FINAL REPORT

INTERLABORATORY VALIDATION OF THE FEMALE PUBERTAL ASSAY

ASSESSMENT OF PUBERTAL DEVELOPMENT AND THYROID FUNCTION IN JUVENILE FEMALE RATS

EPA CONTRACT NUMBER 68-W-01-023
WORK ASSIGNMENT 4-14

March 2006

Prepared for

U.S. ENVIRONMENTAL PROTECTION AGENCY
ENDOCRINE DISRUPTOR SCREENING PROGRAM
WASHINGTON, D.C.

Prepared by

BATTELLE
505 King Avenue
Columbus, Ohio 43201

Interlaboratory Validation of the Female Pubertal Assay

Assessment of Pubertal Development and Thyroid Function in Juvenile Female Rats

EPA CONTRACT NUMBER 68-W-01-023
WORK ASSIGNMENT 4-14

_____ _____

Zhenxu J. Ma, Author Date

_____ _____

Paul I. Feder, Reviewer Date

TABLE OF CONTENTS

Page

LIST OF TABLES

LIST OF FIGURES

SUMMARY AND DISCUSSION

This report discusses the methods and results of the interlaboratory statistical analysis of the female pubertal assay conducted under Work Assignment 4-14 of the USEPA Endocrine Disruptor Screening Program, Interlaboratory Validation of the Female Pubertal Assay. Three laboratories, Argus Laboratories, WIL Laboratories, and Huntingdon Laboratories conducted the assay in accordance with the test method specified by the EPA. Each laboratory tested a corn oil control group and two doses each of three chemicals: DE-71 (30 and 60 mg/kg/day), 2-Chloronitrobenzene (25 and 100 mg/kg/day), and Methoxychlor (12.5 and 50 mg/kg/day) with n=15 juvenile female rats per group. The animals were dosed daily from post natal day 22 to post natal day 42, during which time growth and body weight data and VO status were determined. They were sacrificed on post natal day 42 (and some on PND 43), at which time a suite of organ weights and hormonal concentrations were determined.

The principal results of the statistical analysis are summarized below. Unless specified otherwise, statistically significant results correspond to significance level 0.05 or less.

1. The initial body weights (at PND21) for all treatment groups were about same within individual laboratories. Initial body weights at Argus Laboratories were consistently greater than those at Huntingdon Laboratories, which in turn were consistently greater than those at WIL Laboratories.

2. 2-Chloronitrobenzene and Methoxychlor slowed down body weight growth, at least during portions of the dosing period. The high dose of Methoxychlor was significantly lower than the vehicle control for final body weight and for body weight gain, averaged across all laboratories and for the individual laboratories. However, the low dose of 2-Chloronitrobenzene was significantly higher than the vehicle control for WIL Laboratories, although the high dose did not differ significantly. Figures 2, 5, and 8 indicate that 2-Chloronitrobenzene slowed down growth in the earlier parts of the growth period, with the animals catching up to the control group animals by the end of the growth period. DE-71 did not have a significant effect on body weight growth. Similar changes were observed for final body weight as a percent of control.

3. The test chemicals affected time to vaginal opening. The high dose of 2-Chloronitrobenzene had significantly higher age at vaginal opening than the control group, averaged across all laboratories and at each of the individual laboratories. The high dose of Methoxychlor had significantly lower age at vaginal opening than the vehicle control group, averaged across all laboratories and at each of the individual laboratories. DE-71 had a weaker effect on time to vaginal opening than 2-Chloronitrobenzene or Methoxychlor. The high dose of DE-71 had significantly higher age at vaginal opening than the control group at WIL Laboratories, but not at the other laboratories. For each control group and for most of the chemical groups the animals at Argus Laboratories reached vaginal opening earlier and the animals at WIL Laboratories reached vaginal opening later. At the high dose of Methoxychlor all the laboratories had about the same age at vaginal opening.

4. The high dose of 2-Chloronitrobenzene had significantly higher body weight at vaginal opening than the vehicle control group, averaged across laboratories and at each individual laboratory. The high dose of Methoxychlor had significantly lower body weight at vaginal opening than the vehicle control group, averaged across laboratories and at each individual laboratory. This corresponds to the increased or decreased age at vaginal opening respectively. For the high dose of DE-71 WIL Laboratories had significantly increased age at vaginal opening and body weight at vaginal opening, but not the other laboratories.

5. There were laboratory-to-laboratory differences in organ weights for each of the control and test chemical groups. Organ weights at Argus Laboratories were consistently higher than those at the other two laboratories for paired adrenals, paired kidneys, liver, and pituitary. Organ weights at WIL Laboratories were lower than those at the other two laboratories for paired ovaries and blotted thyroid. Organ weights for Huntingdon Laboratories were lower than those at the other two laboratories for paired kidneys and pituitary. These differences enlarged the laboratory-to-laboratory variation and the associated confidence interval widths, averaged across laboratories.

6. There were laboratory-to-laboratory differences in hormonal assay values for each of the control and test chemical groups. At Argus Laboratories serum thyroxine was consistently high and thyroid stimulating hormone was consistently low. At WIL Laboratories thyroid stimulating hormone was consistently larger than at the other two laboratories. At Huntingdon Laboratories serum thyroxine was relatively low for the 2-Chloronitrobenzene and the Methoxychlor dose groups.

7. Averaged across laboratories the following significant growth and body weight changes relative to controls were observed:

    a. At the high dose of DE-71
        No significant changes

    b. At the high dose of 2-Chloronitrobenzene
        Increased − Age at VO, body weight at VO

    c. At the high dose of Methoxychlor
        Decreased − Final body weight, body weight gain, final body weight as a percent of control, age at VO, body weight at VO

8. Averaged across laboratories the following significant organ weight changes relative to controls were observed:

    a. At the high dose of DE-71
        Increased − Liver

    b. At the high dose of 2-Chloronitrobenzene
        Increased − Liver
        Decreased − Adrenals, ovaries, uterus blotted, uterus wet

c. At the high dose of Methoxychlor
Decreased − Kidneys, liver, ovaries

9. Averaged across laboratories the following significant hormonal assay changes relative to controls were observed:

a. At the high dose of DE-71
Increased – Thyroid stimulating hormone
Decreased − Serum thyroxine

b. At the high dose of 2-Chloronitrobenzene
Decreased – Serum thyroxine

c. At the high dose of Methoxychlor
No significant changes

INTRODUCTION AND BACKGROUND

Study Design

Three laboratories, Argus Laboratories, WIL Laboratories and Huntingdon Laboratories conducted the juvenile female rat pubertal development assay in accordance with the test method specified by the EPA.

Within each laboratory two doses each of three chemicals: DE-71 (30 and 60 mg/kg/day), 2-Chloronitrobenzene (25 and 100 mg/kg/day), and Methoxychlor (12.5 and 50 mg/kg/day) were administered by gavage daily to juvenile female animals from PND22 (post natal day 22) through PND42. In addition, a vehicle control group (corn oil) was simultaneously tested in each laboratory. Argus Laboratories and WIL Laboratories each had one control group. Huntingdon Laboratories had two control groups. The three chemicals and the vehicle control were tested simultaneously at Argus Laboratories and WIL Laboratories. At Huntingdon Laboratories the test was carried out in two groups. DE-71, 2-Chloronitrobenzene, and a vehicle control group were tested together in the first group. Methoxychlor and a second vehicle control group were tested together in the second group. The sample size was n=15 juvenile female rats per group, for a total of seven groups and 105 animals for Argus Laboratories and WIL Laboratories, and a total of eight groups and 120 animals for Huntingdon Laboratories.

Data Used in Analyses

The test method specifies five categories of data:

1. Growth - daily body weights (4 endpoints)
2. Age and body weight at vaginal opening (VO) (4 endpoints)

3. Hormonal analysis (2 endpoints)
    Serum thyroxine (T_4)
    Thyroid stimulating hormone (TSH)
4. Organ weights - 7 organs (8 endpoints)
5. Histology
    Uterine
    Ovarian
    Thyroid
6. Vaginal cytology

Histology and cytology data were not analyzed statistically.

Organs were weighed in pairs when appropriate (ovaries, kidney, and adrenal glands). Uterus was weighed wet and blotted.

All animals attained VO prior to necropsy. All animals survived until final necropsy. At WIL Laboratories and at Argus Laboratories there was one necropsy day, on PND42. At Huntingdon Laboratories 64 animals (8 per treatment group) were sacrificed on PND42 and 56 animals (7 per treatment group) were sacrificed on PND43. For purposes of graphical and tabular summaries the body weight at PND42 was used for all animals, for consistency of comparison. However for purpose of specifying age and body weight at VO for those animals that had VO on day of final sacrifice, age and body weight on day of necropsy (PND42 or PND43) were used.

At Argus Laboratories, five organ weights data values were deleted by quality assurance due to procedural deviations:

Animal 104 - Pituitary
Animal 123 - Adrenals
Animal 129 – Ovaries
Animal 146 - UterusWet and UterusBlotted.

On day of VO for each animal WIL Laboratories and Huntingdon Laboratories determined body weights twice – once for dose determination and a second at clinical observations. In this report the summaries for body weight at VO were based on the dosing body weights. They may differ slightly from summaries based on the clinical observations body weights (e.g. WIL Laboratories).

Deviations from the Statistical Analysis Plan

Huntingdon Laboratories divided its test schedule into two portions. This necessitated that two control groups be run, one in each test portion. The two test portions were:

- Group 1: Corn oil control, DE-71, 2-Chloronitrobenzene
- Group 2: Corn oil control, Methoxychlor

To determine whether there were significant differences between the two control groups, two-sample t-tests were carried out for each response. The results are displayed in Appendix B. One of 15 comparisons was significant at the 5 percent level and three of 15 comparisons were significant at the 10 percent level. This is compatible with random variation. However the signs of the differences in average responses may indicate a systematic difference between control groups. The two hormonal assay averages were greater in group 1 than in group 2. The eight organ weight averages were greater in group 2 than in group 1. The five growth and body weight averages were also greater in group 2 than in group 1.

The principal statistical analyses were divided into two portions, corresponding to the two test portions at Huntingdon Laboratories. For Argus Laboratories and WIL Laboratories the same corn oil control groups were used for each portion.

STATISTICAL METHODS

This section discusses the summaries, displays, and statistical analyses that were used to summarize the results within each laboratory and combined across laboratories. The statistical analysis was based on the test method provided by the EPA but was extended to include comparisons across laboratories.

Outlier Detection and Preliminary Data Summaries Prior to Analysis

Outlier screens were carried out prior to the full analysis. Screens were carried out separately for each laboratory and for each endpoint, based on the untransformed data. Both unadjusted and initial body weight covariate adjusted values were determined for organ weights and for age and body weight at VO, but the outlier screens were carried out based on the unadjusted values only. The outlier screening procedure is described in detail in Appendix A. Appendix A also includes the outlier screening results. Summaries of the raw data by laboratory and group are displayed in Appendix A both with and without the observations that were flagged by the outlier screening procedure and that are considered to be potential outliers. For organ weights, and age and body weight at vaginal opening (VO), summaries of the data by laboratory and group were carried out both with and without potential outliers after adjusting for initial body weights. The summaries of the raw data include N, mean, standard deviation, and CV. The within treatment group CV was calculated as the ratio of the within laboratory residual standard deviation to the least squares mean. The summaries of the unadjusted values also include min and max.

The results of the preliminary outlier screens and the raw summary values were submitted to the EPA for review prior to carrying out the full analysis. The EPA reviewed the list of the potential outliers, as detected by the preliminary outlier screen and divided the screened values into three categories: those that were to be included in all analyses, those that were to be excluded from all analyses, and those that were to be treated as outliers. Table A-1 in Appendix A displays the three categories of screened values.

The results of the principal analyses were similar with and without the outliers. For age at VO, body weight at VO and the organ weights, the results were similar with and without adjustment by centered initial body-weight.

Blocking Variable

At Huntingdon Laboratories the necropsy was divided between PND42 and PND43, as discussed above. A blocking variable was introduced to distinguish these two necropsy days (Block ≡ 0 if PND = 42 and Block ≡ 1 if PND = 43). This was accounted for in the statistical analysis.

Heterogeneity of Residual Variance Among the Laboratories and Treatment Groups

Preliminary tests for heterogeneity of variance were carried out on the data excluding the values flagged by the outlier screen and identified by the EPA as outliers, separately for the two test portions.

For each endpoint the extent of heterogeneity of variability was assessed across laboratories and treatment groups within laboratories. The data were combined across laboratories and a three factor mixed effects analysis of variance model was fitted to the data, including the factors laboratory (random), treatment (fixed), and laboratory×treatment interaction (random). For organ weight responses and for age and body weight at vaginal opening (VO), mean centered initial body weight (i.e., initial body weight minus mean initial body weight over all the test groups within the test portion) and (mean centered initial body weight) ×laboratory interaction were included in the model as covariates.

Four versions of the model were fitted to test for heterogeneity of residual variance.

1. Separate variances for each laboratory and each treatment group (3×5=15 or 3×3=9 variances)
2. Separate variances for each laboratory and chemical (or control) (3×3=9 or 3×2=6 variances)
3. Separate variances for each laboratory (3×1=3 variances)
4. Common variances across all groups

These models were compared by likelihood ratio tests. For each response variable, the model was selected that had the simplest variance structure that was not a significantly worse fit than a more complex variance structure. The subsequent analyses were carried out based on the selected variance models.

Data Summaries - Full Analysis

Data summaries include tables and figures, patterned after those specified in the EPA test method. The tables and figures specified in the test method were extended to provide comparisons across laboratories.

Summary tables were prepared including all the data (except those specified by the EPA to be excluded -- Appendix Table A-1) and additionally excluding the values identified as outliers. The summary tables that excluded outliers were prepared only for those responses for which there was at least one outlier within an individual laboratory. (Note that responses for which an outlier was excluded for any chemical and treatment group were included in the "excluded outlier" summaries for all chemicals and treatment groups). Summary figures include all the data (except those specified by the EPA to be excluded -- Appendix Table A-1). These summary tables and figures were generated based on the statistics produced by the analysis of variance and covariance models that are discussed at the end of the report.

Tables were prepared to display summary values for the four categories of responses enumerated above. Tables 1-A, 1-B compare the model fits for the alternative covariance structures, for test portions 1 and 2 respectively. Tables 2-25 display summaries of the results within the control groups and the treatment groups and their comparisons. Initial body weight at PND21, final body weight, body weight gain, final body weight as percent of control, and hormonal analyses were summarized without adjustment for initial body weight at PND21. Age and body weight at VO, and organ weight variables were summarized with and without adjustment for initial body weight at PND21. Each table corresponds to a single chemical and the associated control group. Some tables display results from each laboratory separately. Other tables display results combined across all three laboratories. The standard errors associated with the summary results within laboratories incorporate only within laboratory variability. The within laboratory coefficient of variation (CV) was calculated as the ratio of the within laboratory residual standard deviation to the least squares mean. This represents the CV among the individual responses within a laboratory. The standard errors associated with summary results combined across laboratories incorporate laboratory-to-laboratory variation as well as within laboratory variation. The results combined across laboratories include an estimate of the coefficient of variation (CV) across laboratories. The among laboratories CV was approximated as CV≈ $[\sqrt{3}(\text{stderr})/(\text{LS mean})]\times 100\%$, where "stderr" is the combined laboratories standard error of the least squares mean (LS mean). This represents the CV among the within laboratory mean responses.

Figures 1-12 display the means and ±2 standard error bars for the daily body weights from PND21 to PND42. Each figure includes three groups, the control and the two doses of a single chemical. Within each plot the mean age of the controls at VO is indicated as a vertical reference line on the PND axis. Figures were prepared for the individual laboratories, as well as combined across the three laboratories.

Figures 13-38 display the least squares means ± 2 standard errors for each of the eight treatment groups (two control groups (one for each test portion) and two treatment groups for each of the three test chemicals) within each laboratory and combined across laboratories. The standard errors associated with summary results within laboratories incorporate only within laboratory variability. The standard errors associated with summary results combined across laboratories incorporate lab-to-lab variability as well as within laboratory variability.

Each figure contains eight groups of bars, each group corresponding to a control or test chemical dose group. Each group includes four bars, corresponding to each of the three

laboratories and to the laboratories combined. Each bar is centered at the least squares mean with width of 2 standard errors above and below the least squares mean. All figures are presented at the end of the report.

Analysis of Variance and Covariance

For each of the responses summarized in Tables 2-25, analysis of variance models were fitted to the data to estimate treatment group effects within individual laboratories and combined across laboratories. For initial body weight, final body weight, body weight gain, final body weight as a percent of control, and the two hormonal assays, only the unadjusted responses were analyzed. For age and body weight at VO and for organ weight responses the unadjusted responses were analyzed as well as the covariate adjusted responses, using mean centered initial body weight at PND21 as the covariate adjustment factor.

Analyses were carried out based on all the data and after omitting outliers. The (possibly heterogeneous) residual variance structures assumed in these analyses were those arrived at as discussed above and are summarized in Tables 1-A and 1-B. Separate analyses were carried out for each test portion.

For each response an analysis of variance model with the selected covariance structure was fitted to the combined data across laboratories and the control group and the one or two test chemicals within the test portion. Treatment group was a fixed effect, and laboratory, and laboratory×treatment group interaction were fixed effects for some models and random effects for others.

For the covariate adjusted responses the factors covariate (mean centered PND21 initial body weight) and covariate×laboratory interaction were included in the models as fixed effects. For calculating summaries within individual laboratories, laboratory, treatment group, and laboratory×treatment group interaction were treated as fixed effects. For calculating summaries combined across laboratories, treatment group was treated as a fixed effect, and laboratory and laboratory×treatment group interaction were treated as random effects.

Least squares means and associated standard errors and 95% confidence intervals for individual treatment groups, and comparisons of each treatment group with its corresponding control group were calculated based on the analysis of variance or analysis of covariance models. The standard approach for calculating least-squares means across two blocks and associated standard errors gives equal weight to each of the two blocks. However the PND42 block includes about half the observations in Huntingdon Laboratories and all the observations in Argus Laboratories and WIL Laboratories. The PND43 block includes about half the observations only in Huntingdon Laboratories. The standard least squares mean calculation substantially over weights the observations in the PND43 block and substantially under weights the observations in the PND42 block. Proper weights needed to be constructed so that for the least squares means combined across laboratories, equal weights were given to each of the three laboratories and within Huntingdon Laboratories, equal weights were given to each of the two blocks. The least squares means, standard errors, and CVs are displayed in Tables 2-25 and in Figures 13-38.

Significance levels for the comparisons were based on two-sample two-sided t-tests. The least squares means, standard errors, CVs, sample sizes, and confidence intervals are displayed in the tables and figures within each laboratory or combined across laboratories. Results significant at the 0.05 significance level are indicated by "*".

The standard errors and confidence intervals for the least squares means within individual laboratories reflect only within laboratory variation. To estimate these effects and their standard errors, the laboratory and laboratory×treatment group factors were treated as fixed effects. The least squares means and associated standard errors for treatment groups within laboratories and comparisons between test chemical dose groups and controls within laboratories were determined based on the within laboratory variation.

The standard errors and confidence intervals for the least squares means combined across laboratories reflect laboratory-to-laboratory variation and as well as within laboratory variation. To estimate these effects and their standard errors, laboratory and laboratory×treatment group factors were treated as random effects and least squares means and associated standard errors for individual treatment groups combined across laboratories and comparisons between treatment groups and control, combined across laboratories, were determined.

STATISTICAL ANALYSIS RESULTS

Outlier screens were carried out on all data including all the treatment groups (seven for Argus Laboratories and WIL Laboratories and eight for Huntingdon Laboratories) separately for each laboratory. The results are displayed in Appendix A. The categorization of the screened potential outliers, as specified by EPA, is displayed in Table A-1. Some of these potential outliers were included in all the analyses, some were excluded from all the analyses, and the remainder were treated as outliers (i.e. included and excluded).

Normal probability plots of the studentized residuals are displayed in Figure sets A-1, A-2, and A-3 (one set per laboratory). These normal probability plots generally showed good agreement with normal distribution assumptions. No data transformations were carried out.

Preliminary summary results with and without potential outliers were calculated for individual laboratories based on a fixed effects analysis of variance model assuming different residual variances among the treatment groups. For age and body weight at VO, and organ weight responses, summary results after adjustment for the body weight at PND21 were also calculated for individual laboratories by incorporating mean centered body weight at PND21 as a covariate. These preliminary results are presented in Appendix A, Tables A-2, A-3 and A-4.

Body weight growth from PND21 through PND42 is displayed in Figures 1-12. Each figure corresponds to a single chemical and either a single laboratory or combined across laboratories. Figures 1-3 corresponds to WIL Laboratories, Figures 4-6 correspond to Argus Laboratories, Figures 7-9 correspond to Huntingdon Laboratories, and Figures 10-12 correspond to the averages combined across laboratories.

The initial body weights (at PND21) were about same for all treatment groups within an individual laboratory, but differed from laboratory to laboratory (Argus Laboratories > Huntingdon Laboratories > WIL Laboratories). As the PND increased, body weight growth differed among the treatment groups within individual laboratories. In general the high dose group within each chemical had reduced body weight growth compared to the control group. There was one instance in which the low dose group of a chemical had a slightly faster or equal body weight growth than the vehicle control. This was the low dose of 2-Chloronitrobenzene in WIL Laboratories.

Tests for heterogeneity of variance were carried out on the data excluding the outliers, separately for the two portions of data. The results of the models fits and the likelihood ratio tests for heterogeneity are summarized in Tables 1-A and 1-B. Based on the likelihood ratio tests, the proper residual covariance models were selected, and the further data summaries and statistical analyses were carried out using these selected models.

Analysis of variance models were fitted to all the data for each endpoint, as specified in the methods section. For age and body weight at VO, and organ weight responses, additional analysis of variance models including covariance adjustment (mean centered body weight at PND21) were also fitted to the data. Tables 2-A to 4-C (a total of 9 tables) present individual laboratories results for body weight responses, and age and body weight at VO. Each table corresponds to a chemical and laboratory combination. Tables 2-A, 2-B, 2-C correspond to DE-71; Tables 3-A, 3-B, 3-C correspond to 2-Chloronitrobenzene; Tables 4-A, 4-B, 4-C correspond to Methoxychlor. Similarly for Tables 5-10. Tables 5-A to 7-C (a total of 9 tables) present individual laboratories results for organ weight responses. Tables 8-A to 10-C (a total of 9 tables) present individual laboratories results for hormonal analysis endpoints. Each table contains results for a single chemical and an individual laboratory. Results for the three laboratories combined are summarized in Tables 11 to 19. Each table contains results for a single chemical.

The least squares means and associated 95% confidence intervals based on the analysis of variance model fits are displayed in Figures 13 to 38. Figures 13 through 28 display the unadjusted responses. Figures 28 through 38 display the covariate adjusted responses. Each figure summarizes the responses across all laboratories, chemicals, and dose groups within chemicals for a single response.

The analysis results based on all the data are summarized below. Significance is at the 0.05 level.

Body Weights

For initial body weight (Tables 2A-4C and Tables 11-13; Figure 13), all treatment groups within individual laboratories were similar. Initial body weights at Argus Laboratories were about 4 grams higher than those at Huntingdon Laboratories, and 10 grams higher than those at WIL Laboratories.

For final body weight (Tables 2A-4C and Tables 11-13; Figure 14), the high dose of Methoxychlor was significantly lower than the vehicle control averaged across all three

laboratories and for Huntingdon and for WIL Laboratories. The low dose of 2-Chloronitrobenzene was significantly higher than the vehicle control for WIL Laboratories. The same results were observed for body weight gain (Figure 15) and for final body weight as percent of control (Figure 16). In addition, the high dose of Methoxychlor was significantly lower than the vehicle control in body weight gain for Argus Laboratories. The final body weights for Argus Laboratories were higher than those for the other two laboratories.

Age and Body Weight at Vaginal Opening (VO)

For age and body weight at VO (Tables 2A-4C and Tables 11-13; Figures 17 and 18, and 29 and 30), the figures and tables show that the high dose of 2-Chloronitrobenzene was significantly higher than the vehicle control averaged across laboratories and for each individual laboratory. The high dose of Methoxychlor was significantly lower than the vehicle control averaged across laboratories and for each individual laboratory. Other test chemical doses were similar to the vehicle control for individual laboratories and averaged across laboratories. For all treatment groups except the high dose of Methoxychlor, Argus Laboratories laboratory reached VO earlier than the other laboratories (nearly 2 days earlier on average). For the high dose of Methoxychlor all the laboratories had about same age at VO. The results were nearly the same after covariate adjustment.

Organ Weights

Organ weights were analyzed with and without covariate adjustment (Tables 5a-7c and Tables 14-16; and Figures 19-26 and 31-38). In general the results with and without covariates were in agreement.

For some organs there was clear separation among laboratories, across all treatment groups. The organ weights for Argus Laboratories were higher for nearly all treatment groups than for the other two laboratories for paired adrenals, paired kidneys, liver, pituitary, blotted uterus, and wet uterus. The organ weights for WIL Laboratories were lower for nearly all treatment groups than for the other two laboratories for paired ovaries and for blotted thyroid. The organ weights for Huntingdon Laboratories were lower for nearly all treatment groups than for the other laboratories for paired kidneys, liver, and pituitary. The relatively large differences among laboratories contributed to relatively large laboratory-to-laboratory variation and therefore to relatively wide 95% confidence intervals associated with the overall least squares means across laboratories.

Significant differences between the test chemicals and the vehicle control are summarized below. Unless specified otherwise, the results agree whether or not covariate adjustment was carried out.

The organ weights for both doses of DE-71 were significantly higher than the vehicle control for liver averaged across laboratories and for each individual laboratory. In addition, the high DE-71 dose had a significantly lower pituitary weight at WIL Laboratories (Table 14 and Tables 5a-5c).

The organ weights for both doses of 2-Chloronitrobenzene were significantly higher than the vehicle control for liver averaged across laboratories and for each individual laboratory. The high dose of 2-Chloronitrobenzene was significantly lower than vehicle control averaged across laboratories for paired adrenals, blotted uterus, paired ovaries and wet uterus, and for pituitary after covariate adjustment. In addition, for Argus Laboratories, the high dose of this chemical was significantly lower than the vehicle control for blotted uterus. For WIL Laboratories, the high dose of this chemical was significantly lower than the vehicle control for paired adrenals, pituitary, and paired ovaries after covariate adjustment. For Huntingdon Laboratories, the low dose of 2-Chloronitrobenzene was significantly lower for paired ovaries and the high dose was significantly lower for paired adrenals, blotted uterus, paired ovaries and pituitary (Table 15 and Tables 6a-6c).

The organ weights for both doses of Methoxychlor were significantly lower than the vehicle control for paired kidneys and liver averaged across laboratories. The low dose of this chemical was significantly higher than the vehicle control averaged across laboratories for wet uterus. The high dose of this chemical was significantly lower than the vehicle control averaged across laboratories, for paired ovaries. In addition, for Argus Laboratories, the high dose of this chemical was significantly higher than the vehicle control for paired adrenals. For WIL Laboratories the high dose of this chemical was significantly lower than the vehicle control for liver. For Huntingdon Laboratories the low dose of the chemical was significantly lower than the vehicle control for paired kidneys and liver. The high dose of the chemical was significantly lower than the vehicle control for paired ovaries, paired kidneys and liver (Table 16 and Tables 7a-7c).

Hormonal Analysis

For serum thryroxine (Tables 8a-10c and Tables 17-19; Figure 27), the two doses of DE-71 had significantly lower values than the vehicle control averaged across laboratories and for each individual laboratory. The high dose of 2-Chloronitrobenzene was significantly lower than the vehicle control averaged across laboratories and for Argus Laboratories. In addition, both doses of 2-Chloronitrobenzene were significantly lower than the vehicle control for Huntingdon Laboratories. For all treatment groups, Argus Laboratories had higher values than the other two laboratories. As a consequence, the among laboratories variation was larger than within-laboratory variation and the 95% confidence intervals across laboratories were about twice as wide as those for individual laboratories.

For thyroid stimulating hormone (Tables 8a-10c and Tables 17-19; Figure 28), the high dose of DE-71 had significantly higher values than the vehicle control averaged across laboratories and for each individual laboratory. The low dose of DE-71 had significantly higher values than the vehicle control averaged across laboratories and for each individual laboratory. The high dose of 2-Chloronitrobenzene was significantly higher than the vehicle control for WIL Laboratories and Huntingdon Laboratories. For all treatment groups WIL Laboratories had considerably higher values than the other two laboratories and Huntingdon Laboratories had slightly higher values than Argus Laboratories. The among laboratories variation was larger than the within-laboratory variation and so for most treatment groups the 95% confidence intervals

across laboratories were about twice as wide as the confidence intervals within individual laboratories.

Analysis results after excluding outliers

Additional analyses of variance were carried out after excluding outliers for the responses which had at least one outlying value. The results are summarized in Tables 20a-22c, and Tables 23-25. These results were similar to those based on all the data except for the following:

The high dose of Methoxychlor was significantly lower than the vehicle control for pituitary averaged across laboratories and at Huntingdon Laboratories.

The low dose of 2-Chloronitrobenze was significantly lower than the vehicle control for pituitary at Huntingdon Laboratories

Table 1a. Likelihoods for Various Heterogeneous Covariance Structures, Likelihood Ratio Goodness of Fit Statistics, and Selections of Covariance Structure. By Parameter for Treatment Group 1 (Corn Oil, DE-71, and 2-Chloronitrobenzene) [1,2]

Parameter	Selected Covariance Structure	-2LogLikelihood				Likelihood Ratio Test					
		Lab* TestChem* DoseLevel (L*T*D)	Lab* TestChem (L*T)	Lab (L)	All (A)	(L*T*D)-(L*T)	p_value (Chisq,df=6)	(L*T)-(L)	p_value (Chisq,df=6)	(L)-(A)	p_value (Chisq,df=2)
Adrenals	L	-1434.0	-1431.0	-1423.7	-1382.2	2.9559	0.81437	7.2819	0.29556	41.485	0.00000
Age at VO	All	928.7	936.6	946.1	950.8	7.9758	0.23988	9.4438	0.15011	4.685	0.09610
BodyWeight Gain	All	1684.9	1693.1	1701.3	1702.1	8.1861	0.22478	8.1548	0.22698	0.810	0.66695
BodyWeight at VO	L	1710.3	1717.3	1727.6	1734.8	7.0196	0.31904	10.2475	0.11461	7.212	0.02716
Final Body Weight (% of control)	All	1536.1	1541.9	1550.1	1552.1	5.8281	0.44272	8.1782	0.22533	2.031	0.36222
Final BodyWeight	All	1752.8	1758.0	1766.3	1768.9	5.2380	0.51367	8.3398	0.21425	2.564	0.27741
Initial BodyWeight	L	1295.9	1296.8	1303.3	1334.7	0.8423	0.99089	6.5260	0.36691	31.424	0.00000
Kidneys	L*T	-167.4	-155.0	-136.0	-116.2	12.4098	0.05343	18.9892	0.00418	19.843	0.00005
Liver	L	747.5	753.2	765.1	771.1	5.6791	0.46008	11.9589	0.06289	6.000	0.04978
Ovaries	L*T*D	-1216.1	-1200.5	-1189.3	-1169.7	15.5450	0.01642	11.2621	0.08061	19.620	0.00005
Pituitary	L*T	-1997.9	-1992.4	-1979.3	-1872.1	5.5193	0.47913	13.0701	0.04194	107.157	0.00000
T4	L*T*D	527.8	544.5	627.3	638.3	16.6707	0.01057	82.8555	0.00000	10.955	0.00418
TSH	L*T*D	963.2	985.5	1029.5	1100.4	22.2744	0.00108	43.9711	0.00000	70.904	0.00000
ThyroidBlotted	L	-1796.0	-1784.0	-1774.1	-1763.4	12.0449	0.06097	9.9189	0.12811	10.708	0.00473
UterusBlotted	All	-405.9	-403.0	-399.4	-395.3	2.8983	0.82149	3.6746	0.72061	4.058	0.13148
UterusWet	L*T	-319.6	-313.4	-300.6	-290.9	6.2245	0.39852	12.8187	0.04601	9.704	0.00781

1. A mixed effects model was fitted to the data separately for each parameter, in which laboratory, laboratory by test chemical and dose level interaction were random effects, test chemical and dose level interaction and block were fixed effects. Three heterogeneous covariance structure models and a homogenous covariance were compared.
2. The steps for selecting a covariance structure were: starting from the most complex structure in (L*T*D), if (L*T*D) was statistically significant better than the next less complex one in L*T, then (L*T*D) was selected. Otherwise (L*T) was compared with (L) to determine whether (L*T) was a better structure. If so, (L*T) was selected. Otherwise (L) was compared with the homogenous model (All). If (L) was better than (All) then (L) was selected. If not, (All) was selected.

Table 1b. Likelihoods for Various Heterogeneous Covariance Structures, Likelihood Ratio Goodness of Fit Statistics, and Selections of Covariance Structure. By Parameter for Treatment Group 2 (Corn Oil and Methoxychlor) [1,2]

Parameter	Selected Covariance Structure[2]	-2LogLikelihood				Likelihood Ratio Test					
		Lab* TestChem* DoseLevel (L*T*D)	Lab* TestChem (L*T)	Lab (L)	All (A)	(L*T*D)-(L*T)	p_value (Chisq,df=3)	(L*T)-(L)	p_value (Chisq,df=3)	(L)-(A)	p_value (Chisq,df=2)
Adrenals	L	-864.3	-861.5	-854.9	-837.4	2.7958	0.42418	6.6546	0.08376	17.4777	0.00016
Age at VO	L*T*D	499.7	546.1	558.1	558.2	46.3452	0.00000	12.0435	0.00724	0.0591	0.97087
BodyWeight Gain	All	1018.5	1025.1	1028.2	1028.4	6.6532	0.08381	3.0024	0.39125	0.2745	0.87175
BodyWeight at VO	L*T*D	970.3	1009.7	1014.7	1015.9	39.4543	0.00000	4.9726	0.17381	1.1847	0.55303
Final Body Weight (% of control)	All	904.9	910.7	913.7	915.3	5.7184	0.12615	3.0413	0.38530	1.5514	0.46038
Final BodyWeight	All	1041.5	1046.3	1049.5	1051.5	4.7768	0.18889	3.1984	0.36204	2.0402	0.36056
Initial BodyWeight	L	777.6	778.4	780.3	797.2	0.8654	0.83377	1.8087	0.61305	16.9419	0.00021
Kidneys	L*T	-103.6	-98.6	-86.6	-62.7	4.9936	0.17227	12.0504	0.00721	23.8807	0.00001
Liver	L	359.9	365.1	370.7	377.3	5.1395	0.16186	5.6789	0.12832	6.5819	0.03722
Ovaries	L	-666.6	-664.3	-660.9	-648.5	2.3269	0.50738	3.3357	0.34270	12.3899	0.00204
Pituitary	L	-1163.2	-1160.4	-1152.8	-1114.9	2.8216	0.41996	7.5798	0.05554	37.9200	0.00000
T4	All	413.5	420.0	424.3	427.1	6.5281	0.08856	4.3047	0.23039	2.8196	0.24420
TSH	L	521.7	523.7	531.4	562.2	1.9783	0.57692	7.7620	0.05120	30.7282	0.00000
ThyroidBlotted	L	-1021.3	-1015.9	-1011.2	-994.9	5.4406	0.14223	4.6030	0.20329	16.3313	0.00028
UterusBlotted	All	-239.1	-237.9	-236.1	-233.7	1.1177	0.77280	1.8060	0.61363	2.3914	0.30250
UterusWet	L	-98.9	-94.6	-93.1	-81.5	4.2629	0.23443	1.5039	0.68137	11.5996	0.00303

1. A mixed effects model was fitted to the data separately for each parameter, in which laboratory, laboratory by test chemical and dose level interaction were random effects, test chemical and dose level interaction and block were fixed effects. Three heterogeneous covariance structure models and a homogenous covariance were compared.
2. The steps for selecting a covariance structure were: starting from the most complex structure in (L*T*D), if (L*T*D) was statistically significant better than the next less complex one in L*T, then (L*T*D) was selected. Otherwise (L*T) was compared with (L) to determine whether (L*T) was a better structure. If so, (L*T) was selected. Otherwise (L) was compared with the homogenous model (All). If (L) was better than (All) then (L) was selected. If not, (All) was selected.

Table 2a. Summary Statistics for Corn Oil and Test Chemical DE-71 in Female Pubertal Assay for Body Weight, and Age and Weight at VO for Argus Laboratory[1,6].

Parameter	Corn Oil				DE-71 (30 mg/kg/day)				DE-71 (60 mg/kg/day)			
	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N
Initial BodyWeight	56.994	1.499	10.1	15	57.008	1.499	10.1	15	57.068	1.499	10.1	15
Final BodyWeight[2]	169.650	3.382	7.6	15	167.183	3.382	7.7	15	170.116	3.382	7.6	15
BodyWeight Gain	112.655	3.017	10.3	15	110.175	3.017	10.5	15	113.049	3.017	10.2	15
Final body weight as percent of control[3]	99.312	2.076	8.0	15	97.868	2.076	8.1	15	99.586	2.076	8.0	15
Age at VO[4]	31.562	0.524	6.4	15	32.495	0.524	6.2	15	32.362	0.524	6.2	15
BodyWeight at VO[4]	109.665	4.008	14.1	15	115.065	4.008	13.4	15	114.265	4.008	13.5	15
Adj. Age at VO[5]	31.548	0.533	6.0	15	32.481	0.533	5.9	15	32.347	0.534	5.9	15
Adj. BodyWeight at VO[5]	103.101	3.755	13.1	15	108.483	3.757	12.4	15	107.603	3.763	12.6	15

1. Least squares means and standard errors were estimated based on a mixed effects model applied to the data for control, two doses of DE-71, and two doses of 2-Chloronitrobenzene.
2. Body weight at PND42 was summarized when animals were necropsied.
3. Final body weight as percent of control was calculated for each animal as the ratio of its final body weight over the mean of the final body weights within the control group (in percent).
4. All animals had VO before necropsy.
5. Least squares means and standard errors for Adj. age and body weight at VO were estimated based on a mixed effects model with mean centered initial body weight as a covariate.
6. Within laboratory CV was calculated as residual standard deviation/LS Mean.

* --- Significantly different from corn oil at the 0.05 level.

Table 2b. Summary Statistics for Corn Oil and Test Chemical DE-71 in Female Pubertal Assay for Body Weight, and Age and Weight at VO for WIL Laboratory[1,6].

Parameter	Corn Oil				DE-71 (30 mg/kg/day)				DE-71 (60 mg/kg/day)			
	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N
Initial BodyWeight	45.941	0.791	6.4	15	46.014	0.791	6.4	15	46.734	0.791	6.3	15
Final BodyWeight[2]	158.823	3.382	8.2	15	161.803	3.382	8.0	15	160.016	3.382	8.1	15
BodyWeight Gain	112.882	3.017	10.2	15	115.789	3.017	10.0	15	113.282	3.017	10.2	15
Final body weight as percent of control[3]	99.312	2.076	8.0	15	101.176	2.076	7.9	15	100.059	2.076	7.9	15
Age at VO[4]	34.229	0.524	5.9	15	35.029	0.524	5.7	15	35.829*	0.524	5.6	15
BodyWeight at VO[4]	115.599	3.173	10.5	15	123.165	3.173	9.9	15	126.359*	3.173	9.6	15
Adj. Age at VO[5]	32.335	0.694	5.9	15	33.157	0.690	5.8	15	34.178*	0.653	5.6	15
Adj. BodyWeight at VO[5]	111.737	4.411	10.9	15	119.347	4.385	10.2	15	122.962*	4.148	9.9	15

1. Least squares means and standard errors were estimated based on a mixed effects model applied to the data for control, two doses of DE-71, and two doses of 2-Chloronitrobenzene.
2. Body weight at PND42 was summarized when animals were necropsied.
3. Final body weight as percent of control was calculated for each animal as the ratio of its final body weight over the mean of the final body weights within the control group (in percent).
4. All animals had VO before necropsy.
5. Least squares means and standard errors for Adj. age and body weight at VO were estimated based on a mixed effects model with mean centered initial body weight as a covariate.
6. Within laboratory CV was calculated as residual standard deviation/LS Mean.

* --- Significantly different from corn oil at the 0.05 level.

Table 2c. Summary Statistics for Corn Oil and Test Chemical DE-71 in Female Pubertal Assay for Body Weight, and Age and Weight at VO for Huntingdon Laboratory[1,6].

Parameter	Corn Oil				DE-71 (30 mg/kg/day)				DE-71 (60 mg/kg/day)			
	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N
Initial BodyWeight	52.024	1.422	10.2	15	52.617	1.422	10.1	15	52.704	1.422	10.1	15
Final BodyWeight[2]	159.524	3.464	8.1	15	163.371	3.464	7.9	15	162.611	3.464	8.0	15
BodyWeight Gain	107.500	3.090	10.7	15	110.754	3.090	10.4	15	109.907	3.090	10.5	15
Final body weight as percent of control[3]	101.238	2.126	7.9	15	103.679	2.126	7.7	15	103.197	2.126	7.7	15
Age at VO[4]	32.895	0.537	6.1	15	33.962	0.537	5.9	15	33.029	0.537	6.1	15
BodyWeight at VO[4]	114.102	2.805	9.2	15	120.596	2.805	8.7	15	114.036	2.805	9.2	15
Adj. Age at VO[5]	32.901	0.510	5.8	15	34.046	0.511	5.6	15	33.124	0.511	5.8	15
Adj. BodyWeight at VO[5]	114.069	2.566	8.4	15	120.072	2.570	8.0	15	113.441	2.571	8.5	15

1. Least squares means and standard errors were estimated based on a mixed effects model applied to the data for control, two doses of DE-71, and two doses of 2-Chloronitrobenzene.
2. Body weight at PND42 was summarized whether animals were necropsied at PND42 or PND43.
3. Final body weight as percent of control was calculated for each animal as the ratio of its final body weight over the mean of the final body weights within the control group (in percent).
4. All animals had VO before necropsy.
5. Least squares means and standard errors for Adj. age and body weight at VO were estimated based on a mixed effects model with mean centered initial body weight as a covariate.
6. Within laboratory CV was calculated as residual standard deviation/LS Mean.

* --- Significantly different from corn oil at the 0.05 level.

Table 3a. Summary Statistics for Corn Oil and Test Chemical 2-Chloronitrobenzene in Female Pubertal Assay for Body Weight, and Age and Weight at VO for Argus Laboratory[1,6].

Parameter	Corn Oil				2-Chloronitrobenzene (25 mg/kg/day)				2-Chloronitrobenzene (100 mg/kg/day)			
	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N
Initial BodyWeight	56.994	1.499	10.1	15	57.554	1.499	10.0	15	57.234	1.499	10.0	15
Final BodyWeight[2]	169.650	3.382	7.6	15	171.516	3.382	7.6	15	169.383	3.382	7.6	15
BodyWeight Gain	112.655	3.017	10.3	15	113.962	3.017	10.1	15	112.149	3.017	10.3	15
Final body weight as percent of control[3]	99.312	2.076	8.0	15	100.406	2.076	7.9	15	99.156	2.076	8.0	15
Age at VO[4]	31.562	0.524	6.4	15	32.162	0.524	6.2	15	34.895*	0.524	5.8	15
BodyWeight at VO[4]	109.665	4.008	14.1	15	116.465	4.008	13.3	15	127.065*	4.008	12.2	15
Adj. Age at VO[5]	31.548	0.533	6.0	15	32.142	0.541	5.9	15	34.879*	0.536	5.5	15
Adj. BodyWeight at VO[5]	103.101	3.755	13.1	15	109.154	3.814	12.4	15	120.181*	3.780	11.2	15

1. Least squares means and standard errors were estimated based on a mixed effects model applied to the data for control, two doses of DE-71, and two doses of 2-Chloronitrobenzene.
2. Body weight at PND42 was summarized when animals were necropsied.
3. Final body weight as percent of control was calculated for each animal as the ratio of its final body weight over the mean of the final body weights within the control group (in percent).
4. All animals had VO before necropsy.
5. Least squares means and standard errors for Adj. age and body weight at VO were estimated based on a mixed effects model with mean centered initial body weight as a covariate.
6. Within laboratory CV was calculated as residual standard deviation/LS Mean.

* --- Significantly different from corn oil at the 0.05 level.

Table 3b. Summary Statistics for Corn Oil and Test Chemical 2-Chloronitrobenzene in Female Pubertal Assay for Body Weight, and Age and Weight at VO for WIL Laboratory[1,6].

Parameter	Corn Oil				2-Chloronitrobenzene (25 mg/kg/day)				2-Chloronitrobenzene (100 mg/kg/day)			
	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N
Initial BodyWeight	45.941	0.791	6.4	15	46.901	0.791	6.3	15	46.568	0.791	6.4	15
Final BodyWeight[2]	158.823	3.382	8.2	15	168.610*	3.382	7.7	15	162.343	3.382	8.0	15
BodyWeight Gain	112.882	3.017	10.2	15	121.709*	3.017	9.5	15	115.775	3.017	10.0	15
Final body weight as percent of control[3]	99.312	2.076	8.0	15	105.433*	2.076	7.5	15	101.514	2.076	7.8	15
Age at VO[4]	34.229	0.524	5.9	15	34.629	0.524	5.8	15	36.762*	0.524	5.5	15
BodyWeight at VO[4]	115.599	3.173	10.5	15	124.085	3.173	9.8	15	130.945*	3.173	9.3	15
Adj. Age at VO[5]	32.335	0.694	5.9	15	33.029	0.644	5.8	15	35.061*	0.661	5.4	15
Adj. BodyWeight at VO[5]	111.737	4.411	10.9	15	120.786*	4.096	10.1	15	127.451*	4.202	9.5	15

1. Least squares means and standard errors were estimated based on a mixed effects model applied to the data for control, two doses of DE-71, and two doses of 2-Chloronitrobenzene.
2. Body weight at PND42 was summarized when animals were necropsied.
3. Final body weight as percent of control was calculated for each animal as the ratio of its final body weight over the mean of the final body weights within the control group (in percent).
4. All animals had VO before necropsy.
5. Least squares means and standard errors for Adj. age and body weight at VO were estimated based on a mixed effects model with mean centered initial body weight as a covariate.
6. Within laboratory CV was calculated as residual standard deviation/LS Mean.

* --- Significantly different from corn oil at the 0.05 level.

Table 3c. Summary Statistics for Corn Oil and Test Chemical 2-Chloronitrobenzene in Female Pubertal Assay for Body Weight, and Age and Weight at VO for Huntingdon Laboratory[1,6].

Parameter	Corn Oil				2-Chloronitrobenzene (25 mg/kg/day)				2-Chloronitrobenzene (100 mg/kg/day)			
	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N
Initial BodyWeight	52.024	1.422	10.2	15	52.377	1.422	10.2	15	52.230	1.422	10.2	15
Final BodyWeight[2]	159.524	3.464	8.1	15	159.591	3.464	8.1	15	155.224	3.464	8.3	15
BodyWeight Gain	107.500	3.090	10.7	15	107.214	3.090	10.8	15	102.994	3.090	11.2	15
Final body weight as percent of control[3]	101.238	2.126	7.9	15	101.280	2.126	7.9	15	98.509	2.126	8.1	15
Age at VO[4]	32.895	0.537	6.1	15	33.895	0.537	5.9	15	38.695*	0.537	5.2	15
BodyWeight at VO[4]	114.102	2.805	9.2	15	117.176	2.805	9.0	15	137.809*	2.805	7.6	15
Adj. Age at VO[5]	32.901	0.510	5.8	15	33.948	0.510	5.6	15	38.728*	0.510	4.9	15
Adj. BodyWeight at VO[5]	114.069	2.566	8.4	15	116.850	2.568	8.2	15	137.605*	2.567	7.0	15

1. Least squares means and standard errors were estimated based on a mixed effects model applied to the data for control, two doses of DE-71, and two doses of 2-Chloronitrobenzene.
2. Body weight at PND42 was summarized whether animals were necropsied at PND42 or PND43.
3. Final body weight as percent of control was calculated for each animal as the ratio of its final body weight over the mean of the final body weights within the control group (in percent).
4. All animals had VO before necropsy.
5. Least squares means and standard errors for Adj. age and body weight at VO were estimated based on a mixed effects model with mean centered initial body weight as a covariate.
6. Within laboratory CV was calculated as residual standard deviation/LS Mean.

* --- Significantly different from corn oil at the 0.05 level.

Table 4a. Summary Statistics for Corn Oil and Test Chemical Methoxychlor in Female Pubertal Assay for Body Weight, and Age and Weight at VO for Argus Laboratory[1,6].

Parameter	Corn Oil				Methoxychlor (12.5 mg/kg/day)				Methoxychlor (50 mg/kg/day)			
	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N
Initial BodyWeight	56.564	1.472	9.9	15	55.671	1.472	10.1	15	56.744	1.472	9.9	15
Final BodyWeight[2]	170.821	3.319	7.4	15	164.021	3.319	7.7	15	161.821	3.319	7.8	15
BodyWeight Gain	114.257	3.077	10.2	15	108.350	3.077	10.8	15	105.077*	3.077	11.1	15
Final body weight as percent of control[3]	100.053	2.003	7.6	15	96.070	2.003	7.9	15	94.782	2.003	8.0	15
Age at VO[4]	31.494	0.415	5.1	15	32.027	0.670	8.1	15	27.561*	0.220	3.0	15
BodyWeight at VO[4]	109.906	3.356	11.7	15	109.706	4.576	16.1	15	85.972*	2.733	12.2	15
Adj. Age at VO[5]	31.502	0.449	5.1	15	32.035	0.685	8.1	15	27.569*	0.283	3.1	15
Adj. BodyWeight at VO[5]	103.632	3.008	10.1	15	104.654	4.073	14.5	15	79.453*	2.292	9.0	15

1. Least squares means and standard errors were estimated based on a mixed effects model applied to the data for control and two doses of Methoxychlor.
2. Body weight at PND42 was summarized when animals were necropsied.
3. Final body weight as percent of control was calculated for each animal as the ratio of its final body weight over the mean of the final body weights within the control group (in percent).
4. All animals had VO before necropsy.
5. Least squares means and standard errors for Adj. age and body weight at VO were estimated based on a mixed effects model with mean centered initial body weight as a covariate.
6. Within laboratory CV was calculated as residual standard deviation/LS Mean.

* --- Significantly different from corn oil at the 0.05 level.

Table 4b. Summary Statistics for Corn Oil and Test Chemical Methoxychlor in Female Pubertal Assay for Body Weight, and Age and Weight at VO for WIL Laboratory[1,6].

Parameter	Corn Oil				Methoxychlor (12.5 mg/kg/day)				Methoxychlor (50 mg/kg/day)			
	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N
Initial BodyWeight	45.511	0.809	6.5	15	46.578	0.809	6.4	15	46.358	0.809	6.4	15
Final BodyWeight[2]	159.994	3.319	7.9	15	160.728	3.319	7.9	15	150.654*	3.319	8.4	15
BodyWeight Gain	114.484	3.077	10.2	15	114.150	3.077	10.2	15	104.297*	3.077	11.2	15
Final body weight as percent of control[3]	100.053	2.003	7.6	15	100.512	2.003	7.6	15	94.212*	2.003	8.1	15
Age at VO[4]	34.161	0.594	6.7	15	33.961	0.504	5.7	15	27.094*	0.159	2.2	15
BodyWeight at VO[4]	115.839	2.750	9.1	15	116.759	3.879	12.8	15	74.459*	1.499	7.5	15
Adj. Age at VO[5]	34.500	0.693	6.7	15	34.244	0.584	5.7	15	27.389*	0.338	2.1	15
Adj. BodyWeight at VO[5]	125.055	3.497	8.6	15	124.453	4.303	12.2	15	82.467*	2.061	4.3	15

1. Least squares means and standard errors were estimated based on a mixed effects model applied to the data for control and two doses of Methoxychlor.
2. Body weight at PND42 was summarized when animals were necropsied.
3. Final body weight as percent of control was calculated for each animal as the ratio of its final body weight over the mean of the final body weights within the control group (in percent).
4. All animals had VO before necropsy.
5. Least squares means and standard errors for Adj. age and body weight at VO were estimated based on a mixed effects model with mean centered initial body weight as a covariate.
6. Within laboratory CV was calculated as residual standard deviation/LS Mean.

* --- Significantly different from corn oil at the 0.05 level.

Table 4c. Summary Statistics for Corn Oil and Test Chemical Methoxychlor in Female Pubertal Assay for Body Weight, and Age and Weight at VO for Huntingdon Laboratory[1,6].

Parameter	Corn Oil				Methoxychlor (12.5 mg/kg/day)				Methoxychlor (50 mg/kg/day)			
	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N
Initial BodyWeight	53.884	1.413	9.6	15	53.144	1.413	9.7	15	54.051	1.413	9.6	15
Final BodyWeight[2]	165.429	3.450	7.6	15	159.242	3.450	7.9	15	155.755*	3.450	8.1	15
BodyWeight Gain	111.544	3.198	10.5	15	106.097	3.198	11.0	15	101.704*	3.198	11.5	15
Final body weight as percent of control[3]	99.905	2.082	7.6	15	96.168	2.082	7.9	15	94.063*	2.082	8.1	15
Age at VO[4]	33.617	0.613	7.0	15	32.484	0.486	5.7	15	27.417*	0.156	1.9	15
BodyWeight at VO[4]	119.843	3.223	10.2	15	109.683*	3.200	11.0	15	81.957*	1.473	6.1	15
Adj. Age at VO[5]	33.556	0.634	7.2	15	32.449	0.471	5.5	15	27.350*	0.165	1.9	15
Adj. BodyWeight at VO[5]	118.404	3.287	10.5	15	108.841*	2.747	9.6	15	80.383*	1.157	4.5	15

1. Least squares means and standard errors were estimated based on a mixed effects model applied to the data for control and two doses of Methoxychlor.
2. Body weight at PND42 was summarized whether animals were necropsied at PND42 or PND43
3. Final body weight as percent of control was calculated for each animal as the ratio of its final body weight over the mean of the final body weights within the control group (in percent).
4. All animals had VO before necropsy.
5. Least squares means and standard errors for Adj. age and body weight at VO were estimated based on a mixed effects model with mean centered initial body weight as a covariate.
6. Within laboratory CV was calculated as residual standard deviation/LS Mean.

* --- Significantly different from corn oil at the 0.05 level.

Table 5a. Summary Statistics for Corn Oil and Test Chemical DE-71 in Female Pubertal Assay for Unadjusted and Body-Weight Adjusted Organ Weights for Argus Laboratory [1,2,3,4].

	Corn Oil				DE-71 (30 mg/kg/day)				DE-71 (60 mg/kg/day)			
Parameter	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N
Adrenals	0.047	0.003	28.4	15	0.049	0.003	27.2	15	0.050	0.003	26.4	15
Kidneys	1.655	0.086	20.0	15	1.710	0.046	10.4	15	1.754	0.046	10.2	15
Liver	8.462	0.389	17.7	15	10.644*	0.389	14.0	15	12.063*	0.389	12.4	15
Ovaries	0.083	0.005	25.5	15	0.078	0.005	23.2	15	0.080	0.004	17.3	15
Pituitary	0.013	0.001	17.5	14	0.012	0.001	42.9	15	0.011	0.001	48.2	15
ThyroidBlotted	0.019	0.001	21.5	15	0.022	0.001	19.2	15	0.022	0.001	18.9	15
UterusBlotted	0.327	0.023	27.0	15	0.350	0.024	25.3	14	0.303	0.023	29.1	15
UterusWet	0.374	0.034	34.4	15	0.384	0.034	32.4	14	0.347	0.033	36.0	15
Adj. Adrenals	0.047	0.004	28.1	15	0.049	0.004	26.9	15	0.051	0.004	26.1	15
Adj. Kidneys	1.565	0.081	19.3	15	1.619	0.045	9.2	15	1.662	0.045	9.0	15
Adj. Liver	8.191	0.410	18.0	15	10.372*	0.410	14.2	15	11.788*	0.411	12.5	15
Adj. Ovaries	0.089	0.006	25.3	15	0.084	0.006	24.3	15	0.086	0.003	10.3	15
Adj. Pituitary	0.014	0.001	15.3	14	0.013	0.001	38.0	15	0.012	0.001	42.2	15
Adj. ThyroidBlotted	0.018	0.001	22.0	15	0.021	0.001	19.5	15	0.021	0.001	19.2	15
Adj. UterusBlotted	0.317	0.024	27.6	15	0.338	0.026	25.9	14	0.293	0.025	29.8	15
Adj. UterusWet	0.368	0.037	35.2	15	0.378	0.037	33.1	14	0.341	0.036	36.7	15

1. Least squares means and standard errors were estimated based on a mixed effects model applied to the data for control, two doses of DE-71, and two doses of 2-Chloronitrobenzene.
2. Least squares means and standard errors for Adj. organ weights were estimated based on a mixed effects model with mean centered initial body weight as a covariate.
3. Within laboratory CV was calculated as residual standard deviation/LS Mean.
4. Significantly differences from corn oil at the 0.05 level were marked by "*".

Table 5b. Summary Statistics for Corn Oil and Test Chemical DE-71 in Female Pubertal Assay for Unadjusted and Body-Weight Adjusted Organ Weights for WIL Laboratory [1,2,3,4].

	Corn Oil				DE-71 (30 mg/kg/day)				DE-71 (60 mg/kg/day)			
Parameter	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N
Adrenals	0.042	0.001	12.0	15	0.043	0.001	11.7	15	0.040	0.001	12.6	15
Kidneys	1.612	0.047	11.2	15	1.644	0.028	6.4	15	1.600	0.028	6.6	15
Liver	7.940	0.327	15.8	15	9.949*	0.327	12.6	15	10.652*	0.327	11.8	15
Ovaries	0.063	0.004	21.9	15	0.062	0.003	18.1	15	0.059	0.003	20.6	15
Pituitary	0.010	0.000	16.2	15	0.010	0.000	13.9	15	0.009*	0.000	14.9	15
ThyroidBlotted	0.013	0.001	21.2	15	0.013	0.001	21.0	15	0.012	0.001	22.4	15
UterusBlotted	0.288	0.023	30.6	15	0.284	0.023	31.1	15	0.248	0.023	35.7	15
UterusWet	0.327	0.028	32.9	15	0.318	0.025	29.6	15	0.295	0.025	31.9	15
Adj. Adrenals	0.045	0.002	10.7	15	0.047	0.002	10.4	15	0.043	0.002	11.2	15
Adj. Kidneys	1.641	0.060	11.4	15	1.673	0.044	6.3	15	1.625	0.041	6.5	15
Adj. Liver	8.214	0.456	15.3	15	10.220*	0.453	12.3	15	10.889*	0.428	11.5	15
Adj. Ovaries	0.072	0.005	20.1	15	0.071	0.004	13.7	15	0.066	0.004	14.4	15
Adj. Pituitary	0.010	0.001	16.3	15	0.010	0.001	14.0	15	0.009*	0.000	15.0	15
Adj. ThyroidBlotted	0.012	0.001	22.5	15	0.012	0.001	22.3	15	0.012	0.001	23.7	15
Adj. UterusBlotted	0.341	0.032	25.7	15	0.336	0.032	26.1	15	0.294	0.030	29.8	15
Adj. UterusWet	0.369	0.035	26.7	15	0.359	0.034	25.6	15	0.332	0.032	27.8	15

1. Least squares means and standard errors were estimated based on a mixed effects model applied to the data for control, two doses of DE-71, and two doses of 2-Chloronitrobenzene.
2. Least squares means and standard errors for Adj. organ weights were estimated based on a mixed effects model with mean centered initial body weight as a covariate.
3. Within laboratory CV was calculated as residual standard deviation/LS Mean.
4. Significantly differences from corn oil at the 0.05 level were marked by "*".

Table 5c. Summary Statistics for Corn Oil and Test Chemical DE-71 in Female Pubertal Assay for Unadjusted and Body-Weight Adjusted Organ Weights for Huntingdon Laboratory [1,2,3,4].

	Corn Oil				DE-71 (30 mg/kg/day)				DE-71 (60 mg/kg/day)			
Parameter	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N
Adrenals	0.041	0.002	21.6	15	0.040	0.002	22.5	15	0.037	0.002	23.8	15
Kidneys	1.481	0.040	10.0	15	1.468	0.040	10.2	15	1.490	0.040	10.0	15
Liver	7.501	0.326	16.3	15	9.588*	0.326	12.7	15	10.922*	0.326	11.2	15
Ovaries	0.092	0.004	17.1	15	0.085	0.003	14.4	15	0.083	0.004	17.6	15
Pituitary	0.009	0.000	16.8	15	0.009	0.000	15.8	15	0.008	0.000	16.8	15
ThyroidBlotted	0.021	0.001	20.1	15	0.023	0.001	18.9	15	0.025	0.001	17.6	15
UterusBlotted	0.322	0.024	27.5	15	0.324	0.024	27.3	15	0.325	0.024	27.2	15
UterusWet	0.343	0.024	25.7	15	0.340	0.035	38.5	15	0.352	0.035	37.2	15
Adj. Adrenals	0.041	0.002	21.5	15	0.040	0.002	22.4	15	0.037	0.002	23.8	15
Adj. Kidneys	1.481	0.037	9.3	15	1.458	0.035	9.1	15	1.478	0.035	9.0	15
Adj. Liver	7.497	0.290	14.4	15	9.519*	0.290	11.4	15	10.844*	0.290	10.0	15
Adj. Ovaries	0.092	0.004	15.6	15	0.085	0.003	14.9	15	0.082	0.004	17.9	15
Adj. Pituitary	0.009	0.000	16.1	15	0.009	0.000	15.6	15	0.008	0.000	16.6	15
Adj. ThyroidBlotted	0.021	0.001	18.4	15	0.023	0.001	17.5	15	0.024	0.001	16.3	15
Adj. UterusBlotted	0.322	0.023	27.2	15	0.323	0.023	27.1	15	0.324	0.023	27.0	15
Adj. UterusWet	0.343	0.025	25.9	15	0.340	0.035	38.7	15	0.352	0.035	37.4	15

1. Least squares means and standard errors were estimated based on a mixed effects model applied to the data for control, two doses of DE-71, and two doses of 2-Chloronitrobenzene.
2. Least squares means and standard errors for Adj. organ weights were estimated based on a mixed effects model with mean centered initial body weight as a covariate.
3. Within laboratory CV was calculated as residual standard deviation/LS Mean.
4. Significantly differences from corn oil at the 0.05 level were marked by "*".

Table 6a. Summary Statistics for Corn Oil and Test Chemical 2-Chloronitrobenzene in Female Pubertal Assay for Unadjusted and Body-Weight Adjusted Organ Weights for Argus Laboratory [1,2,3,4].

Parameter	Corn Oil				2-Chloronitrobenzene (25 mg/kg/day)				2-Chloronitrobenzene (100 mg/kg/day)			
	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N
Adrenals	0.047	0.003	28.4	15	0.053	0.003	24.9	15	0.050	0.003	26.6	15
Kidneys	1.655	0.086	20.0	15	1.820	0.102	21.7	15	1.706	0.102	23.1	15
Liver	8.462	0.389	17.7	15	10.943*	0.389	13.7	15	13.455*	0.389	11.1	15
Ovaries	0.083	0.005	25.5	15	0.091	0.006	25.4	15	0.083	0.009	42.2	15
Pituitary	0.013	0.001	17.5	14	0.012	0.001	34.1	15	0.012	0.001	34.2	15
ThyroidBlotted	0.019	0.001	21.5	15	0.020	0.001	20.6	15	0.020	0.001	21.1	15
UterusBlotted	0.327	0.023	27.0	15	0.317	0.023	27.9	15	0.262*	0.023	33.8	15
UterusWet	0.374	0.034	34.4	15	0.367	0.034	35.2	15	0.305	0.034	42.3	15
Adj. Adrenals	0.047	0.004	28.1	15	0.054	0.004	24.7	15	0.051	0.004	26.3	15
Adj. Kidneys	1.565	0.081	19.3	15	1.719	0.105	22.9	15	1.610	0.104	24.4	15
Adj. Liver	8.191	0.410	18.0	15	10.643*	0.417	13.9	15	13.172*	0.413	11.2	15
Adj. Ovaries	0.089	0.006	25.3	15	0.098	0.006	23.4	15	0.090	0.010	41.6	15
Adj. Pituitary	0.014	0.001	15.3	14	0.013	0.001	31.0	15	0.013	0.001	31.2	15
Adj. ThyroidBlotted	0.018	0.001	22.0	15	0.019	0.001	21.1	15	0.019	0.001	21.6	15
Adj. UterusBlotted	0.317	0.024	27.6	15	0.306	0.025	28.6	15	0.251*	0.025	34.8	15
Adj. UterusWet	0.368	0.037	35.2	15	0.361	0.037	36.0	15	0.299	0.037	43.5	15

1. Least squares means and standard errors were estimated based on a mixed effects model applied to the data for control, two doses of DE-71, and two doses of 2-Chloronitrobenzene.
2. Least squares means and standard errors for Adj. organ weights were estimated based on a mixed effects model with mean centered initial body weight as a covariate.
3. Within laboratory CV was calculated as residual standard deviation/LS Mean.
4. Significantly differences from corn oil at the 0.05 level were marked by "*".

Table 6b. Summary Statistics for Corn Oil and Test Chemical 2-Chloronitrobenzene in Female Pubertal Assay for Unadjusted and Body-Weight Adjusted Organ Weights for WIL Laboratory [1,2,3,4].

	Corn Oil				2-Chloronitrobenzene (25 mg/kg/day)				2-Chloronitrobenzene (100 mg/kg/day)			
Parameter	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N
Adrenals	0.042	0.001	12.0	15	0.044	0.001	11.5	15	0.038*	0.001	13.3	15
Kidneys	1.612	0.047	11.2	15	1.697	0.041	9.3	15	1.687	0.041	9.3	15
Liver	7.940	0.327	15.8	15	10.526*	0.327	11.9	15	12.435*	0.327	10.1	15
Ovaries	0.063	0.004	21.9	15	0.063	0.002	13.7	15	0.054	0.003	21.1	15
Pituitary	0.010	0.000	16.2	15	0.010	0.000	12.5	15	0.009*	0.000	13.8	15
ThyroidBlotted	0.013	0.001	21.2	15	0.012	0.001	23.3	15	0.012	0.001	23.9	15
UterusBlotted	0.288	0.023	30.6	15	0.299	0.023	29.6	15	0.251	0.023	35.2	15
UterusWet	0.327	0.028	32.9	15	0.320	0.021	23.8	14	0.294	0.020	25.9	15
Adj. Adrenals	0.045	0.002	10.7	15	0.047	0.002	10.3	15	0.041*	0.002	11.8	15
Adj. Kidneys	1.641	0.060	11.4	15	1.721	0.050	9.0	15	1.712	0.051	9.1	15
Adj. Liver	8.214	0.456	15.3	15	10.755*	0.423	11.7	15	12.680*	0.434	9.9	15
Adj. Ovaries	0.072	0.005	20.1	15	0.071	0.004	13.4	15	0.062*	0.004	17.5	15
Adj. Pituitary	0.010	0.001	16.3	15	0.010	0.000	12.6	15	0.009*	0.000	13.9	15
Adj. ThyroidBlotted	0.012	0.001	22.5	15	0.011	0.001	24.6	15	0.011	0.001	25.4	15
Adj. UterusBlotted	0.341	0.032	25.7	15	0.343	0.030	25.5	15	0.298	0.030	29.3	15
Adj. UterusWet	0.369	0.035	26.7	15	0.358	0.031	21.9	14	0.332	0.030	23.6	15

1. Least squares means and standard errors were estimated based on a mixed effects model applied to the data for control, two doses of DE-71, and two doses of 2-Chloronitrobenzene.
2. Least squares means and standard errors for Adj. organ weights were estimated based on a mixed effects model with mean centered initial body weight as a covariate.
3. Within laboratory CV was calculated as residual standard deviation/LS Mean.
4. Significantly differences from corn oil at the 0.05 level were marked by "*".

Table 6c. Summary Statistics for Corn Oil and Test Chemical 2-Chloronitrobenzene in Female Pubertal Assay for Unadjusted and Body-Weight Adjusted Organ Weights for Huntingdon Laboratory [1,2,3,4].

	Corn Oil				2-Chloronitrobenzene (25 mg/kg/day)				2-Chloronitrobenzene (100 mg/kg/day)			
Parameter	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N
Adrenals	0.041	0.002	21.6	15	0.035	0.002	25.3	15	0.033*	0.002	27.0	15
Kidneys	1.481	0.040	10.0	15	1.435	0.041	10.6	15	1.470	0.041	10.4	15
Liver	7.501	0.326	16.3	15	9.296*	0.326	13.1	15	11.259*	0.326	10.8	15
Ovaries	0.092	0.004	17.1	15	0.077*	0.003	15.6	15	0.074*	0.003	12.4	15
Pituitary	0.009	0.000	16.8	15	0.008	0.001	41.5	15	0.006*	0.001	56.3	15
ThyroidBlotted	0.021	0.001	20.1	15	0.021	0.001	20.9	15	0.021	0.001	20.7	15
UterusBlotted	0.322	0.024	27.5	15	0.288	0.024	30.7	15	0.243*	0.024	36.4	15
UterusWet	0.343	0.024	25.7	15	0.320	0.037	43.1	15	0.263	0.037	52.5	15
Adj. Adrenals	0.041	0.002	21.5	15	0.035	0.002	25.2	15	0.033*	0.002	27.0	15
Adj. Kidneys	1.481	0.037	9.3	15	1.429	0.029	7.5	15	1.467	0.029	7.3	15
Adj. Liver	7.497	0.290	14.4	15	9.253*	0.290	11.7	15	11.232*	0.290	9.6	15
Adj. Ovaries	0.092	0.004	15.6	15	0.076*	0.003	14.1	15	0.074*	0.002	9.5	15
Adj. Pituitary	0.009	0.000	16.1	15	0.008	0.001	40.0	15	0.006*	0.001	54.2	15
Adj. ThyroidBlotted	0.021	0.001	18.4	15	0.020	0.001	19.3	15	0.021	0.001	19.0	15
Adj. UterusBlotted	0.322	0.023	27.2	15	0.287	0.023	30.5	15	0.242*	0.023	36.1	15
Adj. UterusWet	0.343	0.025	25.9	15	0.320	0.037	43.5	15	0.263	0.037	53.0	15

1. Least squares means and standard errors were estimated based on a mixed effects model applied to the data for control, two doses of DE-71, and two doses of 2-Chloronitrobenzene.
2. Least squares means and standard errors for Adj. organ weights were estimated based on a mixed effects model with mean centered initial body weight as a covariate.
3. Within laboratory CV was calculated as residual standard deviation/LS Mean.
4. Significantly differences from corn oil at the 0.05 level were marked by "*".

Table 7a. Summary Statistics for Corn Oil and Test Chemical Methoxychlor in Female Pubertal Assay for Unadjusted and Body-Weight Adjusted Organ Weights for Argus Laboratory [1,2,3,4].

	Corn Oil				Methoxychlor (12.5 mg/kg/day)				Methoxychlor (50 mg/kg/day)			
Parameter	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N
Adrenals	0.046	0.003	21.4	15	0.047	0.003	21.0	14	0.054*	0.003	18.4	15
Kidneys	1.671	0.086	19.8	15	1.599	0.046	11.0	15	1.623	0.046	10.8	15
Liver	8.576	0.284	12.7	15	8.187	0.284	13.3	15	7.906	0.284	13.8	15
Ovaries	0.083	0.005	24.6	15	0.087	0.005	23.4	14	0.078	0.005	26.2	15
Pituitary	0.013	0.001	28.3	14	0.011	0.001	33.3	15	0.013	0.001	28.9	15
ThyroidBlotted	0.019	0.001	19.6	15	0.018	0.001	21.6	15	0.020	0.001	19.1	15
UterusBlotted	0.327	0.022	26.1	15	0.378	0.022	22.6	15	0.336	0.022	25.5	15
UterusWet	0.381	0.036	34.9	15	0.468	0.036	28.4	15	0.395	0.036	33.7	15
Adj. Adrenals	0.045	0.003	22.0	15	0.046	0.003	21.5	14	0.053*	0.003	18.8	15
Adj. Kidneys	1.605	0.083	19.0	15	1.546	0.047	10.5	15	1.554	0.050	10.5	15
Adj. Liver	8.151	0.284	12.0	15	7.843	0.274	12.4	15	7.465	0.286	13.1	15
Adj. Ovaries	0.084	0.006	24.5	15	0.088	0.006	23.4	14	0.079	0.006	26.1	15
Adj. Pituitary	0.014	0.001	24.8	14	0.012	0.001	29.4	15	0.014	0.001	25.4	15
Adj. ThyroidBlotted	0.019	0.001	19.9	15	0.017	0.001	21.8	15	0.019	0.001	19.4	15
Adj. UterusBlotted	0.317	0.025	27.0	15	0.370	0.024	23.1	15	0.325	0.025	26.3	15
Adj. UterusWet	0.371	0.040	36.1	15	0.460	0.039	29.2	15	0.384	0.040	34.9	15

1. Least squares means and standard errors were estimated based on a mixed effects model applied to the data for control and two doses of Methoxychlor.
2. Least squares means and standard errors for Adj. organ weights were estimated based on a mixed effects model with mean centered initial body weight as a covariate.
3. Within laboratory CV was calculated as residual standard deviation/LS Mean.
4. Significantly differences from corn oil at the 0.05 level were marked by "*".

Table 7b. Summary Statistics for Corn Oil and Test Chemical Methoxychlor in Female Pubertal Assay for Unadjusted and Body-Weight Adjusted Organ Weights for WIL Laboratory [1,2,3,4].

	Corn Oil				Methoxychlor (12.5 mg/kg/day)				Methoxychlor (50 mg/kg/day)			
Parameter	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N
Adrenals	0.041	0.001	13.5	15	0.043	0.001	13.1	15	0.045	0.001	12.6	15
Kidneys	1.627	0.047	11.1	15	1.590	0.031	7.5	15	1.522	0.031	7.8	15
Liver	8.054	0.271	12.9	15	7.767	0.271	13.4	15	7.144*	0.271	14.6	15
Ovaries	0.063	0.003	19.9	15	0.062	0.003	20.2	15	0.060	0.003	21.0	15
Pituitary	0.010	0.000	16.7	15	0.010	0.000	17.5	15	0.009	0.000	18.1	15
ThyroidBlotted	0.013	0.001	23.3	15	0.012	0.001	26.6	15	0.012	0.001	24.9	15
UterusBlotted	0.288	0.022	29.7	15	0.330	0.022	25.9	15	0.325	0.022	26.3	15
UterusWet	0.334	0.033	36.8	15	0.409	0.033	30.1	15	0.402	0.033	30.6	15
Adj. Adrenals	0.045	0.002	12.1	15	0.046	0.002	11.9	15	0.048	0.002	11.4	15
Adj. Kidneys	1.682	0.068	11.4	15	1.636	0.049	7.1	15	1.570	0.050	7.4	15
Adj. Liver	8.338	0.440	12.5	15	8.004	0.396	13.1	15	7.391*	0.404	14.1	15
Adj. Ovaries	0.065	0.005	19.6	15	0.063	0.005	20.0	15	0.061	0.005	20.7	15
Adj. Pituitary	0.010	0.001	17.4	15	0.009	0.001	18.2	15	0.009	0.001	18.9	15
Adj. ThyroidBlotted	0.012	0.001	25.1	15	0.011	0.001	28.6	15	0.011	0.001	26.7	15
Adj. UterusBlotted	0.325	0.036	26.4	15	0.360	0.033	23.8	15	0.356	0.033	24.0	15
Adj. UterusWet	0.376	0.052	32.7	15	0.444	0.047	27.7	15	0.438	0.048	28.1	15

1. Least squares means and standard errors were estimated based on a mixed effects model applied to the data for control and two doses of Methoxychlor.
2. Least squares means and standard errors for Adj. organ weights were estimated based on a mixed effects model with mean centered initial body weight as a covariate.
3. Within laboratory CV was calculated as residual standard deviation/LS Mean.
4. Significantly differences from corn oil at the 0.05 level were marked by "*".

Table 7c. Summary Statistics for Corn Oil and Test Chemical Methoxychlor in Female Pubertal Assay for Unadjusted and Body-Weight Adjusted Organ Weights for Huntingdon Laboratory [1,2,3,4].

Parameter	Corn Oil				Methoxychlor (12.5 mg/kg/day)				Methoxychlor (50 mg/kg/day)			
	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N
Adrenals	0.049	0.002	16.2	15	0.045	0.002	17.7	15	0.045	0.002	17.7	15
Kidneys	1.470	0.032	7.9	15	1.384*	0.029	7.5	15	1.353*	0.029	7.6	15
Liver	7.899	0.189	8.7	15	7.078*	0.189	9.7	15	6.986*	0.189	9.9	15
Ovaries	0.092	0.004	14.1	14	0.090	0.004	14.4	15	0.080*	0.004	16.3	15
Pituitary	0.009	0.001	22.9	15	0.009	0.001	23.1	15	0.008	0.001	26.1	15
ThyroidBlotted	0.022	0.002	25.9	15	0.022	0.002	26.2	15	0.023	0.002	24.2	15
UterusBlotted	0.334	0.023	25.6	15	0.344	0.023	24.8	15	0.315	0.023	27.1	15
UterusWet	0.371	0.054	53.3	15	0.421	0.054	47.1	15	0.353	0.054	56.1	15
Adj. Adrenals	0.048	0.002	16.4	15	0.044	0.002	17.8	15	0.044	0.002	17.9	15
Adj. Kidneys	1.454	0.026	6.4	15	1.373*	0.029	7.8	15	1.336*	0.030	8.0	15
Adj. Liver	7.877	0.194	8.8	15	7.065*	0.191	9.8	15	6.962*	0.195	10.0	15
Adj. Ovaries	0.093	0.004	13.9	14	0.090	0.004	14.4	15	0.080*	0.004	16.2	15
Adj. Pituitary	0.009	0.001	23.3	15	0.009	0.001	23.4	15	0.008	0.001	26.5	15
Adj. ThyroidBlotted	0.021	0.002	26.2	15	0.021	0.002	26.3	15	0.023	0.002	24.5	15
Adj. UterusBlotted	0.336	0.024	25.5	15	0.345	0.024	24.8	15	0.316	0.024	27.1	15
Adj. UterusWet	0.378	0.056	52.8	15	0.424	0.055	47.0	15	0.360	0.056	55.5	15

1. Least squares means and standard errors were estimated based on a mixed effects model applied to the data for control and two doses of Methoxychlor.
2. Least squares means and standard errors for Adj. organ weights were estimated based on a mixed effects model with mean centered initial body weight as a covariate.
3. Within laboratory CV was calculated as residual standard deviation/LS Mean.
4. Significantly differences from corn oil at the 0.05 level were marked by "*".

Table 8a. Summary Statistics for Corn Oil and Test Chemical DE-71 in Female Pubertal Assay for Hormonal Parameters for Argus Laboratory [1,2,3].

Parameter	Corn Oil				DE-71 (30 mg/kg/day)				DE-71 (60 mg/kg/day)			
	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N
Serum Thyroxine	7.984	0.348	16.9	15	4.682*	0.125	10.1	15	4.154*	0.159	14.6	15
Thyroid stimulating hormone	3.341	0.315	35.8	15	4.923*	0.528	41.2	15	4.650*	0.274	22.2	15

1. Least squares means and standard errors were estimated based on a mixed effects model applied to the data for control, two doses of DE-71, and two doses of 2-Chloronitrobenzene.
2. Within laboratory CV was calculated as residual standard deviation/LS Mean.
3. Significantly differences from corn oil at the 0.05 level were marked by "*".

Table 8b. Summary Statistics for Corn Oil and Test Chemical DE-71 in Female Pubertal Assay for Hormonal Parameters for WIL Laboratory [1,2,3].

Parameter	Corn Oil				DE-71 (30 mg/kg/day)				DE-71 (60 mg/kg/day)			
	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N
Serum Thyroxine	5.179	0.362	27.0	15	1.348*	0.120	33.8	15	0.911*	0.054	20.8	15
Thyroid stimulating hormone	8.062	0.554	26.4	15	11.355*	1.115	38.0	15	14.042*	1.734	47.8	15

1. Least squares means and standard errors were estimated based on a mixed effects model applied to the data for control, two doses of DE-71, and two doses of 2-Chloronitrobenzene.
2. Within laboratory CV was calculated as residual standard deviation/LS Mean.
3. Significantly differences from corn oil at the 0.05 level were marked by "*".

Table 8c. Summary Statistics for Corn Oil and Test Chemical DE-71 in Female Pubertal Assay for Hormonal Parameters for Huntingdon Laboratory [1,2,3].

Parameter	Corn Oil				DE-71 (30 mg/kg/day)				DE-71 (60 mg/kg/day)			
	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N
Serum Thyroxine	5.399	0.330	23.5	15	1.579*	0.140	32.7	15	0.733*	0.099	47.5	15
Thyroid stimulating hormone	4.816	0.295	21.9	15	6.470*	0.689	40.7	15	7.043*	0.555	29.8	15

1. Least squares means and standard errors were estimated based on a mixed effects model applied to the data for control, two doses of DE-71, and two doses of 2-Chloronitrobenzene.
2. Within laboratory CV was calculated as residual standard deviation/LS Mean.
3. Significantly differences from corn oil at the 0.05 level were marked by "*".

Table 9a. Summary Statistics for Corn Oil and Test Chemical 2-Chloronitrobenzene in Female Pubertal Assay for Hormonal Parameters for Argus Laboratory [1,2,3].

Parameter	Corn Oil				2-Chloronitrobenzene (25 mg/kg/day)				2-Chloronitrobenzene (100 mg/kg/day)			
	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N
Serum Thyroxine	7.984	0.348	16.9	15	7.192	0.430	23.1	15	6.876*	0.319	17.9	15
Thyroid stimulating hormone	3.341	0.315	35.8	15	4.229	0.682	62.2	15	3.712	0.265	26.9	15

1. Least squares means and standard errors were estimated based on a mixed effects model applied to the data for control, two doses of DE-71, and two doses of 2-Chloronitrobenzene.
2. Within laboratory CV was calculated as residual standard deviation/LS Mean.
3. Significantly differences from corn oil at the 0.05 level were marked by "*".

Table 9b. Summary Statistics for Corn Oil and Test Chemical 2-Chloronitrobenzene in Female Pubertal Assay for Hormonal Parameters for WIL Laboratory [1,2,3].

Parameter	Corn Oil				2-Chloronitrobenzene (25 mg/kg/day)				2-Chloronitrobenzene (100 mg/kg/day)			
	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N
Serum Thyroxine	5.179	0.362	27.0	15	5.086	0.214	16.2	15	4.819	0.217	17.3	15
Thyroid stimulating hormone	8.062	0.554	26.4	15	9.242	0.653	27.2	15	10.395*	0.681	25.2	15

1. Least squares means and standard errors were estimated based on a mixed effects model applied to the data for control, two doses of DE-71, and two doses of 2-Chloronitrobenzene.
2. Within laboratory CV was calculated as residual standard deviation/LS Mean.
3. Significantly differences from corn oil at the 0.05 level were marked by "*".

Table 9c. Summary Statistics for Corn Oil and Test Chemical 2-Chloronitrobenzene in Female Pubertal Assay for Hormonal Parameters for Huntingdon Laboratory [1,2,3].

Parameter	Corn Oil				2-Chloronitrobenzene (25 mg/kg/day)				2-Chloronitrobenzene (100 mg/kg/day)			
	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N
Serum Thyroxine	5.399	0.330	23.5	15	4.199*	0.248	22.5	15	3.899*	0.160	15.4	15
Thyroid stimulating hormone	4.816	0.295	21.9	15	5.103	0.360	25.9	15	6.036*	0.429	26.6	15

1. Least squares means and standard errors were estimated based on a mixed effects model applied to the data for control, two doses of DE-71, and two doses of 2-Chloronitrobenzene.
2. Within laboratory CV was calculated as residual standard deviation/LS Mean.
3. Significantly differences from corn oil at the 0.05 level were marked by "*".

Table 10a. Summary Statistics for Corn Oil and Test Chemical Methoxychlor in Female Pubertal Assay for Hormonal Parameters for Argus Laboratory [1,2,3].

Parameter	Corn Oil				Methoxychlor (12.5 mg/kg/day)				Methoxychlor (50 mg/kg/day)			
	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N
Serum Thyroxine	7.943	0.299	14.3	15	7.814	0.299	14.6	15	7.701	0.299	14.8	15
Thyroid stimulating hormone	3.490	0.399	43.8	15	4.186	0.399	36.5	15	3.416	0.399	44.8	15

1. Least squares means and standard errors were estimated based on a mixed effects model applied to the data for control and two doses of Methoxychlor.
2. Within laboratory CV was calculated as residual standard deviation/LS Mean.
3. Significantly differences from corn oil at the 0.05 level were marked by "*".

Table 10b. Summary Statistics for Corn Oil and Test Chemical Methoxychlor in Female Pubertal Assay for Hormonal Parameters for WIL Laboratory [1,2,3].

Parameter	Corn Oil				Methoxychlor (12.5 mg/kg/day)				Methoxychlor (50 mg/kg/day)			
	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N
Serum Thyroxine	5.138	0.299	22.1	15	4.965	0.299	22.9	15	5.585	0.299	20.4	15
Thyroid stimulating hormone	8.210	0.693	32.6	15	9.984	0.693	26.8	15	9.050	0.693	29.6	15

1. Least squares means and standard errors were estimated based on a mixed effects model applied to the data for control and two doses of Methoxychlor.
2. Within laboratory CV was calculated as residual standard deviation/LS Mean.
3. Significantly differences from corn oil at the 0.05 level were marked by "*".

Table 10c. Summary Statistics for Corn Oil and Test Chemical Methoxychlor in Female Pubertal Assay for Hormonal Parameters for Huntingdon Laboratory [1,2,3].

Parameter	Corn Oil				Methoxychlor (12.5 mg/kg/day)				Methoxychlor (50 mg/kg/day)			
	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N
Serum Thyroxine	4.766	0.311	23.9	15	4.446	0.311	25.6	15	4.486	0.311	25.4	15
Thyroid stimulating hormone	3.729	0.320	31.4	15	4.543	0.320	25.8	15	4.316	0.320	27.2	15

1. Least squares means and standard errors were estimated based on a mixed effects model applied to the data for control and two doses of Methoxychlor.
2. Within laboratory CV was calculated as residual standard deviation/LS Mean.
3. Significantly differences from corn oil at the 0.05 level were marked by "*".

Table 11. Summary Statistics for Corn Oil and Test Chemical DE-71 in Female Pubertal Assay for Body Weight, and Age and Weight at VO across Laboratories[1,6].

Parameter	Corn Oil				DE-71 (30 mg/kg/day)				DE-71 (60 mg/kg/day)			
	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N
Initial BodyWeight	51.566	3.164	10.6	45	51.733	3.164	10.6	45	52.214	3.164	10.5	45
Final BodyWeight[2]	162.658	3.318	3.5	45	164.112	3.318	3.5	45	164.241	3.318	3.5	45
BodyWeight Gain	111.003	2.764	4.3	45	112.230	2.764	4.3	45	112.070	2.764	4.3	45
Final body weight as percent of control[3]	99.960	1.302	2.3	45	100.914	1.302	2.2	45	100.953	1.302	2.2	45
Age at VO[4]	32.895	0.897	4.7	45	33.829	0.897	4.6	45	33.740	0.897	4.6	45
BodyWeight at VO[4]	113.228	3.031	4.6	45	119.809	3.031	4.4	45	118.036	3.031	4.4	45
Adj. Age at VO[5]	32.279	0.729	3.9	45	33.247	0.728	3.8	45	33.235	0.724	3.8	45
Adj. BodyWeight at VO[5]	109.681	4.251	6.7	45	116.020	4.249	6.3	45	114.268	4.220	6.4	45

1. Least squares means and standard errors were estimated based on a mixed effects model applied to the data for control, two doses of DE-71, and two doses of 2-Chloronitrobenzene.
2. Body weight at PND42 was summarized whether animals were necropsied at PND42 or PND43.
3. Final body weight as percent of control was calculated for each animal as the ratio of its final body weight over the mean of the final body weights within the control group (in percent).
4. All animals had VO before necropsy.
5. Least squares means and standard errors for Adj. age and body weight at VO were estimated based on a mixed effects model with mean centered initial body weight as a covariate.

6. CV was calculated as $\sqrt{3}$*standard error/LS Mean.

* --- Significantly different from corn oil at the 0.05 level.

Table 12. Summary Statistics for Corn Oil and Test Chemical 2-Chloronitrobenzene in Female Pubertal Assay for Body Weight, and Age and Weight at VO across Laboratories[1,6].

Parameter	Corn Oil				2-Chloronitrobenzene (25 mg/kg/day)				2-Chloronitrobenzene (100 mg/kg/day)			
	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N
Initial BodyWeight	51.566	3.164	10.6	45	52.337	3.164	10.5	45	52.043	3.164	10.5	45
Final BodyWeight[2]	162.658	3.318	3.5	45	166.565	3.318	3.5	45	162.310	3.318	3.5	45
BodyWeight Gain	111.003	2.764	4.3	45	114.285	2.764	4.2	45	110.296	2.764	4.3	45
Final body weight as percent of control[3]	99.960	1.302	2.3	45	102.379	1.302	2.2	45	99.733	1.302	2.3	45
Age at VO[4]	32.895	0.897	4.7	45	33.562	0.897	4.6	45	36.784*	0.897	4.2	45
BodyWeight at VO[4]	113.228	3.031	4.6	45	119.093	3.031	4.4	45	132.483*	3.031	4.0	45
Adj. Age at VO[5]	32.279	0.729	3.9	45	33.059	0.724	3.8	45	36.241*	0.725	3.5	45
Adj. BodyWeight at VO[5]	109.681	4.251	6.7	45	115.402	4.218	6.3	45	128.946*	4.228	5.7	45

1. Least squares means and standard errors were estimated based on a mixed effects model applied to the data for control, two doses of DE-71, and two doses of 2-Chloronitrobenzene.
2. Body weight at PND42 was summarized whether animals were necropsied at PND42 or PND43
3. Final body weight as percent of control was calculated for each animal as the ratio of its final body weight over the mean of the final body weights within the control group (in percent).
4. All animals had VO before necropsy.
5. Least squares means and standard errors for Adj. age and body weight at VO were estimated based on a mixed effects model with mean centered initial body weight as a covariate.
6. CV was calculated as $\sqrt{3}$*standard error/LS Mean.

* --- Significantly different from corn oil at the 0.05 level.

Table 13. Summary Statistics for Corn Oil and Test Chemical Methoxychlor in Female Pubertal Assay for Body Weight, and Age and Weight at VO across Laboratories[1,6].

Parameter	Corn Oil				Methoxychlor (12.5 mg/kg/day)				Methoxychlor (50 mg/kg/day)			
	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N
Initial BodyWeight	51.714	3.110	10.4	45	52.059	3.110	10.3	45	52.302	3.110	10.3	45
Final BodyWeight[2]	165.412	2.947	3.1	45	161.328	2.947	3.2	45	156.074*	2.947	3.3	45
BodyWeight Gain	113.397	1.749	2.7	45	109.502	1.749	2.8	45	103.662*	1.749	2.9	45
Final body weight as percent of control[3]	99.996	1.124	1.9	45	97.575	1.124	2.0	45	94.344*	1.124	2.1	45
Age at VO[4]	32.989	0.588	3.1	45	32.860	0.591	3.1	45	27.353*	0.500	3.2	45
BodyWeight at VO[4]	115.297	3.104	4.7	45	112.010	3.403	5.3	45	80.436*	2.750	5.9	45
Adj. Age at VO[5]	33.047	0.640	3.4	45	32.901	0.635	3.3	45	27.396*	0.555	3.5	45
Adj. BodyWeight at VO[5]	115.459	4.836	7.3	45	112.264	4.969	7.7	45	80.547*	4.576	9.8	45

1. Least squares means and standard errors were estimated based on a mixed effects model applied to the data for control and two doses of Methoxychlor.
2. Body weight at PND42 was summarized whether animals were necropsied at PND42 or PND43.
3. Final body weight as percent of control was calculated for each animal as the ratio of its final body weight over the mean of the final body weights within the control group (in percent).
4. All animals had VO before necropsy.
5. Least squares means and standard errors for Adj. age and body weight at VO were estimated based on a mixed effects model with mean centered initial body weight as a covariate.
6. CV was calculated as $\sqrt{3}$*standard error/LS Mean.

* --- Significantly different from corn oil at the 0.05 level.

Table 14. Summary Statistics for Corn Oil and Test Chemical DE-71 in Female Pubertal Assay for Unadjusted and Body-Weight Adjusted Organ Weights across Laboratories [1,2,3,4].

	Corn Oil				DE-71 (30 mg/kg/day)				DE-71 (60 mg/kg/day)			
Parameter	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N
Adrenals	0.044	0.004	14.7	45	0.044	0.004	14.4	45	0.042	0.004	15.3	45
Kidneys	1.598	0.082	8.9	45	1.610	0.079	8.5	45	1.604	0.079	8.6	45
Liver	7.985	0.449	9.7	45	10.070*	0.449	7.7	45	11.203*	0.449	6.9	45
Ovaries	0.079	0.008	16.5	45	0.076	0.007	16.9	45	0.074	0.007	17.4	45
Pituitary	0.011	0.001	19.2	44	0.010	0.001	20.0	45	0.010	0.001	21.3	45
ThyroidBlotted	0.018	0.003	29.2	45	0.019	0.003	27.7	45	0.019	0.003	27.7	45
UterusBlotted	0.312	0.016	9.1	45	0.319	0.017	9.0	44	0.292	0.016	9.7	45
UterusWet	0.347	0.020	9.9	45	0.344	0.021	10.5	44	0.326	0.021	11.0	45
Adj. Adrenals	0.045	0.004	14.9	45	0.046	0.004	14.7	45	0.043	0.004	15.6	45
Adj. Kidneys	1.576	0.074	8.1	45	1.582	0.070	7.7	45	1.580	0.070	7.6	45
Adj. Liver	7.970	0.422	9.2	45	10.029*	0.422	7.3	45	11.161*	0.419	6.5	45
Adj. Ovaries	0.085	0.006	12.2	45	0.081	0.006	12.4	45	0.078	0.006	12.5	45
Adj. Pituitary	0.011	0.001	23.5	44	0.011	0.001	24.4	45	0.010	0.001	26.0	45
Adj. ThyroidBlotted	0.018	0.003	31.1	45	0.018	0.003	29.6	45	0.019	0.003	29.4	45
Adj. UterusBlotted	0.322	0.014	7.6	45	0.327	0.014	7.6	44	0.299	0.014	8.0	45
Adj. UterusWet	0.354	0.018	8.6	45	0.353	0.019	9.5	44	0.333	0.019	9.8	45

1. Least squares means and standard errors were estimated based on a mixed effects model applied to the data for control, two doses of DE-71, and two doses of 2-Chloronitrobenzene.
2. Least squares means and standard errors for Adj. organ weights were estimated based on a mixed effects model with mean centered initial body weight as a covariate.
3. CV was calculated as $\sqrt{3}$*standard error/LS Mean.
4. Significantly differences from corn oil at the 0.05 level were marked by "*".

Table 15. Summary Statistics for Corn Oil and Test Chemical 2-Chloronitrobenzene in Female Pubertal Assay for Unadjusted and Body-Weight Adjusted Organ Weights across Laboratories [1,2,3,4].

	Corn Oil				2-Chloronitrobenzene (25 mg/kg/day)				2-Chloronitrobenzene (100 mg/kg/day)			
Parameter	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N
Adrenals	0.044	0.004	14.7	45	0.044	0.004	14.4	45	0.039*	0.004	16.2	45
Kidneys	1.598	0.082	8.9	45	1.629	0.082	8.7	45	1.631	0.082	8.7	45
Liver	7.985	0.449	9.7	45	10.250*	0.449	7.6	45	12.345*	0.449	6.3	45
Ovaries	0.079	0.008	16.5	45	0.075	0.007	17.1	45	0.068*	0.007	19.0	45
Pituitary	0.011	0.001	19.2	44	0.010	0.001	20.4	45	0.009	0.001	22.6	45
ThyroidBlotted	0.018	0.003	29.2	45	0.018	0.003	30.2	45	0.017	0.003	30.5	45
UterusBlotted	0.312	0.016	9.1	45	0.301	0.016	9.4	45	0.252*	0.016	11.3	45
UterusWet	0.347	0.020	9.9	45	0.335	0.020	10.3	44	0.296*	0.020	11.5	45
Adj. Adrenals	0.045	0.004	14.9	45	0.045	0.004	14.7	45	0.041*	0.004	16.5	45
Adj. Kidneys	1.576	0.074	8.1	45	1.591	0.072	7.9	45	1.602	0.072	7.8	45
Adj. Liver	7.970	0.422	9.2	45	10.171*	0.419	7.1	45	12.277*	0.420	5.9	45
Adj. Ovaries	0.085	0.006	12.2	45	0.079	0.006	12.6	45	0.072*	0.006	13.8	45
Adj. Pituitary	0.011	0.001	23.5	44	0.011	0.002	24.8	45	0.010*	0.002	27.4	45
Adj. ThyroidBlotted	0.018	0.003	31.1	45	0.017	0.003	32.2	45	0.017	0.003	32.6	45
Adj. UterusBlotted	0.322	0.014	7.6	45	0.308	0.014	7.8	45	0.260*	0.014	9.3	45
Adj. UterusWet	0.354	0.018	8.6	45	0.344	0.019	9.3	44	0.305*	0.018	10.4	45

1. Least squares means and standard errors were estimated based on a mixed effects model applied to the data for control, two doses of DE-71, and two doses of 2-Chloronitrobenzene.
2. Least squares means and standard errors for Adj. organ weights were estimated based on a mixed effects model with mean centered initial body weight as a covariate.
3. CV was calculated as $\sqrt{3}$*standard error/LS Mean.
4. Significantly differences from corn oil at the 0.05 level were marked by "*".

Table 16. Summary Statistics for Corn Oil and Test Chemical Methoxychlor in Female Pubertal Assay for Unadjusted and Body-Weight Adjusted Organ Weights across Laboratories [1,2,3,4].

	Corn Oil				Methoxychlor (12.5 mg/kg/day)				Methoxychlor (50 mg/kg/day)			
Parameter	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N
Adrenals	0.045	0.002	8.5	45	0.045	0.002	8.6	44	0.047	0.002	8.1	45
Kidneys	1.597	0.075	8.1	45	1.527*	0.072	8.2	45	1.492*	0.072	8.4	45
Liver	8.208	0.284	6.0	45	7.610*	0.284	6.5	45	7.349*	0.284	6.7	45
Ovaries	0.080	0.008	17.7	44	0.079	0.008	17.8	44	0.072*	0.008	19.5	45
Pituitary	0.011	0.001	16.7	44	0.010	0.001	17.5	45	0.010	0.001	18.1	45
ThyroidBlotted	0.018	0.003	27.9	45	0.017	0.003	30.3	45	0.018	0.003	27.9	45
UterusBlotted	0.316	0.014	7.9	45	0.351	0.014	7.1	45	0.325	0.014	7.7	45
UterusWet	0.358	0.022	10.9	45	0.432*	0.022	9.0	45	0.389	0.022	10.0	45
Adj. Adrenals	0.046	0.002	6.0	45	0.045	0.002	6.0	44	0.048	0.002	5.7	45
Adj. Kidneys	1.586	0.078	8.5	45	1.517*	0.076	8.6	45	1.477*	0.076	8.9	45
Adj. Liver	8.093	0.248	5.3	45	7.530*	0.241	5.5	45	7.235*	0.243	5.8	45
Adj. Ovaries	0.081	0.008	16.6	44	0.080	0.008	16.6	44	0.074*	0.008	18.1	45
Adj. Pituitary	0.011	0.001	22.2	44	0.011	0.001	23.1	45	0.010	0.001	23.9	45
Adj. ThyroidBlotted	0.018	0.003	30.3	45	0.016	0.003	32.7	45	0.018	0.003	30.2	45
Adj. UterusBlotted	0.323	0.014	7.7	45	0.356	0.014	6.7	45	0.330	0.014	7.5	45
Adj. UterusWet	0.368	0.026	12.1	45	0.441*	0.024	9.6	45	0.398	0.025	11.0	45

1. Least squares means and standard errors were estimated based on a mixed effects model applied to the data for control and two doses of Methoxychlor.
2. Least squares means and standard errors for Adj. organ weights were estimated based on a mixed effects model with mean centered initial body weight as a covariate.
3. CV was calculated as $\sqrt{3}$*standard error/LS Mean.
4. Significantly differences from corn oil at the 0.05 level were marked by "*".

Table 17. Summary Statistics for Corn Oil and Test Chemical DE-71 in Female Pubertal Assay for Hormonal Parameters across Laboratories [1,2,3].

Parameter	Corn Oil				DE-71 (30 mg/kg/day)				DE-71 (60 mg/kg/day)			
	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N
Serum Thyroxine	6.196	1.024	28.6	45	2.534*	1.006	68.8	45	1.915*	1.005	90.9	45
Thyroid stimulating hormone	5.556	1.751	54.6	45	7.463*	1.788	41.5	45	7.449*	1.770	41.2	45

1. Least squares means and standard errors were estimated based on a mixed effects model applied to the data for control, two doses of DE-71, and two doses of 2-Chloronitrobenzene.

2. CV was calculated as $\sqrt{3}$*standard error/LS Mean.
3. Significantly differences from corn oil at the 0.05 level were marked by "*".

Table 18. Summary Statistics for Corn Oil and Test Chemical 2-Chloronitrobenzene in Female Pubertal Assay for Hormonal Parameters across Laboratories [1,2,3].

Parameter	Corn Oil				2-Chloronitrobenzene (25 mg/kg/day)				2-Chloronitrobenzene (100 mg/kg/day)			
	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N
Serum Thyroxine	6.196	1.024	28.6	45	5.553	1.018	31.8	45	5.213*	1.013	33.7	45
Thyroid stimulating hormone	5.556	1.751	54.6	45	6.042	1.767	50.7	45	6.536	1.756	46.5	45

1. Least squares means and standard errors were estimated based on a mixed effects model applied to the data for control, two doses of DE-71, and two doses of 2-Chloronitrobenzene.

2. CV was calculated as $\sqrt{3}$*standard error/LS Mean.
3. Significantly differences from corn oil at the 0.05 level were marked by "*".

Table 19. Summary Statistics for Corn Oil and Test Chemical Methoxychlor in Female Pubertal Assay for Hormonal Parameters across Laboratories [1,2,3].

Parameter	Corn Oil				Methoxychlor (12.5 mg/kg/day)				Methoxychlor (50 mg/kg/day)			
	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N
Serum Thyroxine	5.949	1.001	29.1	45	5.741	1.001	30.2	45	5.924	1.001	29.3	45
Thyroid stimulating hormone	5.218	1.721	57.1	45	6.098*	1.721	48.9	45	5.614	1.721	53.1	45

1. Least squares means and standard errors were estimated based on a mixed effects model applied to the data for control, two doses of DE-71, and two doses of 2-Chloronitrobenzene.

2. CV was calculated as $\sqrt{3}$*standard error/LS Mean.
3. Significantly differences from corn oil at the 0.05 level were marked by "*".

Table 20a. Summary Statistics for Corn Oil and DE-71 in Female Pubertal Assay for Unadjusted and Body Weight Adjusted Variables for Argus Laboratory, Outliers Excluded[1,2,3].

Parameter	Corn Oil				DE-71 (30 mg/kg/day)				DE-71 (60 mg/kg/day)			
	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N
Body Weight Gain	112.655	2.943	10.0	15	110.175	2.943	10.2	15	113.049	2.943	10.0	15
Adrenals	0.047	0.003	23.0	15	0.049	0.003	22.0	15	0.050	0.003	21.3	15
Kidneys	1.655	0.086	20.0	15	1.710	0.046	10.4	15	1.754	0.046	10.2	15
Ovaries	0.083	0.005	25.5	15	0.078	0.005	23.2	15	0.080	0.004	17.3	15
Pituitary	0.013	0.001	17.5	14	0.012	0.001	42.8	15	0.011	0.001	48.1	15
UterusWet	0.374	0.034	34.4	15	0.355	0.022	21.5	13	0.323	0.021	23.5	14
Adj. Adrenals	0.047	0.003	22.8	15	0.049	0.003	21.8	15	0.051	0.003	21.2	15
Adj. Kidneys	1.563	0.080	19.3	15	1.617	0.043	9.2	15	1.659	0.043	8.9	15
Adj. Ovaries	0.086	0.006	25.1	15	0.081	0.005	23.5	15	0.084	0.003	13.0	15
Adj. Pituitary	0.014	0.001	15.3	14	0.013	0.001	37.9	15	0.012	0.001	42.1	15
Adj. UterusWet	0.379	0.036	34.2	15	0.360	0.025	21.2	13	0.328	0.024	23.3	14

1. Least squares means and standard errors were estimated based on a mixed effects model applied to the data for control, two doses of DE-71, and two doses of 2-Chloronitrobenzene.
2. Least squares means and standard errors for Adj. variable were estimated based on a mixed effects model with mean centered initial body weight as a covariate.
3. Within laboratory CV was calculated as residual standard deviation/LS Mean.

* --- Significantly different from corn oil at the 0.05 level.

Table 20b. Summary Statistics for Corn Oil and DE-71 in Female Pubertal Assay for Unadjusted and Body Weight Adjusted Variables for WIL Laboratory, Outliers Excluded[1,2,3].

Parameter	Corn Oil				DE-71 (30 mg/kg/day)				DE-71 (60 mg/kg/day)			
	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N
BodyWeight Gain	112.882	2.943	10.0	15	115.789	2.943	9.7	15	113.282	2.943	10.0	15
Adrenals	0.042	0.001	12.0	15	0.043	0.001	11.7	15	0.040	0.001	12.6	15
Kidneys	1.612	0.047	11.2	15	1.644	0.028	6.4	15	1.600	0.028	6.6	15
Ovaries	0.063	0.004	21.9	15	0.062	0.003	18.1	15	0.059	0.003	20.6	15
Pituitary	0.010	0.000	16.1	15	0.010	0.000	13.9	15	0.009*	0.000	14.9	15
UterusWet	0.327	0.028	32.9	15	0.318	0.025	29.6	15	0.295	0.025	31.9	15
Adj. Adrenals	0.045	0.002	10.7	15	0.047	0.002	10.4	15	0.043	0.002	11.2	15
Adj. Kidneys	1.640	0.060	11.4	15	1.673	0.044	6.3	15	1.625	0.041	6.5	15
Adj. Ovaries	0.072	0.005	20.1	15	0.071	0.004	13.7	15	0.066	0.004	14.4	15
Adj. Pituitary	0.010	0.001	16.3	15	0.010	0.001	13.9	15	0.009*	0.000	15.0	15
Adj. UterusWet	0.369	0.035	26.7	15	0.359	0.034	25.7	15	0.331	0.032	27.8	15

1. Least squares means and standard errors were estimated based on a mixed effects model applied to the data for control, two doses of DE-71, and two doses of 2-Chloronitrobenzene.
2. Least squares means and standard errors for Adj. variable were estimated based on a mixed effects model with mean centered initial body weight as a covariate.
3. Within laboratory CV was calculated as residual standard deviation/LS Mean.

* --- Significantly different from corn oil at the 0.05 level.

Table 20c. Summary Statistics for Corn Oil and DE-71 in Female Pubertal Assay for Unadjusted and Body Weight Adjusted Variables for Huntingdon Laboratory, Outliers Excluded[1,2,3].

	Corn Oil				DE-71 (30 mg/kg/day)				DE-71 (60 mg/kg/day)			
Parameter	**LS Mean**	**Std Error**	**CV**	**N**	**LS Mean**	**Std Error**	**CV**	**N**	**LS Mean**	**Std Error**	**CV**	**N**
BodyWeight Gain	107.500	3.015	10.5	15	110.754	3.015	10.2	15	109.907	3.015	10.3	15
Adrenals	0.041	0.002	21.6	15	0.040	0.002	22.5	15	0.037	0.002	23.8	15
Kidneys	1.481	0.040	10.0	15	1.468	0.040	10.2	15	1.490	0.040	10.0	15
Ovaries	0.092	0.004	17.1	15	0.085	0.003	14.4	15	0.083	0.004	17.6	15
Pituitary	0.009	0.000	16.9	15	0.009	0.000	15.8	15	0.008	0.000	16.8	15
UterusWet	0.343	0.024	25.7	15	0.340	0.035	38.5	15	0.352	0.035	37.2	15
Adj. Adrenals	0.041	0.002	21.5	15	0.040	0.002	22.5	15	0.037	0.002	23.8	15
Adj. Kidneys	1.480	0.037	9.3	15	1.457	0.035	9.1	15	1.478	0.035	9.0	15
Adj. Ovaries	0.092	0.004	15.6	15	0.085	0.003	14.9	15	0.082	0.004	17.9	15
Adj. Pituitary	0.009	0.000	16.2	15	0.009	0.000	15.5	15	0.008	0.000	16.5	15
Adj. UterusWet	0.343	0.025	25.9	15	0.340	0.035	38.7	15	0.352	0.035	37.4	15

1. Least squares means and standard errors were estimated based on a mixed effects model applied to the data for control, two doses of DE-71, and two doses of 2-Chloronitrobenzene.
2. Least squares means and standard errors for Adj. variable were estimated based on a mixed effects model with mean centered initial body weight as a covariate.
3. Within laboratory CV was calculated as residual standard deviation/LS Mean.

* --- Significantly different from corn oil at the 0.05 level.

Table 21a. Summary Statistics for Corn Oil and 2-Chloronitrobenzene in Female Pubertal Assay for Unadjusted and Body Weight Adjusted Variables for Argus Laboratory, Outliers Excluded[1,2,3].

Parameter	Corn Oil				2-Chloronitrobenzene (25 mg/kg/day)				2-Chloronitrobenzene (100 mg/kg/day)			
	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N
BodyWeight Gain	112.655	2.943	10.0	15	111.317	3.044	10.1	14	112.149	2.943	10.1	15
Adrenals	0.047	0.003	23.0	15	0.051	0.003	21.2	14	0.046	0.003	23.2	14
Kidneys	1.655	0.086	20.0	15	1.820	0.059	12.4	15	1.825	0.061	12.4	14
Ovaries	0.083	0.005	25.5	15	0.091	0.006	25.4	15	0.075	0.003	13.1	14
Pituitary	0.013	0.001	17.5	14	0.012	0.001	34.0	15	0.012	0.001	34.1	15
UterusWet	0.374	0.034	34.4	15	0.367	0.034	35.2	15	0.305	0.034	42.3	15
Adj. Adrenals	0.047	0.003	22.8	15	0.051	0.003	21.0	14	0.047	0.003	23.0	14
Adj. Kidneys	1.563	0.080	19.3	15	1.717	0.057	11.8	15	1.732	0.058	11.7	14
Adj. Ovaries	0.086	0.006	25.1	15	0.095	0.006	23.9	15	0.078	0.003	14.1	14
Adj. Pituitary	0.014	0.001	15.3	14	0.013	0.001	30.9	15	0.013	0.001	31.1	15
Adj. UterusWet	0.379	0.036	34.2	15	0.373	0.036	34.9	15	0.310	0.036	42.0	15

1. Least squares means and standard errors were estimated based on a mixed effects model applied to the data for control, two doses of DE-71, and two doses of 2-Chloronitrobenzene.
2. Least squares means and standard errors for Adj. variable were estimated based on a mixed effects model with mean centered initial body weight as a covariate.
3. Within laboratory CV was calculated as residual standard deviation/LS Mean.

* --- Significantly different from corn oil at the 0.05 level.

Table 21b. Summary Statistics for Corn Oil and 2-Chloronitrobenzene in Female Pubertal Assay for Unadjusted and Body Weight Adjusted Variables for WIL Laboratory, Outliers Excluded[1,2,3].

Parameter	Corn Oil				2-Chloronitrobenzene (25 mg/kg/day)				2-Chloronitrobenzene (100 mg/kg/day)			
	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N
BodyWeight Gain	112.882	2.943	10.0	15	121.709*	2.943	9.3	15	115.775	2.943	9.7	15
Adrenals	0.042	0.001	12.0	15	0.044	0.001	11.5	15	0.038*	0.001	13.3	15
Kidneys	1.612	0.047	11.2	15	1.697	0.041	9.3	15	1.687	0.041	9.3	15
Ovaries	0.063	0.004	21.9	15	0.063	0.002	13.7	15	0.054	0.003	21.1	15
Pituitary	0.010	0.000	16.1	15	0.010	0.000	12.5	15	0.009*	0.000	13.7	15
UterusWet	0.327	0.028	32.9	15	0.320	0.021	23.8	14	0.294	0.020	25.9	15
Adj. Adrenals	0.045	0.002	10.7	15	0.047	0.002	10.3	15	0.041*	0.002	11.8	15
Adj. Kidneys	1.640	0.060	11.4	15	1.721	0.050	9.0	15	1.712	0.051	9.1	15
Adj. Ovaries	0.072	0.005	20.1	15	0.071	0.004	13.4	15	0.062*	0.004	17.5	15
Adj. Pituitary	0.010	0.001	16.3	15	0.010	0.000	12.5	15	0.009*	0.000	13.8	15
Adj. UterusWet	0.369	0.035	26.7	15	0.357	0.030	21.9	14	0.332	0.030	23.6	15

1. Least squares means and standard errors were estimated based on a mixed effects model applied to the data for control, two doses of DE-71, and two doses of 2-Chloronitrobenzene.
2. Least squares means and standard errors for Adj. variable were estimated based on a mixed effects model with mean centered initial body weight as a covariate.
3. Within laboratory CV was calculated as residual standard deviation/LS Mean.

* --- Significantly different from corn oil at the 0.05 level.

Table 21c. Summary Statistics for Corn Oil and 2-Chloronitrobenzene in Female Pubertal Assay for Unadjusted and Body Weight Adjusted Variables for Huntingdon Laboratory, Outliers Excluded[1,2,3].

Parameter	Corn Oil				2-Chloronitrobenzene (25 mg/kg/day)				2-Chloronitrobenzene (100 mg/kg/day)			
	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N
BodyWeight Gain	107.500	3.015	10.5	15	107.214	3.015	10.5	15	102.994	3.015	10.9	15
Adrenals	0.041	0.002	21.6	15	0.035	0.002	25.3	15	0.033*	0.002	27.0	15
Kidneys	1.481	0.040	10.0	15	1.435	0.041	10.6	15	1.470	0.041	10.4	15
Ovaries	0.092	0.004	17.1	15	0.077*	0.003	15.6	15	0.074*	0.003	12.4	15
Pituitary	0.009	0.000	16.9	15	0.007*	0.000	26.1	14	0.006*	0.000	30.9	15
UterusWet	0.343	0.024	25.7	15	0.320	0.037	43.1	15	0.263	0.037	52.5	15
Adj. Adrenals	0.041	0.002	21.5	15	0.035	0.002	25.2	15	0.033*	0.002	27.0	15
Adj. Kidneys	1.480	0.037	9.3	15	1.428	0.029	7.5	15	1.466	0.029	7.3	15
Adj. Ovaries	0.092	0.004	15.6	15	0.076*	0.003	14.1	15	0.074*	0.002	9.5	15
Adj. Pituitary	0.009	0.000	16.2	15	0.007*	0.000	25.1	14	0.006*	0.000	29.9	15
Adj. UterusWet	0.343	0.025	25.9	15	0.320	0.037	43.5	15	0.263	0.037	53.0	15

1. Least squares means and standard errors were estimated based on a mixed effects model applied to the data for control, two doses of DE-71, and two doses of 2-Chloronitrobenzene.
2. Least squares means and standard errors for Adj. variable were estimated based on a mixed effects model with mean centered initial body weight as a covariate.
3. Within laboratory CV was calculated as residual standard deviation/LS Mean.

* --- Significantly different from corn oil at the 0.05 level.

Table 22a. Summary Statistics for Corn Oil and Methoxychlor in Female Pubertal Assay for Unadjusted and Body Weight Adjusted Variables for Argus Laboratory, Outliers Excluded[1,2,3].

Parameter	Corn Oil				Methoxychlor (12.5 mg/kg/day)				Methoxychlor (50 mg/kg/day)			
	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N
BodyWeight Gain	114.257	3.077	10.2	15	108.350	3.077	10.8	15	105.077*	3.077	11.1	15
Adrenals	0.046	0.003	21.6	15	0.047	0.003	21.1	14	0.054*	0.003	18.5	15
Kidneys	1.671	0.086	19.8	15	1.599	0.046	11.0	15	1.623	0.046	10.8	15
Ovaries	0.083	0.005	24.6	15	0.087	0.005	23.4	14	0.078	0.005	26.2	15
Pituitary	0.013	0.001	28.5	14	0.011	0.001	33.5	15	0.013	0.001	29.1	15
UterusWet	0.381	0.036	34.9	15	0.468	0.036	28.4	15	0.395	0.036	33.7	15
Adj. Adrenals	0.045	0.003	22.1	15	0.046	0.003	21.6	14	0.053*	0.003	18.9	15
Adj. Kidneys	1.605	0.083	19.0	15	1.546	0.047	10.5	15	1.554	0.050	10.5	15
Adj. Ovaries	0.084	0.006	24.5	15	0.088	0.006	23.4	14	0.079	0.006	26.1	15
Adj. Pituitary	0.014	0.001	25.0	14	0.012	0.001	29.6	15	0.014	0.001	25.5	15
Adj. UterusWet	0.371	0.040	36.1	15	0.460	0.039	29.2	15	0.384	0.040	34.9	15

1. Least squares means and standard errors were estimated based on a mixed effects model applied to the data for control and two doses of Methoxychlor.
2. Least squares means and standard errors for Adj. variable were estimated based on a mixed effects model with mean centered initial body weight as a covariate.
3. Within laboratory CV was calculated as residual standard deviation/LS Mean.

* --- Significantly different from corn oil at the 0.05 level.

Table 22b. Summary Statistics for Corn Oil and Methoxychlor in Female Pubertal Assay for Unadjusted and Body Weight Adjusted Variables for WIL Laboratory, Outliers Excluded[1,2,3].

Parameter	Corn Oil				Methoxychlor (12.5 mg/kg/day)				Methoxychlor (50 mg/kg/day)			
	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N
BodyWeight Gain	114.484	3.077	10.2	15	114.150	3.077	10.2	15	104.297*	3.077	11.2	15
Adrenals	0.041	0.001	13.6	15	0.043	0.001	13.1	15	0.044	0.001	12.6	15
Kidneys	1.627	0.047	11.1	15	1.590	0.031	7.5	15	1.522	0.031	7.8	15
Ovaries	0.063	0.003	19.9	15	0.062	0.003	20.2	15	0.060	0.003	21.0	15
Pituitary	0.010	0.000	16.8	15	0.010	0.000	17.6	15	0.009	0.000	18.3	15
UterusWet	0.334	0.033	36.8	15	0.409	0.033	30.1	15	0.402	0.033	30.6	15
Adj. Adrenals	0.045	0.002	12.2	15	0.046	0.002	11.9	15	0.047	0.002	11.5	15
Adj. Kidneys	1.682	0.068	11.4	15	1.636	0.049	7.1	15	1.570	0.050	7.4	15
Adj. Ovaries	0.065	0.005	19.6	15	0.063	0.005	20.0	15	0.061	0.005	20.7	15
Adj. Pituitary	0.010	0.001	17.6	15	0.009	0.001	18.3	15	0.009	0.001	19.1	15
Adj. UterusWet	0.376	0.052	32.7	15	0.444	0.047	27.7	15	0.438	0.048	28.1	15

1. Least squares means and standard errors were estimated based on a mixed effects model applied to the data for control and two doses of Methoxychlor.
2. Least squares means and standard errors for Adj. variable were estimated based on a mixed effects model with mean centered initial body weight as a covariate.
3. Within laboratory CV was calculated as residual standard deviation/LS Mean.

* --- Significantly different from corn oil at the 0.05 level.

Table 22c. Summary Statistics for Corn Oil and Methoxychlor in Female Pubertal Assay for Unadjusted and Body Weight Adjusted Variables for Huntingdon Laboratory, Outliers Excluded[1,2,3].

Parameter	Corn Oil				Methoxychlor (12.5 mg/kg/day)				Methoxychlor (50 mg/kg/day)			
	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N
BodyWeight Gain	111.544	3.198	10.5	15	106.097	3.198	11.0	15	101.704*	3.198	11.5	15
Adrenals	0.047	0.002	13.7	14	0.045	0.002	14.3	15	0.045	0.002	14.3	15
Kidneys	1.470	0.032	7.9	15	1.384*	0.029	7.5	15	1.353*	0.029	7.6	15
Ovaries	0.092	0.004	14.1	14	0.090	0.004	14.4	15	0.080*	0.004	16.3	15
Pituitary	0.010	0.000	15.9	15	0.009	0.000	17.3	14	0.008*	0.000	18.1	15
UterusWet	0.371	0.054	53.3	15	0.421	0.054	47.1	15	0.353	0.054	56.1	15
Adj. Adrenals	0.047	0.002	13.9	14	0.045	0.002	14.4	15	0.045	0.002	14.5	15
Adj. Kidneys	1.454	0.026	6.4	15	1.373*	0.029	7.8	15	1.336*	0.030	8.0	15
Adj. Ovaries	0.093	0.004	13.9	14	0.090	0.004	14.4	15	0.080*	0.004	16.2	15
Adj. Pituitary	0.010	0.000	16.1	15	0.009	0.000	17.5	14	0.008*	0.000	18.4	15
Adj. UterusWet	0.378	0.056	52.8	15	0.424	0.055	47.0	15	0.360	0.056	55.5	15

1. Least squares means and standard errors were estimated based on a mixed effects model applied to the data for control and two doses of Methoxychlor.
2. Least squares means and standard errors for Adj. variable were estimated based on a mixed effects model with mean centered initial body weight as a covariate.
3. Within laboratory CV was calculated as residual standard deviation/LS Mean.

* --- Significantly different from corn oil at the 0.05 level.

Table 23. Summary Statistics for Corn Oil and DE-71 in Female Pubertal Assay for Unadjusted and Body Weight Adjusted Variables across Laboratories, Outliers Excluded[1,2,3].

Parameter	Corn Oil				DE-71 (30 mg/kg/day)				DE-71 (60 mg/kg/day)			
	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N
BodyWeight Gain	111.004	2.786	4.3	45	112.231	2.786	4.3	45	112.071	2.786	4.3	45
Adrenals	0.043	0.003	13.2	45	0.044	0.003	13.0	45	0.042	0.003	13.7	45
Kidneys	1.605	0.089	9.6	45	1.613	0.086	9.2	45	1.606	0.086	9.2	45
Ovaries	0.079	0.007	16.2	45	0.076	0.007	16.5	45	0.074	0.007	17.0	45
Pituitary	0.011	0.001	21.6	44	0.010	0.001	22.9	45	0.010	0.001	24.5	45
UterusWet	0.346	0.018	9.1	45	0.338	0.017	8.6	43	0.317	0.017	9.0	44
Adj. Adrenals	0.045	0.004	13.6	45	0.045	0.004	13.4	45	0.043	0.003	14.2	45
Adj. Kidneys	1.580	0.077	8.5	45	1.583	0.074	8.1	45	1.581	0.074	8.1	45
Adj. Ovaries	0.084	0.005	10.8	45	0.080	0.005	10.7	45	0.077*	0.005	10.8	45
Adj. Pituitary	0.011	0.002	25.4	44	0.011	0.002	26.8	45	0.010	0.002	28.6	45
Adj. UterusWet	0.356	0.017	8.5	45	0.350	0.017	8.3	43	0.328	0.016	8.5	44

1. Least squares means and standard errors were estimated based on a mixed effects model applied to the data for control, two doses of DE-71, and two doses of 2-Chloronitrobenzene.
2. Least squares means and standard errors for Adj. variable were estimated based on a mixed effects model with mean centered initial body weight as a covariate.
3. CV was calculated as $\sqrt{3}$*standard error/LS Mean.

* --- Significantly different from corn oil at the 0.05 level.

Table 24. Summary Statistics for Corn Oil and 2-Chloronitrobenzene in Female Pubertal Assay for Unadjusted and Body Weight Adjusted Variables across Laboratories, Outliers Excluded[1,2,3].

Parameter	Corn Oil				2-Chloronitrobenzene (25 mg/kg/day)				2-Chloronitrobenzene (100 mg/kg/day)			
	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N
BodyWeight Gain	111.004	2.786	4.3	45	113.450	2.798	4.3	44	110.297	2.786	4.4	45
Adrenals	0.043	0.003	13.2	45	0.044	0.003	13.0	44	0.039*	0.003	14.7	44
Kidneys	1.605	0.089	9.6	45	1.643	0.087	9.2	45	1.653	0.087	9.1	44
Ovaries	0.079	0.007	16.2	45	0.075	0.007	16.6	45	0.068*	0.007	18.3	44
Pituitary	0.011	0.001	21.6	44	0.010	0.001	24.4	44	0.009*	0.001	26.7	45
UterusWet	0.346	0.018	9.1	45	0.333	0.018	9.4	44	0.294*	0.018	10.6	45
Adj. Adrenals	0.045	0.004	13.6	45	0.045	0.003	13.5	44	0.040*	0.004	15.2	44
Adj. Kidneys	1.580	0.077	8.5	45	1.606	0.075	8.1	45	1.624	0.075	8.0	44
Adj. Ovaries	0.084	0.005	10.8	45	0.078	0.005	10.9	45	0.071*	0.005	11.5	44
Adj. Pituitary	0.011	0.002	25.4	44	0.010	0.002	28.4	44	0.009*	0.002	31.1	45
Adj. UterusWet	0.356	0.017	8.5	45	0.347	0.018	9.1	44	0.308*	0.018	10.2	45

1. Least squares means and standard errors were estimated based on a mixed effects model applied to the data for control, two doses of DE-71, and two doses of 2-Chloronitrobenzene.
2. Least squares means and standard errors for Adj. variable were estimated based on a mixed effects model with mean centered initial body weight as a covariate.
3. CV was calculated as $\sqrt{3}$*standard error/LS Mean.

* --- Significantly different from corn oil at the 0.05 level.

Table 25. Summary Statistics for Corn Oil and Methoxychlor in Female Pubertal Assay for Unadjusted and Body Weight Adjusted Variables across Laboratories, Outliers Excluded[1,2,3].

Parameter	Corn Oil				Methoxychlor (12.5 mg/kg/day)				Methoxychlor (50 mg/kg/day)			
	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N	LS Mean	Std Error	CV	N
BodyWeight Gain	113.397	1.749	2.7	45	109.502	1.749	2.8	45	103.662*	1.749	2.9	45
Adrenals	0.045	0.002	7.9	44	0.045	0.002	7.9	44	0.047	0.002	7.5	45
Kidneys	1.597	0.075	8.1	45	1.527*	0.072	8.2	45	1.492*	0.072	8.4	45
Ovaries	0.080	0.008	17.7	44	0.079	0.008	17.8	44	0.072*	0.008	19.5	45
Pituitary	0.011	0.001	16.6	44	0.010	0.001	17.8	44	0.010*	0.001	18.1	45
UterusWet	0.358	0.022	10.9	45	0.432*	0.022	9.0	45	0.389	0.022	10.0	45
Adj. Adrenals	0.045	0.001	5.0	44	0.045	0.001	4.8	44	0.047	0.001	4.7	45
Adj. Kidneys	1.586	0.078	8.5	45	1.517*	0.076	8.6	45	1.477*	0.076	8.9	45
Adj. Ovaries	0.081	0.008	16.6	44	0.080	0.008	16.6	44	0.074*	0.008	18.1	45
Adj. Pituitary	0.011	0.001	22.0	44	0.010	0.001	23.5	44	0.010*	0.001	24.0	45
Adj. UterusWet	0.368	0.026	12.1	45	0.441*	0.024	9.6	45	0.398	0.025	11.0	45

1. Least squares means and standard errors were estimated based on a mixed effects model applied to the data for control and two doses of Methoxychlor.
2. Least squares means and standard errors for Adj. variable were estimated based on a mixed effects model with mean centered initial body weight as a covariate.
3. CV was calculated as $\sqrt{3}$*standard error/LS Mean.

* --- Significantly different from corn oil at the 0.05 level.

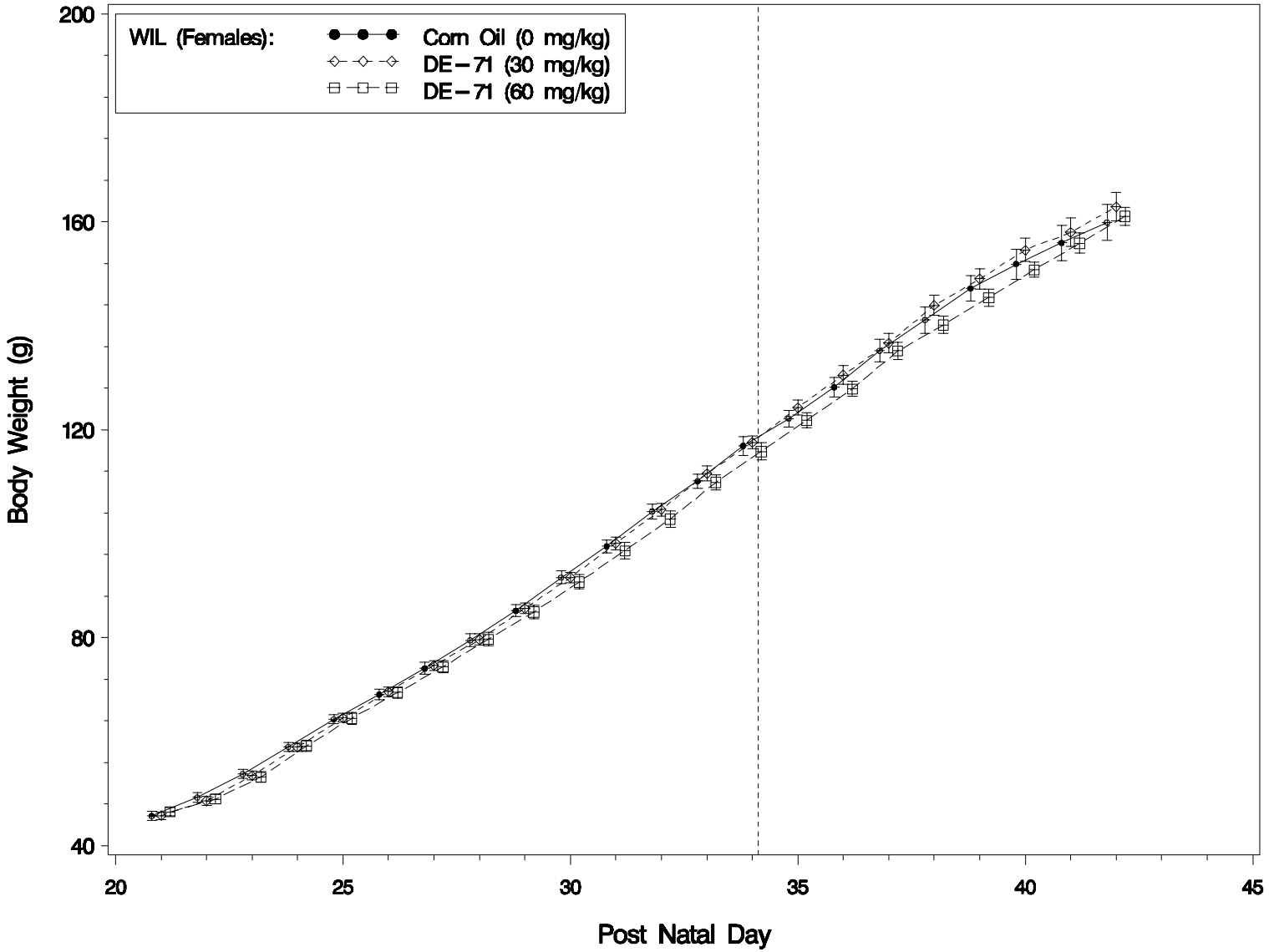

Figure 1. **<u>WIL Females</u> Means (with ± 2 Standard Error Bars) of Body Weights (g) on Each Day from Weaning through Dosing (PND 21 to PND 42) for the Control Group (Corn Oil) and the Two DE-71 Dose Groups. The Reference Line Corresponds to the Mean Age of the Control Group at VO.**

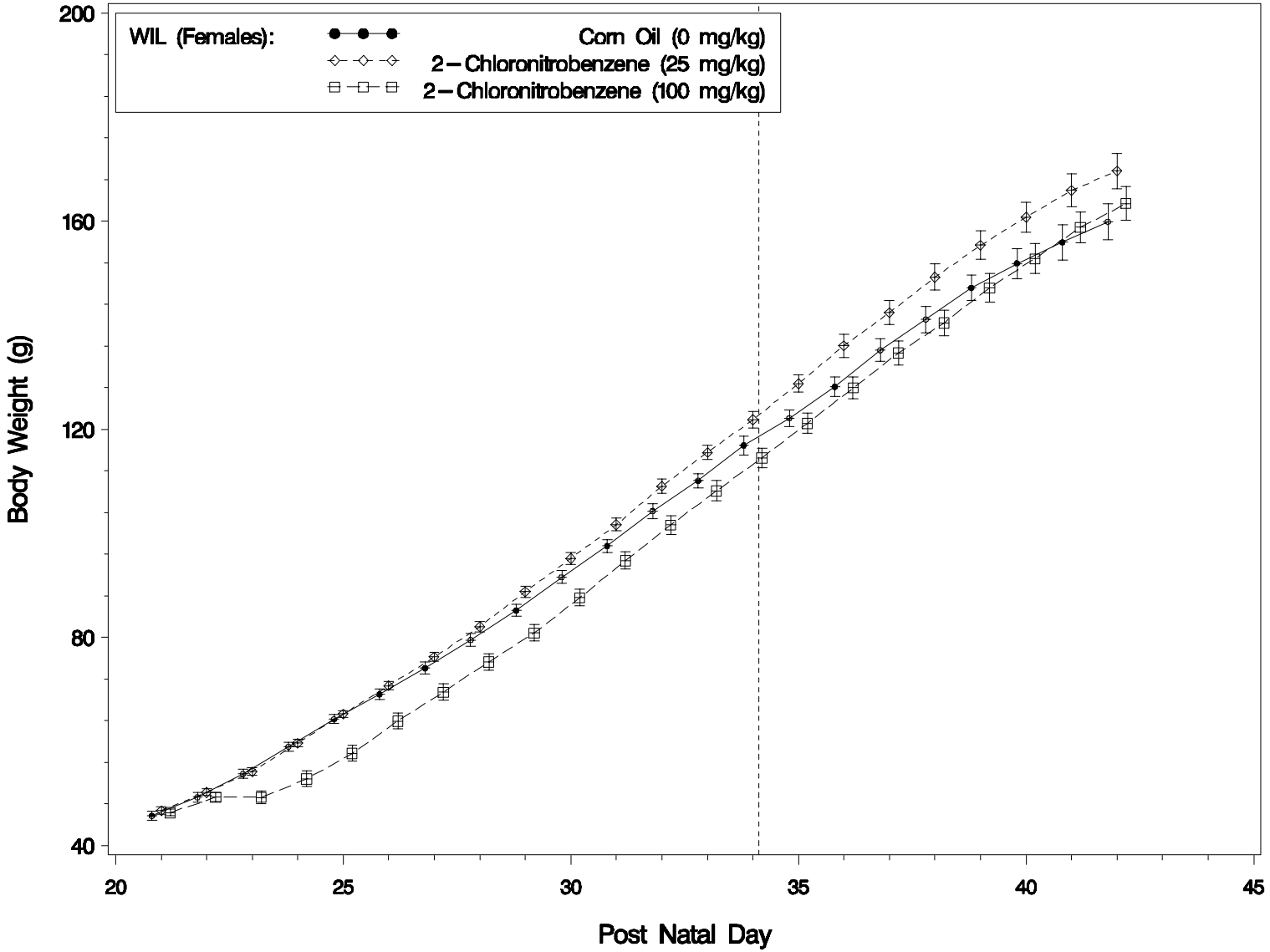

Figure 2. **<u>WIL Females</u> Means (with ± 2 Standard Error Bars) of Body Weights (g) on Each Day from Weaning through Dosing (PND 21 to PND 42) for the Control Group (Corn Oil) and the Two 2-Chloronitrobenzene Dose Groups. The Reference Line Corresponds to the Mean Age of the Control Group at VO.**

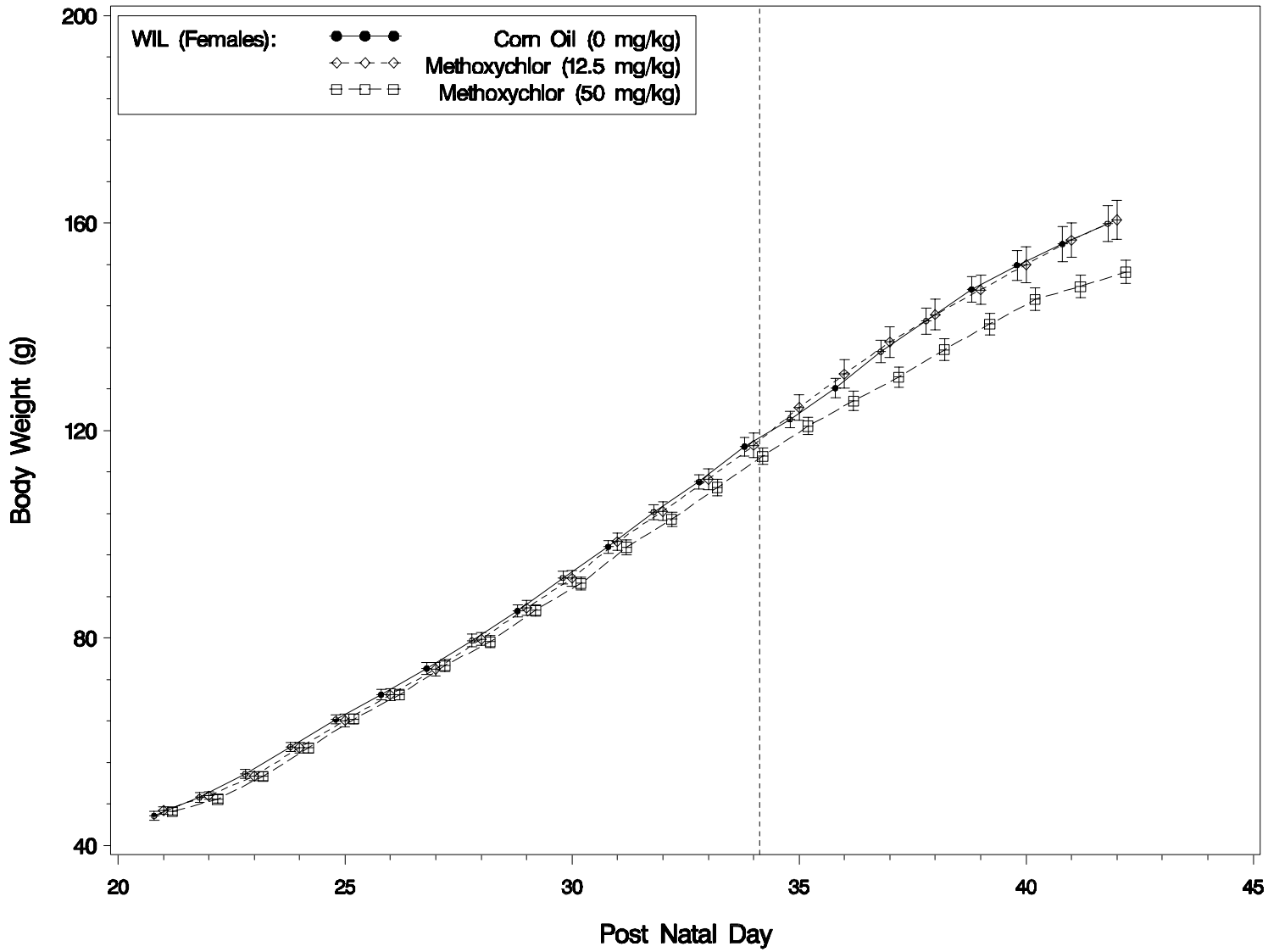

Figure 3. **<u>WIL Females</u> Means (with ± 2 Standard Error Bars) of Body Weights (g) on Each Day from Weaning through Dosing (PND 21 to PND 42) for the Control Group (Corn Oil) and the Two Methoxychlor Dose Groups. The Reference Line Corresponds to the Mean Age of the Control Group at VO.**

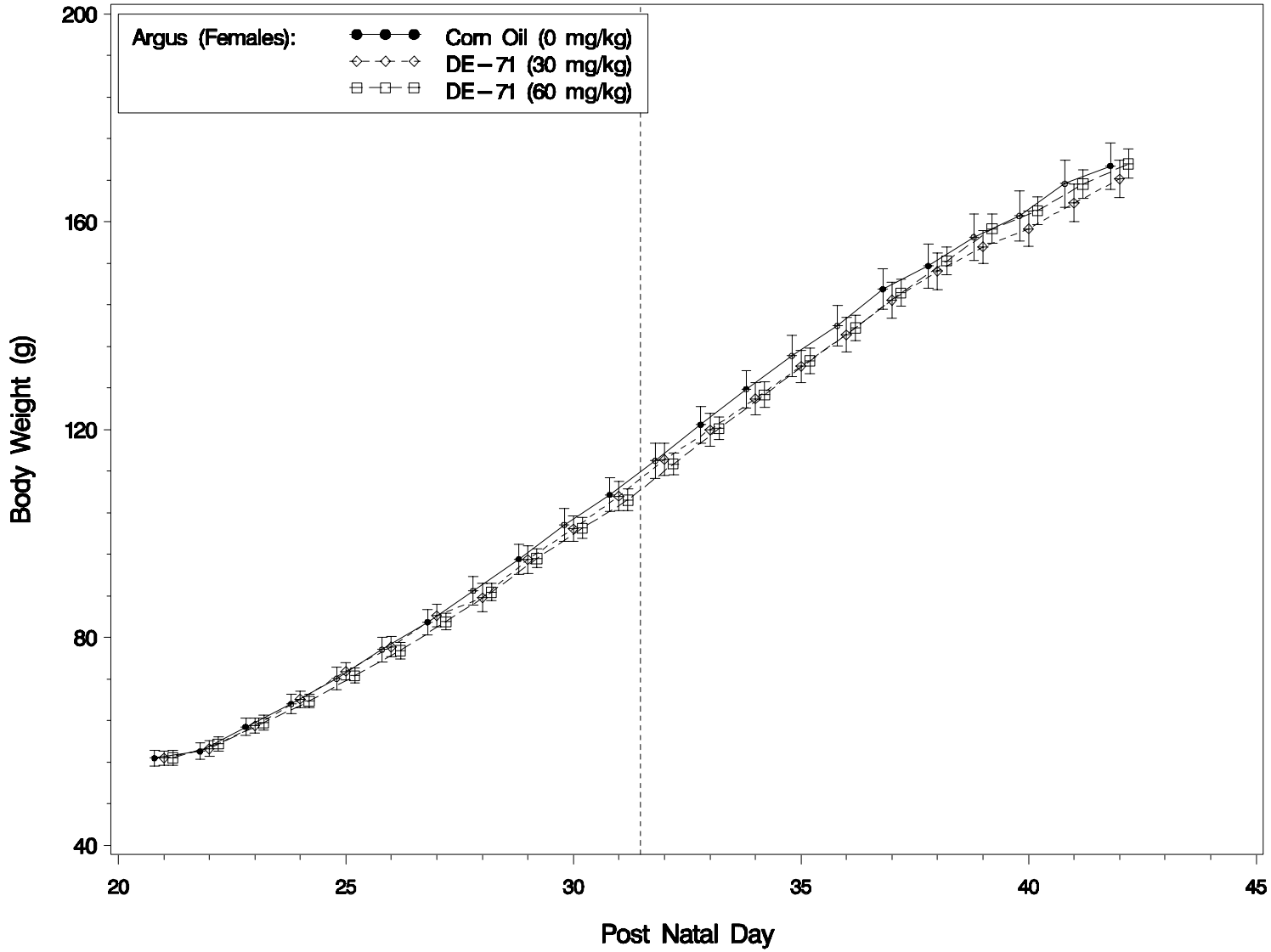

Figure 4. **<u>Argus Females</u> Means (with ± 2 Standard Error Bars) of Body Weights (g) on Each Day from Weaning through Dosing (PND 21 to PND 42) for the Control Group (Corn Oil) and the Two DE-71 Dose Groups. The Reference Line Corresponds to the Mean Age of the Control Group at VO.**

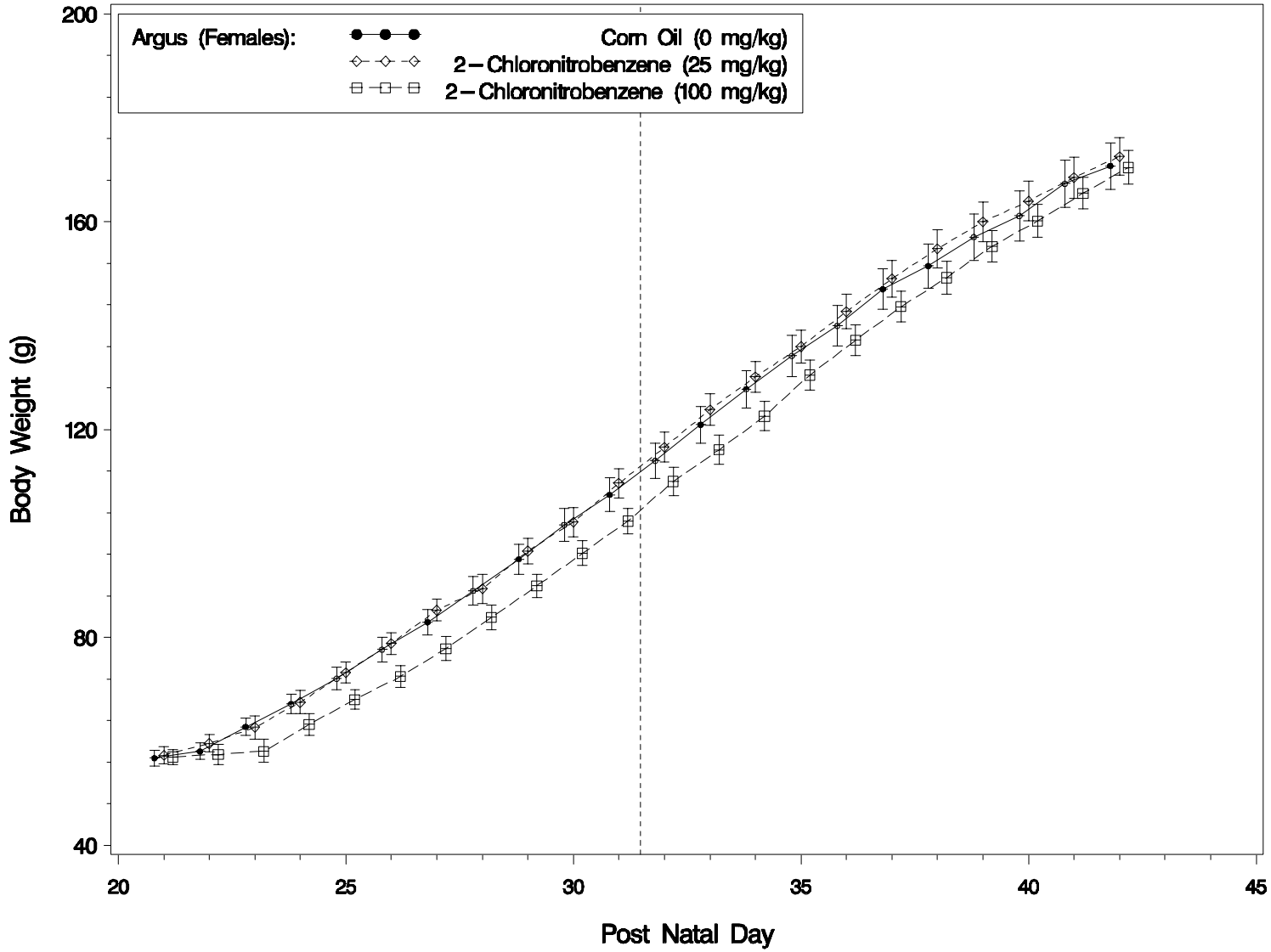

Figure 5. **<u>Argus Females</u> Means (with ± 2 Standard Error Bars) of Body Weights (g) on Each Day from Weaning through Dosing (PND 21 to PND 42) for the Control Group (Corn Oil) and the Two 2-Chloronitrobenzene Dose Groups. The Reference Line Corresponds to the Mean Age of the Control Group at VO.**

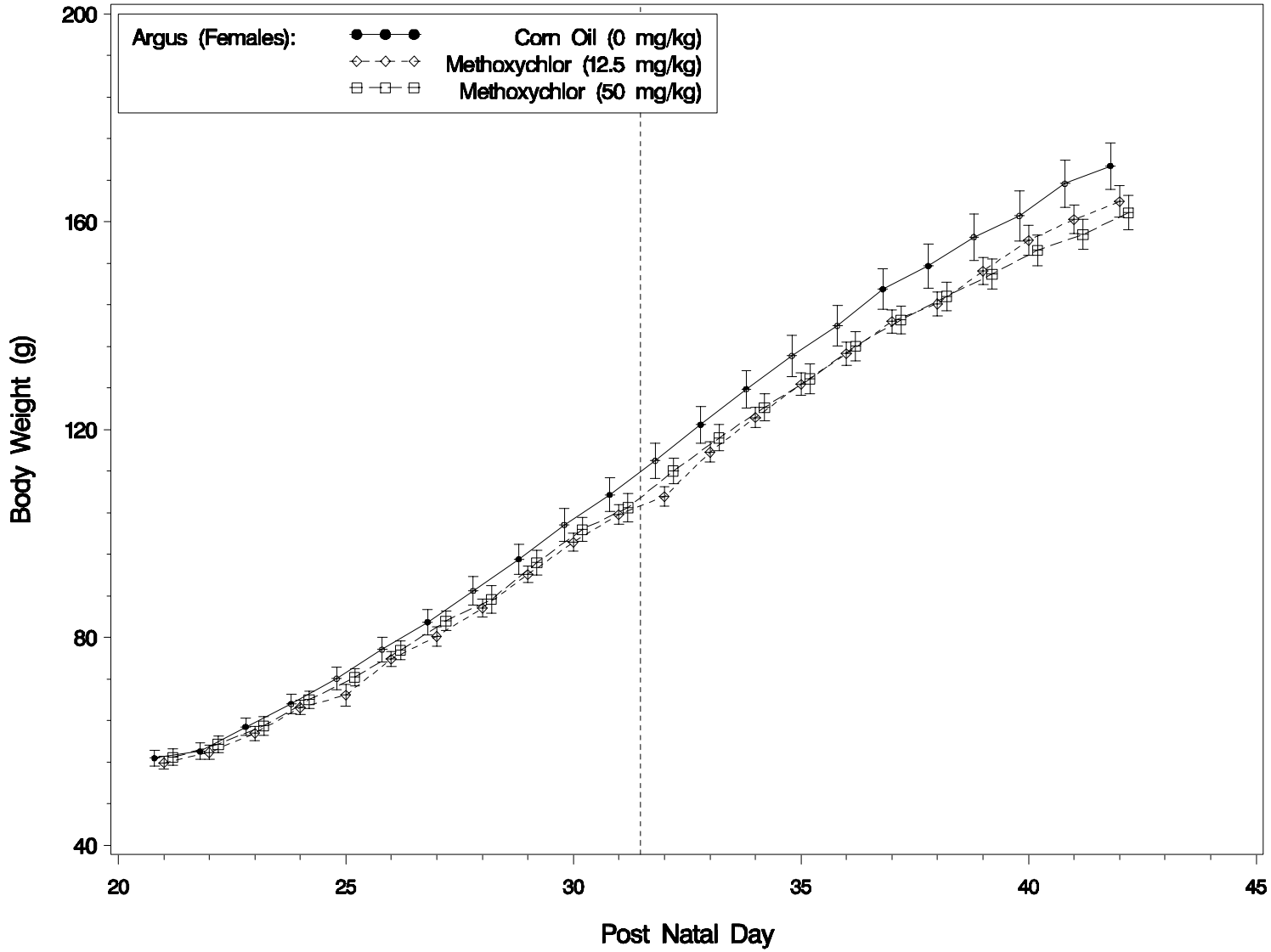

Figure 6. **<u>Argus Females</u> Means (with ± 2 Standard Error Bars) of Body Weights (g) on Each Day from Weaning through Dosing (PND 21 to PND 42) for the Control Group (Corn Oil) and the Two Methoxychlor Dose Groups. The Reference Line Corresponds to the Mean Age of the Control Group at VO.**

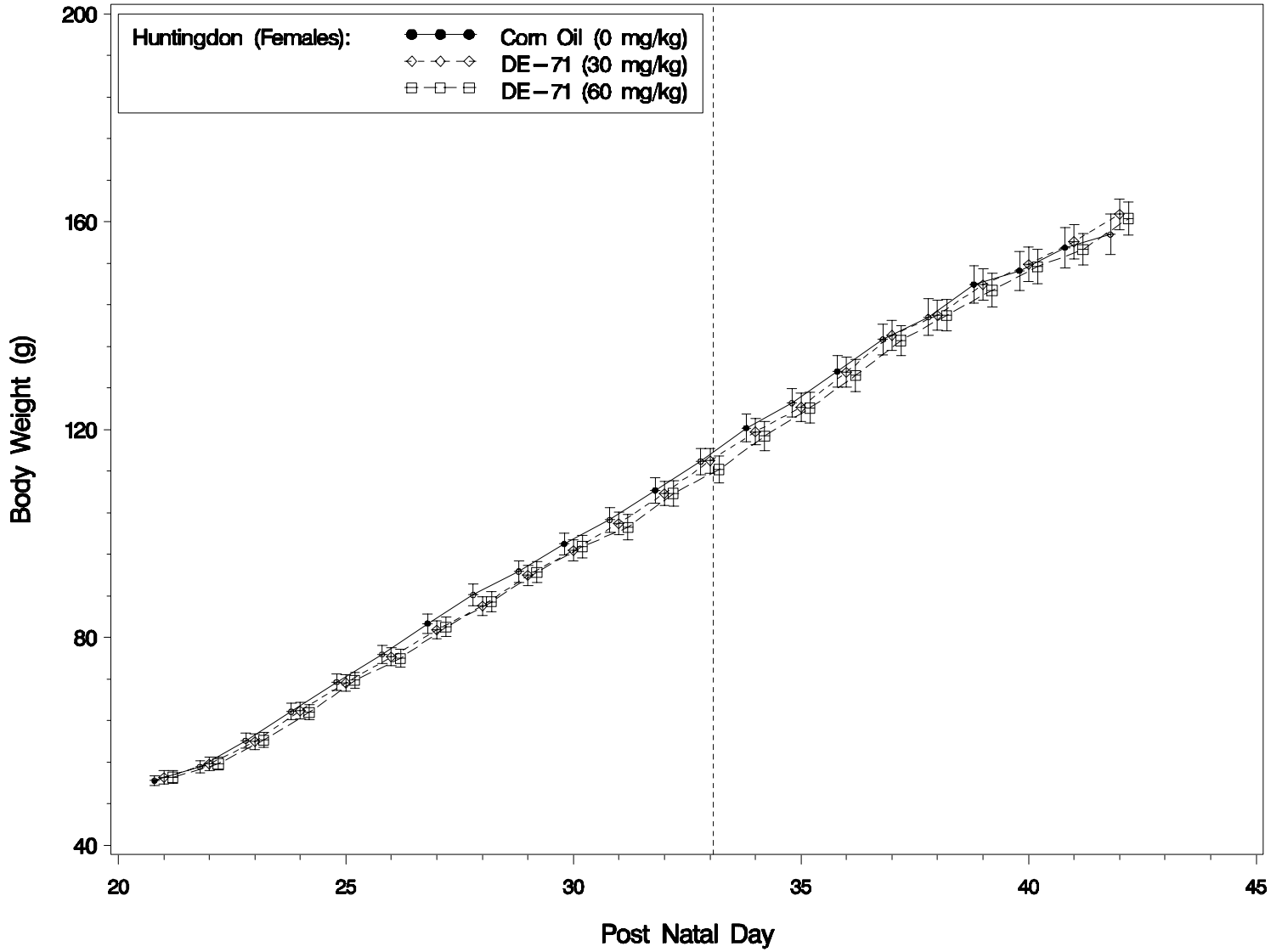

Figure 7. **<u>Huntingdon Females</u> Means (with ± 2 Standard Error Bars) of Body Weights (g) on Each Day from Weaning through Dosing (PND 21 to PND 42) for the Control Group (Corn Oil) and the Two DE-71 Dose Groups. The Reference Line Corresponds to the Mean Age of the Control Group at VO.**

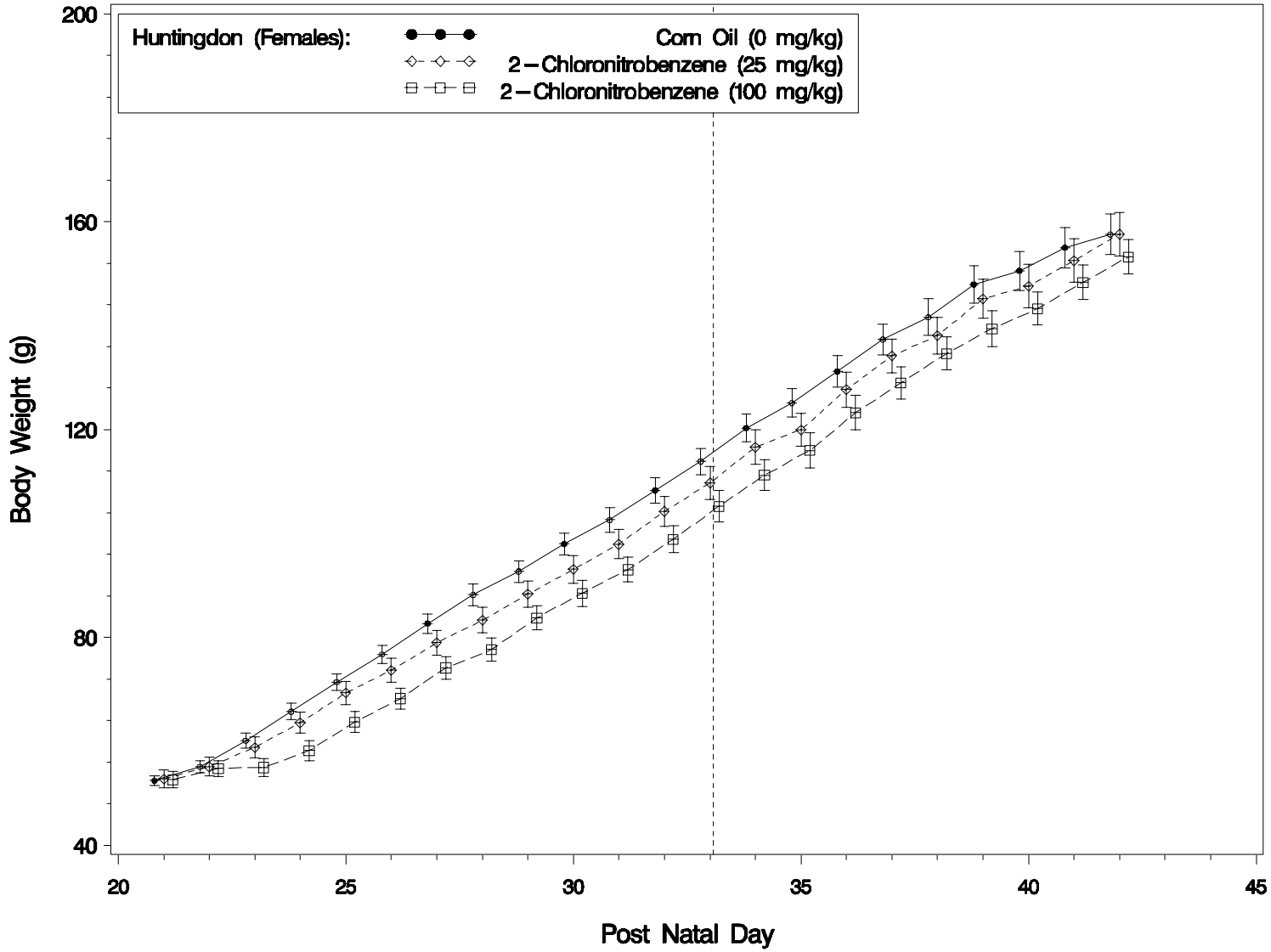

Figure 8. **<u>Huntingdon Females</u> Means (with ± 2 Standard Error Bars) of Body Weights (g) on Each Day from Weaning through Dosing (PND 21 to PND 42) for the Control Group (Corn Oil) and the Two 2-Chloronitrobenzene Dose Groups. The Reference Line Corresponds to the Mean Age of the Control Group at VO.**

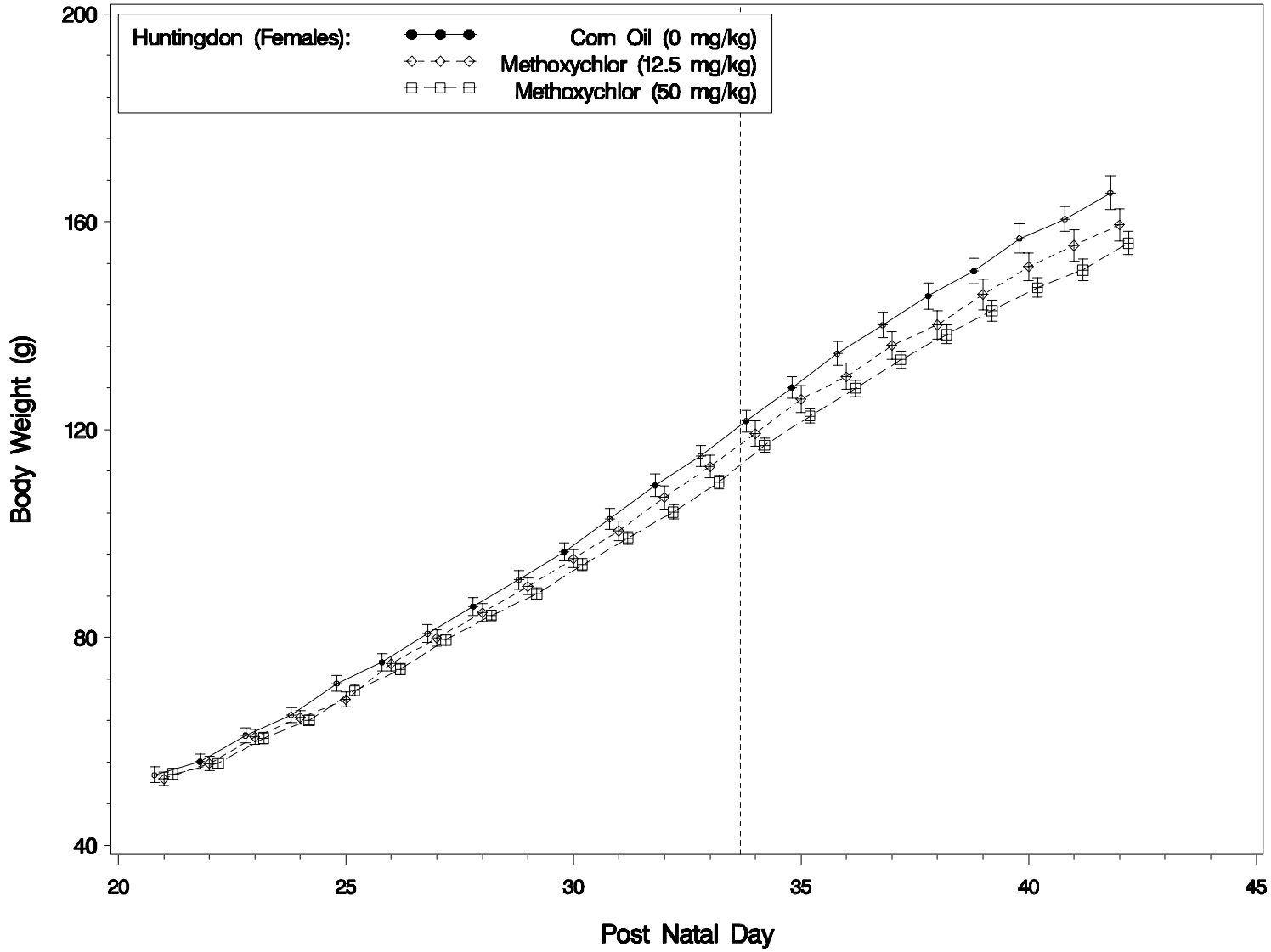

Figure 9. **<u>Huntingdon Females</u> Means (with ± 2 Standard Error Bars) of Body Weights (g) on Each Day from Weaning through Dosing (PND 21 to PND 42) for the Control Group (Corn Oil) and the Two Methoxychlor Dose Groups. The Reference Line Corresponds to the Mean Age of the Control Group at VO.**

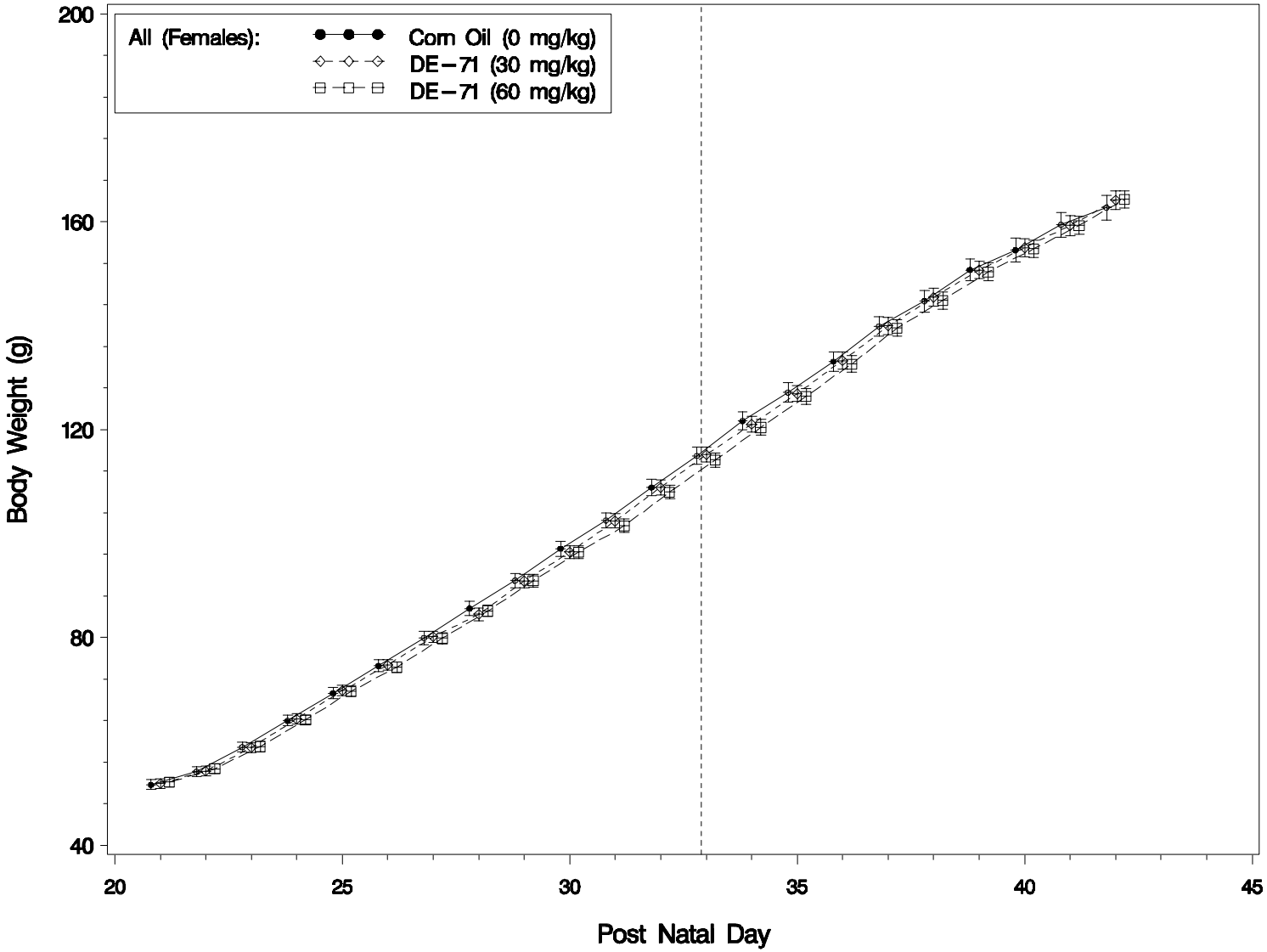

Figure 10. **<u>All Females</u> Means (with ± 2 Standard Error Bars) of Body Weights (g) on Each Day from Weaning through Dosing (PND 21 to PND 42) for the Control Group (Corn Oil) and the Two DE-71 Dose Groups. The Reference Line Corresponds to the Mean Age of the Control Group at VO.**

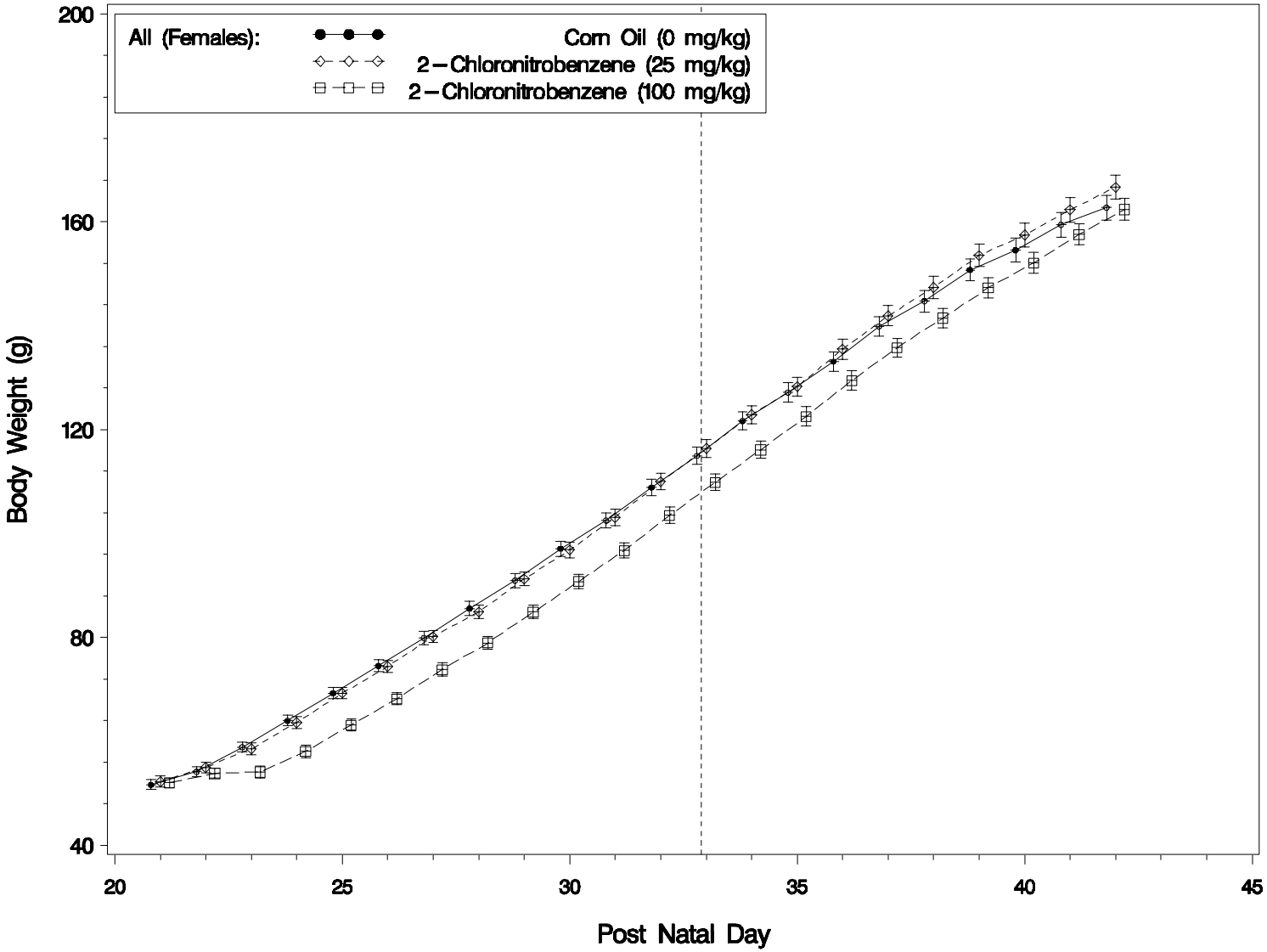

Figure 11. **<u>All Females</u> Means (with ± 2 Standard Error Bars) of Body Weights (g) on Each Day from Weaning through Dosing (PND 21 to PND 42) for the Control Group (Corn Oil) and the Two 2-Chloronitrobenzene Dose Groups. The Reference Line Corresponds to the Mean Age of the Control Group at VO.**

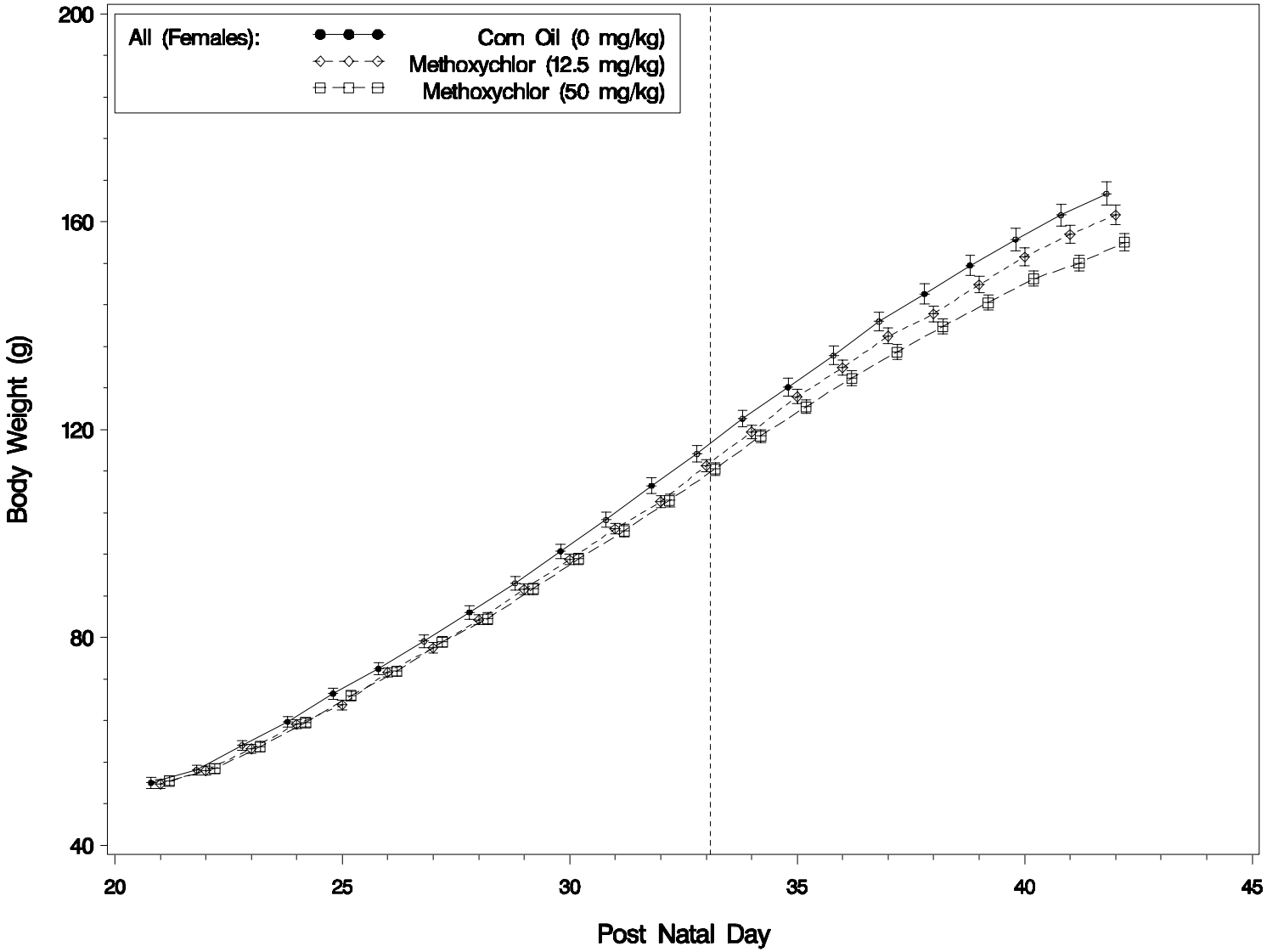

Figure 12. **<u>All Females</u> Means (with ± 2 Standard Error Bars) of Body Weights (g) on Each Day from Weaning through Dosing (PND 21 to PND 42) for the Control Group (Corn Oil) and the Two Methoxychlor Dose Groups. The Reference Line Corresponds to the Mean Age of the Control Group at VO.**

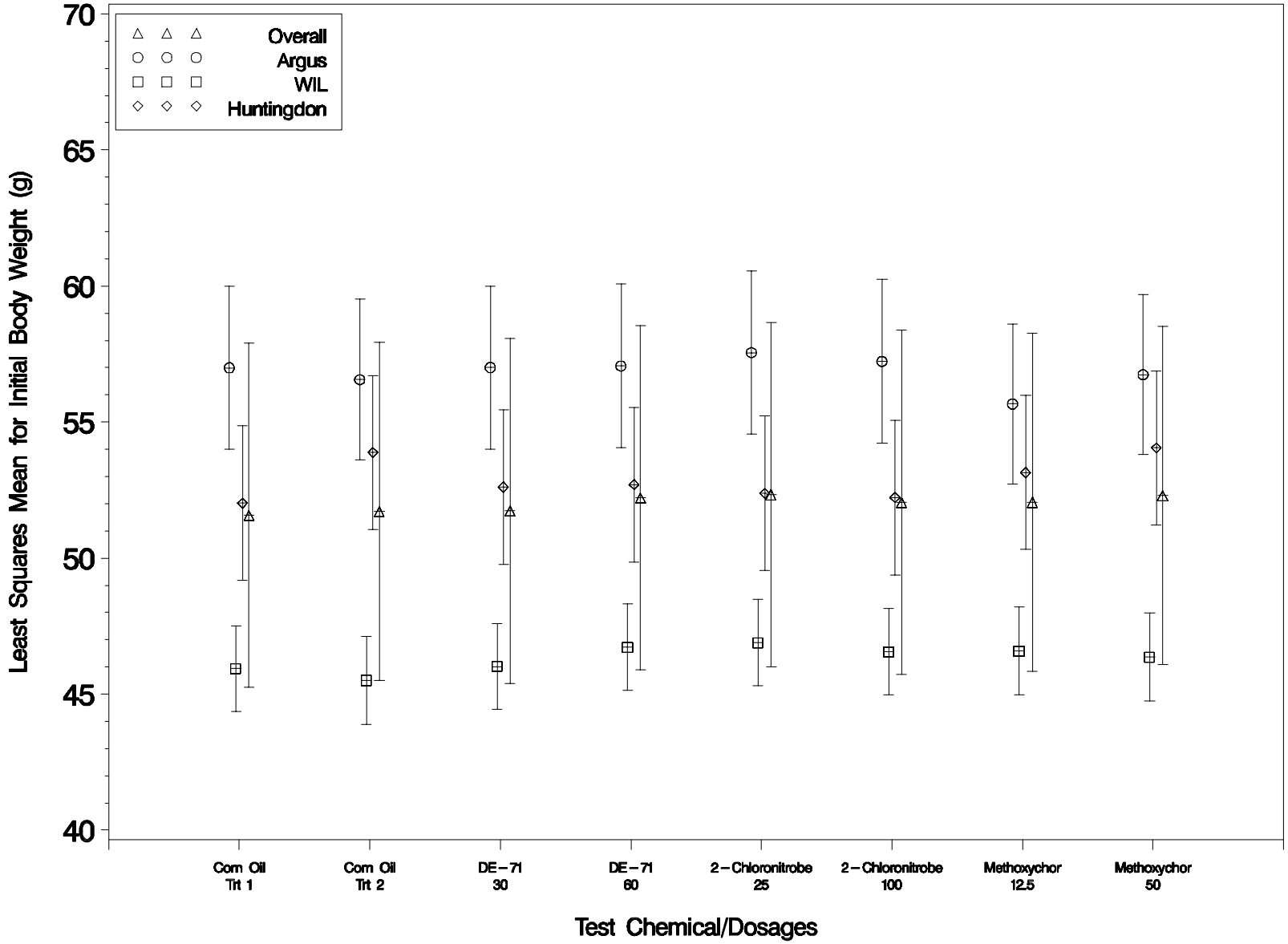

Figure 13. Unadjusted Least Squares Means (with ± 2 Standard Error Bars) for Initial Body Weight (g) for Each Dose Group across Laboratories and for Each Laboratory.

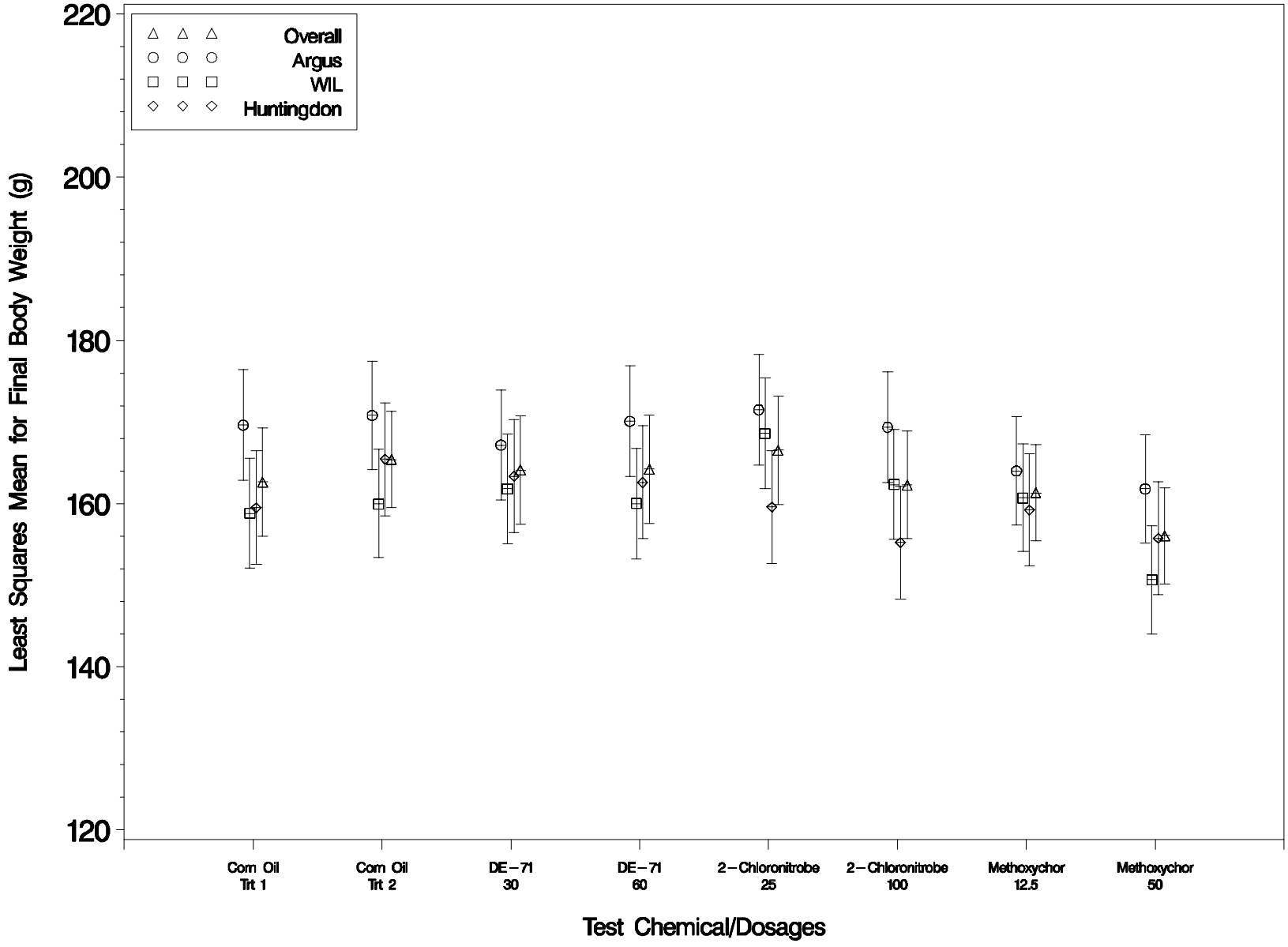

Figure 14. Unadjusted Least Squares Means (with ± 2 Standard Error Bars) for Final Body Weight (g) for Each Dose Group across Laboratories and for Each Laboratory.

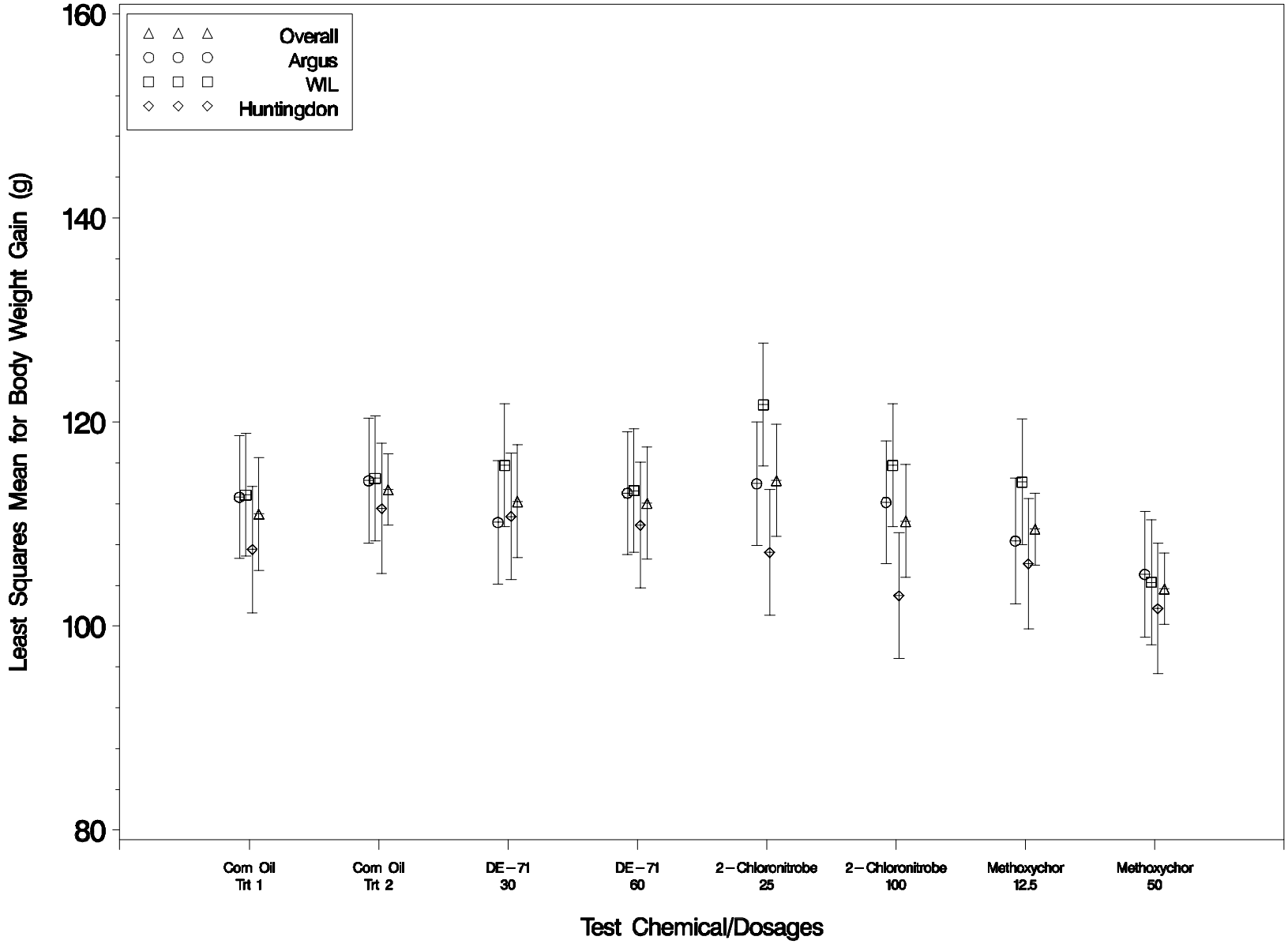

Figure 15. Unadjusted Least Squares Means (with ± 2 Standard Error Bars) for Body Weight Gain (g) for Each Dose Group across Laboratories and for Each Laboratory.

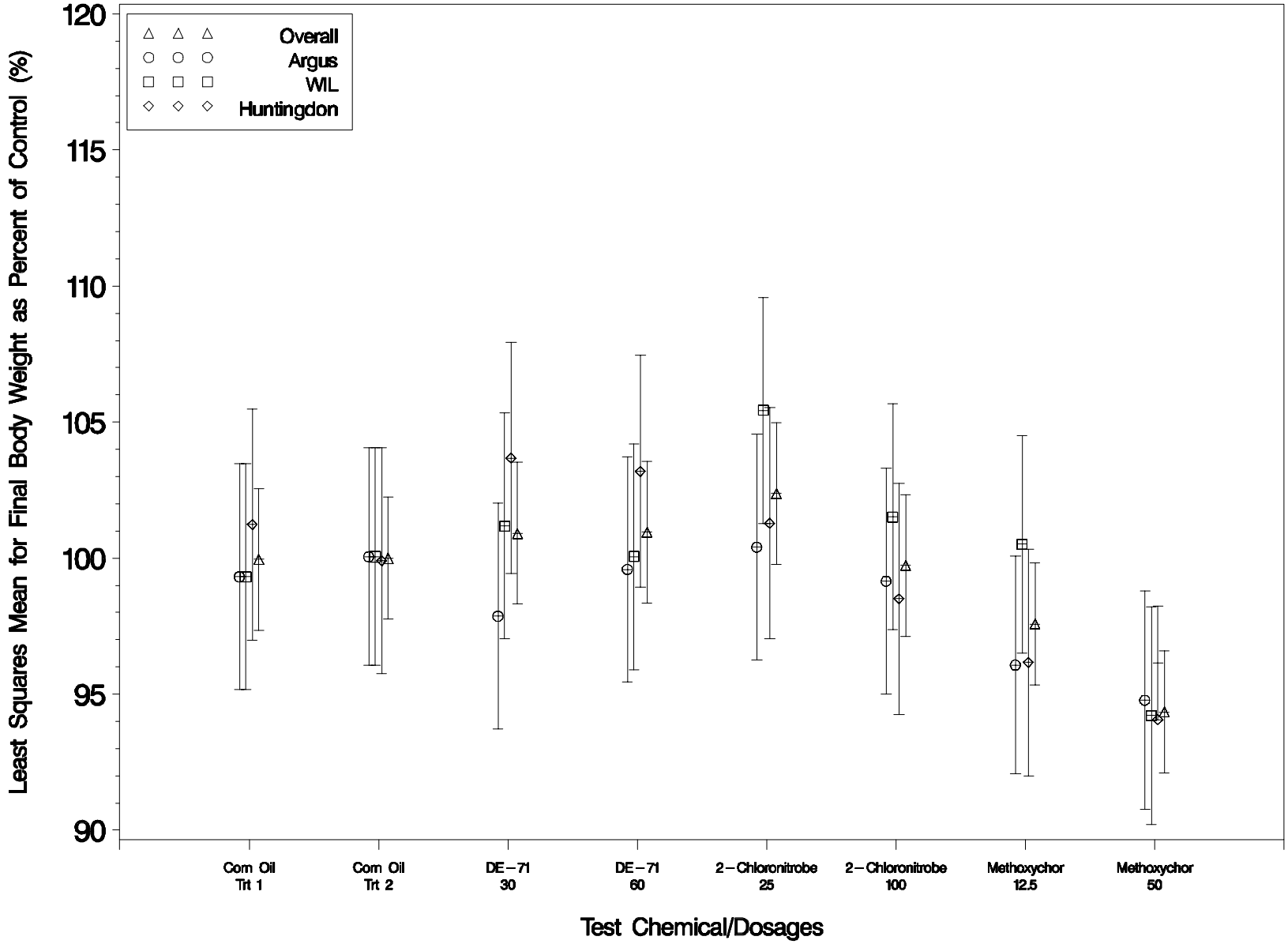

Figure 16. Unadjusted Least Squares Means (with ± 2 Standard Error Bars) for Final Body Weight as Percent of Control (%) for Each Dose Group across Laboratories and for Each Laboratory.

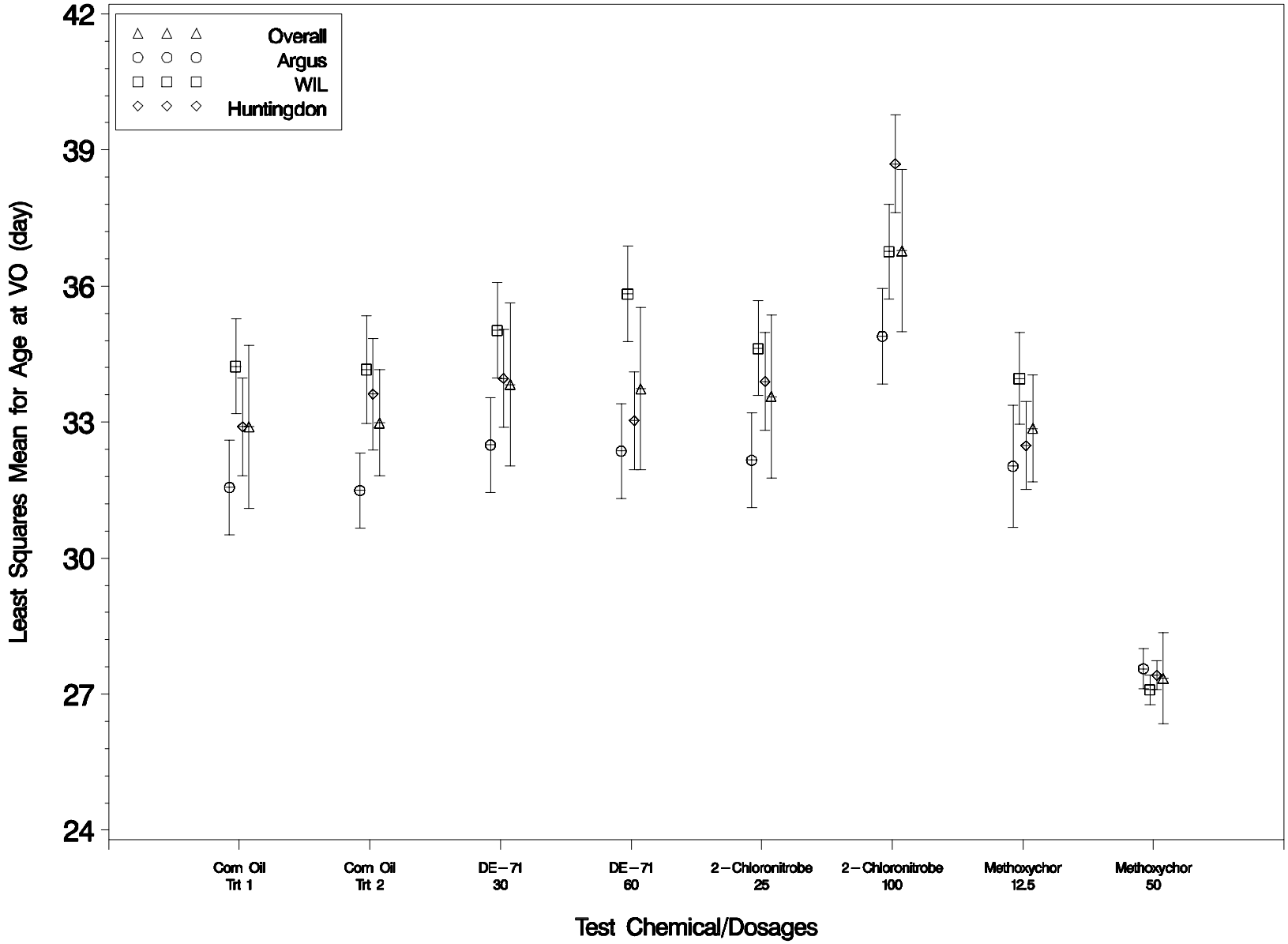

Figure 17. Unadjusted Least Squares Means (with ± 2 Standard Error Bars) for Age at VO (day) for Each Dose Group across Laboratories and for Each Laboratory.

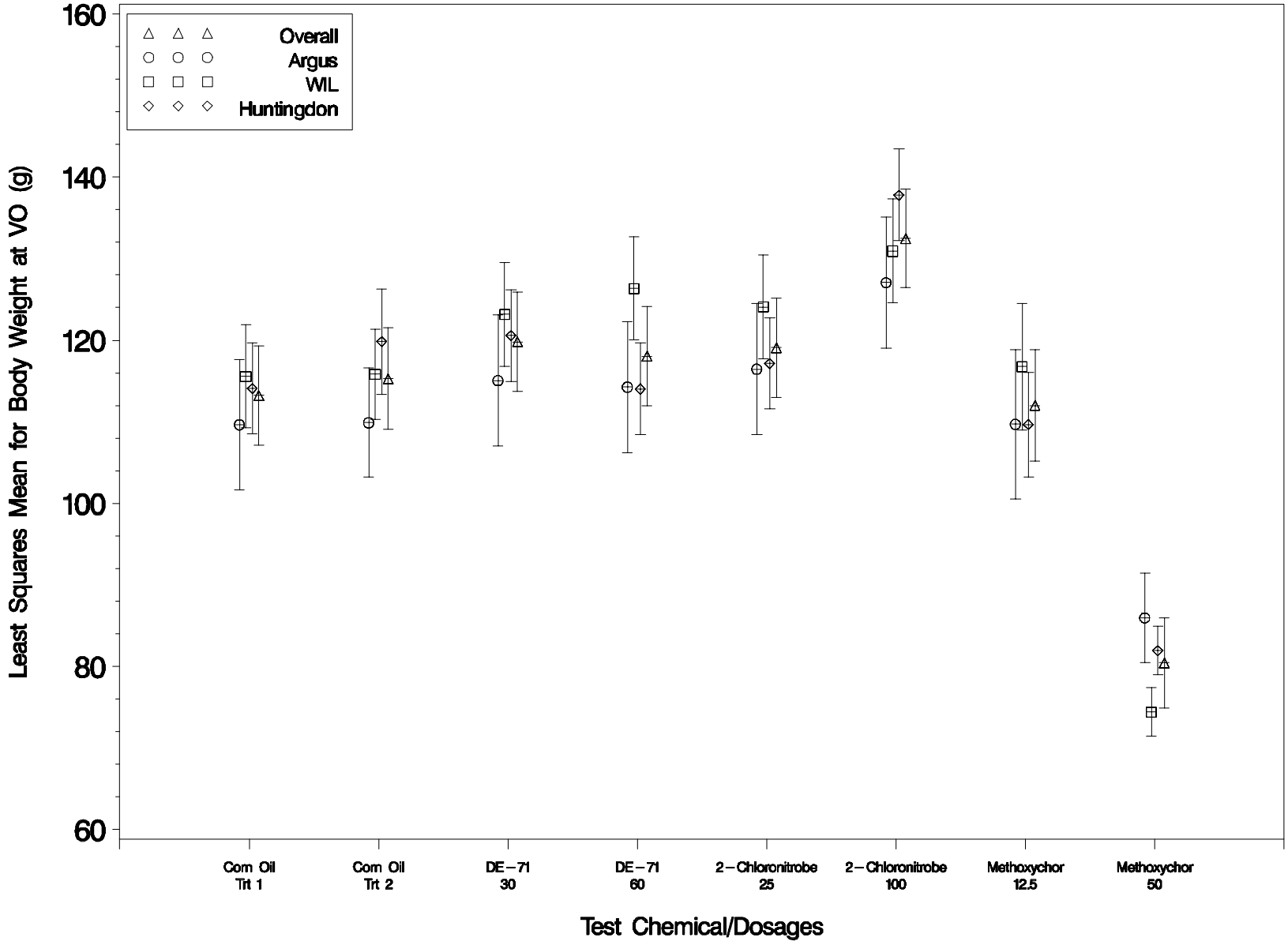

Figure 18. Unadjusted Least Squares Means (with ± 2 Standard Error Bars) for Body Weight at VO (g) for Each Dose Group across Laboratories and for Each Laboratory.

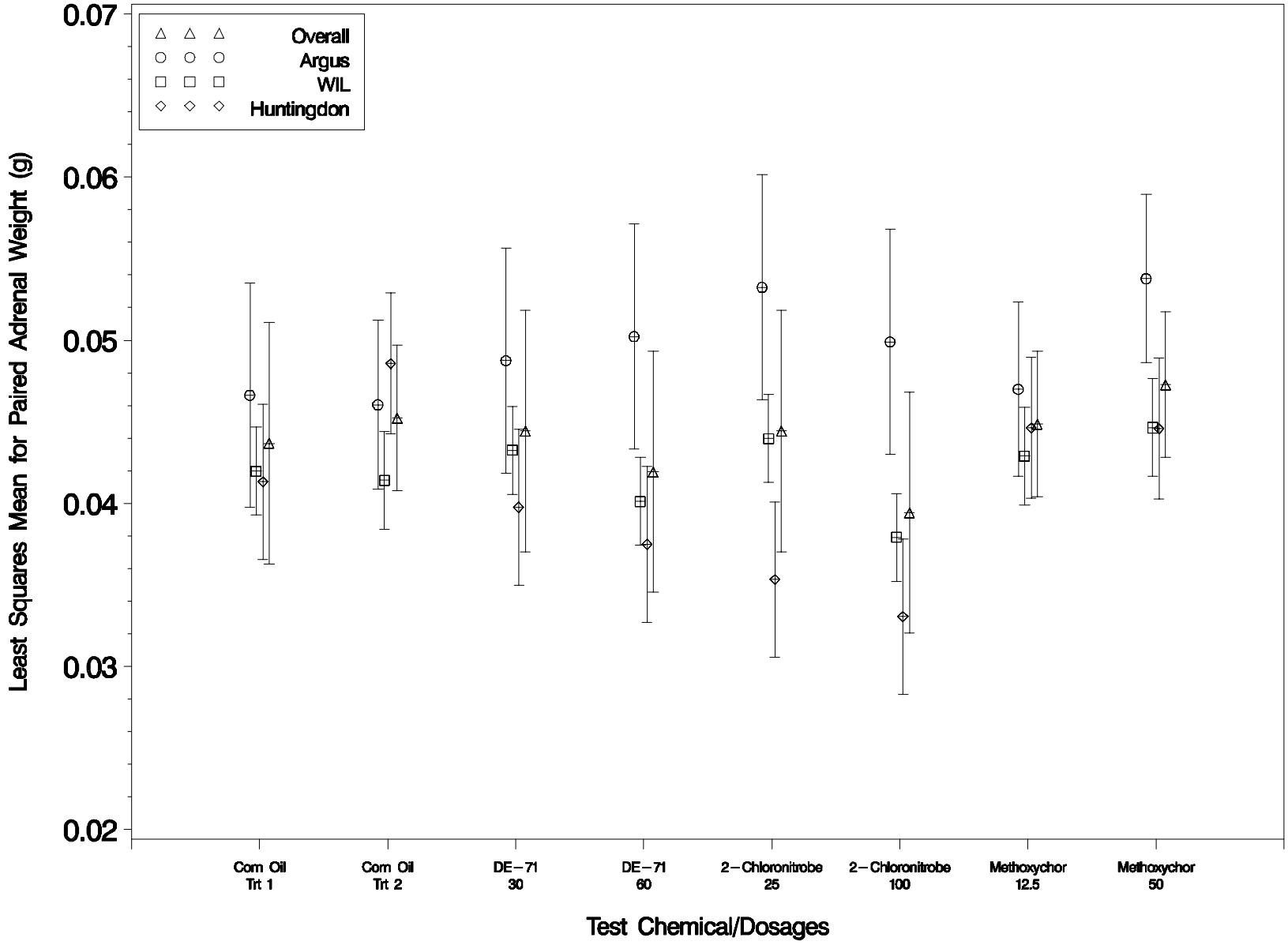

Figure 19. Unadjusted Least Squares Means (with ± 2 Standard Error Bars) for Paired Adrenal Weight (g) for Each Dose Group across Laboratories and for Each Laboratory.

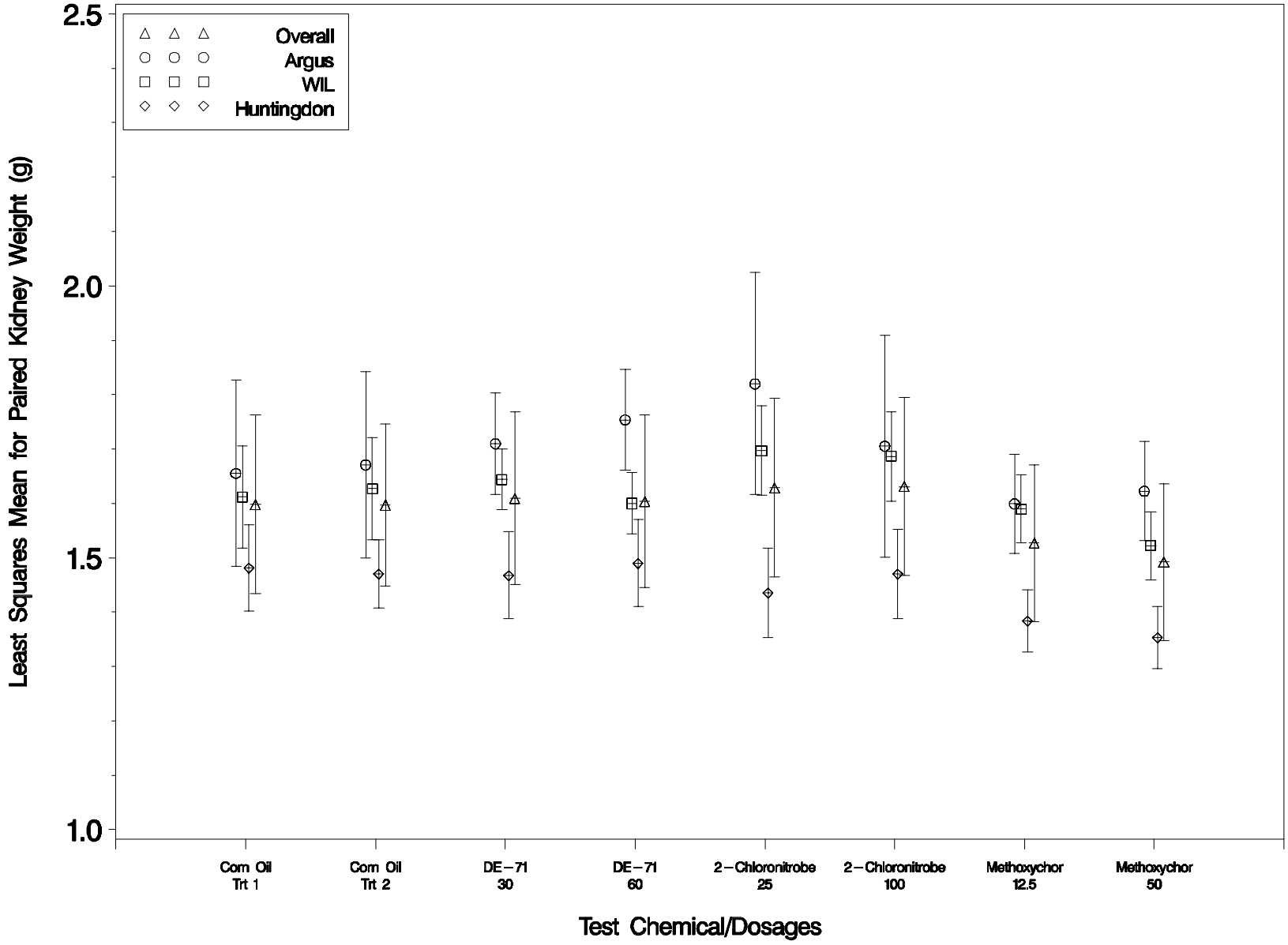

Figure 20. Unadjusted Least Squares Means (with ± 2 Standard Error Bars) for Paired Kidney Weight (g) for Each Dose Group across Laboratories and for Each Laboratory.

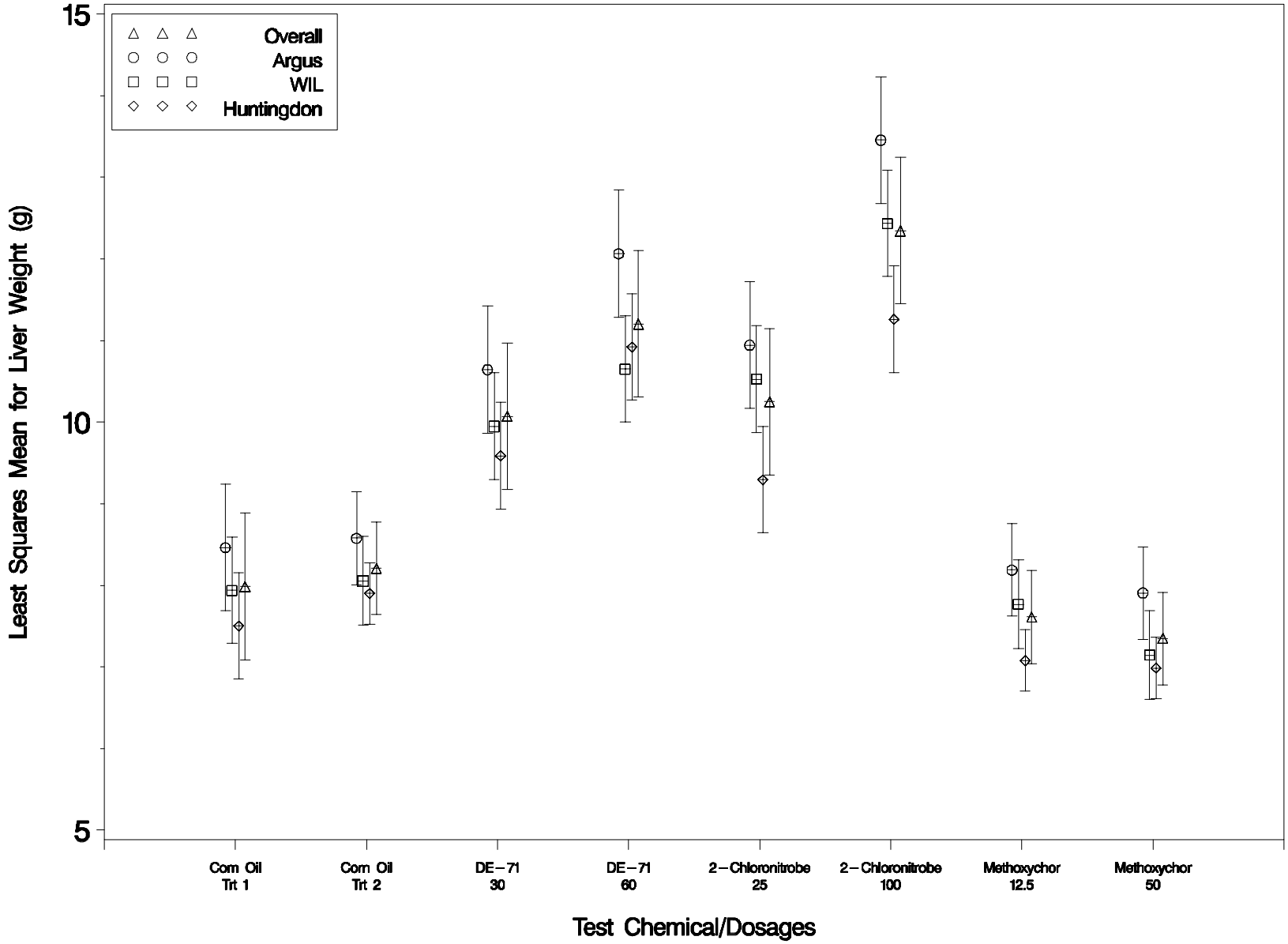

Figure 21. Unadjusted Least Squares Means (with ± 2 Standard Error Bars) for Liver Weight (g) for Each Dose Group across Laboratories and for Each Laboratory.

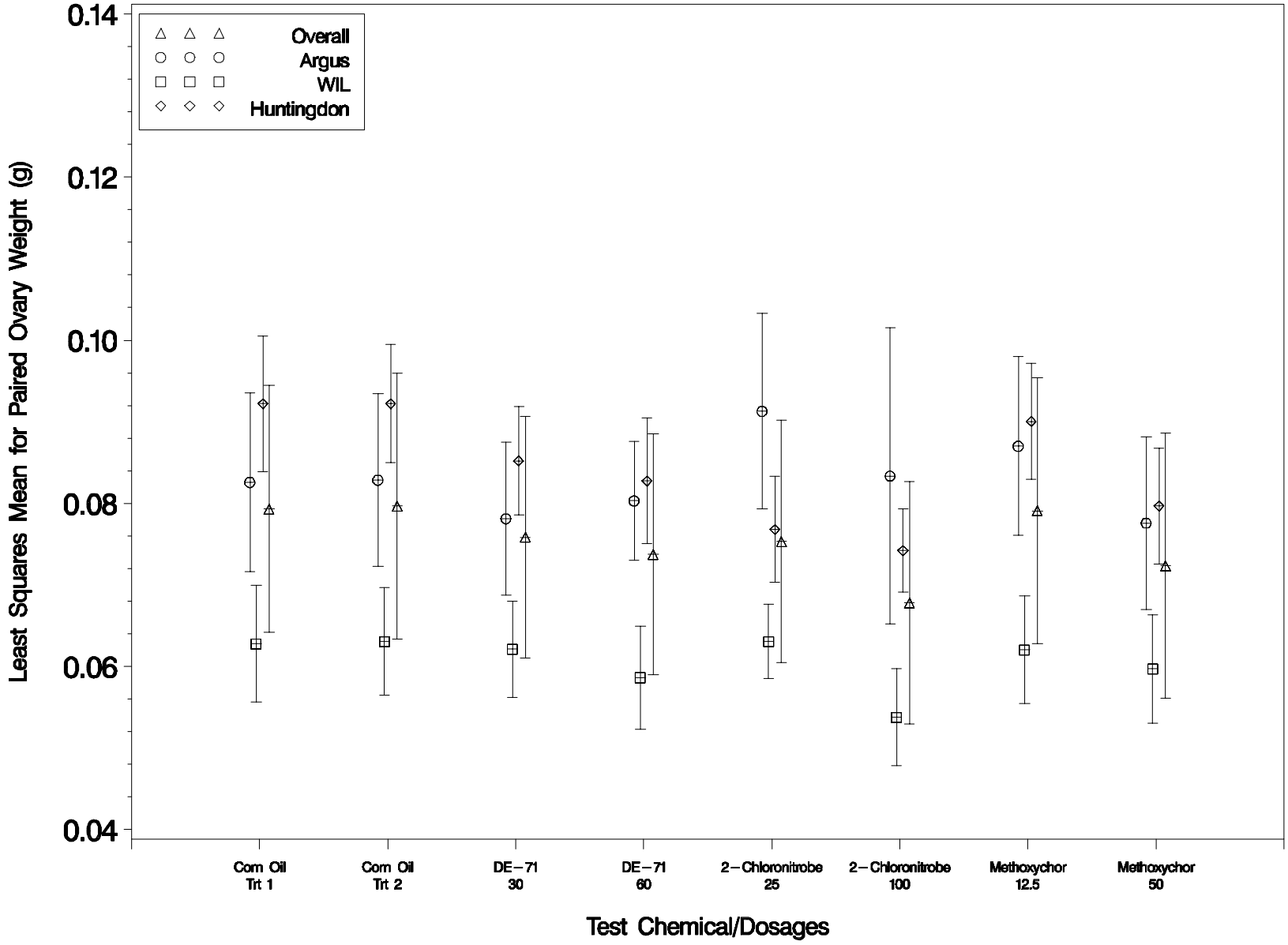

Figure 22. Unadjusted Least Squares Means (with ± 2 Standard Error Bars) for Paired Ovary Weight (g) for Each Dose Group across Laboratories and for Each Laboratory.

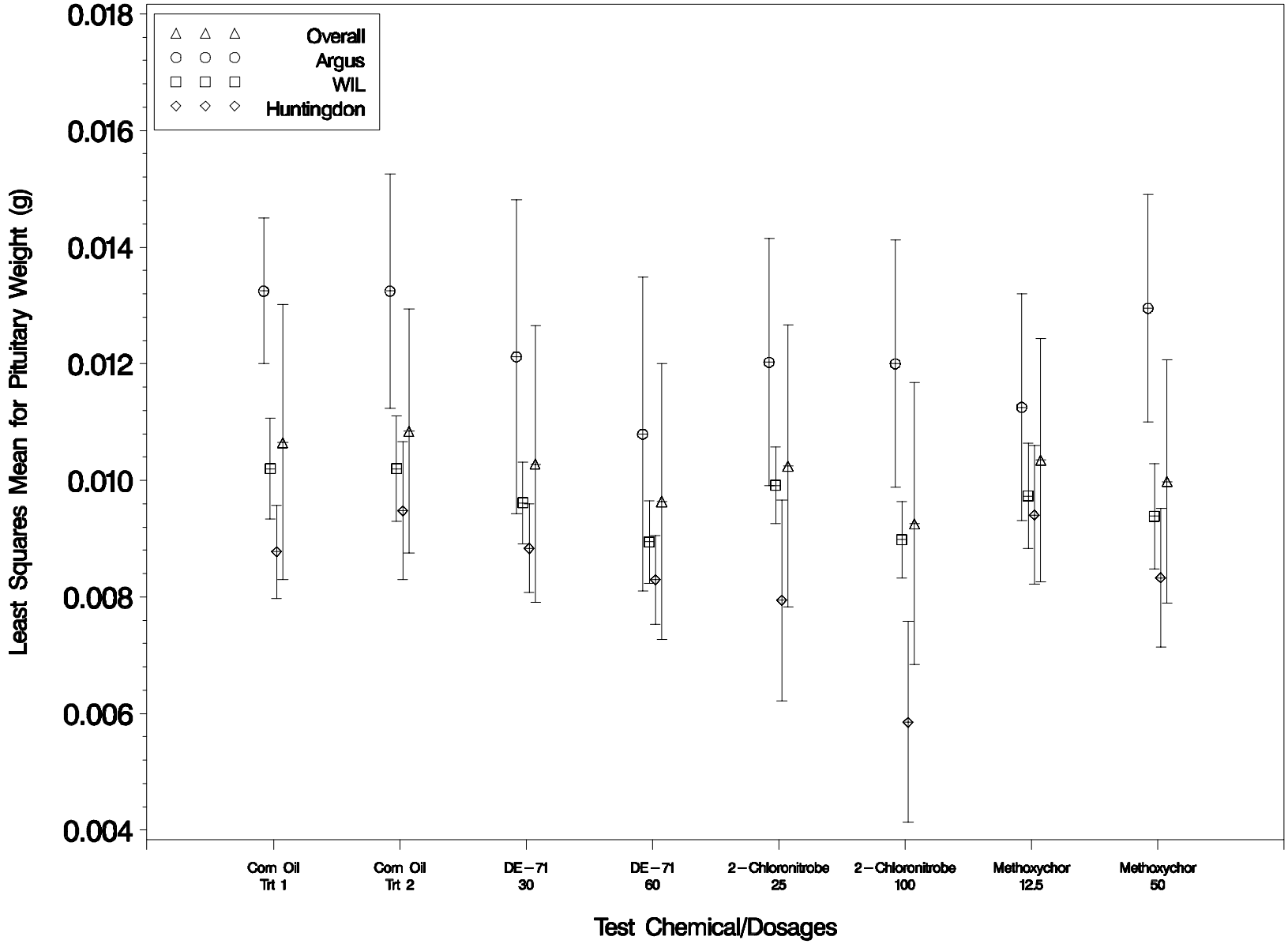

Figure 23. Unadjusted Least Squares Means (with ± 2 Standard Error Bars) for Pituitary Weight (g) for Each Dose Group across Laboratories and for Each Laboratory.

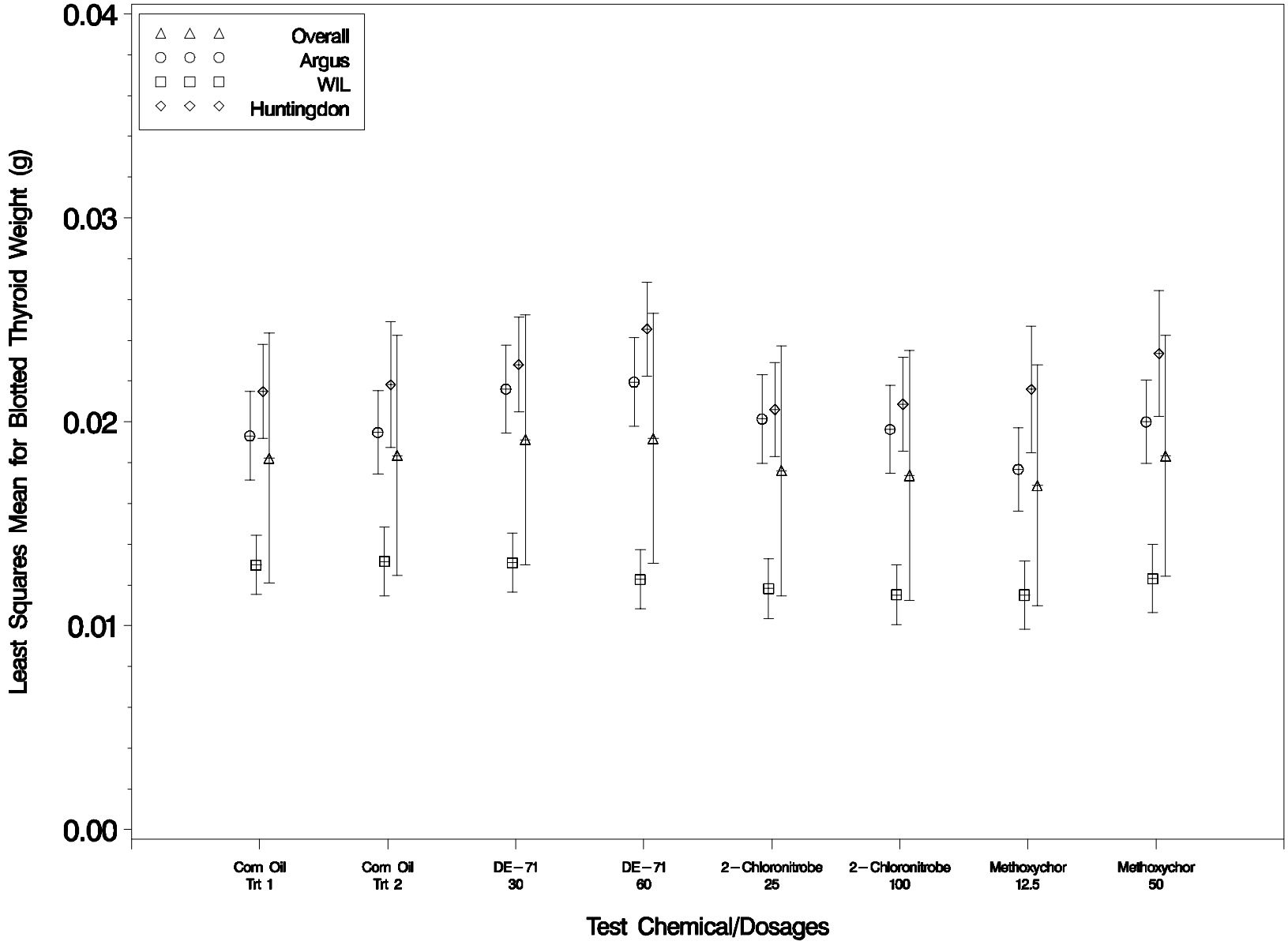

Figure 24. Unadjusted Least Squares Means (with ± 2 Standard Error Bars) for Blotted Thyroid Weight (g) for Each Dose Group across Laboratories and for Each Laboratory.

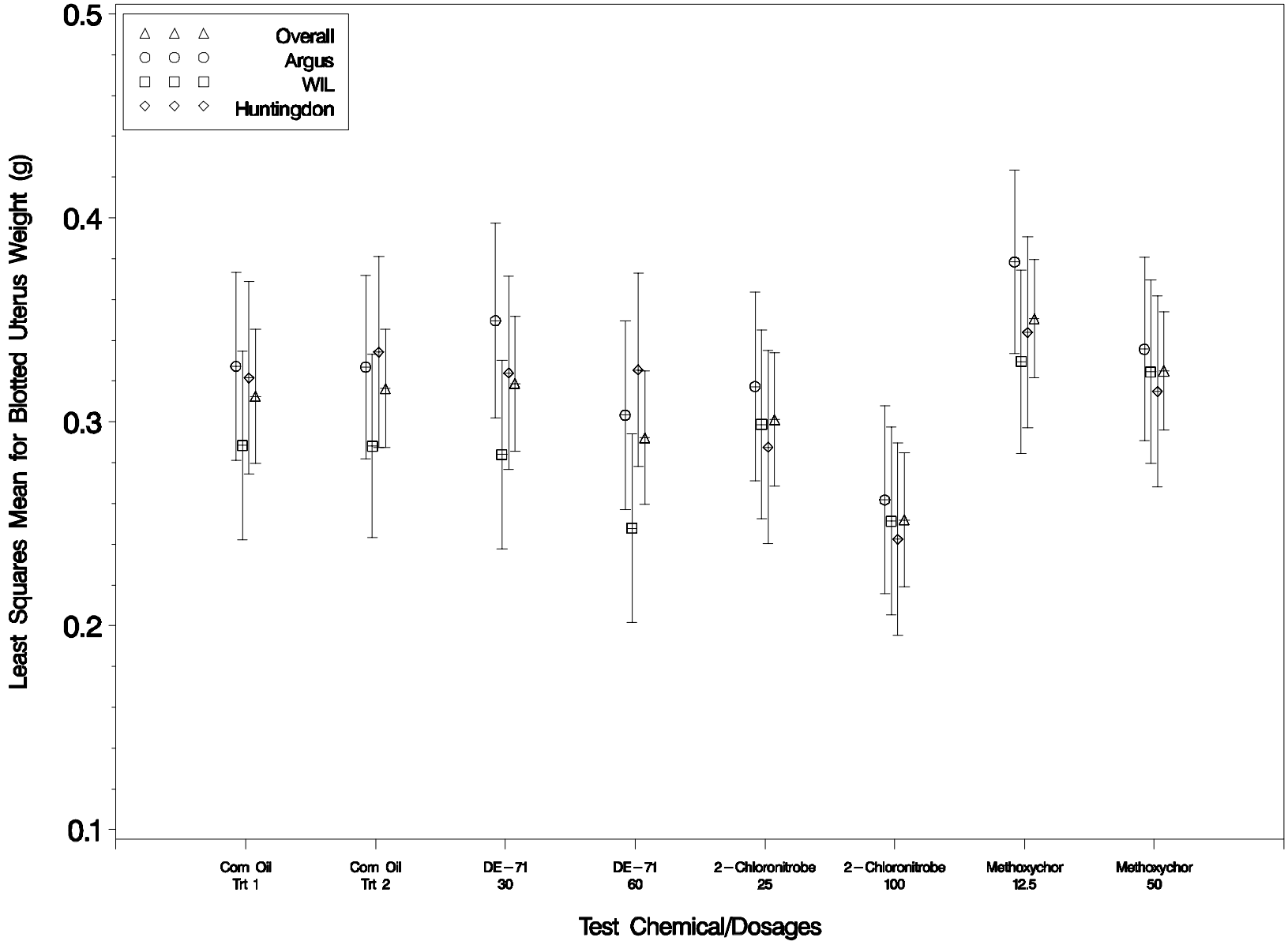

Figure 25. Unadjusted Least Squares Means (with ± 2 Standard Error Bars) for Blotted Uterus Weight (g) for Each Dose Group across Laboratories and for Each Laboratory.

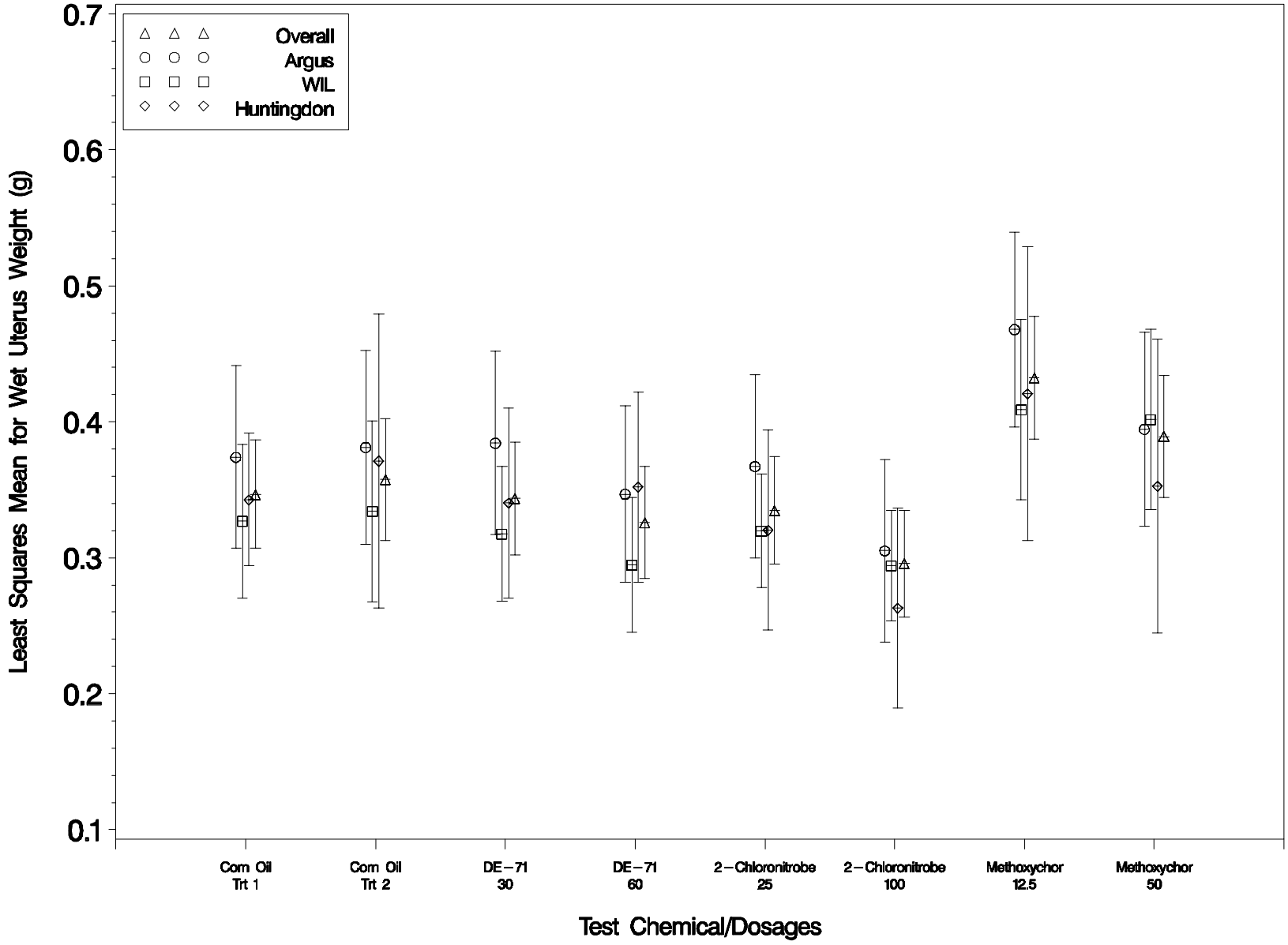

Figure 26. Unadjusted Least Squares Means (with ± 2 Standard Error Bars) for Wet Uterus Weight (g) for Each Dose Group across Laboratories and for Each Laboratory.

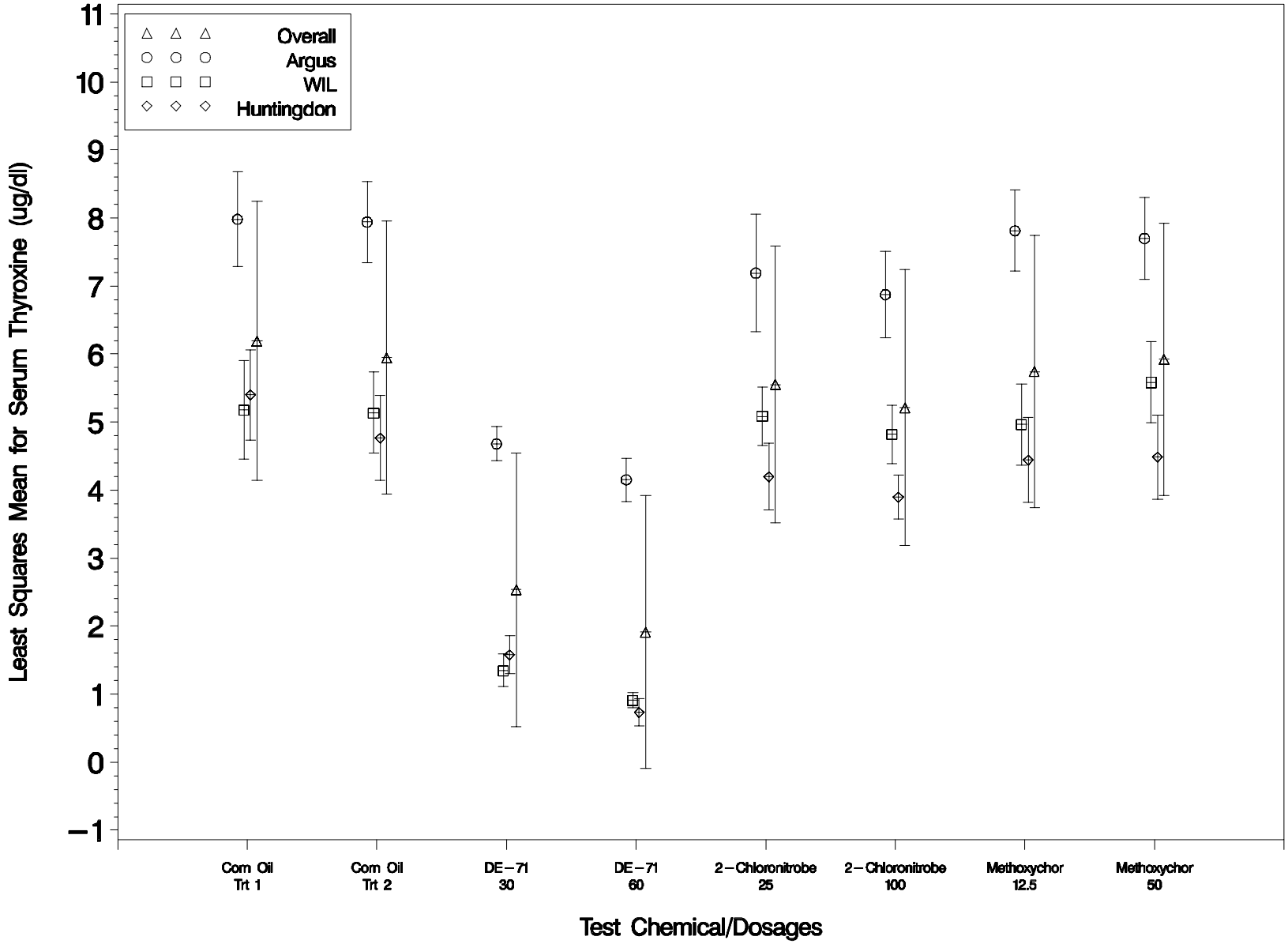

Figure 27. Unadjusted Least Squares Means (with ± 2 Standard Error Bars) for Serum Thyroxine (µg/dl) for Each Dose Group across Laboratories and for Each Laboratory.

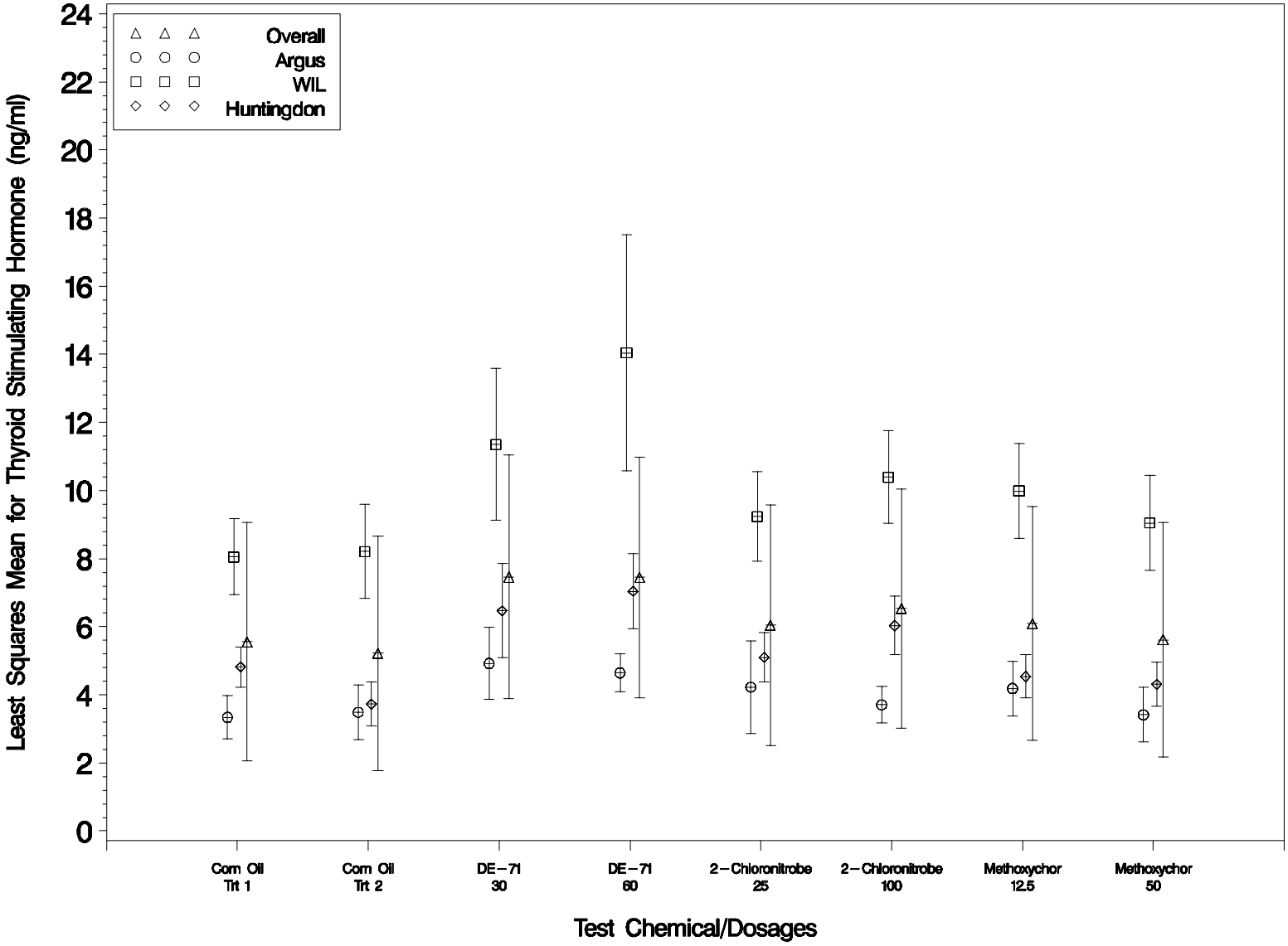

Figure 28. Unadjusted Least Squares Means (with ± 2 Standard Error Bars) for Thyroid Stimulating Hormone (ng/ml) for Each Dose Group across Laboratories and for Each Laboratory.

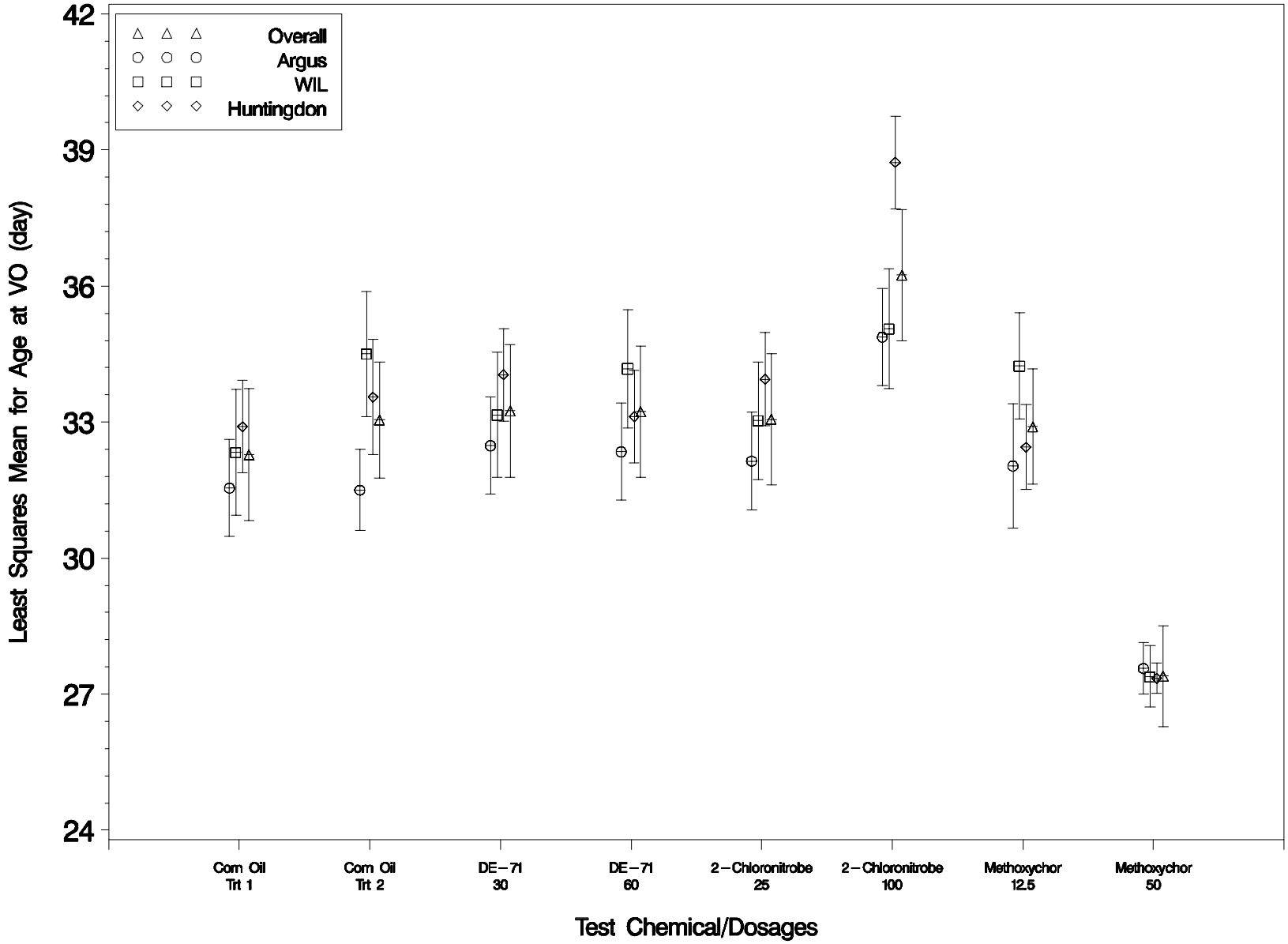

Figure 29. Adjusted Least Squares Means (with ± 2 Standard Error Bars) for Age at VO (day) for Each Dose Group across Laboratories and for Each Laboratory.

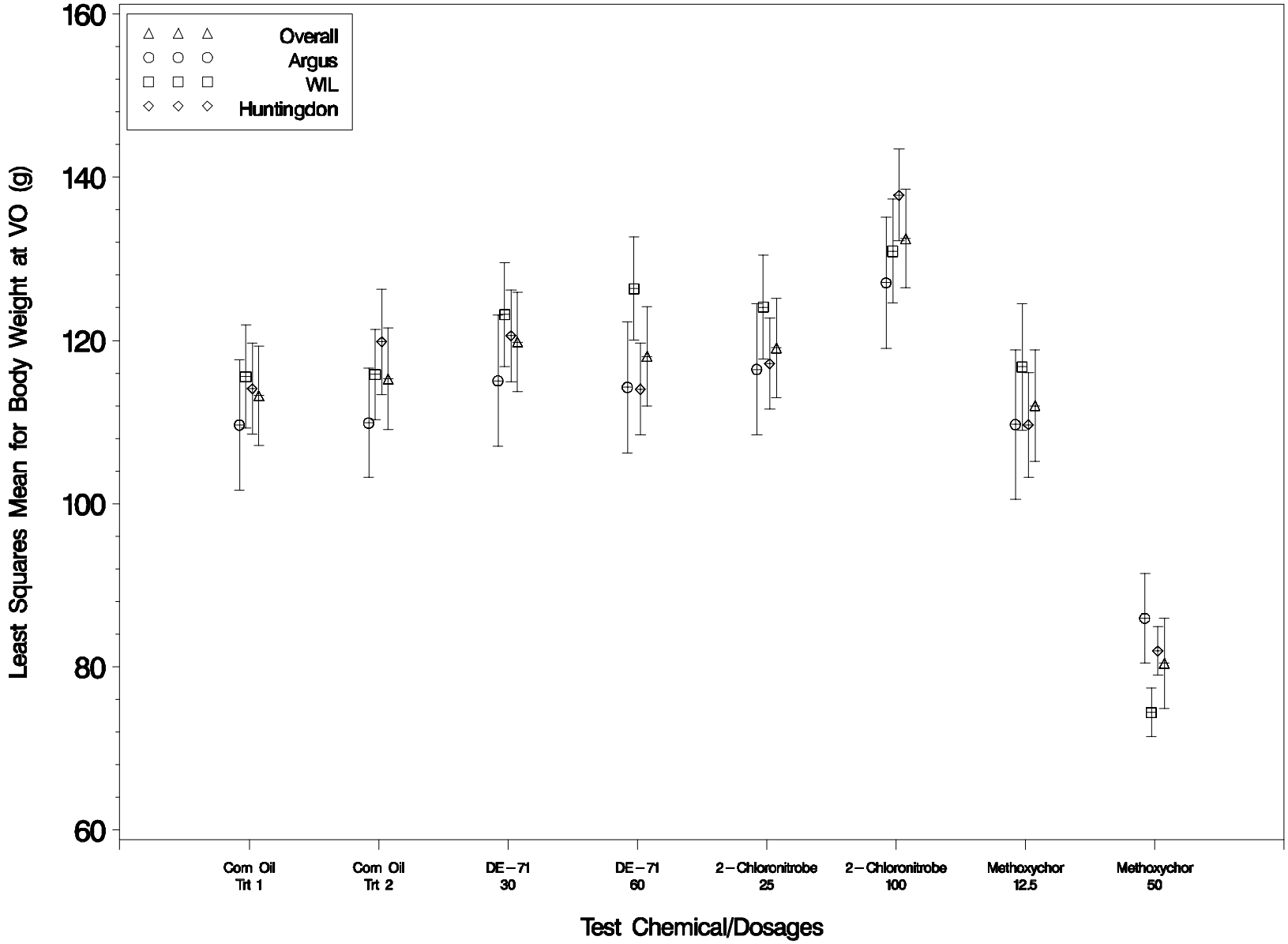

Figure 30. Adjusted Least Squares Means (with ± 2 Standard Error Bars) for Body Weight at VO (g) for Each Dose Group across Laboratories and for Each Laboratory.

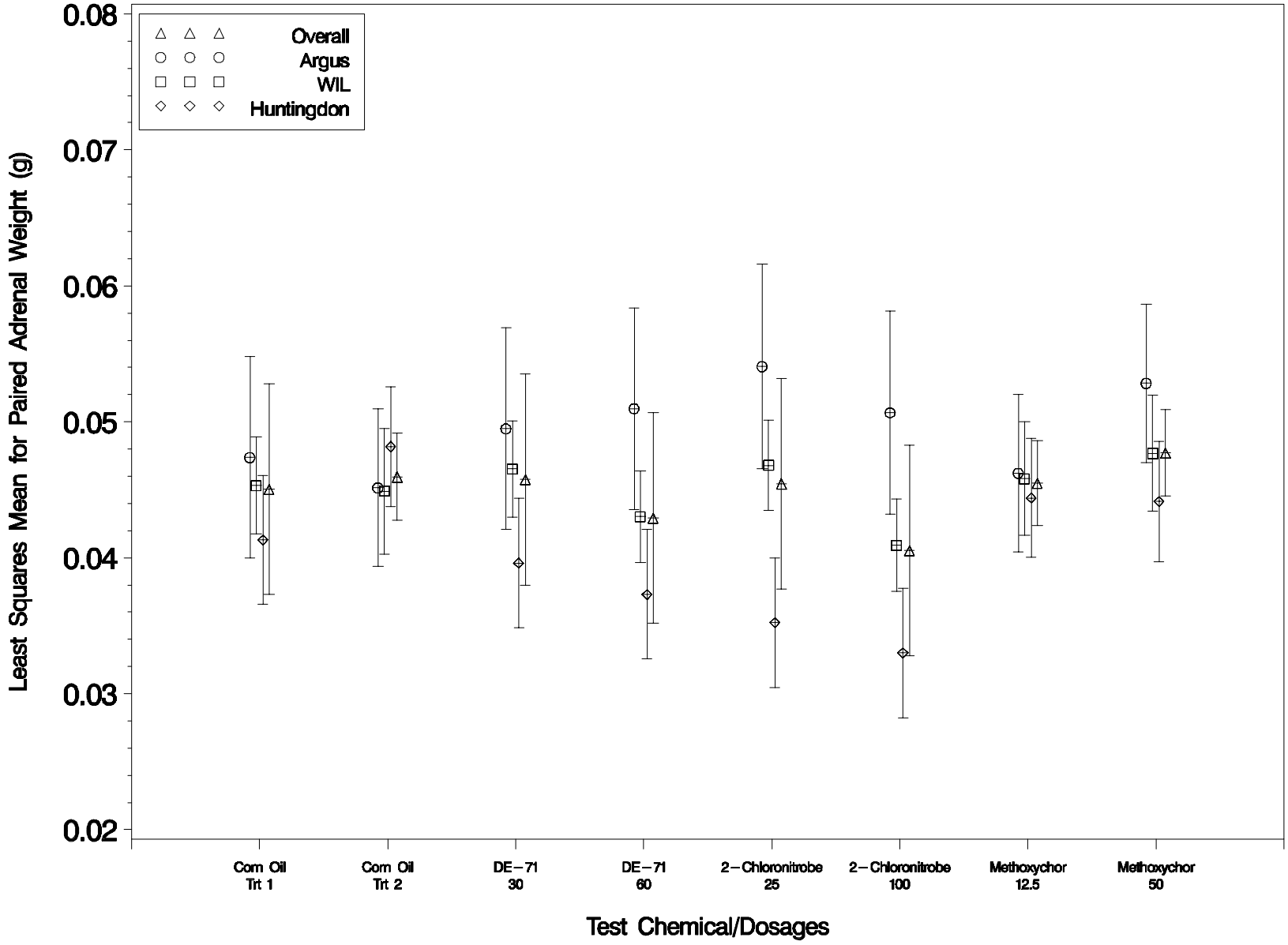

Figure 31. Adjusted Least Squares Means (with ± 2 Standard Error Bars) for Paired Adrenal Weight (g) for Each Dose Group across Laboratories and for Each Laboratory.

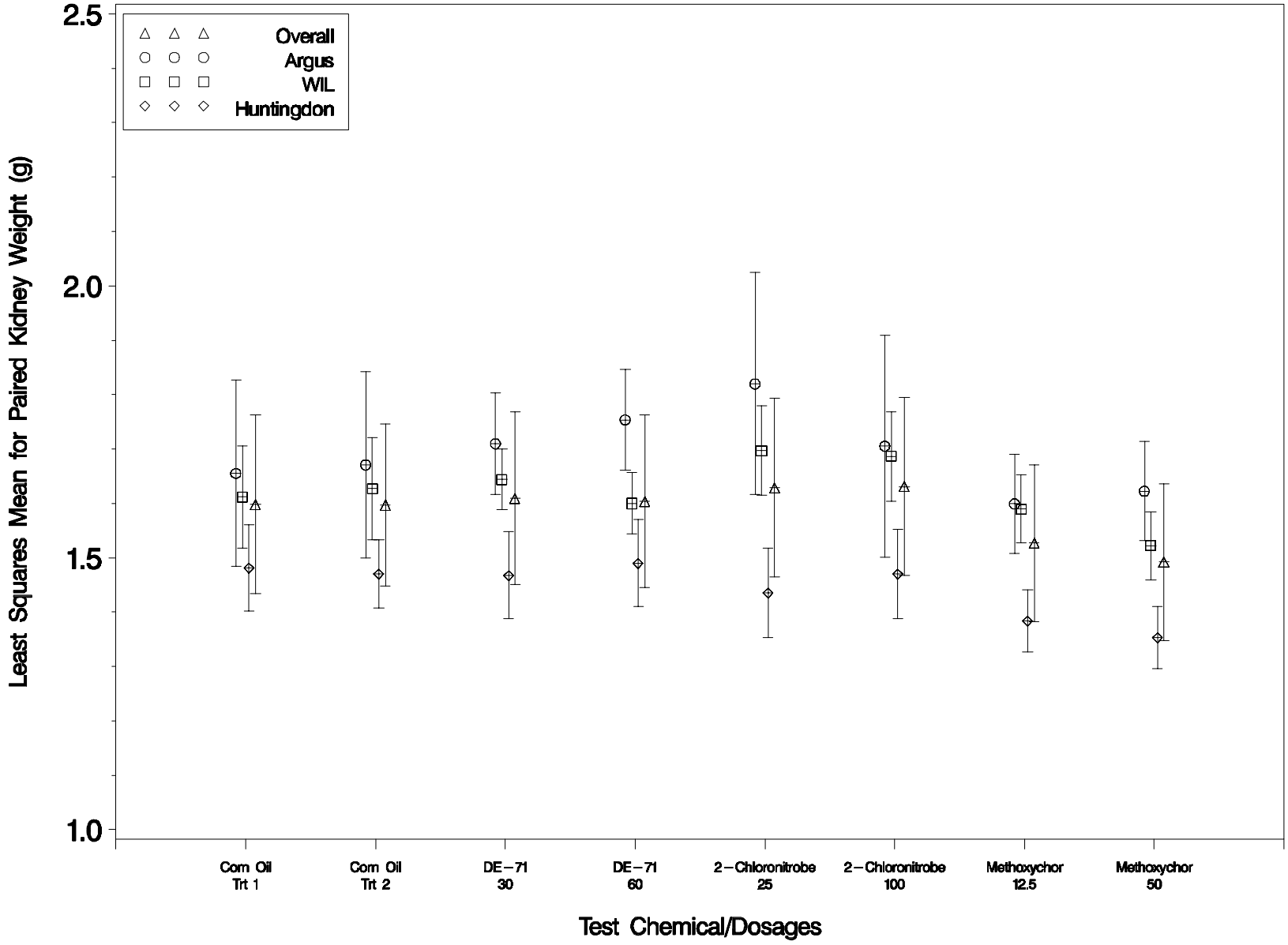

Figure 32. Adjusted Least Squares Means (with ± 2 Standard Error Bars) for Paired Kidney Weight (g) for Each Dose Group across Laboratories and for Each Laboratory.

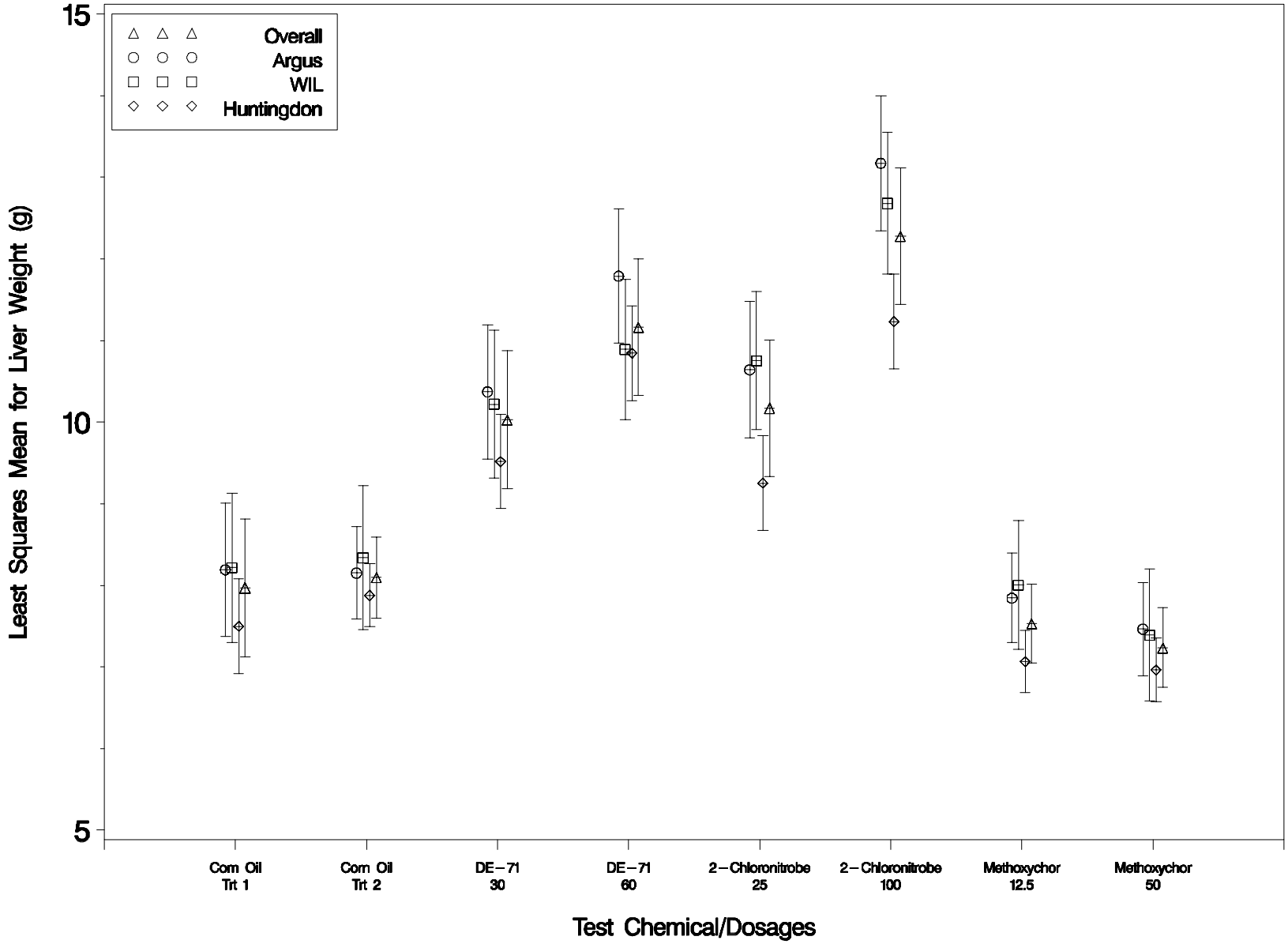

Figure 33. Adjusted Least Squares Means (with ± 2 Standard Error Bars) for Liver Weight (g) for Each Dose Group across Laboratories and for Each Laboratory.

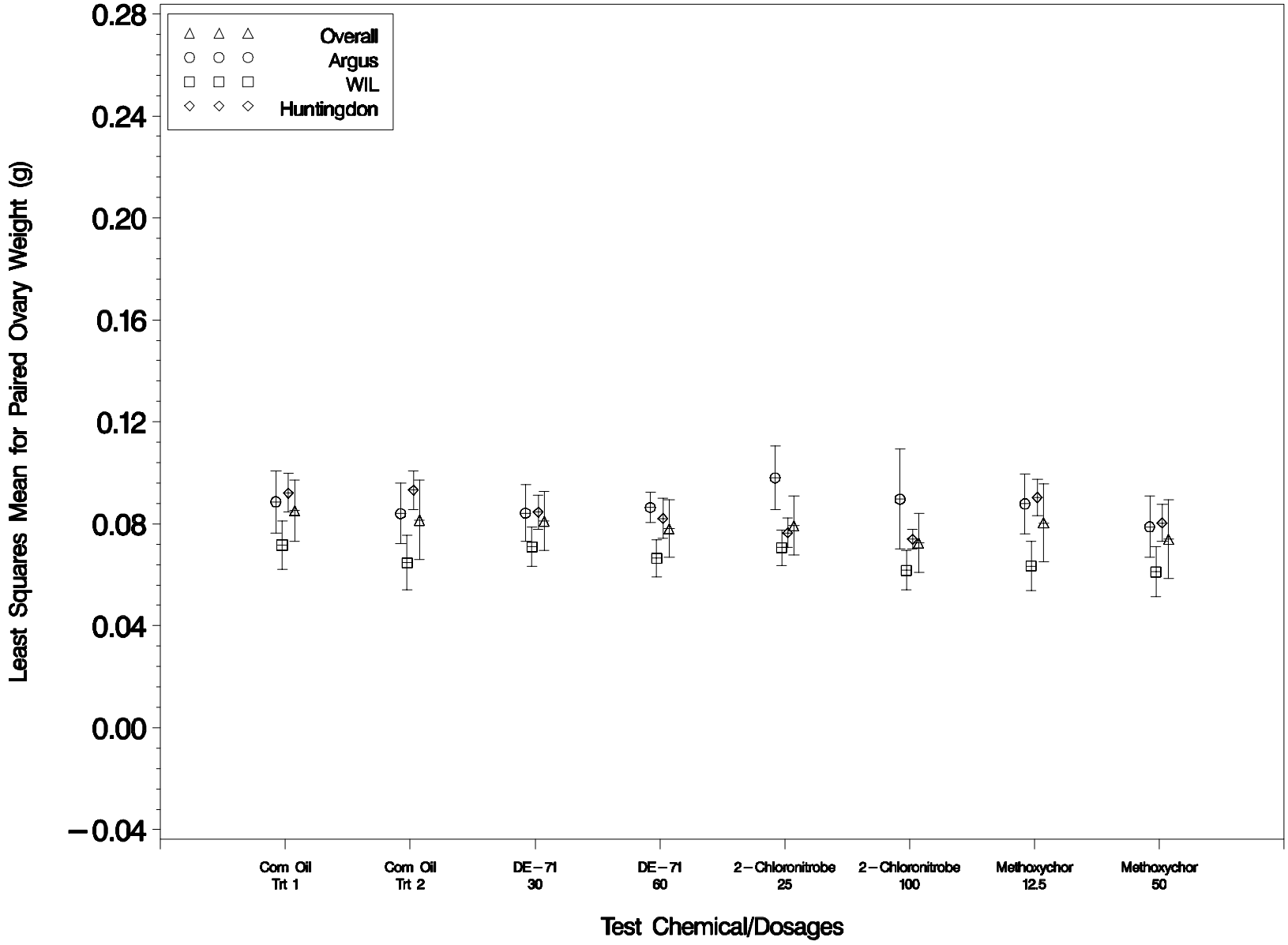

Figure 34. Adjusted Least Squares Means (with ± 2 Standard Error Bars) for Paired Ovary Weight (g) for Each Dose Group across Laboratories and for Each Laboratory.

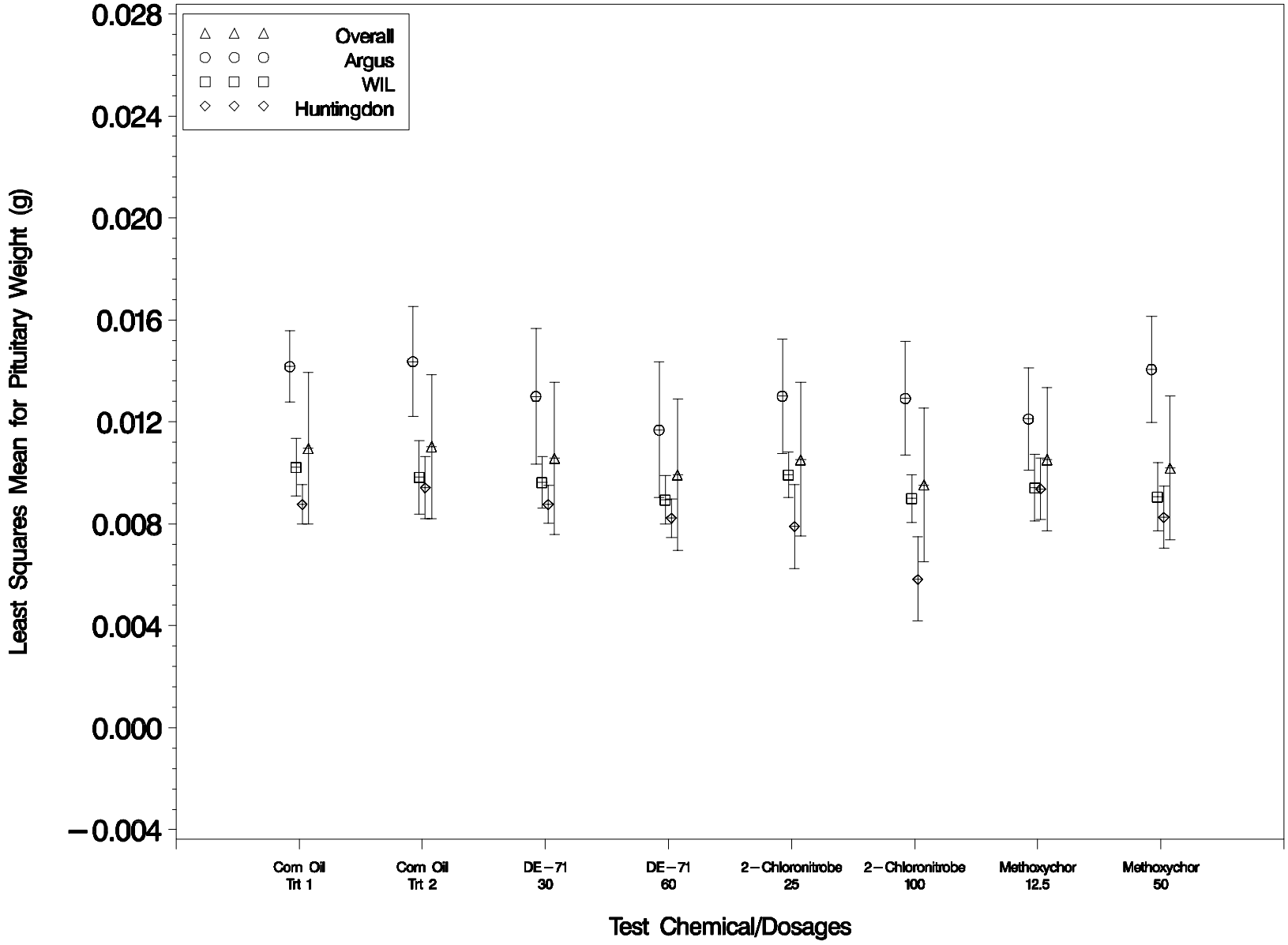

Figure 35. Adjusted Least Squares Means (with ± 2 Standard Error Bars) for Pituitary Weight (g) for Each Dose Group across Laboratories and for Each Laboratory.

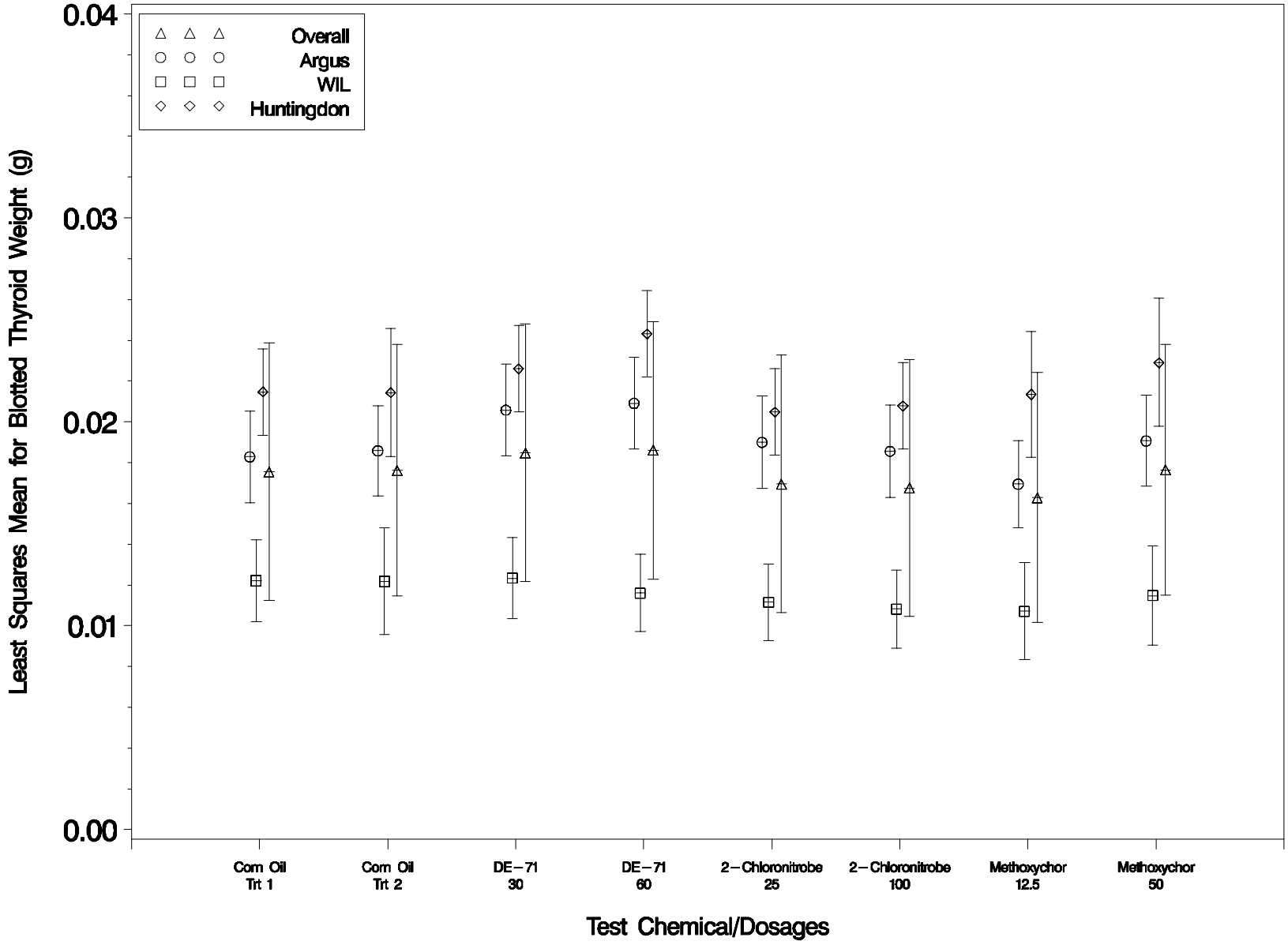

Figure 36. Adjusted Least Squares Means (with ± 2 Standard Error Bars) for Blotted Thyroid Weight (g) for Each Dose Group across Laboratories and for Each Laboratory.

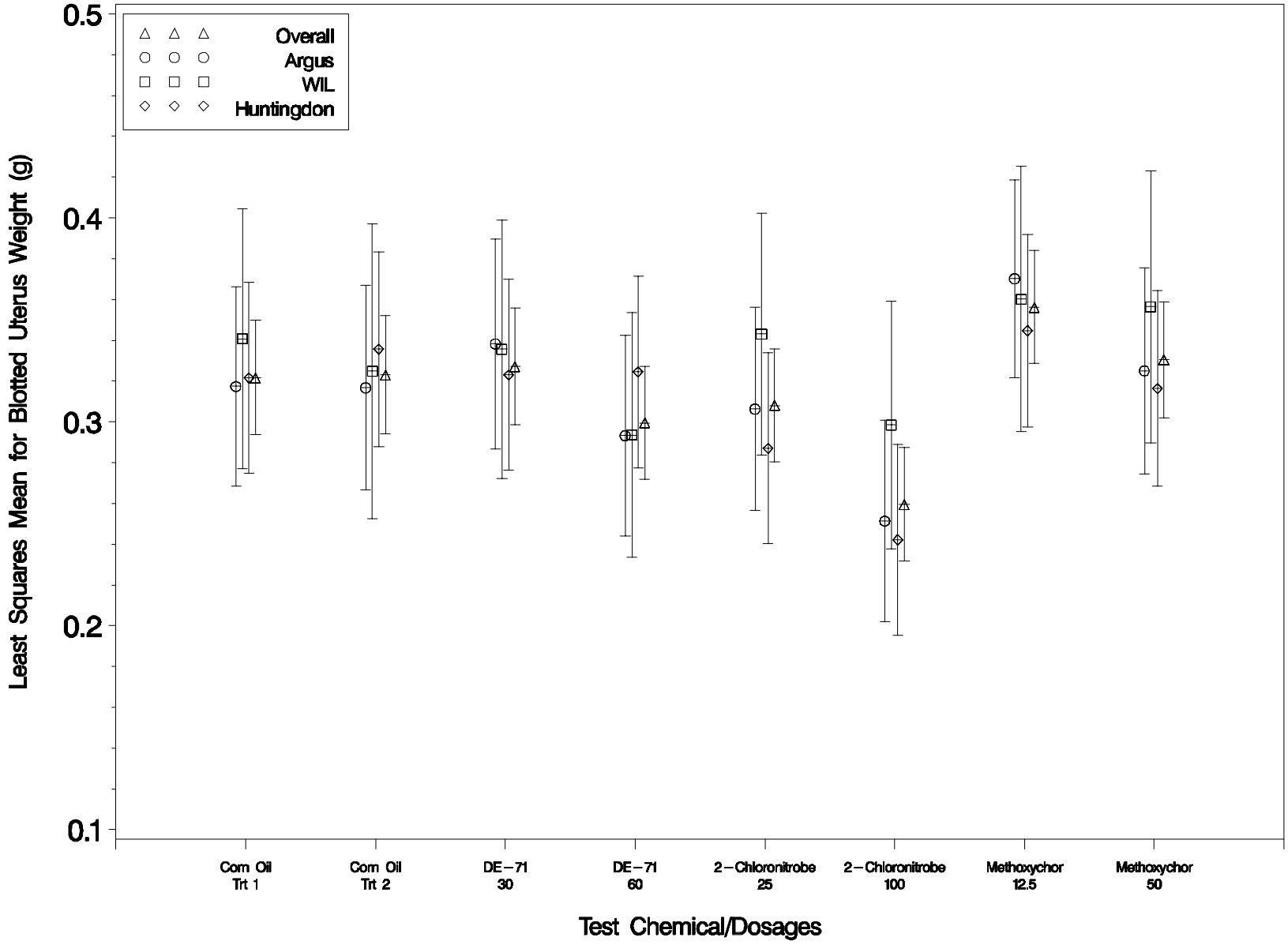

Figure 37. Adjusted Least Squares Means (with ± 2 Standard Error Bars) for Blotted Uterus Weight (g) for Each Dose Group across Laboratories and for Each Laboratory.

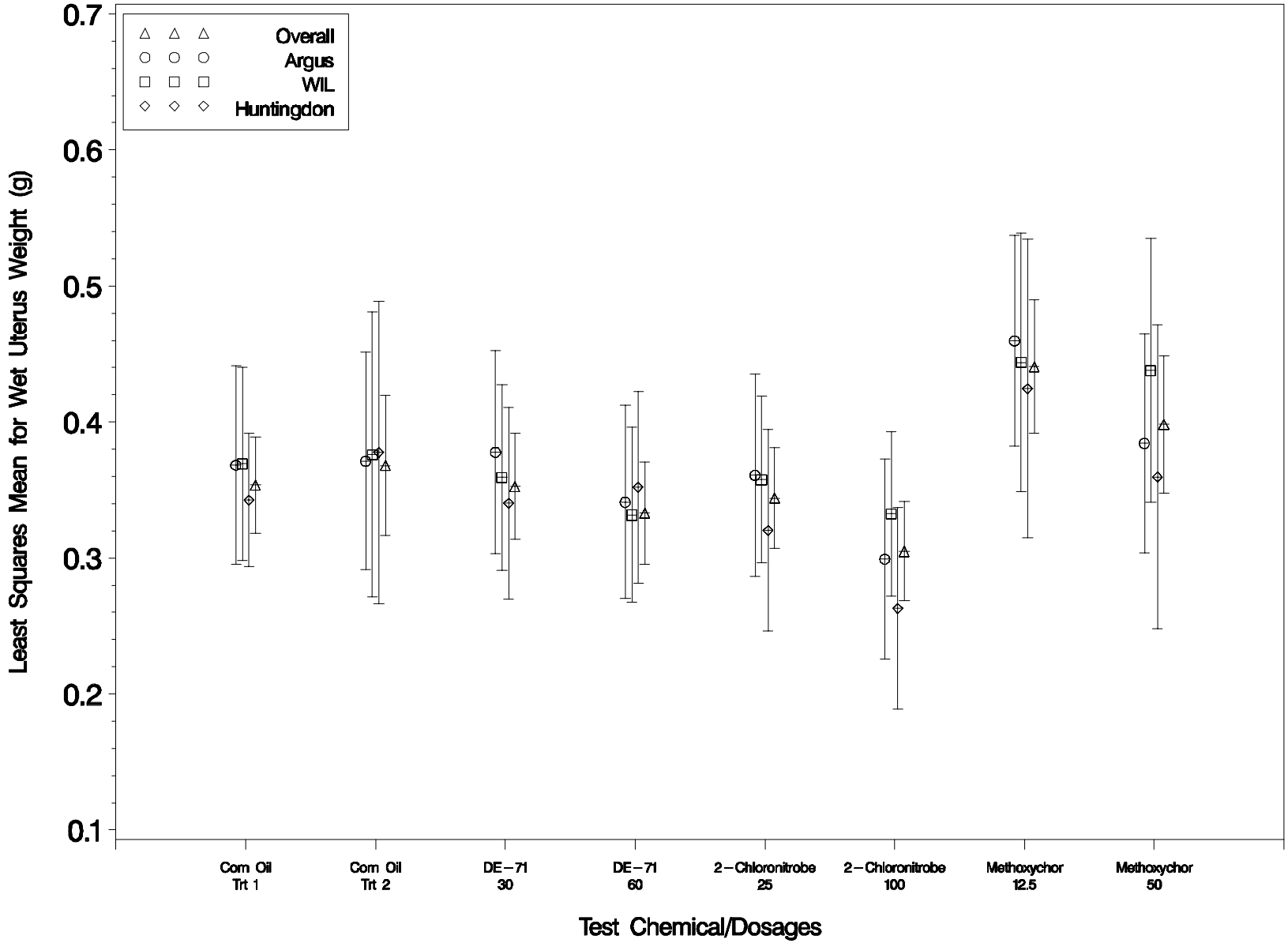

Figure 38. Adjusted Least Squares Means (with ± 2 Standard Error Bars) for Wet Uterus Weight (g) for Each Dose Group across Laboratories and for Each Laboratory.