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3M Environmental Laboratory

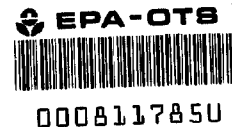
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Final Report- Analytical Study

Single-dose Intravenous Pharmacokinetic Study of T-6246 in Rabbits

In-Vivo Study Reference Number: HWI#6329-159

Study Number: AMDT-042095.1
Test Substance: FC-95 (T-6246)



Name and Address of Sponsor: 3M SCD Division
367 Grove Street
St. Paul, MN 55106

Name and Address of Testing Facility: 3M Environmental Technology & Services
935 Bush Avenue
St. Paul, MN 55106

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Method Numbers and Revisions:

AMDT-M-1-0, Thermal Extraction of Fluoride by means of a Modified
Dohrmann DX2000 Organic Halide Analyzer-Liver
AMDT-M-2-0, Fluoride Measurement by Means of an Orion EA940
Expandable Ion Analyzer
AMDT-M-4-0, Extraction of Fluorochemicals from Rabbit Liver
AMDT-M-8-0, Analysis of Fluoride Using the Skalar Segmented Flow Analyzer
with Ion Selective Electrode
AMDT-M-14-0, Thermal Extraction of Fluoride by Means of a Modified
Dohrmann DX2000 Organic Halide Analyzer-Serum

Initiation Date: See attached protocol

Author: James D. Johnson

Contains No CBI

Approved By:

James D. Johnson
James D. Johnson
Study Director

11/27/95
Completion Date

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page
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of 233

**Exhibit
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State of Minnesota v. 3M Co.,
Court File No. 27-CV-10-28862

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1.0 SUMMARY

Rabbit serum and liver were analyzed for fluorine content at various times after rabbits were dosed intravenously with a single dose of T-6246, a 0.12% solution of FC-95. Doses are expressed as FC-95 equivalents. The fluorine in serum was detected after a single dose of 0.12 mg/kg and after 0.60 mg/kg, but not after a 0.012 mg/kg dose at 28 days post dose. The method is not sensitive enough to detect and measure fluoride after the 0.012 mg/kg dose. The half-life of perfluorooctanesulfonate anion was found to be one month or greater in serum and liver.

The average liver fluoride ion concentration in Group 5 animals (0.60 mg/kg), at day 14 post dose was 1.48 ppm and for four other animals in the same group sacrificed at day 28 the concentration was 1.23 ppm. Thus, the decrease in concentration in liver from 14 days to 28 days post dose is slow; based on just these two points the half-life is greater than 1 month.

2.0 INTRODUCTION

This study was designed to provide information as to whether the perfluorooctanesulfonate anion does go to the liver and other tissues when the material is administered in an intravenous dose, and to ascertain the change in concentration with time after dose in serum and liver.

It is known from studies done previously with rats that the half-life of perfluorooctanesulfonate anion is quite long (>1 month). It was expected that the half-life in rabbits would also be long. Perfluorooctanesulfonate anion is a likely biotransformation product of several fluorochemicals that are to be tested for dermal absorption in other studies. The pharmacokinetics of the perfluorooctanesulfonate anion is very relevant to these dermal absorption studies.

3.0 TEST MATERIALS

3.1 Test, Control, and Reference Substances and Matrices

3.1.1 Analytical Reference Substance: FC-95, lot 161 or 171. They are equivalent.

3.1.2 Analytical Reference Matrix: Bovine liver and bovine serum

3.1.3 Analytical Control Substance: None

3.1.4 Analytical Control Matrix: Bovine liver and bovine serum

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3.2 Source of Materials: 3M ICP/PCP Division For FC-95. Bovine liver from grocery store, bovine serum from Sigma Chemical Company

3.3. Purity and Strength of Reference Substance: Responsibility of Sponsor.

3.4 Stability of Reference Substance: To be determined by Sponsor.

3.5 Storage Conditions for Test Materials: Room temperature for FC-95. For biological samples, the storage is $-20 \pm 10^{\circ}$ C.

3.6 Disposition of Specimens: Biological tissues and fluids will be retained per GLP Regulation for the time period required for studies longer than 28 days.

4.0 EXPERIMENTAL-Overview

Serum and tissues from animals dosed as described (HWI#6329-159), were available for analysis for fluorine compounds. Since perfluorooctanesulfonate anion is not biotransformed, the analysis was accomplished with combustion and subsequent analysis for fluorine. The fluorine data are related directly to perfluorooctanesulfonate concentration. The fluorine analysis of serum collected at different time intervals after dosing provides data which can be interpreted pharmacokinetically. Additional analysis of liver samples provides evidence that the perfluorooctanesulfonate anion is still present at 28 days.

5.0 EXPERIMENTAL - Methods

5.1 AMDT-M-1-0, Thermal Extraction of Fluoride by Means of a Modified Dohrmann DX2000 Organic Halide Analyzer-Liver

5.2 AMDT-M-2-0, Fluoride Measurement by Means of an Orion EA940 Expandable Ion Analyzer

5.3 AMDT-M-4-0, Extraction of Fluorochemicals from Rabbit Liver

5.4 AMDT-M-8-0, Analysis of Fluoride Using the Skalar Segmented Flow Analyzer with Ion Selective Electrode

5.5 AMDT-M-14-0, Thermal Extraction of Fluoride by Means of a Modified Dohrmann DX2000 Organic Halide Analyzer-Serum

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6.0 DATA ANALYSIS

Raw data are shown in Table I (Appendix 9.11). Doses are adjusted for the FC-95 equivalents. The administered dose was T-6246 which is a water solution of 0.12% FC-95. Serum concentrations are obviously not different than the control concentrations for the 0.006 and 0.012 mg/kg doses. The concentration in serum is plotted for Group 4 and Group 5 (see pages 140-141). For Group 5 (0.60 mg/kg dose), if the average concentration is fit to a least square regression $Y=ae^{-kt}$, $r^2=0.95$, $a=1.62$, $k=-1.099 \times 10^{-3}$, $k=0.693$ over $t_{1/2}$, and $t_{1/2}=26$ days. Similarly, $t_{1/2}=48$ days for Group 4. Thus, if Perfluorooctanesulfonate ion is formed from biotransformation, a large portion of the amount formed will be present in the serum at 28 days.

The average liver fluoride ion concentration in Group 5 animals, at day 14 post dose was 1.48 ppm and for four other animals in the same group sacrificed at day 28 the concentration was 1.23 ppm. Thus, the decrease in concentration in liver from 14 days to 28 days post dose is slow; based on just these two points the half-life is greater than 1 month.

Overall, for all time periods the serum and liver levels are as expected for the intravenous dose. The ability to detect levels in liver after an intravenous dose of 120 ug/kg suggests that when perfluorooctanesulfonate is the marker, dermal absorption studies will be quite sensitive.

6.1 Circumstances That May Affect the Quality of the Data: These values for concentration are from combustion analyses of the biological material. The recoveries are based on spiking the biological material with known amounts of FC-95. The fluorine is measured by selective ion electrode and the Orion meter is calibrated over a 5 point range. However, if there is a different response at different concentrations of FC-95 other than the point used as a calibration check, there could be a bias at those concentrations even though the amount of fluorine is being measured accurately. This can come from other variables in the method such as the efficiency of combustion. Thus, the values reported for concentration are not absolute values. The values are certainly sufficient to make the point that the perfluorooctanesulfonate anion is present at 28 days in liver and serum, that the half-life is on the order of a month or longer, and that the method can detect perfluorooctanesulfonate in serum after a dose somewhere between 0.012 and 0.12 mg/kg. This method allows sufficient sensitivity for dermal absorption studies where some of the applied fluorochemical is biotransformed to perfluorooctanesulfonate anion.

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7.0 CONCLUSION

The half-life of perfluorooctanesulfonate in liver and serum after an intravenous dose is one month or greater in rabbits. The perfluorooctanesulfonate anion can be detected by the combustion method and subsequent fluoride analysis at 28 days after either a 0.12 or a 0.60 mg/kg intravenous dose. The 0.012 mg/kg intravenous dose does not provide sufficient fluoride ion for this method. The method would probably be able to detect a dose somewhere between 0.012 and 0.12 mg/kg. Analysis of fluorine at 28 days in liver and serum provides a marker for dermal absorption for dermally applied fluorochemicals that are biotransformed to perfluorooctanesulfonate anion.

8.0 MAINTENANCE OF RAW DATA AND RECORDS

8.1 Raw Data and Data: Raw data, approved protocol, approved final report, appropriate specimens, and electronic data will be maintained in the AMDT Archives.

9.0 APPENDICES

9.1 Protocol and Amendments

9.1.1 Protocol and Final Report: HWI#6329-159 "Single Dose Intravenous Pharmacokinetic Study of T-6246 in Rabbits" (Protocol type TP8084.PK for dosing of animals, tissue collection, etc.)

9.1.2 Analytical protocol AMDT-042095.1

9.2 Signed Reports from Individual Scientists: None

9.3 Quality Assurance Unit Statement: See attached

9.4 Key Personnel Involved in the Study: See attached

9.5 Materials and Equipment: See methods

9.6 Solutions, Reagents, and Standards: See methods

9.7 Sample Preparation: See methods

9.8 Quality Control Practices: See methods

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9.9 Test Methods: See Protocol AMDT-042095.1

9.10 Instrument Settings: See methods

9.11 Data: See attached:

9.11.1 Summary and raw data; ug F⁻ in whole liver as determined by thermal extraction followed by analysis using Orion ion analyzer.

9.11.2 Summary and raw data; ug F⁻ in whole liver as determined by thermal extraction followed by analysis using Skalar segmented flow analyzer with ion selective electrode.

9.11.3 Summary and raw data; ppm F⁻ in serum as determined by thermal extraction followed by analysis using Orion ion analyzer.

9.11.4 Summary and raw data; ppm F⁻ in serum as determined by thermal extraction followed by analysis using Skalar segmented flow analyzer with ion selective electrode.

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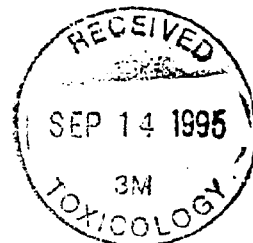
9.1.1 Protocol and Final Report: HWI#6329-159 “Single Dose Intravenous Pharmacokinetic Study of T-6246 in Rabbits” (Protocol type TP8084.PK for dosing of animals, tissue collection, etc.)

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Sponsor:

3M
St. Paul, Minnesota



FINAL REPORT

Study Title:

Single-Dose Intravenous Pharmacokinetic
Study of T-6246 in Rabbits

Author:

Steven M. Glaza

Study Completion Date:

September 14, 1995

Performing Laboratory:

Hazleton Wisconsin, Inc.
3301 Kinsman Boulevard
Madison, Wisconsin 53704

Laboratory Project Identification:

HWI 6329-159

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Phone 608-241-4471

Fax 608-241-7227

EXPRESS-MAIL DELIVERY: 3301 KINSMAN BLVD. MADISON, WI 53704

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QUALITY ASSURANCE STATEMENT

This report has been reviewed by the Quality Assurance Unit of Hazleton Wisconsin, Inc., in accordance with the Food and Drug Administration (FDA) Good Laboratory Practice Regulations, 21 CFR 58.35 (b) (6) (7). The following inspections were conducted and findings reported to the Study Director and management. Written status reports of inspections and findings are issued to Hazleton management monthly according to standard operating procedures.

Inspection Dates		Phase	Date	Date to
From	To		Reported to Study Director	Management
03/22/95	03/22/95	Protocol Review	03/22/95	03/10/95
04/10/95	04/10/95	Protocol Amendment	04/10/95	05/10/95
04/27/95	04/27/95	Animal Observation	04/27/95	05/10/95
07/05/95	07/10/95	Data/Report Review	07/10/95	08/10/95
09/12/95	09/12/95	Report Rereview	09/12/95	10/10/95

Randy Hestey
Representative, Quality Assurance Unit

9.14.95
Date

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HWI 6329-159

STUDY IDENTIFICATION

Single-Dose Intravenous Pharmacokinetic
Study of T-6246 in Rabbits

Test Material	T-6246
Sponsor	3M Toxicology Service Medical Department 3M Center, Bldg. 220-2E-02 P.O. Box 33220 St. Paul, MN 55133-3220
Sponsor's Representative	John L. Butenhoff, PhD 3M Toxicology Service Medical Department 3M Center, Bldg. 220-2E-02 P.O. Box 33220 St. Paul, MN 55133-3220 (612) 733-1962
Study Director	Steven M. Glaza Hazleton Wisconsin, Inc. P.O. Box 7545 Madison, WI 53707-7545 (608) 241-7292
Study Location	Hazleton Wisconsin, Inc. 3301 Kinsman Boulevard Madison, WI 53704
Study Timetable	
Study Initiation Date	March 30, 1995
Experimental (In-life) Start Date	April 4, 1995
In-life End Date	May 1, 1995
Experimental Termination Date	September 14, 1995
Study Completion Date	September 14, 1995

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KEY PERSONNEL

Acute Toxicology

Steven M. Glaza
Study Director
Manager

Francis (Bud) W. McDonald
Study Coordinator

Patricia Padgham
In-life Supervisor

Rose M. Bridge
Report Supervisor

Toxicology Support

Kathy Myers
Manager

Calvin L. Horton
Supervisor

Quality Assurance

Sherry R. W. Petsel
Manager

Laboratory Animal Medicine

Cindy J. Cary, DVM
Diplomate, ACLAM
Supervisor

Anatomical Pathology

Thomas E. Palmer, PhD
Anatomical Pathologist

Jack Serfort/
Deborah L. Pirkel
Supervisors
Necropsy

Anne Mosher
Supervisor
Pathology Data

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SUMMARY

This study was done to assess the level of systemic exposure of T-6246 when administered by a single intravenous injection to rabbits.

The study was conducted using four male and four female acclimated rabbits of the Hra:(NZW)SPF strain for each treatment group as follows:

<u>Group</u>	<u>Test Material</u>	<u>Dose Level (mg/kg)</u>	<u>Number of Animals</u>	
			<u>Males</u>	<u>Females</u>
1 (Control)	Sterile water	0	4	4
2 (Low)	T-6246	5	4	4
3 (Medium)	T-6246	10	4	4
4 (High)	T-6246	100	4*	4
5 (High)	T-6246	500	4*	4

* One animal sacrificed after treatment due to a possible broken back and replaced with another male animal.

The animals received a single intravenous injection of the test material at the indicated dose level into the marginal ear vein of the right ear. The dose volume was 0.5 mL/kg of body weight for Groups 1 through 4 and was 0.75 mL/kg for Group 5. Two animals/sex/dose level were sacrificed on Day 15 and the remaining animals (two animals/sex/dose level) were sacrificed on Day 28.

Clinical observations were conducted predose and at approximately 0.5, 2, and 4 hours after intravenous injection. Additional clinical observations and twice a day mortality checks were conducted daily thereafter until the scheduled sacrifice interval (Day 15 or Day 28). Body weights were determined on Day -7 for randomization purposes, before test or control material administration (Day 1), and at the scheduled sacrifice interval (Day 15 or Day 28). A blood sample (approximately 4 mL) was collected from a marginal ear vein (left ear) of the animals at 4-, 8-, 12-, 24-, and 48-hours post-injection, and on Day 8. An approximate 4-mL blood sample was also collected on Days 15 and 22 for the animals scheduled for sacrifice on Day 28. In addition, at the time of the scheduled sacrifice (Day 15 or Day 28), approximately 20 mL of blood was obtained from each animal. All samples were centrifuged, separated into serum and cellular fractions, and sent to the Sponsor. On Day 15 or 28, the animals were anesthetized with sodium pentobarbital, bled via the posterior vena cava, and exsanguinated. An abbreviated gross necropsy examination was not done, however, tissues were collected. The whole liver, bile, and both kidneys from each animal were collected, weighed (volume only determined for bile), and sent frozen to the Sponsor.

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Intravenous injection of T-6246 did not result in any test material-related changes in body weight gain. All animals appeared clinically normal throughout the study with the exception of one Group 4 and one Group 5 male animals that were sacrificed on Days 2 and 1, respectively, due to injury (possible broken backs). These animals were replaced and the replacement animals appeared clinically normal throughout the study.

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OBJECTIVE

The objective of this study was to assess the level of systemic exposure to the test material, T-6246, when administered as a single intravenous injection to rabbits.

REGULATORY COMPLIANCE

This study was conducted in accordance with the U.S. Food and Drug Administration's Good Laboratory Practice Regulations for Nonclinical Laboratory Studies, 21 CFR 58, with the exception that analysis of the test mixtures for concentration, homogeneity/solubility, and stability was not conducted. All procedures used in this study were in compliance with the Animal Welfare Act Regulations. In the opinion of the Sponsor and study director, the study did not unnecessarily duplicate any previous work.

TEST AND CONTROL MATERIALS

Identification

The test material was identified as T-6246 and described as a clear, colorless liquid. The control material was Sterile Water for Injection, USP (Abbott Laboratories, Lot No. 86-748-DM-02; Exp. April 1, 1996), and was described as a clear, colorless liquid.

Purity and Stability

The Sponsor assumes responsibility for test material purity and stability determinations (including under test conditions). Analysis of the test material mixtures for concentration, homogeneity/solubility, and stability was not conducted or requested by the Sponsor. The purity and stability of the control material were considered to be adequate for the purposes of this study.

Storage and Retention

The test material was stored at room temperature. The control material was stored refrigerated. Any unused test material was returned to the Sponsor after completion of all in-life testing according to Hazleton Wisconsin (HWI) Standard Operating Procedure (SOP). Any remaining vehicle may be used for other testing and will not be discarded after issuance of the final report.

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Safety Precautions

The test and control material handling procedures were according to HWI SOPs and policies.

TEST SYSTEM

Test Animal

Adult albino rabbits of the Hra:(NZW)SPF strain were received from HRP, Inc., Kalamazoo, Michigan on March 8, 1995 and maintained at the Hazleton Wisconsin facility at 3301 Kinsman Boulevard, Madison, Wisconsin.

Housing

After receipt, the animals were acclimated for a period of at least 7 days. During acclimation and throughout the study, the animals were individually housed in screen-bottom stainless steel cages in temperature- and humidity-controlled quarters. Environmental controls for the animal room were set to maintain a temperature of 19° to 23°C, a relative humidity of 50% $\pm$ 20%, and a 12-hour light/12-hour dark lighting cycle. In cases where variations from these conditions existed, they were documented and considered to have had no adverse effect on the study outcome.

Animal Diet

The animals were provided access to water *ad libitum* and a measured amount of Laboratory Rabbit Diet HF #5326, PMI Feeds, Inc. The feed is routinely analyzed by the manufacturer for nutritional components and environmental contaminants. Samples of the water are periodically analyzed by HWI. There were no known contaminants in the feed or water at levels that would have interfered with or affected the results of the study.

Selection of Test Animals

The animals were identified by animal number and corresponding ear tag and were placed into study groups using a stratified body weight randomization program. The randomization body weights were determined on Day -7. The weight variation of the animals for each group of each sex selected for the study did not exceed ± 2 standard deviations of the mean weight, and the mean body weights for each group of each sex were not statistically different at the 5% probability level.

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Study Design

Animals weighing from 2,523 to 3,276 g at initiation of treatment were placed into the following study groups:

<u>Group</u>	<u>Test/Control Material</u>	<u>Dose Level (mg/kg)</u>	<u>Dose Volume (mL/kg)</u>	<u>Number of Animals^a</u>	
				<u>Males</u>	<u>Females</u>
1 (Control)	Sterile water	0	0.5	4	4
2 (Low)	T-6246	5	0.5	4	4
3 (Medium)	T-6246	10	0.5	4	4
4 (High)	T-6246	100	0.5	4*	4
5 (High)	T-6246	500	0.75	4*	4

* One animal sacrificed after treatment due to a possible broken back and replaced with another male animal.

a Two animals/sex/dose level were sacrificed on Day 15. The remaining animals (two animals/sex/dose level) were sacrificed on Day 28.

Justification for Species Selection

Historically, the New Zealand White albino rabbit has been the animal of choice because of the large amount of background information on this species.

PROCEDURES

Dose Preparation and Administration

The test material was diluted with sterile water to achieve a specific concentration for each dose level in Groups 2 to 5. An individual dose of each respective test solution or control was calculated for each animal based on its body weight on the day of treatment. The respective test solution was administered by intravenous injection into the marginal ear vein of the right ear over approximately 22 to 60 seconds. The prepared test solutions were stored at room temperature until administered. After administration, any remaining test solutions were discarded.

Reason for Route of Administration

Intravenous injection is an acceptable route to assess systemic exposure.

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Observations of Animals

Clinical observations were conducted predose and at approximately 0.5, 2, and 4 hours after intravenous injection. Additional clinical observations and twice a day mortality checks were conducted daily thereafter until the scheduled sacrifice interval (Day 15 or Day 28).

Body weights were determined on Day -7 for randomization purposes and before test or control material administration (Day 1). Additional body weights were determined at the scheduled sacrifice interval (Day 15 or Day 28) or at unscheduled sacrifices (when survival exceeded 1 day).

Sample Collections

A blood sample (approximately 4 mL) was collected from the marginal ear vein (left ear) of the animals at 4-, 8-, 12-, 24-, and 48-hours post-injection, and on Day 8. An approximate 4-mL blood sample was also collected on Days 15 and 22 for the animals scheduled for sacrifice on Day 28. In addition, at the time of necropsy, approximately 20 mL of blood was obtained from the posterior vena cava of each animal. All samples were stored at room temperature, and then centrifuged, separated into serum and cellular fractions. These samples were then stored in a freezer set to maintain a temperature of $-20^{\circ}\text{C} \pm 10^{\circ}\text{C}$ until shipped to the Sponsor.

Pathology

The animals sacrificed on Days 1 and 2 due to apparent broken backs were necropsied in the same manner as the animals surviving to the scheduled sacrifices with the exception that they received an abbreviated gross necropsy examination and any abnormalities were recorded.

On Day 15, the first two animals/sex assigned to each dose level (based on the group assignment randomization) were anesthetized with sodium pentobarbital (via injection in the marginal ear vein), bled via the posterior vena cava, and exsanguinated. An abbreviated gross necropsy examination was not done, however, tissues were collected. The whole liver, bile, and both kidneys from each animal were collected, weighed (volume only determined for bile), and immediately placed in a freezer set to maintain a temperature of $-20^{\circ}\text{C} \pm 10^{\circ}\text{C}$. After tissue/bile collection, the animals were discarded. The remaining two animals/sex/dose level were anesthetized, bled, and exsanguinated on Day 28 in the same manner as the animals sacrificed on Day 15.

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Shipment of Tissues

After completion of the in-life phase, the blood samples (serum and cellular fractions), livers, bile, and kidneys were sent frozen (on dry ice) to the Sponsor (James D. Johnson, 3M E.E. & P.C., Bldg. 2-3E-09, 935 Bush Avenue, St. Paul, MN, 55106), along with their corresponding weights or volumes. The Sponsor is responsible for the retention and disposition of the samples. HWI does not accept any responsibility for the analysis of the samples collected in this study nor are these results presented in this report.

Statistical Analyses

No statistical analyses were required by the protocol.

Location of Raw Data, Records, and Final Report

The raw data, records, and an original signed copy of the final report will be retained in the archives of HWI in accordance with HWI SOP.

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RESULTS

Body Weights

Individual body weights are in Table 1. There was no meaningful effect on body weight gain during the study.

Clinical Observations

Individual clinical signs are in Table 2. All animals appeared normal throughout the study with the following exceptions:

- One Group 4 male (No. F54106) treated with T-6246 at 100 mg/kg appeared to have injured its back on Day 2 and was sacrificed, necropsied, and replaced with No. F54099. The replacement animal appeared normal throughout the study.
- One Group 5 male (No. F54076) treated with T-6246 at 500 mg/kg appeared to have injured its back on the day of treatment and was sacrificed, necropsied, and replaced with No. F54112. The replacement animal appeared normal throughout the study.

Pathology

Individual animal pathology comments are presented in Table 3. Individual animal tissue weights and bile volumes are in Table 4. The necropsy of animal No. F54106 revealed the skeletal muscle surrounding the lumbar spinal cord was diffusely dark red. In animal No. F54076, the skeletal muscle surrounding both hind limbs and the sacral spinal cord was diffusely dark red. The remaining animals survived to their scheduled sacrifice and were not examined grossly, although tissues were saved.

Page 15 contains a pathology report by the study pathologist.

DISCUSSION

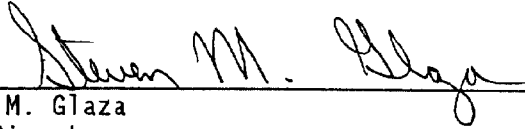
The level of systemic exposure of T-6246 was evaluated in male and female albino rabbits when administered as a single intravenous injection at levels of 5, 10, 100, and 500 mg/kg. There were no test material-related effects in any of the animals following administration of this material.

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HWI 6329-159

SIGNATURE



Steven M. Glaza
Study Director
Acute Toxicology

Date 9-14-95

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PATHOLOGY REPORT

There were two male rabbits sacrificed on Day 1 or Day 2 and necropsied. At necropsy, the skeletal muscle surrounding the lumbar spinal cord in Animal No. F54106 (100 mg/kg of body weight) was diffusely dark red. In Animal No. F54076 (500 mg/kg of body weight), the skeletal muscle surrounding both hind limbs and the sacral spinal cord was diffusely dark red. The findings in these animals are indicative of injury of undetermined etiology to the caudal region of the back. The liver, bile, and both kidneys from these animals were collected as required by protocol. After necropsy, the animals were discarded.


Thomas E. Palmer, PhD
Pathologist

9-14-95
Date

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Table 1
Individual Body Weights (g)

<u>Sex</u>	<u>Animal Number</u>	<u>Random- ization (Day -7)</u>	<u>Initial (Day 1)</u>	<u>Terminal</u>	
				<u>Day 15</u>	<u>Day 28</u>
<u>Group 1 (Control) - Sterile Water for Injection (0 mg/kg)</u>					
Male	F54105	2,603	2,761	2,933	-
	F54075	2,531	2,539	2,703	-
	F54081	2,373	2,526	-	2,874
	F54107	2,544	2,731	-	3,056
Female	F54104	2,665	2,890	3,130	-
	F54086	2,526	2,632	2,775	-
	F54074	2,540	2,703	-	2,990
	F54085	2,553	2,667	-	3,014
<u>Group 2 - T-6246 (5 mg/kg)</u>					
Male	F54083	2,381	2,598	2,538	-
	F54100	2,675	2,869	3,030	-
	F54077	2,459	2,592	-	2,859
	F54094	2,466	2,601	-	2,916
Female	F54091	2,717	2,785	2,996	-
	F54108	2,412	2,622	2,790	-
	F54102	2,690	2,839	-	3,290
	F54097	2,439	2,533	-	2,928
<u>Group 3 - T-6246 (10 mg/kg)</u>					
Male	F54071	2,487	2,523	2,709	-
	F54093	2,652	2,776	2,993	-
	F54095	2,662	2,772	-	3,126
	F54101	2,622	2,642	-	3,162
Female	F54110	2,719	2,802	2,959	-
	F54096	2,772	2,914	3,022	-
	F54090	2,542	2,740	-	3,022
	F54078	2,710	2,842	-	3,244

- Not required.

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Table 1 (Continued)
Individual Body Weights (g)

<u>Sex</u>	<u>Animal Number</u>	<u>Random- ization (Day -7)</u>	<u>Initial (Day 1)</u>	<u>Terminal</u>	
				<u>Day 15</u>	<u>Day 28</u>
<u>Group 4 - T-6246 (100 mg/kg)</u>					
Male	F54088	2,494	2,582	2,771	-
	F54106 ^a	2,677	2,833	2,803 ⁽²⁾	-
	F54089	2,597	2,662	-	2,911
	F54087	2,578	2,665	-	3,060
	F54099	2,360	2,764	3,004	-
Female	F54080	2,498	2,622	2,835	-
	F54092	2,400	2,540	2,667	-
	F54109	2,592	2,657	-	2,979
	F54114	2,776	2,933	-	3,296
<u>Group 5 - T-6246 (500 mg/kg)</u>					
Male	F54076 ^b	2,655	2,678	-	-
	F54113	2,667	2,753	2,896	-
	F54082	2,734	2,843	-	3,216
	F54111	2,547	2,784	-	3,228
	F54112	2,996	3,276	3,530	-
Female	F54098	2,565	2,679	2,856	-
	F54084	2,510	2,600	2,821	-
	F54079	2,468	2,526	-	2,959
	F54116	2,442	2,611	-	3,002

- Not required.

a Animal No. F54106 was originally selected by the randomization program for use in the study and was treated. This animal was sacrificed on Day 2 due to a broken back and was replaced with No. F54099.

() Number in superscripted parentheses indicates the day the body weight was taken.

b Animal No. F54076 was originally selected by the randomization program for use in the study and was treated. This animal was sacrificed on Day 1 due to a broken back and was replaced with No. F54112.

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Table 2
Individual Clinical Signs

Sex	Animal Number	Observation	Hour (Day 1)			Day		
			0.5	2	4	2	3 to 15	16 to 28
Group 1 (Control) - Sterile Water for Injection (0 mg/kg)								
Male	F54105	Appeared normal	✓	✓	✓	✓	✓	*
	F54075	Appeared normal	✓	✓	✓	✓	✓	*
	F54081	Appeared normal	✓	✓	✓	✓	✓	✓
	F54107	Appeared normal	✓	✓	✓	✓	✓	✓
Female	F54104	Appeared normal	✓	✓	✓	✓	✓	*
	F54086	Appeared normal	✓	✓	✓	✓	✓	*
	F54074	Appeared normal	✓	✓	✓	✓	✓	✓
	F54085	Appeared normal	✓	✓	✓	✓	✓	✓
Group 2 - T-6246 (5 mg/kg)								
Male	F54083	Appeared normal	✓	✓	✓	✓	✓	*
	F54100	Appeared normal	✓	✓	✓	✓	✓	*
	F54077	Appeared normal	✓	✓	✓	✓	✓	✓
	F54094	Appeared normal	✓	✓	✓	✓	✓	✓
Female	F54091	Appeared normal	✓	✓	✓	✓	✓	*
	F54108	Appeared normal	✓	✓	✓	✓	✓	*
	F54102	Appeared normal	✓	✓	✓	✓	✓	✓
	F54097	Appeared normal	✓	✓	✓	✓	✓	✓

* Animal sacrificed on Day 15.

✓ Condition existed.

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Table 2 (Continued)
Individual Clinical Signs

Sex	Animal Number	Observation	Hour (Day 1)			Day		
			0.5	2	4	2	3 to 15	16 to 28
<u>Group 3 - T-6246 (10 mg/kg)</u>								
Male	F54071	Appeared normal	✓	✓	✓	✓	✓	*
	F54093	Appeared normal	✓	✓	✓	✓	✓	*
	F54095	Appeared normal	✓	✓	✓	✓	✓	✓
	F54101	Appeared normal	✓	✓	✓	✓	✓	✓
Female	F54110	Appeared normal	✓	✓	✓	✓	✓	*
	F54096	Appeared normal	✓	✓	✓	✓	✓	*
	F54090	Appeared normal	✓	✓	✓	✓	✓	✓
	F54078	Appeared normal	✓	✓	✓	✓	✓	✓
<u>Group 4 - T-6246 (100 mg/kg)</u>								
Male	F54088	Appeared normal	✓	✓	✓	✓	✓	*
	F54106	Appeared normal	✓	✓	✓	-		
		Broken back	-	-	-	✓		
		Moribund sacrifice	-	-	-	✓		
	F54089	Appeared normal	✓	✓	✓	✓	✓	✓
F54087	Appeared normal	✓	✓	✓	✓	✓	✓	
F54099 ^a	Appeared normal	✓	✓	✓	✓	✓	*	
Female	F54080	Appeared normal	✓	✓	✓	✓	✓	*
	F54092	Appeared normal	✓	✓	✓	✓	✓	*
	F54109	Appeared normal	✓	✓	✓	✓	✓	✓
	F54114	Appeared normal	✓	✓	✓	✓	✓	✓

* Animal sacrificed on Day 15.

✓ Condition existed.

- Condition not evident.

^a Replacement animal for Animal No. F54106.

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Table 2 (Continued)
Individual Clinical Signs

Sex	Animal Number	Observation	Hour (Day 1)			Day		
			0.5	2	4	2	3 to 15	16 to 28
<u>Group 5 - T-6246 (500 mg/kg)</u>								
Male	F54076	Appeared normal	✓	✓	✓			
		Broken back	-	-	†			
		Moribund sacrifice	-	-	†			
	F54113	Appeared normal	✓	✓	✓	✓	✓	*
	F54082	Appeared normal	✓	✓	✓	✓	✓	✓
	F54111	Appeared normal	✓	✓	✓	✓	✓	✓
	F54112 ^a	Appeared normal	✓	✓	✓	✓	✓	*
Female	F54098	Appeared normal	✓	✓	✓	✓	✓	*
	F54084	Appeared normal	✓	✓	✓	✓	✓	*
	F54079	Appeared normal	✓	✓	✓	✓	✓	✓
	F54116	Appeared normal	✓	✓	✓	✓	✓	✓

* Animal sacrificed on Day 15.

✓ Condition existed.

- Condition not evident.

† Condition evident at time of 12-hour bleeding interval.

^a Replacement animal for Animal No. F54076.

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Table 3
Individual Pathology Comments

<u>Animal Number</u>	<u>Sex</u>	<u>Test Day</u>		<u>Necropsy Observation</u>
		<u>Died</u>	<u>Sacrificed</u>	
<u>Group 4 - T-6246 (100 mg/kg)</u>				
F54106	M	-	2	The skeletal muscle surrounding the lumbar spinal cord is diffusely dark red.
<u>Group 5 - T-6246 (500 mg/kg)</u>				
F54076	M	-	1	The skeletal muscle surrounding both hind limbs and sacral spinal cord is diffusely dark red.

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Table 4
Individual Animal Tissue Weights and Bile Volumes

<u>Sex</u>	<u>Animal Number</u>	<u>Sacrifice Day</u>	<u>Weight (g)</u>		<u>Bile Volume (mL)</u>
			<u>Liver</u>	<u>Kidneys</u>	
<u>Group 1 (Control) - Sterile Water for Injection (0 mg/kg)</u>					
Male	F54105	15	86.35	14.92	0.6
	F54075	15	60.25	15.97	0.1
	F54081	28	80.597	14.764	1.2
	F54107	28	80.649	15.620	0.4
Female	F54104	15	98.40	16.03	0.7
	F54086	15	77.30	15.23	0.7
	F54074	28	82.895	18.793	1.6
	F54085	28	80.950	14.925	1.3
<u>Group 2 - T-6246 (5 mg/kg)</u>					
Male	F54083	15	73.15	14.87	0.7
	F54100	15	77.90	17.62	0.7
	F54077	28	75.699	17.864	0.3
	F54094	28	78.689	17.213	0.8
Female	F54091	15	84.90	14.92	1.6
	F54108	15	79.90	15.40	0.4
	F54102	28	101.494	18.308	1.7
	F54097	28	73.621	16.214	1.4

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Table 4 (Continued)
Individual Animal Tissue Weights and Bile Volumes

<u>Sex</u>	<u>Animal Number</u>	<u>Sacrifice Day</u>	<u>Weight (g)</u>		<u>Bile Volume (mL)</u>
			<u>Liver</u>	<u>Kidneys</u>	
<u>Group 3 - T-6246 (10 mg/kg)</u>					
Male	F54071	15	77.10	15.88	0.5
	F54093	15	81.40	15.50	0.8
	F54095	28	85.504	15.561	1.2
	F54101	28	85.668	16.120	1.0
Female	F54110	15	83.68	15.79	1.4
	F54096	15	78.10	18.70	1.1
	F54090	28	76.220	15.878	2.1
	F54078	28	83.460	18.130	1.0
<u>Group 4 - T-6246 (100 mg/kg)</u>					
Male	F54088	15	84.26	16.98	0.4
	F54106	2	82.301	16.550	2.0
	F54089	28	71.796	16.434	1.0
	F54087	28	83.710	18.591	0.6
	F54099 ^a	15	82.143	16.038	0.5
Female	F54080	15	75.42	18.32	1.2
	F54092	15	78.36	16.68	*
	F54109	28	73.958	16.915	1.6
	F54114	28	80.966	19.404	2.0

^a Replacement animal for Animal No. F54106.

* This animal had no gallbladder, so no bile was collected.

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Table 4 (Continued)
Individual Animal Tissue Weights and Bile Volumes

<u>Sex</u>	<u>Animal Number</u>	<u>Sacrifice Day</u>	<u>Weight (g)</u>		<u>Bile Volume (mL)</u>
			<u>Liver</u>	<u>Kidneys</u>	
<u>Group 5 - T-6246 (500 mg/kg)</u>					
Male	F54076	1	78.058	14.695	2.0
	F54113	15	91.52	16.57	1.0
	F54082	28	88.965	19.431	1.6
	F54111	28	83.823	19.405	1.5
	F54112 ^a	15	97.824	21.069	1.4
Female	F54098	15	78.95	14.72	1.2
	F54084	15	66.42	13.18	0.8
	F54079	28	83.117	14.785	1.8
	F54116	28	71.962	15.793	2.0

a Replacement animal for Animal No. F54076.

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APPENDIX A

Protocol Deviations
Protocol TP8084.PK
Protocol Amendment No. 1

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Protocol Deviations

<u>Protocol</u>	<u>Actual Procedure</u>
Page 6, 7. Experimental Design, C. Dosing Procedures, (1) Dosing Route. Intravenous injection into the marginal ear vein of the right ear over approximately 30 to 60 seconds.	The rate of injection for one Group 5 female (No. F54098) was 22 seconds. Also, the time for dose administration for one male animal (Group 4, No. F54087) was incorrectly recorded thus the exact duration of dosing can not be determined.

These deviations are not considered to have had an adverse effect on the outcome of the study.

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a **CORNING** Company

Sponsor:

3M
St. Paul, Minnesota

PROTOCOL TP8084.EXT

Study Title:

Single-Dose Intravenous Pharmacokinetic Study
of T-6246 in Rabbits

Date:

March 30, 1995

Performing Laboratory:

Hazleton Wisconsin, Inc.
3301 Kinsman Boulevard
Madison, Wisconsin 53704

Laboratory Project Identification:

HWI 6329-159

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Phone 608-241-4471

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Fax 608-241-7227
MADISON, WI 53704

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Page 2

STUDY IDENTIFICATION

Single-Dose Intravenous Pharmacokinetic Study
of T-6246 in Rabbits

HWI No.	6329-159
Test Material	T-6246
Sponsor	3M Toxicology Service Medical Department 3M Center, Bldg. 220-2E-02 P.O. Box 33220 St. Paul, MN 55133-3220
Sponsor's Representative	John L. Butenhoff, PhD 3M Toxicology Service Medical Department 3M Center, Bldg. 220-2E-02 P.O. Box 33220 St. Paul, MN 55133-3220 (612) 733-1962
Study Director	Steven M. Glaza Hazleton Wisconsin, Inc. P.O. Box 7545 Madison, WI 53707-7545 (608) 241-7292
Study Location	Hazleton Wisconsin, Inc. 3301 Kinsman Boulevard Madison, WI 53704
Proposed Study Timetable	
Experimental Start Date	April 4, 1995
Experimental Termination Date	May 1, 1995
Draft Report Date	June 12, 1995

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Page 3

1. Study
Single-Dose Intravenous Pharmacokinetic Study in Rabbits
2. Purpose
To assess the level of systemic exposure when the test material is administered as a single intravenous injection to rabbits
3. Regulatory Compliance
This study will be conducted in accordance with the following Good Laboratory Practice Regulations/Standards/Guidelines with the exception that analysis of the test material mixtures for concentration, solubility, homogeneity, and stability will not be conducted:
 - ☐ Conduct as a Nonregulated Study
 - ☒ 21 CFR 58 (FDA)
 - ☐ 40 CFR 160 (EPA-FIFRA)
 - ☐ 40 CFR 792 (EPA-TSCA)
 - ☐ C(81)30 (Final) (OECD)
 - ☐ 59 Nohsan No. 3850 (Japanese MAFF)
 - ☐ Notification No. 313 (Japanese MOHW)

All procedures in this protocol are in compliance with the Animal Welfare Act Regulations. In the opinion of the Sponsor and study director, the study does not unnecessarily duplicate any previous work.
4. Quality Assurance
The protocol, study conduct, and the final report will be audited by the Quality Assurance Unit in accordance with Hazleton Wisconsin (HWI) Standard Operating Procedures (SOPs) and policies.
5. Test Material
 - A. Identification
T-6246
 - B. Physical Description
(To be documented in the raw data)
 - C. Purity and Stability
The Sponsor assumes responsibility for purity and stability determinations (including under test conditions). Samples of test material/vehicle mixture(s) for concentration, solubility, homogeneity, and stability analyses will be taken before administration if requested by the Sponsor. These samples (if taken) will be sent to the Sponsor after experimental termination.
 - D. Storage
Room temperature

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E. Reserve Samples

Reserve sample(s) of each batch/lot of test and control materials will be taken for this study.

The test and control material reserve samples will be stored at HWI in a freezer set to maintain a temperature of $-20^{\circ}\text{C} \pm 10^{\circ}\text{C}$ for 10 years per HWI SOP. The Sponsor will be contacted after 10 years for disposition in accordance with the appropriate regulatory Good Laboratory Practices.

F. Retention

Any unused test material will be returned to the Sponsor after completion of the in-life phase of the study.

G. Safety Precautions

As required by HWI SOPs and policies

6. Control Material

A. Identification

Sterile water for injection

B. Physical Description

Clear, colorless liquid

C. Purity and Stability

The purity and stability of this USP grade material is considered adequate for the purposes of this study.

D. Storage

Refrigerated

E. Reserve Samples

See Section 5. E. Reserve Samples

F. Retention

Any remaining control material may be used for other testing and will not be discarded after issuance of the final report.

G. Safety Precautions

As required by HWI SOPs and policies

7. Experimental Design

A. Animals

(1) Species

Rabbit

(2) Strain/Source

Hra:(NZW)SPF/HRP, Inc.

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- (3) Age at Initiation
Adult
- (4) Weight at Initiation
2.5 to 3.5 kg
- (5) Number and Sex
20 males and 20 females
- (6) Identification
Individual numbered ear tag
- (7) Husbandry
 - (a) Housing
Individually, in screen-bottom stainless steel cages (heavy gauge)
 - (b) Food
A measured amount of Laboratory Rabbit Diet HF #5326 (PMI Feeds, Inc.). The food is routinely analyzed by the manufacturer for nutritional components and environmental contaminants.
 - (c) Water
Ad libitum from an automatic system. Samples of the water are analyzed by HWI for total dissolved solids, specified microbiological content, selected elements, heavy metals, organophosphates, and chlorinated hydrocarbons.
 - (d) Contaminants
There are no known contaminants in the food or water that would interfere with this study.
 - (e) Environment
Environmental controls for the animal room will be set to maintain a temperature of 19°C to 23°C, a relative humidity of 50% $\pm$ 20%, and a 12-hour light/12-hour dark cycle.
 - (f) Acclimation
At least 7 days
- (8) Selection of Test Animals
Based on health and body weight according to HWI SOPs. An adequate number of extra animals will be purchased so that no animal in obviously poor health is placed on test. The animals will be placed into study groups using a stratified body weight randomization program within nine days of study initiation.

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(9) Justification for Species Selection

Historically, the New Zealand White albino rabbit has been the animal of choice because of the large amount of background information on this species.

B. Dose Administration(1) Test Groups

<u>Group</u>	<u>Test/Control Material</u>	<u>Dose Level (mg/kg)^a</u>	<u>Number of Animals^b</u>	
			<u>Males</u>	<u>Females</u>
1 (Control)	Sterile water	0	4	4
2 (Low)	T-6246	5	4	4
3 (Medium)	T-6246	10	4	4
4 (High)	T-6246	100	4	4
5 (High)	T-6246	500	4	4

a The dose volume will be 0.5 mL/kg of body weight.

b Two animals/sex/dose level will be sacrificed on Day 15. The remaining animals (two animals/sex/dose level) will be sacrificed on Day 28.

C. Dosing Procedures(1) Dosing Route

Intravenous injection into the marginal ear vein of the right ear over approximately 30 to 60 seconds.

(2) Reason for Dosing Route

Intravenous injection is an acceptable route to assess systemic exposure.

(3) Dosing Duration

Single dose

(4) Dose Preparation

The day of treatment will be designated as Day 1. The Group 1 animals will be treated with sterile water at a dose volume of 0.5 mL/kg. The test material will be diluted with sterile water to achieve a specific concentration for each dose level in Groups 2-5. Individual doses will be calculated based on the animal's body weight taken just before test material administration. The prepared test mixtures will be stored at room temperature until administration.

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D. Observation of Animals**(1) Clinical Observations**

The animals will be observed for clinical signs of toxicity before test or control material administration, at approximately 0.5, 2.0, 4.0 hours post-injection (Day 1), and daily thereafter for clinical signs and twice daily (a.m. and p.m.) for mortality until the scheduled sacrifice interval (Day 15 or Day 28). Observations may be extended when directed by the Study Director.

(2) Body Weights

For randomization, before test or control material injection (Day 1), at the scheduled sacrifice interval (Day 15 or Day 28), and at unscheduled death and sacrifices (when survival exceeds 1 day)

(3) Sample Collections**(a) Frequency**

4-, 8-, 12-, 24-, and 48-hours post-injection, on Days 8, 15, 22, and at the scheduled sacrifice interval (Day 15 or Day 28)

(b) Method of Collection/Number of Animals

Blood samples (approximately 4 mL) will be collected from the marginal ear vein (left ear) of all animals at 4-, 8-, 12-, 24-, and 48-hours post-injection, and on Day 8. Additional samples will be collected on Days 15 and 22 for the animals scheduled for sacrifice on Day 28.

Approximately 20 mL of blood (actual volume to be documented in the raw data) will be obtained from the posterior vena cava at the time of the scheduled sacrifice (Day 15 or Day 28). Approximately 20 mL of blood will be collected from moribund animals during the study, also, if possible.

The samples will be stored at room temperature and then centrifuged, and the separate serum and cellular fractions stored in a freezer set to maintain a temperature of $-20^{\circ}\text{C} \pm 10^{\circ}\text{C}$. The separated serum and cellular fractions will be sent frozen on dry ice to the Sponsor after experimental termination. The Sponsor is responsible for the retention and disposition of the samples.

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Samples will be shipped to:

James D. Johnson
3M E.E. & P.C.
Bldg. 2-3E-09
935 Bush Avenue
St. Paul, MN 55106

James D. Johnson or his alternate will be notified by telephone at (612) 778-5294 prior to the shipment of the samples.

E. Termination

(1) Unscheduled Sacrifices and Deaths

Any animal dying during the study or sacrificed in a moribund condition will be subjected to an abbreviated gross necropsy examination and all abnormalities will be recorded. Animals in a moribund condition will be anesthetized with sodium pentobarbital (via injection in the marginal ear vein), bled via the vena cava, and exsanguinated. Tissues, as described in section 7.E. (3) Sample Collection, will be collected from any animal dying during the study or sacrificed in a moribund condition. After necropsy, the animals will be discarded.

(2) Scheduled Sacrifices

On Day 15, the first two animals/sex assigned to each dose level (based on the group assignment randomization) will be anesthetized with sodium pentobarbital (via injection in the marginal ear vein), bled via the vena cava, and exsanguinated. The remaining two animals/sex/dose level will be anesthetized with sodium pentobarbital (via injection in the marginal ear vein), bled via the vena cava, and exsanguinated on Day 28. An abbreviated gross necropsy examination will not be done, however, tissues (as described in section 7.E. (3) Sample Collection) will be collected.

(3) Sample Collection

The whole liver, bile, and both kidneys from each animal will be collected, weighed (volume only determined for bile), and immediately placed in a freezer set to maintain a temperature of $-20^{\circ}\text{C} \pm 10^{\circ}\text{C}$. After sample collection, the animals will be discarded.

The samples (liver, bile, and kidneys) will be sent frozen on dry ice to the Sponsor after experimental termination. The samples and their corresponding weights or volumes will be shipped to the person listed in Section 7.D.(3).(b). The Sponsor is responsible for the retention and disposition of the samples.

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F. Statistical Analyses

No statistical analyses are required.

8. Report

A final report including those items listed below will be submitted.

Description of the test and control materials

Description of the test system

Procedures

Dates of experimental initiation and termination

Description of any toxic effects

Gross pathology findings (if applicable)

Gross pathology report (if applicable and requested by the Study Director)

Individual animal tissue weights and bile volumes

9. Location of Raw Data, Records, and Final Report

Original data, or copies thereof, will be available at HWI to facilitate auditing the study during its progress and before acceptance of the final report. When the final report is completed, all original paper data, including those item listed below will be retained in the archives of HWI according to HWI SOP.

Protocol and protocol amendments

Dose preparation records

In-life records

Body weights

Dose administration

Observations

Sample collection records

Shipping records

Pathology Records

Study correspondence

Final report (original signed copy)

The following supporting records will be retained at HWI but will not be archived with the study data.

Animal receipt/acclimation records

Water analysis records

Animal room temperature and humidity records

Refrigerator and freezer temperature records

Instrument calibration and maintenance records

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Page 10

PROTOCOL APPROVAL

John L. Butenhoff
John L. Butenhoff, PhD
Sponsor's Representative
3M

4-4-95
Date

Steven M. Glaza
Steven M. Glaza
Study Director
Acute Toxicology
Hazleton Wisconsin, Inc.

3-30-95
Date

Ray Thach
Representative
Quality Assurance Unit
Hazleton Wisconsin, Inc.

(6329-159.protdisk2)

3-30-95
Date

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PROTOCOL TP8084.EXT

Single-Dose Intravenous Pharmacokinetic Study of
T-6246 in Rabbits

HWI 6329-159

Sponsor

3M Toxicology Service
Medical Department
3M Center, Bldg. 220-2E-02
P.O. Box 33220
St. Paul, MN 55133-3220

Contractor

Hazleton Wisconsin, Inc.
3301 Kinsman Boulevard
Madison, WI 53704

Sponsor's Representative

John L. Butenhoff, PhD

Study Director

Steven M. Glaza

Amendment No. 1

This amendment modifies the following portions of the protocol:

Effective April 4, 1995

1. Page 6, 7. Experimental Design; B. Dose Administration; (1) Test Groups.
The test material mixture for Group 5 could not be prepared at the concentration needed to utilize a dose volume of 0.5 mL/kg. Modify footnote "a" in this section with the following underlined addition:
 - a The dose volume will be 0.5 mL/kg of body weight for Groups 1-4 and 0.75 mL/kg for Group 5.

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Phone 608-241-4471

Fax 608-241-7227

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Amendment No. 1

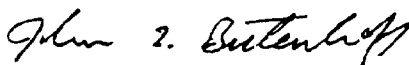
HWI 6329-159
Page 2

Effective April 5, 1995

2. Page 6, 7. Experimental Design; B. Dose Administration; (1) Test Groups.
Animal No. F54076 (Group 5 male) and Animal No. F54106 (Group 4 male)
were sacrificed on Days 1 and 2, respectively, due to injuries (apparent
broken backs). Add the following paragraph to this section:

Due to the sacrifice on Day 1 of one Group 5 male
(Animal No. F54076) and on Day 2 of one Group 4 male
(Animal No. F54106) because of injuries (apparent broken backs),
replacement animals will be treated at the same dose levels in the
same manner as for the initial animals in the study. The
observations (clinical observations, body weights and sample
collections) and the termination of the animals (unscheduled
sacrifices and deaths, scheduled sacrifices, and sample
collection) will be conducted in the same manner as for the other
animals in the study terminating on Day 15.

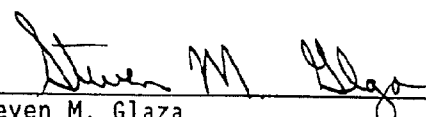
PROTOCOL AMENDMENT APPROVAL



John L. Butenhoff, PhD
Sponsor's Representative
3M Toxicology Service Medical Department

5-2-95

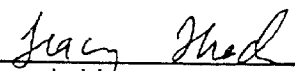
Date



Steven M. Glaza
Study Director
Acute Toxicology
Hazleton Wisconsin, Inc.

4-18-95

Date



Representative
Quality Assurance Unit
Hazleton Wisconsin, Inc.

4.18.95

Date

(6329-159.Aml.dsk3)

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9.1.2 Analytical protocol AMDT-042095.1

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3M Environmental Laboratory

Protocol - Analytical Study

Single-dose Intravenous Pharmacokinetic Study of T-6246 in Rabbits

In-Vivo Study Reference Number: HWI#6329-159

Study Number: AMDT-042095.1

Test Substance: FC-95 (T-6246)

Name and Address of Sponsor: 3M SCD Division
367 Grove Street
St. Paul, MN 55106

Name and Address of Testing Facility:
3M Environmental Technology and Services
935 Bush Avenue
St. Paul, MN 55106

Proposed Initiation Date: July 25, 1995

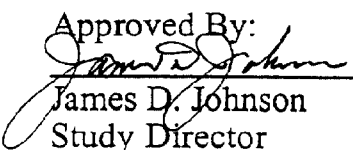
Proposed Completion Date: August 25, 1995

Method Numbers and Revisions:

AMDT-M-1-0, Thermal Extraction of Fluoride by Means of a Modified
Dohrmann DX2000 Organic Halide Analyzer-Liver
AMDT-M-2-0, Fluoride Measurement by Means of an Orion EA940 Expandable
Ion Analyzer
AMDT-M-4-0, Extraction of Fluorochemicals from Rabbit Liver
AMDT-M-8-0, Analysis of Fluoride Using the Skalar Segmented Flow Analyzer
with Ion Selective Electrode
AMDT-M-14-0, Thermal Extraction of Fluoride by Means of a Modified
Dohrmann DX2000 Organic Halide Analyzer-Serum

Author: James D. Johnson

Approved By:


James D. Johnson
Study Director

11/16/95

Date



John Butenhoff, PhD
Sponsor

11/20/95

Date

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1.0 PURPOSE

This study is designed to provide information as to whether the perfluoro-octanesulfonate anion does go to the rabbit liver and other tissues when the material is administered in an intravenous dose, and to ascertain the change in concentration with time after dose in serum and liver.

2.0 TEST MATERIALS

2.1 Test, Control, and Reference Substances and Matrices

2.1.1 Analytical Reference Substance: FC-95, lot 161 or 171. They are equivalent.

2.1.2 Analytical Reference Matrix: Bovine liver and bovine serum

2.1.3 Analytical Control Substance: None

2.1.4 Analytical Control Matrix: Bovine liver and bovine serum

2.2 Source of Materials: 3M ICP/PCP Division (2.1.1), grocery store (2.1.2, 2.1.4 liver), Sigma Chemical Company (2.1.2, 2.1.4 serum)

2.3 Number of Test and Control Samples: Liver and serum from 32 test animals and 8 control animals. Two animals were replaced at 24 hours (animal F54076 was replaced with animal F54112, and animal F54106 was replaced with animal F54099). Other biological tissues (kidney, bile, cellular fraction) will be available for analysis if deemed appropriate by the Study Director.

2.4 Identification of Test and Control Samples: The samples are identified using the HWI animal identification number which consists of a letter and five digit number, plus the tissue identity and day identity (serum).

2.5 Purity and Strength of Reference Substance: To be determined by Sponsor.

2.6 Stability of Reference Substance: To be determined by Sponsor.

2.7 Storage Conditions for Test Materials: Room temperature (2.1.1), $-20 \pm 10^{\circ}\text{C}$ (2.1.2, 2.1.4). Test and Control samples will be received according to AMDT-S-10-0.

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2.8 Disposition of Specimens: Biological tissues and fluids will be retained per GLP Regulation for the time period required for studies longer than 28 days.

2.9 Safety Precautions: Refer to appropriate MSDS. Wear appropriate laboratory attire. Use caution when handling knives for cutting the samples.

3.0 EXPERIMENTAL - Overview

The tissues from animals dosed as described (HWI#6329-159), are available for analysis for fluorine compounds. At the discretion of the Study Director, a series of analytical tests can be performed. The screening for fluoride in liver via combustion (See Methods--next Section) is the appropriate analysis to present definitive data for fluorine in the liver. For these analyses, bovine liver appears to be a good approximation to rabbit liver for matrix spikes and recovery determinations. Since perfluorooctanesulfonate anion is not biotransformed, fluorine content will be an accurate estimate of the concentration of the compound.

4.0 EXPERIMENTAL - Methods

4.1 Liver and Serum screening methods: (attached)

4.1.1 AMDT-M-1-0, Thermal Extraction of Fluoride by Means of a Modified Dohrmann DX2000 Organic Halide Analyzer-Liver

4.1.2 AMDT-M-2-0, Fluoride Measurement by Means of an Orion EA940 Expandable Ion Analyzer

4.1.3 AMDT-M-4-0, Extraction of Fluorochemicals from Rabbit Liver

4.1.4 AMDT-M-8-0, Analysis of Fluoride Using the Skalar Segmented Flow Analyzer with Ion Selective Electrode

4.1.5 AMDT-M-14-0, Thermal Extraction of Fluoride by Means of a Modified Dohrmann DX2000 Organic Halide Analyzer-Serum

5.0 DATA ANALYSIS

5.1 Data Reporting: Data will be reported as a concentration (weight/weight) of fluoride per tissue or fluid, or as FC-95 per tissue or fluid. Statistics used, at the discretion of the Study Director, may include regression analysis of serum concentrations with time and averages and standard deviations of concentrations for

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different dose groups. If necessary, simple statistical tests such as Student's t test may be applied to determine statistical difference. Half-life of disappearance from serum will be determined from the linear regression of the averages of the concentrations at different time points for the post distribution part of the serum concentration versus time curve.

6.0 MAINTENANCE OF RAW DATA AND RECORDS

6.1 Raw Data and Records: Raw data, approved protocol, appropriate specimens, approved final report, and electronic data will be maintained in the AMDT Archives.

7.0 REFERENCES

7.1 AMDT-S-10-0, Sample Tracking System

8.0 ATTACHMENTS

8.1 AMDT-M-1-0, Thermal Extraction of Fluoride by Means of a Modified Dohrmann DX2000 Organic Halide Analyzer-Liver

8.2 AMDT-M-2-0, Fluoride Measurement by Means of an Orion EA940 Expandable Ion Analyzer

8.3 AMDT-M-4-0, Extraction of Fluorochemicals from Rabbit Liver

8.4 AMDT-M-8-0, Analysis of Fluoride Using the Skalar Segmented Flow Analyzer with Ion Selective Electrode

8.5 AMDT-M-14-0, Thermal Extraction of Fluoride by Means of a Modified Dohrmann DX2000 Organic Halide Analyzer-Serum

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3M Environmental Laboratory

Method

Thermal Extraction of Fluoride by Means of a Modified Dohrmann DX2000
Organic Halide Analyzer - Liver

Method Identification Number: AMDT-M-1

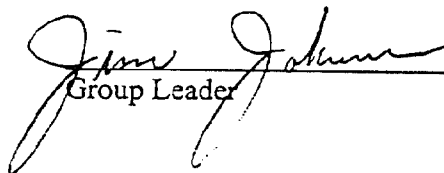
Adoption Date: 10-4-95

Revision Number: 0

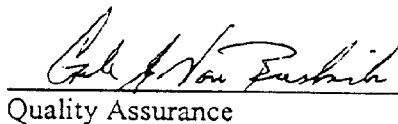
Revision Date: None

Author: Rich Youngblom

Approved by:


Group Leader

10/3/95
Date


Quality Assurance

10-4-95
Date

Software: MS Word 5.1a

Affected Documents: AMDT-M-2 Fluoride Measurement by Means of an Orion EA940
Expandable Ion Analyzer
AMDT-EP-3 Routine Maintenance of a Modified Dohrmann DX2000
Organic Halide Analyzer

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1.0 SCOPE , APPLICABLE COMPOUNDS, AND MATRICES

1.1 Scope: This method is for the operation of a Dohrmann DX2000 when it is used to extract fluoride from various matrices. The fluoride is typically collected in TISAB solution for analysis with an ion selective electrode.

1.2 Applicable Compounds: Fluorochemicals or other fluorinated compounds.

1.3 Matrices: Biological tissues, particularly liver.

2.0 KEYWORDS

2.1 Fluoride, fluorine, extraction, pyrolysis, ionization, ion selective electrode, Dohrmann, halide, DX2000, fluorochemicals.

3.0 PRECAUTIONS

3.1 Glassware and exhaust gases can be extremely hot.

3.2 Glassware is fragile, broken glass may cause injuries.

3.3 Pressurized gases, proper compressed gas handling practices required.

3.4 Solvent based samples may flash, may need to allow them to dry down before starting run.

3.5 Potential biohazards due to the biological matrices. Use appropriate personal protective equipment.

4.0 SUPPLIES AND MATERIALS

4.1 Compressed Oxygen, Hydrocarbon free, regulated to 30 PSI.

4.2 Compressed Helium, High Purity Grade, regulated to 45 PSI.

4.3 Quartz glass sample boat with Teflon™ tubing, Dohrmann 890-097 or equivalent.

4.4 Quartz glass combustion tube, Reliance Glass G-9405-012 or equivalent.

4.5 Orion 940999 Total Ionic Strength Adjustment Buffer (TISAB II) or equivalent.

4.6 Sample collection vials, HDPE.

4.7 Milli-Q™ water

4.8 Polystyrene pipettes.

4.9 Activated Charcoal, E. Merck 2005 or equivalent.

4.10 Hamilton Syringe or equivalent.

4.11 Miscellaneous laboratory glassware

5.0 EQUIPMENT

5.1 Rosemount Dohrmann DX2000 Organic Halide Analyzer, modified for fluoride extraction.

5.2 IBM compatible 386 or 486 computer.

5.3 DX2000 software, version 1.00, modified for fluoride extraction.

5.4 Excel Spreadsheet, version 5.0 or greater

6.0 INTERFERENCES

6.1 Sample size is limited to approximately 150 mg, depending on sample moisture content. This may vary from matrix to matrix.

7.0 SAMPLE HANDLING

7.1 Samples are not to be handled with bare hands. Fluoride may leach from the skin to the sample. Use forceps or probe to transfer tissues.

7.2 Samples of liver are cut from frozen liver and placed in a tared and labeled weigh boat. Use a clean scalpel and cutting board. The cutting board and scalpel should be cleaned with water, methanol, or methanol-water solution after each liver is cut.

8.0 CALIBRATION AND STANDARDIZATION

8.1 Preparation of Calibration Standards

8.1.1 The standards required for each project will need to be appropriate for that individual project. Refer to protocol for that project.

8.1.2 Typically 50-500 ppm FC-95 in methanol standards are used.

8.1.3 For rabbit liver studies, use beef liver as the matrix. Cut a piece of frozen beef liver (100 - 150 mg) and weigh it in a labeled and tared weigh boat.

8.2 Calibration - Overview

The normal calibration is the fluoride curve (AMDT-M-2). However, if an optional spiked liver curve is required the procedure listed below is used.

8.2.1 A calibration curve for the DX2000 is generated by spiking samples with known standards and combusting them using the same methods and matrix type as the samples to be tested.

8.2.2 Typically, three replicates of each standard and five concentrations of standards will be spiked.

8.2.3 Standard curve will be plotted as Mass Spiked F (ug) on the x-axis and Standard Mass Recovered F (ug) on the y-axis. Generate a regression curve and calculate the equation for the line and the r^2 value.

8.2.4 Mass Spiked F (ug) = (Amount spiked in mL) x (Conc. of standard in ppm) x (0.6004)*

*FC-95 is 60.04% F therefore 0.6004 is the factor used to convert FC-95 to F

8.2.5 Standard Mass Recovered F (ug) = (TISAB volume in mL) x (Orion reading in ppm)

8.3 Calibration - Procedure

8.3.1 Start Up

8.3.1.1 Run 2 or more Clean Cycles when starting instrument each day. More clean cycles may be used if the previous samples contained high concentrations of fluoride.

8.3.2 Blanks

8.3.2.1 Prepare sample using the same methods and type of matrix as the test sample.

8.3.2.2 For rabbit studies, use beef liver as the matrix. Prepare at least 3 samples of beef liver (100 - 150 mg) for blanks.

8.3.2.3 Put sample in Dohrmann boat. Combust each sample as described in section 9.0 and analyze sample according to method AMDT-M-2 for the ion selective electrode analysis.

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8.3.2.4 For rabbit studies, the meter reading for a blank sample should be 0.03 ppm or lower before proceeding with the calibration. Burn samples until this limit is reached, or until in the judgement of the operator the reading is stable with respect to historical readings (previous 48 hours).

8.3.2.5 For non-rabbit studies, the blank readings should reach a predetermined ion concentration before proceeding with the calibration.

8.3.2.6 It may be necessary to mix approximately 50 mg of charcoal with the sample to aid combustion.

8.3.3 Standard Curve

8.3.3.1 Weigh out at least 15 matrix samples (5 standards with 3 replicates each) in tared and labeled weigh boats. For rabbit studies, weigh 100-150 mg beef liver samples. Record weights in study data. Store the matrix samples on dry ice or ice packs to keep them frozen until used.

8.3.3.2 Place weighed beef liver sample in Dohrmann sample boat.

8.3.3.3 Start with the lowest standard concentration. Using a Hamilton syringe, eject a fixed quantity of the standard on or in the matrix. For rabbit studies, use 4 uL of standard and eject it on or in the beef liver.

8.3.3.4 At least 3 replicates should be used for the lowest standard concentration; more replicates may be used at the discretion of the analyst.

8.3.3.5 Combust the sample as described in section 9.3 and analyze according to AMDT-M-2.

8.3.3.6 Run all 15 standards. If one replicate is significantly different from the other two replicates, run another sample for that standard. Indicate in data that the new replicate replaces the old replicate and that the new replicate will be used to calculate the regression curve.

8.3.3.7 When all standards have been run, calculate the r^2 . r^2 must be at least 0.95. If it is not at least 0.95, consult with supervisor.

8.3.3.8 A new standard curve should be run when the combustion tube or sample matrix is changed. New standard curve may also be run at the discretion of the analyst.

8.4 Storage Conditions for Standards

8.4.1 Storage requirements for standards are dependent on the individual standards used. Typically, standards are stored at room temperature in plastic screw top bottles.

8.4.2 New FC-95 standards should be prepared at least once a month.

9.0 PROCEDURES

9.1 Typical Operating Conditions:

9.1.1 Combustion tube temperature = 950°C.

9.1.2 Oxygen and Helium flow = 50 cc/minute.

9.1.3 Vaporization/Drying time = 240 seconds.

9.1.4 Bake time = 300 seconds.

9.2 Start Up Procedure:

9.2.1 If the program is not started, start the EOX program on the PC.

9.2.2 Open the SYSTEM SETUP window.

9.2.3 Put the furnace module and the cell in the READY mode.

9.2.4 Close the SYSTEM SETUP window.

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9.2.5 When the oven has reached the READY temperature, run the CLEAN BOAT program found in the CELL CHECK menu.

9.2.6 See AMDT-EP-3 for details of the Dohrmann software.

9.3 Sample Extraction Procedure:

9.3.1 Open the SAMPLE HATCH and place the sample in the BOAT. It may be necessary to mix approximately 50 mg of charcoal with the sample to aid combustion. If this is done, charcoal should also be mixed in while establishing the baseline and when generating the standard curve.

9.3.2 Close SAMPLE HATCH.

9.3.3 Add appropriate volume of TISAB solution or 1:1 TISAB:Milli-Q™ water mixture to a labeled sample collection vial. Typically 0.6 mL to 15 mL are used. For rabbit studies, use 1.0 or 2.0 mL of 1:1 TISAB:Milli-Q™ water mixture.

9.3.4 Place the vial so that the tip of the COMBUSTION TUBE is in the TISAB at least 0.25 inches. Gases released during pyrolysis must bubble through the TISAB.

9.3.5 Run the EOX-SOLIDS program found in the RUN menu.

9.3.6 When the EOX program is finished, remove the collection vial from the combustion tube.

9.3.7 If undiluted TISAB was used to collect the sample, add an equal volume of Milli-Q™ water to the TISAB to make 1:1 TISAB:Milli-Q™.

9.3.8 Rinse the end of the combustion tube with Milli-Q™ water and wipe with a KIMWIP to remove any TISAB remaining on the tube.

9.3.9 Open the sample hatch and remove any remaining ash from the boat. Ash can be removed with a cotton tipped applicator or vacuumed out. It may be necessary to scrap particles off the bottom with a spatula or other similar device. A drop of Milli-Q™ water may be added to the boat to aid in the Clean Cycle.

9.3.10 Close the hatch.

9.3.11 Run the CLEAN BOAT program.

9.3.12 Sample is ready for analysis by ion selective electrode (AMDT-M-2).

9.4 Sample Calculations

9.4.1 Use the standard curve to calculate the sample value.

9.4.2 Sample Mass Recovered F (ug) = (TISAB vol in mL) x $\frac{(\text{Orion reading in ppm} - \text{intercept})}{(\text{Slope})}$

10.0 VALIDATION

10.1 Quality Control

10.1.1 Daily Start Up Check Samples: Once the standard curve is established, each day of analysis is started by analyzing QC samples. The QC samples are to be the same as the lowest concentration spiked samples used to generate the standard curve. Each concentration must be done in triplicate unless the first two replicates are within 20% of the standard curve, then a third replicate is not necessary.

10.2 Precision and Accuracy: See method development analysis and sample analysis in Fluoride Notebooks 2,3, and 5. Precision and accuracy varies when analyzing samples of different matrices and different reference compounds.

10.3 Other Validation Parameters: NA

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11.0 DATA ANALYSIS

11.1 Calculations

11.1.1 For the standard curve, use regression analysis in Excel, version 5.0 or greater.

11.1.2 To calculate the fluoride contraction in the sample, see method AMDT-M-2.

11.2 Analyzing the Data

11.2.1 r^2 must be at least 0.95 or greater. "Outliers" may be excluded if two of the three replicates are within 20% of each other and the outlier is greater than 200% of the average of those two or less than 50% of the average of those two. Any such outliers should be pointed out in the data and noted in the Final Report along with the reason it was considered an outlier.

12.0 ATTACHMENTS

None

13.0 REFERENCES

13.1 Rosemount Dohrmann DX2000 Organic Halide Analyzer Operator's Manual (Manual 915-349, revision B, December 1993)

13.2 AMDT-M-2 Fluoride Measurement by Means of an Orion EA940 Expandable Ion Analyzer

13.3 AMDT-EP-3 Routine Maintenance of a Modified Dohrmann DX2000 Organic Halide Analyzer

14.0 REVISIONS

<u>Revision</u> <u>Number</u>	<u>Reason for Change</u>	<u>Revision</u> <u>Date</u>
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3M Environmental Laboratory

Method

Fluoride Measurement by Means of an Orion EA940 Expandable Ion Analyzer

Method Identification Number: AMDT-M-2

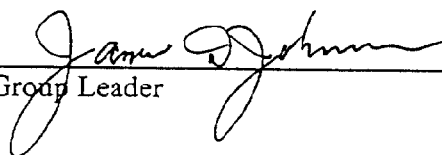
Adoption Date: 10-4-95

Revision Number: 0

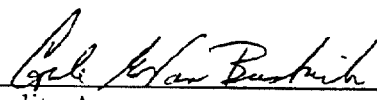
Revision Date: None

Author: Rich Youngblom

Approved By:


Group Leader

10/3/95
Date


Quality Assurance

10-4-95
Date

Software: MS Word 5.1a

Affected Documents: AMDT-M-1 Thermal Extraction of Fluoride by Means of a Modified Dohrmann DX2000 Organic Halide Analyzer

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1.0 SCOPE, APPLICABLE COMPOUNDS, AND MATRICES

1.1 SCOPE: This method is for the calibration and operation of an Orion EA940 Expandable Ion Analyzer.

1.2 APPLICABLE COMPOUNDS: Fluoride.

1.3 APPLICABLE MATRICES: Liquid samples in an appropriate buffer solution. Preferred pH of 6.0.

2.0 KEYWORDS

2.1 Fluoride, fluorine, ion selective electrode

3.0 PRECAUTIONS

3.1 No hazards identified with this method.

4.0 SUPPLIES AND MATERIALS

4.1 Orion 940999 Total Ionic Strength Adjustment Buffer II (TISABII) or equivalent.

4.2 Orion Model 900001 electrode filling solution (AgCl) or equivalent.

4.3 Orion 940907 100 ppm fluoride standard or equivalent.

4.4 Milli-Q™ water or equivalent.

4.5 Magnetic stir bars.

4.6 Lab tissues.

4.7 Sample collection vials.

4.8 Plastic 100 mL volumetric flasks.

4.9 Polystyrene pipettes.

4.10 Miscellaneous laboratory glassware.

5.0 EQUIPMENT

5.1 Orion Model EA940 Expandable Ion Analyzer or equivalent.

5.2 Orion Model 960900 Solid State Combination Fluoride electrode or equivalent.

5.3 Magnetic Stir Plate.

5.4 IBM compatible 386 or 486 computer (only needed if using Orion 3E software).

5.5 Orion RS232 interface cable (only needed if using Orion 3E software).

5.6 Microsoft Excel 5.0 (only needed if using Orion 3E software).

6.0 INTERFERENCES

6.1 It is recommended that the pH be at or near 6.0. A 1:1 mixture of TISAB and sample/Milli-Q™ water will generally bring sample to pH of 6.0.

6.2 Sample temperature may effect fluoride measurement. It is recommended that the sample be at room temperature as the standards were when the meter was calibrated.

6.3 The rate the samples are stirred at should be consistent with the rate the standards were stirred.

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6.4 Air bubbles trapped under electrode can give erroneous readings. Make sure no air is trapped under electrode.

7.0 SAMPLE HANDLING

7.1 No special handling necessary.

8.0 CALIBRATION AND STANDARDIZATION

8.1 Preparation of Calibration Standards

8.1.1 Measure 50 mL of TISAB II into 5 100 mL plastic volumetric flasks.

8.1.2 Label the flasks as 0.05, 0.1, 0.5, 1.0, and 1.5 ppm F⁻, along with the date and your initials.

8.1.3 Pipette 0.05, 0.1, 0.5, 1.0, and 1.5 mL of 100 ppm fluoride standard into the appropriately labeled flasks.

8.1.4 Add approximately 30 mL of Milli-Q™ water to each flask.

8.1.5 Shake the flasks to mix the solutions.

8.1.6 Eliminate air bubbles from the flasks by tipping the flasks on their sides and rolling the air in the flasks over the air bubbles.

8.1.7 Bring the volume in the flasks up to the 100 mL mark with Milli-Q™ water.

8.1.8 Invert and shake the flasks for the final mixing.

8.1.9 Record standards in Standards Log Book.

8.2 Calibration

8.2.1 If necessary, remove tape from electrode filling hole.

8.2.2 Invert probe to wet top seal.

8.2.3 Eject a few drops of filling solution from bottom of electrode to wet lower seal.

8.2.4 Fill the electrode with filling solution.

8.2.5 The meter and the F⁻ electrode are typically calibrated by direct measurement with no blank correction, using standards with concentrations of 0.05, 0.1, 0.5, 1.0, and 1.5 ppm F⁻, following the manufacturer's instructions.

8.2.6 Record the slope in the appropriate log book.

8.2.7 Clean the electrode by rinsing with Milli-Q™ water and wiping the sides down with lab tissues.

8.3 Storage Conditions for Standards

8.3.1 Calibration standards are stored at room temperature.

9.0 PROCEDURES

9.1 Calibration and Measurement, Standard method:

9.1.1 The sample to be measured needs to be mixed with TISAB using the proportions recommended by the TISAB manufacturer.

9.1.2 Place a stir bar in the sample and place the sample on the stir plate.

9.1.3 Allow the sample to mix for a few seconds before inserting the electrode. When the electrode is inserted, make sure there are no air bubbles trapped under the electrode.

9.1.4 The sample should be the same temperature as the calibration standards and stirred at the same rate as the calibration standards.

9.1.5 When the readings have stabilized, record the reading in the appropriate log book.

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9.2 Calibration And Measurement, Using Orion 3E Software:

9.2.1 Calibration:

9.2.1.1 Follow steps 8.2.1 to 8.2.4.

9.2.1.2 Press Function Key #8 (F8).

9.2.1.3 The computer screen will ask you to confirm the number of standards to be used, concentration of the standards, and whether or not a blank is to be included in the calibration. Make any necessary changes to the information presented and click on CONTINUE.

9.2.1.4 Place the electrode in the first standard on the stir plate and click on CONTINUE.

9.2.1.5 Observe the readings on the graphic display on the computer. When the readings have stabilized, press ACCEPT READING.

9.2.1.6 Repeat step 9.2.1.4 and 9.2.1.5 for the remaining standards.

9.2.1.7 After the final standard, the computer will display the slope of the curve, as well as the intercept and correlation. Record the slope, intercept, and correlation in the appropriate log book and click on CONTINUE. The calibration data is automatically copied to C:\Orion\Data\Calib.txt.

9.2.2 Data Spreadsheet:

9.2.2.1 Select either NEW or OPEN from the FILE menu to open a new or existing spreadsheet to store data in.

9.2.2.2 Record the name of the spreadsheet used in the appropriate log book.

9.2.3 Fluoride Measurement:

9.2.3.1 Follow steps 9.2.1 through 9.2.4

9.2.3.2 Enter the name of the sample in the appropriate place on the screen.

9.2.3.3 Click on the NEW SAMPLE button

9.2.3.4 When the readings have stabilized, click on the RECORD button and write the result in the appropriate log book.

10.0 VALIDATION

10.1 Quality Control:

10.2 Precision and Accuracy

10.3 Other Validation Parameters According to Reference 13.2, the range of detection is 0.02 ppm fluoride up to a saturated solution of fluoride.

11.0 DATA ANALYSIS

11.1 Calculations None necessary.

11.2 Analyzing the Data None necessary.

12.0 ATTACHMENTS

None

13.0 REFERENCES

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13.1 Orion Model EA940 Expandable Ion Analyzer Instruction Manual, Orion Research Incorporated, 1991.
13.2 Orion Model 960900 Solid State Combination Fluoride Electrode Instruction Manual, Orion Research Incorporated, 1991.

14.0 REVISIONS

<u>Revision Number</u>	<u>Reason for Change</u>	<u>Revision Date</u>
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3M Environmental Laboratory

Method

Extraction of Fluorochemicals from Rabbit Livers

SOP Identification Number: AMDT-M-4

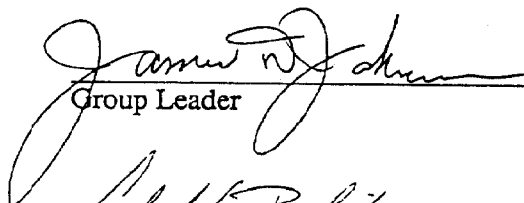
Adoption Date: 10-31-95

Revision Number: 0

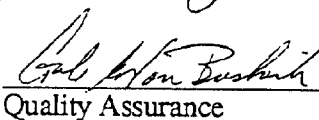
Revision Date: None

Author: Dave Christenson/Cynthia Weber

Approved By:


Group Leader

10-31-95
Date


Quality Assurance

10-31-95
Date

Software: MS Word, 6.0

Affected Documents: M-5, Analysis of Rabbit Extract for Fluorochemicals Using Electrospray Mass Spectroscopy.

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1.0 SCOPE

- 1.1 **Scope:** This method is for the extraction of fluorochemicals from rabbit livers. Ethyl acetate is used to extract fluorochemicals from the livers for analysis by electrospray mass spectroscopy.
- 1.2 **Applicable Compounds:** Fluorochemicals or other fluorinated compounds.
- 1.3 **Matrices:** Rabbit Livers.

2.0 KEYWORDS

- 2.1 Fluorochemicals, rabbit livers, electrospray mass spectrometer, fluorinated compounds, extraction.

3.0 PRECAUTIONS

- 3.1 Use gloves when handling the rabbit livers, they may contain pathogens.

4.0 SUPPLIES AND MATERIALS

- 4.1 **Supplies**
 - 4.1.1 Syringe, capable of measuring 100 μ L
 - 4.1.2 Eppendorf type or disposable pipets
 - 4.1.3 Gloves
 - 4.1.4 Plastic grinding tubes
 - 4.1.5 Plastic centrifuge tubes, 15 mL
 - 4.1.6 Labels
 - 4.1.7 Nitrogen
 - 4.1.8 Timer
 - 4.1.9 Filters, Titan nylon syringe filters, 0.2 μ m.
 - 4.1.10 Analytical pipets: glass volumetric pipets.
 - 4.1.11 Disposable plastic 3 cc syringes.
 - 4.1.12 Crimp cap autovials.
- 4.2 **Reagents**
 - 4.2.1 Aqueous Ammonium Acetate (Aldrich), approx. 250 ppm: Prepare a 2500 ppm aqueous solution of ammonium acetate by adding 250 mg ammonium acetate to a 100 mL volumetric flask and dilute to volume with Milli-Q water. Dilute this solution 1:10 for a 250 ppm solution.
 - 4.2.2 Sodium carbonate/Sodium Bicarbonate Buffer (J.T. Baker), ($\text{Na}_2\text{CO}_3/\text{NaHCO}_3$) 0.25 M: Weigh 26.5 g of sodium carbonate (Na_2CO_3) and 21.0 g of sodium bicarbonate (NaHCO_3) into a 1 L volumetric flask and bring to volume with Milli-Q water.
 - 4.2.3 Dilute acetonitrile solution, dilute acetonitrile 1:1 with Milli-Q water.
 - 4.2.4 Ethyl Acetate
 - 4.2.5 Methanol
 - 4.2.6 Milli-Q water
 - 4.2.7 1H,1H,2H,2H - perfluorooctanesulfonic acid (Aldrich)
 - 4.2.8 FC-95 (3M Specialty Chemical Division)

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5.0 EQUIPMENT

- 5.1 Ultra-Turrax T25 Grinder for grinding liver samples.
- 5.2 Vortex mixer
- 5.3 Centrifuge
- 5.4 Shaker
- 5.5 Analytical Evaporator

6.0 INTERFERENCES

- 6.1 There are no known interferences at this time.

7.0 SAMPLE HANDLING

- 7.1 The rabbit livers are received frozen, and must be kept frozen until the extraction is performed.

8.0 CALIBRATION AND STANDARDIZATION

8.1 Preparation of Internal Standards

- 8.1.1 Prepare an internal standard of approximately 12 ppm 1H,1H,2H,2H-perfluorooctanesulphonic acid to be added to each liver sample.
- 8.1.2 Weigh at least 0.1 g of 1H,1H,2H,2H-perfluorooctanesulphonic acid into a 100 mL volumetric flask. Record the actual weight.
- 8.1.3 Bring it up to volume with methanol, this is the stock standard.
- 8.1.4 To a 250 mL volumetric flask, add 3 mLs of the stock standard and bring to volume with Milli-Q water. Calculate the actual concentration of the standard.

$$\frac{\text{actual mg perfluorooctane-sulphonic acid}}{0.1 \text{ L}} \times \frac{3 \text{ mL}}{250 \text{ mL}} = \text{actual concentration, ppm}$$

8.2 Prepare FC-95 Anion Standards

- 8.2.1 Prepare FC-95 standards for the standard curve.
- 8.2.2 Weigh approximately 100 mg of FC-95 into a 100 mL volumetric flask. Record the actual weight.
- 8.2.3 Bring up to volume with dilute acetonitrile.
- 8.2.4 Dilute the solution with dilute acetonitrile 1:10 for a solution of approximately 100 ppm. Dilute this solution 1:10 with dilute acetonitrile for a solution of approx. 10 ppm.
- 8.2.5 Use the 10 ppm solution to make working standards with values close to 5.0 ppm, 1.0 ppm and 500 ppb.

8.3 Prepare Beef Liver Homogenate to Use for Standards

- 8.3.1 Weigh 40 g of Bovine liver into a 250 mL Nalgene bottle containing 200 mLs Milli-Q water. Grind to a homogenous solution.
- 8.3.2 Add 1 mL of the solution to a 15 mL centrifuge tube. Prepare a total of eight 1 mL aliquots of the solution in 15 mL centrifuge tubes. Be sure to re-suspend solution by shaking it between aliquots.

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- 8.3.3 Spike seven of the 1 mL aliquots with the following amounts of working standards in step 9.12 of the procedure. One 1 mL aliquot serves as the blank.

Working Standard (Approximate Conc.)	uL	Approximate final concentration of FC-95 in liver
-	-	Blank
500 ppb	100	0.292 ppm
500 ppb	200	0.584 ppm
500 ppb	300	0.877 ppm
500 ppb	400	1.168 ppm
1 ppm	500	2.924 ppm
5 ppm	200	5.848 ppm
5 ppm	300	8.772 ppm

- 8.4 Calculate the actual value of the standards:

$$\frac{\text{uL of standard} \times \text{concentration (in ppm)}}{171 \text{ mg liver}^* / 1 \text{ ml homogenate}} = \text{final concentration (ppm) of FC-95 in liver}$$

*Average weight of bovine liver in solution as determined by weighing 1 mL homogenates of 40 mg liver in 200 mL of Milli-Q water. The amount of FC-95 is reported as equivalents of FC-95 potassium salt.

8.5 Calibration

- 8.5.1 Extract the spiked beef liver homogenate following 9.13 to 9.23 of this method. Use these standards to establish your curve on the mass spectrometer.
- 8.5.2 Alternatively, a standard curve may be generated using ratios of responses of the perfluorooctanesulfonate anion and the internal standard anion versus concentration of the perfluorooctanesulfonate anion.

8.6 Storage Conditions for Standards

- 8.6.1 New standards are prepared with each analysis. Standards are stored in covered plastic centrifuge tubes until the analysis on the mass spectrometer is performed.

8.7 Storage Conditions for Standards

- 8.7.1 Beef liver homogenates may be frozen after preparation.

9.0 PROCEDURES

- 9.1 Obtain frozen liver samples. In spent tissue, note that the liver has not been packaged with other tissues.
- 9.2 Use a dissecting scalpel and cut off approximately 1 g of liver.
- 9.3 Weigh the sample directly into a tared plastic grinding tube.
- 9.4 Record the liver weight in the study note book.
- 9.5 Put a label on the vial with the study number, weight, rabbit ID, date and analyst initials.

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- 9.6 Add 2.5 mLs water.
- 9.7 Grind the sample. Put the grinder probe in the sample and grind for about 2 minutes, until the sample is a homogeneous solution with no large chunks.
- 9.8 Rinse the probe off into the sample with 2.5 mLs water using a pipet.
- 9.9 Take the grinder apart and clean it with methanol after each sample. Follow AMDT-EP-22.
- 9.10 Cap the sample and vortex for 15 seconds.
- 9.11 Pipet 1 mL into a 15 mL centrifuge tube. Label the centrifuge tube with the identical information as the grinding tube. (See AMDT-M-4 Worksheet for documenting the remaining steps.)
- 9.12 Spike the beef liver homogenates with the appropriate amount of FC-95 standard as described in 8.3.
- 9.13 Spike the samples and beef liver homogenates with 100 uL of internal standard.
- 9.14 Add 1 mL of the sodium carbonate/sodium bicarbonate buffer and 1 mL ammonium acetate.
- 9.15 Using an analytical pipet, add 5 mL ethyl acetate.
- 9.16 Cap the sample and vortex 20 to 30 seconds.
- 9.17 Put them in the shaker for 20 min.
- 9.18 Centrifuge for 20 to 25 minutes, until the layers are well separated. Set the power on the centrifuge to 25.
- 9.19 Remove 4 mLs of the top organic layer to a fresh 15 mL centrifuge tube with a 5 mL graduated glass pipet. Transfer the label to the fresh tube.
- 9.20 Blow the sample down on the analytical evaporator to near dryness with nitrogen, approximately 30 to 40 minutes.
- 9.21 Bring the remaining sample up in 1 mL dilute acetonitrile with an analytical pipet.
- 9.22 Vortex 15 seconds.
- 9.23 Transfer the sample to a 3 mL syringe. Attach a 0.2 μ m nylon mesh filter, and filter the sample into a fresh centrifuge tube or a autovial. Label the tube or vial with the study number and animal number.
- 9.24 Cap and hold for analysis by electrospray mass spectroscopy.
- 9.25 Complete AMDT-M-4 worksheet and attach to page of study notebook.

10.0 VALIDATION

- 10.1 Quality Control - not applicable
- 10.2 Precision and Accuracy- not applicable
- 10.3 Other Validation Parameters- not applicable

11.0 DATA ANALYSIS

- 11.1 None

12.0 ATTACHMENTS

- 12.1 Worksheet AMDT-M-4

13.0 REFERENCES

- 13.1 AMDT-EP-22 Routine Maintenance of Ultra-Turrax T-25

14.0 REVISIONS

Revision

Number

Reason for Change

Revision

Date

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Worksheet AMDT-M-4[illegible]

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1.0 SCOPE

- 1.1 This method is for the analysis for fluoride, thermally extracted from samples using the Dohrmann DX2000 (AMDT-M-1), and collected in TISAB for analysis with an Ion Selective Electrode (ISE). The analysis is performed using the Skalar Segmented Flow Analyzer with ISE.
- 1.2 Samples can be tissues, serum, biological material, or other materials extracted on the Dohrmann.

2.0 KEYWORDS

- 2.1 Skalar, segmented flow, fluoride.

3.0 PRECAUTIONS

- 3.1 Follow standard laboratory safety practices.

4.0 SUPPLIES AND MATERIALS

4.1 Supplies

- 4.1.1 Sample cups, 4 mL plastic cups with caps
- 4.1.2 Autopipets, oxford or equivalent with plastic tips
- 4.1.3 Polypropylene volumetric flasks, 100 mL
- 4.1.4 Cartridge components, refer to the Skalar Methods for components and part numbers.
- 4.1.5 Sample prefilters, Evergreen

4.2 Reagents

- 4.2.1 Brij 35, 30% S.F.A.S. Detergent
- 4.2.2 TISAB II buffer solution: Purchase TISAB II from Orion. To 1 liter of TISAB II add 2.5 mL or 100 ppm fluoride solution and 1 mL Brij.
- 4.2.3 Sampler rinsing solution: Dilute TISAB II 1:1 with Milli-Q water.
- 4.2.4 Nitric acid solution for decontamination, 1 N (lab grade): Slowly add 64 mLs concentrated nitric acid (HNO_3) to 250 mLs of Milli-Q water. Bring the volume up to 1 L with Milli-Q water.

4.3 Standards

- 4.3.1 Stock solution, 100 ppm F: purchased from Orion.
- 4.3.2 Intermediate standard, 10 ppm: Dilute 10 mLs of stock solution to 100 mLs with Milli-Q water. Use polypropylene volumetric flasks.
- 4.3.3 Working standard: Make up the following working standards by adding the volumes of intermediate or stock standard indicated on the table, using oxford or pumpmate pipets, to 50 mLs of TISAB and diluting to 100 mLs with Milli-Q water.

Working Standard	mLs of Stock Standard	mLs of Intermediate Standard
0.015 ppm	-	0.15
0.03 ppm	-	0.3
0.06 ppm	-	0.6
0.09 ppm	-	0.9
0.12 ppm	-	1.2
0.15 ppm	-	1.5
0.3 ppm	0.3	-
0.6 ppm	0.6	-

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1.2 ppm	1.2	-
1.5 ppm	1.5	-

5.0 EQUIPMENT

- 5.1 Skalar Segmented Flow Auto Analyzer Sans^{Plus} System equipped with ISE

6.0 INTERFERENCES

- 6.1 High concentrations of alkalinity, chloride, phosphate, sulfate or iron can cause interferences.

7.0 SAMPLE HANDLING

- 7.1 Samples should be stored in polyethylene bottles. Samples should be analyzed within 30 days.

8.0 CALIBRATION AND STANDARDIZATION

- 8.1 Preparation of Calibration Standards
- 8.1.1 Prepare calibration standards as in section 4.3.
- 8.2 Calibration
- 8.2.1 The standards are analyzed at the beginning of the run.
- 8.3 Storage Conditions for Standards
- 8.3.1 Standards are stored in capped polypropylene volumetric flasks. New standards are prepared at a minimum of every six months, or as necessary.

9.0 PROCEDURE

- 9.1 Start Up Procedure
- 9.1.1 Clamp down the pumpdecks, air bars and sampler-pump tubing.
- 9.1.2 Put the fluoride electrodes in the electrode chamber.
- 9.1.3 Turn on the power of the sampler, pumps, offset potentiometer and heating bath.
- 9.1.4 Put the reagent-lines in the appropriate bottles.
- 9.1.5 Turn on the interface, computer, display and printer. **Make sure you turn on the interface before the computer.**
- 9.1.6 Let the system stabilize for approximately 30 minutes.
- 9.2 Starting a Run
- 9.2.1 Create a sample table by selecting FILES, TABLE, and CREATE, type in the name of the file, and press ENTER.
- 9.2.2 Print the sample table, inserted in the system table by pushing ESC, PRINT, GROUP 1. This will print the entire run.
- 9.2.3 Dial the sampler settings to the appropriate number of samples, number of seconds for sample wash, and number of seconds for the sample.
- 9.2.4 Fill the sample tray with the standards, samples, washes and drifts. IW and FW/RUNOUT cups on the sampler do not need to be filled.
- 9.2.5 Set the baseline.

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- 9.2.5.1 Select GRAPHICS, REAL TIME. If you cannot get real-time, you may be in the Data Handling Panel. Switch to the Analysis Panel by selecting CONTROL PANEL and pushing F7.
- 9.2.5.2 Use the small screwdriver for the offset potentiometer to set the base line. Adjust the baseline until it is approximately 3/4 inch from the bottom of the screen.
- 9.2.5.3 Check the highest standard and adjust the gain, if necessary, with the interface screw #3.
- 9.2.6 Go to CONTROL PANEL, and to analysis panel. Deselect the analysis that will not be run. (Select or deselect analysis by pressing ENTER.) Press Tab to return to the Analysis Panel.
- 9.2.7 Press the spacebar to bring up the local menu.
- 9.2.8 Select START to start the analysis.
- 9.2.9 Type your ID (initials), the sample table which you created under 9.2.1 (or press ENTER for choices), choose running with or without the system table and select START ANALYSIS.
- 9.2.10 After starting the software, start the sampler. Make sure that the sampler is set to the right number of samples and that the sample/wash/air times are OK.
- 9.2.11 Select GRAPHICS, REAL TIME to view the progress of the analysis.
- 9.3 Loading and Printing the Data-File
 - 9.3.1 Go to CONTROL PANEL, press the spacebar to bring up the local menu and select LOAD. Select AUTOCALCULATION and enter the filename (or highlight the file to be printed and press ENTER).
 - 9.3.2 To view the calibration curve, go to GRAPHICS, CALIBRATION CURVE.
 - 9.3.3 To print the high level curve, push PRINT SCREEN.
 - 9.3.4 To print the low level screen, push ESC to get out of graphics. Select SETTINGS. Change the max y value to approximately 900. Go to CAL CURVE and press ESC, and Enter. Press PRINT SCREEN.
 - 9.3.5 Return to SETTINGS and change the max value back to 4095, go to EDIT, press ENTER and PRINT SCREEN to print sample peaks.
 - 9.3.6 To print the results go to CONTROL PANEL, SPACEBAR, OUTPUT, OUTPUT. Select PRINTER for the Epson or PRN for the Laser.
- 9.4 Shutdown
 - 9.4.1 Put all the reagent-lines in Milli-Q water.
 - 9.4.2 Let the system rinse for approximately 30 minutes.
 - 9.4.3 After the system has rinsed completely, turn off the sampler, pump and offset potentiometer. Turn off the heating bath on weekends. Leave liquid in the lines.
 - 9.4.4 Take the electrode out and soak in 100 ppm F overnight.
 - 9.4.5 Release the pump-decks, air bars and sampler pump-tubing.
 - 9.4.6 Select FILES, press ALT F and select QUIT to exit the program.
 - 9.4.7 On Friday, turn off the computer, display and interface for the weekend.

10.0 VALIDATION

10.1 Quality Control

- 10.1.1 Run a standard (mid to high concentration) every 10 samples. If a significant change in peak height occurs, only the samples before the last acceptable standard will be used. The remaining samples will be reanalyzed.

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10.2 Precision and Accuracy

10.2.1 See Method Validation Report number AMDT-M-8.0.V1

10.3 Other Validation Parameters

10.4 Refer to Method Validation Report Number AMDT-M-8.0.V1

11.0 DATA ANALYSIS

11.1 Calculations

11.1.1 The standard curve is plotted by the Skalar software.

11.1.2 All calculations are done by the Skalar software. r^2 should be 0.995 or better.

11.2 Prepare spreadsheets to summarize data. Include sample volume, weights used etc.

11.3 Write the study number on the printouts, initial, date the printout, and bind together with all package documents and place in the study folder. Make a copy of the summary sheet and tape into the study notebook. Back up all data and spreadsheets onto study disk and backup disks.

11.4 Electronic Data

11.4.1 GLP studies: Electronic data is copied onto the Study floppy disk for each study, and also data is copied onto a floppy disk that is stored in the lab.

11.4.2 Other studies: All data is copied onto a floppy disk that is stored in the lab.

12.0 ATTACHMENTS

None

13.0 REFERENCES

13.1 AMDT-M-1, Thermal Extraction of Fluoride by Means of a Modified Dohrmann DX2000 Organic Halide Analyzer-Liver

13.2 Skalar Methods, #335, Skalar Methods Manual

13.3 AMDT-EP-26, Operation and Maintenance of the Skalar Segmented Flow Analyzer

14.0 REVISIONS

Revision Number	Reason for change	Revision Date
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3M Environmental Laboratory

Method

Thermal Extraction of Fluoride by Means of a Modified Dohrmann DX2000
Organic Halide Analyzer - Serum

Method Identification Number: AMDT-M-14

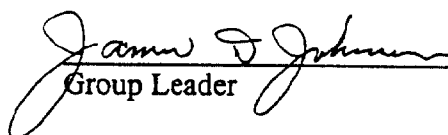
Adoption Date: 10-3-95

Revision Number: 0

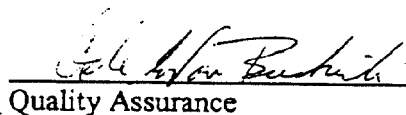
Revision Date: None

Author: Rich Youngblom

Approved by:


Group Leader

10/3/95
Date


Quality Assurance

9-27-95
Date

Software: MS Word 5.1a

Affected Documents: AMDT-M-2 Fluoride Measurement by Means of an Orion EA940
Expandable Ion Analyzer
AMDT-EP-3 Routine Maintenance of a Modified Dohrmann DX2000
Organic Halide Analyzer

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1.0 SCOPE , APPLICABLE COMPOUNDS, AND MATRICES

1.1 Scope: This method is for the operation of a Dohrmann DX2000 when it is used to extract fluoride from various matrices. The fluoride is typically collected in TISAB solution for analysis with an ion selective electrode.

1.2 Applicable Compounds: Fluorochemicals or other fluorinated compounds.

1.3 Matrices: Biological fluids, particularly serum.

2.0 KEYWORDS

2.1 Fluoride, fluorine, extraction, pyrolysis, ionization, ion selective electrode, Dohrmann, halide, DX2000, fluorochemicals.

3.0 PRECAUTIONS

3.1 Glassware and exhaust gases can be extremely hot.

3.2 Glassware is fragile, broken glass may cause injuries.

3.3 Pressurized gases, proper compressed gas handling practices required.

3.4 Solvent based samples may flash, may need to allow them to dry down before starting run.

3.5 Potential biohazards due to the biological matrices. Use appropriate personal protective equipment.

4.0 SUPPLIES AND MATERIALS

4.1 Compressed Oxygen, Hydrocarbon free, regulated to 30 PSI.

4.2 Compressed Helium, High Purity Grade, regulated to 45 PSI.

4.3 Quartz glass sample boat with Teflon™ tubing, Dohrmann 890-097 or equivalent.

4.4 Quartz glass combustion tube, Reliance Glass G-9405-012 or equivalent.

4.5 Orion 940999 Total Ionic Strength Adjustment Buffer (TISAB II) or equivalent.

4.6 Sample collection vials, HDPE.

4.7 Milli-Q™ water

4.8 Polystyrene pipettes.

4.9 Activated Charcoal, E. Merck 2005 or equivalent.

4.10 Hamilton Syringe or equivalent.

4.11 Miscellaneous laboratory glassware

5.0 EQUIPMENT

5.1 Rosemount Dohrmann DX2000 Organic Halide Analyzer, modified for fluoride extraction.

5.2 IBM compatible 386 or 486 computer.

5.3 DX2000 software, version 1.00, modified for fluoride extraction.

5.4 Excel Spreadsheet, version 5.0 or greater

6.0 INTERFERENCES

6.1 Sample size is limited to approximately 100 µl. This may vary from matrix to matrix.

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7.0 SAMPLE HANDLING

7.1 Samples are to be handled with plastic pipettes. A new pipette is to be used for each sample.

8.0 CALIBRATION AND STANDARDIZATION

8.1 Preparation of Calibration Standards

8.1.1 The standards required for each project will need to be appropriate for that individual project. Refer to protocol for that project.

8.1.2 Typically 50-500 ppm FC-95 in methanol standards are used.

8.1.3 For rabbit serum studies, use beef serum as the matrix.

8.2 Calibration - Overview

The normal calibration is the fluoride curve (AMDT-M-2). However, if an optional spiked serum curve is required the procedure listed below is used.

8.2.1 A calibration curve for the DX2000 is generated by spiking samples with known standards and combusting them using the same methods and matrix type as the samples to be tested.

8.2.2 Typically, three replicates of each standard and five concentrations of standards will be spiked.

8.2.3 Standard curve will be plotted as Mass Spiked F (ug) on the x-axis and Standard Mass Recovered F (ug) on the y-axis. Generate a regression curve and calculate the equation for the line and the r^2 value.

8.2.4 Mass Spiked F (ug) = (Amount spiked in mL) x (Conc. of standard in ppm) x (0.6004)*

*FC-95 is 60.04% F therefore 0.6004 is the factor used to convert FC-95 to F

8.2.5 Standard Mass Recovered F (ug) = (TISAB volume in mL) x (Orion reading in ppm)

8.3 Calibration - Procedure

8.3.1 Start Up

8.3.1.1 Run 2 or more Clean Cycles when starting instrument each day. More clean cycles may be used if the previous samples contained high concentrations of fluoride.

8.3.2 Blanks

8.3.2.1 Prepare sample using the same methods and type of matrix as the test sample.

8.3.2.2 For rabbit studies, use beef serum as the matrix.

8.3.2.3 Put serum blank in Dohrmann boat. Combust sample as described in section 9.0 and analyze sample according to method AMDT-M-2 for the ion selective electrode analysis.

8.3.2.4 For rabbit studies, the meter reading for a blank sample should be 0.03 ppm or lower before proceeding with the calibration. Burn samples until this limit is reached, or until in the judgement of the operator the reading is stable with respect to historical readings (previous 48 hours).

8.3.2.5 For non-rabbit studies, the blank readings should reach a predetermined ion concentration before proceeding with the calibration.

8.3.2.6 It may be necessary to mix approximately 50 mg of charcoal with the sample to aid combustion.

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8.3.3 Standard Curve

8.3.3.1 If beef serum is frozen, thaw at least enough to complete the standard curve analysis for the day (≈ 30 mL).

8.3.3.2 Pipette 100 μ L of beef serum into Dohrmann sample boat.

8.3.3.3 Start with the lowest standard concentration. Using a Hamilton syringe, eject a fixed quantity of the standard on or in the matrix. For rabbit studies, use 4 μ L of standard and eject it on or in the beef serum.

8.3.3.4 At least 3 replicates should be used for the lowest standard concentration; more replicates may be used at the discretion of the analyst.

8.3.3.5 Combust the sample as described in section 9.3 and analyze according to AMDT-M-2.

8.3.3.6 Run all 15 standards. If one replicate is significantly different from the other two replicates, run another sample for that standard. Indicate in data that the new replicate replaces the old replicate and that the new replicate will be used to calculate the regression curve.

8.3.3.7 When all standards have been run, calculate the r^2 . r^2 must be at least 0.95. If it is not at least 0.95, consult with supervisor.

8.3.3.8 A new standard curve should be run when the combustion tube or sample matrix is changed. New standard curve may also be run at the discretion of the analyst.

8.4 Storage Conditions for Standards

8.4.1 Storage requirements for standards are dependent on the individual standards used.

Typically, standards are stored at room temperature in plastic screw top bottles.

8.4.2 New FC-95 standards should be prepared at least once a month.

9.0 PROCEDURES

9.1 Typical Operating Conditions:

9.1.1 Combustion tube temperature = 950°C.

9.1.2 Oxygen and Helium flow = 50 cc/minute.

9.1.3 Vaporization/Drying time = 240 seconds.

9.1.4 Bake time = 300 seconds.

9.2 Start Up Procedure:

9.2.1 If the program is not started, start the EOX program on the PC.

9.2.2 Open the SYSTEM SETUP window.

9.2.3 Put the furnace module and the cell in the READY mode.

9.2.4 Close the SYSTEM SETUP window.

9.2.5 When the oven has reached the READY temperature, run the CLEAN BOAT program found in the CELL CHECK menu.

9.2.6 See AMDT-EP-3 for details of the Dohrmann software.

9.3 Sample Extraction Procedure:

9.3.1 Open the SAMPLE HATCH and pipette 100 μ L of sample into the BOAT. It may be necessary to mix approximately 50 mg of charcoal with the sample to aid combustion. If this is done, charcoal should also be mixed in while establishing the baseline and when generating the standard curve.

9.3.2 Close SAMPLE HATCH.

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- 9.3.3 Add appropriate volume of TISAB solution or 1:1 TISAB:Milli-Q™ water mixture to a labeled sample collection vial. Typically 0.6 mL to 15 mL are used. For rabbit studies, use 1.0 or 2.0 mL of 1:1 TISAB:Milli-Q™ water mixture.
- 9.3.4 Place the vial so that the tip of the COMBUSTION TUBE is in the TISAB at least 0.25 inches. Gases released during pyrolysis must bubble through the TISAB.
- 9.3.5 Run the EOX-WATER program found in the RUN menu.
- 9.3.6 When the EOX program is finished, remove the collection vial from the combustion tube.
- 9.3.7 If undiluted TISAB was used to collect the sample, add an equal volume of Milli-Q™ water to the TISAB to make 1:1 TISAB:Milli-Q™.
- 9.3.8 Rinse the end of the combustion tube with Milli-Q™ water and wipe with a KIMWIPE to remove any TISAB remaining on the tube.
- 9.3.9 Open the sample hatch and remove any remaining ash from the boat. Ash can be removed with a cotton tipped applicator and/or vacuumed out. It may be necessary to scrap particles off the bottom with a spatula or other similar device. A drop of Milli-Q™ water may be added to the boat to aid in the Clean Cycle.
- 9.3.10 Close the hatch.
- 9.3.11 Run the CLEAN BOAT program.
- 9.3.12 Sample is ready for analysis by ion selective electrode (AMDT-M-2).

9.4 Sample Calculations

9.4.1 Use the standard curve to calculate the sample value.

9.4.2 Sample Mass Recovered F (ug) = (TISAB vol in mL) × $\frac{(\text{Orion reading in ppm} - \text{intercept})}{(\text{Slope})}$

10.0 VALIDATION

10.1 Quality Control

10.1.1 **Daily Start Up Check Samples:** Once the standard curve is established, each day of analysis is started by analyzing QC samples. The QC samples are to be the same as the lowest concentration spiked samples used to generate the standard curve. Each concentration must be done in triplicate unless the first two replicates are within 20% of the standard curve, then a third replicate is not necessary.

10.2 **Precision and Accuracy:** See method development analysis and sample analysis in Fluoride Notebooks 2,3, and 5. Precision and accuracy varies when analyzing samples of different matrices and different reference compounds.

10.3 **Other Validation Parameters:** NA

11.0 DATA ANALYSIS

11.1 Calculations

11.1.1 For the standard curve, use regression analysis in Excel, version 5.0 or greater.

11.1.2 To calculate the fluoride contraction in the sample, see method AMDT-M-2.

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11.2 Analyzing the Data

11.2.1 r^2 must be at least 0.95 or greater. "Outliers" may be excluded if two of the three replicates are within 20% of each other and the outlier is greater than 200% of the average of those two or less than 50% of the average of those two. Any such outliers should be pointed out in the data and noted in the Final Report along with the reason it was considered an outlier.

12.0 ATTACHMENTS

None

13.0 REFERENCES

13.1 Rosemount Dohrmann DX2000 Organic Halide Analyzer Operator's Manual (Manual 915-349, revision B, December 1993)

13.2 AMDT-M-2 Fluoride Measurement by Means of an Orion EA940 Expandable Ion Analyzer

13.3 AMDT-EP-3 Routine Maintenance of a Modified Dohrmann DX2000 Organic Halide Analyzer

14.0 REVISIONS

<u>Revision Number</u>	<u>Reason for Change</u>	<u>Revision Date</u>
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9.3 Quality Assurance Unit Statement

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Attachment D

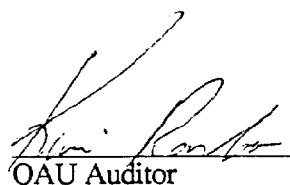
**GLP Study
Quality Assurance Statement**

Completed by: QAU Auditor Original to: Study Director Copies to: QAU Files

Study Title: **Single-dose Intravenous Pharmacokinetic Study of T-6246 in Rabbits**
Study Number: AMDT-042095.1 Name of Auditor: Kari Rambo

This study has been inspected by the Quality Assurance Unit as indicated in the following table.
The findings were reported to the study director and management.

Inspection Dates		Phase	Date Inspection Reported to	
From	To		Management	Study Director
11-13-95	11-13-95	Final Report	11-13-95	11-13-95



QAU Auditor Date 11-13-95

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9.4 Key Personnel Involved in the Study

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3M Environmental Laboratory

Key Personnel

Thermal extraction followed by analysis using Orion ion analyzer:

Jim Johnson
Deb Wright
Rich Youngblom
Deann Plummer

Thermal extraction followed by analysis using Skalar segmented flow analyzer with ion selective electrode:

Jim Johnson
Deb Wright
Rich Youngblom
Deann Plummer

Documentation and Reporting:

Jim Johnson
Rich Youngblom

Quality Assurance Unit:

Gale Van Buskirk
Cynthia Weber
Kari Rambo

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9.11 Data

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9.11.1 Summary and raw data; ug F⁻ in whole liver as determined by thermal extraction followed by analysis using Orion ion analyzer.

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Summary of Combustion Data - Liver
AMDT-042095.1, HWI 6329-159
As Referenced in Final Report section 6.0 *DATA ANALYSIS*

Total μg Fluoride in Whole Liver
Mean per Dose Group per Day Sacrificed*

	μg	Std. Dev.
Control Group, Day 15**	27.1 ± 3.1	
Control Group, Day 28	38.7 ± 16.3	
100 mg/kg dose (T6246), Day 15 (0.12 mg/kg)***	37.4 ± 7.9	
100 mg/kg dose (T6246), Day 28 (0.12 mg/kg)***	29.6 ± 1.3	
500 mg/kg dose (T6246), Day 15 (0.60 mg/kg)***	123.1 ± 14.0	
500 mg/kg dose (T6246), Day 28 (0.60 mg/kg)***	100.5 ± 5.9	

*Calculated as a mean triplicate samples from each of two male and two female rabbits.

**Only two livers analyzed from this group.

***Test material is a 0.12% solution of FC-95, actual dose in parenthesis.

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FC95		Actual	Average		Whole	Total F- in	
ID	%	ppm F-	ppm F-	liver	liver	whole	Dosage
rcvry		in liver	in liver	burned	weight	liver	(mg/kg)
(W/W)		(W/W)		(grams)	(grams)	(ug)	
liver blank-1		0.776		0.113			
liver blank-2		0.500		0.117			
liver blank-3		0.480		0.131			
F54075-1		0.401		0.131	60.3		
F54075-2		0.523	0.412	0.120	60.3	24.8	0.0
F54075-3		0.313		0.132	60.3		
F54081-1		0.308		0.125	80.6		
F54081-2		0.448	0.387	0.116	80.6	31.2	0.0
F54081-3		0.404		0.108	80.6		
F54105-1		0.267		0.151	86.4		
F54105-2		0.431	0.339	0.105	86.4	29.3	0.0
F54105-3		0.319		0.117	86.4		
F54107-1		1.34		0.107	80.6		
F54107-2		0.542	0.780	0.135	80.6	62.9	0.0
F54107-3		0.459		0.129	80.6		
F54074-1		0.350		0.123	82.9		
F54074-2		0.265	0.336	0.144	82.9	27.9	0.0
F54074-3		0.393		0.111	82.9		
F54085-1		0.312		0.149	81.0		
F54085-2		0.272	0.407	0.149	81.0	33.0	0.0
F540853		0.637		0.101	81.0		
Liver Blk-1		0.437		0.097			
Liver Blk-2		0.185		0.148			
Liver Spk-1	40%	0.553		0.110			
Liver Spk-2	45%	0.469		0.145			
Liver Spk-3	40%	0.389		0.156			
Liver Spk-4	39%	0.418		0.142			
Liver Spk-5	54%	0.660		0.125			
blank 1		0.528		0.097			
blank 2		0.334		0.148			
spike-1	91%	1.26		0.110			
spike-2	106%	1.11		0.145			
spike-3	118%	1.15		0.156			
spike-4	97%	1.04		0.142			
spike-5	136%	1.65		0.125			
spike-6	96%	1.06		0.137			
blk 1		0.530		0.153			
blk 2		0.264		0.161			
spk 1	119%	1.15		0.157			
spk 2	113%	1.14		0.150			
spk 3	106%	0.979		0.164			
spk 4	103%	1.11		0.141			
F54082-1		1.22		0.160	89.0		
F54082-2		1.25	1.23	0.163	89.0	109.4	500
F54082-3		1.21		0.156	89.0		
F54111-1		1.21		0.121	83.8		
F54111-2		1.11	1.17	0.115	83.8	97.7	500
F54111-3		1.17		0.136	83.8		

FC95		Actual	Average		Whole	Total F- in	
ID	%	ppm F-	ppm F-	liver	liver	whole	Dosage
	rcvry	in liver	in liver	burned	weight	liver	(mg/kg)
		(W/W)	(W/W)	(grams)	(grams)	(ug)	
F54079-1		1.17		0.157	83.1		
F54079-2		1.20	1.18	0.142	83.1	97.9	500
F54079-3		1.16		0.141	83.1		
F54116-1		1.36		0.154	72.0		
F54116-2		1.33	1.35	0.140	72.0	97.1	500
F54116-3		1.36		0.157	72.0		
F54112-1		1.44		0.134	97.8		
F54112-2		1.55	1.46	0.158	97.8	142.9	500
F54112-3		1.40		0.146	97.8		
F54076-1		1.69		0.139	78.1		
F54076-2		1.81	1.76	0.124	78.1	137.4	500
F54076-3		1.78		0.114	78.1		
F54113-1		1.24		0.145	91.5		
F54113-2		1.33	1.33	0.123	91.5	121.7	500
F54113-3		1.42		0.117	91.5		
F54084-1		1.58		0.134	66.4		
F54084-2		1.73	1.66	0.140	66.4	110.4	500
F54084-3		1.68		0.120	66.4		
F54098-1		1.46		0.135	79.0		
F54098-2		1.39	1.49	0.147	79.0	117.3	500
F54098-3		1.61		0.125	79.0		
F54087-1		0.400		0.130	83.7		
F54087-2		0.346	0.376	0.131	83.7	31.5	100
F54087-3		0.382		0.135	83.7		
F54088-1		1.33		0.134	84.3		
F54088-2		0.485	0.765	0.148	84.3	64.4	100
F54088-3		0.482		0.134	84.3		
LIVER BLK 1		0.259		0.164			
LIVER BLK 2		0.132		0.158			
LIVER SPK 1	89%	1.05		0.128			
LIVER SPK 2	111%	1.30		0.129			
LIVER BLANK		0.243		0.140			
LIVER SPIKE 3	111%	1.27		0.133			
liver blank		0.355		0.111			
F54089-1		0.398		0.153	71.8		
F54089-2		0.394	0.394	0.157	71.8	28.3	100
F54089-3		0.391		0.147	71.8		
F54099-1		0.502		0.139	82.1		
F54099-2		0.504	0.483	0.140	82.1	39.7	100
F54099-3		0.444		0.158	82.1		
F54114-1		0.337		0.157	81.0		
F54114-2		0.372	0.359	0.136	81.0	29.0	100
F54114-3		0.367		0.155	81.0		
F54109-1		0.383		0.133	74.0		
F54109-2		0.387	0.400	0.134	74.0	29.6	100
F54109-3		0.431		0.154	74.0		
F54080-1		0.460		0.132	75.4		
F54080-2		0.475	0.356	0.132	75.4	26.8	100
F54080-3		0.132		0.103	75.4		

FC95		Actual	Average		Whole	Total F- in	
ID	% rcvry	ppm F- in liver (W/W)	ppm F- in liver (W/W)	liver burned (grams)	liver weight (grams)	whole liver (ug)	Dosage (mg/kg)
F54092-1		0.537		0.117	78.4		
F54092-2		0.463	0.478	0.145	78.4	37.4	100
F54092-3		0.433		0.138	78.4		
F54106-1		0.639		0.134	82.3		
F54106-2		0.665	0.634	0.125	82.3	52.2	100
F54106-3		0.598		0.121	82.3		
Blank		0.181		0.133			
Liver spike 1	82%	1.09		0.113			
Liver spike 2	81%	0.755		0.158			
Liver spike 3	85%	0.897		0.144			
Liver spike 4	76%	1.47		0.156			
Liver spike 5	66%	1.36		0.147			
Liver spike 6	70%	1.40		0.152			
liver blank-1		0.549		0.147			
liver blank-2		0.454		0.133			
liver blank-3		0.278		0.110			
liver spike 63-1	103%	1.09		0.143			
liver spike 63-2	96%	1.11		0.132			
liver spike 63-3	159%	1.69		0.143			
liver spike 63-4	101%	1.41		0.108			
F54088-1		0.485		0.145	84.3		
F54088-2		0.655	0.544	0.123	84.3	45.8	100
F54088-3		0.491		0.132	84.3		
liver blank-4		0.292		0.123			
liver spike 63-1	117%	1.30		0.136			
liver spike 63-2	89%	0.972		0.139			
liver spike 63-3	89%	0.922		0.147			
liver spike 63-4	90%	0.910		0.149			

9.11.2 Summary and raw data; ug F⁻ in whole liver as determined by thermal extraction followed by analysis using Skalar segmented flow analyzer with ion selective electrode.

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DDW 6/21/95
Skalar Data

RE: 6329-159 LIVER SAMPLES

AMDT 42095.1

Date of Analysis: 5-23 and 5-24-95

Analyst: DDW

The samples are burned in the Dohrman at 950 C using between 0.1 and 0.2 grams of the liver. The gas is collected in 2.0 mL of 1:1 TISAB/Milli-Q water. The samples are then analyzed on a Skalar Segmented Flow Analyzer using the Ion Specific Electrode (ISE) Method.

TISAB buffer is added to each sample as it proceeds through the system. The sample then goes through a heated mixing coil before the potential between the ion selective electrode and the reference electrode is measured. The signal is amplified and related to the fluoride concentration.

The instrument was calibrated in the ranges of 0.015 - 0.15 ppm and 0.15 - 1.50 ppm fluoride. The standard curve for the high range was plotted using the inverse logarithm option. The standard curve for the low range is linear. All standards and samples were then calculated by the Skalar software using these curves. All results below 0.0001 ppm appear on the raw data as #.####.

A quality control standard was analyzed every 10 samples to check for accuracy and drift.

Raw data is taken from the appropriate calibrated range of the Skalar printout and summarized on an Excel spreadsheet. The final results are adjusted for the collection volume and any subsequent dilutions.

Debra D Wright

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QOW 6/21/95
Skalar

SUMMARY of 6329-159
LIVER SAMPLES
AMDT 42095.1

	Sample ID	Skalar Result (ppm)	DI-TISAB final vol (mL)	Qty Sample (mL or grams)	Actual ppm F- in Sample	Average Actual ppm F- in Sample	Total Tissue Wt (grams)	Total F- per tissue (ug)	Average Total F- per tissue (ug)
GROUP 1 Dose Level : 0	F54075-1	0.03	2.0	0.1311	0.50		60.2500	30.06	
	F54075-2	0.03	2.0	0.1197	0.55	0.52	60.2500	33.32	27.4
	F54075-3	0.02	2.0	0.1318	0.31		60.2500	18.93	
	F54081-1	0.02	2.0	0.1246	0.32		80.597	25.87	
	F54081-2	0.02	2.0	0.1161	0.36	0.33	80.597	29.30	26.8
	F54081-3	0.02	2.0	0.1075	0.31		80.597	25.34	
	F54105-1	0.02	2.0	0.1507	0.25		86.35	21.54	
	F54105-2	0.02	2.0	0.1053	0.46	0.36	86.35	39.53	31.2
	F54105-3	0.02	2.0	0.1173	0.38		86.35	32.39	
	F54107-1	0.45	2.0	0.1069	8.38		80.649	675.67	
	F54107-2	0.05	2.0	0.1351	0.75	3.19	80.649	60.53	257
	F54107-3	0.03	2.0	0.1286	0.43		80.649	34.37	
	F54074-1	0.02	2.0	0.1227	0.37		82.895	31.08	
	F54074-2	0.02	2.0	0.1441	0.25	0.34	82.895	21.05	28.3
	F54074-3	0.02	2.0	0.1110	0.40		82.895	32.86	
	F54085-1	0.02	2.0	0.1485	0.23		80.95	18.97	
	F54085-2	0.02	2.0	0.1490	0.30	1.81	80.95	23.90	45.8
	F54085-3	0.06	2.0	0.1005	1.17		80.95	94.40	
GROUP 4 Dose Level : 100 mg/kg	F54087-1	0.04	2.0	0.1301	0.59		83.71	49.42	
	F54087-2	0.03	2.0	0.1314	0.47	0.52	83.71	39.24	43.7
	F54087-3	0.03	2.0	0.1351	0.51		83.71	42.51	
	F54088-1	0.11	2.0	0.1339	1.70		84.26	143.47	
	F54088-2	0.05	2.0	0.1476	0.66	1.01	84.26	55.26	85.3
	F54088-3	0.05	2.0	0.1344	0.68		84.26	57.30	
	F54092-1	0.06	2.0	0.1169	0.96		78.36	75.61	
	F54092-2	0.05	2.0	0.1453	0.69	0.75	78.36	54.15	58.8
	F54092-3	0.04	2.0	0.1381	0.60		78.36	46.75	
	F54106-1	0.06	2.0	0.1336	0.85		82.301	70.35	
	F54106-2	0.06	2.0	0.1249	0.90	0.82	82.301	74.33	67.8
	F54106-3	0.04	2.0	0.1213	0.71		82.301	58.76	
	F54088-1	0.05	2.0	0.1448	0.72		84.26	60.63	
	F54088-2	0.05	2.0	0.1228	0.89	0.75	84.26	75.07	63.1
	F54088-3	0.04	2.0	0.1317	0.63		84.26	53.49	
	F54089-1	0.03	2.0	0.1532	0.42		71.796	29.81	
	F54089-2	0.03	2.0	0.1568	0.41	0.41	71.796	29.12	29
	F54089-3	0.03	2.0	0.1474	0.39		71.796	28.15	
	F54099-1	0.04	2.0	0.1386	0.56		82.143	46.35	
	F54099-2	0.04	2.0	0.1403	0.53	0.56	82.143	43.21	45.95
	F54099-3	0.05	2.0	0.1575	0.59		82.143	48.29	
	F54114-1	0.03	2.0	0.1573	0.39		80.966	31.19	
	F54114-2	0.03	2.0	0.1359	0.38	0.38	80.966	31.10	31.5
	F54114-3	0.03	2.0	0.1552	0.40		80.966	32.14	
	F54109-1	0.03	2.0	0.1326	0.38		73.958	28.45	
	F54109-2	0.03	2.0	0.1339	0.38	40.30	73.958	28.17	29.9
	F54109-3	0.03	2.0	0.1536	0.45		73.958	33.13	

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HWI-159L.SUM

Page 1

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**SUMMARY of 6329-159
LIVER SAMPLES
AMDT 42095.1**

	Sample ID	Scalar Result (ppm)	DI TISAB final vol (mL)	Qty Sample (mL or grams)	Actual ppm F- in Sample	Average Actual ppm F-	Total Tissue Wt. (grams)	Total F- per tissue (ug)	Average Total F- per tissue
	F54080-1	0.03	2.0	0.1322	0.46		75.42	34.91	
	F54080-2	0.03	2.0	0.1323	0.50	0.32	75.42	37.74	24.2
	F54080-3	ND	2.0	0.1028	ND		75.42	ND	
	F54082-1	0.12	2.0	0.1595	1.44		88.965	128.40	
	F54082-2	0.12	2.0	0.1626	1.48	1.46	88.965	131.75	130
	F54082-3	0.11	2.0	0.1558	1.47		88.965	130.42	
	F54111-1	0.09	2.0	0.1207	1.41		83.823	118.48	
	F54111-2	0.08	2.0	0.1147	1.34	1.42	83.823	112.69	119
	F54111-3	0.10	2.0	0.1360	1.50		83.823	125.36	
	F54079-1	0.11	2.0	0.1571	1.46		83.117	121.58	
	F54079-2	0.11	2.0	0.1420	1.52	1.48	83.117	126.67	123
	F54079-3	0.10	2.0	0.1406	1.46		83.117	121.07	
	F54116-1	0.13	2.0	0.1541	1.71		71.962	122.82	
	F54116-2	0.12	2.0	0.1403	1.68	1.69	71.962	121.15	122
	F54116-3	0.13	2.0	0.1570	1.68		71.962	120.73	
GROUP 5 Dose Level : 500 mg/kg	F54112-1	0.12	2.0	0.1340	1.82		97.824	177.98	
	F54112-2	0.15	2.0	0.1583	1.84	1.82	97.824	180.45	178
	F54112-3	0.13	2.0	0.1458	1.79		97.824	175.25	
	F54076-1	0.15	2.0	0.1385	2.22		78.058	173.59	
	F54076-2	0.15	2.0	0.1243	2.43	2.33	78.058	189.65	182
	F54076-3	0.13	2.0	0.1136	2.35		78.058	183.60	
	F54113-1	0.12	2.0	0.1449	1.65		91.52	151.08	
	F54113-2	0.11	2.0	0.1227	1.85	1.81	91.52	169.17	166
	F54113-3	0.11	2.0	0.1171	1.94		91.52	177.26	
	F54084-1	0.14	2.0	0.1338	2.09		66.42	138.90	
	F54084-2	0.16	2.0	0.1402	2.24	2.18	66.42	148.76	145
	F54084-3	0.13	2.0	0.1200	2.22		66.42	147.23	
	F54098-1	0.13	2.0	0.1346	1.93		78.95	152.03	
	F54098-2	0.14	2.0	0.1469	1.88	1.98	78.95	148.33	156
	F54098-3	0.13	2.0	0.1253	2.12		78.95	167.23	

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HWI-159L.SUM

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1995-06-13 10:27 OutPut of : 950523A1

Operator : DDW

Date of the Analysis : 1995-05-23 10:18

Analysis File Name : C:\SKALAR\DATA\HWIDATA\IVERS\950523A1

Sample #	Sample ID	Skalar Standard (ppm)	Skalar Result (ppm)	% Recovery	DISTISAB final vol (mL)	Qty Sample (mL or grams)	Actual ppm F. in Sample	Total Tissue Wt. (grams)	Total F. per tissue (ug)	ml PC 95 Solution Spiked	Conc (ppm)	Mass Spiked (ug Fe)	Mass Recovered (ug Fe)	% Recovery
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1	Tracer	1.50	1.47	98%										
2	Drift	1.50	1.48	98%										
3	Wash		0.00											
4	Standard 1	0.015	0.02	125%										
5	Standard 2	0.03	0.03	85%										
6	Standard 3	0.06	0.06	100%										
7	Standard 4	0.09	0.09	102%										
8	Standard 5	0.12	0.12	99%										
9	Standard 6	0.15	0.15	103%										
10	Standard 7	0.30	0.29	95%										
11	Standard 8	0.60	0.61	102%										
12	Standard 9	1.20	1.24	103%										
13	Standard 10	1.50	1.46	97%										
14	Drift	1.50	1.53	102%										
15	Wash		0.00											
16	BLK 1		0.05		2.0	0.1332	0.79							
17	BLK 2		0.04		2.0	0.1172	0.60							
18	BLK 3		0.04		2.0	0.1313	0.60							
19	F54075-1		0.03		2.0	0.1311	0.50	60.2500	30.06					
20	F54075-2		0.03		2.0	0.1197	0.55	60.2500	33.32					
21	F54075-3		0.02		2.0	0.1318	0.31	60.2500	18.93					
22	F54081-1		0.02		2.0	0.1246	0.32	80.597	25.87					
23	F54081-2		0.02		2.0	0.1161	0.36	80.597	29.30					
24	F54081-3		0.02		2.0	0.1075	0.31	80.597	25.34					
25	F54105-1		0.02		2.0	0.1507	0.25	86.35	21.54					
26	Drift	1.50	1.53	102%										
27	Wash		0.00											
28	F54105-2		0.02		2.0	0.1053	0.46	86.35	39.53					
29	F54105-3		0.02		2.0	0.1173	0.38	86.35	32.39					
30	F54107-1		0.45		2.0	0.1069	8.38	80.649	675.67					

000173

000093

DDW 6/21/95
 AMDT 42095.1
 Skalar Summer
 6329-159

Sample #	Sample ID	Scalar Standard (ppm)	Scalar Result (ppm)	% Recovery	DIUSAB final vol (ml)	DIUSAB Qty Sample (ml or grams)	Actual ppm P- in Sample	Total Tissue Wt. (grams)	Total P- per tissue (ug)	ml PC 95 Solution Spiked	Conc (ppm)	Mass Spiked (ug P-)	Mass Recovered (ug P-)	% Recovery
31	F54107-2		0.05		2.0	0.1351	0.75	80.649	60.53					
32	F54107-3		0.03		2.0	0.1286	0.43	80.649	34.37					
33	F54074-1		0.02		2.0	0.1227	0.37	82.895	31.08					
34	F54074-2		0.02		2.0	0.1441	0.25	82.895	21.05					
35	F54074-3		0.02		2.0	0.111	0.40	82.895	32.86					
36	F54085-1		0.02		2.0	0.1485	0.23	80.95	18.97					
37	F54085-2		0.02		2.0	0.149	0.30	80.95	23.90					
38	Drift	1.50	1.52	101%										
39	Wash		0.00											
40	F54085-3		0.06		2.0	0.1005	1.17	80.95	94.40					
41	BLK 1		0.02		2.0	0.0971	0.50							
42	BLK 2		0.03		2.0	0.1479	0.39							
43	SPK 1		0.15		2.0	0.1096	2.67			0.004	63.00	0.15	0.29	194%
44	SPK 2		0.10		2.0	0.1446	1.36			0.004	63.00	0.15	0.20	130%
45	SPK 3		0.11		2.0	0.1556	1.39			0.004	63.00	0.15	0.22	143%
46	SPK 4		0.09		2.0	0.1416	1.21			0.004	63.00	0.15	0.17	114%
47	SPK 5		0.12		2.0	0.1246	1.97			0.004	63.00	0.15	0.25	162%
48	SPK 6		0.09		2.0	0.1369	1.32			0.004	63.00	0.15	0.18	119%
49	BLK 1		0.04		2.0	0.153	0.58							
50	Drift	1.50	1.53	102%										
51	Wash		0.00											
52	BLK 2		0.02		2.0	0.1609	0.27							
53	SPK 1		0.11		2.0	0.1568	1.37			0.004	63.00	0.15	0.22	142%
54	SPK 2		0.10		2.0	0.1502	1.35			0.004	63.00	0.15	0.20	134%
55	SPK 3		0.10		2.0	0.1636	1.17			0.004	63.00	0.15	0.19	126%
56	SPK 4		0.11		2.0	0.1412	1.51			0.004	63.00	0.15	0.21	141%
57	F54082-1		0.12		2.0	0.1595	1.44	88.965	128.40					
58	F54082-2		0.12		2.0	0.1626	1.48	88.965	131.75					
59	F54082-3		0.11		2.0	0.1558	1.47	88.965	130.42					
60	F54111-1		0.09		2.0	0.1207	1.41	83.823	118.48					
61	F54111-2		0.08		2.0	0.1147	1.34	83.823	112.69					
62	Drift	1.50	1.51	101%										
63	Wash		0.00											
64	F54111-3		0.10		2.0	0.136	1.50	83.823	125.36					
65	F54079-1		0.11		2.0	0.1571	1.46	83.117	121.58					
66	F54079-2		0.11		2.0	0.142	1.52	83.117	126.67					

000174

000091

Sample #	Sample ID	Skalar Standard (ppm)	Skalar Result (ppm)	% Recovery	DI H2O vol (mL)	DI H2OAB Qty (mL)	Actual ppb F- in Sample	Total Tissue Wt (grams)	Total F- per tissue (ug)	ml. FC 95 Solution Spiked	Conc (ppm)	Mass Spiked (ug F-)	Mass Recovered (ug F-)	% Recovery
67	F54079-3		0.10		2.0	0.1406	1.46	83.117	121.07					
68	F54116-1		0.13		2.0	0.1541	1.71	71.962	122.82					
69	F54116-2		0.12		2.0	0.1403	1.68	71.962	121.15					
70	F54116-3		0.13		2.0	0.157	1.68	71.962	120.73					
71	F54112-1		0.12		2.0	0.134	1.82	97.824	177.98					
72	F54112-2		0.15		2.0	0.1583	1.84	97.824	180.45					
73	F54112-3		0.13		2.0	0.1458	1.79	97.824	175.25					
74	Drift	1.50	1.48	99%										
75	Wash		0.00											
76	F54076-1		0.15		2.0	0.1385	2.22	78.058	173.59					
77	F54076-2		0.15		2.0	0.1243	2.43	78.058	189.65					
78	F54076-3		0.13		2.0	0.1136	2.35	78.058	183.60					
79	F54113-1		0.12		2.0	0.1449	1.65	91.52	151.08					
80	F54113-2		0.11		2.0	0.1227	1.85	91.52	169.17					
81	F54113-3		0.11		2.0	0.1171	1.94	91.52	177.26					
82	F54084-1		0.14		2.0	0.1338	2.09	66.42	138.90					
83	F54084-2		0.16		2.0	0.1402	2.24	66.42	148.76					
84	F54084-3		0.13		2.0	0.12	2.22	66.42	147.23					
85	F54098-1		0.13		2.0	0.1346	1.93	78.95	152.03					
86	Drift	1.50	1.49	99%										
87	Wash		0.00											
88	F54098-2		0.14		2.0	0.1469	1.88	78.95	148.33					
89	F54098-3		0.13		2.0	0.1253	2.12	78.95	167.23					
90	F54087-1		0.04		2.0	0.1301	0.59	83.71	49.42					
91	F54087-2		0.03		2.0	0.1314	0.47	83.71	39.24					
92	F54087-3		0.03		2.0	0.1351	0.51	83.71	42.51					
93	F54088-1		0.11		2.0	0.1339	1.70	84.26	143.47					
94	F54088-2		0.05		2.0	0.1476	0.66	84.26	55.26					
95	F54088-3		0.05		2.0	0.1344	0.68	84.26	57.30					
96	Drift	1.50	1.49	99%										
97	Wash		0.00											

000175

000095

1995-06-13 10:27 OutPut of : 950524A1

Operator : DDW

Date of the Analysis : 1995-05-24 07:50

Analysis File Name : C:\SKALAR\DATA\HWIDATA\IVERS\950524A1

Sample #	Sample ID	Skalar Standard (ppm)	Skalar Result (ppm)	% Recovery	DI-TISAB Qty Sample (ml)	DI-TISAB Qty Sample (ml)	Actual ppb P. in Sample (grams)	Total Tissue Wt (grams)	Total P. per tissue (ug)	ml PC-95 Solution	Skalar Spiked (ug P.)	Mass Spiked (ug P.)	Mass Recovered (ug P.)	% Recovery
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1	Tracer	1.50	1.45	97%										
2	Drift	1.50	1.47	98%										
3	Wash		0.00											
4	Standard 1	0.015	0.02	107%										
5	Standard 2	0.03	0.03	94%										
6	Standard 3	0.06	0.06	101%										
7	Standard 4	0.09	0.09	103%										
8	Standard 5	0.12	0.12	97%										
9	Standard 6	0.15	0.16	103%										
10	Standard 7	0.30	0.28	94%										
11	Standard 8	0.60	0.61	102%										
12	Standard 9	1.20	1.24	103%										
13	Standard 10	1.50	1.46	97%										
14	Drift	1.50	1.50	100%										
15	Wash		0.00											
16	F54092-1		0.06		2.0	0.1169	0.96	78.36	75.61					
17	F54092-2		0.05		2.0	0.1453	0.69	78.36	54.15					
18	F54092-3		0.04		2.0	0.1381	0.60	78.36	46.75					
19	F54106-1		0.06		2.0	0.1336	0.85	82.301	70.35					
20	F54106-2		0.06		2.0	0.1249	0.90	82.301	74.33					
21	F54106-3		0.04		2.0	0.1213	0.71	82.301	58.76					
22	BLK		0.01		2.0	0.1326	0.18							
23	SPK 1		0.08		2.0	0.1133	1.34							
24	SPK 2		0.08		2.0	0.1577	0.99							
25	SPK 3		0.09		2.0	0.1441	1.19							
26	Drift	1.50	1.45	97%										
27	Wash		0.00											
28	SPK 4		0.15		2.0	0.1556	1.89							
29	SPK 5		0.13		2.0	0.1474	1.72							
30	SPK 6		0.14		2.0	0.1518	1.82							

DDW 6/21/95
AMDT 42095.1 J. J. J. J. J.
6329
Skalar
SW

000176

000096

Sample #	Sample ID	Scalar Standard (ppm)	Scalar Result (ppm)	% Recovery	DI H ₂ O Qty (mL)	DI H ₂ O Vol (mL)	Actual P. in Sample (ppm)	Total Tissue Wt. (grams)	Total P. per tissue (ug)	mg PC 95 Solution Spiked	Conc (ppm)	Mass Spiked (ug P.)	Mass Recovered (ug P.)	% Recovery
31	LIVER BLK-1		0.05		2.0	0.1457	0.70							
32	LIVER BLK-2		0.03		2.0	0.1328	0.52							
33	LIVER BLK-3		0.02		2.0	0.1101	0.29							
34	SPK 63-1		0.09		2.0	0.1425	1.25			0.004	63.00	0.15	0.18	118%
35	SPK 63-2		0.09		2.0	0.1316	1.36			0.004	63.00	0.15	0.18	119%
36	SPK 63-3		0.15		2.0	0.1428	2.03			0.004	63.00	0.15	0.29	192%
37	SPK 63-4		0.09		2.0	0.1079	1.73			0.004	63.00	0.15	0.19	123%
38	Drift	1.50	1.49	100%										
39	Wash		0.00											
40	F54088-1		0.05		2.0	0.1448	0.72	84.26	60.63					
41	F54088-2		0.05		2.0	0.1228	0.89	84.26	75.07					
42	F54088-3		0.04		2.0	0.1317	0.63	84.26	53.49					
43	BLK 4		0.02		2.0	0.1227	0.35							
44	SPK 63-1		0.12		2.0	0.1358	1.71			0.004	63.00	0.15	0.23	154%
45	SPK 63-2		0.08		2.0	0.1393	1.22			0.004	63.00	0.15	0.17	112%
46	SPK 63-3		0.08		2.0	0.1468	1.15			0.004	63.00	0.15	0.17	112%
47	SPK 63-4		0.08		2.0	0.1494	1.14			0.004	63.00	0.15	0.17	112%
48	BLK-1		0.02		2.0	0.1643	0.24							
49	BLK-2		0.00		2.0	0.1578	0.06							
50	Drift	1.50	1.49	99%										
51	Wash		0.00											
52	SPK-1		0.08		2.0	0.1283	1.32			0.004	63.00	0.15	0.17	112%
53	SPK-2		0.10		2.0	0.1292	1.49			0.004	63.00	0.15	0.19	127%
54	BLK 3		0.02		2.0	0.1396	0.24							
55	SPK-3		0.10		2.0	0.1325	1.48							
56	SPK-4		0.02		2.0	0.1109	0.30							
57	F54089-1		0.03		2.0	0.1532	0.42	71.796	29.81					
58	F54089-2		0.03		2.0	0.1568	0.41	71.796	29.12					
59	F54089-3		0.03		2.0	0.1474	0.39	71.796	28.15					
60	F54099-1		0.04		2.0	0.1386	0.56	82.143	46.35					
61	F54099-2		0.04		2.0	0.1403	0.53	82.143	43.21					
62	Drift	1.50	1.49	99%										
63	Wash		0.00											
64	F54099-3		0.05		2.0	0.1575	0.59	82.143	48.29					
65	F54114-1		0.03		2.0	0.1573	0.39	80.966	31.19					
66	F54114-2		0.03		2.0	0.1359	0.38	80.966	31.10					

000177

000097

Sample #	Sample ID	Stalar Standard (ppm)	Stalar Result (ppm)	% Recovery	DI TISAB final vol (mL)	DI TISAB Qty Sample (mL)	Actual ppm P. in Sample (ppm)	Total Tissue Wt. per tissue (grams)	Total P. (ug)	mt. FC 95 Solution Spiked (ppm)	FC 95 Soln Spiked (ug/L)	Mass Spiked (ug/L)	Mass Recovered (ug/L)	% Recovery
67	F54114-3		0.03		2.0	0.1552	0.40	80.966	32.14					
68	F54109-1		0.03		2.0	0.1326	0.38	73.958	28.45					
69	F54109-2		0.03		2.0	0.1339	0.38	73.958	28.17					
70	F54109-3		0.03		2.0	0.1536	0.45	73.958	33.13					
71	F54080-1		0.03		2.0	0.1322	0.46	75.42	34.91					
72	F54080-2		0.03		2.0	0.1323	0.50	75.42	37.74					
73	F54080-3		0.00		2.0	0.1028	0.00	75.42	0.00					
74	Drift	1.50	1.47	98%										
75	Wash		0.00											

000178

000098

QOW 6/21/95
AMDT 42095.1
6329-159 Line

3MA01502266

luoride 1.5 Path number : 3
Signal type : Debubbled
Decolor : Yes
system Number : 0
diLute : No
Resample : No
dil Threshold : 4095
diG output : 0
Window event : Off

s1 sTandard : Ignore
s2 sTandard : Ignore
s3 sTandard : Ignore
s4 sTandard : Ignore
s5 sTandard : Ignore
s6 sTandard : 0.150
s7 sTandard : 0.300
s8 sTandard : 0.600
s9 sTandard : 1.200
s10 sTandard : 1.500
Order : Inverse Logarithm
Dimension : PPM
start Value : 500 DU
trigger Limit : 1800 Sec
Peak shape : Pointed
stArt ignore : 60 Sec
eNd ignore : 120 Sec
Measure window : 75 %
Filter : No
Regeneration : No
formUla :
output : ##.###

luoride L Path number : 0
Signal type : Debubbled
Decolor : No
system Number : 0
diLute : No
Resample : No
dil Threshold : 4095
diG output : 0
Window event : Off

000180

000100

995-05-23 15:26

OutPut of : 950523A1

s1 sTandard : 0.015
s2 sTandard : 0.030
s3 sTandard : 0.060
s4 sTandard : 0.090
s5 sTandard : 0.120
s6 sTandard : 0.150
s7 sTandard : Ignore
s8 sTandard : Ignore
s9 sTandard : Ignore
s10 sTandard : Ignore
Order : 2
Dimension : PPM
start Value : 500 DU
trigger Limit : 1800 Sec
Peak shape : Pointed
stArt ignore : 60 Sec
eNd ignore : 120 Sec
Measure window : 75 %
Filter : No
Regeneration : No
formUla : c4:=c3
output : #.####

000181

000101

3MA01502268

2807.0101

Fluoride 1.5

Fluoride L

PPM

PPM

os	Typ	Ident	Ch	Result	F	Time	Ch	Result	F	Time
t	iw	Initial Wash	3	0.060		65	4	#####		0
t		Tracer	3	1.472		213	4	0.5569		0
d		Drift	3	1.476		389	4	0.5576		0
w		Wash	3	0.060		627	4	#####		0
s1		Standard 1	3	0.068		740	4	0.0188		0
s2		Standard 2	3	0.071		916	4	0.0255		0
s3		Standard 3	3	0.088		1090	4	0.0599		0
s4		Standard 4	3	0.108		1264	4	0.0917		0
s5		Standard 5	3	0.127		1442	4	0.1189		0
s6		Standard 6	3	0.154		1616	4	0.1501		0
0	s7	Standard 7	3	0.285		1792	4	0.2516		0
-	s8	Standard 8	3	0.611		1966	4	0.3836		0
2	s9	Standard 9	3	1.238		2140	4	0.5188		0
3	s10	Standard 10	3	1.461		2314	4	0.5552		0
4	d	Drift	3	1.532		2490	4	0.5664		0
5	w	Wash	3	0.060		2723	4	#####		0
6	u	BLK 1	3	0.084		2839	4	0.0527		0
7	u	BLK 2	3	0.076		3014	4	0.0354		0
3	u	BLK 3	3	0.077		3191	4	0.0393		0
9	u	F54075-1	3	0.074		3366	4	0.0327		0
0	u	F54075-2	3	0.075		3541	4	0.0331		0
1	u	F54075-3	3	0.069		3717	4	0.0207		0
2	u	F54081-1	3	0.069		3891	4	0.0200		0
3	u	F54081-2	3	0.069		4065	4	0.0211		0
4	u	F54081-3	3	0.067		4238	4	0.0169		0
5	u	F54105-1	3	0.068		4415	4	0.0188		0
6	d	Drift	3	1.526		4591	4	0.5654		0
7	w	Wash	3	0.060		4832	4	#####		0
3	u	F54105-2	3	0.070		4941	4	0.0241		0
9	u	F54105-3	3	0.070		5115	4	0.0220		0
0	u	F54107-1	3	0.866		5291	4	0.4478		0
1	u	F54107-2	3	0.083		5465	4	0.0507		0
2	u	F54107-3	3	0.072		5640	4	0.0274		0
3	u	F54074-1	3	0.070		5820	4	0.0230		0
4	u	F54074-2	3	0.068		5992	4	0.0183		0
5	u	F54074-3	3	0.070		6166	4	0.0220		0
6	u	F54085-1	3	0.068		6342	4	0.0174		0
7	u	F54085-2	3	0.070		6514	4	0.0220		0
3	d	Drift	3	1.515		6692	4	0.5638		0
9	w	Wash	3	0.060		6925	4	#####		0
0	u	F54085-3	3	0.087		7044	4	0.0586		0
1	u	BLK 1	3	0.071		7216	4	0.0244		0
2	u	BLK 2	3	0.072		7393	4	0.0285		0
3	u	SPK 1	3	0.151		7583	4	0.1464		0
4	u	SPK 2	3	0.112		7744	4	0.0984		0
5	u	SPK 3	3	0.119		7918	4	0.1080		0
6	u	SPK 4	3	0.104		8095	4	0.0860		0
7	u	SPK 5	3	0.130		8271	4	0.1228		0
8	u	SPK 6	3	0.106		8445	4	0.0901		0
9	u	BLK 1	3	0.080		8619	4	0.0446		0
0	d	Drift	3	1.533		8793	4	0.5666		0
1	w	Wash	3	0.060		9030	4	#####		0
2	u	BLK 2	3	0.069		9141	4	0.0218		0
3	u	SPK 1	3	0.119		9319	4	0.1076		0

Use high curve results raws/rs

000182

000102

Fluoride 1.5

Fluoride L

PPM

PPM

os	Typ	Ident	Ch	Result	F	Time	Ch	Result	F	Time
4	u	SPK 2	3	0.114		9495	4	0.1015		0
5	u	SPK 3	3	0.110		9670	4	0.0956		0
6	u	SPK 4	3	0.118		9845	4	0.1065		0
7	u	F54082-1	3	0.124		10020	4	0.1151		0
8	u	F54082-2	3	0.128		10196	4	0.1204		0
9	u	F54082-3	3	0.124		10370	4	0.1142		0
0	u	F54111-1	3	0.103		10546	4	0.0853		0
1	u	F54111-2	3	0.098		10720	4	0.0771		0
2	d	Drift	3	1.512		10894	4	0.5633		0
3	w	Wash	3	0.060		11133	4	#####		0
4	u	F54111-3	3	0.114		11245	4	0.1017		0
5	u	F54079-1	3	0.124		11420	4	0.1149		0
6	u	F54079-2	3	0.119		11595	4	0.1082		0
7	u	F54079-3	3	0.115		11770	4	0.1024		0
8	u	F54116-1	3	0.138		11944	4	0.1315		0
9	u	F54116-2	3	0.127		12118	4	0.1181		0
0	u	F54116-3	3	0.138		12296	4	0.1317		0
1	u	F54112-1	3	0.130		12470	4	0.1219		0
2	u	F54112-2	3	0.150		12645	4	0.1460		0
3	u	F54112-3	3	0.137		12821	4	0.1306		0
4	d	Drift	3	1.483		12995	4	0.5587		0
5	w	Wash	3	0.060		13234	4	#####		0
6	u	F54076-1	3	0.154		13347	4	0.1501		0
7	u	F54076-2	3	0.151		13520	4	0.1462		0
8	u	F54076-3	3	0.139		13697	4	0.1336		0
9	u	F54113-1	3	0.128		13873	4	0.1196		0
0	u	F54113-2	3	0.123		14047	4	0.1134		0
1	u	F54113-3	3	0.123		14221	4	0.1134		0
2	u	F54084-1	3	0.145		14397	4	0.1399		0
3	u	F54084-2	3	0.157		14571	4	0.1530		0
4	u	F54084-3	3	0.139		14747	4	0.1330		0
5	u	F54098-1	3	0.136		14921	4	0.1296		0
6	d	Drift	3	1.490		15095	4	0.5598		0
7	w	Wash	3	0.060		15327	4	#####		0
8	u	F54098-2	3	0.143		15447	4	0.1380		0
9	u	F54098-3	3	0.139		15621	4	0.1327		0
0	u	F54087-1	3	0.077		15796	4	0.0384		0
1	u	F54087-2	3	0.073		15969	4	0.0308		0
2	u	F54087-3	3	0.075		16142	4	0.0343		0
3	u	F54088-1	3	0.123		16322	4	0.1140		0
4	u	F54088-2	3	0.082		16496	4	0.0484		0
5	u	F54088-3	3	0.081		16672	4	0.0457		0
6	d	Drift	3	1.489		16846	4	0.5596		0
7	w	Wash	3	0.060		17079	4	#####		0
8	rw	RunOut Wash	3	0.060		17321	4	#####		0

000183

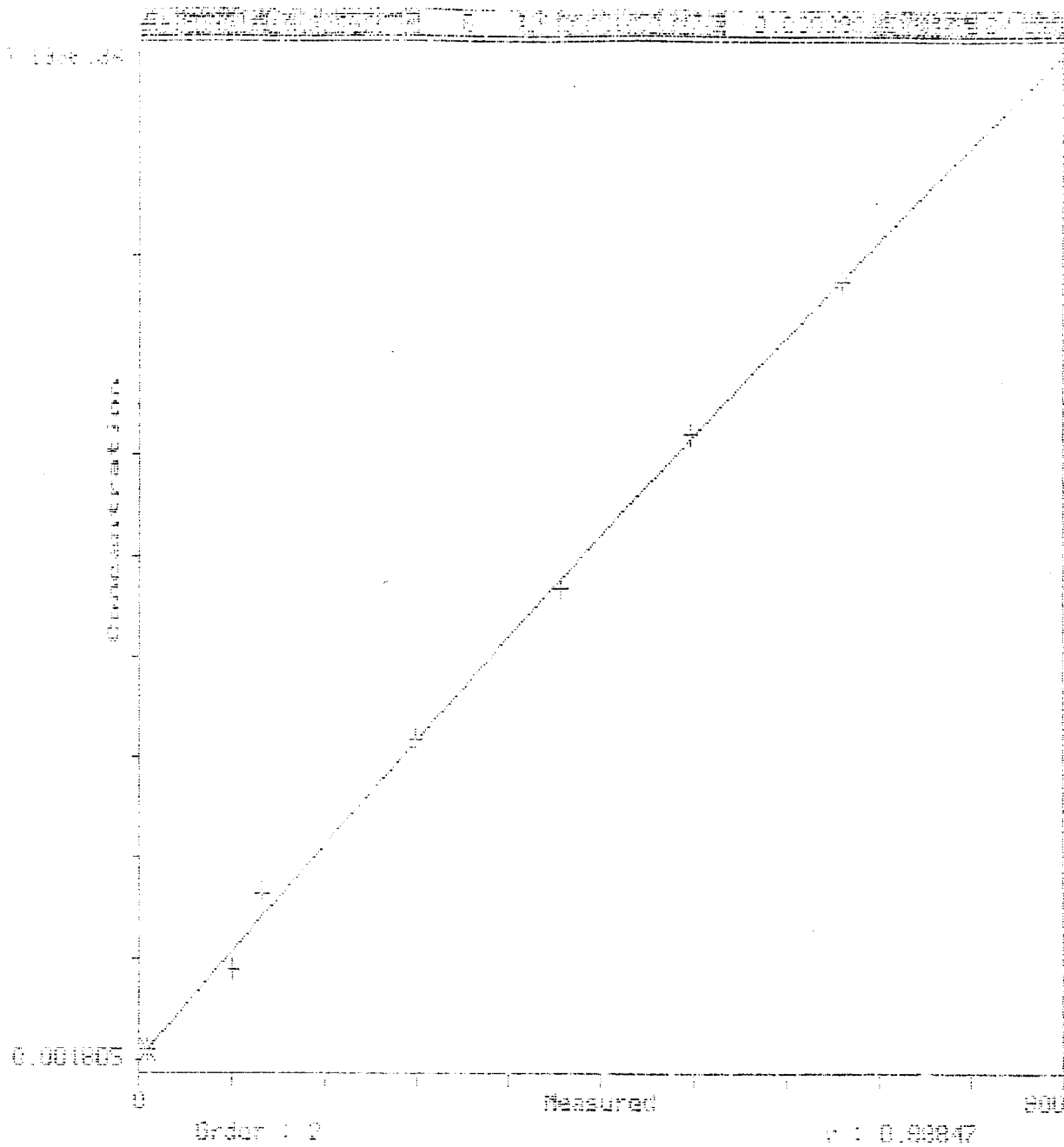
000103

14

3MA01502270

2807.0103

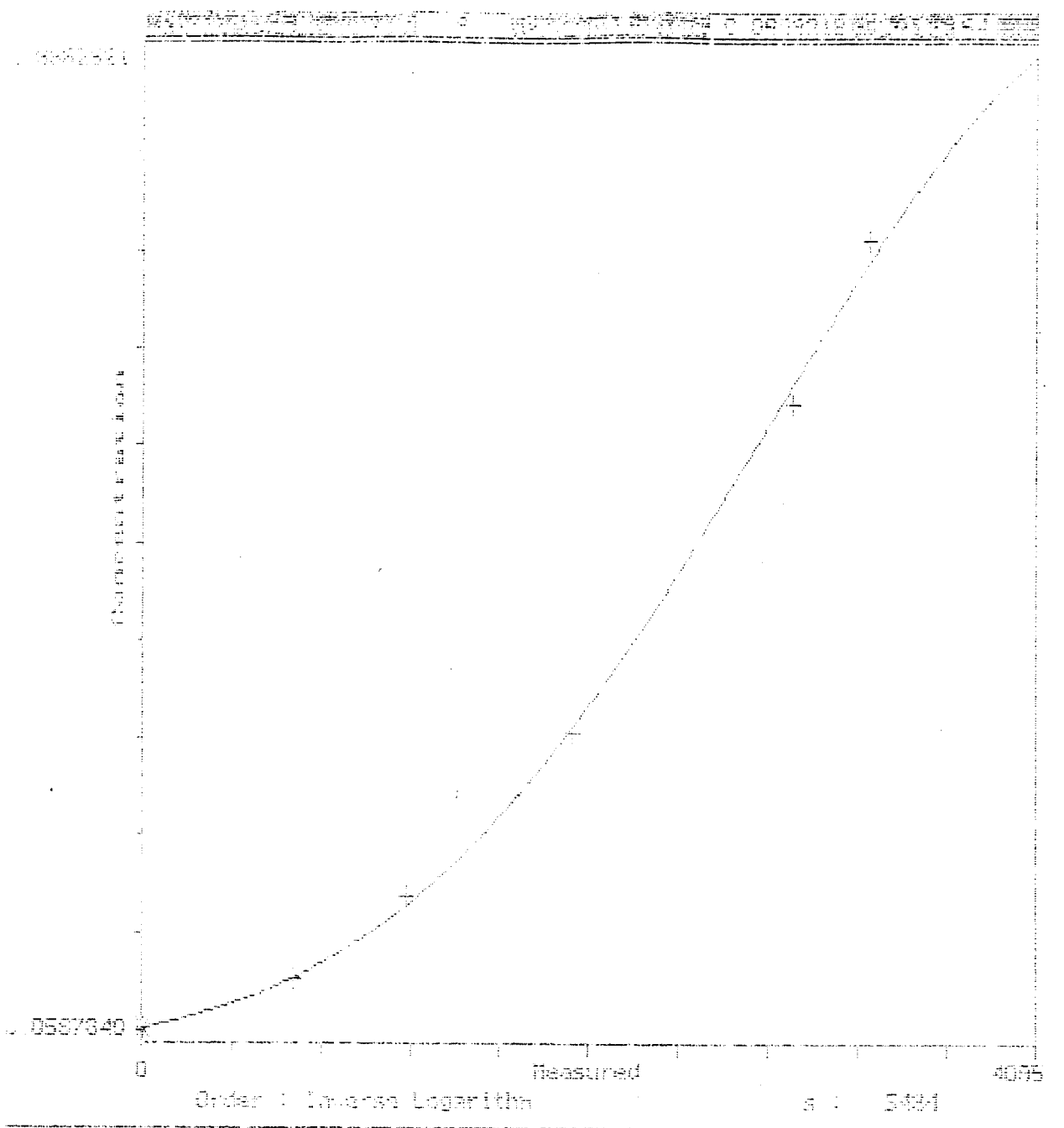
Calibration curve of 99012091 : Fluoride I.



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000184

000101

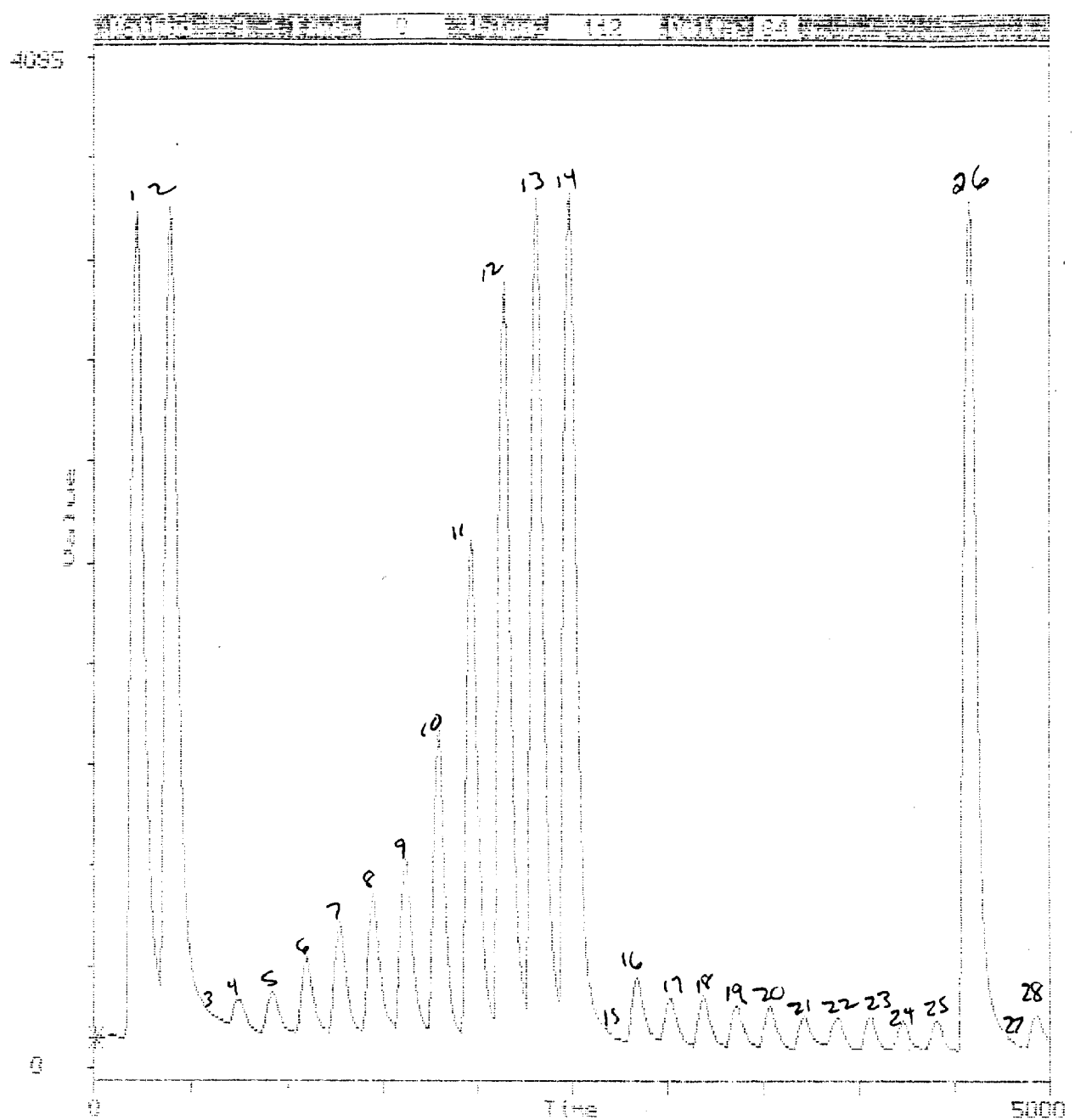


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000185

000105

10

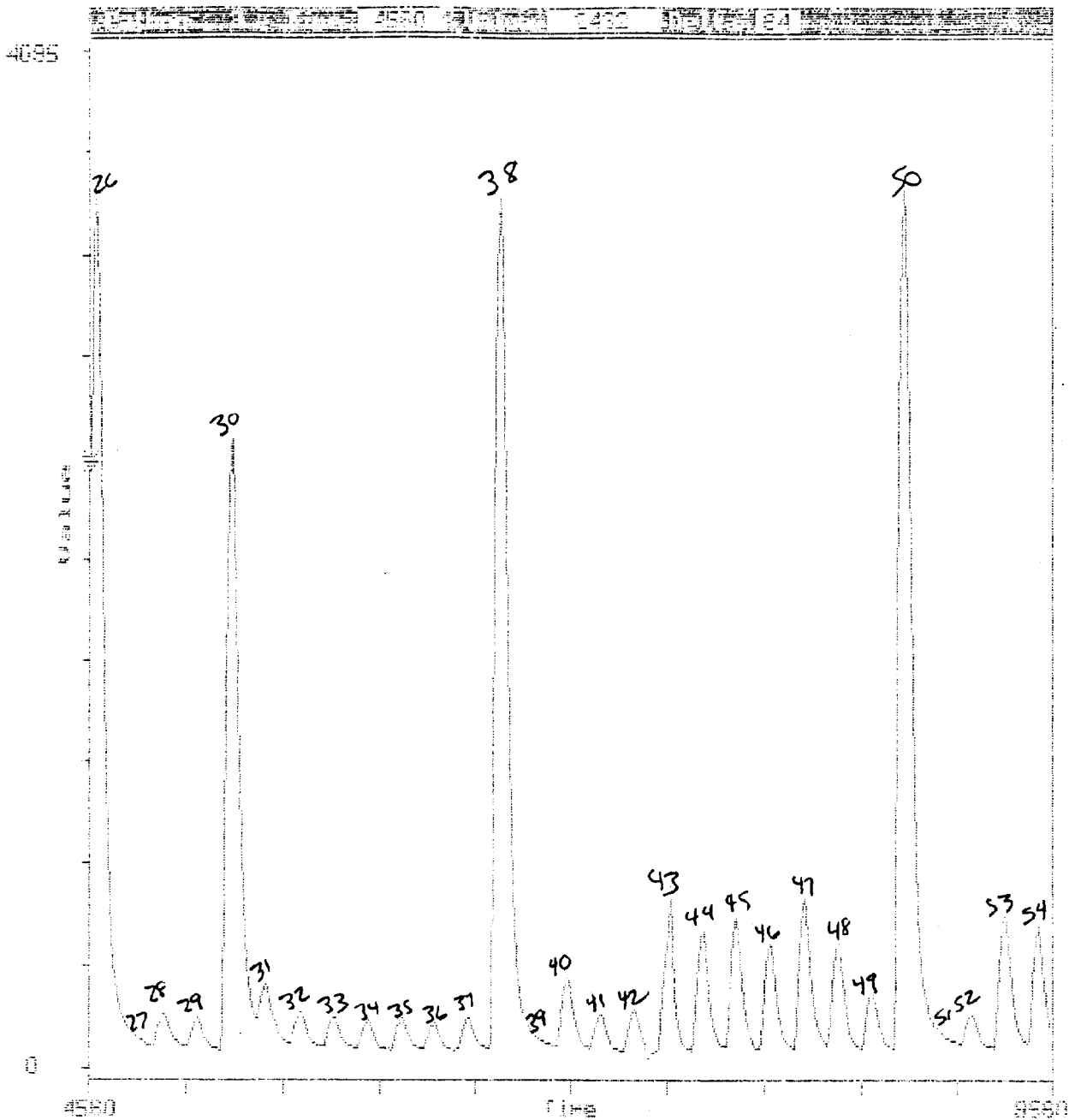


ac-Exit : F1-Help : Ctrl-P-Edit peaks :

BEST COPY AVAILABLE

000186

000106

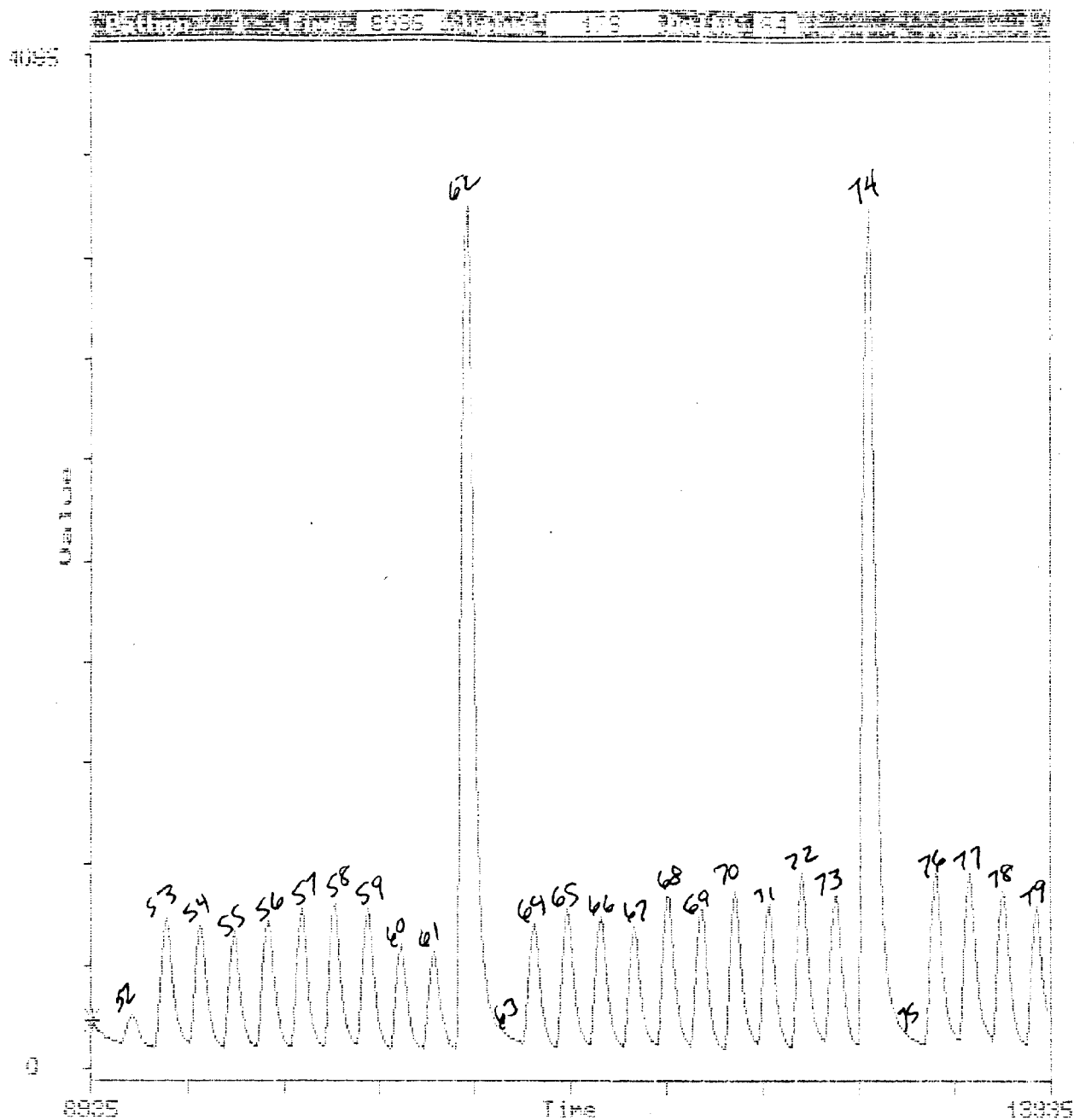


sc=Exit / F1=Help / Ctrl-P=Edit peaks /

1ST COPY AVAILABLE

000187

000107



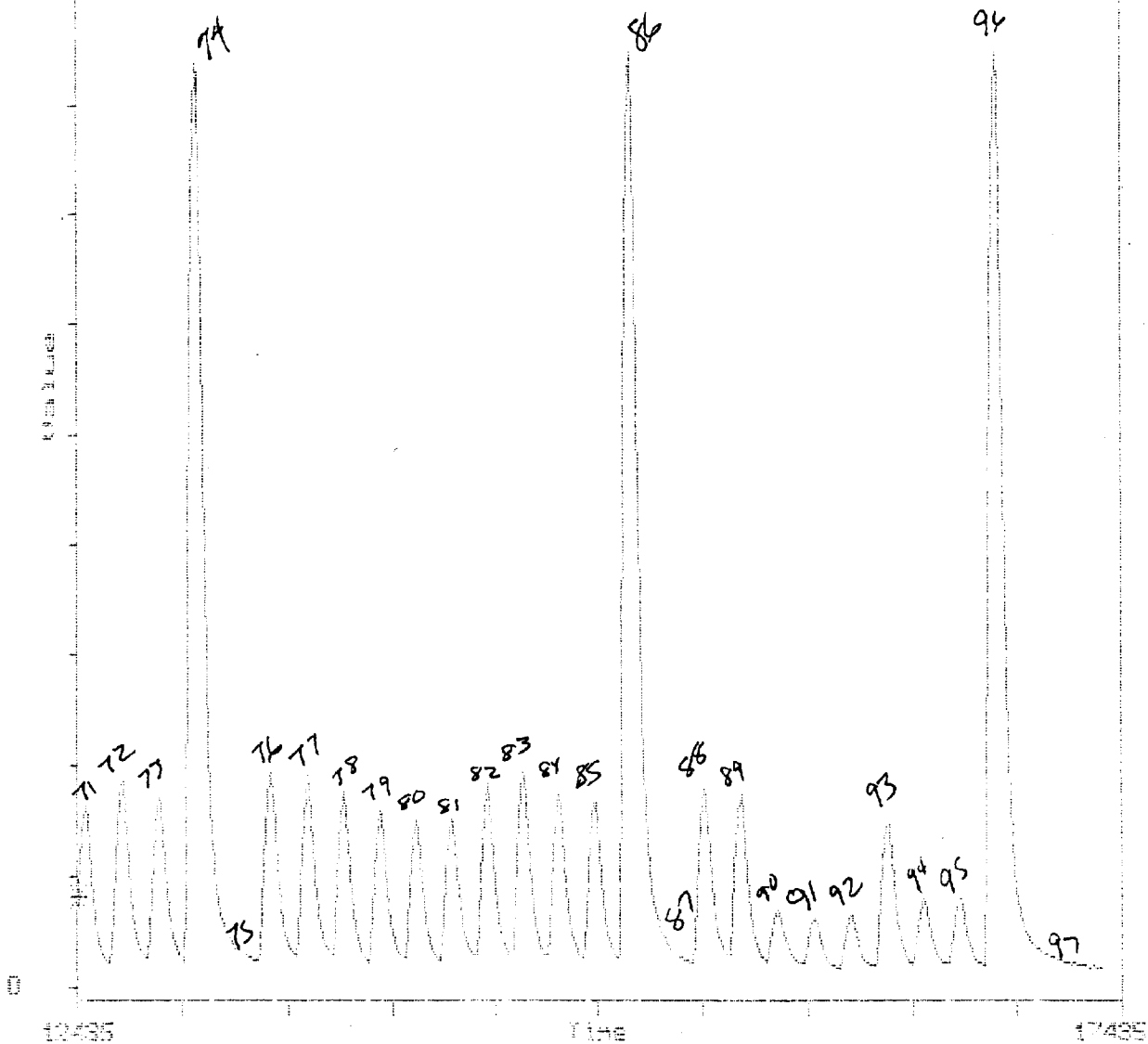
ac=Exit | F1=Help | Ctrl-F=Edit peaks |

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000188

000108

4095



Esc=Exit : F1=Help : Ctrl-P=Edit peak :

BEST COPY AVAILABLE

000189

000109

1995-05-24 12:48

OutPut of : 950524A1

software : version 6.1 c1990,93

operator : EDW

date of the Analysis : 1995-05-24 07:50

analysis File Name : C:\SKALAR\DATA\HWIDATA\LIVERS\950524A1

BEST COPY AVAILABLE

EDW 6/21/95
AMDT 42095.1
6329-159 liver

fluoride 1.5

calibration order = Inverse Logarithm

Slope : s = #####

result = $10^{\left[\frac{x - c1}{s} \right]}$

x = corrected value of the sample
c1 = corrected value of the concentration 1
s = Slope of the electrode

a2 = -0.00000

a1 = 0.00065

a0 = -1.22861

fluoride L

calibration order = 2

correlation : r = 0.99892

result = a2 * x² + a1 * x + a0

a2 = 0.00000

a1 = 0.00021

a0 = -0.00134

amplifier Type : SA1000
 Number : 1
 Sample Time : 50 sec.
 Wash Time : 120 sec.
 Air Time : 1 sec.
 Take up : Single
 sPecial : None
 needle Height : 70 mm.

injector needle Height : 80 mm
 dilution Factor : 10
 dilution Volume : 2.5 ml.
 Resample : 1
 Dilution runs : 1

User file : . TXT
Reproces : No

000190

000110

3MA01502277

2807.0110

995-05-24 12:48

OutPut of : 950524A1

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Fluoride 1.5 Path number : 3
Signal type : Debubbled
Decolor : Yes
system Number : 0
diLute : No
Resample : No
dil Threshold : 4095
diG output : 0
Window event : Off

s1 sStandard : Ignore
s2 sStandard : Ignore
s3 sStandard : Ignore
s4 sStandard : Ignore
s5 sStandard : Ignore
s6 sStandard : 0.150
s7 sStandard : 0.300
s8 sStandard : 0.600
s9 sStandard : 1.200
s10 sStandard : 1.500
Order : Inverse Logarithm
Dimension : PPM
start Value : 500 DU
trigger Limit : 1800 Sec
Peak shape : Pointed
stArt ignore : 60 Sec
eNd ignore : 120 Sec
Measure window : 75 %
Filter : No
Regeneration : No
formUla :
output : ##.###

Fluoride L Path number : 0
Signal type : Debubbled
Decolor : No
system Number : 0
diLute : No
Resample : No
dil Threshold : 4095
diG output : 0
Window event : Off

000191

000111

2807.0111

3MA01502278

s1 sTandard : 0.015
s2 sTandard : 0.030
s3 sTandard : 0.060
s4 sTandard : 0.090
s5 sTandard : 0.120
s6 sTandard : 0.150
s7 sTandard : Ignore
s8 sTandard : Ignore
s9 sTandard : Ignore
s10 sTandard : Ignore
Order : 2
Dimension : PPM
start Value : 500 DU
trigger Limit : 1800 Sec
Peak shape : Pointed
stArt ignore : 60 Sec
eNd ignore : 120 Sec
Measure window : 75 %
Filter : No
Regeneration : No
formUla : c4:=c3
output : #.####

000192

000112

Fluoride 1.5

Fluoride L

PPM

PPM

os	Typ	Ident	Ch	Result	F	Time	Ch	Result	F	Time
t	iw	Initial Wash	3	0.059		65	4	#####		0
t		Tracer	3	1.452		211	4	0.8505		0
d		Drift	3	1.469		387	4	0.8584		0
w		Wash	3	0.059		626	4	#####		0
s1		Standard 1	3	0.067		736	4	0.0160		0
s2		Standard 2	3	0.073		912	4	0.0282		0
s3		Standard 3	3	0.090		1086	4	0.0603		0
s4		Standard 4	3	0.110		1262	4	0.0931		0
s5		Standard 5	3	0.127		1438	4	0.1164		0
s6		Standard 6	3	0.155		1612	4	0.1510		0
0	s7	Standard 7	3	0.283		1788	4	0.2712		0
1	s8	Standard 8	3	0.614		1964	4	0.4713		0
2	s9	Standard 9	3	1.237		2138	4	0.7522		0
3	s10	Standard 10	3	1.462		2312	4	0.8550		0
4	d	Drift	3	1.495		2488	4	0.8710		0
5	w	Wash	3	0.059		2725	4	#####		0
6	u	F54092-1	3	0.088		2838	4	0.0564		0
7	u	F54092-2	3	0.084		3014	4	0.0502		0
8	u	F54092-3	3	0.079		3190	4	0.0412		0
9	u	F54106-1	3	0.088		3367	4	0.0571		0
0	u	F54106-2	3	0.088		3541	4	0.0564		0
1	u	F54106-3	3	0.080		3713	4	0.0433		0
2	u	BLK	3	0.065		3883	4	0.0118		0
3	u	SPK 1	3	0.099		4063	4	0.0760		0
4	u	SPK 2	3	0.101		4241	4	0.0784		0
5	u	SPK 3	3	0.105		4415	4	0.0854		0
6	d	Drift	3	1.454		4589	4	0.8511		0
7	w	Wash	3	0.059		4830	4	#####		0
8	u	SPK 4	3	0.152		4939	4	0.1473		0
9	u	SPK 5	3	0.135		5113	4	0.1269		0
0	u	SPK 6	3	0.144		5291	4	0.1380		0
1	u	LIVER BLK-1	3	0.085		5463	4	0.0515		0
2	u	LIVER BLK-2	3	0.076		5639	4	0.0346		0
3	u	LIVER BLK-3	3	0.067		5813	4	0.0162		0
4	u	SPK 63-1	3	0.108		5992	4	0.0889		0
5	u	SPK 63-2	3	0.108		6168	4	0.0898		0
6	u	SPK 63-3	3	0.150		6342	4	0.1450		0
7	u	SPK 63-4	3	0.110		6516	4	0.0931		0
8	d	Drift	3	1.494		6692	4	0.8707		0
9	w	Wash	3	0.059		6923	4	#####		0
0	u	F54088-1	3	0.085		7040	4	0.0521		0
1	u	F54088-2	3	0.087		7218	4	0.0547		0
2	u	F54088-3	3	0.080		7390	4	0.0418		0
3	u	BLK 4	3	0.069		7566	4	0.0217		0
4	u	SPK 63-1	3	0.127		7742	4	0.1162		0
5	u	SPK 63-2	3	0.105		7916	4	0.0847		0
6	u	SPK 63-3	3	0.105		8092	4	0.0847		0
7	u	SPK 63-4	3	0.105		8268	4	0.0849		0
8	u	BLK-1	3	0.069		8442	4	0.0198		0
9	u	BLK-2	3	0.062		8614	4	0.0049		0
0	d	Drift	3	1.487		8791	4	0.8670		0
1	w	Wash	3	0.059		9029	4	#####		0
2	u	SPK-1	3	0.105		9143	4	0.0847		0
3	u	SPK-2	3	0.112		9317	4	0.0960		0

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000193

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Fluoride 1.5 Fluoride L

PPM

PPM

os	Typ	Ident	Ch	Result	F	Time	Ch	Result	F	Time
4	u	BLK 3	3	0.067		9491	4	0.0166		0
5	u	SPK-3	3	0.114		9669	4	0.0979		0
6	u	SPK-4	3	0.067		9839	4	0.0166		0
7	u	F54089-1	3	0.074		10015	4	0.0318		0
8	u	F54089-2	3	0.074		10193	4	0.0318		0
9	u	F54089-3	3	0.073		10368	4	0.0289		0
0	u	F54099-1	3	0.078		10544	4	0.0391		0
1	u	F54099-2	3	0.077		10718	4	0.0369		0
2	d	Drift	3	1.487		10893	4	0.8670		0
3	w	Wash	3	0.059		11107	4	#####		0
4	u	F54099-3	3	0.082		11244	4	0.0463		0
5	u	F54114-1	3	0.074		11416	4	0.0303		0
6	u	F54114-2	3	0.072		11594	4	0.0261		0
7	u	F54114-3	3	0.074		11768	4	0.0308		0
8	u	F54109-1	3	0.071		11940	4	0.0255		0
9	u	F54109-2	3	0.071		12115	4	0.0255		0
0	u	F54109-3	3	0.076		12296	4	0.0344		0
1	u	F54080-1	3	0.074		12469	4	0.0306		0
2	u	F54080-2	3	0.075		12645	4	0.0331		0
3	u	F54080-3	3	0.059	A	12818	4	#####		0
4	d	Drift	3	1.468		12993	4	0.8578		0
5	w	Wash	3	0.059		13185	4	#####		0
t	rw	RunOut Wash	3	0.059		13468	4	#####		0

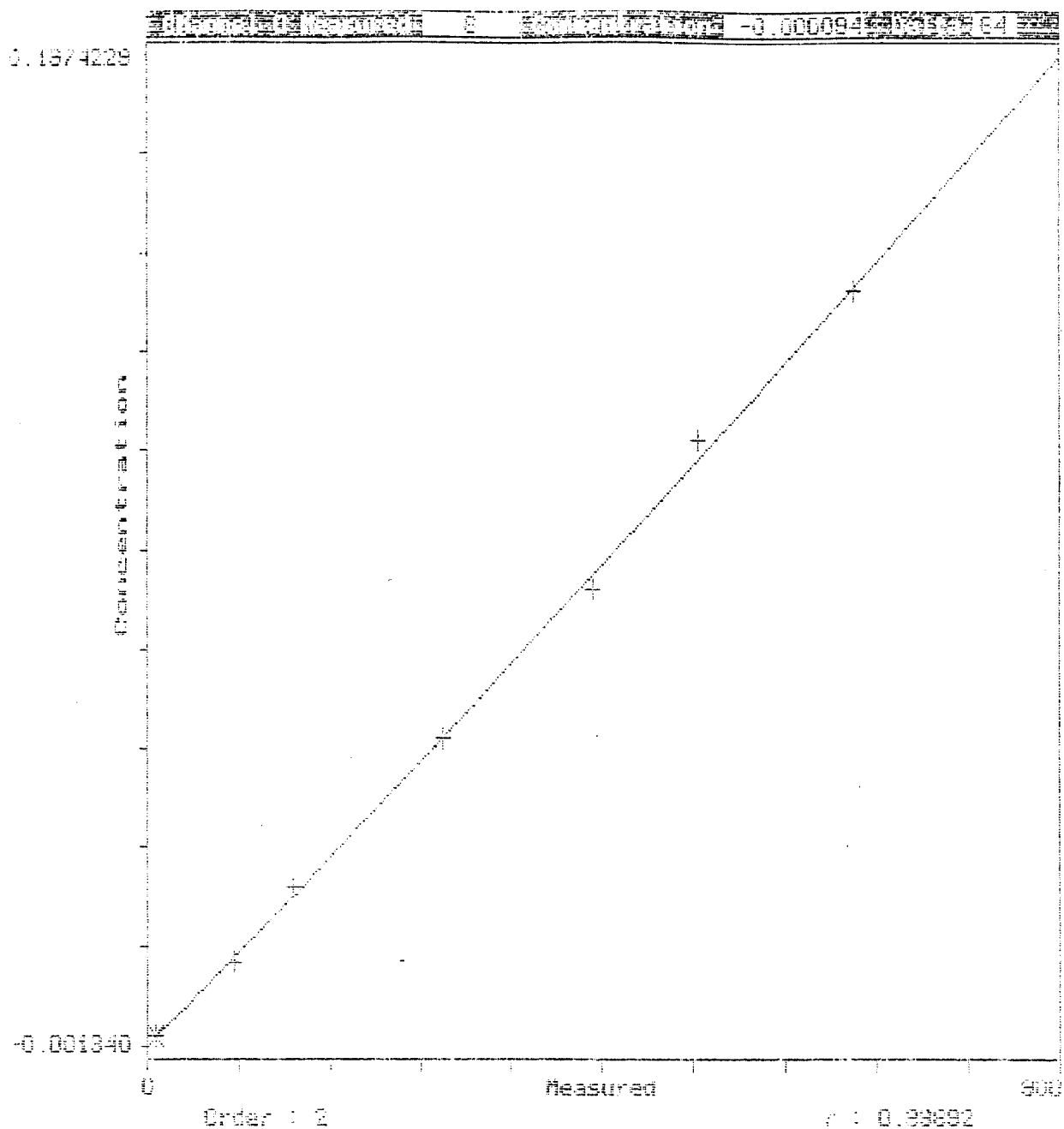
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000194

000114

7.

Calibration curve of 650524A1 : Fluoride L



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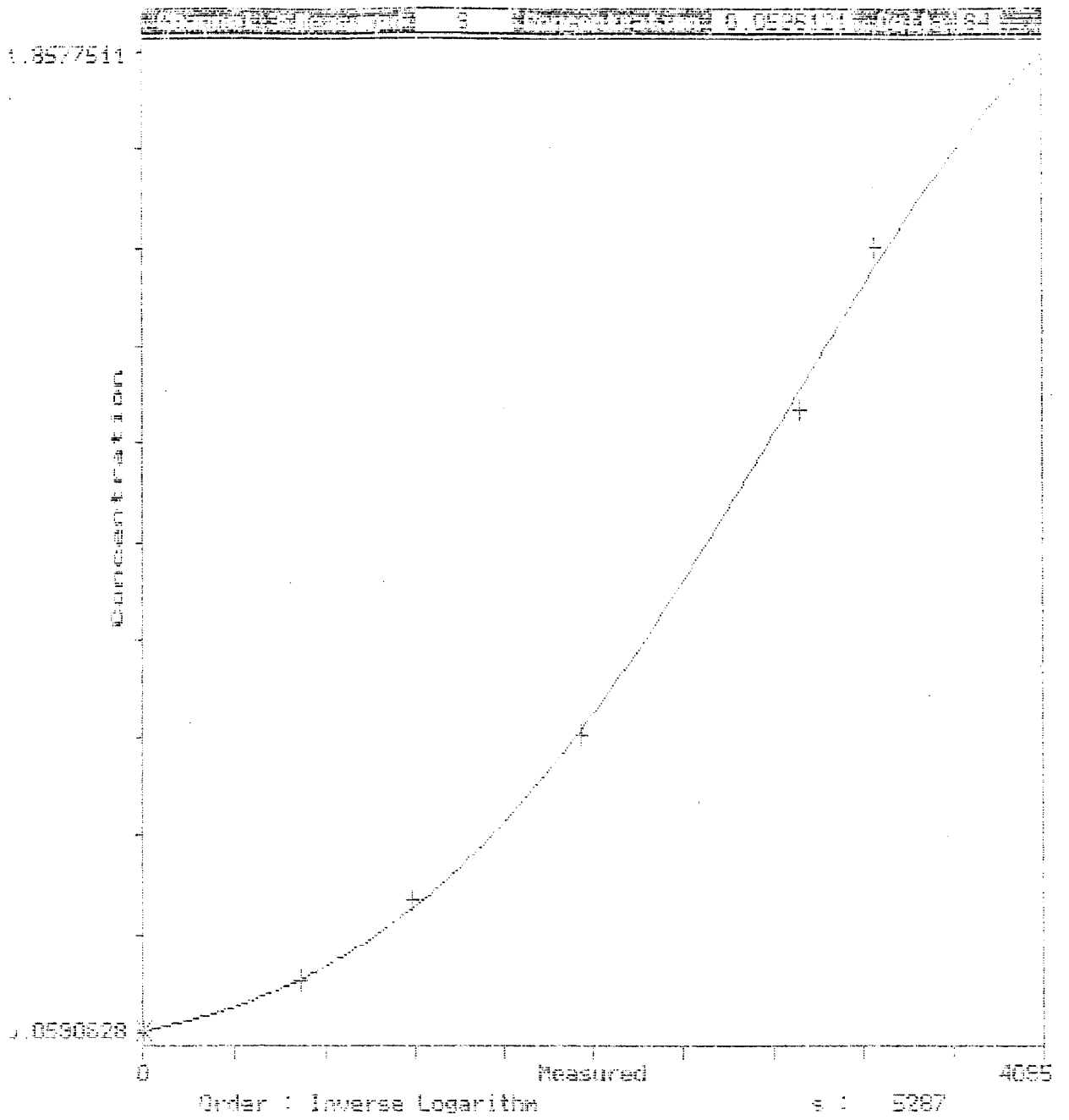
000195

000115

2807.0115

3MA01502282

Calibration curve of 950524A: Fluoride 1.5



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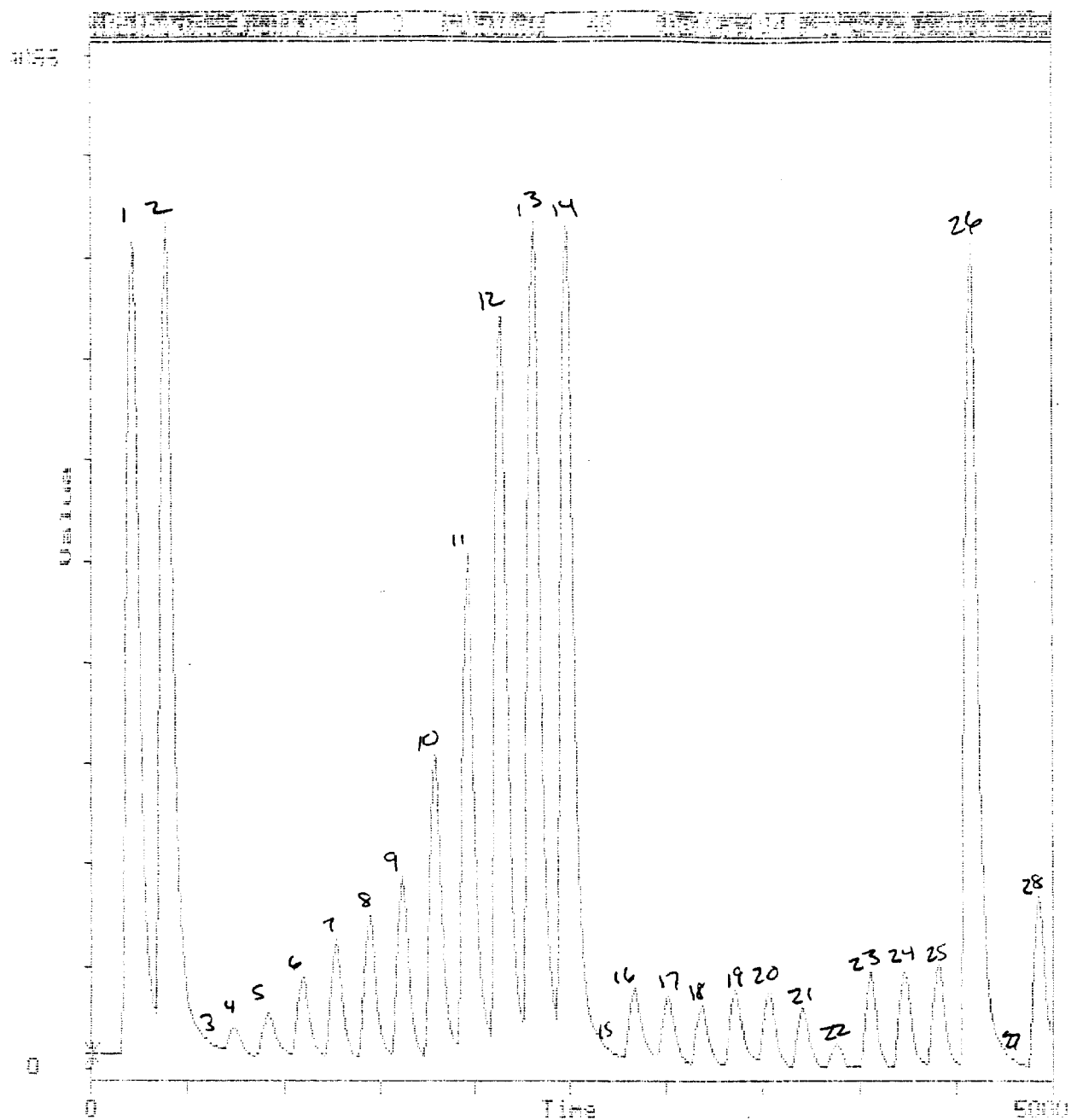
000196

000116

7

3MA01502283

2807.0116

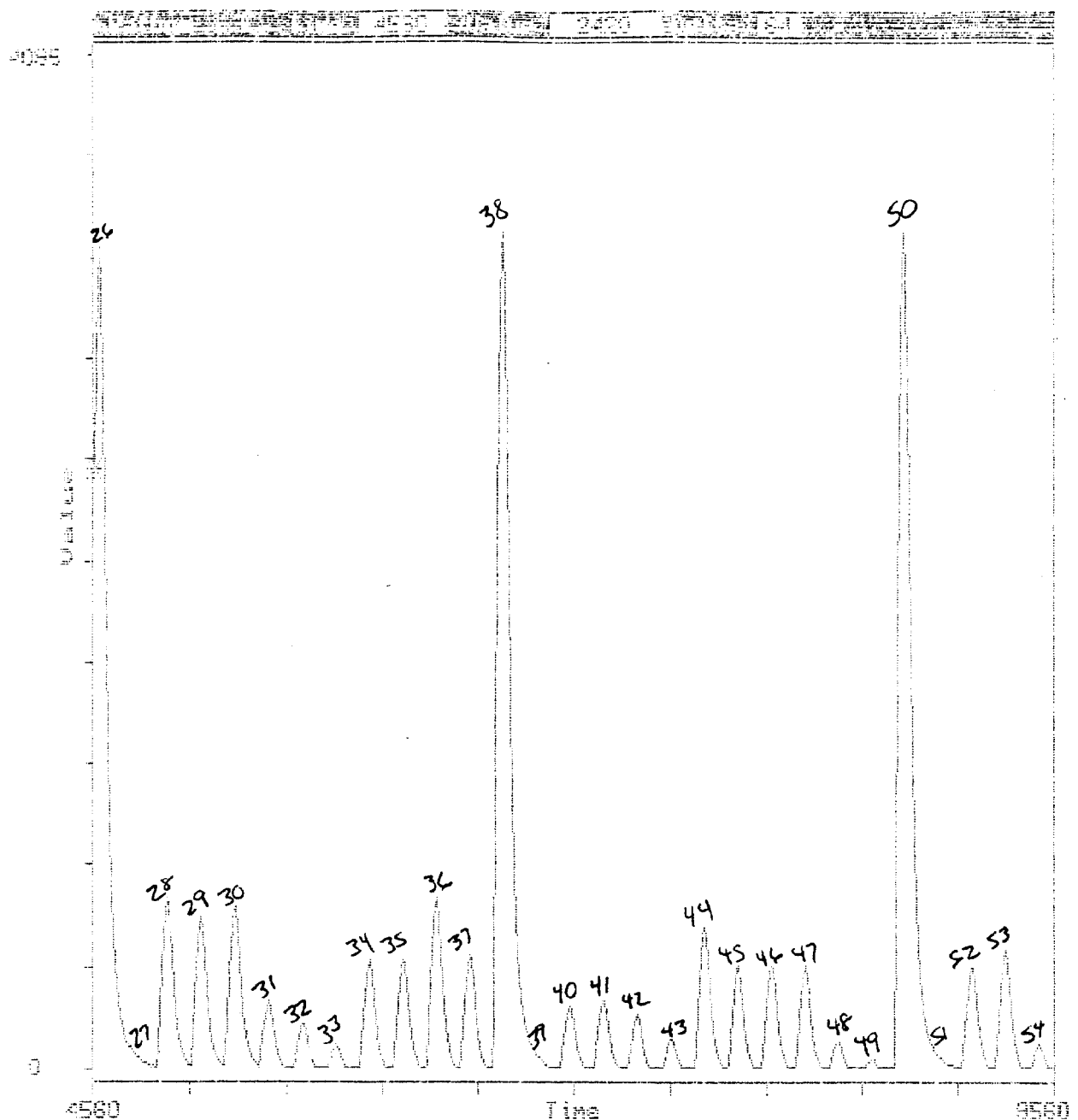


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BEST COPY AVAILABLE

000197

000117



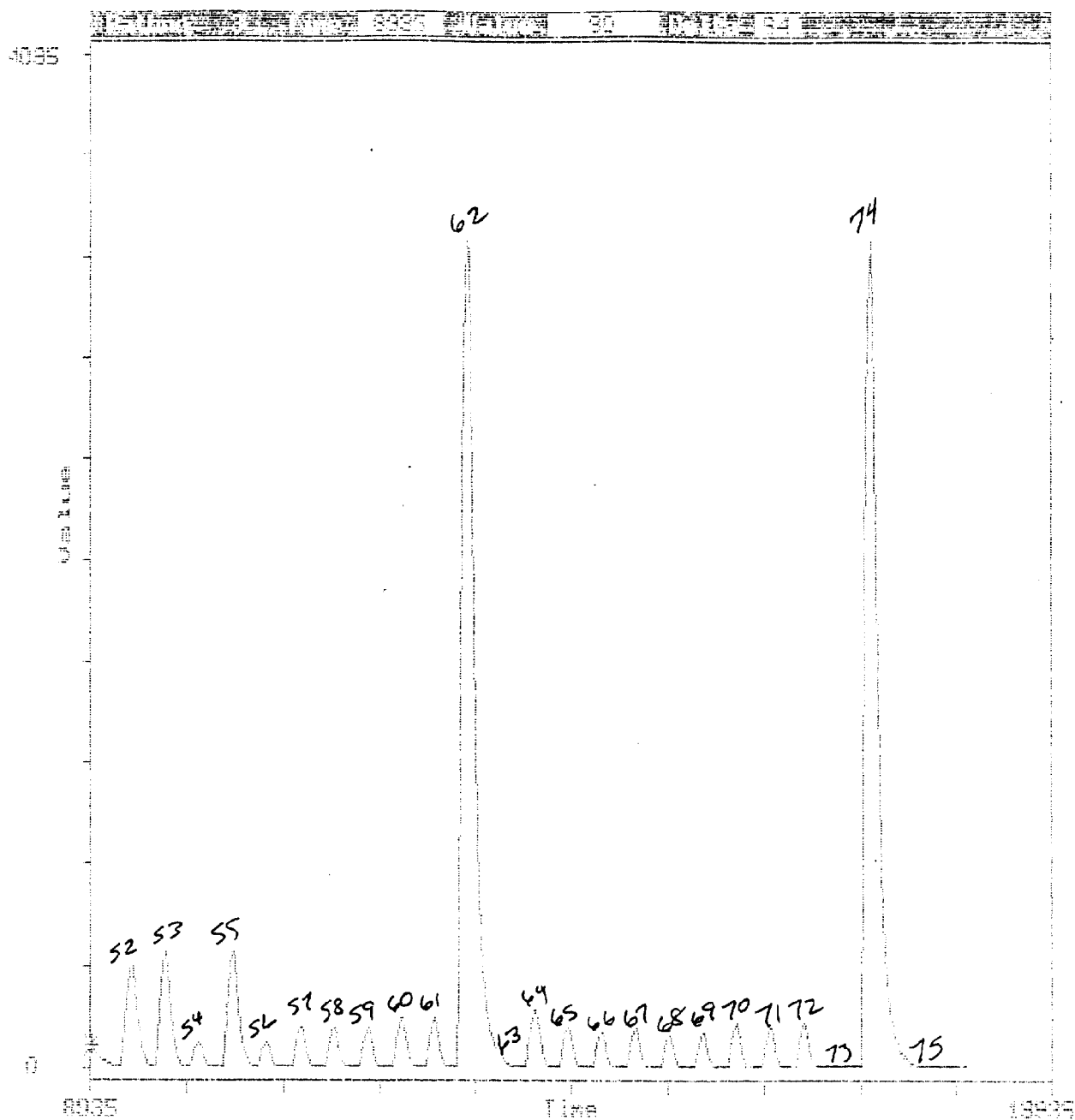
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BEST COPY AVAILABLE

000198

000118

76



Exit | F1=Help | Ctrl-P=Edit peaks |

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000199

006119

20

9.11.3 Summary and raw data; ppm F⁻ in serum as determined by thermal extraction followed by analysis using Orion ion analyzer.

000200

000120

HWI 6329-159
AMDT 042095.1
Dohrmann Serum Analysis
Analysis Dates: 04/28/95 - 05/10/95

All serum samples were thermally extracted by a modified Dohrmann DX2000 Organic Halide Analyzer and collected in a 1:1 milli Q water and TISAB solution. The samples were measured on an Orion EA940 expandable ion analyzer. The Dohrmann was calibrated using 32ppm, 63ppm, 126ppm, and 253ppm FC-95 standards. The Orion was calibrated by direct measurement with no blank correction using 0.05ppm, 0.1ppm, 0.5ppm, 1.0ppm and 1.5ppm F⁻ standards. The slope, intercept, and correlation were recorded in the appropriate logbook.

A summary table is included, showing the ppm F⁻ in each sample (see page 2). The value of "ND" has been entered for any sample with an Orion reading of below 0.05.

Pages 3 - 10 show the excel spreadsheet that was generated when the samples were analyzed. Pages 11 - 18 show the same spreadsheet with "ND" inserted where the Orion reading is below 0.05.

Deann K. Plummer

Page 1 of 18

000201

000121

3MA01502288

2807.0121

FC-95 PK
HWI 6329-159

Fluoride concentration in rabbit serum (ppm F-)

Dosage: 0 mg/kg

Sample	4 hour	8 hour	12 hour	24 hour	48 hour
F54074	ND	ND	ND	ND	ND
F54075	ND	ND	ND	ND	
F54081	ND	ND	ND	ND	
F54085	ND	ND	ND	ND	
F54086	ND	ND	ND	ND	
F54104	ND	ND	ND	ND	ND
F54105	ND	ND	ND	ND	
F54107	ND	ND	ND	ND	

Dosage: 5 mg/kg

Sample	4 hour	8 hour	12 hour	24 hour
F54077	ND	ND	ND	ND
F54083	ND	ND	ND	ND
F54091	ND	ND	ND	ND
F54094	ND	ND	ND	ND
F54097	ND	ND	ND	ND
F54100	ND	ND	ND	ND
F54102	ND	ND	ND	ND
F54108	ND	ND	ND	ND

Dosage: 10 mg/kg

Sample	4 hour	8 hour	12 hour	24 hour
F54071	ND	ND	ND	ND
F54078	ND	ND	ND	ND
F54090	ND	ND	ND	ND
F54093	ND	ND	ND	ND
F54095	ND	ND	ND	ND
F54096	ND	ND	ND	ND
F54101	ND	ND	ND	ND
F54110	ND	1.5	ND	ND

Dosage: 100 mg/kg

Sample	4 hour	8 hour	12 hour	15 hour	24 hour	48 hours	Day 8	Day 22	Day 28
F54080	ND	ND	ND	ND	ND	ND	ND		
F54087	ND	ND	ND	ND	ND	ND	ND	ND	ND
F54088	ND	ND	ND	ND	ND	ND	ND		
F54089	ND	ND	ND	ND	ND	ND	ND	ND	ND
F54092	ND	ND	ND	ND	ND	ND	ND		
F54099	ND	ND	1.5	ND	1.7	ND	ND	ND	
F54106	ND	ND	ND		ND		ND		
F54109	ND	ND	ND	ND	ND	ND	ND	ND	ND
F54114	ND	ND	ND	ND	ND	ND	ND	ND	ND

Dosage: 500 mg/kg

Sample	4 hour	8 hour	12 hour	24 hour	48 hours	Day 8	360 hour	Day 22	Day 28
F54076	ND	ND	ND						
F54079	2.3	ND	ND	1.2	1.2	1.4	1.3	ND	ND
F54082	1.1	1.3	ND	1.1	1.3	1.5	ND	ND	ND
F54084	1.3	ND	ND	1.2	1.8	1.5	1.4		
F54098	ND	1.0	ND	1.3	1.3	1.3	1.1		
F54111	1.9	ND	ND	1.3	1.5	1.3	1.3	ND	ND
F54112	ND	1.2	1.3	1.0	1.3	1.2	ND		
F54113	1.6	ND	ND	1.3	1.4	1.6	1.3		
F54116	2.0	3.4	ND	1.3	1.7	1.3	1.4	ND	ND

000202

000122

2

3MA01502289

2807.0122

384	mL of	Conc.	Actual	Quantity	DI:				
ID	FC95 solution spiked	FC95 solution (ppm)	Meter reading (ppm F-)	sample (mL or grams)	TISAB final vol (mL)	% rcvry (ug/ug)	Actual ppm F- in sample	Mass spiked (ug F-)	Mass rcvrd (ug F-)
serum blank-1			0.036	0.10	2.0		0.72		0.072
serum blank-2			0.020	0.10	2.0		0.40		0.040
serum spike 63-1	0.004	63	0.070	0.10	2.0	93%	1.4	0.15	0.14
serum spike 63-2	0.004	63	0.070	0.10	2.0	92%	1.4	0.15	0.14
serum spike 94.5-1	0.004	94.5	0.063	0.10	2.0	56%	1.3	0.23	0.13
serum spike 94.5-2	0.004	94.5	0.046	0.10	2.0	41%	0.92	0.23	0.092
serum spike 126-1	0.004	126	0.15	0.10	2.0	101%	3.1	0.30	0.31
serum spike 126-2	0.004	126	0.099	0.10	2.0	65%	2.0	0.30	0.20
serum spike 126-3	0.004	126	0.15	0.10	2.0	98%	3.0	0.30	0.30
serum spike 126-4	0.004	126	0.13	0.10	2.0	85%	2.6	0.30	0.26
F54081-4			0.040	0.10	2.0		0.80		0.080
F54075-4			0.032	0.10	2.0		0.65		0.065
F54107-4			0.024	0.10	2.0		0.48		0.048
F54105-4			0.025	0.10	2.0		0.51		0.051
F54074-4			0.034	0.10	2.0		0.67		0.067
Blank 1			0.71	0.10	2.0		14		1.4
Blank 2			0.34	0.10	2.0		6.9		0.69
Blank 3			0.36	0.10	2.0		7.2		0.72
Blank 4			0.084	0.10	2.0		1.7		0.17
Blank 5			0.038	0.10	2.0		0.75		0.075
Blank 6			0.039	0.10	2.0		0.79		0.079
Serum Spk-1	0.004	63	0.055	0.10	2.0	73%	1.1	0.15	0.11
Serum Spk-2	0.004	63	0.068	0.10	2.0	90%	1.4	0.15	0.14
Serum Spk-3	0.004	63	0.073	0.10	2.0	96%	1.5	0.15	0.15
Serum Spk-4	0.004	126	0.10	0.10	2.0	67%	2.0	0.30	0.20
Serum Spk-5	0.004	126	0.11	0.10	2.0	74%	2.2	0.30	0.22
Serum Spk-6	0.004	126	0.11	0.10	2.0	73%	2.2	0.30	0.22
Serum Spk-7	0.004	126	0.11	0.10	2.0	72%	2.2	0.30	0.22
Serum Spk-8	0.004	126	0.098	0.10	2.0	65%	2.0	0.30	0.20
Serum Spk-9	0.004	126	0.12	0.10	2.0	77%	2.3	0.30	0.23
Serum Spk-10	0.004	126	0.10	0.10	2.0	68%	2.1	0.30	0.21
F54085-4			0.045	0.10	2.0		0.90		0.090
F54086-4			0.027	0.10	2.0		0.54		0.054
F54104-4			0.025	0.10	2.0		0.49		0.049
F54077-4			0.021	0.10	2.0		0.42		0.042
F54083-4			0.020	0.10	2.0		0.40		0.040
F54094-4			0.021	0.10	2.0		0.42		0.042
F54100-4			0.020	0.10	2.0		0.41		0.041
F54091-4			0.019	0.10	2.0		0.38		0.038
serum blk 1			0.029	0.10	2.0		0.59		0.059
serum blk 2			0.024	0.10	2.0		0.48		0.048
serum spk 1	0.004	63	0.071	0.10	2.0	94%	1.4	0.15	0.14
serum spk 2	0.004	63	0.072	0.10	2.0	95%	1.4	0.15	0.14
F54097-4			0.022	0.10	2.0		0.45		0.045
F54102-4			0.020	0.10	2.0		0.41		0.041
F54108-4			0.016	0.10	2.0		0.32		0.032
F54071-4			0.017	0.10	2.0		0.34		0.034

000203

000123

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384	mL of FC95 solution spiked	Conc. FC95 solution (ppm)	Actual Meter reading (ppm F-)	Quantity sample (mL or grams)	DI: TISAB final vol (mL)	% rcvry (ug/ug)	Actual ppm F- in sample	Mass spiked (ug F-)	Mass rcvrd (ug F-)
ID									
F54093-4			0.020	0.10	2.0		0.41		0.041
F54095-4			0.016	0.10	2.0		0.32		0.032
F54101-4			0.015	0.10	2.0		0.29		0.029
F54078-4			0.021	0.10	2.0		0.41		0.041
F54090-4			0.020	0.10	2.0		0.39		0.039
F54096-4			0.017	0.10	2.0		0.34		0.034
F54110-4			0.020	0.10	2.0		0.39		0.039
F54087-4			0.025	0.10	2.0		0.50		0.050
F54088-4			0.028	0.10	2.0		0.55		0.055
F54089-4			0.020	0.10	2.0		0.41		0.041
F54106-4			0.032	0.10	2.0		0.63		0.063
F54080-4			0.025	0.10	2.0		0.51		0.051
F54092-4			0.019	0.10	2.0		0.38		0.038
F54109-4			0.021	0.10	2.0		0.42		0.042
F54114-4			0.039	0.10	2.0		0.78		0.078
F54076-4			0.041	0.10	2.0		0.81		0.081
F54082-4			0.057	0.10	2.0		1.1		0.11
F54111-4			0.096	0.10	2.0		1.9		0.19
F54113-4			0.082	0.10	2.0		1.6		0.16
F54079-4			0.12	0.10	2.0		2.3		0.23
F54084-4			0.067	0.10	2.0		1.3		0.13
F54098-4			0.046	0.10	2.0		0.93		0.093
F54116-4			0.10	0.10	2.0		2.0		0.20
F54075-8			0.025	0.10	2.0		0.49		0.049
F54081-8			0.020	0.10	2.0		0.40		0.040
F54105-8			0.021	0.10	2.0		0.43		0.043
F54107-8			0.015	0.10	2.0		0.30		0.030
F54074-8			0.015	0.10	2.0		0.30		0.030
F54085-8			0.021	0.10	2.0		0.43		0.043
F54086-8			0.031	0.10	2.0		0.62		0.062
serum blk 1			0.029	0.10	2.0		0.58		0.058
serum blk 2			0.028	0.10	2.0		0.56		0.056
serum spk 1	0.004	63	0.080	0.10	2.0	106%	1.6	0.15	0.16
serum spk 2	0.004	63	0.069	0.10	2.0	91%	1.4	0.15	0.14
F54104-8			0.031	0.10	2.0		0.62		0.062
F54077-8			0.023	0.10	2.0		0.46		0.046
F54083-8			0.018	0.10	2.0		0.35		0.035
F54094-8			0.025	0.10	2.0		0.51		0.051
F54100-8			0.017	0.10	2.0		0.35		0.035
F54091-8			0.014	0.10	2.0		0.28		0.028
F54097-8			0.014	0.10	2.0		0.28		0.028
F54102-8			0.013	0.10	2.0		0.26		0.026
F54108-8			0.013	0.10	2.0		0.25		0.025
F54071-8			0.015	0.10	2.0		0.30		0.030
F54093-8			0.019	0.10	2.0		0.37		0.037
F54095-8			0.026	0.10	2.0		0.51		0.051
F54101-8			0.016	0.10	2.0		0.32		0.032
F54078-8			0.021	0.10	2.0		0.42		0.042

000204

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384	mL of FC95 solution spiked	Conc. FC95 solution (ppm)	Actual Meter reading (ppm F-)	Quantity sample (mL or grams)	DI: TISAB final vol (mL)	% rcvry (ug/ug)	Actual ppm F- in sample	Mass spiked (ug F-)	Mass rcvrd (ug F-)
ID									
F54090- 8			0.021	0.10	2.0		0.42		0.042
F54096- 8			0.017	0.10	2.0		0.34		0.034
F54110- 8			0.075	0.10	2.0		1.5		0.15
F54087- 8			0.022	0.10	2.0		0.44		0.044
F54088- 8			0.033	0.10	2.0		0.66		0.066
F54089- 8			0.031	0.10	2.0		0.62		0.062
F54080- 8			0.032	0.10	2.0		0.64		0.064
F54106- 8			0.043	0.10	2.0		0.86		0.086
F54092- 8			0.037	0.10	2.0		0.74		0.074
F54109- 8			0.024	0.10	2.0		0.49		0.049
F54114- 8			0.034	0.10	2.0		0.68		0.068
F54076- 8			0.045	0.10	2.0		0.89		0.089
F54082- 8			0.063	0.10	2.0		1.3		0.13
F54111- 8			0.044	0.10	2.0		0.88		0.088
F54113- 8			0.048	0.10	2.0		0.95		0.10
F54079- 8			0.042	0.10	2.0		0.84		0.084
F54084- 8			0.045	0.10	2.0		0.89		0.089
F54098- 8			0.050	0.10	2.0		1.0		0.10
F54116- 8			0.17	0.10	2.0		3.4		0.34
serum blk 1			0.012	0.10	2.0		0.25		0.025
serum blk 2			0.018	0.10	2.0		0.36		0.036
serum spk 1	0.004	63	0.066	0.10	2.0	87%	1.3	0.15	0.13
serum spk 2	0.004	63	0.070	0.10	2.0	93%	1.4	0.15	0.14
F54075-12			0.028	0.10	2.0		0.56		0.056
F54081-12			0.021	0.10	2.0		0.42		0.042
F54105-12			0.026	0.10	2.0		0.53		0.053
F54107-12			0.019	0.10	2.0		0.39		0.039
F54074-12			0.017	0.10	2.0		0.35		0.035
F54085-12			0.018	0.10	2.0		0.37		0.037
F54086-12			0.020	0.10	2.0		0.41		0.041
F54086-12			0.025	0.10	2.0		0.50		0.050
F54077-12			0.038	0.10	2.0		0.76		0.076
F54083-12			0.032	0.10	2.0		0.64		0.064
F54094-12			0.035	0.10	2.0		0.71		0.071
F54100-12			0.022	0.10	2.0		0.44		0.044
F54091-12			0.029	0.10	2.0		0.58		0.058
F54097-12			0.025	0.10	2.0		0.49		0.049
F54102-12			0.022	0.10	2.0		0.44		0.044
F54108-12			0.014	0.10	2.0		0.29		0.029
F54077-12			0.046	0.10	2.0		0.92		0.092
F54071-12			0.021	0.10	2.0		0.41		0.041
F54093-12			0.016	0.10	2.0		0.33		0.033
F54095-12			0.016	0.10	2.0		0.32		0.032
F54101-12			0.020	0.10	2.0		0.40		0.040
F54110-12			0.016	0.10	2.0		0.31		0.031
F54096-12			0.012	0.10	2.0		0.25		0.025
F54090-12			0.017	0.10	2.0		0.34		0.034
F54078-12			0.014	0.10	2.0		0.28		0.028

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384	mL of FC95 solution spiked	Conc. FC95 solution (ppm)	Actual Meter reading (ppm F-)	Quantity sample (mL or grams)	DI: TISAB final vol (mL)	% rcvry (ug/ug)	Actual ppm F- in sample	Mass spiked (ug F-)	Mass rcvrd (ug F-)
ID									
F54088-12			0.025	0.10	2.0		0.51		0.051
F54106-12			0.027	0.10	2.0		0.54		0.054
F54089-12			0.019	0.10	2.0		0.38		0.038
F54087-12			0.019	0.10	2.0		0.37		0.037
F54080-12			0.018	0.10	2.0		0.36		0.036
F54092-12			0.017	0.10	2.0		0.33		0.033
F54109-12			0.021	0.10	2.0		0.41		0.041
F54114-12			0.026	0.10	2.0		0.52		0.052
F54075-12			0.027	0.10	2.0		0.55		0.055
F54113-12			0.022	0.10	2.0		0.44		0.044
F54082-12			0.034	0.10	2.0		0.69		0.069
F54111-12			0.046	0.10	2.0		0.91		0.091
F54098-12			0.042	0.10	2.0		0.84		0.084
F54084-12			0.044	0.10	2.0		0.87		0.087
F54079-12			0.043	0.10	2.0		0.85		0.085
F54116-12			0.047	0.10	2.0		0.94		0.094
Serum Blk-1			0.033	0.10	2.0		0.66		0.066
Serum Blk-2			0.030	0.10	2.0		0.60		0.060
Serum Spk-1	0.004	63	0.034	0.10	2.0	44%	0.67	0.15	0.067
Serum Spk-2	0.004	63	0.040	0.10	2.0	52%	0.79	0.15	0.079
Serum Spk-3	0.004	63	0.050	0.10	2.0	66%	0.99	0.15	0.10
Serum Spk-4	0.004	63	0.054	0.10	2.0	72%	1.1	0.15	0.11
Serum Spk-5	0.004	63	0.083	0.10	2.0	110%	1.7	0.15	0.17
Serum Spk-6	0.004	63	0.053	0.10	2.0	71%	1.1	0.15	0.11
Serum Spk-7	0.004	63	0.049	0.10	2.0	65%	0.99	0.15	0.10
Serum Spk-8	0.004	63	0.055	0.10	2.0	73%	1.1	0.15	0.11
F54105-24			0.041	0.10	2.0		0.81		0.081
F54075-24			0.022	0.10	2.0		0.44		0.044
F54081-24			0.017	0.10	2.0		0.35		0.035
F54107-24			0.015	0.10	2.0		0.30		0.030
F54104-24			0.018	0.10	2.0		0.37		0.037
F54086-24			0.016	0.10	2.0		0.33		0.033
F54074-24			0.013	0.10	2.0		0.27		0.027
Blank 1			0.031	0.10	2.0		0.61		0.061
Blank 2			0.022	0.10	2.0		0.43		0.043
spike 1	0.004	63	0.033	0.10	2.0	43%	0.65	0.15	0.065
spike 2	0.004	63	0.044	0.10	2.0	58%	0.88	0.15	0.088
spike 3	0.004	63	0.047	0.10	2.0	63%	0.95	0.15	0.095
spike 4	0.004	63	0.047	0.10	2.0	62%	0.94	0.15	0.094
spike 5	0.004	63	0.052	0.10	2.0	68%	1.0	0.15	0.10
spike 6	0.004	63	0.051	0.10	2.0	67%	1.0	0.15	0.10
Blank 3			0.036	0.10	2.0		0.72		0.072
Blank 4			0.020	0.10	2.0		0.39		0.039
F54085-24			0.021	0.10	2.0		0.41		0.041
F54083-24			0.019	0.10	2.0		0.38		0.038
F54100-24			0.016	0.10	2.0		0.32		0.032
F54077-24			0.017	0.10	2.0		0.33		0.033
F54094-24			0.015	0.10	2.0		0.31		0.031
F54091-24			0.016	0.10	2.0		0.31		0.031

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4

384	mL of FC95 solution spiked	Conc. FC95 solution (ppm)	Actual Meter reading (ppm F-)	Quantity sample (mL or grams)	DI: TISAB final vol (mL)	% rcvry (ug/ug)	Actual ppm F- in sample	Mass spiked (ug F-)	Mass rcvrd (ug F-)
ID									
F54108-24			0.014	0.10	2.0		0.28		0.028
F54102-24			0.013	0.10	2.0		0.25		0.025
F54097-24			0.020	0.10	2.0		0.40		0.040
F54071-24			0.015	0.10	2.0		0.30		0.030
F54093-24			0.014	0.10	2.0		0.27		0.027
F54095-24			0.013	0.10	2.0		0.26		0.026
F54101-24			0.012	0.10	2.0		0.24		0.024
F54110-24			0.011	0.10	2.0		0.23		0.023
F54096-24			0.013	0.10	2.0		0.26		0.026
F54090-24			0.025	0.10	2.0		0.50		0.050
F54078-24			0.013	0.10	2.0		0.27		0.027
F54088-24			0.014	0.10	2.0		0.27		0.027
F54106-24			0.013	0.10	2.0		0.26		0.026
F54089-24			0.014	0.10	2.0		0.28		0.028
F54087-24			0.014	0.10	2.0		0.27		0.027
F54080-24			0.016	0.10	2.0		0.32		0.032
F54092-24			0.016	0.10	2.0		0.32		0.032
F54109-24			0.015	0.10	2.0		0.31		0.031
F54114-24			0.016	0.10	2.0		0.32		0.032
serum blk 1			0.039	0.10	2.0		0.77		0.077
serum blk 2			0.028	0.10	2.0		0.55		0.055
serum spk 1	0.004	63	0.071	0.10	2.0	94%	1.4	0.15	0.14
serum spk 2	0.004	63	0.082	0.10	2.0	109%	1.6	0.15	0.16
F54113-24			0.064	0.10	2.0		1.3		0.13
F54082-24			0.055	0.10	2.0		1.1		0.11
F54111-24			0.063	0.10	2.0		1.3		0.13
F54098-24			0.064	0.10	2.0		1.3		0.13
F54084-24			0.061	0.10	2.0		1.2		0.12
F54079-24			0.059	0.10	2.0		1.2		0.12
F54115-24			0.064	0.10	2.0		1.3		0.13
F54113-48			0.068	0.10	2.0		1.4		0.14
F54082-48			0.066	0.10	2.0		1.3		0.13
F54111-48			0.073	0.10	2.0		1.5		0.15
F54098-48			0.067	0.10	2.0		1.3		0.13
F54084-48			0.091	0.10	2.0		1.8		0.18
F54079-48			0.059	0.10	2.0		1.2		0.12
F54116-48			0.085	0.10	2.0		1.7		0.17
F54113-192			0.080	0.10	2.0		1.6		0.16
F54082-192			0.073	0.10	2.0		1.5		0.15
F54111-192			0.063	0.10	2.0		1.3		0.13
F54098-192			0.067	0.10	2.0		1.3		0.13
F54079-192			0.068	0.10	2.0		1.4		0.14
F54084-192			0.077	0.10	2.0		1.5		0.15
F54116-192			0.065	0.10	2.0		1.3		0.13
F54113-360			0.065	0.10	2.0		1.3		0.13
F54082-360			0.043	0.10	2.0		0.87		0.087
F54111-360			0.063	0.10	2.0		1.3		0.13
F54098-360			0.054	0.10	2.0		1.1		0.11
F54079-360			0.063	0.10	2.0		1.3		0.13

000207

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384	mL of FC95 solution spiked	Conc. FC95 solution (ppm)	Actual Meter reading (ppm F-)	Quantity sample (mL or grams)	DI: TISAB final vol (mL)	% rcvry (ug/ug)	Actual ppm F- in sample	Mass spiked (ug F-)	Mass rcvrd (ug F-)
ID									
F54084-360			0.069	0.10	2.0		1.4		0.14
F54116-360			0.069	0.10	2.0		1.4		0.14
Serum Blk 1			0.025	0.10	2.0		0.50		0.050
Serum Blk 2			0.032	0.10	2.0		0.65		0.065
Serum Spk 1	0.004	63	0.069	0.10	2.0	91%	1.4	0.15	0.14
Serum Spk 2	0.004	63	0.076	0.10	2.0	101%	1.5	0.15	0.15
F54082-D22			0.046	0.10	2.0		0.91		0.091
F54111-D22			0.041	0.10	2.0		0.82		0.082
F54079-D22			0.040	0.10	2.0		0.81		0.081
F54116-D22			0.045	0.10	2.0		0.89		0.089
F54082-D28			0.048	0.10	2.0		0.96		0.10
F54111-D28			0.036	0.10	2.0		0.71		0.071
F54079-D28			0.033	0.10	2.0		0.66		0.066
F54116-D28			0.036	0.10	2.0		0.73		0.073
F54099-4			0.028	0.10	2.0		0.55		0.055
F54099-8			0.026	0.10	2.0		0.51		0.051
F54099-12			0.074	0.10	2.0		1.5		0.15
F54099-24			0.087	0.10	2.0		1.7		0.17
F54099-48			0.047	0.10	2.0		0.95		0.095
F54099-192			0.033	0.10	2.0		0.67		0.067
F54099-360			0.029	0.10	2.0		0.57		0.057
F54112-4			0.038	0.10	2.0		0.76		0.076
F54112-8			0.059	0.10	2.0		1.2		0.12
F54112-12			0.066	0.10	2.0		1.3		0.13
F54112-24			0.051	0.10	2.0		1.0		0.10
F54112-48			0.066	0.10	2.0		1.3		0.13
F54112-192			0.059	0.10	2.0		1.2		0.12
F54112-360			0.041	0.10	2.0		0.82		0.082
SERUM SPIKE-63-1	0.004	63	0.059	0.10	2.0	78%	1.2	0.15	0.12
SERUM SPIKE-63-2	0.004	63	0.079	0.10	2.0	105%	1.6	0.15	0.16
SERUM SPIKE-63-3	0.004	63	0.074	0.10	2.0	97%	1.5	0.15	0.15
SERUM SPIKE-126-1	0.004	126	0.083	0.10	2.0	55%	1.7	0.30	0.17
SERUM SPIKE-126-2	0.004	126	0.12	0.10	2.0	77%	2.3	0.30	0.23
SERUM SPIKE-126-3	0.004	126	0.12	0.10	2.0	79%	2.4	0.30	0.24
serum blank-1			0.10	0.10	2.0		2.0		0.20
serum blank-2			0.040	0.10	2.0		0.79		0.079
serum blank-3			0.019	0.10	2.0		0.39		0.039
spike 63-1	0.004	63	0.058	0.10	2.0	77%	1.2	0.15	0.12
spike 63-2	0.004	63	0.058	0.10	2.0	77%	1.2	0.15	0.12
spike 63-3	0.004	63	0.092	0.10	2.0	121%	1.8	0.15	0.18
spike 63-4	0.004	63	0.053	0.10	2.0	70%	1.1	0.15	0.11
spike 63-5	0.004	63	0.055	0.10	2.0	73%	1.1	0.15	0.11
spike 63-6	0.004	63	0.058	0.10	2.0	77%	1.2	0.15	0.12
spike 63-7	0.004	63	0.072	0.10	2.0	95%	1.4	0.15	0.14
spike 63-8	0.004	63	0.060	0.10	2.0	79%	1.2	0.15	0.12
Serum blank 1			0.045	0.10	2.0		0.90		0.090
Serum blank 2			0.017	0.10	2.0		0.33		0.033
Serum spike 63-1	0.004	63	0.12	0.10	2.0	153%	2.3	0.15	0.23
Serum spike 63-2	0.004	63	0.21	0.10	2.0	273%	4.1	0.15	0.41

000208

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384	mL of FC95 solution spiked	Conc. FC95 solution (ppm)	Actual Meter reading (ppm F-)	Quantity sample (mL or grams)	DI: TISAB final vol (mL)	% rcvry (ug/ug)	Actual ppm F- in sample	Mass spiked (ug F-)	Mass rcvrd (ug F-)
ID									
Serum blank 1			0.031	0.10	2.0		0.62		0.062
Serum blank 2			0.021	0.10	2.0		0.42		0.042
Serum spike 1	0.004	63	0.074	0.10	2.0	98%	1.5	0.15	0.15
Serum spike 2	0.004	63	0.066	0.10	2.0	87%	1.3	0.15	0.13
Serum spike 3	0.004	63	0.065	0.10	2.0	86%	1.3	0.15	0.13
Serum spike 4	0.004	63	0.060	0.10	2.0	80%	1.2	0.15	0.12
Serum spike 5	0.004	63	0.070	0.10	2.0	93%	1.4	0.15	0.14
Serum spike 6	0.004	63	0.069	0.10	2.0	91%	1.4	0.15	0.14
Serum spike 7	0.004	63	0.068	0.10	2.0	90%	1.4	0.15	0.14
Serum blank 3			0.023	0.10	2.0		0.46		0.046
Serum blank 4			0.020	0.10	2.0		0.41		0.041
F54088-48			0.019	0.10	2.0		0.37		0.037
F54099-48			0.021	0.10	2.0		0.43		0.043
F54089-48			0.017	0.10	2.0		0.34		0.034
F54087-48			0.020	0.10	2.0		0.40		0.040
F54080-48			0.017	0.10	2.0		0.34		0.034
F54092-48			0.016	0.10	2.0		0.32		0.032
F54109-48			0.022	0.10	2.0		0.45		0.045
F54114-48			0.022	0.10	2.0		0.44		0.044
F54088 dy8			0.018	0.10	2.0		0.36		0.036
F54099 dy8			0.014	0.10	2.0		0.28		0.028
serum spike 8	0.004	63	0.059	0.10	2.0	78%	1.2	0.15	0.12
serum spike 9	0.004	63	0.060	0.10	2.0	79%	1.2	0.15	0.12
serum spike 10	0.004	63	0.060	0.10	2.0	79%	1.2	0.15	0.12
SERUM BLK 1			0.031	0.10	2.0		0.62		0.062
SERUM BLK 2			0.016	0.10	2.0		0.32		0.032
SERUM SPK 1	0.004	63	0.056	0.10	2.0	74%	1.1	0.15	0.11
SERUM SPK 2	0.004	63	0.069	0.10	2.0	91%	1.4	0.15	0.14
SERUM SPK 3	0.004	63	0.072	0.10	2.0	95%	1.4	0.15	0.14
F54089-DY8			0.026	0.10	2.0		0.52		0.052
F54087-DY8			0.029	0.10	2.0		0.59		0.059
F54080-DY8			0.029	0.10	2.0		0.59		0.059
F54092-DY8			0.036	0.10	2.0		0.73		0.073
F54109-DY8			0.028	0.10	2.0		0.56		0.056
F54114-DY8			0.035	0.10	2.0		0.69		0.069
F54088-15			0.010	0.10	2.0		0.21		0.021
F54099-15			0.026	0.10	2.0		0.52		0.052
F54089-15			0.022	0.10	2.0		0.43		0.043
F54087-15			0.021	0.10	2.0		0.43		0.043
F54080-15			0.019	0.10	2.0		0.39		0.039
F54092-15			0.022	0.10	2.0		0.44		0.044
F54109-15			0.025	0.10	2.0		0.50		0.050
F54114-15			0.020	0.10	2.0		0.40		0.040
F54089-D22			0.019	0.10	2.0		0.39		0.039
F54087-D22			0.018	0.10	2.0		0.36		0.036
F54109-D22			0.019	0.10	2.0		0.37		0.037
F54114-D22			0.019	0.10	2.0		0.39		0.039
F54089-d28			0.018	0.10	2.0		0.36		0.036
F54087-d28			0.018	0.10	2.0		0.35		0.035

000209

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384	mL of FC95 solution spiked	Conc. FC95 solution (ppm)	Actual Meter reading (ppm F-)	Quantity sample (mL or grams)	DI: TISAB final vol (mL)	% rcvry (ug/ug)	Actual ppm F- in sample	Mass spiked (ug F-)	Mass rcvrd (ug F-)
ID									
F54109-d28			0.020	0.10	2.0		0.41		0.041
F54114-d28			0.017	0.10	2.0		0.33		0.033
SERUM SPIKE 63-4	0.004	63	0.031	0.10	2.0	41%	0.62	0.15	0.062
SERUM SPIKE 63-5	0.004	63	0.049	0.10	2.0	65%	0.98	0.15	0.10
SERUM SPIKE 63-6	0.004	63	0.061	0.10	2.0	81%	1.2	0.15	0.12
SERUM SPIKE 63-7	0.004	63	0.059	0.10	2.0	78%	1.2	0.15	0.12
SERUM BLK 1			0.031	0.10	2.0		0.62		0.062
SERUM BLK 2			0.017	0.10	2.0		0.34		0.034
SERUM SPK 63-1	0.004	63	0.061	0.10	2.0	81%	1.2	0.15	0.12
SERUM SPK 63-2	0.004	63	0.078	0.10	2.0	103%	1.6	0.15	0.16
SERUM SPK 63-3	0.004	63	0.062	0.10	2.0	82%	1.2	0.15	0.12
F54105-48			0.021	0.10	2.0		0.42		0.042
F54075-48			0.026	0.10	2.0		0.52		0.052

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000130

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384	mL of FC95 solution spiked	Conc. FC95 solution (ppm)	Actual Meter reading (ppm F-)	Quantity sample (mL or grams)	DI: TISAB final vol (mL)	% rcvry (ug/ug)	Actual ppm F- in sample	Mass spiked (ug F-)	Mass rcvrd (ug F-)
ID									
serum blank-1			0.036	0.10	2.0		ND		
serum blank-2			0.020	0.10	2.0		ND		
serum spike 63-1	0.004	63	0.070	0.10	2.0	93%	1.4	0.15	0.14
serum spike 63-2	0.004	63	0.070	0.10	2.0	92%	1.4	0.15	0.14
serum spike 94.5-1	0.004	94.5	0.063	0.10	2.0	56%	1.3	0.23	0.13
serum spike 94.5-2	0.004	94.5	0.046	0.10	2.0	41%	0.92	0.23	0.092
serum spike 126-1	0.004	126	0.15	0.10	2.0	101%	3.1	0.30	0.31
serum spike 126-2	0.004	126	0.099	0.10	2.0	65%	2.0	0.30	0.20
serum spike 126-3	0.004	126	0.15	0.10	2.0	98%	3.0	0.30	0.30
serum spike 126-4	0.004	126	0.13	0.10	2.0	85%	2.6	0.30	0.26
F54081-4			0.040	0.10	2.0		ND		ND
F54075-4			0.032	0.10	2.0		ND		ND
F54107-4			0.024	0.10	2.0		ND		ND
F54105-4			0.025	0.10	2.0		ND		ND
F54074-4			0.034	0.10	2.0		ND		ND
Blank 1			0.71	0.10	2.0		14		1.4
Blank 2			0.34	0.10	2.0		6.9		0.69
Blank 3			0.36	0.10	2.0		7.2		0.72
Blank 4			0.084	0.10	2.0		1.7		0.17
Blank 5			0.038	0.10	2.0		ND		ND
Blank 6			0.039	0.10	2.0		ND		ND
Serum Spk-1	0.004	63	0.055	0.10	2.0	73%	1.1	0.15	0.11
Serum Spk-2	0.004	63	0.068	0.10	2.0	90%	1.4	0.15	0.14
Serum Spk-3	0.004	63	0.073	0.10	2.0	96%	1.5	0.15	0.15
Serum Spk-4	0.004	126	0.10	0.10	2.0	67%	2.0	0.30	0.20
Serum Spk-5	0.004	126	0.11	0.10	2.0	74%	2.2	0.30	0.22
Serum Spk-6	0.004	126	0.11	0.10	2.0	73%	2.2	0.30	0.22
Serum Spk-7	0.004	126	0.11	0.10	2.0	72%	2.2	0.30	0.22
Serum Spk-8	0.004	126	0.098	0.10	2.0	65%	2.0	0.30	0.20
Serum Spk-9	0.004	126	0.12	0.10	2.0	77%	2.3	0.30	0.23
Serum Spk-10	0.004	126	0.10	0.10	2.0	68%	2.1	0.30	0.21
F54085-4			0.045	0.10	2.0		ND		ND
F54086-4			0.027	0.10	2.0		ND		ND
F54104-4			0.025	0.10	2.0		ND		ND
F54077-4			0.021	0.10	2.0		ND		ND
F54083-4			0.020	0.10	2.0		ND		ND
F54094-4			0.021	0.10	2.0		ND		ND
F54100-4			0.020	0.10	2.0		ND		ND
F54091-4			0.019	0.10	2.0		ND		ND
serum blk 1			0.029	0.10	2.0		ND		ND
serum blk 2			0.024	0.10	2.0		ND		ND
serum spk 1	0.004	63	0.071	0.10	2.0	94%	1.4	0.15	0.14
serum spk 2	0.004	63	0.072	0.10	2.0	95%	1.4	0.15	0.14
F54097-4			0.022	0.10	2.0		ND		ND
F54102-4			0.020	0.10	2.0		ND		ND
F54108-4			0.016	0.10	2.0		ND		ND
F54071-4			0.017	0.10	2.0		ND		ND

000211

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384 ID	mL of FC95 solution spiked	Conc. FC95 solution (ppm)	Actual Meter reading (ppm F-)	Quantity sample (mL or grams)	DI: TISAB final vol (mL)	% rcvry (ug/ug)	Actual ppm F- in sample	Mass spiked (ug F-)	Mass rcvrd (ug F-)
F54093-4			0.020	0.10	2.0		ND		ND
F54095-4			0.016	0.10	2.0		ND		ND
F54101-4			0.015	0.10	2.0		ND		ND
F54078-4			0.021	0.10	2.0		ND		ND
F54090-4			0.020	0.10	2.0		ND		ND
F54096-4			0.017	0.10	2.0		ND		ND
F54110-4			0.020	0.10	2.0		ND		ND
F54087-4			0.025	0.10	2.0		ND		ND
F54088-4			0.028	0.10	2.0		ND		ND
F54089-4			0.020	0.10	2.0		ND		ND
F54106-4			0.032	0.10	2.0		ND		ND
F54080-4			0.025	0.10	2.0		ND		ND
F54092-4			0.019	0.10	2.0		ND		ND
F54109-4			0.021	0.10	2.0		ND		ND
F54114-4			0.039	0.10	2.0		ND		ND
F54076-4			0.041	0.10	2.0		ND		ND
F54082-4			0.057	0.10	2.0		1.1		0.11
F54111-4			0.096	0.10	2.0		1.9		0.19
F54113-4			0.082	0.10	2.0		1.6		0.16
F54079-4			0.12	0.10	2.0		2.3		0.23
F54084-4			0.067	0.10	2.0		1.3		0.13
F54098-4			0.046	0.10	2.0		ND		ND
F54116-4			0.10	0.10	2.0		2.0		0.20
F54075-8			0.025	0.10	2.0		ND		ND
F54081-8			0.020	0.10	2.0		ND		ND
F54105-8			0.021	0.10	2.0		ND		ND
F54107-8			0.015	0.10	2.0		ND		ND
F54074-8			0.015	0.10	2.0		ND		ND
F54085-8			0.021	0.10	2.0		ND		ND
F54086-8			0.031	0.10	2.0		ND		ND
serum blk 1			0.029	0.10	2.0		ND		ND
serum blk 2			0.028	0.10	2.0		ND		ND
serum spk 1	0.004	63	0.080	0.10	2.0	106%	1.6	0.15	0.16
serum spk 2	0.004	63	0.069	0.10	2.0	91%	1.4	0.15	0.14
F54104-8			0.031	0.10	2.0		ND		ND
F54077-8			0.023	0.10	2.0		ND		ND
F54083-8			0.018	0.10	2.0		ND		ND
F54094-8			0.025	0.10	2.0		ND		ND
F54100-8			0.017	0.10	2.0		ND		ND
F54091-8			0.014	0.10	2.0		ND		ND
F54097- 8			0.014	0.10	2.0		ND		ND
F54102- 8			0.013	0.10	2.0		ND		ND
F54108- 8			0.013	0.10	2.0		ND		ND
F54071- 8			0.015	0.10	2.0		ND		ND
F54093 - 8			0.019	0.10	2.0		ND		ND
F54095 - 8			0.026	0.10	2.0		ND		ND
F54101- 8			0.016	0.10	2.0		ND		ND
F54078- 8			0.021	0.10	2.0		ND		ND

000212

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384 ID	mL of FC95 solution spiked	Conc. FC95 solution (ppm)	Actual Meter reading (ppm F-)	Quantity sample (mL or grams)	DI: TISAB final vol (mL)	% rcvry (ug/ug)	Actual ppm F- in sample	Mass spiked (ug F-)	Mass rcvrd (ug F-)
F54090- 8			0.021	0.10	2.0		ND		ND
F54096- 8			0.017	0.10	2.0		ND		ND
F54110- 8			0.075	0.10	2.0		1.5		0.15
F54087- 8			0.022	0.10	2.0		ND		ND
F54088- 8			0.033	0.10	2.0		ND		ND
F54089- 8			0.031	0.10	2.0		ND		ND
F54080- 8			0.032	0.10	2.0		ND		ND
F54106- 8			0.043	0.10	2.0		ND		ND
F54092- 8			0.037	0.10	2.0		ND		ND
F54109- 8			0.024	0.10	2.0		ND		ND
F54114- 8			0.034	0.10	2.0		ND		ND
F54076- 8			0.045	0.10	2.0		ND		ND
F54082- 8			0.063	0.10	2.0		1.3		0.13
F54111- 8			0.044	0.10	2.0		ND		ND
F54113- 8			0.048	0.10	2.0		ND		ND
F54079- 8			0.042	0.10	2.0		ND		ND
F54084- 8			0.045	0.10	2.0		ND		ND
F54098- 8			0.050	0.10	2.0		1.0		0.10
F54116- 8			0.17	0.10	2.0		3.4		0.34
serum blk 1			0.012	0.10	2.0		ND		ND
serum blk 2			0.018	0.10	2.0		ND		ND
serum spk 1	0.004	63	0.066	0.10	2.0	87%	1.3	0.15	0.13
serum spk 2	0.004	63	0.070	0.10	2.0	93%	1.4	0.15	0.14
F54075-12			0.028	0.10	2.0		ND		ND
F54081-12			0.021	0.10	2.0		ND		ND
F54105-12			0.026	0.10	2.0		ND		ND
F54107-12			0.019	0.10	2.0		ND		ND
F54074-12			0.017	0.10	2.0		ND		ND
F54085-12			0.018	0.10	2.0		ND		ND
F54086-12			0.020	0.10	2.0		ND		ND
F54086-12			0.025	0.10	2.0		ND		ND
F54077-12			0.038	0.10	2.0		ND		ND
F54083-12			0.032	0.10	2.0		ND		ND
F54094-12			0.035	0.10	2.0		ND		ND
F54100-12			0.022	0.10	2.0		ND		ND
F54091-12			0.029	0.10	2.0		ND		ND
F54097-12			0.025	0.10	2.0		ND		ND
F54102-12			0.022	0.10	2.0		ND		ND
F54108-12			0.014	0.10	2.0		ND		ND
F54077-12			0.046	0.10	2.0		ND		ND
F54071-12			0.021	0.10	2.0		ND		ND
F54093-12			0.016	0.10	2.0		ND		ND
F54095-12			0.016	0.10	2.0		ND		ND
F54101-12			0.020	0.10	2.0		ND		ND
F54110-12			0.016	0.10	2.0		ND		ND
F54096-12			0.012	0.10	2.0		ND		ND
F54090-12			0.017	0.10	2.0		ND		ND
F54078-12			0.014	0.10	2.0		ND		ND

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384	mL of FC95 solution spiked	Conc. FC95 solution (ppm)	Actual Meter reading (ppm F-)	Quantity sample (mL or grams)	DI: TISAB final vol (mL)	% rcvry (ug/ug)	Actual ppm F- in sample	Mass spiked (ug F-)	Mass rcvrd (ug F-)
F54088-12			0.025	0.10	2.0		ND		ND
F54106-12			0.027	0.10	2.0		ND		ND
F54089-12			0.019	0.10	2.0		ND		ND
F54087-12			0.019	0.10	2.0		ND		ND
F54080-12			0.018	0.10	2.0		ND		ND
F54092-12			0.017	0.10	2.0		ND		ND
F54109-12			0.021	0.10	2.0		ND		ND
F54114-12			0.026	0.10	2.0		ND		ND
F54076-12			0.027	0.10	2.0		ND		ND
F54113-12			0.022	0.10	2.0		ND		ND
F54082-12			0.034	0.10	2.0		ND		ND
F54111-12			0.046	0.10	2.0		ND		ND
F54098-12			0.042	0.10	2.0		ND		ND
F54084-12			0.044	0.10	2.0		ND		ND
F54079-12			0.043	0.10	2.0		ND		ND
F54116-12			0.047	0.10	2.0		ND		ND
Serum Blk-1			0.033	0.10	2.0		ND		ND
Serum Blk-2			0.030	0.10	2.0		ND		ND
Serum Spk-1	0.004	63	0.034	0.10	2.0	44%	0.67	0.15	0.067
Serum Spk-2	0.004	63	0.040	0.10	2.0	52%	0.79	0.15	0.079
Serum Spk-3	0.004	63	0.050	0.10	2.0	66%	0.99	0.15	0.10
Serum Spk-4	0.004	63	0.054	0.10	2.0	72%	1.1	0.15	0.11
Serum Spk-5	0.004	63	0.083	0.10	2.0	110%	1.7	0.15	0.17
Serum Spk-6	0.004	63	0.053	0.10	2.0	71%	1.1	0.15	0.11
Serum Spk-7	0.004	63	0.049	0.10	2.0	65%	0.99	0.15	0.10
Serum Spk-8	0.004	63	0.055	0.10	2.0	73%	1.1	0.15	0.11
F54105-24			0.041	0.10	2.0		ND		ND
F54075-24			0.022	0.10	2.0		ND		ND
F54081-24			0.017	0.10	2.0		ND		ND
F54107-24			0.015	0.10	2.0		ND		ND
F54104-24			0.018	0.10	2.0		ND		ND
F54086-24			0.016	0.10	2.0		ND		ND
F54074-24			0.013	0.10	2.0		ND		ND
Blank 1			0.031	0.10	2.0		ND		ND
Blank 2			0.022	0.10	2.0		ND		ND
spike 1	0.004	63	0.033	0.10	2.0	43%	0.65	0.15	0.065
spike 2	0.004	63	0.044	0.10	2.0	58%	0.88	0.15	0.088
spike 3	0.004	63	0.047	0.10	2.0	63%	0.95	0.15	0.095
spike 4	0.004	63	0.047	0.10	2.0	62%	0.94	0.15	0.094
spike 5	0.004	63	0.052	0.10	2.0	68%	1.0	0.15	0.10
spike 6	0.004	63	0.051	0.10	2.0	67%	1.0	0.15	0.10
Blank 3			0.036	0.10	2.0		ND		ND
Blank 4			0.020	0.10	2.0		ND		ND
F54085-24			0.021	0.10	2.0		ND		ND
F54083-24			0.019	0.10	2.0		ND		ND
F54100-24			0.016	0.10	2.0		ND		ND
F54077-24			0.017	0.10	2.0		ND		ND
F54094-24			0.015	0.10	2.0		ND		ND
F54091-24			0.016	0.10	2.0		ND		ND

000134

000214

384 ID	mL of FC95 solution spiked	Conc. FC95 solution (ppm)	Actual Meter reading (ppm F-)	Quantity sample (mL or grams)	DI: TISAB final vol (mL)	% rcvry (ug/ug)	Actual ppm F- in sample	Mass spiked (ug F-)	Mass rcvrd (ug F-)
F54108-24			0.014	0.10	2.0		ND		ND
F54102-24			0.013	0.10	2.0		ND		ND
F54097-24			0.020	0.10	2.0		ND		ND
F54071-24			0.015	0.10	2.0		ND		ND
F54093-24			0.014	0.10	2.0		ND		ND
F54095-24			0.013	0.10	2.0		ND		ND
F54101-24			0.012	0.10	2.0		ND		ND
F54110-24			0.011	0.10	2.0		ND		ND
F54096-24			0.013	0.10	2.0		ND		ND
F54090-24			0.025	0.10	2.0		ND		ND
F54078-24			0.013	0.10	2.0		ND		ND
F54088-24			0.014	0.10	2.0		ND		ND
F54106-24			0.013	0.10	2.0		ND		ND
F54089-24			0.014	0.10	2.0		ND		ND
F54087-24			0.014	0.10	2.0		ND		ND
F54080-24			0.016	0.10	2.0		ND		ND
F54092-24			0.016	0.10	2.0		ND		ND
F54109-24			0.015	0.10	2.0		ND		ND
F54114-24			0.016	0.10	2.0		ND		ND
serum blk 1			0.039	0.10	2.0		ND		ND
serum blk 2			0.028	0.10	2.0		ND		ND
serum spk 1	0.004	63	0.071	0.10	2.0	94%	1.4	0.15	0.14
serum spk 2	0.004	63	0.082	0.10	2.0	109%	1.6	0.15	0.16
F54113-24			0.064	0.10	2.0		1.3		0.13
F54082-24			0.055	0.10	2.0		1.1		0.11
F54111-24			0.063	0.10	2.0		1.3		0.13
F54098-24			0.064	0.10	2.0		1.3		0.13
F54084-24			0.061	0.10	2.0		1.2		0.12
F54079-24			0.059	0.10	2.0		1.2		0.12
F54116-24			0.064	0.10	2.0		1.3		0.13
F54113-48			0.068	0.10	2.0		1.4		0.14
F54082-48			0.066	0.10	2.0		1.3		0.13
F54111-48			0.073	0.10	2.0		1.5		0.15
F54098-48			0.067	0.10	2.0		1.3		0.13
F54084-48			0.091	0.10	2.0		1.8		0.18
F54079-48			0.059	0.10	2.0		1.2		0.12
F54116-48			0.085	0.10	2.0		1.7		0.17
F54113-192			0.080	0.10	2.0		1.6		0.16
F54082-192			0.073	0.10	2.0		1.5		0.15
F54111-192			0.063	0.10	2.0		1.3		0.13
F54098-192			0.067	0.10	2.0		1.3		0.13
F54079-192			0.068	0.10	2.0		1.4		0.14
F54084-192			0.077	0.10	2.0		1.5		0.15
F54116-192			0.065	0.10	2.0		1.3		0.13
F54113-360			0.065	0.10	2.0		1.3		0.13
F54082-360			0.043	0.10	2.0		ND		0.087
F54111-360			0.063	0.10	2.0		1.3		0.13
F54098-360			0.054	0.10	2.0		1.1		0.11
F54079-360			0.063	0.10	2.0		1.3		0.13

000215

000125

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384 ID	mL of FC95 solution spiked	Conc. FC95 solution (ppm)	Actual Meter reading (ppm F-)	Quantity sample (mL or grams)	DI: TISAB final vol. (mL)	% rcvry (ug/ug)	Actual ppm F- in sample	Mass spiked (ug F-)	Mass rcvrd (ug F-)
F54084-360			0.069	0.10	2.0		1.4		0.14
F54116-360			0.069	0.10	2.0		1.4		0.14
Serum Blk 1			0.025	0.10	2.0		ND		ND
Serum Blk 2			0.032	0.10	2.0		ND		ND
Serum Spk 1	0.004	63	0.069	0.10	2.0	91%	1.4	0.15	0.14
Serum Spk 2	0.004	63	0.076	0.10	2.0	101%	1.5	0.15	0.15
F54082-D22			0.046	0.10	2.0		ND		ND
F54111-D22			0.041	0.10	2.0		ND		ND
F54079-D22			0.040	0.10	2.0		ND		ND
F54116-D22			0.045	0.10	2.0		ND		ND
F54082-D28			0.048	0.10	2.0		ND		ND
F54111-D28			0.036	0.10	2.0		ND		ND
F54079-D28			0.033	0.10	2.0		ND		ND
F54116-D28			0.036	0.10	2.0		ND		ND
F54099-4			0.028	0.10	2.0		ND		ND
F54099-8			0.026	0.10	2.0		ND		ND
F54099-12			0.074	0.10	2.0		1.5		0.15
F54099-24			0.087	0.10	2.0		1.7		0.17
F54099-48			0.047	0.10	2.0		ND		ND
F54099-192			0.033	0.10	2.0		ND		ND
F54099-360			0.029	0.10	2.0		ND		ND
F54112-4			0.038	0.10	2.0		ND		ND
F54112-8			0.059	0.10	2.0		1.2		0.12
F54112-12			0.066	0.10	2.0		1.3		0.13
F54112-24			0.051	0.10	2.0		1.0		0.10
F54112-48			0.066	0.10	2.0		1.3		0.13
F54112-192			0.059	0.10	2.0		1.2		0.12
F54112-360			0.041	0.10	2.0		ND		ND
SERUM SPIKE-63-1	0.004	63	0.059	0.10	2.0	78%	1.2	0.15	0.12
SERUM SPIKE-63-2	0.004	63	0.079	0.10	2.0	105%	1.6	0.15	0.16
SERUM SPIKE-63-3	0.004	63	0.074	0.10	2.0	97%	1.5	0.15	0.15
SERUM SPIKE-126-1	0.004	126	0.083	0.10	2.0	55%	1.7	0.30	0.17
SERUM SPIKE-126-2	0.004	126	0.12	0.10	2.0	77%	2.3	0.30	0.23
SERUM SPIKE-126-3	0.004	126	0.12	0.10	2.0	79%	2.4	0.30	0.24
serum blank-1			0.10	0.10	2.0		2.0		0.20
serum blank-2			0.040	0.10	2.0		ND		ND
serum blank-3			0.019	0.10	2.0		ND		ND
spike 63-1	0.004	63	0.058	0.10	2.0	77%	1.2	0.15	0.12
spike 63-2	0.004	63	0.058	0.10	2.0	77%	1.2	0.15	0.12
spike 63-3	0.004	63	0.092	0.10	2.0	121%	1.8	0.15	0.18
spike 63-4	0.004	63	0.053	0.10	2.0	70%	1.1	0.15	0.11
spike 63-5	0.004	63	0.055	0.10	2.0	73%	1.1	0.15	0.11
spike 63-6	0.004	63	0.058	0.10	2.0	77%	1.2	0.15	0.12
spike 63-7	0.004	63	0.072	0.10	2.0	95%	1.4	0.15	0.14
spike 63-8	0.004	63	0.060	0.10	2.0	79%	1.2	0.15	0.12
Serum blk 1			0.045	0.10	2.0		ND		ND
Serum blk 2			0.017	0.10	2.0		ND		ND
Serum spike 63-1	0.004	63	0.12	0.10	2.0	153%	2.3	0.15	0.23
Serum spike 63-2	0.004	63	0.21	0.10	2.0	273%	4.1	0.15	0.41

000216

000135

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384 ID	mL of FC95 solution spiked	Conc. FC95 solution (ppm)	Actual Meter reading (ppm F-)	Quantity sample (mL or grams)	DI: TISAB final vol (mL)	% rcvry (ug/ug)	Actual ppm F- in sample	Mass spiked (ug F-)	Mass rcvrd (ug F-)
Serum blank 1			0.031	0.10	2.0		ND		ND
Serum blank 2			0.021	0.10	2.0		ND		ND
Serum spike 1	0.004	63	0.074	0.10	2.0	98%	1.5	0.15	0.15
Serum spike 2	0.004	63	0.066	0.10	2.0	87%	1.3	0.15	0.13
Serum spike 3	0.004	63	0.065	0.10	2.0	86%	1.3	0.15	0.13
Serum spike 4	0.004	63	0.060	0.10	2.0	80%	1.2	0.15	0.12
Serum spike 5	0.004	63	0.070	0.10	2.0	93%	1.4	0.15	0.14
Serum spike 6	0.004	63	0.069	0.10	2.0	91%	1.4	0.15	0.14
Serum spike 7	0.004	63	0.068	0.10	2.0	90%	1.4	0.15	0.14
Serum blank 3			0.023	0.10	2.0		ND		ND
Serum blank 4			0.020	0.10	2.0		ND		ND
F54088-48			0.019	0.10	2.0		ND		ND
F54099-48			0.021	0.10	2.0		ND		ND
F54089-48			0.017	0.10	2.0		ND		ND
F54087-48			0.020	0.10	2.0		ND		ND
F54080-48			0.017	0.10	2.0		ND		ND
F54092-48			0.016	0.10	2.0		ND		ND
F54109-48			0.022	0.10	2.0		ND		ND
F54114-48			0.022	0.10	2.0		ND		ND
F54088 dy8			0.018	0.10	2.0		ND		ND
F54099 dy8			0.014	0.10	2.0		ND		ND
serum spike 8	0.004	63	0.059	0.10	2.0	78%	1.2	0.15	0.12
serum spike 9	0.004	63	0.060	0.10	2.0	79%	1.2	0.15	0.12
serum spike 10	0.004	63	0.060	0.10	2.0	79%	1.2	0.15	0.12
SERUM BLK 1			0.031	0.10	2.0		ND		ND
SERUM BLK 2			0.016	0.10	2.0		ND		ND
SERUM SPK 1	0.004	63	0.056	0.10	2.0	74%	1.1	0.15	0.11
SERUM SPK 2	0.004	63	0.069	0.10	2.0	91%	1.4	0.15	0.14
SERUM SPK 3	0.004	63	0.072	0.10	2.0	95%	1.4	0.15	0.14
F54089-DY8			0.026	0.10	2.0		ND		ND
F54087-DY8			0.029	0.10	2.0		ND		ND
F54080-DY8			0.029	0.10	2.0		ND		ND
F54092-DY8			0.036	0.10	2.0		ND		ND
F54109-DY8			0.028	0.10	2.0		ND		ND
F54114-DY8			0.035	0.10	2.0		ND		ND
F54088-15			0.010	0.10	2.0		ND		ND
F54099-15			0.026	0.10	2.0		ND		ND
F54089-15			0.022	0.10	2.0		ND		ND
F54087-15			0.021	0.10	2.0		ND		ND
F54080-15			0.019	0.10	2.0		ND		ND
F54092-15			0.022	0.10	2.0		ND		ND
F54109-15			0.025	0.10	2.0		ND		ND
F54114-15			0.020	0.10	2.0		ND		ND
F54089-D22			0.019	0.10	2.0		ND		ND
F54087-D22			0.018	0.10	2.0		ND		ND
F54109-D22			0.019	0.10	2.0		ND		ND
F54114-D22			0.019	0.10	2.0		ND		ND
F54089-d28			0.018	0.10	2.0		ND		ND
F54087-d28			0.018	0.10	2.0		ND		ND

000217

000137

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384 ID	mL of FC95 solution spiked	Conc. FC95 solution (ppm)	Actual Meter reading (ppm F-)	Quantity sample (mL or grams)	DI: TISAB final vol (mL)	% rcvry (ug/ug)	Actual ppm F- in sample	Mass spiked (ug F-)	Mass rcvrd (ug F-)
F54109-d28			0.020	0.10	2.0		ND		ND
F54114-d28			0.017	0.10	2.0		ND		ND
SERUM SPIKE 63-4	0.004	63	0.031	0.10	2.0	41%	0.62	0.15	0.062
SERUM SPIKE 63-5	0.004	63	0.049	0.10	2.0	65%	0.98	0.15	0.10
SERUM SPIKE 63-6	0.004	63	0.061	0.10	2.0	81%	1.2	0.15	0.12
SERUM SPIKE 63-7	0.004	63	0.059	0.10	2.0	78%	1.2	0.15	0.12
SERUM BLK 1			0.031	0.10	2.0		ND		ND
SERUM BLK 2			0.017	0.10	2.0		ND		ND
SERUM SPK 63-1	0.004	63	0.061	0.10	2.0	81%	1.2	0.15	0.12
SERUM SPK 63-2	0.004	63	0.078	0.10	2.0	103%	1.6	0.15	0.16
SERUM SPK 63-3	0.004	63	0.062	0.10	2.0	82%	1.2	0.15	0.12
F54105-48			0.021	0.10	2.0		ND		ND
F54075-48			0.026	0.10	2.0		ND		ND

000218

000138

18

HWI 6329-159, AMDT 042095.1

ppm F- in serum

Control	4 hour	8 hour	12 hour	24 hour
F54074	0.670	0.304	0.346	0.268
F54075	0.645	0.490	0.558	0.440
F54081	0.800	0.398	0.416	0.346
F54085	0.898	0.428	0.366	0.412
F54086	0.542	0.616	0.408	0.328
F54104	0.492	0.616	0.502	0.366
F54105	0.509	0.426	0.528	0.812
F54107	0.484	0.304	0.388	0.304

Summary of Orion serum analysis without entering "ND". This summary is used to determine the relative half life, therefore it is appropriate to use values which are less than the detection limit.

5 mg/kg	4 hour	8 hour	12 hour	24 hour
F54077	0.416	0.458	0.839	0.330
F54083	0.400	0.352	0.636	0.380
F54091	0.384	0.282	0.576	0.314
F54094	0.418	0.506	0.708	0.308
F54097	0.446	0.278	0.492	0.400
F54100	0.408	0.346	0.442	0.324
F54102	0.406	0.258	0.436	0.250
F54108	0.318	0.254	0.288	0.278

10 mg/kg	4 hour	8 hour	12 hour	24 hour
F54071	0.336	0.302	0.412	0.302
F54093	0.408	0.374	0.328	0.274
F54095	0.316	0.514	0.320	0.256
F54101	0.290	0.322	0.404	0.240
F54078	0.412	0.424	0.284	0.266
F54090	0.390	0.424	0.342	0.500
F54096	0.336	0.342	0.246	0.264
F54110	0.392	1.500	0.312	0.226

100 mg/kg	4 hour	8 hour	12 hour	24 hour	48 hour	192 hour	360 hour	528 hour	672 hour
F54080	0.508	0.638	0.358	0.320					
F54087	0.496	0.438	0.372	0.270	0.398	0.588	0.426	0.362	0.350
F54088	0.552	0.662	0.508	0.274	0.336	0.524	0.434	0.390	0.360
F54089	0.406	0.624	0.380	0.278					
F54092	0.376	0.740	0.332	0.322					
F54099	0.552	0.514	1.478	1.748	0.948	0.666	0.572		
F54106	0.630	0.860	0.536	0.256					
F54109	0.418	0.488	0.410	0.306	0.446	0.564	0.500	0.374	0.406
F54114	0.776	0.676	0.524	0.322	0.438	0.694	0.400	0.390	0.330

500 mg/kg	4 hour	8 hour	12 hour	24 hour	48 hour	192 hour	360 hour	528 hour	672 hour
F54076	0.810	0.890	0.546						
F54079	2.320	0.838	0.852	1.170	1.184	1.364	1.266	0.808	0.660
F54082	1.130	1.254	0.686	1.104	1.318	1.458	0.866	0.912	0.964
F54084	1.344	0.890	0.870	1.222	1.824	1.546	1.370		
F54098	0.926	1.000	0.836	1.276	1.332	1.344	1.078		
F54111	1.914	0.878	0.912	1.252	1.452	1.256	1.252	0.822	0.710
F54112	0.758	1.184	1.310	1.022	1.314	1.184	0.822		
F54113	1.638	0.954	0.436	1.276	1.364	1.596	1.292		
F54116	2.040	3.440	0.940	1.286	1.706	1.292	1.380	0.890	0.728

00013

000219

11-30-88

11-88-11
AM

ppm F- in Serum (Group 4)

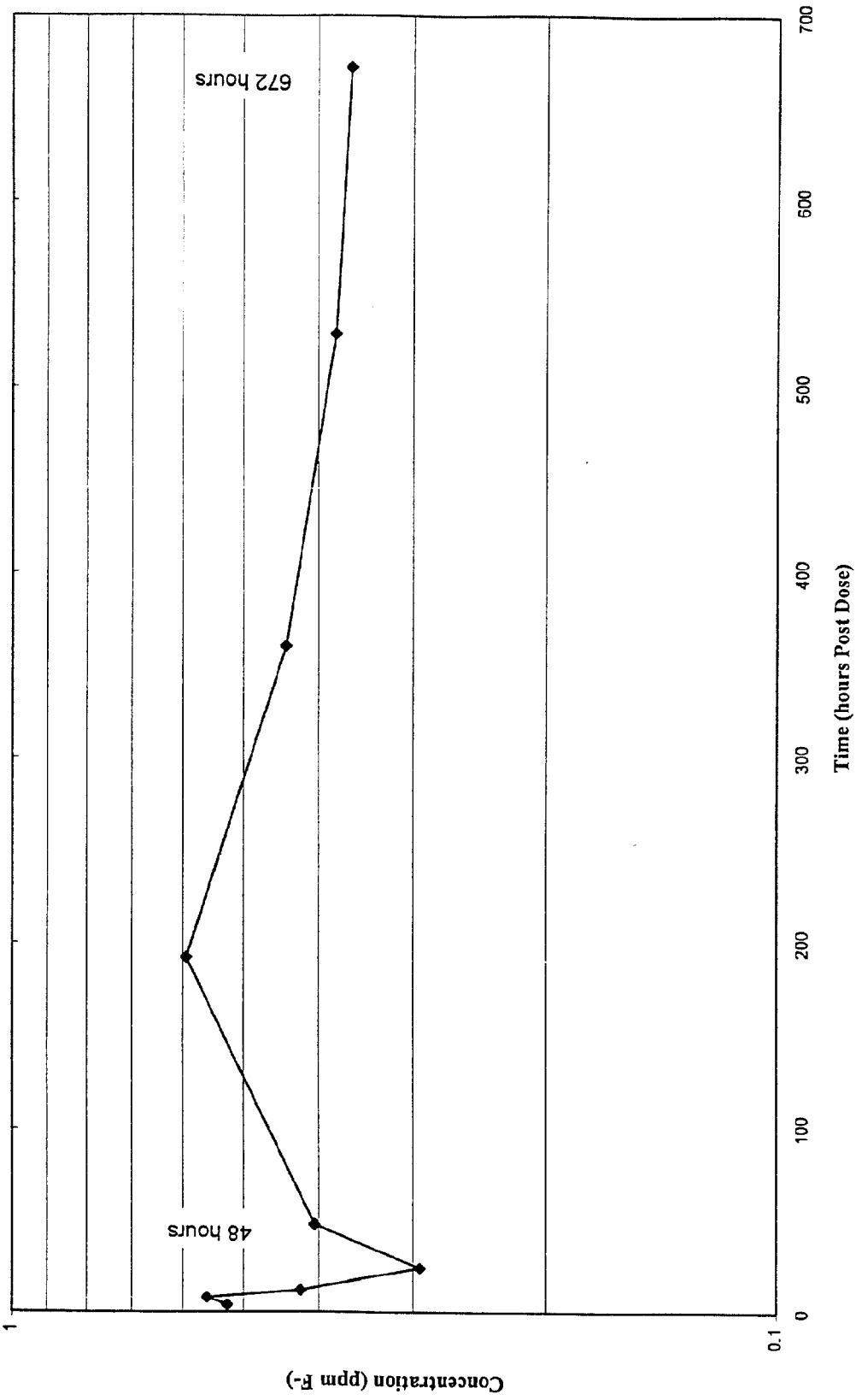


Figure 2

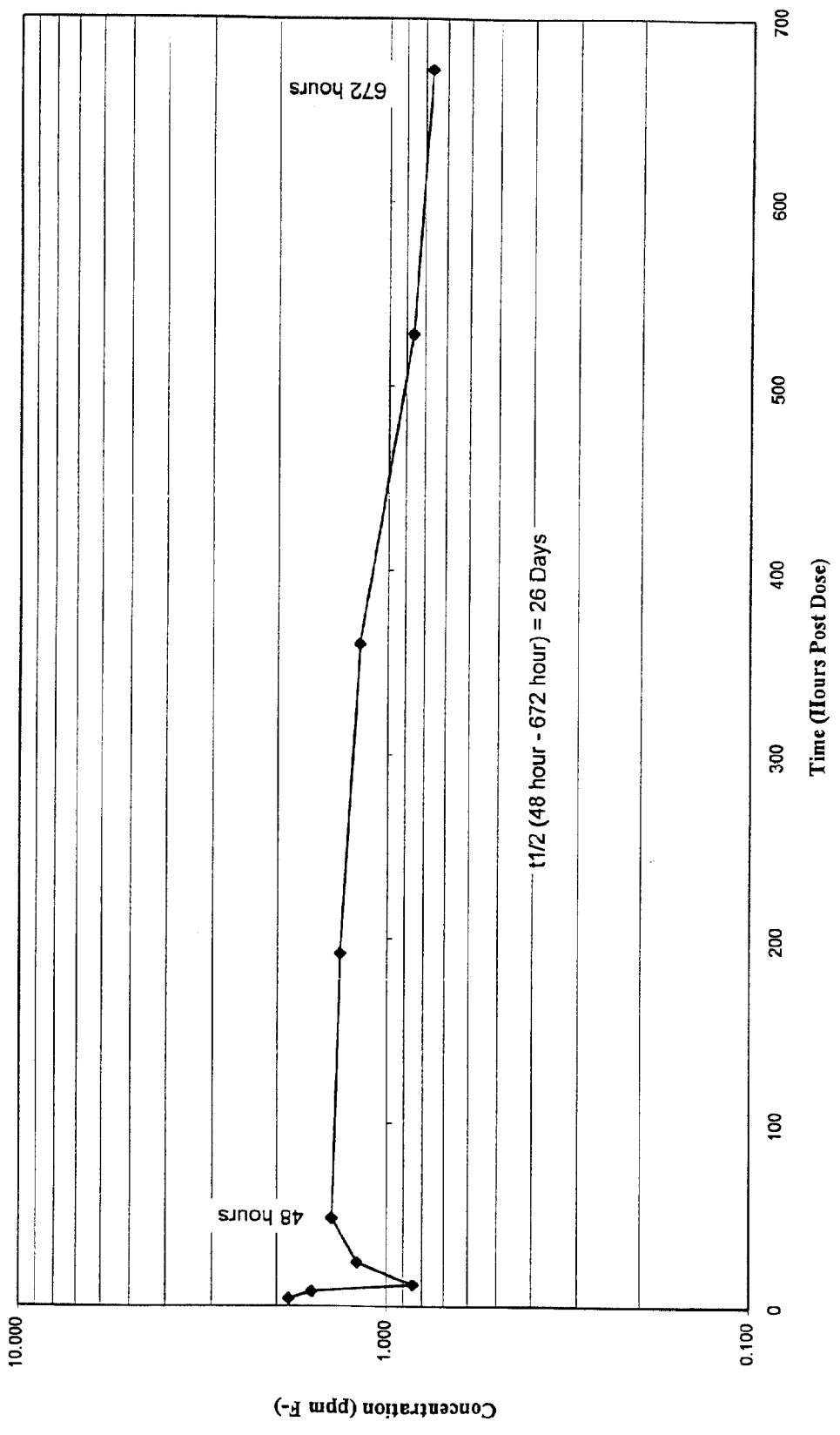
11-28-88
Dy

3MA01502308

2807.0141

Figure 1

ppm F- in serum (Group 5)



000221

000141

9.11.4 Summary and raw data; ppm F⁻ in serum as determined by thermal extraction followed by analysis using Skalar segmented flow analyzer with ion selective electrode.

000222

000142

RE: 6329-159 SERUM SAMPLES

AMDT 42095.1

Date of Analysis: May 4, 8, 9, 11, 24 and May 25, 1995

Analyst: DDW

The samples are burned in the Dohrman at 950 C using 0.10 mL of the serum. The gas is collected in 2.0 mL of 1:1 TISAB/Milli-Q water. The samples are then analyzed on a Skalar Segmented Flow Analyzer using the Ion Specific Electrode (ISE) Method.

TISAB buffer is added to each sample as it proceeds through the system. The sample then goes through a heated mixing coil before the potential between the ion selective electrode and the reference electrode is measured. The signal is amplified and related to the fluoride concentration.

The instrument was calibrated in the ranges of 0.015 - 0.15 ppm and 0.15 - 1.50 ppm fluoride. The standard curve for the high range was plotted using the inverse logarithm option. The standard curve for the low range is linear. All standards and samples were then calculated by the Skalar software using these curves. All results below 0.0001 ppm appear on the raw data as #.####.

A quality control standard was analyzed every 10 samples to check for accuracy and drift.

Raw data is taken from the appropriate calibrated range of the Skalar printout and summarized on an Excel spreadsheet. The final results are adjusted for the collection volume and any subsequent dilutions.



000143

000223

Proc. 1 of 91

SUMMARY of 6329-159
SERUM SAMPLES
AMDT 42095.1

	Sample ID	Fluoride	Fluoride	Fluoride	Fluoride	Fluoride	Fluoride	Fluoride	Fluoride	Fluoride
		In Sample (ppm) 4 hr	In Sample (ppm) 8 hr	In Sample (ppm) 12 hr	In Sample (ppm) 24 hr	In Sample (ppm) 48 hr	In Sample (ppm) 192 hr	In Sample (ppm) 360 hr	In Sample (ppm) 528 hr	In Sample (ppm) 672 hr
GROUP 1 Dose Level : 0	F54074	0.51	0.35	0.42	0.70					
	F54075	0.61	0.64	0.63	0.47	0.52				
	F54080	0.84	0.40	0.43	0.40					
	F54085	0.98	0.62	0.29	0.00					
	F54085				0.31					
	F54086			0.70	0.35					
	F54104	0.58	0.73	0.81	0.47					
	F54105	0.34	0.55	0.60	1.08	0.36				
	F54107	0.46	0.31	0.40	0.31					
GROUP 2 Dose Level : 5 mg/kg	F54077	0.53	0.58	1.22	0.34					
	F54077			0.39						
	F54083	0.33	0.43	0.98	0.00					
	F54083				0.42					
	F54091	0.36	0.12	0.90	0.28					
	F54094	0.36	0.45	1.03	0.27					
	F54097	0.40	0.05	0.67	0.48					
	F54100	0.39	0.41	0.62	0.00					
	F54100				0.31					
	F54102	0.38	0.29	0.46	0.18					
GROUP 3 Dose Level : 10 mg/kg	F54071	0.24	0.16	0.00	0.24					
	F54078	0.39	0.22	0.32	0.52					
	F54090	0.28	0.20	0.49	1.02					
	F54093	0.43	0.29	0.00	0.21					
	F54095	0.24	0.41	0.00	0.42					
	F54096	0.13	0.00	0.04	0.23					
	F54101	0.15	0.13	0.00	0.34					
	F54110	0.25	1.85	0.00	0.30					
GROUP 4 Dose Level : 100 mg/kg	F54080	0.56	0.73	0.53	1.21	0.28	0.65	0.21		
	F54080	0.57								
	F54087	0.50	0.41	0.64	0.81	0.38	0.66	0.35	0.27	0.34
	F54088	0.40	0.64	0.79	0.48	0.31	0.32	0.00		
	F54089	0.36	0.75	0.65	0.99	0.22	0.49	0.33	0.32	0.23
	F54092	0.28	0.87	0.44	1.02	0.19	0.73	0.43		
	F54099	0.63	0.60	1.79	2.15	1.14	0.74	0.61		
	F54099					0.47	0.34	0.53		
	F54106	0.68	1.05	0.96	0.88					
	F54109	0.32	0.67	0.64	0.78	0.43	0.56	0.50	0.29	0.34
	F54114	0.86	0.80	0.72	0.64	0.46	0.73	0.29	0.34	0.36

SUMMARY of 6329-159
SERUM SAMPLES
AMDT 42095.1

	Sample	Fluoride	Fluoride	Fluoride	Fluoride	Fluoride	Fluoride	Fluoride	Fluoride	Fluoride
	ID	In Sample	In Sample	In Sample	In Sample	In Sample	In Sample	In Sample	In Sample	In Sample
		(ppm)	(ppm)	(ppm)	(ppm)	(ppm)	(ppm)	(ppm)	(ppm)	(ppm)
GROUP 5 Dose Level : 500 mg/kg	F54076	0.92	1.17	0.68						
	F54079	2.94	1.36	1.25	1.00	1.05	1.28	1.36	1.07	0.86
	F54082	1.40	1.75	0.95	0.86	1.37	1.28	0.71	1.17	1.21
	F54084	1.78	1.44	1.30	1.03	1.73	1.46	1.40		
	F54098	1.25	1.58	1.39	1.10	1.37	1.25	1.04		
	F54111	2.42	1.19	1.40	1.18	1.52	1.02	1.22	1.14	0.89
	F54112	1.05	1.47	1.65	1.25	1.63	1.45	0.90		
	F54113	2.23	1.40	0.66	1.17	1.44	1.55	1.17		
	F54116	2.61	4.56	1.32	1.20	1.69	1.15	1.92	1.08	1.00

1995-06-21 10:11 OutPut of : 950504A1

Operator : DDW

Date of the Analysis : 1995-05-04 08:18

Analysis File Name : C:\SKALAR\DATA\HWIDATA\SERUM\950504A1

Sample #	Sample ID	Skalar Standard (ppm)	Skalar Result (ppm)	% Recovery	DI TISAB QV Sample Analyte (mL)	Actual in Sample (ppm)	mL FC 95 Solution Spiked (ug FC)	Conc (ppm)	Mass Recovered (ug FC)	% Recovery
1	Tracer	1.50	1.46	97%						
2	Drift	1.50	1.47	98%						
3	Wash		0.00							
4	Standard 1	0.015	0.015	100%						
5	Standard 2	0.03	0.03	101%						
6	Standard 3	0.06	0.06	99%						
7	Standard 4	0.09	0.09	99%						
8	Standard 5	0.12	0.12	102%						
9	Standard 6	0.15	0.15	99%						
10	Standard 7	0.30	0.29	96%						
11	Standard 8	0.60	0.61	102%						
12	Standard 9	1.20	1.23	102%						
13	Standard 10	1.50	1.47	98%						
14	Drift	1.50	1.47	98%						
15	Wash		0.00							
16	Blk 1		0.04		2.0	0.10	0.77	0.004	0.15	91%
17	Blk 2		0.02		2.0	0.10	0.48	0.004	0.15	97%
18	Spk 63-1		0.07		2.0	0.10	1.37	0.004	0.23	65%
19	Spk 63-2		0.07		2.0	0.10	1.47	0.004	0.23	38%
20	Spk 94.5-1		0.07		2.0	0.10	1.46	0.004	0.30	113%
21	Spk 94.5-2		0.04		2.0	0.10	0.87	0.004	0.30	62%
22	Spk 126-1		0.17		2.0	0.10	3.42	0.004	0.30	89%
23	Spk 126-2		0.09		2.0	0.10	1.87	0.004	0.30	95%
24	Spk 126-3		0.13		2.0	0.10	2.69	0.004	0.30	
25	Spk 126-4		0.14		2.0	0.10	2.86	0.004	0.30	
26	Drift	1.50	1.43	95%						
27	Wash		0.00							
28	F54081-4		0.04		2.0	0.10	0.84			
29	F54075-4		0.03		2.0	0.10	0.61			
30	F54107-4		0.02		2.0	0.10	0.46			
31	F54105-4		0.02		2.0	0.10	0.34			

DDW 4/22/95
 ANDT 42095.1
 Skalar Summary
 6329-159 Serum

000226

000146

Sample #	Sample ID	Skalar Standard (ppm)	Skalar Result (ppm)	% Recovery	DI (SAB) final vol (mL)	DI (SAB) Qty Sample (mL or grams)	Actual ppm F. in Sample	mL FC-95 Solution Spiked	Conc. FC-95 Soln. (ppm)	Mass Spiked (ug F.)	Mass Recovered (ug F.)	% Recovery
32	F54074-4		0.03		2.0	0.10	0.51					
33	Blk-1		0.83		2.0	0.10	16.56					
34	Blk-2		0.40		2.0	0.10	8.04					
35	Spk 63-1		0.08		2.0	0.10	1.53	0.004	63.00	0.15	0.15	101%
36	Spk 63-2		0.09		2.0	0.10	1.86	0.004	63.00	0.15	0.19	123%
37	Spk 63-3		0.10		2.0	0.10	1.93	0.004	63.00	0.15	0.19	127%
38	Drift	1.50	1.46	98%								
39	Wash		0.00									
40	Spk 126-1		0.14		2.0	0.10	2.79	0.004	126.00	0.30	0.28	92%
41	Spk 126-2		0.14		2.0	0.10	2.83	0.004	126.00	0.30	0.28	94%
42	Spk 126-3		0.14		2.0	0.10	2.74	0.004	126.00	0.30	0.27	90%
43	Spk 126-4		0.15		2.0	0.10	2.93	0.004	126.00	0.30	0.29	97%
44	Spk 126-5		0.13		2.0	0.10	2.58	0.004	126.00	0.30	0.26	85%
45	Spk 126-6		0.15		2.0	0.10	3.07	0.004	126.00	0.30	0.31	101%
46	Spk 126-7		0.12		2.0	0.10	2.36					
47	F54085-4		0.05		2.0	0.10	0.98					
48	F54080-4		0.03		2.0	0.10	0.56					
49	F54104-4		0.03		2.0	0.10	0.58					
50	Drift	1.50	1.47	98%								
51	Wash		0.00									
52	F54077-4		0.03		2.0	0.10	0.53					
53	F54083-4		0.02		2.0	0.10	0.33					
54	F54094-4		0.02		2.0	0.10	0.36					
55	F54100-4		0.02		2.0	0.10	0.39					
56	F54091-4		0.02		2.0	0.10	0.36					
57	Blk 1		0.02		2.0	0.10	0.44					
58	Blk 2		0.01		2.0	0.10	0.26					
59	Spk 1		0.08		2.0	0.10	1.60					
60	Spk 2		0.08		2.0	0.10	1.67					
61	F54097-4		0.02		2.0	0.10	0.40					
62	Drift	1.50	1.44	96%								
63	Wash		0.00									
64	F54102-4		0.02		2.0	0.10	0.38					
65	F54092-4		0.01		2.0	0.10	0.28					
66	F54080-4		0.03		2.0	0.10	0.57					
67	F54106-4		0.03		2.0	0.10	0.68					

000227

000147

Sample #	Sample ID	Skalar Standard (ppm)	Skalar Result (ppm)	% Recovery	DITISAB final vol (mL)	DITISAB Qty Sample (mL or grams)	Actual ppm F ₂ in Sample	mL FC 95 Solution Spiked	Conc (ppm)	Mass Spiked (ug F ₂)	Mass Recovered (ug F ₂)	% Recovery
68	F54089-4		0.02		2.0	0.10	0.36					
69	F54088-4		0.02		2.0	0.10	0.40					
70	F54087-4		0.02		2.0	0.10	0.50					
71	F54086-4		0.01		2.0	0.10	0.25					
72	F54096-4		0.01		2.0	0.10	0.13					
73	F54090-4		0.01		2.0	0.10	0.28					
74	Drift	1.50	1.46	97%								
75	Wash		0.00									
76	F54078-4		0.02		2.0	0.10	0.39					
77	F54101-4		0.01		2.0	0.10	0.15					
78	F54095-4		0.01		2.0	0.10	0.24					
79	F54093-4		0.02		2.0	0.10	0.43					
80	F54071-4		0.01		2.0	0.10	0.24					
81	F54108-4		0.01		2.0	0.10	0.20					
82	F54116-4		0.13		2.0	0.10	2.61					
83	F54098-4		0.06		2.0	0.10	1.25					
84	F54084-4		0.09		2.0	0.10	1.78					
85	F54079-4		0.15		2.0	0.10	2.94					
86	Drift	1.50	1.48	99%								
87	Wash		0.00									
88	F54113-4		0.11		2.0	0.10	2.23					
89	F54111-4		0.12		2.0	0.10	2.42					
90	F54082-4		0.07		2.0	0.10	1.40					
91	F54076-4		0.05		2.0	0.10	0.92					
92	F54114-4		0.04		2.0	0.10	0.86					
93	F54109-4		0.02		2.0	0.10	0.32					
94	Drift	1.50	1.47	98%								
95	Wash		0.00									

* TE 00009/21.95

000228

000148

DDW 6/22/95
AMDT 42095.1
Skalar Summar
6329-159 SW

HWI-159B.XLS

1995-06-21 10:15 OutPut of : 950504B1

Operator : DDW

Date of the Analysis : 1995-05-04 13:07

Analysis File Name : C:\SKALAR\DATA\HWI\DATA\SERUM\950504B1

Sample #	Sample ID	Standard (ppm)	Skalar Result (ppm)	% Recovery	DELTASAB Anal Vol (mL)	Qty Sample (mL or grams)	Actual ppm in Sample	ml Solution Spiked	Conc (ppm)	Mass Spiked (ug/L)	Mass Recovered (ug/L)	% Recovery
1	Tracer	1.50	1.47	98%								
2	Drift	1.50	1.47	98%								
3	Wash		0.00									
4	Standard 1	0.015	0.014	93%								
5	Standard 2	0.03	0.03	104%								
6	Standard 3	0.06	0.06	103%								
7	Standard 4	0.09	0.09	97%								
8	Standard 5	0.12	0.12	101%								
9	Standard 6	0.15	0.15	100%								
10	Standard 7	0.30	0.29	97%								
11	Standard 8	0.60	0.61	101%								
12	Standard 9	1.20	1.23	102%								
13	Standard 10	1.50	1.48	98%								
14	Drift	1.50	1.45	97%								
15	Wash		0.00									
16	F54075-8		0.03		2.0	0.10	0.64					
17	F54081-8		0.02		2.0	0.10	0.40					
18	F54105-8		0.03		2.0	0.10	0.55					
19	F54107-8		0.02		2.0	0.10	0.31					
20	F54074-8		0.02		2.0	0.10	0.35					
21	F54085-8		0.03		2.0	0.10	0.62					
22	F54086-8		0.04		2.0	0.10	0.71					
23	BLK-1		0.02		2.0	0.10	0.42					
24	BLK-2		0.07		2.0	0.10	1.33					
25	SPK 1		0.10		2.0	0.10	2.00	0.004	63.00	0.15	0.20	132%
26	Drift	1.50	1.44	96%								
27	Wash		0.00									
28	SPK 2		0.08		2.0	0.10	1.55					
29	F54104-8		0.04		2.0	0.10	0.73					
30	F54077-8		0.03		2.0	0.10	0.58					
31	F54083-8		0.02		2.0	0.10	0.43					

Page 1

000229

000119

7

3MA01502316

2807.0149

Sample #	Sample ID	Standard (ppm)	Skalar Result (ppm)	% Recovery	DI/TISAB Final Vol (mL)	DI/TISAB Qty Sample (mL or grams)	Actual ppm F- in Sample	mL FC 95 Solution Spiked	Conc (ppm)	Mass Spiked (ug F-)	Mass Recovered (ug F-)	% Recovery
32	F54094-8		0.02		2.0	0.10	0.45					
33	F54100-8		0.02		2.0	0.10	0.41					
34	F54091-8		0.01		2.0	0.10	0.12					
35	F54097-8		0.00		2.0	0.10	0.05					
36	F54102-8		0.01		2.0	0.10	0.29					
37	F54108-8		0.00		2.0	0.10	0.01					
38	Drift	1.50	1.40	93%								
39	Wash		0.00									
40	F54071-8		0.01		2.0	0.10	0.16					
41	F54093-8		0.01		2.0	0.10	0.29					
42	F54095-8		0.02		2.0	0.10	0.41					
43	F54101-8		0.01		2.0	0.10	0.13					
44	F54078-8		0.01		2.0	0.10	0.22					
45	F54090-8		0.01		2.0	0.10	0.20					
46	F54096-8		0.00		2.0	0.10	0.00					
47	F54110-8		0.09		2.0	0.10	1.85					
48	F54087-8		0.02		2.0	0.10	0.41					
49	F54088-8		0.03		2.0	0.10	0.64					
50	Drift	1.50	1.48	99%								
51	Wash		0.00									
52	F54089-8		0.04		2.0	0.10	0.75					
53	F54106-8		0.05		2.0	0.10	1.05					
54	F54080-8		0.04		2.0	0.10	0.73					
55	F54092-8		0.04		2.0	0.10	0.87					
56	F54109-8		0.03		2.0	0.10	0.67					
57	F54114-8		0.04		2.0	0.10	0.80					
58	F54076-8		0.06		2.0	0.10	1.17					
59	F54082-8		0.09		2.0	0.10	1.75					
60	F54111-8		0.06		2.0	0.10	1.19					
61	F54113-8		0.07		2.0	0.10	1.40					
62	Drift	1.50	1.51	101%								
63	Wash		0.00									
64	F54079-8		0.07		2.0	0.10	1.36					
65	F54084-8		0.07		2.0	0.10	1.44					
66	F54098-8		0.08		2.0	0.10	1.58					
67	F54116-8		0.23		2.0	0.10	4.56					

000230

000150

Sample #	Sample ID	Skalar Standard (ppm)	Skalar Result (ppm)	% Recovery	DITISAB final vol (mL)	QTY Sample (mL or grams)	Actual ppb F ₂ in Sample	ml FC 95 Solution	Conc FC 95 Soln (ppm)	Mass Spiked (ug F ₂)	Mass Recovered (ug F ₂)	% Recovery
68	Drift	1.50	1.51	101%								
69	Wash		0.00									

000231

000151

1995-06-13 13:25 OutPut of : 950508A1

Operator : DDW

Date of the Analysis : 1995-05-08 07:30

Analysis File Name : C:\SKALAR\DATA\HWIDATA\ISERUM\950508A1

Sample #	Sample ID	Scalar Standard (ppm)	Scalar Result (ppm)	% Recovery	DI TISAB final vol (ml)	DI TISAB Qty Sample (ml or frame)	Actual ppm F- in Sample	ml FC 95 Solution Spiked	Conc (ppm)	Mass Spiked (ug F-)	Mass Recovered (ug F-)	% Recovery
1	Tracer	1.5	1.45	96%								
2	Drift	1.5	1.47	98%								
3	Wash		0.00									
4	Standard 1	0.015	0.014	93%								
5	Standard 2	0.03	0.03	104%								
6	Standard 3	0.06	0.06	100%								
7	Standard 4	0.09	0.09	104%								
8	Standard 5	0.12	0.12	96%								
9	Standard 6	0.15	0.15	103%								
10	Standard 7	0.3	0.29	96%								
11	Standard 8	0.6	0.61	101%								
12	Standard 9	1.2	1.24	103%								
13	Standard 10	1.5	1.46	98%								
14	Drift	1.50	1.47	98%								
15	Wash		0.00									
16	Blk 1		0.03				0.60					
17	Blk 2		0.01				0.26					
18	Spk 1		0.08				1.66					
19	Spk 2		0.09				1.77					
20	F54075-12		0.03				0.63					
21	F54081-12		0.02				0.43					
22	F54105-12		0.03				0.60	0.004	63.00	0.15	0.17	110%
23	F54107-12		0.02				0.40	0.004	63.00	0.15	0.18	117%
24	F54074-12		0.02				0.42					
25	F54085-12		0.01				0.29					
26	Drift	1.50	1.45	97%								
27	Wash		0.00									
28	F54086-12		0.04				0.70					
29	F54104-12		0.04				0.81					
30	F54077-12		0.06				1.22					
31	F54083-12		0.05				0.98					

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DDW 7/22/95
 AMDT 4209 S.1
 Skalar Summary
 6329-159 Sum

000232

000152

10

Sample #	Sample ID	Scalar Standard (ppm)	Stair Result (ppm)	% Recovery	DI/TISAB Qry Sample final vol (mL)	(mL or grams)	Actual in Sample	mL FC 95 Solution Spiked	Conc (ppm)	Mass Spiked (ug/L)	Mass Recovered (ug/L)	% Recovery
32	F54094-12		0.05		2.0	0.10	1.03					
33	F54100-12		0.03		2.0	0.10	0.62					
34	F54091-12		0.04		2.0	0.10	0.90					
35	F54097-12		0.03		2.0	0.10	0.67					
36	F54102-12		0.02		2.0	0.10	0.46					
37	F54108-12		0.01		2.0	0.10	0.20					
38	Drift	1.50	1.47	98%								
39	Wash		0.00									
40	F54077-12		0.02		2.0	0.10	0.39					
41	F54071-12		0.00		2.0	0.10	0.00					
42	F54093-12		0.00		2.0	0.10	0.00					
43	F54095-12		0.00		2.0	0.10	0.00					
44	F54101-12		0.00		2.0	0.10	0.00					
45	F54110-12		0.00		2.0	0.10	0.00					
46	F54096-12		0.00		2.0	0.10	0.04					
47	F54090-12		0.02		2.0	0.10	0.49					
48	F54078-12		0.02		2.0	0.10	0.32					
49	F54088-12		0.04		2.0	0.10	0.79					
50	Drift	1.50	1.46	97%								
51	Wash		0.00									
52	F54106-12		0.05		2.0	0.10	0.96					
53	F54089-12		0.03		2.0	0.10	0.65					
54	F54087-12		0.03		2.0	0.10	0.64					
55	F54080-12		0.03		2.0	0.10	0.53					
56	F54092-12		0.02		2.0	0.10	0.44					
57	F54109-12		0.03		2.0	0.10	0.64					
58	F54114-12		0.04		2.0	0.10	0.72					
59	F54076-12		0.03		2.0	0.10	0.68					
60	F54113-12		0.03		2.0	0.10	0.66					
61	F54082-12		0.05		2.0	0.10	0.95					
62	Drift	1.50	1.44	96%								
63	Wash		0.00									
64	F54111-12		0.07		2.0	0.10	1.40					
65	F54098-12		0.07		2.0	0.10	1.39					
66	F54084-12		0.07		2.0	0.10	1.30					
67	F54079-12		0.06		2.0	0.10	1.25					

000233

000153

Sample #	Sample ID	Scalar Standard (ppm)	Scalar Result (ppm)	% Recovery	DI/TISAB final vol (mL)	QTY Sample (mL or grams)	Actual ppm F. in Sample	mL FC 93 Solution	Conc Spiked (ppm)	Mass Spiked (ug F.)	Mass Recovered (ug F.)	% Recovery
68	F54116-12		0.07		2.0	0.10	1.32					
69	Drift	1.50	1.52	101%								
70	Wash		0.00									

000234

000154

1995-06-13 10:27 OutPut of : 950509A1

Operator : DDW

Date of the Analysis : 1995-05-09 09:48

Analysis File Name : C:\SKALAR\DATA\HWIDATA\SERUM950509A1

Sample #	Sample ID	Standard (ppm)	Scalar Result (ppm)	% Recovery	Final Vol (ul)	DI-HSAB QTY Sample (ml or grams)	Actual ppm F ₂ in Sample	ml FC 95 Solution Spiked	Conc (ppm)	Mass Spiked (ug F ₂)	Mass Recovered (ug F ₂)	% Recovery
1	Tracer	1.5	1.47	98%								
2	Drift	1.5	1.50	100%								
3	Wash		0.00									
4	Standard 1	0.015	0.014	94%								
5	Standard 2	0.03	0.03	106%								
6	Standard 3	0.06	0.06	98%								
7	Standard 4	0.09	0.09	101%								
8	Standard 5	0.12	0.12	99%								
9	Standard 6	0.15	0.15	102%								
10	Standard 7	0.3	0.29	97%								
11	Standard 8	0.6	0.61	101%								
12	Standard 9	1.2	1.23	103%								
13	Standard 10	1.5	1.47	98%								
14	Drift	1.5	1.55	103%								
15	Wash		0.00									
16	Serum blk 1		0.05		2.0	0.10	0.90					
17	Serum blk 2		0.03		2.0	0.10	0.62					
18	Serum spk 1		0.04		2.0	0.10	0.87					
19	Serum spk 2		0.05		2.0	0.10	0.91					
20	Serum spk 3		0.06		2.0	0.10	1.17					
21	Serum spk 4		0.07		2.0	0.10	1.30					
22	Serum spk 5		0.10		2.0	0.10	2.03					
23	Serum spk 6		0.07		2.0	0.10	1.43					
24	Serum spk 7		0.06		2.0	0.10	1.27					
25	Serum spk 8		0.07		2.0	0.10	1.46					
26	Drift	1.50	1.51	101%								
27	Wash		0.00									
28	F54105-24		0.05		2.0	0.10	1.08					
29	F54075-24		0.02		2.0	0.10	0.47					
30	F54081-24		0.02		2.0	0.10	0.40					
31	F54107-24		0.02		2.0	0.10	0.31					

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122143
 AMDT 42095.1
 Skalar Summary
 6329-159 - Serum

000235

000155

Sample #	Sample ID	Standard (ppm)	Std	Result (ppm)	% Recovery	DITISAB Qv Sample (mL or grams)	Actual (ppm F- in Sample)	mL FC-95 Solution Spiked	Conc (ppm)	Mass Spiked (ug F-)	Mass Recovered (ug F-)	% Recovery
32	F54104-24		0.02	0.02		2.0	0.10	0.47				
33	F54086-24		0.02	0.02		2.0	0.10	0.35				
34	F54074-24		0.04	0.04		2.0	0.10	0.70				
35	F54085-24		0.00	0.00		2.0	0.10	0.00				
36	F54083-24		0.00	0.00		2.0	0.10	0.00				
37	F54100-24		0.00	0.00		2.0	0.10	0.00				
38	Drift	1.50	1.47		98%							
39	Wash		0.00									
40	Blk 1		0.03			2.0	0.10	0.62				
41	Blk 2		0.01			2.0	0.10	0.27				
42	Spk 1		0.04			2.0	0.10	0.80				
43	Spk 2		0.06			2.0	0.10	1.11				
44	Spk 3		0.06			2.0	0.10	1.16	0.004	63.00	0.15	53%
45	Spk 4		0.06			2.0	0.10	1.18	0.004	63.00	0.15	73%
46	Spk 5		0.07			2.0	0.10	1.35	0.004	63.00	0.15	76%
47	Spk 6		0.07			2.0	0.10	1.32	0.004	63.00	0.15	78%
48	Blk 3		0.04			2.0	0.10	0.82	0.004	63.00	0.15	89%
49	F54085-24		0.02			2.0	0.10	0.31	0.004	63.00	0.15	87%
50	Drift	1.50	1.51		100%							
51	Wash		0.00									
52	F54083-24		0.02			2.0	0.10	0.42				
53	F54100-24		0.02			2.0	0.10	0.31				
54	F54077-24		0.02			2.0	0.10	0.34				
55	F54094-24		0.01			2.0	0.10	0.27				
56	F54091-24		0.01			2.0	0.10	0.28				
57	F54108-24		0.01			2.0	0.10	0.27				
58	F54102-24		0.01			2.0	0.10	0.18				
59	F54097-24		0.02			2.0	0.10	0.48				
60	F54071-24		0.01			2.0	0.10	0.24				
61	F54093-24		0.01			2.0	0.10	0.21				
62	Drift	1.50	1.49		100%							
63	Wash		0.00									
64	F54095-24		0.02			2.0	0.10	0.42				
65	F54101-24		0.02			2.0	0.10	0.34				
66	F54110-24		0.02			2.0	0.10	0.30				
67	F54096-24		0.01			2.0	0.10	0.23				

000236

000156

Sample #	Sample ID	Skalar Standard (ppm)	Skalar Result (ppm)	% Recovery	DI TISAB QTY Sample (mL)	final vol (mL)	(mL or grams)	Actual ppb P. in Sample	mL FC 93 Solution	Conc (ppm)	Mass Spiked (ug P.)	Mass Recovered (ug P.)	% Recovery
68	F54090-24		0.05		2.0		0.10	1.02					
69	F54078-24		0.03		2.0		0.10	0.52					
70	F54088-24		0.02		2.0		0.10	0.48					
71	F54106-24		0.81		2.0		0.10	16.10					
72	F54089-24		0.44		2.0		0.10	8.70					
73	F54087-24		0.57		2.0		0.10	11.48					
74	Drift	1.50	0.22	15%									
75	Wash		0.00										
76	F54080-24		0.06		2.0		0.10	1.21					
77	F54092-24		0.05		2.0		0.10	1.02					
78	F54109-24		0.04		2.0		0.10	0.78					
79	F54114-24		0.03		2.0		0.10	0.64					
80	Blk 1		0.02		2.0		0.10	0.41					
81	Blk 2		0.01		2.0		0.10	0.29					
82	Spk 1		0.09		2.0		0.10	1.75	0.004	63.00	0.15	0.17	115%
83	Spk 2		0.11		2.0		0.10	2.13	0.004	63.00	0.15	0.21	141%
84	F54113-24		0.06		2.0		0.10	1.17					
85	F54082-24		0.04		2.0		0.10	0.86					
86	Drift	1.50	1.42	95%									
87	Wash		0.00										
88	F54111-24		0.06		2.0		0.10	1.18					
89	F54098-24		0.05		2.0		0.10	1.10					
90	F54084-24		0.05		2.0		0.10	1.03					
91	F54079-24		0.05		2.0		0.10	1.00					
92	F54116-24		0.06		2.0		0.10	1.20					
93	Drift	1.50	1.46	97%									
94	Wash		0.00										
1	Tracer	1.50	1.51	101%									
2	Drift	1.50	1.52	101%									
3	Wash		0.00										
4	F54106-24		0.04		2.0		0.10	0.88					
5	F54089-24		0.05		2.0		0.10	0.99					
6	F54087-24		0.04		2.0		0.10	0.81					
7	Drift	1.50	1.62	108%									
8	Wash		0.00										

samples not
loaded -
run next
tray Q000.

000237

000157

serum - 124-2
ANDT 42095J
Stalor Summary
6329159 Serum

HWI-159E.XLS

1995-06-13 10:27 OutPut of : 950511A1

Operator : DDW

Date of the Analysis : 1995-05-11 08:16

Analysis File Name : C:\SKALAR\DATA\HWIDATA\ISERUM\950511A1

Sample #	Sample ID	Stator Standard (ppm)	Stator Result (ppm)	% Recovery	DI TISAB final vol (mL)	Qty Sample (mL or grams)	Actual ppm F- in Sample	mL FC-95 Solution Spiked	Conc (ppm)	Mass Spiked (ug F-)	Mass Recovered (ug F-)	% Recovery
1	Tracer	1.50	1.47	98%								
2	Drift	1.50	1.47	98%								
3	Wash		0.00									
4	Standard 1	0.015	0.016	109%								
5	Standard 2	0.03	0.03	96%								
6	Standard 3	0.06	0.06	98%								
7	Standard 4	0.09	0.09	102%								
8	Standard 5	0.12	0.12	100%								
9	Standard 6	0.15	0.15	102%								
10	Standard 7	0.30	0.29	96%								
11	Standard 8	0.60	0.61	101%								
12	Standard 9	1.20	1.23	103%								
13	Standard 10	1.50	1.47	98%								
14	Drift	1.50	1.51	101%								
15	Wash		0.00									
16	F54113-48		0.07		2.0	0.10	1.44					
17	F54082-48		0.07		2.0	0.10	1.37					
18	F54111-48		0.08		2.0	0.10	1.52					
19	F54098-48		0.07		2.0	0.10	1.37					
20	F54084-48		0.09		2.0	0.10	1.73					
21	F54079-48		0.05		2.0	0.10	1.05					
22	F54116-48		0.08		2.0	0.10	1.69					
23	F54113-192		0.08		2.0	0.10	1.55					
24	F54082-192		0.06		2.0	0.10	1.28					
25	F54111-192		0.05		2.0	0.10	1.02					
26	Drift	1.50	1.44	96%								
27	Wash		0.00									
28	F54098-192		0.06		2.0	0.10	1.25					
29	F54079-192		0.06		2.0	0.10	1.28					
30	F54084-192		0.07		2.0	0.10	1.46					
31	F54116-192		0.06		2.0	0.10	1.15					

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000238

000158

Sample #	Sample ID	Standard (ppm)	Scalar	Stable Result (ppm)	% Recovery	DIETASAB final vol (mL)	DIETASAB Qty Sample (mL or grams)	Actual ppb F	mL FC 95 Solution	Conc (ppm)	Mass Spiked (ug F)	Mass Recovered (ug F)	% Recovery
32	F54113-360			0.06		2.0	0.10	1.17					
33	F54082-360			0.04		2.0	0.10	0.71					
34	F54111-360			0.06		2.0	0.10	1.22					
35	F54098-360			0.05		2.0	0.10	1.04					
36	F54079-360			0.07		2.0	0.10	1.36					
37	F54084-360			0.07		2.0	0.10	1.40					
38	Drift	1.50		1.48	99%								
39	Wash			0.00									
40	F54116-360			0.10		2.0	0.10	1.92					
41	BLK 1			0.02		2.0	0.10	0.38					
42	SPK 1			0.07		2.0	0.10	1.45					
43	SPK 2			0.10		2.0	0.10	2.00	0.004	63.00	0.15	0.15	96%
44	F54082-D22			0.06		2.0	0.10	1.17	0.004	63.00	0.15	0.20	132%
45	F54111-D22			0.06		2.0	0.10	1.14					
46	F54079-D22			0.05		2.0	0.10	1.07					
47	F54116-D22			0.05		2.0	0.10	1.08					
48	F54082-D28			0.06		2.0	0.10	1.21					
49	F54111-D28			0.04		2.0	0.10	0.89					
50	Drift	1.50		1.52	101%								
51	Wash			0.00									
52	F54079-D28			0.04		2.0	0.10	0.86					
53	F54116-D28			0.05		2.0	0.10	1.00					
54	F54099-4			0.03		2.0	0.10	0.63					
55	F54099-8			0.03		2.0	0.10	0.60					
56	F54099-12			0.09		2.0	0.10	1.79					
57	F54099-24			0.11		2.0	0.10	2.15					
58	F54099-48			0.06		2.0	0.10	1.14					
59	F54099-192			0.04		2.0	0.10	0.74					
60	F54099-360			0.03		2.0	0.10	0.61					
61	F54099-361			0.00		2.0	0.10	0.00					
62	Drift	1.50		1.50	100%								
63	Wash			0.00									
64	F54112-4			0.05		2.0	0.10	1.05					
65	F54112-8			0.07		2.0	0.10	1.47					
66	F54112-12			0.08		2.0	0.10	1.65					
67	F54112-24			0.06		2.0	0.10	1.25					

Blank inserted in tray - no such sample exists.
0006/21/95

000239

000179

Sample #	Sample ID	Skalar Standard (ppm)	Skalar Result (ppm)	% Recovery	DITISAR final vol (mL)	DITISAR Qty Sample (mL or grams)	Actual ppm P. in Sample	ml. FC-95 Solution Spiked	Conc (ppm)	Mass Spiked (ug P.)	Mass Recovered (ug P.)	% Recovery
68	F54112-48		0.08		2.0	0.10	1.63					
69	F54112-192		0.07		2.0	0.10	1.45					
70	F54112-360		0.05		2.0	0.10	0.90					
71	SPK 63-1		0.08		2.0	0.10	1.50	0.004	63.00	0.15	0.15	99%
72	SPK 63-2		0.10		2.0	0.10	1.95	0.004	63.00	0.15	0.19	129%
73	SPK 63-3		0.07		2.0	0.10	1.38	0.004	63.00	0.15	0.14	91%
74	Drift	1.50	1.47	98%								
75	Wash		0.00									
76	SPK 126-1		0.11		2.0	0.10	2.12	0.004	126.00	0.30	0.21	70%
77	SPK 126-2		0.15		2.0	0.10	2.90	0.004	126.00	0.30	0.29	96%
78	SPK 126-3		0.15		2.0	0.10	3.07	0.004	126.00	0.30	0.31	102%
79	Drift	1.50	1.50	100%								
80	Wash		0.00									

000240

000160

1995-06-13 12:41 OutPut of : 950524A1

Operator : DDW

Date of the Analysis : 1995-05-24 11:39

Analysis File Name : C:\SKALAR\DATA\HW\DATA\SERUM\950524A1

Sample ID	Sample	Skalar Standard (ppm)	Skalar Result (ppm)	% Recovery	DISTAB final vol (mL)	QTY Sample (mL or grams)	Actual in Sample (ppm F)	ml. FC 95 Solution Spiked (ppm)	Conc (ppm)	Mass Spiked (ug F)	Mass Recovered (ug F)	% Recovery
1	Tracer	1.5	1.45	97%								
2	Drift	1.5	1.47	98%								
3	Wash		0.00									
4	Standard 1	0.015	0.018	120%								
5	Standard 2	0.03	0.03	92%								
6	Standard 3	0.06	0.06	95%								
7	Standard 4	0.09	0.09	105%								
8	Standard 5	0.12	0.12	99%								
9	Standard 6	0.15	0.16	103%								
10	Standard 7	0.3	0.28	95%								
11	Standard 8	0.6	0.61	102%								
12	Standard 9	1.2	1.24	104%								
13	Standard 10	1.5	1.46	97%								
14	Drift	1.50	1.44	96%								
15	Wash		0.00									
16	BLK 1		0.03		2.0	0.10	0.66	0.004	63.00	0.15	0.17	111%
17	BLK 2		0.02		2.0	0.10	0.34	0.004	63.00	0.15	0.15	101%
18	SPK 63-1		0.08		2.0	0.10	1.69	0.004	63.00	0.15	0.15	102%
19	SPK 63-2		0.08		2.0	0.10	1.52	0.004	63.00	0.15	0.15	90%
20	SPK 63-3		0.08		2.0	0.10	1.54	0.004	63.00	0.15	0.14	114%
21	SPK 63-4		0.07		2.0	0.10	1.37	0.004	63.00	0.15	0.17	110%
22	SPK 63-5		0.09		2.0	0.10	1.72	0.004	63.00	0.15	0.17	109%
23	SPK 63-6		0.08		2.0	0.10	1.66	0.004	63.00	0.15	0.15	
24	SPK 63-7		0.08		2.0	0.10	1.64	0.004	63.00	0.15	0.16	
25	BLK 3		0.03		2.0	0.10	0.53					
26	Drift	1.50	1.46	97%								
27	Wash		0.00									
28	BLK 4		0.03		2.0	0.10	0.55					

Review 1221110
 And 42095+1
 Skalar Summary
 6329-159 Sum

000241

000161

Sample #	Sample ID	Standard (ppm)	Scalar Result (ppm)	% Recovery	DISTAB final vol (mL)	Qty Sample (mL or grams)	Actual ppm F ₁ In Sample	nd. FC 95 Solution	FC 95 Soln (ppm)	Mass Spiked (ug F ₁)	Mass Recovered (ug F ₁)	% Recovery
29	F54088-48		0.02		2.0	0.10	0.31					
30	F54099-48		0.02		2.0	0.10	0.47					
31	F54089-48		0.01		2.0	0.10	0.22					
32	F54087-48		0.02		2.0	0.10	0.38					
33	F54080-48		0.01		2.0	0.10	0.28					
34	F54092-48		0.01		2.0	0.10	0.19					
35	F54109-48		0.02		2.0	0.10	0.43					
36	F54114-48		0.02		2.0	0.10	0.46					
37	F54088-DY8		0.02		2.0	0.10	0.32					
38	Drift	1.50	1.49	99%								
39	Wash		0.00									
40	F54099-DY8		0.02		2.0	0.10	0.34					
41	SPK 63-8		0.08		2.0	0.10	1.62	0.004	63.00	0.15	0.16	107%
42	SPK 63-9		0.08		2.0	0.10	1.55	0.004	63.00	0.15	0.15	102%
43	SPK 63-10		0.08		2.0	0.10	1.58	0.004	63.00	0.15	0.16	104%
44	BLK 1		0.03		2.0	0.10	0.55					
45	BLK 2		0.01		2.0	0.10	0.17					
46	SPK 63-1		0.06		2.0	0.10	1.19	0.004	63.00	0.15	0.12	79%
47	SPK 63-2		0.08		2.0	0.10	1.53	0.004	63.00	0.15	0.15	101%
48	SPK 63-3		0.08		2.0	0.10	1.68	0.004	63.00	0.15	0.17	111%
49	F54089-DY8		0.02		2.0	0.10	0.49					
50	Drift	1.50	1.47	98%								
51	Wash		0.00									
52	F54087-DY8		0.03		2.0	0.10	0.66					
53	F54080-DY8		0.03		2.0	0.10	0.65					
54	F54092-DY8		0.04		2.0	0.10	0.73					
55	F54109-DY8		0.03		2.0	0.10	0.56					
56	F54114-DY8		0.04		2.0	0.10	0.73					
57	F54088-D15		0.00		2.0	0.10	0.00					
58	F54099-D15		0.03		2.0	0.10	0.53					
59	F54089-D15		0.02		2.0	0.10	0.33					
60	F54087-D15		0.02		2.0	0.10	0.35					
61	F54080-D15		0.01		2.0	0.10	0.21					

000242

000162

20

Sample #	Sample ID	Skalar Standard (ppm)	Skalar Result (ppm)	% Recovery	DITISAB final vol (mL)	Qr Sample (mL or grams)	Actual ppb in Sample	ml FCYS Solution Spiked	Conc (ppm)	Mass Spiked (ug/L)	Mass Recovered (ug/L)	% Recovery
62	Drift	1.50	1.47	98%								
63	Wash		0.00									
64	F54092-D15		0.02		2.0	0.10	0.43					
65	F54109-D15		0.02		2.0	0.10	0.50					
66	F54114-D15		0.01		2.0	0.10	0.29					
67	F54089-D22		0.02		2.0	0.10	0.32					
68	F54087-D22		0.01		2.0	0.10	0.27					
69	F54109-D22		0.01		2.0	0.10	0.29					
70	F54114-D22		0.02		2.0	0.10	0.34					
71	F54089-D28		0.01		2.0	0.10	0.23					
72	F54087-D28		0.02		2.0	0.10	0.34					
73	F54109-D28		0.02		2.0	0.10	0.34					
74	Drift	1.50	1.46	97%								
75	Wash		0.00									
76	F54114-D28		0.02		2.0	0.10	0.36					
77	SPK 63-4		0.04		2.0	0.10	0.76	0.004	63.00	0.15	0.08	50%
78	SPK 63-5		0.06		2.0	0.10	1.22	0.004	63.00	0.15	0.12	81%
79	SPK 63-6		0.08		2.0	0.10	1.53	0.004	63.00	0.15	0.15	101%
80	SPK 63-7		0.08		2.0	0.10	1.50	0.004	63.00	0.15	0.15	99%
81	F54105-48HR		0.02		2.0	0.10	0.36					
82	F54075-48HR		0.03		2.0	0.10	0.52					
83	Drift	1.50	1.41	94%								
84	Wash		0.00									

000243

000163

OutPut of : 950504A1

UDW - 122195
 AMBT 42095.1
 6329-159 Serva

BEST COPY AVAILABLE

Analysis File Name : C:\SKALAR\DATA\HWIDATA\SERUM\950504A1

```
calibration order = Inverse Logarithm
```

$$\text{result} = 10^{\left[\frac{x - c1}{s} \right]}$$

x = corrected value of the sample
 $c1$ = corrected value of the concentration 1
 s = Slope of the electrode

```
2 = -0.00000
1 = 0.00063
0 = -1.24458
```

```
calibration order = 2
```

Correlation : $r = 0.99928$

```
result = a2 * x2 + a1 * x + a0
```

```

2 =      0.00000
1 =      0.00018
0 =     -0.00141

```

```

amplifier      Type      : SA1000
                Number    : 1
                Sample Time : 50 sec.
                Wash Time   : 120 sec.
                Air Time    : 1 sec.
                Take up     : Single
                sPecial     : None
                needle Height : 70 mm.

```

```

iluter          needle Height      : 80      mm
                dilution Factor   : 10
                dilution Volume    : 2.5     ml.
                Resample            : 1
                Dilution runs      : 1

```

```
User file :      . TXT
Reproces  : No
```

000164

000244

22

3MA01502331

2807.0164

luoride 1.5 Path number : 3
Signal type : Debubbled
Decolor : Yes
system Number : 0
diLute : No
Resample : No
dil Threshold : 4095
diG output : 0
Window event : Off

BEST COPY AVAILABLE

s1 sTandard : Ignore
s2 sTandard : Ignore
s3 sTandard : Ignore
s4 sTandard : Ignore
s5 sTandard : Ignore
s6 sTandard : 0.150
s7 sTandard : 0.300
s8 sTandard : 0.600
s9 sTandard : 1.200
s10 sTandard : 1.500
Order : Inverse Logarithm
Dimension : PPM
start Value : 500 DU
trigger Limit : 1800 Sec
Peak shape : Pointed
stArt ignore : 60 Sec
eNd ignore : 120 Sec
Measure window : 75 %
Filter : No
Regeneration : No
formUla :
output : ##.###

luoride L Path number : 0
Signal type : Debubbled
Decolor : No
system Number : 0
diLute : No
Resample : No
dil Threshold : 4095
diG output : 0
Window event : Off

000245

000165

23

s1 sTandard : 0.015
s2 sTandard : 0.030
s3 sTandard : 0.060
s4 sTandard : 0.090
s5 sTandard : 0.120
s6 sTandard : 0.150
s7 sTandard : Ignore
s8 sTandard : Ignore
s9 sTandard : Ignore
s10 sTandard : Ignore
Order : 2
Dimension : PPM
start Value : 500 DU
trigger Limit : 1800 Sec
Peak shape : Pointed
stArt ignore : 60 Sec
eNd ignore : 120 Sec
Measure window : 75 %
Filter : No
Regeneration : No
formUla : c4:=c3
output : #.####

BEST COPY AVAILABLE

000246

000166

24

Fluoride 1.5 Fluoride L

PPM PPM

Pos	Typ	Ident	Ch	Result	F	Time	Ch	Result	F	Time
1	t	Initial Wash	3	0.057		65	4	#####		0
2	t	Tracer	3	1.462		212	4	1.0733		0
3	d	Drift	3	1.467		387	4	1.0775		0
4	w	Wash	3	0.057		629	4	#####		0
5	s1	Standard 1	3	0.065		740	4	0.0150		0
6	s2	Standard 2	3	0.073		915	4	0.0304		0
7	s3	Standard 3	3	0.090		1087	4	0.0594		0
8	s4	Standard 4	3	0.109		1263	4	0.0891		0
9	s5	Standard 5	3	0.132		1436	4	0.1221		0
10	s6	Standard 6	3	0.153		1611	4	0.1490		0
11	s7	Standard 7	3	0.288		1787	4	0.2865		0
12	s8	Standard 8	3	0.609		1961	4	0.5232		0
13	s9	Standard 9	3	1.226		2137	4	0.9080		0
14	s10	Standard 10	3	1.474		2313	4	1.0831		0
15	d	Drift	3	1.472		2487	4	1.0810		0
16	w	Wash	3	0.057		2729	4	#####		0
17	u	Blk 1	3	0.077		2838	4	0.0385		0
18	u	Blk 2	3	0.070		3013	4	0.0242		0
19	u	Spk 63-1	3	0.095		3188	4	0.0686		0
20	u	Spk 63-2	3	0.098		3364	4	0.0736		0
21	u	Spk 94.5-1	3	0.098		3538	4	0.0732		0
22	u	Spk 94.5-2	3	0.080		3714	4	0.0433		0
23	u	Spk 126-1	3	0.171		3888	4	0.1698		0
24	u	Spk 126-2	3	0.112		4062	4	0.0937		0
25	u	Spk 126-3	3	0.142		4238	4	0.1343		0
26	u	Spk 126-4	3	0.149		4414	4	0.1431		0
27	d	Drift	3	1.425		4588	4	1.0452		0
28	w	Wash	3	0.057		4756	4	#####		0
29	u	F54081-4	3	0.079		4938	4	0.0420		0
30	u	F54075-4	3	0.073		5113	4	0.0306		0
31	u	F54107-4	3	0.069		5291	4	0.0229		0
32	u	F54105-4	3	0.066		5465	4	0.0172		0
33	u	F54074-4	3	0.070		5641	4	0.0255		0
34	u	Blk-1	3	0.828		5815	4	0.6608		0
35	u	Blk-2	3	0.402		5989	4	0.3788		0
36	u	Spk 63-1	3	0.100		6165	4	0.0767		0
37	u	Spk 63-2	3	0.111		6339	4	0.0929		0
38	u	Spk 63-3	3	0.113		6515	4	0.0963		0
39	d	Drift	3	1.464		6689	4	1.0750		0
40	w	Wash	3	0.057		6911	4	#####		0
41	u	Spk 126-1	3	0.146		7040	4	0.1397		0
42	u	Spk 126-2	3	0.147		7215	4	0.1417		0
43	u	Spk 126-3	3	0.144		7390	4	0.1368		0
44	u	Spk 126-4	3	0.151		7566	4	0.1467		0
45	u	Spk 126-5	3	0.138		7740	4	0.1292		0
46	u	Spk 126-6	3	0.157		7916	4	0.1533		0
47	u	Spk 126-7	3	0.129		8092	4	0.1179		0
48	u	F54085-4	3	0.083		8266	4	0.0492		0
49	u	F54080-4	3	0.072		8442	4	0.0278		0
50	u	F54104-4	3	0.072		8623	4	0.0291		0
51	d	Drift	3	1.467		8790	4	1.0775		0
52	w	Wash	3	0.057		9032	4	#####		0
53	u	F54077-4	3	0.071		9138	4	0.0265		0
54	u	F54083-4	3	0.066		9314	4	0.0163		0

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000247

000167

25

Fluoride 1.5

Fluoride L

PPM

PPM

Pos	Typ	Ident	Ch	Result	F	Time	Ch	Result	F	Time
4	u	F54094-4	3	0.067		9488	4	0.0181		0
5	u	F54100-4	3	0.067		9666	4	0.0196		0
6	u	F54091-4	3	0.067		9842	4	0.0181		0
7	u	Blk 1	3	0.069		10016	4	0.0220		0
8	u	Blk 2	3	0.064		10191	4	0.0130		0
9	u	Spk 1	3	0.103		10367	4	0.0800		0
0	u	Spk 2	3	0.105		10543	4	0.0835		0
1	u	F54097-4	3	0.067		10717	4	0.0200		0
2	d	Drift	3	1.436		10891	4	1.0537		0
3	w	Wash	3	0.057		11066	4	#####		0
4	u	F54102-4	3	0.067		11241	4	0.0192		0
5	u	F54092-4	3	0.064		11419	4	0.0141		0
6	u	F54080-4	3	0.072		11591	4	0.0287		0
7	u	F54106-4	3	0.075		11769	4	0.0340		0
8	u	F541089-4	3	0.067		11942	4	0.0181		0
9	u	F541088-4	3	0.067		12116	4	0.0200		0
0	u	F541087-4	3	0.070		12291	4	0.0248		0
1	u	F541110-4	3	0.064		12462	4	0.0123		0
2	u	F54096-4	3	0.061		12642	4	0.0064		0
3	u	F54090-4	3	0.064		12818	4	0.0138		0
4	d	Drift	3	1.455		12992	4	1.0681		0
5	w	Wash	3	0.057		13159	4	#####		0
6	u	F54078-4	3	0.067		13342	4	0.0194		0
7	u	F54101-4	3	0.061		13516	4	0.0076		0
8	u	F54095-4	3	0.063		13692	4	0.0120		0
9	u	F54093-4	3	0.068		13868	4	0.0213		0
0	u	F54071-4	3	0.063		14042	4	0.0118		0
1	u	F54108-4	3	0.062		14213	4	0.0102		0
2	u	F54116-4	3	0.139		14393	4	0.1307		0
3	u	F54098-4	3	0.091		14568	4	0.0624		0
4	u	F54084-4	3	0.108		14744	4	0.0889		0
5	u	F54079-4	3	0.152		14919	4	0.1471		0
6	d	Drift	3	1.478		15093	4	1.0857		0
7	w	Wash	3	0.057		15332	4	#####		0
8	u	F54113-4	3	0.124		15444	4	0.1114		0
9	u	F54111-4	3	0.131		15619	4	0.1210		0
0	u	F54082-4	3	0.096		15795	4	0.0702		0
1	u	F54076-4	3	0.082		15967	4	0.0460		0
2	u	F54114-4	3	0.080		16145	4	0.0431		0
3	u	F54109-4	3	0.065		16319	4	0.0160		0
4	d	Drift	3	1.468		16493	4	1.0780		0
5	w	Wash	3	0.057		16650	4	#####		0
t	rw	RunOut Wash	3	0.057		16968	4	#####		0

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2x DCW to 5/4/95

000248

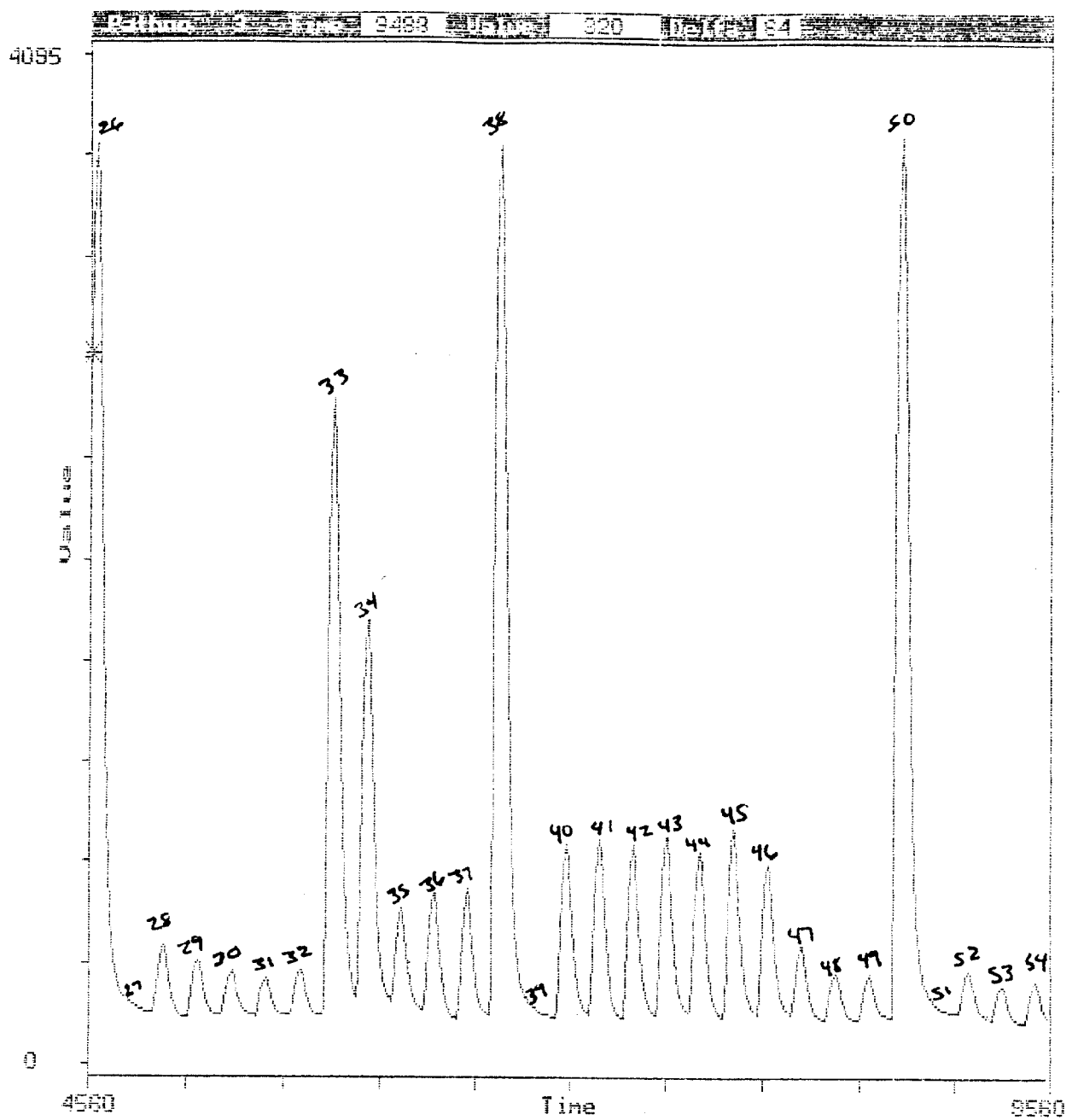
000168

24

3MA01502335

2807.0168

Raw data of 850504A1 : Fluoride 1.5

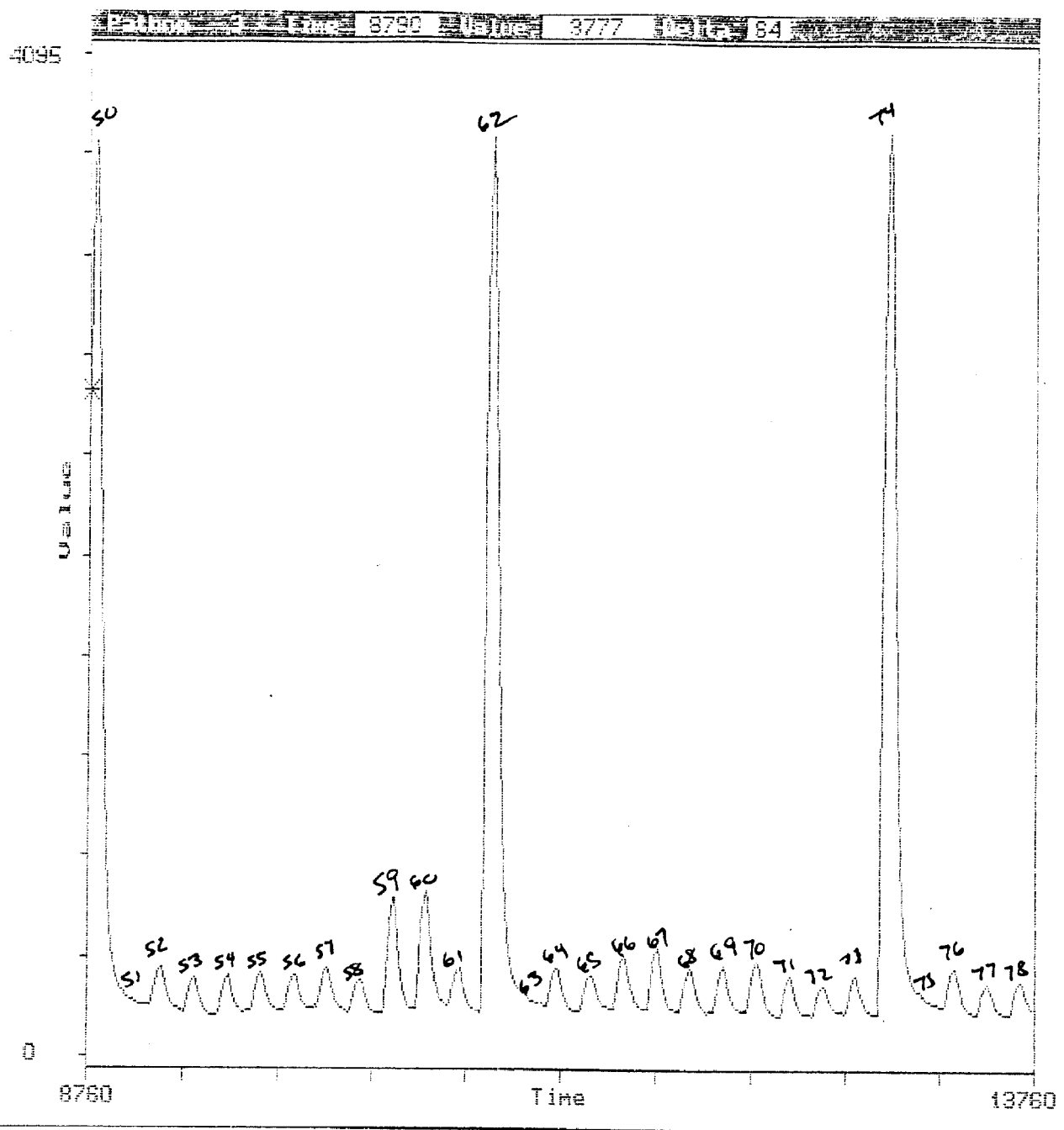


sc=Exit | F1=Help | Ctrl-P=Edit peaks |

000249

000172

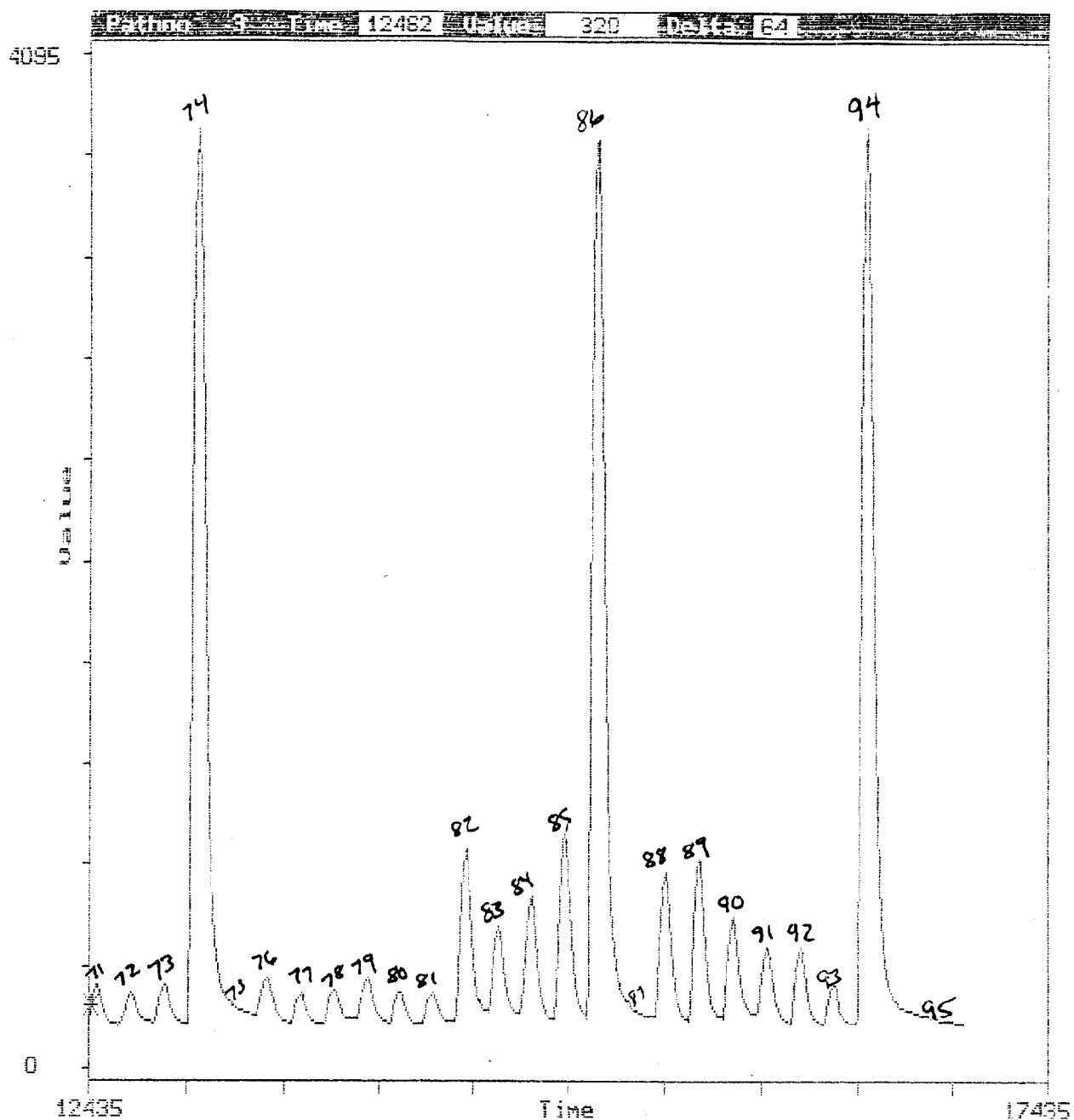
Raw data of 950504A1 : Fluoride 1.5



sc=Exit | F1=Help | Ctrl-P=Edit peaks |

000250

000173



sc=Exit : F1=Help : Ctrl-P=Edit peaks :

000251

000174

17

995-05-04 16:48

OutPut of : 950504B1

DDW 4/22/95
AMDT 42095
6329-159 Su

oftware : version 6.1 c1990,93

perator : DDW

BEST COPY AVAILABLE

ate of the Analysis : 1995-05-04 13:07

alysis File Name : C:\SKALAR\DATA\HWIDATA\SERUM\950504B1

luoride 1.5

alibration order = Inverse Logarithm

lope : $S = \#.#####$

result = $10^{\left[\frac{x - c1}{s} \right]}$

x = corrected value of the sample
 $c1$ = corrected value of the concentration 1
 s = Slope of the electrode

2 = -0.00000

1 = 0.00062

0 = -1.24651

luoride L

alibration order = 2

orrelation : $r = 0.99962$

esult = $a2 * x^2 + a1 * x + a0$

2 = 0.00000

1 = 0.00020

0 = -0.00460

ampler Type : SA1000
 Number : 1
 Sample Time : 50 sec.
 Wash Time : 120 sec.
 Air Time : 1 sec.
 Take up : Single
 sPecial : None
 needle Height : 70 mm.

iluter needle Height : 80 mm
 dilution Factor : 10
 dilution Volume : 2.5 ml.
 Resample : 1
 Dilution runs : 1

User file : . TXT
Reproces : No

000252

000175

23

3MA01502339

2807.0172

fluoride 1.5 Path number : 3
Signal type : Debubbled
Decolor : Yes
system Number : 0
diLute : No
Resample : No
dil Threshold : 4095
diG output : 0
Window event : Off

BEST COPY AVAILABLE

s1 sTandard : Ignore
s2 sTandard : Ignore
s3 sTandard : Ignore
s4 sTandard : Ignore
s5 sTandard : Ignore
s6 sTandard : 0.150
s7 sTandard : 0.300
s8 sTandard : 0.600
s9 sTandard : 1.200
s10 sTandard : 1.500
Order : Inverse Logarithm
Dimension : PPM
start Value : 500 DU
trigger Limit : 1800 Sec
Peak shape : Pointed
stArt ignore : 60 Sec
eNd ignore : 120 Sec
Measure window : 75 %
Filter : No
Regeneration : No
formUla :
output : ##.###

fluoride L Path number : 0
Signal type : Debubbled
Decolor : No
system Number : 0
diLute : No
Resample : No
dil Threshold : 4095
diG output : 0
Window event : Off

000253**000176**

44

995-05-04 16:48

OutPut of : 950504B1

s1 sTandard : 0.015
s2 sTandard : 0.030
s3 sTandard : 0.060
s4 sTandard : 0.090
s5 sTandard : 0.120
s6 sTandard : 0.150
s7 sTandard : Ignore
s8 sTandard : Ignore
s9 sTandard : Ignore
s10 sTandard : Ignore
Order : 2
Dimension : PPM
start Value : 500 DU
trigger Limit : 1800 Sec
Peak shape : Pointed
stArt ignore : 60 Sec
eNd ignore : 120 Sec
Measure window : 75 %
Filter : No
Regeneration : No
formUla : c4:=c3
output : #.####

000254

000177

25

3MA01502341

2807.0174

Fluoride 1.5 Fluoride L

PPM PPM

Pos	Typ	Ident	Ch	Result	F	Time	Ch	Result	F	Time
1	iw	Initial Wash	3	0.057		65	4	#####		0
2	t	Tracer	3	1.467		212	4	0.8037		0
3	d	Drift	3	1.473		388	4	0.8066		0
4	w	Wash	3	0.057		629	4	#####		0
5	s1	Standard 1	3	0.065		740	4	0.0140		0
6	s2	Standard 2	3	0.073		910	4	0.0311		0
7	s3	Standard 3	3	0.089		1089	4	0.0615		0
8	s4	Standard 4	3	0.105		1264	4	0.0877		0
9	s5	Standard 5	3	0.128		1440	4	0.1206		0
10	s6	Standard 6	3	0.153		1614	4	0.1501		0
11	s7	Standard 7	3	0.291		1790	4	0.2729		0
12	s8	Standard 8	3	0.605		1964	4	0.4486		0
13	s9	Standard 9	3	1.228		2138	4	0.7030		0
14	s10	Standard 10	3	1.475		2314	4	0.8073		0
15	d	Drift	3	1.448		2488	4	0.7951		0
16	w	Wash	3	0.057		2709	4	#####		0
17	u	F54075-8	3	0.073		2837	4	0.0319		0
18	u	F54081-8	3	0.067		3013	4	0.0199		0
19	u	F54105-8	3	0.071		3186	4	0.0274		0
20	u	F54107-8	3	0.065		3361	4	0.0154		0
21	u	F54074-8	3	0.066		3541	4	0.0176		0
22	u	F54085-8	3	0.073		3712	4	0.0311		0
23	u	F54086-8	3	0.075		3891	4	0.0357		0
24	u	BLK-1	3	0.068		4067	4	0.0211		0
25	u	BLK-2	3	0.092		4241	4	0.0663		0
26	u	SPK 1	3	0.113		4415	4	0.1002		0
27	d	Drift	3	1.439		4589	4	0.7912		0
28	w	Wash	3	0.057		4828	4	#####		0
29	u	SPK 2	3	0.098		4941	4	0.0774		0
30	u	F54104-8	3	0.075		5112	4	0.0366		0
31	u	F54077-8	3	0.072		5301	4	0.0292		0
32	u	F54083-8	3	0.068		5461	4	0.0217		0
33	u	F54094-8	3	0.069		5642	4	0.0227		0
34	u	F54100-8	3	0.067		5813	4	0.0203		0
35	u	F54091-8	3	0.061		5987	4	0.0061		0
36	u	F54097-8	3	0.060		6169	4	0.0027		0
37	u	F54102-8	3	0.065		6339	4	0.0146		0
38	u	F54108-8	3	0.059		6513	4	0.0004		0
39	d	Drift	3	1.397		6690	4	0.7727		0
40	w	Wash	3	0.057		6854	4	#####		0
41	u	F54071-8	3	0.062		7040	4	0.0081		0
42	u	F54093-8	3	0.065		7214	4	0.0144		0
43	u	F54095-8	3	0.067		7392	4	0.0203		0
44	u	F54101-8	3	0.061		7562	4	0.0063		0
45	u	F54078-8	3	0.063		7740	4	0.0108		0
46	u	F54090-8	3	0.063		7916	4	0.0101		0
47	u	F54096-8	3	0.058		8088	4	#####		0
48	u	F54110-8	3	0.108		8266	4	0.0923		0
49	u	F54087-8	3	0.068		8441	4	0.0207		0
50	u	F54088-8	3	0.073		8615	4	0.0321		0
51	d	Drift	3	1.481		8790	4	0.8103		0
52	w	Wash	3	0.057		8938	4	#####		0
53	u	F54089-8	3	0.076		9141	4	0.0376		0
54	u	F54106-8	3	0.084		9315	4	0.0525		0

BEST COPY AVAILABLE

000255

000178

Fluoride 1.5

Fluoride L

PPM

PPM

os	Typ	Ident	Ch	Result	F	Time	Ch	Result	F	Time
4	u	F54080-8	3	0.075		9491	4	0.0364		0
5	u	F54092-8	3	0.079		9667	4	0.0433		0
6	u	F54109-8	3	0.074		9841	4	0.0333		0
7	u	F54114-8	3	0.077		10015	4	0.0402		0
8	u	F54076-8	3	0.087		10193	4	0.0585		0
9	u	F54082-8	3	0.105		10367	4	0.0877		0
0	u	F54111-8	3	0.088		10543	4	0.0593		0
1	u	F54113-8	3	0.094		10717	4	0.0700		0
2	d	Drift	3	1.512		10891	4	0.8247		0
3	w	Wash	3	0.057		11093	4	#####		0
4	u	F54079-8	3	0.093		11240	4	0.0681		0
5	u	F54084-8	3	0.095		11416	4	0.0718		0
6	u	F54098-8	3	0.099		11591	4	0.0792		0
7	u	F54116-8	3	0.228		11766	4	0.2236		0
8	d	Drift	3	1.512		11941	4	0.8245		0
9	w	Wash	3	0.057		12097	4	#####		0
t	rw	RunOut Wash	3	0.057		12416	4	#####		0

BEST COPY AVAILABLE

000256

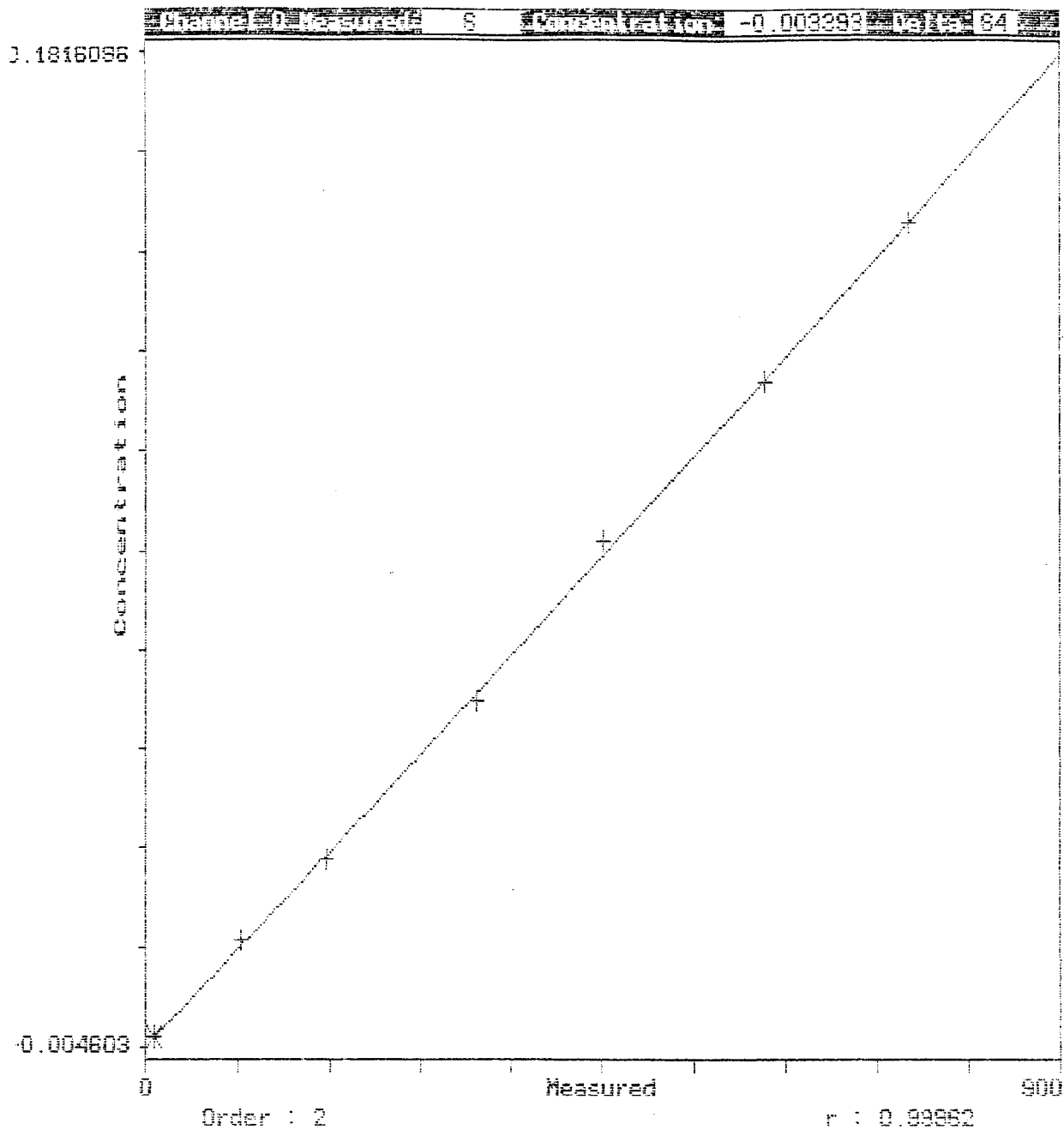
000179

m

3MA01502343

2807.0176

Calibration curve of 95050481 : Fluoride L



BEST COPY AVAILABLE

000257

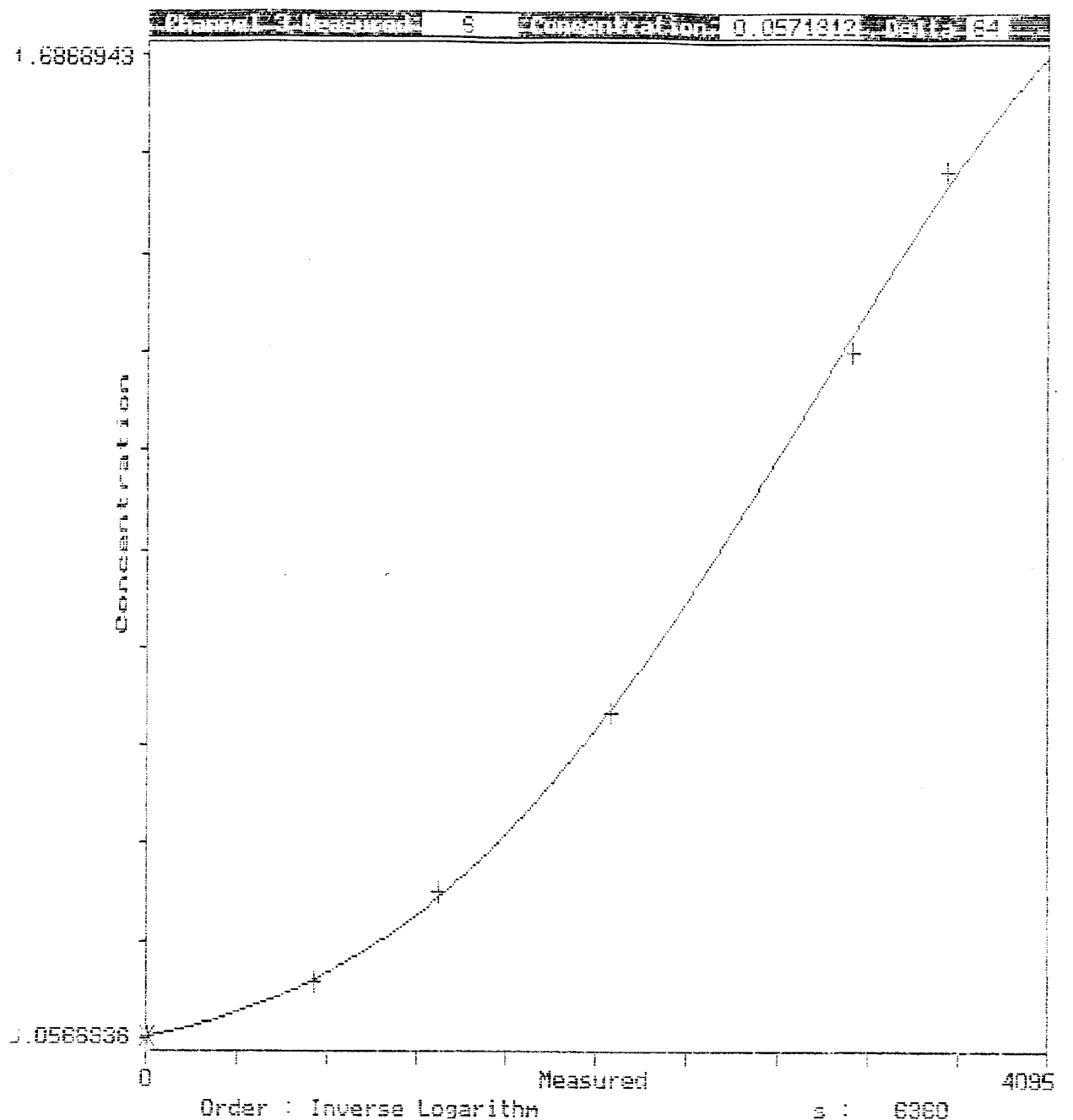
000180

28

3MA01502344

2807.0177

Calibration curve of 950504B1 : Fluoride 1.5



BEST COPY AVAILABLE

000258

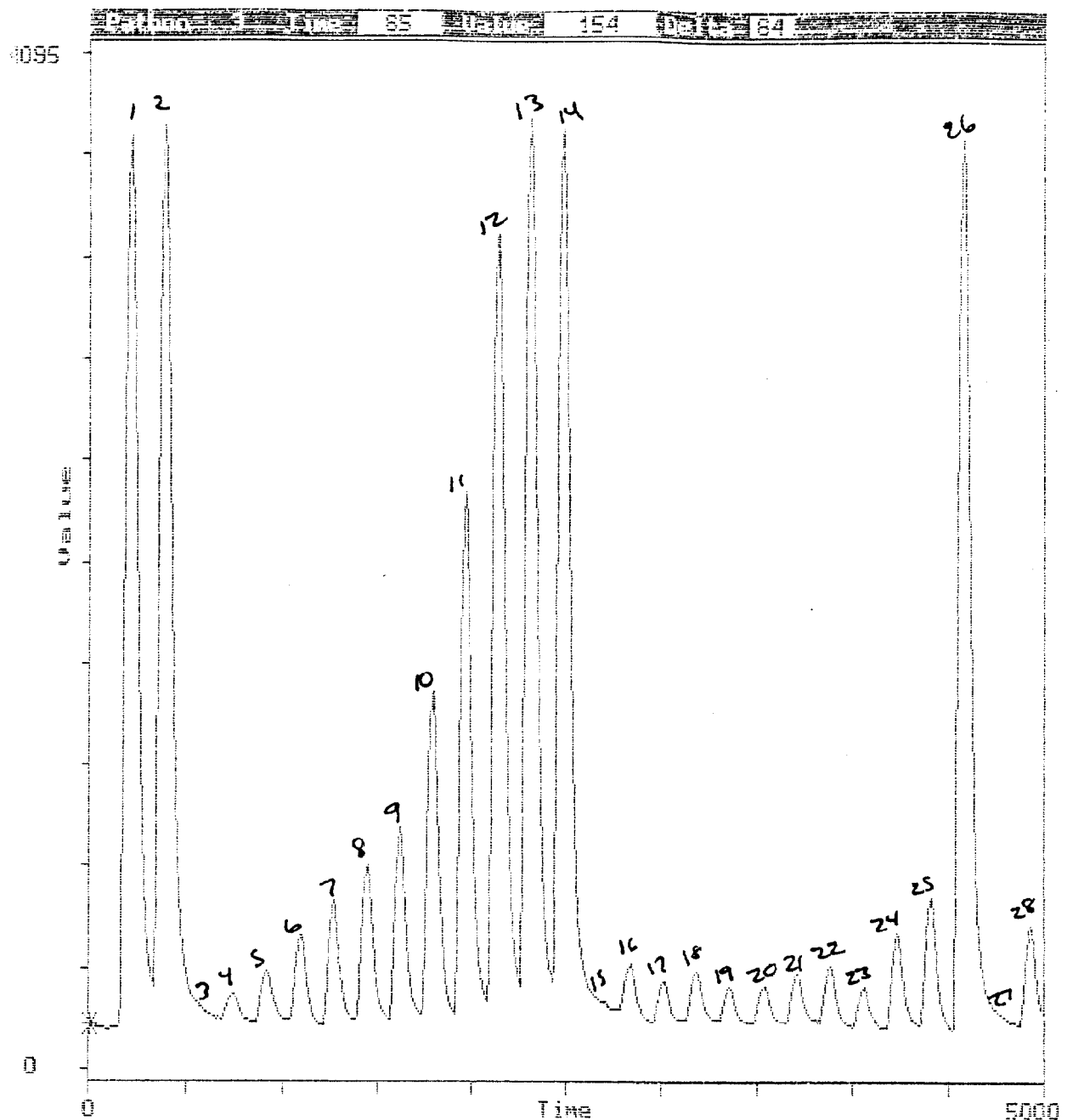
000181

39

3MA01502345

2807.0178

Raw data of 950504B1 : Fluoride 1.5



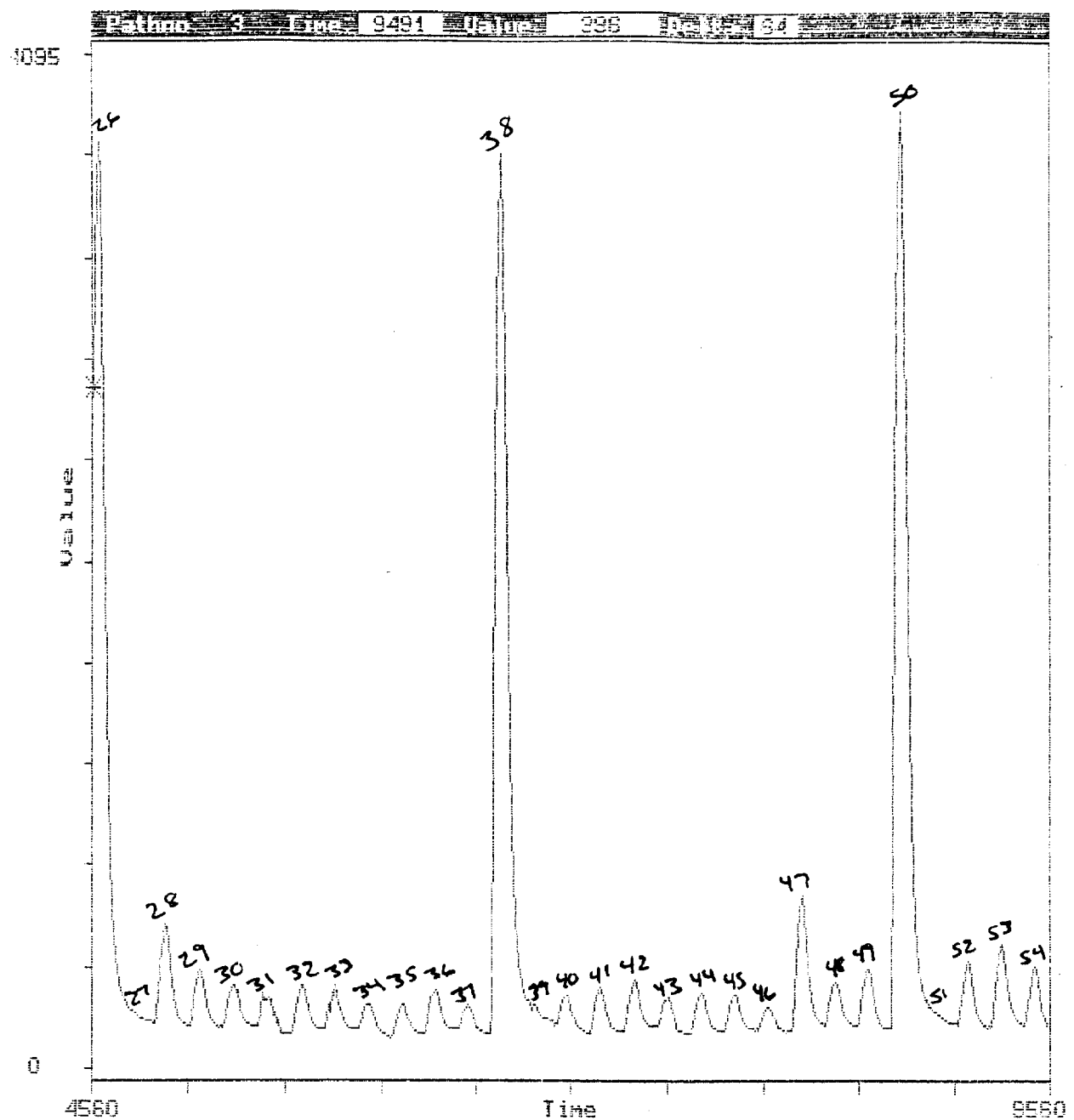
ec=Exit ; F1=Help ; Ctrl-P=Edit peaks ;

000259

000182

45

Raw data of 95050481 : Fluoride 1.5



sc=Exit ! F1=Help ! Ctrl-P=Edit peaks !

000260

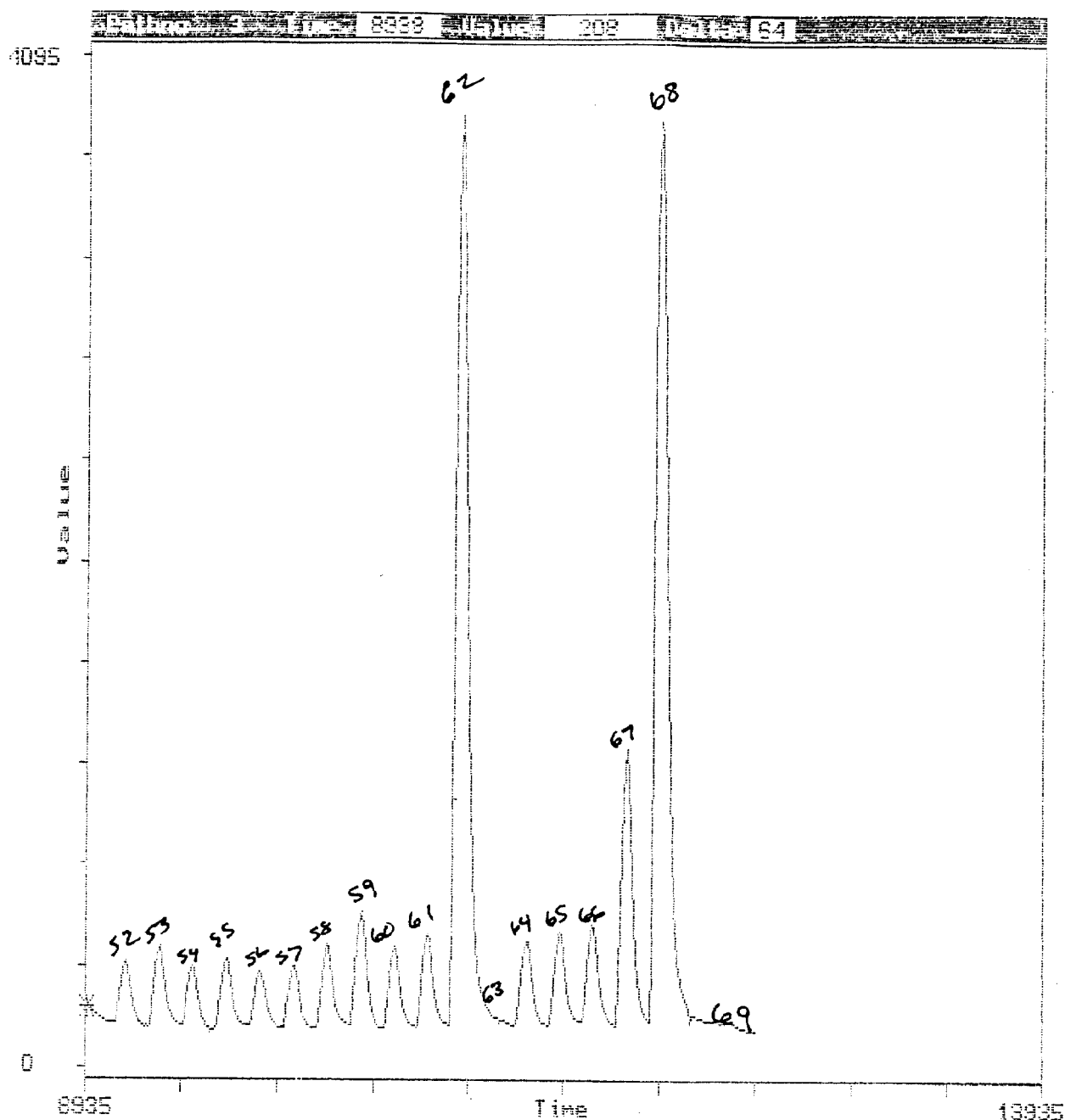
000183

711

3MA01502347

2807.0180

BEST COPY AVAILABLE



sc=Exit ; F1=Help ; Ctrl-P=Edit peaks ;

000261

000184

15

QOW 6/22/95
AMDT 42095.1
6329-159 Ser

```
software : version 6.1  c1990,93
```

operator : DDW

BEST COPY AVAILABLE

Date of the Analysis : 1995-05-08 07:30

Analysis File Name : C:\SKALAR\DATA\HWIDATA\SERUM\950508A1

fluoride 1.5

```
calibration order = Inverse Logarithm
```

```
Slope      : S = #####
```

$$\text{result} = 10^{\left[\frac{x - c1}{s} \right]}$$

x = corrected value of the sample
 $c1$ = corrected value of the concentration 1
 s = Slope of the electrode

$$t_2 = -0.00000$$

1	=	0.00066
---	---	---------

$$C_0 = -1.26704$$

fluoride L

```
calibration order = 2
```

Correlation : $r = 0.99873$

```
result = a2 * x2 + a1 * x + a0
```

$$.2 = -0.00000$$
$$.1 = 0.00021$$
$$.0 = -0.00833$$

```

ampler          Type          : SA1000
                  Number       : 1
                  Sample Time  : 50 sec.
                  Wash Time    : 120 sec.
                  Air Time     : 1 sec.
                  Take up      : Single
                  sPecial      : None
                  needle Height : 70 mm.

```

```

diluter      needle Height      : 80      mm
              dilution Factor   : 10
              dilution Volume   : 2.5     ml.
              Resample           : 1
              Dilution runs     : 1
              ,
              User file          :          . TXT
              Reproces           : No

```

000262

000185

3MA01502349

2807.0182

995-05-08 12:46

OutPut of : 950508A1

luoride 1.5 Path number : 3
 Signal type : Debubbled
 Decolor : Yes
 system Number : 0
 diLute : No
 Resample : No
 dil Threshold : 4095
 diG output : 0
 Window event : Off

BEST COPY AVAILABLE

s1 sTandard : Ignore
s2 sTandard : Ignore
s3 sTandard : Ignore
s4 sTandard : Ignore
s5 sTandard : Ignore
s6 sTandard : 0.150
s7 sTandard : 0.300
s8 sTandard : 0.600
s9 sTandard : 1.200
s10 sTandard : 1.500
Order : Inverse Logarithm
Dimension : PPM
start Value : 500 DU
trigger Limit : 1800 Sec
Peak shape : Pointed
stArt ignore : 60 Sec
eNd ignore : 120 Sec
Measure window : 75 %
Filter : No
Regeneration : No
formUla :
output : ##.###

luoride L Path number : 0
 Signal type : Debubbled
 Decolor : No
 system Number : 0
 diLute : No
 Resample : No
 dil Threshold : 4095
 diG output : 0
 Window event : Off

000263

000186

3MA01502350

2807.0183

995-05-08 12:46

OutPut of : 950508A1

s1 sTandard : 0.015
s2 sTandard : 0.030
s3 sTandard : 0.060
s4 sTandard : 0.090
s5 sTandard : 0.120
s6 sTandard : 0.150
s7 sTandard : Ignore
s8 sTandard : Ignore
s9 sTandard : Ignore
s10 sTandard : Ignore
Order : 2
Dimension : PPM
start Value : 500 DU
trigger Limit : 1800 Sec
Peak shape : Pointed
stArt ignore : 60 Sec
eNd ignore : 120 Sec
Measure window : 75 %
Filter : No
Regeneration : No
formUla : c4:=c3
output : #.####

000264

000187

3MA01502351

2807.0184

Fluoride 1.5 Fluoride L

PPM PPM

Pos	Typ	Ident	Ch	Result	F	Time	Ch	Result	F	Time
1	iw	Initial Wash	3	0.054		65	4	#####		0
2	t	Tracer	3	1.447		210	4	0.7320		0
3	d	Drift	3	1.466		384	4	0.7393		0
4	w	Wash	3	0.054		625	4	#####		0
5	s1	Standard 1	3	0.063		734	4	0.0139		0
6	s2	Standard 2	3	0.071		910	4	0.0313		0
7	s3	Standard 3	3	0.086		1086	4	0.0597		0
8	s4	Standard 4	3	0.107		1260	4	0.0932		0
9	s5	Standard 5	3	0.124		1436	4	0.1156		0
10	s6	Standard 6	3	0.154		1611	4	0.1514		0
11	s7	Standard 7	3	0.287		1785	4	0.2640		0
12	s8	Standard 8	3	0.607		1961	4	0.4282		0
13	s9	Standard 9	3	1.239		2134	4	0.6557		0
14	s10	Standard 10	3	1.464		2309	4	0.7386		0
15	d	Drift	3	1.474		2485	4	0.7425		0
16	w	Wash	3	0.054		2718	4	#####		0
17	u	Blk 1	3	0.071		2835	4	0.0298		0
18	u	Blk 2	3	0.063		3010	4	0.0128		0
19	u	Spk 1	3	0.100		3187	4	0.0829		0
20	u	Spk 2	3	0.104		3362	4	0.0883		0
21	u	F54075-12	3	0.071		3538	4	0.0315		0
22	u	F54081-12	3	0.067		3712	4	0.0217		0
23	u	F54105-12	3	0.071		3886	4	0.0298		0
24	u	F54107-12	3	0.066		4057	4	0.0198		0
25	u	F54074-12	3	0.066		4235	4	0.0209		0
26	u	F54085-12	3	0.063		4402	4	0.0143		0
27	d	Drift	3	1.454		4588	4	0.7348		0
28	w	Wash	3	0.054		4778	4	#####		0
29	u	F54086-12	3	0.073		4937	4	0.0352		0
30	u	F54104-12	3	0.076		5110	4	0.0403		0
31	u	F54077-12	3	0.087		5286	4	0.0610		0
32	u	F54083-12	3	0.081		5467	4	0.0492		0
33	u	F54094-12	3	0.082		5637	4	0.0514		0
34	u	F54100-12	3	0.071		5813	4	0.0309		0
35	u	F54091-12	3	0.078		5991	4	0.0448		0
36	u	F54097-12	3	0.072		6165	4	0.0335		0
37	u	F54102-12	3	0.067		6337	4	0.0232		0
38	u	F54108-12	3	0.062		6515	4	0.0100		0
39	d	Drift	3	1.467		6687	4	0.7399		0
40	w	Wash	3	0.054		6853	4	#####		0
41	u	F54077-12	3	0.066		7037	4	0.0194		0
42	u	F54071-12	3	0.054 A		7212	4	#####		0
43	u	F54093-12	3	0.054 A		7387	4	#####		0
44	u	F54095-12	3	0.054 A		7562	4	#####		0
45	u	F54101-12	3	0.054 A		7737	4	#####		0
46	u	F54110-12	3	0.054 A		7912	4	#####		0
47	u	F54096-12	3	0.058		8088	4	0.0021		0
48	u	F54090-12	3	0.068		8264	4	0.0243		0
49	u	F54078-12	3	0.064		8438	4	0.0160		0
50	u	F54088-12	3	0.075		8611	4	0.0397		0
51	d	Drift	3	1.457		8789	4	0.7356		0
52	w	Wash	3	0.054		8995	4	#####		0
53	u	F54106-12	3	0.080		9141	4	0.0478		0
54	u	F54089-12	3	0.072		9315	4	0.0326		0

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000188

000265

Fluoride 1.5

Fluoride L

PPM

PPM

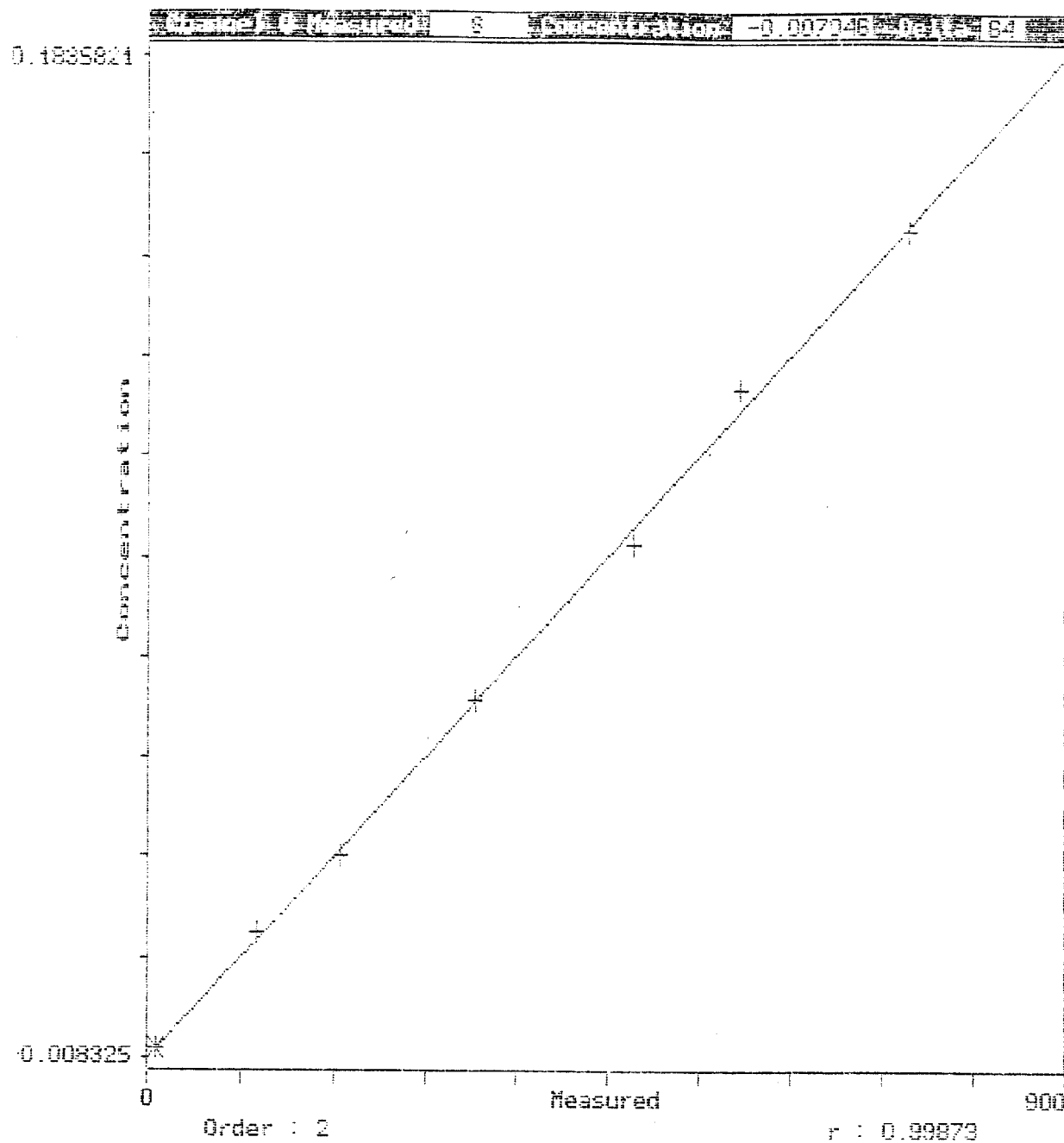
Pos	Typ	Ident	Ch	Result	F	Time	Ch	Result	F	Time
4	u	F54087-12	3	0.072		9491	4	0.0320		0
5	u	F54080-12	3	0.069		9664	4	0.0266		0
6	u	F54092-12	3	0.067		9839	4	0.0222		0
7	u	F54109-12	3	0.072		10017	4	0.0322		0
8	u	F54114-12	3	0.074		10193	4	0.0362		0
9	u	F54076-12	3	0.073		10367	4	0.0341		0
0	u	F54113-12	3	0.072		10540	4	0.0330		0
1	u	F54082-12	3	0.080		10716	4	0.0475		0
2	d	Drift	3	1.442		10890	4	0.7301		0
3	w	Wash	3	0.054		11058	4	#####		0
4	u	F54111-12	3	0.092		11242	4	0.0701		0
5	u	F54098-12	3	0.092		11418	4	0.0697		0
6	u	F54084-12	3	0.089		11590	4	0.0650		0
7	u	F54079-12	3	0.088		11764	4	0.0623		0
8	u	F54116-12	3	0.090		11943	4	0.0659		0
9	d	Drift	3	1.515		12116	4	0.7597		0
0	w	Wash	3	0.054		12348	4	#####		0
t	rw	RunOut Wash	3	0.054		12591	4	#####		0

BEST COPY AVAILABLE

000266

000189

Calibration curve of 950508A1 : Fluoride L



BEST COPY AVAILABLE

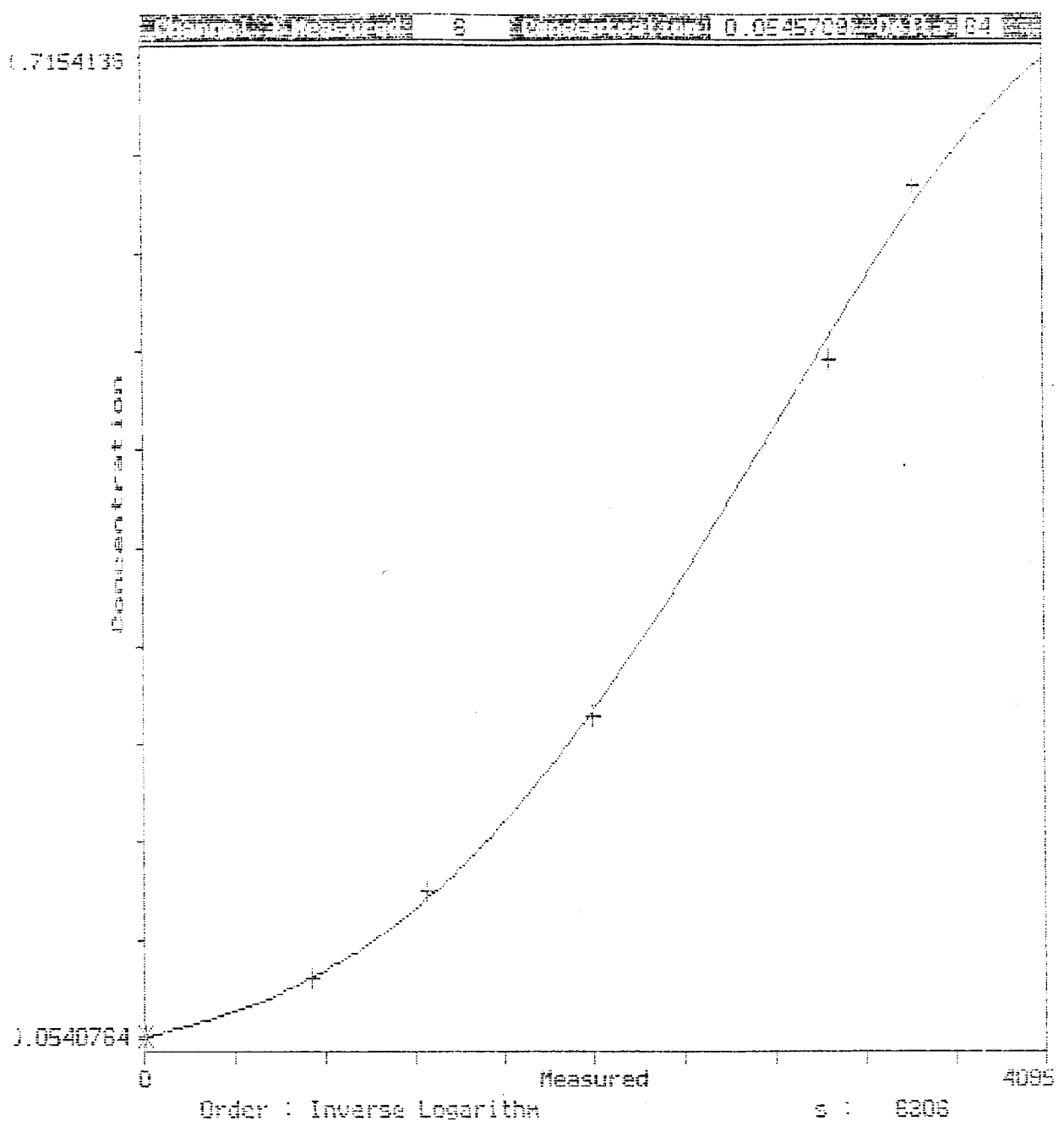
000267

000190

2807.0187

3MA01502354

Calibration curve of 950508A1 : Fluoride 1.5

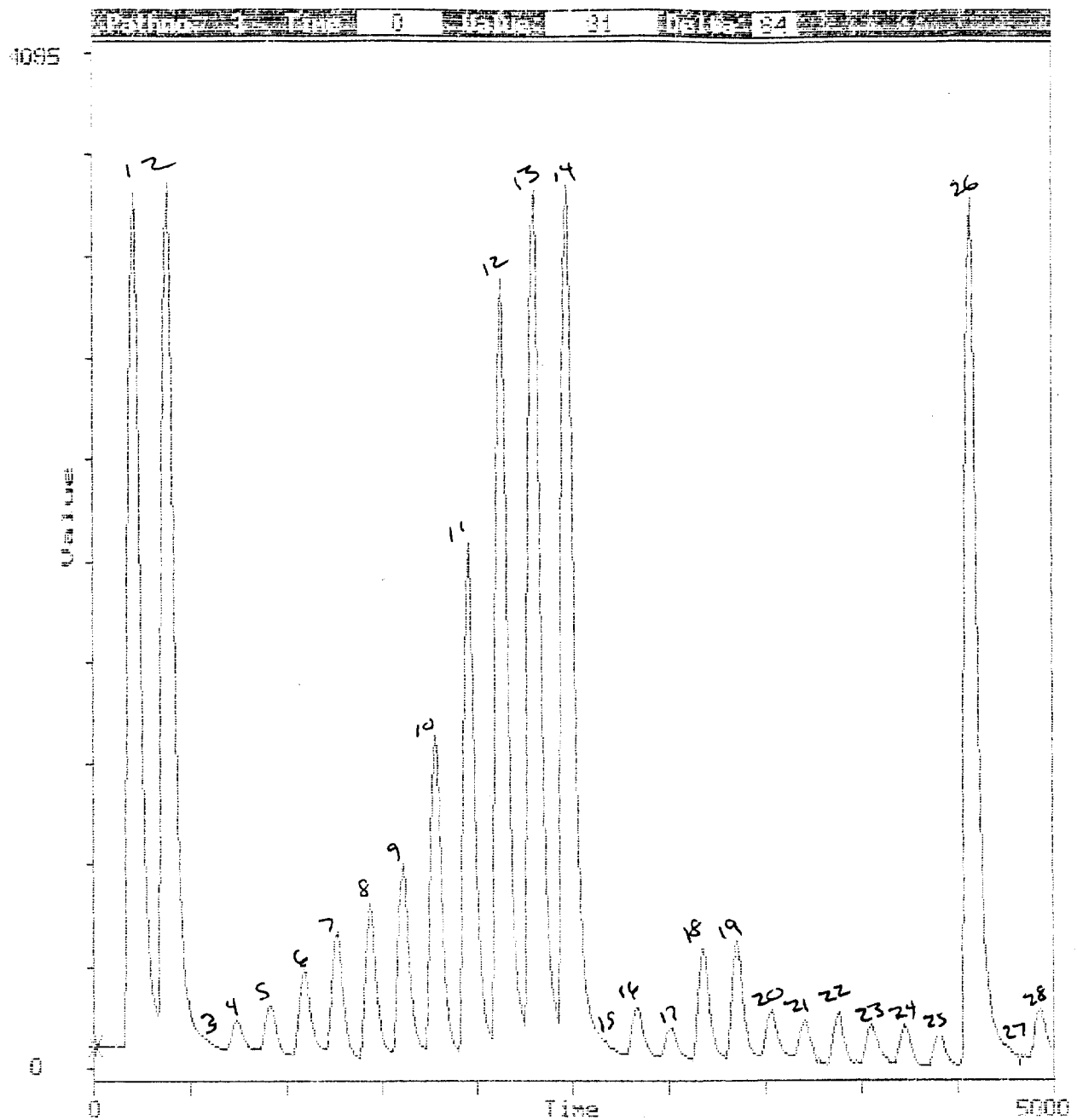


BEST COPY AVAILABLE

000268

000191

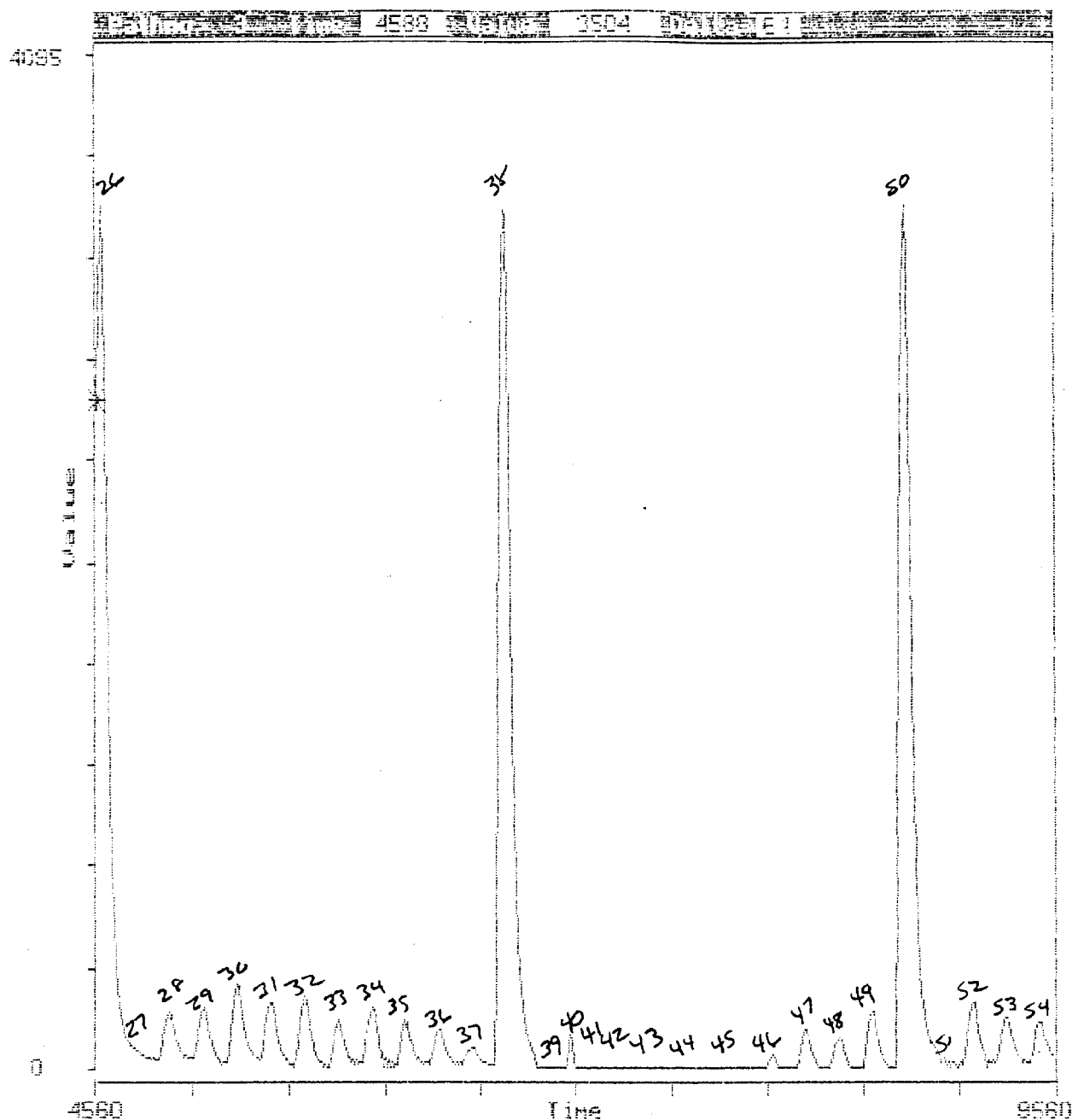
BEST COPY AVAILABLE



Esc=Exit : F1=Help : Ctrl-P=Edit peaks :

000269

000192

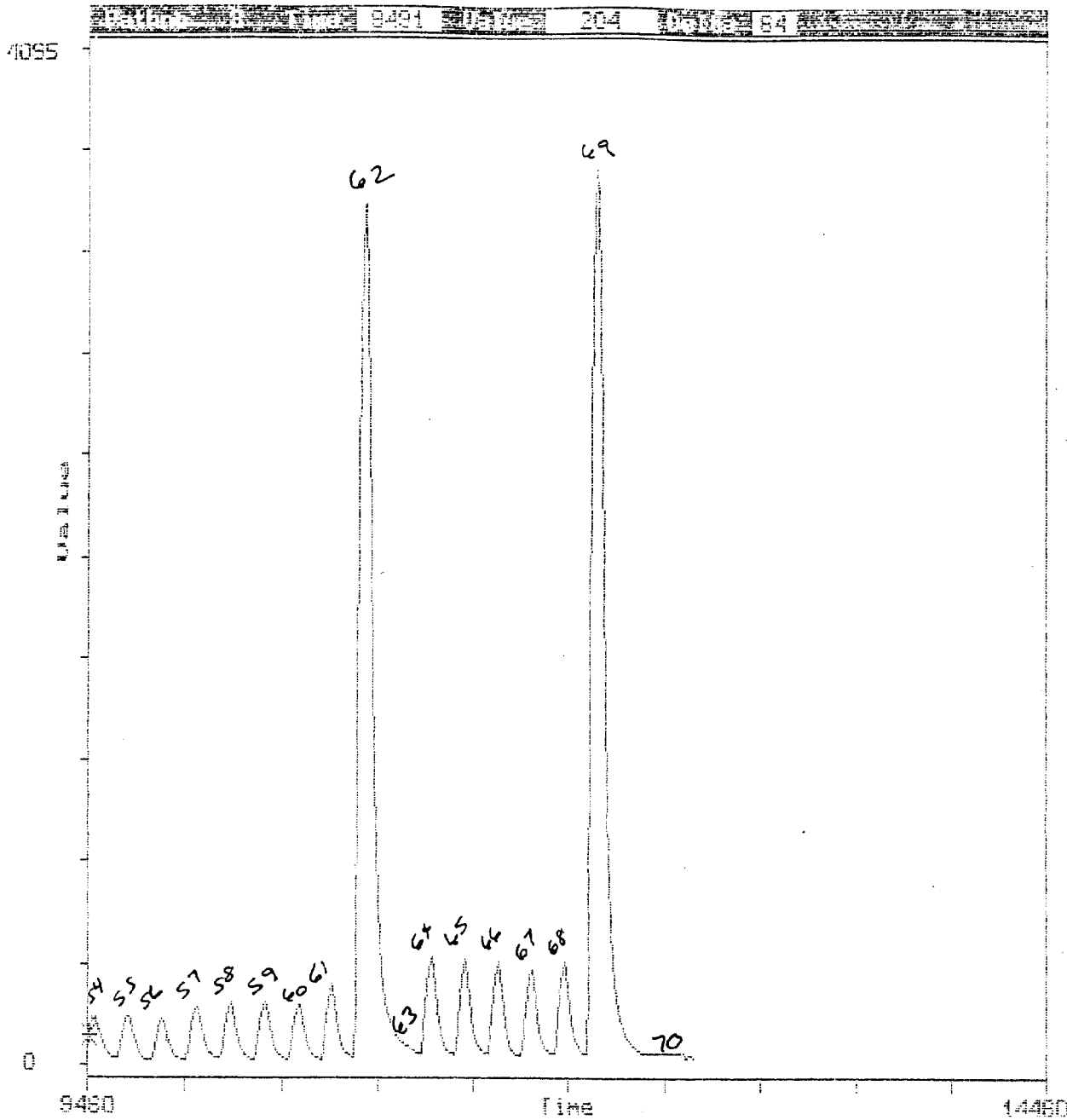


BEST COPY AVAILABLE

sc=Exit | F1=Help | Ctrl-P=Edit peaks |

000270

000193



BEST COPY AVAILABLE

sc=Exit : F1=Help : Ctrl-P=Edit peaks :

000271

00019

DDW 6/22/95
AMDT 42095.1
6329-159 Sewi

luoride 1.5 Path number : 3
Signal type : Debubbled
Decolor : Yes
system Number : 0
diLute : No
Resample : No
dil Threshold : 4095
diG output : 0
Window event : Off

BEST COPY AVAILABLE

s1 sTandard : Ignore
s2 sTandard : Ignore
s3 sTandard : Ignore
s4 sTandard : Ignore
s5 sTandard : Ignore
s6 sTandard : 0.150
s7 sTandard : 0.300
s8 sTandard : 0.600
s9 sTandard : 1.200
s10 sTandard : 1.500
Order : Inverse Logarithm
Dimension : PPM
start Value : 500 DU
trigger Limit : 1800 Sec
Peak shape : Pointed
stArt ignore : 60 Sec
eNd ignore : 120 Sec
Measure window : 75 %
Filter : No
Regeneration : No
formUla :
output : ##.###

luoride L Path number : 0
Signal type : Debubbled
Decolor : No
system Number : 0
diLute : No
Resample : No
dil Threshold : 4095
diG output : 0
Window event : Off

000273

000196

995-05-09 15:09

OutPut of : 950509A1

```
s1  sTandard :    0.015
s2  sTandard :    0.030
s3  sTandard :    0.060
s4  sTandard :    0.090
s5  sTandard :    0.120
s6  sTandard :    0.150
s7  sTandard : Ignore
s8  sTandard : Ignore
s9  sTandard : Ignore
s10 sTandard : Ignore
Order : 2
Dimension : PPM
start Value : 500 DU
trigger Limit : 1800 Sec
Peak shape : Pointed
stArt ignore : 60 Sec
eNd ignore : 120 Sec
Measure window : 75 %
Filter : No
Regeneration : No
formUla : c4:=c3
output : #.####
```

000274

00019'

3MA01502361

2807.0194

Fluoride 1.5

Fluoride L

PPM

PPM

os	Typ	Ident	Ch	Result	F	Time	Ch	Result	F	Time
t	iw	Initial Wash	3	0.057		65	4	#####		0
t		Tracer	3	1.474		209	4	0.7917		0
d		Drift	3	1.502		384	4	0.8031		0
w		Wash	3	0.057		626	4	#####		0
s1		Standard 1	3	0.065		734	4	0.0141		0
s2		Standard 2	3	0.074		910	4	0.0318		0
s3		Standard 3	3	0.088		1082	4	0.0588		0
s4		Standard 4	3	0.107		1260	4	0.0908		0
s5		Standard 5	3	0.128		1435	4	0.1193		0
s6		Standard 6	3	0.153		1610	4	0.1503		0
0	s7	Standard 7	3	0.290		1787	4	0.2726		0
1	s8	Standard 8	3	0.606		1960	4	0.4494		0
2	s9	Standard 9	3	1.233		2135	4	0.6983		0
3	s10	Standard 10	3	1.468		2310	4	0.7892		0
4	d	Drift	3	1.548		2484	4	0.8224		0
5	w	Wash	3	0.057		2726	4	#####		0
6	u	Serum blk 1	3	0.080		2839	4	0.0451		0
7	u	Serum blk 2	3	0.073		3011	4	0.0312		0
8	u	Serum spk 1	3	0.080		3189	4	0.0436		0
9	u	Serum spk 2	3	0.081		3361	4	0.0457		0
0	u	Serum spk 3	3	0.088		3537	4	0.0584		0
1	u	Serum spk 4	3	0.091		3712	4	0.0650		0
2	u	Serum spk 5	3	0.115		3887	4	0.1016		0
3	u	Serum spk 6	3	0.095		4062	4	0.0713		0
4	u	Serum spk 7	3	0.090		4236	4	0.0633		0
5	u	Serum spk 8	3	0.096		4413	4	0.0728		0
6	d	Drift	3	1.509		4587	4	0.8060		0
7	w	Wash	3	0.057		4813	4	#####		0
8	u	F54105-24	3	0.085		4939	4	0.0541		0
9	u	F54075-24	3	0.070		5111	4	0.0236		0
0	u	F54081-24	3	0.068		5282	4	0.0202		0
1	u	F54107-24	3	0.066		5464	4	0.0153		0
2	u	F54104-24	3	0.070		5635	4	0.0236		0
3	u	F54086-24	3	0.067		5814	4	0.0175		0
4	u	F54074-24	3	0.075		5994	4	0.0352		0
5	u	F54085-24	3	0.055	A	6162	4	#####		0
6	u	F54083-24	3	0.055		6336	4	#####		0
7	u	F54100-24	3	0.055		6508	4	#####		0
8	d	Drift	3	1.472		6688	4	0.7909		0
9	w	Wash	3	0.057		6927	4	#####		0
0	u	Blk 1	3	0.073		7038	4	0.0310		0
1	u	Blk 2	3	0.065		7210	4	0.0137		0
2	u	Spk 1	3	0.078		7391	4	0.0402		0
3	u	Spk 2	3	0.086		7565	4	0.0553		0
4	u	Spk 3	3	0.087		7739	4	0.0578		0
5	u	Spk 4	3	0.088		7912	4	0.0592		0
6	u	Spk 5	3	0.093		8091	4	0.0674		0
7	u	Spk 6	3	0.092		8263	4	0.0658		0
8	u	Blk 3	3	0.078		8439	4	0.0412		0
9	u	F54085-24	3	0.066		8615	4	0.0155		0
0	d	Drift	3	1.506		8789	4	0.8050		0
1	w	Wash	3	0.057		9028	4	#####		0
2	u	F54083-24	3	0.068		9142	4	0.0208		0
3	u	F54100-24	3	0.066		9313	4	0.0153		0

BEST COPY AVAILABLE

000198

000275

SC

Fluoride 1.5

Fluoride L

PPM

PPM

os	Typ	Ident	Ch	Result	F	Time	Ch	Result	F	Time
4	u	F54077-24	3	0.067		9489	4	0.0169		0
5	u	F54094-24	3	0.065		9663	4	0.0133		0
6	u	F54091-24	3	0.065		9842	4	0.0139		0
7	u	F54108-24	3	0.065		10012	4	0.0135		0
8	u	F54102-24	3	0.063		10188	4	0.0090		0
9	u	F54097-24	3	0.070		10364	4	0.0242		0
0	u	F54071-24	3	0.064		10540	4	0.0121		0
1	u	F54093-24	3	0.064		10716	4	0.0106		0
2	d	Drift	3	1.493		10890	4	0.7997		0
3	w	Wash	3	0.057		11098	4	#####		0
4	u	F54095-24	3	0.068		11236	4	0.0208		0
5	u	F54101-24	3	0.067		11414	4	0.0171		0
6	u	F54110-24	3	0.066		11590	4	0.0151		0
7	u	F54096-24	3	0.064		11772	4	0.0117		0
8	u	F54090-24	3	0.084		11943	4	0.0510		0
9	u	F54078-24	3	0.071		12115	4	0.0261		0
0	u	F54088-24	3	0.070		12282	4	0.0242		0
1	u	F54106-24	3	0.805		12480	4	0.5348		0
2	u	F54089-24	3	0.435		12655	4	0.3636		0
3	u	F54087-24	3	0.574		12830	4	0.4347		0
4	d	Drift	3	0.223		13006	4	0.2195		0
5	w	Wash	3	0.057		13117	4	#####		0
6	u	F54080-24	3	0.089		13335	4	0.0606		0
7	u	F54092-24	3	0.084		13517	4	0.0510		0
8	u	F54109-24	3	0.077		13693	4	0.0389		0
9	u	F54114-24	3	0.074		13865	4	0.0322		0
0	u	Blk 1	3	0.068		14042	4	0.0204		0
1	u	Blk 2	3	0.066		14218	4	0.0145		0
2	u	Spk 1	3	0.105		14392	4	0.0873		0
3	u	Spk 2	3	0.118		14568	4	0.1063		0
4	u	F54113-24	3	0.088		14743	4	0.0584		0
5	u	F54082-24	3	0.079		14918	4	0.0430		0
6	d	Drift	3	1.423		15092	4	0.7713		0
7	w	Wash	3	0.057		15331	4	#####		0
8	u	F54111-24	3	0.088		15442	4	0.0592		0
9	u	F54098-24	3	0.086		15618	4	0.0549		0
0	u	F54084-24	3	0.084		15794	4	0.0514		0
1	u	F54079-24	3	0.083		15968	4	0.0500		0
2	u	F54116-24	3	0.088		16145	4	0.0598		0
3	d	Drift	3	1.457		16318	4	0.7849		0
4	w	Wash	3	0.057		16558	4	#####		0
rt	rw	RunOut Wash	3	0.057		16793	4	#####		0

BEST COPY AVAILABLE

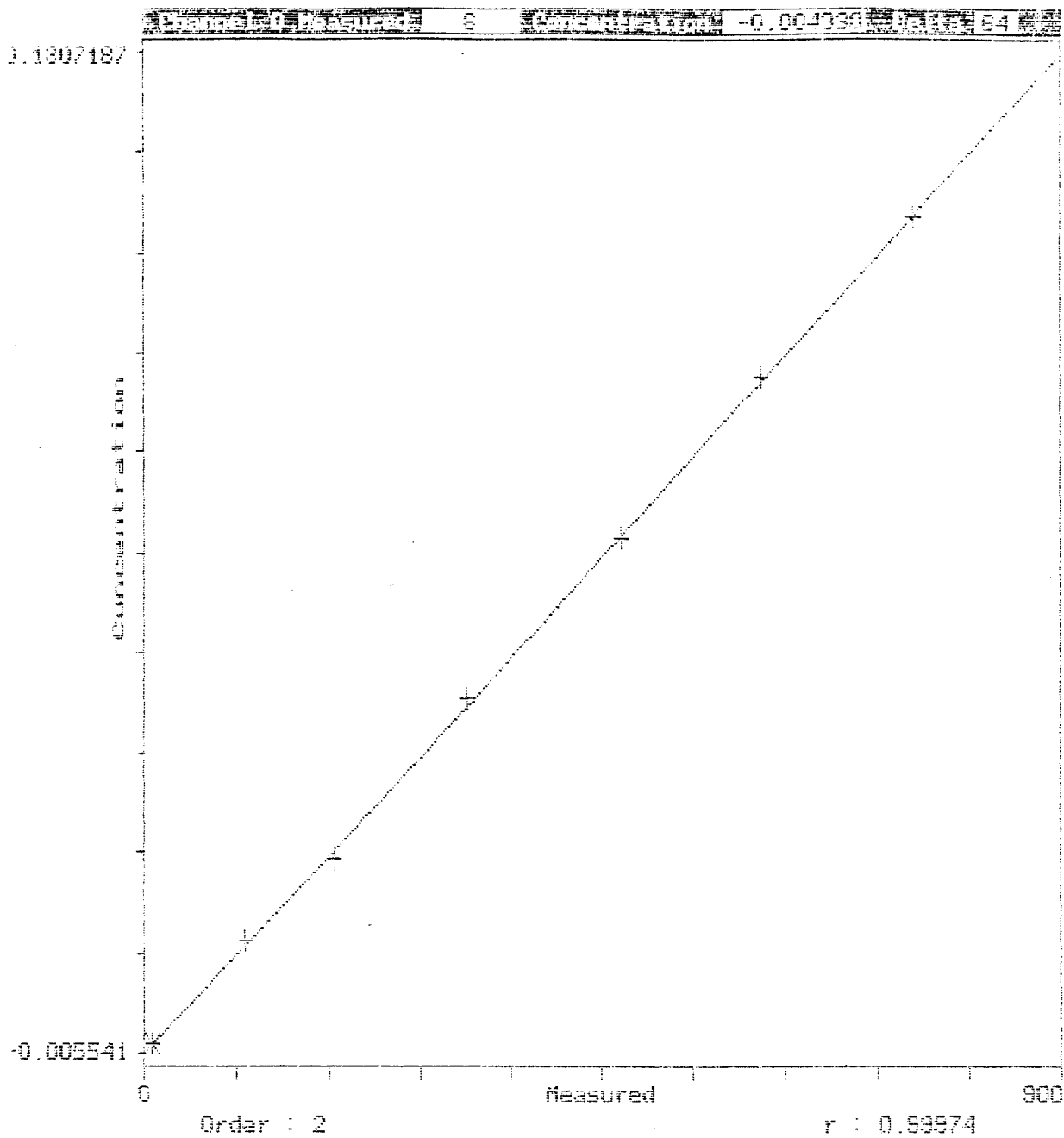
— 0 cup not filled completely
DOW 3/9/95

000276

000199

BEST COPY AVAILABLE

Calibration curve of 850508A1 : Fluoride L

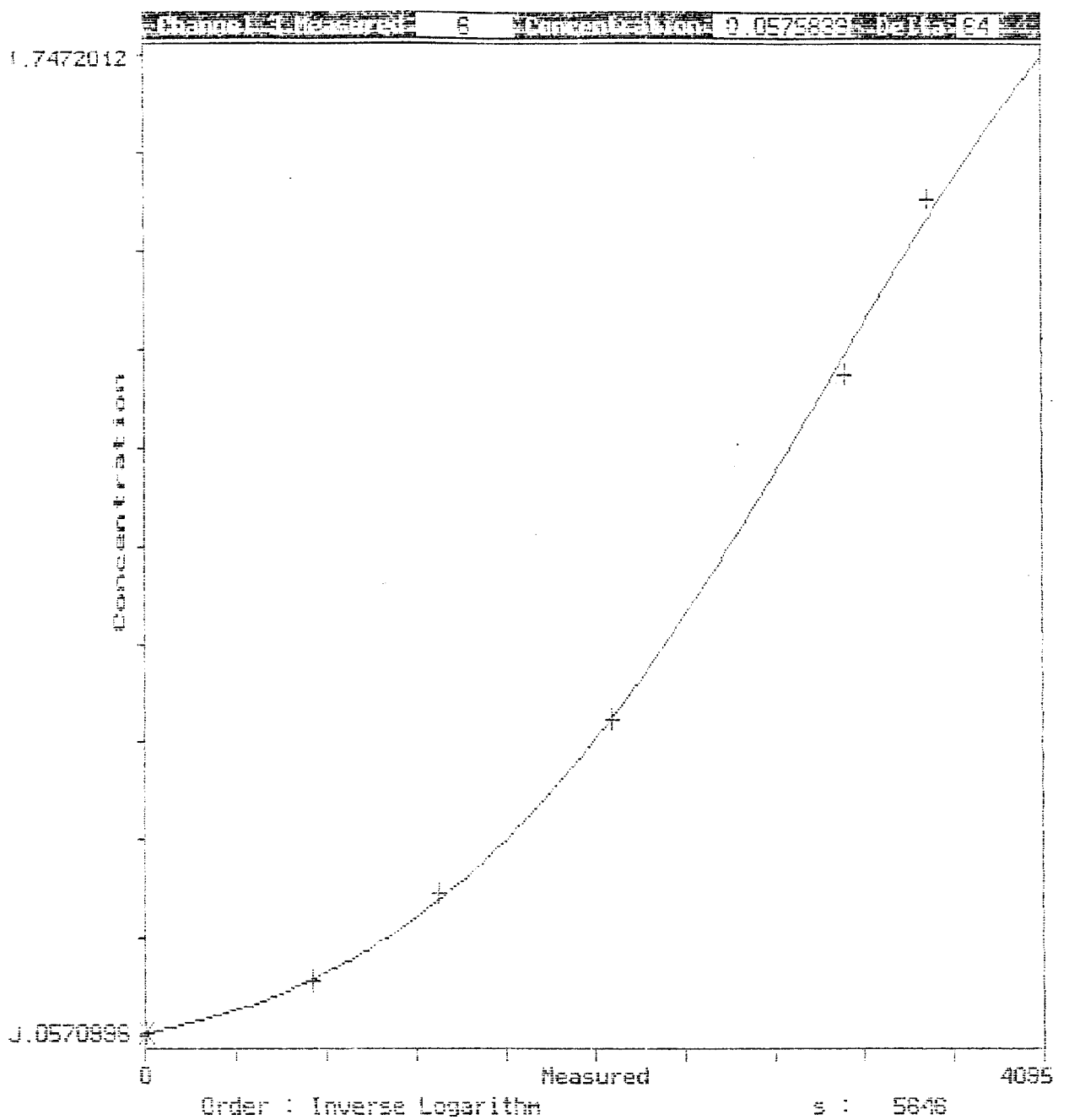


000277

000200

2807.0197

3MA01502364



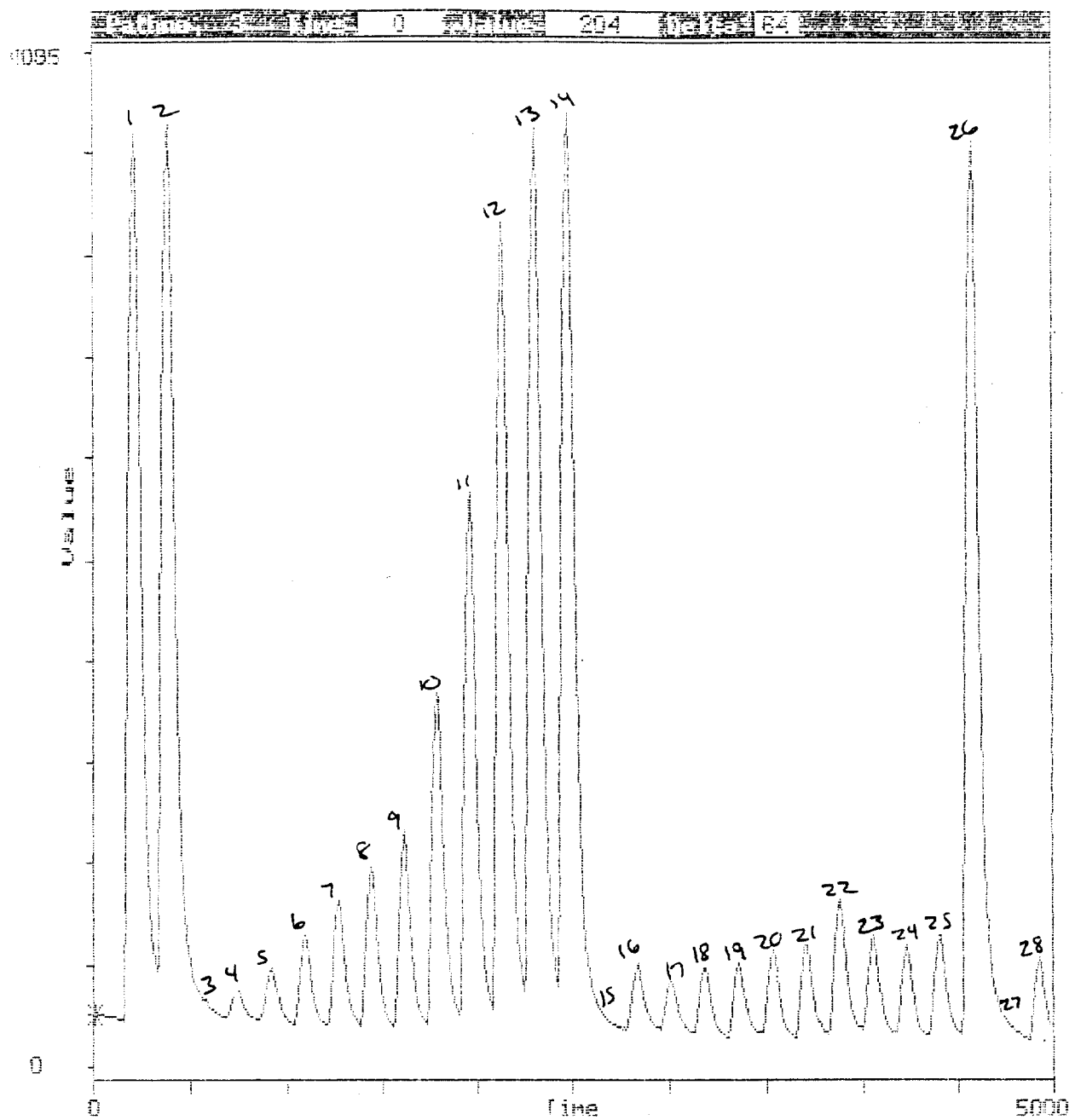
BEST COPY AVAILABLE

000278

000201

5'

BEST COPY AVAILABLE

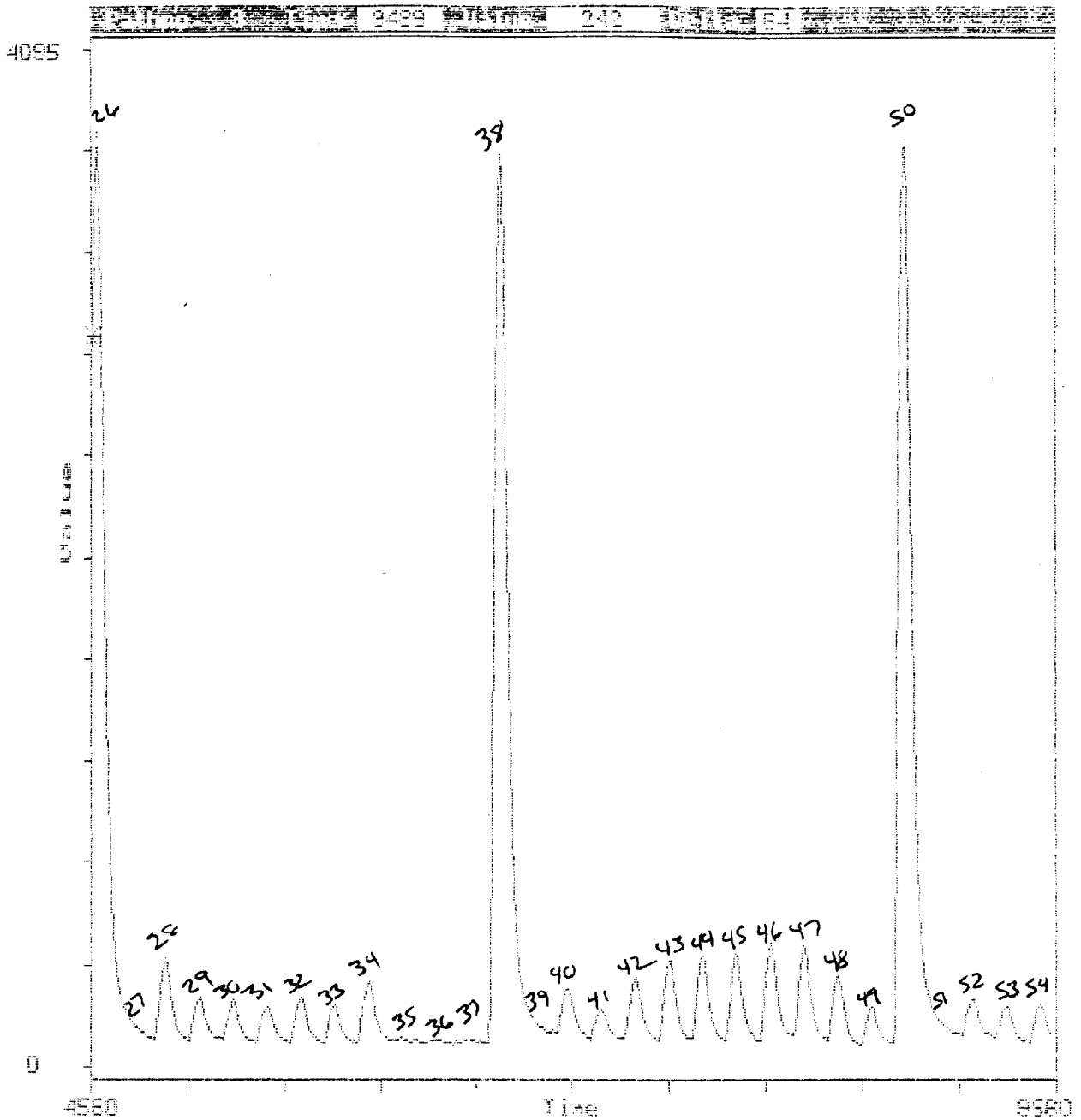


sc=Exit | F1=Help | Ctrl-P=Edit peaks |

000279

000202

Raw data of 85850841 : Fluoride 1.5

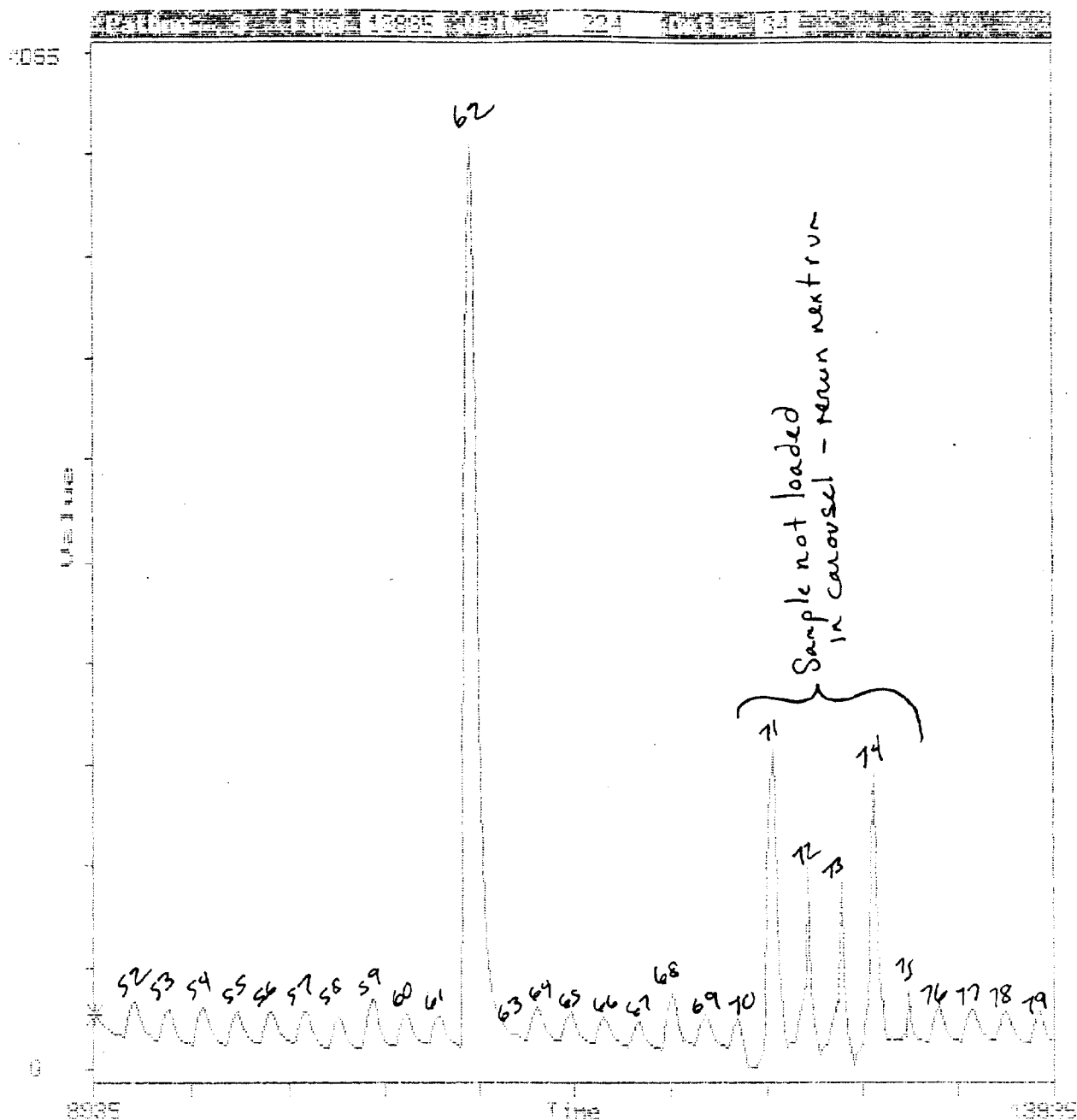


sc=Exit : F1=Help : Ctrl-P=Edit peaks :

000280

000203

BEST COPY AVAILABLE

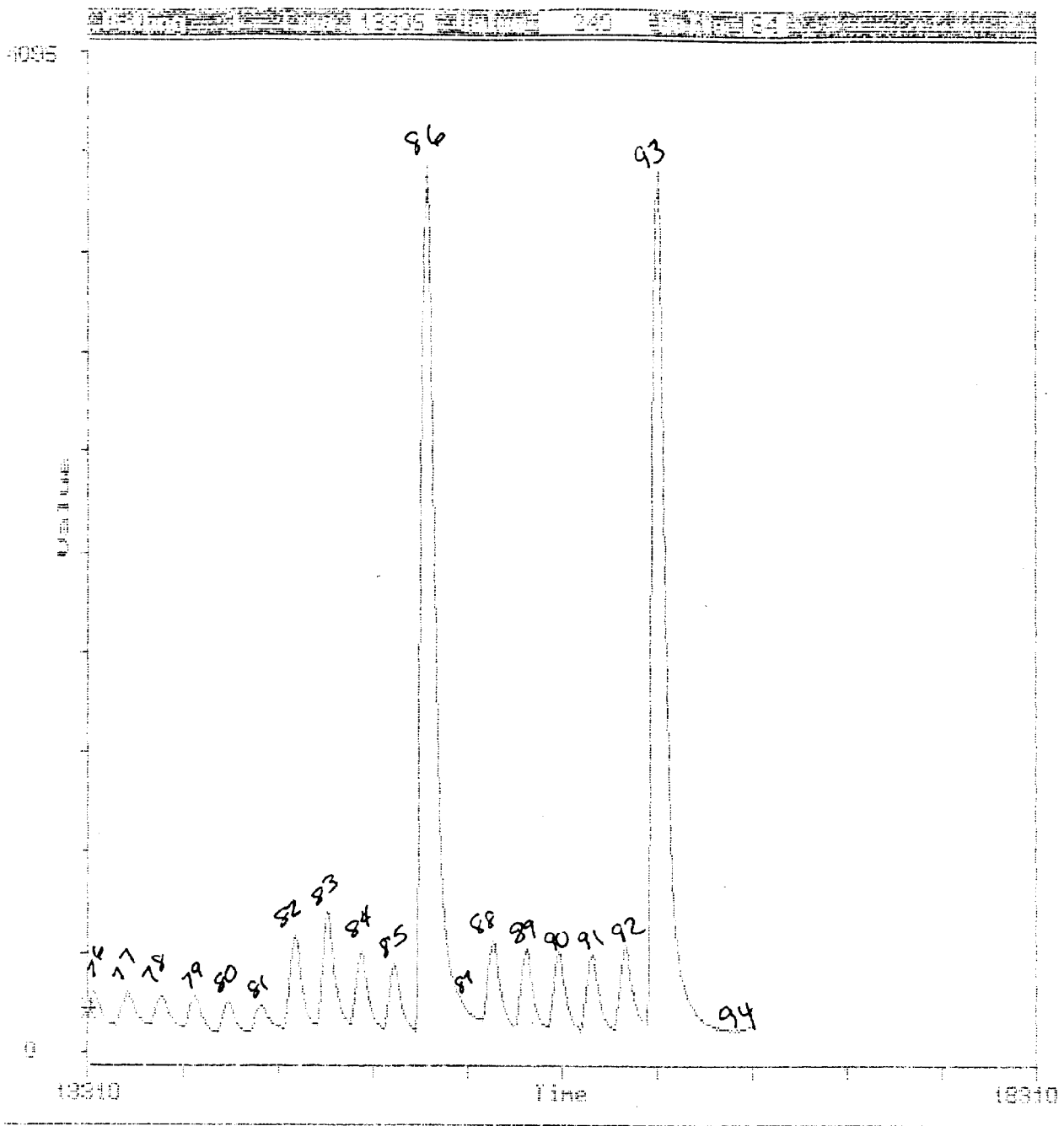


sc=Exit | F1=Help | Ctrl-P=Edit peaks |

000281

000204

BEST COPY AVAILABLE



ac=Exit | F1=Help | Ctrl-P=Edit peaks |

000282

000205

61

OutPut of : 950509B1

```
software : version 6.1  c1990,93
```

operator : DDW

ate of the Analysis : 1995-05-09 15:08

Analysis File Name : C:\SKALAR\DATA\HWIDATA\SERUM\950509B1

'luoride 1.5

calibration original time-date stamp : 1995-05-09 09:48

```
calibration order = Inverse Logarithm
```

Slope : S = #####

$$\text{result} = 10 \left[\frac{x - c1}{s} \right]$$

x = corrected value of the sample
 $c1$ = corrected value of the concentration 1
 s = Slope of the electrode

```

:2 = -0.000000

```

1 = 0.00061

$$10 = -1.24329$$

fluoride L

```

calibration original time-date stamp : 1995-05-09 09:48

```

```
calibration order = 2
```

Correlation : $r = 0.99974$

```
result = a2 * x2 + a1 * x + a0
```

$$2 = 0.00000$$
$$.1 = 0.00020$$
$$C_0 = -0.00554$$

```

amplifier      Type      : SA1000
                Number    : 1
                Sample Time : 50 sec.
                Wash Time   : 120 sec.
                Air Time    : 1 sec.
                Take up     : Single
                sPECIAL     : None
                needle Height : 70 mm.

```

```

diluter      needle Height   : 80      mm
              dilution Factor : 10
              dilution Volume  : 2.5    ml.
              Resample         : 1
              Dilution runs    : 1

```

```
User file : . TXT
Reproces : No
```

BEST COPY AVAILABLE

000283

000206

3MA01502370

2807.0203

fluoride 1.5 Path number : 3
Signal type : Debubbled
Decolor : Yes
system Number : 0
diLute : No
Resample : No
dil Threshold : 4095
diG output : 0
Window event : Off

s1 sTandard : Ignore
s2 sTandard : Ignore
s3 sTandard : Ignore
s4 sTandard : Ignore
s5 sTandard : Ignore
s6 sTandard : 0.150
s7 sTandard : 0.300
s8 sTandard : 0.600
s9 sTandard : 1.200
s10 sTandard : 1.500
Order : Inverse Logarithm
Dimension : PPM
start Value : 500 DU
trigger Limit : 1800 Sec
Peak shape : Pointed
stArt ignore : 60 Sec
eNd ignore : 120 Sec
Measure window : 75 %
Filter : No
Regeneration : No
formUla :
output : ##.###

fluoride L Path number : 0
Signal type : Debubbled
Decolor : No
system Number : 0
diLute : No
Resample : No
dil Threshold : 4095
diG output : 0
Window event : Off

BEST COPY AVAILABLE

000284

000207

s1 sTandard : 0.015
s2 sTandard : 0.030
s3 sTandard : 0.060
s4 sTandard : 0.090
s5 sTandard : 0.120
s6 sTandard : 0.150
s7 sTandard : Ignore
s8 sTandard : Ignore
s9 sTandard : Ignore
s10 sTandard : Ignore
Order : 2
Dimension : PPM
start Value : 500 DU
trigger Limit : 1800 Sec
Peak shape : Pointed
stArt ignore : 60 Sec
eNd ignore : 120 Sec
Measure window : 75 %
Filter : No
Regeneration : No
formUla : c4:=c3
output : #.####

000285

000208

66

Fluoride 1.5 Fluoride L
PPM PPM

os	Typ	Ident	Ch	Result	F	Time	Ch	Result	F	Time
t	iw	Initial Wash	3	0.057		65	4	#####		0
t		Tracer	3	1.509		212	4	0.8062		0
d		Drift	3	1.520		386	4	0.8106		0
w		Wash	3	0.057		651	4	#####		0
u		F54106-24	3	0.080		745	4	0.0438		0
u		F54089-24	3	0.083		944	4	0.0494		0
u		F54087-24	3	0.078		1093	4	0.0406		0
d		Drift	3	1.619		1262	4	0.8540		0
w		Wash	3	0.057		1503	4	#####		0
t	rw	Run out wash	3	0.057		1737	4	#####		0

BEST COPY AVAILABLE

000286

000286

Fluoride 1.5

Fluoride L

PPM

PPM

os	Typ	Ident	Ch	Result	F	Time	Ch	Result	F	Time
t	iw	Initial Wash	3	0.057		65	4	#####		0
t		Tracer	3	1.490		212	4	0.7985		0
d		Drift	3	1.482		386	4	0.7951		0
w		Wash	3	0.057		551	4	#####		0
u		F54106-24	3	0.113		751	4	0.0989		0
u		F54089-24	3	0.159		926	4	0.1577		0
u		F54087-24	3	0.108		1101	4	0.0916		0
d		Drift	3	1.609		1262	4	0.8493		0
w		Wash	3	0.057		1503	4	#####		0
t	rw	Run out wash	3	0.057		1737	4	#####		0

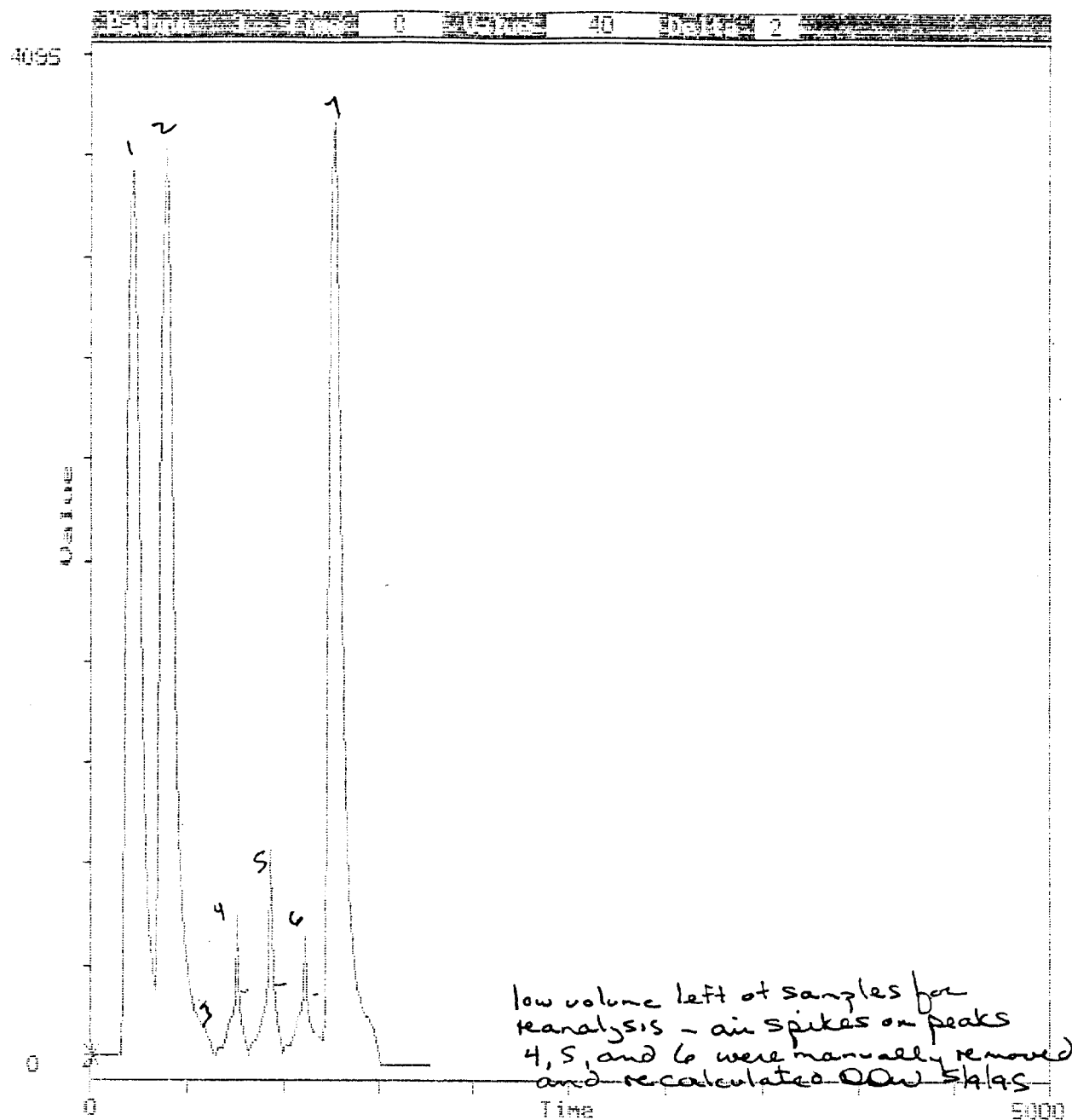
BEST COPY AVAILABLE

low volumes left for reanalysis
are spikes present in peaks
4-6. Manually remove, recalc
and reprint 5/1/95 ODU

000287

000210

BEST COPY AVAILABLE



sc=Exit | F1=Help | Ctrl-P=Edit peaks |

000288

000211

1.0

DDW 6/22/95
AMDT 42095.
6329-159 Sew

luoride 1.5 Path number : 3
Signal type : Debubbled
Decolor : Yes
system Number : 0
diLute : No
Resample : No
dil Threshold : 4095
diG output : 0
Window event : Off

BEST COPY AVAILABLE

s1 sTandard : Ignore
s2 sTandard : Ignore
s3 sTandard : Ignore
s4 sTandard : Ignore
s5 sTandard : Ignore
s6 sTandard : 0.150
s7 sTandard : 0.300
s8 sTandard : 0.600
s9 sTandard : 1.200
s10 sTandard : 1.500
Order : Inverse Logarithm
Dimension : PPM
start Value : 500 DU
trigger Limit : 1800 Sec
Peak shape : Pointed
stArt ignore : 60 Sec
eNd ignore : 120 Sec
Measure window : 75 %
Filter : No
Regeneration : No
formUla :
output : ##.###

luoride L Path number : 0
Signal type : Debubbled
Decolor : No
system Number : 0
diLute : No
Resample : No
dil Threshold : 4095
diG output : 0
Window event : Off

000290

000213

995-05-11 13:19

OutPut of : 950511A1

s1 sTandard : 0.015
s2 sTandard : 0.030
s3 sTandard : 0.060
s4 sTandard : 0.090
s5 sTandard : 0.120
s6 sTandard : 0.150
s7 sTandard : Ignore
s8 sTandard : Ignore
s9 sTandard : Ignore
s10 sTandard : Ignore
Order : 2
Dimension : PPM
start Value : 500 DU
trigger Limit : 1800 Sec
Peak shape : Pointed
stArt ignore : 60 Sec
eNd ignore : 120 Sec
Measure window : 75 %
Filter : No
Regeneration : No
formUla : c4:=c3
output : #.####

000291

000214

2807.0211

3MA01502378

Fluoride 1.5

Fluoride L

PPM

PPM

Pos	Typ	Ident	Ch	Result	F	Time	Ch	Result	F	Time
1	iw	Initial Wash	3	0.057		65	4	#####		0
2	t	Tracer	3	1.472		208	4	0.7342		0
3	d	Drift	3	1.472		382	4	0.7342		0
4	w	Wash	3	0.057		624	4	#####		0
5	s1	Standard 1	3	0.064		729	4	0.0164		0
6	s2	Standard 2	3	0.070		913	4	0.0287		0
7	s3	Standard 3	3	0.085		1085	4	0.0586		0
8	s4	Standard 4	3	0.107		1260	4	0.0921		0
9	s5	Standard 5	3	0.127		1435	4	0.1194		0
10	s6	Standard 6	3	0.153		1610	4	0.1498		0
11	s7	Standard 7	3	0.289		1784	4	0.2642		0
12	s8	Standard 8	3	0.607		1959	4	0.4285		0
13	s9	Standard 9	3	1.233		2133	4	0.6527		0
14	s10	Standard 10	3	1.468		2309	4	0.7329		0
15	d	Drift	3	1.509		2484	4	0.7476		0
16	w	Wash	3	0.057		2725	4	#####		0
17	u	F54113-48	3	0.094		2836	4	0.0722		0
18	u	F54082-48	3	0.091		3011	4	0.0685		0
19	u	F54111-48	3	0.096		3185	4	0.0758		0
20	u	F54098-48	3	0.091		3359	4	0.0685		0
21	u	F54084-48	3	0.103		3537	4	0.0863		0
22	u	F54079-48	3	0.082		3711	4	0.0523		0
23	u	F54116-48	3	0.101		3887	4	0.0844		0
24	u	F54113-192	3	0.097		4061	4	0.0775		0
25	u	F54082-192	3	0.089		4237	4	0.0639		0
26	u	F54111-192	3	0.081		4413	4	0.0512		0
27	d	Drift	3	1.435		4585	4	0.7213		0
28	w	Wash	3	0.057		4732	4	#####		0
29	u	F54098-192	3	0.088		4936	4	0.0626		0
30	u	F54079-192	3	0.089		5111	4	0.0639		0
31	u	F54084-192	3	0.094		5286	4	0.0729		0
32	u	F54116-192	3	0.085		5458	4	0.0573		0
33	u	F54113-360	3	0.085		5638	4	0.0586		0
34	u	F54082-360	3	0.073		5810	4	0.0353		0
35	u	F54111-360	3	0.087		5984	4	0.0611		0
36	u	F54098-360	3	0.082		6164	4	0.0519		0
37	u	F54079-360	3	0.091		6336	4	0.0681		0
38	u	F54084-360	3	0.092		6513	4	0.0699		0
39	d	Drift	3	1.481		6686	4	0.7374		0
40	w	Wash	3	0.057		6926	4	#####		0
41	u	F54116-360	3	0.109		7039	4	0.0959		0
42	u	BLK 1	3	0.065		7213	4	0.0188		0
43	u	SPK 1	3	0.094		7387	4	0.0727		0
44	u	SPK 2	3	0.112		7565	4	0.1002		0
45	u	F54082-D22	3	0.085		7739	4	0.0586		0
46	u	F54111-D22	3	0.084		7912	4	0.0569		0
47	u	F54079-D22	3	0.083		8085	4	0.0536		0
48	u	F54116-D22	3	0.083		8263	4	0.0540		0
49	u	F54082-D28	3	0.087		8438	4	0.0607		0
50	u	F54111-D28	3	0.078		8614	4	0.0447		0
51	d	Drift	3	1.519		8787	4	0.7510		0
52	w	Wash	3	0.057		9027	4	#####		0
53	u	F54079-D28	3	0.077		9138	4	0.0431		0
54	u	F54116-D28	3	0.081		9314	4	0.0502		0

BEST COPY AVAILABLE

000215

000292

Fluoride 1.5

Fluoride L

PPM

PPM

BEST COPY AVAILABLE

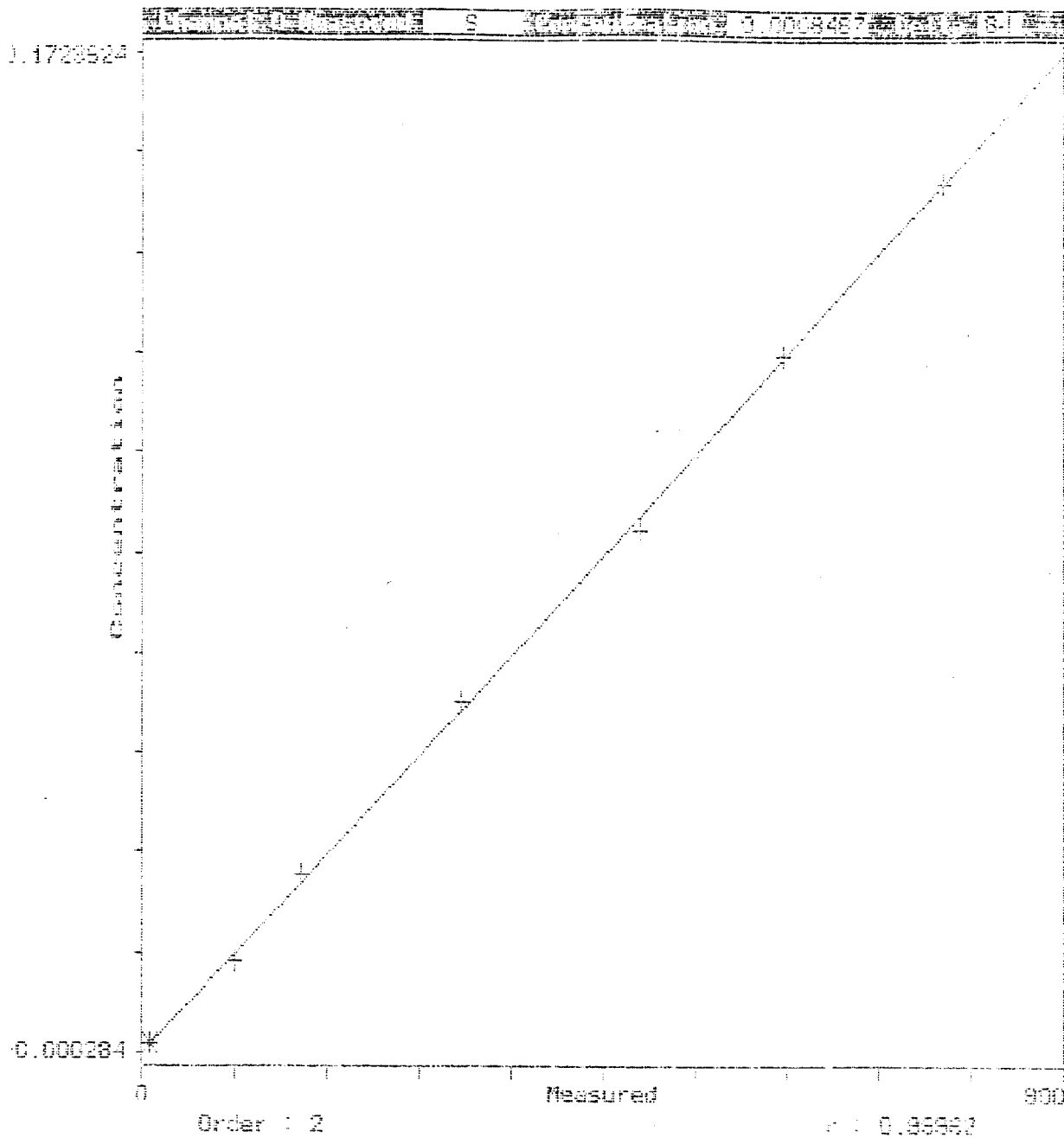
os	Typ	Ident	Ch	Result	F	Time	Ch	Result	F	Time
4	u	F54099-4	3	0.071		9490	4	0.0317		0
5	u	F54099-8	3	0.070		9662	4	0.0298		0
6	u	F54099-12	3	0.105		9840	4	0.0894		0
7	u	F54099-24	3	0.118		10015	4	0.1075		0
3	u	F54099-48	3	0.084		10190	4	0.0569		0
9	u	F54099-192	3	0.074		10362	4	0.0371		0
0	u	F54099-360	3	0.070		10538	4	0.0306		0
1	u	F54099-361	3	0.054	A	10715	4	#####	0	0
2	d	Drift	3	1.504		10888	4	0.7457		0
3	w	Wash	3	0.057		11129	4	#####		0
4	u	F54112-4	3	0.082		11237	4	0.0527		0
5	u	F54112-8	3	0.094		11415	4	0.0735		0
6	u	F54112-12	3	0.100		11591	4	0.0827		0
7	u	F54112-24	3	0.088		11765	4	0.0624		0
8	u	F54112-48	3	0.100		11941	4	0.0815		0
9	u	F54112-192	3	0.094		12115	4	0.0725		0
0	u	F54112-360	3	0.078		12289	4	0.0452		0
1	u	SPK 63-1	3	0.095		12465	4	0.0750		0
2	u	SPK 63-2	3	0.110		12641	4	0.0973		0
3	u	SPK 63-3	3	0.092		12817	4	0.0689		0
4	d	Drift	3	1.469		12989	4	0.7334		0
5	w	Wash	3	0.057		13166	4	#####		0
6	u	SPK 126-1	3	0.117		13342	4	0.1061		0
7	u	SPK 126-2	3	0.149		13518	4	0.1452		0
8	u	SPK 126-3	3	0.157		13692	4	0.1537		0
9	d	Drift	3	1.496		13865	4	0.7427		0
0	w	Wash	3	0.057		14107	4	#####		0
t	rw	RunOut Wash	3	0.057		14340	4	#####		0

Blank inserted - no suc!
sample exists OnQw!

000293

000216

Calibration curve of 99051191 : Fluoride L



BEST COPY AVAILABLE

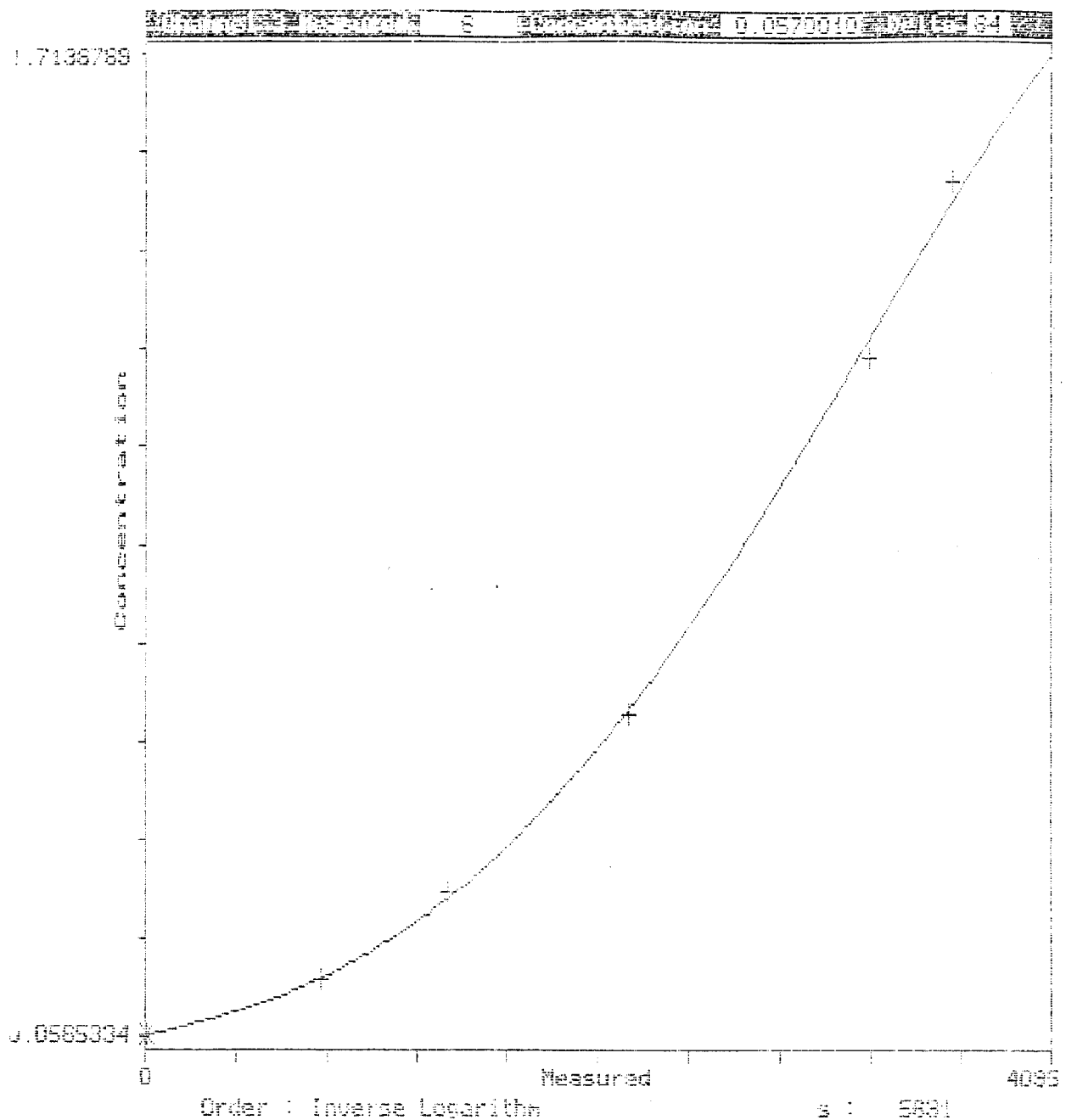
000294

000217

2807.0214

3MA01502381

Calibration curve of 950511A1 : Fluoride 1.5



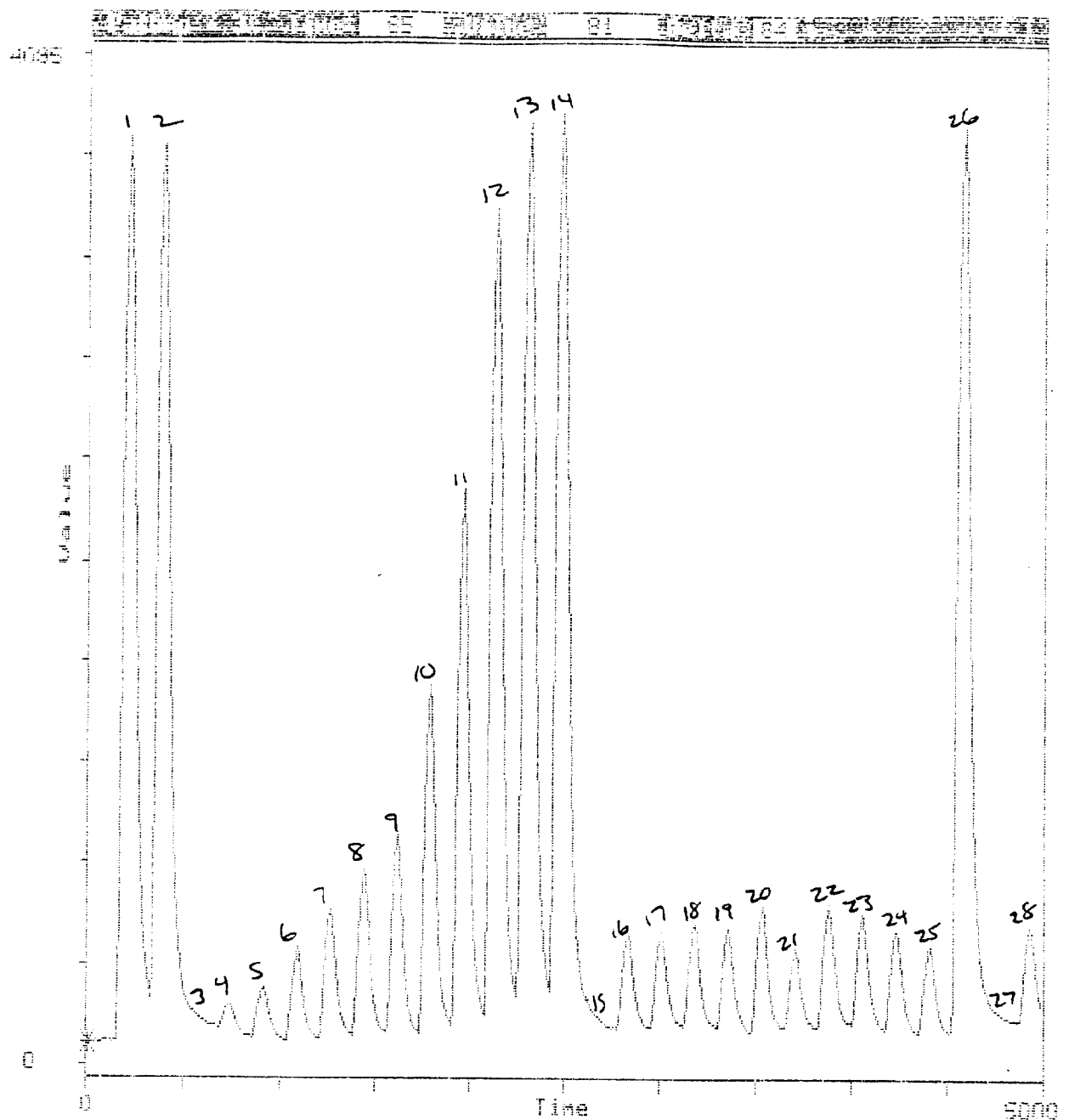
EST COPY AVAILABLE

000295

000218

2807.0215

3MA01502382

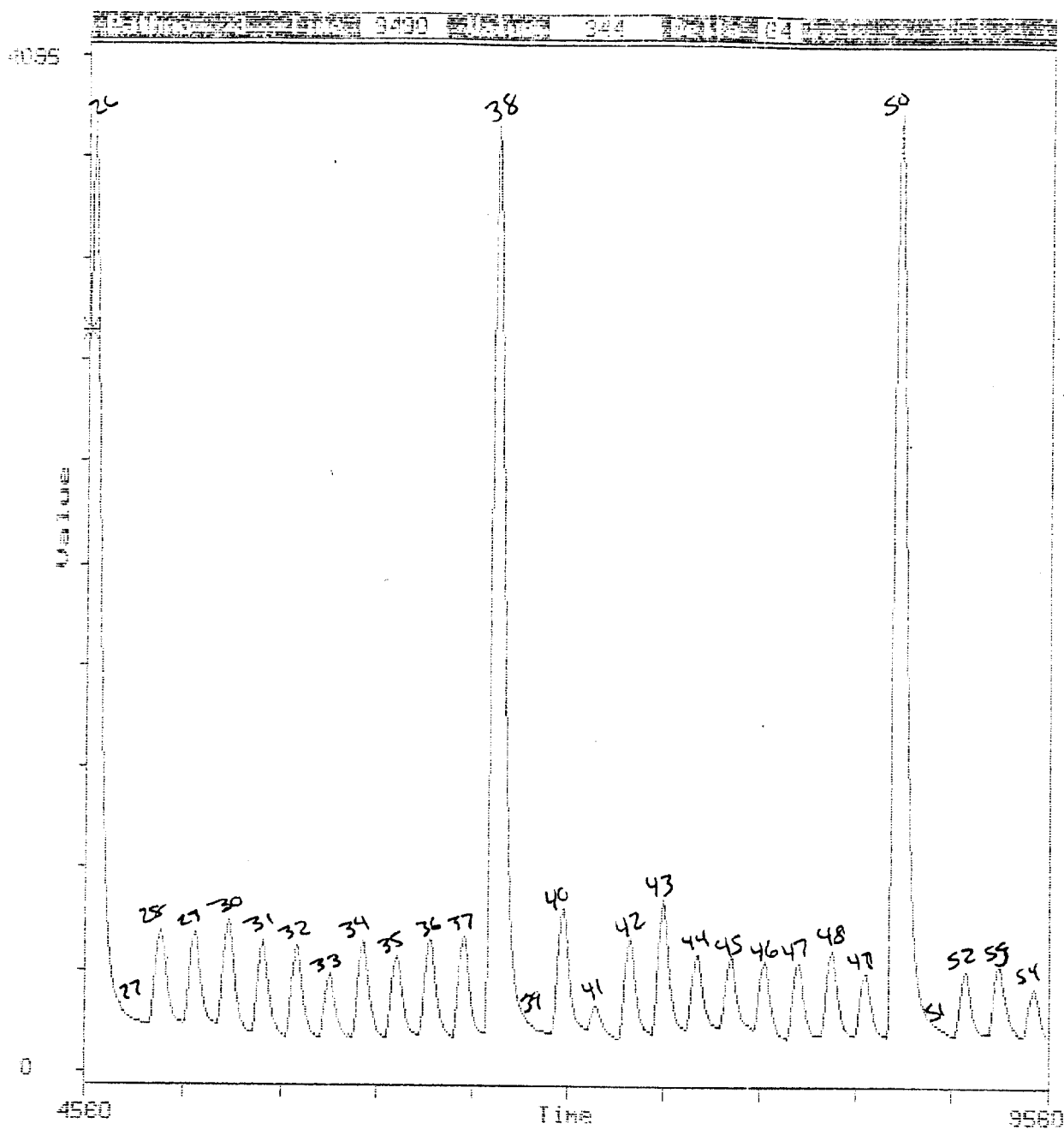


sc-Exit : F1-Help : Ctrl-P=Edit peaks :

BEST COPY AVAILABLE

000296

000219



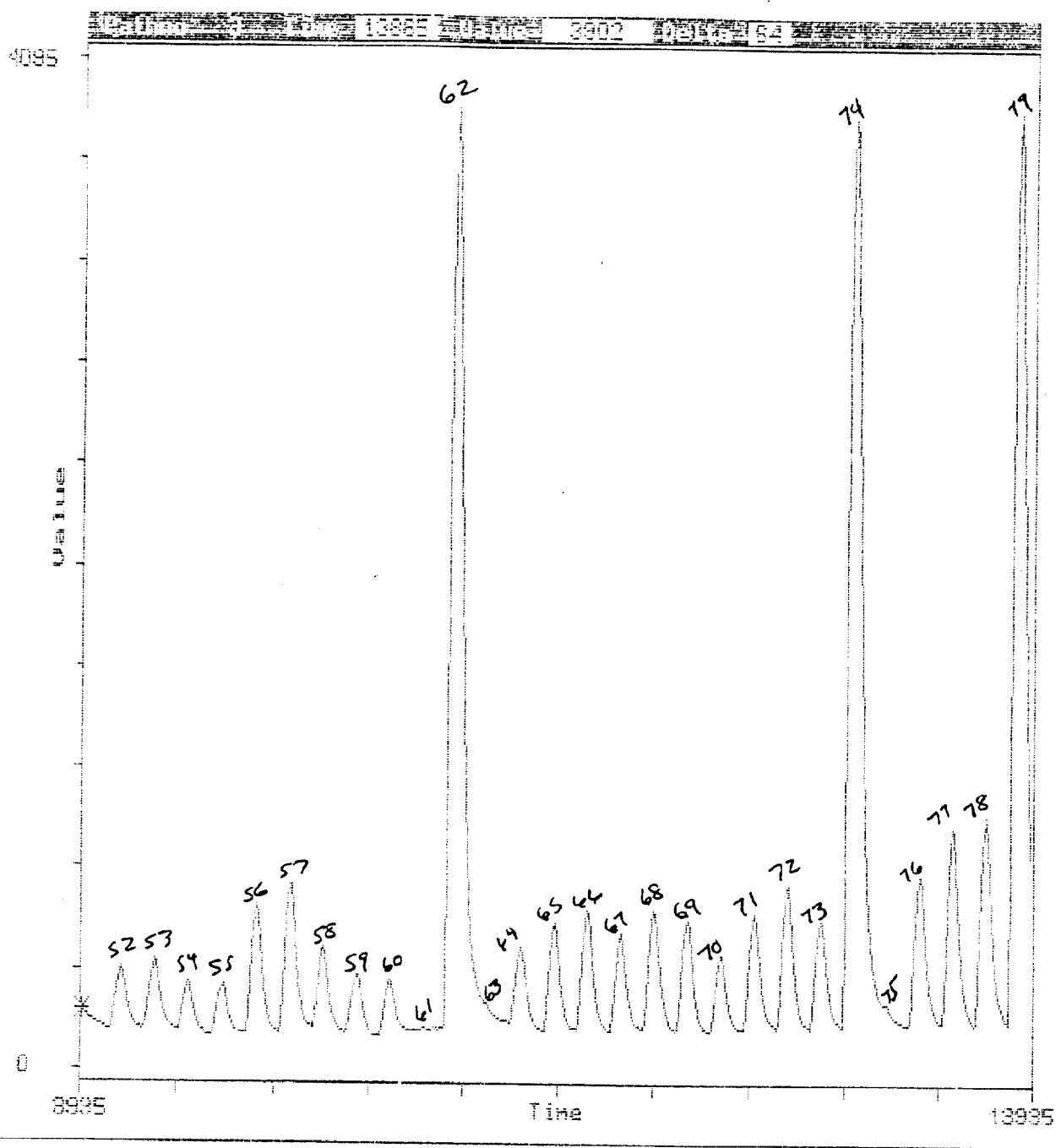
sc=Exit : F1=Help : Ctrl-P=Edit peaks :

BEST COPY AVAILABLE

000297

000220

Raw data of 950511A1 : Fluoride 1.5



sc=Exit / F1=Help / Ctrl-P=Edit peaks /

BEST COPY AVAILABLE

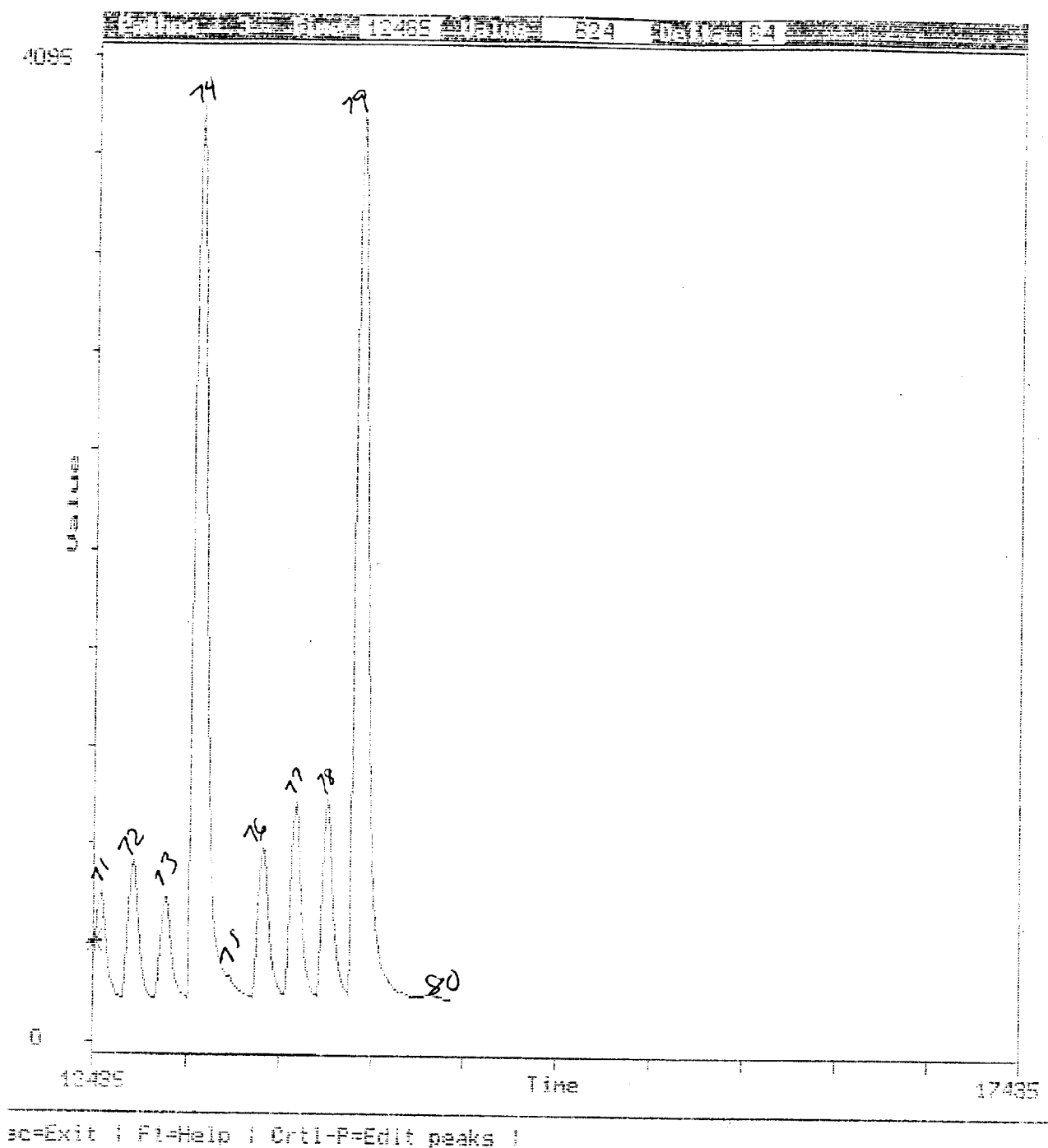
000298

000221

2807.0218

3MA01502385

Raw data of 95051101 : Fluoride 1.5



BEST COPY AVAILABLE

000299

000222

2807.0219

3MA01502386

995-05-24 16:00

OutPut of : 950524A1

DDW 6/22/95
AMDT 42095.1
6329-159 Sewn

Software : version 6.1 c1990,93

Operator : DDW

BEST COPY AVAILABLE

Date of the Analysis : 1995-05-24 11:39

Analysis File Name : C:\SKALAR\DATA\HWIDATA\SERUM\950524A1

Fluoride 1.5

Calibration order = Inverse Logarithm

Slope : S = #.#####

Result = $10^{\left[\frac{x - c1}{s} \right]}$
x = corrected value of the sample
c1 = corrected value of the concentration 1
s = Slope of the electrode

2 = -0.00000
1 = 0.00064
0 = -1.22588

Fluoride L

Calibration order = 2

Correlation : r = 0.99786

Result = a2 * x² + a1 * x + a0

2 = -0.00000
1 = 0.00025
0 = -0.00699

Amplifier Type : SA1000
Number : 1
Sample Time : 50 sec.
Wash Time : 120 sec.
Air Time : 1 sec.
Take up : Single
Special : None
Needle Height : 70 mm.

Diluter
Needle Height : 80 mm
Dilution Factor : 10
Dilution Volume : 2.5 ml.
Resample : 1
Dilution runs : 1

User file : . TXT
Reprocess : No

000300

000223

3MA01502387

2807.0220

BEST COPY AVAILABLE

luoride 1.5 Path number : 3
Signal type : Debubbled
Decolor : Yes
system Number : 0
diLute : No
Resample : No
dil Threshold : 4095
diG output : 0
Window event : Off

s1 sTandard : Ignore
s2 sTandard : Ignore
s3 sTandard : Ignore
s4 sTandard : Ignore
s5 sTandard : Ignore
s6 sTandard : 0.150
s7 sTandard : 0.300
s8 sTandard : 0.600
s9 sTandard : 1.200
s10 sTandard : 1.500
Order : Inverse Logarithm
Dimension : PPM
start Value : 500 DU
trigger Limit : 1800 Sec
Peak shape : Pointed
stArt ignore : 60 Sec
eNd ignore : 120 Sec
Measure window : 75 %
Filter : No
Regeneration : No
formUla :
output : ##.###

luoride L Path number : 0
Signal type : Debubbled
Decolor : No
system Number : 0
diLute : No
Resample : No
dil Threshold : 4095
diG output : 0
Window event : Off

000301

000224

995-05-24 16:01

OutPut of : 950524A1

s1 sTandard : 0.015
s2 sTandard : 0.030
s3 sTandard : 0.060
s4 sTandard : 0.090
s5 sTandard : 0.120
s6 sTandard : 0.150
s7 sTandard : Ignore
s8 sTandard : Ignore
s9 sTandard : Ignore
s10 sTandard : Ignore
Order : 2
Dimension : PPM
start Value : 500 DU
trigger Limit : 1800 Sec
Peak shape : Pointed
stArt ignore : 60 Sec
eNd ignore : 120 Sec
Measure window : 75 %
Filter : No
Regeneration : No
formUla : c4:=c3
output : #.####

000302

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3MA01502389

2807.0222

Fluoride 1.5 Fluoride L

PPM PPM

os	Typ	Ident	Ch	Result	F	Time	Ch	Result	F	Time
t	iw	Initial Wash	3	0.059		65	4	#####		0
t		Tracer	3	1.452		215	4	0.4057		0
d		Drift	3	1.469		389	4	0.4054		0
w		Wash	3	0.059		621	4	#####		0
s1		Standard 1	3	0.069		740	4	0.0180		0
s2		Standard 2	3	0.073		916	4	0.0276		0
s3		Standard 3	3	0.087		1090	4	0.0569		0
s4		Standard 4	3	0.109		1269	4	0.0945		0
s5		Standard 5	3	0.127		1442	4	0.1182		0
s6		Standard 6	3	0.155		1618	4	0.1498		0
0	s7	Standard 7	3	0.284		1790	4	0.2417		0
.	s8	Standard 8	3	0.612		1965	4	0.3431		0
2	s9	Standard 9	3	1.242		2140	4	0.4037		0
3	s10	Standard 10	3	1.458		2314	4	0.4056		0
4	d	Drift	3	1.442		2490	4	0.4058		0
5	w	Wash	3	0.059		2728	4	#####		0
6	u	BLK 1	3	0.075		2841	4	0.0330		0
7	u	BLK 2	3	0.068		3015	4	0.0168		0
3	u	SPK 63-1	3	0.103		3191	4	0.0843		0
9	u	SPK 63-2	3	0.098		3365	4	0.0761		0
0	u	SPK 63-3	3	0.098		3539	4	0.0768		0
1	u	SPK 63-4	3	0.093		3715	4	0.0683		0
2	u	SPK 63-5	3	0.104		3891	4	0.0860		0
3	u	SPK 63-6	3	0.102		4067	4	0.0829		0
4	u	SPK 63-7	3	0.101		4243	4	0.0821		0
5	u	BLK 3	3	0.072		4415	4	0.0264		0
6	d	Drift	3	1.455		4591	4	0.4056		0
7	w	Wash	3	0.059		4831	4	#####		0
3	u	BLK 4	3	0.073		4939	4	0.0273		0
9	u	F54088-48	3	0.068		5118	4	0.0156		0
0	u	F54099-48	3	0.071		5290	4	0.0233		0
1	u	F54089-48	3	0.066		5466	4	0.0110		0
2	u	F54087-48	3	0.069		5644	4	0.0192		0
3	u	F54080-48	3	0.067		5812	4	0.0141		0
4	u	F54092-48	3	0.066		5988	4	0.0095		0
.	u	F54109-48	3	0.070		6168	4	0.0216		0
6	u	F54114-48	3	0.071		6344	4	0.0228		0
7	u	F54088-DY8	3	0.068		6517	4	0.0158		0
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1	u	SPK 63-8	3	0.101		7218	4	0.0812		0
2	u	SPK 63-9	3	0.099		7393	4	0.0774		0
3	u	SPK 63-10	3	0.100		7568	4	0.0790		0
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6	u	SPK 63-1	3	0.088		8093	4	0.0597		0
7	u	SPK 63-2	3	0.098		8267	4	0.0765		0
3	u	SPK 63-3	3	0.102		8443	4	0.0838		0
9	u	F54089-DY8	3	0.072		8619	4	0.0247		0
0	d	Drift	3	1.471		8793	4	0.4054		0
1	w	Wash	3	0.059		9028	4	#####		0
2	u	F54087-DY8	3	0.075		9143	4	0.0328		0
.	u	F54080-DY8	3	0.075		9319	4	0.0323		0

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Fluoride 1.5

Fluoride L

PPM

PPM

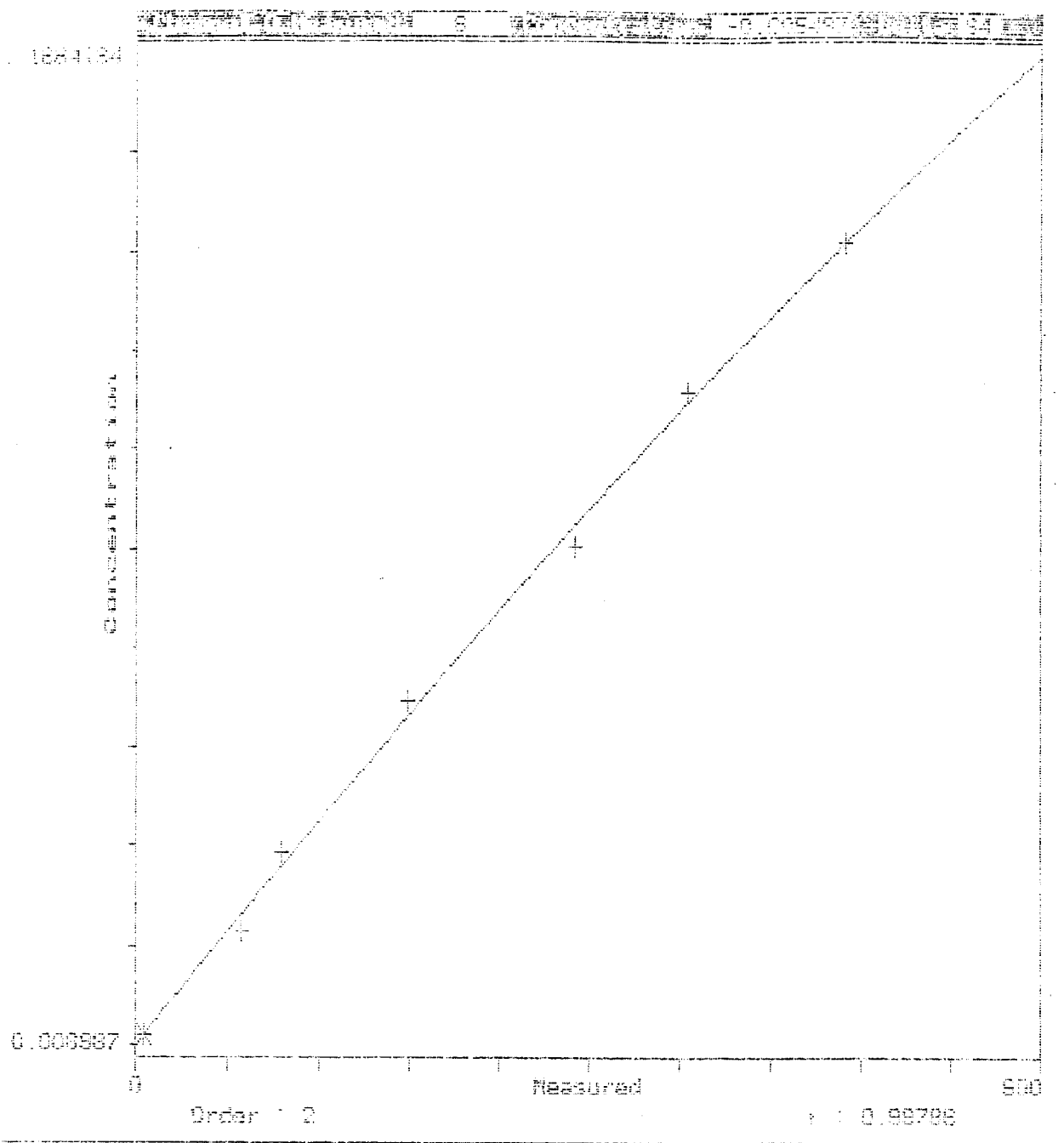
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6	u	F54114-DY8	3	0.077		9843	4	0.0365		0
7	u	F54088-D15	3	0.061		10022	4	#####		0
8	u	F54099-D15	3	0.073		10194	4	0.0266		0
9	u	F54089-D15	3	0.068		10370	4	0.0165		0
0	u	F54087-D15	3	0.069		10542	4	0.0175		0
1	u	F54080-D15	3	0.066		10718	4	0.0107		0
2	d	Drift	3	1.469		10893	4	0.4054		0
3	w	Wash	3	0.059		11133	4	#####		0
4	u	F54092-D15	3	0.070		11244	4	0.0216		0
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6	u	F54114-D15	3	0.068		11594	4	0.0146		0
7	u	F54089-D22	3	0.068		11767	4	0.0158		0
8	u	F54087-D22	3	0.067		11944	4	0.0134		0
9	u	F54109-D22	3	0.068		12118	4	0.0146		0
0	u	F54114-D22	3	0.069		12296	4	0.0170		0
1	u	F54089-D28	3	0.066		12466	4	0.0114		0
2	u	F54087-D28	3	0.068		12642	4	0.0168		0
3	u	F54109-D28	3	0.069		12822	4	0.0170		0
4	d	Drift	3	1.455		12994	4	0.4056		0
5	w	Wash	3	0.059		13222	4	#####		0
6	u	F54114-D28	3	0.069		13345	4	0.0182		0
7	u	SPK 63-4	3	0.078		13515	4	0.0379		0
8	u	SPK 63-5	3	0.089		13695	4	0.0610		0
9	u	SPK 63-6	3	0.098		13872	4	0.0763		0
0	u	SPK 63-7	3	0.097		14045	4	0.0750		0
1	u	F54105-48HR	3	0.069		14224	4	0.0180		0
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3	d	Drift	3	1.411		14569	4	0.4060		0
4	w	Wash	3	0.059		14810	4	#####		0
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000304

000227

Calibration curve of 950524A1 : Fluoride L



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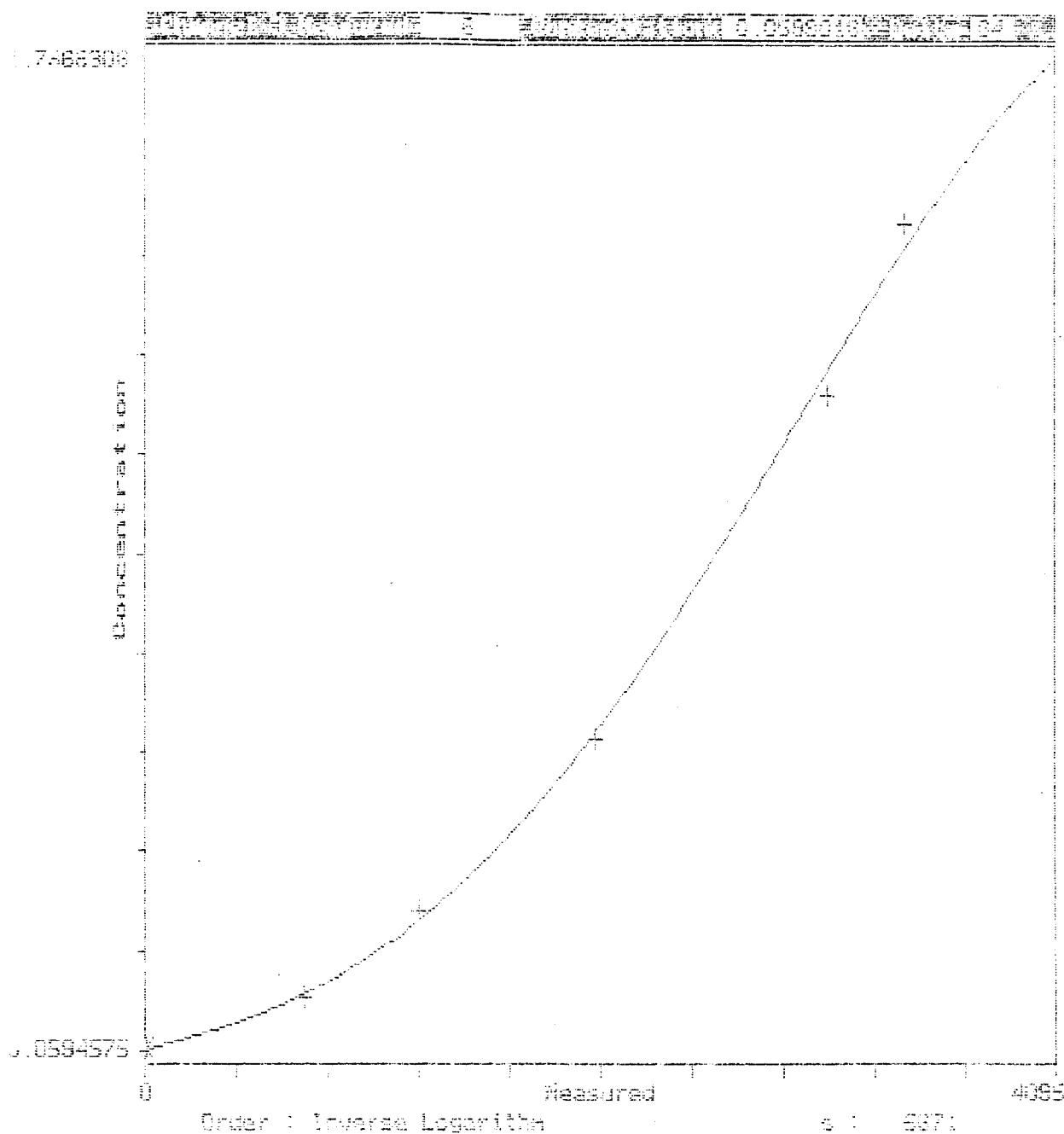
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Calibration curve of 95052401 : Fluoride 1.5



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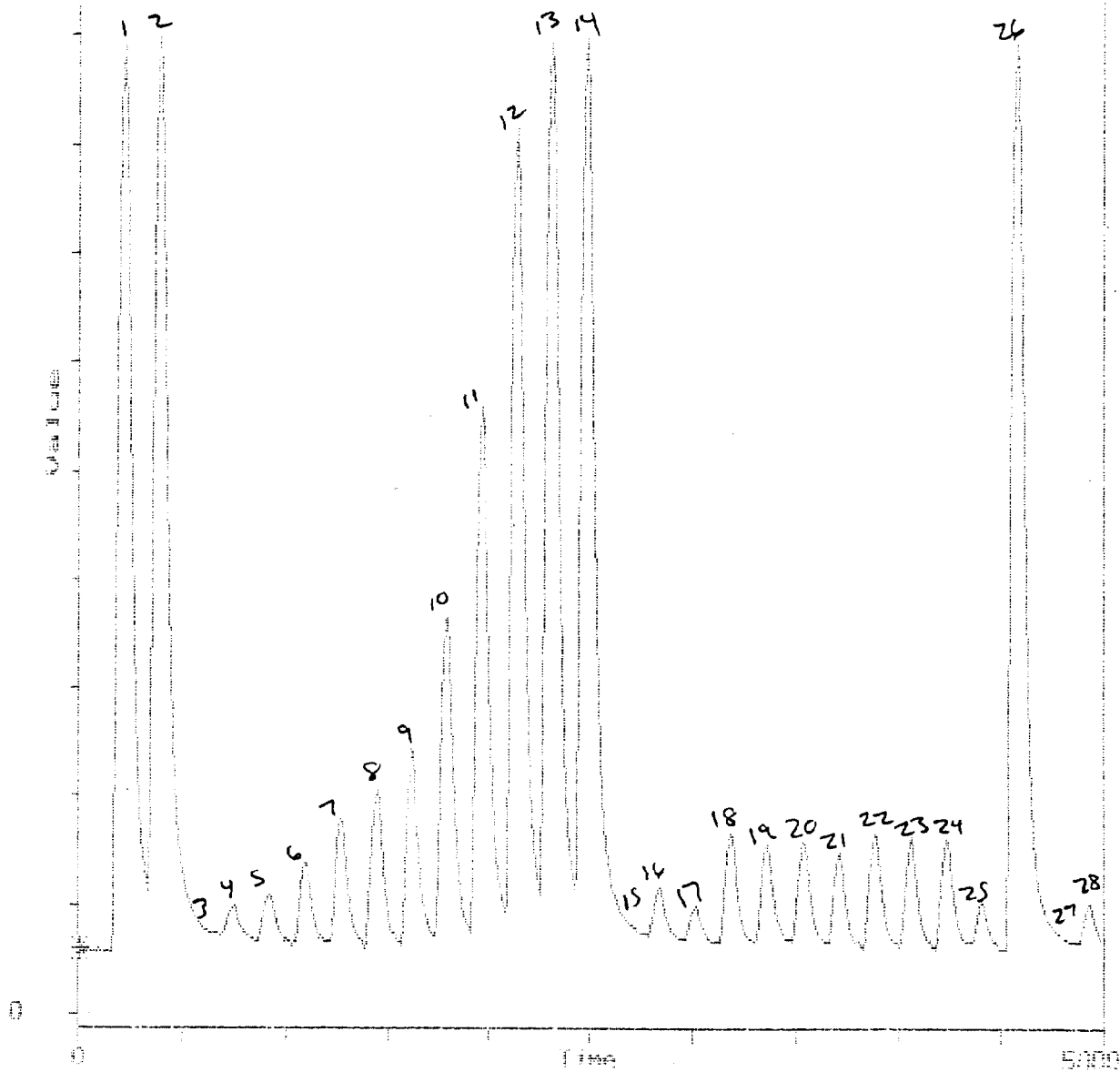
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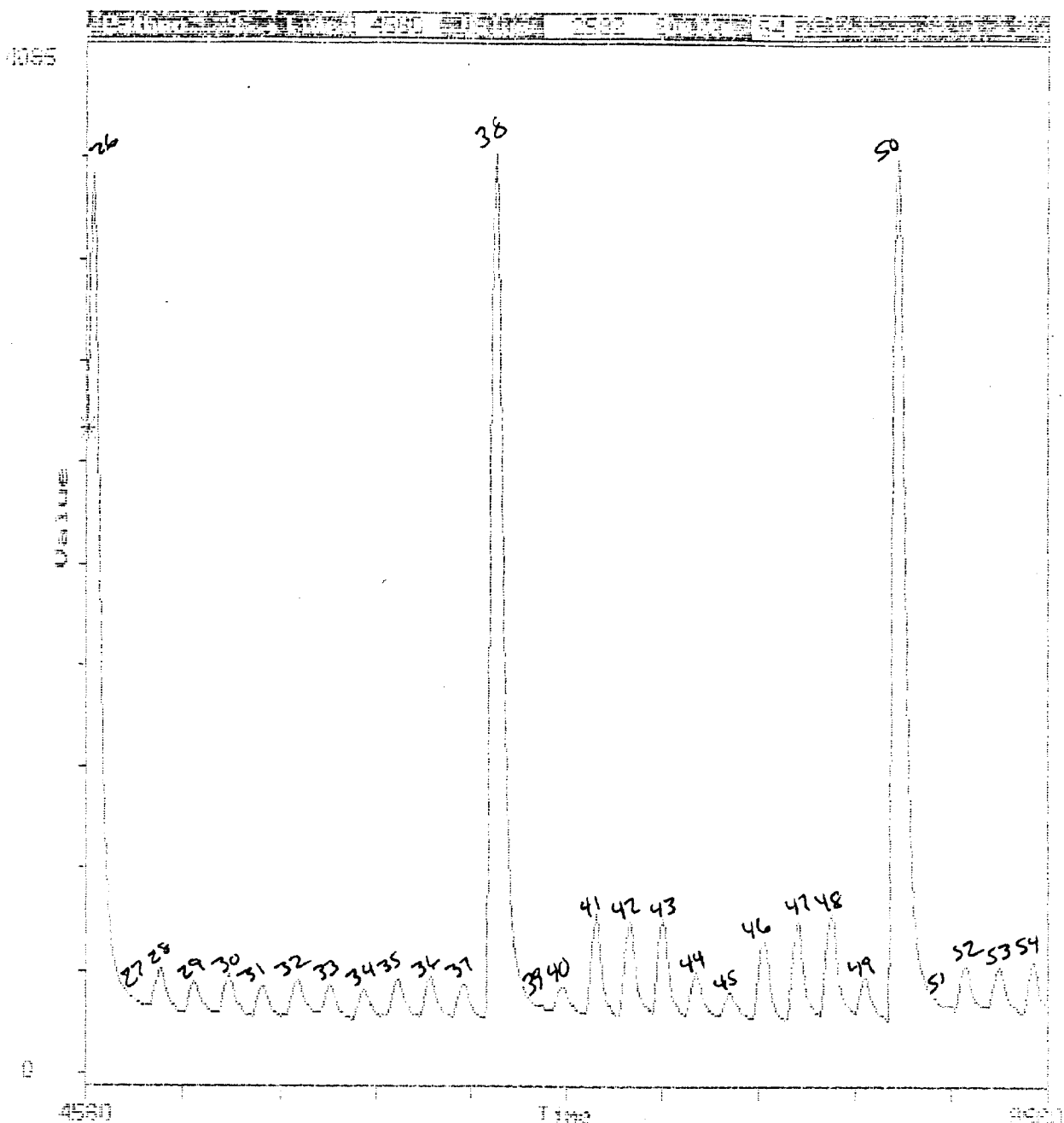


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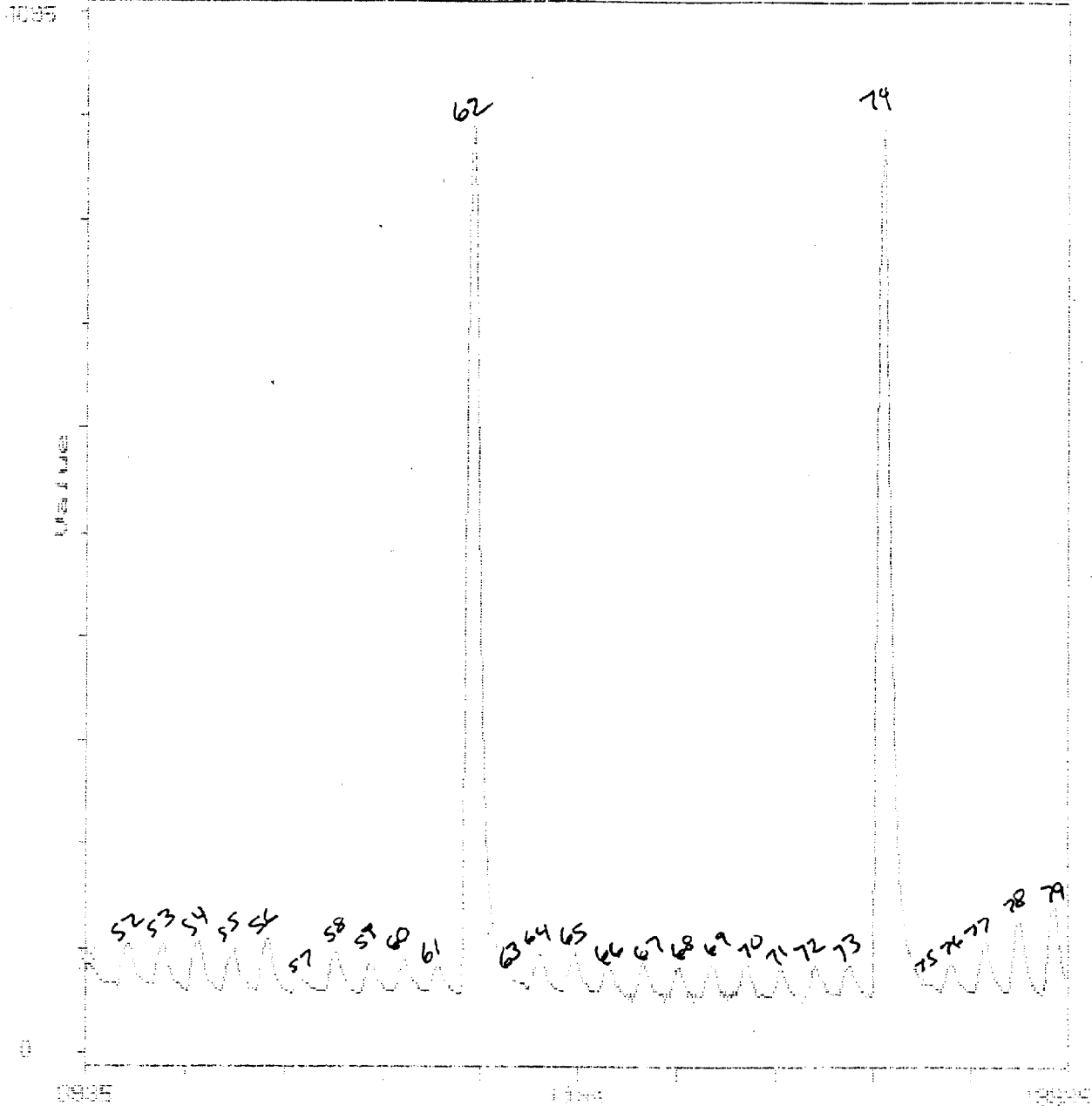


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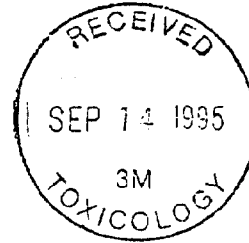


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3M
St. Paul, Minnesota



FINAL REPORT

Study Title:

Single-Dose Intravenous Pharmacokinetic
Study of T-6246 in Rabbits

Author:

Steven M. Glaza

Study Completion Date:

September 14, 1995

Performing Laboratory:

Hazleton Wisconsin, Inc.
3301 Kinsman Boulevard
Madison, Wisconsin 53704

Laboratory Project Identification:

HWI 6329-159

Page 1 of 38

Phone 608-241-4471

Fax 608-241-7227

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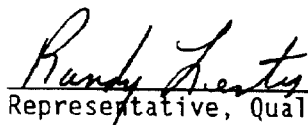
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QUALITY ASSURANCE STATEMENT

This report has been reviewed by the Quality Assurance Unit of Hazleton Wisconsin, Inc., in accordance with the Food and Drug Administration (FDA) Good Laboratory Practice Regulations, 21 CFR 58.35 (b) (6) (7). The following inspections were conducted and findings reported to the Study Director and management. Written status reports of inspections and findings are issued to Hazleton management monthly according to standard operating procedures.

Inspection Dates		Phase	Date	Date
From	To		Reported to Study Director	to Management
03/22/95	03/22/95	Protocol Review	03/22/95	03/10/95
04/10/95	04/10/95	Protocol Amendment	04/10/95	05/10/95
04/27/95	04/27/95	Animal Observation	04/27/95	05/10/95
07/05/95	07/10/95	Data/Report Review	07/10/95	08/10/95
09/12/95	09/12/95	Report Rereview	09/12/95	10/10/95


Representative, Quality Assurance Unit

9.14.95
Date

000312

HWI 6329-159

STUDY IDENTIFICATION

Single-Dose Intravenous Pharmacokinetic
Study of T-6246 in Rabbits

Test Material	T-6246
Sponsor	3M Toxicology Service Medical Department 3M Center, Bldg. 220-2E-02 P.O. Box 33220 St. Paul, MN 55133-3220
Sponsor's Representative	John L. Butenhoff, PhD 3M Toxicology Service Medical Department 3M Center, Bldg. 220-2E-02 P.O. Box 33220 St. Paul, MN 55133-3220 (612) 733-1962
Study Director	Steven M. Glaza Hazleton Wisconsin, Inc. P.O. Box 7545 Madison, WI 53707-7545 (608) 241-7292
Study Location	Hazleton Wisconsin, Inc. 3301 Kinsman Boulevard Madison, WI 53704
Study Timetable	
Study Initiation Date	March 30, 1995
Experimental (In-life) Start Date	April 4, 1995
In-life End Date	May 1, 1995
Experimental Termination Date	September 14, 1995
Study Completion Date	September 14, 1995

000313

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KEY PERSONNEL

Acute Toxicology

Steven M. Glaza
Study Director
Manager

Francis (Bud) W. McDonald
Study Coordinator

Patricia Padgham
In-life Supervisor

Rose M. Bridge
Report Supervisor

Toxicology Support

Kathy Myers
Manager

Calvin L. Horton
Supervisor

Quality Assurance

Sherry R. W. Petzel
Manager

Laboratory Animal Medicine

Cindy J. Cary, DVM
Diplomate, ACLAM
Supervisor

Anatomical Pathology

Thomas E. Palmer, PhD
Anatomical Pathologist

Jack Serfort/
Deborah L. Pirkel
Supervisors
Necropsy

Anne Mosher
Supervisor
Pathology Data

000314

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000315

SUMMARY

This study was done to assess the level of systemic exposure of T-6246 when administered by a single intravenous injection to rabbits.

The study was conducted using four male and four female acclimated rabbits of the Hra:(NZW)SPF strain for each treatment group as follows:

<u>Group</u>	<u>Test Material</u>	<u>Dose Level (mg/kg)</u>	<u>Number of Animals</u>	
			<u>Males</u>	<u>Females</u>
1 (Control)	Sterile water	0	4	4
2 (Low)	T-6246	5	4	4
3 (Medium)	T-6246	10	4	4
4 (High)	T-6246	100	4*	4
5 (High)	T-6246	500	4*	4

* One animal sacrificed after treatment due to a possible broken back and replaced with another male animal.

The animals received a single intravenous injection of the test material at the indicated dose level into the marginal ear vein of the right ear. The dose volume was 0.5 mL/kg of body weight for Groups 1 through 4 and was 0.75 mL/kg for Group 5. Two animals/sex/dose level were sacrificed on Day 15 and the remaining animals (two animals/sex/dose level) were sacrificed on Day 28.

Clinical observations were conducted predose and at approximately 0.5, 2, and 4 hours after intravenous injection. Additional clinical observations and twice a day mortality checks were conducted daily thereafter until the scheduled sacrifice interval (Day 15 or Day 28). Body weights were determined on Day -7 for randomization purposes, before test or control material administration (Day 1), and at the scheduled sacrifice interval (Day 15 or Day 28). A blood sample (approximately 4 mL) was collected from a marginal ear vein (left ear) of the animals at 4-, 8-, 12-, 24-, and 48-hours post-injection, and on Day 8. An approximate 4-mL blood sample was also collected on Days 15 and 22 for the animals scheduled for sacrifice on Day 28. In addition, at the time of the scheduled sacrifice (Day 15 or Day 28), approximately 20 mL of blood was obtained from each animal. All samples were centrifuged, separated into serum and cellular fractions, and sent to the Sponsor. On Day 15 or 28, the animals were anesthetized with sodium pentobarbital, bled via the posterior vena cava, and exsanguinated. An abbreviated gross necropsy examination was not done, however, tissues were collected. The whole liver, bile, and both kidneys from each animal were collected, weighed (volume only determined for bile), and sent frozen to the Sponsor.

000316

HWI 6329-159

Intravenous injection of T-6246 did not result in any test material-related changes in body weight gain. All animals appeared clinically normal throughout the study with the exception of one Group 4 and one Group 5 male animals that were sacrificed on Days 2 and 1, respectively, due to injury (possible broken backs). These animals were replaced and the replacement animals appeared clinically normal throughout the study.

000317

OBJECTIVE

The objective of this study was to assess the level of systemic exposure to the test material, T-6246, when administered as a single intravenous injection to rabbits.

REGULATORY COMPLIANCE

This study was conducted in accordance with the U.S. Food and Drug Administration's Good Laboratory Practice Regulations for Nonclinical Laboratory Studies, 21 CFR 58, with the exception that analysis of the test mixtures for concentration, homogeneity/solubility, and stability was not conducted. All procedures used in this study were in compliance with the Animal Welfare Act Regulations. In the opinion of the Sponsor and study director, the study did not unnecessarily duplicate any previous work.

TEST AND CONTROL MATERIALS

Identification

The test material was identified as T-6246 and described as a clear, colorless liquid. The control material was Sterile Water for Injection, USP (Abbott Laboratories, Lot No. 86-748-DM-02; Exp. April 1, 1996), and was described as a clear, colorless liquid.

Purity and Stability

The Sponsor assumes responsibility for test material purity and stability determinations (including under test conditions). Analysis of the test material mixtures for concentration, homogeneity/solubility, and stability was not conducted or requested by the Sponsor. The purity and stability of the control material were considered to be adequate for the purposes of this study.

Storage and Retention

The test material was stored at room temperature. The control material was stored refrigerated. Any unused test material was returned to the Sponsor after completion of all in-life testing according to Hazleton Wisconsin (HWI) Standard Operating Procedure (SOP). Any remaining vehicle may be used for other testing and will not be discarded after issuance of the final report.

000318

Safety Precautions

The test and control material handling procedures were according to HWI SOPs and policies.

TEST SYSTEM

Test Animal

Adult albino rabbits of the Hra:(NZW)SPF strain were received from HRP, Inc., Kalamazoo, Michigan on March 8, 1995 and maintained at the Hazleton Wisconsin facility at 3301 Kinsman Boulevard, Madison, Wisconsin.

Housing

After receipt, the animals were acclimated for a period of at least 7 days. During acclimation and throughout the study, the animals were individually housed in screen-bottom stainless steel cages in temperature- and humidity-controlled quarters. Environmental controls for the animal room were set to maintain a temperature of 19° to 23°C, a relative humidity of 50% $\pm$ 20%, and a 12-hour light/12-hour dark lighting cycle. In cases where variations from these conditions existed, they were documented and considered to have had no adverse effect on the study outcome.

Animal Diet

The animals were provided access to water *ad libitum* and a measured amount of Laboratory Rabbit Diet HF #5326, PMI Feeds, Inc. The feed is routinely analyzed by the manufacturer for nutritional components and environmental contaminants. Samples of the water are periodically analyzed by HWI. There were no known contaminants in the feed or water at levels that would have interfered with or affected the results of the study.

Selection of Test Animals

The animals were identified by animal number and corresponding ear tag and were placed into study groups using a stratified body weight randomization program. The randomization body weights were determined on Day -7. The weight variation of the animals for each group of each sex selected for the study did not exceed ± 2 standard deviations of the mean weight, and the mean body weights for each group of each sex were not statistically different at the 5% probability level.

000319

Study Design

Animals weighing from 2,523 to 3,276 g at initiation of treatment were placed into the following study groups:

<u>Group</u>	<u>Test/Control Material</u>	<u>Dose Level (mg/kg)</u>	<u>Dose Volume (mL/kg)</u>	<u>Number of Animals^a</u>	
				<u>Males</u>	<u>Females</u>
1 (Control)	Sterile water	0	0.5	4	4
2 (Low)	T-6246	5	0.5	4	4
3 (Medium)	T-6246	10	0.5	4	4
4 (High)	T-6246	100	0.5	4*	4
5 (High)	T-6246	500	0.75	4*	4

- * One animal sacrificed after treatment due to a possible broken back and replaced with another male animal.
- ^a Two animals/sex/dose level were sacrificed on Day 15. The remaining animals (two animals/sex/dose level) were sacrificed on Day 28.

Justification for Species Selection

Historically, the New Zealand White albino rabbit has been the animal of choice because of the large amount of background information on this species.

PROCEDURES

Dose Preparation and Administration

The test material was diluted with sterile water to achieve a specific concentration for each dose level in Groups 2 to 5. An individual dose of each respective test solution or control was calculated for each animal based on its body weight on the day of treatment. The respective test solution was administered by intravenous injection into the marginal ear vein of the right ear over approximately 22 to 60 seconds. The prepared test solutions were stored at room temperature until administered. After administration, any remaining test solutions were discarded.

Reason for Route of Administration

Intravenous injection is an acceptable route to assess systemic exposure.

000320

Observations of Animals

Clinical observations were conducted predose and at approximately 0.5, 2, and 4 hours after intravenous injection. Additional clinical observations and twice a day mortality checks were conducted daily thereafter until the scheduled sacrifice interval (Day 15 or Day 28).

Body weights were determined on Day -7 for randomization purposes and before test or control material administration (Day 1). Additional body weights were determined at the scheduled sacrifice interval (Day 15 or Day 28) or at unscheduled sacrifices (when survival exceeded 1 day).

Sample Collections

A blood sample (approximately 4 mL) was collected from the marginal ear vein (left ear) of the animals at 4-, 8-, 12-, 24-, and 48-hours post-injection, and on Day 8. An approximate 4-mL blood sample was also collected on Days 15 and 22 for the animals scheduled for sacrifice on Day 28. In addition, at the time of necropsy, approximately 20 mL of blood was obtained from the posterior vena cava of each animal. All samples were stored at room temperature, and then centrifuged, separated into serum and cellular fractions. These samples were then stored in a freezer set to maintain a temperature of $-20^{\circ}\text{C} \pm 10^{\circ}\text{C}$ until shipped to the Sponsor.

Pathology

The animals sacrificed on Days 1 and 2 due to apparent broken backs were necropsied in the same manner as the animals surviving to the scheduled sacrifices with the exception that they received an abbreviated gross necropsy examination and any abnormalities were recorded.

On Day 15, the first two animals/sex assigned to each dose level (based on the group assignment randomization) were anesthetized with sodium pentobarbital (via injection in the marginal ear vein), bled via the posterior vena cava, and exsanguinated. An abbreviated gross necropsy examination was not done, however, tissues were collected. The whole liver, bile, and both kidneys from each animal were collected, weighed (volume only determined for bile), and immediately placed in a freezer set to maintain a temperature of $-20^{\circ}\text{C} \pm 10^{\circ}\text{C}$. After tissue/bile collection, the animals were discarded. The remaining two animals/sex/dose level were anesthetized, bled, and exsanguinated on Day 28 in the same manner as the animals sacrificed on Day 15.

000321

Shipment of Tissues

After completion of the in-life phase, the blood samples (serum and cellular fractions), livers, bile, and kidneys were sent frozen (on dry ice) to the Sponsor (James D. Johnson, 3M E.E. & P.C., Bldg. 2-3E-09, 935 Bush Avenue, St. Paul, MN, 55106), along with their corresponding weights or volumes. The Sponsor is responsible for the retention and disposition of the samples. HWI does not accept any responsibility for the analysis of the samples collected in this study nor are these results presented in this report.

Statistical Analyses

No statistical analyses were required by the protocol.

Location of Raw Data, Records, and Final Report

The raw data, records, and an original signed copy of the final report will be retained in the archives of HWI in accordance with HWI SOP.

000322

RESULTS

Body Weights

Individual body weights are in Table 1. There was no meaningful effect on body weight gain during the study.

Clinical Observations

Individual clinical signs are in Table 2. All animals appeared normal throughout the study with the following exceptions:

- One Group 4 male (No. F54106) treated with T-6246 at 100 mg/kg appeared to have injured its back on Day 2 and was sacrificed, necropsied, and replaced with No. F54099. The replacement animal appeared normal throughout the study.
- One Group 5 male (No. F54076) treated with T-6246 at 500 mg/kg appeared to have injured its back on the day of treatment and was sacrificed, necropsied, and replaced with No. F54112. The replacement animal appeared normal throughout the study.

Pathology

Individual animal pathology comments are presented in Table 3. Individual animal tissue weights and bile volumes are in Table 4. The necropsy of animal No. F54106 revealed the skeletal muscle surrounding the lumbar spinal cord was diffusely dark red. In animal No. F54076, the skeletal muscle surrounding both hind limbs and the sacral spinal cord was diffusely dark red. The remaining animals survived to their scheduled sacrifice and were not examined grossly, although tissues were saved.

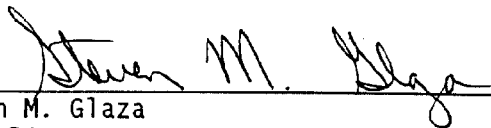
Page 15 contains a pathology report by the study pathologist.

DISCUSSION

The level of systemic exposure of T-6246 was evaluated in male and female albino rabbits when administered as a single intravenous injection at levels of 5, 10, 100, and 500 mg/kg. There were no test material-related effects in any of the animals following administration of this material.

000323

SIGNATURE



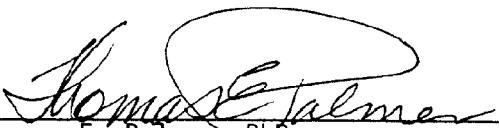
Steven M. Glaza
Study Director
Acute Toxicology

Date 9-14-95

000324

PATHOLOGY REPORT

There were two male rabbits sacrificed on Day 1 or Day 2 and necropsied. At necropsy, the skeletal muscle surrounding the lumbar spinal cord in Animal No. F54106 (100 mg/kg of body weight) was diffusely dark red. In Animal No. F54076 (500 mg/kg of body weight), the skeletal muscle surrounding both hind limbs and the sacral spinal cord was diffusely dark red. The findings in these animals are indicative of injury of undetermined etiology to the caudal region of the back. The liver, bile, and both kidneys from these animals were collected as required by protocol. After necropsy, the animals were discarded.


Thomas E. Palmer, PhD
Pathologist

9-14-95
Date

(6329-159.1hm)
051295

000325

Table 1
Individual Body Weights (g)

<u>Sex</u>	<u>Animal Number</u>	<u>Random- ization (Day -7)</u>	<u>Initial (Day 1)</u>	<u>Terminal</u>	
				<u>Day 15</u>	<u>Day 28</u>
<u>Group 1 (Control) - Sterile Water for Injection (0 mg/kg)</u>					
Male	F54105	2,603	2,761	2,933	-
	F54075	2,531	2,539	2,703	-
	F54081	2,373	2,526	-	2,874
	F54107	2,544	2,731	-	3,056
Female	F54104	2,665	2,890	3,130	-
	F54086	2,526	2,632	2,775	-
	F54074	2,540	2,703	-	2,990
	F54085	2,553	2,667	-	3,014

Group 2 - T-6246 (5 mg/kg)

Male	F54083	2,381	2,598	2,538	-
	F54100	2,675	2,869	3,030	-
	F54077	2,459	2,592	-	2,859
	F54094	2,466	2,601	-	2,916
Female	F54091	2,717	2,785	2,996	-
	F54108	2,412	2,622	2,790	-
	F54102	2,690	2,839	-	3,290
	F54097	2,439	2,533	-	2,928

Group 3 - T-6246 (10 mg/kg)

Male	F54071	2,487	2,523	2,709	-
	F54093	2,652	2,776	2,993	-
	F54095	2,662	2,772	-	3,126
	F54101	2,622	2,642	-	3,162
Female	F54110	2,719	2,802	2,959	-
	F54096	2,772	2,914	3,022	-
	F54090	2,542	2,740	-	3,022
	F54078	2,710	2,842	-	3,244

- Not required.

000326

Table 1 (Continued)
Individual Body Weights (g)

<u>Sex</u>	<u>Animal Number</u>	<u>Random- ization (Day -7)</u>	<u>Initial (Day 1)</u>	<u>Terminal</u>	
				<u>Day 15</u>	<u>Day 28</u>
<u>Group 4 - T-6246 (100 mg/kg)</u>					
Male	F54088	2,494	2,582	2,771	-
	F54106 ^a	2,677	2,833	2,803 ⁽²⁾	-
	F54089	2,597	2,662	-	2,911
	F54087	2,578	2,665	-	3,060
	F54099	2,360	2,764	3,004	-
Female	F54080	2,498	2,622	2,835	-
	F54092	2,400	2,540	2,667	-
	F54109	2,592	2,657	-	2,979
	F54114	2,776	2,933	-	3,296

Group 5 - T-6246 (500 mg/kg)

Male	F54076 ^b	2,655	2,678	-	-
	F54113	2,667	2,753	2,896	-
	F54082	2,734	2,843	-	3,216
	F54111	2,547	2,784	-	3,228
	F54112	2,996	3,276	3,530	-
Female	F54098	2,565	2,679	2,856	-
	F54084	2,510	2,600	2,821	-
	F54079	2,468	2,526	-	2,959
	F54116	2,442	2,611	-	3,002

- Not required.

a Animal No. F54106 was originally selected by the randomization program for use in the study and was treated. This animal was sacrificed on Day 2 due to a broken back and was replaced with No. F54099.

() Number in superscripted parentheses indicates the day the body weight was taken.

b Animal No. F54076 was originally selected by the randomization program for use in the study and was treated. This animal was sacrificed on Day 1 due to a broken back and was replaced with No. F54112.

000327

Table 2
Individual Clinical Signs

Sex	Animal Number	Observation	Hour (Day 1)			Day		
			0.5	2	4	2	3 to 15	16 to 28
<u>Group 1 (Control) - Sterile Water for Injection (0 mg/kg)</u>								
Male	F54105	Appeared normal	✓	✓	✓	✓	✓	*
	F54075	Appeared normal	✓	✓	✓	✓	✓	*
	F54081	Appeared normal	✓	✓	✓	✓	✓	✓
	F54107	Appeared normal	✓	✓	✓	✓	✓	✓
Female	F54104	Appeared normal	✓	✓	✓	✓	✓	*
	F54086	Appeared normal	✓	✓	✓	✓	✓	*
	F54074	Appeared normal	✓	✓	✓	✓	✓	✓
	F54085	Appeared normal	✓	✓	✓	✓	✓	✓
<u>Group 2 - T-6246 (5 mg/kg)</u>								
Male	F54083	Appeared normal	✓	✓	✓	✓	✓	*
	F54100	Appeared normal	✓	✓	✓	✓	✓	*
	F54077	Appeared normal	✓	✓	✓	✓	✓	✓
	F54094	Appeared normal	✓	✓	✓	✓	✓	✓
Female	F54091	Appeared normal	✓	✓	✓	✓	✓	*
	F54108	Appeared normal	✓	✓	✓	✓	✓	*
	F54102	Appeared normal	✓	✓	✓	✓	✓	✓
	F54097	Appeared normal	✓	✓	✓	✓	✓	✓

* Animal sacrificed on Day 15.

✓ Condition existed.

000328

Table 2 (Continued)
Individual Clinical Signs

Sex	Animal Number	Observation	Hour (Day 1)			Day		
			0.5	2	4	2	3 to 15	16 to 28
Group 3 - T-6246 (10 mg/kg)								
Male	F54071	Appeared normal	✓	✓	✓	✓	✓	*
	F54093	Appeared normal	✓	✓	✓	✓	✓	*
	F54095	Appeared normal	✓	✓	✓	✓	✓	✓
	F54101	Appeared normal	✓	✓	✓	✓	✓	✓
Female	F54110	Appeared normal	✓	✓	✓	✓	✓	*
	F54096	Appeared normal	✓	✓	✓	✓	✓	*
	F54090	Appeared normal	✓	✓	✓	✓	✓	✓
	F54078	Appeared normal	✓	✓	✓	✓	✓	✓
Group 4 - T-6246 (100 mg/kg)								
Male	F54088	Appeared normal	✓	✓	✓	✓	✓	*
	F54106	Appeared normal	✓	✓	✓	-		
		Broken back	-	-	-	✓		
		Moribund sacrifice	-	-	-	✓		
	F54089	Appeared normal	✓	✓	✓	✓	✓	✓
F54087	Appeared normal	✓	✓	✓	✓	✓	✓	
F54099 ^a	Appeared normal	✓	✓	✓	✓	✓	*	
Female	F54080	Appeared normal	✓	✓	✓	✓	✓	*
	F54092	Appeared normal	✓	✓	✓	✓	✓	*
	F54109	Appeared normal	✓	✓	✓	✓	✓	✓
	F54114	Appeared normal	✓	✓	✓	✓	✓	✓

* Animal sacrificed on Day 15.

✓ Condition existed.

- Condition not evident.

^a Replacement animal for Animal No. F54106.

000329

Table 2 (Continued)
Individual Clinical Signs

<u>Sex</u>	<u>Animal Number</u>	<u>Observation</u>	<u>Hour (Day 1)</u>			<u>Day</u>		
			<u>0.5</u>	<u>2</u>	<u>4</u>	<u>2</u>	<u>3 to 15</u>	<u>16 to 28</u>
<u>Group 5 - T-6246 (500 mg/kg)</u>								
Male	F54076	Appeared normal	✓	✓	✓			
		Broken back	-	-	†			
		Moribund sacrifice	-	-	†			
	F54113	Appeared normal	✓	✓	✓	✓	✓	*
	F54082	Appeared normal	✓	✓	✓	✓	✓	✓
F54111	Appeared normal	✓	✓	✓	✓	✓	✓	
F54112 ^a	Appeared normal	✓	✓	✓	✓	✓	*	
Female	F54098	Appeared normal	✓	✓	✓	✓	✓	*
	F54084	Appeared normal	✓	✓	✓	✓	✓	*
	F54079	Appeared normal	✓	✓	✓	✓	✓	✓
	F54116	Appeared normal	✓	✓	✓	✓	✓	✓

* Animal sacrificed on Day 15.

✓ Condition existed.

- Condition not evident.

† Condition evident at time of 12-hour bleeding interval.

^a Replacement animal for Animal No. F54076.

000330

Table 3
Individual Pathology Comments

<u>Animal Number</u>	<u>Sex</u>	<u>Test Day</u>		<u>Necropsy Observation</u>
		<u>Died</u>	<u>Sacrificed</u>	
<u>Group 4 - T-6246 (100 mg/kg)</u>				
F54106	M	-	2	The skeletal muscle surrounding the lumbar spinal cord is diffusely dark red.
<u>Group 5 - T-6246 (500 mg/kg)</u>				
F54076	M	-	1	The skeletal muscle surrounding both hind limbs and sacral spinal cord is diffusely dark red.

000331

Table 4
Individual Animal Tissue Weights and Bile Volumes

<u>Sex</u>	<u>Animal Number</u>	<u>Sacrifice Day</u>	<u>Weight (g)</u>		<u>Bile Volume (mL)</u>
			<u>Liver</u>	<u>Kidneys</u>	
<u>Group 1 (Control) - Sterile Water for Injection (0 mg/kg)</u>					
Male	F54105	15	86.35	14.92	0.6
	F54075	15	60.25	15.97	0.1
	F54081	28	80.597	14.764	1.2
	F54107	28	80.649	15.620	0.4
Female	F54104	15	98.40	16.03	0.7
	F54086	15	77.30	15.23	0.7
	F54074	28	82.895	18.793	1.6
	F54085	28	80.950	14.925	1.3
<u>Group 2 - T-6246 (5 mg/kg)</u>					
Male	F54083	15	73.15	14.87	0.7
	F54100	15	77.90	17.62	0.7
	F54077	28	75.699	17.864	0.3
	F54094	28	78.689	17.213	0.8
Female	F54091	15	84.90	14.92	1.6
	F54108	15	79.90	15.40	0.4
	F54102	28	101.494	18.308	1.7
	F54097	28	73.621	16.214	1.4

000332

Table 4 (Continued)
Individual Animal Tissue Weights and Bile Volumes

<u>Sex</u>	<u>Animal Number</u>	<u>Sacrifice Day</u>	<u>Weight (g)</u>		<u>Bile Volume (mL)</u>
			<u>Liver</u>	<u>Kidneys</u>	
<u>Group 3 - T-6246 (10 mg/kg)</u>					
Male	F54071	15	77.10	15.88	0.5
	F54093	15	81.40	15.50	0.8
	F54095	28	85.504	15.561	1.2
	F54101	28	85.668	16.120	1.0
Female	F54110	15	83.68	15.79	1.4
	F54096	15	78.10	18.70	1.1
	F54090	28	76.220	15.878	2.1
	F54078	28	83.460	18.130	1.0
<u>Group 4 - T-6246 (100 mg/kg)</u>					
Male	F54088	15	84.26	16.98	0.4
	F54106	2	82.301	16.550	2.0
	F54089	28	71.796	16.434	1.0
	F54087	28	83.710	18.591	0.6
	F54099 ^a	15	82.143	16.038	0.5
Female	F54080	15	75.42	18.32	1.2
	F54092	15	78.36	16.68	*
	F54109	28	73.958	16.915	1.6
	F54114	28	80.966	19.404	2.0

^a Replacement animal for Animal No. F54106.

* This animal had no gallbladder, so no bile was collected.

000333

Table 4 (Continued)
Individual Animal Tissue Weights and Bile Volumes

<u>Sex</u>	<u>Animal Number</u>	<u>Sacrifice Day</u>	<u>Weight (g)</u>		<u>Bile Volume (mL)</u>
			<u>Liver</u>	<u>Kidneys</u>	
<u>Group 5 - T-6246 (500 mg/kg)</u>					
Male	F54076	1	78.058	14.695	2.0
	F54113	15	91.52	16.57	1.0
	F54082	28	88.965	19.431	1.6
	F54111	28	83.823	19.405	1.5
	F54112 ^a	15	97.824	21.069	1.4
Female	F54098	15	78.95	14.72	1.2
	F54084	15	66.42	13.18	0.8
	F54079	28	83.117	14.785	1.8
	F54116	28	71.962	15.793	2.0

^a Replacement animal for Animal No. F54076.

000334

APPENDIX A

Protocol Deviations
Protocol TP8084.PK
Protocol Amendment No. 1

000335

Protocol Deviations

<u>Protocol</u>	<u>Actual Procedure</u>
Page 6, 7. Experimental Design, C. Dosing Procedures, (1) Dosing Route. Intravenous injection into the marginal ear vein of the right ear over approximately 30 to 60 seconds.	The rate of injection for one Group 5 female (No. F54098) was 22 seconds. Also, the time for dose administration for one male animal (Group 4, No. F54087) was incorrectly recorded thus the exact duration of dosing can not be determined.

These deviations are not considered to have had an adverse effect on the outcome of the study.

000336



HAZLETON
W I S C O N S I N
POST OFFICE BOX 7545
MADISON, WI 53707-7545

a **CORNING** Company

Sponsor:

3M
St. Paul, Minnesota

PROTOCOL TP8084.EXT

Study Title:

Single-Dose Intravenous Pharmacokinetic Study
of T-6246 in Rabbits

Date:

March 30, 1995

Performing Laboratory:

Hazleton Wisconsin, Inc.
3301 Kinsman Boulevard
Madison, Wisconsin 53704

Laboratory Project Identification:

HWI 6329-159

000337

Phone 608-241-3471

EXPRESS MAIL DELIVERY

3301 KINSMAN BLVD

Fax 608-241-7227
MADISON, WI 53704

3MA01502424

2807.0257

STUDY IDENTIFICATION

Single-Dose Intravenous Pharmacokinetic Study
of T-6246 in Rabbits

HWI No.	6329-159
Test Material	T-6246
Sponsor	3M Toxicology Service Medical Department 3M Center, Bldg. 220-2E-02 P.O. Box 33220 St. Paul, MN 55133-3220
Sponsor's Representative	John L. Butenhoff, PhD 3M Toxicology Service Medical Department 3M Center, Bldg. 220-2E-02 P.O. Box 33220 St. Paul, MN 55133-3220 (612) 733-1962
Study Director	Steven M. Glaza Hazleton Wisconsin, Inc. P.O. Box 7545 Madison, WI 53707-7545 (608) 241-7292
Study Location	Hazleton Wisconsin, Inc. 3301 Kinsman Boulevard Madison, WI 53704
Proposed Study Timetable	
Experimental Start Date	April 4, 1995
Experimental Termination Date	May 1, 1995
Draft Report Date	June 12, 1995

000338

1. Study
Single-Dose Intravenous Pharmacokinetic Study in Rabbits
2. Purpose
To assess the level of systemic exposure when the test material is administered as a single intravenous injection to rabbits
3. Regulatory Compliance
This study will be conducted in accordance with the following Good Laboratory Practice Regulations/Standards/Guidelines with the exception that analysis of the test material mixtures for concentration, solubility, homogeneity, and stability will not be conducted:

- ☐ Conduct as a Nonregulated Study
- ☒ 21 CFR 58 (FDA)
- ☐ 40 CFR 160 (EPA-FIFRA)
- ☐ 40 CFR 792 (EPA-TSCA)
- ☐ C(81)30 (Final) (OECD)
- ☐ 59 Nohsan No. 3850 (Japanese MAFF)
- ☐ Notification No. 313 (Japanese MOHW)

All procedures in this protocol are in compliance with the Animal Welfare Act Regulations. In the opinion of the Sponsor and study director, the study does not unnecessarily duplicate any previous work.

4. Quality Assurance
The protocol, study conduct, and the final report will be audited by the Quality Assurance Unit in accordance with Hazleton Wisconsin (HWI) Standard Operating Procedures (SOPs) and policies.
5. Test Material
 - A. Identification
T-6246
 - B. Physical Description
(To be documented in the raw data)
 - C. Purity and Stability
The Sponsor assumes responsibility for purity and stability determinations (including under test conditions). Samples of test material/vehicle mixture(s) for concentration, solubility, homogeneity, and stability analyses will be taken before administration if requested by the Sponsor. These samples (if taken) will be sent to the Sponsor after experimental termination.
 - D. Storage
Room temperature

000339

E. Reserve Samples

Reserve sample(s) of each batch/lot of test and control materials will be taken for this study.

The test and control material reserve samples will be stored at HWI in a freezer set to maintain a temperature of $-20^{\circ}\text{C} \pm 10^{\circ}\text{C}$ for 10 years per HWI SOP. The Sponsor will be contacted after 10 years for disposition in accordance with the appropriate regulatory Good Laboratory Practices.

F. Retention

Any unused test material will be returned to the Sponsor after completion of the in-life phase of the study.

G. Safety Precautions

As required by HWI SOPs and policies

6. Control Material

A. Identification

Sterile water for injection

B. Physical Description

Clear, colorless liquid

C. Purity and Stability

The purity and stability of this USP grade material is considered adequate for the purposes of this study.

D. Storage

Refrigerated

E. Reserve Samples

See Section 5. E. Reserve Samples

F. Retention

Any remaining control material may be used for other testing and will not be discarded after issuance of the final report.

G. Safety Precautions

As required by HWI SOPs and policies

7. Experimental Design

A. Animals

(1) Species

Rabbit

(2) Strain/Source

Hra:(NZW)SPF/HRP, Inc.

000340

- (3) Age at Initiation
Adult
- (4) Weight at Initiation
2.5 to 3.5 kg
- (5) Number and Sex
20 males and 20 females
- (6) Identification
Individual numbered ear tag
- (7) Husbandry
 - (a) Housing
Individually, in screen-bottom stainless steel cages (heavy gauge)
 - (b) Food
A measured amount of Laboratory Rabbit Diet HF #5326 (PMI Feeds, Inc.). The food is routinely analyzed by the manufacturer for nutritional components and environmental contaminants.
 - (c) Water
Ad libitum from an automatic system. Samples of the water are analyzed by HWI for total dissolved solids, specified microbiological content, selected elements, heavy metals, organophosphates, and chlorinated hydrocarbons.
 - (d) Contaminants
There are no known contaminants in the food or water that would interfere with this study.
 - (e) Environment
Environmental controls for the animal room will be set to maintain a temperature of 19°C to 23°C, a relative humidity of 50% $\pm$ 20%, and a 12-hour light/12-hour dark cycle.
 - (f) Acclimation
At least 7 days
- (8) Selection of Test Animals
Based on health and body weight according to HWI SOPs. An adequate number of extra animals will be purchased so that no animal in obviously poor health is placed on test. The animals will be placed into study groups using a stratified body weight randomization program within nine days of study initiation.

000341

(9) Justification for Species Selection

Historically, the New Zealand White albino rabbit has been the animal of choice because of the large amount of background information on this species.

B. Dose Administration(1) Test Groups

<u>Group</u>	<u>Test/Control Material</u>	<u>Dose Level (mg/kg)^a</u>	<u>Number of Animals^b</u>	
			<u>Males</u>	<u>Females</u>
1 (Control)	Sterile water	0	4	4
2 (Low)	T-6246	5	4	4
3 (Medium)	T-6246	10	4	4
4 (High)	T-6246	100	4	4
5 (High)	T-6246	500	4	4

a The dose volume will be 0.5 mL/kg of body weight.

b Two animals/sex/dose level will be sacrificed on Day 15. The remaining animals (two animals/sex/dose level) will be sacrificed on Day 28.

C. Dosing Procedures(1) Dosing Route

Intravenous injection into the marginal ear vein of the right ear over approximately 30 to 60 seconds.

(2) Reason for Dosing Route

Intravenous injection is an acceptable route to assess systemic exposure.

(3) Dosing Duration

Single dose

(4) Dose Preparation

The day of treatment will be designated as Day 1. The Group 1 animals will be treated with sterile water at a dose volume of 0.5 mL/kg. The test material will be diluted with sterile water to achieve a specific concentration for each dose level in Groups 2-5. Individual doses will be calculated based on the animal's body weight taken just before test material administration. The prepared test mixtures will be stored at room temperature until administration.

000342

D. Observation of Animals**(1) Clinical Observations**

The animals will be observed for clinical signs of toxicity before test or control material administration, at approximately 0.5, 2.0, 4.0 hours post-injection (Day 1), and daily thereafter for clinical signs and twice daily (a.m. and p.m.) for mortality until the scheduled sacrifice interval (Day 15 or Day 28). Observations may be extended when directed by the Study Director.

(2) Body Weights

For randomization, before test or control material injection (Day 1), at the scheduled sacrifice interval (Day 15 or Day 28), and at unscheduled death and sacrifices (when survival exceeds 1 day)

(3) Sample Collections**(a) Frequency**

4-, 8-, 12-, 24-, and 48-hours post-injection, on Days 8, 15, 22, and at the scheduled sacrifice interval (Day 15 or Day 28)

(b) Method of Collection/Number of Animals

Blood samples (approximately 4 mL) will be collected from the marginal ear vein (left ear) of all animals at 4-, 8-, 12-, 24-, and 48-hours post-injection, and on Day 8. Additional samples will be collected on Days 15 and 22 for the animals scheduled for sacrifice on Day 28.

Approximately 20 mL of blood (actual volume to be documented in the raw data) will be obtained from the posterior vena cava at the time of the scheduled sacrifice (Day 15 or Day 28). Approximately 20 mL of blood will be collected from moribund animals during the study, also, if possible.

The samples will be stored at room temperature and then centrifuged, and the separate serum and cellular fractions stored in a freezer set to maintain a temperature of $-20^{\circ}\text{C} \pm 10^{\circ}\text{C}$. The separated serum and cellular fractions will be sent frozen on dry ice to the Sponsor after experimental termination. The Sponsor is responsible for the retention and disposition of the samples.

000343

Samples will be shipped to:

James D. Johnson
3M E.E. & P.C.
Bldg. 2-3E-09
935 Bush Avenue
St. Paul, MN 55106

James D. Johnson or his alternate will be notified by telephone at (612) 778-5294 prior to the shipment of the samples.

E. Termination

(1) Unscheduled Sacrifices and Deaths

Any animal dying during the study or sacrificed in a moribund condition will be subjected to an abbreviated gross necropsy examination and all abnormalities will be recorded. Animals in a moribund condition will be anesthetized with sodium pentobarbital (via injection in the marginal ear vein), bled via the vena cava, and exsanguinated. Tissues, as described in section 7.E. (3) Sample Collection, will be collected from any animal dying during the study or sacrificed in a moribund condition. After necropsy, the animals will be discarded.

(2) Scheduled Sacrifices

On Day 15, the first two animals/sex assigned to each dose level (based on the group assignment randomization) will be anesthetized with sodium pentobarbital (via injection in the marginal ear vein), bled via the vena cava, and exsanguinated. The remaining two animals/sex/dose level will be anesthetized with sodium pentobarbital (via injection in the marginal ear vein), bled via the vena cava, and exsanguinated on Day 28. An abbreviated gross necropsy examination will not be done, however, tissues (as described in section 7.E. (3) Sample Collection) will be collected.

(3) Sample Collection

The whole liver, bile, and both kidneys from each animal will be collected, weighed (volume only determined for bile), and immediately placed in a freezer set to maintain a temperature of $-20^{\circ}\text{C} \pm 10^{\circ}\text{C}$. After sample collection, the animals will be discarded.

The samples (liver, bile, and kidneys) will be sent frozen on dry ice to the Sponsor after experimental termination. The samples and their corresponding weights or volumes will be shipped to the person listed in Section 7.D.(3).(b). The Sponsor is responsible for the retention and disposition of the samples.

000344

F. Statistical Analyses

No statistical analyses are required.

8. Report

A final report including those items listed below will be submitted.

Description of the test and control materials

Description of the test system

Procedures

Dates of experimental initiation and termination

Description of any toxic effects

Gross pathology findings (if applicable)

Gross pathology report (if applicable and requested by the Study Director)

Individual animal tissue weights and bile volumes

9. Location of Raw Data, Records, and Final Report

Original data, or copies thereof, will be available at HWI to facilitate auditing the study during its progress and before acceptance of the final report. When the final report is completed, all original paper data, including those item listed below will be retained in the archives of HWI according to HWI SOP.

Protocol and protocol amendments

Dose preparation records

In-life records

Body weights

Dose administration

Observations

Sample collection records

Shipping records

Pathology Records

Study correspondence

Final report (original signed copy)

The following supporting records will be retained at HWI but will not be archived with the study data.

Animal receipt/acclimation records

Water analysis records

Animal room temperature and humidity records

Refrigerator and freezer temperature records

Instrument calibration and maintenance records

000345

PROTOCOL APPROVAL

John L. Butenhoff
John L. Butenhoff, PhD
Sponsor's Representative
3M

4-4-95
Date

Steven M. Glaza
Steven M. Glaza
Study Director
Acute Toxicology
Hazleton Wisconsin, Inc.

3-30-95
Date

Gay Shach
Representative
Quality Assurance Unit
Hazleton Wisconsin, Inc.

(6329-159.protdsk2)

3-30-95
Date

000346



a CORNING Company

PROTOCOL TP8084.EXT

Single-Dose Intravenous Pharmacokinetic Study of
T-6246 in Rabbits

HWI 6329-159

Sponsor

3M Toxicology Service
Medical Department
3M Center, Bldg. 220-2E-02
P.O. Box 33220
St. Paul, MN 55133-3220

Contractor

Hazleton Wisconsin, Inc.
3301 Kinsman Boulevard
Madison, WI 53704

Sponsor's Representative

John L. Butenhoff, PhD

Study Director

Steven M. Glaza

Amendment No. 1

This amendment modifies the following portions of the protocol:

Effective April 4, 1995

1. Page 6, 7. Experimental Design; B. Dose Administration; (1) Test Groups.
The test material mixture for Group 5 could not be prepared at the concentration needed to utilize a dose volume of 0.5 mL/kg. Modify footnote "a" in this section with the following underlined addition:
 - a The dose volume will be 0.5 mL/kg of body weight for Groups 1-4 and 0.75 mL/kg for Group 5.

000347

Phone 608-241-4471

Fax 608-241-7227

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Amendment No. 1

HWI 6329-159
Page 2

Effective April 5, 1995

2. Page 6, 7. Experimental Design; B. Dose Administration; (1) Test Groups.
Animal No. F54076 (Group 5 male) and Animal No. F54106 (Group 4 male)
were sacrificed on Days 1 and 2, respectively, due to injuries (apparent
broken backs). Add the following paragraph to this section:

Due to the sacrifice on Day 1 of one Group 5 male
(Animal No. F54076) and on Day 2 of one Group 4 male
(Animal No. F54106) because of injuries (apparent broken backs),
replacement animals will be treated at the same dose levels in the
same manner as for the initial animals in the study. The
observations (clinical observations, body weights and sample
collections) and the termination of the animals (unscheduled
sacrifices and deaths, scheduled sacrifices, and sample
collection) will be conducted in the same manner as for the other
animals in the study terminating on Day 15.

PROTOCOL AMENDMENT APPROVAL

John L. Butenhoff

John L. Butenhoff, PhD
Sponsor's Representative
3M Toxicology Service Medical Department

5-2-95
Date

Steven M. Glaza

Steven M. Glaza
Study Director
Acute Toxicology
Hazleton Wisconsin, Inc.

4-18-95
Date

Judy Thod

Representative
Quality Assurance Unit
Hazleton Wisconsin, Inc.

4.18.95
Date

(6329-159.Aml.dsk3)

000348

Calibration curve of 950504A1 : Fluoride L

Channel 1 Measured: 6 Concentration: -0.000355 0.001851733

Concentration

Order : 2

Measured

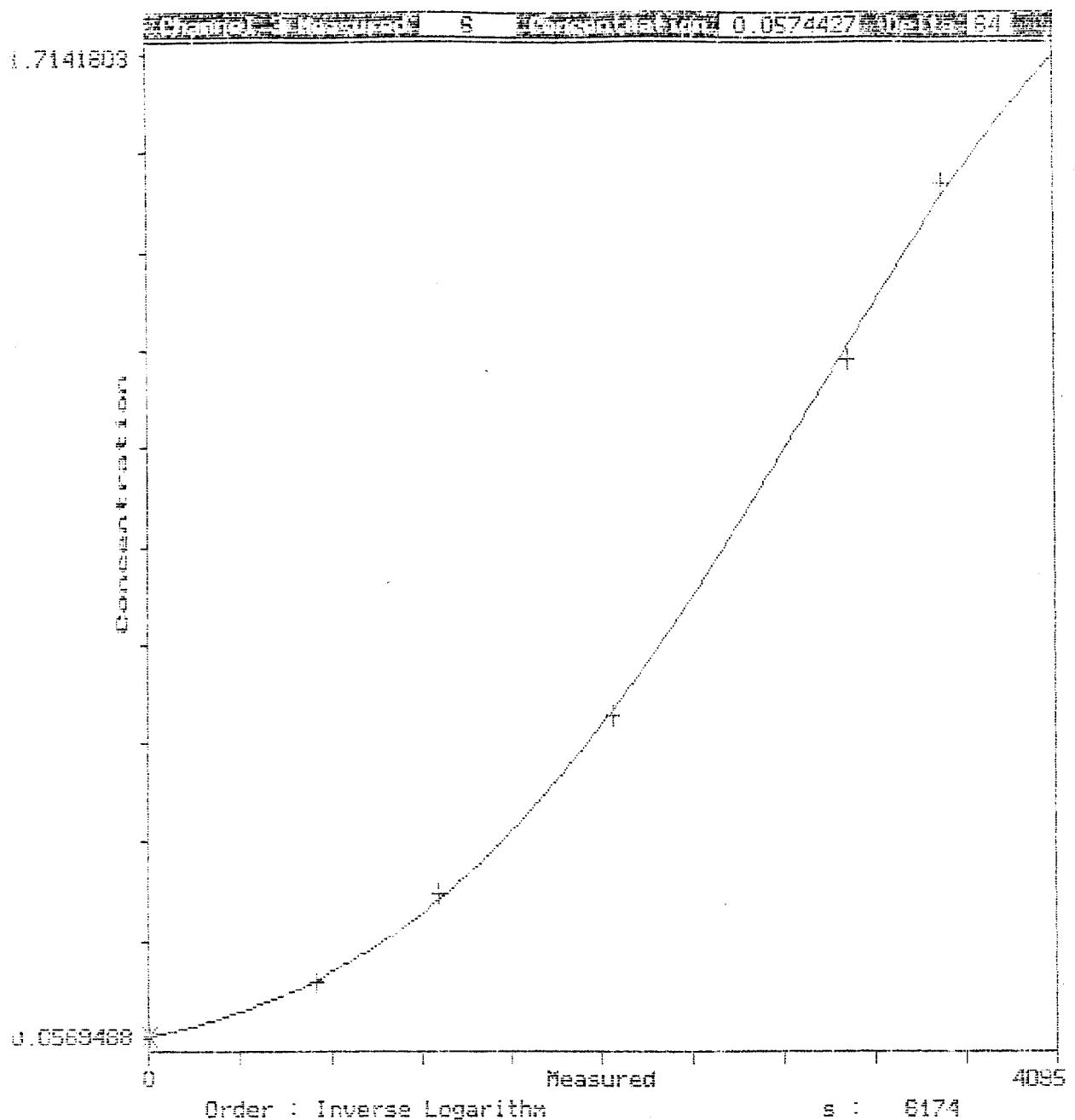
$r : 0.99928$

0.001409

900

Measured	Concentration
0	0.001409
100	0.001450
200	0.001491
300	0.001532
400	0.001573
500	0.001614
600	0.001655
700	0.001696
800	0.001737
900	0.001778

Calibration curve of 850504A1 : Fluoride 1.5



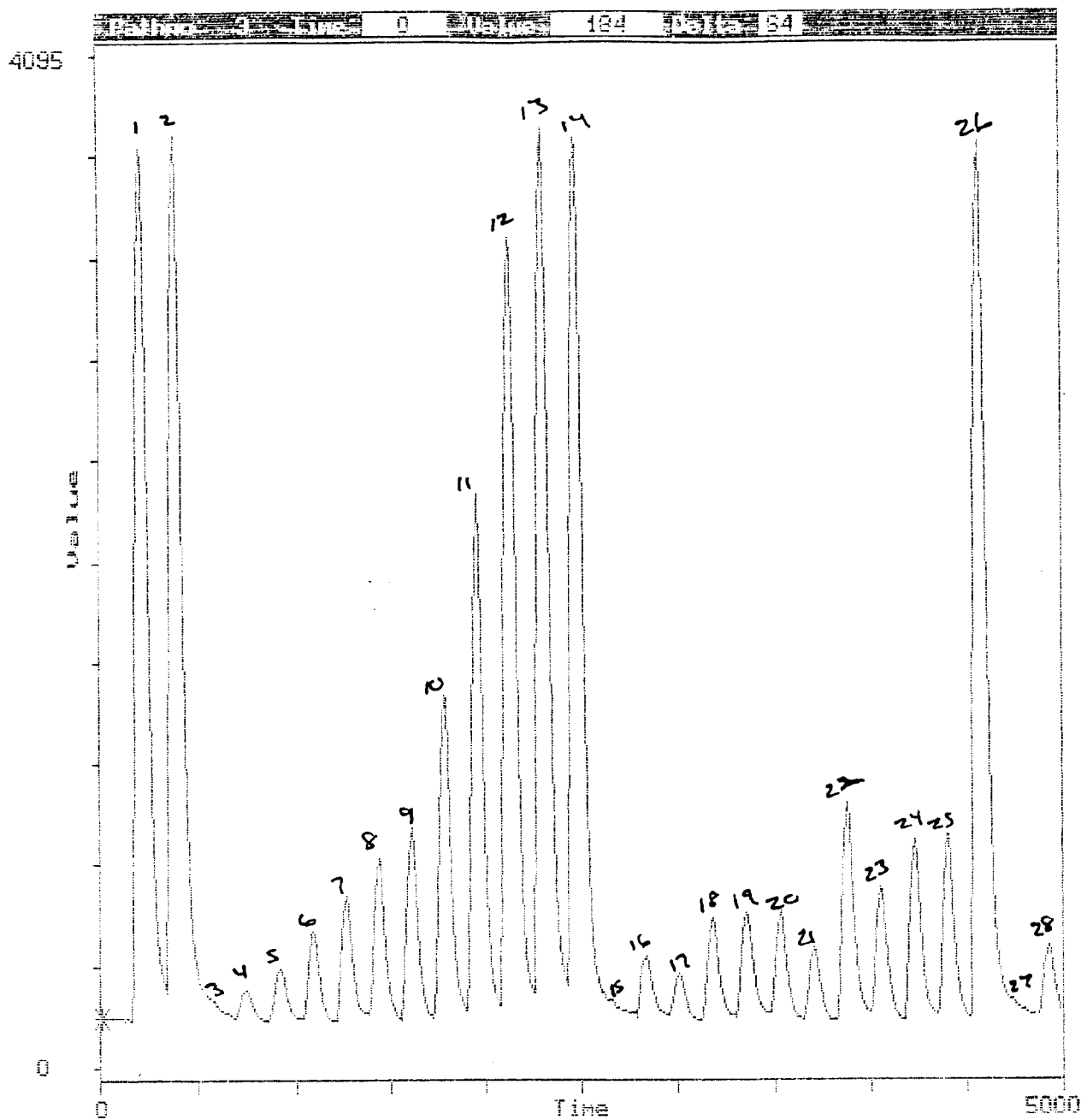
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Esc=Exit | F1=Help | Ctrl-P=Edit peaks |

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