MEMORANDUM

To: Timothy Leighton, EPA; Diana Hsieh, EPA

From: Jonathan Cohen, ICF

Date: September 18, 2019

Re: Statistical Review of the AEATF II Airless Sprayer Study

Contents

1. Introduction and Summary

In June 2019, AEATF II submitted the final report for their study "A Study for Measurement of Potential Dermal and Inhalation Exposure During the Application of Paint Containing an Antimicrobial using an Airless Sprayer." ICF was asked by EPA to analyze the airless sprayer study data to investigate the relationship between dermal and inhalation exposures and the pesticide product usage when professionals paint rooms with latex paint using an airless sprayer. In this study, professional painters painted the surfaces (walls, ceiling, unhung doors) of two purpose-built modules constructed to simulate houses with bedrooms, bathrooms, kitchen, hallways, closets with shelving, etc., and one purpose-built module module constructed to simulate and office building with small and large offices, conference rooms, and hallways. The painters were asked to paint the rooms and hallways using an airless sprayer as they normally would using airless sprayer painting equipment provided by study personnel. Note that much of the SAS code used for these analyses and

some of the following description was adapted from Sarkar's SAS code (which, in turn, was based on code provided by the AHETF) and his June 2010 Statistical Review "Review of Statistical Analyses in Agricultural Handler Exposure Task Force (AHETF) Monographs."

The report for the main study describes the experimental study methodology and the measurements in detail. Briefly, the study was carried out at a test site in Orlando, Florida. Monitoring of the professional painters was conducted indoors where 18 subjects separately used an airless sprayer to paint rooms in the modules. The square footage of the three modules varied between approximately 2,600 and 3,100 square feet with 8 or 10 foot ceilings.

The study used 18 volunteers from the professional house and commercial structures painting industry and thus 18 Monitoring Events (MEs). The volunteers painted the rooms using either 10, 15, or 30 gallons of paint (determined by weight). The three volumes of paint were each randomly assigned to six volunteers. In each group, three of the subjects were randomly chosen to paint with a paint containing the preservative propiconazole (PPZ) at a concentration of 1,200 ppm and the other three painted with a paint containing PPZ at a concentration of 12,000 ppm. Modules were painted on alternate days with untinted and tinted paint.

In this memorandum the main analyses use data from all 18 MEs in the six paint volume and PPZ concentration groups. For some analyses, we also present separate analyses for the 6 MEs in each paint volume group and for the 9 MEs in each PPZ concentration group; detailed results by groups are available upon request. Thus we define six groups of MEs:

- All: All 18 MEs
- Conc 1200 ppm: The 9 MEs in the Low concentration group (1200 ppm PPZ)
- Conc 12000 ppm: The 9 MEs in the High concentration group (12000 ppm PPZ)
- Vol 10 gals: The 6 MEs in the Low volume group (10 gallons paint)
- Vol 15 gals: The 6 MEs in the Mid volume group (15 gallons paint)
- Vol 30 gals: The 6 MEs in the High volume group (30 gallons paint)

Most of the statistical analyses presented in this memorandum only use the exposure measurements, the paint volumes, and the amounts of PPZ used. The only other factor that was controlled for in the study was whether or not the paint was tinted. This factor and any other factors affecting exposure are treated as random effects. In section 9 of this memorandum we present residual plots to illustrate the possible impacts of these uncontrolled factors on the estimated exposures calculated from the linear regression model.

Each subject was given inner and outer dosimeters and a painter's hat to wear, in addition to a 5" by 8" single layer of inner dosimeter material to be worn underneath the hat. Gloves were not worn. They also wore their own shoes. Each subject was given a low-volume, personal air-sampling pump attached to an OVS sampling tube with glass filter and XAD2 sorbent placed in the subject's breathing zone. Each subject was also given a second low-volume, personal air-sampling pump attached to a Parallel Particle Impactor (PPI) containing a 37 mm PVC filter and 37 mm support pad, which was also placed in the subject's breathing zone. The OVS sampler is designed to capture total inhalable residue and the PPI sampler is designed to capture respirable particles. Subjects also wore safety glasses and a fitted half-face respirator. The outer and inner dosimeters were each sectioned into six sections: lower arm, upper arm, lower leg, upper leg, front torso and rear torso. In the analytical laboratory, the mass of PPZ was measured on each inner and

outer dosimeter section, the OVS tubes and PPI Sampler filters, painter's hat, painter's hat inner dosimeter, hand wash, and face and neck wash.

The exposure measurements were corrected for the average percentage recovery of field fortification samples from the set of field fortification samples. Adjustments were not made if the average percentage recovery was above 100% for the field fortification set. The residues from the hand wash and face and neck wipes were also corrected for removal efficiency using the average removal efficiency of the BIT measured in the hand wash removal efficiency study (GPL Study 130503). In that study, removal efficiencies for BIT were measured on subjects that had 100 µL aliquots of paint applied between both their palms. Ten subjects had base paint applied to their palms that contained 154 ppm BIT, and the average removal efficiency for that group was 73.3%. Ten subjects had paint applied to their palms that contained 547 ppm BIT, and the average removal efficiency for that group was 60.3%. For this PPZ study, the main analyses used the lower removal efficiency value of 60%. In section 13 of this memorandum we compare the estimated dermal exposure confidence intervals for the means and 95th percentiles using the selected 60% removal efficiency with confidence intervals computed assuming the 73% removal efficiency value.

The face/neck wipes were also corrected using a correction factor of 1.43 to account for the area of the face covered by the safety glasses and the respirator.

These analyses used the corrected measurements. Excel spreadsheets containing the data in the report was supplied by the Study Director and used for these analyses. Some of the numerical results may differ a little from those in the study report because of rounding conventions and because of a slightly different treatment of non-detect values, as discussed below.

The dermal exposure data were used to develop exposure measurements for the following dermal exposure routes:

- **Long Dermal**. This case represents the dermal exposure to a person wearing long pants and a long-sleeved shirt, without gloves and without a hat. This is the sum of the mass from the six inner dosimeters, hand wash, the face/neck wipes, the painter's hat, and the painter's hat inner dosimeter.
- **Short Dermal**. This case represents the dermal exposure to a person wearing short pants and a short-sleeved shirt, without gloves and without a hat. This is the sum of the mass from the six inner dosimeters, the outer dosimeters for the lower leg and lower arm, hand wash, the face/neck wipes, the painter's hat, and the painter's hat inner dosimeter.
- **Long Short Dermal**. This case represents the dermal exposure to a person wearing long pants and a short-sleeved shirt, without gloves and without a hat. This is the sum of the mass from the six inner dosimeters, the outer dosimeters for the lower arm, hand wash, the face/neck wipes, the painter's hat, and the painter's hat inner dosimeter.
- **Hands Only**. This case represents the dermal exposure to the hands only and is the mass from hand wash.

Total inhalable Inhalation exposure was measured by the OVS sampler using the total residue from the air sampling tube glass fiber filters. Inhalation exposure for respirable particles was measured using the PPI sampler. The OVS sample residue was found by summing the residues from between 2 and 6 sections for each ME. The PPI sample residue was found by summing the residues from between 1 and 3 sections for each ME. The exposure concentration (mg/m^3) was calculated by dividing the corrected residue mass by the volume of air drawn.

The following inhalation exposure metrics are analyzed in this memorandum:

- **Inhalation (OVS Total) Concentration (mg/m^3).** Concentration measured by the OVS Sampler.
- **Inhalation (OVS Total) Dose (mg).** Inhalation (OVS Total) Concentration (mg/m^3) × Air Sampling Duration (hr) × Breathing Rate for Light Activity (m^3/hr). A breathing rate of 1 m^3/hr is assumed.
- **8-Hour Time Weighted Average (TWA) Inhalation (OVS Total) Concentration (mg/m^3).** Average inhalation (OVS Total) concentration over eight hours that includes this period of painting activity. Inhalation (OVS Total) Concentration (mg/m^3) × Air Sampling Duration (hr) / 8 (hr).
- **Inhalation (PPI Total) Concentration (mg/m^3).** Concentration measured by the PPI Sampler.
- **Inhalation (PPI Total) Dose (mg).** Inhalation (PPI Total) Concentration (mg/m^3) × Air Sampling Duration (hr) × Breathing Rate for Light Activity (m^3/hr). A breathing rate of 1 m^3/hr is assumed.
- **8-Hour Time Weighted Average (TWA) Inhalation (PPI Total) Concentration (mg/m^3).** Average inhalation (PPI Total) concentration over eight hours that includes this period of painting activity. Inhalation (OVS Total) Concentration (mg/m^3) × Air Sampling Duration (hr) / 8 (hr).

Some of the measured residue values were below the level of quantitation (LOQ), and some were also below the level of detection (LOD). Such values are called "non-detects." None of the residues for dermal exposure (hand wash, face/neck wipes, inner and outer dosimeters including painter hats) were non-detects. There were no PVC filter sections with residues below the detection limit (LOQ = 0.1 µg, LOD = 0.03 µg).

There were 77 OVS tube front sections and 77 OVS tube back sections. There were four OVS tube front sections with residues below the detection limit (LOQ = 2 µg, LOD = 0.6 µg). There were 74 OVS tube back sections (i.e., all but 3) with residues below the detection limit. In the study report, the OVS tube sections with values below the LOD were assigned a value of 0, and the OVS tube sections with values below the LOQ but above the LOD were assigned a value of 1 µg. For this memorandum we used different assignments more consistent with these upper bounds: The OVS tube sections with values below the LOD of 0.6 µg were assigned a value of 0.3 µg, half the LOD. The OVS tube sections with values below the LOQ of 2 µg but above the LOD of 0.6 µg were assigned a value of 1.3 µg, the midpoint of the LOD and LOQ. These choices have little impact on the results because each OVS sample is the sum of several residue values, there were only four non-detects for the front sections, and most of the back sections were below the LOD. Unless otherwise stated, for most of the analyses of OVS residues in this memorandum, we used these midpoint values to replace the non-detect values and then added these midpoint values to the other measured residues from the same ME. For some of the analyses we also calculated the minimum and maximum residue adding the other measured residues for the same ME to the minimum and maximum for the non-detect sections. For sections below the LOD, the minimum residue is 0 µg and the maximum residue is 0.6 µg. For sections above the LOD but below the LOQ, the minimum residue is 0.6 µg and the maximum residue is 2.0 µg. See sections 5 and 9 below for analyses of the impact of these non-detects. The impact is small.

In this memorandum we present the analysis of the unit or normalized exposure defined as the dermal or inhalation exposure divided by the pounds of active ingredient handled. Estimates of the arithmetic and geometric means and standard deviation as well as the 95th percentile are computed using the empirical data as well as a lognormal simple random sampling model. Unlike some of the other studies previously analyzed, we did not use lognormal mixed models since there are no cluster or random effects. Each group is assumed to be a simple random sample of subjects. The empirical model calculates statistics for all the unit exposure measurements assuming the data are statistically independent. The lognormal simple random sampling model calculates statistics for all the unit exposure measurements, assuming the unit exposure measurements are statistically independent with a lognormal distribution.

We used analysis of variance to compare the geometric means of the unit exposures for the two concentration groups "Conc 1200 ppm" and "Conc 12000 ppm." We also used analysis of variance to compare the geometric means of the unit exposures for the three volume groups "Vol 10 gals," "Vol 15 gals," and "Vol 30 gals." We assumed that the unit exposures for the 18 MEs are log-normally distributed with different geometric means for each group and possibly different geometric standard deviations. These analyses showed that there were statistically significant differences (at the 5% significance level) between the two concentration groups for Long Dermal, Hands Only, Inhalation (PPI Total) Dose, and Inhalation (PPI Total) Time-weighted Average. These analyses also showed that there were statistically significant differences (at the 5% significance level) between the three volume groups for Inhalation (OVS Total) Concentration and Inhalation (PPI Total) Concentration. For this reason we present results by concentration or volume group, as well as overall (the group "All"), for several of the most important statistical analyses. Group-specific results are not reported for all the analyses to limit the size of the memorandum, but are available upon request.

For each summary statistic we present confidence intervals. We also compute the fold relative accuracies of the summary statistics and compare them with the (primary) study design benchmark of 3-fold accuracy, which was always met for the various arithmetic mean and 95th percentile estimates of All MEs combined. Although not presented in this memorandum, the highest K-factor across groups and exposure modes was 3.05 for the empirical 95th percentile exposure of Hands Only exposure in the group "Conc 12000 ppm" using the parametric bootstrap. To evaluate the statistical models we present quantile-quantile plots of the data to determine whether the normalized exposure should be treated as being normally or lognormally distributed.

The statistical models for the normalized exposure assume that the mean value of the logarithm of the exposure is equal to an intercept plus the slope times the logarithm of the amount of active ingredient used, where the slope equals 1. To test this "log-log-linearity with a slope of 1" assumption, the lognormal simple random sampling model with a slope term was fitted to the data and a 95% confidence interval for the slope was calculated. A statistical test was used to determine if the slope was 1 or 0, corresponding either to a valid normalized exposure model or to a case where the exposure is independent of the amount of active ingredient used. We applied this test to each exposure metric using the lognormal simple random sampling model. We also present quantile-quantile plots of the residuals from the lognormal simple random sampling model with a slope term to evaluate the fitted models. We also evaluated quadratic regression models.

The slopes for the different exposure routes ranged from 0.74 to 0.93 and the confidence intervals for the slope all excluded 0 and in about half of the cases included 1. The upper bounds were all less than 1.1. Thus the assumption of independence was always rejected and the assumption of log-log-linearity with slope 1 was rejected in about half of the cases.

A secondary objective is for meeting 80% power for detecting log-log-linearity with a slope of 1. This objective is approximately met if the widths of the confidence intervals for the slope based on the lognormal model are at most 1.4. The results show that the observed widths were all less than 1.4. Therefore the secondary objective of meeting 80% power for detecting proportionality was met.

To evaluate whether additional descriptor variables could improve the model estimates, we plotted the regression residuals against several candidate variables, such as the use of different types of equipment or the monitored minutes. These residual plots mostly showed a weak relationship between the studentized residuals and the other descriptor variables. As an exception, for Inhalation (OVS Total) Conc and Inhalation (PPI Total) Conc, the residuals tended to be lower for the high numbers of minutes monitored or amount of paint used, which may suggest the need for alternative models to also take into account the minutes of monitoring and the amount of paint used. The best alternative approach

is complicated by the fact that the experimental design and regression model accounts for the amount of active ingredient used, which increases with the amount of paint used and with the concentration.

Finally we evaluated and compared several alternative statistical model formulations. In addition to the above linear and quadratic models for the logarithm of exposure we considered linear regression models with extra terms for the concentration or paint volume, log-log-logistic and three-parameter logistic models for exposure, and a gamma model for exposure. We used the Akaike Information Criterion to compare the goodness-of-fit, penalizing potentially over-parametrized models with more parameters, and plotted the observed and predicted values. The linear model performed best for five of the exposure routes, the quadratic model performed best for two of the exposure routes, and the best models for the other three routes were the linear model adjusted for concentration or volume and the gamma model.

2. Summary Statistics of Exposure per Pound of Active Ingredient Handled

Table 1 to Table 10 summarize the normalized exposure data (per lb active ingredient handled) with the summary statistics from the 18 (all concentrations), or 9 (specific concentrations) measurements for each concentration group, or 6 (specific paint volumes) measurements for each volume group, and each dermal and inhalation exposure route. These analyses assume that the exposure measurements within each subset come from some unspecified distribution for that subset.

Table 1. Summary statistics for normalized long dermal exposure (mg/lb AI) using empirical sampling model

Statistic	All	Conc 1200 ppm	Conc 12000 ppm	Vol 10 gals	Vol 15 gals	Vol 30 gals
Arithmetic Mean	43.429	53.157	33.702	48.870	45.077	36.341
Arithmetic Standard Deviation	20.248	22.677	12.003	29.840	13.496	14.910
Geometric Mean	39.525	48.807	32.009	41.686	43.246	34.252
Geometric Standard Deviation	1.553	1.564	1.398	1.862	1.382	1.436
Min	18.937	23.854	18.937	18.937	27.498	23.854
5%	18.937	23.854	18.937	18.937	27.498	23.854
10%	23.854	23.854	18.937	18.937	27.498	23.854
25%	27.586	33.141	27.498	27.264	31.236	27.586
50%	37.452	50.267	27.706	38.568	46.991	30.424
75%	58.317	63.995	41.763	76.422	58.317	41.763
90%	76.422	93.464	58.317	93.464	59.429	63.995
95%	93.464	93.464	58.317	93.464	59.429	63.995
Max	93.464	93.464	58.317	93.464	59.429	63.995

Table 2. Summary statistics for normalized short dermal exposure (mg/lb AI) using empirical sampling model

Statistic	All	Conc 1200 ppm	Conc 12000 ppm	Vol 10 gals	Vol 15 gals	Vol 30 gals
Arithmetic Mean	104.420	129.906	78.934	100.421	122.849	89.991
Arithmetic Standard Deviation	55.386	64.846	29.194	65.688	52.465	51.825
Geometric Mean	92.307	114.606	74.347	87.596	113.437	79.152
Geometric Standard Deviation	1.658	1.733	1.444	1.711	1.561	1.729
Min	42.013	48.441	42.013	51.418	61.694	42.013
5%	42.013	48.441	42.013	51.418	61.694	42.013
10%	48.441	48.441	42.013	51.418	61.694	42.013
25%	61.694	73.394	57.629	57.629	74.797	48.441
50%	83.740	118.786	74.797	79.935	123.635	75.403
75%	130.199	179.899	86.477	105.143	146.380	118.786
90%	206.950	228.464	130.199	228.464	206.950	179.899
95%	228.464	228.464	130.199	228.464	206.950	179.899
Max	228.464	228.464	130.199	228.464	206.950	179.899

Table 3. Summary statistics for normalized long short dermal exposure (mg/lb AI) using empirical sampling model

Statistic	All	Conc 1200 ppm	Conc 12000 ppm	Vol 10 gals	Vol 15 gals	Vol 30 gals
Arithmetic Mean	63.499	78.196	48.803	66.041	71.908	52.548
Arithmetic Standard Deviation	32.450	36.624	20.258	41.879	26.163	30.090
Geometric Mean	56.665	70.263	45.698	57.128	67.224	47.377
Geometric Standard Deviation	1.622	1.658	1.449	1.770	1.528	1.593
Min	29.025	29.746	29.025	29.025	33.637	29.746
5%	29.025	29.746	29.025	29.025	33.637	29.746
10%	29.746	29.746	29.025	29.025	33.637	29.746
25%	38.201	49.169	36.481	40.560	49.169	36.481
50%	51.554	82.842	40.560	49.522	77.494	41.755
75%	85.577	103.120	53.939	85.577	90.535	53.939
90%	111.614	142.040	90.535	142.040	103.120	111.614
95%	142.040	142.040	90.535	142.040	103.120	111.614
Max	142.040	142.040	90.535	142.040	103.120	111.614

Table 4. Summary statistics for normalized hands only dermal exposure (mg/lb AI) using empirical sampling model

Statistic	All	Conc 1200 ppm	Conc 12000 ppm	Vol 10 gals	Vol 15 gals	Vol 30 gals
Arithmetic Mean	26.056	33.893	18.218	30.900	26.748	20.518
Arithmetic Standard Deviation	13.963	14.968	7.216	22.340	8.626	4.889
Geometric Mean	23.097	31.155	17.123	24.083	25.545	20.030
Geometric Standard Deviation	1.645	1.548	1.443	2.214	1.401	1.273
Min	9.440	14.713	9.440	9.440	17.115	14.713
5%	9.440	14.713	9.440	9.440	17.115	14.713
10%	12.405	14.713	9.440	9.440	17.115	14.713
25%	16.780	24.683	15.022	12.405	17.375	16.780
50%	23.673	29.183	17.115	24.605	26.933	20.175
75%	34.132	38.002	17.375	52.207	34.132	24.345
90%	52.207	62.138	34.132	62.138	38.002	26.920
95%	62.138	62.138	34.132	62.138	38.002	26.920
Max	62.138	62.138	34.132	62.138	38.002	26.920

Table 5. Summary statistics for normalized inhalation (OVS total) concentration exposure ((mg/m^3)/lb AI) using empirical sampling model

Statistic	All	Conc 1200 ppm	Conc 12000 ppm	Vol 10 gals	Vol 15 gals	Vol 30 gals
Arithmetic Mean	0.5206	0.5382	0.5029	0.7065	0.5548	0.3004
Arithmetic Standard Deviation	0.2054	0.2357	0.1827	0.1343	0.1328	0.0823
Geometric Mean	0.4784	0.4909	0.4661	0.6957	0.5413	0.2907
Geometric Standard Deviation	1.5557	1.5911	1.5601	1.2126	1.2782	1.3318
Min	0.1845	0.2506	0.1845	0.5572	0.3998	0.1845
5%	0.1845	0.2506	0.1845	0.5572	0.3998	0.1845
10%	0.2506	0.2506	0.1845	0.5572	0.3998	0.1845
25%	0.3532	0.3532	0.4155	0.5614	0.4155	0.2506
50%	0.5528	0.5524	0.5572	0.7078	0.5528	0.2964
75%	0.6951	0.7482	0.6673	0.8299	0.6951	0.3532
90%	0.8299	0.8747	0.7130	0.8747	0.7130	0.4216
95%	0.8747	0.8747	0.7130	0.8747	0.7130	0.4216
Max	0.8747	0.8747	0.7130	0.8747	0.7130	0.4216

Table 6. Summary statistics for normalized inhalation (OVS total) dose exposure (mg/lb AI) using empirical sampling model

Statistic	All	Conc 1200 ppm	Conc 12000 ppm	Vol 10 gals	Vol 15 gals	Vol 30 gals
Arithmetic Mean	0.9922	1.0591	0.9254	1.0419	1.0694	0.8654
Arithmetic Standard Deviation	0.3198	0.3359	0.3074	0.4073	0.3314	0.2065
Geometric Mean	0.9486	1.0150	0.8865	0.9821	1.0303	0.8436
Geometric Standard Deviation	1.3540	1.3576	1.3530	1.4457	1.3415	1.2877
Min	0.5780	0.6724	0.5780	0.6895	0.7596	0.5780
5%	0.5780	0.6724	0.5780	0.6895	0.7596	0.5780
10%	0.6724	0.6724	0.5780	0.6895	0.7596	0.5780
25%	0.7596	0.8455	0.7336	0.7336	0.7894	0.6724
50%	0.9192	0.9359	0.8609	0.8532	0.9693	0.9192
75%	1.1453	1.3183	0.9626	1.5588	1.3183	0.9586
90%	1.5631	1.5631	1.6104	1.5631	1.6104	1.1453
95%	1.6104	1.5631	1.6104	1.5631	1.6104	1.1453
Max	1.6104	1.5631	1.6104	1.5631	1.6104	1.1453

Table 7. Summary statistics for normalized inhalation (OVS total) time-weighted average concentration exposure ((mg/m^3)/lb AI) using empirical sampling model

Statistic	All	Conc 1200 ppm	Conc 12000 ppm	Vol 10 gals	Vol 15 gals	Vol 30 gals
Arithmetic Mean	0.1240	0.1324	0.1157	0.1302	0.1337	0.1082
Arithmetic Standard Deviation	0.0400	0.0420	0.0384	0.0509	0.0414	0.0258
Geometric Mean	0.1186	0.1269	0.1108	0.1228	0.1288	0.1054
Geometric Standard Deviation	1.3540	1.3576	1.3530	1.4457	1.3415	1.2877
Min	0.0722	0.0840	0.0722	0.0862	0.0949	0.0722
5%	0.0722	0.0840	0.0722	0.0862	0.0949	0.0722
10%	0.0840	0.0840	0.0722	0.0862	0.0949	0.0722
25%	0.0949	0.1057	0.0917	0.0917	0.0987	0.0840
50%	0.1149	0.1170	0.1076	0.1066	0.1212	0.1149
75%	0.1432	0.1648	0.1203	0.1948	0.1648	0.1198
90%	0.1954	0.1954	0.2013	0.1954	0.2013	0.1432
95%	0.2013	0.1954	0.2013	0.1954	0.2013	0.1432
Max	0.2013	0.1954	0.2013	0.1954	0.2013	0.1432

Table 8. Summary statistics for normalized inhalation (PPI Total) concentration exposure ((mg/m^3)/lb AI) using empirical sampling model

Statistic	All	Conc 1200 ppm	Conc 12000 ppm	Vol 10 gals	Vol 15 gals	Vol 30 gals
Arithmetic Mean	0.0643	0.0758	0.0529	0.0847	0.0760	0.0323
Arithmetic Standard Deviation	0.0335	0.0374	0.0263	0.0396	0.0157	0.0102
Geometric Mean	0.0559	0.0672	0.0465	0.0764	0.0746	0.0307
Geometric Standard Deviation	1.7659	1.7100	1.7658	1.6746	1.2384	1.4534
Min	0.0158	0.0286	0.0158	0.0355	0.0546	0.0158
5%	0.0158	0.0286	0.0158	0.0355	0.0546	0.0158
10%	0.0275	0.0286	0.0158	0.0355	0.0546	0.0158
25%	0.0395	0.0404	0.0355	0.0523	0.0619	0.0275
50%	0.0582	0.0770	0.0523	0.0805	0.0783	0.0341
75%	0.0848	0.0901	0.0708	0.1231	0.0848	0.0404
90%	0.1231	0.1364	0.0980	0.1364	0.0980	0.0421
95%	0.1364	0.1364	0.0980	0.1364	0.0980	0.0421
Max	0.1364	0.1364	0.0980	0.1364	0.0980	0.0421

Table 9. Summary statistics for normalized inhalation (PPI Total) dose exposure (mg/lb AI) using empirical sampling model

Statistic	All	Conc 1200 ppm	Conc 12000 ppm	Vol 10 gals	Vol 15 gals	Vol 30 gals
Arithmetic Mean	0.1225	0.1472	0.0978	0.1269	0.1484	0.0922
Arithmetic Standard Deviation	0.0585	0.0548	0.0538	0.0822	0.0490	0.0234
Geometric Mean	0.1107	0.1394	0.0879	0.1071	0.1422	0.0891
Geometric Standard Deviation	1.5876	1.4083	1.5944	1.8825	1.3713	1.3577
Min	0.0497	0.0915	0.0497	0.0514	0.1037	0.0497
5%	0.0497	0.0915	0.0497	0.0514	0.1037	0.0497
10%	0.0514	0.0915	0.0497	0.0514	0.1037	0.0497
25%	0.0847	0.1085	0.0688	0.0688	0.1074	0.0847
50%	0.1079	0.1190	0.0847	0.0961	0.1343	0.0981
75%	0.1499	0.1835	0.1074	0.1877	0.1835	0.1085
90%	0.2271	0.2615	0.2271	0.2615	0.2271	0.1137
95%	0.2615	0.2615	0.2271	0.2615	0.2271	0.1137
Max	0.2615	0.2615	0.2271	0.2615	0.2271	0.1137

Table 10. Summary statistics for normalized inhalation (PPI Total) time-weighted average concentration exposure ((mg/m^3)/lb AI) using empirical sampling model

Statistic	All	Conc 1200 ppm	Conc 12000 ppm	Vol 10 gals	Vol 15 gals	Vol 30 gals
Arithmetic Mean	0.0153	0.0184	0.0122	0.0159	0.0185	0.0185
Arithmetic Standard Deviation	0.0073	0.0069	0.0067	0.0103	0.0061	0.0061
Geometric Mean	0.0138	0.0174	0.0110	0.0134	0.0178	0.0178
Geometric Standard Deviation	1.5876	1.4083	1.5944	1.8825	1.3713	1.3713
Min	0.0062	0.0114	0.0062	0.0064	0.0130	0.0130
5%	0.0062	0.0114	0.0062	0.0064	0.0130	0.0130
10%	0.0064	0.0114	0.0062	0.0064	0.0130	0.0130
25%	0.0106	0.0136	0.0086	0.0086	0.0134	0.0134
50%	0.0135	0.0149	0.0106	0.0120	0.0168	0.0168
75%	0.0187	0.0229	0.0134	0.0235	0.0229	0.0229
90%	0.0284	0.0327	0.0284	0.0327	0.0284	0.0284
95%	0.0327	0.0327	0.0284	0.0327	0.0284	0.0284
Max	0.0327	0.0327	0.0284	0.0327	0.0284	0.0284

The results also show the high proportions of the dermal exposure from hands only. Based on the arithmetic means for All, the overall percentages of exposure from hands only are about 60% of the Long Dermal, 25% of Short Dermal, and 41% of Long Short Dermal. For the 1200 ppm concentration group, the corresponding percentages of exposure from hands only are about 64% of the Long Dermal, 26% of Short Dermal, and 43% of Long Short Dermal. For the 12000 ppm concentration group, the corresponding percentages of exposure from hands only are about 54% of the Long Dermal, 23% of Short Dermal, and 37% of Long Short Dermal. For the 10 gallon volume group, the corresponding percentages of exposure from hands only are about 63% of the Long Dermal, 31% of Short Dermal, and 47% of Long Short Dermal. For the 15 gallon volume group, the corresponding percentages of exposure from hands only are about 59% of the Long Dermal, 22% of Short Dermal, and 37% of Long Short Dermal. For the 30 gallon volume group, the corresponding percentages of exposure from hands only are about 57% of the Long Dermal, 23% of Short Dermal, and 39% of Long Short Dermal.

3. Compare Concentration and Volume Groups

The results in Tables 1 to 10 show differences between the normalized exposure statistics for the two concentration groups “Conc 1200 ppm” and “Conc 12000 ppm” and the differences for the three volume groups “Vol 10 gals,” “Vol 15 gals” and “Vol 30 gals.” To compare these groups, an analysis of variance was performed to test whether the geometric means were statistically significantly different at the 5% significance level. Because later analyses in this memorandum confirm that log-normal distributions provide a better fit to the data than normal distributions, this analysis used the logarithms of the normalized exposure and tested whether the population means of the logarithms of the normalized exposure are the same across the two or three groups. This is equivalent to testing whether the geometric means of the normalized exposure are the same across the groups. The one way analysis of variance (ANOVA) test assumes that the geometric standard deviations of the normalized exposure are the same across the groups, which is the same as

assuming that the variances of the logarithms of the normalized exposure are the same across the groups. The Welch's ANOVA test avoids this equal variance assumption.

The p-values for these ANOVA tests are shown in Table 11, separately for the concentration and volume groups. These analyses show that there were statistically significant differences (at the 5% significance level) between the two concentration groups for Long Dermal, Hands Only, Inhalation (PPI Total) Dose, and Inhalation (PPI Total) Time-weighted Average. These analyses also show that there were statistically significant differences (at the 5% significance level) between the three volume groups for Inhalation (OVS Total) Concentration and Inhalation (PPI Total) Concentration.

Table 11. P-values for testing differences in geometric means for different concentration or volume groups

Exposure Route	Concentrations		Volumes	
	ANOVA	Welch's ANOVA	ANOVA	Welch's ANOVA
Long Dermal	0.038	0.039	0.643	0.532
Short Dermal	0.067	0.070	0.473	0.467
Long Short Dermal	0.056	0.058	0.483	0.450
Hands Only	0.006	0.006	0.703	0.405
Inhalation (OVS Total) Conc	0.812	0.812	0.000	0.001
Inhalation (OVS Total) Dose	0.359	0.359	0.519	0.468
Inhalation (OVS Total) 8-hr TWA	0.359	0.359	0.519	0.468
Inhalation (PPI Total) Conc	0.177	0.178	0.001	0.003
Inhalation (PPI Total) Dose	0.030	0.031	0.219	0.088
Inhalation (PPI Total) 8-hr TWA	0.030	0.031	0.219	0.088

To illustrate the differences between the concentration groups and between the volume groups, the following Figure 1 is a scatter plot of the natural logarithm of the Long Dermal exposure plotted against the natural logarithm of the pounds of active ingredient. The data points are labeled to show the concentration and volume groups. The letters l, m, and h in upper or lower case show the three volume groups for l = low = 10 gals, m = mid = 15 gals, and h = high = 30 gals. Lower case letters show the low concentration MEs (1200 ppm) and upper case letter show the high concentration MEs (12000 ppm).

Also shown is a regression line fitted to all 18 MEs (see Section 9 for details about the regression analyses). This plot shows that the pounds of active ingredient varies very little across the three MEs for a given concentration and volume combination but there are relatively large differences in the pounds of active ingredient between the concentration or volume groups. This follows from the fact that by design the amount of active ingredient increases with the concentration and with the volume of paint used. Because of the variation across concentration and volume groups, for several of the analyses in this memorandum we present separate results for each concentration and volume groups as well as the overall results from all 18 MEs. We do not present detailed results by group for all the statistical analyses but they can be made available upon request. Scatter plots with regression lines for all the exposure routes are presented in Section 9.

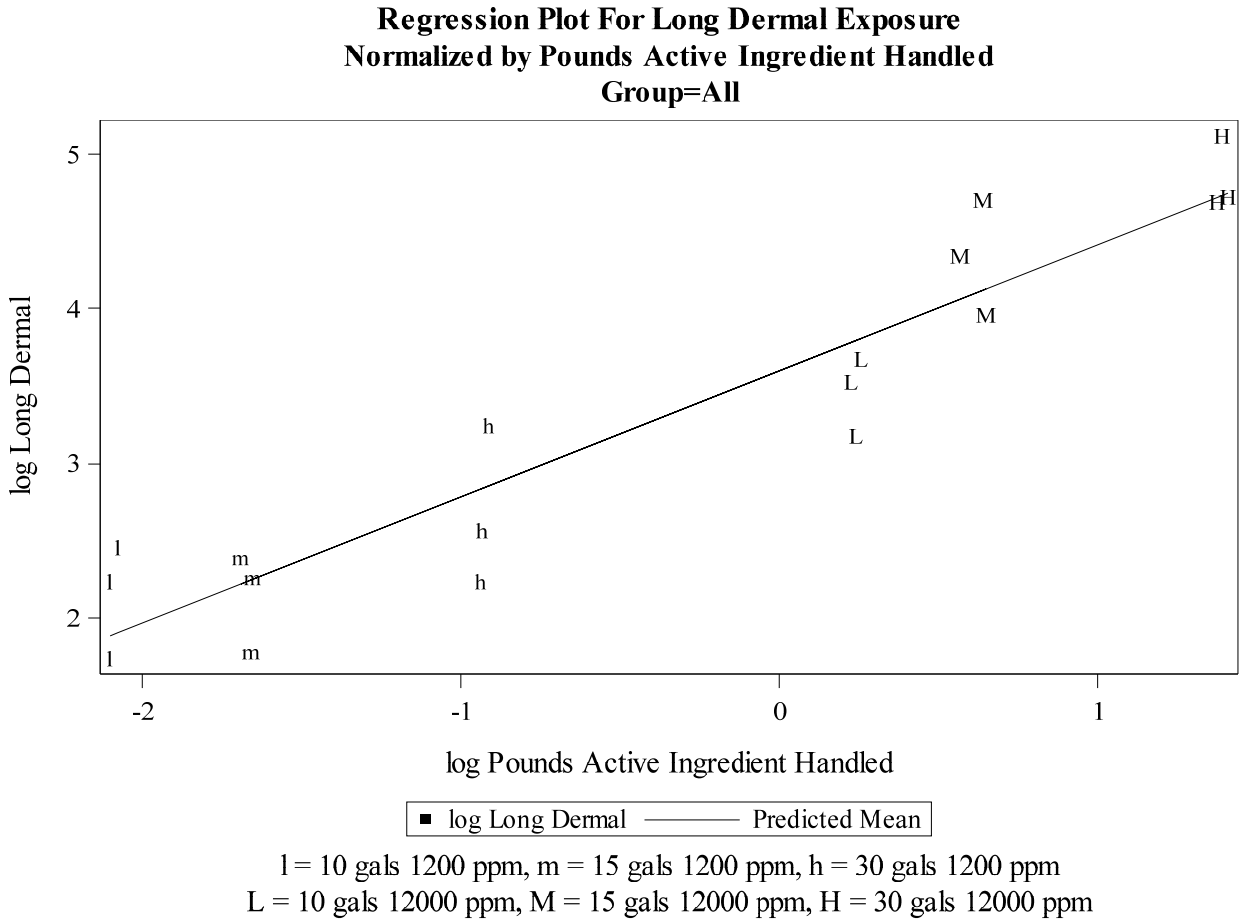


Figure 1. Regression plot for Long Dermal exposure (mg).

4. Statistical Models

The statistical analyses of the normalized exposure use the following two alternative statistical models. Let X be the normalized exposure and X = exp(Y) so that Y = log (X), where log denotes the natural logarithm. LnGM is the log of the geometric mean. Let Z95 be the 95th percentile of a standard normal distribution, approximately 1.645.

- Empirical simple random sampling model. Code "s." Assumes that all the values of X were randomly drawn from an unspecified distribution. Gives empirical estimates such as in Tables 1 to 14 above.
  - Y = LnGM + Error. Error is independent and identically distributed with mean 0 and the same variance for every measurement.
  - AMs = Arithmetic mean of X values
  - GMs = Geometric mean of X values = exp(LnGM) (= GMu)
  - GSDs = Geometric standard deviation of X values (= GSDu)
  - P95s = 95th percentile of X values

- Lognormal simple random sampling model. Code "u." Assumes that all the values of X were randomly drawn from a lognormal distribution.
  - Y = LnGM + Error. Error is normally distributed with mean 0, variance Vu, and standard deviation Su = √Vu.
  - AMu = Modeled arithmetic mean of X values = exp(LnGM) exp(½ Vu)
  - GMu = Modeled geometric mean of X values = exp(LnGM)
  - GSDu = Modeled geometric standard deviation of X values = exp(Su)
  - P95u = Modeled 95th percentile of X values = exp(LnGM) exp(Z95×Su)

Table 12 to Table 17 present the arithmetic mean and 95th percentile estimates from the lognormal simple random sampling model, together with 95% confidence intervals, for all the exposure routes and for each concentration and volume group. These are the values of AMu and P95u. The other summary statistics are presented in more detail below.

Table 12. Arithmetic mean and 95th percentile estimates from lognormal simple random sampling model for normalized exposure for All

Exposure Route	Clothing	Arithmetic Mean (95% Confidence Interval)	95th Percentile (95% Confidence Interval)
Dermal (mg/lb AI)	Long Dermal	43.55 (35.29, 53.87)	81.57 (59.27, 111.31)
	Short Dermal	104.89 (82.04, 134.41)	212.01 (146.94, 302.93)
	Long Short Dermal	63.70 (50.44, 80.64)	125.61 (88.43, 176.76)
	Hands Only	26.15 (20.54, 33.37)	52.39 (36.51, 74.45)
Inhalation (OVS Total) Concentration ((mg/m^3)/lb AI)		0.527 (0.427, 0.653)	0.990 (0.718, 1.352)
Inhalation (OVS Total) Dose (mg/lb AI)		0.993 (0.8362 1.144)	1.562 (1.253, 1.934)
Inhalation (OVS Total) 8-hr TWA ((mg/m^3)/lb AI)		0.124 (0.108, 0.143)	0.195 (0.157, 0.242)
Inhalation (PPI Total) Concentration ((mg/m^3)/lb AI)		0.0657 (0.0497, 0.0874)	0.1425 (0.0943, 0.2129)
Inhalation (PPI Total) Dose (mg/lb AI)		0.1232 (0.0987, 0.1542)	0.2368 (0.1693, 0.3281)
Inhalation (PPI Total) 8-hr TWA ((mg/m^3)/lb AI)		0.0154 (0.0123, 0.0193)	0.0296 (0.0212, 0.0410)

Table 13. Arithmetic mean and 95th percentile estimates from lognormal simple random sampling model for normalized exposure for Conc 1200 ppm

Exposure Route	Clothing	Arithmetic Mean (95% Confidence Interval)	95th Percentile (95% Confidence Interval)
Dermal (mg/lb AI)	Long Dermal	53.94 (39.80, 73.86)	101.85 (63.44, 160.96)
	Short Dermal	133.33 (90.89, 199.00)	283.25 (158.23, 497.38)
	Long Short Dermal	79.86 (56.34, 114.95)	161.48 (94.53, 271.02)
	Hands Only	34.27 (25.49, 46.51)	63.90 (40.25, 99.92)
Inhalation (OVS Total) Concentration ((mg/m^3)/lb AI)		0.547 (0.399, 0.759)	1.054 (0.645, 1.695)
Inhalation (OVS Total) Dose (mg/lb AI)		1.064 (0.868, 1.308)	1.678 (1.214, 2.295)
Inhalation (OVS Total) 8-hr TWA ((mg/m^3)/lb AI)		0.133 (0.109, 0.163)	0.210 (0.152, 0.287)
Inhalation (PPI Total) Concentration ((mg/m^3)/lb AI)		0.0776 (0.0535, 0.1144)	0.1624 (0.0920, 0.2813)
Inhalation (PPI Total) Dose (mg/lb AI)		0.1478 (0.1176, 0.1867)	0.2447 (0.1703, 0.3474)
Inhalation (PPI Total) 8-hr TWA ((mg/m^3)/lb AI)		0.0185 (0.0147, 0.0233)	0.0306 (0.0213, 0.0434)

Table 14. Arithmetic mean and 95th percentile estimates from lognormal simple random sampling model for normalized exposure for Conc 12000 ppm

Exposure Route	Clothing	Arithmetic Mean (95% Confidence Interval)	95th Percentile (95% Confidence Interval)
Dermal (mg/lb AI)	Long Dermal	33.85 (27.09, 42.50)	55.53 (39.14, 78.49)
	Short Dermal	79.54 (62.20, 102.18)	136.10 (92.70, 198.97)
	Long Short Dermal	48.95 (38.18, 63.05)	84.12 (57.10, 123.41)
	Hands Only	18.31 (14.33, 23.51)	31.30 (21.34, 45.72)
Inhalation (OVS Total) Concentration ((mg/m^3)/lb AI)		0.515 (0.380, 0.701)	0.969 (0.609, 1.534)
Inhalation (OVS Total) Dose (mg/lb AI)		0.928 (0.759, 1.138)	1.458 (1.063, 1.992)
Inhalation (OVS Total) 8-hr TWA ((mg/m^3)/lb AI)		0.116 (0.095, 0.142)	0.182 (0.133, 0.249)
Inhalation (PPI Total) Concentration ((mg/m^3)/lb AI)		0.0547 (0.0369, 0.0823)	0.1186 (0.0655, 0.2133)

Exposure Route	Clothing	Arithmetic Mean (95% Confidence Interval)	95th Percentile (95% Confidence Interval)
Inhalation (PPI Total) Dose (mg/lb AI)		0.0980 (0.0713, 0.1358)	0.1894 (0.1163, 0.3067)
Inhalation (PPI Total) 8-hr TWA ((mg/m^3)/lb AI)		0.0123 (0.0089, 0.0170)	0.0237 (0.0145, 0.0383)

Table 15. Arithmetic mean and 95th percentile estimates from lognormal simple random sampling model for normalized exposure for Vol 10 gals

Exposure Route	Clothing	Arithmetic Mean (95% Confidence Interval)	95th Percentile (95% Confidence Interval)
Dermal (mg/lb AI)	Long Dermal	50.57 (29.59, 88.52)	115.88 (52.64, 246.75)
	Short Dermal	101.19 (64.24, 161.86)	211.95 (107.16, 407.34)
	Long Short Dermal	67.25 (41.32, 111.26)	146.18 (70.79, 292.80)
	Hands Only	33.03 (16.22, 70.95)	89.04 (32.45, 234.11)
Inhalation (OVS Total) Concentration ((mg/m^3)/lb AI)		0.709 (0.607, 0.831)	0.955 (0.748, 1.208)
Inhalation (OVS Total) Dose (mg/lb AI)		1.051 (0.778, 1.433)	1.801 (1.128, 2.819)
Inhalation (OVS Total) 8-hr TWA ((mg/m^3)/lb AI)		0.131 (0.097, 0.179)	0.225 (0.141, 0.352)
Inhalation (PPI Total) Concentration ((mg/m^3)/lb AI)		0.0872 (0.0566, 0.1368)	0.1784 (0.0927, 0.3339)
Inhalation (PPI Total) Dose (mg/lb AI)		0.1309 (0.0758, 0.2318)	0.3033 (0.1359, 0.6546)
Inhalation (PPI Total) 8-hr TWA ((mg/m^3)/lb AI)		0.0164 (0.0095, 0.0290)	0.0379 (0.0170, 0.0818)

Table 16. Arithmetic mean and 95th percentile estimates from lognormal simple random sampling model for normalized exposure for Vol 15 gals

Exposure Route	Clothing	Arithmetic Mean (95% Confidence Interval)	95th Percentile (95% Confidence Interval)
Dermal (mg/lb AI)	Long Dermal	45.57 (35.01, 59.36)	73.66 (48.52, 108.86)
	Short Dermal	125.25 (86.48, 182.01)	235.92 (132.89, 403.68)
	Long Short Dermal	73.54 (51.75, 104.71)	134.96 (78.15, 225.02)
	Hands Only	27.04 (20.52, 35.67)	44.50 (28.80, 66.88)

Exposure Route	Clothing	Arithmetic Mean (95% Confidence Interval)	95th Percentile (95% Confidence Interval)
Inhalation (OVS Total) Concentration ((mg/m^3)/lb AI)		0.558 (0.458, 0.681)	0.811 (0.591, 1.090)
Inhalation (OVS Total) Dose (mg/lb AI)		1.076 (0.848, 1.367)	1.670 (1.144, 2.381)
Inhalation (OVS Total) 8-hr TWA ((mg/m^3)/lb AI)		0.134 (0.106, 0.171)	0.209 (0.143, 0.298)
Inhalation (PPI Total) Concentration ((mg/m^3)/lb AI)		0.0763 (0.0643, 0.0907)	0.1060 (0.0805, 0.1372)
Inhalation (PPI Total) Dose (mg/lb AI)		0.1494 (0.1156, 0.1933)	0.2390 (0.1590, 0.3498)
Inhalation (PPI Total) 8-hr TWA ((mg/m^3)/lb AI)		0.0187 (0.0145, 0.0242)	0.0299 (0.0199, 0.0437)

Table 17. Arithmetic mean and 95th percentile estimates from lognormal simple random sampling model for normalized exposure for Vol 30 gals.

Exposure Route	Clothing	Arithmetic Mean (95% Confidence Interval)	95th Percentile (95% Confidence Interval)
Dermal (mg/lb AI)	Long Dermal	36.57 (27.09, 49.44)	62.09 (38.33, 97.43)
	Short Dermal	91.94 (57.17, 149.61)	194.72 (93.83, 385.08)
	Long Short Dermal	52.80 (35.53, 79.04)	101.91 (54.76, 182.07)
	Hands Only	20.62 (16.94, 25.16)	29.80 (21.59, 40.27)
Inhalation (OVS Total) Concentration ((mg/m^3)/lb AI)		0.303 (0.239, 0.384)	0.466 (0.318, 0.666)
Inhalation (OVS Total) Dose (mg/lb AI)		0.871 (0.708, 1.073)	1.279 (0.913, 1.752)
Inhalation (OVS Total) 8-hr TWA ((mg/m^3)/lb AI)		0.109 (0.089, 0.134)	0.160 (0.114, 0.219)
Inhalation (PPI Total) Concentration ((mg/m^3)/lb AI)		0.039 (0.0241, 0.0450)	0.0568 (0.0345, 0.0905)
Inhalation (PPI Total) Dose (mg/lb AI)		0.0933 (0.0725, 0.1202)	0.1473 (0.0979, 0.2155)
Inhalation (PPI Total) 8-hr TWA ((mg/m^3)/lb AI)		0.0117 (0.0091, 0.0150)	0.0184 (0.0122, 0.0269)

For each group and exposure route, the two statistical models were fitted to the observed data and the summary statistics listed above were calculated together with 95% confidence intervals. The 95% confidence intervals in Tables 12 to 17 were computed using a parametric bootstrap. For these calculations, the parametric bootstrap simulations were all generated from the fitted lognormal simple random sampling model, even for the empirical summary statistics, on the basis that the lognormal simple random sampling model is the best choice for modeling the data, even if the summary statistics are developed from a simpler statistical model. For example, in Tables 1 to 10, the empirical

arithmetic means are presented, which are the arithmetic means of the 18 measurements for the "All" group, the 9 measurements in both concentration groups "Conc 1200 ppm" and "Conc 12000 ppm," and the 6 measurements in each of the three volume groups "Vol 10 gals, "Vol 15 gals", and "Vol 30 gals." To estimate the uncertainty of those empirical arithmetic means, data are simulated from the lognormal simple random sampling model to calculate the parametric bootstrap confidence intervals. The arithmetic means in Tables 12 to 17 are estimated using the lognormal simple random sampling model, which is also used to estimate the confidence intervals in Tables 12 to 17. The unit exposure estimates (from the lognormal simple random sampling model) displayed in Tables 12 to 17 are recommended over the empirical arithmetic means and 95th percentiles displayed in Tables 1 to 10.

The algorithm used was as follows:

Step 1:
Assume that there are N subjects in a data subset. (N = 18 for the "All" group, N = 9 for the concentration groups, and N = 6 for the volume groups.)
Simulate N random variables Y, X from the estimated lognormal distribution superimposed upon the observed sampling structure ---;

Y = LnGM + RanNor(Seed)×Sr

X = exp(Y)

where:

LnGM = natural logarithm of fitted geometric mean

Sr = natural logarithm of fitted geometric standard deviation

Step 2:
For Y:

Calculate GMs = exp(EAM)

Calculate GSDs = exp(Su)

Calculate AMu = GMs×exp(0.5×Su×Su)

Calculate P95u = GMs× exp(Z95×Su)

where:

EAM = sample arithmetic mean of Y = AMu

Su = standard deviation of Y

For X:

Calculate arithmetic mean AMs

Calculate 95th percentile P95s

Step 3: Repeat Steps 1 and 2 10,000 times.

Steps 1 to 3 result in 10,000 values each for each of GSDs, GMs, AMs, AMu, P95s, and P95u. 95% confidence intervals can be defined for each parameter by the 2.5th and 97.5th percentiles (lower and upper, respectively) of the bootstrap distribution of that corresponding parameter. Note that by definition, GSDs = GSDu and GMs = GMu.

5. Non-detects

For all the analyses presented in this memorandum except for Table 18 and Table 29, measurements below the LOQ or LOD were replaced by the mid-value, the midpoint of the lowest and highest possible value for that measurement. This

only impacts the OVS sampler data since all other values were above the LOQ. In Table 18 we investigated the impact on the summary statistics of the exposure values below the LOQ, i.e., censored values.

None of the residues for dermal exposure (hand wash, face/neck wipes, inner and outer dosimeters including painter hats) were non-detects. There were no PVC filter sections with residues below the detection limit (LOQ = 0.1 µg, LOD = 0.03 µg).

There were 77 OVS tube front sections and 77 OVS tube back sections. There were four OVS tube front sections with residues below the detection limit (LOQ = 2 µg, LOD = 0.6 µg). There were 74 OVS tube back sections (i.e., all but 3) with residues below the detection limit. In the study report, the OVS tube sections with values below the LOD were assigned a value of 0, and the OVS tube sections with values below the LOQ but above the LOD were assigned a value of 1 µg. For this memorandum we used different assignments more consistent with these upper bounds: The OVS tube sections with values below the LOD of 0.6 µg were assigned a value of 0.3 µg, half the LOD. The OVS tube sections with values below the LOQ of 2 µg but above the LOD of 0.6 µg were assigned a value of 1.3 µg, the midpoint of the LOD and LOQ. These choices have little impact on the results because each OVS sample is the sum of several residue values, there were only four non-detects for the front sections, and most of the back sections were below the LOD. Unless otherwise stated, for most of the analyses of OVS residues in this memorandum, we used these midpoint values to replace the non-detect values and then added these midpoint values to the other measured residues from the same ME. For some of the analyses we also calculated the minimum and maximum residue adding the other measured residues for the same ME to the minimum and maximum for the non-detect sections. For sections below the LOD, the minimum residue is 0 µg and the maximum residue is 0.6 µg. For sections above the LOD but below the LOQ, the minimum residue is 0.6 µg and the maximum residue is 2.0 µg.

for the Inhalation (OVS Total) exposure metrics, we used the approach in the last paragraph to compute the arithmetic mean and 95th percentiles using the recommended substitution of the midpoint value for section values below the LOQ and compared those results to estimates using the alternative substitutions of the minimum and maximum for that non-detect section. We also investigated a censored maximum likelihood statistical method described in the following paragraph.

The lognormal simple random sampling model assumes that the exposure values are independent and identically lognormally distributed. For uncensored values with a mass m, the mass is between a lower bound of m and an upper bound of m. For censored mass values, the mass value is known to be between a lower bound and an upper bound. The SAS procedure LIFEREG was used to fit the lognormal model to the combined censored and uncensored data using the maximum likelihood method. The procedure produces estimates of the geometric mean and geometric standard deviation for the fitted lognormal distribution.

To calculate confidence intervals for the arithmetic means and 95th percentiles, a parametric bootstrap method was used. This is exactly the same bootstrap method that was used for the original case where the non-detects were replaced by the midpoint value. 10,000 values of the unit exposure were simulated from the fitted lognormal distribution, and for each simulation, the geometric mean and geometric standard deviation were calculated and used to calculate the arithmetic mean (AMu) and 95th percentile (P95u) of the corresponding lognormal distribution. The simulated unit exposures are all uncensored numerical values even though the corresponding residues can be lower than the LOQs. The confidence intervals for the AMu and P95u range from the 2.5th percentile to the 97.5th percentile.

Results for all the exposure metrics are presented in Table 18. The results are compared for the default substitution of the midpoint value (“mid value”) the alternative substitutions of the maximum value (“max value”) and minimum value

("min value"), and estimates calculated using the maximum likelihood method for censored data, referred to as "Censored data MLE."

Table 18. Exposure summary statistics for Inhalation (OVS Total) calculated using alternative estimated exposures for values below the LOQ*

Exposure Route	Method for Substituting Values Below the LOQ**	Arithmetic Mean	95th Percentile
Inhalation (OVS total) concentration ((mg/m^3)/lb AI)	Substitute mid value	0.5274 (0.4271, 0.6529)	0.9895 (0.7182, 1.3518)
	Substitute max value	0.5446 (0.4416, 0.6732)	1.0187 (0.7407, 1.3892)
	Substitute min value	0.5104 (0.4121, 0.6338)	0.9635 (0.6967, 1.3211)
	Censored data MLE	0.5242 (0.4274, 0.6444)	0.9682 (0.7094, 1.3107)
Inhalation (OVS total) dose (mg/lb AI)	Substitute mid value	0.9931 (0.8624, 1.1441)	1.5616 (1.2535, 1.9340)
	Substitute max value	1.0267 (0.8914, 1.1829)	1.6147 (1.2960, 2.0002)
	Substitute min value	0.9598 (0.8320, 1.1075)	1.5160 (1.2139, 1.8821)
	Censored data MLE	0.9899 (0.8634, 1.1354)	1.5373 (1.2423, 1.8917)
Inhalation (OVS Total) 8-hr TWA ((mg/m^3)/lb AI)	Substitute mid value	0.1241 (0.1078, 0.1430)	0.1952 (0.1567, 0.2418)
	Substitute max value	0.1283 (0.1114, 0.1479)	0.2018 (0.1620, 0.2500)
	Substitute min value	0.1200 (0.1040, 0.1384)	0.1895 (0.1517, 0.2353)
	Censored data MLE	0.1237 (0.1079, 0.1419)	0.1922 (0.1553, 0.2365)

*There were no non-detects for dermal or Inhalation (PPI Total) exposure.
**For each OVS tube section below the LOD (0.6 µg), the mid value residue is 0.3 µg, the max value residue is 0.6 µg, and the min value residue is 0 µg. For each OVS tube section above the LOD but below the LOQ (2.0 µg), the mid value residue is 1.3 µg, the max value residue is 2.0 µg, and the min value is 0.6 µg.

The results in Table 18 show small impacts of the alternative substitution approaches for treating values below the LOQ on the unit exposure arithmetic mean and 95th percentile.

6. Fold Relative Accuracy

Fold relative accuracy (*fRA*) is a measure that can be used to determine how well a statistic can describe its population parameter. Let us assume θ is a parameter and T is the sample statistic of θ (i.e., an estimate of θ). If the 2.5th and 97.5th percentiles of the sampling distribution of T can be denoted by $T_{2.5}$ and $T_{97.5}$, respectively, then the 95th percentile of sample fold relative accuracy can be theoretically calculated using the following formula provided in the AHETF Governing Document (AHETF, 2007, pg. 136 and AHETF, 2011, pg. 120):

$$fRA_{95} = \text{Max}\,(T_{97.5} / \theta, \theta / T_{2.5})$$

The actual value of θ is unknown. Thus, fRA_{95} was calculated by substituting θ with T. If the fRA_{95} of a statistic were equal to 3, then it would be correct to say: "At least 95% of the time the sample statistic will be accurate to within 3-fold of the population value". According to the AHETF Governing Document, the statistical design of the exposure monitoring study should be adequate to produce a fRA_{95} less than or equal to 3. Thus the confidence intervals calculated

in the above algorithm can be used to estimate the fold relative accuracy and compare the observed fRA with the study design benchmark of 3. If the observed fold relative accuracy is greater than 3, this means that the experiment did not meet the benchmark, which would be due to differences between the distributions of the data used to design the study and the experimental data collected in the study. If the fold relative accuracy benchmark is not met, then it might be desirable to collect more data for this scenario in order to meet the benchmark. The fRA_{95} is also referred to as the K-factor.

Following HSRB recommendations, confidence intervals were estimated using both a parametric bootstrap approach, as described above, and the following non-parametric bootstrap approach. The non-parametric bootstrap method should be more robust since it does not assume that the fitted parametric model is the correct one. For the non-parametric bootstrap, exactly the same algorithm was used except that Step 1 above was replaced by the following:

Step 1:
Simulate N random variables Y, X by resampling at random with replacement from the original data:

The original exposure data are X(1), X(2), …, X(N), where N is the number of subjects in the data set.
Sample N values at random with replacement from the exposure values X(1), X(2), …, X(N). This gives the N simulated random variables X.
Y = log(X).

7. Detailed Summary Statistics with Confidence Intervals and Fold Relative Accuracy

Table 19 to Table 28 present the estimates, parametric and non-parametric confidence intervals and fold relative accuracy values for all the summary statistics for the All group. All these analyses use non-detects substituted by the mid-value; this only impacts the analyses of the OVS Total exposure metrics.

Table 19. Arithmetic mean, geometric mean, geometric standard deviation, and 95th percentiles (with 95% confidence intervals and fold relative accuracy), for different statistical models of the normalized long dermal exposure (mg/lb AI) using All data

		Parametric Bootstrap			Non-parametric Bootstrap		
Parameter	Estimate	Lower Bound	Upper Bound	Fold Relative Accuracy	Lower Bound	Upper Bound	Fold Relative Accuracy
GSDs	1.55	1.34	1.80	1.16	1.36	1.70	1.14
GMs	39.53	32.38	48.36	1.22	32.44	48.45	1.23
AMs	43.43	35.09	53.49	1.24	34.89	52.93	1.24
AMu	43.55	35.29	53.87	1.24	34.82	53.48	1.25
P95s	93.46	58.78	146.75	1.59	59.43	93.46	1.57
P95u	81.57	59.27	111.31	1.38	57.64	105.14	1.42

Table 20. Arithmetic mean, geometric mean, geometric standard deviation, and 95th percentiles (with 95% confidence intervals and fold relative accuracy), for different statistical models of the normalized short dermal exposure (mg/lb AI) using All data

		Parametric Bootstrap			Non-parametric Bootstrap		
Parameter	Estimate	Lower Bound	Upper Bound	Fold Relative Accuracy	Lower Bound	Upper Bound	Fold Relative Accuracy
GSDs	1.66	1.40	1.97	1.19	1.43	1.83	1.16
GMs	92.31	73.43	116.37	1.26	73.95	116.03	1.26
AMs	104.42	81.58	133.38	1.28	81.14	130.36	1.29
AMu	104.89	82.04	134.41	1.28	80.98	132.59	1.30
P95s	228.46	145.56	416.00	1.82	146.38	228.46	1.56
P95u	212.01	146.94	302.93	1.44	142.80	281.26	1.48

Table 21. Arithmetic mean, geometric mean, geometric standard deviation, and 95th percentiles (with 95% confidence intervals and fold relative accuracy), for different statistical models of the normalized long short dermal exposure (mg/lb AI) using All data

		Parametric Bootstrap			Non-parametric Bootstrap		
Parameter	Estimate	Lower Bound	Upper Bound	Fold Relative Accuracy	Lower Bound	Upper Bound	Fold Relative Accuracy
GSDs	1.62	1.38	1.91	1.18	1.42	1.77	1.14
GMs	56.66	45.52	70.73	1.25	45.71	70.84	1.25
AMs	63.50	50.13	80.01	1.27	49.62	78.81	1.28
AMu	63.70	50.44	80.64	1.27	49.50	80.04	1.29
P95s	142.04	87.63	239.46	1.69	90.53	142.04	1.57
P95u	125.61	88.43	176.76	1.42	85.55	164.87	1.47

Table 22. Arithmetic mean, geometric mean, geometric standard deviation, and 95th percentiles (with 95% confidence intervals and fold relative accuracy), for different statistical models of the normalized hands only exposure (mg/lb AI) using All data

		Parametric Bootstrap			Non-parametric Bootstrap		
Parameter	Estimate	Lower Bound	Upper Bound	Fold Relative Accuracy	Lower Bound	Upper Bound	Fold Relative Accuracy
GSDs	1.65	1.40	1.95	1.18	1.40	1.85	1.18
GMs	23.10	18.44	29.02	1.26	18.48	28.99	1.26
AMs	26.06	20.42	33.11	1.28	20.21	32.78	1.29
AMu	26.15	20.54	33.37	1.28	20.20	33.21	1.29
P95s	62.14	36.17	101.75	1.72	34.19	62.14	1.82
P95u	52.39	36.51	74.45	1.43	35.12	71.05	1.49

Table 23. Arithmetic mean, geometric mean, geometric standard deviation, and 95th percentiles (with 95% confidence intervals and fold relative accuracy), for different statistical models of the normalized inhalation (OVS total) concentration exposure ((mg/m³)/lb AI) using All data

		Parametric Bootstrap			Non-parametric Bootstrap		
Parameter	Estimate	Lower Bound	Upper Bound	Fold Relative Accuracy	Lower Bound	Upper Bound	Fold Relative Accuracy
GSDs	1.556	1.345	1.807	1.16	1.351	1.722	1.15
GMs	0.478	0.392	0.586	1.22	0.390	0.578	1.23
AMs	0.521	0.425	0.648	1.25	0.430	0.613	1.21
AMu	0.527	0.427	0.653	1.24	0.433	0.621	1.22
P95s	0.875	0.712	1.784	2.04	0.713	0.875	1.23
P95u	0.990	0.718	1.352	1.38	0.773	1.173	1.28

Table 24. Arithmetic mean, geometric mean, geometric standard deviation, and 95th percentiles (with 95% confidence intervals and fold relative accuracy), for different statistical models of the normalized inhalation (OVS total) dose exposure (mg/lb AI) using All data

		Parametric Bootstrap			Non-parametric Bootstrap		
Parameter	Estimate	Lower Bound	Upper Bound	Fold Relative Accuracy	Lower Bound	Upper Bound	Fold Relative Accuracy
GSDs	1.354	1.225	1.501	1.11	1.223	1.442	1.11
GMs	0.949	0.827	1.090	1.15	0.830	1.086	1.15
AMs	0.992	0.861	1.141	1.15	0.855	1.140	1.16
AMu	0.993	0.862	1.144	1.15	0.855	1.143	1.16
P95s	1.610	1.246	2.339	1.45	1.318	1.610	1.22
P95u	1.562	1.253	1.934	1.25	1.197	1.880	1.30

Table 25. Arithmetic mean, geometric mean, geometric standard deviation, and 95th percentiles (with 95% confidence intervals and fold relative accuracy), for different statistical models of the normalized inhalation (OVS total) time-weighted average concentration exposure ((mg/m³)/lb AI) using All data

		Parametric Bootstrap			Non-parametric Bootstrap		
Parameter	Estimate	Lower Bound	Upper Bound	Fold Relative Accuracy	Lower Bound	Upper Bound	Fold Relative Accuracy
GSDs	1.354	1.225	1.501	1.11	1.223	1.442	1.11
GMs	0.119	0.103	0.136	1.15	0.104	0.136	1.15
AMs	0.124	0.108	0.143	1.15	0.107	0.142	1.16
AMu	0.124	0.108	0.143	1.15	0.107	0.143	1.16
P95s	0.201	0.156	0.292	1.45	0.165	0.201	1.22
P95u	0.195	0.157	0.242	1.25	0.150	0.235	1.30

Table 26. Arithmetic mean, geometric mean, geometric standard deviation, and 95th percentiles (with 95% confidence intervals and fold relative accuracy), for different statistical models of the normalized inhalation (PPI Total) concentration exposure ((mg/m³)/lb AI) using All data

		Parametric Bootstrap			Non-parametric Bootstrap		
Parameter	Estimate	Lower Bound	Upper Bound	Fold Relative Accuracy	Lower Bound	Upper Bound	Fold Relative Accuracy
GSDs	1.7659	1.4642	2.1414	1.21	1.4631	2.0358	1.21
GMs	0.0559	0.0432	0.0726	1.30	0.0434	0.0717	1.29
AMs	0.0643	0.0493	0.0866	1.35	0.0500	0.0799	1.29
AMu	0.0657	0.0497	0.0874	1.33	0.0506	0.0821	1.30
P95s	0.1364	0.0933	0.3041	2.23	0.0901	0.1364	1.51
P95u	0.1425	0.0943	0.2129	1.51	0.0983	0.1858	1.45

Table 27. Arithmetic mean, geometric mean, geometric standard deviation, and 95th percentiles (with 95% confidence intervals and fold relative accuracy), for different statistical models of the normalized inhalation (PPI Total) dose exposure (mg/lb AI) using All data

		Parametric Bootstrap			Non-parametric Bootstrap		
Parameter	Estimate	Lower Bound	Upper Bound	Fold Relative Accuracy	Lower Bound	Upper Bound	Fold Relative Accuracy
GSDs	1.5876	1.3634	1.8571	1.17	1.3574	1.7704	1.17
GMs	0.1107	0.0898	0.1368	1.24	0.0901	0.1364	1.23
AMs	0.1225	0.0980	0.1529	1.25	0.0978	0.1501	1.25
AMu	0.1232	0.0987	0.1542	1.25	0.0981	0.1520	1.26
P95s	0.2615	0.1679	0.4385	1.68	0.1835	0.2615	1.42
P95u	0.2368	0.1693	0.3281	1.40	0.1637	0.3088	1.45

Table 28. Arithmetic mean, geometric mean, geometric standard deviation, and 95th percentiles (with 95% confidence intervals and fold relative accuracy), for different statistical models of the normalized inhalation (PPI Total) time-weighted average concentration exposure ((mg/m³)/lb AI) using All data

		Parametric Bootstrap			Non-parametric Bootstrap		
Parameter	Estimate	Lower Bound	Upper Bound	Fold Relative Accuracy	Lower Bound	Upper Bound	Fold Relative Accuracy
GSDs	1.5876	1.3634	1.8571	1.17	1.3574	1.7704	1.17
GMs	0.0138	0.0112	0.0171	1.24	0.0113	0.0171	1.23
AMs	0.0153	0.0123	0.0191	1.25	0.0122	0.0188	1.25
AMu	0.0154	0.0123	0.0193	1.25	0.0123	0.0190	1.26
P95s	0.0327	0.0210	0.0548	1.68	0.0229	0.0327	1.42
P95u	0.0296	0.0212	0.0410	1.40	0.0205	0.0386	1.45

Tables 19 to 28 show that the study benchmark design value of 3 for the fold relative accuracy was met in every case. In fact, this benchmark was also met for every case in the five concentration and volume groups with the sole exception of a value of 3.05 for the hands only exposure empirical 95th percentile in the group “Vol 10 gals” using the parametric bootstrap.

8. Empirical Quantile Plots

Quantile-quantile plots of the normalized exposure values were used to evaluate whether the data were lognormally distributed, as implied by the assumed statistical lognormal models. These plots were intended to help determine whether the data supported using untransformed normalized exposure values (exposure per pound AI) or log-transformed values or neither. The plots are not intended to evaluate the fitted regression models for the un-normalized exposure to be described in Section 9 below, for which the residual quantile plots were developed.

In each case the quantile-quantile plot compared the observed quantiles of the measured values with the corresponding quantiles of a normal or lognormal distribution. A perfect fit would imply that the plotted values lie in a straight line. The quantile-quantile plots for all exposure routes are presented in Figure 2 to Figure 21. Although in some cases the difference between the normal and log-normal fits is small, the plots seems to show a little better fit for the lognormal distributions, supporting the use of the log-transformed exposure values over the untransformed values.

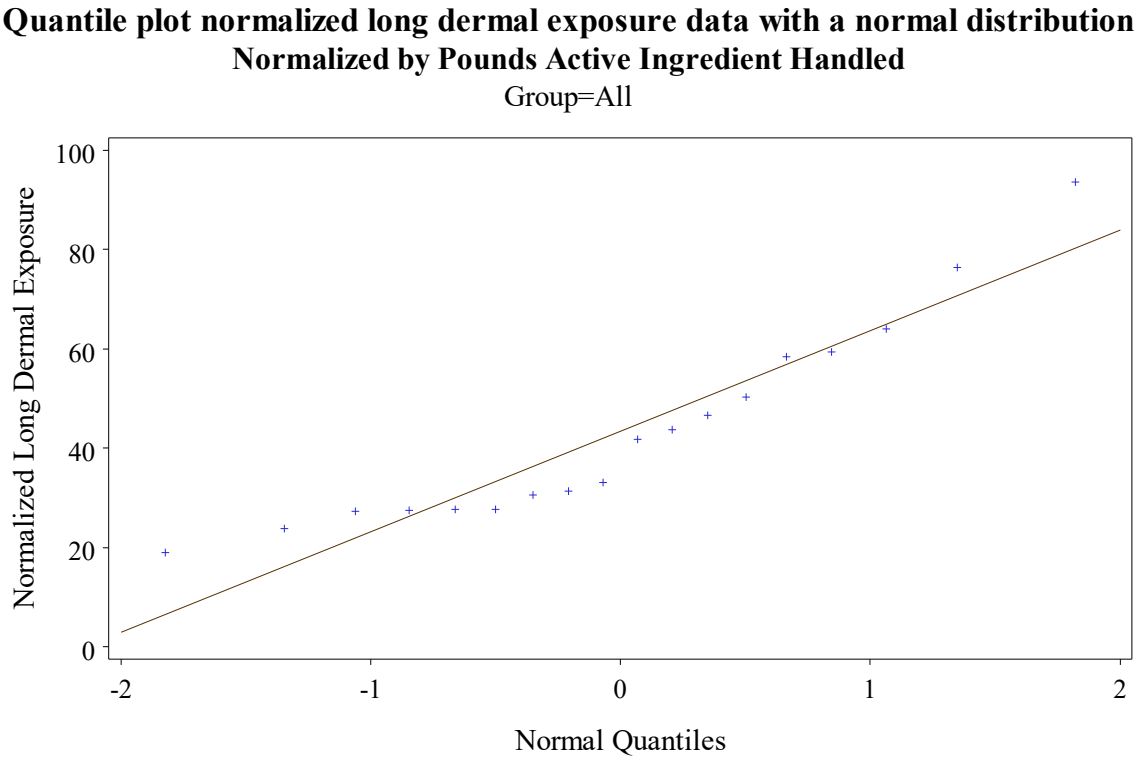


Figure 2. Empirical quantile plot for Long Dermal, with a normal distribution

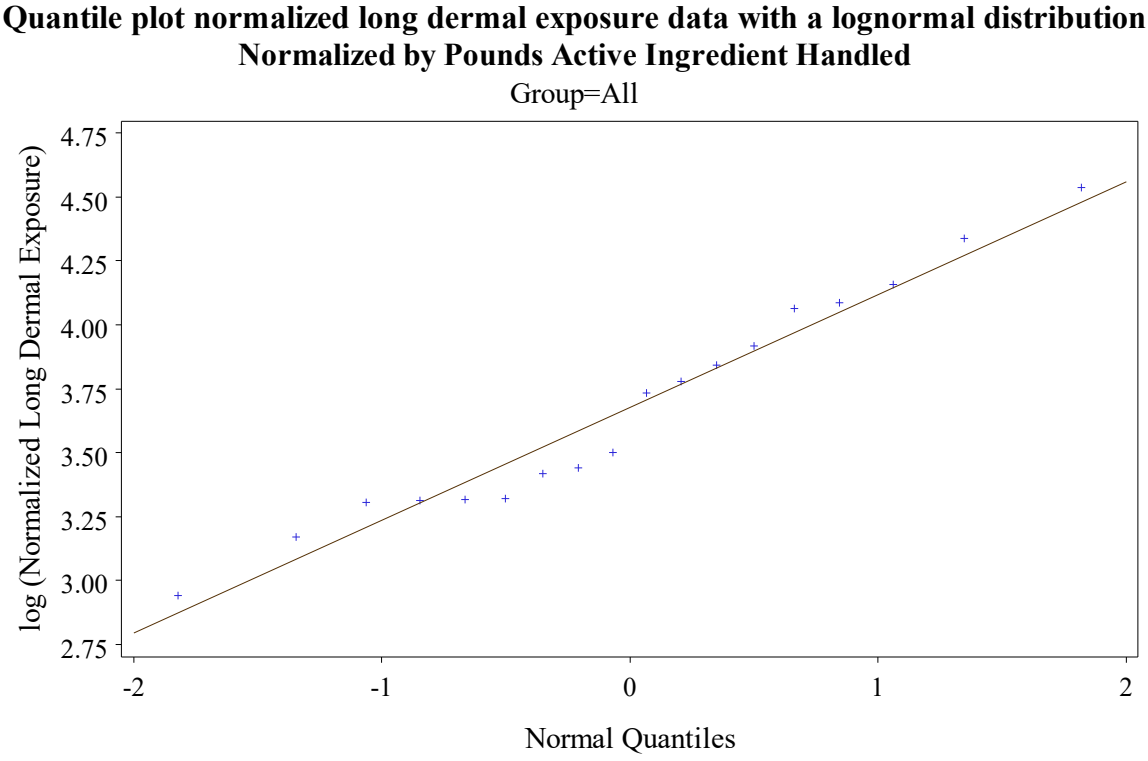


Figure 3. Empirical quantile plot for Long Dermal, with a lognormal distribution

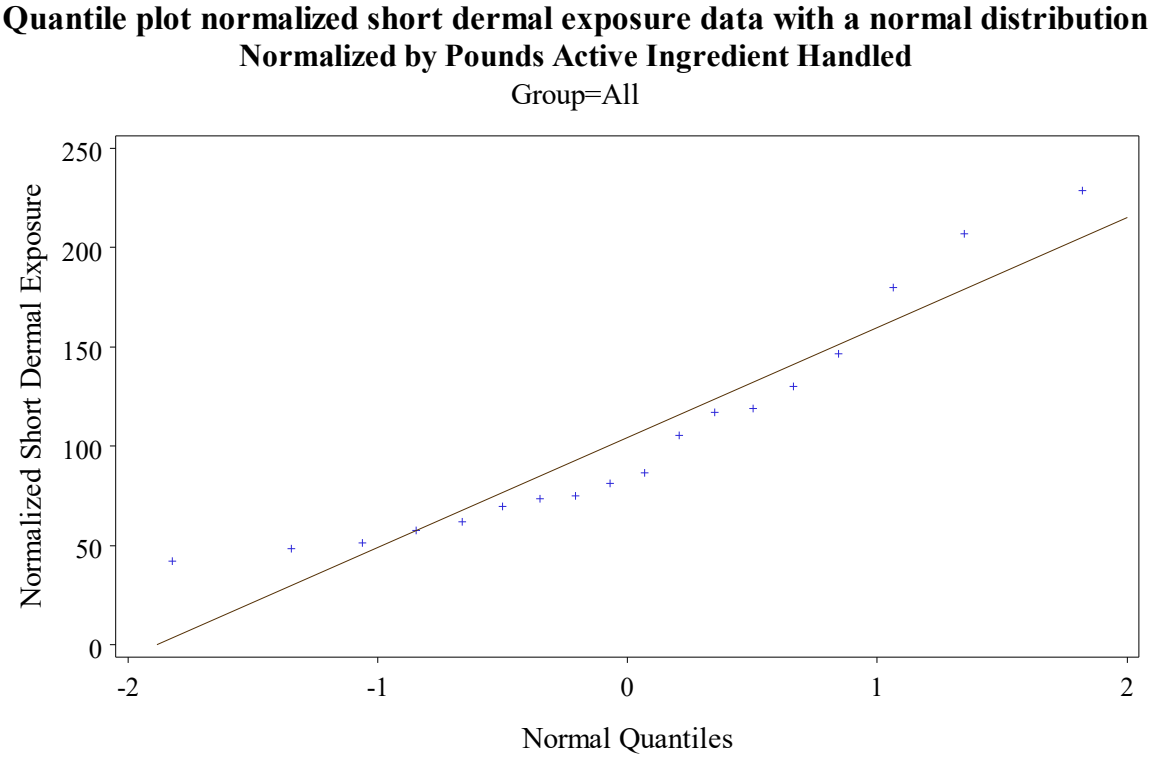


Figure 4. Empirical quantile plot for Short Dermal, with a normal distribution

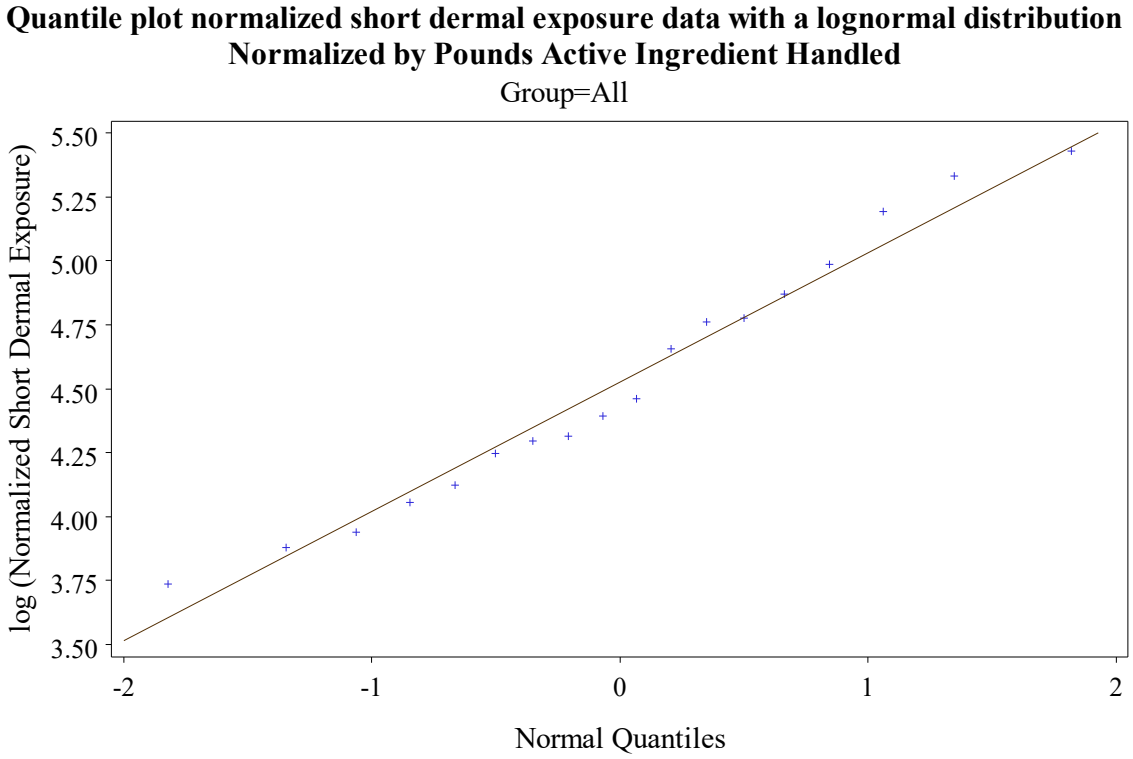


Figure 5. Empirical quantile plot for Short Dermal, with a lognormal distribution

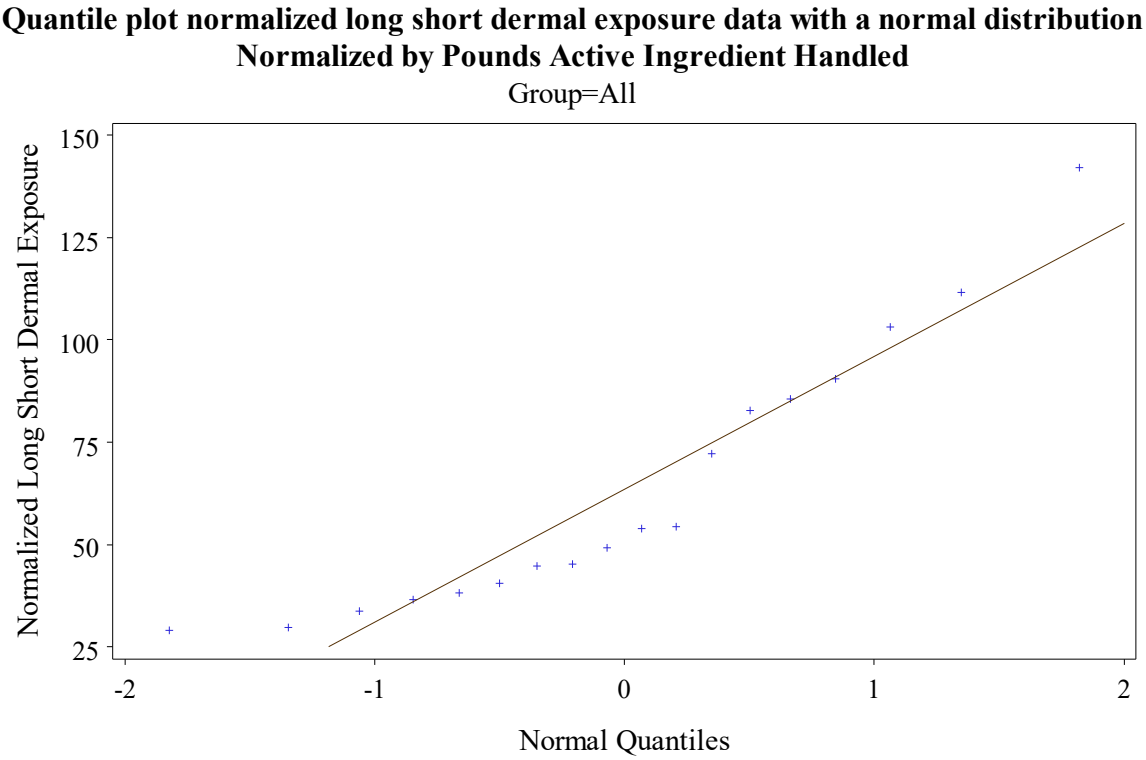


Figure 6. Empirical quantile plot for Long Short Dermal, with a normal distribution

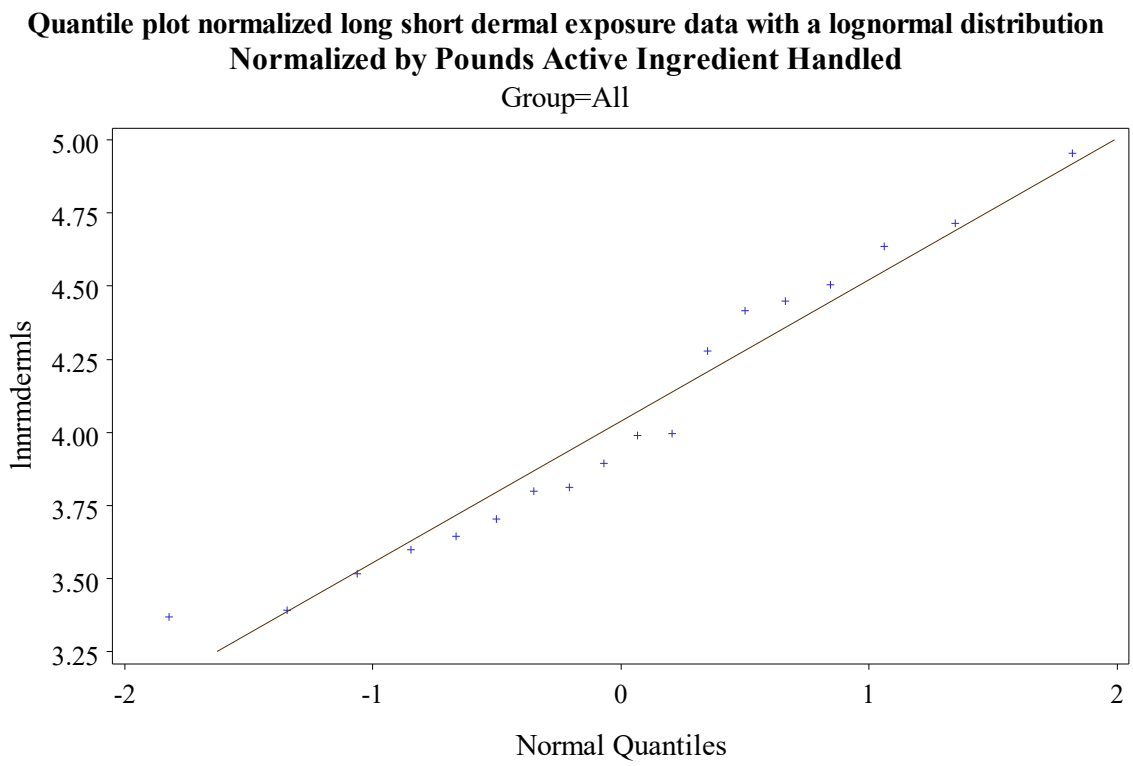


Figure 7. Empirical quantile plot for Long Short Dermal, with a lognormal distribution

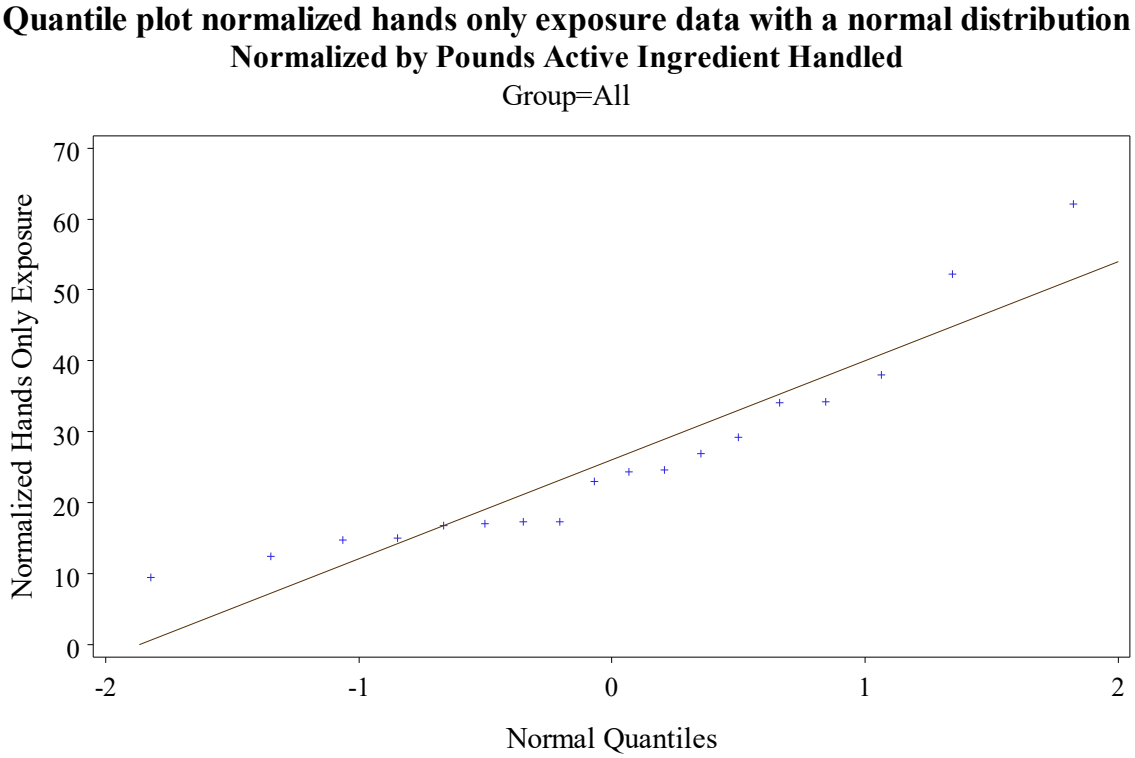


Figure 8. Empirical quantile plot for Hands Only, with a normal distribution

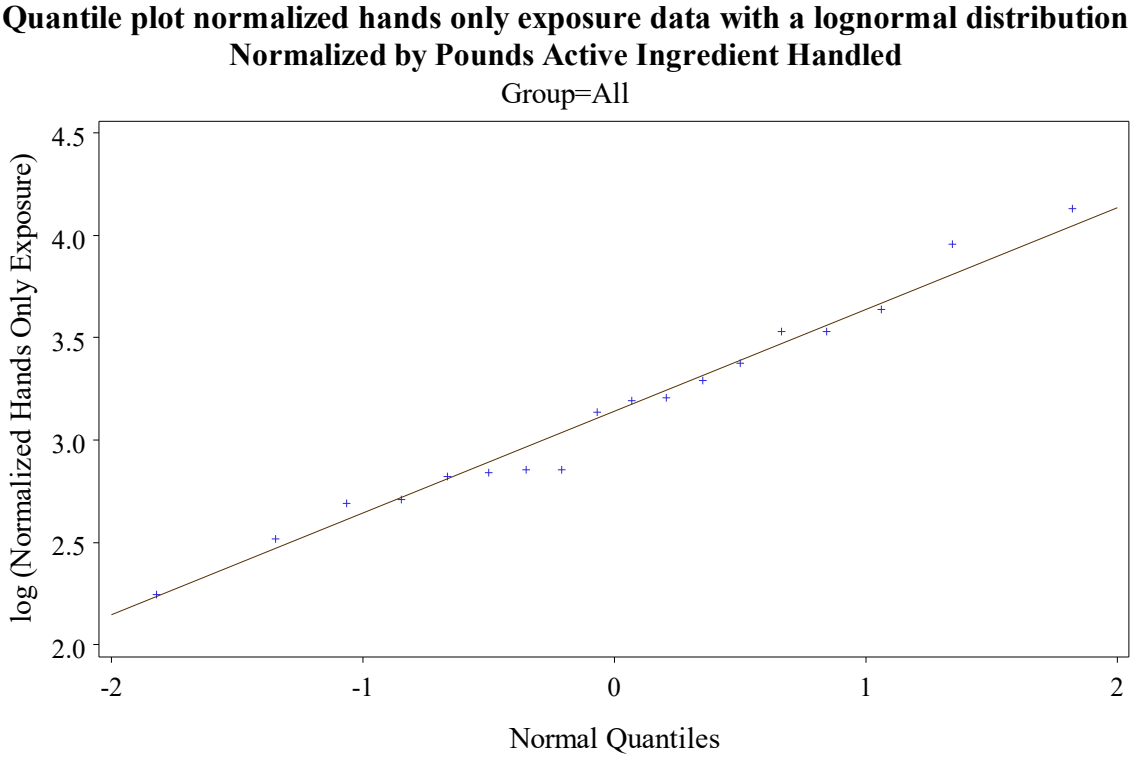


Figure 9. Empirical quantile plot for Hands Only, with a lognormal distribution

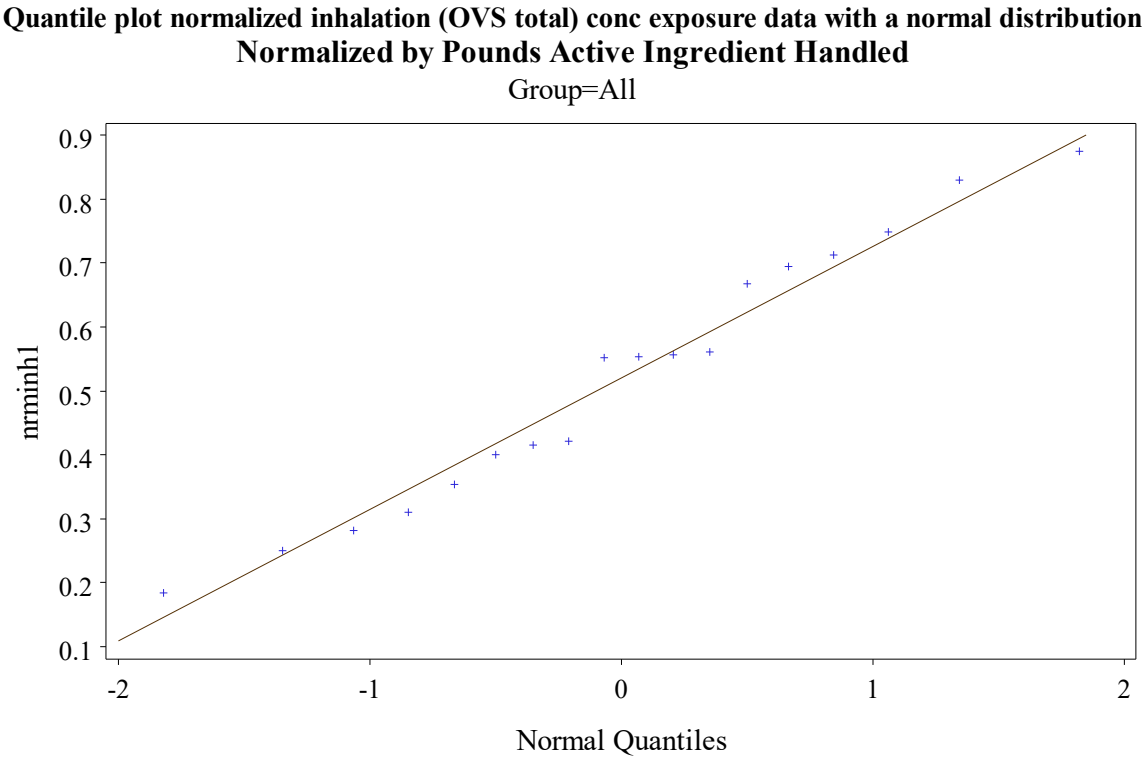


Figure 10. Empirical quantile plot for Inhalation (OVS Total) Concentration, with a normal distribution

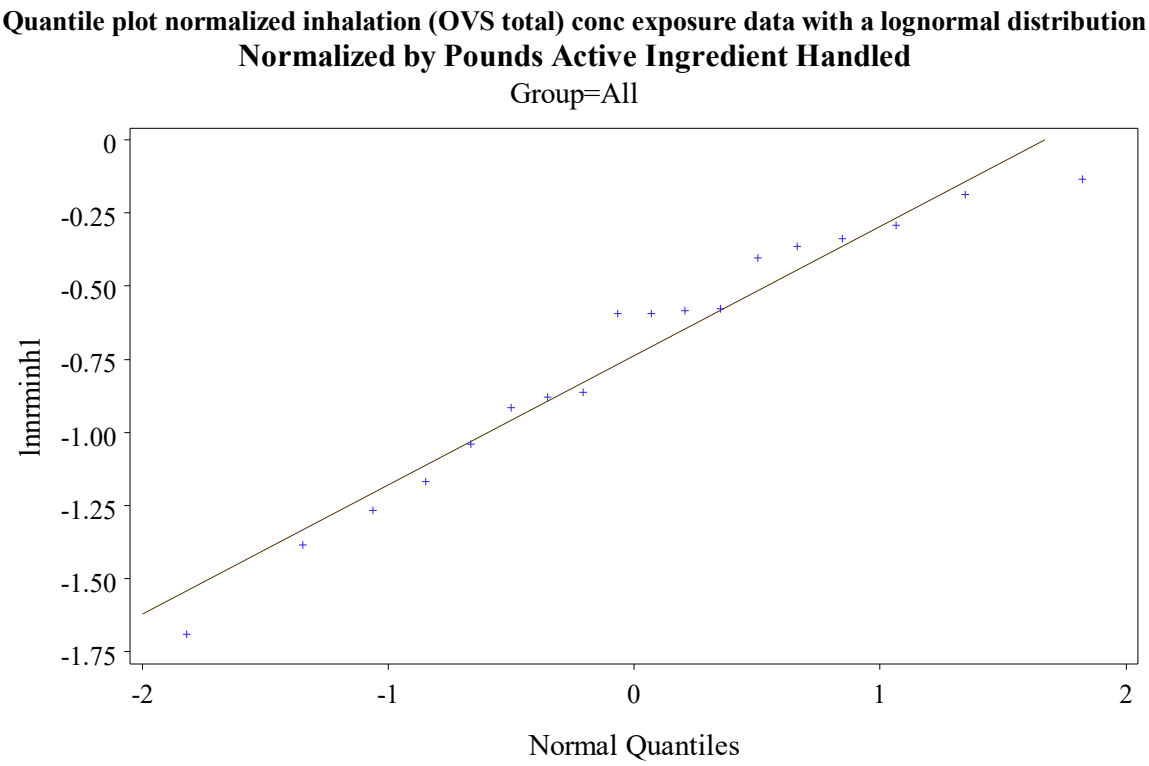


Figure 11. Empirical quantile plot for Inhalation (OVS Total) Concentration, with a lognormal distribution

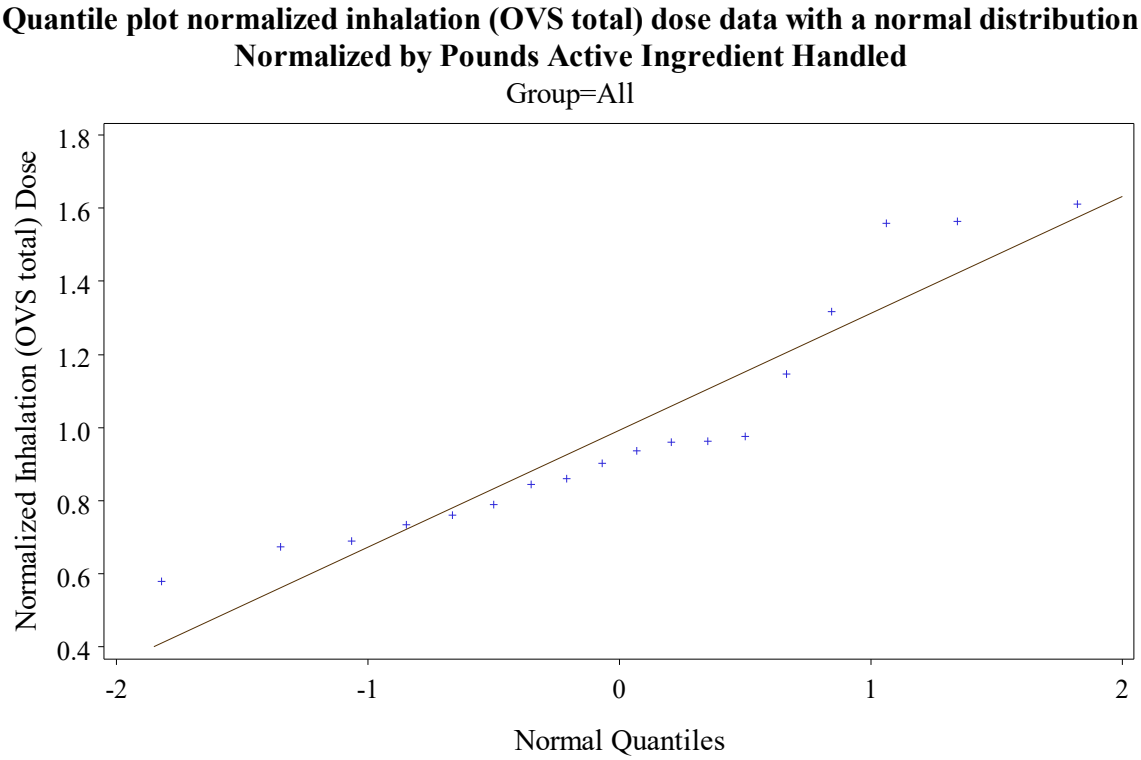


Figure 12. Empirical quantile plot for Inhalation (OVS Total) Dose, with a normal distribution

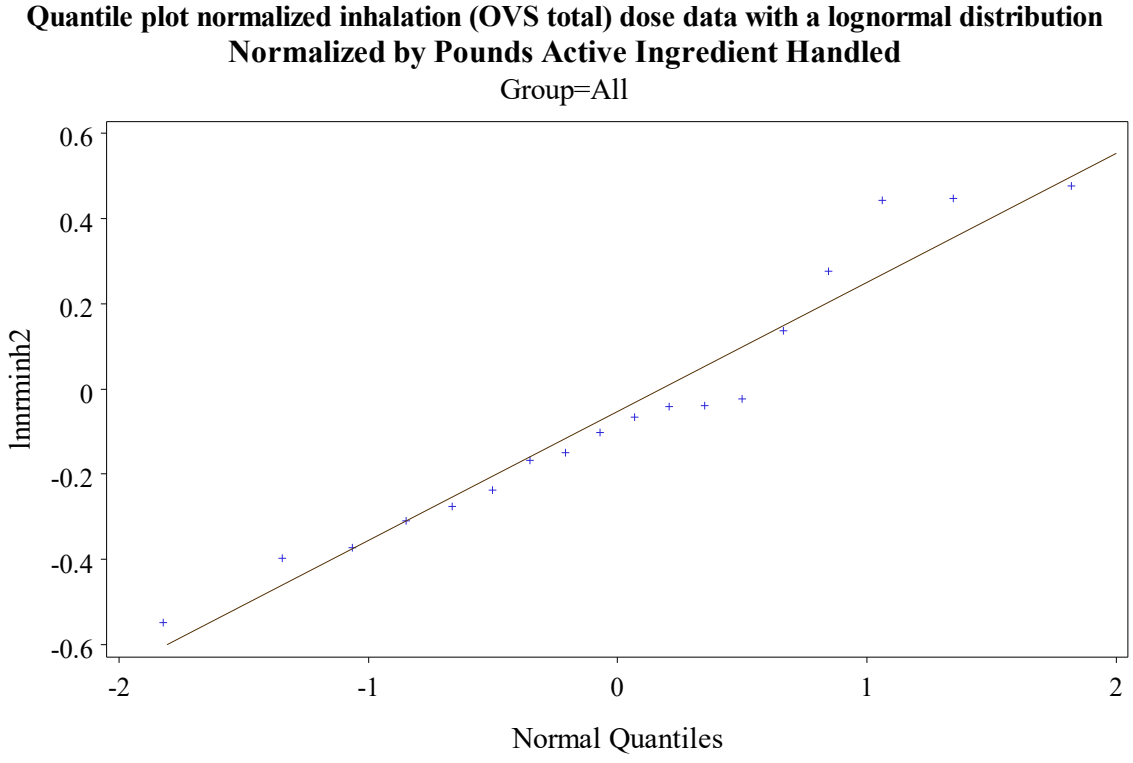


Figure 13. Empirical quantile plot for Inhalation (OVS Total) Dose, with a lognormal distribution

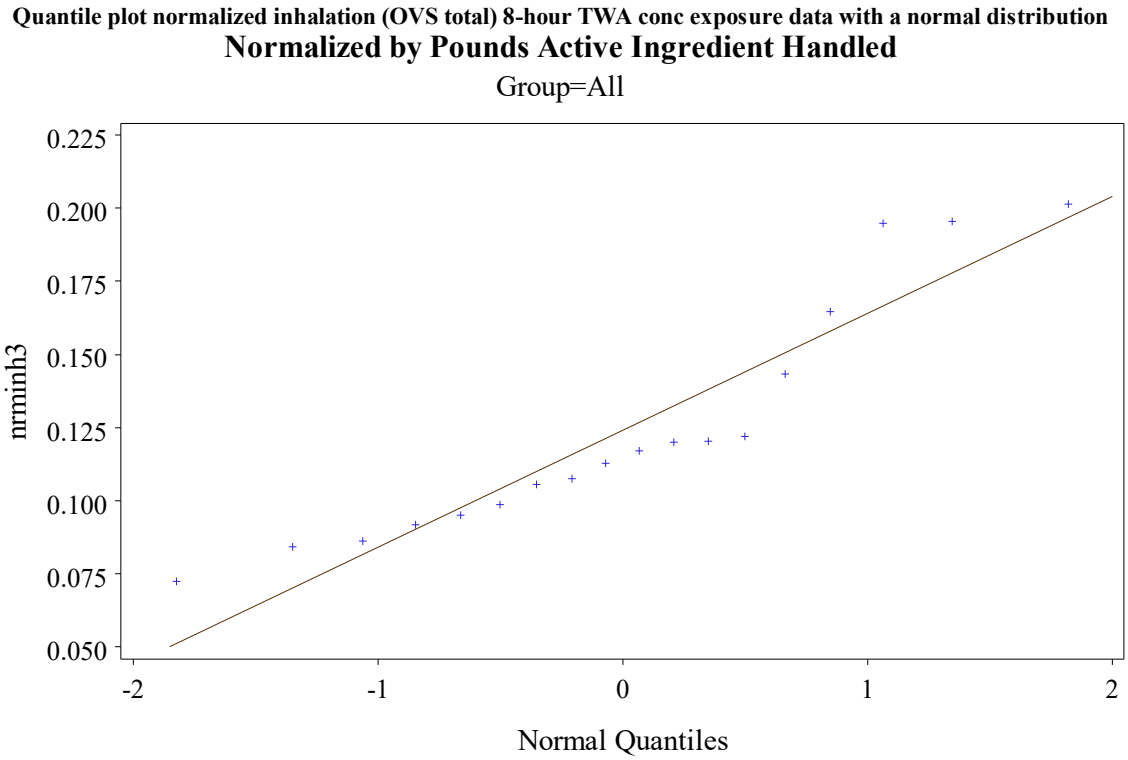


Figure 14. Empirical quantile plot for Inhalation (OVS Total) Time-weighted Average Conc, with a normal distribution

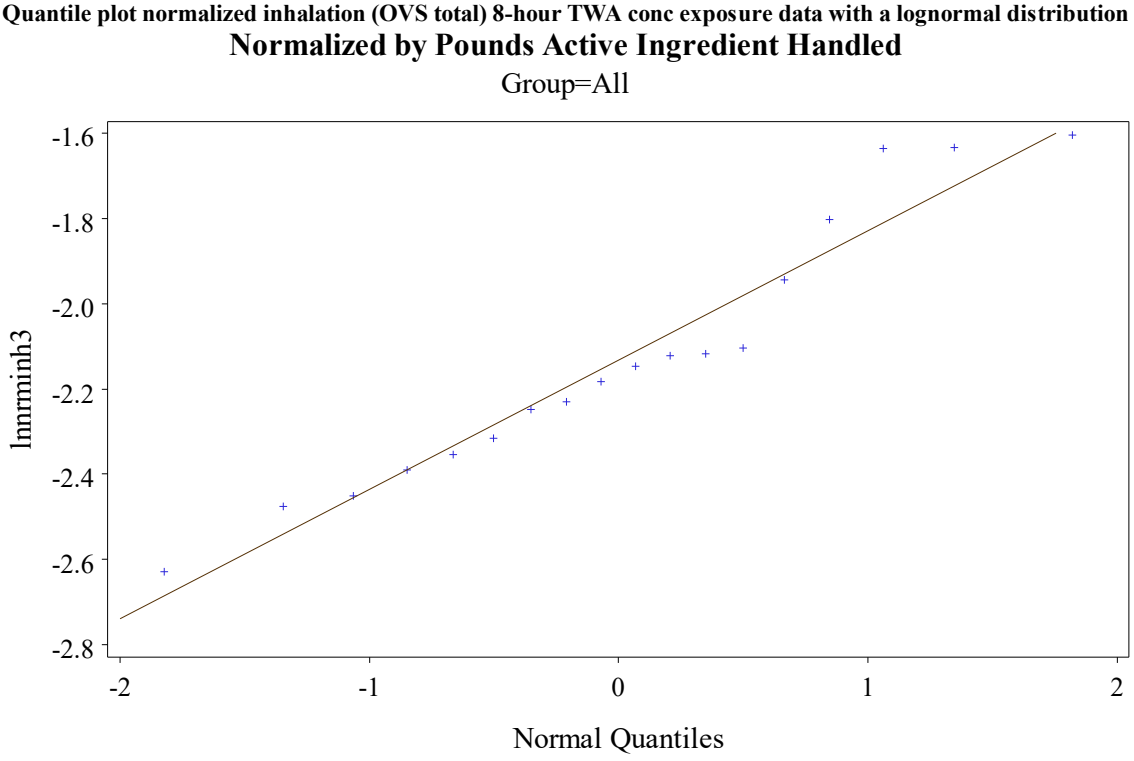


Figure 15. Empirical quantile plot for Inhalation (OVS Total) Time-weighted Average Conc, with a lognormal distribution

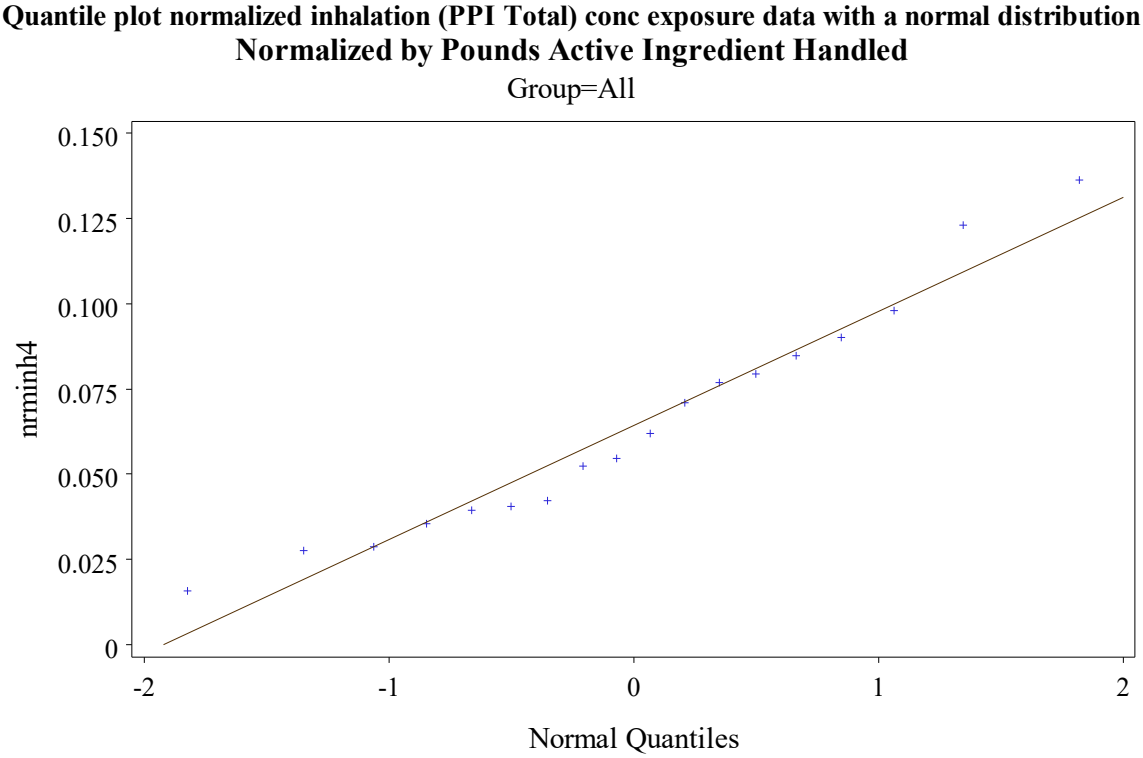


Figure 16. Empirical quantile plot for Inhalation (PPI Total) Concentration, with a normal distribution

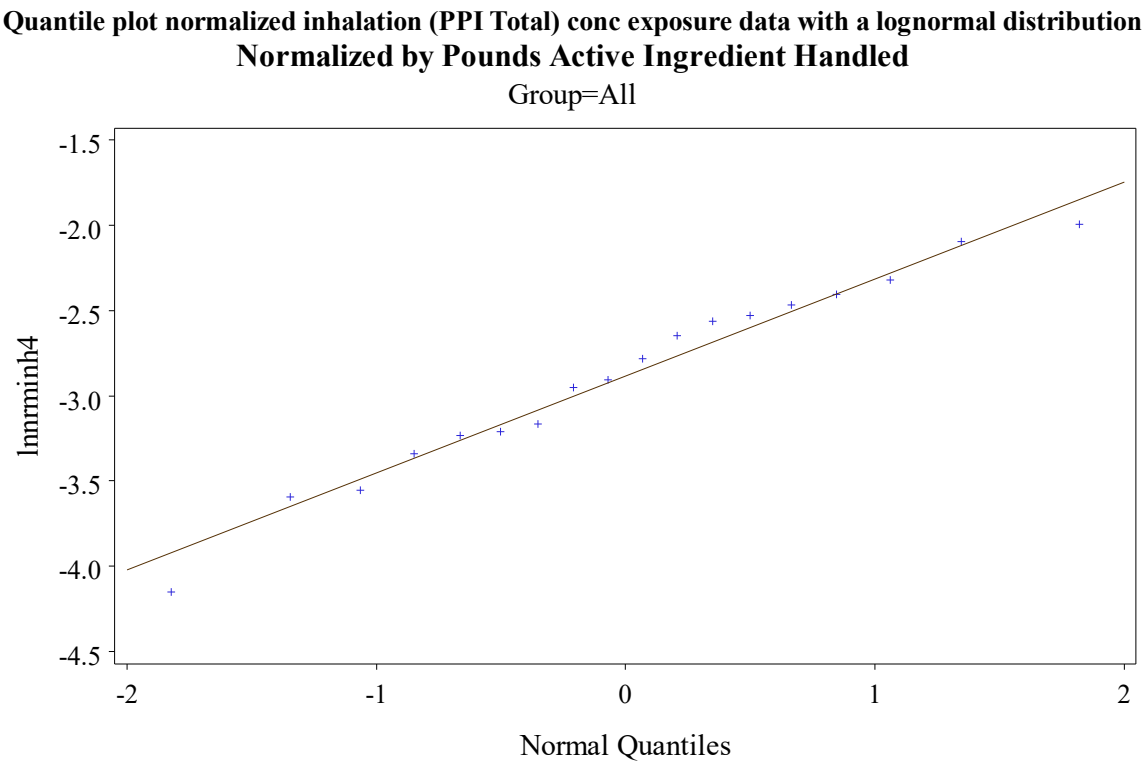


Figure 17. Empirical quantile plot for Inhalation (PPI Total) Concentration, with a lognormal distribution

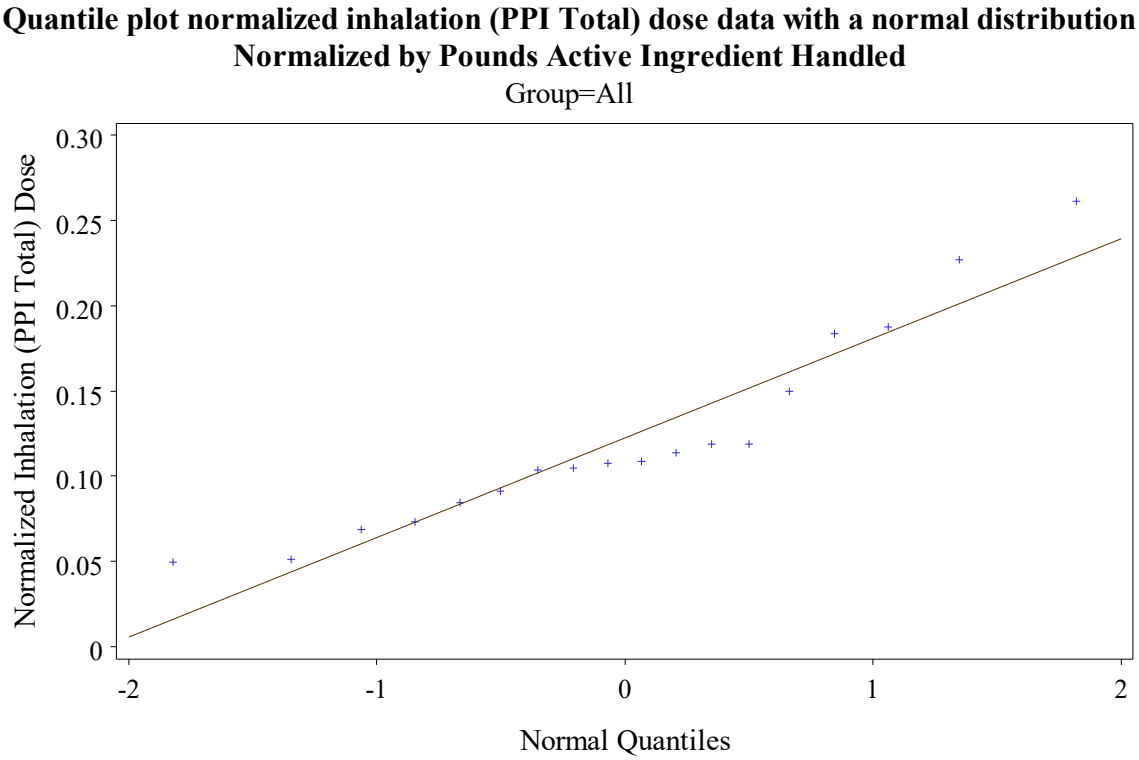


Figure 18. Empirical quantile plot for Inhalation (PPI Total) Dose, with a normal distribution

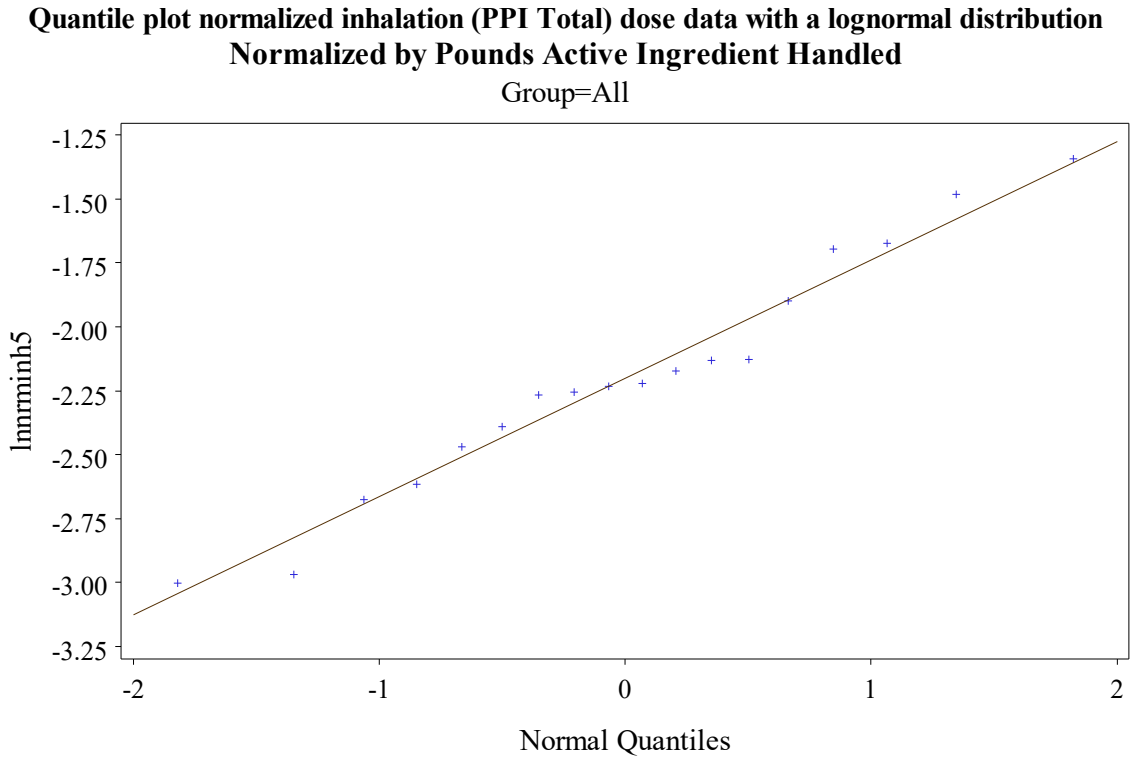


Figure 19. Empirical quantile plot for Inhalation (PPI Total) Dose, with a lognormal distribution

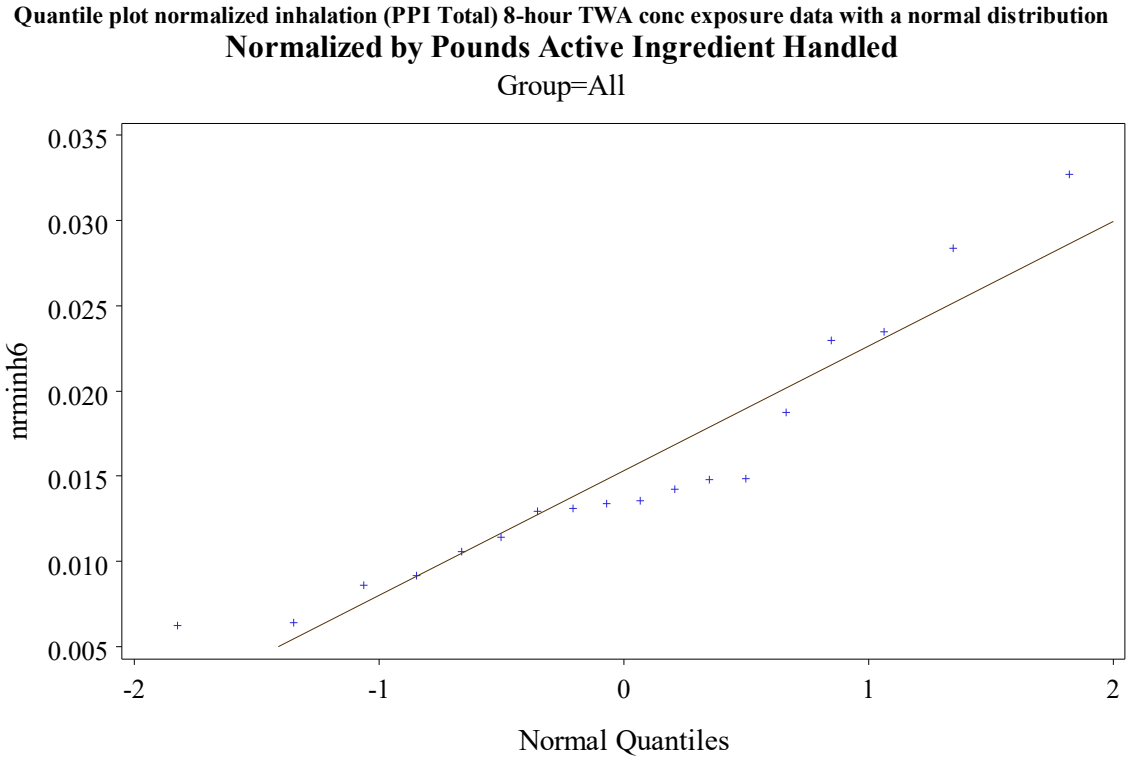


Figure 20. Empirical quantile plot for Inhalation (PPI Total) Time-Weighted Average Conc, with a normal distribution

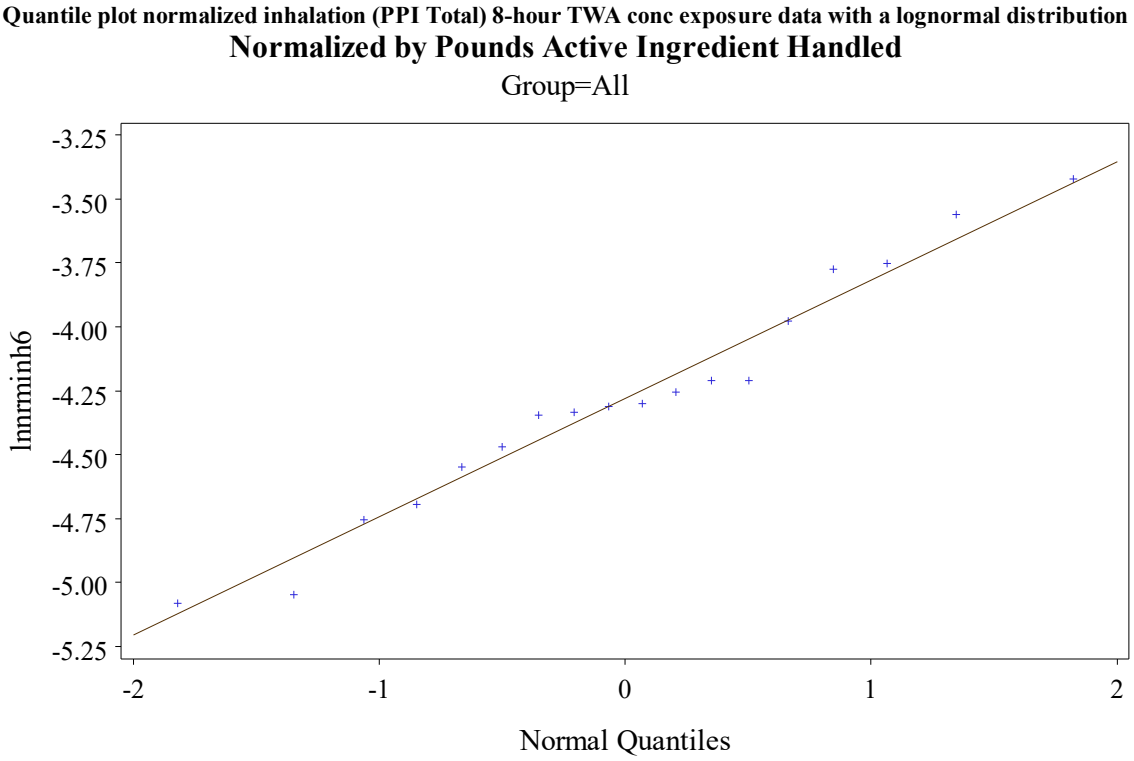


Figure 21. Empirical quantile plot for Inhalation (PPI Total) Time-Weighted Average Conc, with a normal distribution

9. Log-log-Linearity Analyses and Estimated Log-log Slopes

The use of the normalized or unit exposure is based on the assumption that the exposure is proportional to the normalizing variable pounds of active ingredient handled. Exact proportionality is defined as

Exposure = K × Pounds of Active Ingredient,

where K is the proportionality constant. Exact proportionality implies that

Normalized Exposure = Exposure / Pounds of Active Ingredient = K,

so that if the pounds of active ingredient is doubled, then the exposure is exactly doubled, which is not a reasonable assumption due to the variability of exposure for any given amount of active ingredient. Instead of exact proportionality we allow for random multiplicative error terms, which do not depend on the amount of active ingredient, so that

Exposure = K × Pounds of Active Ingredient × Multiplicative Errors, or

Normalized Exposure = K × Multiplicative Errors.

Since the above quantile plots generally support the assumption that the normalized exposure is lognormally distributed, we can take natural logarithms of both sides to get a log-log-linear model of the form

Log (Exposure) = Intercept + 1 × Log (Pounds of Active Ingredient) + Error Terms.

The statistical analyses of log-log-linearity, previously referred to as proportionality, is based on the following more general log-log-linear statistical model:

Linear Model

Log (Exposure) = Intercept + Slope × Log (Pounds of Active Ingredient) + Random Error.

The Random Error terms are assumed to be normally distributed with a mean of zero and a variance of Varerror. The error terms are also assumed to be independent of the amount of active ingredient, which is the explanatory variable in this regression model. The values of Intercept, Slope, and Varerror are parameters of the fitted model. This linear model is for the Exposure rather than the Normalized Exposure (Exposure / AI).

Using this model, taking exponentials of both sides gives

Exposure = $e^{\text{Intercept}} \times (\text{Pounds of Active Ingredient})^{\text{Slope}} \times e^{\text{Random Error}}$, so that

E{Exposure | AI} = Expected Exposure Given the Pounds of Active Ingredient

= C × (Pounds of Active Ingredient)$^{\text{Slope}}$, where

C = Expected Value $\{e^{\text{Intercept}} \times e^{\text{Random Error}}\} = e^{\text{Intercept}} \times e^{\text{Varerror}/2}$

The value of E{Exposure | AI} is the arithmetic mean of the distribution of exposures for a future set of randomly selected consumers or workers that are all pouring exactly the same amount of active ingredient, AI. The parameters Intercept and Varerror are unknown, but are estimated by fitting the linear model to the solid pour data.

Therefore, the expected exposure given the AI will be proportional to the pounds of active ingredient if and only if the Slope in the linear model equals 1. Note that the proportionality constant is C, which is very different to the estimated value of Slope.

Lognormal Model

If the value of Slope in the linear model is 1, then

Log (Exposure) = Intercept + 1 × Log (Pounds of Active Ingredient) + Random Error,

so that

Log (Normalized Exposure) = Log(Exposure / Pounds of Active Ingredient)

= Intercept + Random Error,

This statistical model is exactly the same as the lognormal simple random sampling model that was defined above.

The same calculations that we used for the linear model give

E{Exposure | AI} = Expected Exposure Given the Pounds of Active Ingredient

= C* × (Pounds of Active Ingredient), where

C* = Expected Value $\{e^{Intercept^* \times Random\ Error}\} = e^{Intercept^*} \times e^{Varerror^*/2}$

These parameters are shown with asterisks to emphasize that they will in general be different from the ones for the model with a slope parameter not necessarily equal to 1.

Test for log-log-linearity with slope 1

Proportionality, or log-log-linearity with slope 1, of exposure to the pounds of active ingredient is statistically modeled by assuming a Slope equal to 1 in the linear model.

Possible alternative models include the same formulation with a slope of zero, implying that the exposure does not depend upon the amount of active ingredient handled, even though the amount of active ingredient handled varied between the subjects as part of the study design. Other possible models include the same model with a slope not equal to zero or one, the quadratic models discussed below, or models with more complicated relationships between the exposure and the experimental conditions. To evaluate and test whether the slope is zero, one, or other possible values, we fitted the above linear model and computed confidence intervals for the slope.

Table 29 shows the 95% confidence intervals for the slope calculated from the above linear model. A confidence interval that includes one but not zero supports the use of unit exposures. A confidence interval that includes zero but not one suggests that the exposure does not depend on the amount of active ingredient handled. A confidence interval that

includes both zero and one suggests that either the basic statistical model is incorrect or there are not enough data to statistically infer whether the slope is zero or one. This table also shows the widths of the confidence intervals used to evaluate the second benchmark for post-hoc power discussed in the next sub-section. The table also shows the values of the threshold amount of active ingredient (pounds) and the corresponding estimated exposure, to be described and discussed below in Section 11. Threshold values were not computed for the censored data models.

There were several non-detects for the inhalation (OVS Total) exposure routes. The rows marked "Substitute mid value" calculate the slope estimates after replacing each non-detect residue for a section by the midpoint of the lowest and highest possible value for that residue. The rows marked "Censored data MLE" calculate the slope estimates for the linear model using a censored maximum likelihood statistical method and the lower and upper bounds for each non-detect that were calculated as described in Section 5. This procedure was implemented using the LIFEREG SAS procedure.

Table 29. 95 percent confidence intervals for the slope of log exposure versus log pounds active ingredient handled

Exposure Route	Treatment of Non-detects	Estimate	Lower	Upper	Width	Threshold	Exposure
Long Dermal (mg)	Not applicable	0.816	0.663	0.969	0.305	0.584	25.437
Short Dermal (mg)	Not applicable	0.820	0.635	1.005	0.370	0.593	62.200
Long Short Dermal (mg)	Not applicable	0.811	0.639	0.983	0.344	0.585	37.270
Hands Only (mg)	Not applicable	0.752	0.595	0.910	0.314	0.551	14.412
Inhalation (OVS Total) Concentration (mg/m^3)	Substitute mid value	0.868	0.700	1.036	0.335	0.620	0.327
	Censored data MLE	0.868	0.722	1.014	0.293		
Inhalation (OVS Total) Dose (mg)	Substitute mid value	0.927	0.808	1.045	0.237	0.648	0.644
	Censored data MLE	0.927	0.824	1.030	0.207		
Inhalation (OVS Total) Time-Weighted Average Concentration (mg/m^3)	Substitute mid value	0.927	0.808	1.045	0.237	0.648	0.080
	Censored data MLE	0.927	0.824	1.030	0.207		
Inhalation (PPI Total) Concentration (mg/m^3)	Not applicable	0.739	0.551	0.928	0.378	0.549	0.0361
Inhalation (PPI Total) Dose (mg)	Not applicable	0.795	0.639	0.952	0.312	0.573	0.0706

Exposure Route	Treatment of Non-detects	Estimate	Lower	Upper	Width	Threshold	Exposure
Inhalation (PPI Total) Time-Weighted Average Concentration (mg/m^3)	Not applicable	0.795	0.639	0.952	0.312	0.573	0.0088

Table 29 gives the slopes for all the exposure routes. The slopes range from 0.74 to 0.93 and the confidence intervals for the slope exclude 0 and in about half of the cases include 1. The upper bounds are all less than 1.1. Thus the assumption of independence was always rejected and the assumption of log-log-linearity with slope 1 was rejected in about half of the cases.

Suppose that the study had a (post-hoc) power of at least 80% for detecting "proportionality" (i.e., log-log-linearity with a slope of 1) under the null hypothesis of independence (slope = 0). It follows that the confidence intervals have an approximate width of 1.4 or less. The results in Table 29 show that observed widths are all below 1.4. The maximum width was about 0.4. Therefore, based on the confidence intervals, the secondary objective of meeting the 80% power for detecting proportionality was met.

Quantile plots for residuals

To evaluate the fitted linear regression models we created quantile-quantile[1] plots of the studentized residuals for each fitted model. The residual is the observed value of log exposure minus the predicted value. The studentized residual is the residual divided by its standard error. For these analyses we used the internally studentized residual where the estimated standard error is calculated using all the data. An alternative approach that is sometimes preferred when checking for outliers in small samples is to use the externally studentized residual where the estimated standard error is calculated after excluding the data point. If the plotted points lie close to the straight line then the model assumptions for the linear model are supported. Furthermore, a standard rule of thumb identifies statistical outliers as cases where the studentized residual is above +3 or below −3 (a stricter criterion of ±2 is sometimes used, and more complex statistical outlier tests taking into account the sample size are also available). These quantile-quantile plots are for the Linear Model. Quantile-quantile plots for the Lognormal Model were presented in the even-numbered Figures 1-20 above, since in that case both the predicted values and the standard errors are the same for every ME. The quantile-quantile plots for all exposure routes other than the OVS and PPI Total Time-weighted average exposure are shown in

[1] These quantile plots compare the distribution of the studentized residuals to a standard normal distribution. Some authors prefer a more exact approach where the distribution of the studentized residuals is compared to a t distribution. That method is not easily available using current SAS software.

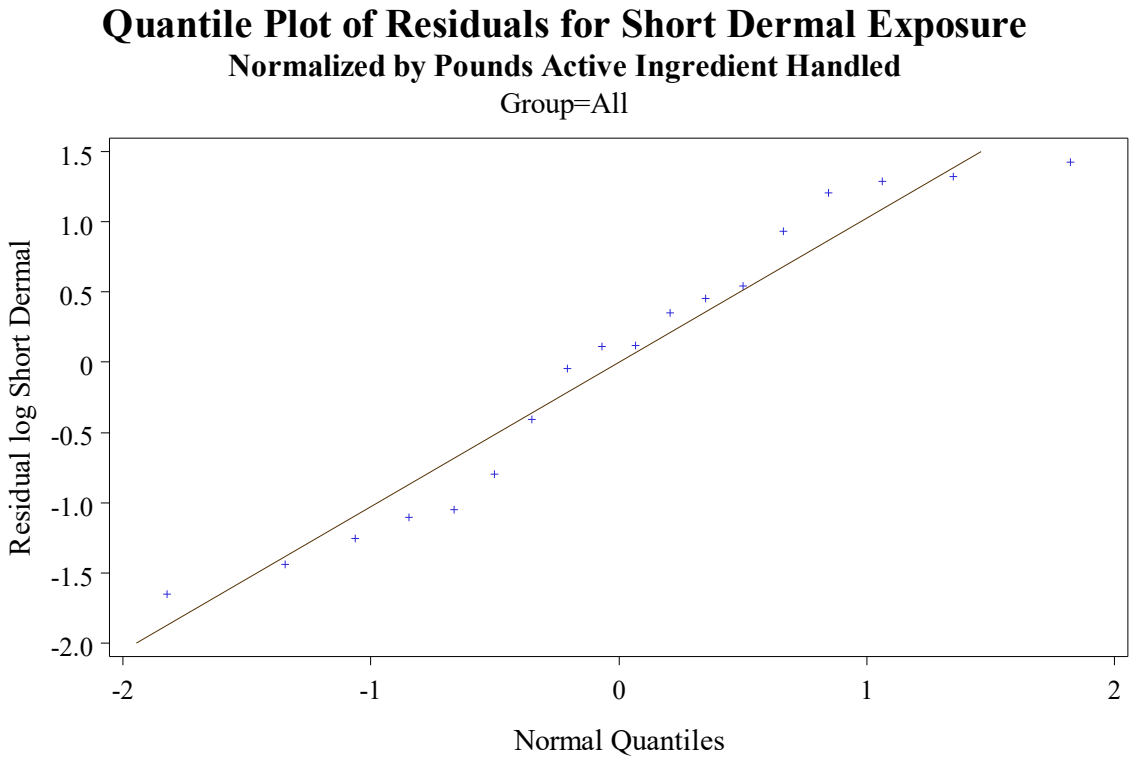


Figure 22. Quantile plot of residuals from linear model for Short Dermal

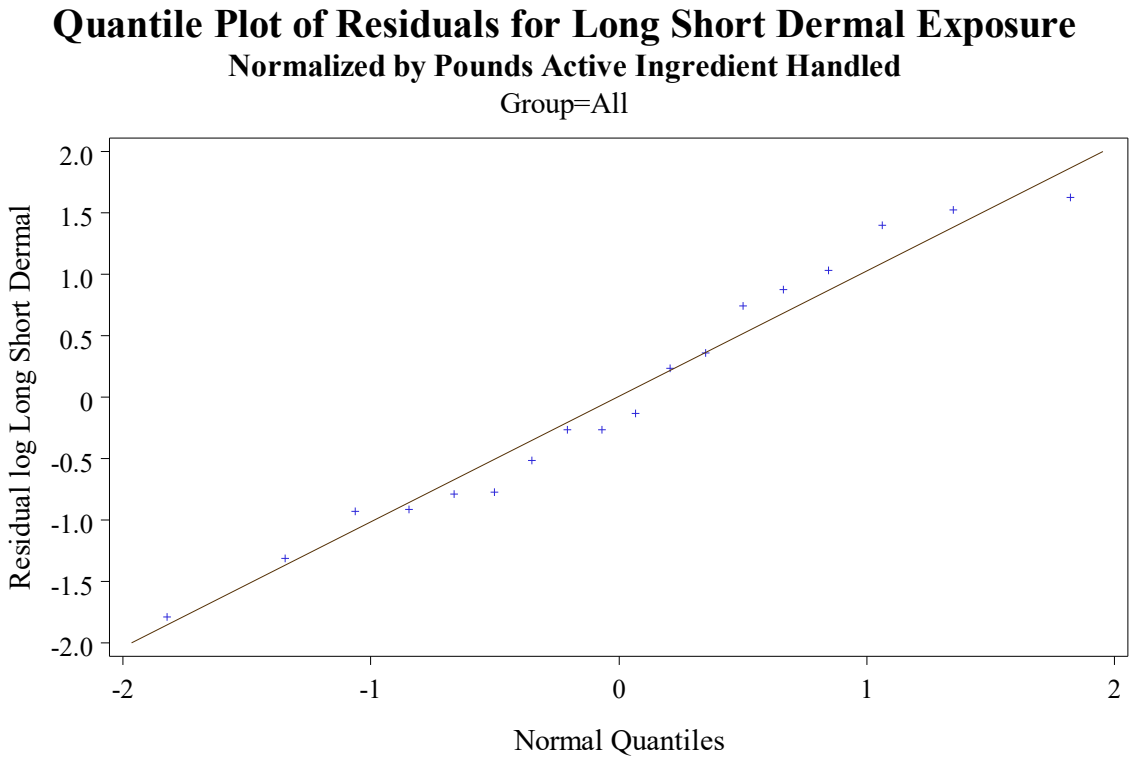


Figure 23. Quantile plot of residuals from linear model for Long Short Dermal

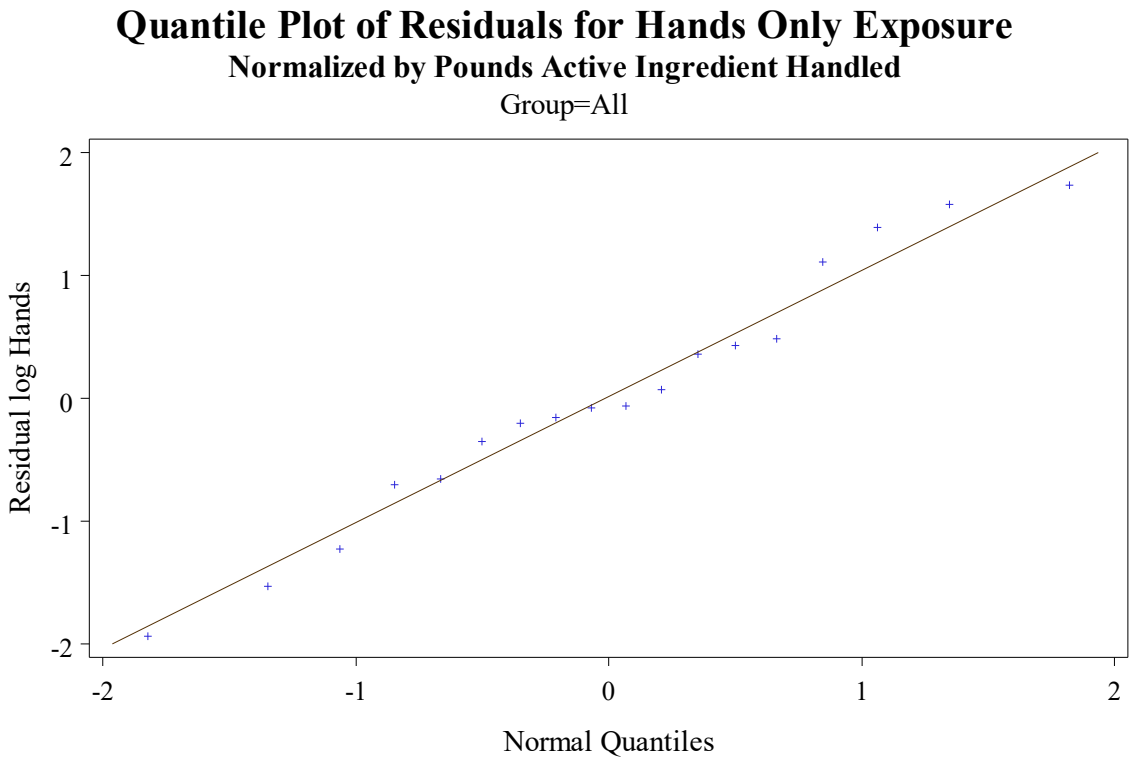


Figure 24. Quantile plot of residuals from linear model for Hands Only

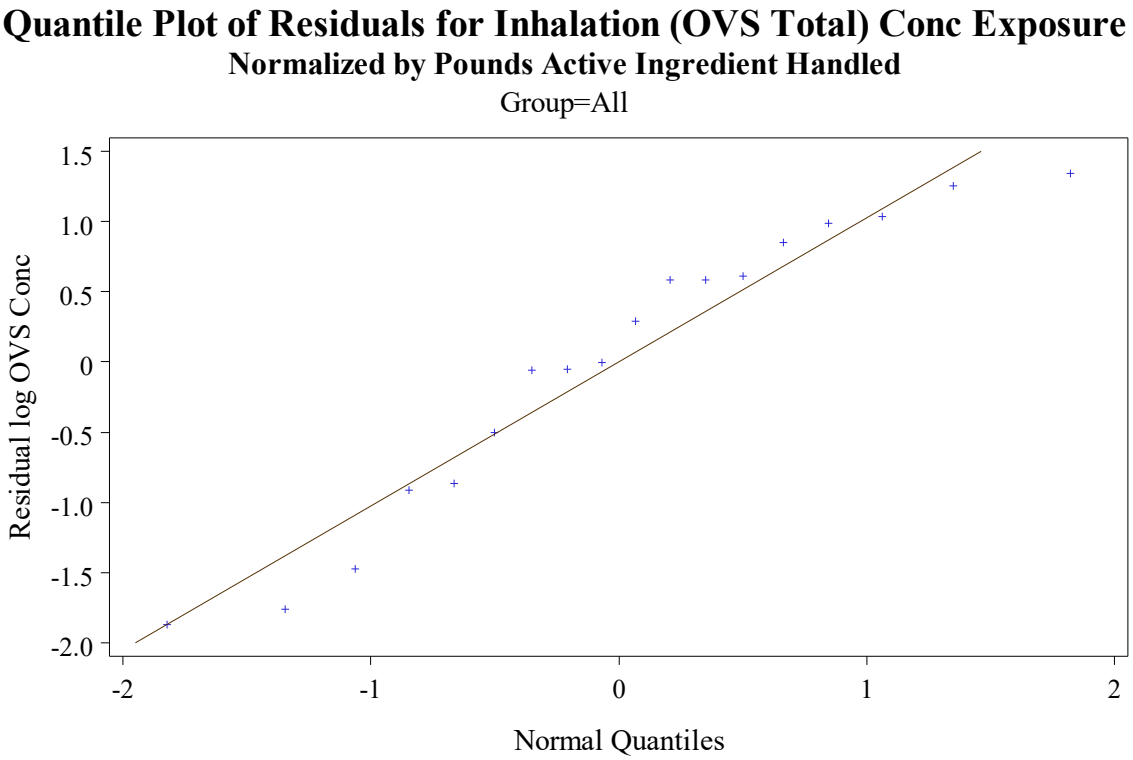


Figure 25. Quantile plot of residuals from linear model for Inhalation (OVS Total) Concentration

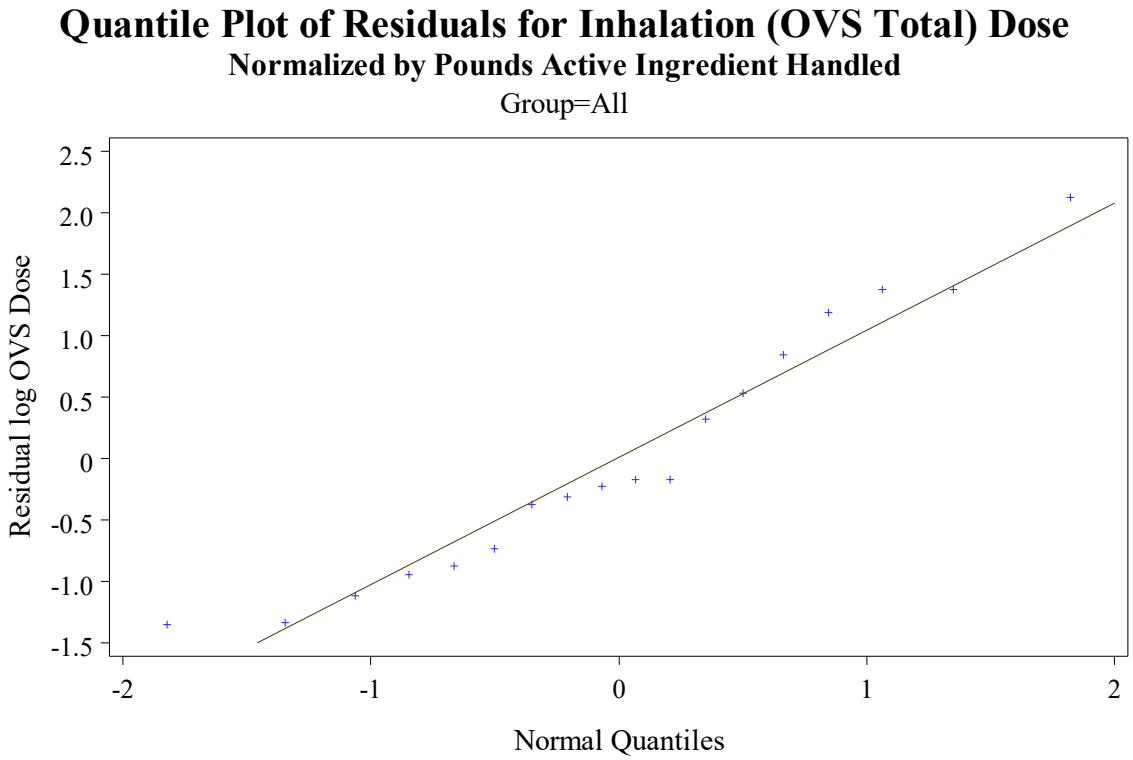


Figure 26. Quantile plot of residuals from linear model for Inhalation (OVS Total) Dose

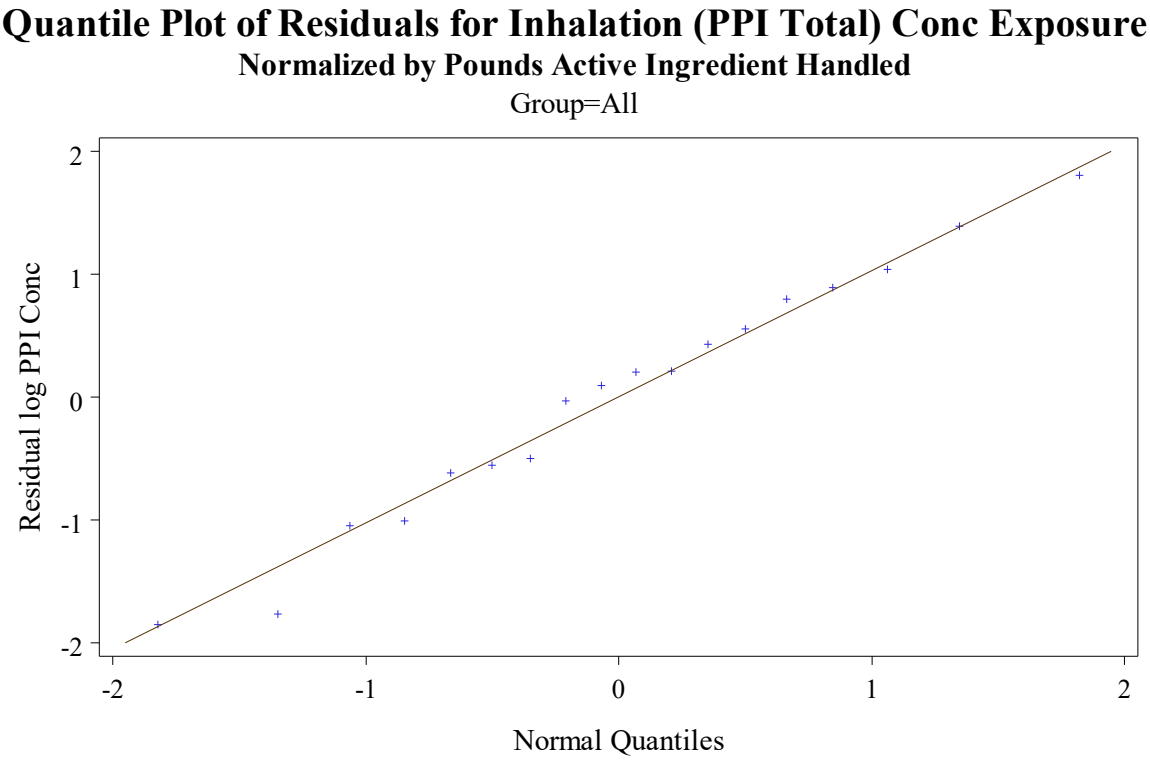


Figure 27. Quantile plot of residuals from linear model for Inhalation (PPI Total) Concentration

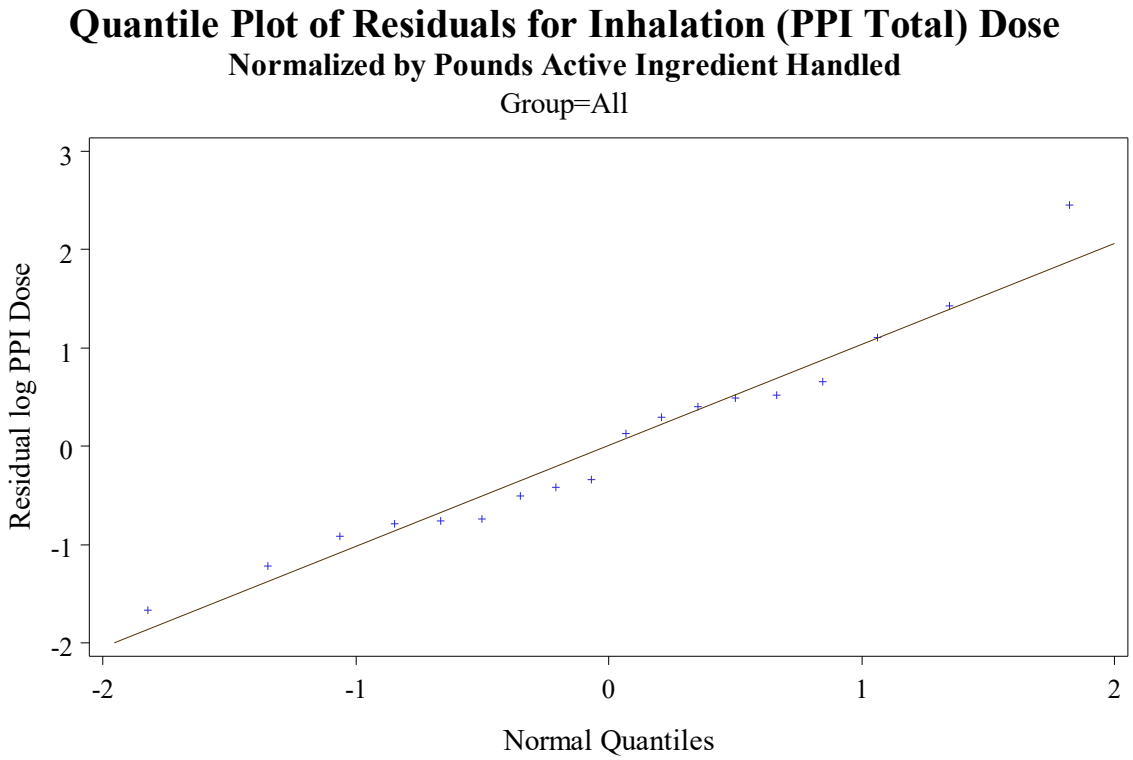


Figure 28. Quantile plot of residuals from linear model for Inhalation (PPI Total) Dose

The quantile-quantile plots of the studentized residuals are reasonably close to the straight line. None of the studentized residuals exceeded the standard outlier cutoff of ±3.

Regression plots

The lognormal linear regression results for all the exposure routes are shown below using the mid value substitution method for non-detect values. The data points are labeled to show the concentration and volume groups. The letters l, m, and h in upper or lower case show the three volume groups for l = low = 10 gals, m = mid = 15 gals, and h = high = 30 gals. Lower case letters show the low concentration MEs (1200 ppm) and upper case letter show the high concentration MEs (12000 ppm).

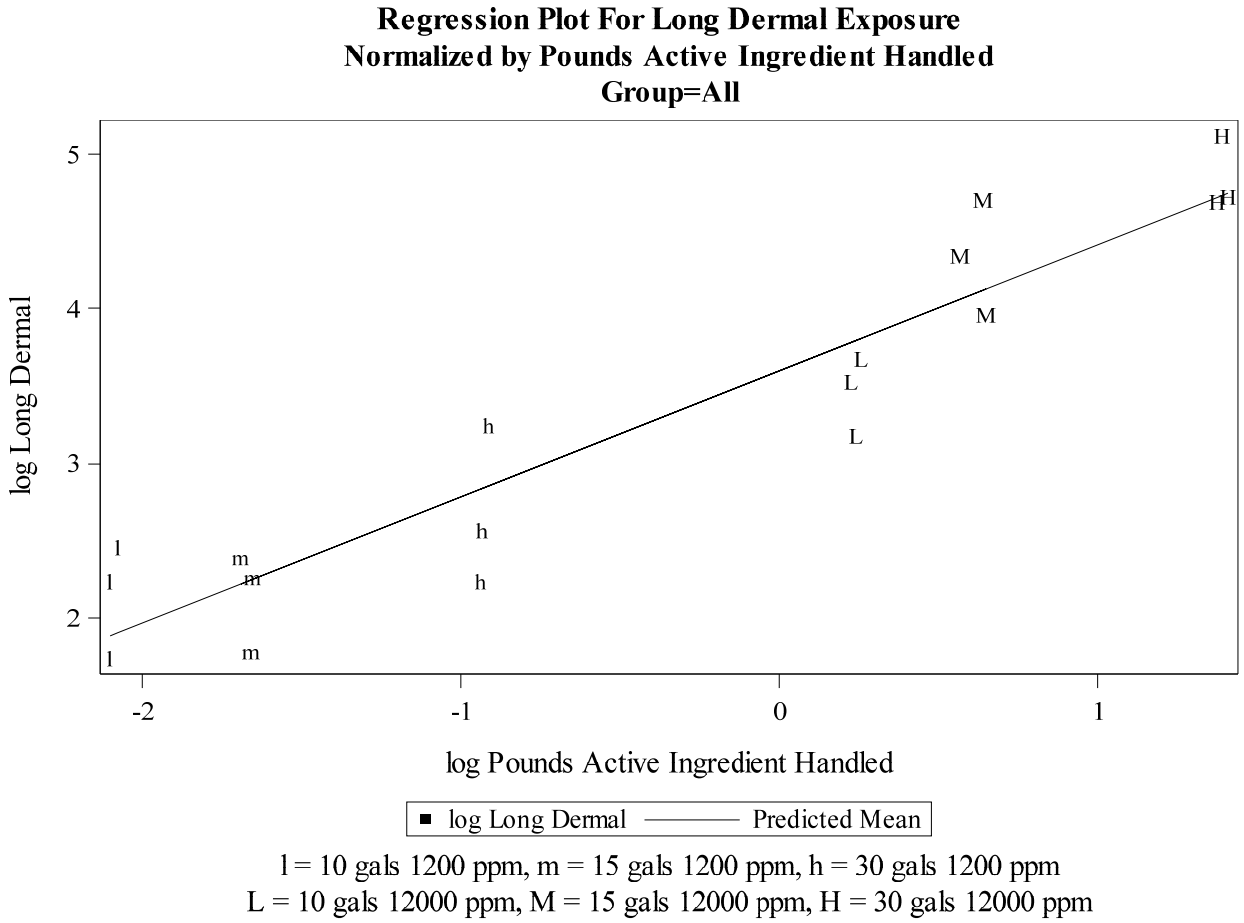


Figure 29. Regression plot for Long Dermal Exposure (mg)

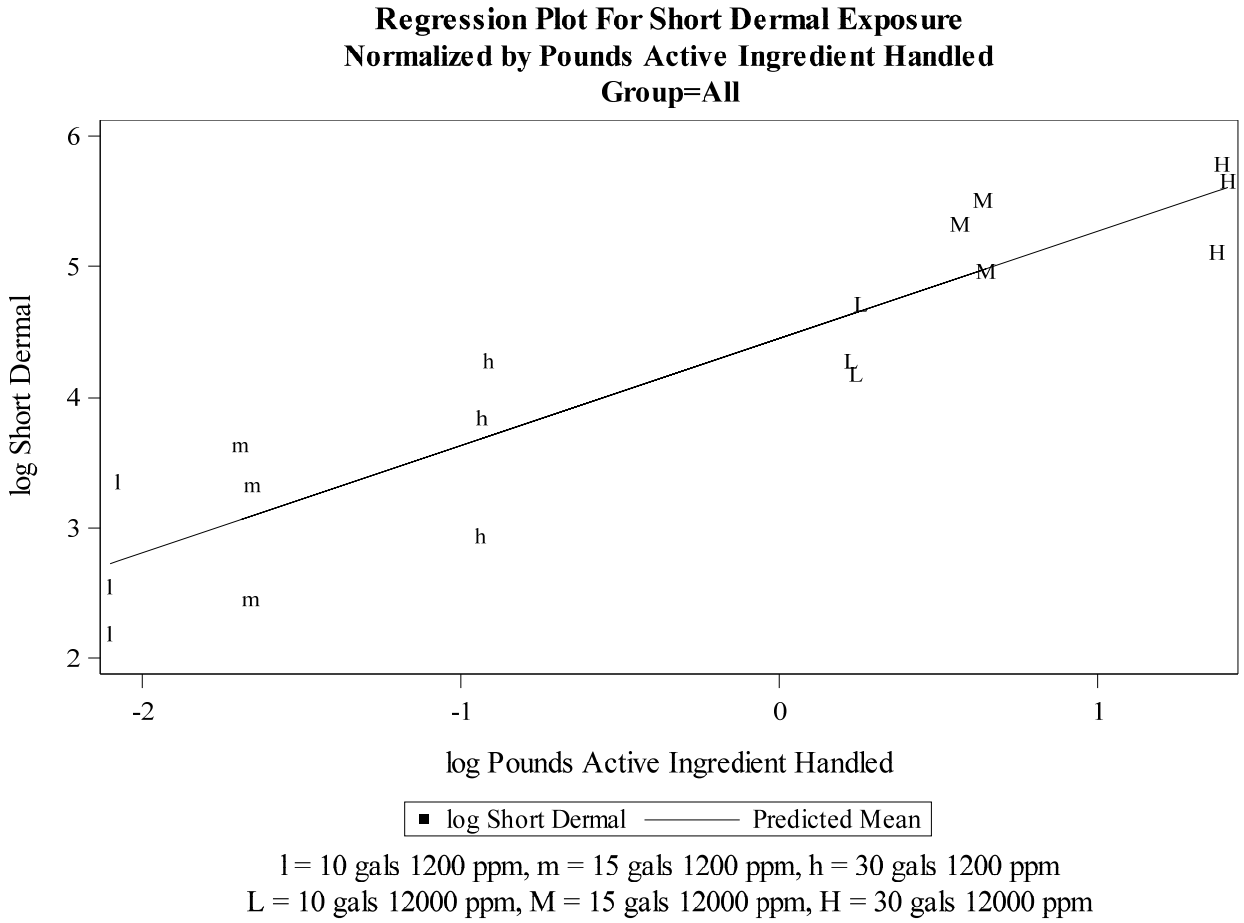


Figure 30. Regression plot for Short Dermal Exposure (mg)

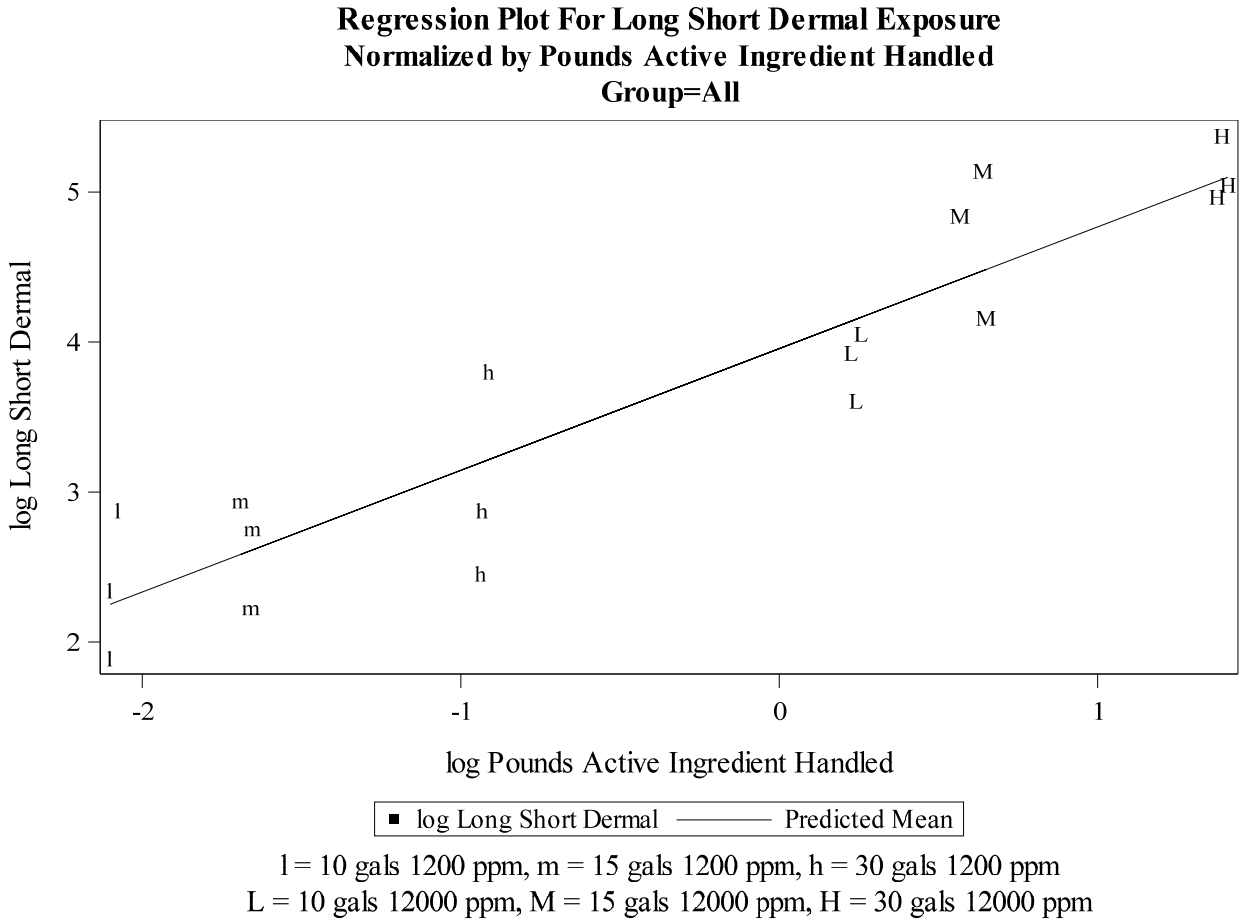


Figure 31. Regression plot for Long Short Dermal Exposure (mg)

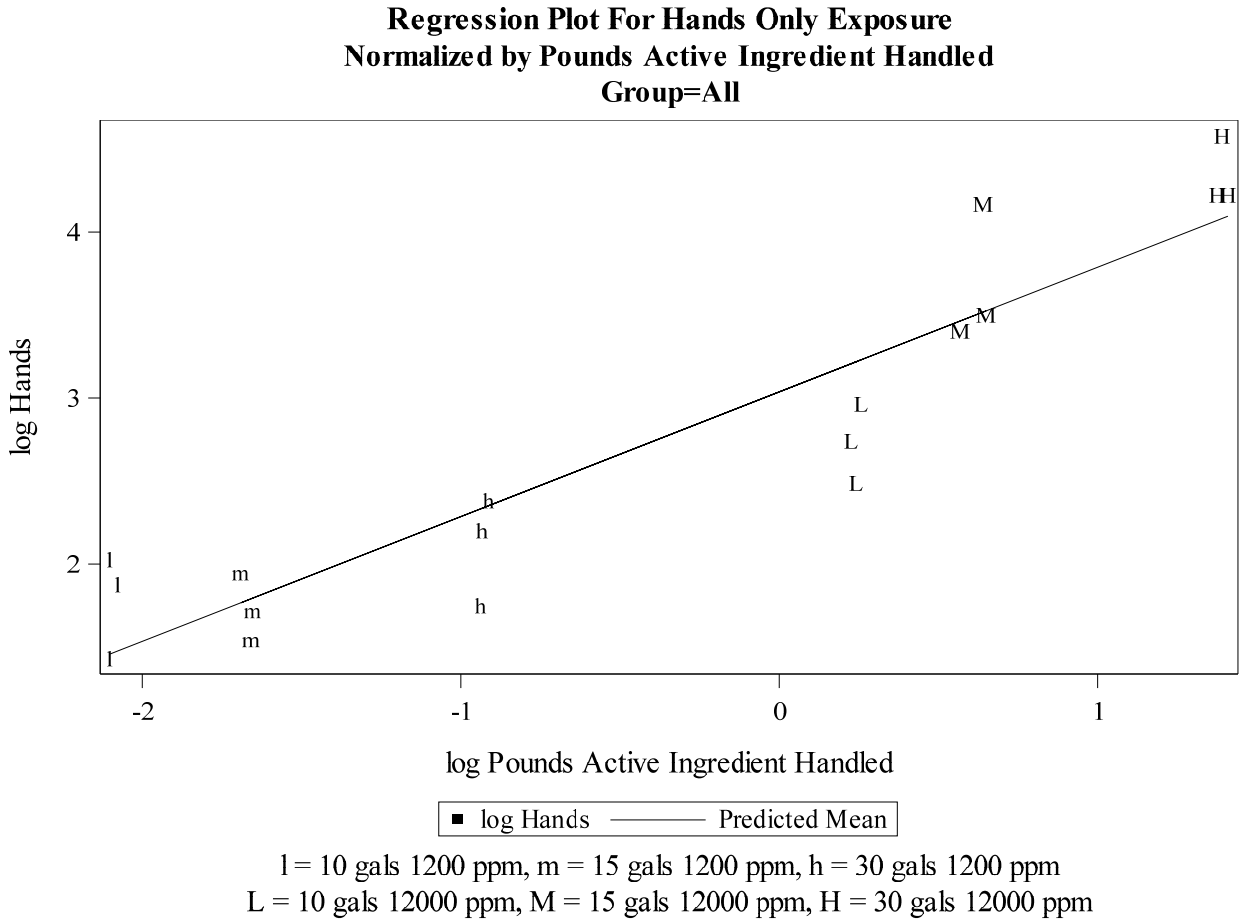


Figure 32. Regression plot for Hands Only Exposure (mg)

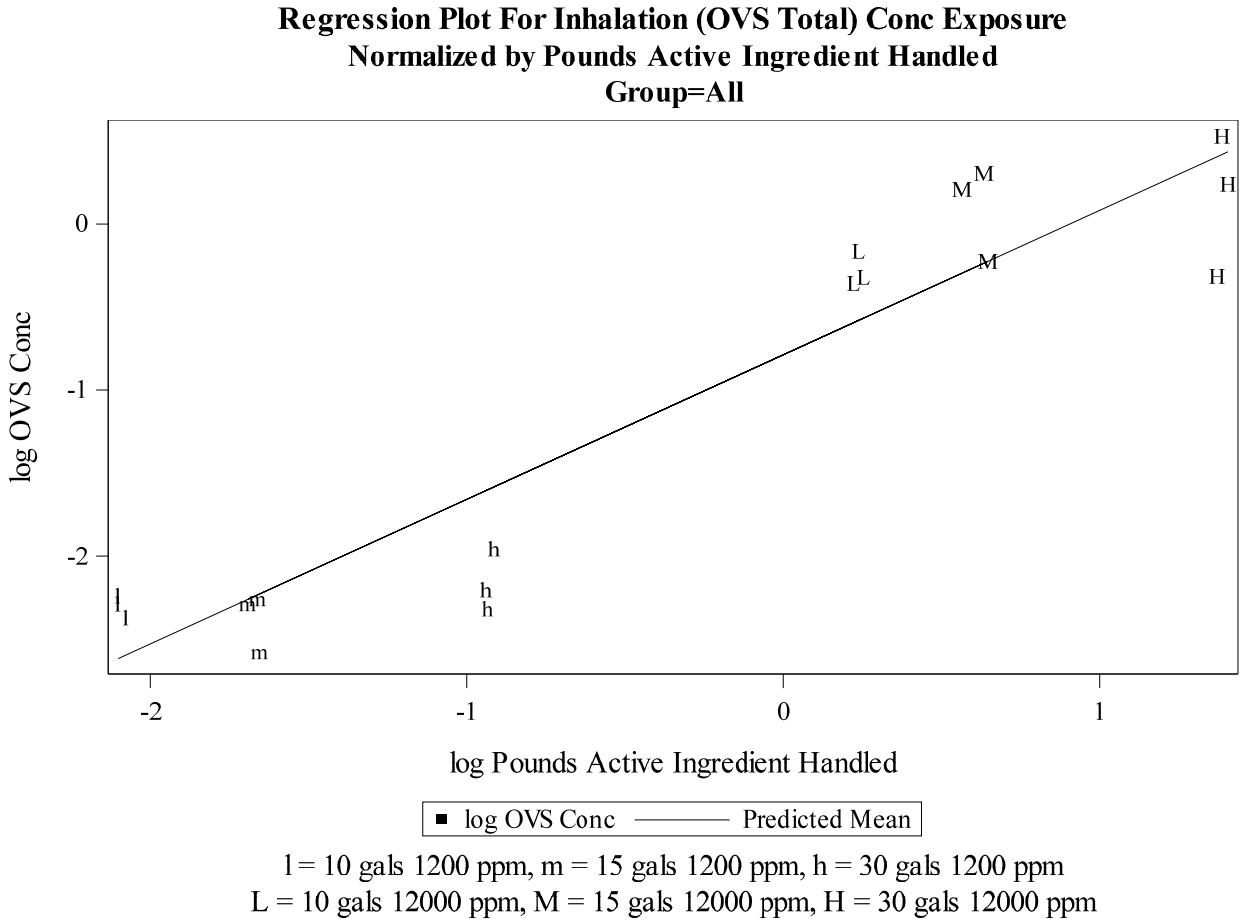


Figure 33. Regression plot for Inhalation (OVS Total) Concentration Exposure (mg/m^3)

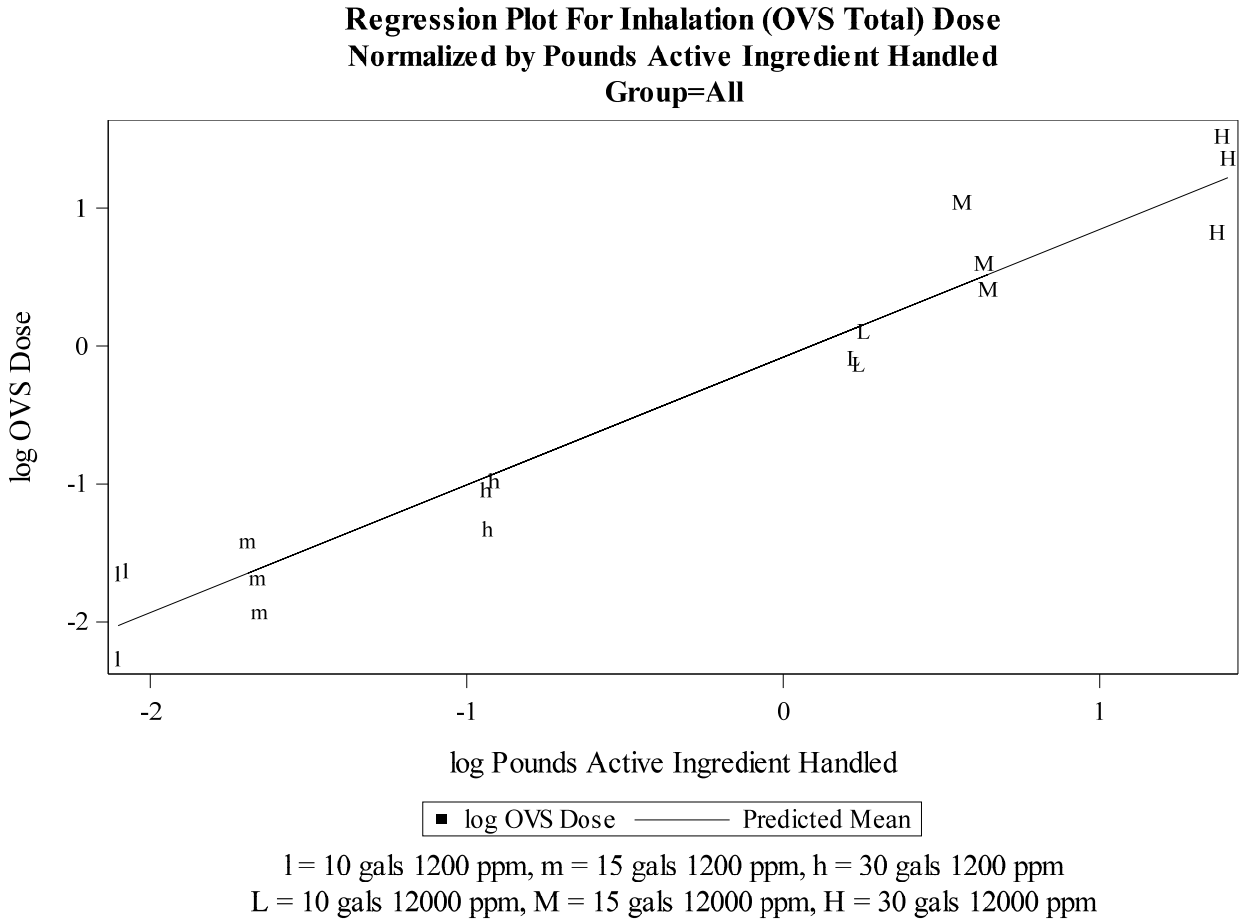


Figure 34. Regression plot for Inhalation (OVS Total) Dose (mg)

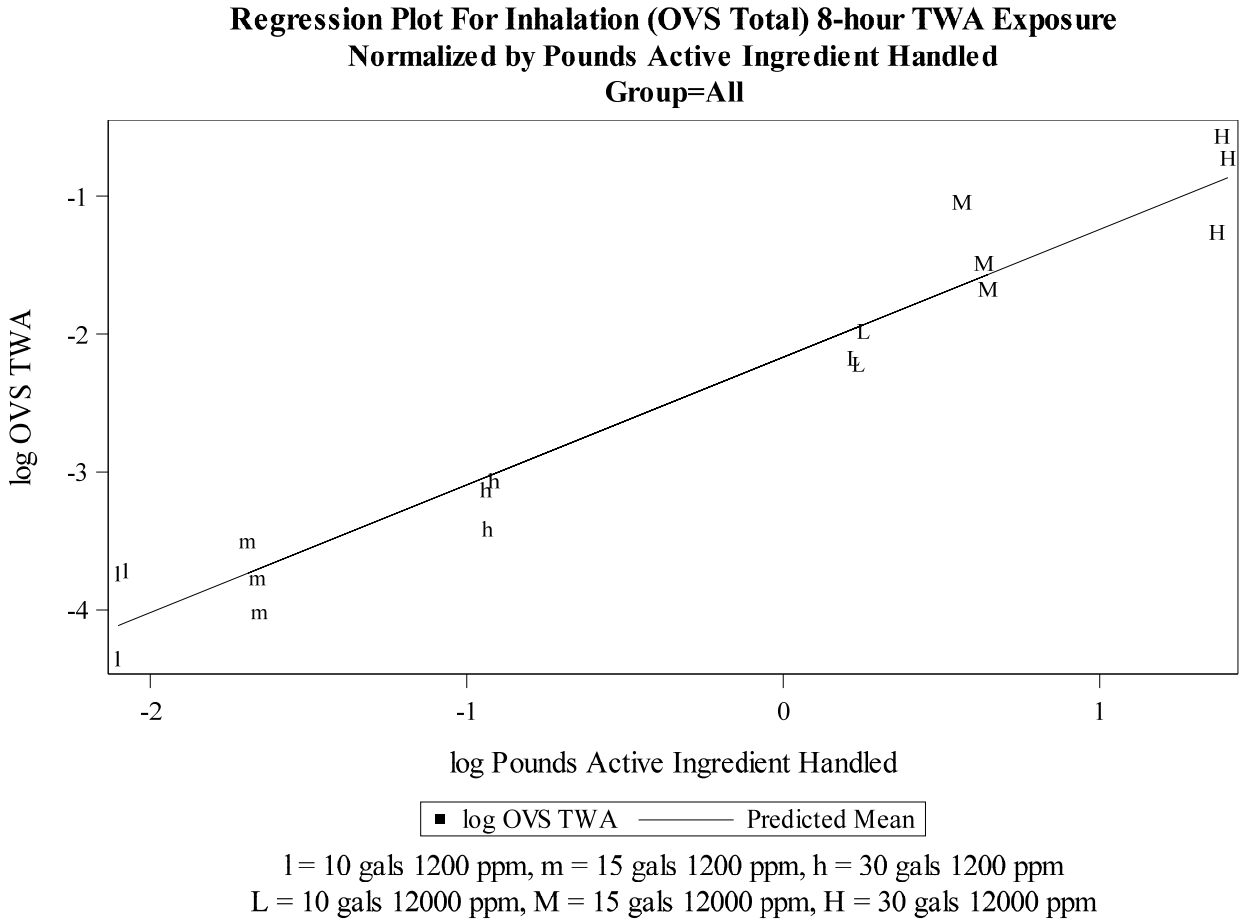


Figure 35. Regression plot for Inhalation (OVS Total) Time-Weighted Average Exposure (mg/m^3)

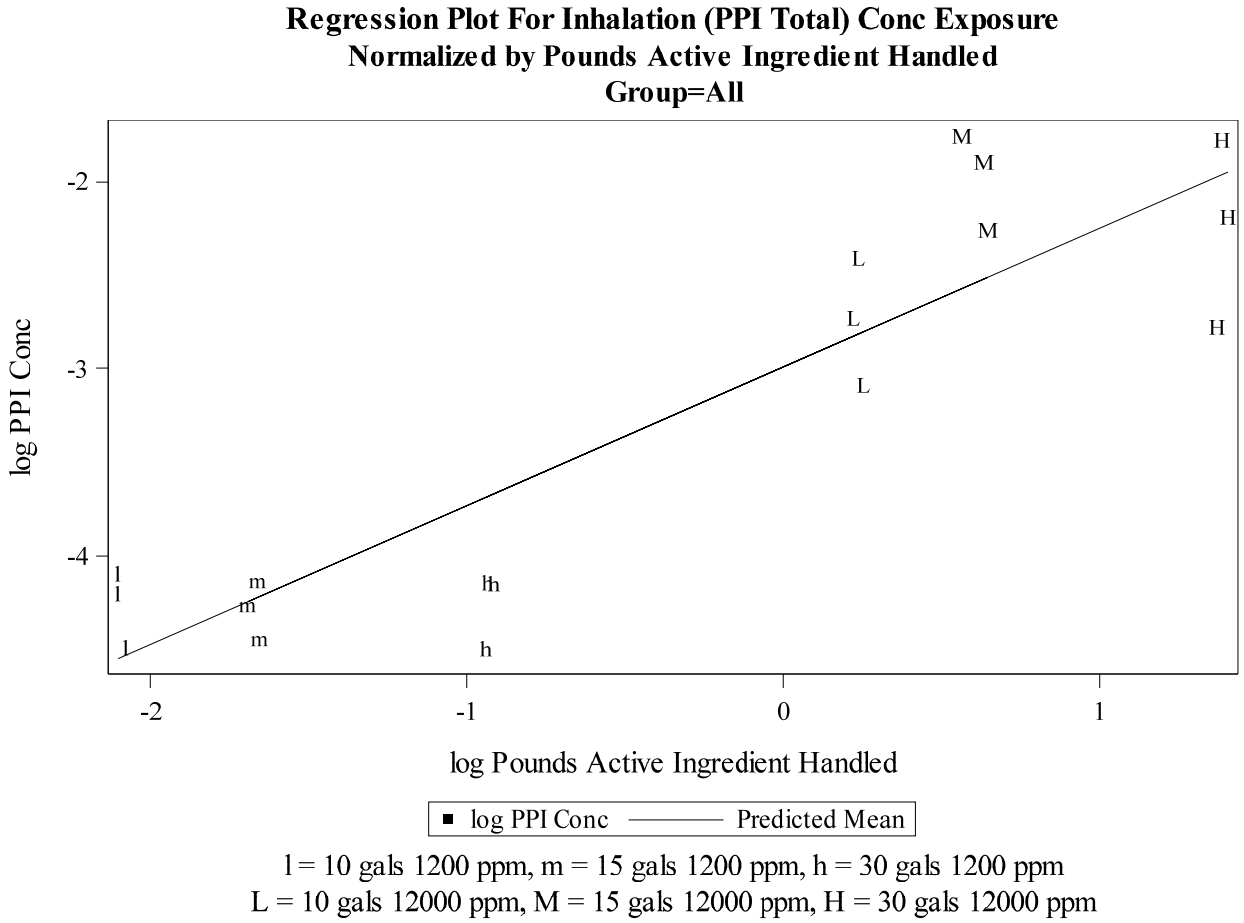


Figure 36. Regression plot for Inhalation (PPI Total) Concentration Exposure (mg/m^3)

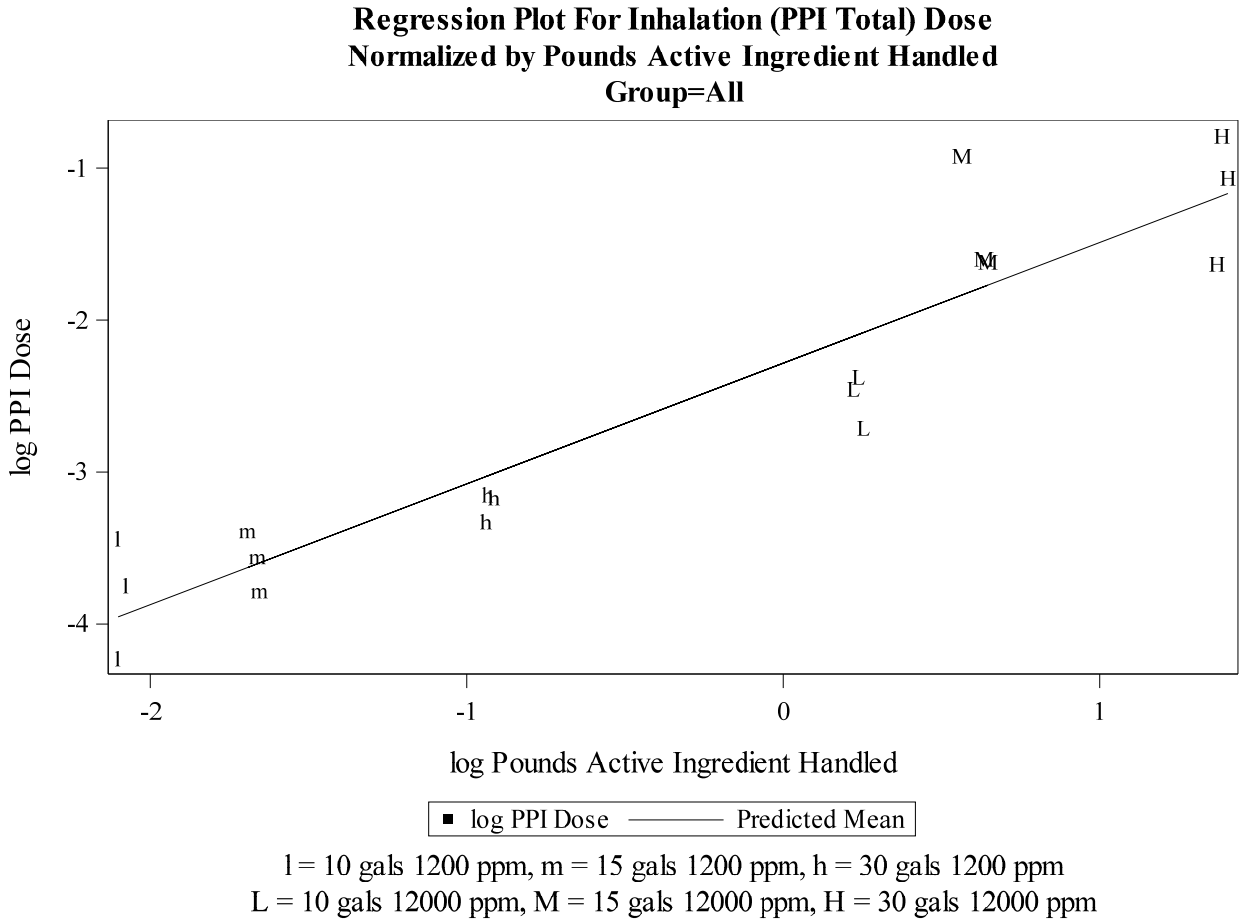


Figure 37. Regression plot for Inhalation (PPI Total) Dose (mg)

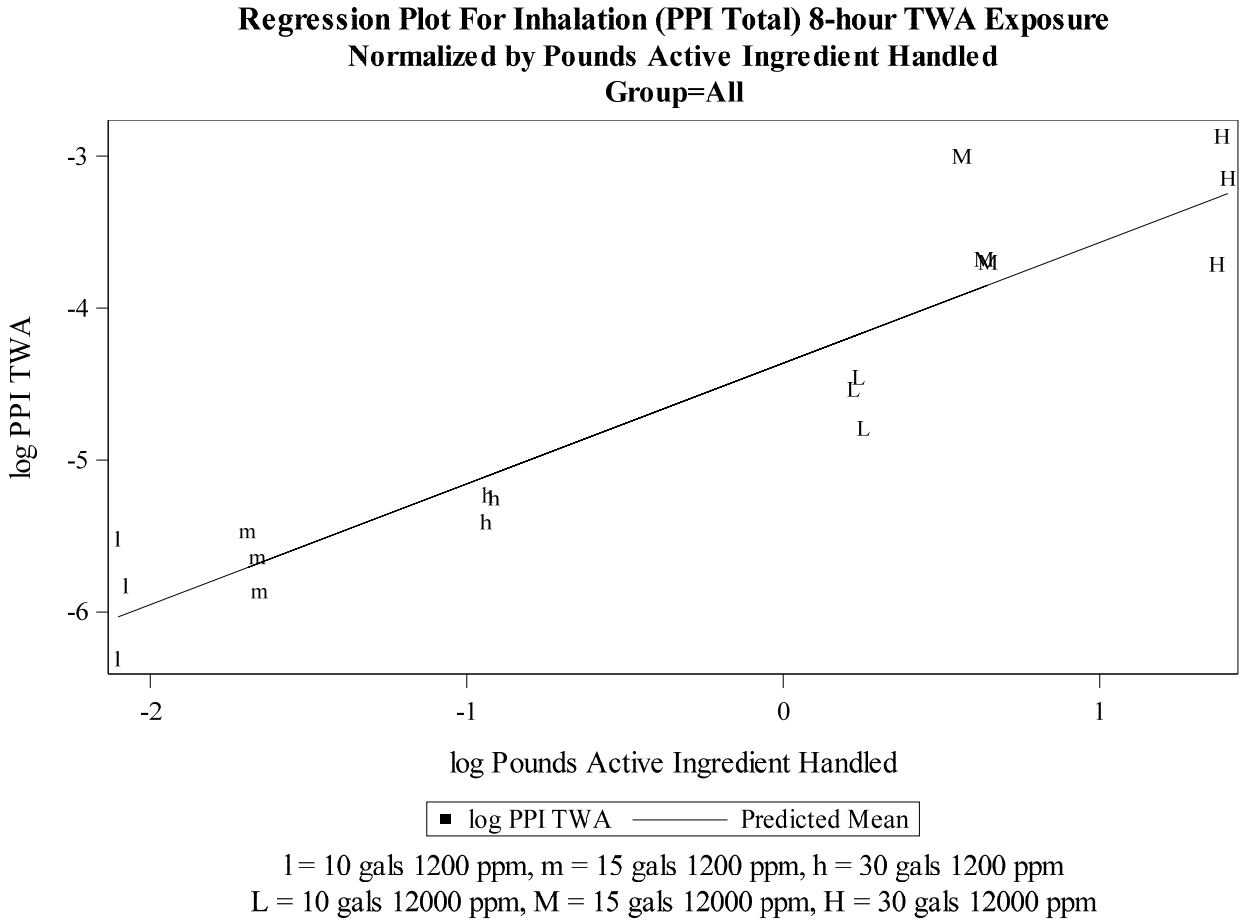


Figure 38. Regression plot for Inhalation (PPI Total) Time-weighted Average Exposure (mg/m^3)

Residual Plots

To evaluate some possible improvements to the linear regression model, we plotted the studentized residuals against some of the other measured values for each ME. We only present the results for Long Dermal Exposure, Inhalation (OVS Total) Conc Exposure and Inhalation (PPI Total) Conc Exposure to avoid a voluminous report. The measured values we considered are monitored minutes, amount (pounds) of paint used, average temperature (calculated as the average of the reported minimum and maximum temperature), average relative humidity (calculated as the average of the reported minimum and maximum relative humidity), the use of a fan, ladder, or wrench, and the spray tip or tips used. Sometimes more than one spray tip type was used. The plotted points are marked using the ME number.

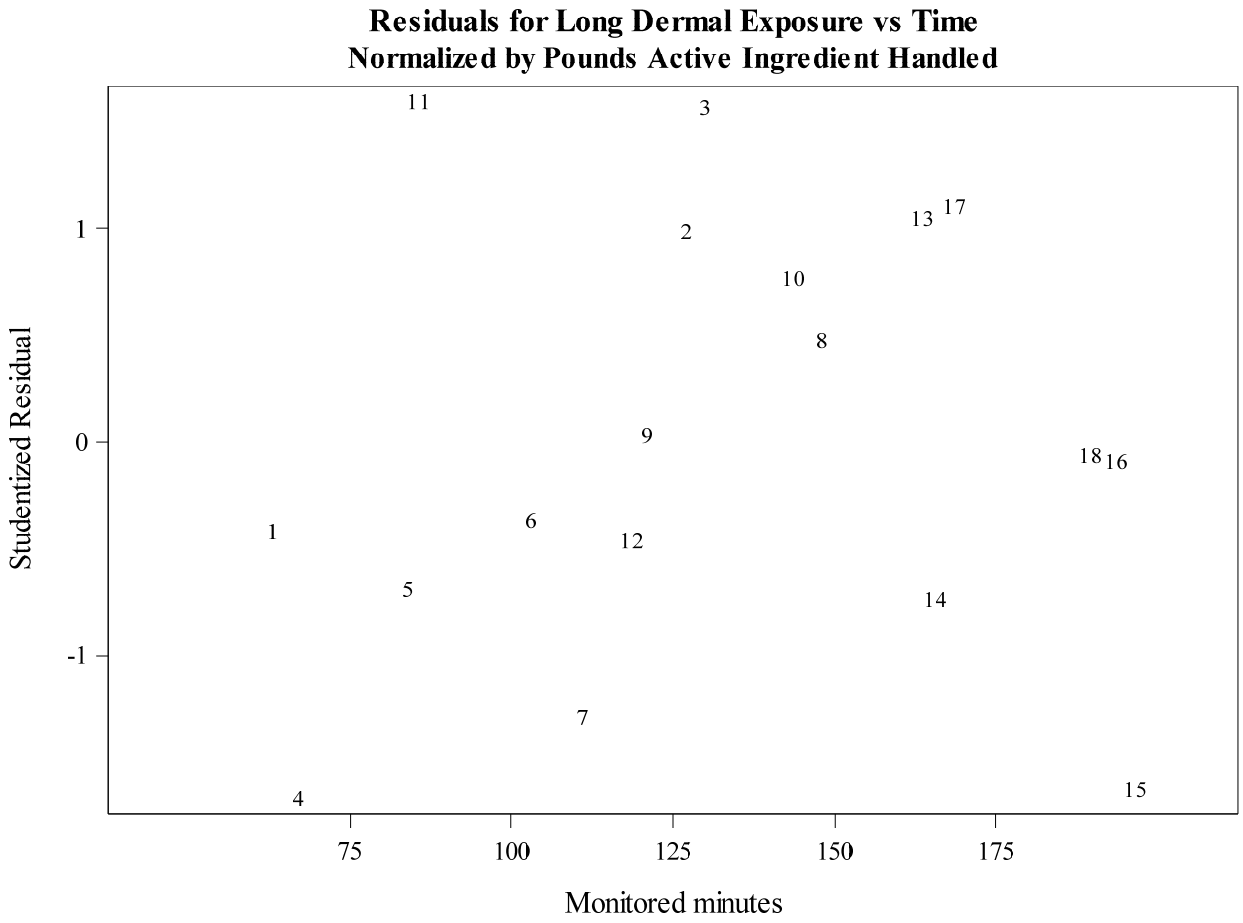


Figure 39. Residuals for Long Dermal Exposure versus monitored minutes

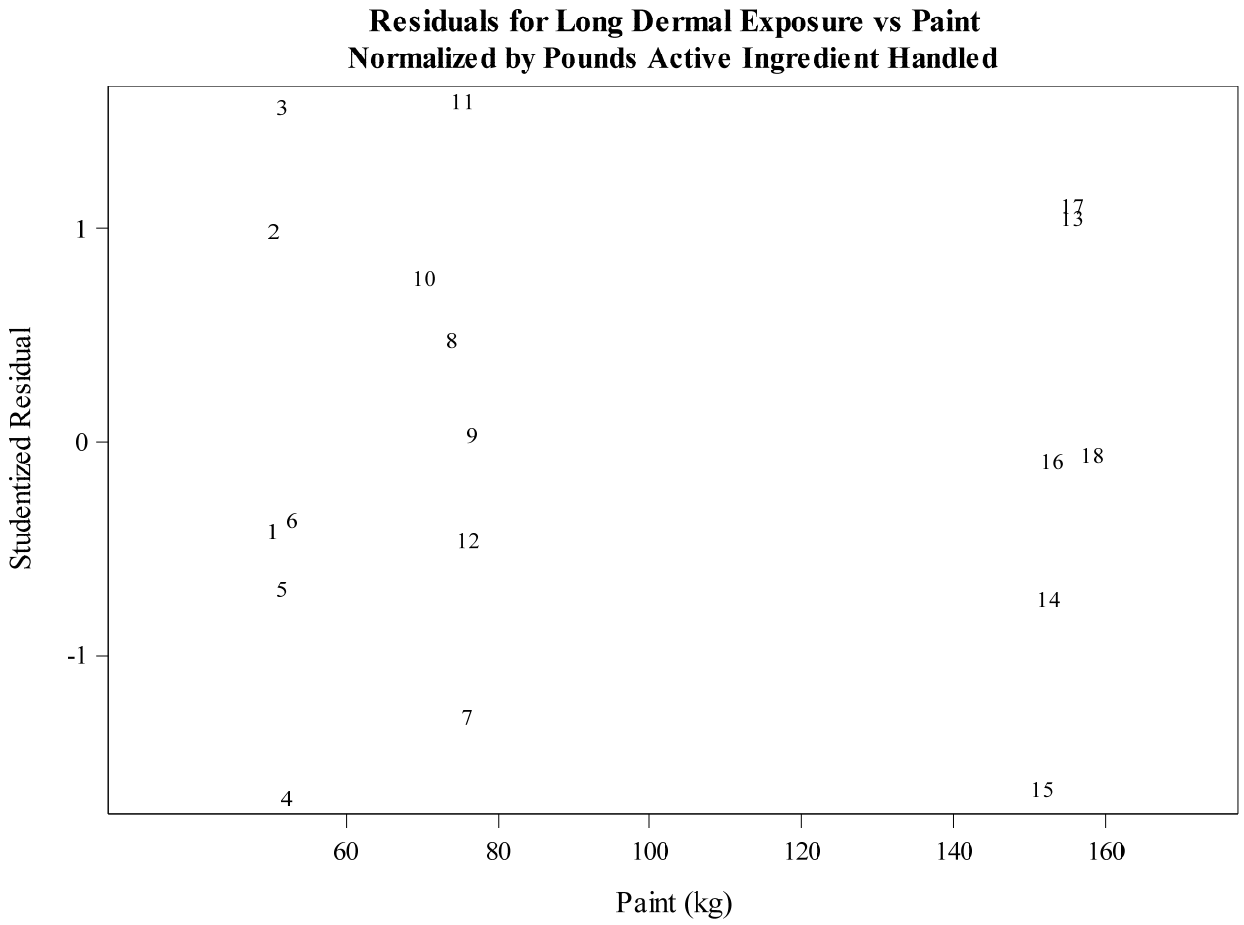


Figure 40. Residuals for Long Dermal Exposure versus amount of paint handled

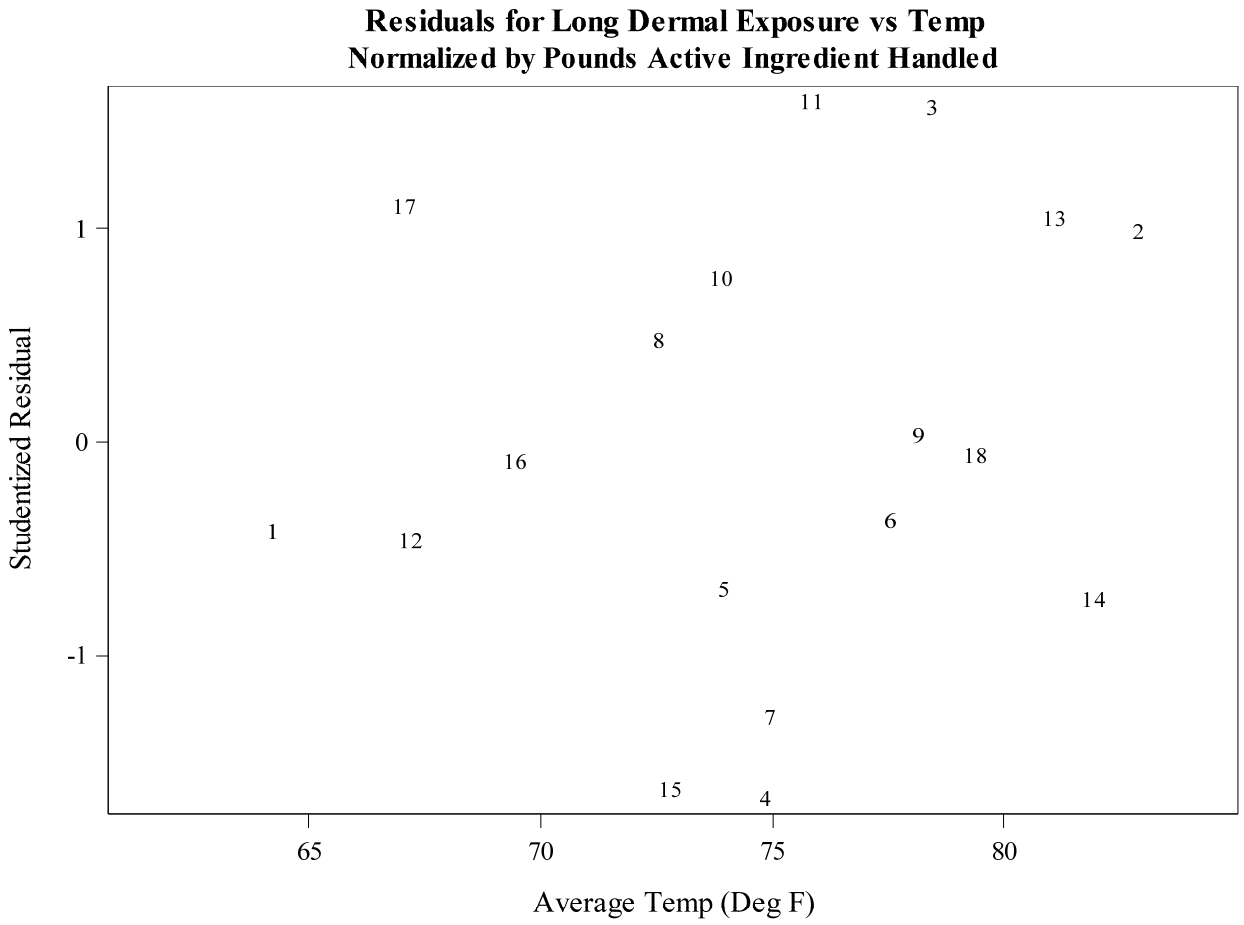


Figure 41. Residuals for Long Dermal Exposure versus average temperature

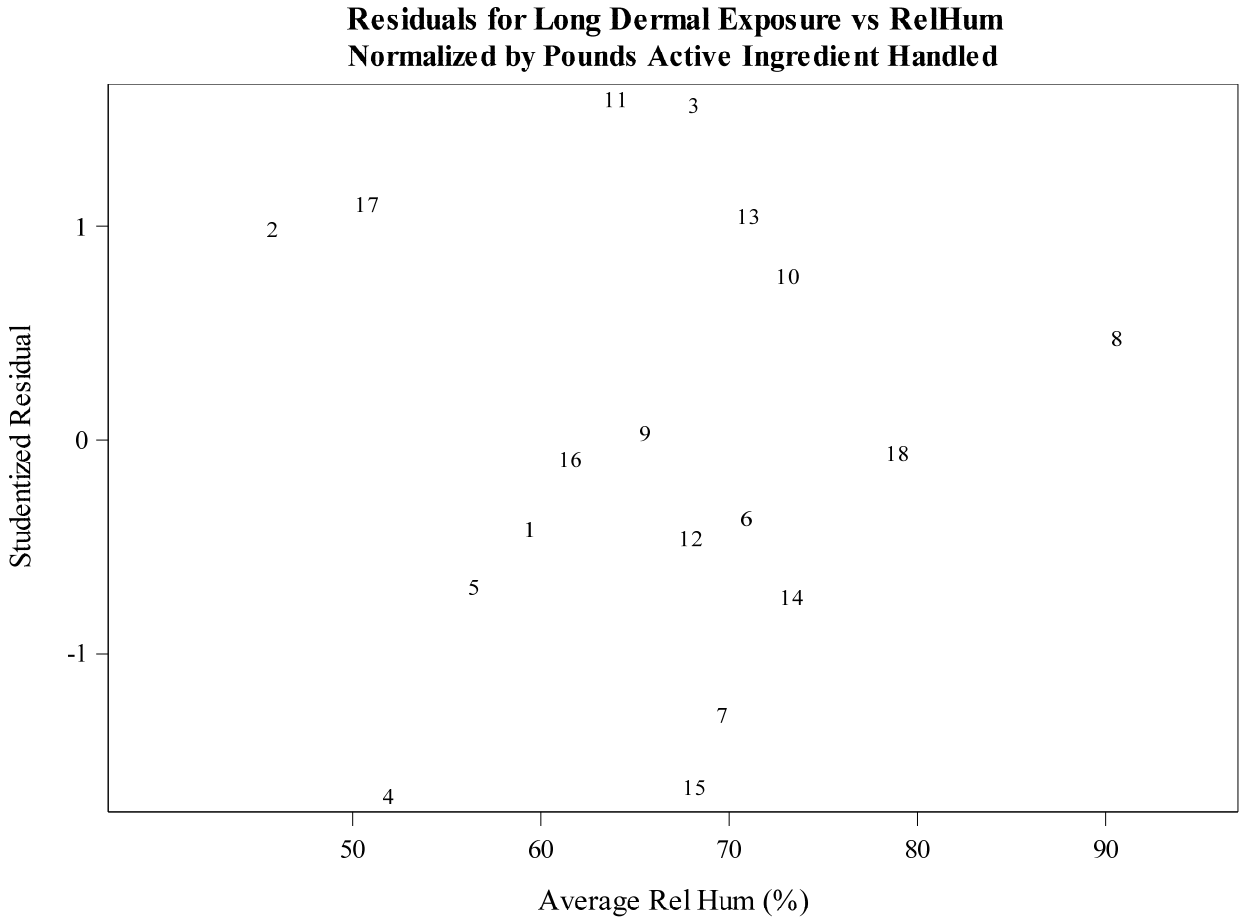


Figure 42. Residuals for Long Dermal Exposure versus average relative humidity

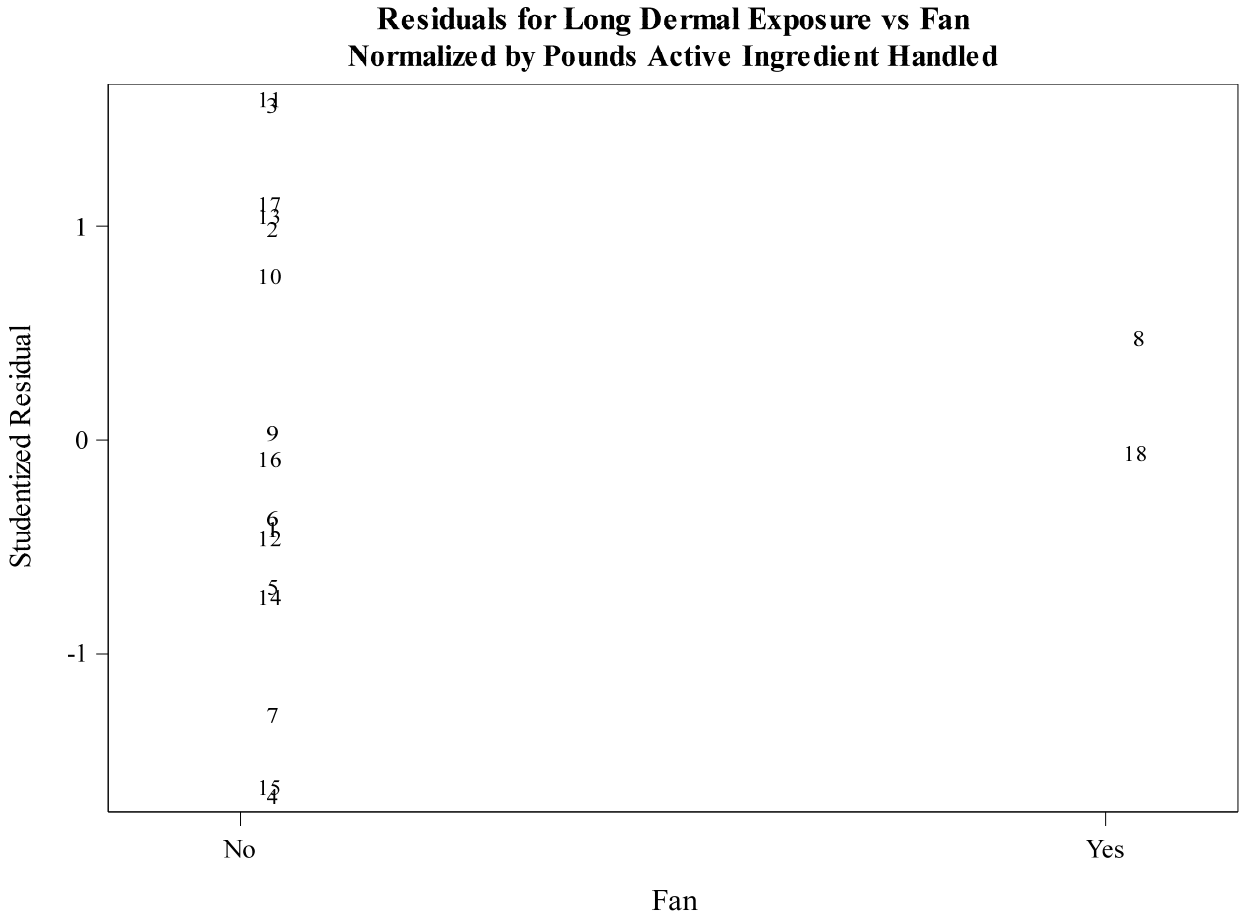


Figure 43. Residuals for Long Dermal Exposure versus use of fan

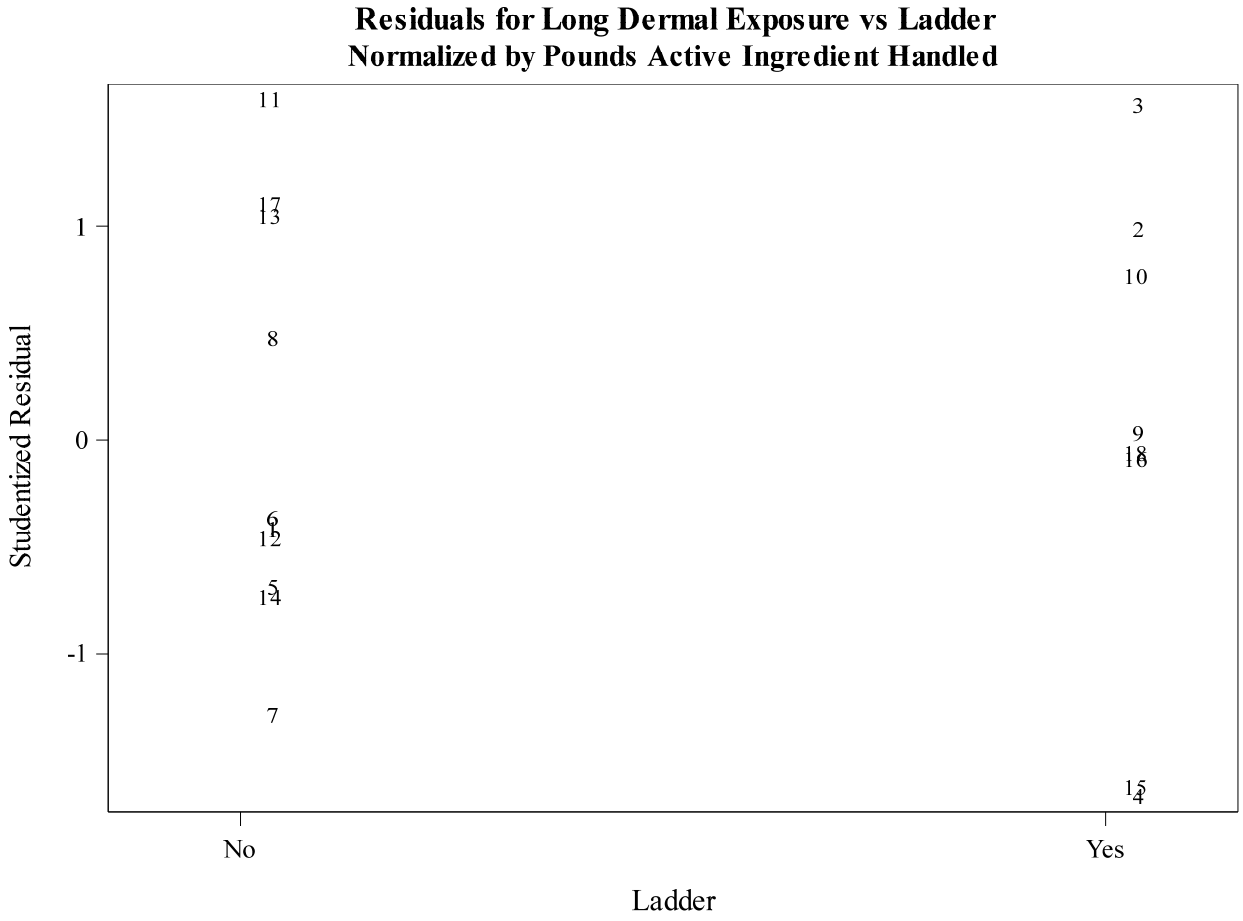


Figure 44. Residuals for Long Dermal Exposure versus use of ladder

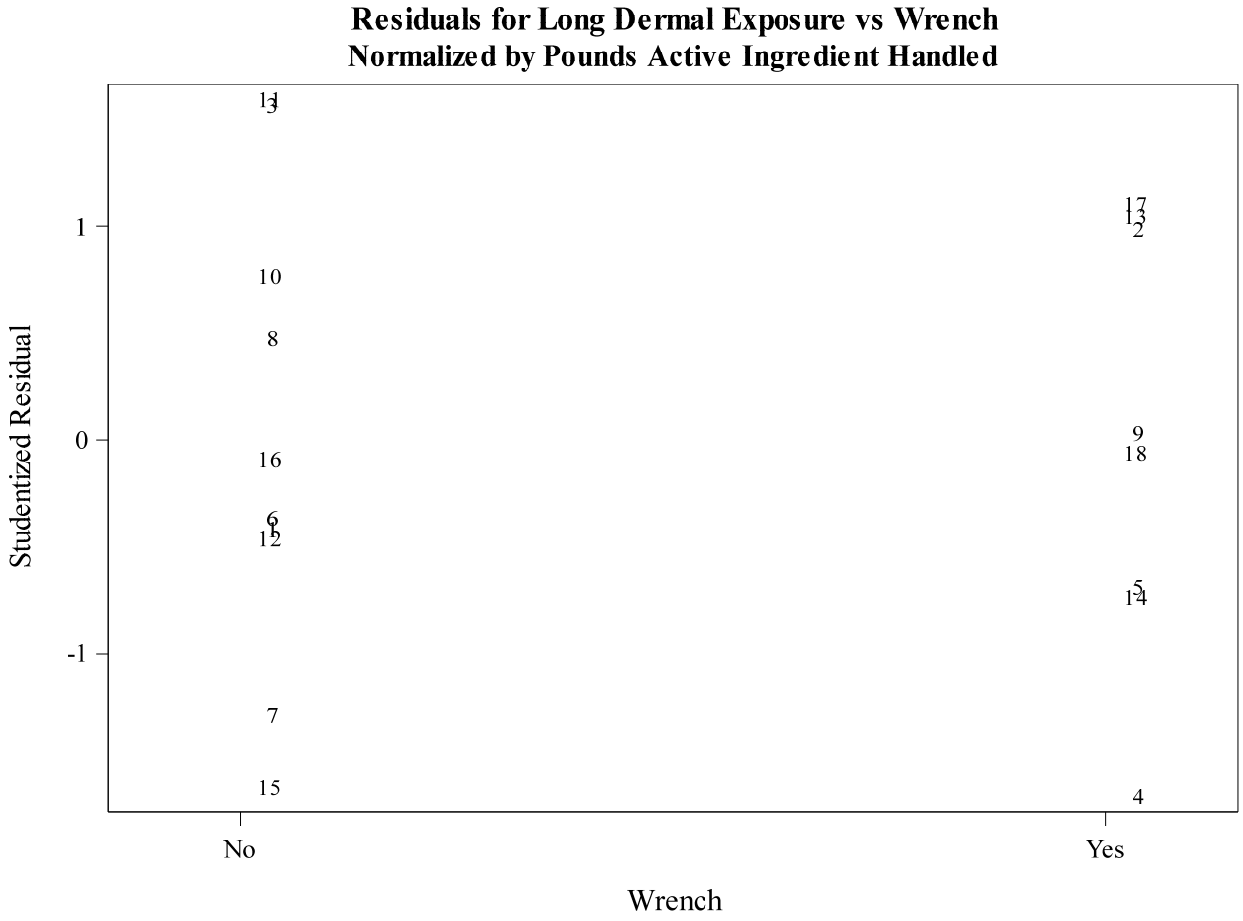


Figure 45. Residuals for Long Dermal Exposure versus use of wrench

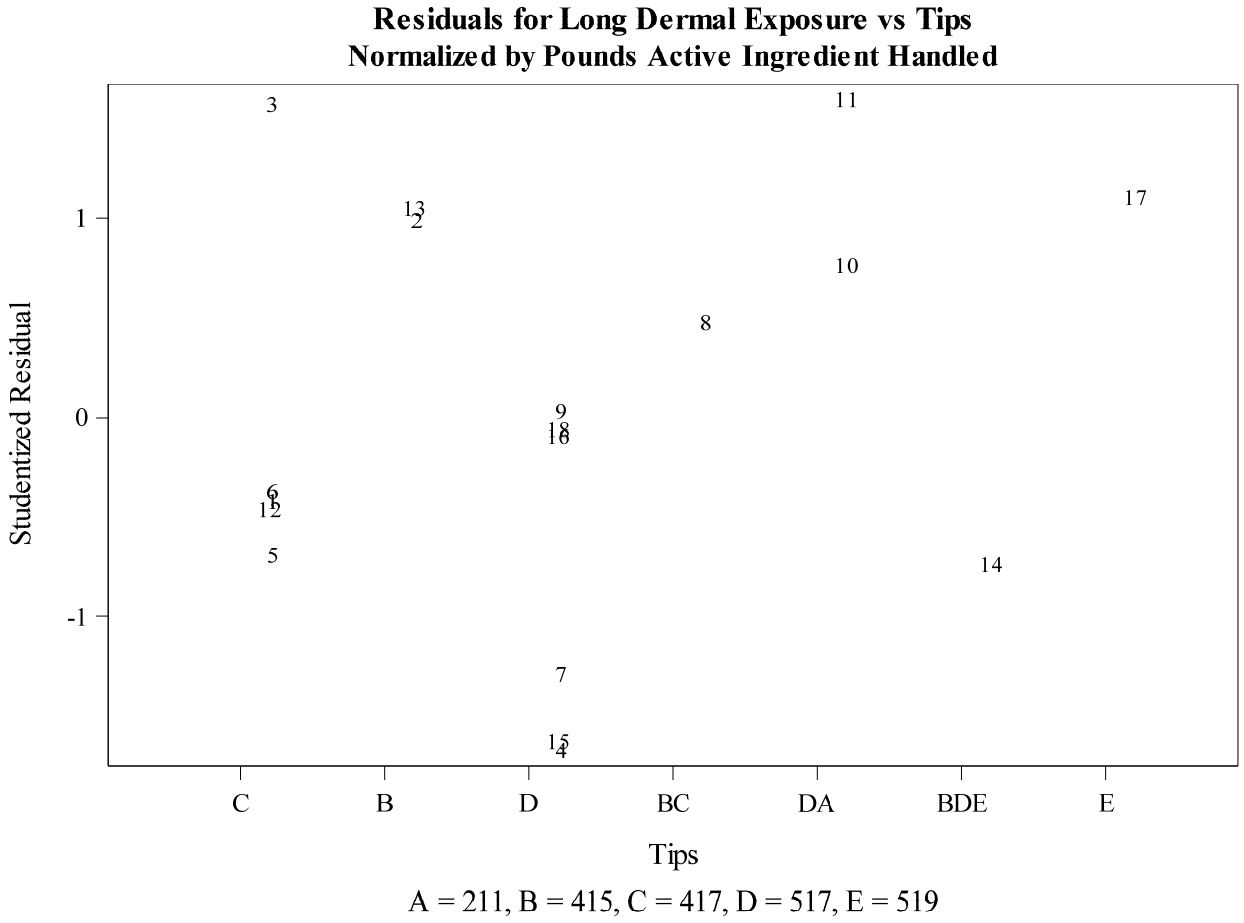


Figure 46. Residuals for Long Dermal Exposure versus spray tips used

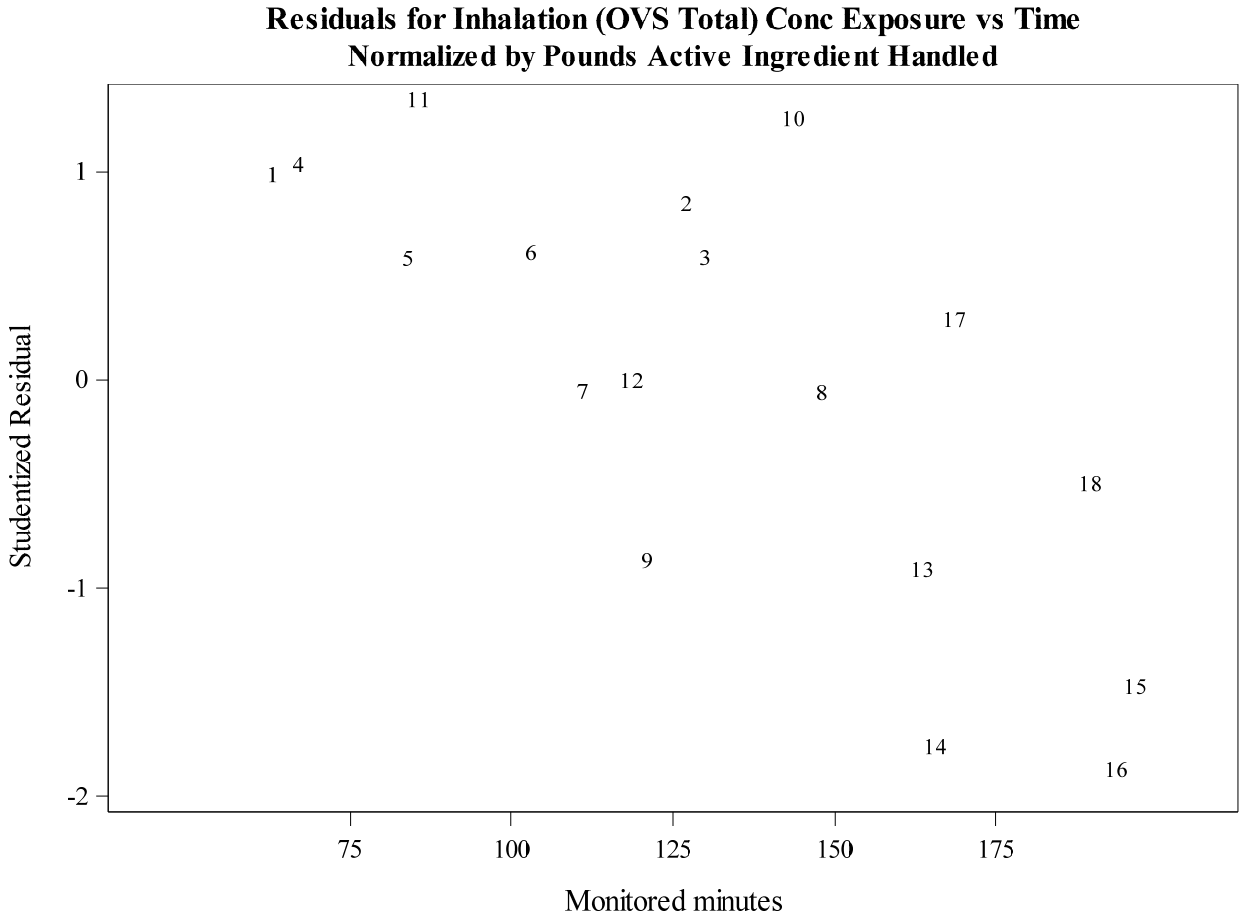


Figure 47. Residuals for Inhalation (OVS Total) Concentration versus monitored minutes

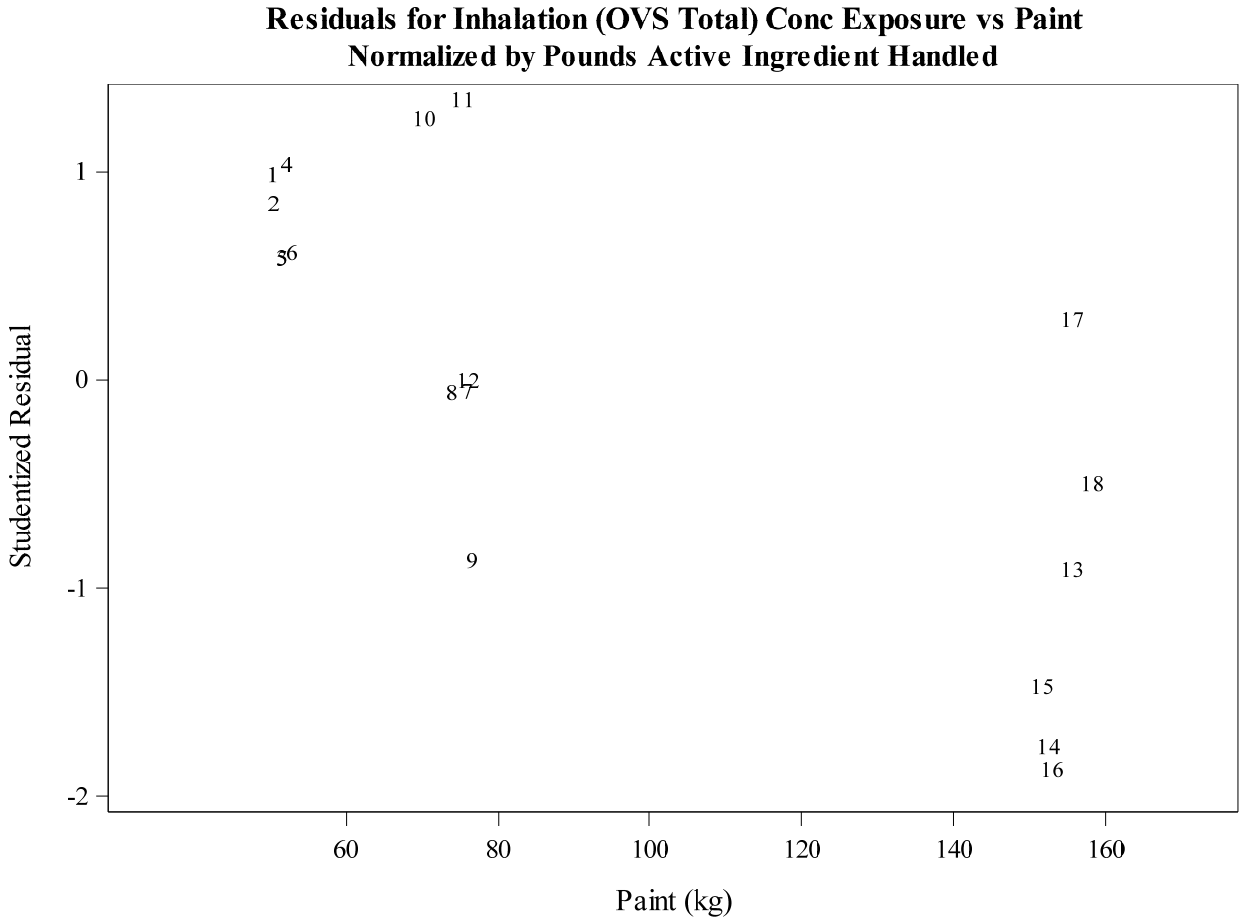


Figure 48. Residuals for Inhalation (OVS Total) Concentration versus amount of paint handled

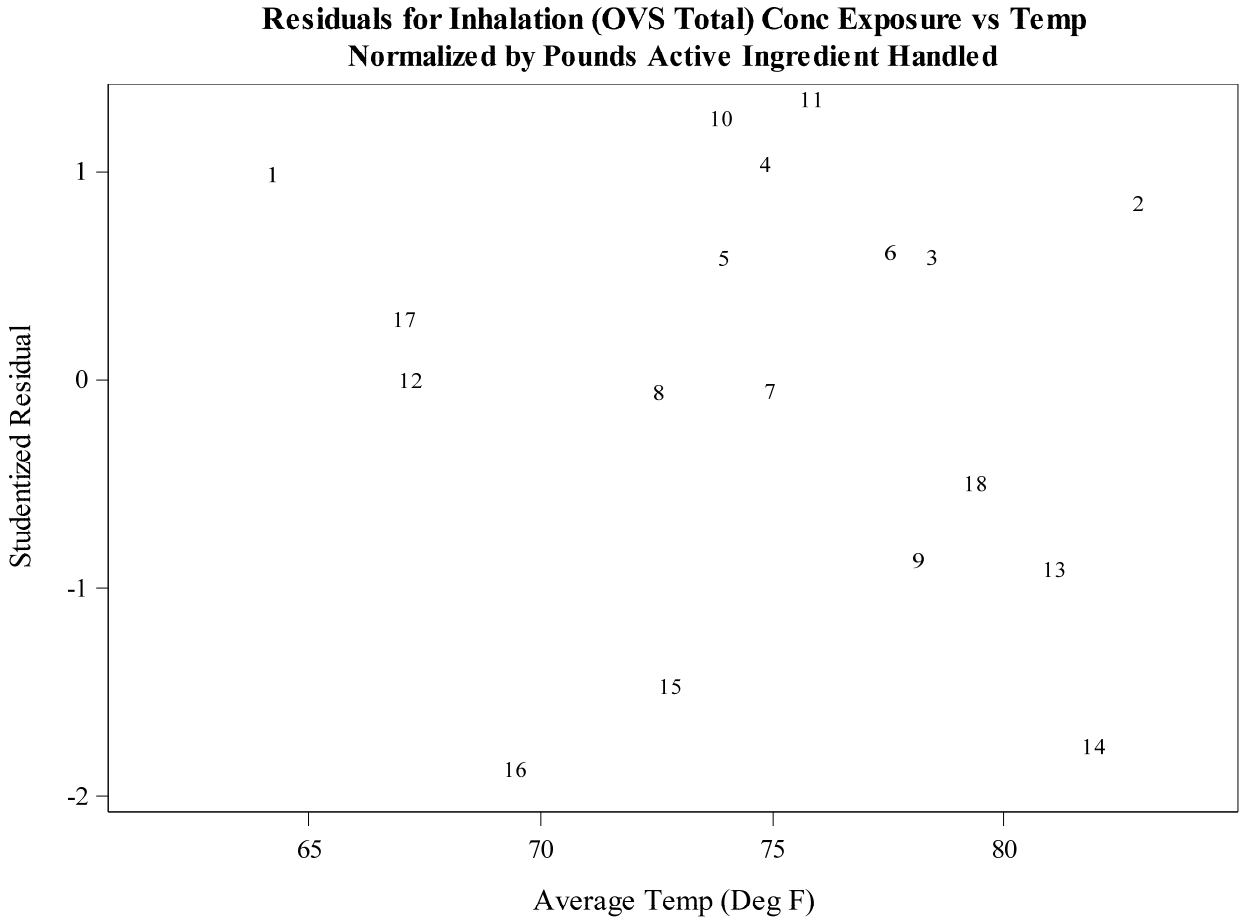


Figure 49. Residuals for Inhalation (OVS Total) Concentration versus average temperature

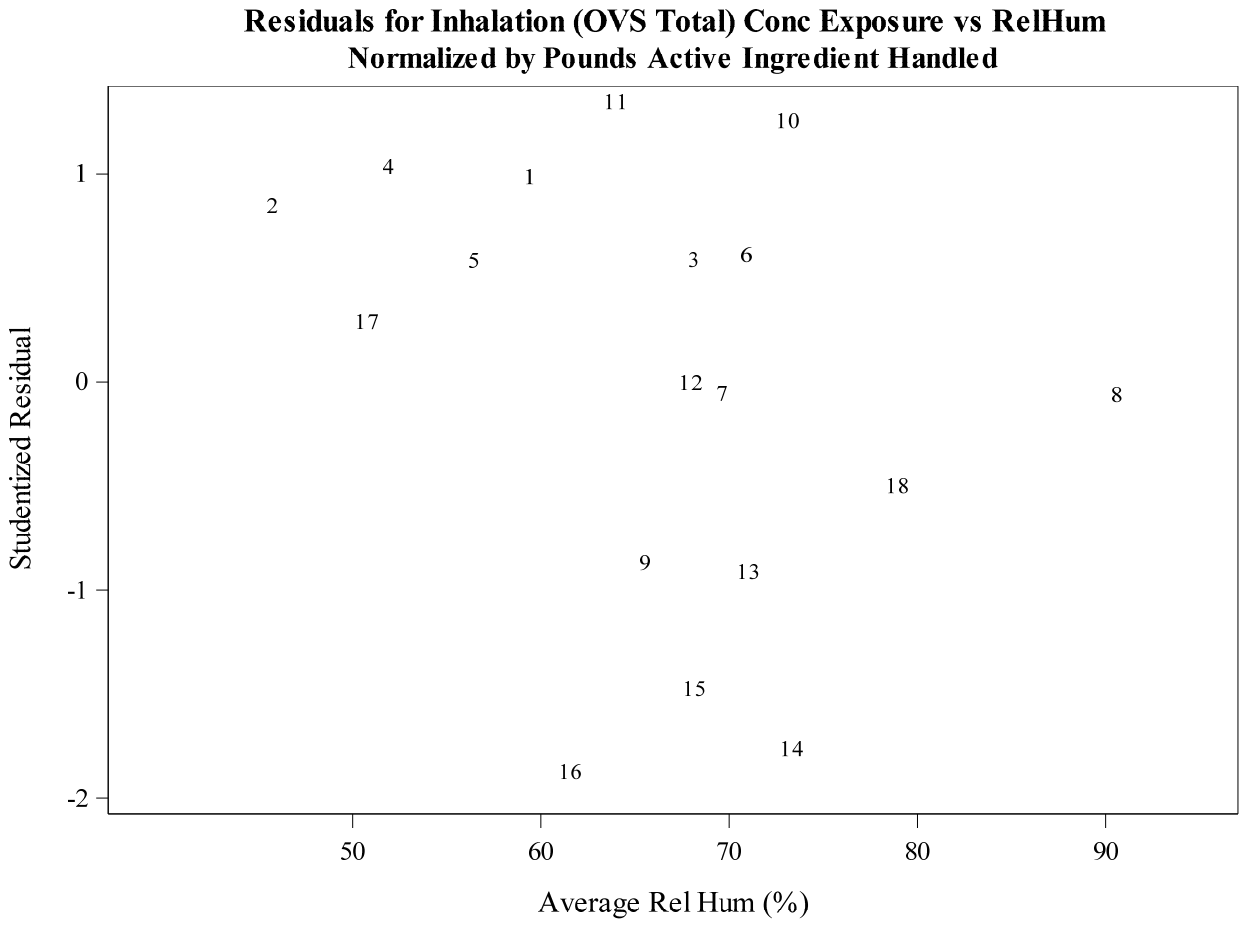


Figure 50. Residuals for Inhalation (OVS Total) Concentration versus average relative humidity

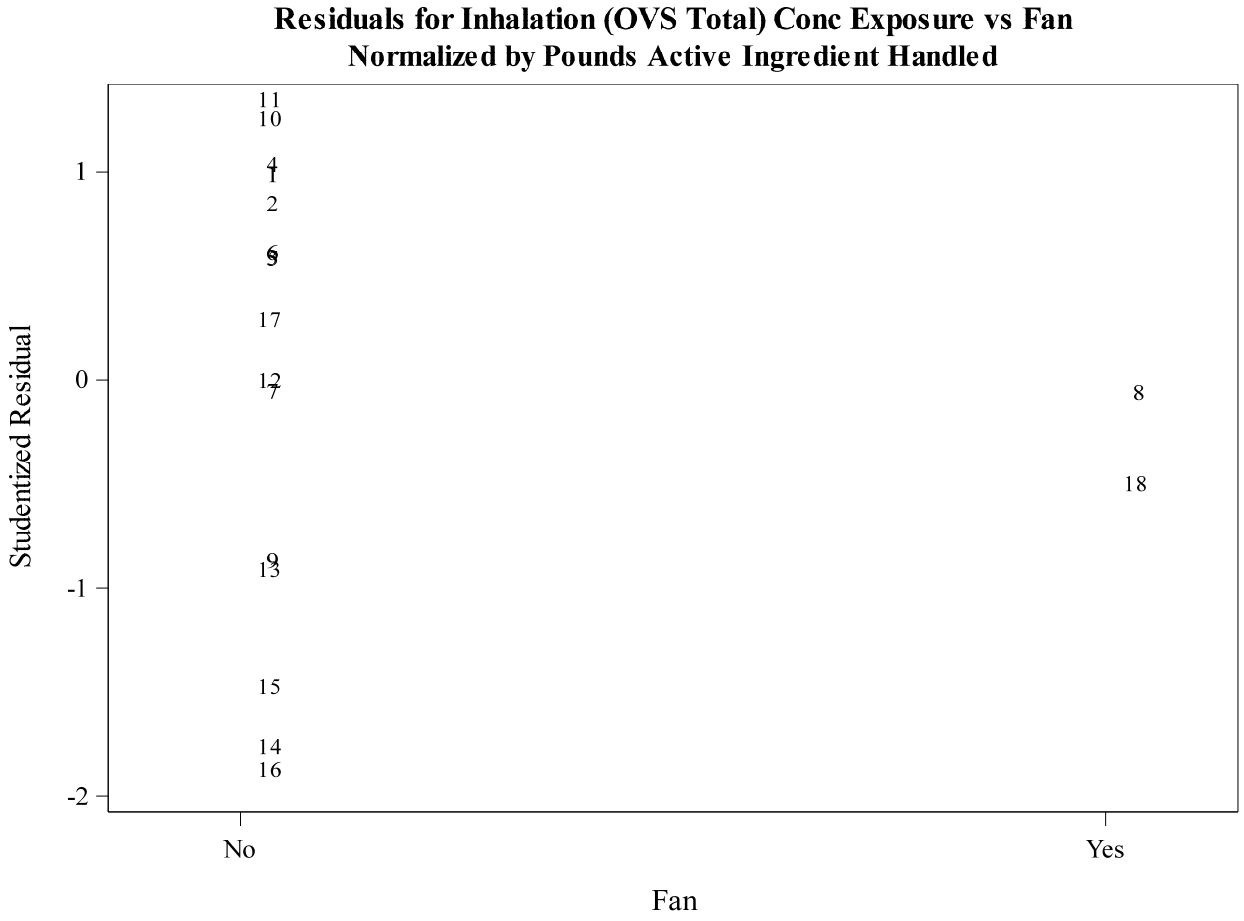


Figure 51. Residuals for Inhalation (OVS Total) Concentration versus use of fan

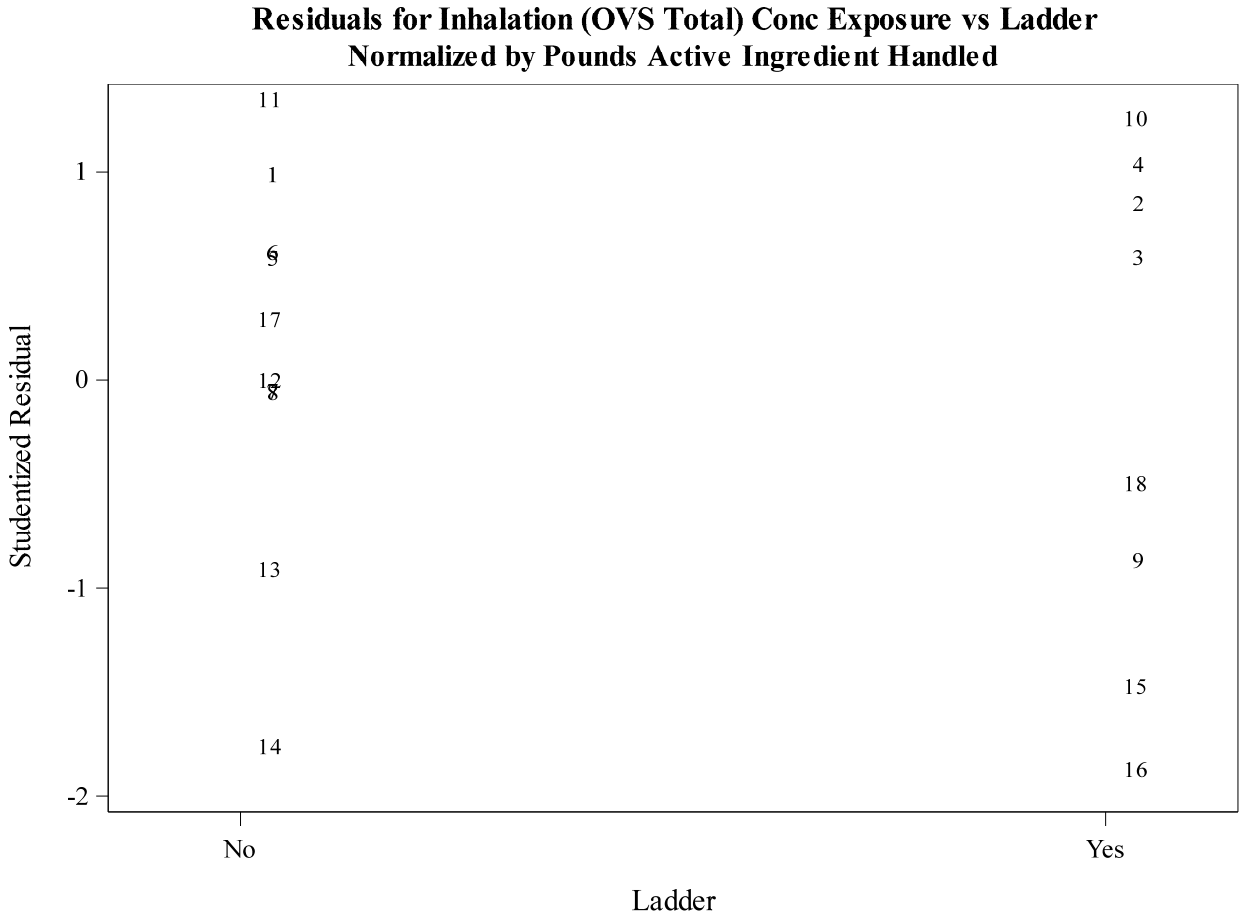


Figure 52. Residuals for Inhalation (OVS Total) Concentration versus use of ladder

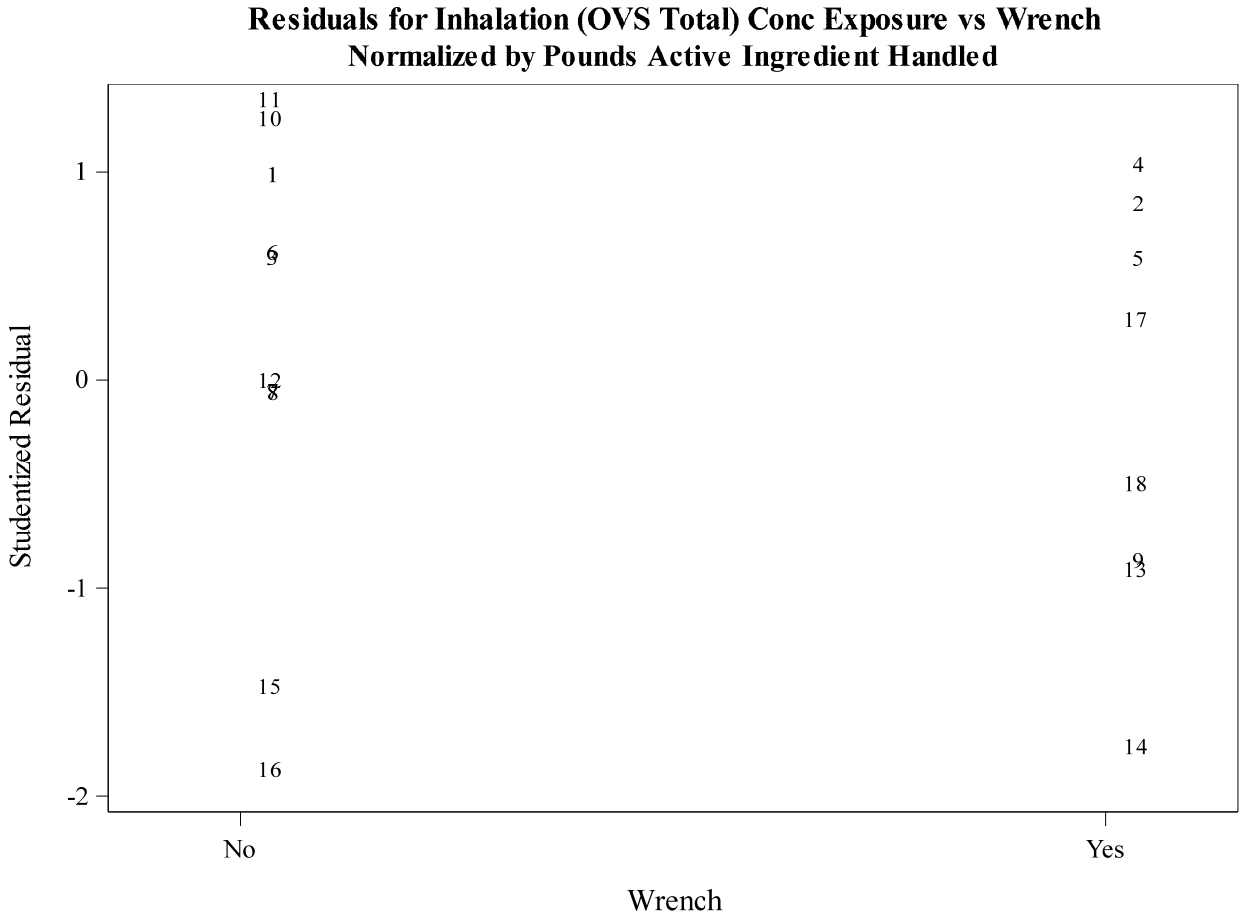


Figure 53. Residuals for Inhalation (OVS Total) Concentration versus use of wrench

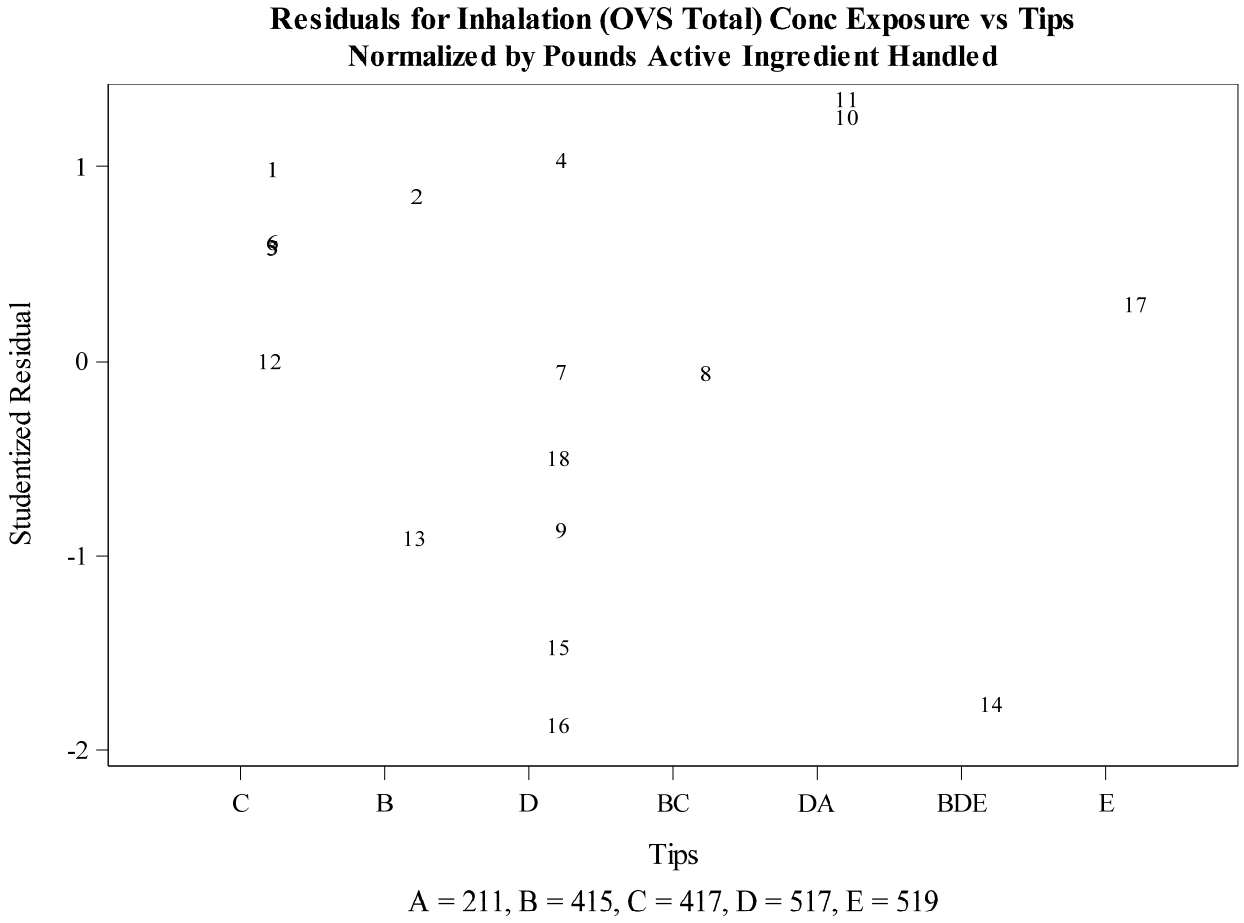


Figure 54. Residuals for Inhalation (OVS Total) Concentration versus spray tips used

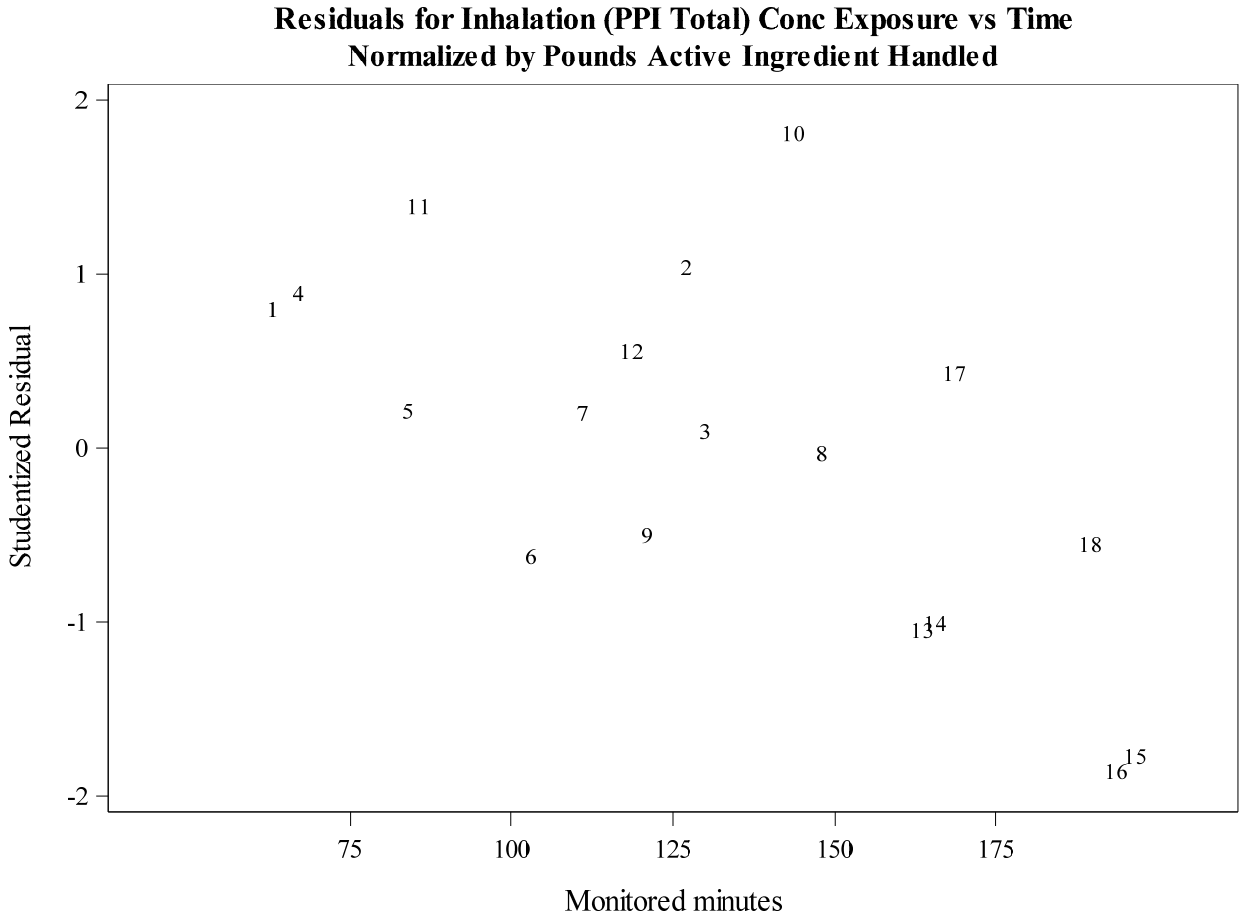


Figure 55. Residuals for Inhalation (PPI Total) Concentration versus monitored minutes

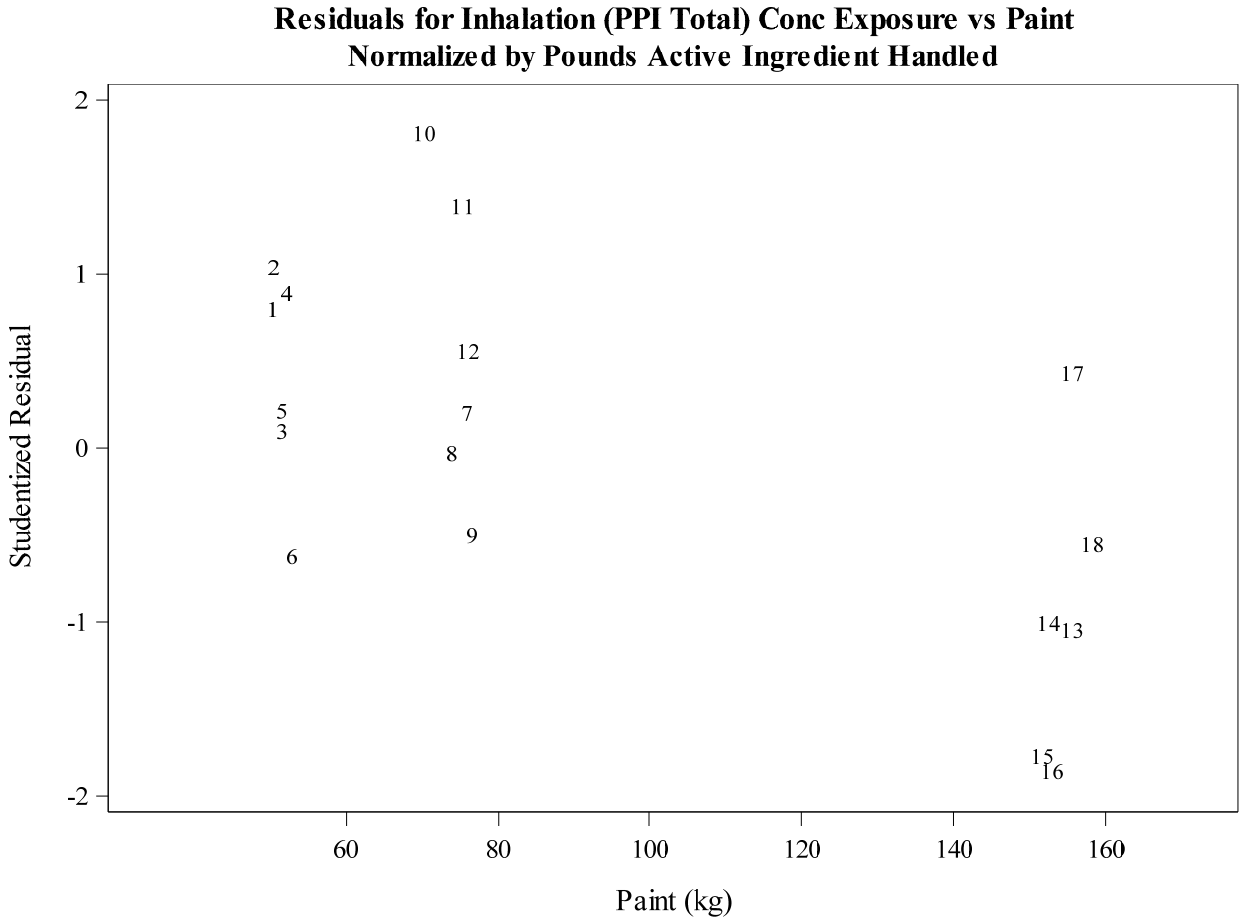


Figure 56. Residuals for Inhalation (PPI Total) Concentration versus amount of paint handled

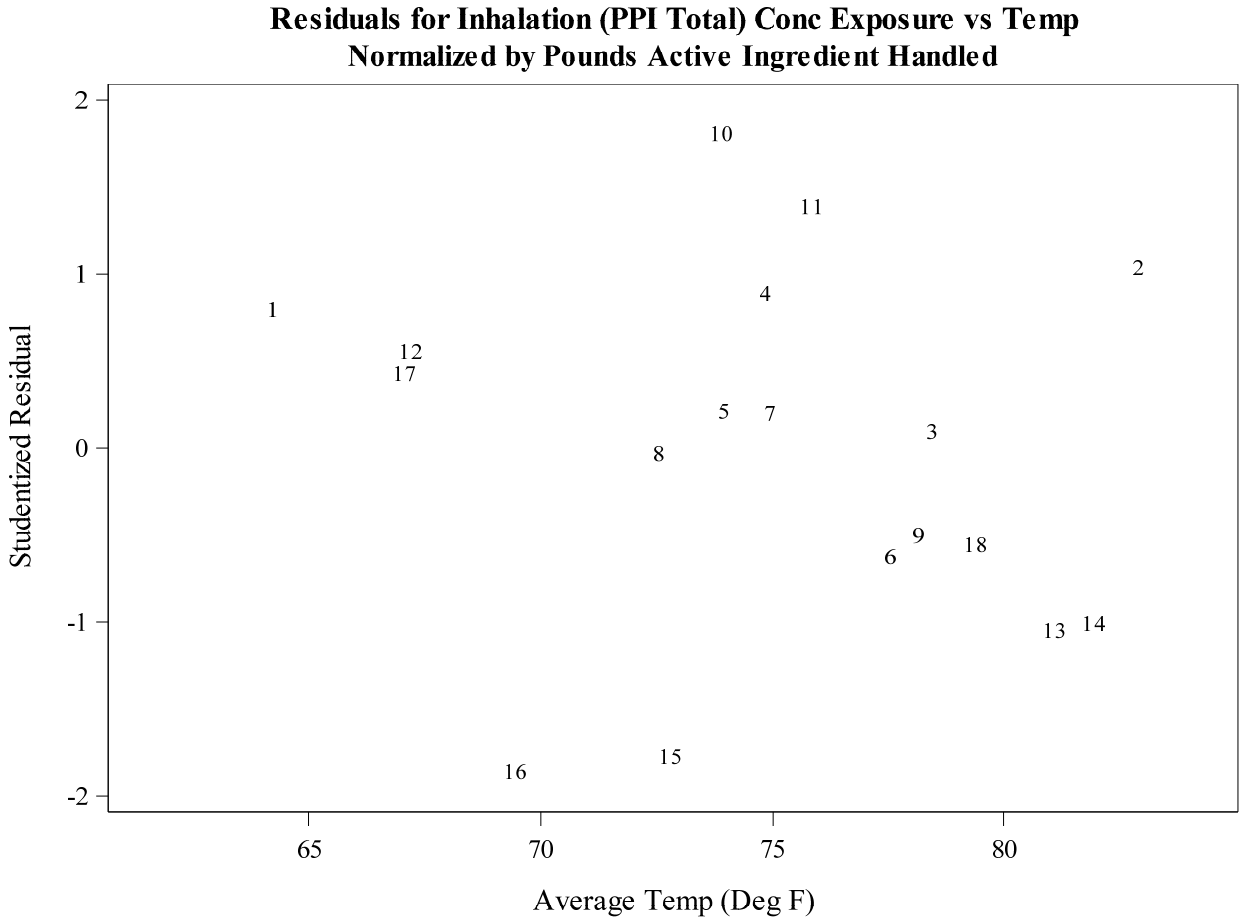


Figure 57. Residuals for Inhalation (PPI Total) Concentration versus average temperature

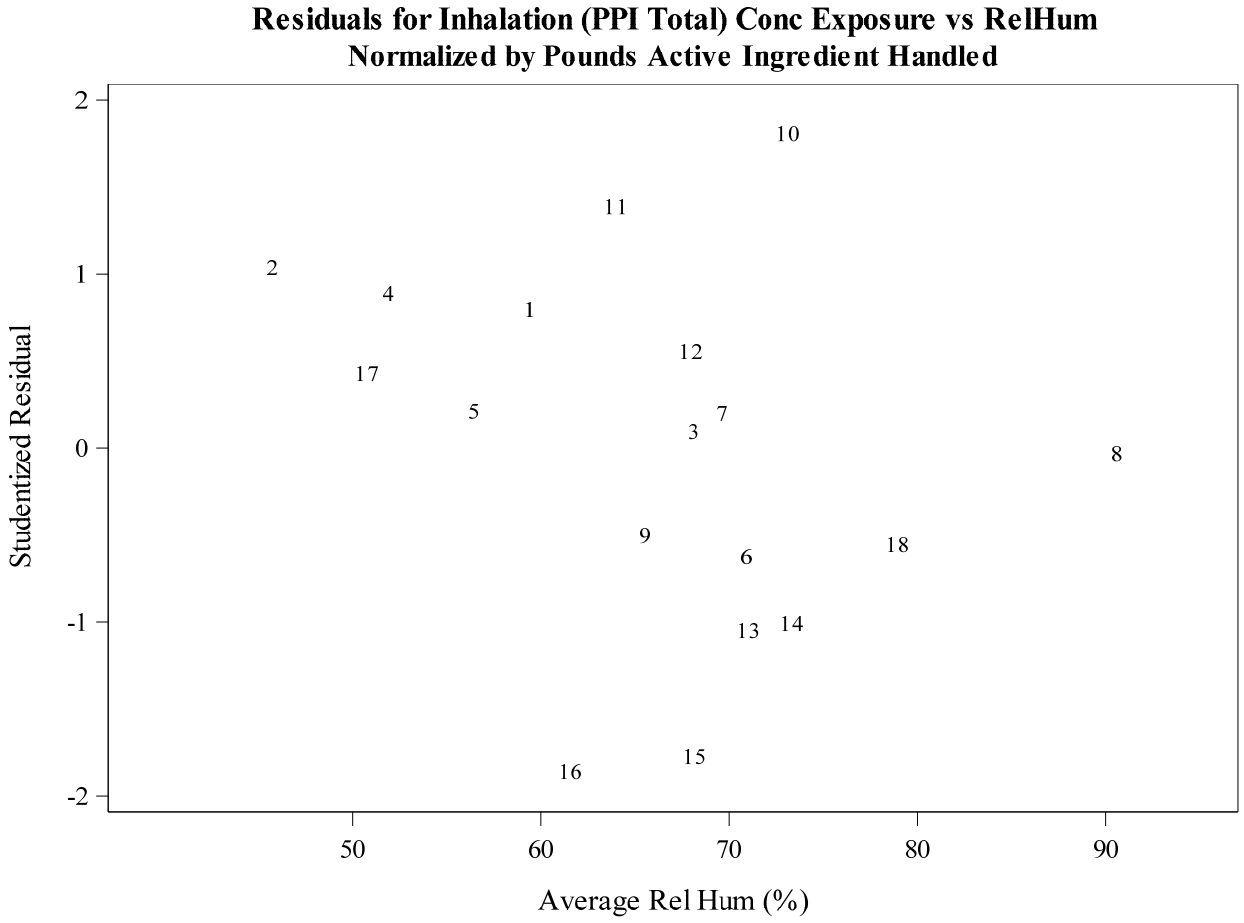


Figure 58. Residuals for Inhalation (PPI Total) Concentration versus average relative humidity

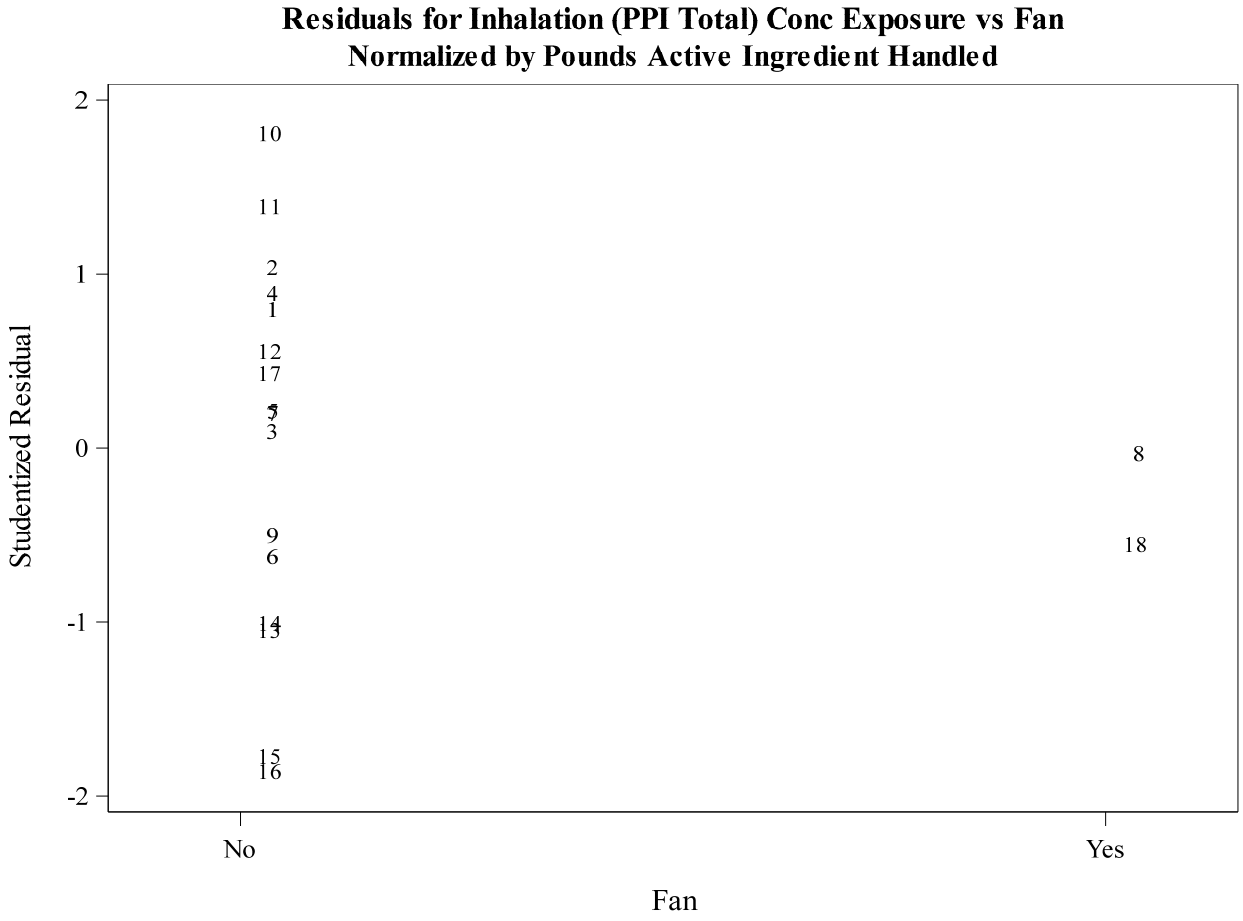


Figure 59. Residuals for Inhalation (PPI Total) Concentration versus use of fan

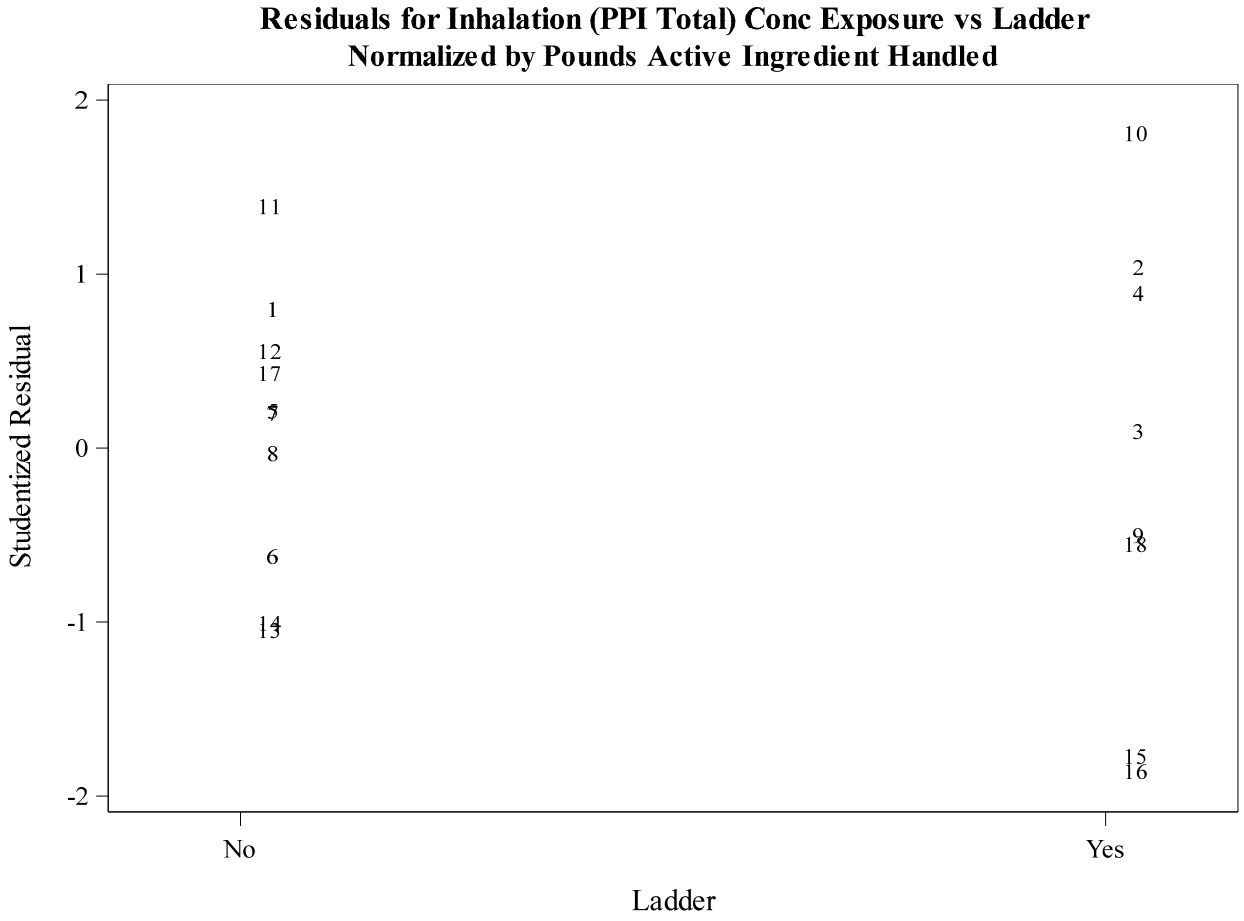


Figure 60. Residuals for Inhalation (PPI Total) Concentration versus use of ladder

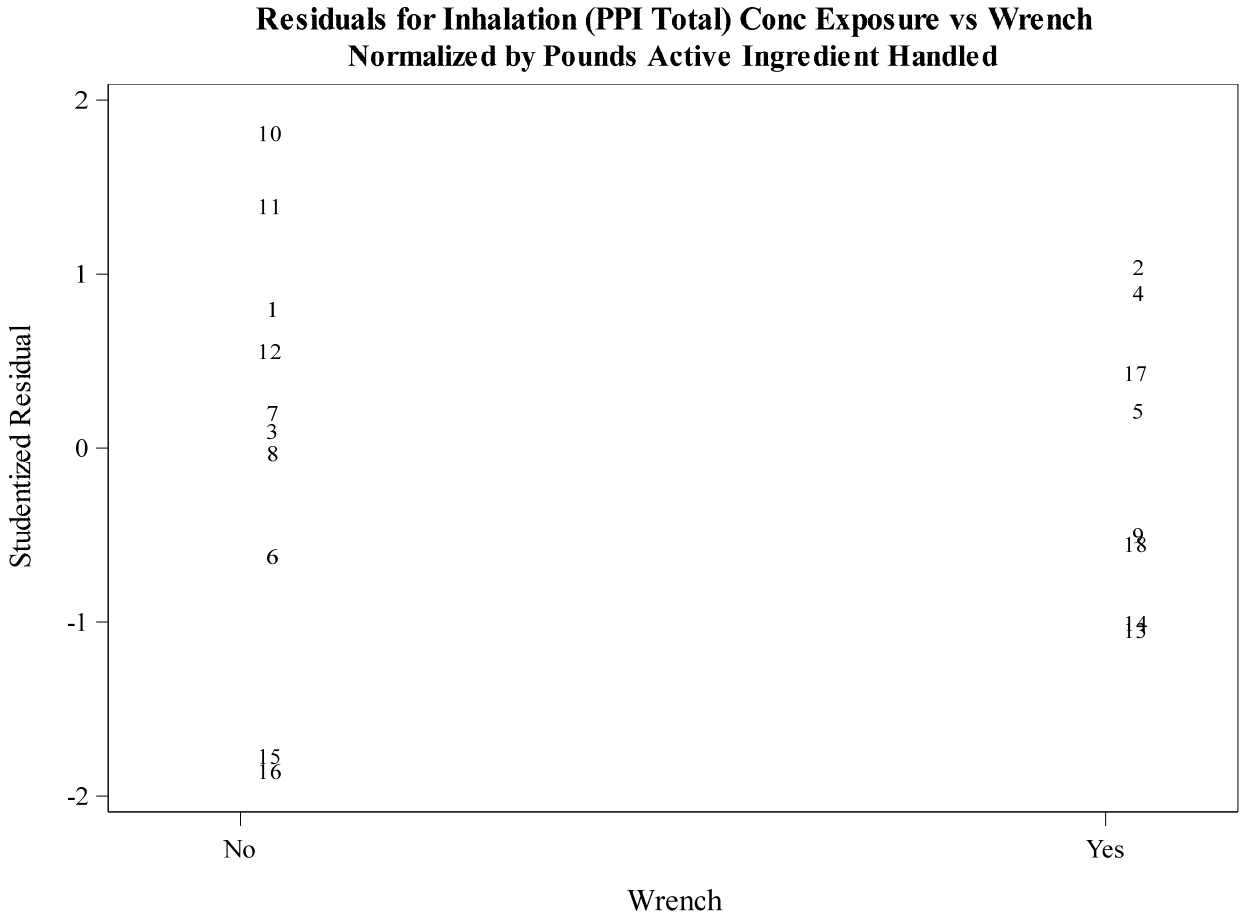


Figure 61. Residuals for Inhalation (PPI Total) Concentration versus use of wrench

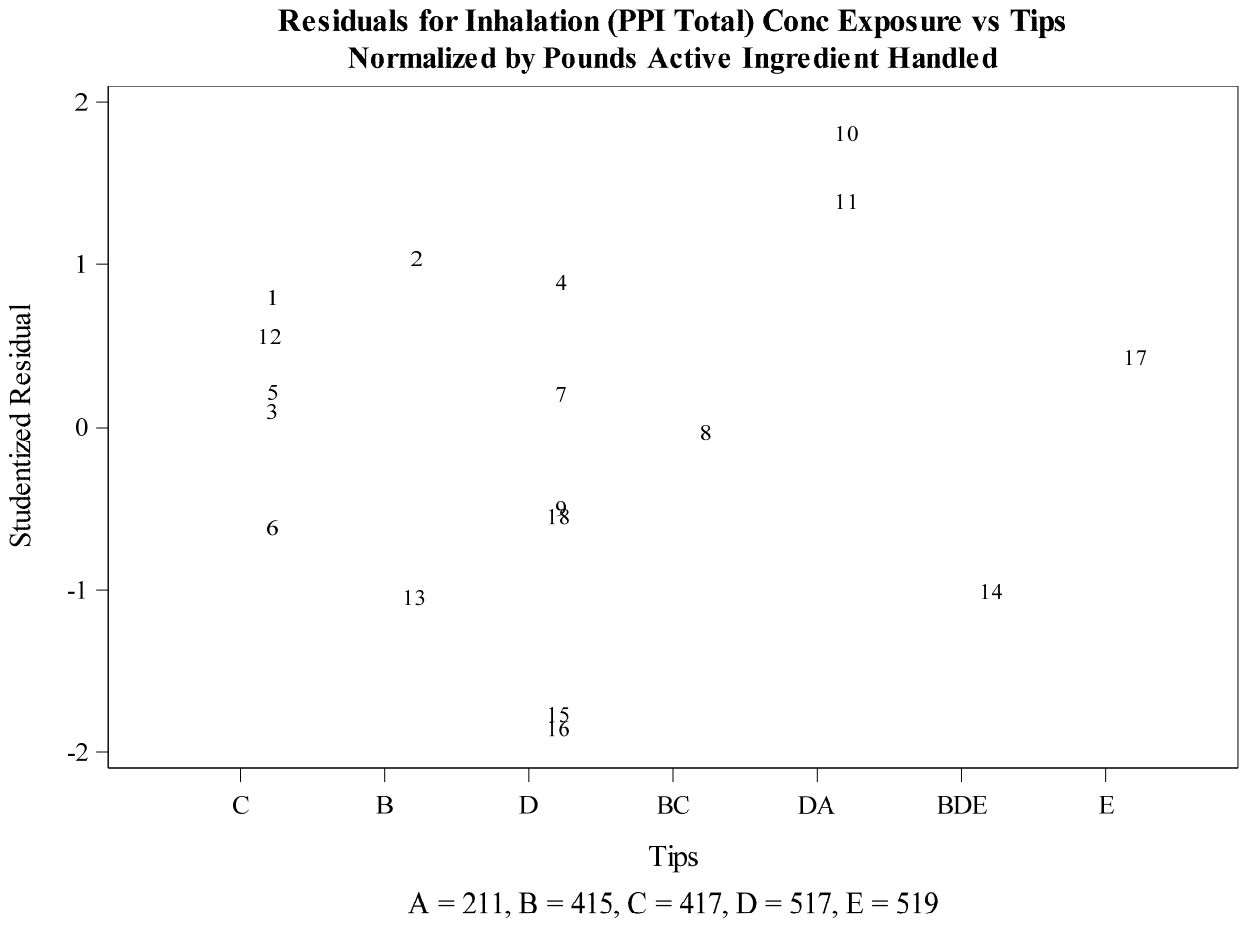


Figure 62. Residuals for Inhalation (PPI Total) Concentration versus spray tips used

These residual plots mostly show a weak relationship between the studentized residuals and the other descriptor variables. As an exception, for Inhalation (OVS Total) Conc and Inhalation (PPI Total) Conc, the residuals tend to be lower for the high numbers of minutes monitored or amount of paint used, which may suggest the need for alternative models to also take into account the minutes of monitoring and the amount of paint used. The best alternative approach is complicated by the fact that the experimental design and regression model accounts for the amount of active ingredient used, which increases with the amount of paint used and with the concentration.

10. Quadratic models

The log-log-linearity test was based on a linear model for log exposure versus log pounds active ingredient handled. The HSRB suggested that a quadratic model should also be considered.

There are two quadratic models that could be considered. Since the original linear model is of the form

Log (Exposure) = Intercept + Slope × Log (Pounds of Active Ingredient) + Error Terms,

the main quadratic model is of the form

Log (Exposure) = Intercept + Slope × Log (Pounds of Active Ingredient) + Quad × {Log (Pounds of Active Ingredient)}^{2}

+ Error Terms.

Note that the quadratic term is the square of the logarithm of the pounds of active ingredient rather than the logarithm of the square; the latter approach produces an ill-defined model with two multiples of the logarithm of the pounds of active ingredient.

Another approach might be to consider a quadratic model for exposure:

$$\text{Exposure} = \text{Intercept} + \text{Slope} \times (\text{Pounds of Active Ingredient}) + \text{Quad} \times (\text{Pounds of Active Ingredient})^2 + \text{Error Terms}.$$

We do not recommend this second approach for these data since the exposures are known to be non-negative and the quantile plots for hands only exposure data are better modeled using a log-normal distribution than using a normal distribution. Furthermore, unless the intercept is zero, this model predicts a nonzero exposure when the pounds of active ingredient is zero, and so a more realistic (though possibly poorer-fitting) model of this form would have a zero intercept. For other exposure data a log-log-linearity test could be carried out by fitting the zero intercept model

$$\text{Exposure} = \text{Slope} \times (\text{Pounds of Active Ingredient}) + \text{Quad} \times (\text{Pounds of Active Ingredient})^2 + \text{Error Terms}$$

and testing if Quad equals zero.

The parsimony principle suggests that the appropriate statistical procedure for this study is to first fit the quadratic regression model for the logarithm of the exposure

$$\text{Log (Exposure)} = \text{Intercept} + \text{Slope} \times \text{Log (Pounds of Active Ingredient)} + \text{Quad} \times \{\text{Log (Pounds of Active Ingredient)}\}^2 + \text{Error Terms}.$$

If the coefficient Quad is statistically significant at the 5% level, which is equivalent to requiring that the 95% confidence interval does not include zero, than the quadratic model is supported. Otherwise the linear model should be used.

Table 30 presents the quadratic coefficient Quad from the fitted quadratic regression models for all the exposure routes using All data. Coefficients for the Intercept and Slope are shown under model 2 in Tables 31 to 40 below.

Table 30. Quadratic coefficients with 95% confidence intervals for quadratic regression models for the log exposure versus log pounds active ingredient handled

Exposure Route	Estimate	Lower Bound	Upper Bound
Long Dermal	0.126	-0.035	0.288
Short Dermal	-0.004	-0.217	0.208
Long Short Dermal	0.079	-0.114	0.272
Hands Only	0.210	0.070	0.349
Inhalation (OVS Total) Concentration	0.021	-0.171	0.214
Inhalation (OVS Total) Dose	0.077	-0.052	0.207

Exposure Route	Estimate	Lower Bound	Upper Bound
Inhalation (OVS Total) Time-weighted Average	0.077	-0.052	0.207
Inhalation (PPI Total) Concentration	0.035	-0.182	0.251
Inhalation (PPI Total) Dose	0.094	-0.078	0.266
Inhalation (PPI Total) Time-weighted Average	0.094	-0.078	0.266

Except for the Hands Only Exposure, the 95% confidence intervals for Quad include zero, the quadratic coefficient is not statistically significant and the quadratic models are not supported.

11. Threshold Analyses

As shown above, two statistical models were fitted to the dermal exposure data and can be used to estimate the conditional mean exposure, i.e., the expected exposure conditional on the amount of active ingredient, E{Exposure | AI}.

Linear Model

Log (Exposure) = Intercept + Slope × Log (Pounds of Active Ingredient) + Random Error,

which implies

Equation 1: E{Exposure | AI} = Expected Exposure Given the Pounds of Active Ingredient $= C \times AI^{Slope}$,

where

$C = e^{Intercept} \times e^{Varerror/2}$.

Lognormal Model

If the value of Slope in the linear model is 1, then

Log (Normalized Exposure) = Log(Exposure / Pounds of Active Ingredient)

= Intercept* + Random Error,

which implies

Equation 2: E{Exposure | AI} = Expected Exposure Given the Pounds of Active Ingredient = C* × AI,

where

$C^* = e^{Intercept^*} \times e^{Vararror^*/2}$.

(The parameters for the lognormal model are asterisked). If Slope equals 1 then the two models are identical.

These two statistical models can be compared by calculating the threshold value of the pounds of active ingredient at which both models predict the same conditional mean exposure.

Define Threshold = $\left(\frac{C}{C^*}\right)^{\frac{1}{1-Slope}}$.

Thus E(X | AI) for the lognormal model > E(X | AI) for the linear model if and only if

$C^* \times AI > C \times AI^{Slope}$, which is true if and only if

Either Slope < 1 and AI > Threshold

Or Slope > 1 and AI < Threshold.

These are the conditions under which the lognormal model overestimates exposure compared to the linear model.

The most useful case is when slope < 1. If so, the lognormal model is "more conservative" (i.e., predicts higher exposure) when the pounds of active ingredient is high (more specifically, above the threshold). When the pounds of active ingredient is below the threshold, then either the linear model equation $C \times AI^{Slope}$ can be used to estimate the conditional mean exposure, or instead one can use the upper bound C* × Threshold. If AI = Threshold, then the estimates of the conditional mean exposure are the same.

The Threshold pounds of AI values and corresponding exposure values C* × Threshold were tabulated together with the estimated slopes in Table 29 above.

We now have two estimates of the conditional mean exposure for a given amount of active ingredient, equations 1 and 2. The graphs in Figure 63 to Figure 66 below compare the conditional mean exposure estimates for all four exposure routes. The conditional mean exposure is plotted against the pounds of active ingredient. The brown curve gives the estimates for the linear model in equation 1. The green line gives the estimates for the lognormal model in equation 2. The two estimates are equal if the pounds of active ingredient equals the Threshold value. The data points are labeled to show the concentration and volume groups. The letters l, m, and h in upper or lower case show the three volume groups for l = low = 10 gals, m = mid = 15 gals, and h = high = 30 gals. Lower case letters show the low concentration MEs (1200 ppm) and upper case letter show the high concentration MEs (12000 ppm).

For all the cases the estimated slope is less than 1. As proven above, the conditional mean exposure from the lognormal model will be greater than the conditional mean exposure from the linear model for amounts of active ingredient above the threshold (right hand side of the graph). The conditional mean exposure from the lognormal model will be less than the conditional mean exposure from the linear model for amounts of active ingredient below the threshold (left hand side of the graph).

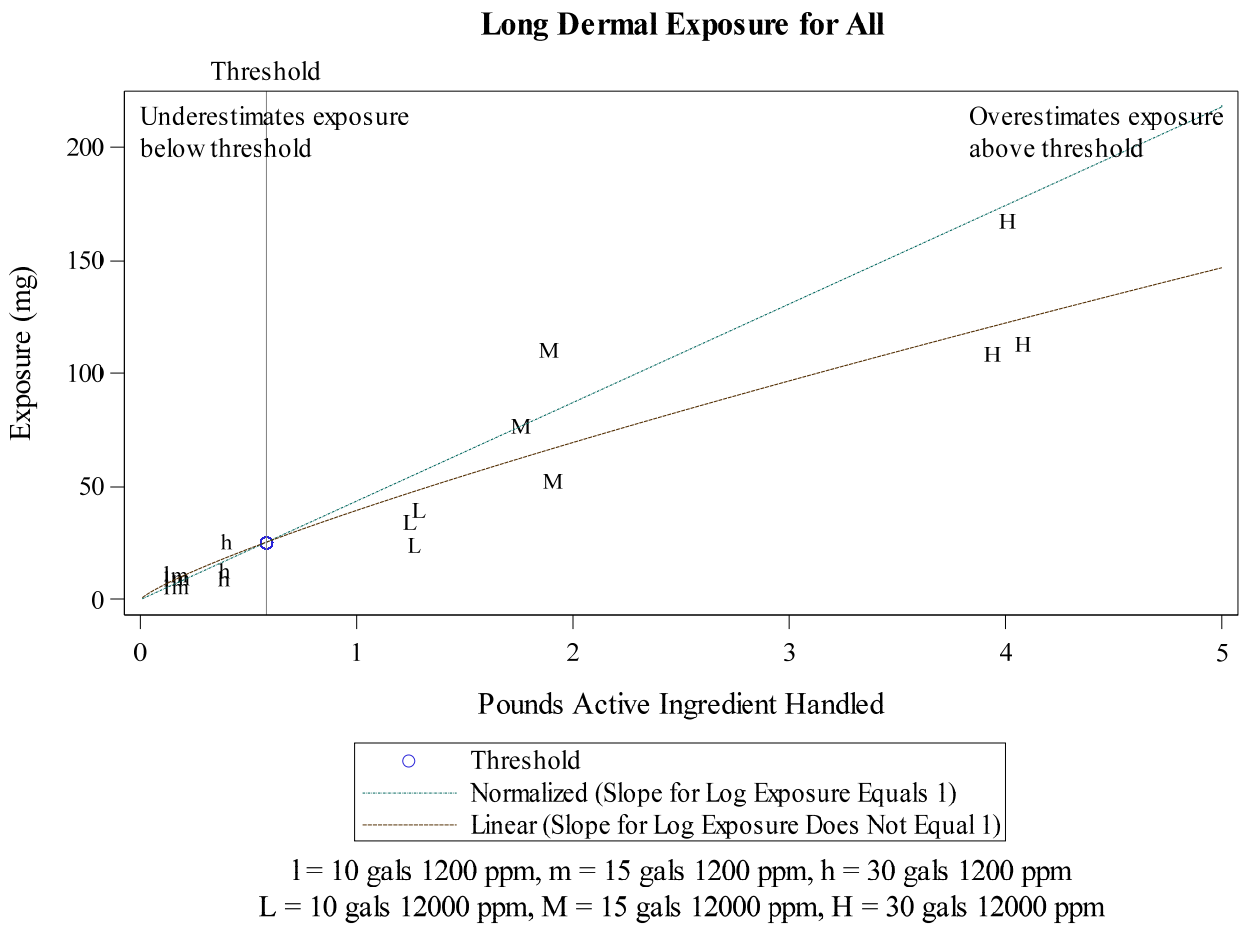
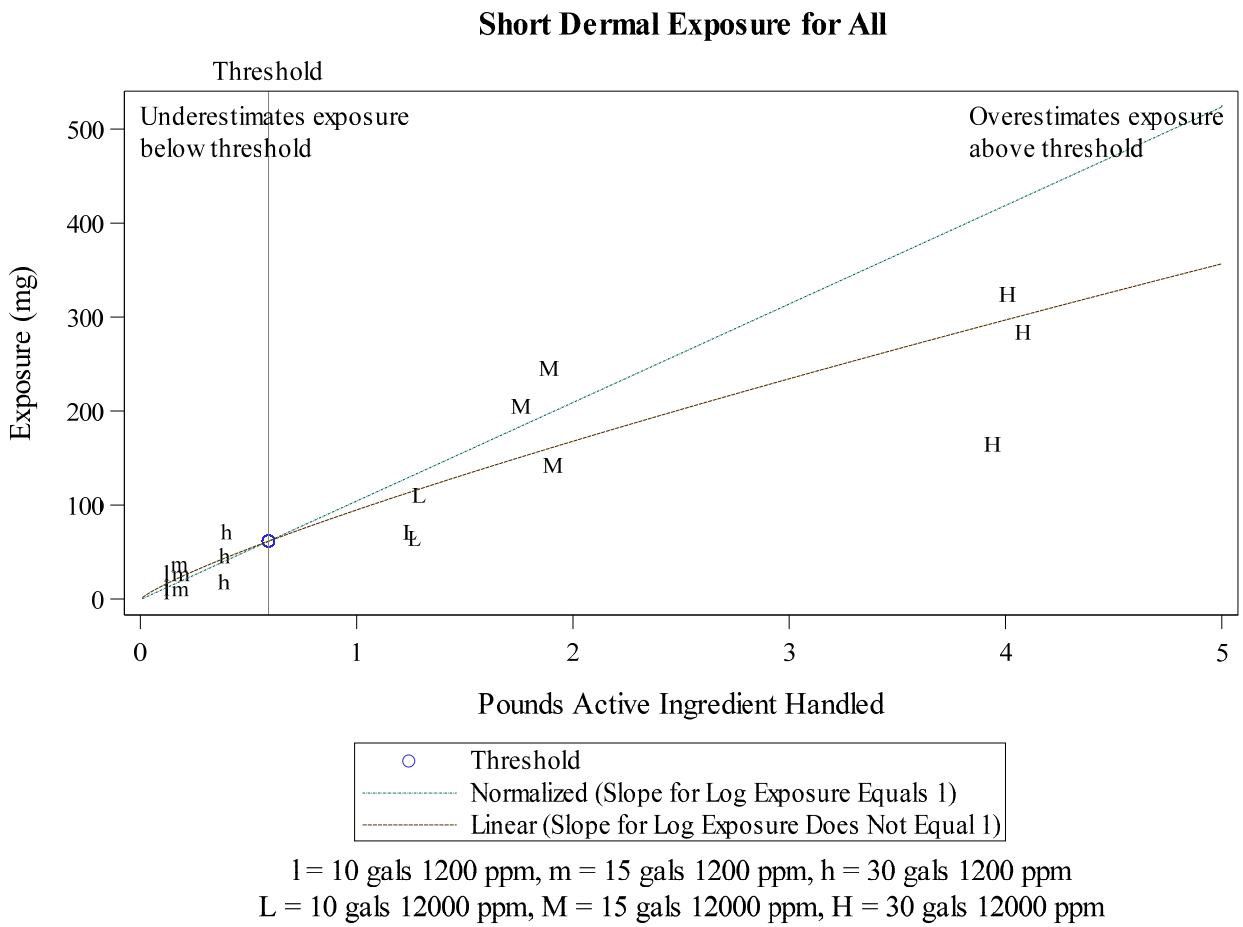


Figure 63. Threshold plot for Long Dermal Exposure (mg)



l = 10 gals 1200 ppm, m = 15 gals 1200 ppm, h = 30 gals 1200 ppm
L = 10 gals 12000 ppm, M = 15 gals 12000 ppm, H = 30 gals 12000 ppm

Figure 64. Threshold plot for Short Dermal Exposure (mg)

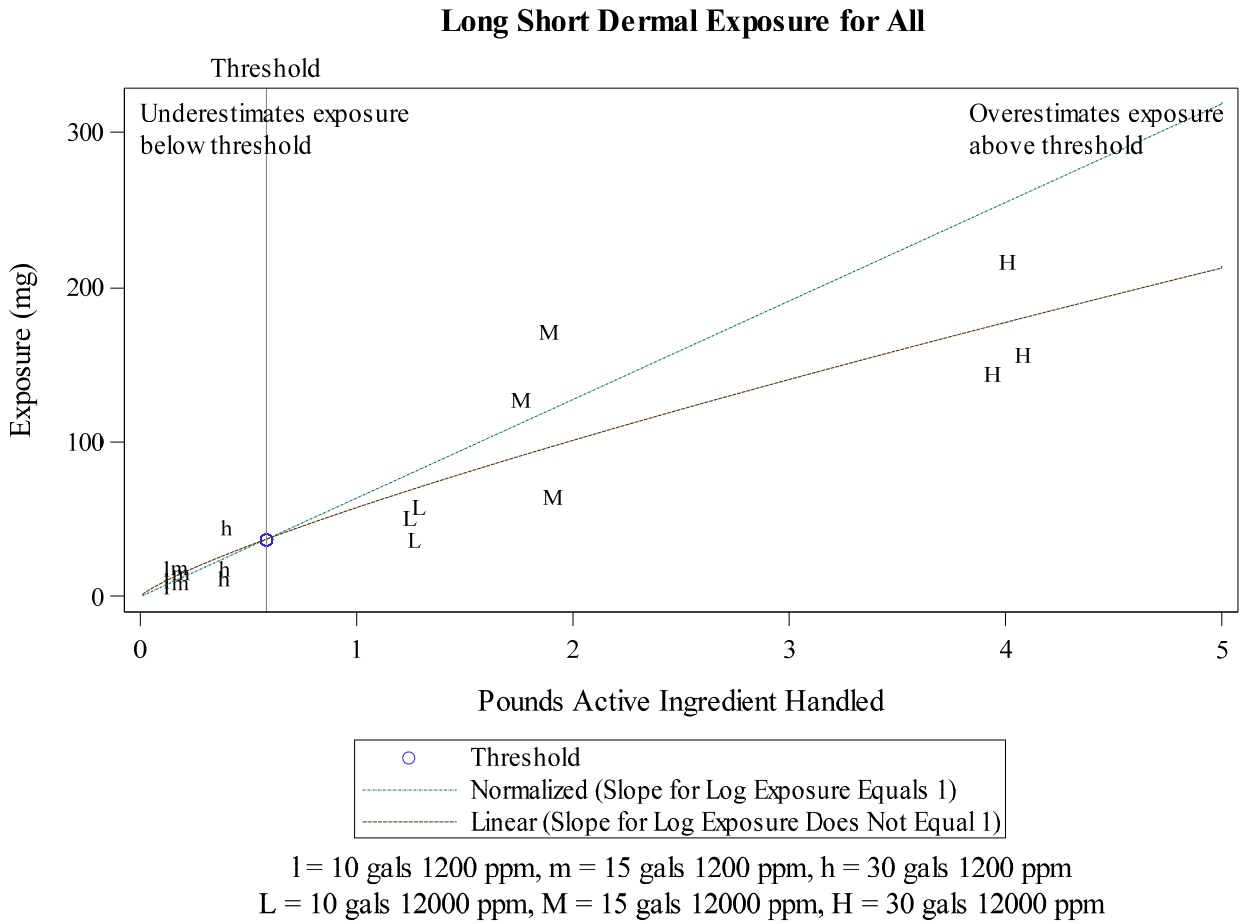
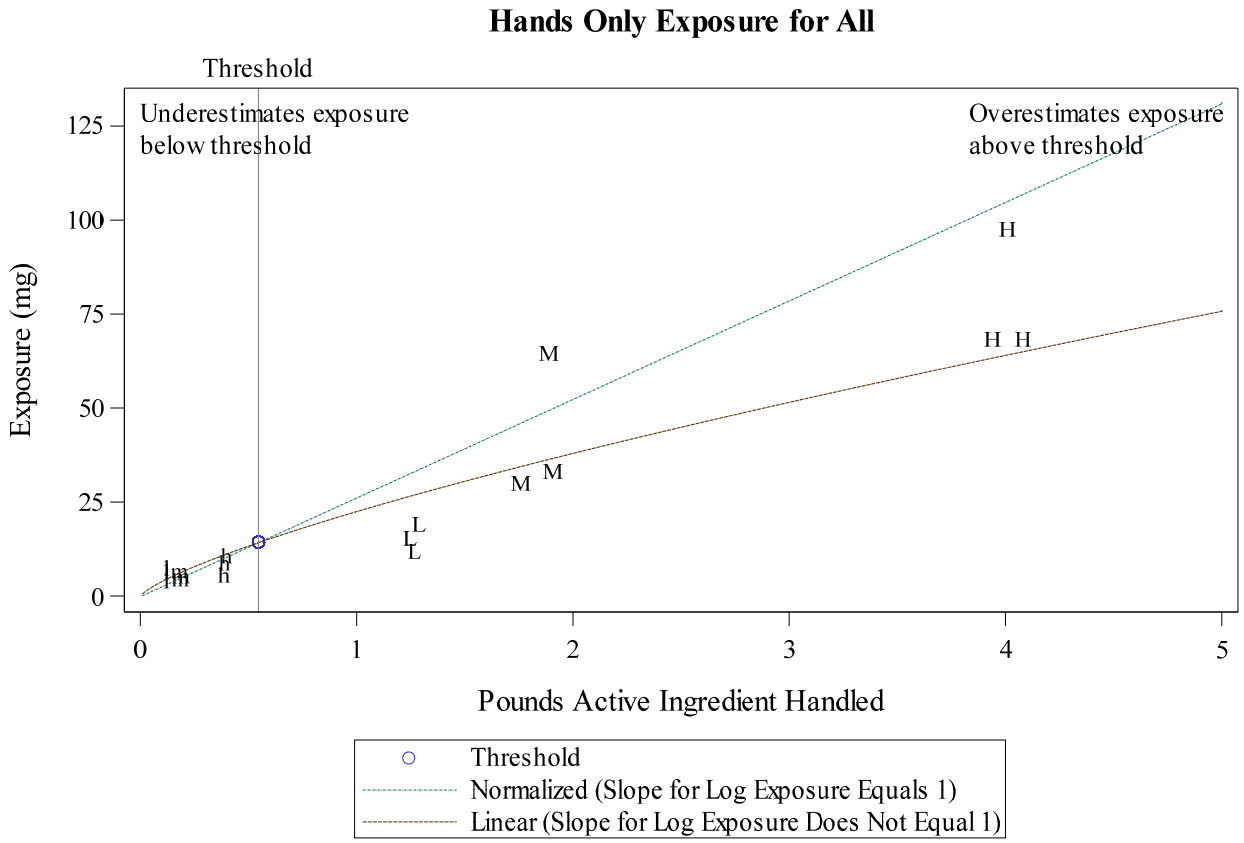
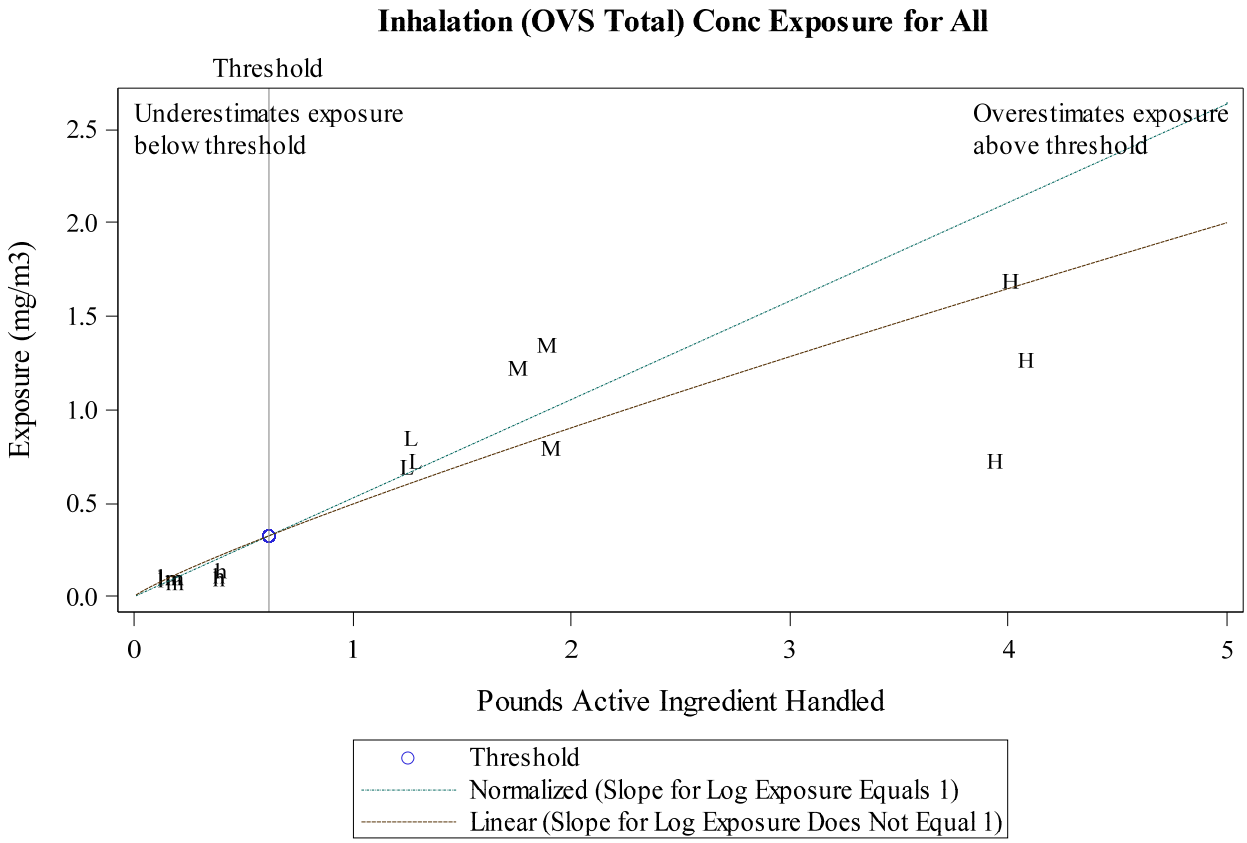


Figure 65. Threshold plot for Long Short Dermal Exposure (mg)



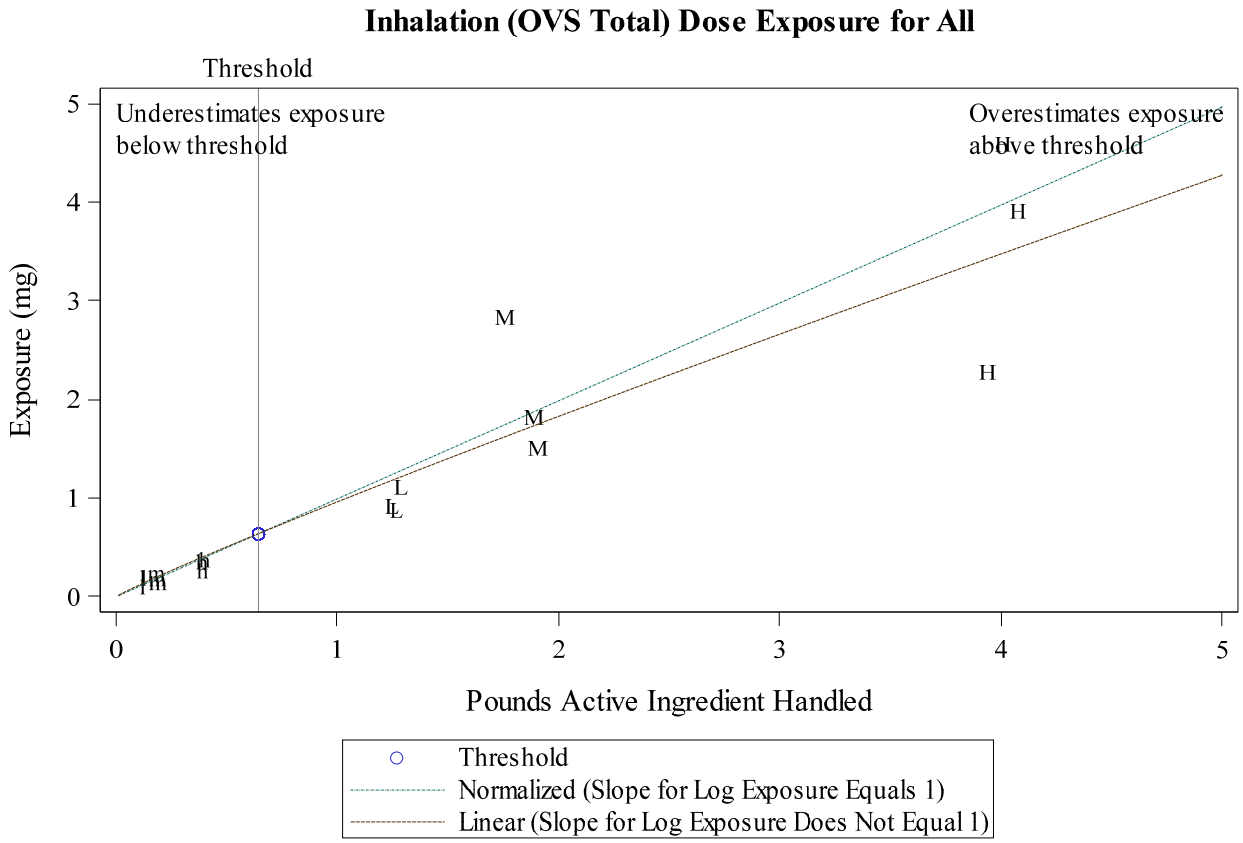
l = 10 gals 1200 ppm, m = 15 gals 1200 ppm, h = 30 gals 1200 ppm
L = 10 gals 12000 ppm, M = 15 gals 12000 ppm, H = 30 gals 12000 ppm

Figure 66. Threshold plot for Hands Only Exposure (mg)



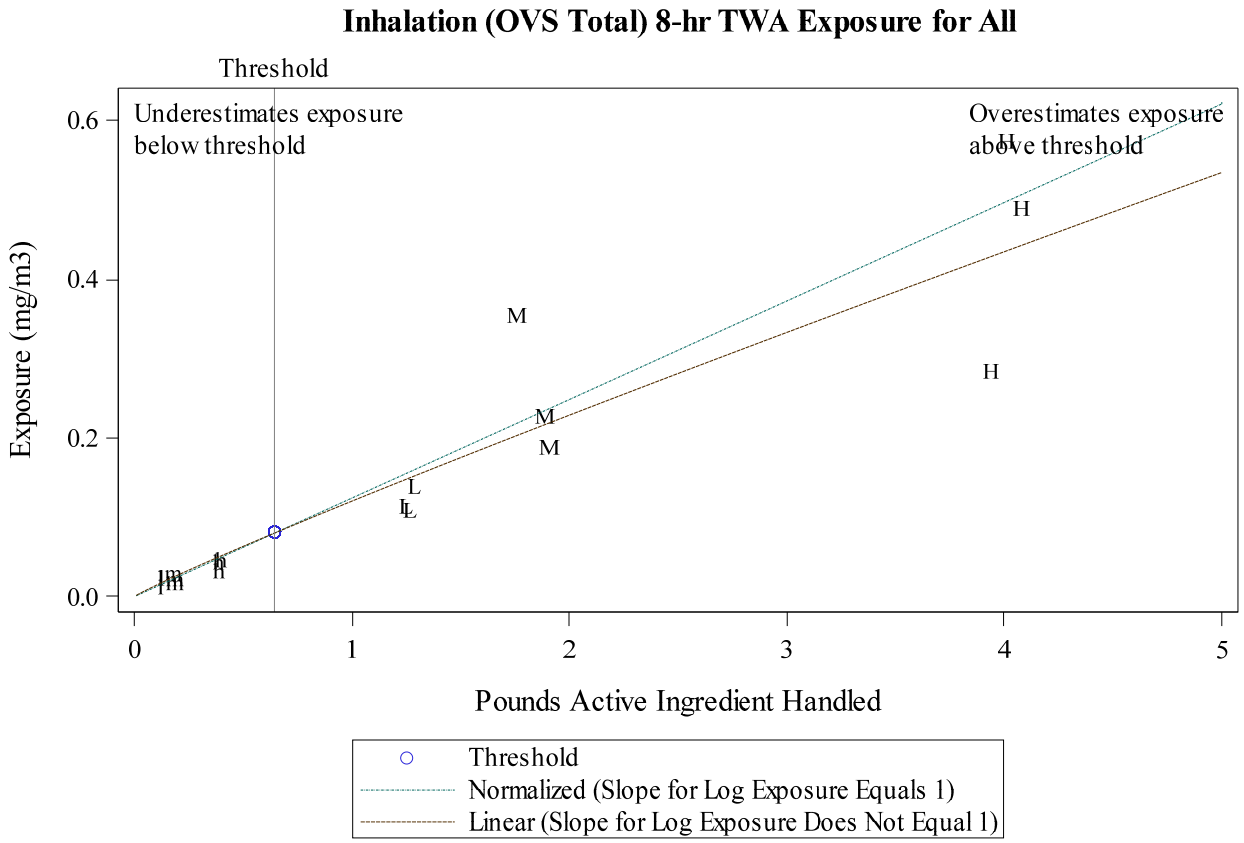
l = 10 gals 1200 ppm, m = 15 gals 1200 ppm, h = 30 gals 1200 ppm
L = 10 gals 12000 ppm, M = 15 gals 12000 ppm, H = 30 gals 12000 ppm

Figure 67. Threshold plot for Inhalation (OVS Total) Conc Exposure (mg/m^3)



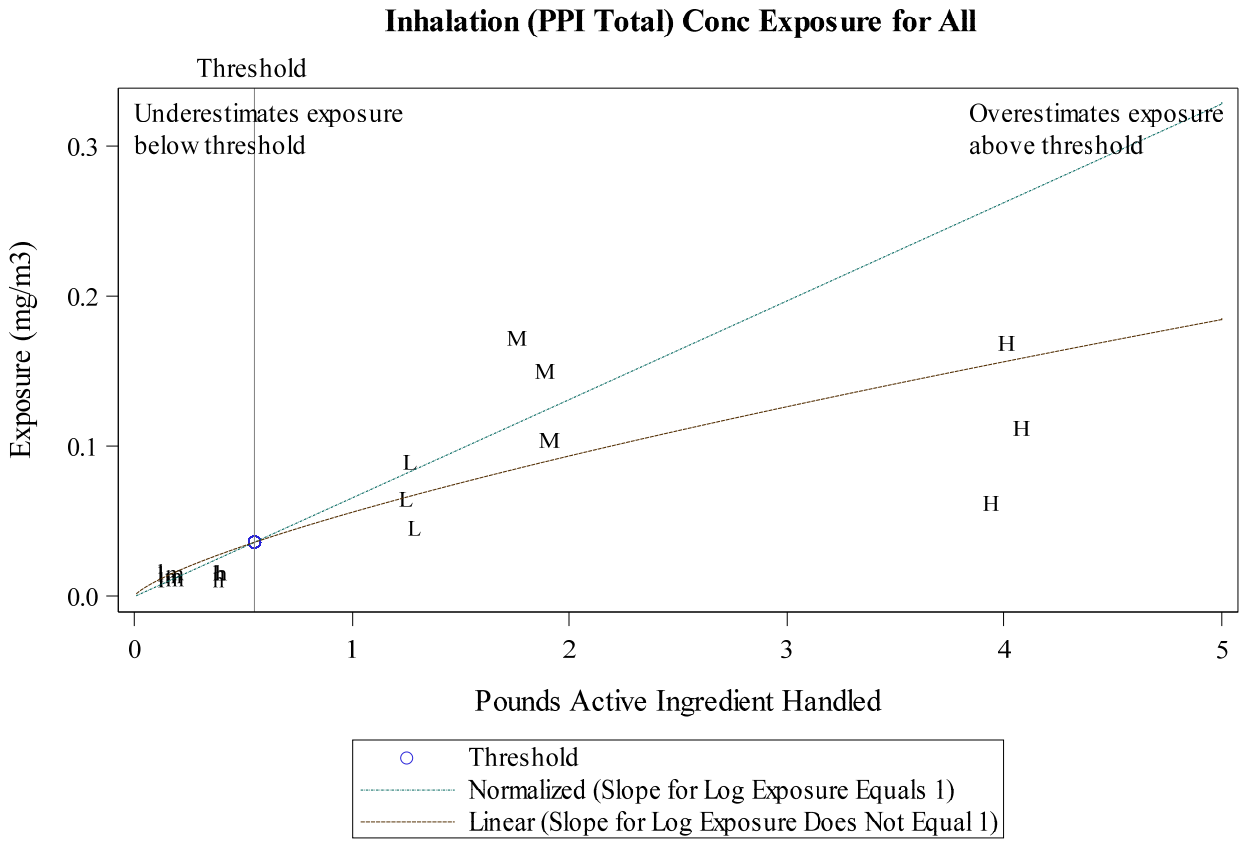
l = 10 gals 1200 ppm, m = 15 gals 1200 ppm, h = 30 gals 1200 ppm
L = 10 gals 12000 ppm, M = 15 gals 12000 ppm, H = 30 gals 12000 ppm

Figure 68. Threshold plot for Inhalation (OVS Total) Dose (mg)



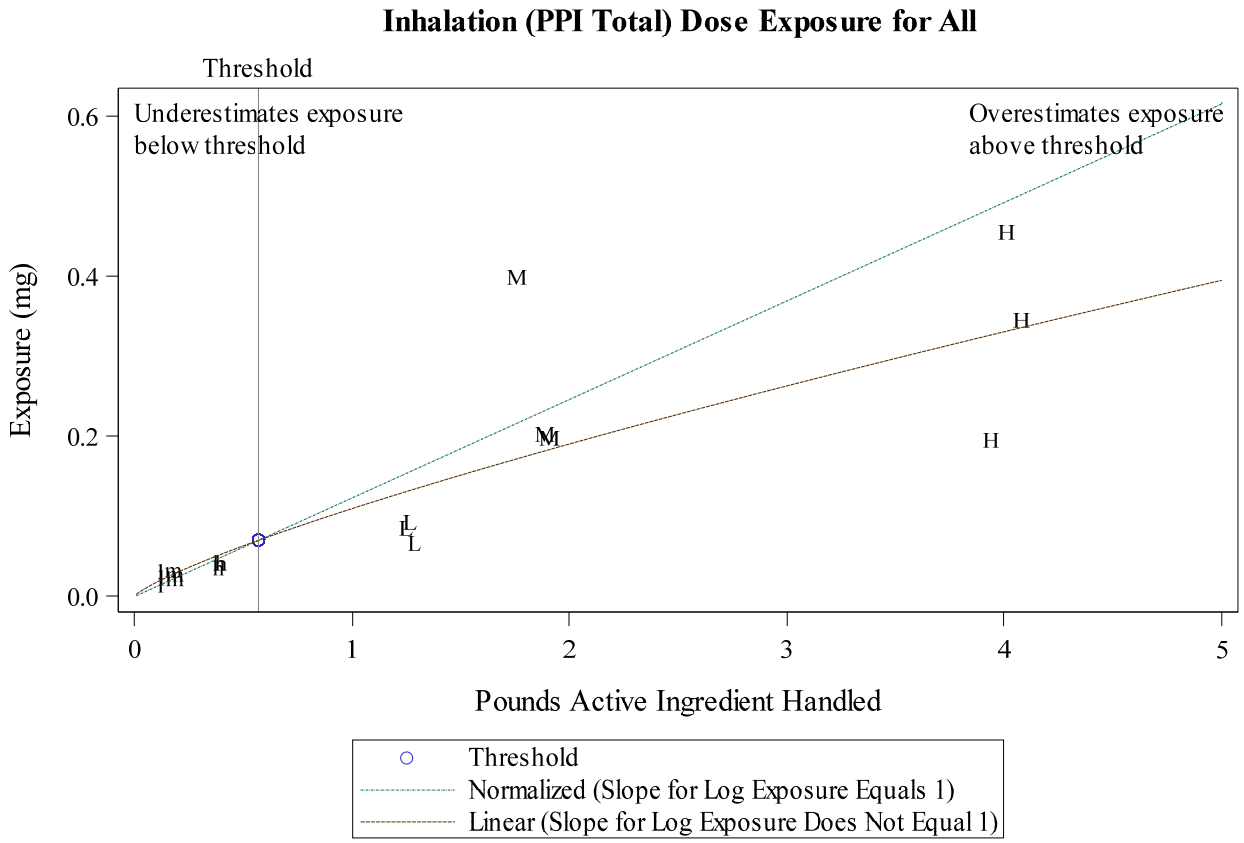
1 = 10 gals 1200 ppm, m = 15 gals 1200 ppm, h = 30 gals 1200 ppm
L = 10 gals 12000 ppm, M = 15 gals 12000 ppm, H = 30 gals 12000 ppm

Figure 69. Threshold plot for Inhalation (OVS Total) Time-weighted Average (mg/m^3)



l = 10 gals 1200 ppm, m = 15 gals 1200 ppm, h = 30 gals 1200 ppm
L = 10 gals 12000 ppm, M = 15 gals 12000 ppm, H = 30 gals 12000 ppm

Figure 70. Threshold plot for Inhalation (PPI Total) Conc Exposure (mg/m^3)



l = 10 gals 1200 ppm, m = 15 gals 1200 ppm, h = 30 gals 1200 ppm
L = 10 gals 12000 ppm, M = 15 gals 12000 ppm, H = 30 gals 12000 ppm

Figure 71. Threshold plot for Inhalation (PPI Total) Dose (mg)

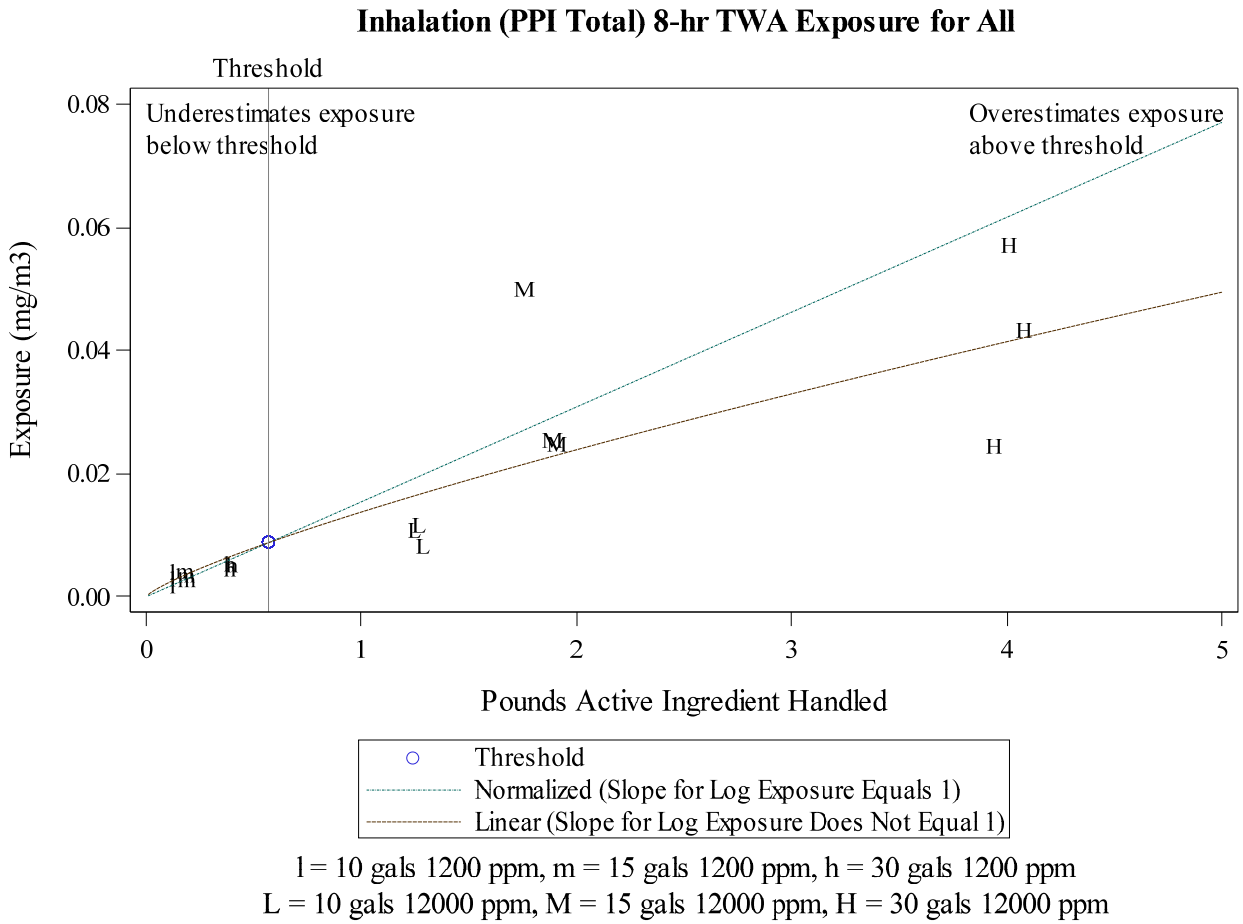


Figure 72. Threshold plot for Inhalation (PPI Total) Time-weighted Average (mg/m^3)

12. Alternative Statistical Approaches

In this section we present and compare some alternative statistical approaches including several that were suggested by the HSRB (in their review of the study protocol).

For estimating the 95th percentile of the normalized or unit exposure, our preferred approach is to fit a lognormal statistical model. HSRB recommended consideration of a quantile regression approach, which would provide confidence intervals for the 95th percentile assuming a simple random sample from an unspecified distribution. This is exactly the same as the above calculations of the confidence intervals for P95s calculated using the non-parametric bootstrap approach (see Table 19 to Table 28). The quantile regression approach could also be applied to the exposure to estimate the 95th percentile of the exposure as a linear or non-linear function of the amount of active ingredient. We chose not to apply the latter approach due to its complexity and because it would not be consistent with the modeling approaches used for estimating the arithmetic mean.

For estimating the dependence of exposure on the amount of active ingredient, our main model was the linear model described above, where the mean log(exposure) is a linear function of the log(amount of active ingredient). All logarithms in this memorandum are natural logarithms. This model is described by the equation:

Model 1: Log(Exposure) = $\mu + \beta$ log(AI) + Error

We also considered a quadratic model, but found the quadratic term to be non-significant except for Hands Only exposure. This model is described by the equation:

Model 2: Log(Exposure) = $\mu + \beta \log(AI) + \gamma \{\log(AI)\}^2$ + Error

To account for the effects of concentration and volume, we can consider adding these variables to the linear model, as categorical variables. These models are described by the equations:

Model 3: Log(Exposure) = $\mu + \beta \log(AI) + \alpha_1$ Ind1 + α_2 Ind2 + Error, where for concentration 1200 ppm, Ind1 = 1 and Ind2 = 0, and for concentration 12000 ppm, Ind1 = 0 and Ind2 = 1.

Model 4: Log(Exposure) = $\mu + \beta \log(AI) + \alpha_1$ Ind1 + α_2 Ind2 + α_3 Ind3 + Error, where for 10 gallons, Ind1 = 1, Ind2 = 0, and Ind3 = 0, for 15 gallons, Ind1 = 0, Ind2 = 1, and Ind3 = 0, and for 30 gallons, Ind1 = 0, Ind2 = 0, and Ind3 = 1.

Models 3 and 4 can easily be rewritten using a linear model for the concentration and a quadratic model for the volume, allowing other concentrations and volumes to be modeled.

The HSRB suggested including non-linear functions of the log-log-logistic or logistic forms:

Model 5. Log-log-logistic: Exposure = $\delta + \dfrac{\alpha - \delta}{1 + \gamma \exp\{\beta \log(AI)\}}$ + Error.

Model 6. 3-parameter logistic: Exposure = $\dfrac{C}{1 + \exp\{\alpha + \beta \times AI\}}$ + Error.

Since there is no background exposure in most of these scenarios, we will assume $\delta = 0$ for the log-log-logistic model. A major problem with using the log-log-logistic model is that the mean exposure is bounded above, which is possibly unrealistic.

For each of the above models, the errors are assumed to be normally distributed.

Another HRSB suggestion was to fit a gamma model instead of a log-normal model. We chose to assume a log link, so that the exposure has a gamma distribution with a mean $\exp(\mu + \beta \log(AI)$ and variance = $(\text{mean})^2/\phi$. This is model 7.

The fitted model parameters and confidence intervals are presented in Table 31 to Table 40 below. Note that the nonlinear models 6 and 7 were fitted using SAS's iterative procedure NLIN and it is possible that better estimates of the parameters could have been obtained using different starting points for the estimated parameters.

Model Parameters

Table 31. Alternative fitted statistical models for Long Dermal Exposure (mg)

Model	Parameter	Estimate	Lower Bound	Upper Bound
1. Linear regression of Ln(exposure) on Ln(AaiH)	μ	3.6018	3.4007	3.8029

Model	Parameter	Estimate	Lower Bound	Upper Bound
	β	0.8160	0.6633	0.9687
2. Quadratic regression of Ln(exposure) on Ln(AaiH)	μ	3.4236	3.1262	3.7209
	β	0.9165	0.7226	1.1105
	γ	0.1264	-0.0348	0.2876
3. Regression of Ln(exposure) on Ln(AaiH) and conc	μ	3.5857	2.8812	4.2903
	α_1	0.0247	-1.0097	1.0591
	α_2	0.0000		
	β	0.8069	0.3939	1.2199
4. Regression of Ln(exposure) on Ln(AaiH) and gallons	μ	3.6703	3.3034	4.0373
	α_1	-0.0944	-0.6139	0.4251
	α_2	-0.1104	-0.6173	0.3965
	α_3	0.0000		
	β	0.8166	0.6395	0.9938
5. Log-log logistic regression of exposure on AaiH	**α**	338.6904	-810.8015	1488.1824
	γ	8.1899	-22.3848	38.7647
	β	-1.1820	-2.5014	0.1374
6. 3-parameter logistic regression of exposure on AaiH	**α**	3.1895	1.6179	4.7611
	c	132.1071	108.6345	155.5798
	β	-1.8732	-2.9395	-0.8068
7. Gamma model for exposure	**μ**	3.6636	3.4924	3.8348
	β	0.8109	0.6858	0.9359
	ϕ	7.9890	4.2119	15.1531

Table 32. Alternative fitted statistical models for Short Dermal Exposure (mg)

Model	Parameter	Estimate	Lower Bound	Upper Bound
1. Linear regression of Ln(exposure) on Ln(AaiH)	μ	4.4517	4.2083	4.6951
	β	0.8202	0.6354	1.0050
2. Quadratic regression of Ln(exposure) on Ln(AaiH)	μ	4.4577	4.0657	4.8498
	β	0.8168	0.5611	1.0725
	γ	-0.0043	-0.2168	0.2082
3. Regression of Ln(exposure) on Ln(AaiH) and conc	μ	4.5267	3.6748	5.3785
	α_1	-0.1152	-1.3658	1.1353
	α_2	0.0000		
	β	0.8627	0.3634	1.3620
4. Regression of Ln(exposure) on Ln(AaiH) and gallons	μ	4.6327	4.2075	5.0580
	α_1	-0.2184	-0.8204	0.3837
	α_2	-0.3336	-0.9211	0.2539
	α_3	0.0000		
	β	0.8130	0.6077	1.0183
5. Log-log logistic regression of exposure on AaiH	**α**	485.9756	-417.4013	1389.3524
	γ	3.9306	-5.6646	13.5257
	β	-1.1130	-2.2658	0.0398
6. 3-parameter logistic regression of exposure on AaiH	**α**	2.8994	1.3335	4.4653
	c	263.8047	209.9731	317.6363
	β	-1.9891	-3.1431	-0.8351
7. Gamma model for exposure	**μ**	4.5327	4.3282	4.7373
	β	0.7955	0.6394	0.9515
	ϕ	5.6476	2.9930	10.6567

Table 33. Alternative fitted statistical models for Long Short Dermal (mg)

Model	Parameter	Estimate	Lower Bound	Upper Bound
1. Linear regression of Ln(exposure) on Ln(AaiH)	μ	3.9601	3.7334	4.1868
	β	0.8113	0.6392	0.9834
2. Quadratic regression of Ln(exposure) on Ln(AaiH)	μ	3.8485	3.4924	4.2046
	β	0.8742	0.6420	1.1065
	γ	0.0791	-0.1139	0.2722
3. Regression of Ln(exposure) on Ln(AaiH) and conc	μ	3.9327	3.1386	4.7267
	α_1	0.0422	-1.1236	1.2080
	α_2	0.0000		
	β	0.7958	0.3303	1.2612
4. Regression of Ln(exposure) on Ln(AaiH) and gallons	μ	4.1097	3.7067	4.5128
	α_1	-0.2087	-0.7793	0.3619
	α_2	-0.2377	-0.7945	0.3191
	α_3	0.0000		
	β	0.8133	0.6188	1.0079
5. Log-log logistic regression of exposure on AaiH	**α**	335.0161	-383.8257	1053.8580
	γ	4.8640	-7.8036	17.5316
	β	-1.1992	-2.5555	0.1570
6. 3-parameter logistic regression of exposure on AaiH	**α**	3.0982	1.3597	4.8368
	c	174.7637	139.2293	210.2981
	β	-1.9816	-3.1994	-0.7638
7. Gamma model for exposure	**μ**	4.0389	3.8447	4.2332
	β	0.8027	0.6579	0.9475
	ϕ	6.2338	3.2982	11.7823

Table 34. Alternative fitted statistical models for Hands Only Exposure (mg)

Model	Parameter	Estimate	Lower Bound	Upper Bound
1. Linear regression of Ln(exposure) on Ln(AaiH)	μ	3.0386	2.8315	3.2456
	β	0.7523	0.5952	0.9095
2. Quadratic regression of Ln(exposure) on Ln(AaiH)	μ	2.7430	2.4863	2.9997
	β	0.9190	0.7516	1.0864
	γ	0.2096	0.0705	0.3487
3. Regression of Ln(exposure) on Ln(AaiH) and conc	μ	3.1523	2.4298	3.8747
	α_1	-0.1748	-1.2354	0.8858
	α_2	0.0000		
	β	0.8168	0.3933	1.2402
4. Regression of Ln(exposure) on Ln(AaiH) and gallons	μ	3.1039	2.7288	3.4789
	α_1	-0.0470	-0.5779	0.4839
	α_2	-0.1631	-0.6811	0.3550
	α_3	0.0000		
	β	0.7407	0.5596	0.9217
5. Log-log logistic regression of exposure on AaiH	**α**	1.309E+07	7.980E+06	1.821E+07
	γ	6.781E+05		
	β	-1.0120	-1.3266	-0.6974
6. 3-parameter logistic regression of exposure on AaiH	**α**	3.3707	1.7312	5.0102
	C	80.1038	66.3767	93.8309
	β	-1.8251	-2.9080	-0.7422
7. Gamma model for exposure	**μ**	3.1084	2.9325	3.2843
	β	0.7572	0.6323	0.8821

Model	Parameter	Estimate	Lower Bound	Upper Bound
	ϕ	7.5336	3.9749	14.2784

Table 35. Alternative fitted statistical models for Inhalation (OVS Total) Conc Exposure (mg/m³)

Model	Parameter	Estimate	Lower Bound	Upper Bound
1. Linear regression of Ln(exposure) on Ln(AaiH)	μ	-0.7913	-1.0122	-0.5704
	β	0.8679	0.7002	1.0356
2. Quadratic regression of Ln(exposure) on Ln(AaiH)	μ	-0.8212	-1.1764	-0.4660
	β	0.8848	0.6531	1.1164
	γ	0.0212	-0.1713	0.2137
3. Regression of Ln(exposure) on Ln(AaiH) and conc	μ	-1.9117	-2.3389	-1.4846
	α_1	1.7222	1.0952	2.3493
	α_2	0.0000		
	β	0.2329	-0.0174	0.4833
4. Regression of Ln(exposure) on Ln(AaiH) and gallons	μ	-0.6261	-0.8537	-0.3986
	α_1	-0.6040	-0.9261	-0.2819
	α_2	0.2415	-0.0728	0.5559
	α_3	0.0000		
	β	0.9765	0.8667	1.0864
5. Log-log logistic regression of exposure on AaiH	**α**	1.3086	0.9302	1.6871
	γ	1.0687	-0.0676	2.2050
	β	-2.3387	-4.3332	-0.3443
6. 3-parameter logistic regression of exposure on AaiH	**α**	3.2139	1.2027	5.2250
	c	1.2302	0.9949	1.4654
	β	-2.9347	-4.7359	-1.1336

Model	Parameter	Estimate	Lower Bound	Upper Bound
7. Gamma model for exposure	**μ**	-0.7152	-0.8980	-0.5323
	β	0.8768	0.7385	1.0152
	ϕ	7.0578	3.7272	13.3646

Table 36. Alternative fitted statistical models for Inhalation (OVS Total) Dose (mg)

Model	Parameter	Estimate	Lower Bound	Upper Bound
1. Linear regression of Ln(exposure) on Ln(AaiH)	μ	-0.0827	-0.2387	0.0733
	β	0.9267	0.8083	1.0451
2. Quadratic regression of Ln(exposure) on Ln(AaiH)	μ	-0.1915	-0.4302	0.0473
	β	0.9880	0.8323	1.1437
	γ	0.0771	-0.0523	0.2065
3. Regression of Ln(exposure) on Ln(AaiH) and conc	μ	-0.2336	-0.7733	0.3060
	α_1	0.2319	-0.5603	1.0242
	α_2	0.0000		
	β	0.8412	0.5249	1.1575
4. Regression of Ln(exposure) on Ln(AaiH) and gallons	μ	-0.0020	-0.2824	0.2784
	α_1	-0.1543	-0.5512	0.2427
	α_2	-0.0721	-0.4595	0.3152
	α_3	0.0000		
	β	0.9397	0.8043	1.0750
5. Log-log logistic regression of exposure on AaiH	**α**	1.371E+06	8.340E+05	1.909E+06
	γ	1.419E+06		
	β	-0.9571	-1.2759	-0.6384
6. 3-parameter logistic regression of exposure on AaiH	**α**	3.1298	1.4328	4.8268

Model	Parameter	Estimate	Lower Bound	Upper Bound
	c	3.6596	2.9116	4.4075
	β	-1.7706	-2.9291	-0.6121
7. Gamma model for exposure	**μ**	-0.0415	-0.1788	0.0958
	β	0.9281	0.8268	1.0294
	ϕ	12.4540	6.5357	23.7316

Table 37. Alternative fitted statistical models for Inhalation (OVS Total) Time-weighted Average (mg/m^3)

Model	Parameter	Estimate	Lower Bound	Upper Bound
1. Linear regression of Ln(exposure) on Ln(AaiH)	μ	-2.1622	-2.3182	-2.0062
	β	0.9267	0.8083	1.0451
2. Quadratic regression of Ln(exposure) on Ln(AaiH)	μ	-2.2709	-2.5097	-2.0322
	β	0.9880	0.8323	1.1437
	γ	0.0771	-0.0523	0.2065
3. Regression of Ln(exposure) on Ln(AaiH) and conc	μ	-2.3131	-2.8527	-1.7734
	α_1	0.2319	-0.5603	1.0242
	α_2	0.0000		
	β	0.8412	0.5249	1.1575
4. Regression of Ln(exposure) on Ln(AaiH) and gallons	μ	-2.0814	-2.3618	-1.8010
	α_1	-0.1543	-0.5512	0.2427
	α_2	-0.0721	-0.4595	0.3152
	α_3	0.0000		
	β	0.9397	0.8043	1.0750
5. Log-log logistic regression of exposure on AaiH	**α**	1.2794	-4.1340	6.6928
	γ	9.8311	-34.6700	54.3322
	β	-1.2141	-2.7039	0.2758

Model	Parameter	Estimate	Lower Bound	Upper Bound
6. 3-parameter logistic regression of exposure on AaiH	**α**	3.1298	1.4328	4.8268
	c	0.4574	0.3640	0.5509
	β	-1.7706	-2.9291	-0.6121
7. Gamma model for exposure	**μ**	-2.1209	-2.2582	-1.9836
	β	0.9281	0.8268	1.0294
	ϕ	12.4540	6.5357	23.7316

Table 38. Alternative fitted statistical models for Inhalation (PPI Total) Conc Exposure (mg/m^3)

Model	Parameter	Estimate	Lower Bound	Upper Bound
1. Linear regression of Ln(exposure) on Ln(AaiH)	μ	-2.9903	-3.2389	-2.7416
	β	0.7395	0.5507	0.9282
2. Quadratic regression of Ln(exposure) on Ln(AaiH)	μ	-3.0392	-3.4381	-2.6403
	β	0.7671	0.5069	1.0273
	γ	0.0347	-0.1815	0.2509
3. Regression of Ln(exposure) on Ln(AaiH) and conc	μ	-4.0275	-4.6614	-3.3935
	α_1	1.5943	0.6636	2.5250
	α_2	0.0000		
	β	0.1517	-0.2199	0.5233
4. Regression of Ln(exposure) on Ln(AaiH) and gallons	μ	-2.6807	-2.9898	-2.3716
	α_1	-0.7660	-1.2036	-0.3284
	α_2	-0.0408	-0.4677	0.3862
	α_3	0.0000		
	β	0.8389	0.6897	0.9881
5. Log-log logistic regression of exposure on AaiH	**α**	0.1281	0.1009	0.1553

Model	Parameter	Estimate	Lower Bound	Upper Bound
	γ	26.3224	-479.7074	532.3523
	β	-14.1799	-95.2161	66.8564
6. 3-parameter logistic regression of exposure on AaiH	**α**	3.8562	-0.1804	7.8928
	c	0.1287	0.0970	0.1604
	β	-3.4284	-6.8342	-0.0225
7. Gamma model for exposure	**μ**	-2.8852	-3.0940	-2.6763
	β	0.7633	0.6059	0.9207
	ϕ	5.4048	2.8665	10.1906

Table 39. Alternative fitted statistical models for Inhalation (PPI Total) Dose (mg)

Model	Parameter	Estimate	Lower Bound	Upper Bound
1. Linear regression of Ln(exposure) on Ln(AaiH)	μ	-2.2845	-2.4902	-2.0788
	β	0.7955	0.6393	0.9516
2. Quadratic regression of Ln(exposure) on Ln(AaiH)	μ	-2.4176	-2.7348	-2.1004
	β	0.8705	0.6636	1.0773
	γ	0.0943	-0.0776	0.2663
3. Regression of Ln(exposure) on Ln(AaiH) and conc	μ	-2.3401	-3.0603	-1.6200
	α_1	0.0855	-0.9717	1.1427
	α_2	0.0000		
	β	0.7639	0.3418	1.1860
4. Regression of Ln(exposure) on Ln(AaiH) and gallons	μ	-2.0572	-2.3980	-1.7164
	α_1	-0.3148	-0.7973	0.1676
	α_2	-0.3639	-0.8347	0.1069
	α_3	0.0000		
	β	0.7979	0.6334	0.9625

Model	Parameter	Estimate	Lower Bound	Upper Bound
5. Log-log logistic regression of exposure on AaiH	**α**	0.3189	0.2303	0.4074
	γ	16.1675	-30.5333	62.8683
	β	-7.6093	-16.5349	1.3162
6. 3-parameter logistic regression of exposure on AaiH	**α**	4.5153	0.2565	8.7740
	c	0.3332	0.2449	0.4215
	β	-3.0263	-5.9495	-0.1032
7. Gamma model for exposure	**μ**	-2.2037	-2.3864	-2.0210
	β	0.8151	0.6803	0.9498
	ϕ	7.0305	3.7130	13.3121

Table 40. Alternative fitted statistical models for Inhalation (PPI Total) Time-weighted average (mg/m^3)

Model	Parameter	Estimate	Lower Bound	Upper Bound
1. Linear regression of Ln(exposure) on Ln(AaiH)	μ	-4.3640	-4.5697	-4.1582
	β	0.7955	0.6393	0.9516
2. Quadratic regression of Ln(exposure) on Ln(AaiH)	μ	-4.4970	-4.8142	-4.1798
	β	0.8705	0.6636	1.0773
	γ	0.0943	-0.0776	0.2663
3. Regression of Ln(exposure) on Ln(AaiH) and conc	μ	-4.4196	-5.1397	-3.6994
	α_1	0.0855	-0.9717	1.1427
	α_2	0.0000		
	β	0.7639	0.3418	1.1860
4. Regression of Ln(exposure) on Ln(AaiH) and gallons	μ	-4.1367	-4.4775	-3.7959
	α_1	-0.3148	-0.7973	0.1676
	α_2	-0.3639	-0.8347	0.1069

Model	Parameter	Estimate	Lower Bound	Upper Bound
	α_3	0.0000		
	β	0.7979	0.6334	0.9625
5. Log-log logistic regression of exposure on AaiH	**α**	0.0399	0.0288	0.0509
	γ	16.1676	-30.5335	62.8687
	β	-7.6094	-16.5350	1.3163
6. 3-parameter logistic regression of exposure on AaiH	**α**	4.5153	0.2565	8.7741
	c	0.0416	0.0306	0.0527
	β	-3.0264	-5.9495	-0.1032
7. Gamma model for exposure	**μ**	-4.2831	-4.4659	-4.1004
	β	0.8151	0.6803	0.9498
	ϕ	7.0305	3.7130	13.3122

Model Comparisons

One way to compare the fit of the 7 models presented above is to use the Akaike Information Criterion (AIC), which takes minus twice the log-likelihood and then makes an adjustment or penalty for the number of parameters in the model. To properly apply this approach to the seven models it was first necessary to re-express all of them using the same dependent variable, ln(exposure), since models 1 to 4 were specified using ln(exposure) but models 5 to 7 were specified using exposure. The following two tables compare the AIC values for the various Dermal and Inhalation exposure measures. The smaller values of the AIC suggest a better-fitting model.

Table 41. Akaike Information Criteria values for alternative models for Dermal Exposure

Model	Long Dermal	Short Dermal	Long Short Dermal	Hands Only
1. Linear regression of Ln(exposure) on Ln(AaiH)	20.38	27.25	24.69	21.42
2. Quadratic regression of Ln(exposure) on Ln(AaiH)	19.30	29.25	25.79	14.01
3. Regression of Ln(exposure) on Ln(AaiH) and conc	22.37	29.21	26.68	23.28

Model	Long Dermal	Short Dermal	Long Short Dermal	Hands Only
4. Regression of Ln(exposure) on Ln(AaiH) and gallons	24.05	29.36	27.42	24.83
5. Log-log logistic regression of exposure on AaiH	43.80	44.72	46.94	42.86
6. 3-parameter logistic regression of exposure on AaiH	41.02	42.22	44.36	39.29
7. Gamma model for exposure	20.43	26.98	25.10	21.53

Table 42. Akaike Information Criteria values for alternative models for Inhalation Exposure

Model	OVS Total Conc	OVS Total Dose	OVS Total TWA	PPI Total Conc	PPI Total Dose	PPI Total TWA
1. Linear regression of Ln(exposure) on Ln(AaiH)	23.76	11.24	11.24	28.02	21.20	21.20
2. Quadratic regression of Ln(exposure) on Ln(AaiH)	25.70	11.40	11.40	29.88	21.62	21.62
3. Regression of Ln(exposure) on Ln(AaiH) and conc	4.35	12.77	12.77	18.57	23.16	23.16
4. Regression of Ln(exposure) on Ln(AaiH) and gallons	6.84	14.36	14.36	17.87	21.39	21.39
5. Log-log logistic regression of exposure on AaiH	42.61	50.14	49.98	46.86	55.02	55.02

Model	OVS Total Conc	OVS Total Dose	OVS Total TWA	PPI Total Conc	PPI Total Dose	PPI Total TWA
6. 3-parameter logistic regression of exposure on AaiH	41.11	49.76	49.76	47.37	55.05	55.05
7. Gamma model for exposure	22.76	12.17	12.17	27.82	22.83	22.83

Based on the AIC, the best-fitting models are: model 1 (linear model for ln(exposure)) for Long Short Dermal, OVS Dose, OVS TWA, PPI Dose and PPI TWA; model 2 (quadratic model for ln(exposure)) for Long Dermal and Hands Only; model 3 (linear model for ln(exposure) and conc) for OVS Conc; model 4 (linear model for ln(exposure) and gallons) for PPI Conc; and model 7 (gamma) for Short Dermal. Models 5 and 6 fitted poorly.

The following figures are scatterplots comparing the observed and predicted values of ln(exposure) for the different statistical models. It can be seen that the models other than models 5 and 6 tend to give very similar predictions.

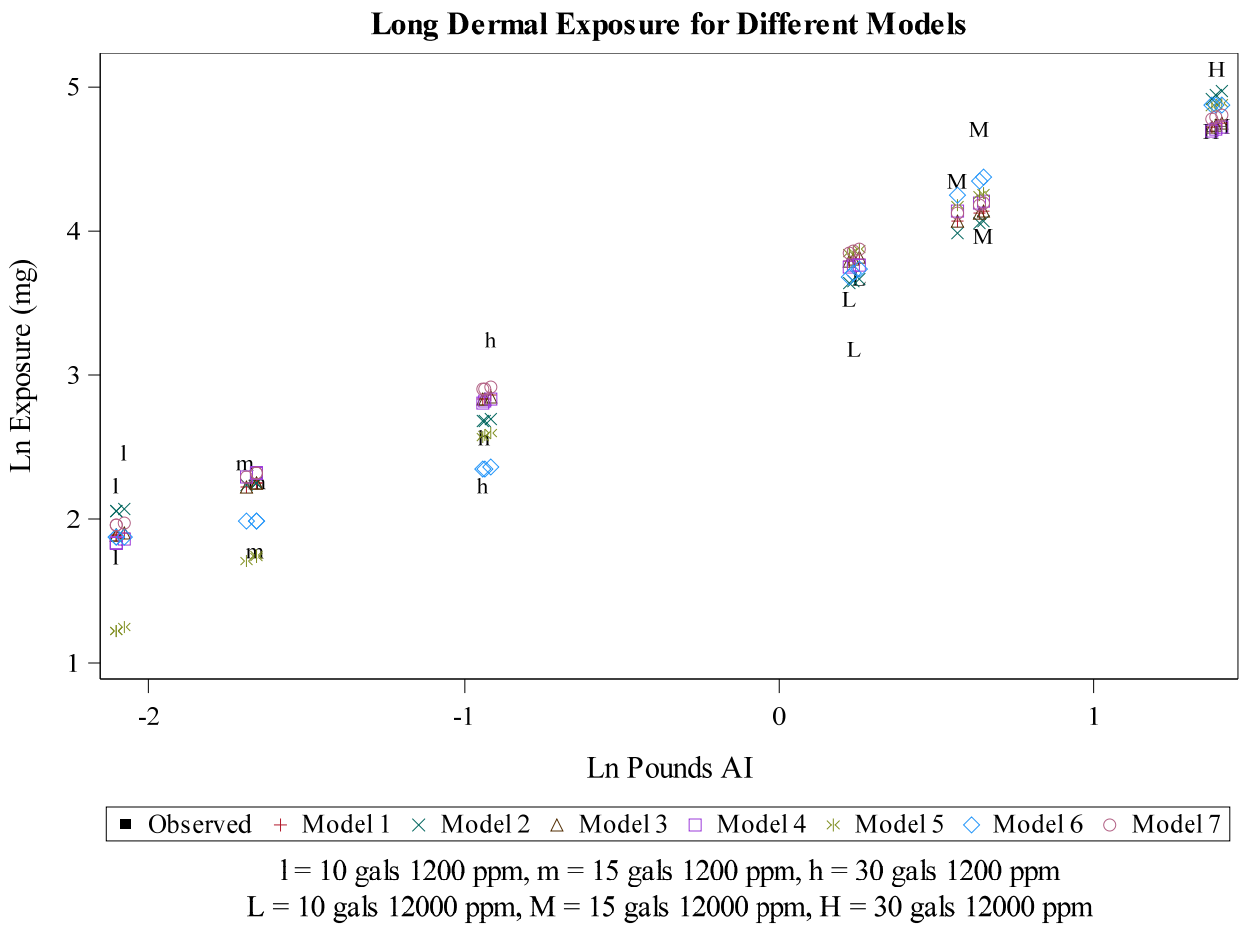


Figure 73. Comparisons of predicted log Long Dermal Exposure for different statistical models

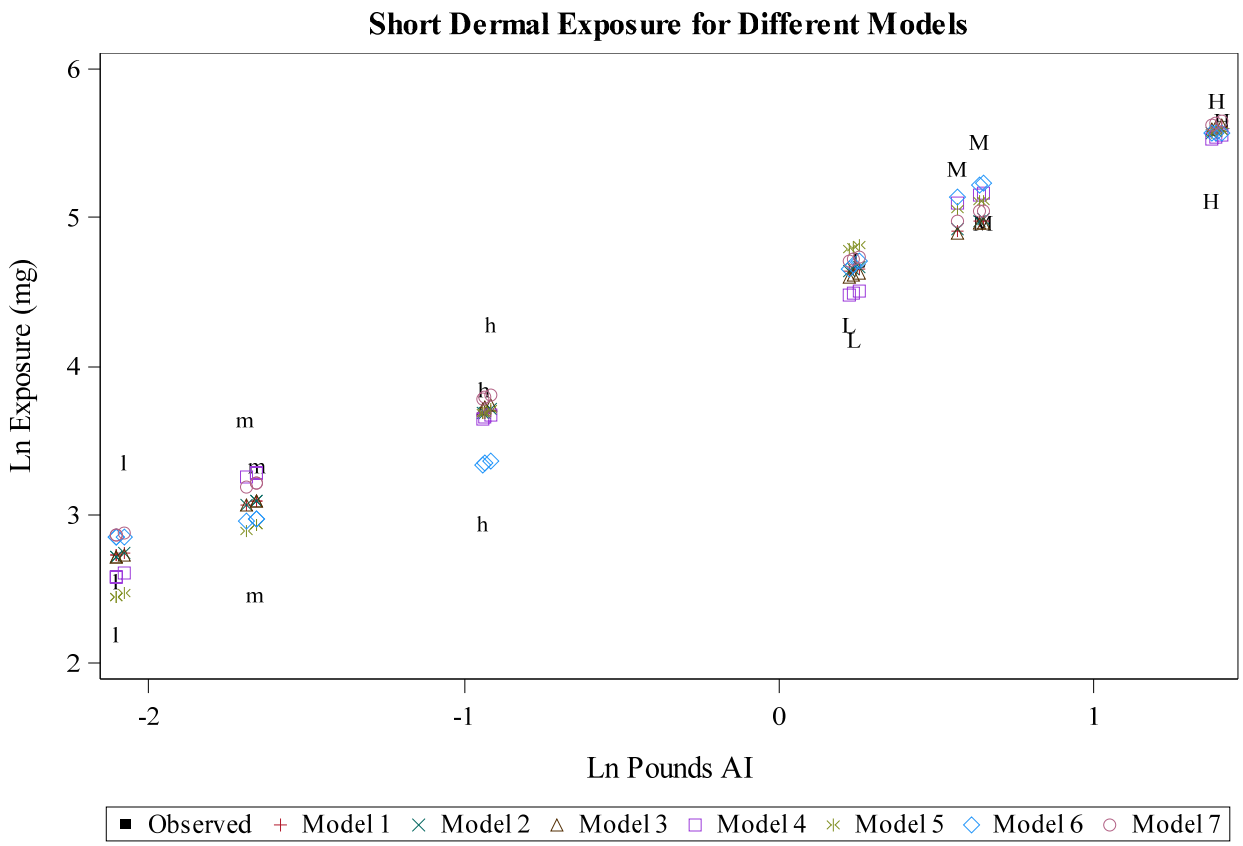


Figure 74. Comparisons of predicted log Long Dermal Exposure for different statistical models

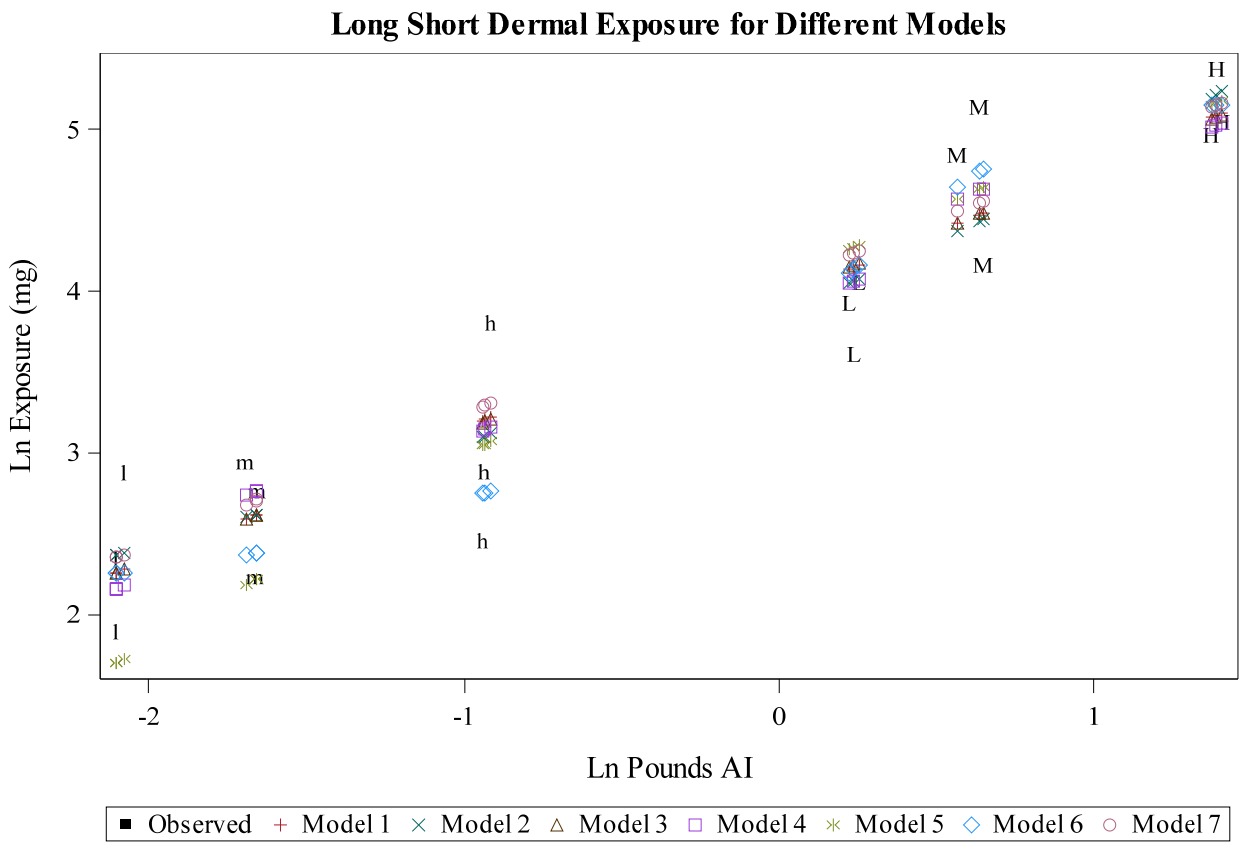


Figure 75. Comparisons of predicted log Short Dermal Exposure for different statistical models

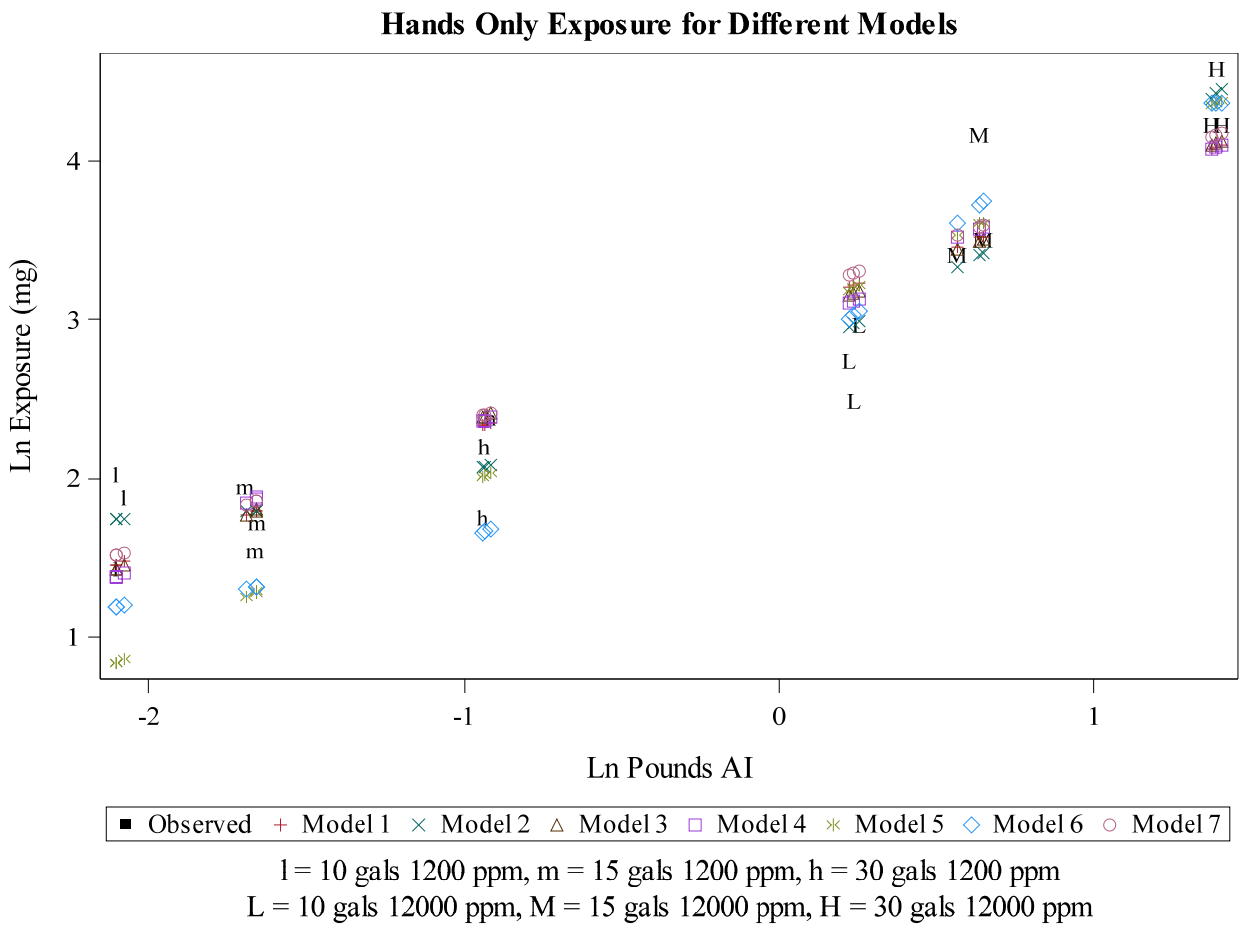


Figure 76. Comparisons of predicted log Hands Only Exposure for different statistical models

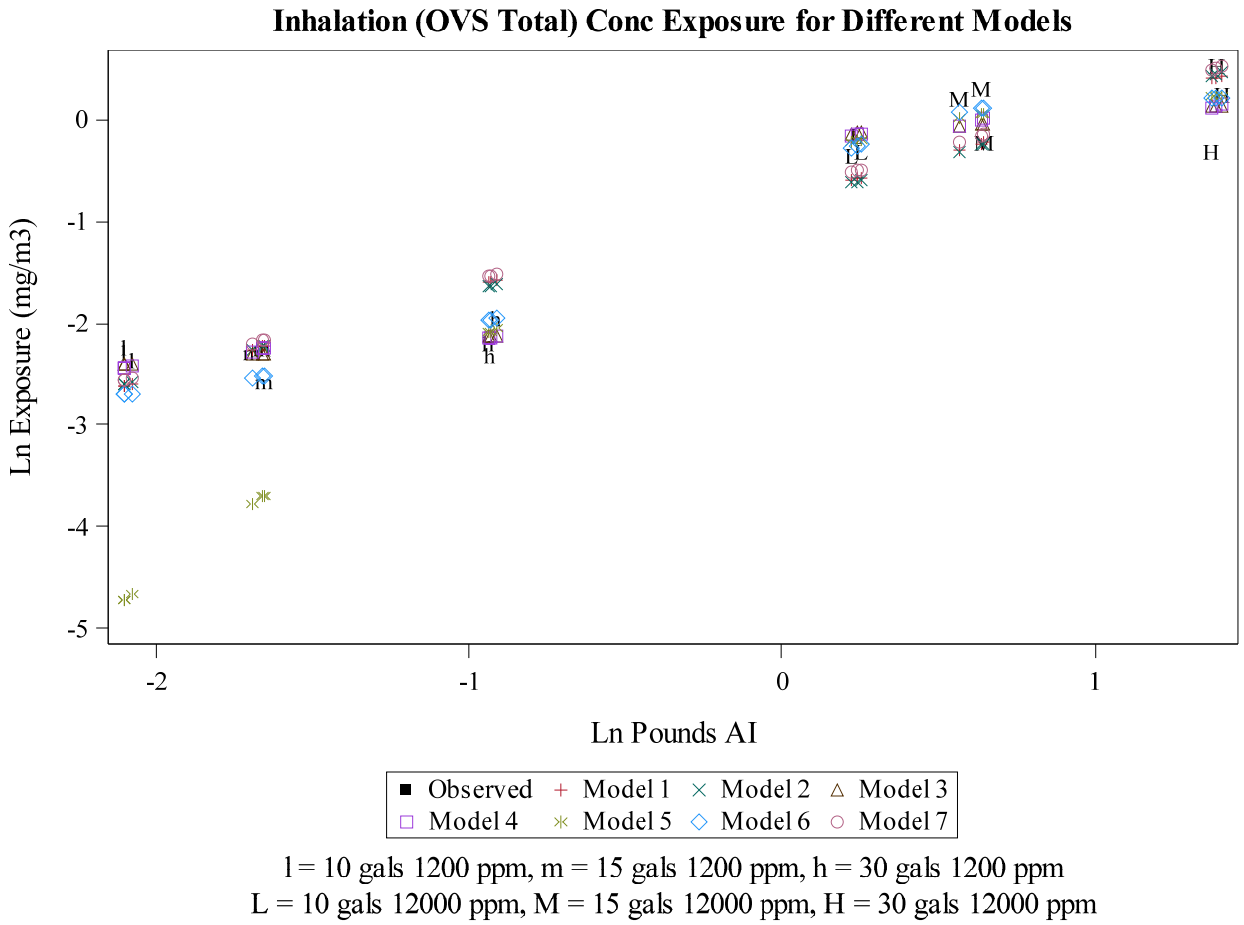


Figure 77. Comparisons of predicted log Inhalation (OVS Total) Conc Exposure for different statistical models

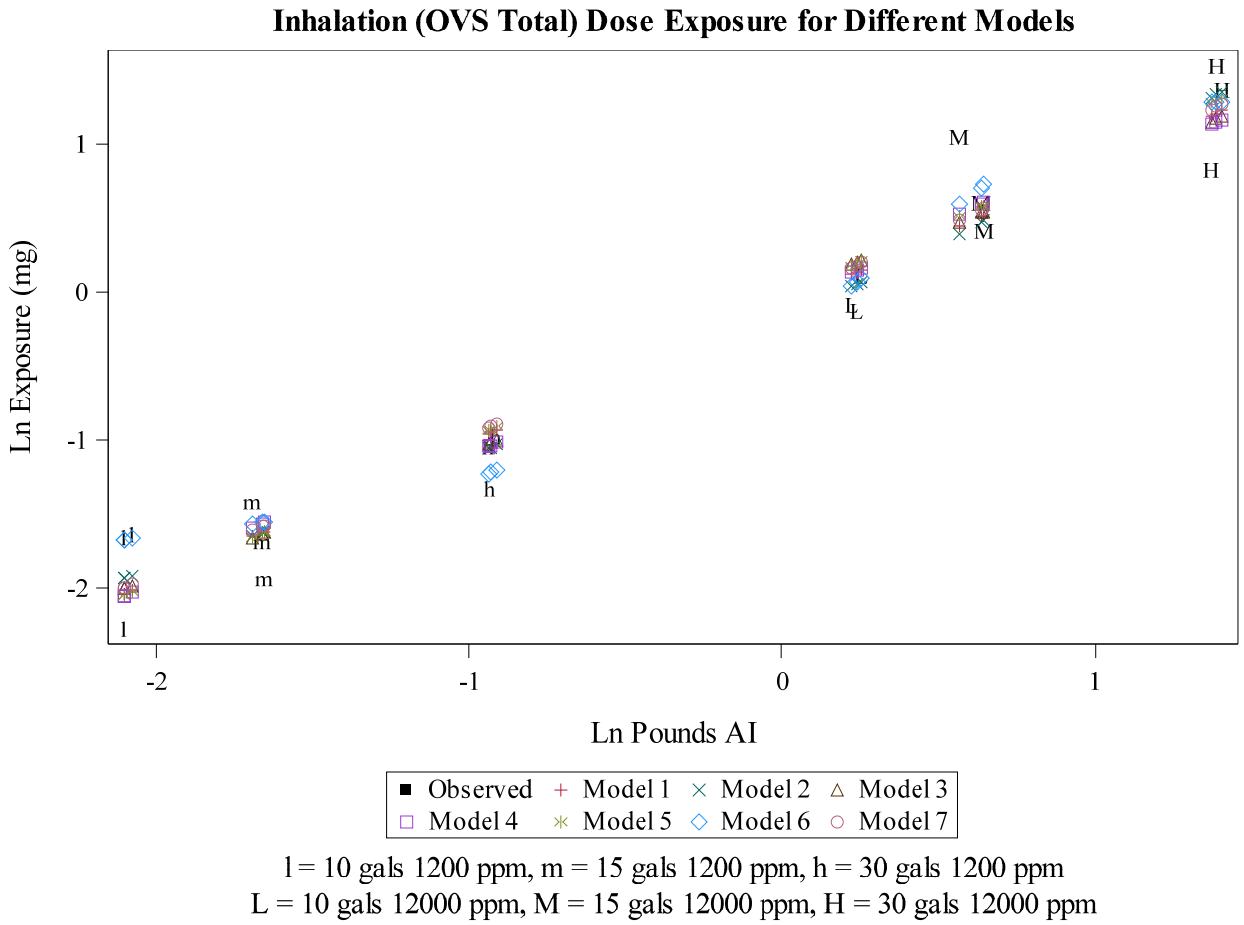


Figure 78. Comparisons of predicted log Inhalation (OVS Total) Dose for different statistical models

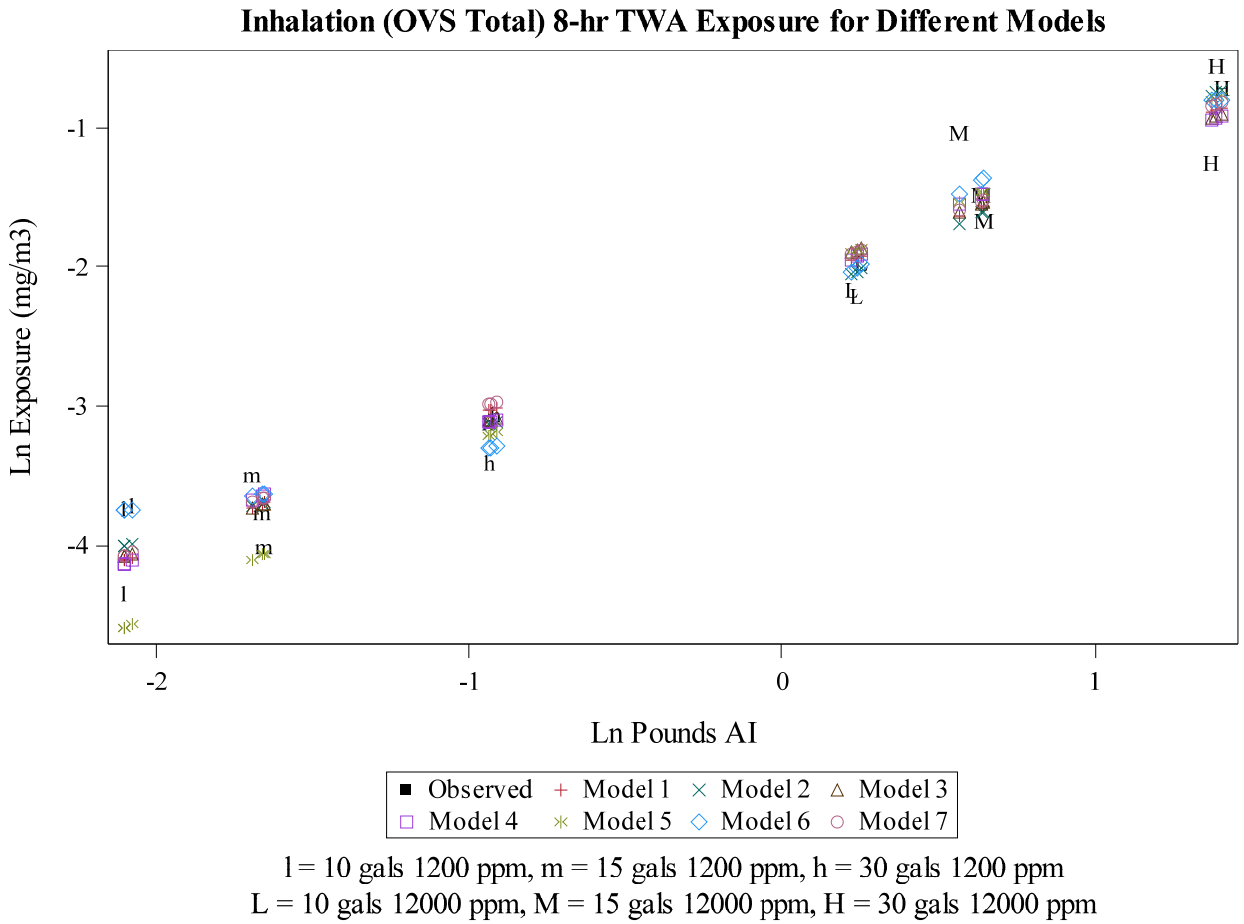


Figure 79. Comparisons of predicted log Inhalation (OVS Total) Time-weighted Average Exposure for different statistical models

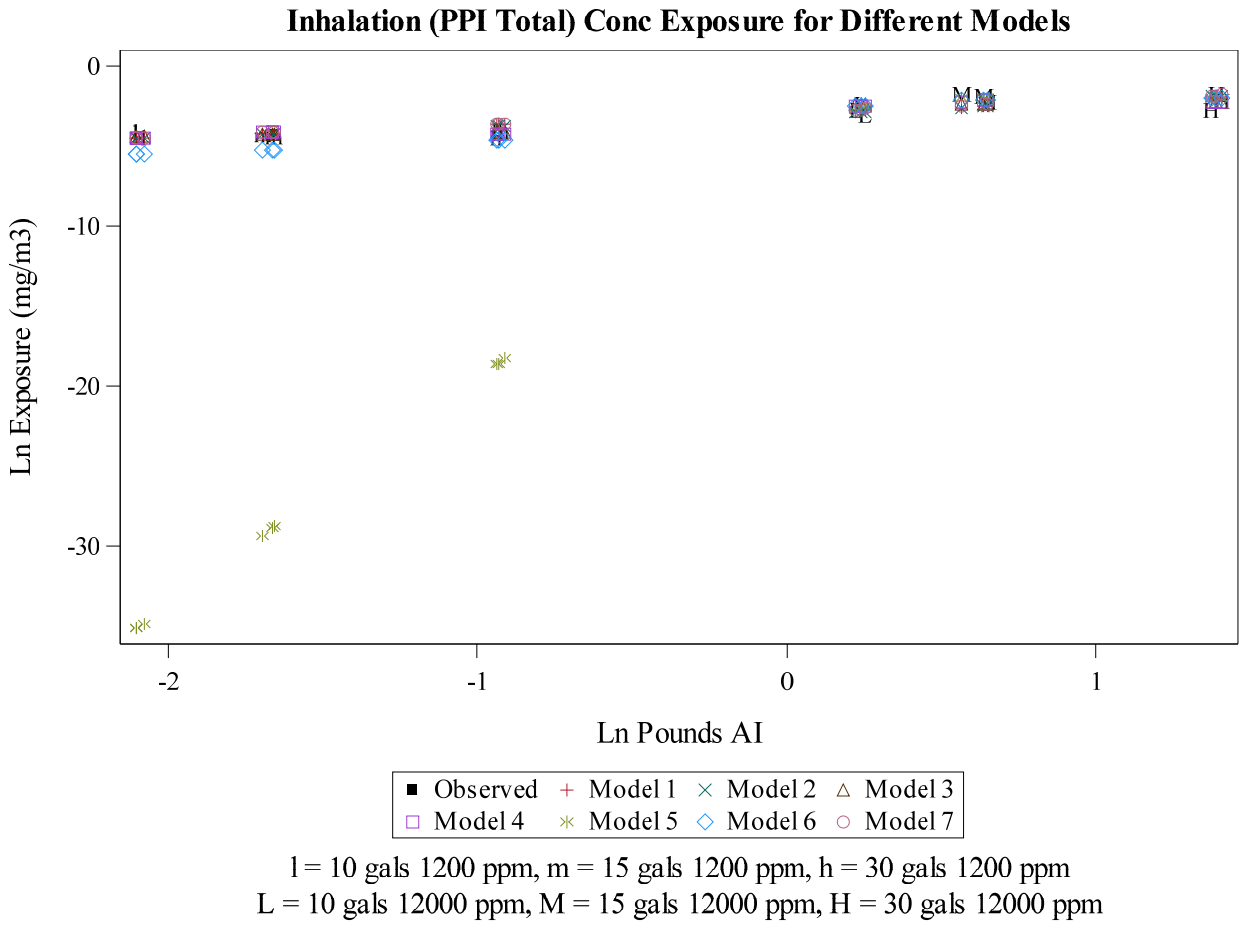


Figure 80. Comparisons of predicted log Inhalation (PPI Total) Conc Exposure for different statistical models

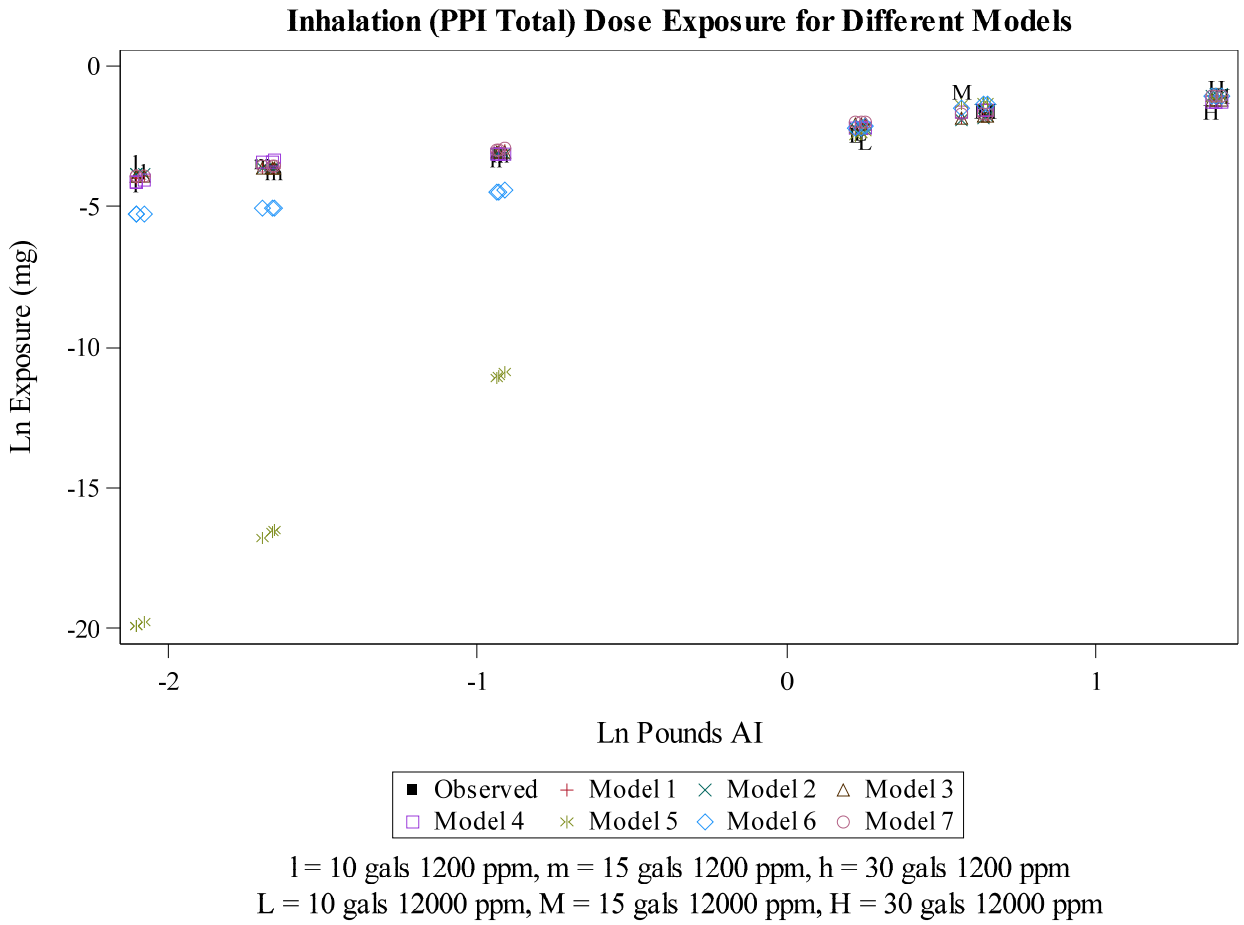


Figure 81. Comparisons of predicted log Inhalation (PPI Total) Dose for different statistical models

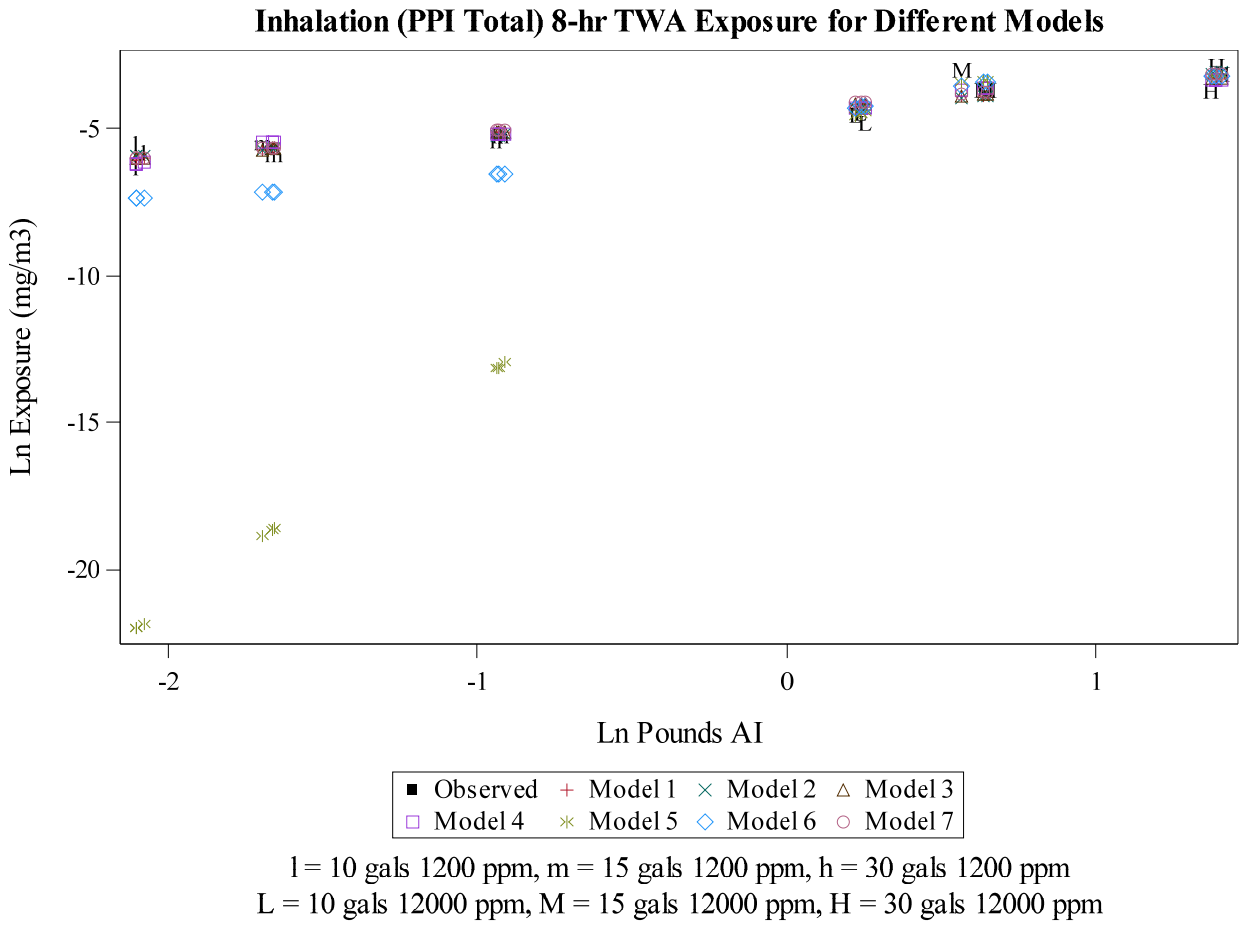


Figure 82. Comparisons of predicted log Inhalation (PPI Total) Time-weighted Average for different statistical models

13. Alternative Removal Efficiency Estimates

Finally we present some estimates of the impact of the removal efficiency estimate on the dermal exposure arithmetic mean and 95th percentile confidence intervals. The airless sprayer study report assumed a removal efficiency of 60% based on the hand wash removal efficiency study using BIT at the higher concentration (547 ppm). A reasonable alternative is to use a removal efficiency value of 73% from the same hand wash removal efficiency study using BIT at the lower concentration (154 ppm). The arithmetic means and 95th percentile values are reduced since the hand and face/neck residues are divided by a larger number. The dosimeter and hat residues are unaffected.

Table 43. Impact of alternative wipe/wash removal efficiency estimates on confidence intervals for the arithmetic means and 95th percentiles of dermal exposure

Exposure Route	Clothing	Removal Efficiency	Arithmetic Mean (95% Confidence Interval)	95th Percentile (95% Confidence Interval)
Dermal (mg/lb AI)	Long Dermal	60%	43.55 (35.29, 53.87)	81.57 (59.27, 111.31)
		73%	38.44 (31.17, 47.51)	71.89 (52.28, 98.01)
	Short Dermal	60%	104.89 (82.04, 134.41)	212.01 (146.94, 302.93)
		73%	99.77 (77.67, 128.47)	203.71 (140.29, 292.88)
	Long Short Dermal	60%	63.70 (50.44, 80.64)	125.61 (88.43, 176.76)

Exposure Route	Clothing	Removal Efficiency	Arithmetic Mean (95% Confidence Interval)	95th Percentile (95% Confidence Interval)
		73%	58.57 (46.22, 74.43)	116.30 (81.52, 164.36)
	Hands Only	60%	26.15 (20.54, 33.37)	52.39 (36.51, 74.45)
		73%	21.49 ((16.88. 27.43)	43.06 (30.01, 61.19)