FOCUS work group on degradation kinetics

Overview and parent kinetics

Presentation at the

3rd European Modelling Workshop

Catania, Sicily, 17-19 February 2004

Introduction

- The degradation rates of parent and metabolites are important variables in assessing environmental exposure and movement to water
- Assumptions used in calculating degradation rates can significantly affect these assessments
- Need for harmonisation

Introduction

- FOCUS (an organization co-sponsored by the EU and industry) established a work group to provide guidance on calculation of degradation rates of parent and metabolites
  - laboratory studies
  - field studies
  - water sediment studies

FOCUS WORK GROUP ON DEGRADATION KINETICS

- Group of 13 scientists chaired by Jos Boesten
  - research institutes
  - regulatory agencies
  - academia
  - industry
- Six meetings starting in September 2002
- Essentially complete final report (will be submitted to the FOCUS Steering Committee in early March)

Work Group Members

Jos Boesten

Karin Aden

Claude Beigel

Sabine Beulke

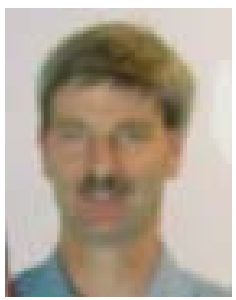
Martin Dust

Jeremy Dyson

Inge Fomsgaard

Russell Jones

Sylvia Karlsson



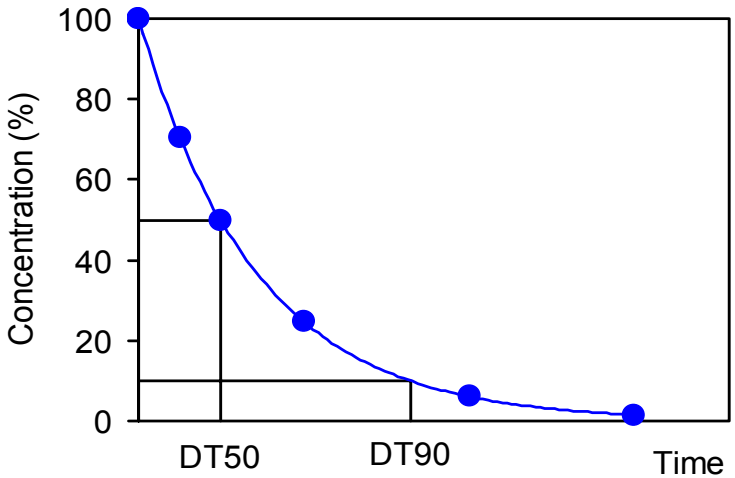
Ton van der Linden

Oriol Magrans Soria

Otto Richter

Guy Soulas

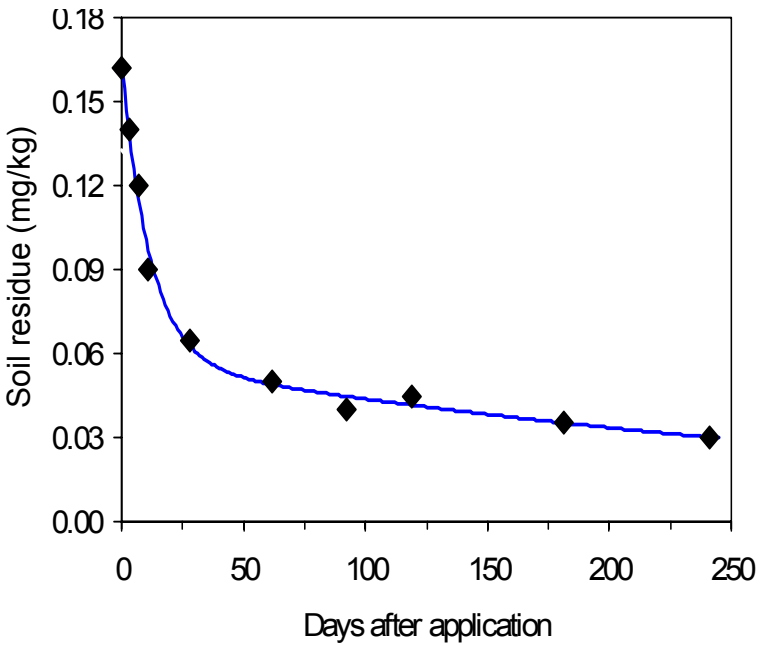
Types of Kinetics



Single first-order (SFO)

Time for decrease from 100% to 50% same as time for decrease from 50% to 25%

DT90 = 3.32 x DT50



Bi-phasic

Degradation initially fast, then slower

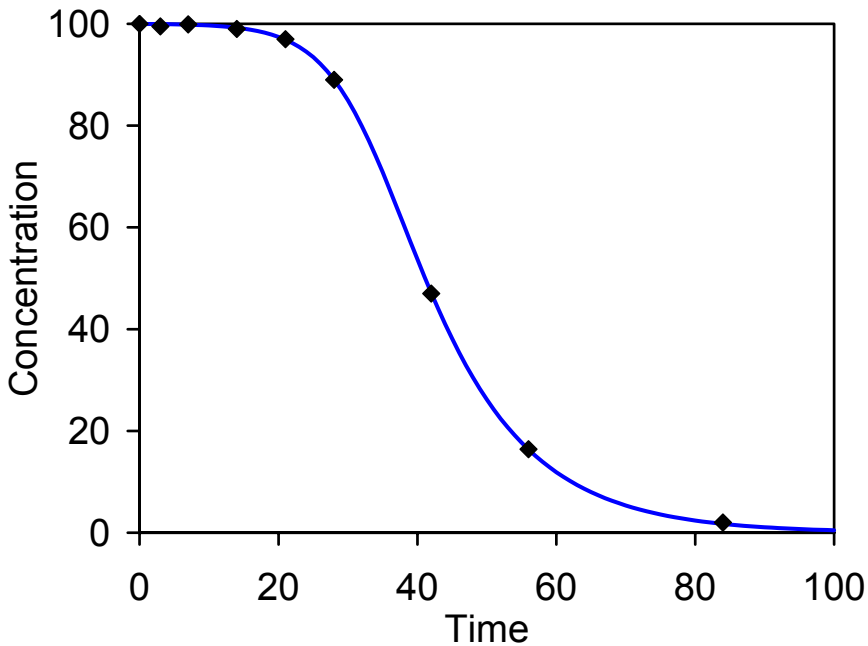
e.g. due to declining microbial activity (artefact!), increasing sorption

Gustafson and Holden (FOMC)

Hockey-stick (HS)

Bi-exponential (DFOP)

Types of kinetics



Lag-phase

Degradation initially slow, then faster

e.g. due to inappropriate storage before study (artefact!), adaptation of micro-organisms

Modified Hockey-stick model

Logistic model

Goodness of Fit

- Aim to identify statistical measure that matches expert judgement

- No single statistical measure was found to be universally valid

➔ Acceptability of fits are judged on the basis of a Chi^2 test and visual assessment

Chi^2 Test (variant)

$$\chi^2 = \sum \frac{(C - O)^2}{(err/100 \times \overline{O})^2}$$

C = calculated value
O = observed value
$\overline{O}$ = mean of all observed values
err = measurement error percentage

If χ^2 > tabulated value then the model is not appropriate at the chosen level of significance (usually 5%)

Error unknown
→ Calculate error level at which test is passed

Model with smallest error percentage is best-fit model

Visual Inspection

- Graph of predicted and observed concentrations *vs* time

- Graph of residuals *vs* time (for kinetic models for exposure assessment, consider only the residues through the DT90)

Spreadsheet for parent SFO and FOMC

Version 1.0
Parameter optimisation for SFO kinetics with Excel Solver Add-In
Visual assessment and chi2-test
For datasets without replicates, optimisation of two parameters (M0 and k)

User input, all other cells calculated or automated
Optimise using Solver (click on grey button)

Name of dataset: **Example dataset L3**

No	Time	Observed	Calculated
1	0	97.80	74.87
2	3	60.00	69.41
3	7	51.00	62.73
4	14	43.00	52.56
5	30	35.00	35.08
6	60	22.00	16.44
7	91	15.00	7.51
8	120	12.00	3.61
9			
10			
11			
12			
13			
14			
15			
16			
17			
18			
19			
20			
21			
22			
23			
24			
25			

SFO parameters and endpoints

1. Enter starting values in cell E17 and E18
2. Optimise parameters by pressing button

M0	74.87	**DT50**	27.4
k	0.025	**DT90**	91.1

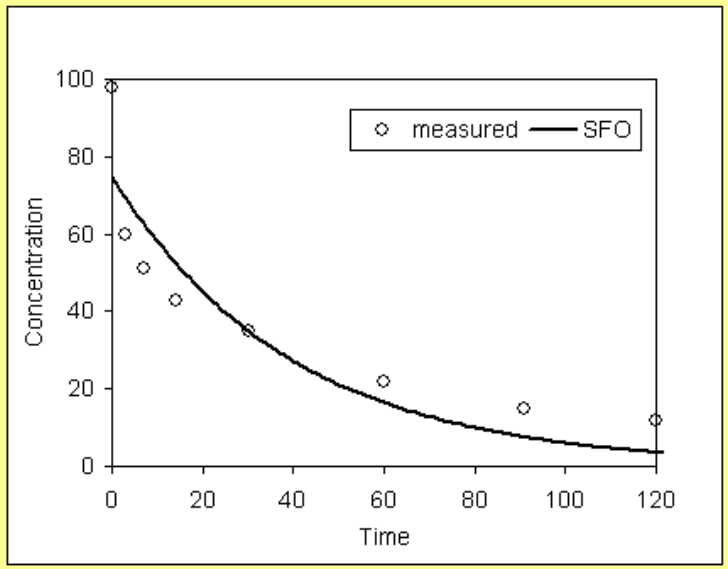
1000.727 **Residual Sum of Squares**

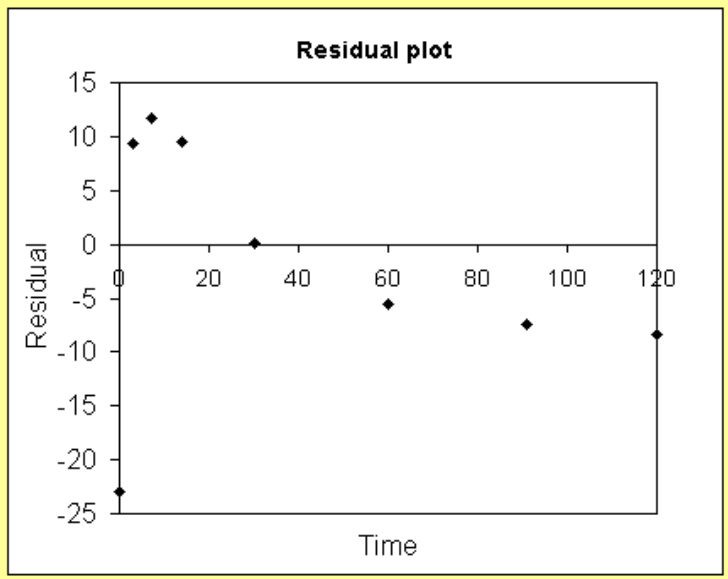
Optimise SFO parameters

Chi2 Test SFO **passed**

1000.727	**Residual Sum of Squares**
8	**Number of observations**
2	**Number of parameters**
42.0	**Average of observed**
21.2	**% Error**
8.91	**Scaled Error**
12.592	**Chi2 calculated**
12.592	**Chi2 Table**
0.000	**Chi2 calculated - Chi2 Table**

Calculate % error at which test passed





Objectives for Parent Kinetic Analysis

- DT50 and DT90 values used to trigger additional studies
  - Chose best-fit model kinetics on statistical and visual analysis
- Endpoints to calculate predicted environmental concentrations in groundwater and surface water
  - Standard versions of most fate models use SFO
  - Preference for SFO when an adequate fit is obtained
  - Correction procedures if an adequate fit is not obtained

Estimating Endpoints Used as Trigger Values

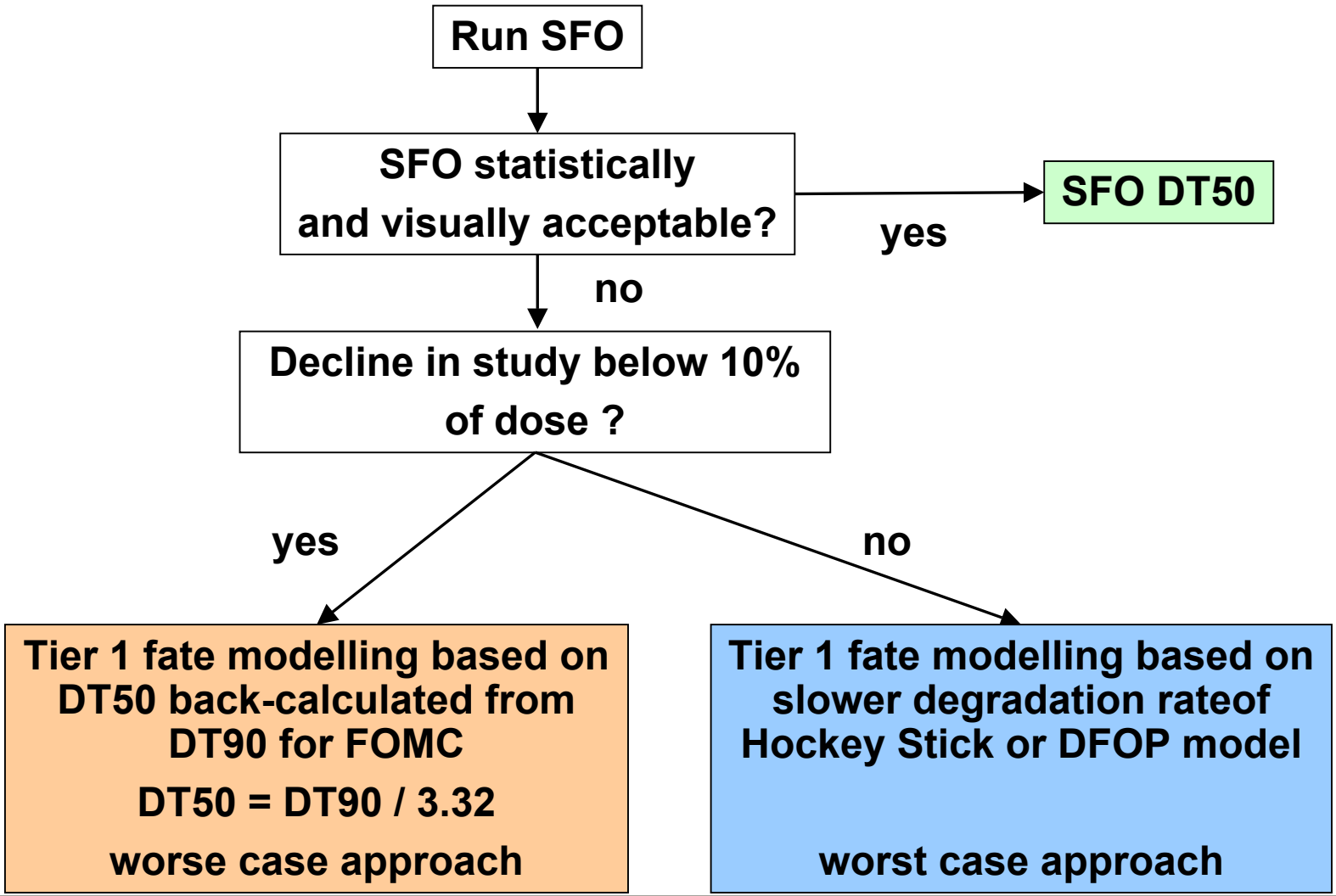
- Run SFO and FOMC.

  If fit for SFO is better, then use SFO

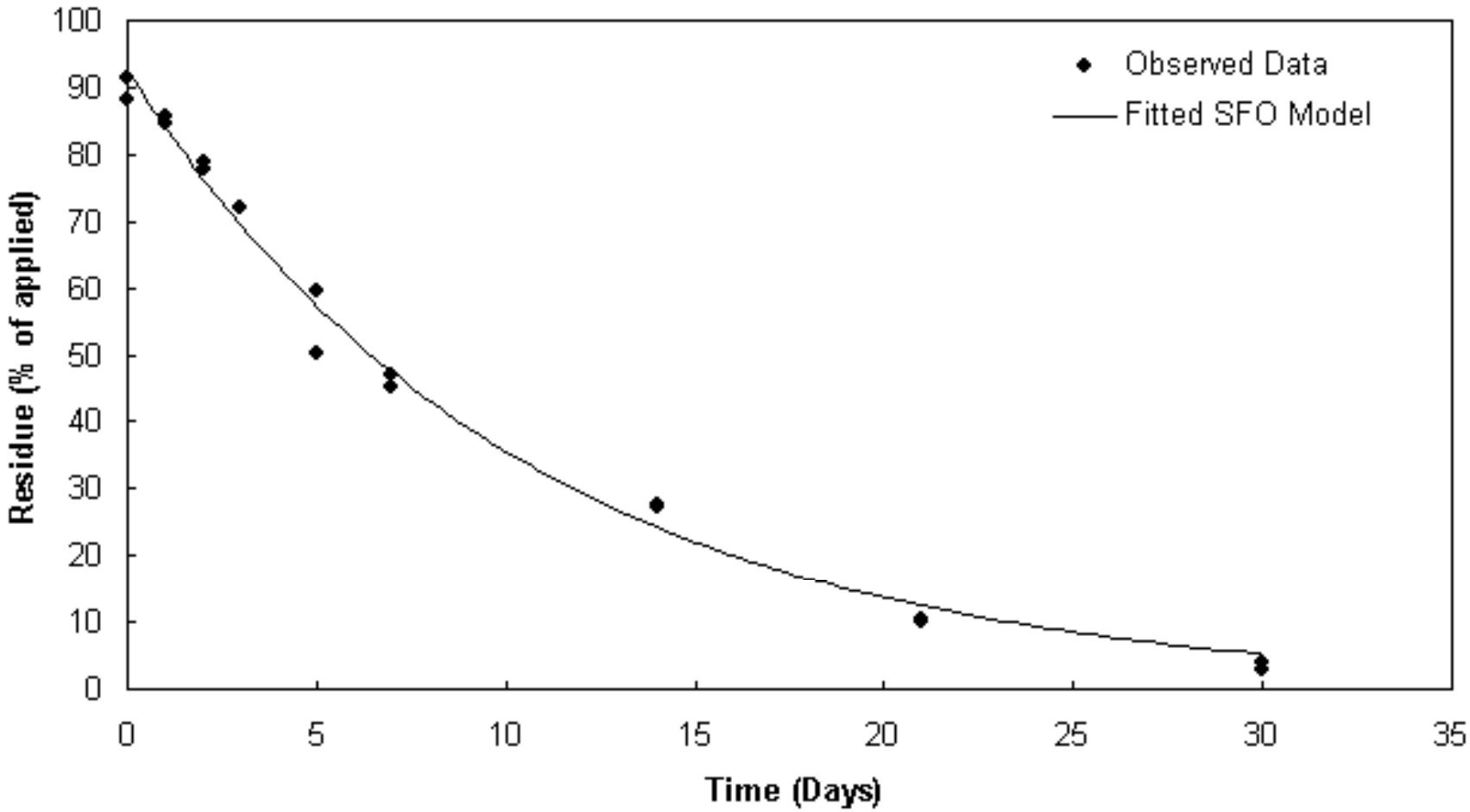
- If FOMC is better, run DFOP. Use whichever model gives the best fit (lowest error in Chi^2 test)

- Assess by visual inspection whether the best fit model provides an acceptable description of the data

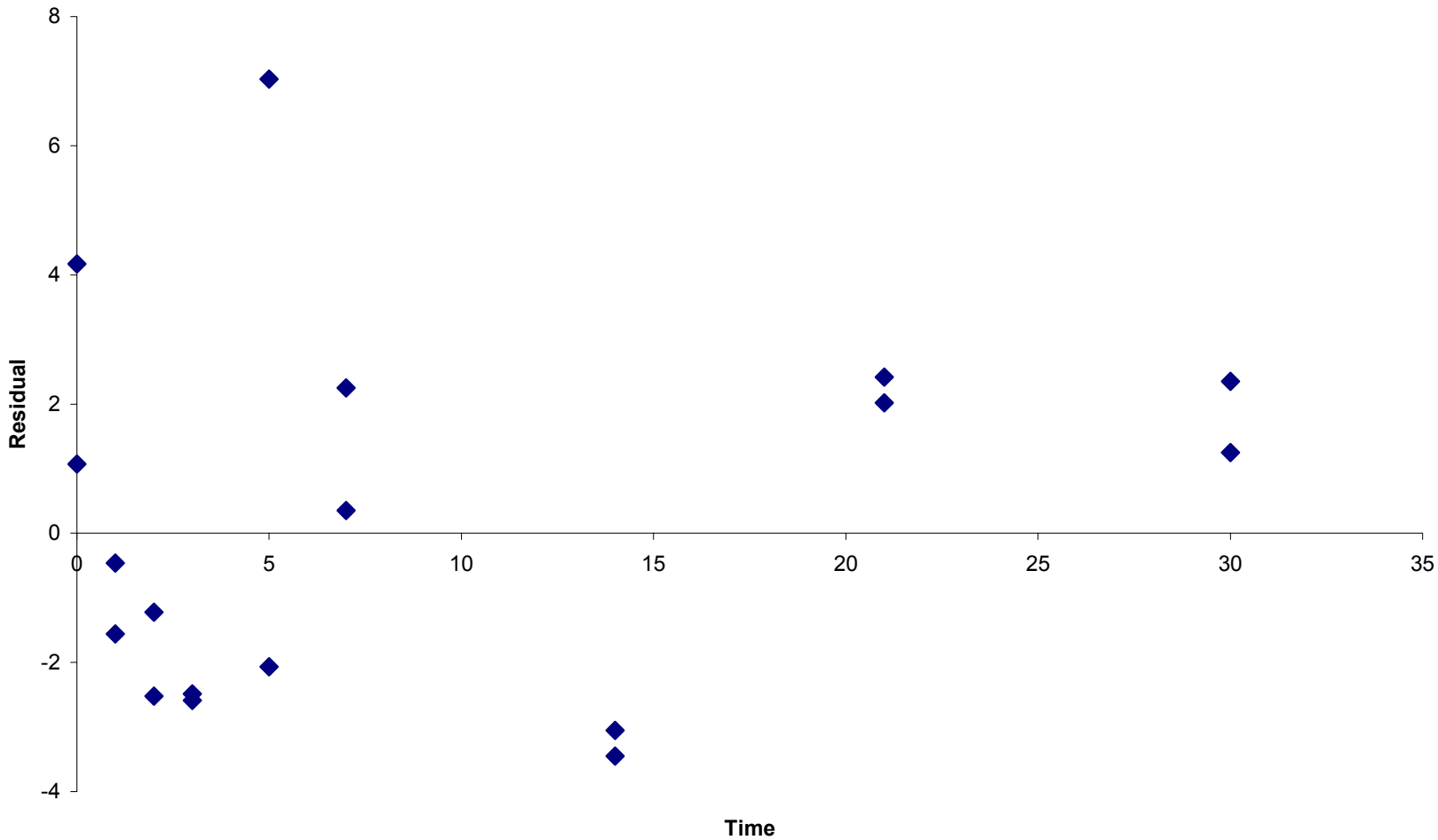
Parent Endoints for Exposure Modelling



Example A (laboratory study)



Example A (laboratory study)

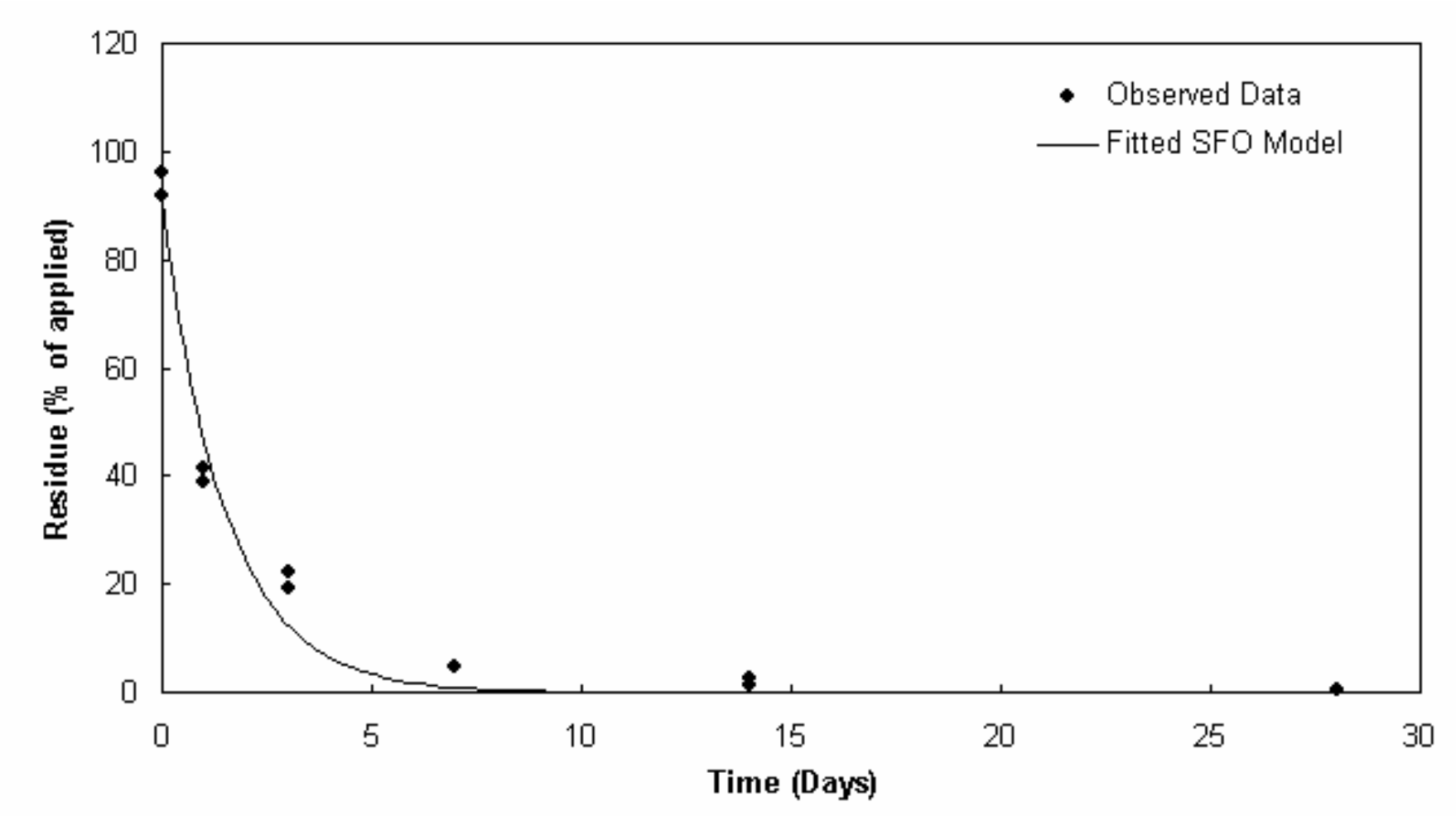


Example A (laboratory study)

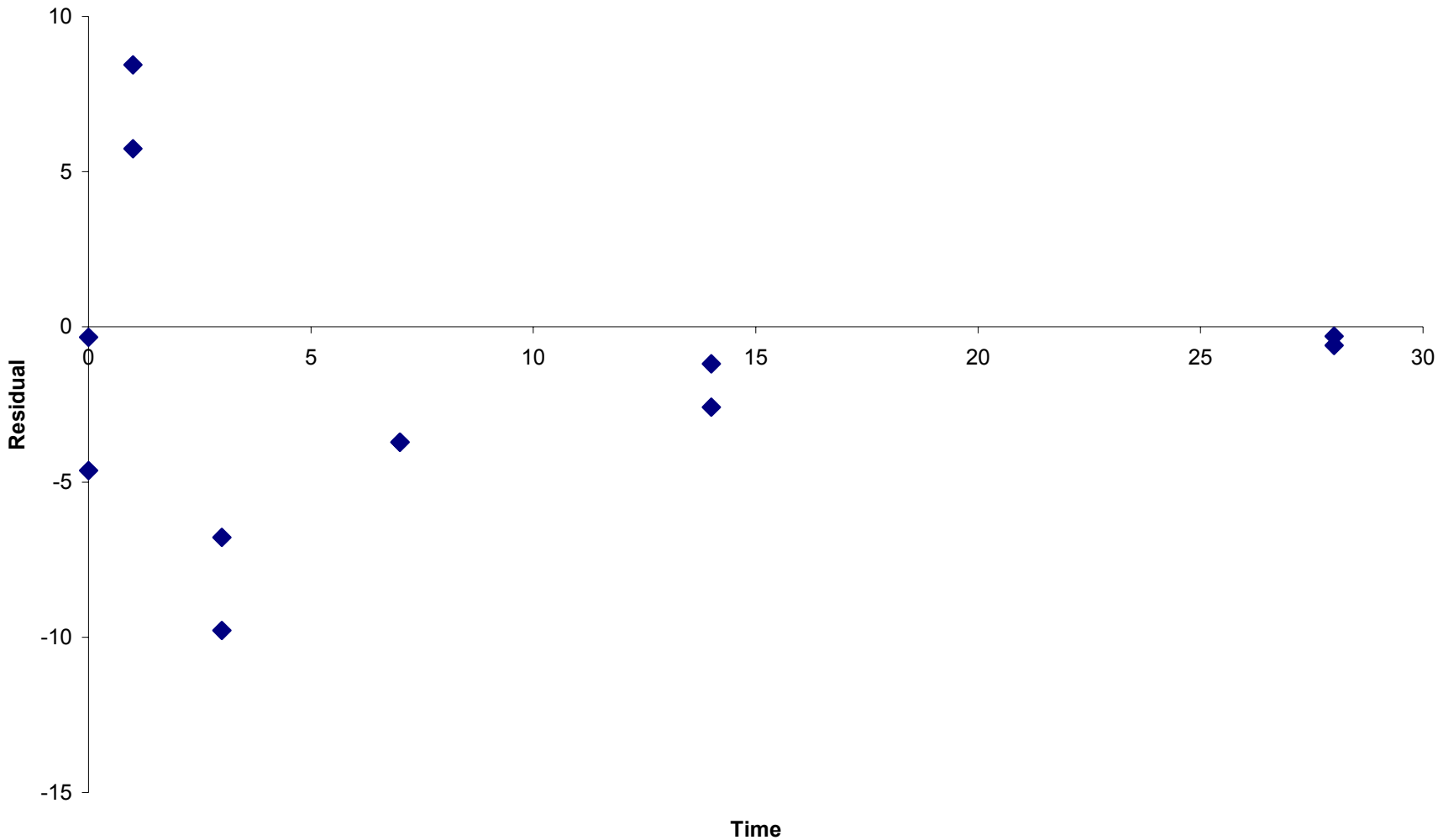
- Conclusions
  - Chi^2 error value for SFO is 4%
  - No systematic error apparent in residual plots
  - Well behaved data-set, very limited scatter in the measured data
  - **SFO appropriate for use in modelling**

- Additional Information
  - No improvement in Chi^2 error or residual pattern with FOMC

Example B (laboratory study)



Example B (laboratory study)

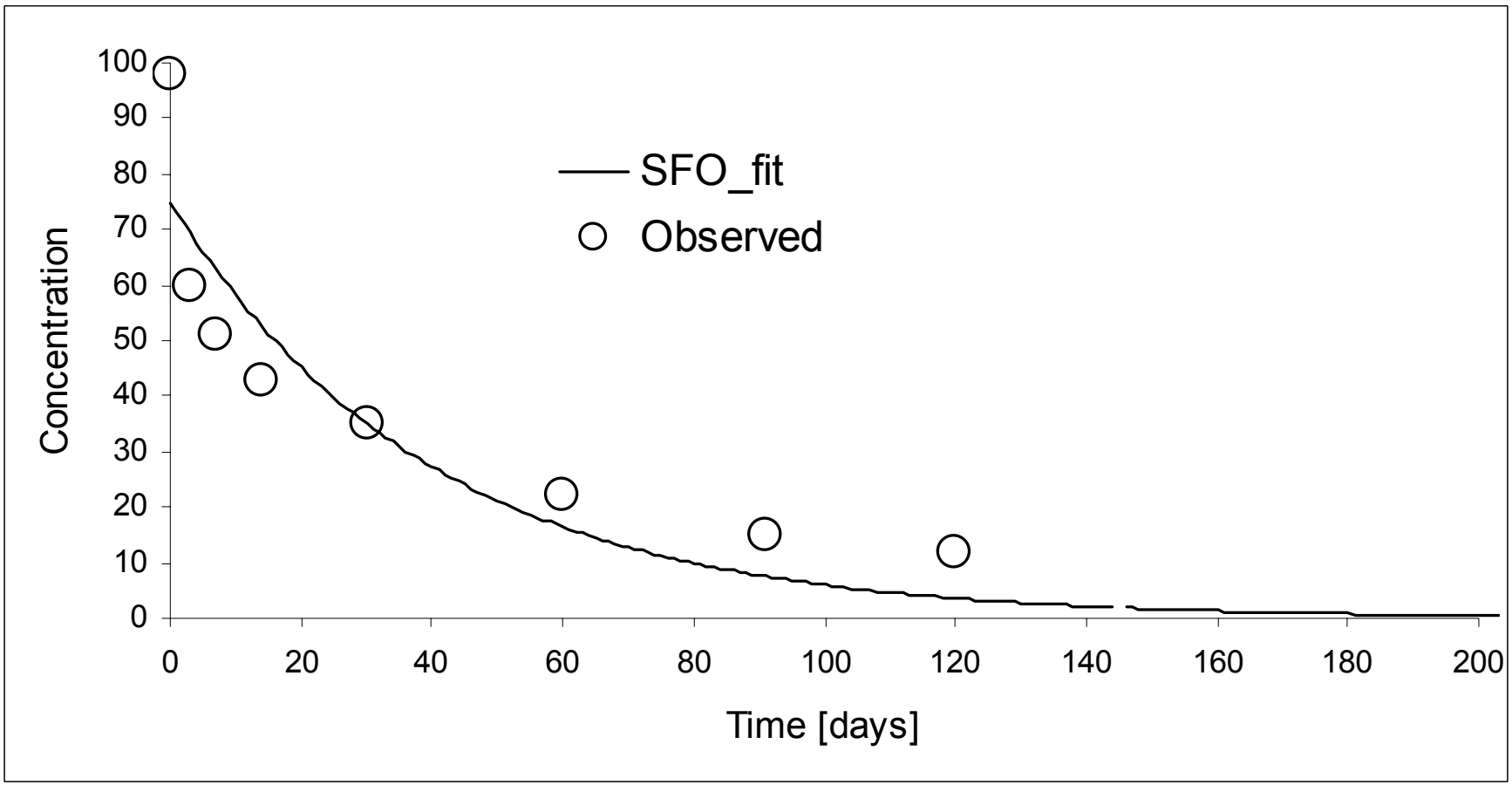


Example B (laboratory study)

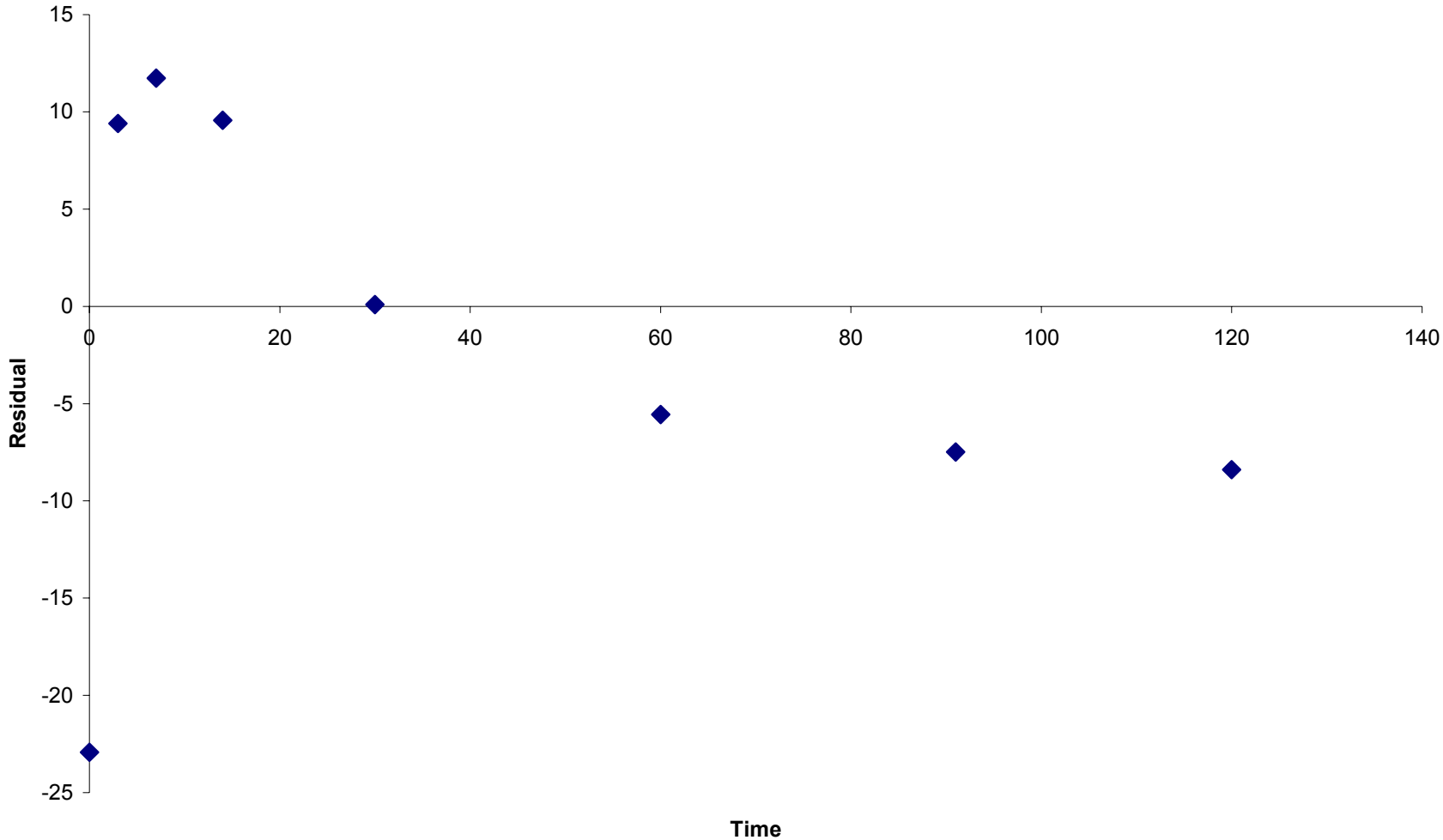
- Conclusions
  - Chi^2 error value for SFO is 15%
  - No systematic error apparent in residual plots up to DT90 (~5 days), underestimation afterwards
  - **SFO appropriate for use in modelling**

- Additional Information
  - Chi^2 error value for FOMC is 7%
  - No improvement in residual pattern with FOMC up to DT90

Example C (laboratory study)



Example C (laboratory study)



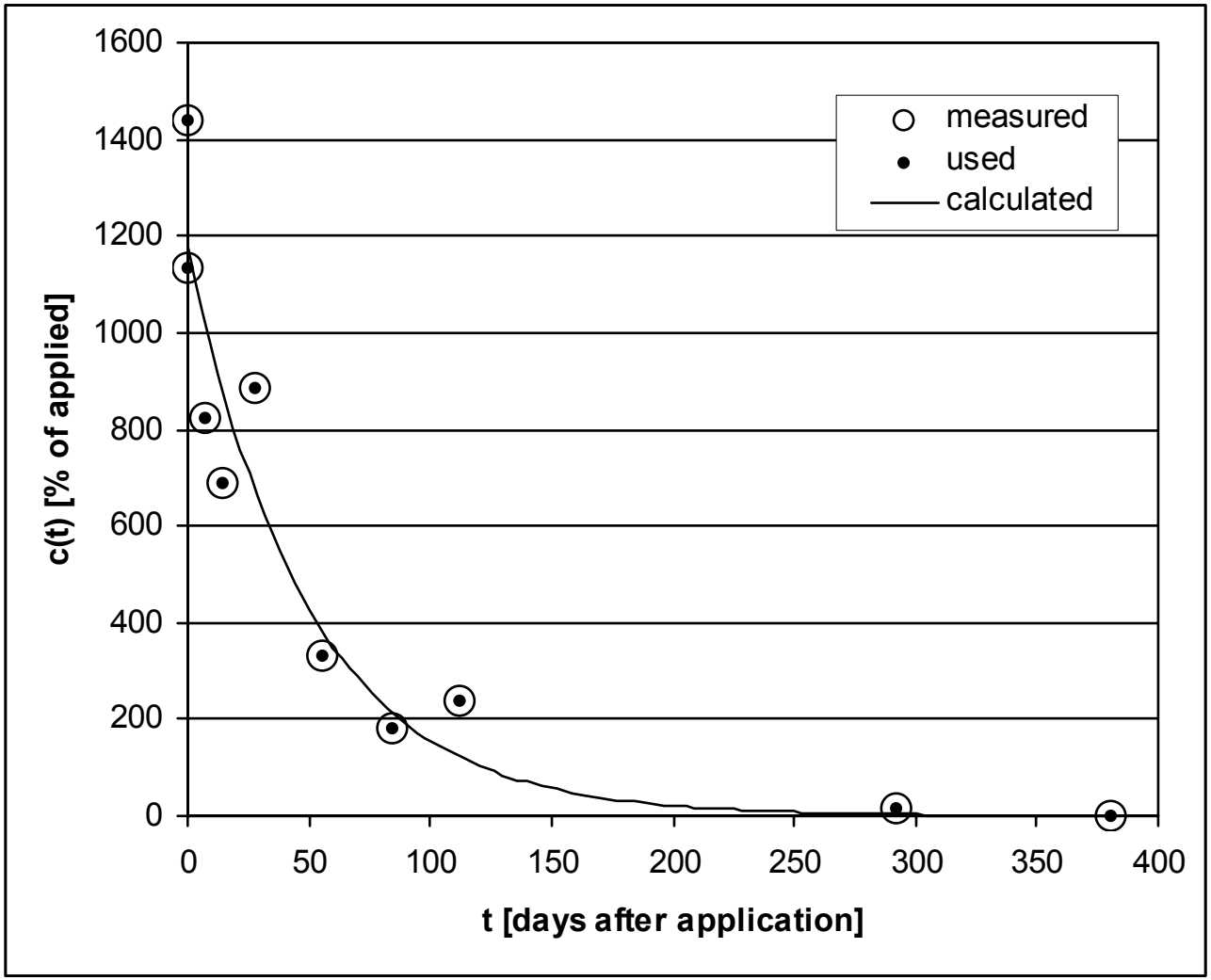
Example C (laboratory study)

- Conclusions-SFO
  - Chi^2 error value for SFO is 22%
  - SFO misses measured initial concentration
  - Residual plot indicates systematic deviation for later sampling dates in period up to DT90
  - **SFO inappropriate for use in modelling**

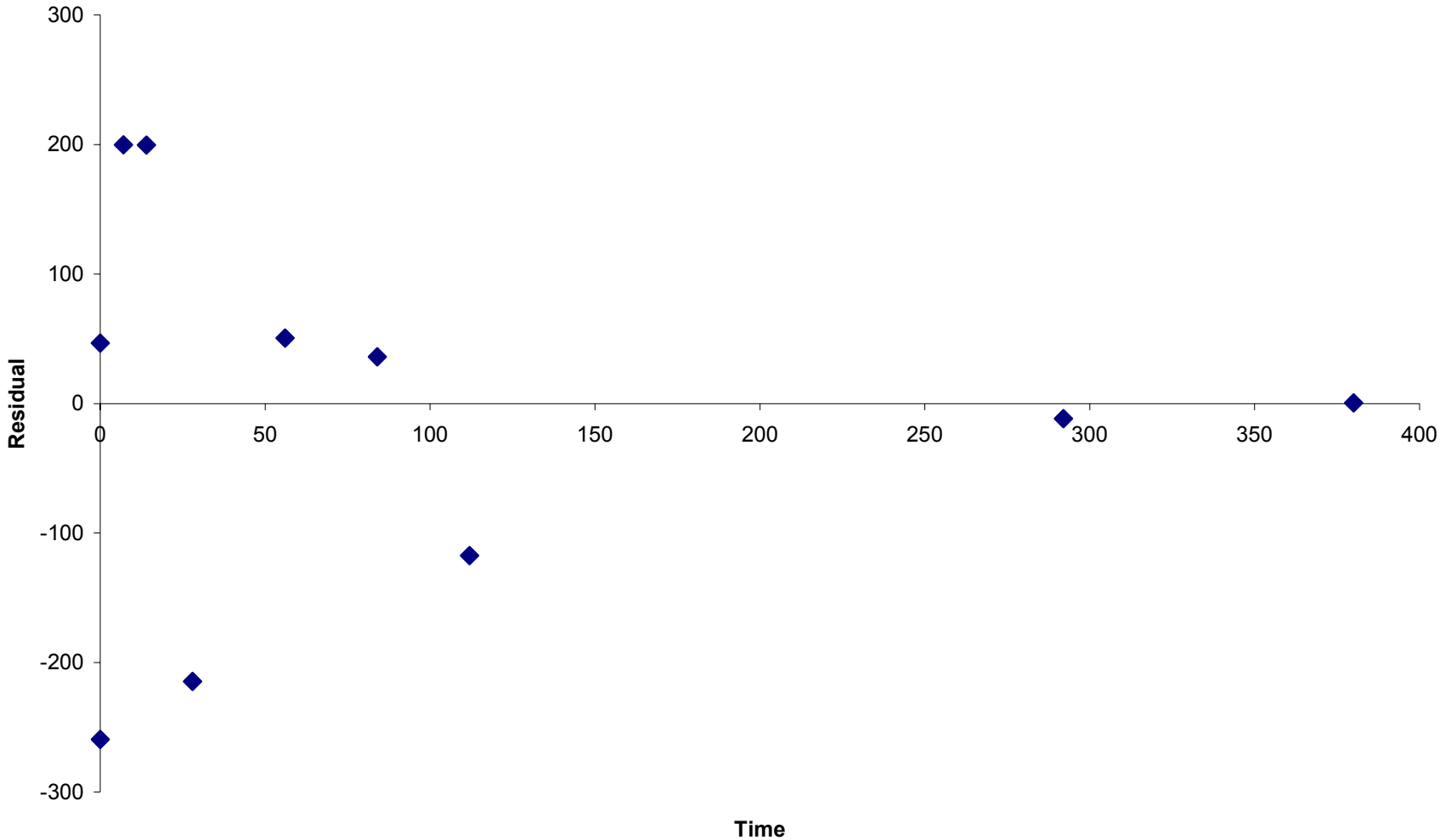
Example C (laboratory study)

- Conclusions-FOMC
  - Chi^2 error value for FOMC drops to 8%
  - Better description of initial concentration
  - No improvement with regard to random nature of residuals, however overall smaller absolute deviations compared to SFO
  - **Use bi-phasic kinetics approaches for modelling**
    - DT90 FOMC/3.32 or higher tier approaches

Example D (field study)



Example D (field study)



Example D (field study)

- Conclusions-SFO
  - Chi^2 error value for SFO is 22%
  - Residuals plots indicate no systematic error of the SFO model, rather that the observed pattern is most likely due to scatter of early measurements
  - **SFO appropriate for use in modelling, confirm against bi-phasic kinetics**

Example D (field study)

- Conclusions-FOMC
  - No improvement in Chi^2 error value
  - No improvement in residual pattern

Other Topics in the Report

- General data issues
  - Replicates
  - Data transformation and weighting
  - Outliers
  - Data below LOD and LOQ
  - Time zero samples

Other Topics in the Report

- Metabolites
- Water sediment studies
- Use of kinetic endpoints in regulatory assessments
  - when averages are desired, use geometric mean
    - same value when half-lives and degradation rates are averaged
    - best description of averages of entire degradation curves

Other Topics in the Report

- Discussion of statistical measures
- Normalization of field data
- Higher tier approaches if degradation is bi-phasic
- Reporting of results
- Review of software packages