DOCUMENT 29

AR226-1924

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Results to Date from the PFOA Worker Study

Ammonium Perfluorooctonoate: Cross-Sectional Surveillance of Clinical Measures of General Health Status Related to a Serum Biomarker of Exposure and Retrospective Cohort Analyses in a Polymer Production Plant

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EPA 00575

EXHIBIT 2

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Agenda

- Purpose of Study
- General methodology
- Results to date (clinical pathology parameters)
- Summary
- Timeline
- Further Work

EPA 00576

Purpose of Study

- Primary objectives :
  - Develop statistical models that *describe the relationship of serum PFOA to health outcome variables* suggested by previous animal and worker studies, taking into account potential confounders and effect modifiers.
  - Conduct retrospective cohort mortality analyses using appropriate stratification based on estimated past exposures to PFOA.

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General Methodology

- Voluntary participation across all areas of the plant
- Cross-sectional design, that is, "snapshot" of both the exposure marker and the health outcome variables
  - Cross-sectional studies address "person and place", but not "time"—the descriptive triad of epidemiology
  - No data collected over time, no baseline
  - Cannot determine causality, only identify associations
- Logistic, linear, and quadratic regression analyses for modeling
- Deciles of exposure used for internal comparisons

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Results from Clinical Chemistries

- 1,024 employees participated in the cross-sectional health surveillance
  - All participants have received their individual serum PFOA levels and medical test results
  - 62 parameters have been analyzed
- Not all of the questionnaire data have been analyzed, but these analyses are underway
- Restrospective cohort analyses not completed
  - NDI data received Dec. 21, 2004

EPA 00579

General Findings

- Most of the parameters measured were within normal reference ranges and not associated with serum PFOA levels.
- There were statistically significant ($p \leq 0.05$) modest increases in some cholesterol fractions (total, LDL) and triglycerides with higher concentrations of serum PFOA.
- HDL cholesterol was not associated with serum PFOA levels.
  - As expected, age, body mass index, and alcohol consumption were also contributors to increases in lipids.
- CRP levels (C-reactive protein) were not associated with serum PFOA levels.

EPA 00580

General Findings

- There were no consistent relationships between results of liver tests and serum PFOA concentrations.
  - Different responses in males and females
  - Alcohol consumption was a factor, but inconsistent as to category and between genders
- There were statistically significant, but slight, increases in uric acid and iron with higher concentrations of serum PFOA.
  - Increased uric acid has been associated with increased lipids.

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Serum PFOA Levels By Work Assignment

Work Assignment	Serum PFOA (ppb)			
	Number in Group	Median	Min	Max
Works in PFOA areas	259	490	17	9550
Previously worked in PFOA areas	264	200	9	2590
Occasionally works in PFOA areas	160	180	8	2070
Never assigned to PFOA areas	342	110	5	963
Total Participants	1025			

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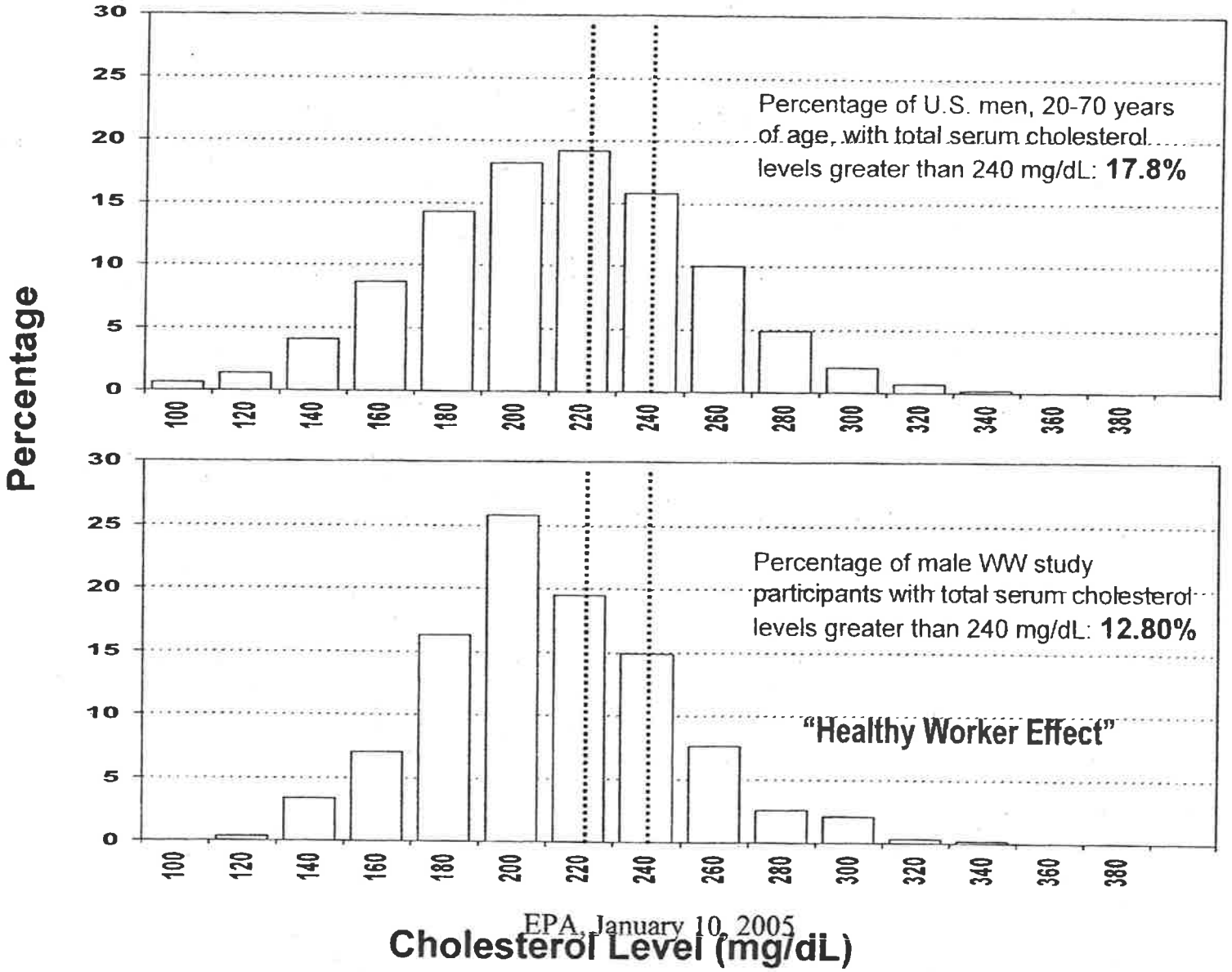
Context for Cholesterol Levels

- Male study participants' total cholesterol and LDL levels were compared to U.S. males using NHANES data.
- Study participants had a smaller percentage of males with high cholesterol than the U.S. population, except for the top decile of serum PFOA.

EPA 00583

Overall Comparison of Male Washington Works Study Participants with the General US Population



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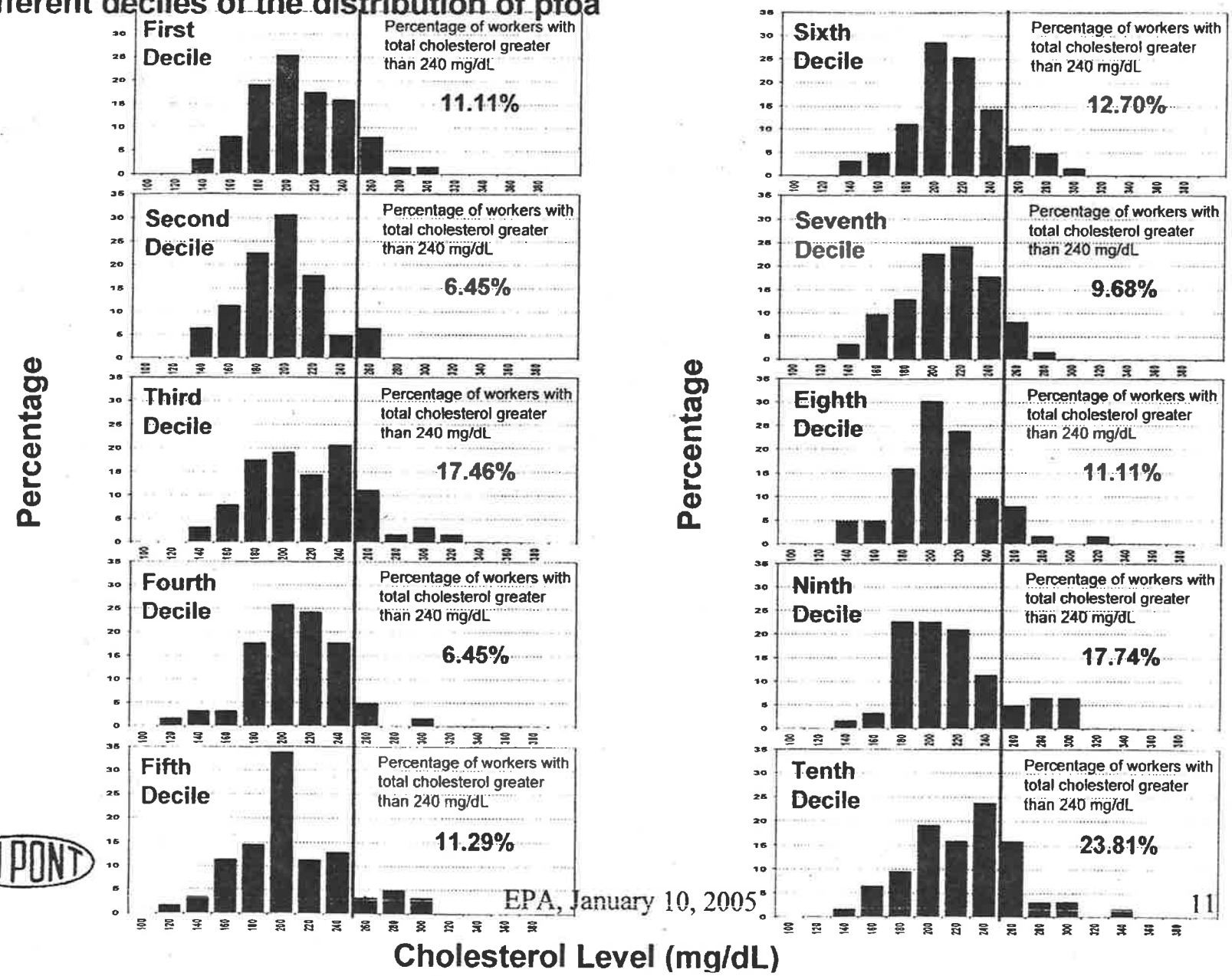
Comparison of Washington Works Workers Compared to US Population

Distribution of total cholesterol level of non-medicated male workers exposed to different deciles of the distribution of pfoa



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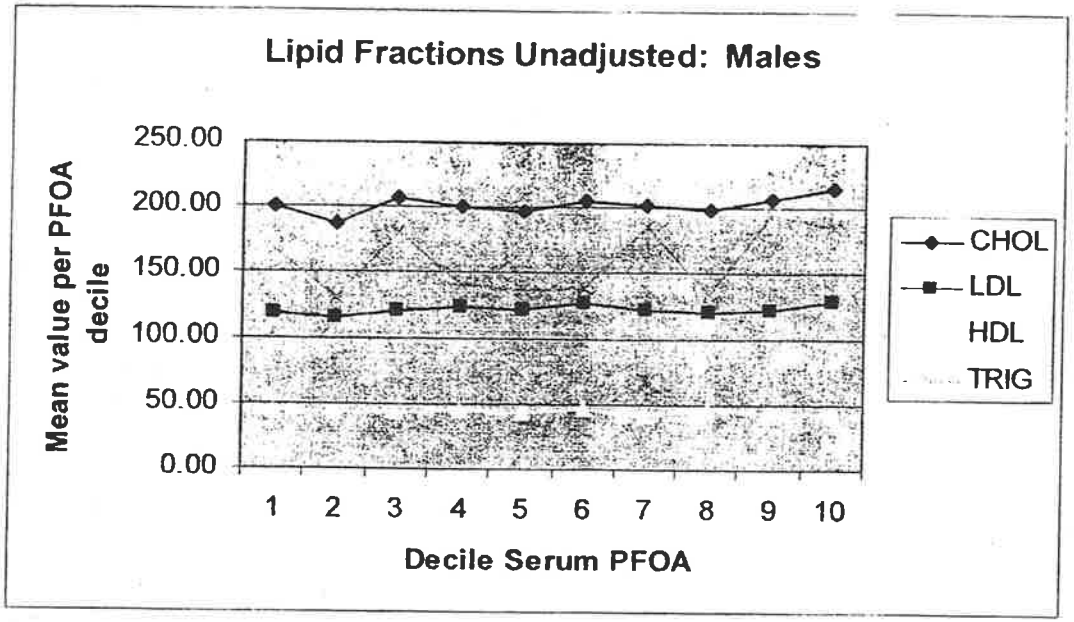
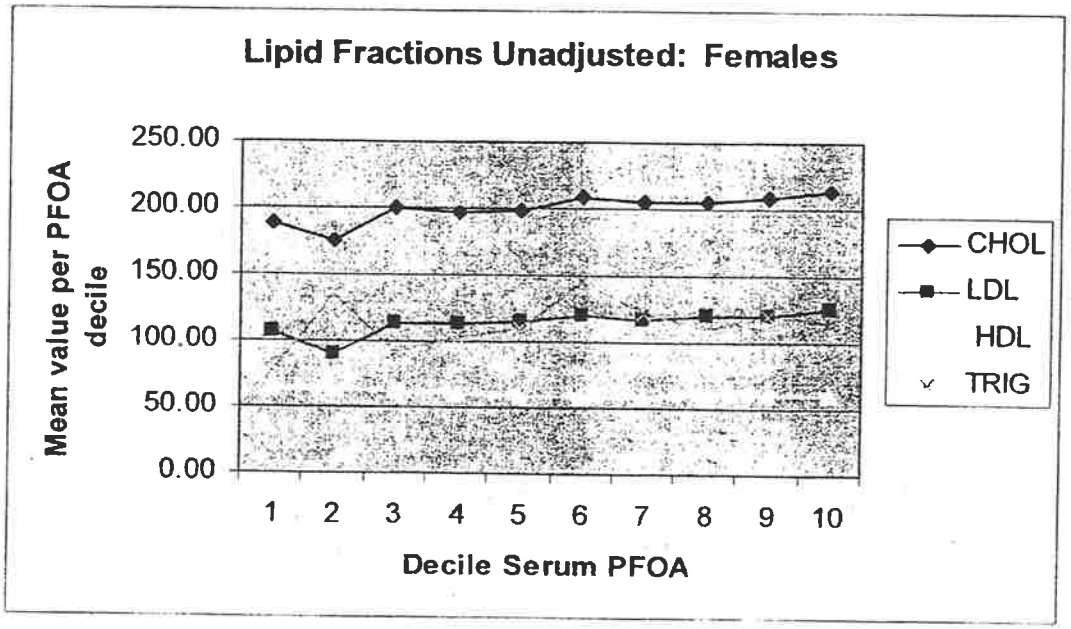
Excludes those on lipid-lowering meds

Simple charts of mean unadjusted lipid values for exposure decile indicate a small increase in last decile. Modeling ***that accounts for known risk factors*** provides more information.





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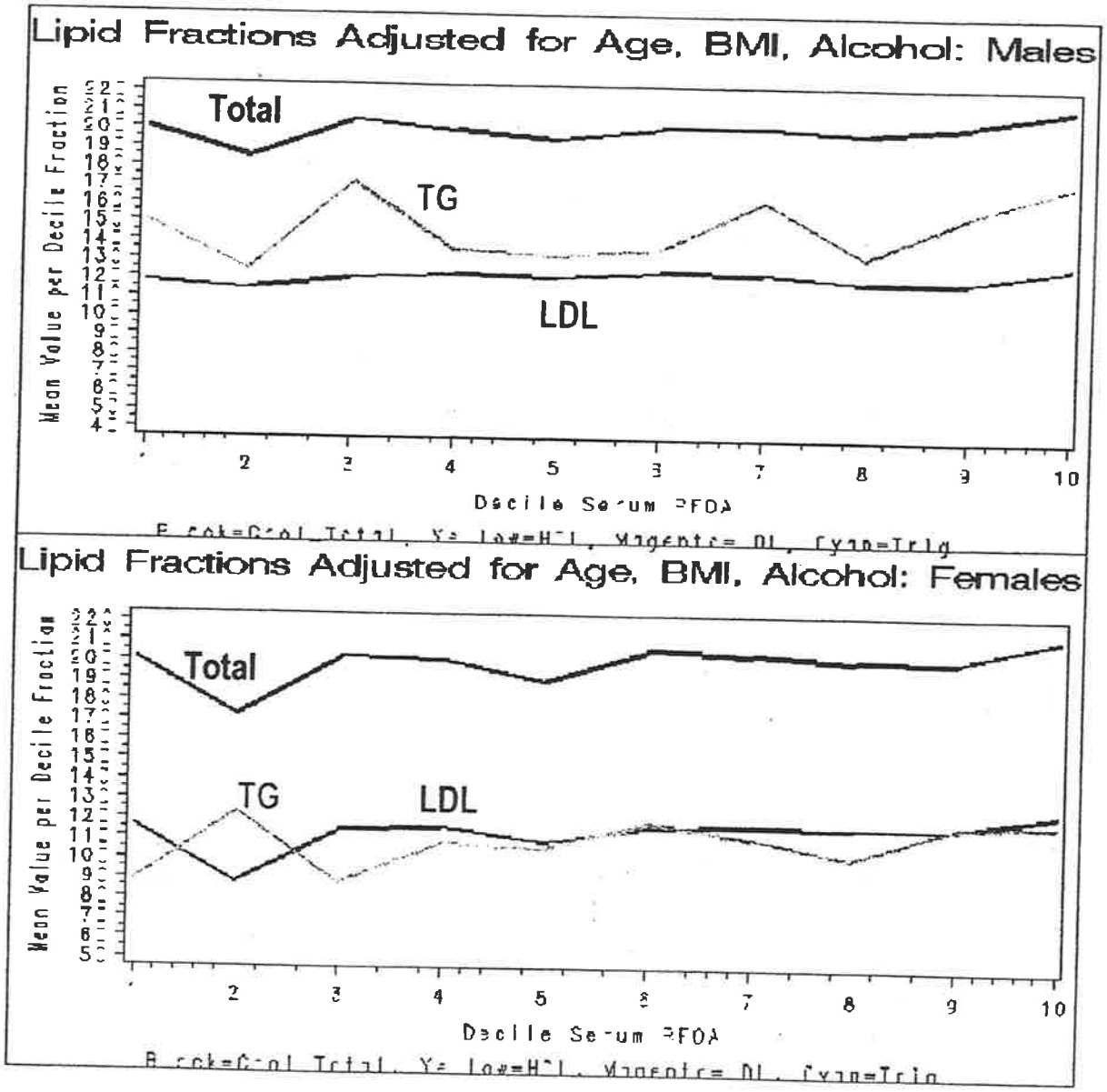
Mean adjusted lipid values for serum PFOA levels indicate a modest increase in highest decile (>1000 ppb)



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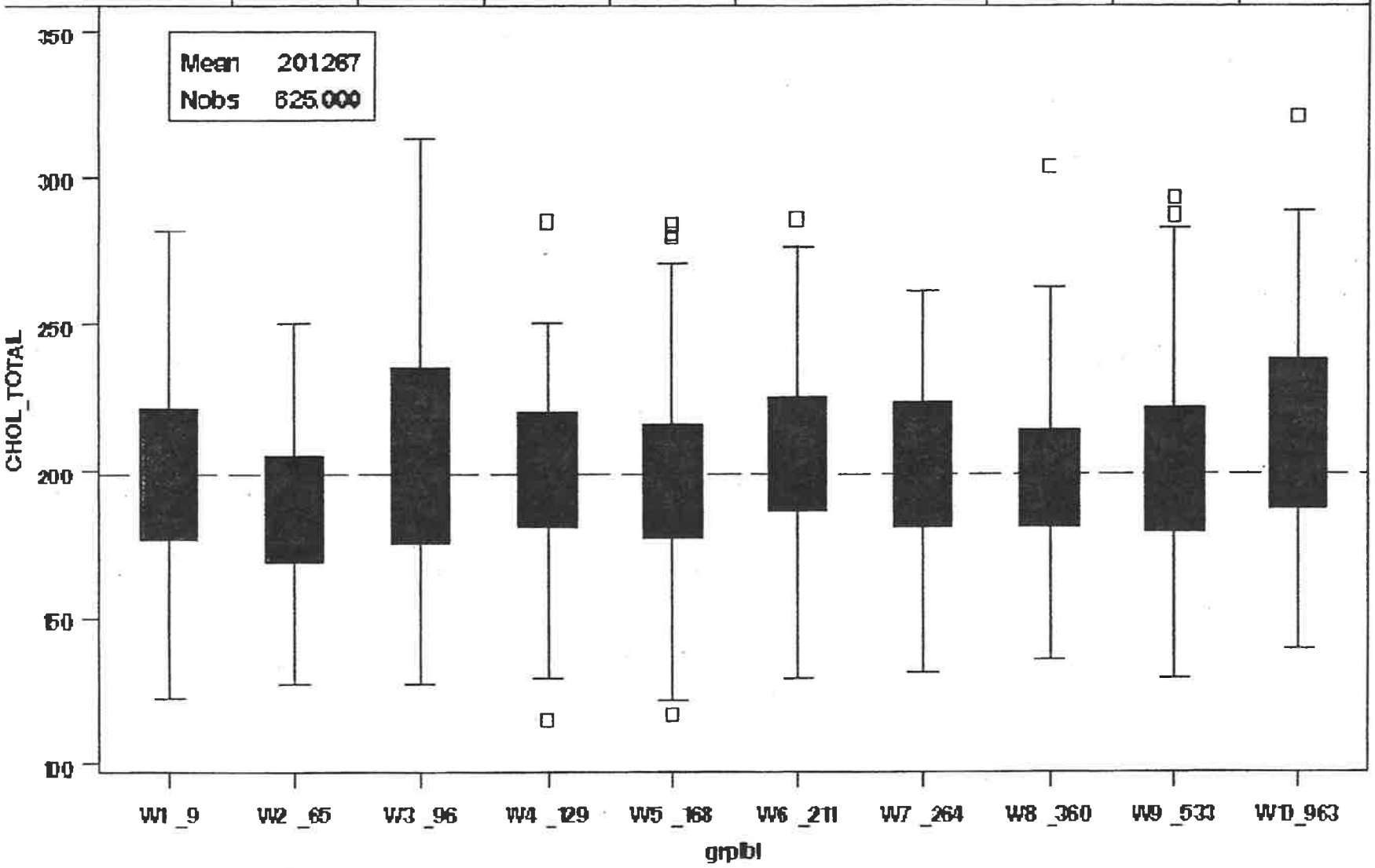
CHOL_TOTAL by PFOA Quantile

Sex=M, Heartmeds=N, WW 2004

	W1 _9	W2 _65	W3 _96	W4 _129	W5 _168	W6 _211	W7 _264	W8 _360	W9 _533	W10_963
Mean	198.823	187.016	205.629	199.857	196.306	204.635	200.871	198.873	206.097	214.587
Std Dev	32.345	28.787	39.434	31.099	37.476	32.835	30.472	31.022	36.740	36.646



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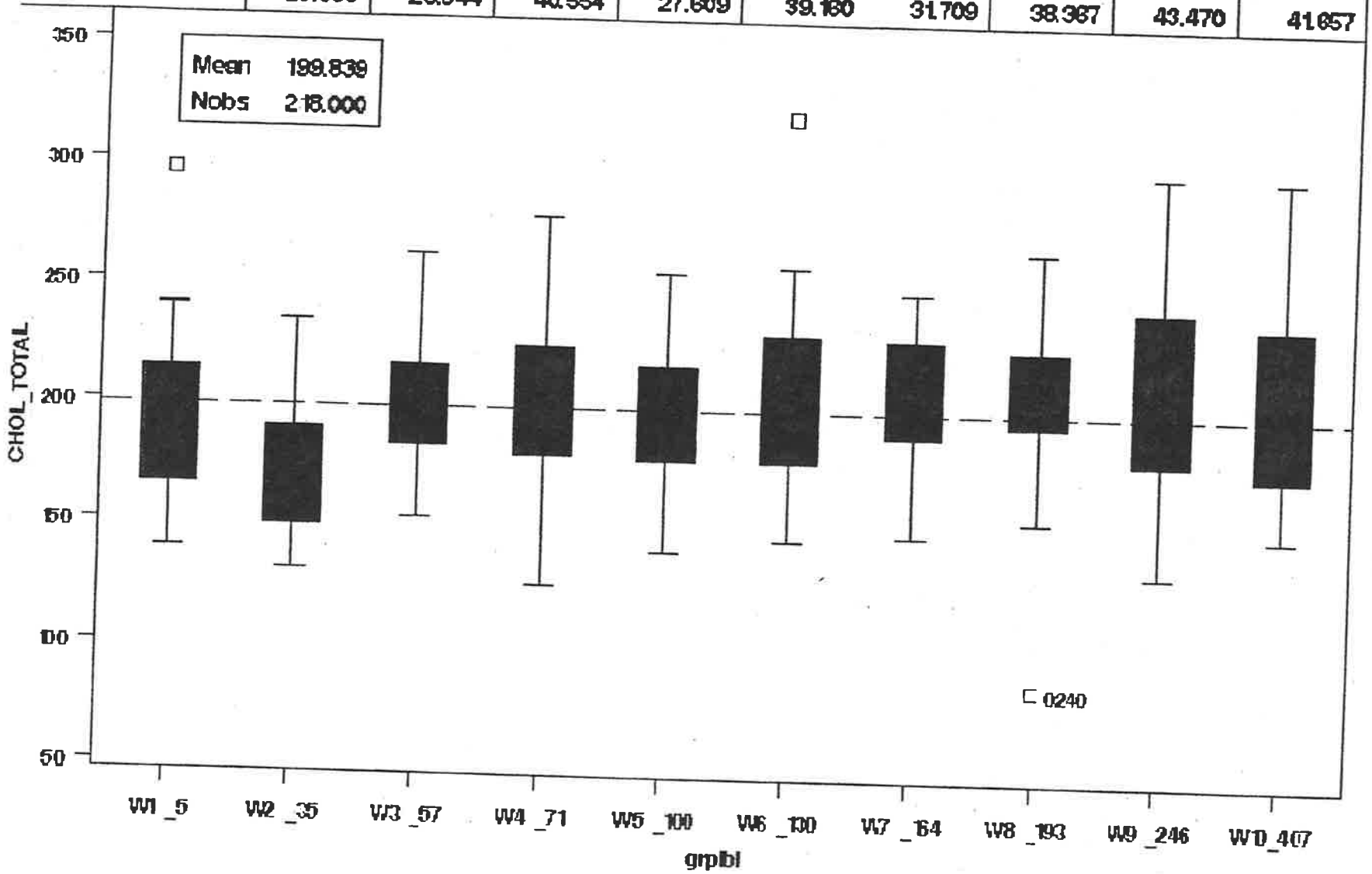
CHOL_TOTAL by PFOA Quantile

Sex=F, Heartmeds=N, WU 2004

	W1 _5	W2 _35	W3 _57	W4 _71	W5 _100	W6 _130	W7 _164	W8 _193	W9 _246	W10_407
Mean	190.667	171.045	201.727	197.318	195.150	208.478	205.636	208.045	208.000	213.091
Std Dev	38.111	28.550	28.944	40.554	27.609	39.160	31.709	38.367	43.470	41.657



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LOG_Chol_Total: MALES, WW 2004

Results of Regression Modeling

Where Sex=M, Heartmeds=NO

Source	DF	SS	MS	FValue	ProbF
Model	4	0.78955	0.19739	6.88	<.0001
Error	620	17.78688	0.02869	–	–
Corrected Total	624	18.57643	–	–	–

Parameter Estimates

Variable	DF	Estimate	StdErr	tValue	Probt	Sex=M
Intercept	1	4.99553	0.06366	78.47	<.0001	Meds=NO
LOG_PFOA	1	0.02307	0.00623	3.70	0.0002	
BMI	1	0.00357	0.00158	2.27	0.0238	
AGE	1	0.00153	0.00077841	1.97	0.0491	
ALC6	1	-0.07070	0.03469	-2.04	0.0420	
R-Square	0.042503					

Where Sex=M, Heartmeds=B (B=all subjects)

Source	DF	SS	MS	FValue	ProbF
Model	2	0.43865	0.21932	7.11	0.0009
Error	778	23.98564	0.03083	–	–
Corrected Total	780	24.42429	–	–	–

Parameter Estimates

Variable	DF	Estimate	StdErr	tValue	Probt	Sex=M
Intercept	1	5.17480	0.03196	161.93	<.0001	Meds=B
LOG_PFOA	1	0.01921	0.00574	3.34	0.0009	
ALC6	1	-0.05789	0.03170	-1.83	0.0683	
R-Square	0.017960					

EPA 00590

LOG_Chol_Total : FEMALES, WW 2004
Results of Regression Modeling

Source	DF	SS	MS	FValue	ProbF
Model	4	1.00313	0.25078	7.73	<.0001
Error	213	6.91462	0.03246	_	_
Corrected Total	217	7.91775	_	_	_

Parameter Estimates: Sex=F, Heartmeds=NO

Variable	DF	Estimate	StdErr	tValue	Probt
Intercept	1	4.84428	0.08752	55.35	<.0001
LOG_PFOA	1	0.02381	0.01161	2.05	0.0415
BMI	1	0.00413	0.00195	2.11	0.0358
AGE	1	0.00474	0.00141	3.36	0.0009
ALC2	1	0.39119	0.18144	2.16	0.0322
R-Square	0.126694				

Source	DF	SS	MS	FValue	ProbF
Model	4	1.04587	0.26147	8.36	<.0001
Error	238	7.43958	0.03126	_	_
Corrected Total	242	8.48546	_	_	_

Parameter Estimates: Sex=F, Heartmeds=B

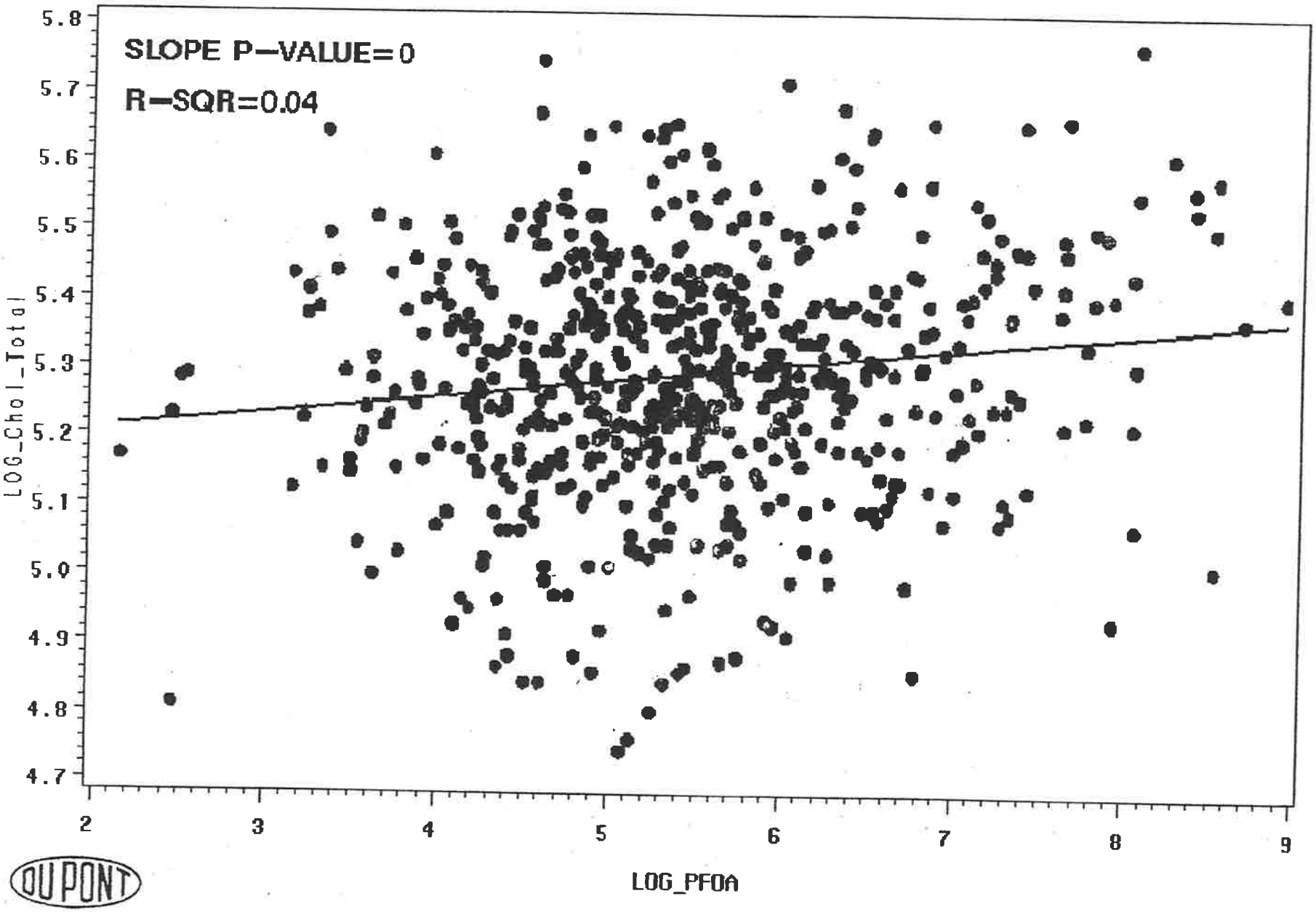
Variable	DF	Estimate	StdErr	tValue	Probt
Intercept	1	4.86657	0.07935	61.33	<.0001
LOG_PFOA	1	0.02283	0.01067	2.14	0.0334
BMI	1	0.00475	0.00178	2.68	0.0080
AGE	1	0.00383	0.00127	3.01	0.0029
ALC2	1	0.40589	0.17787	2.28	0.0234
R-Square	0.123255				

EPA 00591

LOG_Chol_Total vs LOG_PFOA : WW 2004, Terms=LogPFOA BMI AGE

ALO6

Where Sex=M, Heartmeds=NO



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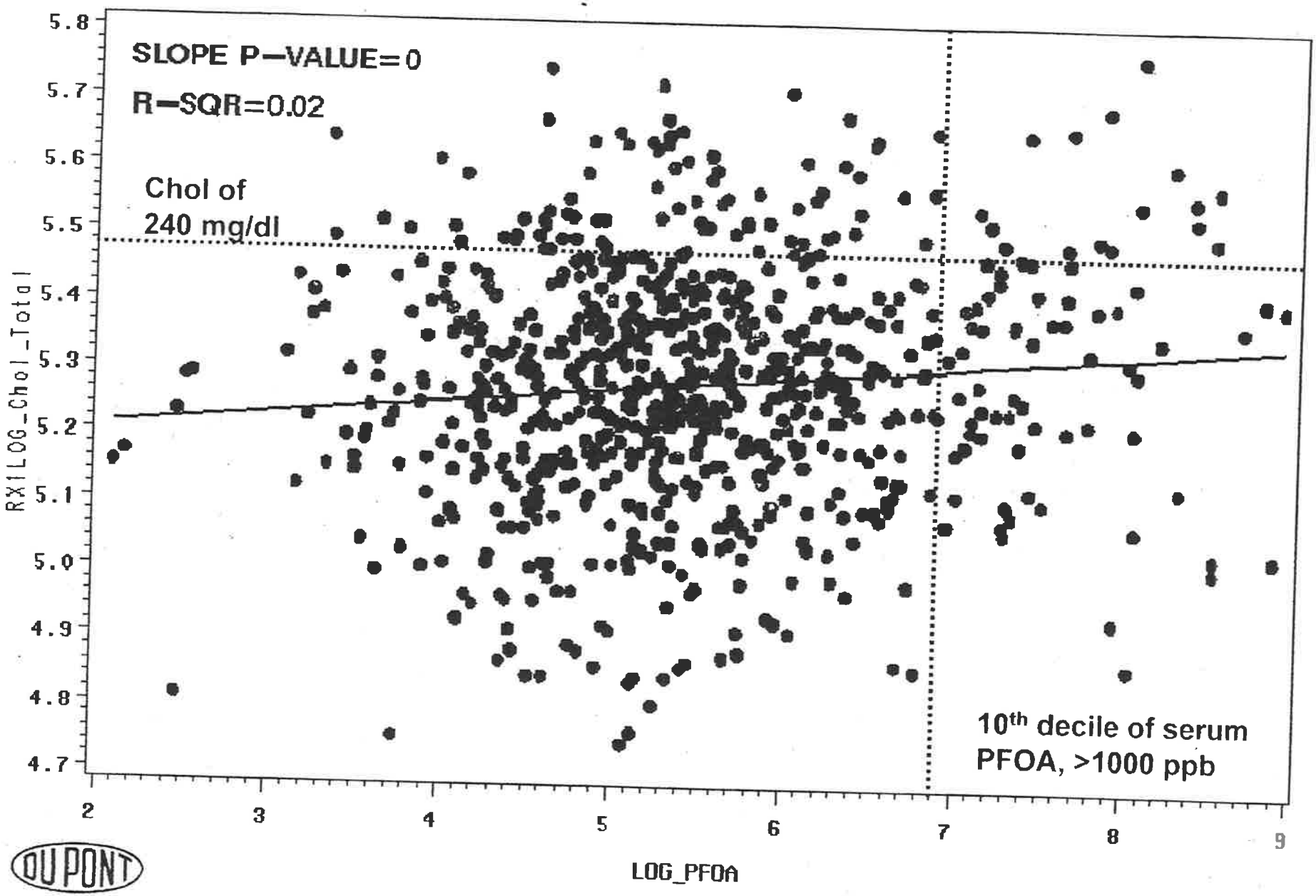
EPA 00592

LOG_Chol_Total vs LOG_PFOA : WW 2004, Terms=LogPFOA ALC6

Where Sex=M, Heartmeds=B



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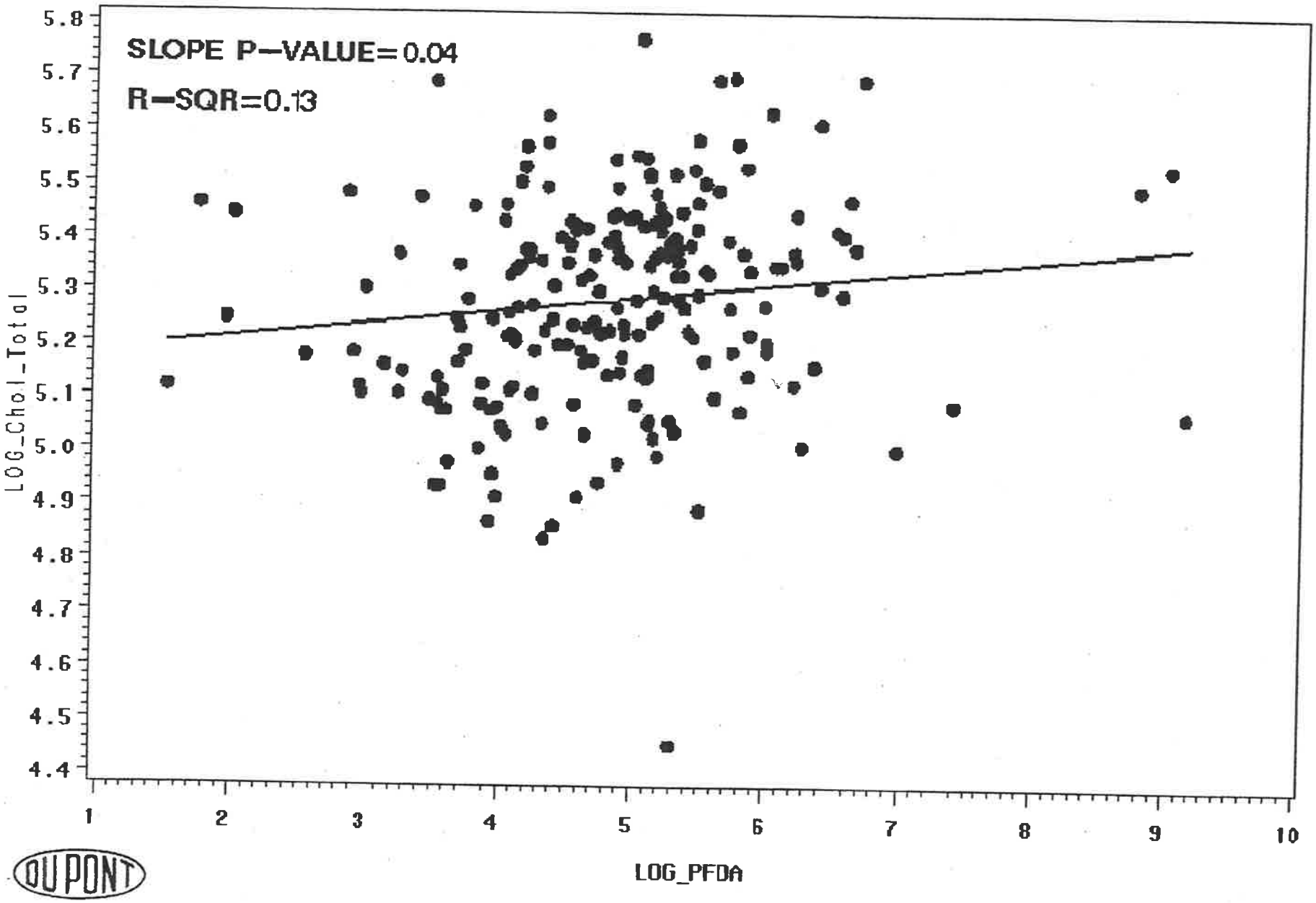
EPA 00593

LOG_Chol_Total vs LOG_PFOA : WW 2004, Terms= LogPFOA BMI AGE ALC2

Where Sex=F, Heartmeds=NO,



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EPA 00594

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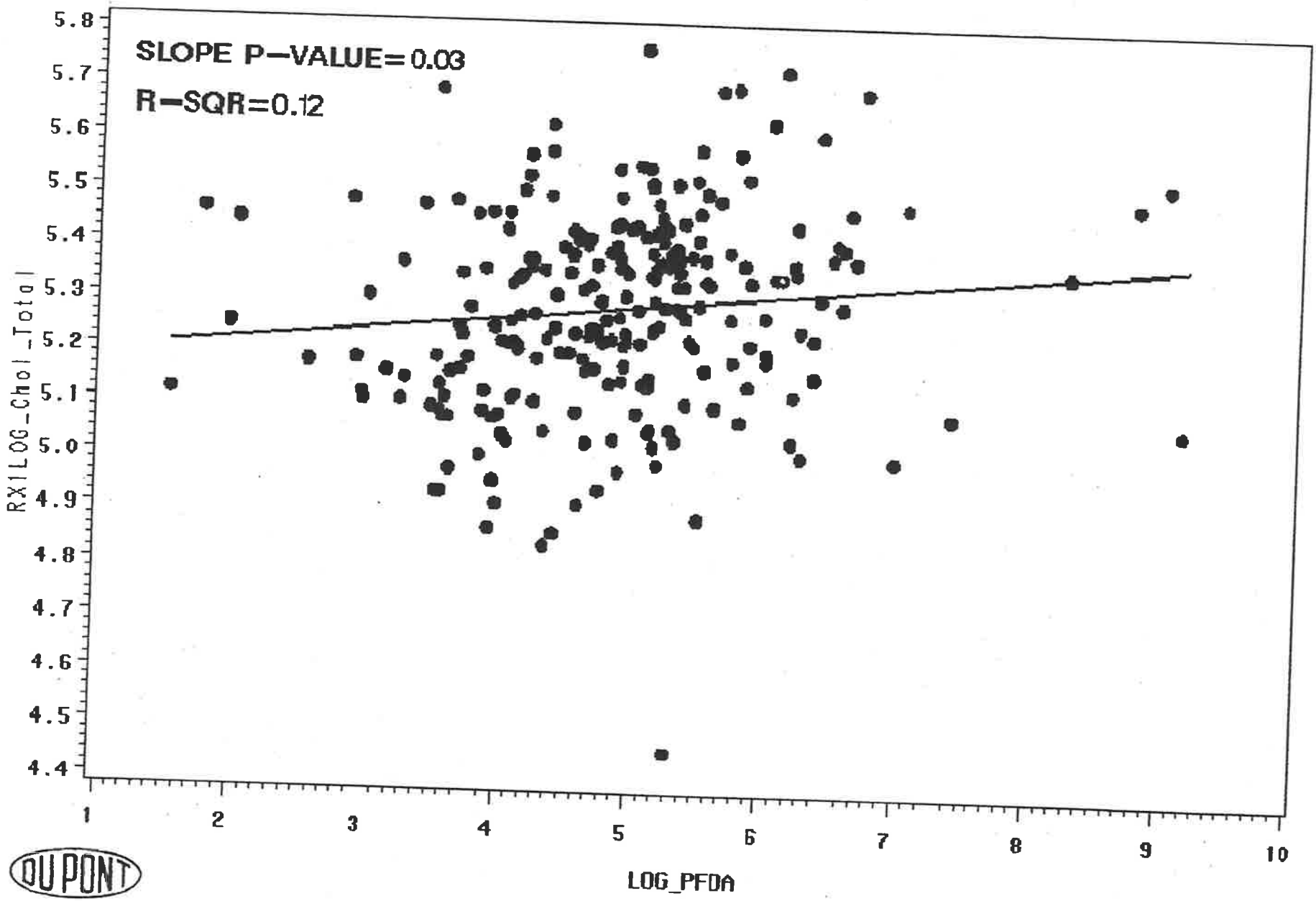
LOG_Chol_Total vs LOG_PFOA : WW 2004, Terms= LogPFOA BMI AGE ALC2

Where Sex=F, Heartmeds=B



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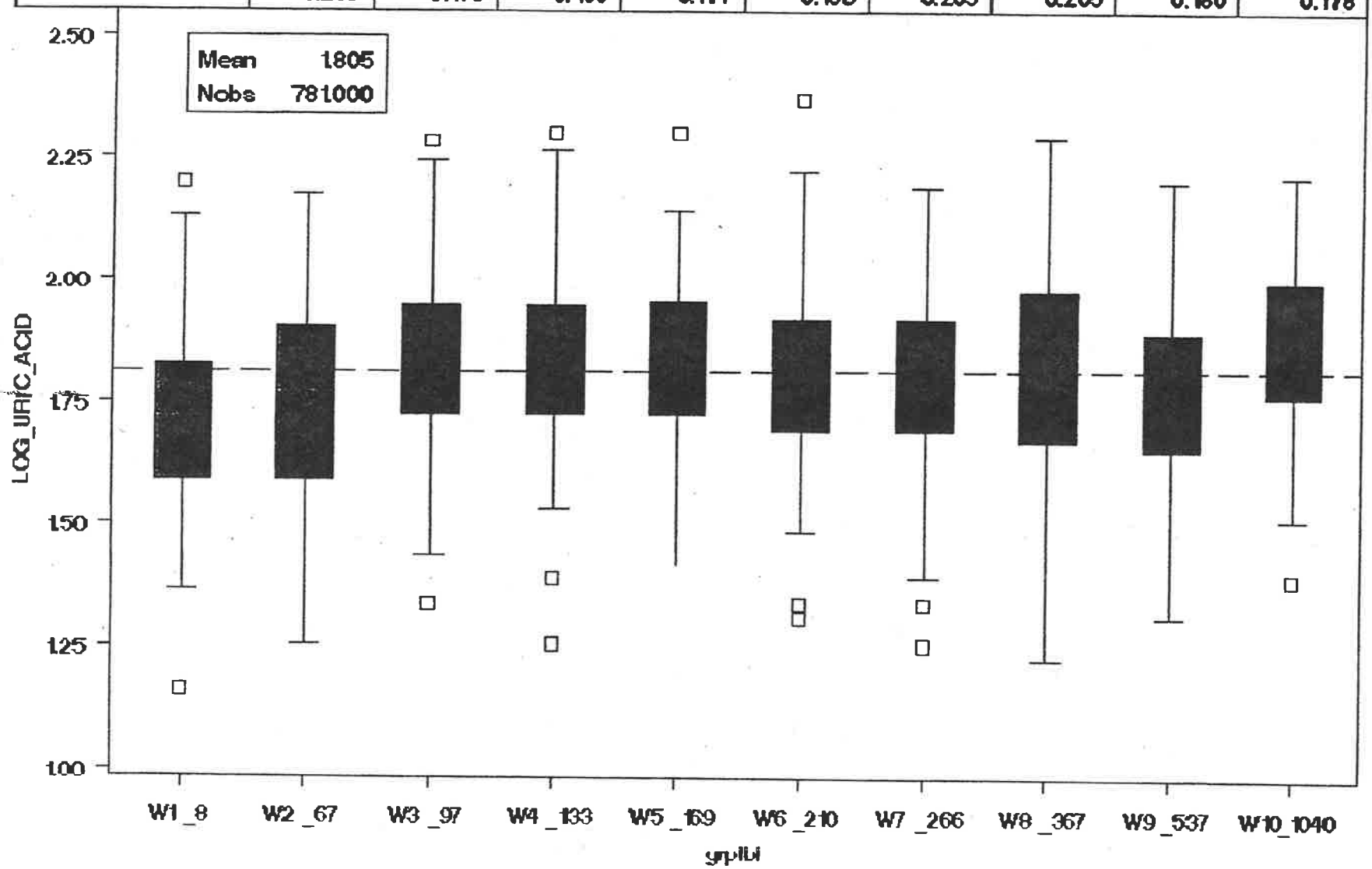
URIC_ACID by PFOA Quantile

Sex=M, Heartmeds=B, WW 2004

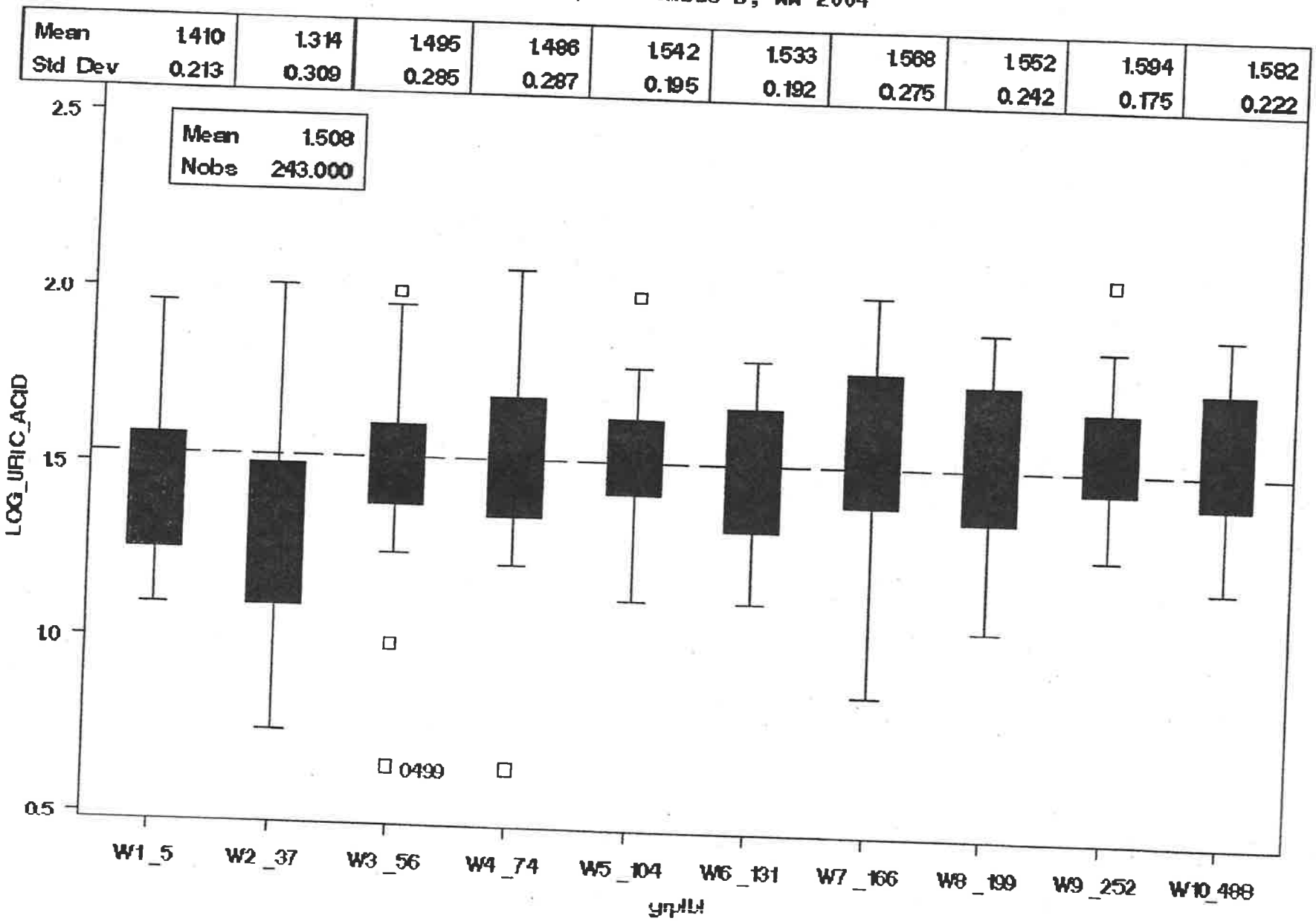
	W1_8	W2_67	W3_97	W4_133	W5_169	W6_210	W7_266	W8_367	W9_537	W10_1040
Mean	1.735	1.755	1.822	1.828	1.820	1.805	1.810	1.816	1.777	1.875
Std Dev	0.198	0.209	0.179	0.183	0.177	0.189	0.205	0.205	0.180	0.178



EPA 00596

URIC_ACID by PFOA Quantile

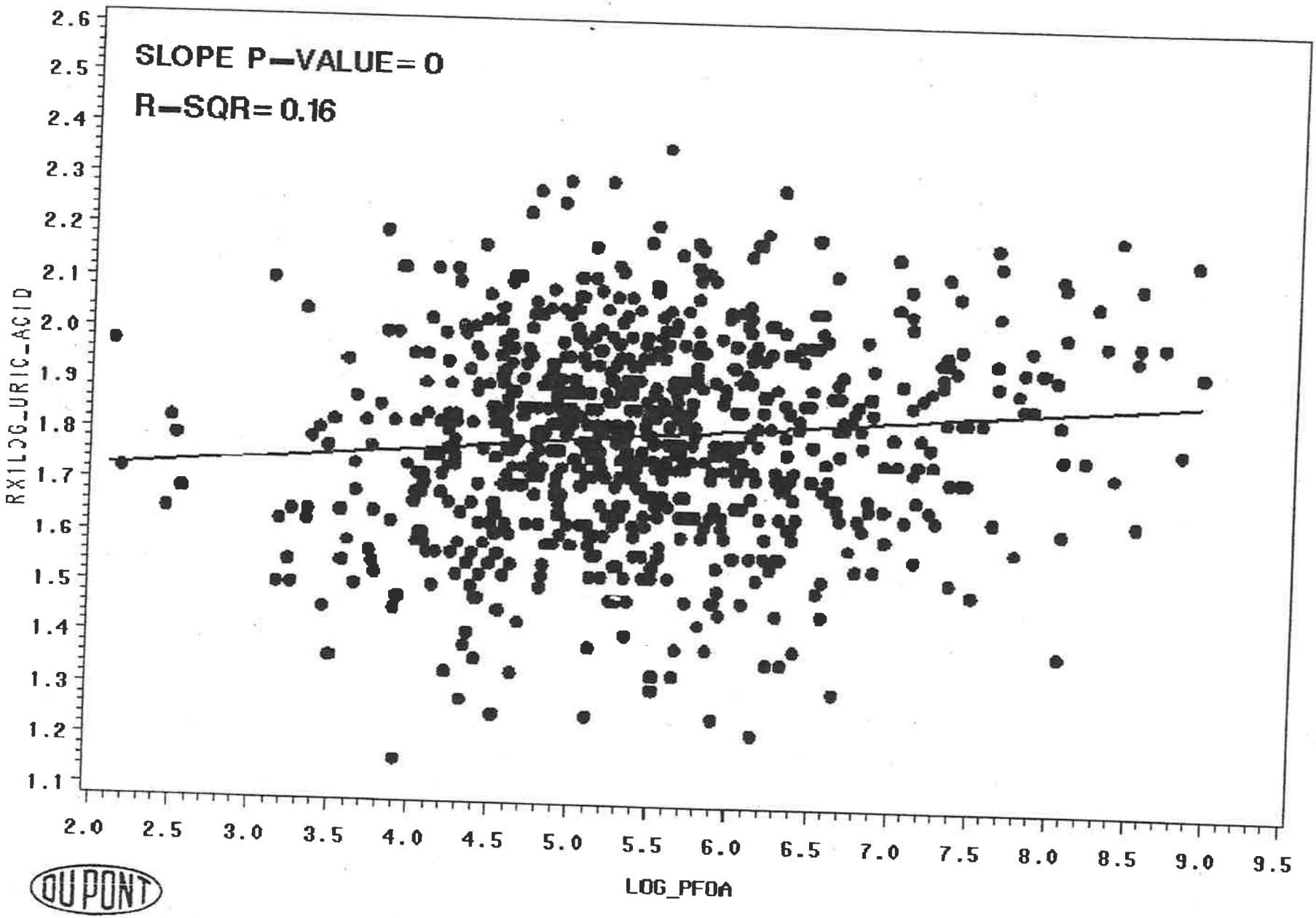
Sex=F, Heartmeds=B, WW 2004



EPA 00597

LOG_URIC_ACID vs LOG_PFOA: WW 2004, terms=LogPFOA BMI ALC4

Where Sex=M, Heartmeds=R



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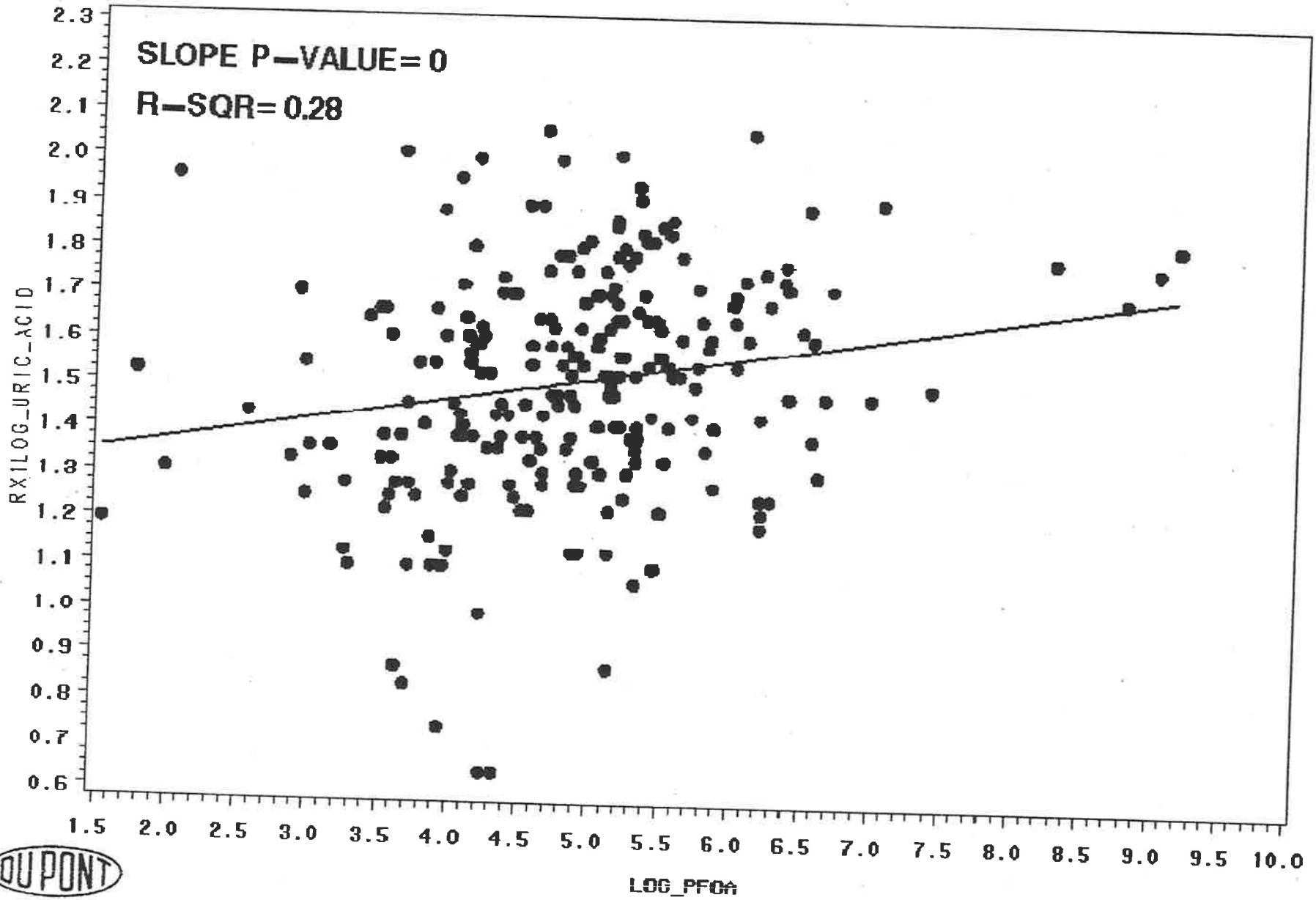
EPA 00598

LOG_URIC_ACID vs LOG_PFOA: WW 2004, Terms= LogPFOA BMI AGE

Where Sex=F, Heartmeds=B



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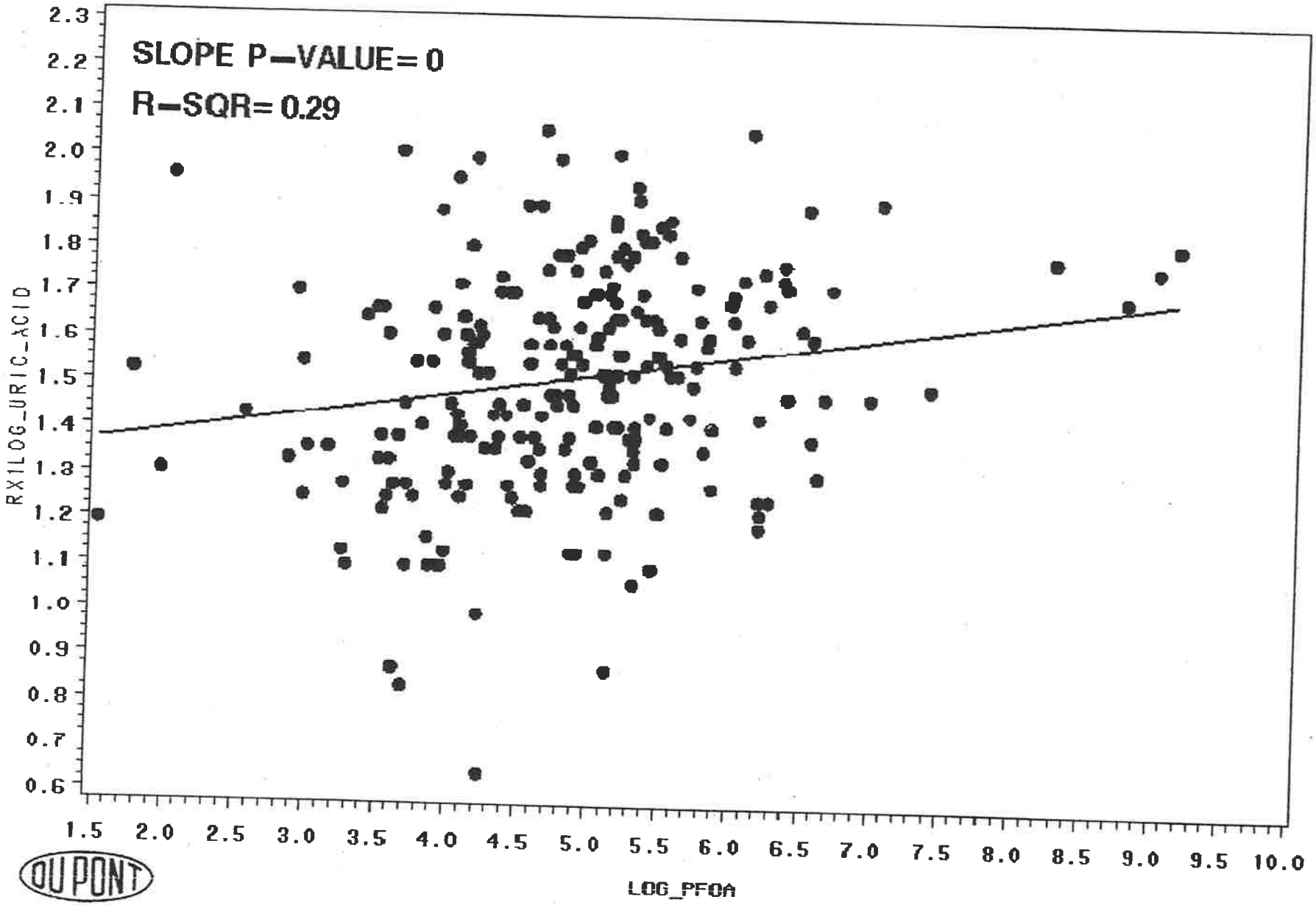
EPA 00599

LOG_URIC_ACID vs LOG_PFOA: CLEANED, Terms= LogPFOA BMI AGE

Where Sex=F, Heartmeds=B



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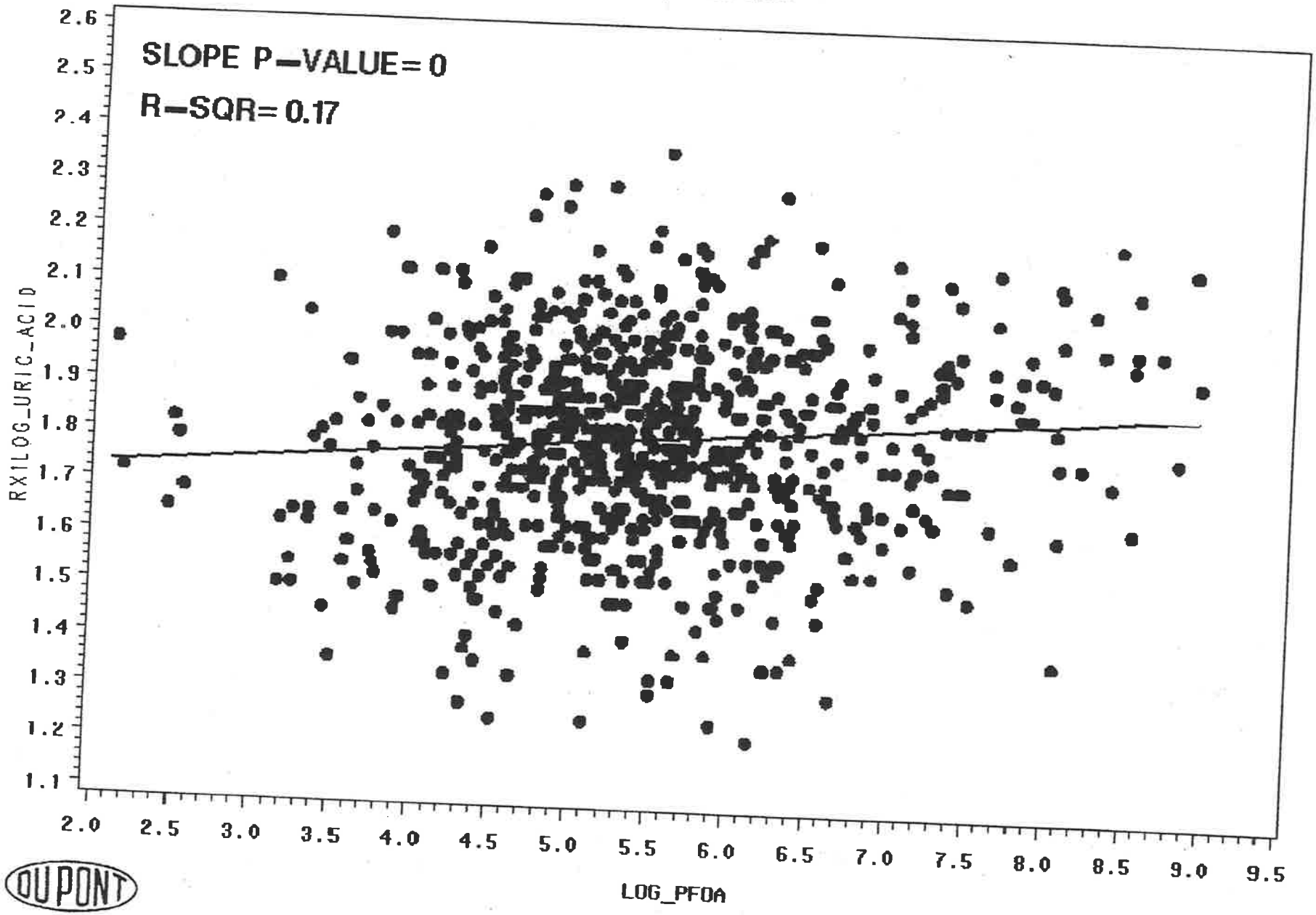
EPA 00600

LOG_URIC_ACID vs LOG_PFOA: CLEANED, Terms=LogPFOA BMI ALC4

Where Sex=M, Heartmeds=B



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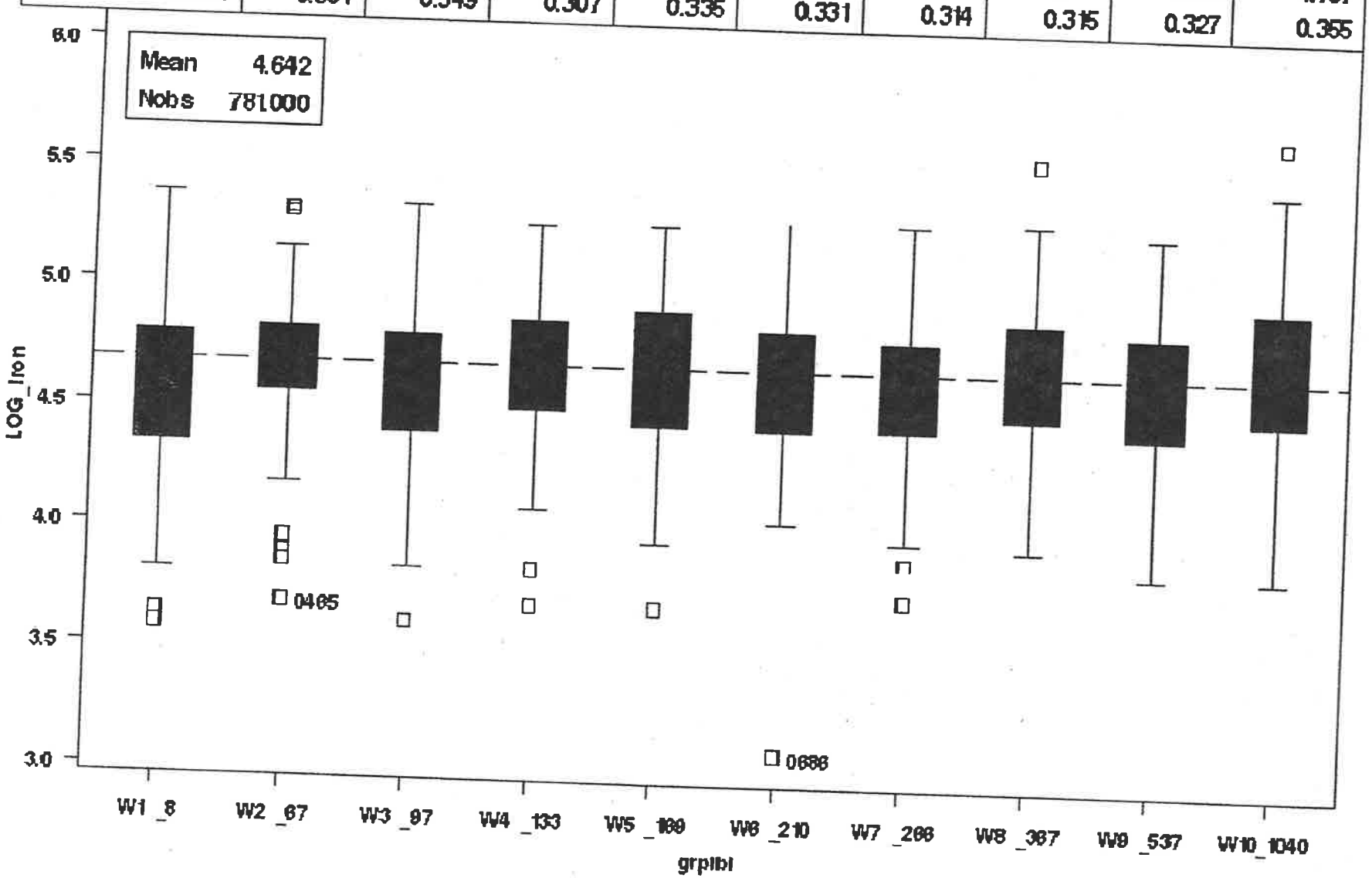
EPA 00601

IRON by PFOA Quantile

Sex=M, Heartmeds=B, NW 2004

	W1 _8	W2 _67	W3 _97	W4 _133	W5 _189	W6 _210	W7 _288	W8 _367	W9 _537	W10_1040
Mean	4.545	4.670	4.568	4.672	4.668	4.621	4.616	4.699	4.622	4.737
Std Dev	0.364	0.304	0.349	0.307	0.335	0.331	0.314	0.315	0.327	0.355

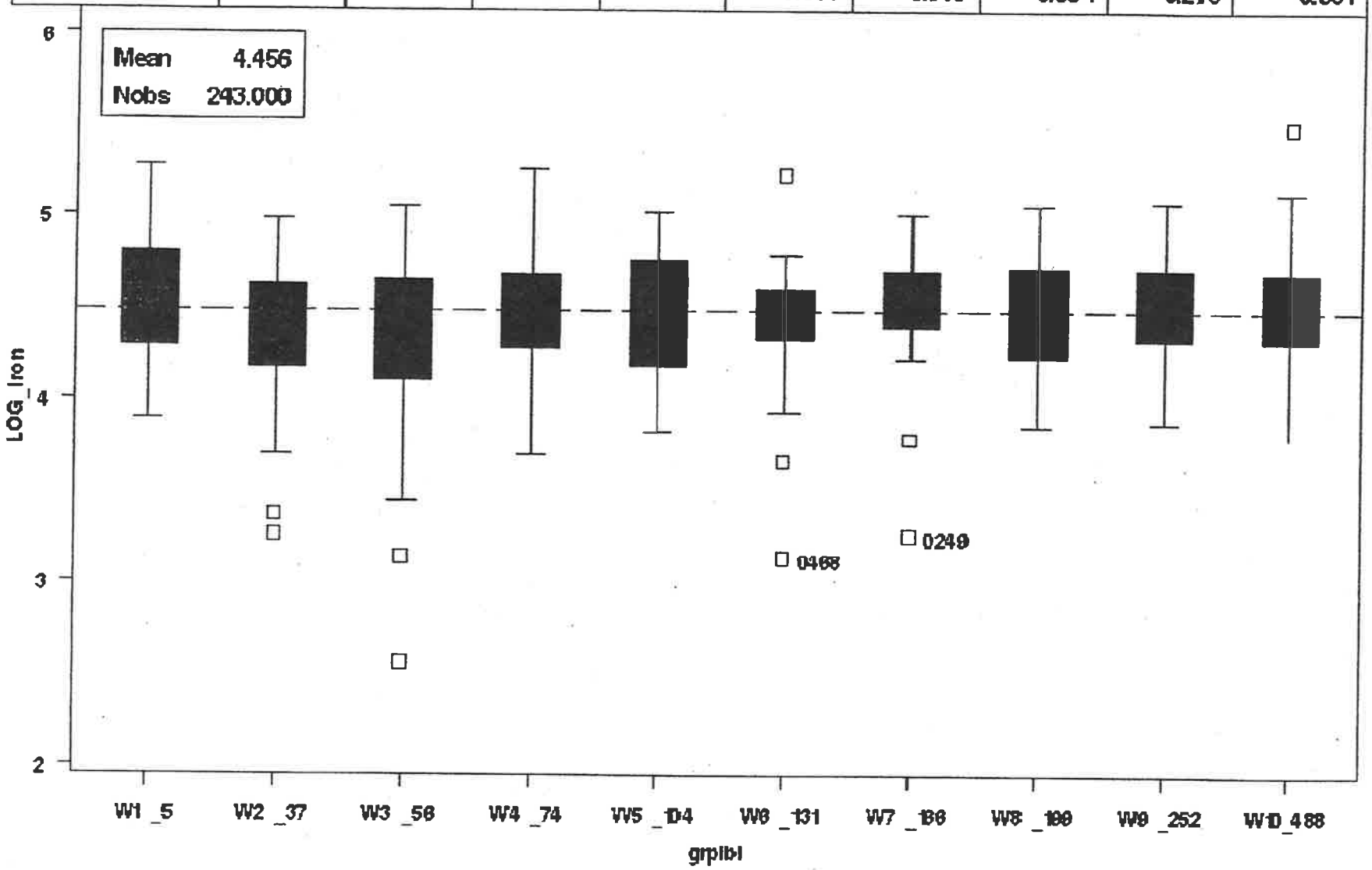


EPA 00602

IRON by PFOA Quantile

Sex=F, Heartmeds=B, WW 2004

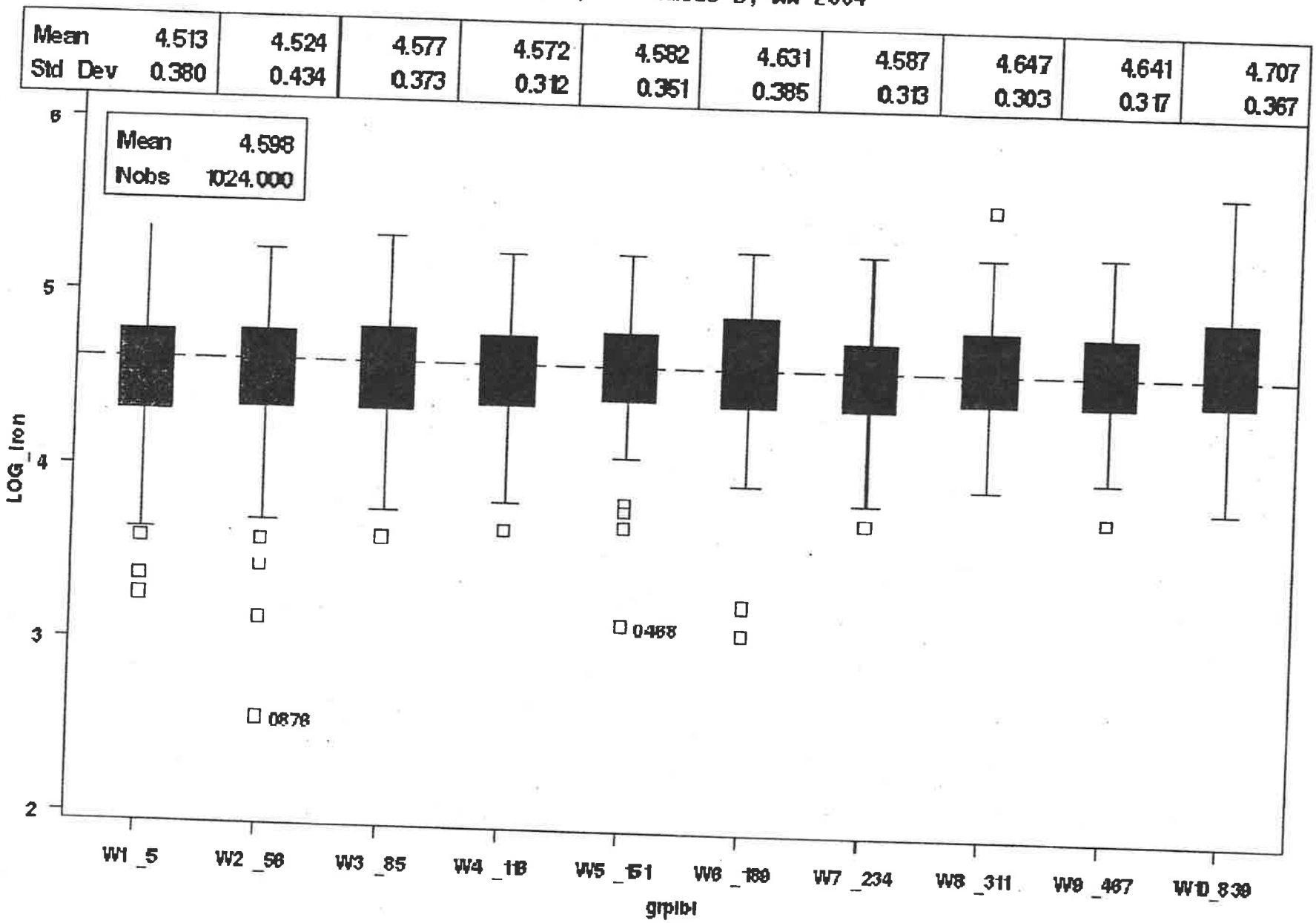
Mean	4.566	4.362	4.269	4.474	4.471	4.393	4.454	4.457	4.520	4.592
Std Dev	0.359	0.445	0.583	0.401	0.345	0.395	0.389	0.334	0.278	0.354



EPA 00603

IRON by PFOA Quantile

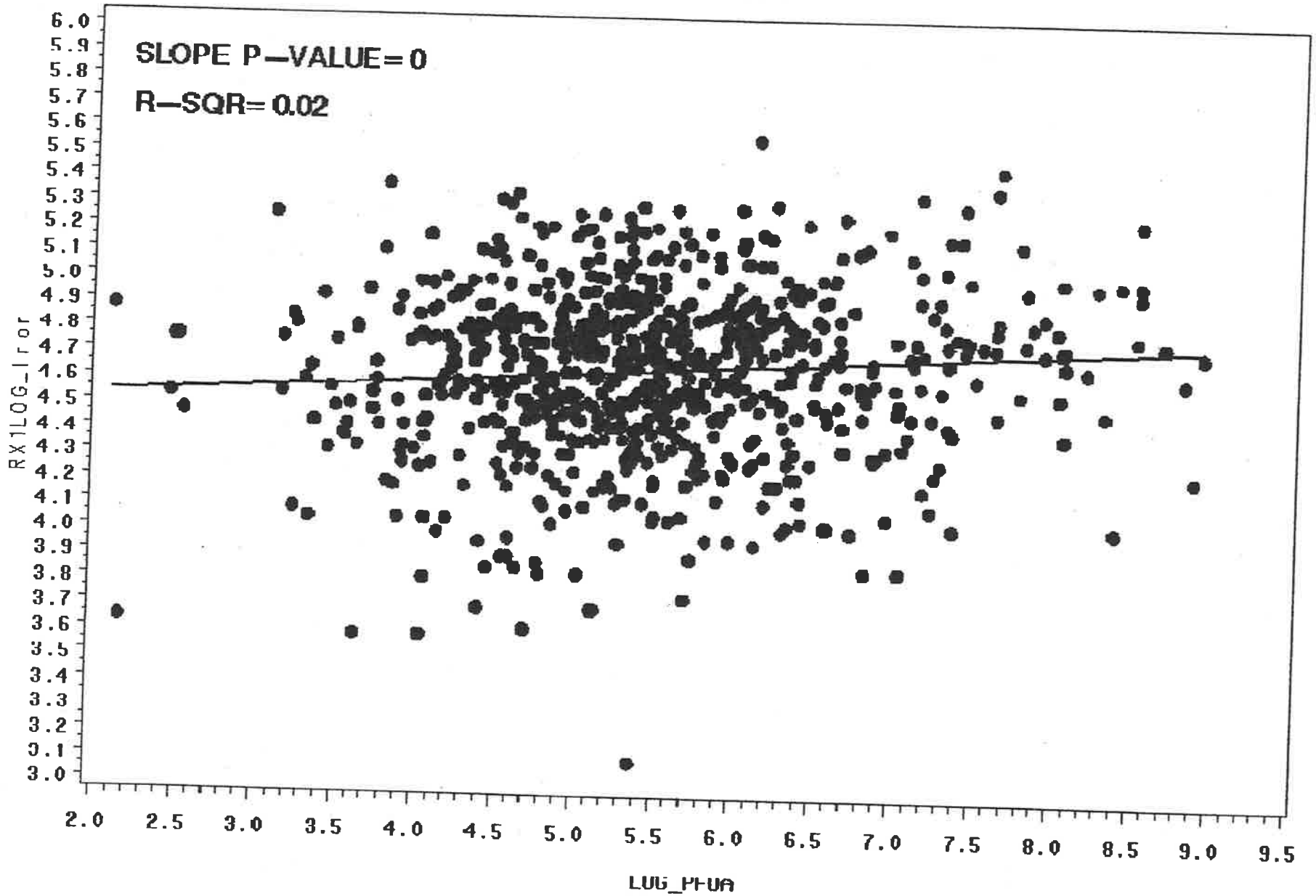
Sex=B, Heartmeds=B, WW 2004



EPA 00604

LOG_Iron vs LOG_PFOA: CLEANED, Terms= LogPFOA BMI

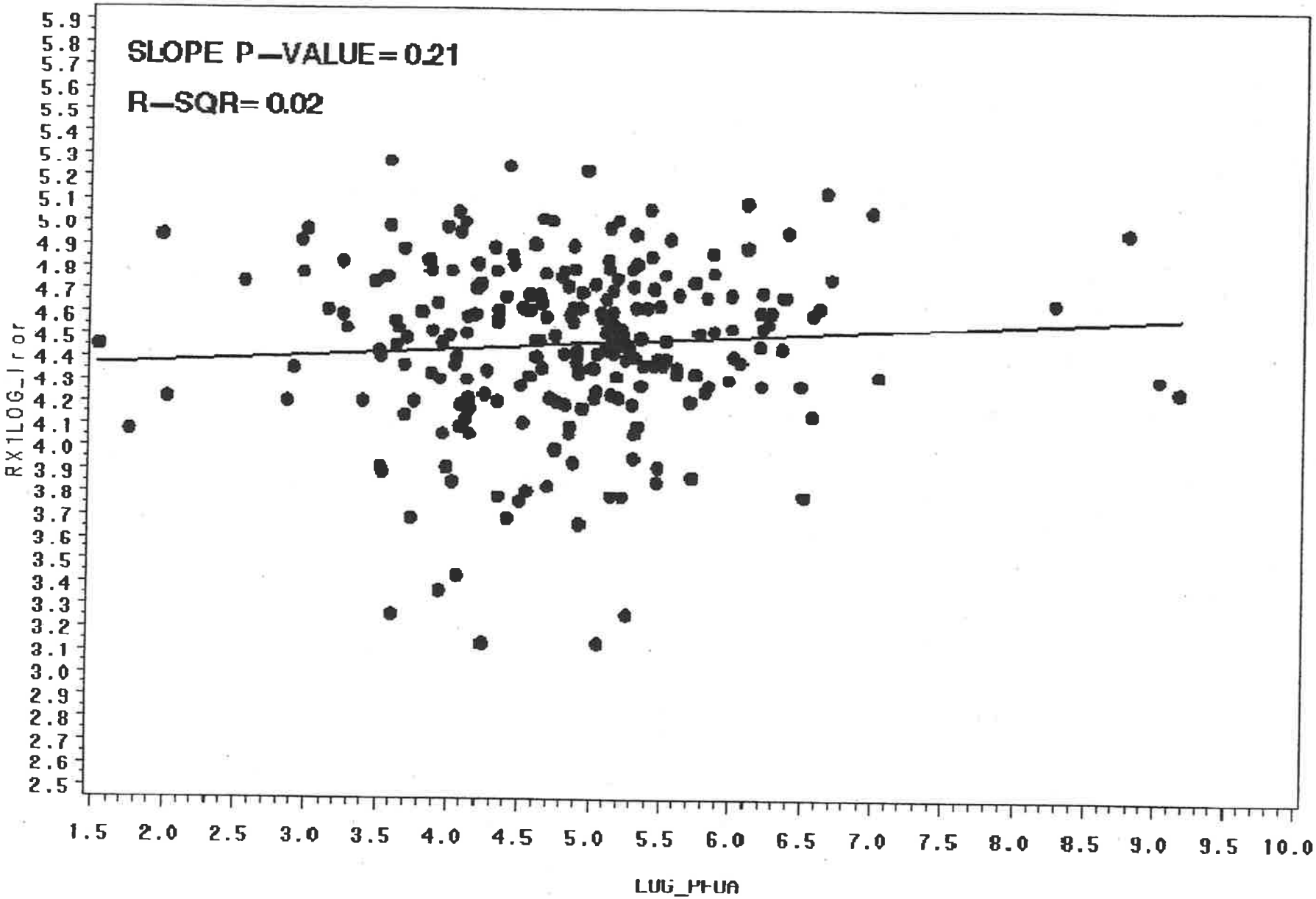
Where Sex=M, Heartmeds=B



EPA 00605

LOG_Iron vs LOG_PFOA: CLEANED, Terms= LogPFOA BMI

Where Sex=F, Heartmeds=B



EPA 00606

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Summary

- *To date, there are no human health effects known to be caused by PFOA; several statistical observations merit further study.*
  - Statistically significant associations are seen with serum PFOA levels and some serum lipid fractions, uric acid, and iron.
  - These associations were only seen in those study participants with the highest serum PFOA levels, which were equal to or greater than 1000 ppb.
  - DuPont, in collaboration with outside experts, is committed to conducting the studies that are necessary to understand the significance of these observations.

EPA, January 10, 2005

EPA 00607

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Timeline 2004

Epidemiology Study Timeline	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	1Q 05	2Q 05
Design, identification of contractors, approvals from review boards											
Operations and logistics planning, employee communications											
Clinical examinations, blood draw											
Electronic data capture/transfer/QA											
Initiate statistical analyses, draft methods, outline results section, meet with ERB											
Draft Final Report (Cross-sectional analyses)											
Draft Final Report (Cohort Mortality analyses)											

EPA, January 10, 2005

EPA 00608

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Plans for Further Work

DuPont Medical, Epidemiology, and Toxicology will work with medical and scientific advisors to design studies to answer remaining questions:

Are these observations reproducible?

Are similar associations seen in other worker populations?

Is there a cause and effect?

Is there a biological basis of these associations?

EPA 00609