

AR 226 - 0651

# PFOS

Repeat Dose - 1b

000101



200 Girard Street, Suite 200, Gaithersburg, MD 20877  
301-921-0168 Fax: 301-977-0433

Client: 3M MEDICAL DEPARTMENT  
3M CENTER  
BUILDING 220-2E-02  
ST. PAUL, MN 55133-3220  
(651) 575-3161  
Attention: ANDREW SEACAT

Date Collected: 02/20/1999-02/26/2000  
Date Received: 04/18/2000  
Date Reported: 05/02/2000

Client No. 1492

Study: 6 MONTH PFOS STUDY Species: CYNOMOLGUS

| Accession No. | Spec. ID | Gp | Sex | Age | TSH, SI<br>UIU/ML | CHOLEST<br>MG/DL | HDL-DIR<br>MG/DL | LDL-DIR<br>MG/DL | VLDL<br>MG/DL |
|---------------|----------|----|-----|-----|-------------------|------------------|------------------|------------------|---------------|
| A 0098138     | I05508M  | 1  |     |     | 0.45              | 105              | 50               | 53               | 2             |
| A 0098139     | I05519M  | 1  |     |     | 0.32              | 145              | 72               | 73               | 0             |
| A 0098140     | I05527M  | 1  |     |     | 0.42              | 143              | 44               | 97               | 2             |
| A 0098141     | I05530F  | 1  |     |     | 0.43              | 124              | 56               | 68               | 0             |
| A 0098142     | I05531F  | 1  |     |     | 0.19              | 116              | 47               | 66               | 3             |
| A 0098143     | I05535F  | 1  |     |     | 0.59              | 171              | 42               | 128              | 1             |
| A 0098144     | I05544F  | 1  |     |     | 0.80              | 99               | 32               | 65               | 2             |
| Mean          |          |    |     |     | .457              | 129              | 49               | 78.6             | 1.4           |
| S.D.          |          |    |     |     | .195              | 25.4             | 12.6             | 25.6             | 1.1           |

Group 1

|           |         |   |  |  |      |      |      |      |     |
|-----------|---------|---|--|--|------|------|------|------|-----|
| A 0098145 | I05514M | 2 |  |  | 0.64 | 115  | 43   | 72   | 0   |
| A 0098146 | I05515M | 2 |  |  | 0.69 | 80   | 37   | 41   | 2   |
| A 0098147 | I05516M | 2 |  |  | 0.49 | 73   | 32   | 36   | 5   |
| A 0098148 | I05521M | 2 |  |  | 0.41 | 67   | 34   | 33   | 0   |
| A 0098149 | I05541F | 2 |  |  | 0.51 | 92   | 48   | 40   | 4   |
| A 0098150 | I05547F | 2 |  |  | 0.43 | 84   | 36   | 48   | 0   |
| A 0098151 | I05550F | 2 |  |  | 0.34 | 82   | 25   | 51   | 6   |
| Mean      |         |   |  |  | .501 | 84.7 | 36.4 | 45.9 | 2.4 |
| S.D.      |         |   |  |  | .125 | 15.6 | 7.5  | 13.1 | 2.6 |

Group 2

|                 |      |       |     |     |     |
|-----------------|------|-------|-----|-----|-----|
| Reference Range | .2 - | 101 - | 0 - | 0 - | 0 - |
|                 | 2.6  | 240   | 0   | 0   | 0   |



200 Girard Street, Suite 200, Gaithersburg, MD 20877  
301-921-0168 Fax: 301-977-0433

Client: 3M MEDICAL DEPARTMENT  
3M CENTER  
BUILDING 220-2E-02  
ST. PAUL, MN 55133-3220  
(651) 575-3161  
Attention: ANDREW SEACAT

Date Collected: 02/20/1999-02/26/2000  
Date Received: 04/18/2000  
Date Reported: 05/02/2000

Client No. 1492

Study: 6 MONTH PFOS STUDY Species: CYNOMOLGUS

| Accession No. | Spec. ID | Gp | Sex | Age | TSH, SI<br>UIU/ML | CHOLEST<br>MG/DL | HDL-DIR<br>MG/DL | LDL-DIR<br>MG/DL | VLDL<br>MG/DL |
|---------------|----------|----|-----|-----|-------------------|------------------|------------------|------------------|---------------|
| A 0098152     | I05510M  | 3  |     |     | 0.83              | 115              | 48               | 66               | 1             |
| A 0098153     | I05518M  | 3  |     |     | 0.83              | 98               | 44               | 54               | 0             |
| A 0098154     | I05524M  | 3  |     |     | 0.54              | 110              | 37               | 72               | 1             |
| A 0098155     | I05528M  | 3  |     |     | 0.60              | 116              | 31               | 76               | 9             |
| A 0098156     | I05532F  | 3  |     |     | 0.76              | 91               | 23               | 68               | 0             |
| A 0098157     | I05538F  | 3  |     |     | 0.46              | 88               | 32               | 53               | 3             |
| A 0098158     | I05545F  | 3  |     |     | 0.34              | 74               | 24               | 50               | 0             |
| A 0098159     | I05548F  | 3  |     |     | 0.32              | 74               | 31               | 42               | 1             |
| Mean          |          |    |     |     | .585              | 95.8             | 33.8             | 60.1             | 1.9           |
| S.D.          |          |    |     |     | .207              | 17               | 8.8              | 12               | 3             |

Group 3

|           |         |   |  |  |      |      |     |      |     |
|-----------|---------|---|--|--|------|------|-----|------|-----|
| A 0098160 | I05506M | 4 |  |  | 0.73 | 56   | 14  | 42   | 0   |
| A 0098161 | I05507M | 4 |  |  | 0.72 | 25   | 8   | 16   | 1   |
| A 0098162 | I05512M | 4 |  |  | 1.15 | 27   | 11  | 16   | 0   |
| A 0098163 | I05534F | 4 |  |  | 1.25 | 59   | 16  | 40   | 3   |
| A 0098164 | I05536F | 4 |  |  | 1.75 | 53   | 18  | 31   | 4   |
| A 0098165 | I05540F | 4 |  |  | 0.89 | 57   | 16  | 41   | 0   |
| A 0098166 | I05551F | 4 |  |  | 0.86 | 61   | 22  | 35   | 4   |
| Mean      |         |   |  |  | 1.05 | 48.3 | 15  | 31.6 | 1.7 |
| S.D.      |         |   |  |  | .368 | 15.4 | 4.6 | 11.3 | 1.9 |

Group 4

|                 |      |       |     |     |     |
|-----------------|------|-------|-----|-----|-----|
| Reference Range | .2 - | 101 - | 0 - | 0 - | 0 - |
|                 | 2.6  | 240   | 0   | 0   | 0   |



200 Girard Street, Suite 200, Gaithersburg, MD 20877  
301-921-0168 Fax: 301-977-0433

Client: 3M MEDICAL DEPARTMENT  
3M CENTER  
BUILDING 220-2E-02  
ST. PAUL, MN 55133-3220  
(651) 575-3161  
Attention: ANDREW SEACAT

Date Collected: 02/20/1999-02/26/2000  
Date Received: 04/18/2000  
Date Reported: 05/02/2000

Client No. 1492

Study: 6 MONTH PFOS STUDY Species: CYNOMOLGUS

| Accession No. | Spec. ID | Gp | Sex | Age | TSH, SI<br>UIU/ML | CHOLEST<br>MG/DL | HDL-DIR<br>MG/DL | LDL-DIR<br>MG/DL | VLDL<br>MG/DL |
|---------------|----------|----|-----|-----|-------------------|------------------|------------------|------------------|---------------|
| A 0098167     | I05533F  | 4R |     |     | 0.85              | 117              | 51               | 61               | 5             |
| A 0098168     | I05542F  | 4R |     |     | 0.60              | 124              | 50               | 46               | 28            |
| A 0098169     | I05511M  | 4R |     |     | 0.65              | 89               | 45               | 44               | 0             |
| A 0098170     | I05522M  | 4R |     |     | 0.93              | 106              | 37               | 68               | 1             |
| Mean          |          |    |     |     | .758              | 109              | 45.8             | 54.8             | 8.5           |
| S.D.          |          |    |     |     | .158              | 15.3             | 6.4              | 11.6             | 13.2          |

Group 4 WK52 RECOVERY

|                 |      |       |     |     |     |
|-----------------|------|-------|-----|-----|-----|
| Reference Range | .2 - | 101 - | 0 - | 0 - | 0 - |
|                 | 2.6  | 240   | 0   | 0   | 0   |

Approved \_\_\_\_\_  
Page 3 of 3

Date 5/2/00

000104

Andrew M. Seacat, Ph.D.  
3M Medical Dept.  
3M Center, Building 220-2E-02  
St. Paul, MN 55133-3220  
Phone: (612) 575-3161  
FAX: (612) 733-1773  
e-mail: amseacat1@mmm.com

3/6/2000

Peter J. Thomford, Ph.D.  
Study Director, Toxicology  
Covance Laboratories Inc.  
3301 Kinsman Blvd.  
Madison WI 53704  
Phone: 608-241-7202  
Fax: 608-242-2736

Re: 26-week capsule toxicity study with perfluorooctane sulfonic acid potassium salt (PFOS; T-6295) in Cynomolgus Monkeys. Covance Study Number: 6329-223,

Peter,

3M requests information from the study records of 6329-223 for the methods used and the dates of specific hormone determinations conducted by Ani Lytics Incorporated, Gaithersburg, MD. Specifically, we need more information on the methods of determination for T3, T4, free T3, free T4 and TSH. An explanation of the zero values for TSH is requested. What is the limit of detection (LOD) and limit of quantitation (LOQ) for TSH in the method used, and should the zero values be replaced with <LOD or < LOQ. Furthermore, we need to understand the high T3 values reported for the day 37 samples (reference, appendix 6 of Draft interim Report from Covance), for which the T3 values were high in all dose groups. The date that the tests were performed on each sample is also requested. Ani Lytics is being copied on this request in order to expedite the transfer of information.

Sincerely,

Andrew M. Seacat Ph.D.  
Study Monitor

cc: Dr. Saroj Das  
Ani Lytics  
200 Girard Street, Suite 200  
Gaithersburg, Maryland 20877  
Telephone No.: 301-921-0168  
Facsimile No.: 301-977-0433



200 Girard Street, Suite 200, Gaithersburg, MD 20877  
301-921-0168 800-237-2815

05 April 2000

Andrew Seacat, Ph.D.  
3M Medical Department  
3M Center, Building 220-2E-02  
St. Paul, MN 55133-3220

Dear Dr. Seacat,

REF: Fax dated 3/20/00  
TSH analysis in Cynos

I want to bring to your attention that primate TSH analysis at AniLytics, Inc. has always been performed using anti-human TSH polyclonal antibody. During our telephone conversation I told you that as of 1998 all human TSH testing is being done using monoclonal antibody, therefore these test reagents can not be used in primates. For this reason we initiated an inhouse TSH assay procedure utilizing polyclonal antibody. The reagent source and other information on each of the assays mentioned in your letter along with result reporting policy are inclosed.

As I indicated to you, primates in general have quite low TSH levels. Therefore it will be necessary to increase the specimen volume in the TSH test system. At least 0.5ml but preferably 1.0ml serum will be good.

Sincerely,

A handwritten signature in dark ink, appearing to read "Saroj R. Das". The signature is fluid and cursive, with a horizontal line drawn underneath the name.

Saroj R. Das, M.S., Ph.D.  
Director

cc: Peter J. Thomford, Ph.D.  
Study Director, Toxicology  
Covance Laboratories, Inc.  
3301 Kinsman Blvd.  
Madison, WI 53704

000106 .



200 Girard Street, Suite 200, Gaithersburg, MD 20877  
301-921-0168 800-237-2815

#### RESULT REPORTING POLICY

Linear regression curve correlation coefficient of 0.99 or greater accepted.

Results observed over the highest calibrator concentration repeated on appropriate dilution.

Lowest limit of quantitation is the lowest calibrator concentration. Values below this concentration are computer generated based on the standard curve. These values are reported. In some assays the exact calibration range is kit lot number specific.

A zero value indicates that the counts bound for the sample/s were same as or close to or > zero standard counts.

000107



200 Girard Street, Suite 200, Gaithersburg, MD 20877  
301-921-0168 800-237-2815

ANALYTE: NonHuman Primate  
Thyroid Stimulating Hormone (TSH)

PROCEDURE: Double Antibody RIA  
Inhouse Procedure

REAGENTS:

Human TSH standard (Ref WHO standard 68/38)  
Sigma-Aldrich Inc. Cat. #T-4651

Rabbit-anti human TSH (polyclonal)  
Sigma-Aldrich Inc. Cat. #T-4651

Radiolabeled HTSH  
Covance Laboratories, Inc., Vienna, VA

CALIBRATION RANGE: 0.4 to 50 mIu/ml. (Low end sensitivity is  
dependent upon the integrity of the iodinated hormone.)

RESULTS: mIu/ml  
Computer generated values reported below low end sensitivity of the  
curve.

COMMENT: Overall TSH levels in NHP are extremely low so it is  
difficult to know if this test offers significant clinical  
information.

000108



200 Girard Street, Suite 200, Gaithersburg, MD 20877  
301-921-0168 800-237-2815

ANALYTE: Free T4

PROCEDURE: Coat-A-Count RIA

REAGENT SOURCE: Diagnostic Products Corporation, CA.

CALIBRATION RANGE: 0.1 to 10 ng/dl (kit lot # specific)

RESULTS: ng/dl  
Computer generated values reported below the standard.

000109



200 Girard Street, Suite 200, Gaithersburg, MD 20877  
301-921-0168 800-237-2815

ANALYTE: Total T4

PROCEDURE: RIA Coated Tube Assay

REAGENT SOURCE: DPC, CA.

CALIBRATION RANGE: 1 to 24 ug/dl

RESULTS: ug/dl  
Computer generated values reported below 1 ug/dl.

000110



200 Girard Street, Suite 200, Gaithersburg, MD 20877  
301-921-0168 800-237-2815

ANALYTE: Free T3

PROCEDURE: Coat-A-Count RIA

REAGENT SOURCE: DPC, CA.

CALIBRATION RANGE: 0.5 - 42 pg/ml (kit lot # specific)

RESULTS: pg/ml  
computer generated values reported below the lowest  
standard curve calibrator concentration.

000111



200 Girard Street, Suite 200, Gaithersburg, MD 20877  
301-921-0168 800-237-2815

ANALYTE: Total T3

PROCEDURE: Radioimmunoassay (RIA)  
Coated Tube Assay

REAGENT SOURCE: Diagnostic Products Corporation (DPC), CA.

CALIBRATION RANGE: 20 to 600 ng/dl

RESULTS: ng/dl  
Computer generated values reported below 20 ng/dl

000112