the covariance matrix could not be created.

χ^2

Parameter	Error %	Degrees of Freedom
All data	nd	nd
Parent	nd	nd

Decay Times:

Compartment	DT50 (overall days)	DT90 (overall days)	k1 DT50 (days)	k2 DT50 (days)
Parent	38.4	364	28.8	140

Additional Statistics:

Parameter	r^2 (Obs v Pred)	Efficiency
All data	0.9603	0.9603
Parent	0.9603	0.9603

Parameter Correlation:

	Parent_0	k1	k2	tb
Parent_0	1	0.2261	-0.03779	-0.01956
k1	0.2261	1	-0.6502	-0.2869
k2	-0.03779	-0.6502	1	-0.1476
tb	-0.01956	-0.2869	-0.1476	1

Observed v. Predicted:

Compartment Parent

Time (days)	Value (%)	Predicted Value	Residual
15	105.6	105.6	0.000864
30	81.22	79.01	2.214
45	68.58	73.37	-4.781
60	70.7	68.12	2.576

Sequence Creation Information:
Fit generated by CAKE version 3.3 (Release)
running on R version 3.0.0 (2013-04-03)

Report Information:
Report generated by CAKE version 3.3 (Release)
CAKE developed by Tessella Ltd, Abingdon, Oxfordshire, UK, sponsored by Syngenta
Running on .NET version 4.0.30319.42000

Data set: Experiment 1 (FOMC)

Study date: Montag, 7. Dezember 2020
Report generated: Montag, 7. Dezember 2020

Model Setup:

Topology: Parent only
Optimiser: IRLS (IRLS Its. 10, IRLS Tol. 1E-05, Max. Its. 100, Tol. 1E-05)
SANN Max Iterations: 10000
Extra Solver Option: Use If Required

Initial Values of Sequence Parameters:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
alpha_Parent	0.1	0 to (unbounded)	No
beta_Parent	0.01	0 to (unbounded)	No

Fit step: Final

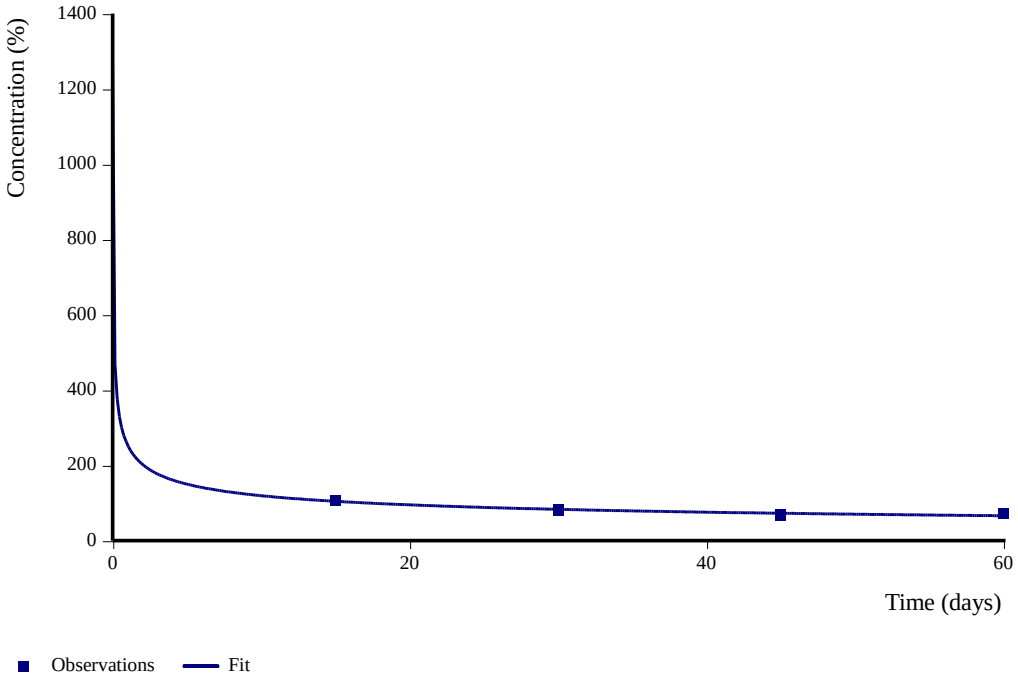
Used Extra Solver: Yes

Reference Table:

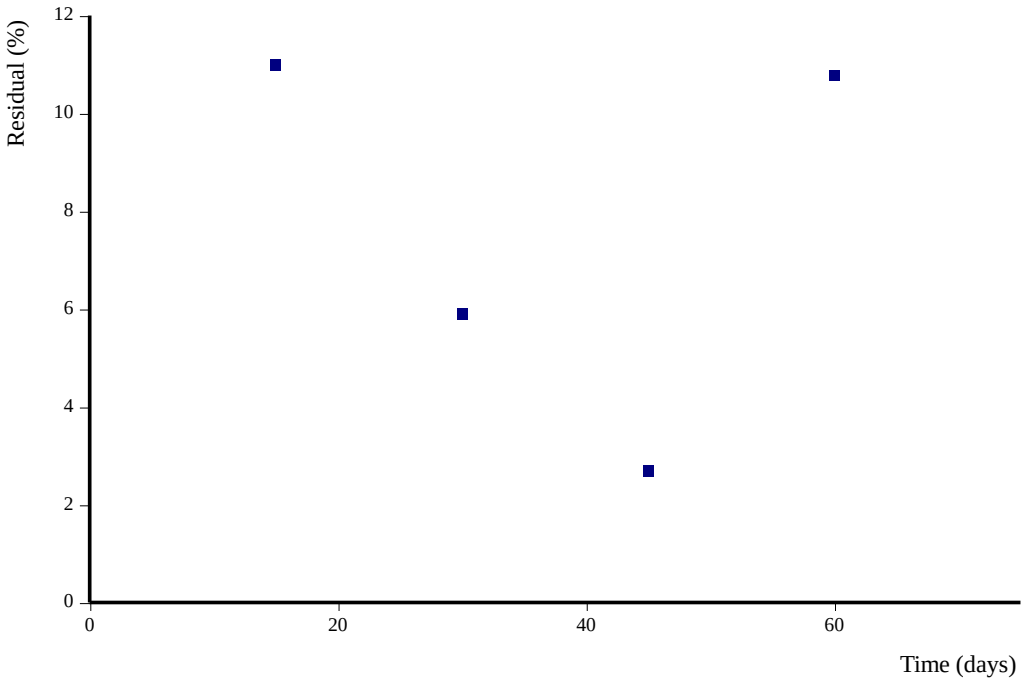
Compartment	Name
Parent	Parent

Graphical Summary:

Observations and Fitted Model:



Residuals:



Initial Values for this Step:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
alpha_Parent	0.1	0 to (unbounded)	No
beta_Parent	0.01	0 to (unbounded)	No

Estimated Values:

Parameter	Value	σ	Prob. > t	Lower (90%) CI	Upper (90%) CI	Lower (95%) CI	Upper (95%) CI
Parent_0	1.26E+003	795.9	N/A	-3762	6.29E+003	-8850	1.14E+004
alpha	0.3299	0.0745	N/A	-0.1405	0.8002	-0.6167	1.276
beta	0.007817	0.005087	N/A	-0.0243	0.03994	-0.05682	0.072

χ^2

Parameter	Error %	Degrees of Freedom
All data	10.5	1
Parent	10.5	1

Decay Times:

Compartment	DT50 (days)	DT90 (days)	DT90 / 3.32 (days)
Parent	0.0561	8.4	2.53E+03

Additional Statistics:

Parameter	r^2 (Obs v Pred)	Efficiency
All data	0.9507	0.6779
Parent	0.9507	0.6779

Parameter Correlation:

	Parent_0	alpha	beta
Parent_0	1	0.9386	-0.2638
alpha	0.9386	1	0.07924
beta	-0.2638	0.07924	1

Observed v. Predicted:

Compartment Parent

Time (days)	Value (%)	Predicted Value	Residual
15	105.6	94.66	10.98
30	81.22	75.31	5.91
45	68.58	65.89	2.698
60	70.7	59.92	10.78

Sequence Creation Information:
Fit generated by CAKE version 3.3 (Release)
running on R version 3.0.0 (2013-04-03)

Report Information:
Report generated by CAKE version 3.3 (Release)
CAKE developed by Tessella Ltd, Abingdon, Oxfordshire, UK, sponsored by Syngenta
Running on .NET version 4.0.30319.42000

1,4-dioxane

Data set: Experiment 1 (SFO)

Study date: Donnerstag, 1. Oktober 2020
Report generated: Donnerstag, 1. Oktober 2020

Model Setup:

Topology: Parent only
Optimiser: IRLS (IRLS Its. 10, IRLS Tol. 1E-05, Max. Its. 100, Tol. 1E-05)
SANN Max Iterations: 10000
Extra Solver Option: Use If Required

Initial Values of Sequence Parameters:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k_Parent	0.1	0 to (unbounded)	No

Fit step: Final

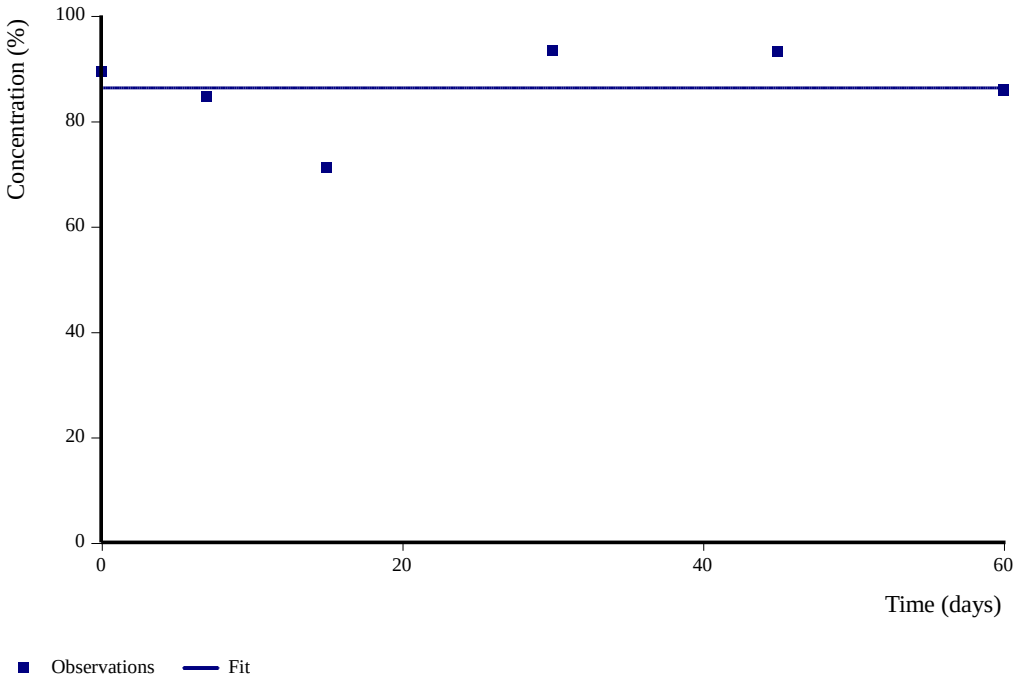
Used Extra Solver: No

Reference Table:

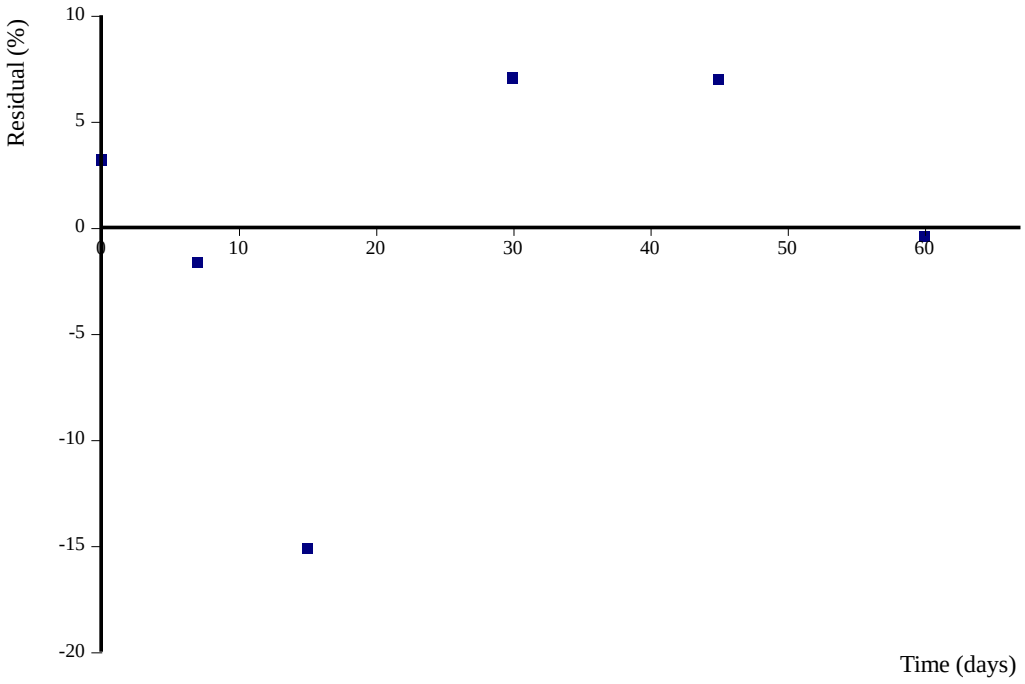
Compartment	Name
Parent	Parent

Graphical Summary:

Observations and Fitted Model:



Residuals:



Initial Values for this Step:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k_Parent	0.1	0 to (unbounded)	No

Estimated Values:

Parameter	Value	σ	Prob. > t	Lower (90%) CI	Upper (90%) CI	Lower (95%) CI	Upper (95%) CI
Parent_0	86.23	5.986	N/A	73.47	98.99	69.61	102.9
k_Parent	2.20E-014	0.002062	0.5	-0.004396	0.004396	-0.005726	0.006

χ^2

Parameter	Error %	Degrees of Freedom
All data	6.95	4
Parent	6.95	4

Decay Times:

Compartment	DT50 (days)	DT90 (days)
Parent	>10,000	>10,000

Additional Statistics:

Parameter	r^2 (Obs v Pred)	Efficiency
All data	0.07442	1.323E-06
Parent	0.07442	1.323E-06

Parameter Correlation:

	Parent_0	k_Parent
Parent_0	1	0.7773
k_Parent	0.7773	1

Observed v. Predicted:

Compartment Parent

Time (days)	Value (%)	Predicted Value	Residual
0	89.4	86.23	3.167
7	84.6	86.23	-1.633
15	71.1	86.23	-15.13
30	93.3	86.23	7.067
45	93.2	86.23	6.967
60	85.8	86.23	-0.4334

Sequence Creation Information:
Fit generated by CAKE version 3.3 (Release)
running on R version 3.0.0 (2013-04-03)

Report Information:
Report generated by CAKE version 3.3 (Release)
CAKE developed by Tessella Ltd, Abingdon, Oxfordshire, UK, sponsored by Syngenta
Running on .NET version 4.0.30319.42000

Data set: Experiment 1 (DFOP)

Study date: Donnerstag, 1. Oktober 2020
Report generated: Donnerstag, 1. Oktober 2020

Model Setup:

Topology: Parent only
Optimiser: IRLS (IRLS Its. 10, IRLS Tol. 1E-05, Max. Its. 100, Tol. 1E-05)
SANN Max Iterations: 10000
Extra Solver Option: Use If Required

Initial Values of Sequence Parameters:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k1_Parent	0.1	0 to (unbounded)	No
k2_Parent	0.01	0 to (unbounded)	No
g_Parent	0.5	0 to 1	No

Fit step: Final

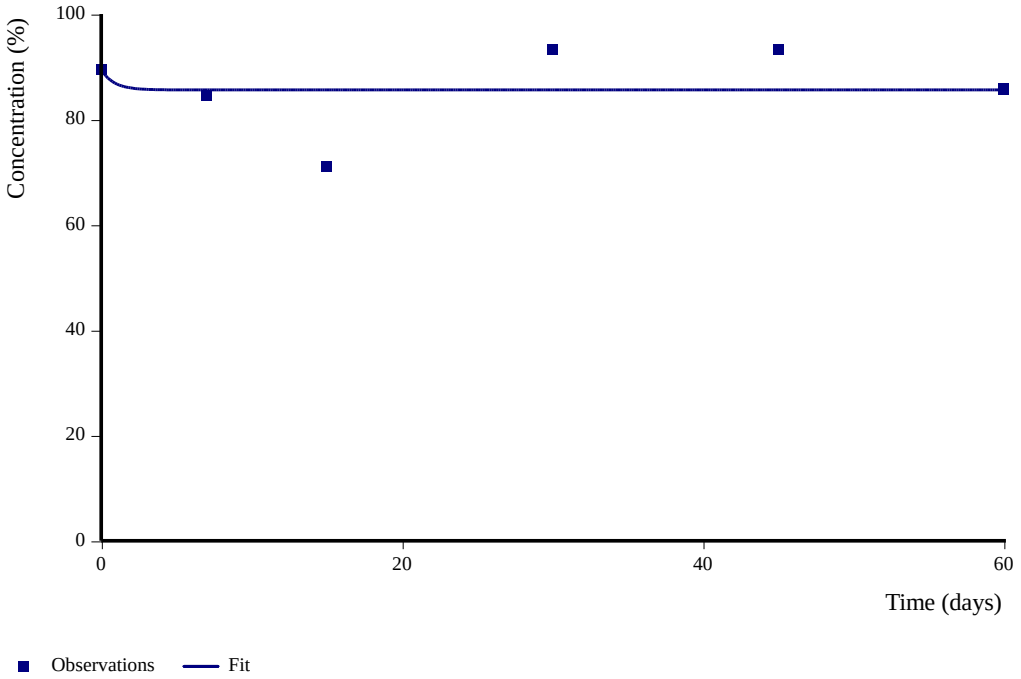
Used Extra Solver: Yes

Reference Table:

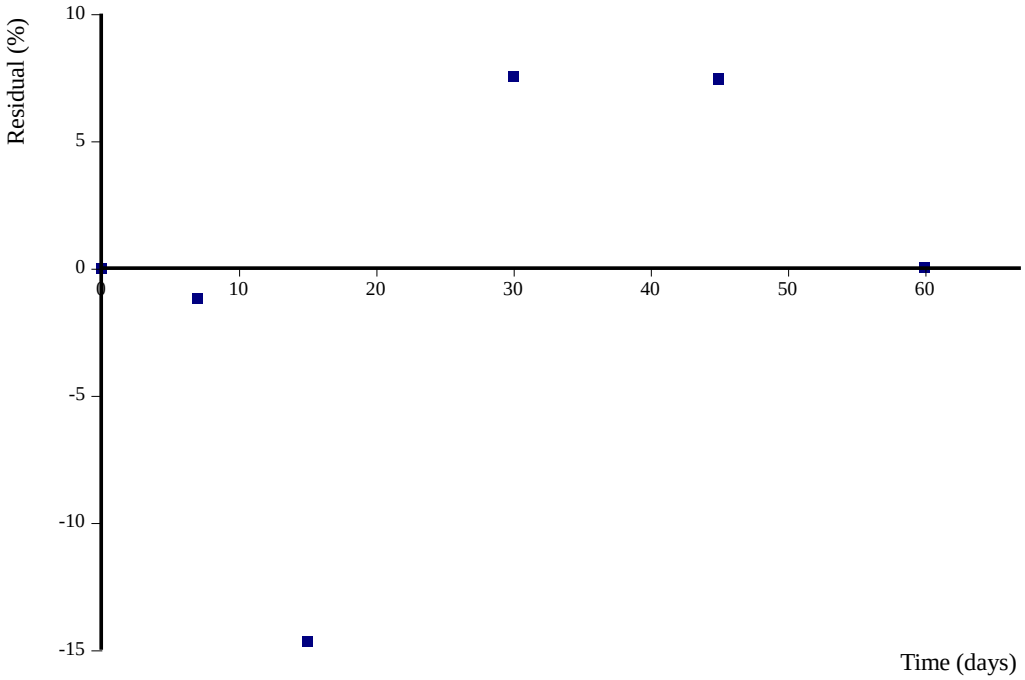
Compartment	Name
Parent	Parent

Graphical Summary:

Observations and Fitted Model:



Residuals:



Initial Values for this Step:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k1_Parent	0.1	0 to (unbounded)	No
k2_Parent	0.01	0 to (unbounded)	No
g_Parent	0.5	0 to 1	No

Estimated Values:

Parameter	Value	σ	Prob. > t	Lower (90%) CI	Upper (90%) CI	Lower (95%) CI	Upper (95%) CI
Parent_0	89.4	12.81	N/A	51.99	126.8	34.27	144.5
k1_Parent	1.187	58.53	0.4928	-169.7	172.1	-250.6	253
k2_Parent	9.50E-015	0.003419	0.5	-0.009983	0.009983	-0.01471	0.015
g_Parent	0.04251	0.1817	N/A	-0.488	0.573	-0.7392	0.824

χ^2

Parameter	Error %	Degrees of Freedom
All data	8.59	2
Parent	8.59	2

Decay Times:

Compartment	DT50 (overall days)	DT90 (overall days)	k1 DT50 (days)	k2 DT50 (days)
Parent	>10,000	>10,000	0.584	>10,000

Additional Statistics:

Parameter	r^2 (Obs v Pred)	Efficiency
All data	0.03535	0.03488
Parent	0.03535	0.03488

Parameter Correlation:

	Parent_0	k1_Parent	k2_Parent	g_Parent
Parent_0	1	0.006738	-6.271E-05	0.7554
k1_Parent	0.006738	1	0.01142	-0.004865
k2_Parent	-6.271E-05	0.01142	1	-0.5522
g_Parent	0.7554	-0.004865	-0.5522	1

Observed v. Predicted:

Compartment Parent

Time (days)	Value (%)	Predicted Value	Residual
0	89.4	89.4	0.0002961
7	84.6	85.78	-1.179
15	71.1	85.78	-14.68
30	93.3	85.78	7.521
45	93.2	85.78	7.421
60	85.8	85.78	0.02136

Sequence Creation Information:
Fit generated by CAKE version 3.3 (Release)
running on R version 3.0.0 (2013-04-03)

Report Information:
Report generated by CAKE version 3.3 (Release)
CAKE developed by Tessella Ltd, Abingdon, Oxfordshire, UK, sponsored by Syngenta
Running on .NET version 4.0.30319.42000

Data set: Experiment 1 (HS)

Study date: Donnerstag, 1. Oktober 2020
Report generated: Donnerstag, 1. Oktober 2020

Model Setup:

Topology: Parent only
Optimiser: IRLS (IRLS Its. 10, IRLS Tol. 1E-05, Max. Its. 100, Tol. 1E-05)
SANN Max Iterations: 10000
Extra Solver Option: Use If Required

Initial Values of Sequence Parameters:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k1_Parent	0.1	0 to (unbounded)	No
k2_Parent	0.01	0 to (unbounded)	No
tb_Parent	Automatic	0 to (unbounded)	No

Fit step: Final

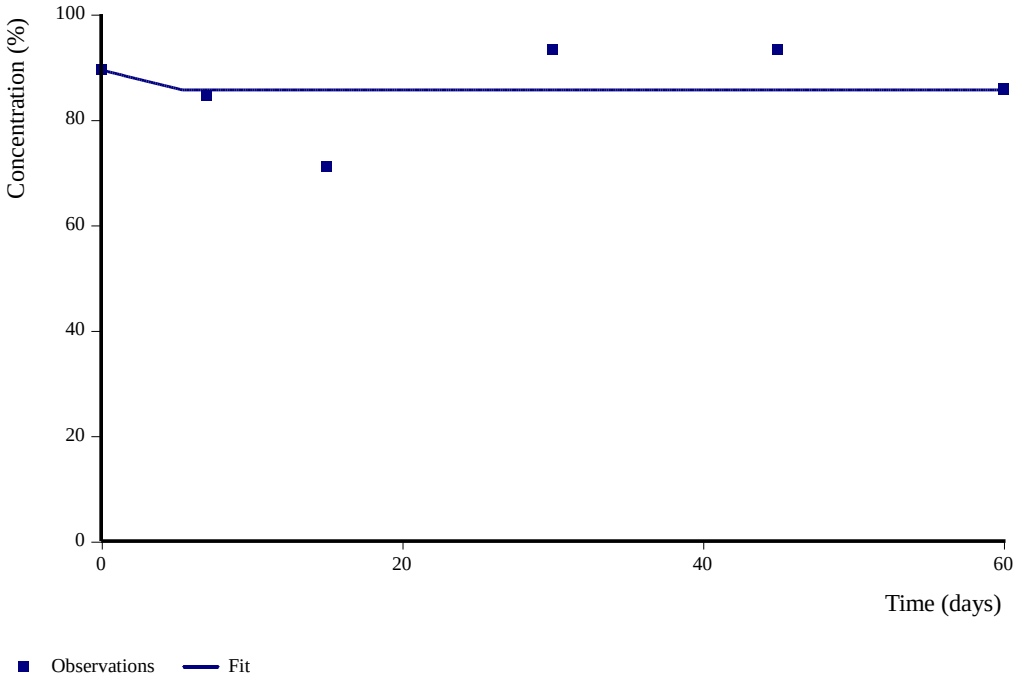
Used Extra Solver: Yes

Reference Table:

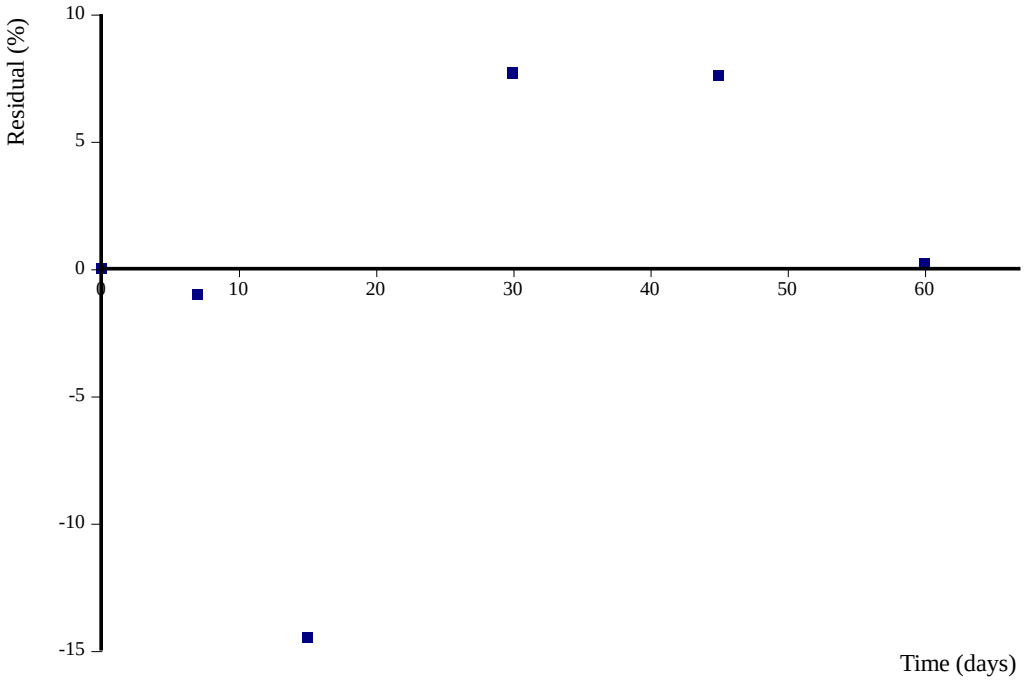
Compartment	Name
Parent	Parent

Graphical Summary:

Observations and Fitted Model:



Residuals:



Initial Values for this Step:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k1_Parent	0.1	0 to (unbounded)	No
k2_Parent	0.01	0 to (unbounded)	No
tb_Parent	15.37	0 to (unbounded)	No

Estimated Values:

Parameter	Value	σ	Prob. > t	Lower (90%) CI	Upper (90%) CI	Lower (95%) CI	Upper (95%) CI
Parent_0	89.4	12.92	N/A	51.68	127.1	33.82	145
k1	0.008052	0.04454	0.4366	-0.122	0.1381	-0.1836	0.2
k2	3.05E-011	0.003582	0.5	-0.01046	0.01046	-0.01541	0.015
tb	5.395	26.11	N/A	-70.85	81.64	-106.9	117.7

χ^2

Parameter	Error %	Degrees of Freedom
All data	8.59	2
Parent	8.59	2

Decay Times:

Compartment	DT50 (overall days)	DT90 (overall days)	k1 DT50 (days)	k2 DT50 (days)
Parent	>10,000	>10,000	86.1	>10,000

Additional Statistics:

Parameter	r^2 (Obs v Pred)	Efficiency
All data	0.03535	0.03535
Parent	0.03535	0.03535

Parameter Correlation:

	Parent_0	k1	k2	tb
Parent_0	1	0.5054	-0.03782	0.1293
k1	0.5054	1	-0.1469	-0.662
k2	-0.03782	-0.1469	1	-0.2958
tb	0.1293	-0.662	-0.2958	1

Observed v. Predicted:

Compartment Parent

Time (days)	Value (%)	Predicted Value	Residual
0	89.4	89.4	-0.0003654
7	84.6	85.6	-1.001
15	71.1	85.6	-14.5
30	93.3	85.6	7.699
45	93.2	85.6	7.599
60	85.8	85.6	0.1985

Sequence Creation Information:
Fit generated by CAKE version 3.3 (Release)
running on R version 3.0.0 (2013-04-03)

Report Information:
Report generated by CAKE version 3.3 (Release)
CAKE developed by Tessella Ltd, Abingdon, Oxfordshire, UK, sponsored by Syngenta
Running on .NET version 4.0.30319.42000

Melamine

Data set: Experiment 1 (SFO)

Study date: Montag, 19. Oktober 2020
Report generated: Montag, 19. Oktober 2020

Model Setup:

Topology: Parent only
Optimiser: IRLS (IRLS Its. 10, IRLS Tol. 1E-05, Max. Its. 100, Tol. 1E-05)
SANN Max Iterations: 10000
Extra Solver Option: Use If Required

Initial Values of Sequence Parameters:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k_Parent	0.1	0 to (unbounded)	No

Fit step: Final

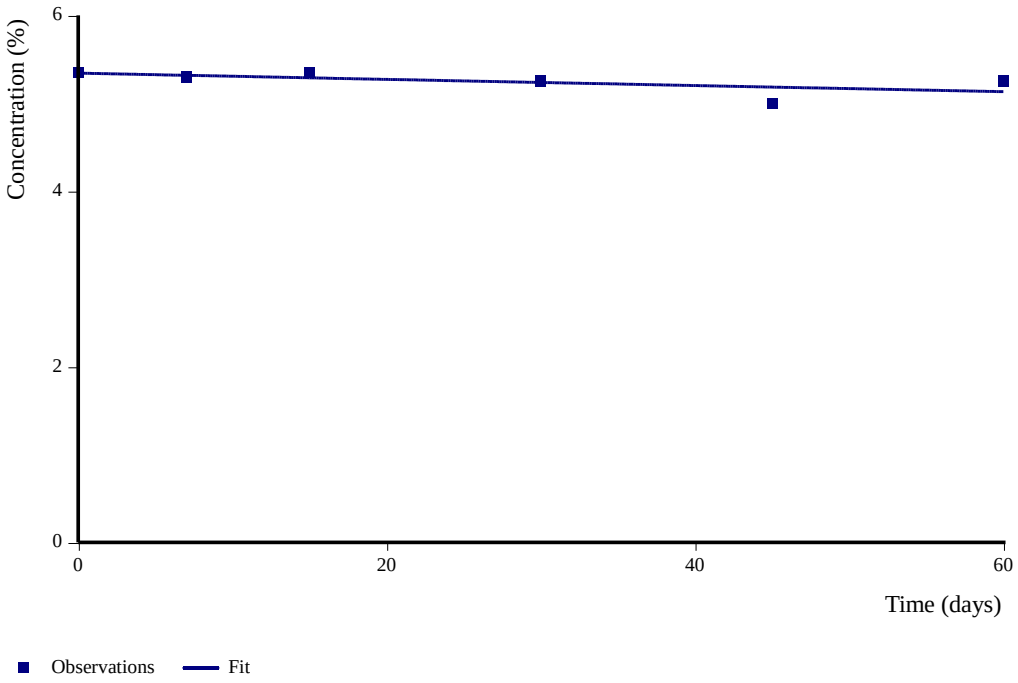
Used Extra Solver: No

Reference Table:

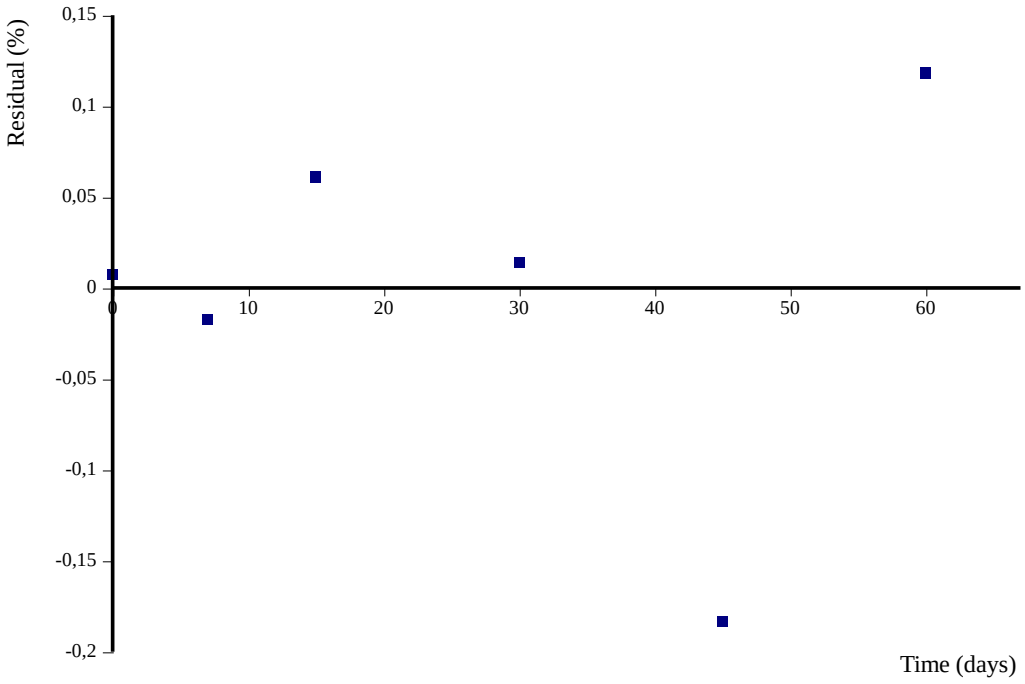
Compartment	Name
Parent	Parent

Graphical Summary:

Observations and Fitted Model:



Residuals:



Initial Values for this Step:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k_Parent	0.1	0 to (unbounded)	No

Estimated Values:

Parameter	Value	σ	Prob. > t	Lower (90%) CI	Upper (90%) CI	Lower (95%) CI	Upper (95%) CI
Parent_0	5.342	0.07446	N/A	5.184	5.501	5.136	5.549
k_Parent	6.71E-004	4.21E-004	0.09306	-0.0002262	0.001567	-0.0004973	0.002

χ^2

Parameter	Error %	Degrees of Freedom
All data	1.41	4
Parent	1.41	4

Decay Times:

Compartment	DT50 (days)	DT90 (days)
Parent	1.03E+03	3.43E+03

Additional Statistics:

Parameter	r^2 (Obs v Pred)	Efficiency
All data	0.3884	0.3884
Parent	0.3884	0.3884

Parameter Correlation:

	Parent_0	k_Parent
Parent_0	1	0.7717
k_Parent	0.7717	1

Observed v. Predicted:

Compartment Parent

Time (days)	Value (%)	Predicted Value	Residual
0	5.35	5.342	0.0076
7	5.3	5.317	-0.01738
15	5.35	5.289	0.06107
30	5.25	5.236	0.01401
45	5	5.184	-0.1836
60	5.25	5.132	0.1183

Sequence Creation Information:
Fit generated by CAKE version 3.3 (Release)
running on R version 3.0.0 (2013-04-03)

Report Information:
Report generated by CAKE version 3.3 (Release)
CAKE developed by Tessella Ltd, Abingdon, Oxfordshire, UK, sponsored by Syngenta
Running on .NET version 4.0.30319.42000

Data set: Experiment 1 (DFOP)

Study date: Montag, 19. Oktober 2020
Report generated: Montag, 19. Oktober 2020

Model Setup:

Topology: Parent only
Optimiser: IRLS (IRLS Its. 10, IRLS Tol. 1E-05, Max. Its. 100, Tol. 1E-05)
SANN Max Iterations: 10000
Extra Solver Option: Use If Required

Initial Values of Sequence Parameters:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k1_Parent	0.1	0 to (unbounded)	No
k2_Parent	0.01	0 to (unbounded)	No
g_Parent	0.5	0 to 1	No

Fit step: Final

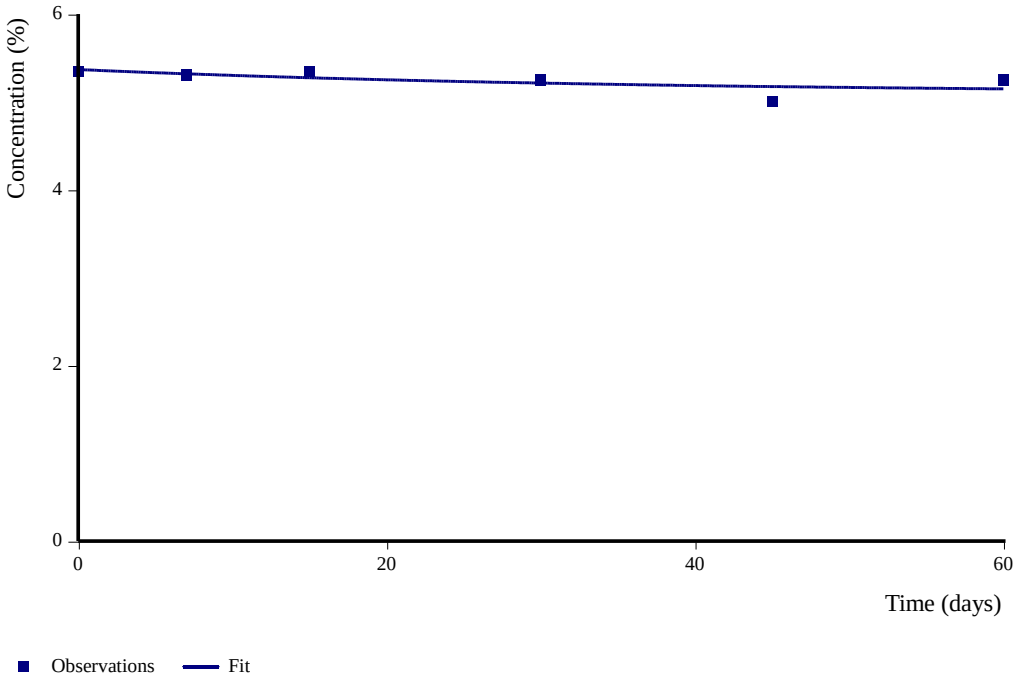
Used Extra Solver: No

Reference Table:

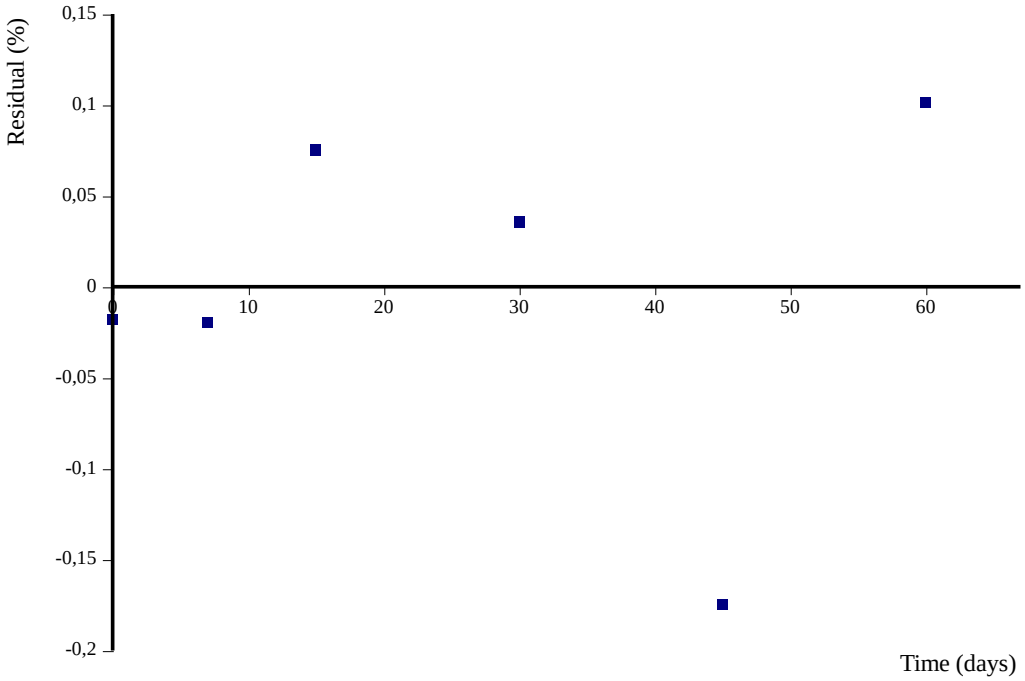
Compartment	Name
Parent	Parent

Graphical Summary:

Observations and Fitted Model:



Residuals:



Initial Values for this Step:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k1_Parent	0.1	0 to (unbounded)	No
k2_Parent	0.01	0 to (unbounded)	No
g_Parent	0.5	0 to 1	No

Estimated Values:

Parameter	Value	σ	Prob. > t	Lower (90%) CI	Upper (90%) CI	Lower (95%) CI	Upper (95%) CI
Parent_0	5.368	0.1492	N/A	4.932	5.804	4.726	6.01
k1_Parent	0.0285	0.6988	0.4856	-2.012	2.069	-2.978	3.035
k2_Parent	3.05E-014	0.01675	0.5	-0.0489	0.0489	-0.07206	0.072
g_Parent	0.04989	1.596	N/A	-4.611	4.71	-6.817	6.917

χ^2

Parameter	Error %	Degrees of Freedom
All data	1.71	2
Parent	1.71	2

Decay Times:

Compartment	DT50 (overall days)	DT90 (overall days)	k1 DT50 (days)	k2 DT50 (days)
Parent	>10,000	>10,000	24.3	>10,000

Additional Statistics:

Parameter	r^2 (Obs v Pred)	Efficiency
All data	0.4311	0.4311
Parent	0.4311	0.4311

Parameter Correlation:

	Parent_0	k1_Parent	k2_Parent	g_Parent
Parent_0	1	0.44	0.3607	-0.3694
k1_Parent	0.44	1	0.9872	-0.9934
k2_Parent	0.3607	0.9872	1	-0.9985
g_Parent	-0.3694	-0.9934	-0.9985	1

Observed v. Predicted:

Compartment Parent

Time (days)	Value (%)	Predicted Value	Residual
0	5.35	5.368	-0.01805
7	5.3	5.32	-0.01961
15	5.35	5.275	0.07509
30	5.25	5.214	0.03583
45	5	5.175	-0.1746
60	5.25	5.149	0.1013

Sequence Creation Information:
Fit generated by CAKE version 3.3 (Release)
running on R version 3.0.0 (2013-04-03)

Report Information:
Report generated by CAKE version 3.3 (Release)
CAKE developed by Tessella Ltd, Abingdon, Oxfordshire, UK, sponsored by Syngenta
Running on .NET version 4.0.30319.42000

Data set: Experiment 1 (HS)

Study date: Montag, 19. Oktober 2020
Report generated: Montag, 19. Oktober 2020

Model Setup:

Topology: Parent only
Optimiser: IRLS (IRLS Its. 10, IRLS Tol. 1E-05, Max. Its. 100, Tol. 1E-05)
SANN Max Iterations: 10000
Extra Solver Option: Use If Required

Initial Values of Sequence Parameters:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k1_Parent	0.1	0 to (unbounded)	No
k2_Parent	0.01	0 to (unbounded)	No
tb_Parent	Automatic	0 to (unbounded)	No

Fit step: Final

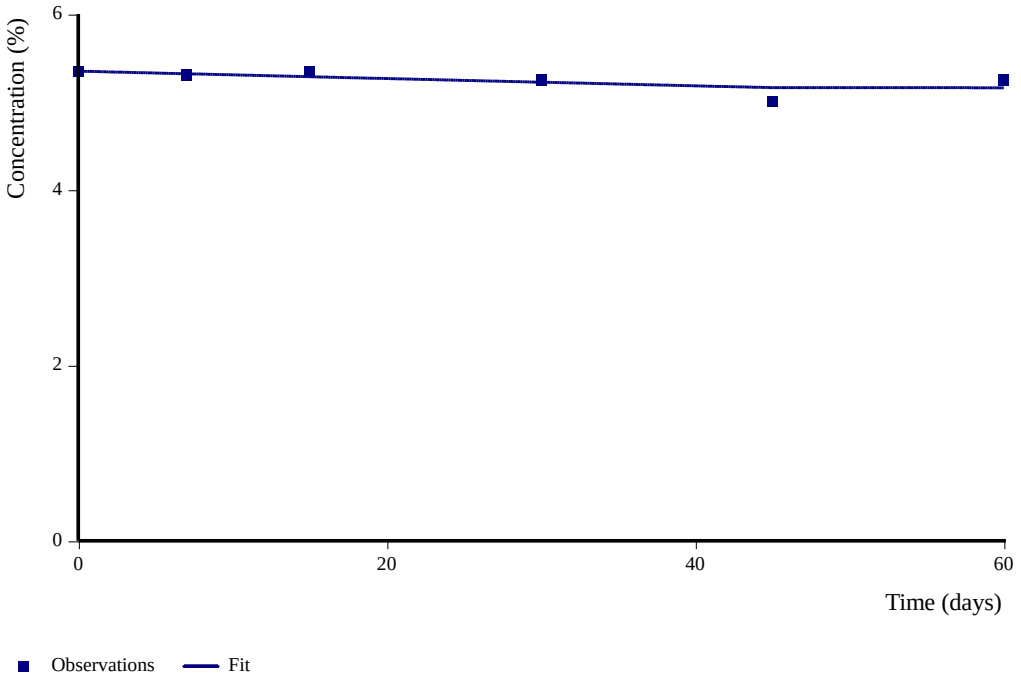
Used Extra Solver: No

Reference Table:

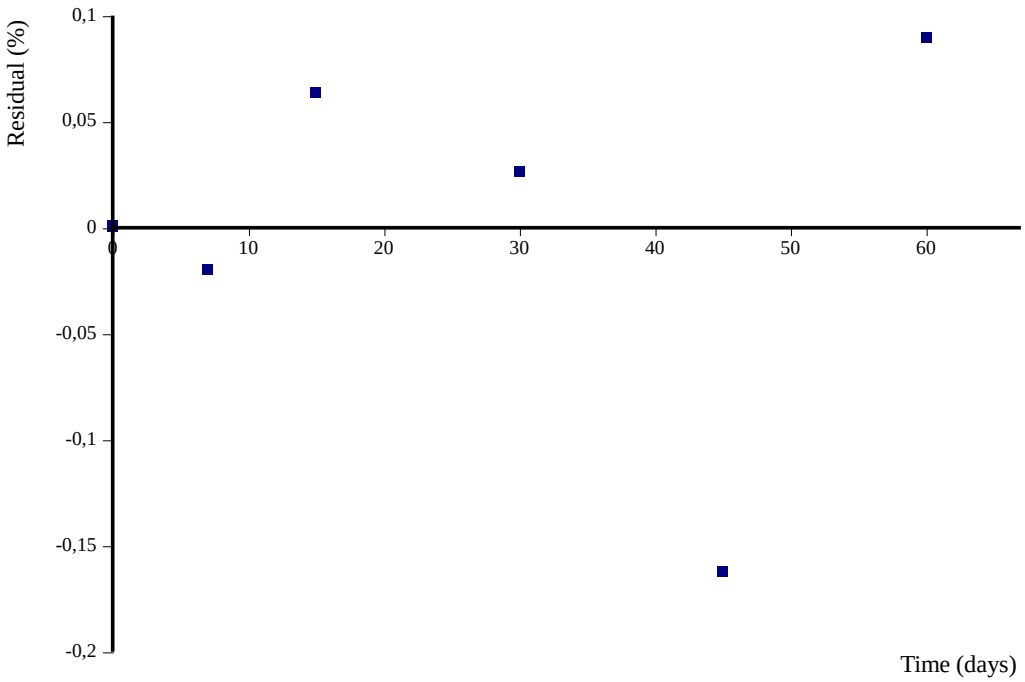
Compartment	Name
Parent	Parent

Graphical Summary:

Observations and Fitted Model:



Residuals:



Initial Values for this Step:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k1_Parent	0.1	0 to (unbounded)	No
k2_Parent	0.01	0 to (unbounded)	No
tb_Parent	18.4	0 to (unbounded)	No

Estimated Values:

Parameter	Value	σ	Prob. > t	Lower (90%) CI	Upper (90%) CI	Lower (95%) CI	Upper (95%) CI
Parent_0	5.349	0.1082	N/A	5.033	5.665	4.884	5.815
k1	7.93E-004	0.001193	0.2874	-0.002692	0.004278	-0.004342	0.006
k2	1.22E-005	0.002456	0.4982	-0.00716	0.007184	-0.01056	0.011
tb	45.1	104.5	N/A	-260	350.1	-404.4	494.6

χ^2

Parameter	Error %	Degrees of Freedom
All data	1.55	2
Parent	1.55	2

Decay Times:

Compartment	DT50 (overall days)	DT90 (overall days)	k1 DT50 (days)	k2 DT50 (days)
Parent	>10,000	>10,000	874	>10,000

Additional Statistics:

Parameter	r^2 (Obs v Pred)	Efficiency
All data	0.5514	0.5359
Parent	0.5514	0.5359

Parameter Correlation:

	Parent_0	k1	k2	tb
Parent_0	1	0.7552	-0.1046	-0.4133
k1	0.7552	1	-0.1935	-0.7826
k2	-0.1046	-0.1935	1	-0.1846
tb	-0.4133	-0.7826	-0.1846	1

Observed v. Predicted:

Compartment Parent

Time (days)	Value (%)	Predicted Value	Residual
0	5.35	5.349	0.0006768
7	5.3	5.32	-0.01971
15	5.35	5.286	0.06393
30	5.25	5.224	0.02644
45	5	5.162	-0.1621
60	5.25	5.16	0.08951

Sequence Creation Information:
Fit generated by CAKE version 3.3 (Release)
running on R version 3.0.0 (2013-04-03)

Report Information:
Report generated by CAKE version 3.3 (Release)
CAKE developed by Tessella Ltd, Abingdon, Oxfordshire, UK, sponsored by Syngenta
Running on .NET version 4.0.30319.42000

Data set: Experiment 1 (FOMC)

Study date: Montag, 19. Oktober 2020
Report generated: Montag, 19. Oktober 2020

Model Setup:

Topology: Parent only
Optimiser: IRLS (IRLS Its. 10, IRLS Tol. 1E-05, Max. Its. 100, Tol. 1E-05)
SANN Max Iterations: 10000
Extra Solver Option: Use If Required

Initial Values of Sequence Parameters:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
alpha_Parent	0.1	0 to (unbounded)	No
beta_Parent	0.01	0 to (unbounded)	No

Fit step: Final

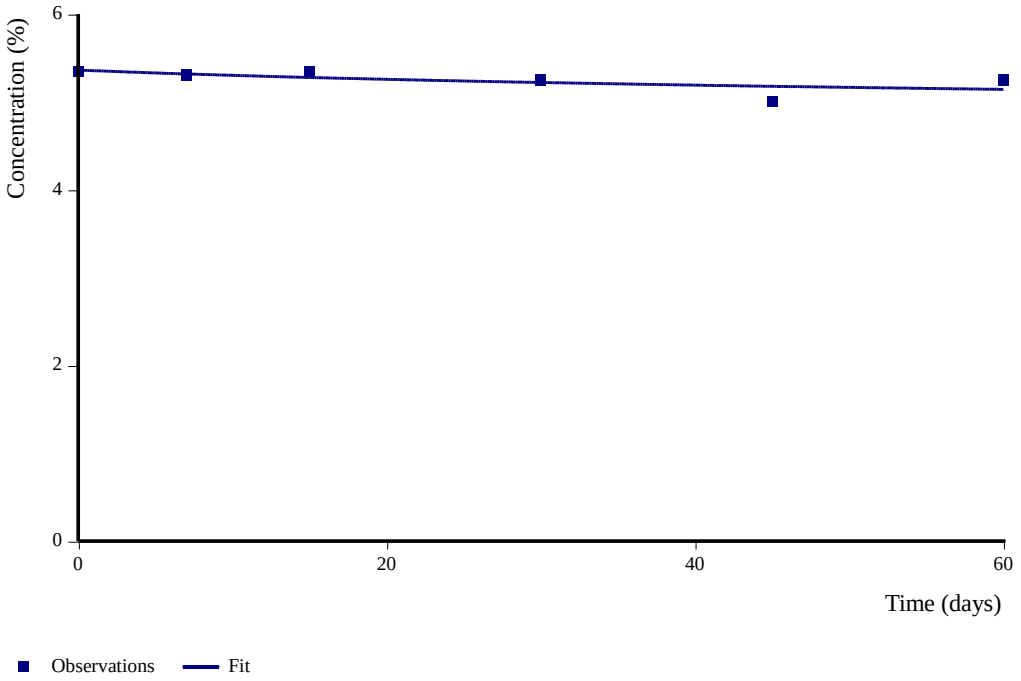
Used Extra Solver: No

Reference Table:

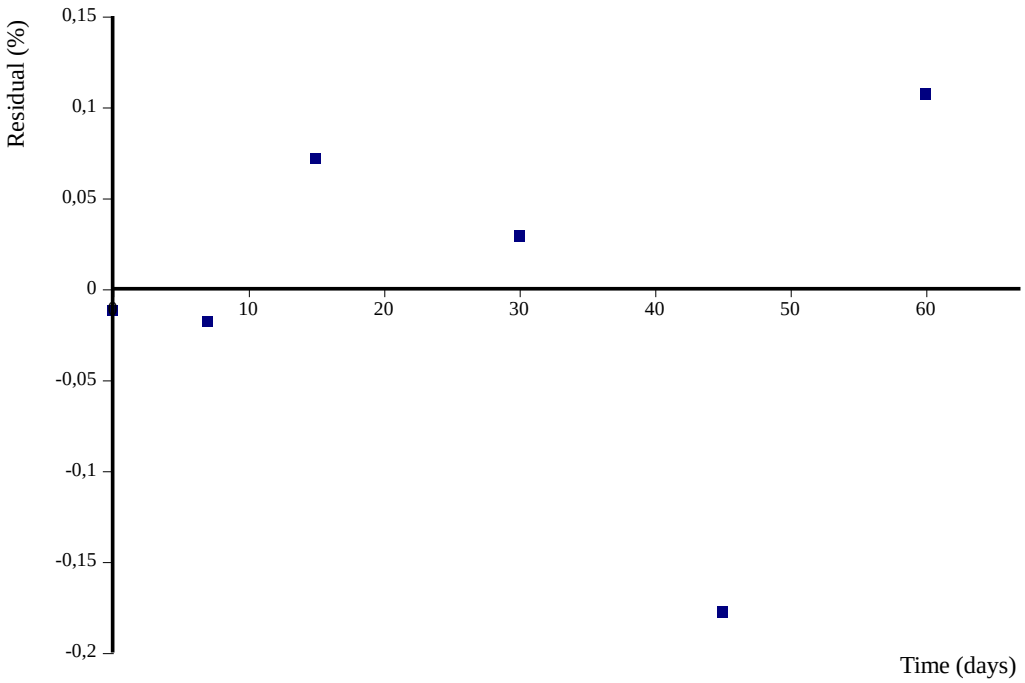
Compartment	Name
Parent	Parent

Graphical Summary:

Observations and Fitted Model:



Residuals:



Initial Values for this Step:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
alpha_Parent	0.1	0 to (unbounded)	No
beta_Parent	0.01	0 to (unbounded)	No

Estimated Values:

Parameter	Value	σ	Prob. > t	Lower (90%) CI	Upper (90%) CI	Lower (95%) CI	Upper (95%) CI
Parent_0	5.362	0.1198	N/A	5.08	5.644	4.981	5.743
alpha	0.03539	0.1511	N/A	-0.3203	0.391	-0.4456	0.516
beta	26.66	193.7	N/A	-429.1	482.4	-589.7	643

χ^2

Parameter	Error %	Degrees of Freedom
All data	1.52	3
Parent	1.52	3

Decay Times:

Compartment	DT50 (days)	DT90 (days)	DT90 / 3.32 (days)
Parent	>10,000	>10,000	>10,000

Additional Statistics:

Parameter	r^2 (Obs v Pred)	Efficiency
All data	0.4174	0.4174
Parent	0.4174	0.4174

Parameter Correlation:

	Parent_0	alpha	beta
Parent_0	1	-0.5201	-0.6296
alpha	-0.5201	1	0.9872
beta	-0.6296	0.9872	1

Observed v. Predicted:

Compartment Parent

Time (days)	Value (%)	Predicted Value	Residual
0	5.35	5.362	-0.01213
7	5.3	5.318	-0.01807
15	5.35	5.278	0.07191
30	5.25	5.221	0.02905
45	5	5.178	-0.1777
60	5.25	5.143	0.107

Sequence Creation Information:
Fit generated by CAKE version 3.3 (Release)
running on R version 3.0.0 (2013-04-03)

Report Information:
Report generated by CAKE version 3.3 (Release)
CAKE developed by Tessella Ltd, Abingdon, Oxfordshire, UK, sponsored by Syngenta
Running on .NET version 4.0.30319.42000

Urotropin

Data set: Experiment 1 (SFO)

Study date: Montag, 19. Oktober 2020
Report generated: Montag, 19. Oktober 2020

Model Setup:

Topology: Parent only
Optimiser: IRLS (IRLS Its. 10, IRLS Tol. 1E-05, Max. Its. 100, Tol. 1E-05)
SANN Max Iterations: 10000
Extra Solver Option: Use If Required

Initial Values of Sequence Parameters:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k_Parent	0.1	0 to (unbounded)	No

Fit step: Final

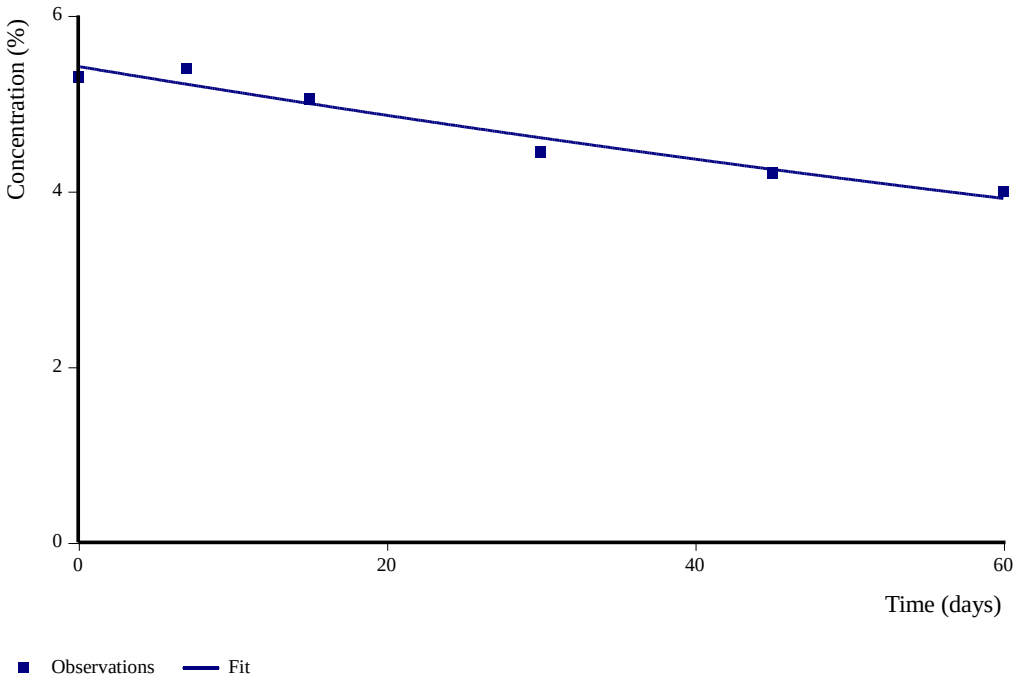
Used Extra Solver: No

Reference Table:

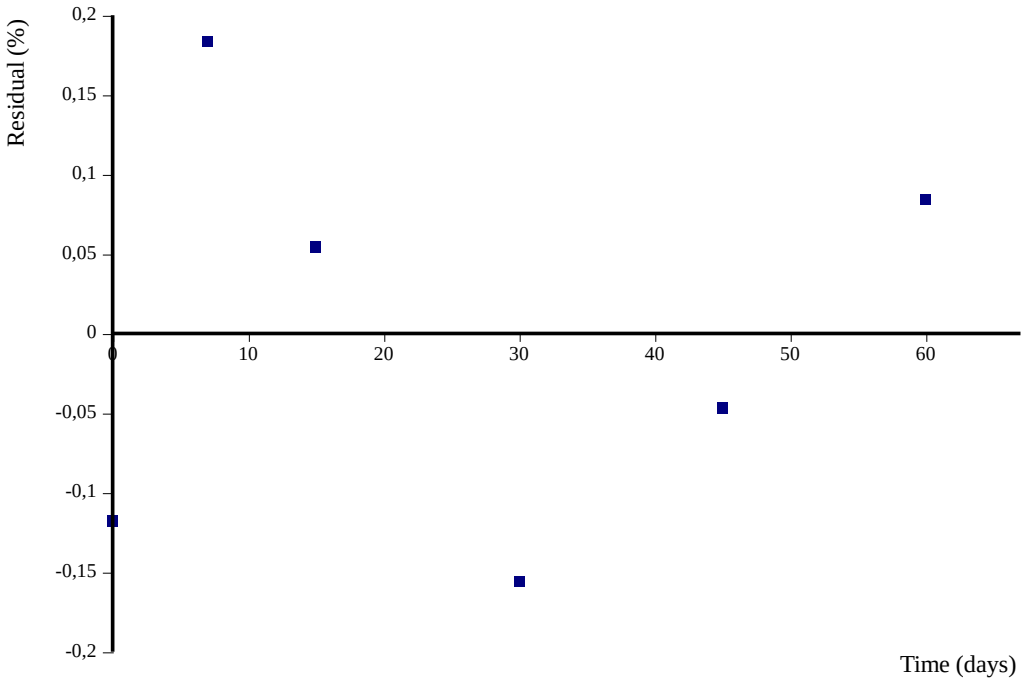
Compartment	Name
Parent	Parent

Graphical Summary:

Observations and Fitted Model:



Residuals:



Initial Values for this Step:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k_Parent	0.1	0 to (unbounded)	No

Estimated Values:

Parameter	Value	σ	Prob. > t	Lower (90%) CI	Upper (90%) CI	Lower (95%) CI	Upper (95%) CI
Parent_0	5.418	0.09897	N/A	5.207	5.629	5.143	5.693
k_Parent	0.005412	6.21E-004	4.78E-004	0.004088	0.006736	0.003687	0.007

χ^2

Parameter	Error %	Degrees of Freedom
All data	1.99	4
Parent	1.99	4

Decay Times:

Compartment	DT50 (days)	DT90 (days)
Parent	128	426

Additional Statistics:

Parameter	r^2 (Obs v Pred)	Efficiency
All data	0.9524	0.9524
Parent	0.9524	0.9524

Parameter Correlation:

	Parent_0	k_Parent
Parent_0	1	0.7326
k_Parent	0.7326	1

Observed v. Predicted:

Compartment Parent

Time (days)	Value (%)	Predicted Value	Residual
0	5.3	5.418	-0.118
7	5.4	5.217	0.1834
15	5.05	4.996	0.05442
30	4.45	4.606	-0.1561
45	4.2	4.247	-0.04697
60	4	3.916	0.08416

Sequence Creation Information:
Fit generated by CAKE version 3.3 (Release)
running on R version 3.0.0 (2013-04-03)

Report Information:
Report generated by CAKE version 3.3 (Release)
CAKE developed by Tessella Ltd, Abingdon, Oxfordshire, UK, sponsored by Syngenta
Running on .NET version 4.0.30319.42000

Data set: Experiment 1 (DFOP)

Study date: Montag, 19. Oktober 2020
Report generated: Montag, 19. Oktober 2020

Model Setup:

Topology: Parent only
Optimiser: IRLS (IRLS Its. 10, IRLS Tol. 1E-05, Max. Its. 100, Tol. 1E-05)
SANN Max Iterations: 10000
Extra Solver Option: Use If Required

Initial Values of Sequence Parameters:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k1_Parent	0.1	0 to (unbounded)	No
k2_Parent	0.01	0 to (unbounded)	No
g_Parent	0.5	0 to 1	No

Fit step: Final

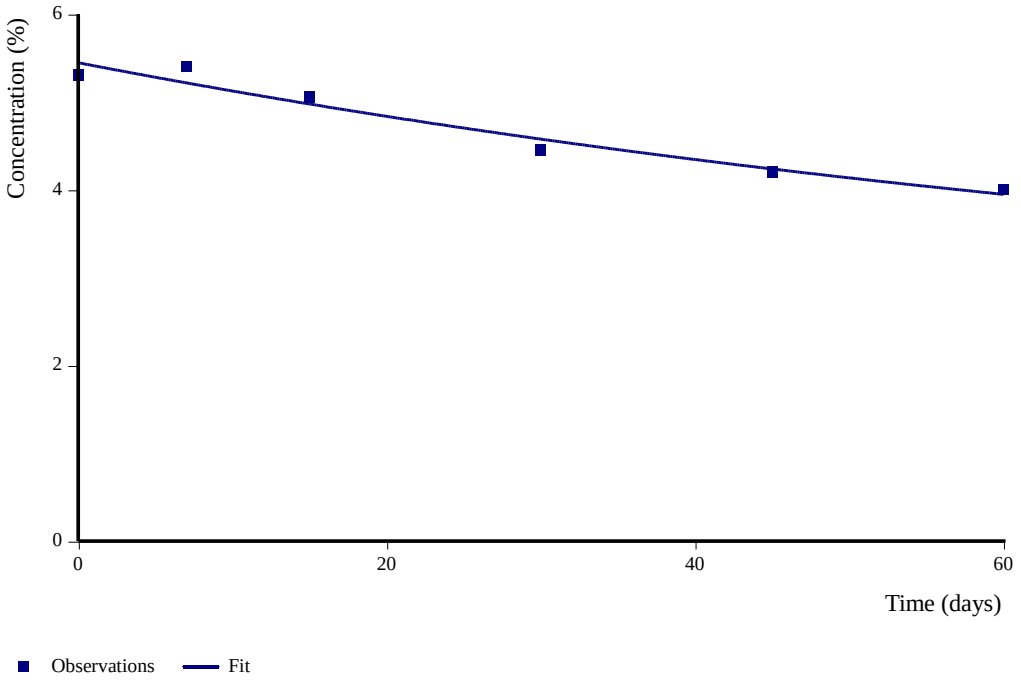
Used Extra Solver: No

Reference Table:

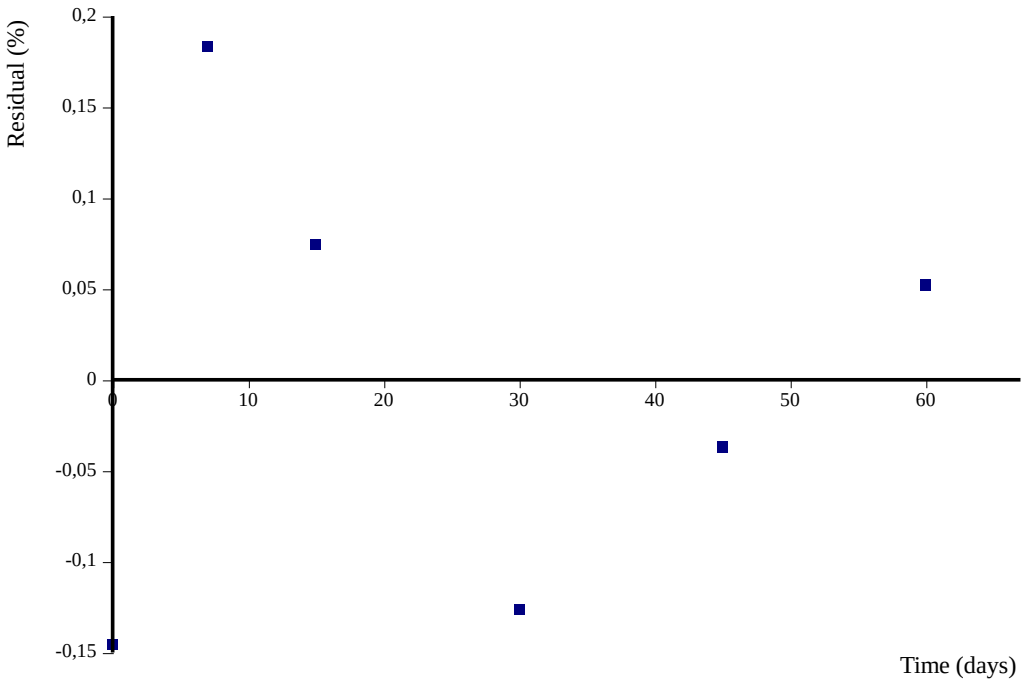
Compartment	Name
Parent	Parent

Graphical Summary:

Observations and Fitted Model:



Residuals:



Initial Values for this Step:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k1_Parent	0.1	0 to (unbounded)	No
k2_Parent	0.01	0 to (unbounded)	No
g_Parent	0.5	0 to 1	No

Estimated Values:

Parameter	Value	σ	Prob. > t	Lower (90%) CI	Upper (90%) CI	Lower (95%) CI	Upper (95%) CI
Parent_0	5.446	0.1895	N/A	4.892	5.999	4.63	6.261
k1_Parent	0.01082	0.3274	0.4883	-0.9451	0.9668	-1.398	1.419
k2_Parent	2.92E-022	0.324	0.5	-0.9461	0.9461	-1.394	1.394
g_Parent	0.5758	29.57	N/A	-85.77	86.92	-126.7	127.8

χ^2

Parameter	Error %	Degrees of Freedom
All data	2.45	2
Parent	2.45	2

Decay Times:

Compartment	DT50 (overall days)	DT90 (overall days)	k1 DT50 (days)	k2 DT50 (days)
Parent	187	>10,000	64	>10,000

Additional Statistics:

Parameter	r^2 (Obs v Pred)	Efficiency
All data	0.9546	0.9546
Parent	0.9546	0.9546

Parameter Correlation:

	Parent_0	k1_Parent	k2_Parent	g_Parent
Parent_0	1	0.4691	0.4383	-0.4502
k1_Parent	0.4691	1	0.9982	-0.9994
k2_Parent	0.4383	0.9982	1	-0.9997
g_Parent	-0.4502	-0.9994	-0.9997	1

Observed v. Predicted:

Compartment Parent

Time (days)	Value (%)	Predicted Value	Residual
0	5.3	5.446	-0.1458
7	5.4	5.217	0.183
15	5.05	4.976	0.0741
30	4.45	4.576	-0.1264
45	4.2	4.237	-0.03682
60	4	3.948	0.0519

Sequence Creation Information:
Fit generated by CAKE version 3.3 (Release)
running on R version 3.0.0 (2013-04-03)

Report Information:
Report generated by CAKE version 3.3 (Release)
CAKE developed by Tessella Ltd, Abingdon, Oxfordshire, UK, sponsored by Syngenta
Running on .NET version 4.0.30319.42000

Data set: Experiment 1 (HS)

Study date: Montag, 19. Oktober 2020
Report generated: Montag, 19. Oktober 2020

Model Setup:

Topology: Parent only
Optimiser: IRLS (IRLS Its. 10, IRLS Tol. 1E-05, Max. Its. 100, Tol. 1E-05)
SANN Max Iterations: 10000
Extra Solver Option: Use If Required

Initial Values of Sequence Parameters:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k1_Parent	0.1	0 to (unbounded)	No
k2_Parent	0.01	0 to (unbounded)	No
tb_Parent	Automatic	0 to (unbounded)	No

Fit step: Final

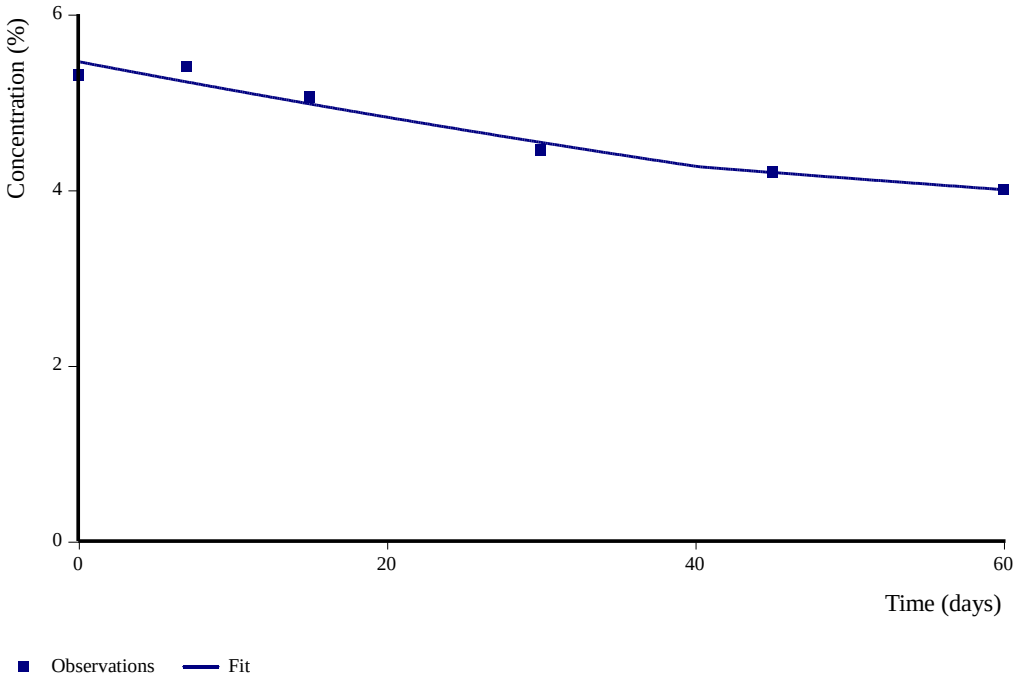
Used Extra Solver: Yes

Reference Table:

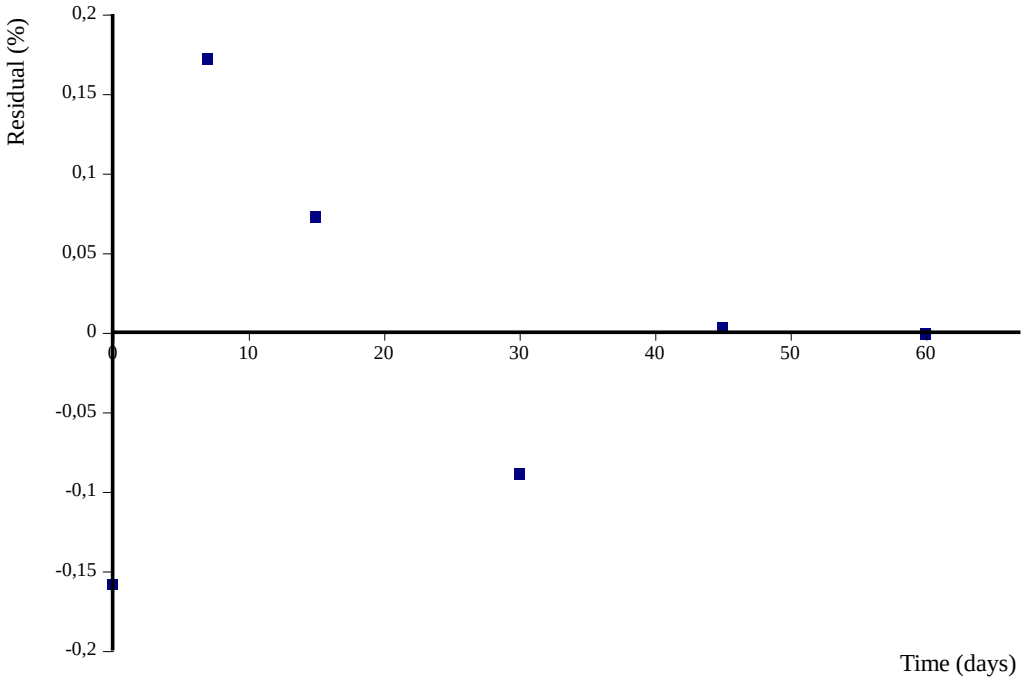
Compartment	Name
Parent	Parent

Graphical Summary:

Observations and Fitted Model:



Residuals:



Initial Values for this Step:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
k1_Parent	0.1	0 to (unbounded)	No
k2_Parent	0.01	0 to (unbounded)	No
tb_Parent	41.98	0 to (unbounded)	No

Estimated Values:

Parameter	Value	σ	Prob. > t	Lower (90%) CI	Upper (90%) CI	Lower (95%) CI	Upper (95%) CI
Parent_0	5.458	0.1429	N/A	5.041	5.876	4.844	6.073
k1	0.00615	0.00161	0.0311	0.001449	0.01085	-0.0007764	0.013
k2	0.003191	0.004265	0.2662	-0.009264	0.01564	-0.01516	0.022
tb	40.3	25.67	N/A	-34.67	115.3	-70.17	150.8

χ^2

Parameter	Error %	Degrees of Freedom
All data	2.25	2
Parent	2.25	2

Decay Times:

Compartment	DT50 (overall days)	DT90 (overall days)	k1 DT50 (days)	k2 DT50 (days)
Parent	180	684	113	217

Additional Statistics:

Parameter	r^2 (Obs v Pred)	Efficiency
All data	0.9617	0.9617
Parent	0.9617	0.9617

Parameter Correlation:

	Parent_0	k1	k2	tb
Parent_0	1	0.7204	-0.02432	-0.2473
k1	0.7204	1	-0.03322	-0.5725
k2	-0.02432	-0.03322	1	-0.6457
tb	-0.2473	-0.5725	-0.6457	1

Observed v. Predicted:

Compartment Parent

Time (days)	Value (%)	Predicted Value	Residual
0	5.3	5.458	-0.1584
7	5.4	5.228	0.1716
15	5.05	4.977	0.07258
30	4.45	4.539	-0.08884
45	4.2	4.197	0.003067
60	4	4.001	-0.0007962

Sequence Creation Information:
Fit generated by CAKE version 3.3 (Release)
running on R version 3.0.0 (2013-04-03)

Report Information:
Report generated by CAKE version 3.3 (Release)
CAKE developed by Tessella Ltd, Abingdon, Oxfordshire, UK, sponsored by Syngenta
Running on .NET version 4.0.30319.42000

Data set: Experiment 1 (FOMC)

Study date: Montag, 19. Oktober 2020
Report generated: Montag, 19. Oktober 2020

Model Setup:

Topology: Parent only
Optimiser: IRLS (IRLS Its. 10, IRLS Tol. 1E-05, Max. Its. 100, Tol. 1E-05)
SANN Max Iterations: 10000
Extra Solver Option: Use If Required

Initial Values of Sequence Parameters:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
alpha_Parent	0.1	0 to (unbounded)	No
beta_Parent	0.01	0 to (unbounded)	No

Fit step: Final

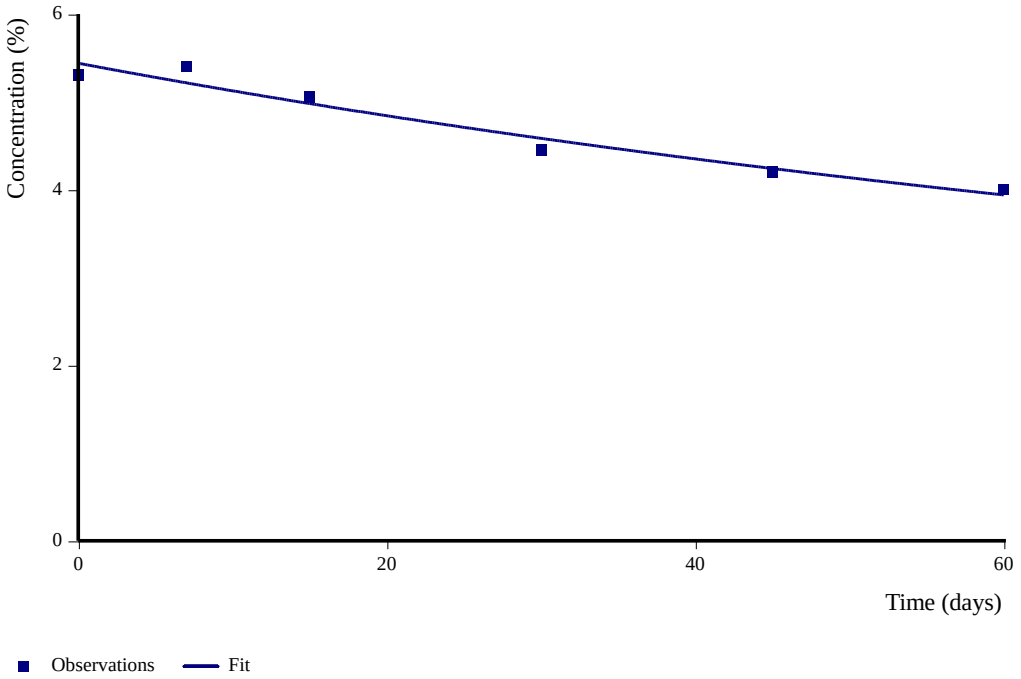
Used Extra Solver: No

Reference Table:

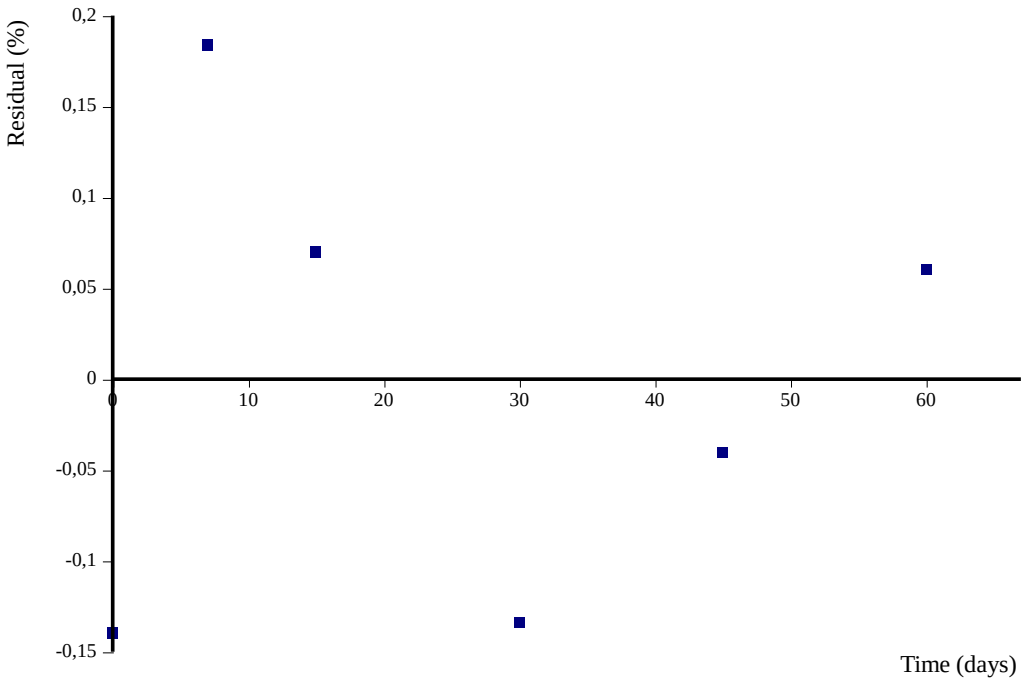
Compartment	Name
Parent	Parent

Graphical Summary:

Observations and Fitted Model:



Residuals:



Initial Values for this Step:

Parameter	Initial Value	Bounds	Fixed
Parent_0	100	0 to (unbounded)	No
alpha_Parent	0.1	0 to (unbounded)	No
beta_Parent	0.01	0 to (unbounded)	No

Estimated Values:

Parameter	Value	σ	Prob. > t	Lower (90%) CI	Upper (90%) CI	Lower (95%) CI	Upper (95%) CI
Parent_0	5.44	0.1426	N/A	5.104	5.775	4.986	5.894
alpha	1.324	5.166	N/A	-10.83	13.48	-15.12	17.77
beta	217.5	949.6	N/A	-2017	2.45E+003	-2805	3.24E+003

χ^2

Parameter	Error %	Degrees of Freedom
All data	2.16	3
Parent	2.16	3

Decay Times:

Compartment	DT50 (days)	DT90 (days)	DT90 / 3.32 (days)
Parent	150	1.02E+03	3.07E+03

Additional Statistics:

Parameter	r^2 (Obs v Pred)	Efficiency
All data	0.9539	0.9539
Parent	0.9539	0.9539

Parameter Correlation:

	Parent_0	alpha	beta
Parent_0	1	-0.5735	-0.5937
alpha	-0.5735	1	0.9994
beta	-0.5937	0.9994	1

Observed v. Predicted:

Compartment Parent

Time (days)	Value (%)	Predicted Value	Residual
0	5.3	5.44	-0.1397
7	5.4	5.216	0.1838
15	5.05	4.98	0.07016
30	4.45	4.584	-0.1341
45	4.2	4.24	-0.04044
60	4	3.94	0.06044

Sequence Creation Information:
Fit generated by CAKE version 3.3 (Release)
running on R version 3.0.0 (2013-04-03)

Report Information:
Report generated by CAKE version 3.3 (Release)
CAKE developed by Tessella Ltd, Abingdon, Oxfordshire, UK, sponsored by Syngenta
Running on .NET version 4.0.30319.42000