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DETERMINATION OF PARTITION COEFFICIENT AND HYDROLYSIS AS A FUNCTION OF pH

[redacted] **PROJECT NUMBER:** [redacted]

AUTHOR: [redacted]

STUDY SPONSOR:

[redacted]

[redacted]

TEST FACILITY:

[redacted]

QUALITY ASSURANCE REPORT

This study type is classed as short-term. Inspection of the routine and repetitive procedures that constitute the study is carried out as a continuous process designed to encompass the major phases at or about the time this study was in progress.

This report has been audited by [redacted] and is considered to be an accurate account of the data generated and of the procedures followed.

In each case, the outcome of QA evaluation is reported to the Study Director and Management on the day of evaluation. Audits of study documentation, and process inspections appropriate to the type and schedule of this study were as follows:

Protocol Compliance Audit
Partition Coefficient
Draft Report Audit
Final Report Audit

§ Evaluation specific to this study

[redacted] DATE: ....

[redacted]

GLP COMPLIANCE STATEMENT

With the exception of the hydrolysis as a function of pH calculation the work described was performed in compliance with UK GLP standards (Schedule 1, Good Laboratory Practice Regulations 1999 (SI 1999/3106 as amended by SI 2004/0994)). These Regulations are in accordance with GLP standards published as OECD Principles on Good Laboratory Practice (revised 1997, ENV/MC/CHEM(98)17); and are in accordance with, and implement, the requirements of Directives 2004/9/EC and 2004/10/EC.

These international standards are acceptable to the Regulatory agencies of the following countries: Australia, Austria, Belgium, Canada, the Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Israel, Italy, Japan, Republic of Korea, Luxembourg, Mexico, The Netherlands, New Zealand, Norway, Poland, Portugal, Slovenia, South Africa, Spain, Sweden, Switzerland, Turkey, the United Kingdom, and the United States of America.

This report fully and accurately reflects the procedures used and data generated.

[redacted] DATE: ....

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DETERMINATION OF PARTITION COEFFICIENT AND HYDROLYSIS AS A FUNCTION OF pH

SUMMARY

Partition Coefficient. <2.00, $\log_{10} P_{ow}$ <0.3, using the HPLC method, Method 117 of the OECD Guidelines for Testing of Chemicals, 13 April 2004.

Hydrolysis as a Function of pH. Testing was not carried out according to Method 111 of the OECD Guidelines for Testing of Chemicals, 13 April 2004. For further detailed information refer to Section 5 of this report.

[redacted]

DETERMINATION OF PARTITION COEFFICIENT AND HYDROLYSIS AS A FUNCTION OF pH

1. INTRODUCTION

The partition coefficient and hydrolysis as a function of pH of the test material have been determined or estimated.

Methods employed (where applicable) complied with those specified in the current OECD Guidelines for Testing of Chemicals.

2. TEST MATERIAL

2.1 Description, Identification and Storage Conditions

Sponsor's identification : [redacted]
Description :
Lot number :
Date received :
Storage conditions :

The integrity of supplied data relating to the identity, purity and stability of the test material is the responsibility of the Sponsor.

3. ARCHIVES

Unless instructed otherwise by the Sponsor, all original data and the final report will be retained for five years, after which instructions will be sought as to further retention or disposal.

4. PARTITION COEFFICIENT

4.1 Method

The determination was carried out using the HPLC Method 117, of the OECD Guidelines for Testing of Chemicals, 13 April 2004.

4.1.1 Procedure

4.1.1.1 Preliminary estimate

A preliminary assessment of the partition coefficient was made based on the approximate solubilities of the test material in n-octanol and water. This was carried out by visual assessment.

4.1.1.2 Definitive test

Preparation of sample solution

Test material (0.1123 g) was diluted to 100 ml with mobile phase.

Preparation of reference solutions

The dead time was determined by measuring the retention time of thiourea (purity* >99%, 23.0 mg/l solution in mobile phase).

A solution of reference standards (see following table) was prepared in mobile phase.

Table 4.1

Standard	Purity (%)*	Concentration (mg/l)
	99+	5.13 x 10^3
	≥99	3.02 x 10^3
	≥99	218
	99.98	5.05 x 10^3
	>99	3.00 x 10^3
	≥99.0	416

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* Value quoted by supplier

Determination of retention time

The sample, thiourea and reference standard solutions were injected in duplicate using the following HPLC parameters:

Chromatograph

Column :
Column temperature : 40°C
Mobile phase : methanol:water (75:25 v/v)
pH of mobile phase : 7.4
Flow-rate : 1.0 ml/min
UV detector wavelength : 240 nm
Injection volume : 100 µl

Construction of calibration curve

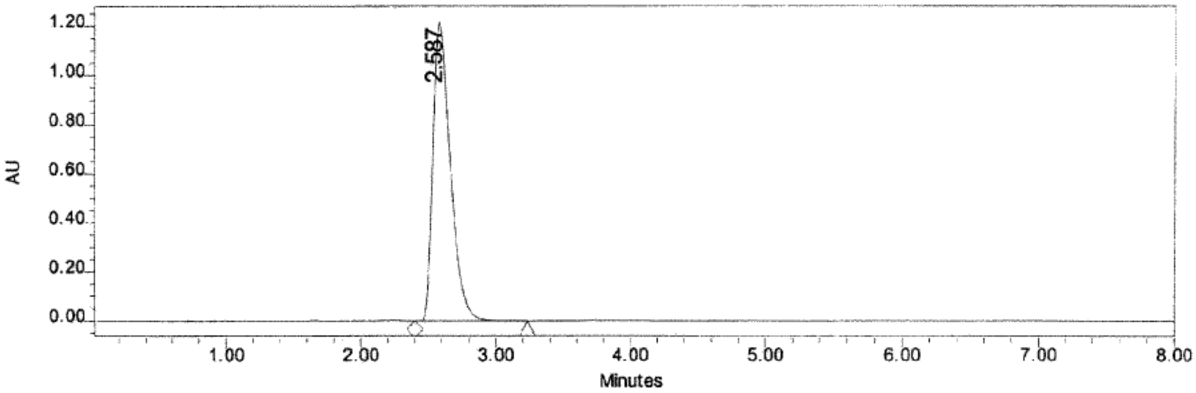
A calibration curve was constructed from the retention time data of the thiourea and reference standard solutions (Figure 4.1). The capacity factors (k) for the reference standards were calculated using Equation 4.2. $\text{Log}_{10}\ P_{ow}$ values of the reference standards are those quoted in Method 117 of the OECD Guidelines for Testing of Chemicals, 13 April 2004.

Partition coefficient of sample

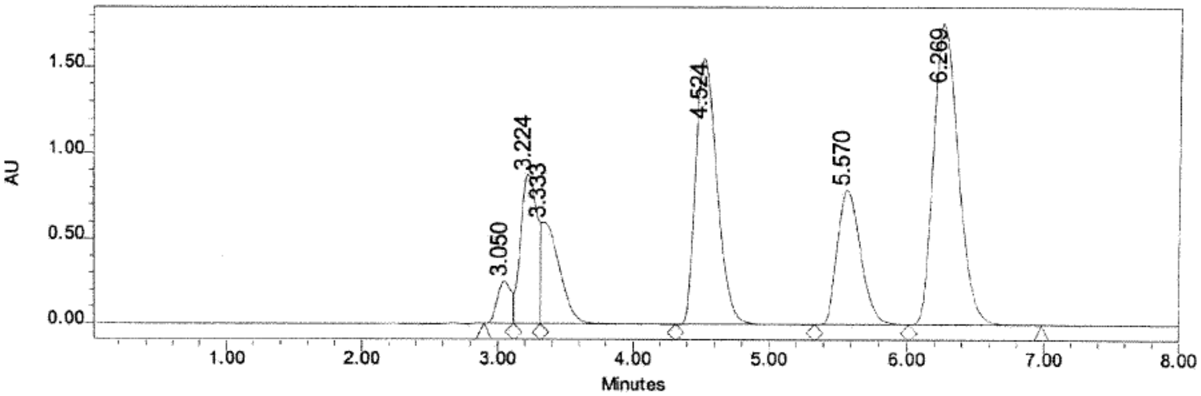
The capacity factor was calculated using Equation 4.2 and the $\log_{10} P_{ow}$ value determined with reference to the calibration curve (Figure 4.1).

Typical Chromatography

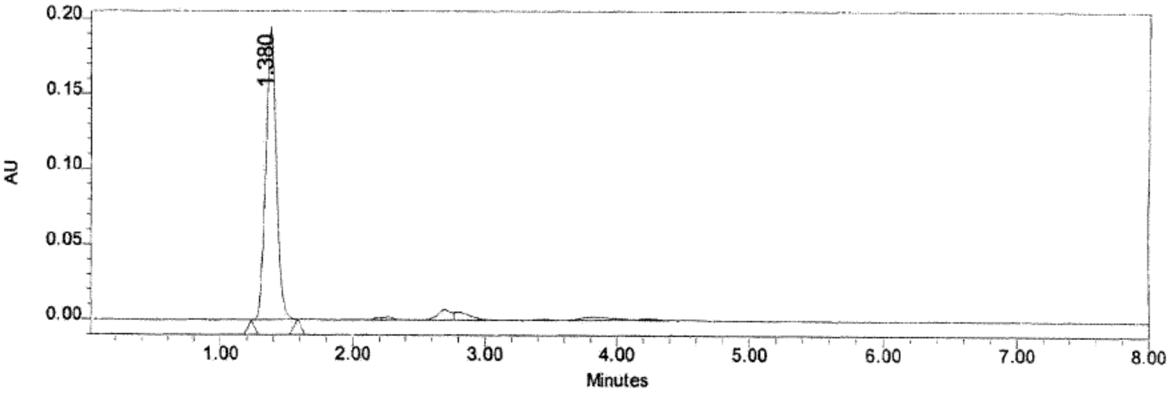
Dead Time



Reference Standards



Sample



4.1.2 Calculation

4.1.2.1 Preliminary estimate

The preliminary estimate of the partition coefficient was calculated using Equation 4.1.

Equation 4.1

$$P_{OW}\ \text{estimate} = \frac{\text{solubility of the test material in n - octanol}}{\text{solubility of the test material in water}}$$

4.1.2.2 Capacity factor

The capacity factor was determined using Equation 4.2.

Equation 4.2

$$k = \frac{t_r - t_0}{t_0}$$

where:

k = capacity factor
t_r = retention time (min)
t_0 = dead time (min)

4.2 Results

4.2.1 Preliminary estimate

Approximate solubility in n-octanol: $<9.00 \times 10^{-3}$ g/l
Approximate solubility in water: >994 g/l
Approximate P_{ow}: $<9.06 \times 10^{-6}$
$\text{Log}_{10}\ P_{ow}$: <-5.04

4.2.2 Definitive test

Calibration

The retention times of thiourea and the retention times, capacity factors (k) and $\log_{10} P_{ow}$ values for the reference standards are shown in the following tables:

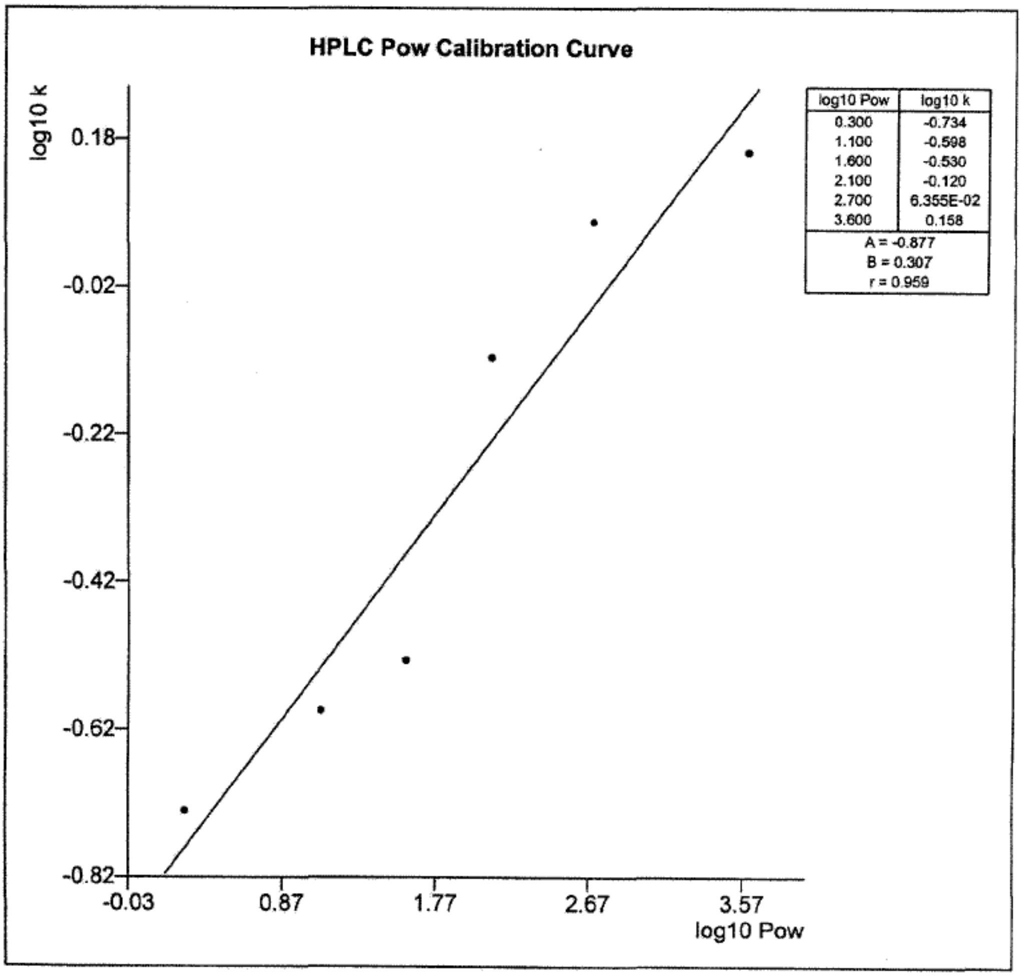
Table 4.2

Dead Time	Retention Time (mins)		Mean Retention Time (mins)
	Injection 1	Injection 2	
Thiourea	2.572	2.587	2.580

Table 4.3

Standard	Retention Time (mins)		Mean Retention Time (mins)	Capacity Factor (k)	$\log_{10} k$	$\log_{10} P_{ow}$
	Injection 1	Injection 2				
	3.050	3.060	3.055	0.184	-0.734	0.3
	3.224	3.238	3.231	0.253	-0.598	1.1
	3.333	3.350	3.342	0.295	-0.530	1.6
	4.524	4.551	4.538	0.759	-0.210	2.1
	5.570	5.561	5.566	1.16	6.36×10^{-2}	2.7
	6.269	6.320	6.295	1.44	0.158	3.6

Figure 4.1 Calibration Curve



Partition coefficient of sample

The retention times, capacity factors and $\log_{10} P_{ow}$ values determined for the sample are shown in the following table:

Table 4.4

Injection	Retention Time (mins)	Capacity Factor (k)	Log_{10} k	$\text{Log}_{10} P_{ow}$
1	1.380	-0.465	<2.00	<0.3
2	1.386	-0.463	<2.00	<0.3

$\text{Log}_{10} P_{ow}$: <0.3
Partition coefficient: <2.00

4.3 Discussion

Substances having a $\log_{10} P_{ow}$ greater than 3 are regarded as having the potential to bioaccumulate in the environment.

Testing was carried out at approximately neutral pH due to the complex nature of the test material which had numerous functional groups and to simulate environmental conditions.

Testing was carried out using the HPLC method since the test material is a complex reaction mixture/polymer. This is the preferred method for materials of this nature. The test material eluted around the dead time of the HPLC column and thus a limit value was obtained. It should be noted that the test material is only approximately 32% polymer with a significant amount of impurities present (>10%) and dispersed in water. This type of material/mixture is not generally considered suitable for Physico-Chemical testing. However, the result obtained does support the visual estimation of partition coefficient also carried out.

4.4 Conclusion

The partition coefficient of the test material has been determined to be <2.00, $\log_{10} P_{ow}$ <0.3.

5. HYDROLYSIS AS A FUNCTION OF pH

5.1 Summary

Testing was not carried out according to Method 111 of the OECD Guidelines for Testing of Chemicals, 13 April 2004, predominantly due to the complex chemical structure and nature of the test material.

The test material was a complex reaction mixture/polymer dispersed in water. There were numerous chemical structures for the test material possible. Method 111 is not suitable for complex mixtures/reaction polymers.

The test material also had a significant level of impurities present (>10%) further adding to the difficulty of performing a hydrolysis test.

Finally, the test material was of low purity, . It is not practicable to apply Method 111 to materials of such low purity. Additionally, methods of analysis of adequate accuracy or specificity were not available to fully distinguish between the polymer components, impurities and any possible degradation products.

It was therefore considered appropriate to supply additional information in the form of a computer-based estimate. Using the software (HYDROWIN Program, Version 1.67, Copyright US EPA 2000) with a base structure of one repetition of any sub groups and half lives of 19.855 and 198.564 days were obtained for pH 8 and 7 respectively.

Appendix 1 Statement of GLP Compliance in accordance with Directive 2004/9/EC