



STUDY REPORT
90 DAY OECD INHALATION STUDY ON
SPRAGUE-DAWLEY RATS TO CHARACTERIZE
TOXICITY OF MAINSTREAM AEROSOL FROM
ZURICH FPD 4.2 CIGARETTES AND COMPARISON
TO 3R4F MAINSTREAM AEROSOL TOXICITY
STUDY NUMBER 15006

PART 2 – STATISTICAL REPORT FOR METABOLIC
ANALYTE PROFILING OF BRONCHIOALVEOLAR
LAVAGE FLUID (BALF)

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Some notes on the analysis performed:

Planned Size is the number of samples that should have been measured (one sample per animal).

Measured Size is the actual number of samples for which the measurement could be performed (exclude missing and QNS).

LDD is the least detectable dose and LLOQ is the lower limit of quantitation.

The lower limit of quantitation (LLQ) is defined as the maximum between LDD and LLOQ.

UQL is the upper limit of quantitation.

Valid Size is the number of samples for which the measurement was within LLQ and ULQ.

Values below LLQ are replaced by $LLQ / 2$ for the computation of statistics.

Values above ULQ are replaced by $1.1 * ULQ$.

P-values must be interpreted with great care (exploratory study, no adjustment for the alpha-level is performed).

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 1

Apolipoprotein A-I (Apo A-I)

Unit = ug/mL

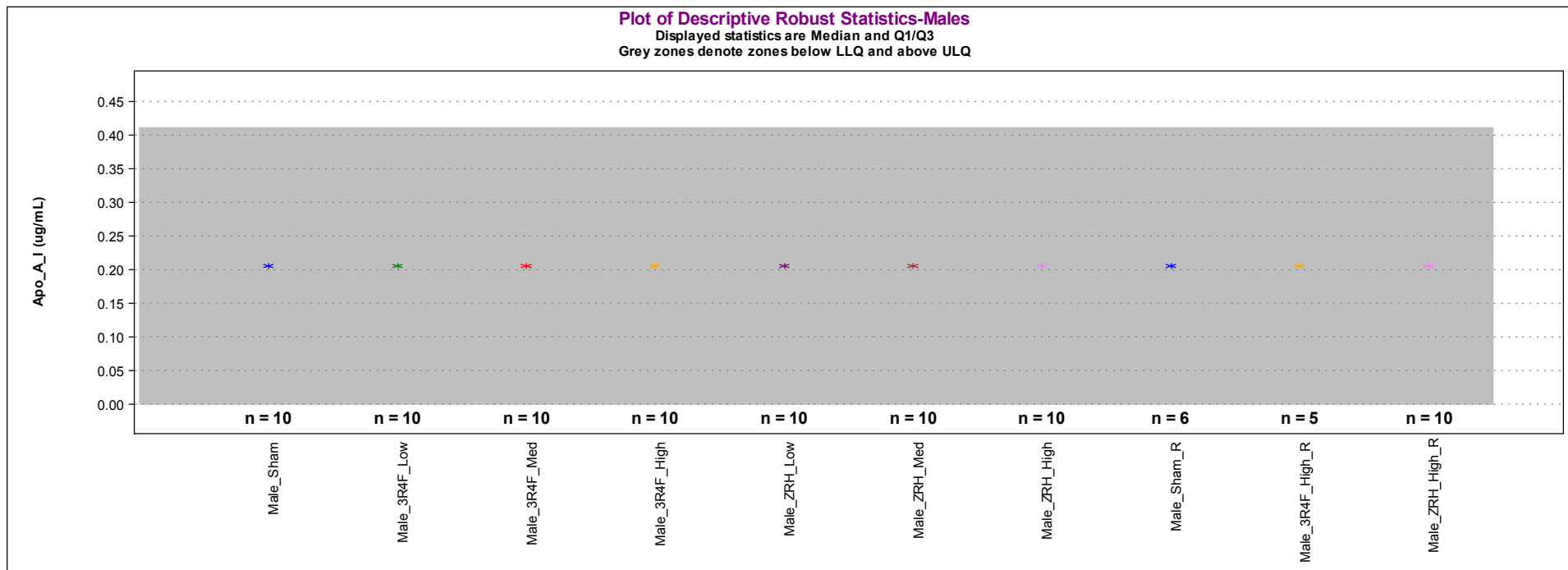
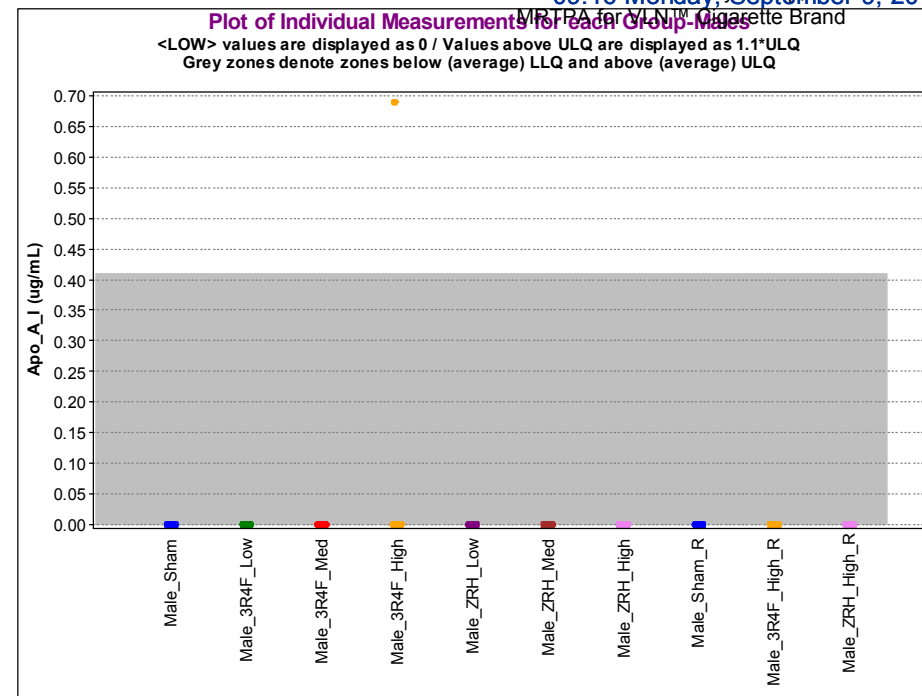
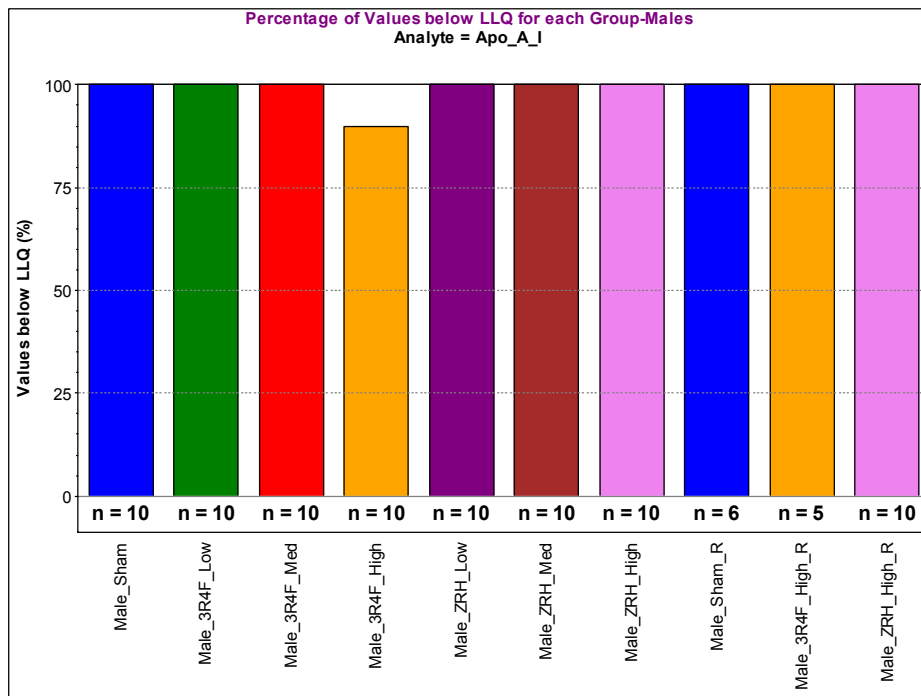
Descriptive Statistics by Exposure Duration and Treatment Type**Analyte = Apo_A_I**

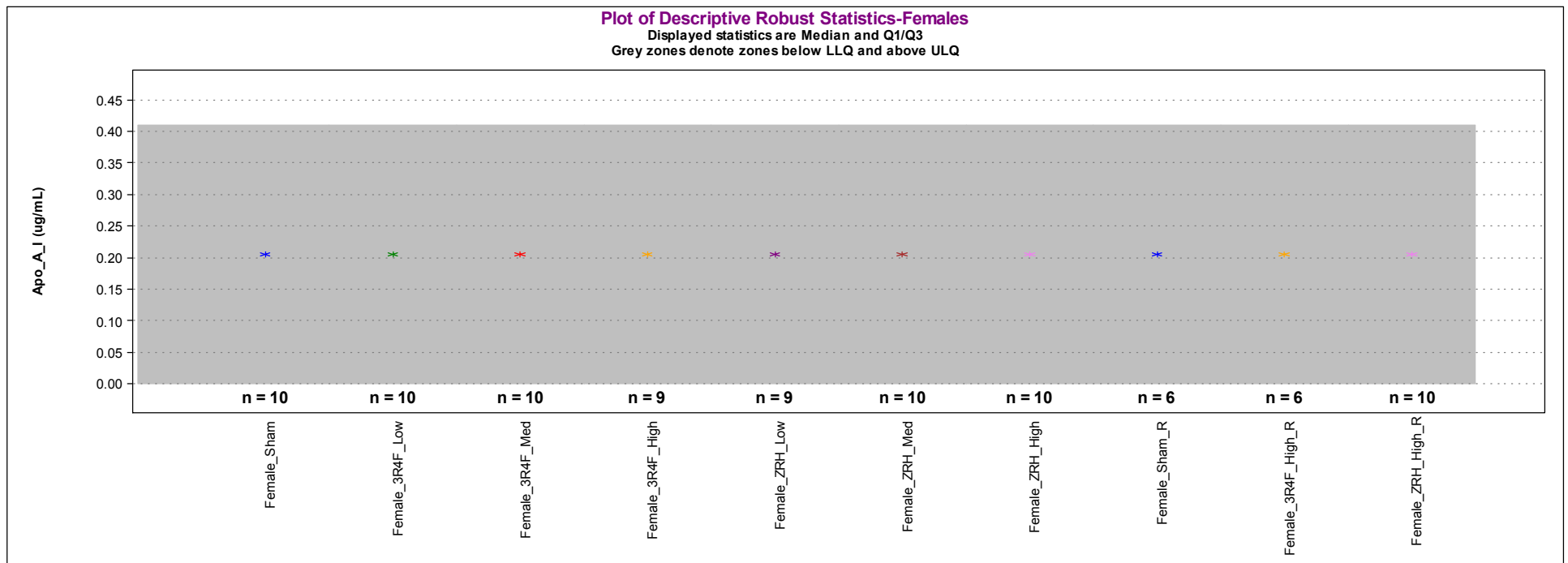
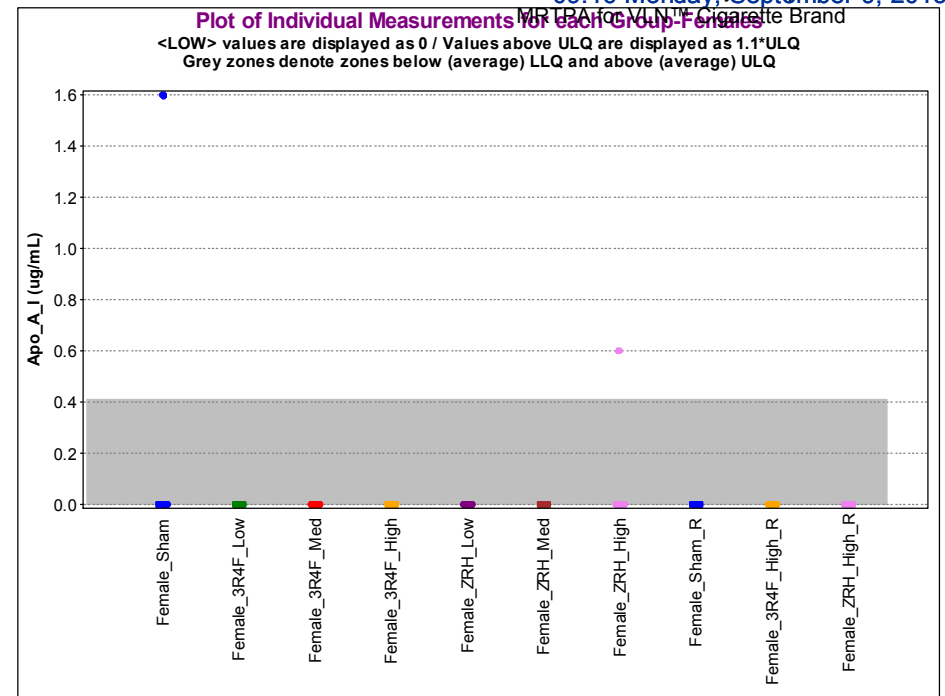
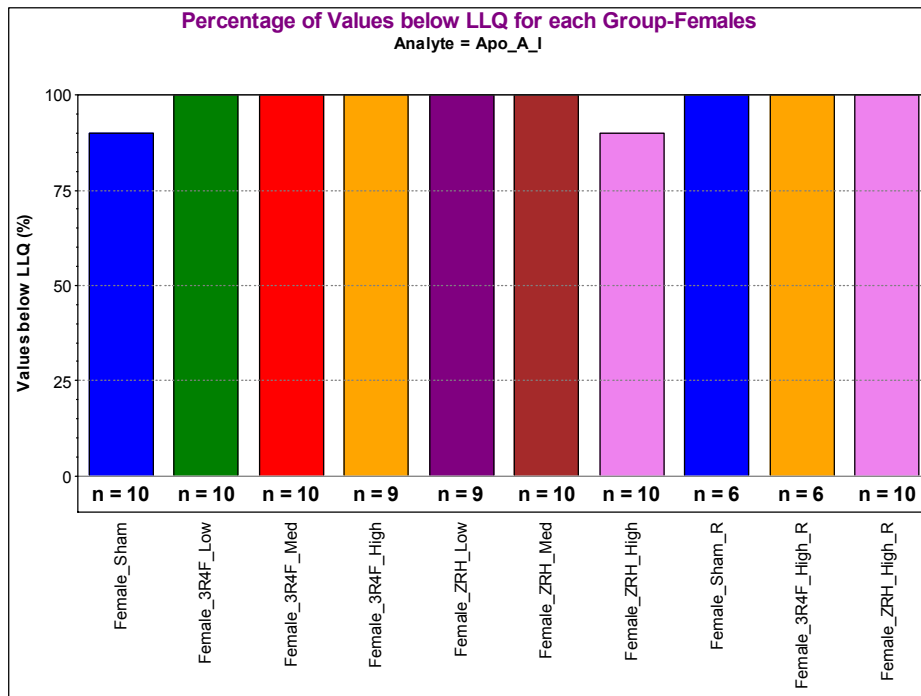
Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	10	0	0	0.41	.
Male	3	3R4F Low	10	10	10	0	0	0.41	.
Male	3	3R4F Medium	10	10	10	0	0	0.41	.
Male	3	3R4F High	10	10	9	1	0	0.41	.
Male	3	ZRH Low	10	10	10	0	0	0.41	.
Male	3	ZRH Medium	10	10	10	0	0	0.41	.
Male	3	ZRH High	10	10	10	0	0	0.41	.
Male	4.5	Sham Recovery	6	6	6	0	0	0.41	.
Male	4.5	3R4F High Recovery	5	5	5	0	0	0.41	.
Male	4.5	ZRH High Recovery	10	10	10	0	0	0.41	.
Female	3	Sham	10	10	9	1	0	0.41	.
Female	3	3R4F Low	10	10	10	0	0	0.41	.
Female	3	3R4F Medium	10	10	10	0	0	0.41	.
Female	3	3R4F High	9	9	9	0	0	0.41	.
Female	3	ZRH Low	9	9	9	0	0	0.41	.
Female	3	ZRH Medium	10	10	10	0	0	0.41	.
Female	3	ZRH High	10	10	9	1	0	0.41	.
Female	4.5	Sham Recovery	6	6	6	0	0	0.41	.
Female	4.5	3R4F High Recovery	6	6	6	0	0	0.41	.
Female	4.5	ZRH High Recovery	10	10	10	0	0	0.41	.

Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = Apo_A_I

Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	0.205	0.205	0.205	0.205	0.205	0.205	0.000	0.000	0.0	.	.	0.41	.
Male	3	3R4F Low	0.205	0.205	0.205	0.205	0.205	0.205	0.000	0.000	0.0	.	.	0.41	.
Male	3	3R4F Medium	0.205	0.205	0.205	0.205	0.205	0.205	0.000	0.000	0.0	.	.	0.41	.
Male	3	3R4F High	0.205	0.205	0.205	0.205	0.690	0.254	0.153	0.049	60.5	3.162	10.000	0.41	.
Male	3	ZRH Low	0.205	0.205	0.205	0.205	0.205	0.205	0.000	0.000	0.0	.	.	0.41	.
Male	3	ZRH Medium	0.205	0.205	0.205	0.205	0.205	0.205	0.000	0.000	0.0	.	.	0.41	.
Male	3	ZRH High	0.205	0.205	0.205	0.205	0.205	0.205	0.000	0.000	0.0	.	.	0.41	.
Male	4.5	Sham Recovery	0.205	0.205	0.205	0.205	0.205	0.205	0.000	0.000	0.0	.	.	0.41	.
Male	4.5	3R4F High Recovery	0.205	0.205	0.205	0.205	0.205	0.205	0.000	0.000	0.0	.	.	0.41	.
Male	4.5	ZRH High Recovery	0.205	0.205	0.205	0.205	0.205	0.205	0.000	0.000	0.0	.	.	0.41	.
Female	3	Sham	0.205	0.205	0.205	0.205	1.600	0.345	0.441	0.140	128.1	3.162	10.000	0.41	.
Female	3	3R4F Low	0.205	0.205	0.205	0.205	0.205	0.205	0.000	0.000	0.0	.	.	0.41	.
Female	3	3R4F Medium	0.205	0.205	0.205	0.205	0.205	0.205	0.000	0.000	0.0	.	.	0.41	.
Female	3	3R4F High	0.205	0.205	0.205	0.205	0.205	0.205	0.000	0.000	0.0	.	.	0.41	.
Female	3	ZRH Low	0.205	0.205	0.205	0.205	0.205	0.205	0.000	0.000	0.0	.	.	0.41	.
Female	3	ZRH Medium	0.205	0.205	0.205	0.205	0.205	0.205	0.000	0.000	0.0	.	.	0.41	.
Female	3	ZRH High	0.205	0.205	0.205	0.205	0.600	0.245	0.125	0.040	51.1	3.162	10.000	0.41	.
Female	4.5	Sham Recovery	0.205	0.205	0.205	0.205	0.205	0.205	0.000	0.000	0.0	.	.	0.41	.
Female	4.5	3R4F High Recovery	0.205	0.205	0.205	0.205	0.205	0.205	0.000	0.000	0.0	.	.	0.41	.
Female	4.5	ZRH High Recovery	0.205	0.205	0.205	0.205	0.205	0.205	0.000	0.000	0.0	.	.	0.41	.





Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = Apo_A_I

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	1.000000
---- Sham vs. 3R4F Medium for Male	1.000000
---- Sham vs. 3R4F High for Male	0.317311
---- Sham vs. ZRH Low for Male	1.000000
---- Sham vs. ZRH Medium for Male	1.000000
---- Sham vs. ZRH High for Male	1.000000
---- ZRH Low vs. 3R4F Medium for Male	1.000000
---- ZRH Medium vs. 3R4F High for Male	0.317311
---- ZRH High vs. 3R4F High for Male	0.317311
---- Sham Recovery vs. 3R4F High Recovery for Male	1.000000
---- Sham Recovery vs. ZRH High Recovery for Male	1.000000
---- Sham vs. Sham Recovery for Male	1.000000
---- 3R4F High vs. 3R4F High Recovery for Male	0.479500
---- ZRH High vs. ZRH High Recovery for Male	1.000000
---- 3R4F High Recovery vs. ZRH High Recovery for Male	1.000000
---- Sham vs. 3R4F Low for Female	0.317311
---- Sham vs. 3R4F Medium for Female	0.317311
---- Sham vs. 3R4F High for Female	0.342782
---- Sham vs. ZRH Low for Female	0.342782
---- Sham vs. ZRH Medium for Female	0.317311
---- Sham vs. ZRH High for Female	0.942166
---- ZRH Low vs. 3R4F Medium for Female	1.000000
---- ZRH Medium vs. 3R4F High for Female	1.000000
---- ZRH High vs. 3R4F High for Female	0.342782
---- Sham Recovery vs. 3R4F High Recovery for Female	1.000000
---- Sham Recovery vs. ZRH High Recovery for Female	1.000000
---- Sham vs. Sham Recovery for Female	0.438578

Unadjusted P-values Obtained by Kruskal-Wallis Test
Analyte = Apo_A_I

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	1.000000
---- ZRH High vs. ZRH High Recovery for Female	0.317311
---- 3R4F High Recovery vs. ZRH High Recovery for Female	1.000000

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 3

CD40 (CD40)

Unit = pg/mL

Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = CD40

Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	10	0	0	2.5	.
Male	3	3R4F Low	10	10	10	0	0	2.5	.
Male	3	3R4F Medium	10	10	10	0	0	2.5	.
Male	3	3R4F High	10	10	10	0	0	2.5	.
Male	3	ZRH Low	10	10	10	0	0	2.5	.
Male	3	ZRH Medium	10	10	10	0	0	2.5	.
Male	3	ZRH High	10	10	10	0	0	2.5	.
Male	4.5	Sham Recovery	6	6	6	0	0	2.5	.
Male	4.5	3R4F High Recovery	5	5	5	0	0	2.5	.
Male	4.5	ZRH High Recovery	10	10	10	0	0	2.5	.
Female	3	Sham	10	10	10	0	0	2.5	.
Female	3	3R4F Low	10	10	10	0	0	2.5	.
Female	3	3R4F Medium	10	10	10	0	0	2.5	.
Female	3	3R4F High	9	9	9	0	0	2.5	.
Female	3	ZRH Low	9	9	9	0	0	2.5	.
Female	3	ZRH Medium	10	10	10	0	0	2.5	.
Female	3	ZRH High	10	10	10	0	0	2.5	.
Female	4.5	Sham Recovery	6	6	6	0	0	2.5	.
Female	4.5	3R4F High Recovery	6	6	6	0	0	2.5	.
Female	4.5	ZRH High Recovery	10	10	10	0	0	2.5	.

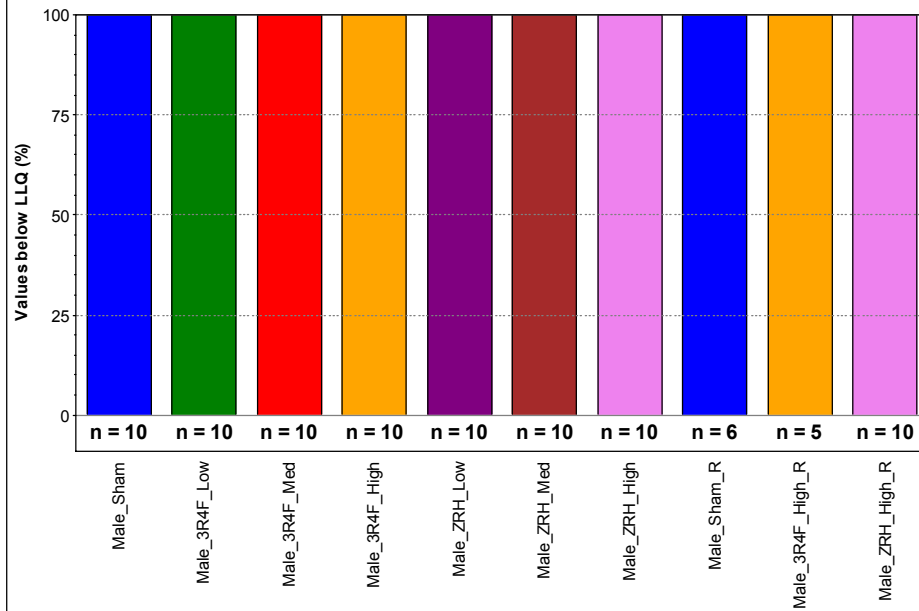
Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = CD40

Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	1.250	1.250	1.250	1.250	1.250	1.250	0.000	0.000	0.0	.	.	2.5	.
Male	3	3R4F Low	1.250	1.250	1.250	1.250	1.250	1.250	0.000	0.000	0.0	.	.	2.5	.
Male	3	3R4F Medium	1.250	1.250	1.250	1.250	1.250	1.250	0.000	0.000	0.0	.	.	2.5	.
Male	3	3R4F High	1.250	1.250	1.250	1.250	1.250	1.250	0.000	0.000	0.0	.	.	2.5	.
Male	3	ZRH Low	1.250	1.250	1.250	1.250	1.250	1.250	0.000	0.000	0.0	.	.	2.5	.
Male	3	ZRH Medium	1.250	1.250	1.250	1.250	1.250	1.250	0.000	0.000	0.0	.	.	2.5	.
Male	3	ZRH High	1.250	1.250	1.250	1.250	1.250	1.250	0.000	0.000	0.0	.	.	2.5	.
Male	4.5	Sham Recovery	1.250	1.250	1.250	1.250	1.250	1.250	0.000	0.000	0.0	.	.	2.5	.
Male	4.5	3R4F High Recovery	1.250	1.250	1.250	1.250	1.250	1.250	0.000	0.000	0.0	.	.	2.5	.
Male	4.5	ZRH High Recovery	1.250	1.250	1.250	1.250	1.250	1.250	0.000	0.000	0.0	.	.	2.5	.
Female	3	Sham	1.250	1.250	1.250	1.250	1.250	1.250	0.000	0.000	0.0	.	.	2.5	.
Female	3	3R4F Low	1.250	1.250	1.250	1.250	1.250	1.250	0.000	0.000	0.0	.	.	2.5	.
Female	3	3R4F Medium	1.250	1.250	1.250	1.250	1.250	1.250	0.000	0.000	0.0	.	.	2.5	.
Female	3	3R4F High	1.250	1.250	1.250	1.250	1.250	1.250	0.000	0.000	0.0	.	.	2.5	.
Female	3	ZRH Low	1.250	1.250	1.250	1.250	1.250	1.250	0.000	0.000	0.0	.	.	2.5	.
Female	3	ZRH Medium	1.250	1.250	1.250	1.250	1.250	1.250	0.000	0.000	0.0	.	.	2.5	.
Female	3	ZRH High	1.250	1.250	1.250	1.250	1.250	1.250	0.000	0.000	0.0	.	.	2.5	.
Female	4.5	Sham Recovery	1.250	1.250	1.250	1.250	1.250	1.250	0.000	0.000	0.0	.	.	2.5	.
Female	4.5	3R4F High Recovery	1.250	1.250	1.250	1.250	1.250	1.250	0.000	0.000	0.0	.	.	2.5	.
Female	4.5	ZRH High Recovery	1.250	1.250	1.250	1.250	1.250	1.250	0.000	0.000	0.0	.	.	2.5	.

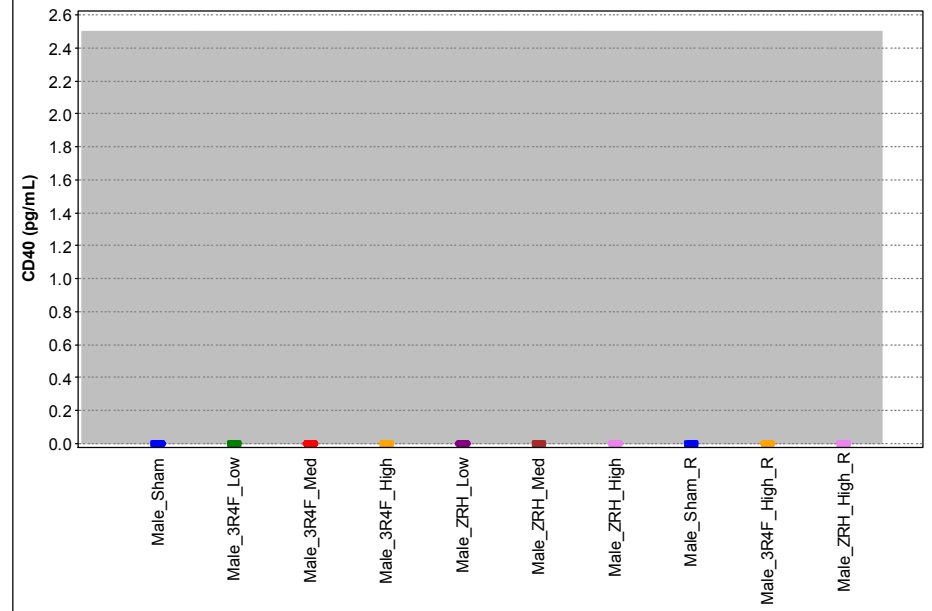
Percentage of Values below LLQ for each Group-Males

Analyte = CD40



Plot of Individual Measurements for each Group-Males

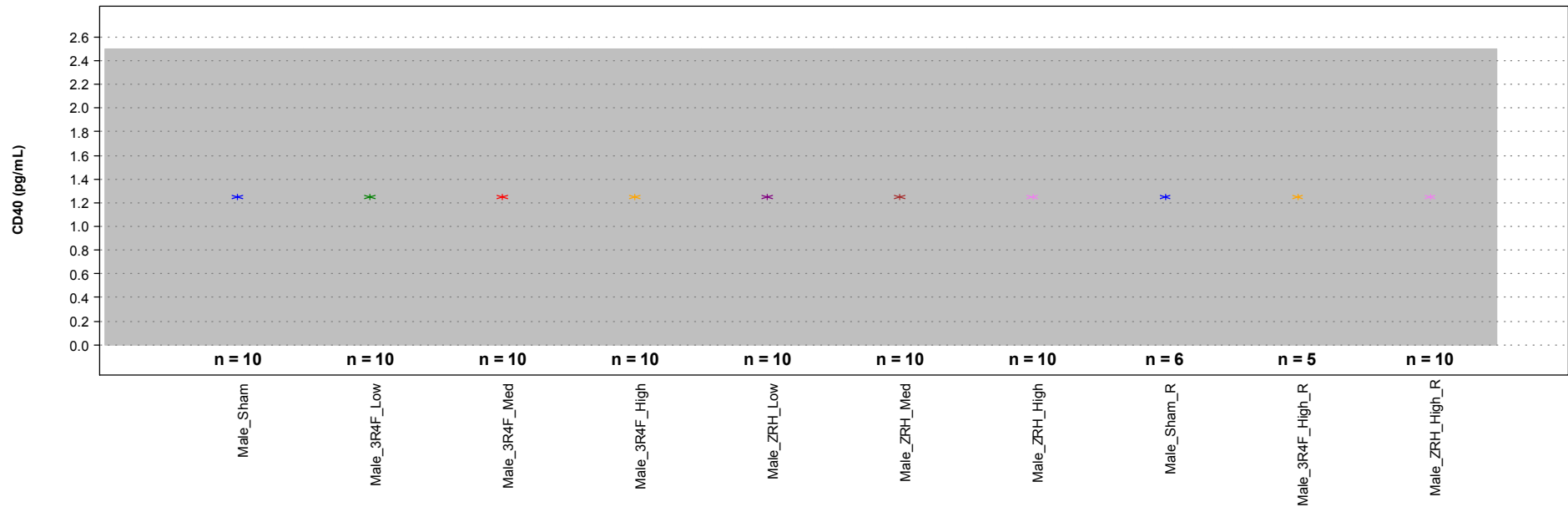
<LOW> values are displayed as 0 / Values above ULQ are displayed as 1.1*ULQ
Grey zones denote zones below (average) LLQ and above (average) ULQ

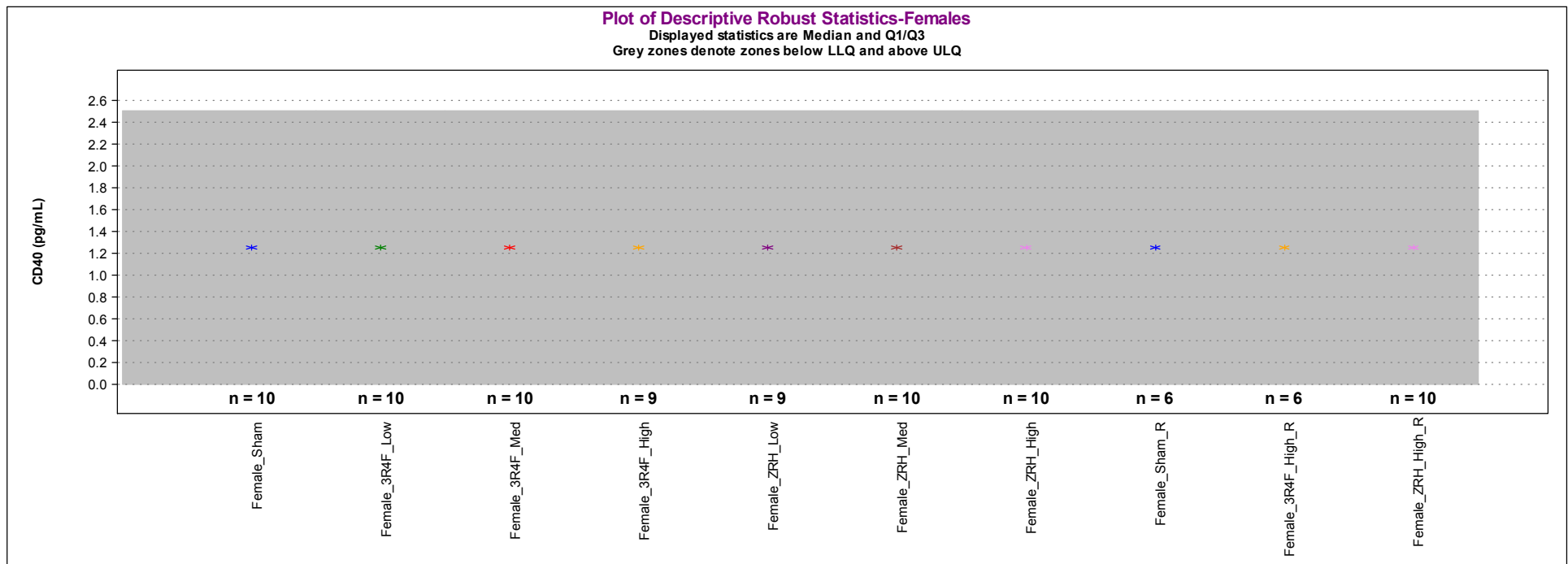
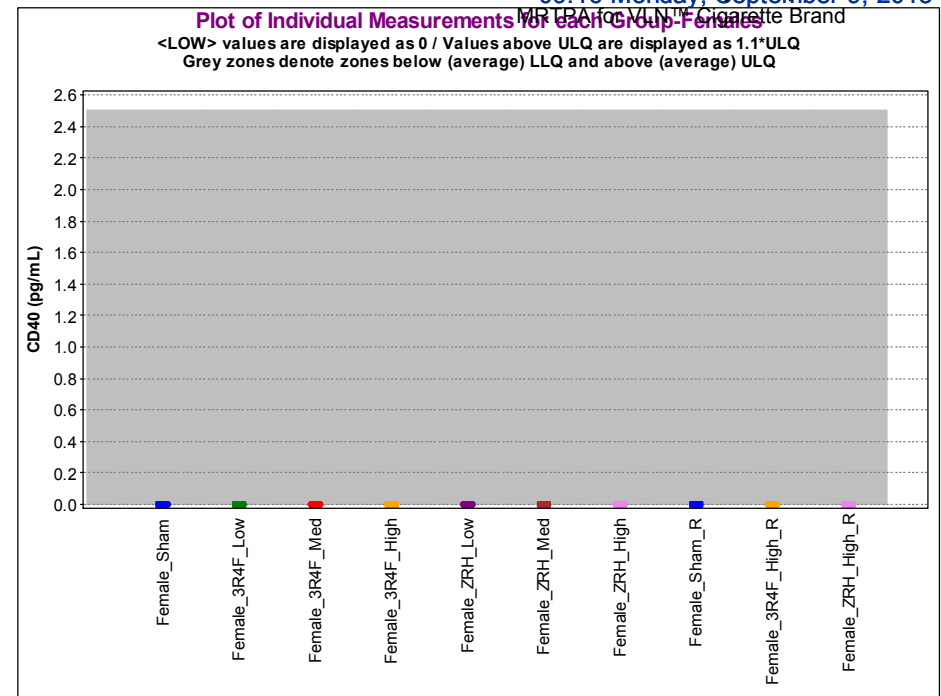
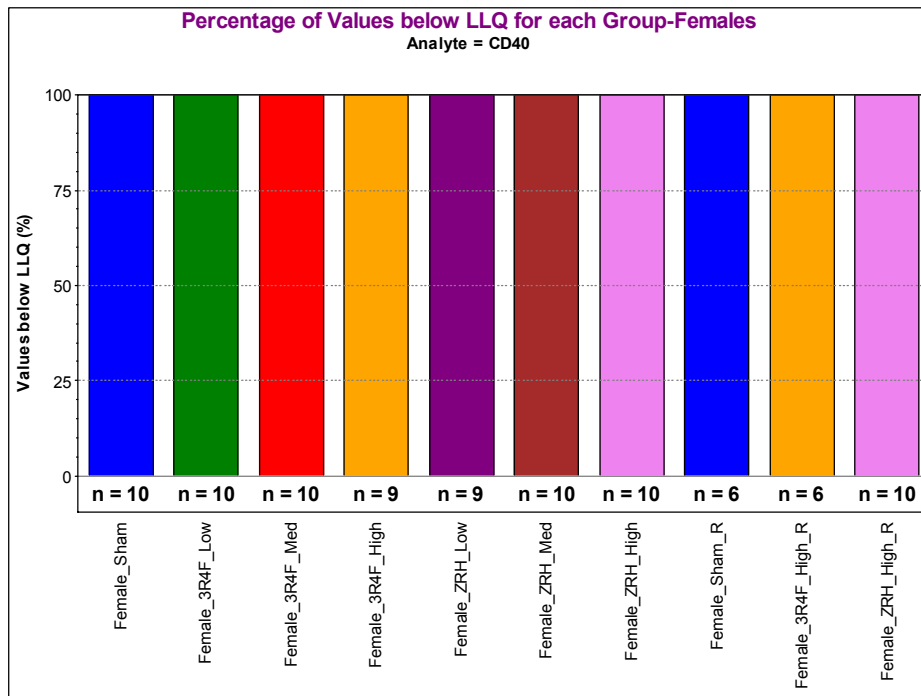


Plot of Descriptive Robust Statistics-Males

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ





Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = CD40

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	1.000000
---- Sham vs. 3R4F Medium for Male	1.000000
---- Sham vs. 3R4F High for Male	1.000000
---- Sham vs. ZRH Low for Male	1.000000
---- Sham vs. ZRH Medium for Male	1.000000
---- Sham vs. ZRH High for Male	1.000000
---- ZRH Low vs. 3R4F Medium for Male	1.000000
---- ZRH Medium vs. 3R4F High for Male	1.000000
---- ZRH High vs. 3R4F High for Male	1.000000
---- Sham Recovery vs. 3R4F High Recovery for Male	1.000000
---- Sham Recovery vs. ZRH High Recovery for Male	1.000000
---- Sham vs. Sham Recovery for Male	1.000000
---- 3R4F High vs. 3R4F High Recovery for Male	1.000000
---- ZRH High vs. ZRH High Recovery for Male	1.000000
---- 3R4F High Recovery vs. ZRH High Recovery for Male	1.000000
---- Sham vs. 3R4F Low for Female	1.000000
---- Sham vs. 3R4F Medium for Female	1.000000
---- Sham vs. 3R4F High for Female	1.000000
---- Sham vs. ZRH Low for Female	1.000000
---- Sham vs. ZRH Medium for Female	1.000000
---- Sham vs. ZRH High for Female	1.000000
---- ZRH Low vs. 3R4F Medium for Female	1.000000
---- ZRH Medium vs. 3R4F High for Female	1.000000
---- ZRH High vs. 3R4F High for Female	1.000000
---- Sham Recovery vs. 3R4F High Recovery for Female	1.000000
---- Sham Recovery vs. ZRH High Recovery for Female	1.000000
---- Sham vs. Sham Recovery for Female	1.000000

Unadjusted P-values Obtained by Kruskal-Wallis Test
Analyte = CD40

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	1.000000
---- ZRH High vs. ZRH High Recovery for Female	1.000000
---- 3R4F High Recovery vs. ZRH High Recovery for Female	1.000000

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 4

CD40 Ligand (CD40-L)

Unit = pg/mL

Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = CD40_L

Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	6	4	0	86	.
Male	3	3R4F Low	10	10	3	7	0	86	.
Male	3	3R4F Medium	10	10	1	9	0	86	.
Male	3	3R4F High	10	10	2	8	0	86	.
Male	3	ZRH Low	10	10	7	3	0	86	.
Male	3	ZRH Medium	10	10	6	4	0	86	.
Male	3	ZRH High	10	10	8	2	0	86	.
Male	4.5	Sham Recovery	6	6	3	3	0	86	.
Male	4.5	3R4F High Recovery	5	5	2	3	0	86	.
Male	4.5	ZRH High Recovery	10	10	8	2	0	86	.
Female	3	Sham	10	10	1	9	0	86	.
Female	3	3R4F Low	10	10	0	10	0	86	.
Female	3	3R4F Medium	10	10	0	10	0	86	.
Female	3	3R4F High	9	9	0	9	0	86	.
Female	3	ZRH Low	9	9	3	6	0	86	.
Female	3	ZRH Medium	10	10	5	5	0	86	.
Female	3	ZRH High	10	10	5	5	0	86	.
Female	4.5	Sham Recovery	6	6	2	4	0	86	.
Female	4.5	3R4F High Recovery	6	6	3	3	0	86	.
Female	4.5	ZRH High Recovery	10	10	6	4	0	86	.

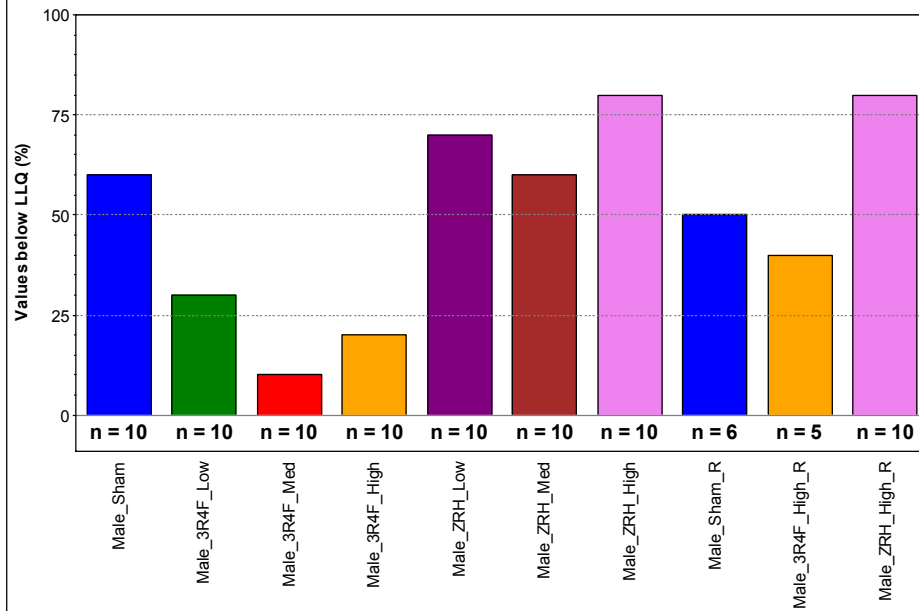
Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = CD40_L

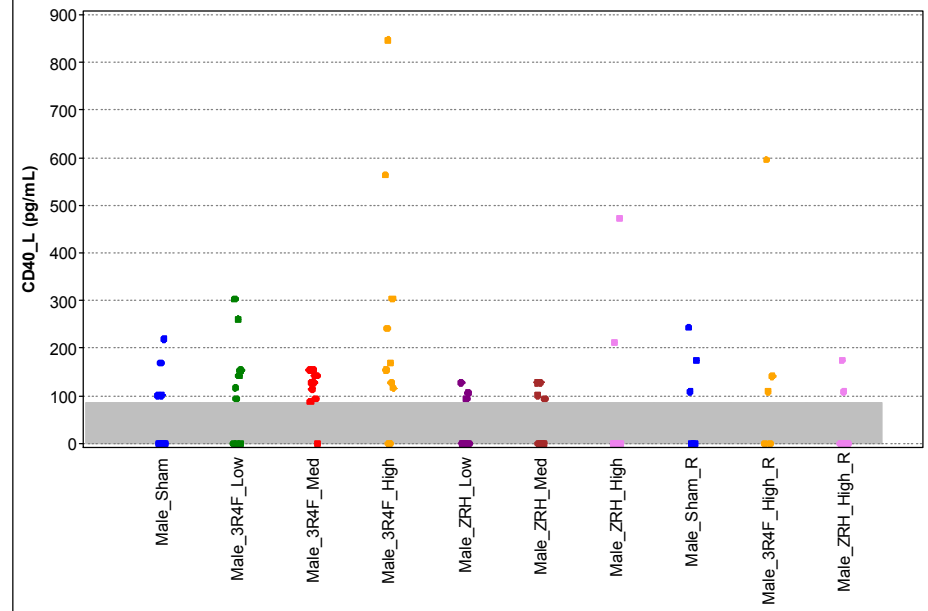
Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	43.000	43.000	43.000	101.000	220.000	84.900	63.576	20.104	74.9	1.420	1.028	86	.
Male	3	3R4F Low	43.000	43.000	129.500	154.000	303.000	135.400	89.608	28.337	66.2	0.822	-0.074	86	.
Male	3	3R4F Medium	43.000	94.000	128.000	142.000	155.000	118.900	35.275	11.155	29.7	-1.146	1.083	86	.
Male	3	3R4F High	43.000	117.000	162.000	304.000	847.000	261.200	256.166	81.007	98.1	1.659	2.333	86	.
Male	3	ZRH Low	43.000	43.000	43.000	94.000	128.000	62.900	33.057	10.454	52.6	1.272	-0.054	86	.
Male	3	ZRH Medium	43.000	43.000	43.000	101.000	128.000	70.900	37.462	11.847	52.8	0.744	-1.458	86	.
Male	3	ZRH High	43.000	43.000	43.000	43.000	473.000	102.900	140.468	44.420	136.5	2.519	6.316	86	.
Male	4.5	Sham Recovery	43.000	43.000	76.000	175.000	244.000	109.500	84.436	34.471	77.1	0.913	-0.682	86	.
Male	4.5	3R4F High Recovery	43.000	43.000	109.000	141.000	596.000	186.400	232.890	104.152	124.9	2.054	4.337	86	.
Male	4.5	ZRH High Recovery	43.000	43.000	43.000	43.000	175.000	62.800	44.547	14.087	70.9	2.277	4.765	86	.
Female	3	Sham	43.000	93.000	116.000	147.000	971.000	193.900	274.711	86.871	141.7	3.090	9.672	86	.
Female	3	3R4F Low	89.000	89.000	111.500	170.000	253.000	137.800	60.255	19.054	43.7	1.105	-0.074	86	.
Female	3	3R4F Medium	89.000	116.000	145.000	170.000	875.000	237.800	248.139	78.469	104.3	2.340	5.379	86	.
Female	3	3R4F High	157.000	282.000	366.000	422.000	938.000	403.556	222.826	74.275	55.2	1.934	4.769	86	.
Female	3	ZRH Low	43.000	43.000	89.000	120.000	537.000	138.333	156.420	52.140	113.1	2.542	6.851	86	.
Female	3	ZRH Medium	43.000	43.000	68.000	120.000	338.000	102.900	93.216	29.477	90.6	2.096	4.737	86	.
Female	3	ZRH High	43.000	43.000	66.000	93.000	829.000	143.100	242.592	76.714	169.5	3.086	9.642	86	.
Female	4.5	Sham Recovery	43.000	43.000	122.500	136.000	136.000	100.500	45.750	18.678	45.5	-0.769	-1.995	86	.
Female	4.5	3R4F High Recovery	43.000	43.000	92.000	141.000	209.000	103.333	70.602	28.823	68.3	0.535	-1.505	86	.
Female	4.5	ZRH High Recovery	43.000	43.000	43.000	212.000	251.000	108.900	92.578	29.276	85.0	0.896	-1.244	86	.

Percentage of Values below LLQ for each Group-Males

Analyte = CD40_L

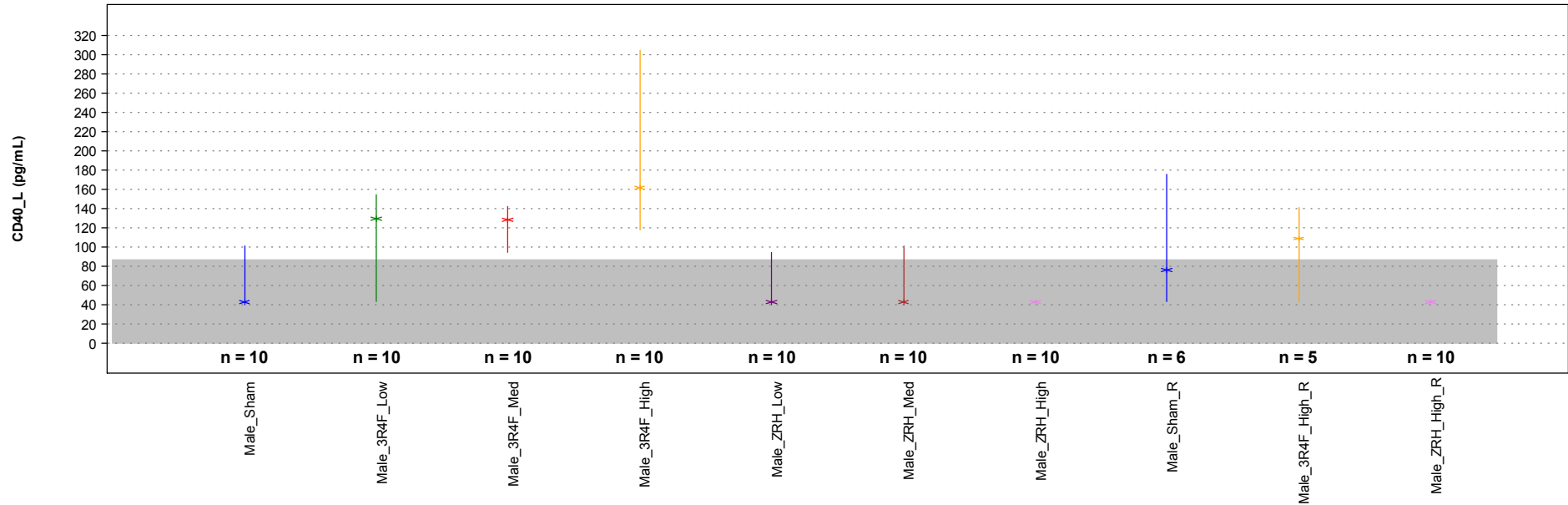
**Plot of Individual Measurements for each Group-Males**

<LOW> values are displayed as 0 / Values above ULQ are displayed as 1.1*ULQ
 Grey zones denote zones below (average) LLQ and above (average) ULQ

**Plot of Descriptive Robust Statistics-Males**

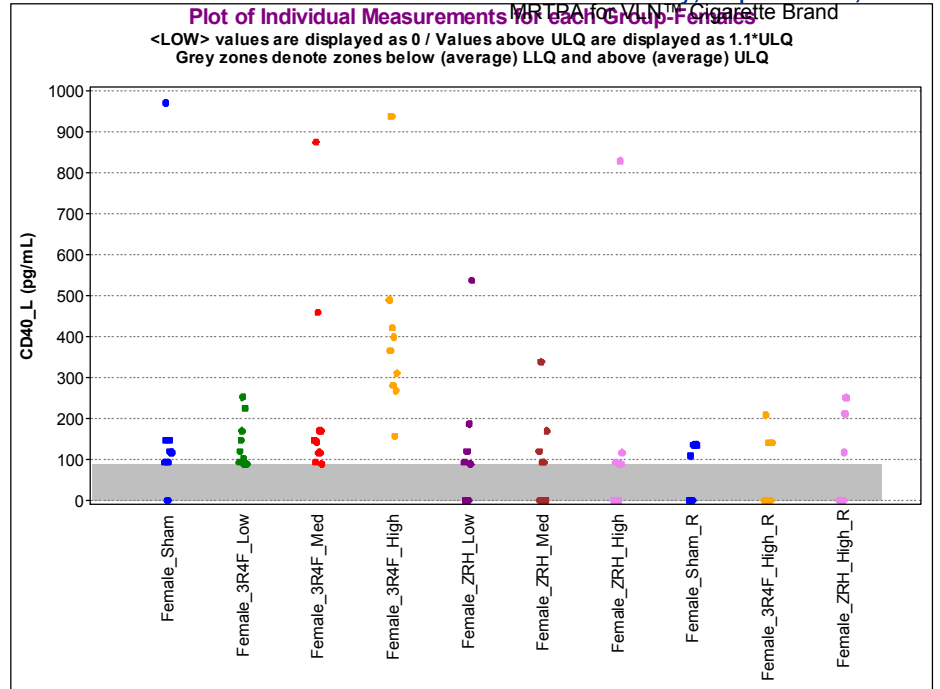
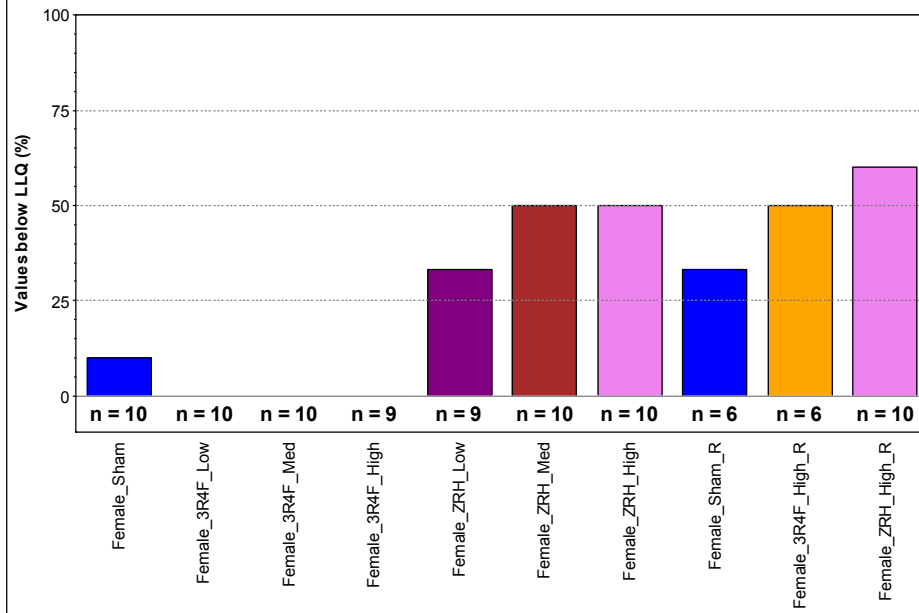
Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



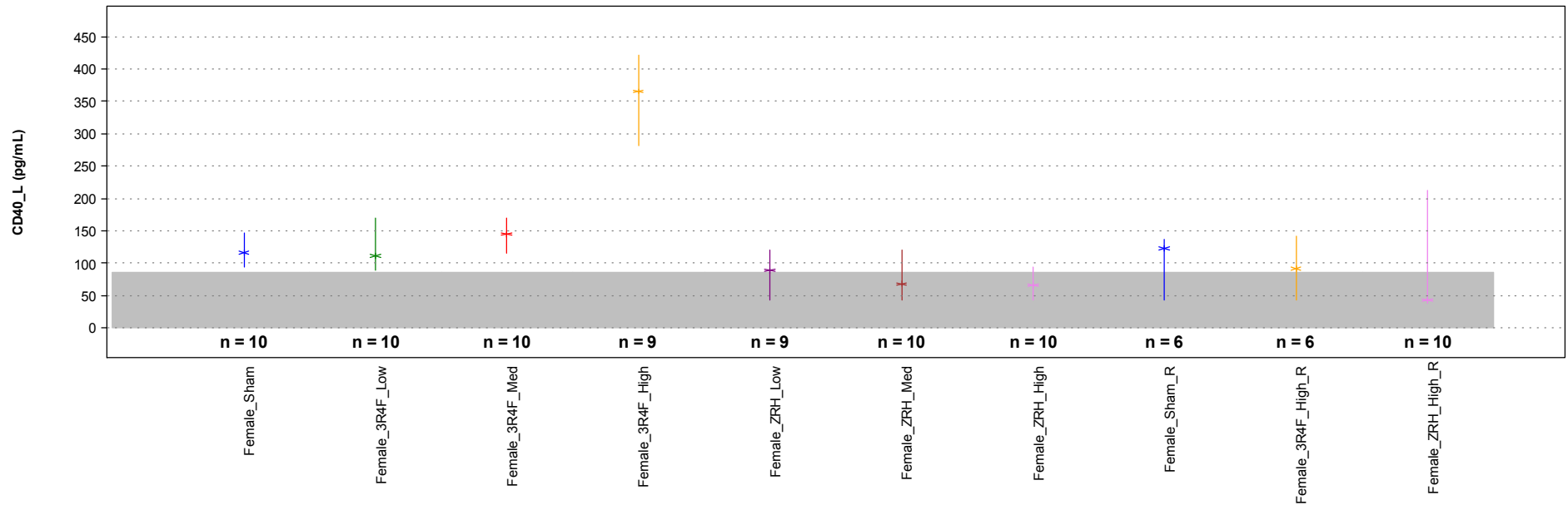
Percentage of Values below LLQ for each Group-Females

Analyte = CD40_L

**Plot of Descriptive Robust Statistics-Females**

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = CD40_L

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	0.177526
---- Sham vs. 3R4F Medium for Male	0.104266
---- Sham vs. 3R4F High for Male	0.025906
---- Sham vs. ZRH Low for Male	0.534459
---- Sham vs. ZRH Medium for Male	0.797504
---- Sham vs. ZRH High for Male	0.513915
---- ZRH Low vs. 3R4F Medium for Male	0.004810
---- ZRH Medium vs. 3R4F High for Male	0.009839
---- ZRH High vs. 3R4F High for Male	0.023727
---- Sham Recovery vs. 3R4F High Recovery for Male	0.773386
---- Sham Recovery vs. ZRH High Recovery for Male	0.186289
---- Sham vs. Sham Recovery for Male	0.472894
---- 3R4F High vs. 3R4F High Recovery for Male	0.322828
---- ZRH High vs. ZRH High Recovery for Male	0.828784
---- 3R4F High Recovery vs. ZRH High Recovery for Male	0.125242
---- Sham vs. 3R4F Low for Female	0.939286
---- Sham vs. 3R4F Medium for Female	0.268490
---- Sham vs. 3R4F High for Female	0.003207
---- Sham vs. ZRH Low for Female	0.284653
---- Sham vs. ZRH Medium for Female	0.164120
---- Sham vs. ZRH High for Female	0.025386
---- ZRH Low vs. 3R4F Medium for Female	0.085031
---- ZRH Medium vs. 3R4F High for Female	0.000979
---- ZRH High vs. 3R4F High for Female	0.002294
---- Sham Recovery vs. 3R4F High Recovery for Female	0.615059
---- Sham Recovery vs. ZRH High Recovery for Female	0.727061
---- Sham vs. Sham Recovery for Female	0.661098

Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = CD40_L

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	0.002085
---- ZRH High vs. ZRH High Recovery for Female	0.933994
---- 3R4F High Recovery vs. ZRH High Recovery for Female	1.000000

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 2

C-Reactive Protein Rat (CRP Rat)

Unit = ug/mL

Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = CRP_Rat

Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	0	10	0	0.026	.
Male	3	3R4F Low	10	10	0	10	0	0.026	.
Male	3	3R4F Medium	10	10	0	10	0	0.026	.
Male	3	3R4F High	10	10	0	10	0	0.026	.
Male	3	ZRH Low	10	10	0	10	0	0.026	.
Male	3	ZRH Medium	10	10	0	10	0	0.026	.
Male	3	ZRH High	10	10	0	10	0	0.026	.
Male	4.5	Sham Recovery	6	6	0	6	0	0.026	.
Male	4.5	3R4F High Recovery	5	5	0	5	0	0.026	.
Male	4.5	ZRH High Recovery	10	10	0	10	0	0.026	.
Female	3	Sham	10	10	0	10	0	0.026	.
Female	3	3R4F Low	10	10	0	10	0	0.026	.
Female	3	3R4F Medium	10	10	0	10	0	0.026	.
Female	3	3R4F High	9	9	0	9	0	0.026	.
Female	3	ZRH Low	9	9	0	9	0	0.026	.
Female	3	ZRH Medium	10	10	0	10	0	0.026	.
Female	3	ZRH High	10	10	0	10	0	0.026	.
Female	4.5	Sham Recovery	6	6	0	6	0	0.026	.
Female	4.5	3R4F High Recovery	6	6	0	6	0	0.026	.
Female	4.5	ZRH High Recovery	10	10	0	10	0	0.026	.

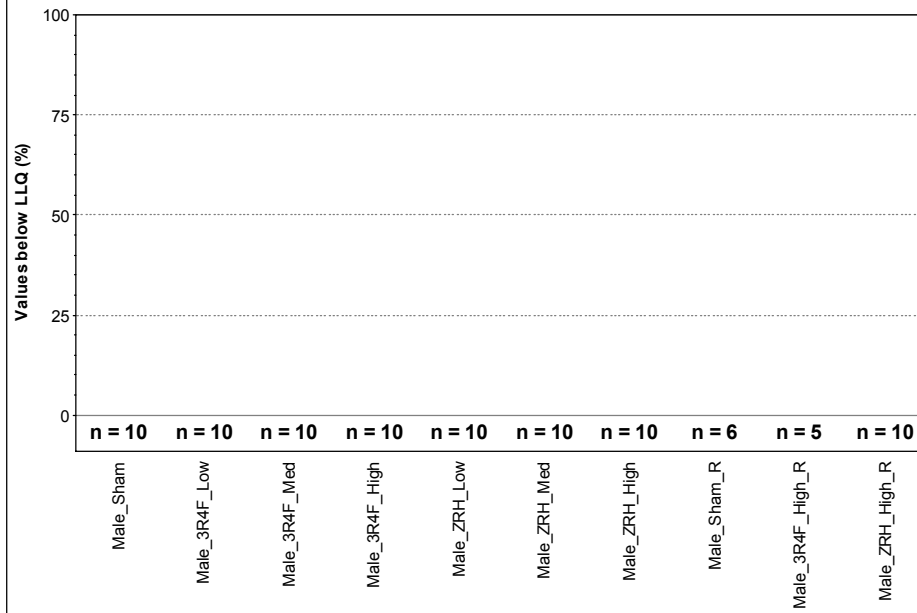
Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = CRP_Rat

Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	0.047	0.120	0.150	0.280	1.800	0.351	0.523	0.165	149.0	2.883	8.627	0.026	.
Male	3	3R4F Low	0.093	0.120	0.215	0.280	0.830	0.279	0.228	0.072	81.6	1.871	3.530	0.026	.
Male	3	3R4F Medium	0.078	0.120	0.140	0.170	0.240	0.143	0.046	0.014	32.0	0.768	1.452	0.026	.
Male	3	3R4F High	0.052	0.110	0.130	0.270	0.370	0.179	0.106	0.033	59.2	0.754	-0.715	0.026	.
Male	3	ZRH Low	0.063	0.082	0.125	0.170	0.520	0.168	0.141	0.044	83.5	2.083	4.512	0.026	.
Male	3	ZRH Medium	0.069	0.100	0.140	0.380	0.920	0.263	0.267	0.085	101.7	1.976	3.905	0.026	.
Male	3	ZRH High	0.078	0.120	0.175	0.300	0.460	0.220	0.137	0.043	62.2	0.898	-0.402	0.026	.
Male	4.5	Sham Recovery	0.110	0.120	0.150	0.170	0.210	0.152	0.038	0.016	25.2	0.521	-0.957	0.026	.
Male	4.5	3R4F High Recovery	0.079	0.091	0.160	0.230	0.280	0.168	0.087	0.039	51.8	0.304	-2.118	0.026	.
Male	4.5	ZRH High Recovery	0.110	0.110	0.130	0.180	0.420	0.175	0.102	0.032	58.3	1.968	3.420	0.026	.
Female	3	Sham	0.100	0.140	0.150	0.180	0.830	0.219	0.217	0.069	99.2	3.024	9.354	0.026	.
Female	3	3R4F Low	0.110	0.130	0.180	0.250	0.330	0.198	0.077	0.024	39.0	0.571	-1.000	0.026	.
Female	3	3R4F Medium	0.069	0.076	0.111	0.140	0.590	0.154	0.156	0.049	101.7	2.923	8.891	0.026	.
Female	3	3R4F High	0.084	0.094	0.110	0.180	0.710	0.225	0.222	0.074	98.6	1.787	2.235	0.026	.
Female	3	ZRH Low	0.078	0.140	0.170	0.210	0.710	0.236	0.193	0.064	81.8	2.228	5.289	0.026	.
Female	3	ZRH Medium	0.082	0.110	0.250	0.320	0.890	0.281	0.237	0.075	84.1	2.150	5.504	0.026	.
Female	3	ZRH High	0.095	0.140	0.200	0.280	0.560	0.248	0.148	0.047	59.8	1.300	1.025	0.026	.
Female	4.5	Sham Recovery	0.120	0.130	0.150	0.220	0.530	0.217	0.157	0.064	72.7	2.200	4.941	0.026	.
Female	4.5	3R4F High Recovery	0.120	0.150	0.195	0.250	0.310	0.203	0.069	0.028	34.0	0.519	-0.420	0.026	.
Female	4.5	ZRH High Recovery	0.080	0.098	0.135	0.240	0.310	0.169	0.084	0.027	49.8	0.638	-1.250	0.026	.

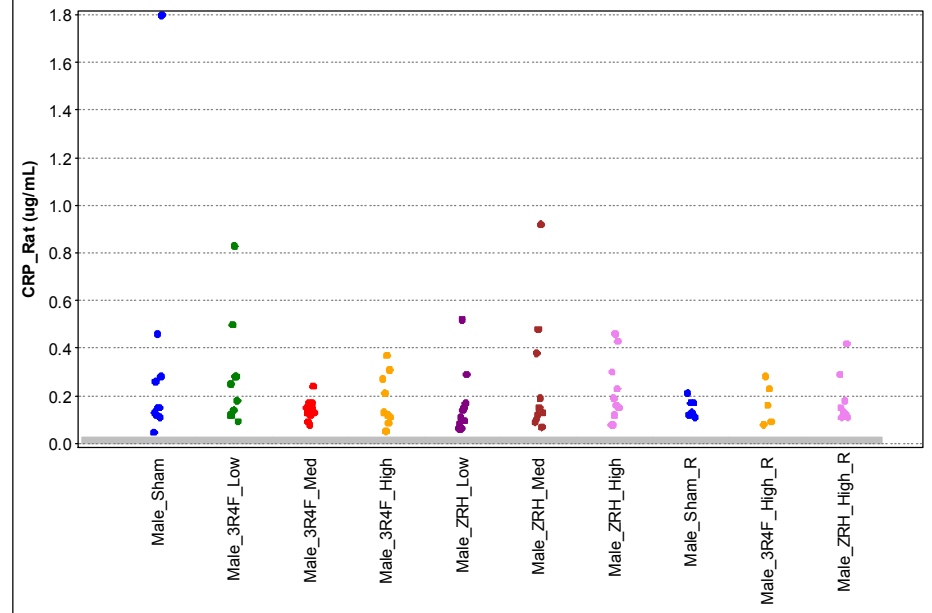
Percentage of Values below LLQ for each Group-Males

Analyte = CRP_Rat



Plot of Individual Measurements for each Group-Males

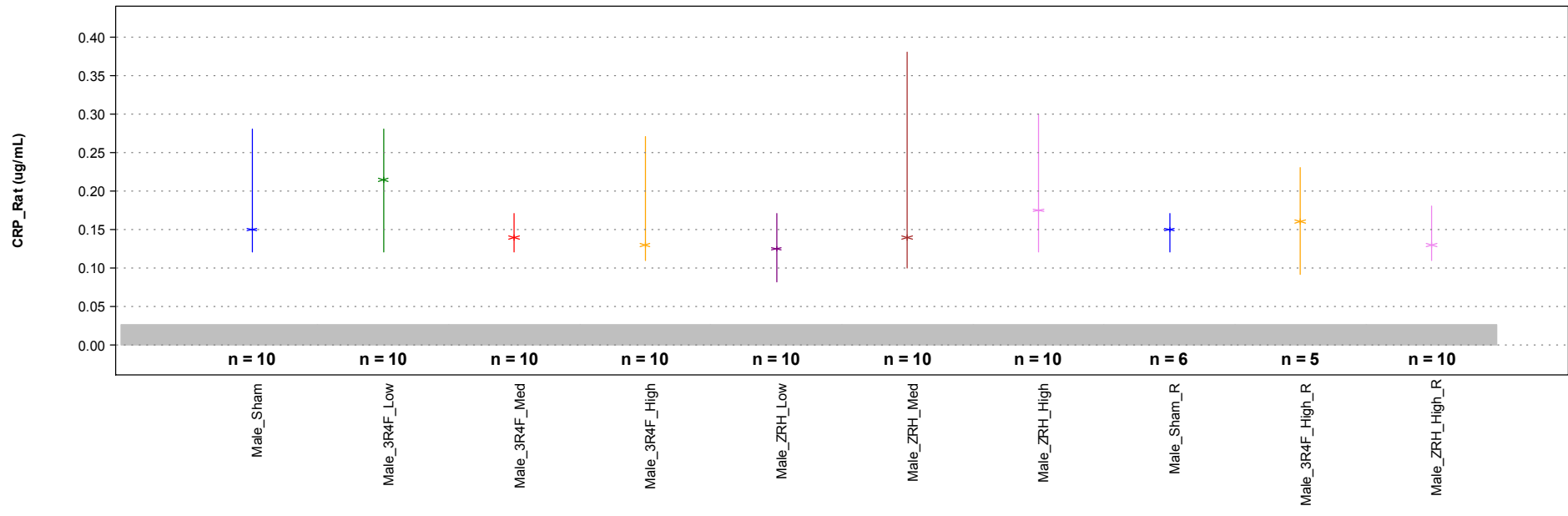
<LOW> values are displayed as 0 / Values above ULQ are displayed as 1.1*ULQ
 Grey zones denote zones below (average) LLQ and above (average) ULQ



Plot of Descriptive Robust Statistics-Males

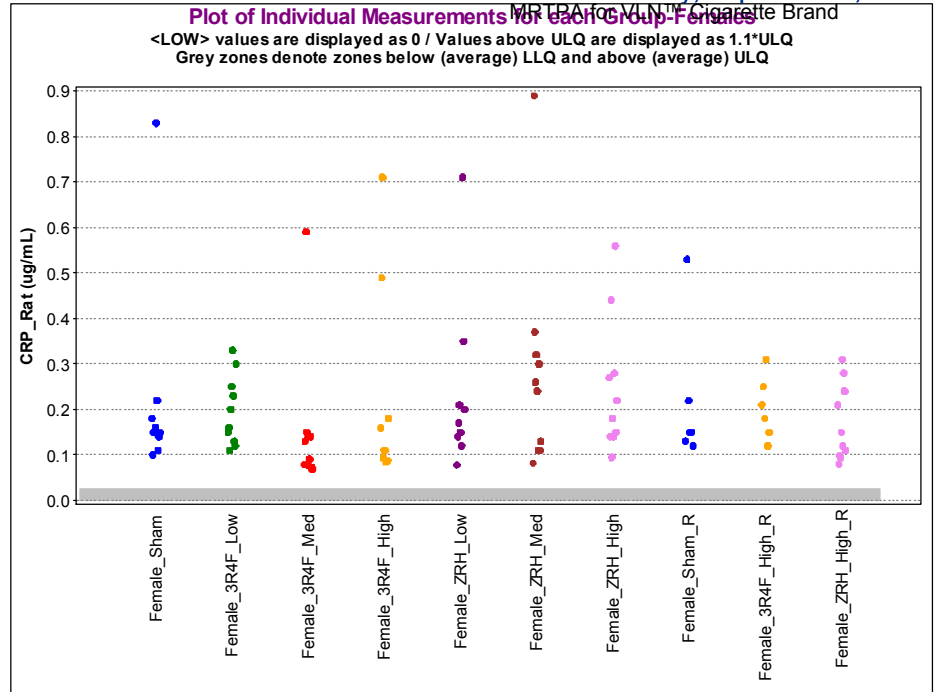
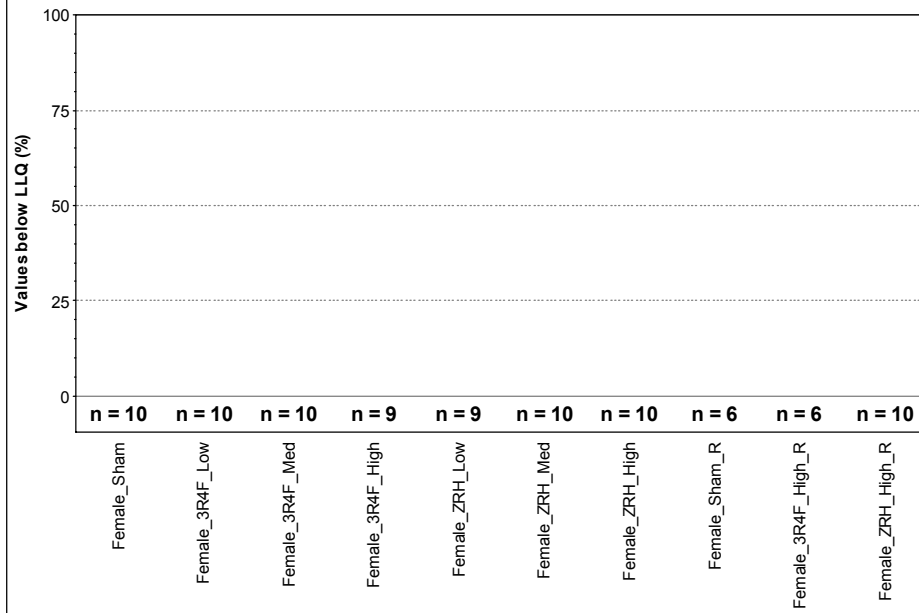
Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Percentage of Values below LLQ for each Group-Females

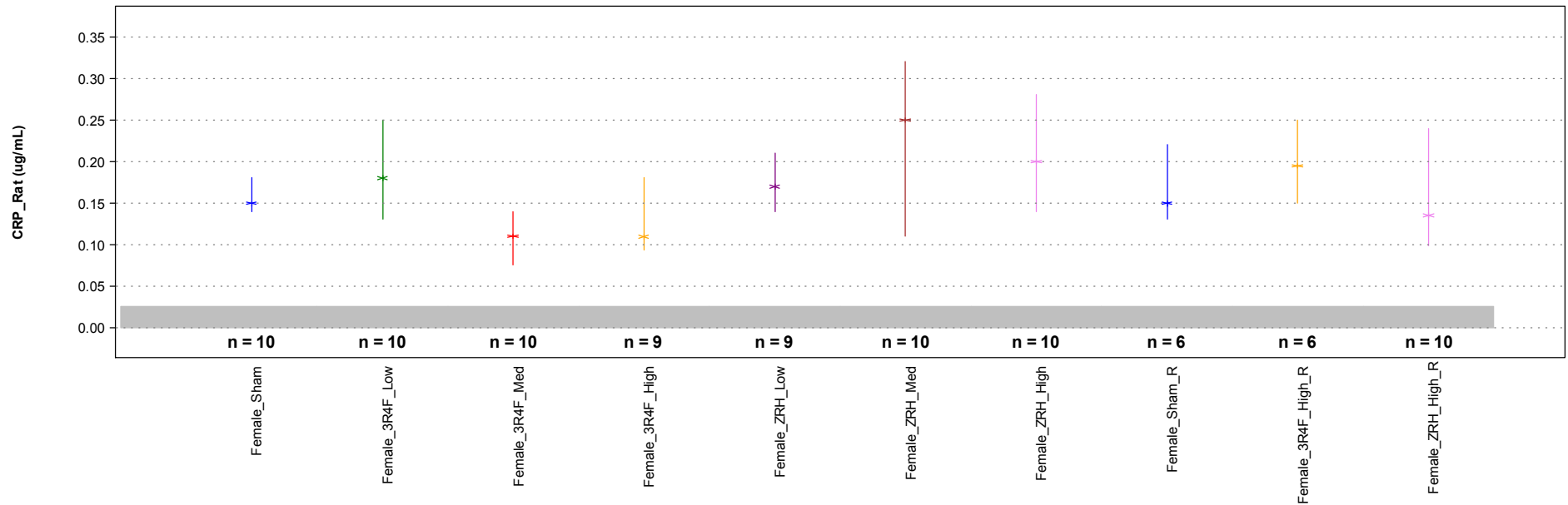
Analyte = CRP_Rat



Plot of Descriptive Robust Statistics-Females

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = CRP_Rat

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	0.704502
---- Sham vs. 3R4F Medium for Male	0.424555
---- Sham vs. 3R4F High for Male	0.544288
---- Sham vs. ZRH Low for Male	0.343613
---- Sham vs. ZRH Medium for Male	0.761847
---- Sham vs. ZRH High for Male	0.879514
---- ZRH Low vs. 3R4F Medium for Male	0.648913
---- ZRH Medium vs. 3R4F High for Male	0.677012
---- ZRH High vs. 3R4F High for Male	0.520052
---- Sham Recovery vs. 3R4F High Recovery for Male	1.000000
---- Sham Recovery vs. ZRH High Recovery for Male	0.826238
---- Sham vs. Sham Recovery for Male	0.624206
---- 3R4F High vs. 3R4F High Recovery for Male	0.902437
---- ZRH High vs. ZRH High Recovery for Male	0.362899
---- 3R4F High Recovery vs. ZRH High Recovery for Male	0.805644
---- Sham vs. 3R4F Low for Female	0.425259
---- Sham vs. 3R4F Medium for Female	0.024973
---- Sham vs. 3R4F High for Female	0.412158
---- Sham vs. ZRH Low for Female	0.681636
---- Sham vs. ZRH Medium for Female	0.448324
---- Sham vs. ZRH High for Female	0.381794
---- ZRH Low vs. 3R4F Medium for Female	0.044983
---- ZRH Medium vs. 3R4F High for Female	0.325056
---- ZRH High vs. 3R4F High for Female	0.205070
---- Sham Recovery vs. 3R4F High Recovery for Female	0.571793
---- Sham Recovery vs. ZRH High Recovery for Female	0.414216
---- Sham vs. Sham Recovery for Female	0.956067

Unadjusted P-values Obtained by Kruskal-Wallis Test
Analyte = CRP_Rat

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	0.215104
---- ZRH High vs. ZRH High Recovery for Female	0.198258
---- 3R4F High Recovery vs. ZRH High Recovery for Female	0.276658

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 6

Epidermal Growth Factor Mouse (EGF Mouse)

Unit = pg/mL

Descriptive Statistics by Exposure Duration and Treatment Type

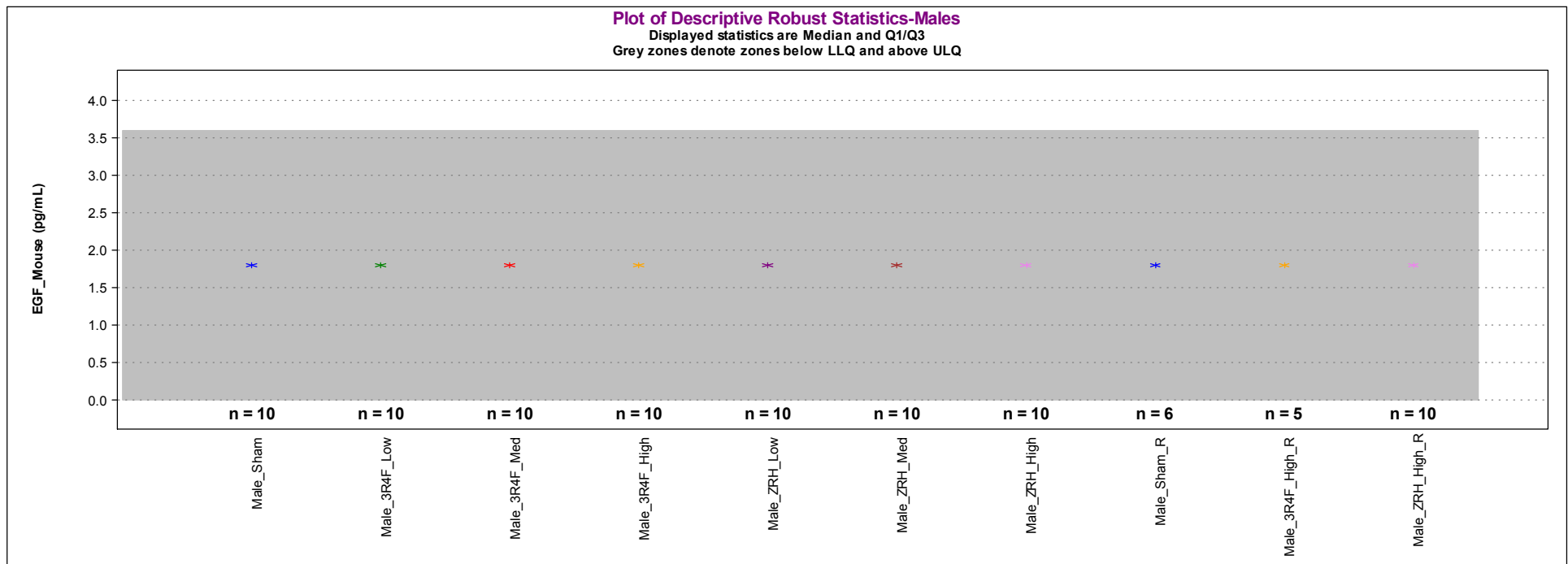
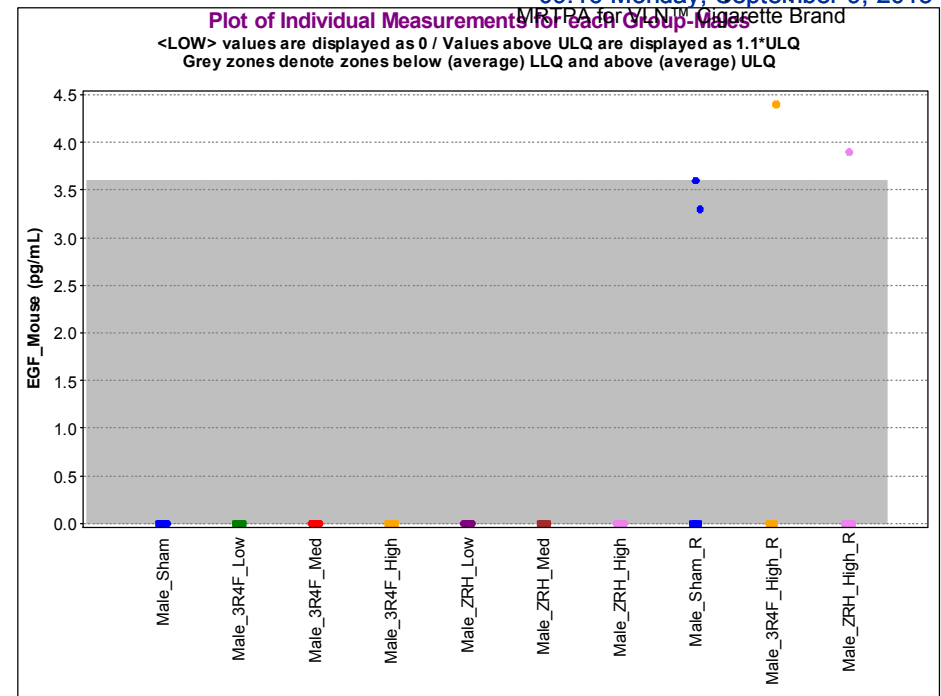
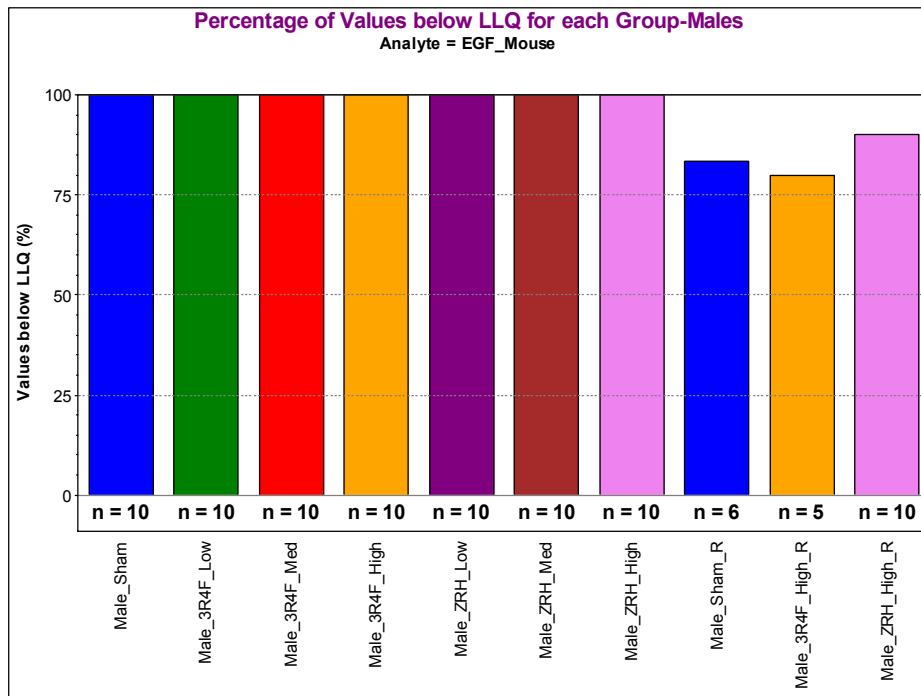
Analyte = EGF_Mouse

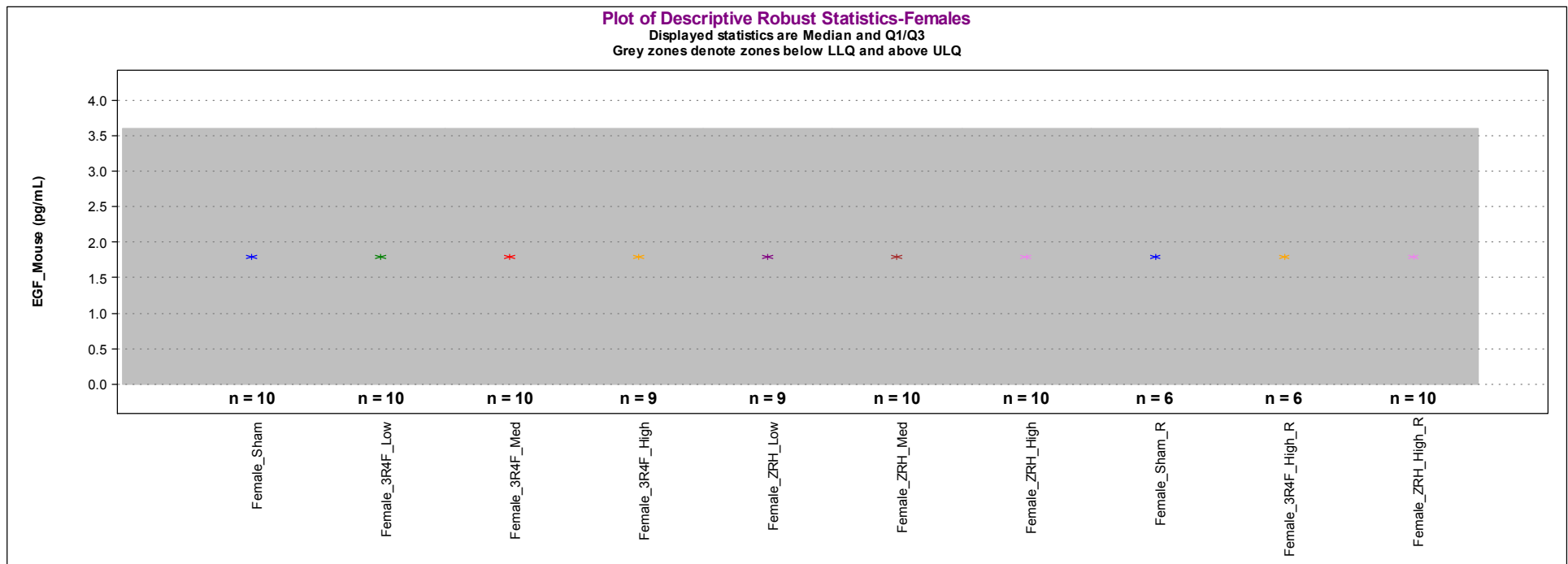
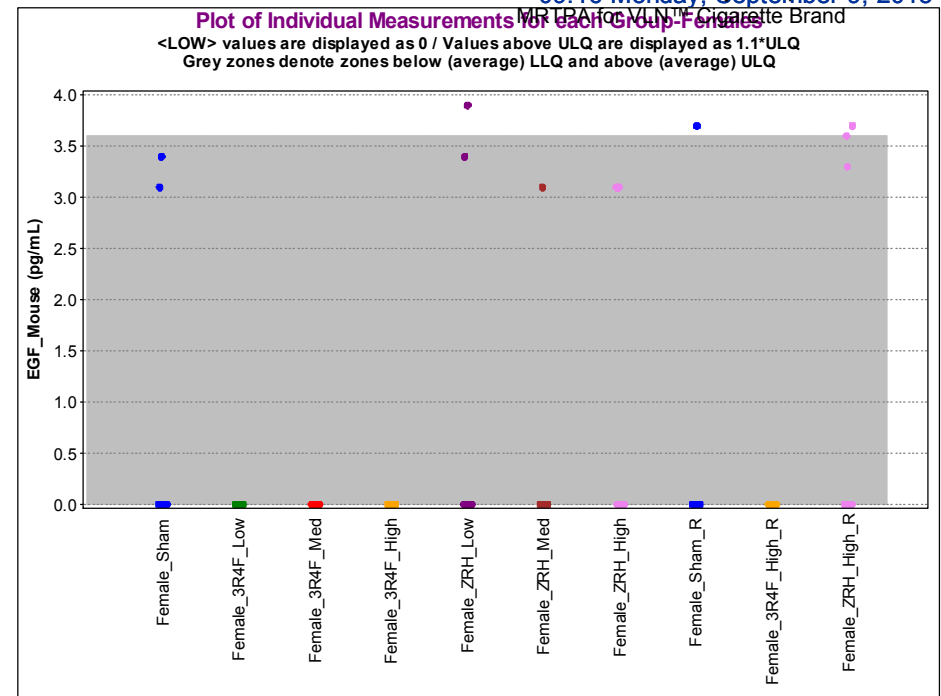
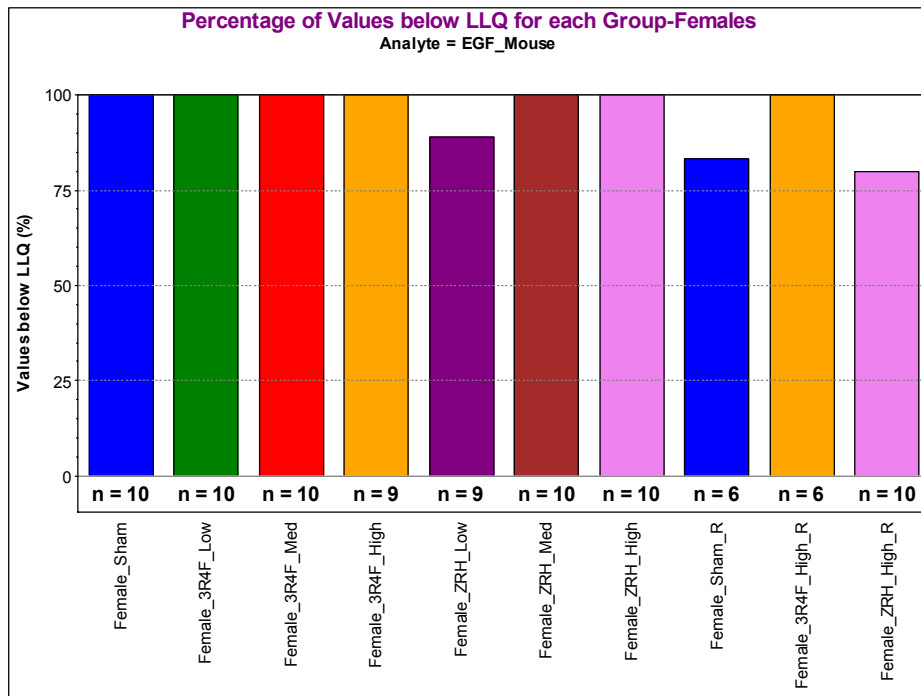
Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	10	0	0	3.6	.
Male	3	3R4F Low	10	10	10	0	0	3.6	.
Male	3	3R4F Medium	10	10	10	0	0	3.6	.
Male	3	3R4F High	10	10	10	0	0	3.6	.
Male	3	ZRH Low	10	10	10	0	0	3.6	.
Male	3	ZRH Medium	10	10	10	0	0	3.6	.
Male	3	ZRH High	10	10	10	0	0	3.6	.
Male	4.5	Sham Recovery	6	6	5	1	0	3.6	.
Male	4.5	3R4F High Recovery	5	5	4	1	0	3.6	.
Male	4.5	ZRH High Recovery	10	10	9	1	0	3.6	.
Female	3	Sham	10	10	10	0	0	3.6	.
Female	3	3R4F Low	10	10	10	0	0	3.6	.
Female	3	3R4F Medium	10	10	10	0	0	3.6	.
Female	3	3R4F High	9	9	9	0	0	3.6	.
Female	3	ZRH Low	9	9	8	1	0	3.6	.
Female	3	ZRH Medium	10	10	10	0	0	3.6	.
Female	3	ZRH High	10	10	10	0	0	3.6	.
Female	4.5	Sham Recovery	6	6	5	1	0	3.6	.
Female	4.5	3R4F High Recovery	6	6	6	0	0	3.6	.
Female	4.5	ZRH High Recovery	10	10	8	2	0	3.6	.

Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = EGF_Mouse

Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	1.800	1.800	1.800	1.800	1.800	1.800	0.000	0.000	0.0	.	.	3.6	.
Male	3	3R4F Low	1.800	1.800	1.800	1.800	1.800	1.800	0.000	0.000	0.0	.	.	3.6	.
Male	3	3R4F Medium	1.800	1.800	1.800	1.800	1.800	1.800	0.000	0.000	0.0	.	.	3.6	.
Male	3	3R4F High	1.800	1.800	1.800	1.800	1.800	1.800	0.000	0.000	0.0	.	.	3.6	.
Male	3	ZRH Low	1.800	1.800	1.800	1.800	1.800	1.800	0.000	0.000	0.0	.	.	3.6	.
Male	3	ZRH Medium	1.800	1.800	1.800	1.800	1.800	1.800	0.000	0.000	0.0	.	.	3.6	.
Male	3	ZRH High	1.800	1.800	1.800	1.800	1.800	1.800	0.000	0.000	0.0	.	.	3.6	.
Male	4.5	Sham Recovery	1.800	1.800	1.800	1.800	3.600	2.100	0.735	0.300	35.0	2.449	6.000	3.6	.
Male	4.5	3R4F High Recovery	1.800	1.800	1.800	1.800	4.400	2.320	1.163	0.520	50.1	2.236	5.000	3.6	.
Male	4.5	ZRH High Recovery	1.800	1.800	1.800	1.800	3.900	2.010	0.664	0.210	33.0	3.162	10.000	3.6	.
Female	3	Sham	1.800	1.800	1.800	1.800	1.800	1.800	0.000	0.000	0.0	.	.	3.6	.
Female	3	3R4F Low	1.800	1.800	1.800	1.800	1.800	1.800	0.000	0.000	0.0	.	.	3.6	.
Female	3	3R4F Medium	1.800	1.800	1.800	1.800	1.800	1.800	0.000	0.000	0.0	.	.	3.6	.
Female	3	3R4F High	1.800	1.800	1.800	1.800	1.800	1.800	0.000	0.000	0.0	.	.	3.6	.
Female	3	ZRH Low	1.800	1.800	1.800	1.800	3.900	2.033	0.700	0.233	34.4	3.000	9.000	3.6	.
Female	3	ZRH Medium	1.800	1.800	1.800	1.800	1.800	1.800	0.000	0.000	0.0	.	.	3.6	.
Female	3	ZRH High	1.800	1.800	1.800	1.800	1.800	1.800	0.000	0.000	0.0	.	.	3.6	.
Female	4.5	Sham Recovery	1.800	1.800	1.800	1.800	3.700	2.117	0.776	0.317	36.6	2.449	6.000	3.6	.
Female	4.5	3R4F High Recovery	1.800	1.800	1.800	1.800	1.800	1.800	0.000	0.000	0.0	.	.	3.6	.
Female	4.5	ZRH High Recovery	1.800	1.800	1.800	1.800	3.700	2.170	0.780	0.247	36.0	1.783	1.434	3.6	.





Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = EGF_Mouse

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	1.000000
---- Sham vs. 3R4F Medium for Male	1.000000
---- Sham vs. 3R4F High for Male	1.000000
---- Sham vs. ZRH Low for Male	1.000000
---- Sham vs. ZRH Medium for Male	1.000000
---- Sham vs. ZRH High for Male	1.000000
---- ZRH Low vs. 3R4F Medium for Male	1.000000
---- ZRH Medium vs. 3R4F High for Male	1.000000
---- ZRH High vs. 3R4F High for Male	1.000000
---- Sham Recovery vs. 3R4F High Recovery for Male	0.786544
---- Sham Recovery vs. ZRH High Recovery for Male	0.777297
---- Sham vs. Sham Recovery for Male	0.196706
---- 3R4F High vs. 3R4F High Recovery for Male	0.157299
---- ZRH High vs. ZRH High Recovery for Male	0.317311
---- 3R4F High Recovery vs. ZRH High Recovery for Male	0.534561
---- Sham vs. 3R4F Low for Female	1.000000
---- Sham vs. 3R4F Medium for Female	1.000000
---- Sham vs. 3R4F High for Female	1.000000
---- Sham vs. ZRH Low for Female	0.291841
---- Sham vs. ZRH Medium for Female	1.000000
---- Sham vs. ZRH High for Female	1.000000
---- ZRH Low vs. 3R4F Medium for Female	0.291841
---- ZRH Medium vs. 3R4F High for Female	1.000000
---- ZRH High vs. 3R4F High for Female	1.000000
---- Sham Recovery vs. 3R4F High Recovery for Female	0.317311
---- Sham Recovery vs. ZRH High Recovery for Female	0.936490
---- Sham vs. Sham Recovery for Female	0.196706

Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = EGF_Mouse

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	1.000000
---- ZRH High vs. ZRH High Recovery for Female	0.146793
---- 3R4F High Recovery vs. ZRH High Recovery for Female	0.257899

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 5

Eotaxin

Unit = pg/mL

Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = Eotaxin

Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	0	10	0	1.2	.
Male	3	3R4F Low	10	10	0	10	0	1.2	.
Male	3	3R4F Medium	10	10	0	10	0	1.2	.
Male	3	3R4F High	10	10	0	10	0	1.2	.
Male	3	ZRH Low	10	10	0	10	0	1.2	.
Male	3	ZRH Medium	10	10	0	10	0	1.2	.
Male	3	ZRH High	10	10	0	10	0	1.2	.
Male	4.5	Sham Recovery	6	6	0	6	0	1.2	.
Male	4.5	3R4F High Recovery	5	5	0	5	0	1.2	.
Male	4.5	ZRH High Recovery	10	10	0	10	0	1.2	.
Female	3	Sham	10	10	0	10	0	1.2	.
Female	3	3R4F Low	10	10	0	10	0	1.2	.
Female	3	3R4F Medium	10	10	0	10	0	1.2	.
Female	3	3R4F High	9	9	0	9	0	1.2	.
Female	3	ZRH Low	9	9	0	9	0	1.2	.
Female	3	ZRH Medium	10	10	0	10	0	1.2	.
Female	3	ZRH High	10	10	0	10	0	1.2	.
Female	4.5	Sham Recovery	6	6	0	6	0	1.2	.
Female	4.5	3R4F High Recovery	6	6	0	6	0	1.2	.
Female	4.5	ZRH High Recovery	10	10	0	10	0	1.2	.

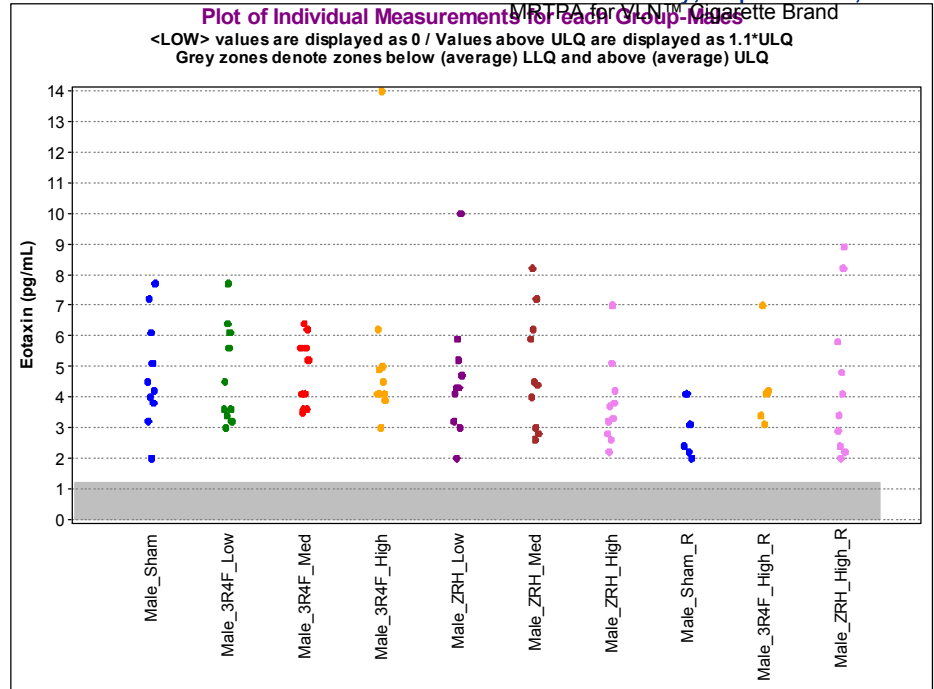
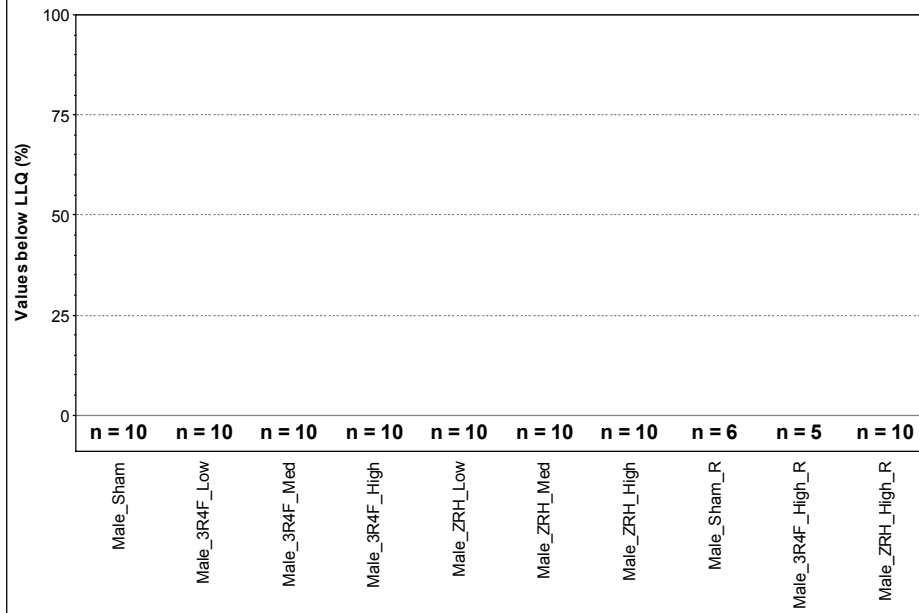
Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = Eotaxin

Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	2.000	3.800	4.350	6.100	7.700	4.780	1.778	0.562	37.2	0.355	-0.460	1.2	.
Male	3	3R4F Low	3.000	3.400	4.050	6.100	7.700	4.710	1.631	0.516	34.6	0.688	-0.882	1.2	.
Male	3	3R4F Medium	3.500	3.600	4.650	5.600	6.400	4.790	1.131	0.358	23.6	0.186	-1.831	1.2	.
Male	3	3R4F High	3.000	4.100	4.300	5.000	14.000	5.380	3.143	0.994	58.4	2.761	8.115	1.2	.
Male	3	ZRH Low	2.000	3.200	4.300	5.200	10.000	4.670	2.183	0.690	46.7	1.686	4.053	1.2	.
Male	3	ZRH Medium	2.600	3.000	4.450	6.200	8.200	4.880	1.926	0.609	39.5	0.468	-0.955	1.2	.
Male	3	ZRH High	2.200	2.800	3.500	4.200	7.000	3.790	1.403	0.444	37.0	1.429	2.351	1.2	.
Male	4.5	Sham Recovery	2.000	2.200	2.750	4.100	4.100	2.983	0.941	0.384	31.5	0.416	-2.201	1.2	.
Male	4.5	3R4F High Recovery	3.100	3.400	4.100	4.200	7.000	4.360	1.547	0.692	35.5	1.744	3.340	1.2	.
Male	4.5	ZRH High Recovery	2.000	2.400	3.750	5.800	8.900	4.470	2.465	0.780	55.2	0.931	-0.373	1.2	.
Female	3	Sham	2.600	3.400	5.100	7.200	17.000	7.020	5.240	1.657	74.6	1.416	0.701	1.2	.
Female	3	3R4F Low	1.900	3.000	5.650	7.400	29.000	7.440	7.869	2.488	105.8	2.737	8.078	1.2	.
Female	3	3R4F Medium	3.500	4.000	4.650	6.500	6.500	4.930	1.190	0.376	24.1	0.447	-1.514	1.2	.
Female	3	3R4F High	2.300	3.900	4.400	4.900	6.900	4.378	1.260	0.420	28.8	0.483	1.881	1.2	.
Female	3	ZRH Low	1.900	3.300	4.400	4.600	7.200	4.367	1.576	0.525	36.1	0.343	0.356	1.2	.
Female	3	ZRH Medium	2.300	2.800	4.450	8.000	9.700	5.370	2.828	0.894	52.7	0.478	-1.569	1.2	.
Female	3	ZRH High	2.600	3.000	3.350	5.000	9.100	4.250	2.090	0.661	49.2	1.746	2.536	1.2	.
Female	4.5	Sham Recovery	4.100	4.200	4.250	4.600	5.500	4.483	0.527	0.215	11.8	1.936	3.775	1.2	.
Female	4.5	3R4F High Recovery	2.500	3.100	3.600	4.300	5.000	3.683	0.935	0.382	25.4	0.197	-1.323	1.2	.
Female	4.5	ZRH High Recovery	2.200	2.200	2.700	4.600	5.500	3.230	1.269	0.401	39.3	0.985	-0.794	1.2	.

Percentage of Values below LLQ for each Group-Males

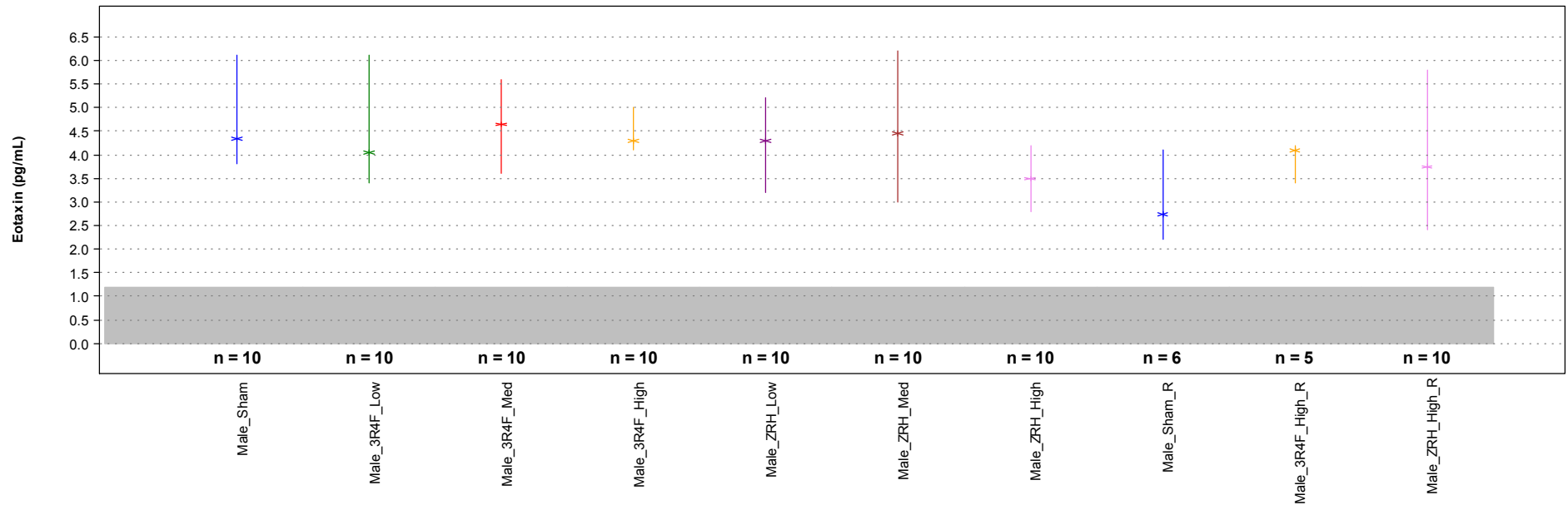
Analyte = Eotaxin



Plot of Descriptive Robust Statistics-Males

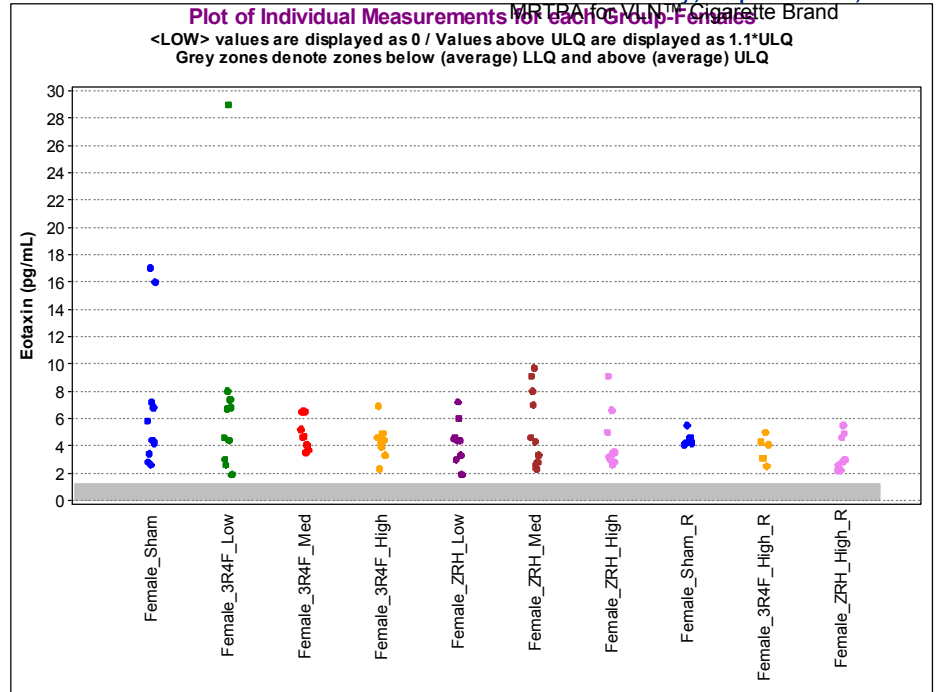
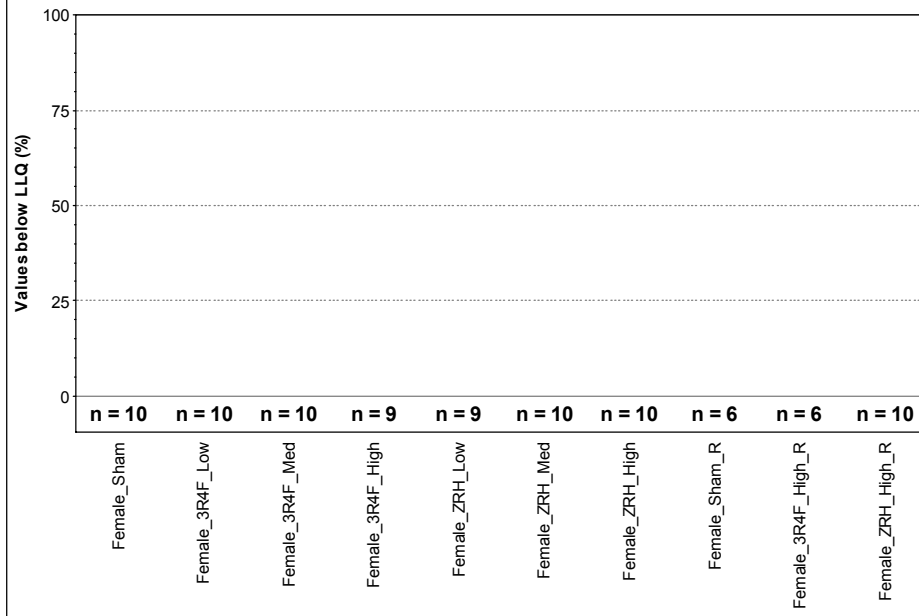
Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Percentage of Values below LLQ for each Group-Females

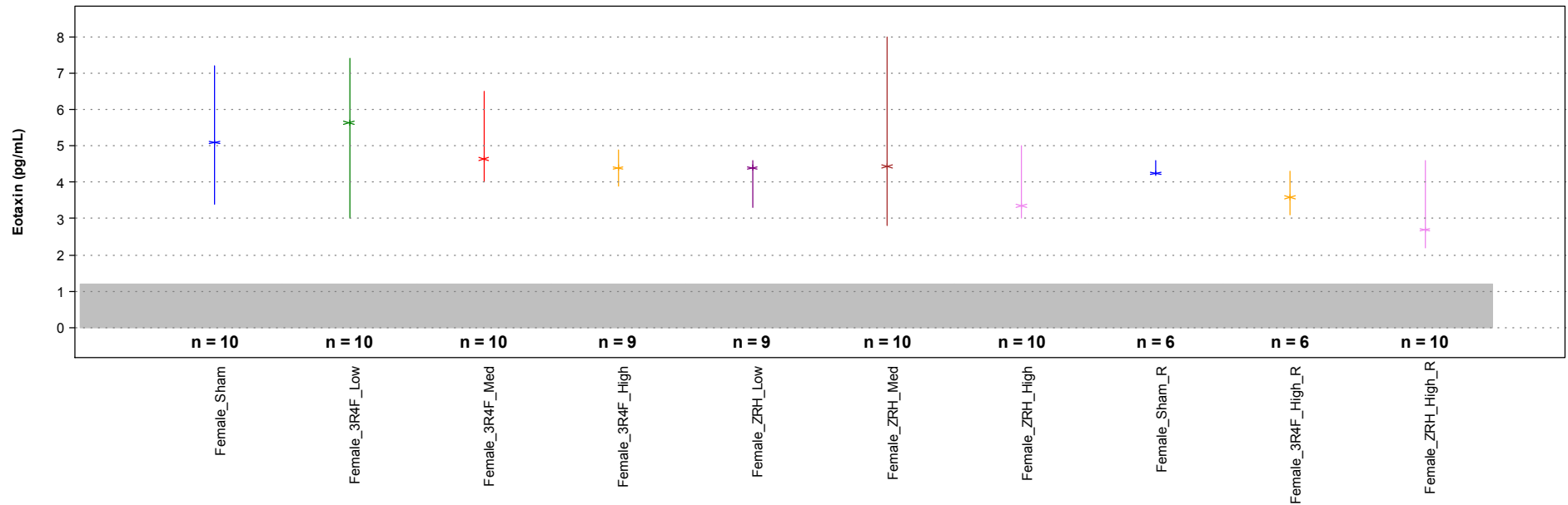
Analyte = Eotaxin



Plot of Descriptive Robust Statistics-Females

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = Eotaxin

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	0.761934
---- Sham vs. 3R4F Medium for Male	0.939675
---- Sham vs. 3R4F High for Male	0.909552
---- Sham vs. ZRH Low for Male	0.820397
---- Sham vs. ZRH Medium for Male	0.969816
---- Sham vs. ZRH High for Male	0.129991
---- ZRH Low vs. 3R4F Medium for Male	0.569587
---- ZRH Medium vs. 3R4F High for Male	0.849715
---- ZRH High vs. 3R4F High for Male	0.069223
---- Sham Recovery vs. 3R4F High Recovery for Male	0.079344
---- Sham Recovery vs. ZRH High Recovery for Male	0.252295
---- Sham vs. Sham Recovery for Male	0.044477
---- 3R4F High vs. 3R4F High Recovery for Male	0.496691
---- ZRH High vs. ZRH High Recovery for Male	0.791260
---- 3R4F High Recovery vs. ZRH High Recovery for Male	0.712813
---- Sham vs. 3R4F Low for Female	0.969816
---- Sham vs. 3R4F Medium for Female	0.705034
---- Sham vs. 3R4F High for Female	0.413601
---- Sham vs. ZRH Low for Female	0.486711
---- Sham vs. ZRH Medium for Female	0.649902
---- Sham vs. ZRH High for Female	0.198089
---- ZRH Low vs. 3R4F Medium for Female	0.346473
---- ZRH Medium vs. 3R4F High for Female	0.712821
---- ZRH High vs. 3R4F High for Female	0.368477
---- Sham Recovery vs. 3R4F High Recovery for Female	0.146686
---- Sham Recovery vs. ZRH High Recovery for Female	0.101961
---- Sham vs. Sham Recovery for Female	0.513941

Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = Eotaxin

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	0.287982
---- ZRH High vs. ZRH High Recovery for Female	0.074672
---- 3R4F High Recovery vs. ZRH High Recovery for Female	0.231101

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 9

Fibroblast Growth Factor 9 (FGF-9)

Unit = ng/mL

Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = FGF_9

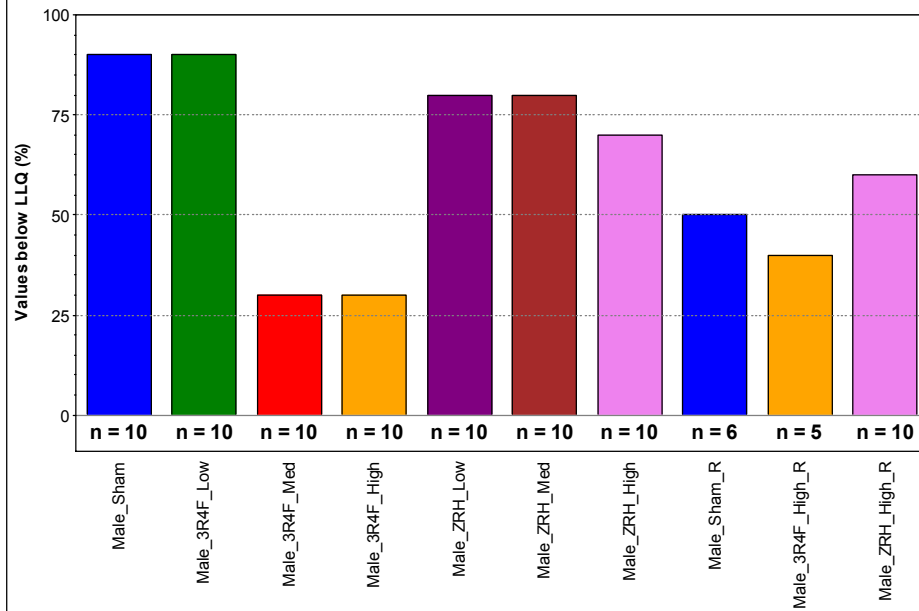
Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	9	1	0	0.57	.
Male	3	3R4F Low	10	10	9	1	0	0.57	.
Male	3	3R4F Medium	10	10	3	7	0	0.57	.
Male	3	3R4F High	10	10	3	7	0	0.57	.
Male	3	ZRH Low	10	10	8	2	0	0.57	.
Male	3	ZRH Medium	10	10	8	2	0	0.57	.
Male	3	ZRH High	10	10	7	3	0	0.57	.
Male	4.5	Sham Recovery	6	6	3	3	0	0.57	.
Male	4.5	3R4F High Recovery	5	5	2	3	0	0.57	.
Male	4.5	ZRH High Recovery	10	10	6	4	0	0.57	.
Female	3	Sham	10	10	8	2	0	0.57	.
Female	3	3R4F Low	10	10	5	5	0	0.57	.
Female	3	3R4F Medium	10	10	1	9	0	0.57	.
Female	3	3R4F High	9	9	2	7	0	0.57	.
Female	3	ZRH Low	9	9	8	1	0	0.57	.
Female	3	ZRH Medium	10	10	10	0	0	0.57	.
Female	3	ZRH High	10	10	7	3	0	0.57	.
Female	4.5	Sham Recovery	6	6	1	5	0	0.57	.
Female	4.5	3R4F High Recovery	6	6	3	3	0	0.57	.
Female	4.5	ZRH High Recovery	10	10	4	6	0	0.57	.

Descriptive Statistics by Exposure Duration and Treatment Type**Analyte = FGF_9**

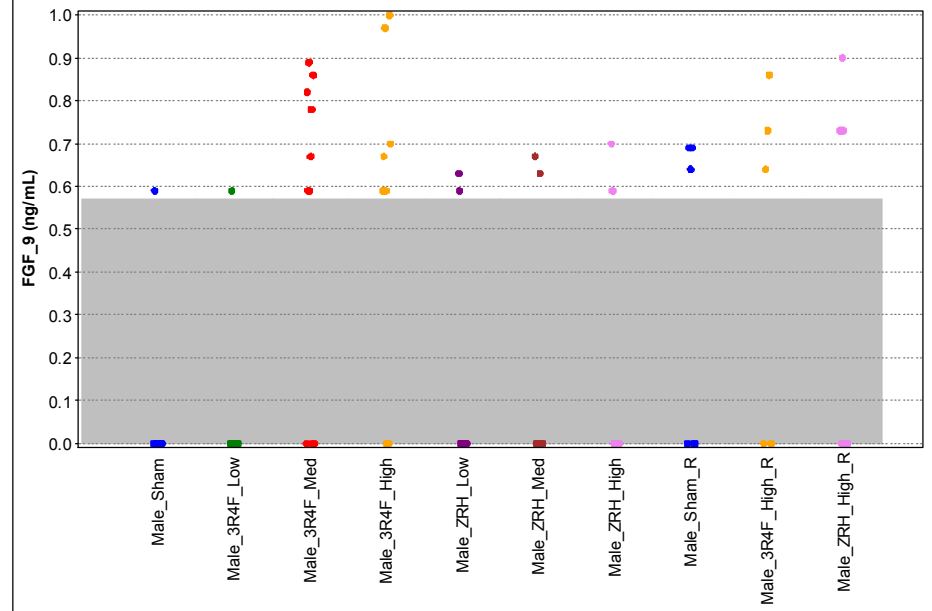
Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	0.285	0.285	0.285	0.285	0.590	0.316	0.096	0.031	30.6	3.162	10.000	0.57	.
Male	3	3R4F Low	0.285	0.285	0.285	0.285	0.590	0.316	0.096	0.031	30.6	3.162	10.000	0.57	.
Male	3	3R4F Medium	0.285	0.285	0.630	0.820	0.890	0.606	0.244	0.077	40.3	-0.420	-1.531	0.57	.
Male	3	3R4F High	0.285	0.285	0.590	0.700	1.000	0.597	0.260	0.082	43.6	0.226	-0.802	0.57	.
Male	3	ZRH Low	0.285	0.285	0.285	0.285	0.630	0.350	0.137	0.043	39.2	1.800	1.551	0.57	.
Male	3	ZRH Medium	0.285	0.285	0.285	0.285	0.670	0.358	0.154	0.049	43.1	1.795	1.522	0.57	.
Male	3	ZRH High	0.285	0.285	0.285	0.590	0.700	0.388	0.168	0.053	43.3	1.165	-0.569	0.57	.
Male	4.5	Sham Recovery	0.285	0.285	0.463	0.690	0.690	0.479	0.213	0.087	44.6	0.029	-3.256	0.57	.
Male	4.5	3R4F High Recovery	0.285	0.285	0.640	0.730	0.860	0.560	0.263	0.118	47.0	-0.210	-2.661	0.57	.
Male	4.5	ZRH High Recovery	0.285	0.285	0.285	0.730	0.900	0.480	0.256	0.081	53.4	0.630	-1.741	0.57	.
Female	3	Sham	0.285	0.285	0.285	0.285	0.670	0.362	0.162	0.051	44.8	1.779	1.406	0.57	.
Female	3	3R4F Low	0.285	0.285	0.433	0.610	0.720	0.461	0.189	0.060	41.1	0.168	-2.206	0.57	.
Female	3	3R4F Medium	0.285	0.650	0.730	0.850	1.100	0.744	0.220	0.069	29.5	-0.483	1.695	0.57	.
Female	3	3R4F High	0.285	0.610	0.670	0.720	0.780	0.606	0.188	0.063	31.1	-1.326	0.264	0.57	.
Female	3	ZRH Low	0.285	0.285	0.285	0.285	0.650	0.326	0.122	0.041	37.4	3.000	9.000	0.57	.
Female	3	ZRH Medium	0.285	0.285	0.285	0.285	0.285	0.285	0.000	0.000	0.0	.	.	0.57	.
Female	3	ZRH High	0.285	0.285	0.285	0.580	0.650	0.382	0.156	0.049	41.0	1.087	-0.967	0.57	.
Female	4.5	Sham Recovery	0.285	0.670	0.730	0.750	0.790	0.659	0.187	0.076	28.4	-2.221	5.117	0.57	.
Female	4.5	3R4F High Recovery	0.285	0.285	0.443	0.640	0.860	0.493	0.244	0.100	49.5	0.564	-1.425	0.57	.
Female	4.5	ZRH High Recovery	0.285	0.285	0.630	0.750	1.100	0.574	0.282	0.089	49.2	0.435	-0.595	0.57	.

Percentage of Values below LLQ for each Group-Males

Analyte = FGF_9

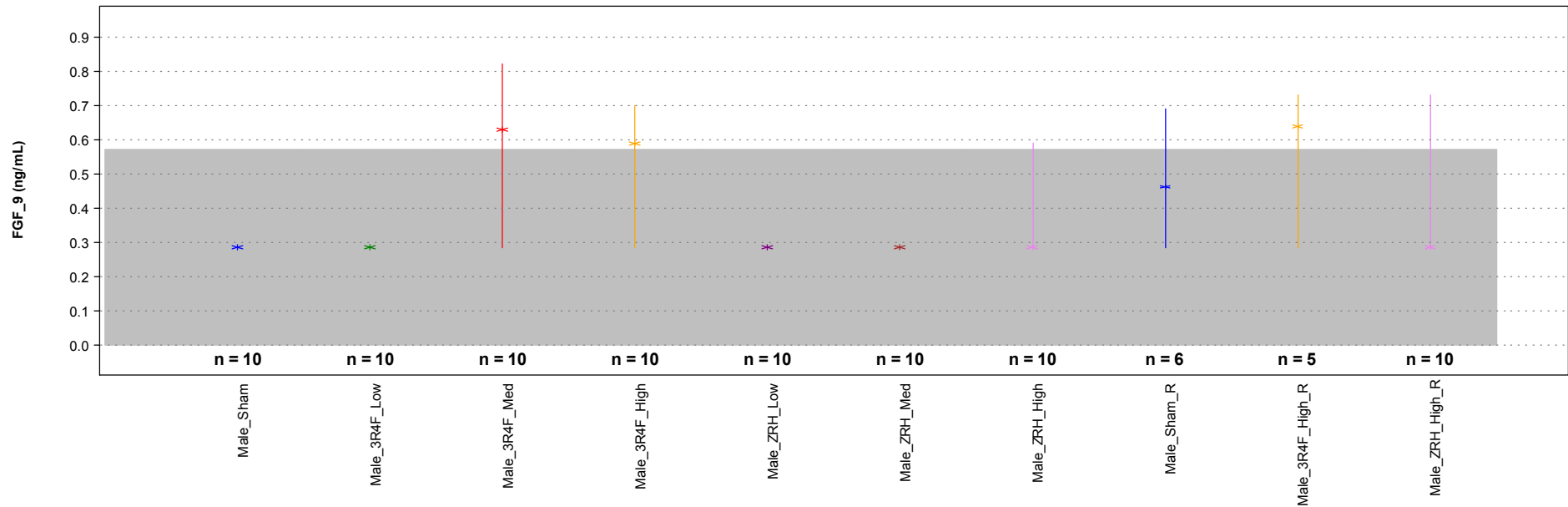
**Plot of Individual Measurements for each Group-Males**

<LOW> values are displayed as 0 / Values above ULQ are displayed as 1.1*ULQ
Grey zones denote zones below (average) LLQ and above (average) ULQ

**Plot of Descriptive Robust Statistics-Males**

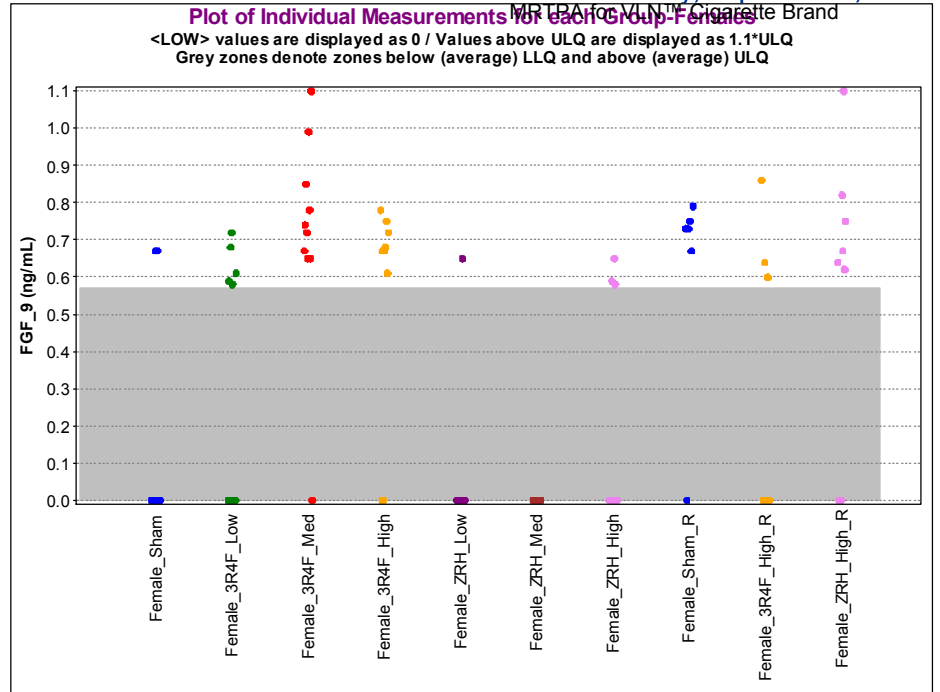
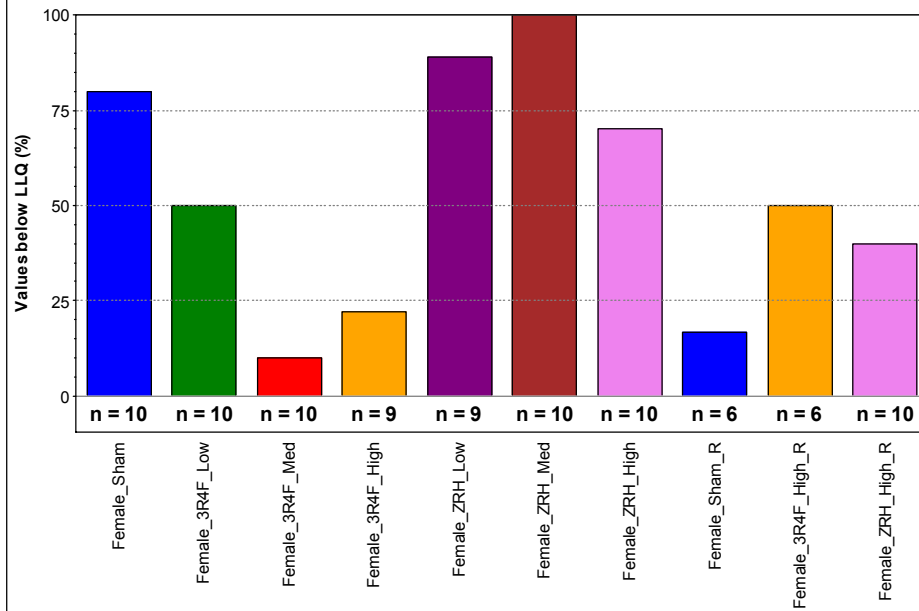
Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



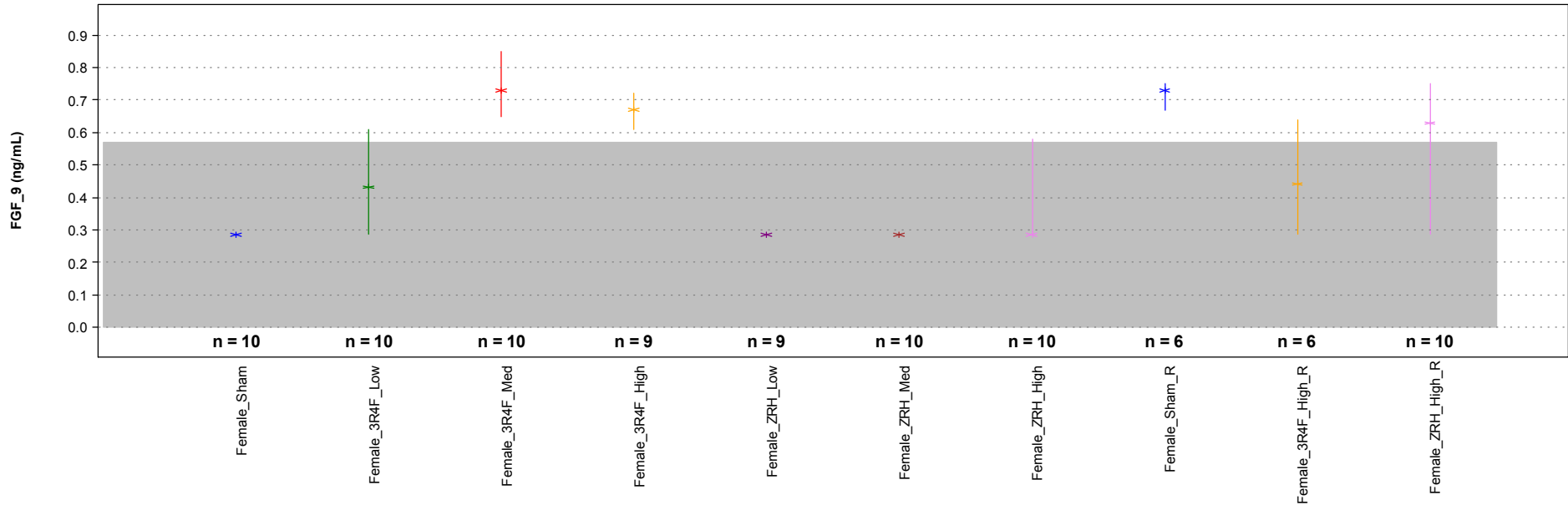
Percentage of Values below LLQ for each Group-Females

Analyte = FGF_9

**Plot of Descriptive Robust Statistics-Females**

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = FGF_9

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	1.000000
---- Sham vs. 3R4F Medium for Male	0.005465
---- Sham vs. 3R4F High for Male	0.006080
---- Sham vs. ZRH Low for Male	0.503216
---- Sham vs. ZRH Medium for Male	0.465643
---- Sham vs. ZRH High for Male	0.254751
---- ZRH Low vs. 3R4F Medium for Male	0.016219
---- ZRH Medium vs. 3R4F High for Male	0.034448
---- ZRH High vs. 3R4F High for Male	0.060840
---- Sham Recovery vs. 3R4F High Recovery for Male	0.500581
---- Sham Recovery vs. ZRH High Recovery for Male	0.718712
---- Sham vs. Sham Recovery for Male	0.054090
---- 3R4F High vs. 3R4F High Recovery for Male	1.000000
---- ZRH High vs. ZRH High Recovery for Male	0.327964
---- 3R4F High Recovery vs. ZRH High Recovery for Male	0.638419
---- Sham vs. 3R4F Low for Female	0.214079
---- Sham vs. 3R4F Medium for Female	0.001953
---- Sham vs. 3R4F High for Female	0.010065
---- Sham vs. ZRH Low for Female	0.519975
---- Sham vs. ZRH Medium for Female	0.146233
---- Sham vs. ZRH High for Female	0.842399
---- ZRH Low vs. 3R4F Medium for Female	0.000743
---- ZRH Medium vs. 3R4F High for Female	0.000954
---- ZRH High vs. 3R4F High for Female	0.007424
---- Sham Recovery vs. 3R4F High Recovery for Female	0.165124
---- Sham Recovery vs. ZRH High Recovery for Female	0.377355
---- Sham vs. Sham Recovery for Female	0.005756

Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = FGF_9

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	0.229654
---- ZRH High vs. ZRH High Recovery for Female	0.068697
---- 3R4F High Recovery vs. ZRH High Recovery for Female	0.533119

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 10

Fibroblast Growth Factor basic (FGF-basic)

Unit = ng/mL

Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = FGF_basic

Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	10	0	0	3.1	.
Male	3	3R4F Low	10	10	10	0	0	3.1	.
Male	3	3R4F Medium	10	10	10	0	0	3.1	.
Male	3	3R4F High	10	10	10	0	0	3.1	.
Male	3	ZRH Low	10	10	10	0	0	3.1	.
Male	3	ZRH Medium	10	10	10	0	0	3.1	.
Male	3	ZRH High	10	10	10	0	0	3.1	.
Male	4.5	Sham Recovery	6	6	6	0	0	3.1	.
Male	4.5	3R4F High Recovery	5	5	2	3	0	3.1	.
Male	4.5	ZRH High Recovery	10	10	7	3	0	3.1	.
Female	3	Sham	10	10	3	7	0	3.1	.
Female	3	3R4F Low	10	10	7	3	0	3.1	.
Female	3	3R4F Medium	10	10	7	3	0	3.1	.
Female	3	3R4F High	9	9	5	4	0	3.1	.
Female	3	ZRH Low	9	9	4	5	0	3.1	.
Female	3	ZRH Medium	10	10	5	5	0	3.1	.
Female	3	ZRH High	10	10	5	5	0	3.1	.
Female	4.5	Sham Recovery	6	6	4	2	0	3.1	.
Female	4.5	3R4F High Recovery	6	6	2	4	0	3.1	.
Female	4.5	ZRH High Recovery	10	10	9	1	0	3.1	.

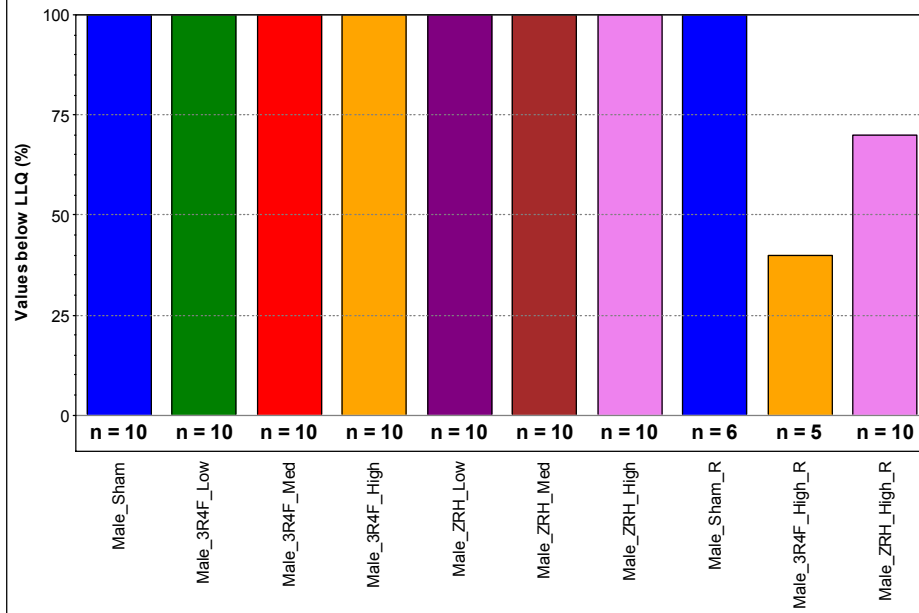
Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = FGF_basic

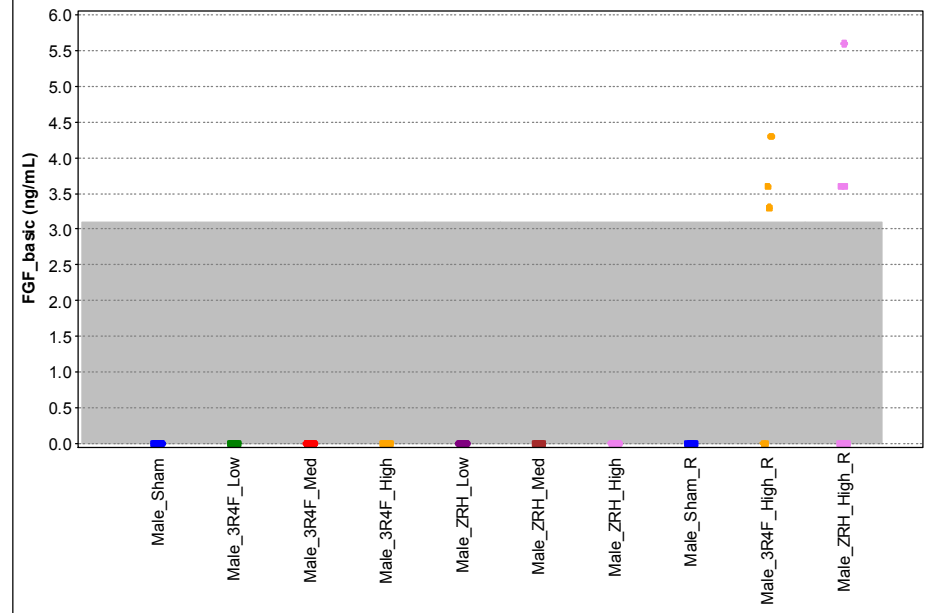
Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	1.550	1.550	1.550	1.550	1.550	1.550	0.000	0.000	0.0	.	.	3.1	.
Male	3	3R4F Low	1.550	1.550	1.550	1.550	1.550	1.550	0.000	0.000	0.0	.	.	3.1	.
Male	3	3R4F Medium	1.550	1.550	1.550	1.550	1.550	1.550	0.000	0.000	0.0	.	.	3.1	.
Male	3	3R4F High	1.550	1.550	1.550	1.550	1.550	1.550	0.000	0.000	0.0	.	.	3.1	.
Male	3	ZRH Low	1.550	1.550	1.550	1.550	1.550	1.550	0.000	0.000	0.0	.	.	3.1	.
Male	3	ZRH Medium	1.550	1.550	1.550	1.550	1.550	1.550	0.000	0.000	0.0	.	.	3.1	.
Male	3	ZRH High	1.550	1.550	1.550	1.550	1.550	1.550	0.000	0.000	0.0	.	.	3.1	.
Male	4.5	Sham Recovery	1.550	1.550	1.550	1.550	1.550	1.550	0.000	0.000	0.0	.	.	3.1	.
Male	4.5	3R4F High Recovery	1.550	1.550	3.300	3.600	4.300	2.860	1.250	0.559	43.7	-0.218	-2.605	3.1	.
Male	4.5	ZRH High Recovery	1.550	1.550	1.550	3.600	5.600	2.365	1.421	0.449	60.1	1.639	1.943	3.1	.
Female	3	Sham	1.550	1.550	3.100	3.700	4.400	2.945	1.040	0.329	35.3	-0.464	-1.203	3.1	.
Female	3	3R4F Low	1.550	1.550	1.550	3.100	4.400	2.205	1.098	0.347	49.8	1.328	0.181	3.1	.
Female	3	3R4F Medium	1.550	1.550	1.550	3.100	3.700	2.085	0.875	0.277	42.0	1.157	-0.616	3.1	.
Female	3	3R4F High	1.550	1.550	1.550	3.700	4.400	2.528	1.198	0.399	47.4	0.506	-1.864	3.1	.
Female	3	ZRH Low	1.550	1.550	3.700	4.400	4.900	3.033	1.454	0.485	47.9	-0.045	-2.241	3.1	.
Female	3	ZRH Medium	1.550	1.550	2.325	3.100	3.700	2.445	0.969	0.306	39.6	0.185	-2.176	3.1	.
Female	3	ZRH High	1.550	1.550	2.325	3.700	4.400	2.635	1.184	0.374	44.9	0.237	-2.059	3.1	.
Female	4.5	Sham Recovery	1.550	1.550	1.550	3.300	4.300	2.300	1.204	0.492	52.4	1.256	-0.169	3.1	.
Female	4.5	3R4F High Recovery	1.550	1.550	3.600	3.600	4.000	2.983	1.121	0.458	37.6	-0.881	-1.842	3.1	.
Female	4.5	ZRH High Recovery	1.550	1.550	1.550	1.550	3.600	1.755	0.648	0.205	36.9	3.162	10.000	3.1	.

Percentage of Values below LLQ for each Group-Males

Analyte = FGF_basic

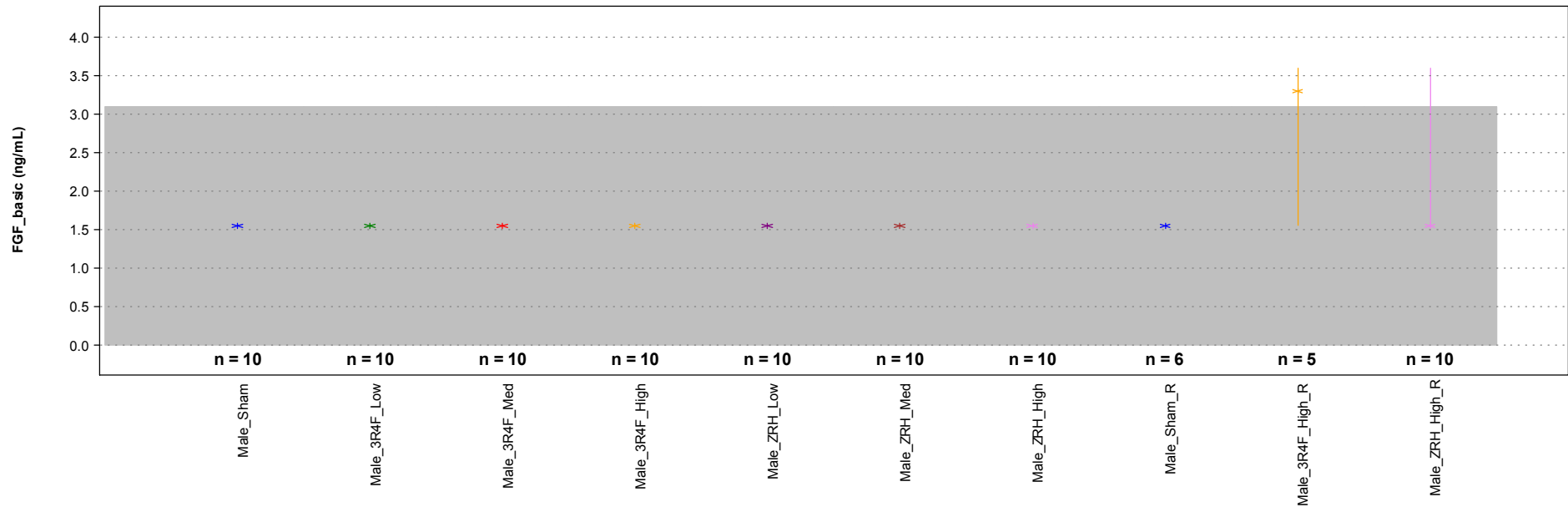
**Plot of Individual Measurements for each Group-Males**

<LOW> values are displayed as 0 / Values above ULQ are displayed as 1.1*ULQ
 Grey zones denote zones below (average) LLQ and above (average) ULQ

**Plot of Descriptive Robust Statistics-Males**

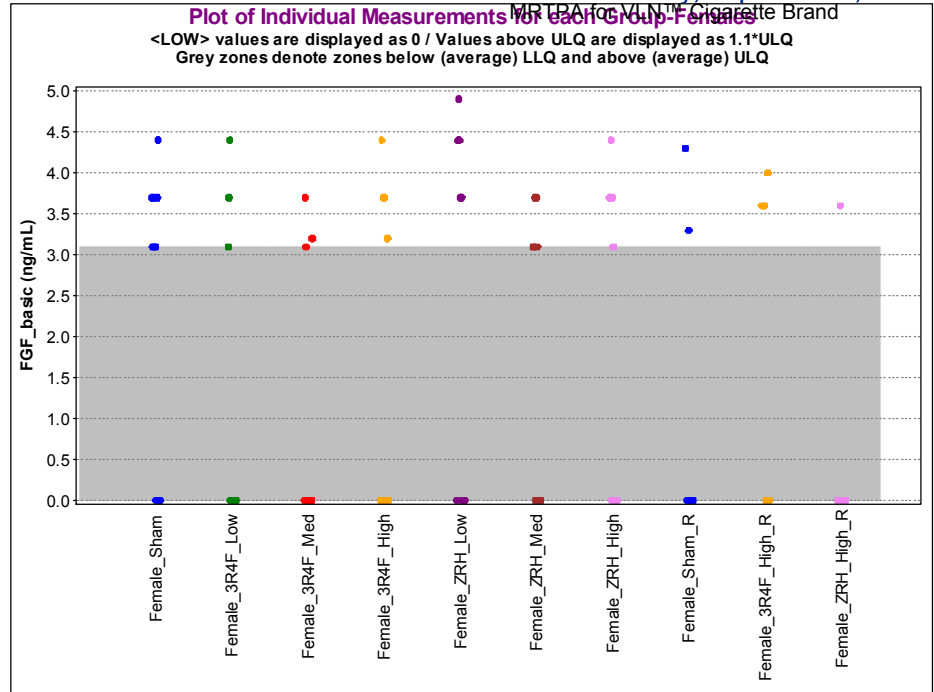
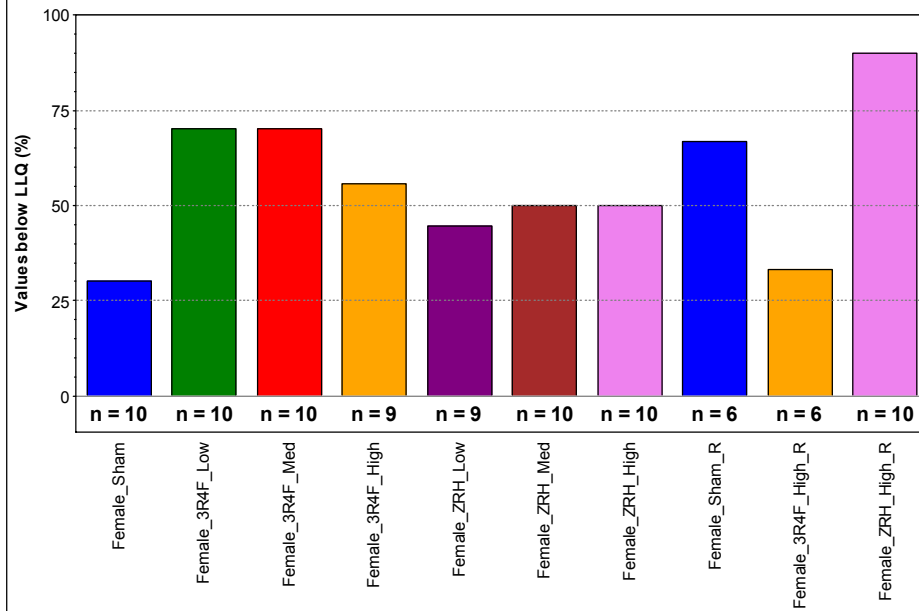
Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



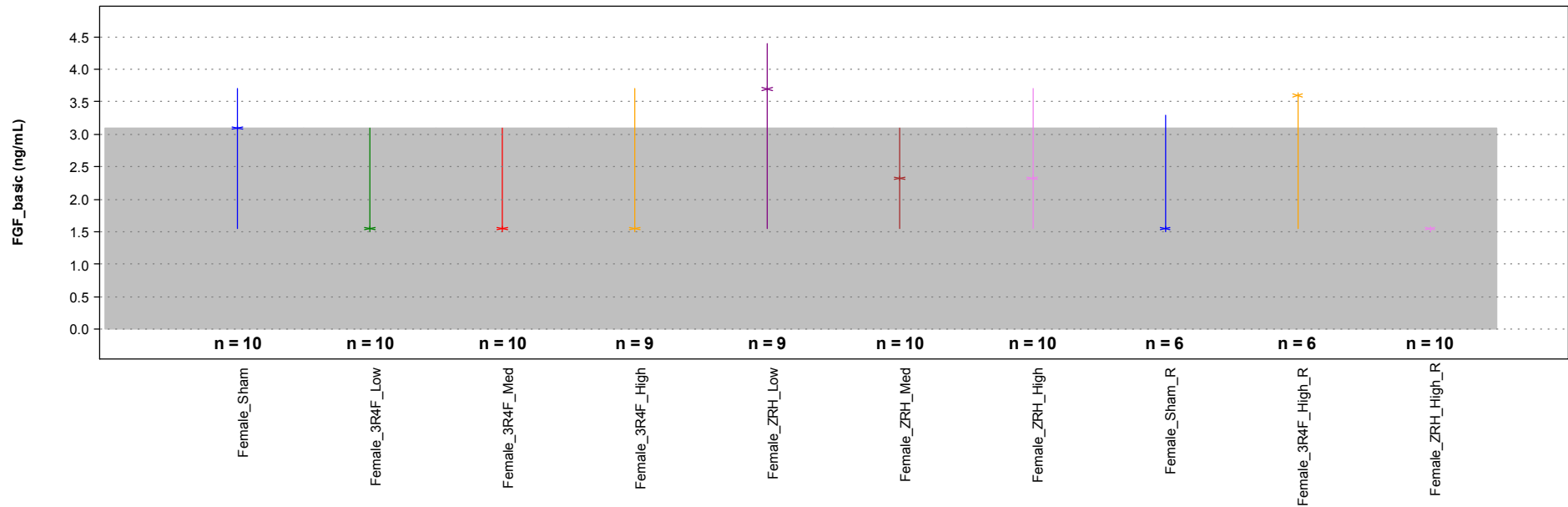
Percentage of Values below LLQ for each Group-Females

Analyte = FGF_basic

**Plot of Descriptive Robust Statistics-Females**

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = FGF_basic

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	1.000000
---- Sham vs. 3R4F Medium for Male	1.000000
---- Sham vs. 3R4F High for Male	1.000000
---- Sham vs. ZRH Low for Male	1.000000
---- Sham vs. ZRH Medium for Male	1.000000
---- Sham vs. ZRH High for Male	1.000000
---- ZRH Low vs. 3R4F Medium for Male	1.000000
---- ZRH Medium vs. 3R4F High for Male	1.000000
---- ZRH High vs. 3R4F High for Male	1.000000
---- Sham Recovery vs. 3R4F High Recovery for Male	0.036628
---- Sham Recovery vs. ZRH High Recovery for Male	0.151494
---- Sham vs. Sham Recovery for Male	1.000000
---- 3R4F High vs. 3R4F High Recovery for Male	0.008630
---- ZRH High vs. ZRH High Recovery for Male	0.067889
---- 3R4F High Recovery vs. ZRH High Recovery for Male	0.404950
---- Sham vs. 3R4F Low for Female	0.142343
---- Sham vs. 3R4F Medium for Female	0.079837
---- Sham vs. 3R4F High for Female	0.547839
---- Sham vs. ZRH Low for Female	0.671438
---- Sham vs. ZRH Medium for Female	0.263416
---- Sham vs. ZRH High for Female	0.633011
---- ZRH Low vs. 3R4F Medium for Female	0.100907
---- ZRH Medium vs. 3R4F High for Female	0.755609
---- ZRH High vs. 3R4F High for Female	0.858322
---- Sham Recovery vs. 3R4F High Recovery for Female	0.301211
---- Sham Recovery vs. ZRH High Recovery for Female	0.265373
---- Sham vs. Sham Recovery for Female	0.305059

Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = FGF_basic

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	0.617507
---- ZRH High vs. ZRH High Recovery for Female	0.044608
---- 3R4F High Recovery vs. ZRH High Recovery for Female	0.019631

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 7

Factor VII

Unit = ng/mL

Descriptive Statistics by Exposure Duration and Treatment Type

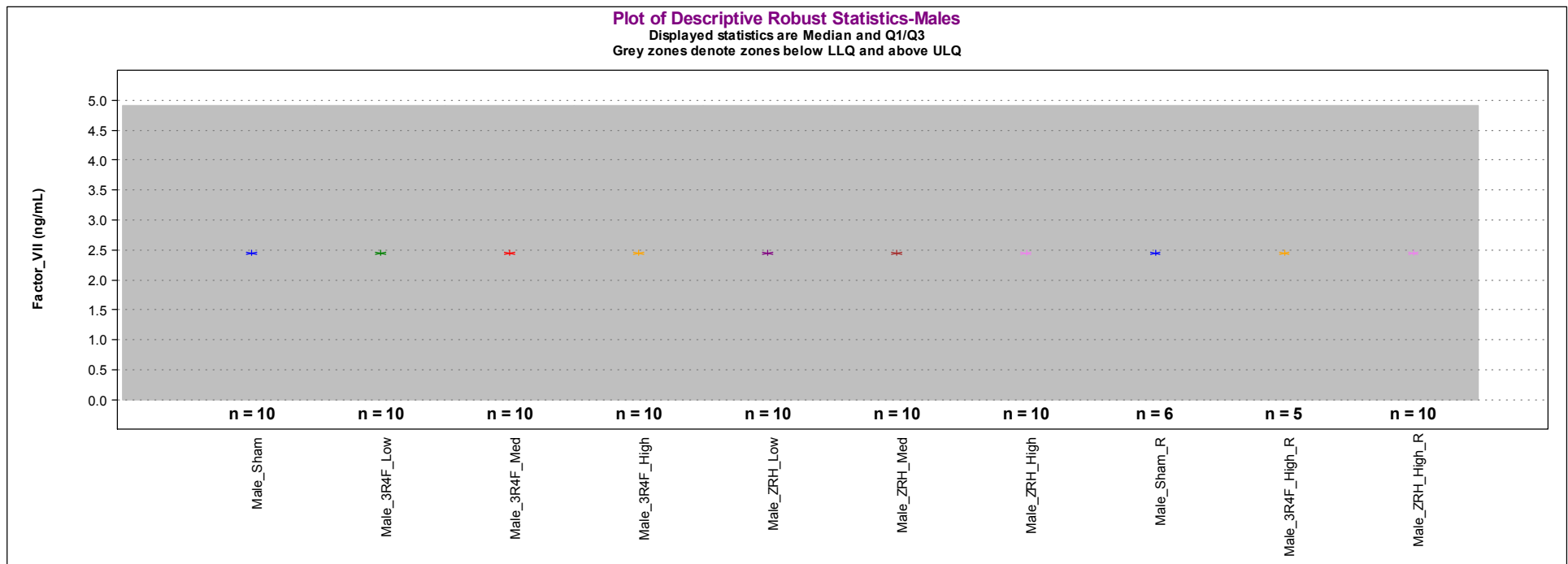
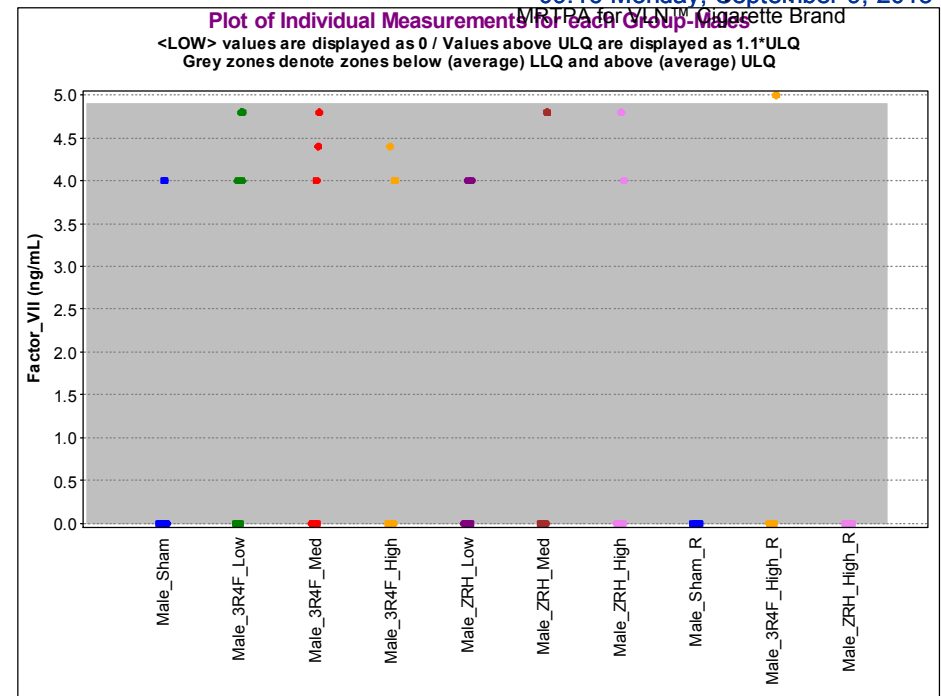
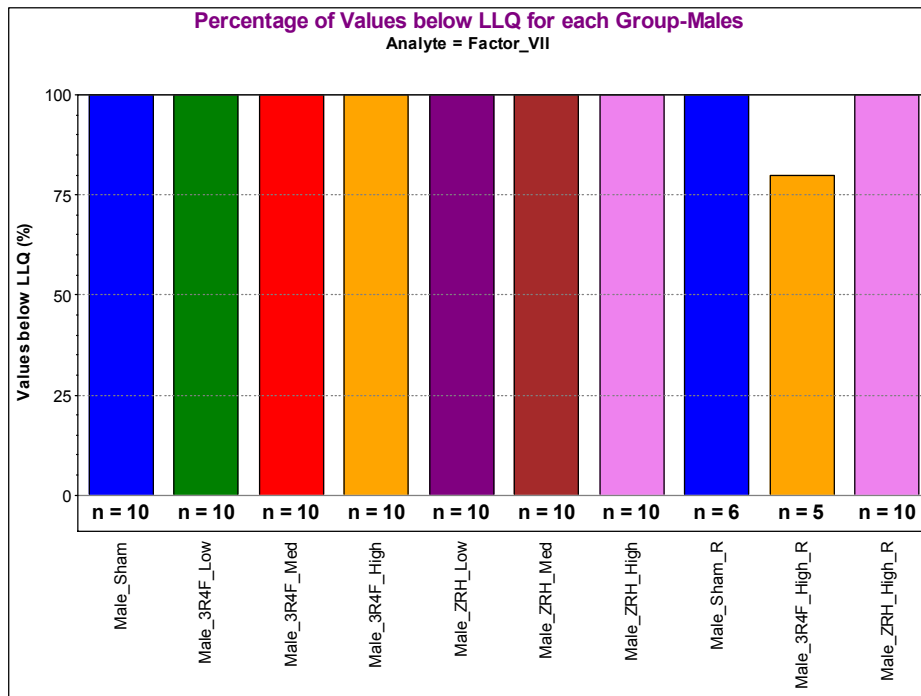
Analyte = Factor_VII

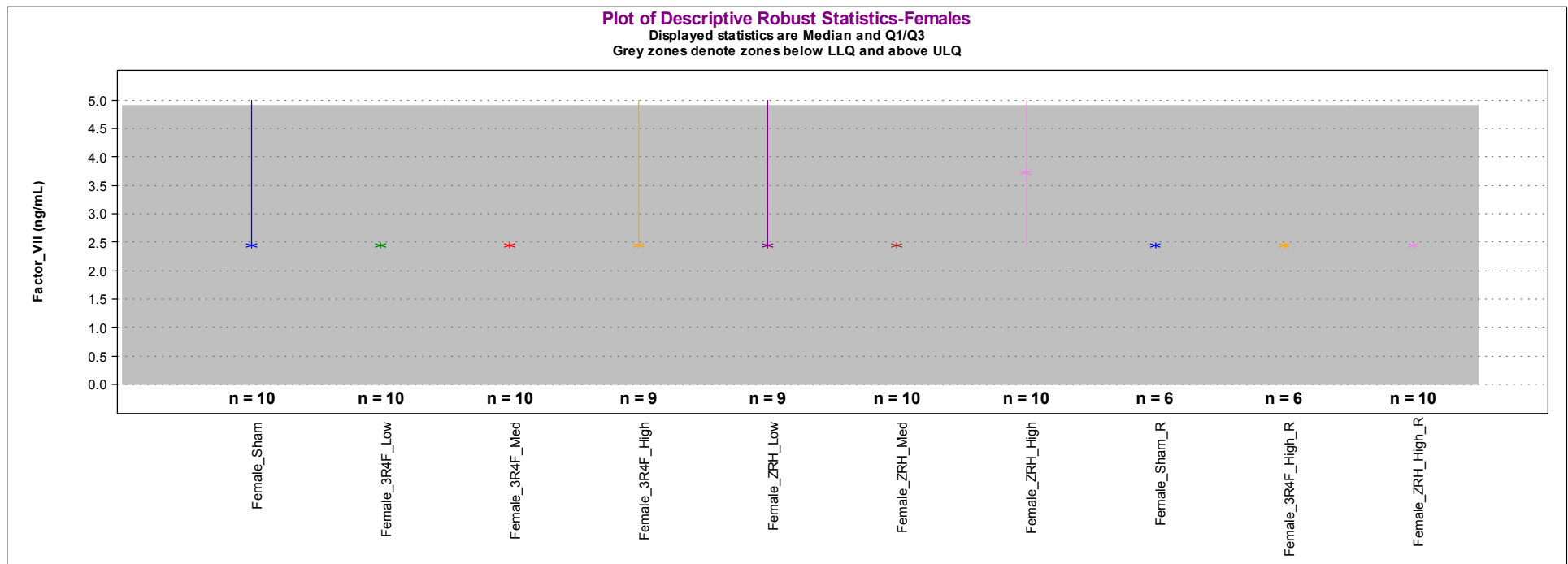
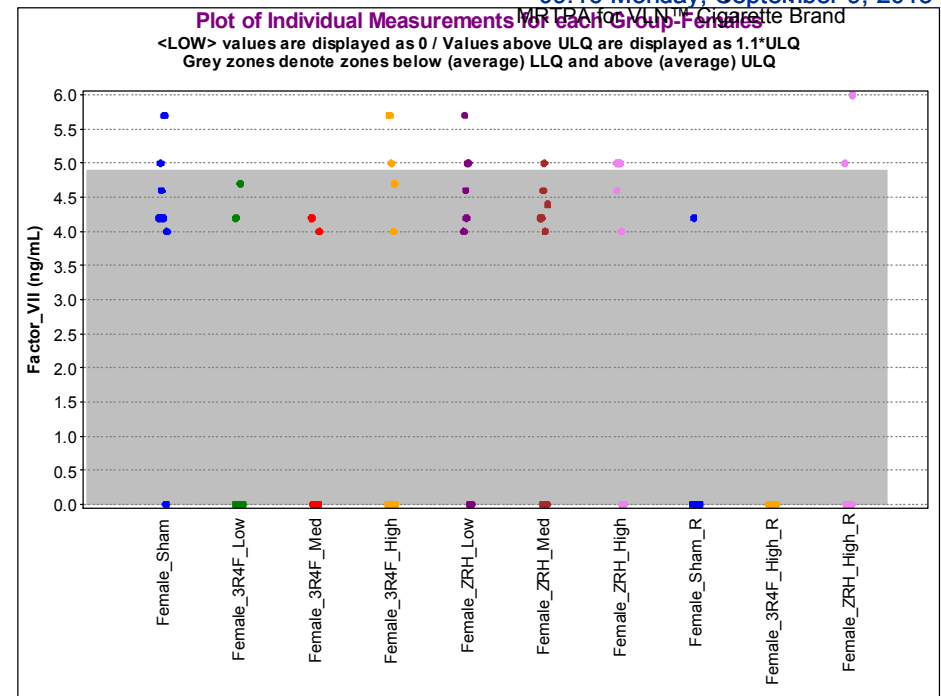
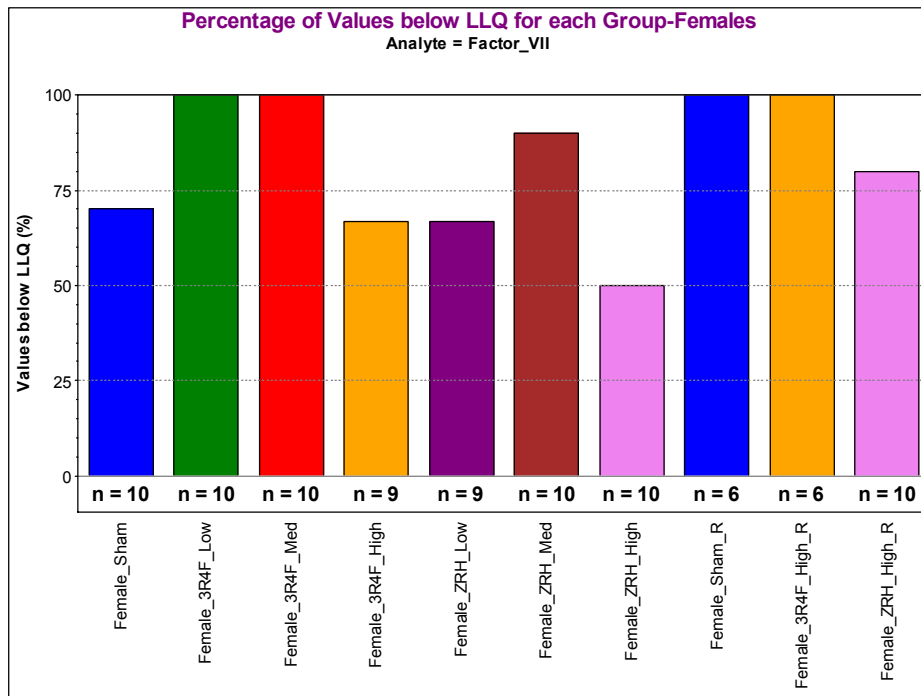
Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	10	0	0	4.9	.
Male	3	3R4F Low	10	10	10	0	0	4.9	.
Male	3	3R4F Medium	10	10	10	0	0	4.9	.
Male	3	3R4F High	10	10	10	0	0	4.9	.
Male	3	ZRH Low	10	10	10	0	0	4.9	.
Male	3	ZRH Medium	10	10	10	0	0	4.9	.
Male	3	ZRH High	10	10	10	0	0	4.9	.
Male	4.5	Sham Recovery	6	6	6	0	0	4.9	.
Male	4.5	3R4F High Recovery	5	5	4	1	0	4.9	.
Male	4.5	ZRH High Recovery	10	10	10	0	0	4.9	.
Female	3	Sham	10	10	7	3	0	4.9	.
Female	3	3R4F Low	10	10	10	0	0	4.9	.
Female	3	3R4F Medium	10	10	10	0	0	4.9	.
Female	3	3R4F High	9	9	6	3	0	4.9	.
Female	3	ZRH Low	9	9	6	3	0	4.9	.
Female	3	ZRH Medium	10	10	9	1	0	4.9	.
Female	3	ZRH High	10	10	5	5	0	4.9	.
Female	4.5	Sham Recovery	6	6	6	0	0	4.9	.
Female	4.5	3R4F High Recovery	6	6	6	0	0	4.9	.
Female	4.5	ZRH High Recovery	10	10	8	2	0	4.9	.

Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = Factor_VII

Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	2.450	2.450	2.450	2.450	2.450	2.450	0.000	0.000	0.0	.	.	4.9	.
Male	3	3R4F Low	2.450	2.450	2.450	2.450	2.450	2.450	0.000	0.000	0.0	.	.	4.9	.
Male	3	3R4F Medium	2.450	2.450	2.450	2.450	2.450	2.450	0.000	0.000	0.0	.	.	4.9	.
Male	3	3R4F High	2.450	2.450	2.450	2.450	2.450	2.450	0.000	0.000	0.0	.	.	4.9	.
Male	3	ZRH Low	2.450	2.450	2.450	2.450	2.450	2.450	0.000	0.000	0.0	.	.	4.9	.
Male	3	ZRH Medium	2.450	2.450	2.450	2.450	2.450	2.450	0.000	0.000	0.0	.	.	4.9	.
Male	3	ZRH High	2.450	2.450	2.450	2.450	2.450	2.450	0.000	0.000	0.0	.	.	4.9	.
Male	4.5	Sham Recovery	2.450	2.450	2.450	2.450	2.450	2.450	0.000	0.000	0.0	.	.	4.9	.
Male	4.5	3R4F High Recovery	2.450	2.450	2.450	2.450	5.000	2.960	1.140	0.510	38.5	2.236	5.000	4.9	.
Male	4.5	ZRH High Recovery	2.450	2.450	2.450	2.450	2.450	2.450	0.000	0.000	0.0	.	.	4.9	.
Female	3	Sham	2.450	2.450	2.450	5.000	5.700	3.355	1.470	0.465	43.8	1.096	-0.947	4.9	.
Female	3	3R4F Low	2.450	2.450	2.450	2.450	2.450	2.450	0.000	0.000	0.0	.	.	4.9	.
Female	3	3R4F Medium	2.450	2.450	2.450	2.450	2.450	2.450	0.000	0.000	0.0	.	.	4.9	.
Female	3	3R4F High	2.450	2.450	2.450	5.000	5.700	3.456	1.522	0.507	44.0	0.921	-1.446	4.9	.
Female	3	ZRH Low	2.450	2.450	2.450	5.000	5.700	3.378	1.406	0.469	41.6	0.940	-1.326	4.9	.
Female	3	ZRH Medium	2.450	2.450	2.450	2.450	5.000	2.705	0.806	0.255	29.8	3.162	10.000	4.9	.
Female	3	ZRH High	2.450	2.450	3.725	5.000	5.000	3.725	1.344	0.425	36.1	-0.000	-2.571	4.9	.
Female	4.5	Sham Recovery	2.450	2.450	2.450	2.450	2.450	2.450	0.000	0.000	0.0	.	.	4.9	.
Female	4.5	3R4F High Recovery	2.450	2.450	2.450	2.450	2.450	2.450	0.000	0.000	0.0	.	.	4.9	.
Female	4.5	ZRH High Recovery	2.450	2.450	2.450	2.450	6.000	3.060	1.307	0.413	42.7	1.920	2.382	4.9	.





Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = Factor_VII

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	1.000000
---- Sham vs. 3R4F Medium for Male	1.000000
---- Sham vs. 3R4F High for Male	1.000000
---- Sham vs. ZRH Low for Male	1.000000
---- Sham vs. ZRH Medium for Male	1.000000
---- Sham vs. ZRH High for Male	1.000000
---- ZRH Low vs. 3R4F Medium for Male	1.000000
---- ZRH Medium vs. 3R4F High for Male	1.000000
---- ZRH High vs. 3R4F High for Male	1.000000
---- Sham Recovery vs. 3R4F High Recovery for Male	0.273322
---- Sham Recovery vs. ZRH High Recovery for Male	1.000000
---- Sham vs. Sham Recovery for Male	1.000000
---- 3R4F High vs. 3R4F High Recovery for Male	0.157299
---- ZRH High vs. ZRH High Recovery for Male	1.000000
---- 3R4F High Recovery vs. ZRH High Recovery for Male	0.157299
---- Sham vs. 3R4F Low for Female	0.067889
---- Sham vs. 3R4F Medium for Female	0.067889
---- Sham vs. 3R4F High for Female	0.881152
---- Sham vs. ZRH Low for Female	1.000000
---- Sham vs. ZRH Medium for Female	0.233546
---- Sham vs. ZRH High for Female	0.664175
---- ZRH Low vs. 3R4F Medium for Female	0.053588
---- ZRH Medium vs. 3R4F High for Female	0.187275
---- ZRH High vs. 3R4F High for Female	0.816690
---- Sham Recovery vs. 3R4F High Recovery for Female	1.000000
---- Sham Recovery vs. ZRH High Recovery for Female	0.257899
---- Sham vs. Sham Recovery for Female	0.151494

Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = Factor_VII

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	0.128735
---- ZRH High vs. ZRH High Recovery for Female	0.258736
---- 3R4F High Recovery vs. ZRH High Recovery for Female	0.257899

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 8

Fibrinogen

Unit = ug/mL

Descriptive Statistics by Exposure Duration and Treatment Type

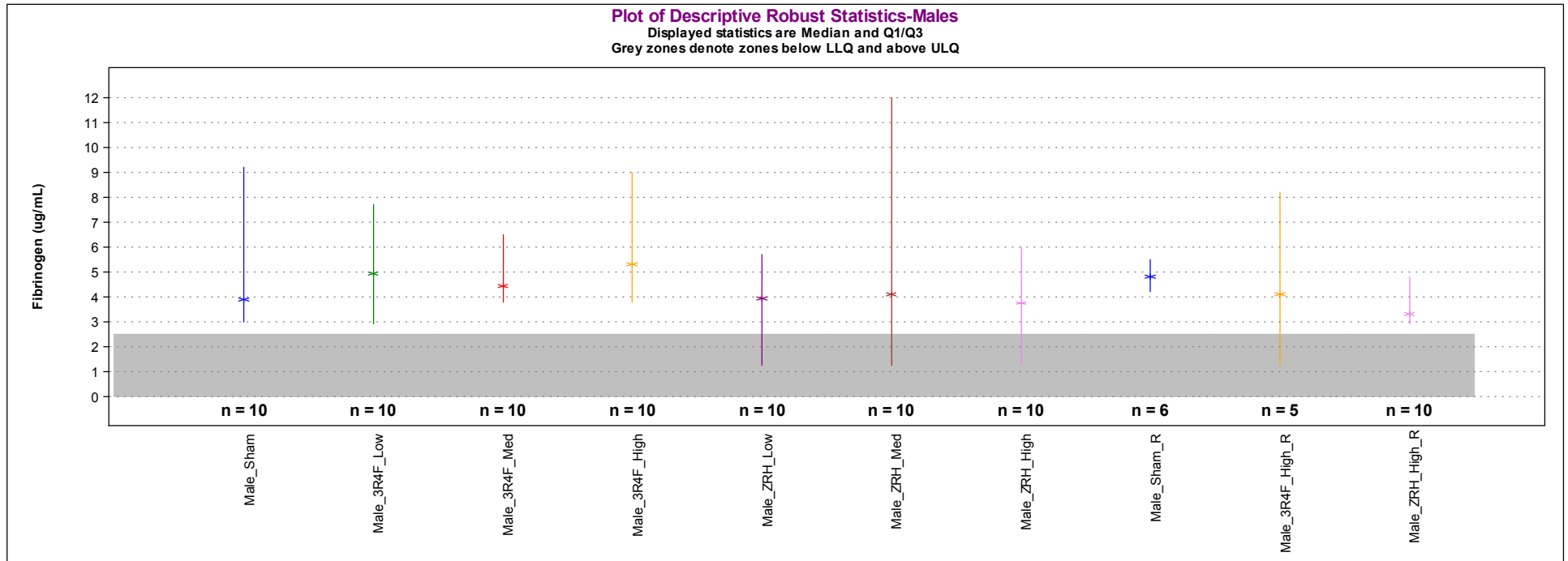
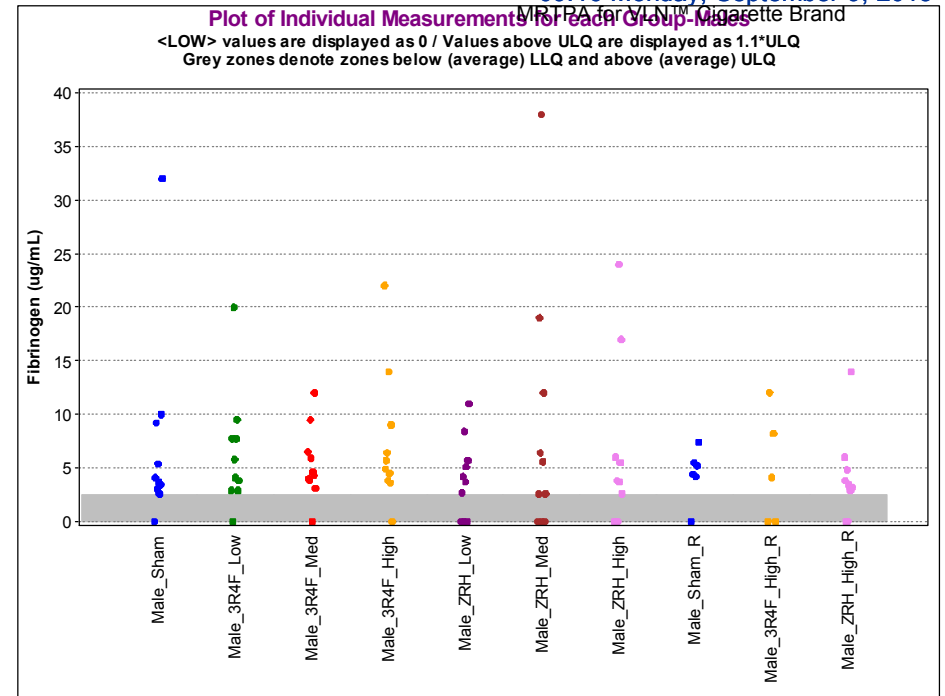
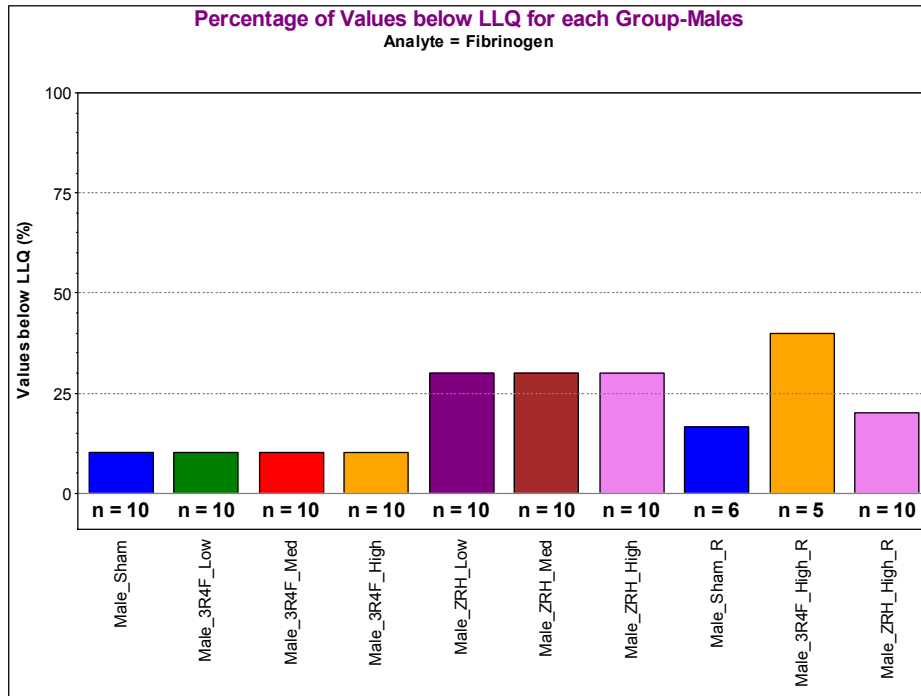
Analyte = Fibrinogen

Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	1	9	0	2.5	.
Male	3	3R4F Low	10	10	1	9	0	2.5	.
Male	3	3R4F Medium	10	10	1	9	0	2.5	.
Male	3	3R4F High	10	10	1	9	0	2.5	.
Male	3	ZRH Low	10	10	3	7	0	2.5	.
Male	3	ZRH Medium	10	10	3	7	0	2.5	.
Male	3	ZRH High	10	10	3	7	0	2.5	.
Male	4.5	Sham Recovery	6	6	1	5	0	2.5	.
Male	4.5	3R4F High Recovery	5	5	2	3	0	2.5	.
Male	4.5	ZRH High Recovery	10	10	2	8	0	2.5	.
Female	3	Sham	10	10	5	5	0	2.5	.
Female	3	3R4F Low	10	10	1	9	0	2.5	.
Female	3	3R4F Medium	10	10	0	10	0	2.5	.
Female	3	3R4F High	9	9	0	9	0	2.5	.
Female	3	ZRH Low	9	9	2	7	0	2.5	.
Female	3	ZRH Medium	10	10	2	8	0	2.5	.
Female	3	ZRH High	10	10	1	9	0	2.5	.
Female	4.5	Sham Recovery	6	6	3	3	0	2.5	.
Female	4.5	3R4F High Recovery	6	6	1	5	0	2.5	.
Female	4.5	ZRH High Recovery	10	10	5	5	0	2.5	.

Descriptive Statistics by Exposure Duration and Treatment Type

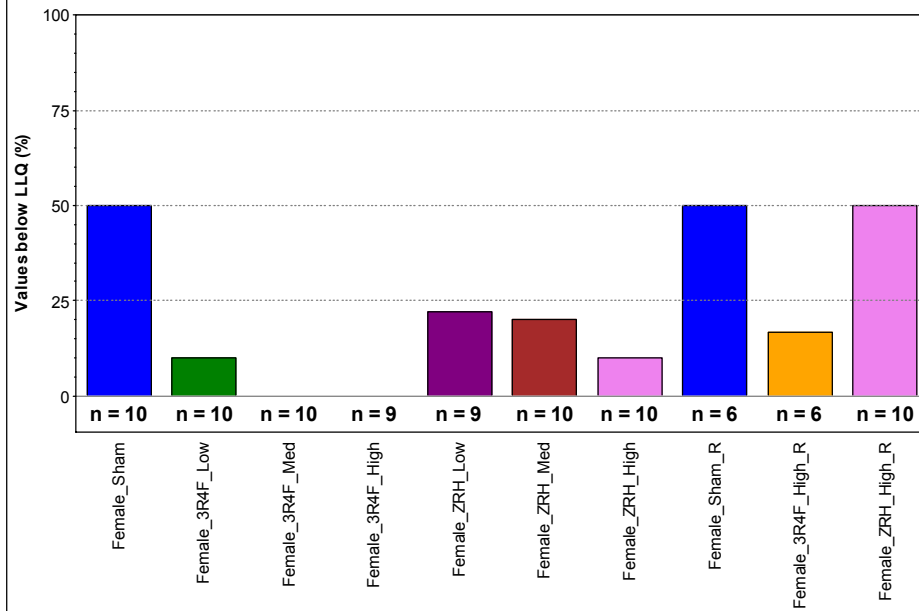
Analyte = Fibrinogen

Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	1.250	3.000	3.900	9.200	32.000	7.465	9.067	2.867	121.5	2.642	7.462	2.5	.
Male	3	3R4F Low	1.250	2.900	4.950	7.700	20.000	6.565	5.386	1.703	82.0	1.927	4.454	2.5	.
Male	3	3R4F Medium	1.250	3.800	4.450	6.500	12.000	5.495	3.173	1.003	57.7	1.042	0.875	2.5	.
Male	3	3R4F High	1.250	3.800	5.300	9.000	22.000	7.515	6.173	1.952	82.1	1.716	2.862	2.5	.
Male	3	ZRH Low	1.250	1.250	3.950	5.700	11.000	4.455	3.247	1.027	72.9	0.971	0.384	2.5	.
Male	3	ZRH Medium	1.250	1.250	4.100	12.000	38.000	8.995	11.692	3.697	130.0	2.038	4.211	2.5	.
Male	3	ZRH High	1.250	1.250	3.750	6.000	24.000	6.635	7.678	2.428	115.7	1.769	2.279	2.5	.
Male	4.5	Sham Recovery	1.250	4.200	4.800	5.500	7.400	4.658	2.020	0.825	43.4	-0.667	1.818	2.5	.
Male	4.5	3R4F High Recovery	1.250	1.250	4.100	8.200	12.000	5.360	4.678	2.092	87.3	0.712	-1.259	2.5	.
Male	4.5	ZRH High Recovery	1.250	2.900	3.300	4.800	14.000	4.380	3.670	1.161	83.8	2.320	6.217	2.5	.
Female	3	Sham	1.250	1.250	1.975	3.600	5.600	2.665	1.688	0.534	63.3	0.729	-0.974	2.5	.
Female	3	3R4F Low	1.250	3.500	4.700	7.000	10.000	5.055	2.568	0.812	50.8	0.615	0.179	2.5	.
Female	3	3R4F Medium	3.100	3.300	3.850	4.900	15.000	5.110	3.569	1.129	69.8	2.870	8.599	2.5	.
Female	3	3R4F High	3.200	4.400	5.100	6.800	37.000	10.356	11.523	3.841	111.3	2.020	3.480	2.5	.
Female	3	ZRH Low	1.250	3.400	4.100	5.800	10.000	4.778	3.080	1.027	64.5	0.723	-0.377	2.5	.
Female	3	ZRH Medium	1.250	2.600	6.950	13.000	13.000	6.850	4.840	1.531	70.7	0.256	-1.624	2.5	.
Female	3	ZRH High	1.250	3.700	5.300	8.000	15.000	6.255	3.936	1.245	62.9	1.138	1.826	2.5	.
Female	4.5	Sham Recovery	1.250	1.250	2.025	4.300	10.000	3.475	3.422	1.397	98.5	1.834	3.378	2.5	.
Female	4.5	3R4F High Recovery	1.250	2.700	4.050	7.300	16.000	5.892	5.376	2.195	91.2	1.701	3.033	2.5	.
Female	4.5	ZRH High Recovery	1.250	1.250	2.025	5.600	16.000	3.965	4.591	1.452	115.8	2.371	6.113	2.5	.

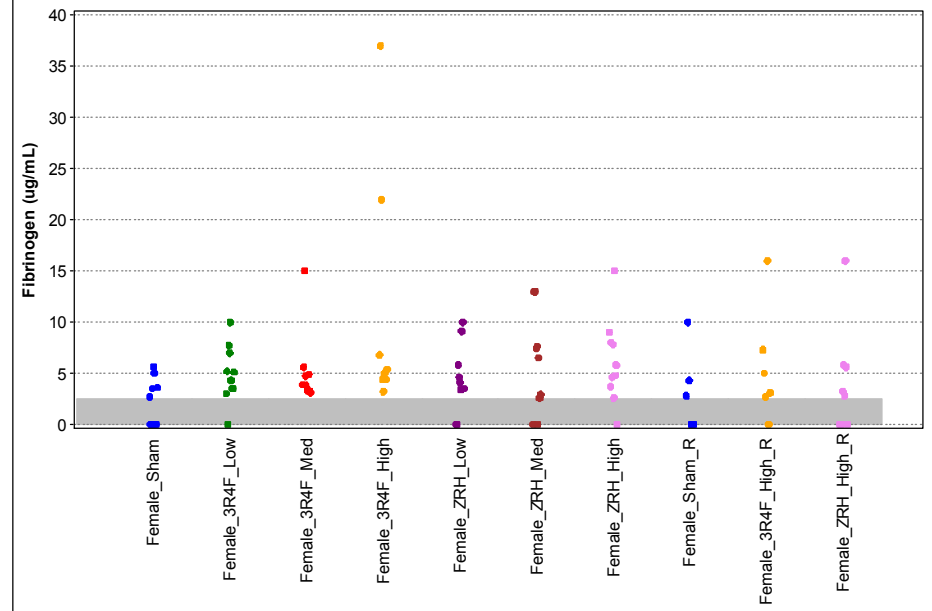


Percentage of Values below LLQ for each Group-Females

Analyte = Fibrinogen

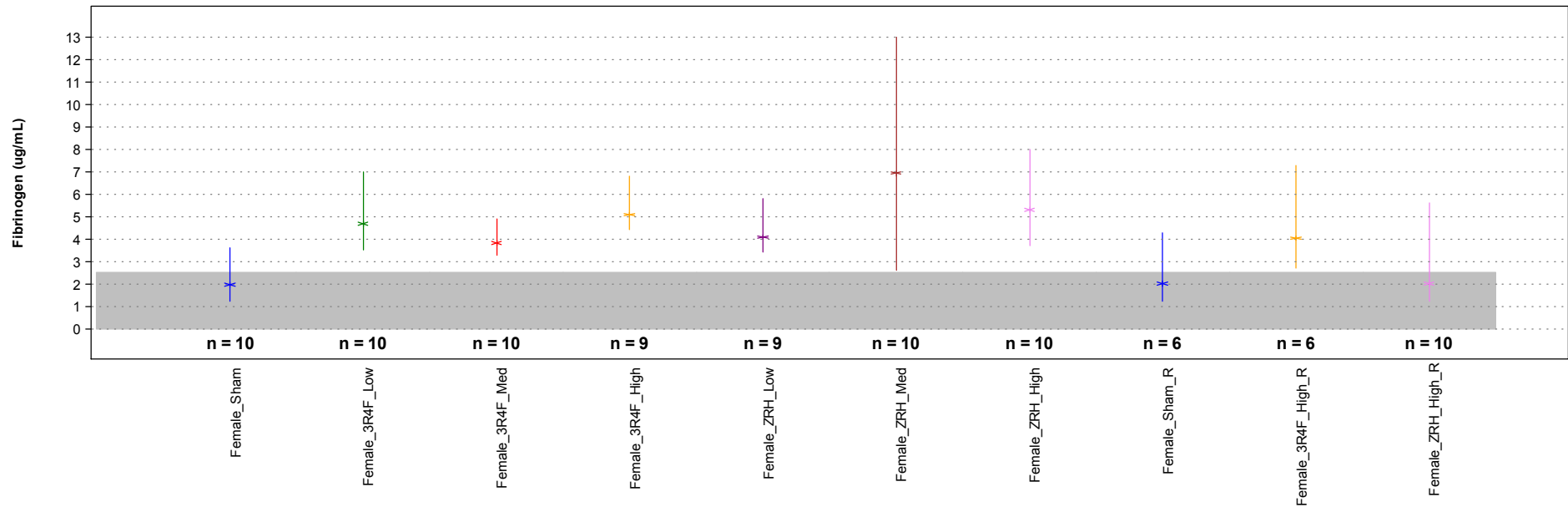
**Plot of Individual Measurements for each Group-Females**

<LOW> values are displayed as 0 / Values above ULQ are displayed as 1.1*ULQ
 Grey zones denote zones below (average) LLQ and above (average) ULQ

**Plot of Descriptive Robust Statistics-Females**

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = Fibrinogen

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	0.820330
---- Sham vs. 3R4F Medium for Male	0.623046
---- Sham vs. 3R4F High for Male	0.427181
---- Sham vs. ZRH Low for Male	0.595175
---- Sham vs. ZRH Medium for Male	0.790256
---- Sham vs. ZRH High for Male	0.676204
---- ZRH Low vs. 3R4F Medium for Male	0.342883
---- ZRH Medium vs. 3R4F High for Male	0.543526
---- ZRH High vs. 3R4F High for Male	0.323742
---- Sham Recovery vs. 3R4F High Recovery for Male	0.853812
---- Sham Recovery vs. ZRH High Recovery for Male	0.276303
---- Sham vs. Sham Recovery for Male	0.786112
---- 3R4F High vs. 3R4F High Recovery for Male	0.460827
---- ZRH High vs. ZRH High Recovery for Male	0.760351
---- 3R4F High Recovery vs. ZRH High Recovery for Male	0.804606
---- Sham vs. 3R4F Low for Female	0.034861
---- Sham vs. 3R4F Medium for Female	0.047408
---- Sham vs. 3R4F High for Female	0.006536
---- Sham vs. ZRH Low for Female	0.121199
---- Sham vs. ZRH Medium for Female	0.044293
---- Sham vs. ZRH High for Female	0.015816
---- ZRH Low vs. 3R4F Medium for Female	0.967393
---- ZRH Medium vs. 3R4F High for Female	0.743319
---- ZRH High vs. 3R4F High for Female	0.743863
---- Sham Recovery vs. 3R4F High Recovery for Female	0.289363
---- Sham Recovery vs. ZRH High Recovery for Female	0.907689
---- Sham vs. Sham Recovery for Female	0.862034

Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = Fibrinogen

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	0.288413
---- ZRH High vs. ZRH High Recovery for Female	0.077959
---- 3R4F High Recovery vs. ZRH High Recovery for Female	0.315812

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 11

Granulocyte Chemotactic Protein-2 Rat (GCP-2 Rat)

Unit = ng/mL

Descriptive Statistics by Exposure Duration and Treatment Type

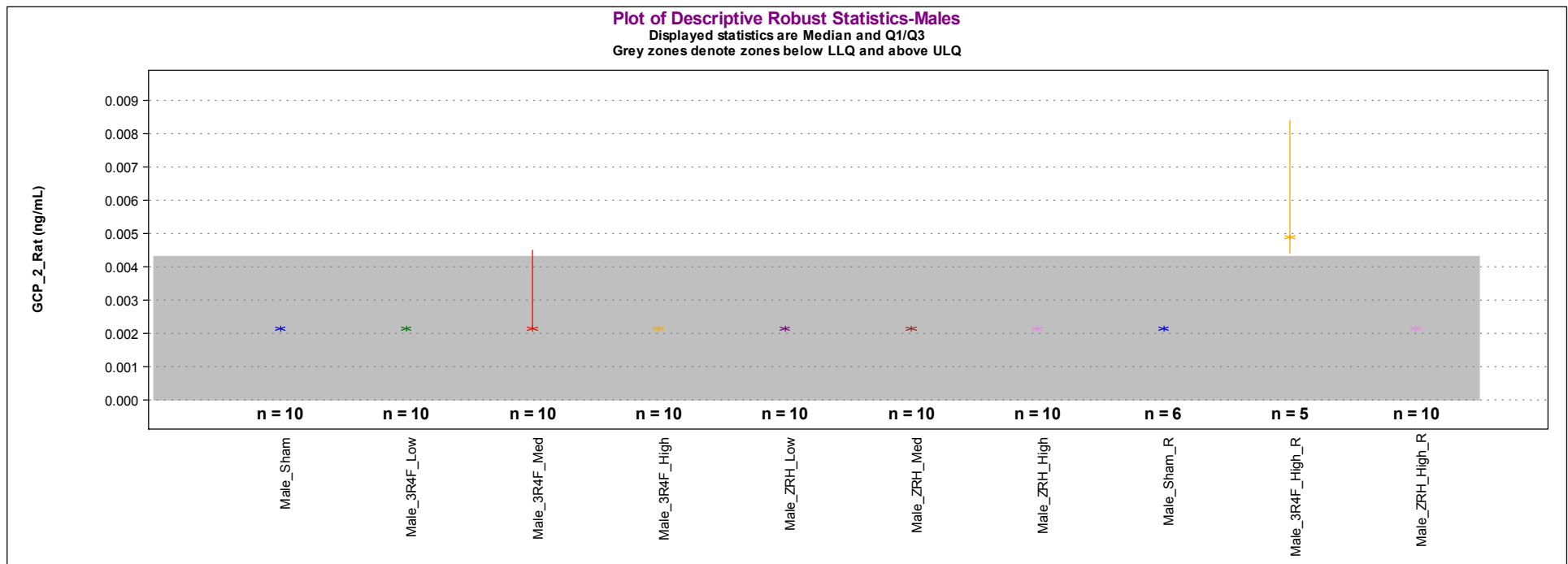
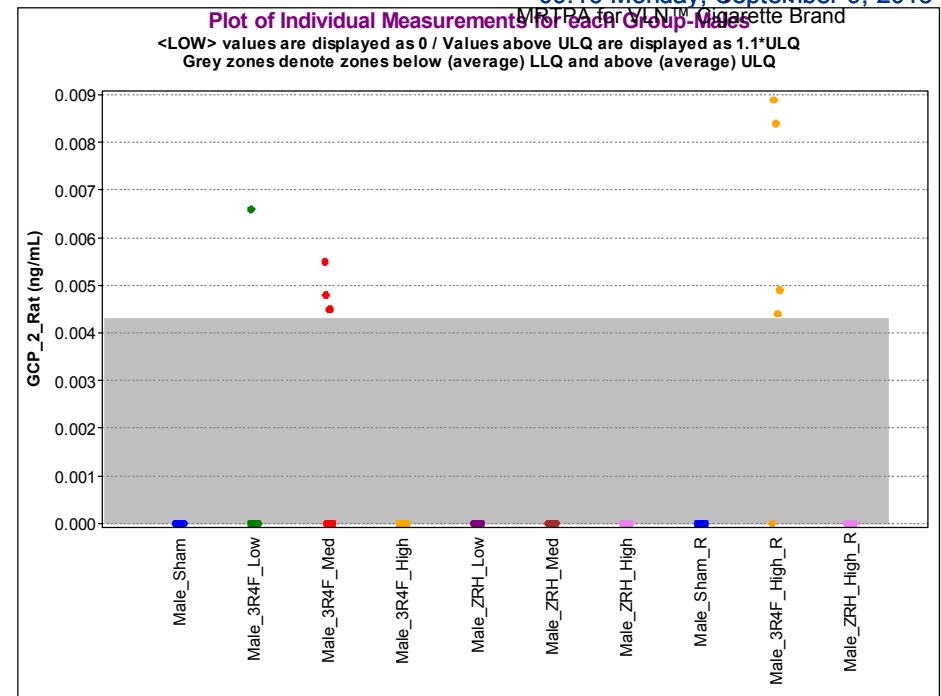
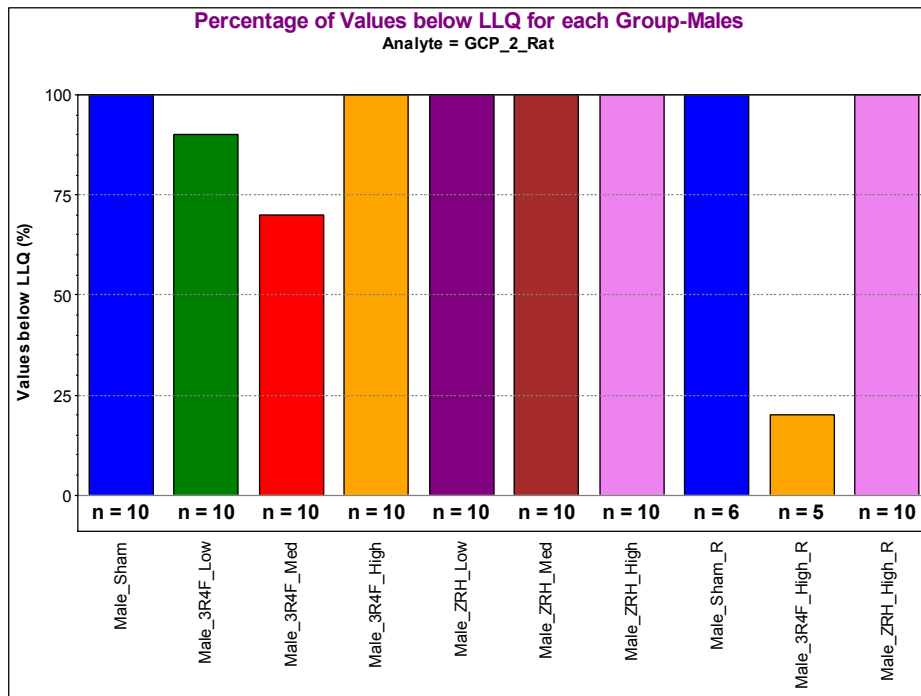
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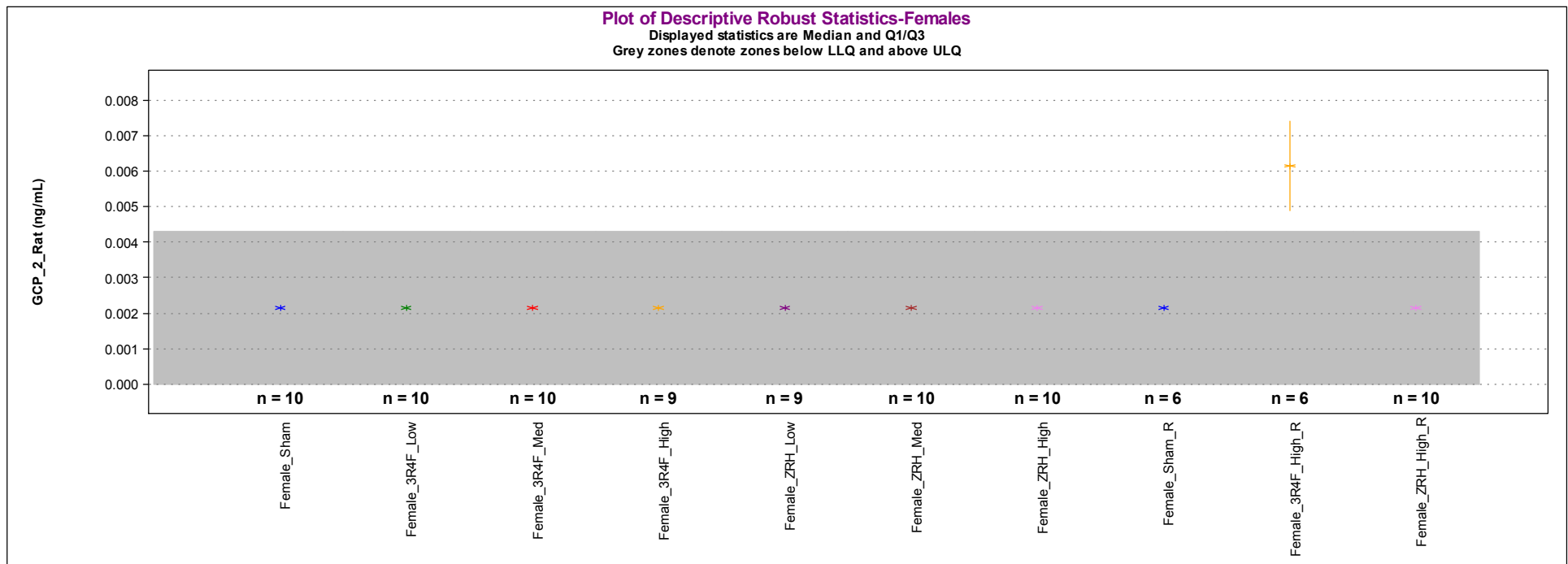
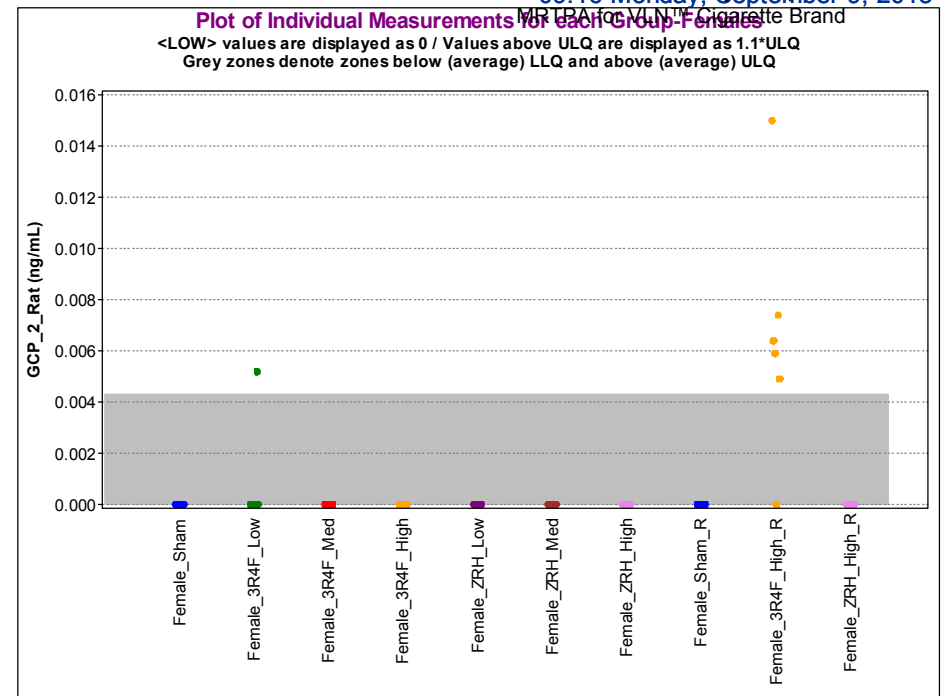
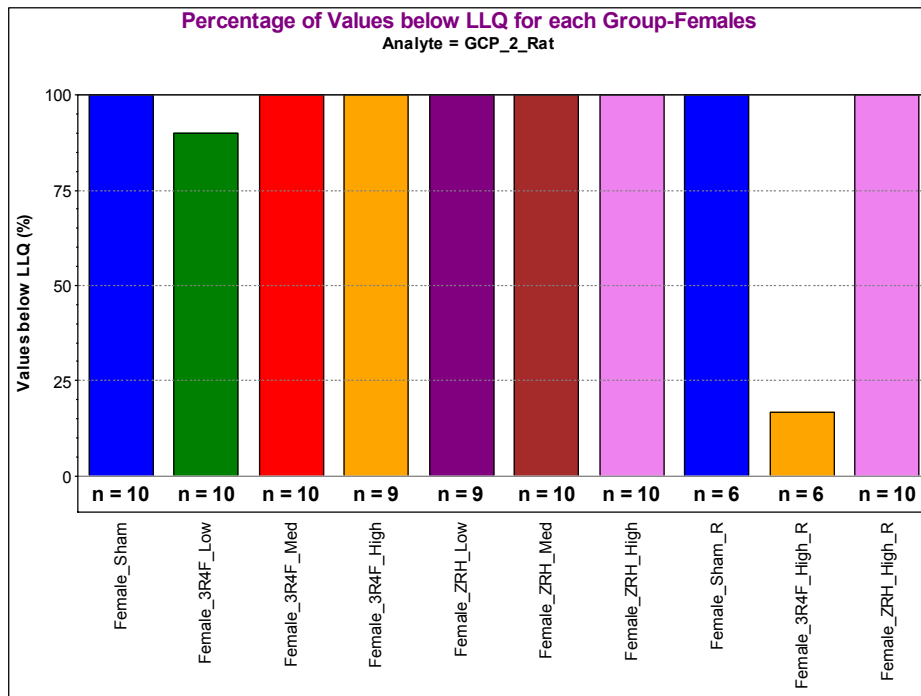
Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	10	0	0	0.004	.
Male	3	3R4F Low	10	10	9	1	0	0.004	.
Male	3	3R4F Medium	10	10	7	3	0	0.004	.
Male	3	3R4F High	10	10	10	0	0	0.004	.
Male	3	ZRH Low	10	10	10	0	0	0.004	.
Male	3	ZRH Medium	10	10	10	0	0	0.004	.
Male	3	ZRH High	10	10	10	0	0	0.004	.
Male	4.5	Sham Recovery	6	6	6	0	0	0.004	.
Male	4.5	3R4F High Recovery	5	5	1	4	0	0.004	.
Male	4.5	ZRH High Recovery	10	10	10	0	0	0.004	.
Female	3	Sham	10	10	10	0	0	0.004	.
Female	3	3R4F Low	10	10	9	1	0	0.004	.
Female	3	3R4F Medium	10	10	10	0	0	0.004	.
Female	3	3R4F High	9	9	9	0	0	0.004	.
Female	3	ZRH Low	9	9	9	0	0	0.004	.
Female	3	ZRH Medium	10	10	10	0	0	0.004	.
Female	3	ZRH High	10	10	10	0	0	0.004	.
Female	4.5	Sham Recovery	6	6	6	0	0	0.004	.
Female	4.5	3R4F High Recovery	6	6	1	5	0	0.004	.
Female	4.5	ZRH High Recovery	10	10	10	0	0	0.004	.

Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = GCP_2_Rat

Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	0.002	0.002	0.002	0.002	0.002	0.002	0.000	0.000	0.0	.	.	0.004	.
Male	3	3R4F Low	0.002	0.002	0.002	0.002	0.007	0.003	0.001	0.000	54.2	3.162	10.000	0.004	.
Male	3	3R4F Medium	0.002	0.002	0.002	0.005	0.006	0.003	0.001	0.000	45.8	1.160	-0.608	0.004	.
Male	3	3R4F High	0.002	0.002	0.002	0.002	0.002	0.002	0.000	0.000	0.0	.	.	0.004	.
Male	3	ZRH Low	0.002	0.002	0.002	0.002	0.002	0.002	0.000	0.000	0.0	.	.	0.004	.
Male	3	ZRH Medium	0.002	0.002	0.002	0.002	0.002	0.002	0.000	0.000	0.0	.	.	0.004	.
Male	3	ZRH High	0.002	0.002	0.002	0.002	0.002	0.002	0.000	0.000	0.0	.	.	0.004	.
Male	4.5	Sham Recovery	0.002	0.002	0.002	0.002	0.002	0.002	0.000	0.000	0.0	.	.	0.004	.
Male	4.5	3R4F High Recovery	0.002	0.004	0.005	0.008	0.009	0.006	0.003	0.001	49.5	0.002	-1.930	0.004	.
Male	4.5	ZRH High Recovery	0.002	0.002	0.002	0.002	0.002	0.002	0.000	0.000	0.0	.	.	0.004	.
Female	3	Sham	0.002	0.002	0.002	0.002	0.002	0.002	0.000	0.000	0.0	.	.	0.004	.
Female	3	3R4F Low	0.002	0.002	0.002	0.002	0.005	0.002	0.001	0.000	39.3	3.162	10.000	0.004	.
Female	3	3R4F Medium	0.002	0.002	0.002	0.002	0.002	0.002	0.000	0.000	0.0	.	.	0.004	.
Female	3	3R4F High	0.002	0.002	0.002	0.002	0.002	0.002	0.000	0.000	0.0	.	.	0.004	.
Female	3	ZRH Low	0.002	0.002	0.002	0.002	0.002	0.002	0.000	0.000	0.0	.	.	0.004	.
Female	3	ZRH Medium	0.002	0.002	0.002	0.002	0.002	0.002	0.000	0.000	0.0	.	.	0.004	.
Female	3	ZRH High	0.002	0.002	0.002	0.002	0.002	0.002	0.000	0.000	0.0	.	.	0.004	.
Female	4.5	Sham Recovery	0.002	0.002	0.002	0.002	0.002	0.002	0.000	0.000	0.0	.	.	0.004	.
Female	4.5	3R4F High Recovery	0.002	0.005	0.006	0.007	0.015	0.007	0.004	0.002	62.2	1.476	3.199	0.004	.
Female	4.5	ZRH High Recovery	0.002	0.002	0.002	0.002	0.002	0.002	0.000	0.000	0.0	.	.	0.004	.





Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = GCP_2_Rat

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	0.317311
---- Sham vs. 3R4F Medium for Male	0.068157
---- Sham vs. 3R4F High for Male	1.000000
---- Sham vs. ZRH Low for Male	1.000000
---- Sham vs. ZRH Medium for Male	1.000000
---- Sham vs. ZRH High for Male	1.000000
---- ZRH Low vs. 3R4F Medium for Male	0.068157
---- ZRH Medium vs. 3R4F High for Male	1.000000
---- ZRH High vs. 3R4F High for Male	1.000000
---- Sham Recovery vs. 3R4F High Recovery for Male	0.011164
---- Sham Recovery vs. ZRH High Recovery for Male	1.000000
---- Sham vs. Sham Recovery for Male	1.000000
---- 3R4F High vs. 3R4F High Recovery for Male	0.001669
---- ZRH High vs. ZRH High Recovery for Male	1.000000
---- 3R4F High Recovery vs. ZRH High Recovery for Male	0.001669
---- Sham vs. 3R4F Low for Female	0.317311
---- Sham vs. 3R4F Medium for Female	1.000000
---- Sham vs. 3R4F High for Female	1.000000
---- Sham vs. ZRH Low for Female	1.000000
---- Sham vs. ZRH Medium for Female	1.000000
---- Sham vs. ZRH High for Female	1.000000
---- ZRH Low vs. 3R4F Medium for Female	1.000000
---- ZRH Medium vs. 3R4F High for Female	1.000000
---- ZRH High vs. 3R4F High for Female	1.000000
---- Sham Recovery vs. 3R4F High Recovery for Female	0.007397
---- Sham Recovery vs. ZRH High Recovery for Female	1.000000
---- Sham vs. Sham Recovery for Female	1.000000

Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = GCP_2_Rat

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	0.001593
---- ZRH High vs. ZRH High Recovery for Female	1.000000
---- 3R4F High Recovery vs. ZRH High Recovery for Female	0.000978

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 13

Growth Hormone (GH)

Unit = ng/mL

Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = GH

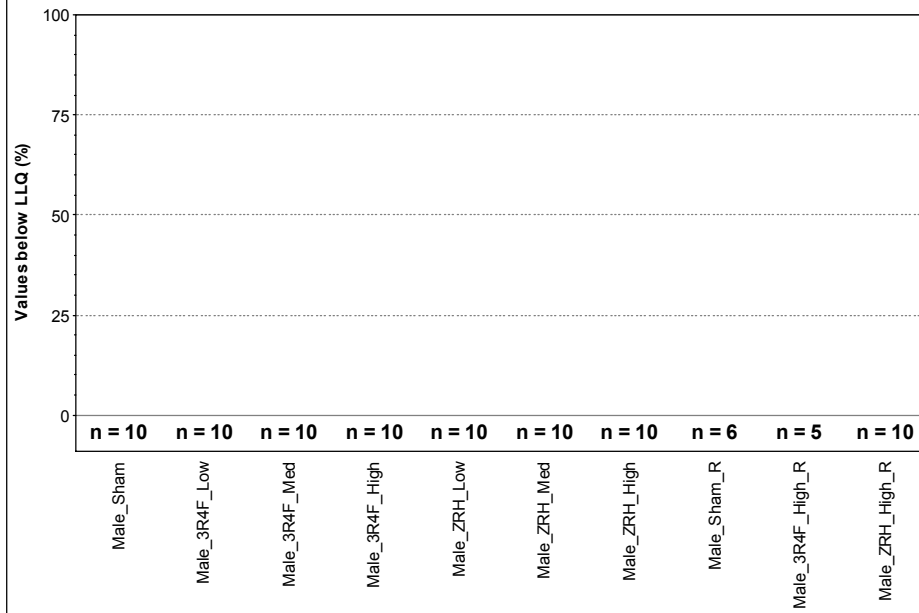
Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	0	10	0	0.38	.
Male	3	3R4F Low	10	10	0	10	0	0.38	.
Male	3	3R4F Medium	10	10	0	10	0	0.38	.
Male	3	3R4F High	10	10	0	10	0	0.38	.
Male	3	ZRH Low	10	10	0	10	0	0.38	.
Male	3	ZRH Medium	10	10	0	10	0	0.38	.
Male	3	ZRH High	10	10	0	10	0	0.38	.
Male	4.5	Sham Recovery	6	6	0	6	0	0.38	.
Male	4.5	3R4F High Recovery	5	5	0	5	0	0.38	.
Male	4.5	ZRH High Recovery	10	10	0	10	0	0.38	.
Female	3	Sham	10	10	0	10	0	0.38	.
Female	3	3R4F Low	10	10	0	10	0	0.38	.
Female	3	3R4F Medium	10	10	0	10	0	0.38	.
Female	3	3R4F High	9	9	0	9	0	0.38	.
Female	3	ZRH Low	9	9	0	9	0	0.38	.
Female	3	ZRH Medium	10	10	0	10	0	0.38	.
Female	3	ZRH High	10	10	0	10	0	0.38	.
Female	4.5	Sham Recovery	6	6	0	6	0	0.38	.
Female	4.5	3R4F High Recovery	6	6	0	6	0	0.38	.
Female	4.5	ZRH High Recovery	10	10	0	10	0	0.38	.

Descriptive Statistics by Exposure Duration and Treatment Type**Analyte = GH**

Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	1.000	1.100	1.250	1.700	2.000	1.370	0.340	0.108	24.8	0.935	-0.511	0.38	.
Male	3	3R4F Low	1.200	1.200	1.400	1.700	2.500	1.520	0.408	0.129	26.8	1.689	3.306	0.38	.
Male	3	3R4F Medium	1.100	1.100	1.350	1.600	1.900	1.400	0.294	0.093	21.0	0.588	-0.974	0.38	.
Male	3	3R4F High	1.000	1.200	1.300	1.700	2.000	1.410	0.345	0.109	24.4	0.465	-1.038	0.38	.
Male	3	ZRH Low	0.900	1.200	1.200	1.400	5.000	1.590	1.207	0.382	75.9	3.076	9.610	0.38	.
Male	3	ZRH Medium	0.930	1.300	1.400	1.500	2.400	1.463	0.379	0.120	25.9	1.663	4.753	0.38	.
Male	3	ZRH High	1.100	1.200	1.250	1.400	9.000	2.030	2.452	0.775	120.8	3.147	9.928	0.38	.
Male	4.5	Sham Recovery	0.950	1.000	1.100	1.200	1.700	1.175	0.272	0.111	23.1	1.904	3.986	0.38	.
Male	4.5	3R4F High Recovery	1.100	1.200	1.200	1.400	1.400	1.260	0.134	0.060	10.6	0.166	-2.407	0.38	.
Male	4.5	ZRH High Recovery	0.870	1.100	1.300	1.400	1.500	1.227	0.200	0.063	16.3	-0.507	-0.709	0.38	.
Female	3	Sham	0.840	0.940	0.995	1.000	2.200	1.091	0.397	0.125	36.4	2.953	9.057	0.38	.
Female	3	3R4F Low	0.800	0.900	0.960	1.000	1.100	0.947	0.084	0.027	8.8	-0.016	0.510	0.38	.
Female	3	3R4F Medium	0.840	0.910	0.980	1.000	1.100	0.960	0.077	0.024	8.1	0.036	-0.010	0.38	.
Female	3	3R4F High	0.860	0.940	0.960	0.960	1.500	1.004	0.189	0.063	18.8	2.787	8.138	0.38	.
Female	3	ZRH Low	0.830	0.870	0.940	0.990	1.600	0.998	0.234	0.078	23.4	2.625	7.377	0.38	.
Female	3	ZRH Medium	0.730	0.840	0.895	0.960	1.200	0.906	0.131	0.041	14.4	1.108	2.174	0.38	.
Female	3	ZRH High	0.910	0.910	0.955	1.000	1.200	0.987	0.096	0.030	9.7	1.475	1.714	0.38	.
Female	4.5	Sham Recovery	0.930	1.100	1.200	1.200	2.000	1.272	0.372	0.152	29.3	1.983	4.564	0.38	.
Female	4.5	3R4F High Recovery	0.870	0.910	0.975	1.200	1.300	1.038	0.172	0.070	16.6	0.849	-1.098	0.38	.
Female	4.5	ZRH High Recovery	0.950	1.100	1.200	1.300	1.500	1.202	0.178	0.056	14.8	0.135	-0.702	0.38	.

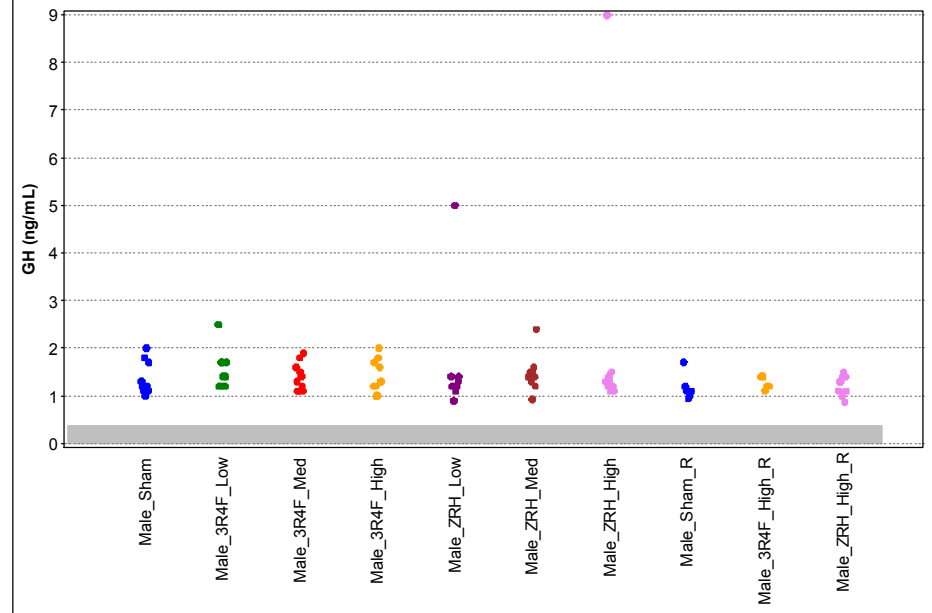
Percentage of Values below LLQ for each Group-Males

Analyte = GH



Plot of Individual Measurements for each Group-Males

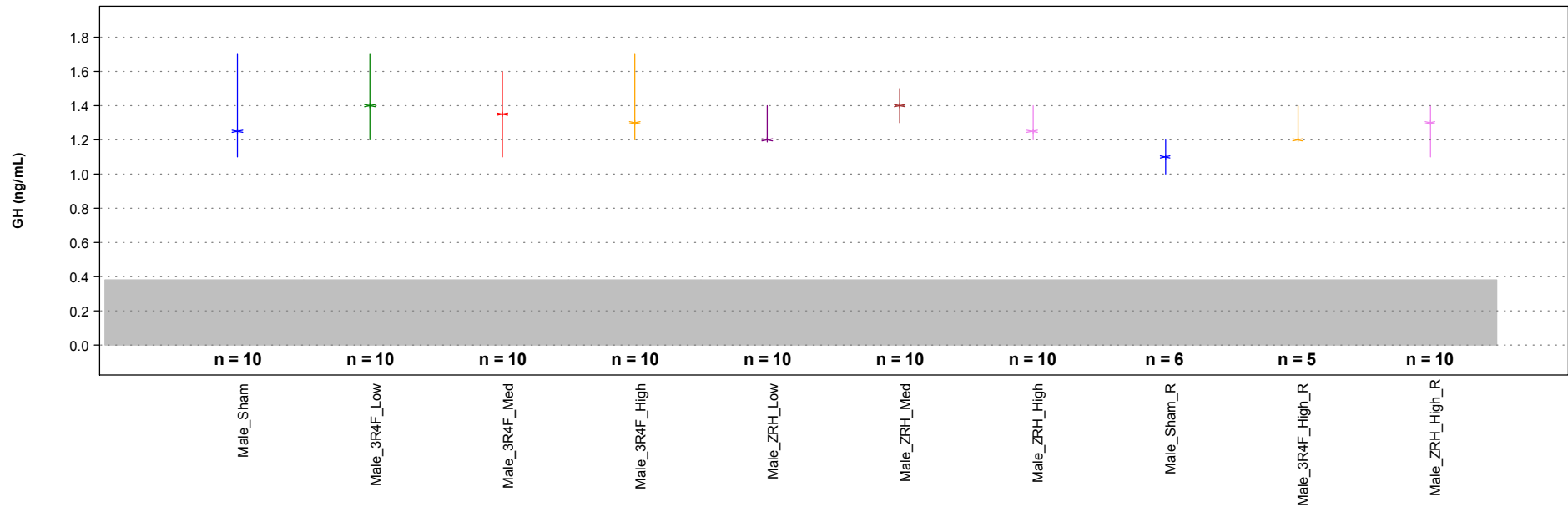
<LOW> values are displayed as 0 / Values above ULQ are displayed as 1.1*ULQ
 Grey zones denote zones below (average) LLQ and above (average) ULQ



Plot of Descriptive Robust Statistics-Males

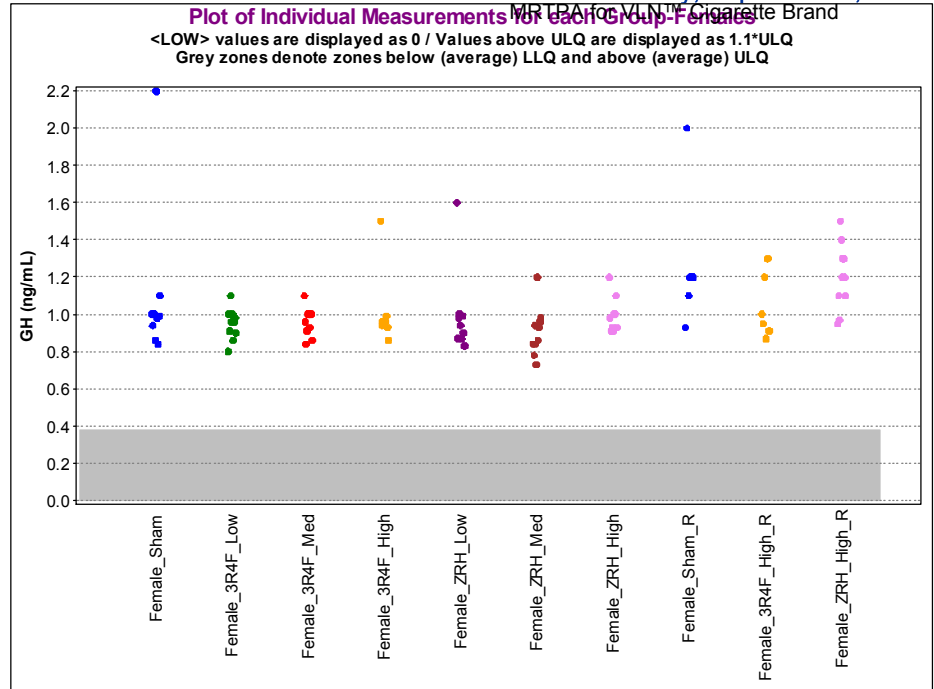
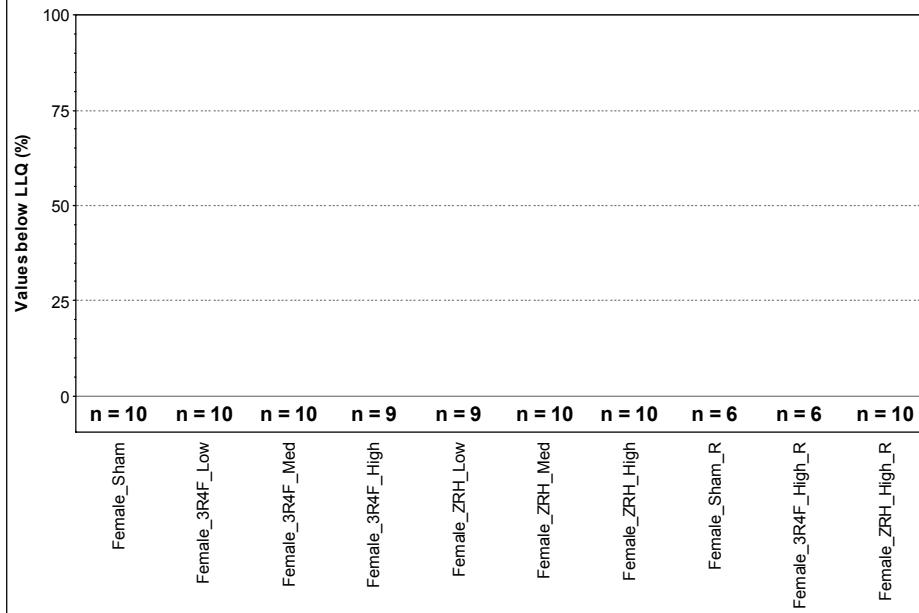
Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



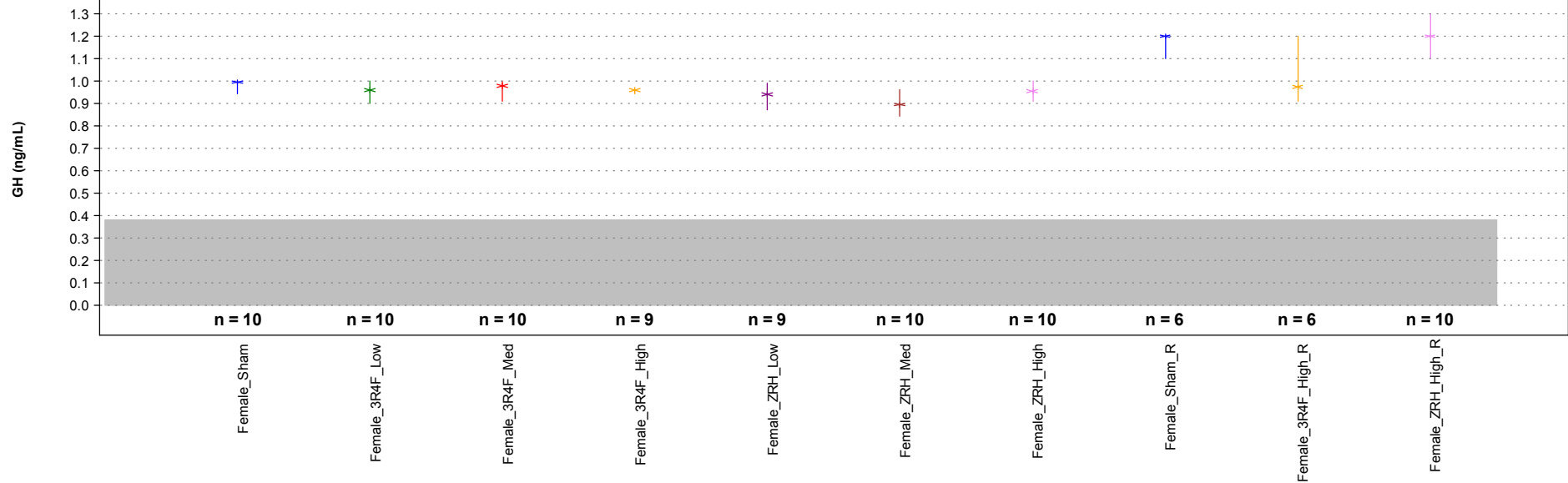
Percentage of Values below LLQ for each Group-Females

Analyte = GH

**Plot of Descriptive Robust Statistics-Females**

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = GH

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	0.335830
---- Sham vs. 3R4F Medium for Male	0.730893
---- Sham vs. 3R4F High for Male	0.789157
---- Sham vs. ZRH Low for Male	0.877807
---- Sham vs. ZRH Medium for Male	0.361807
---- Sham vs. ZRH High for Male	0.877995
---- ZRH Low vs. 3R4F Medium for Male	0.490528
---- ZRH Medium vs. 3R4F High for Male	0.732274
---- ZRH High vs. 3R4F High for Male	0.702020
---- Sham Recovery vs. 3R4F High Recovery for Male	0.191896
---- Sham Recovery vs. ZRH High Recovery for Male	0.410376
---- Sham vs. Sham Recovery for Male	0.124083
---- 3R4F High vs. 3R4F High Recovery for Male	0.535517
---- ZRH High vs. ZRH High Recovery for Male	0.617976
---- 3R4F High Recovery vs. ZRH High Recovery for Male	0.803196
---- Sham vs. 3R4F Low for Female	0.303086
---- Sham vs. 3R4F Medium for Female	0.615225
---- Sham vs. 3R4F High for Female	0.250070
---- Sham vs. ZRH Low for Female	0.285510
---- Sham vs. ZRH Medium for Female	0.036847
---- Sham vs. ZRH High for Female	0.646785
---- ZRH Low vs. 3R4F Medium for Female	0.509704
---- ZRH Medium vs. 3R4F High for Female	0.108676
---- ZRH High vs. 3R4F High for Female	1.000000
---- Sham Recovery vs. 3R4F High Recovery for Female	0.221509
---- Sham Recovery vs. ZRH High Recovery for Female	0.825068
---- Sham vs. Sham Recovery for Female	0.071602

Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = GH

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	0.722483
---- ZRH High vs. ZRH High Recovery for Female	0.006204
---- 3R4F High Recovery vs. ZRH High Recovery for Female	0.090320

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 12

Granulocyte-Macrophage Colony-Stimulating Factor (GM-CSF)

Unit = pg/mL

Descriptive Statistics by Exposure Duration and Treatment Type

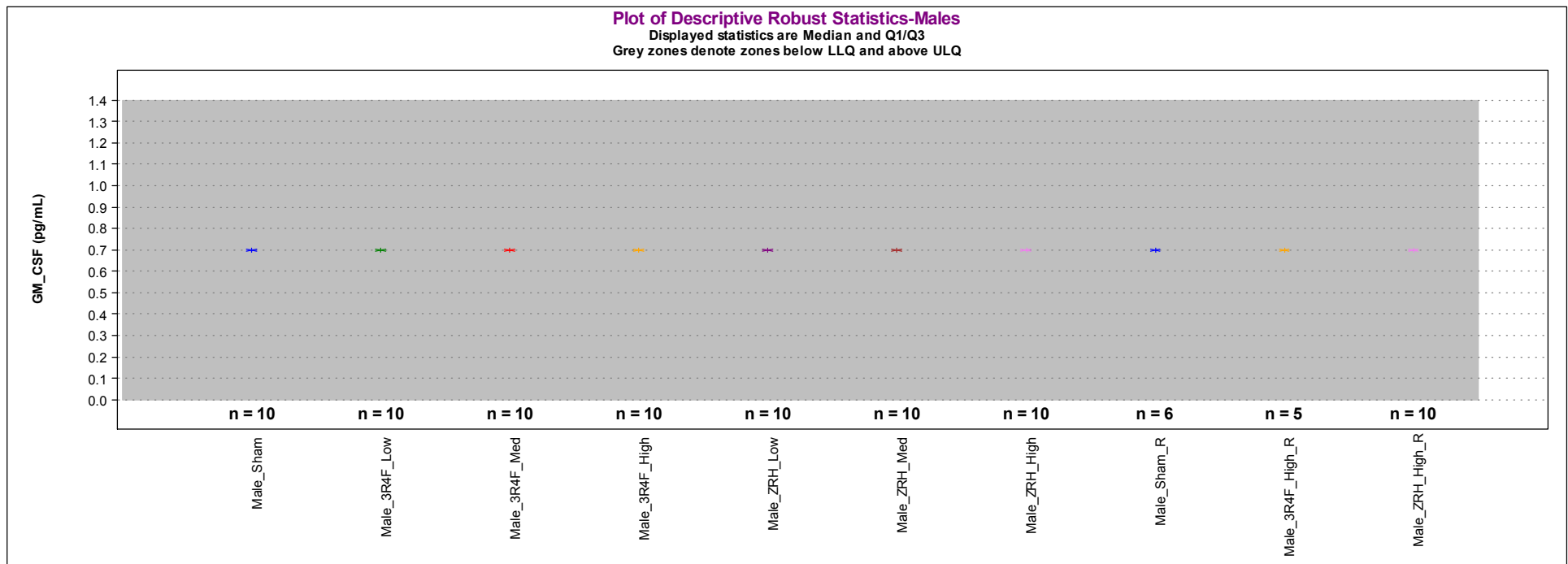
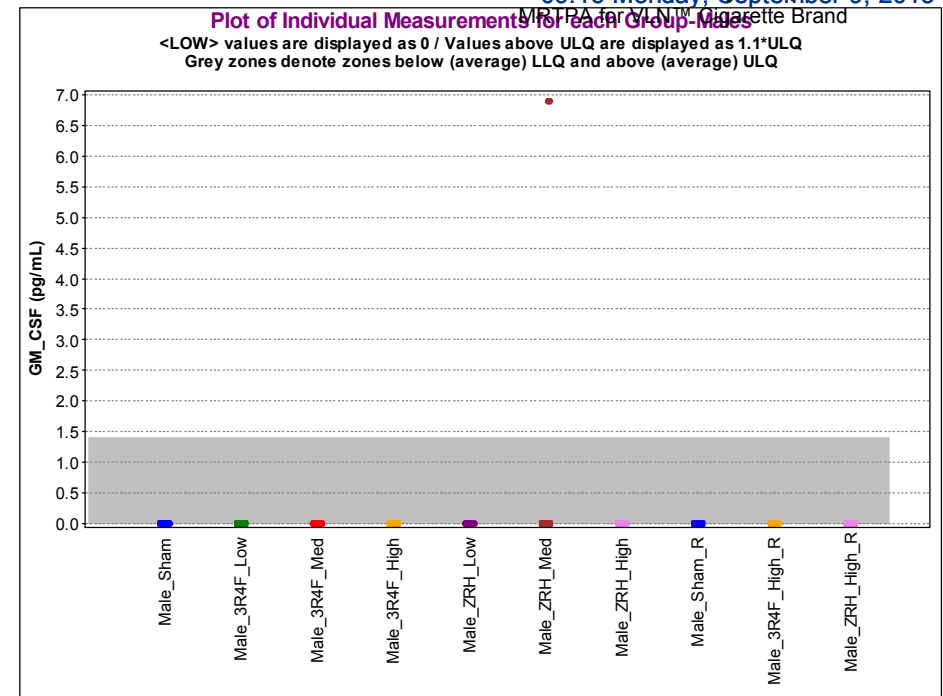
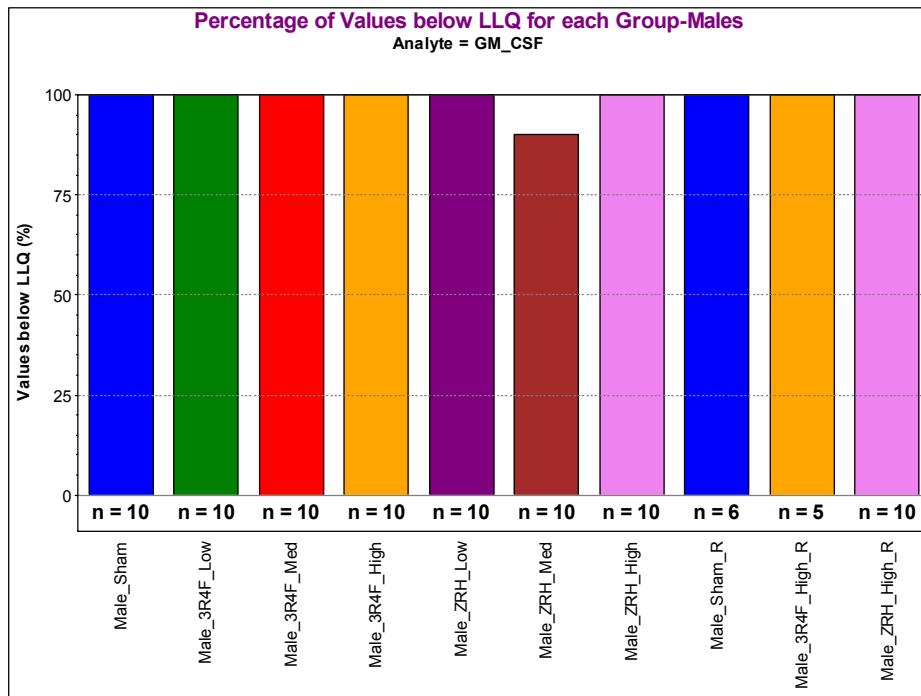
Analyte = GM_CSF

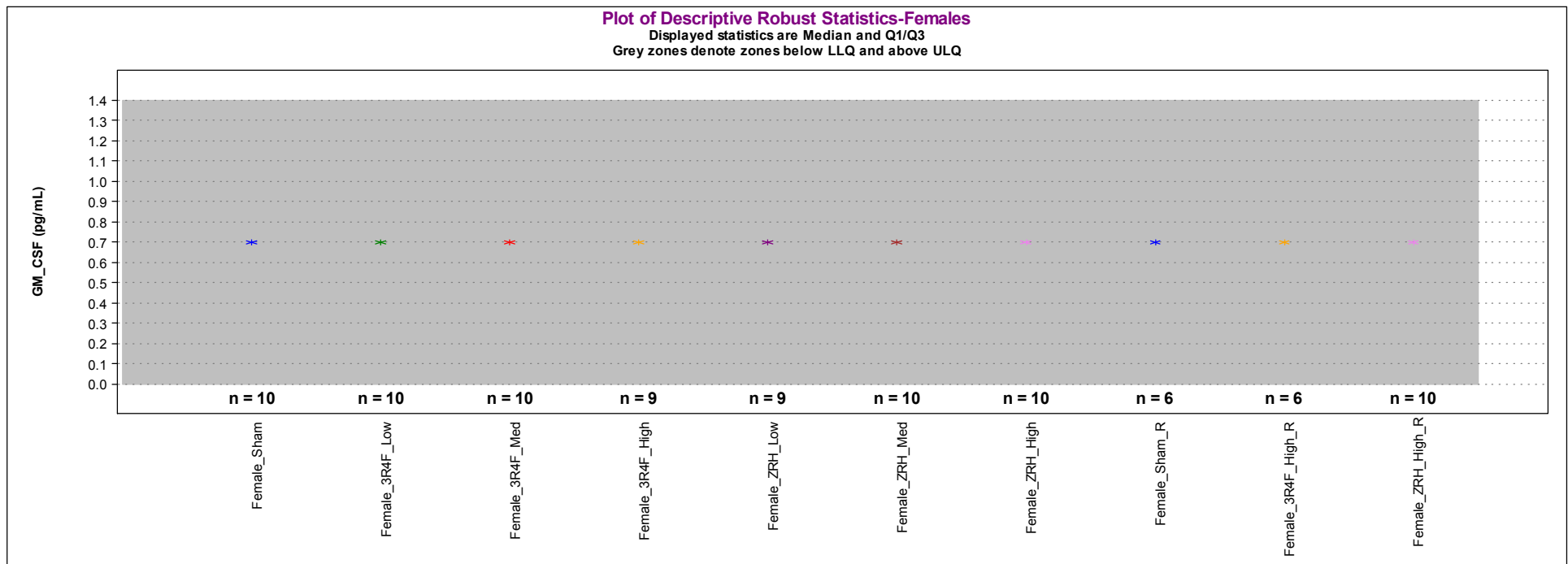
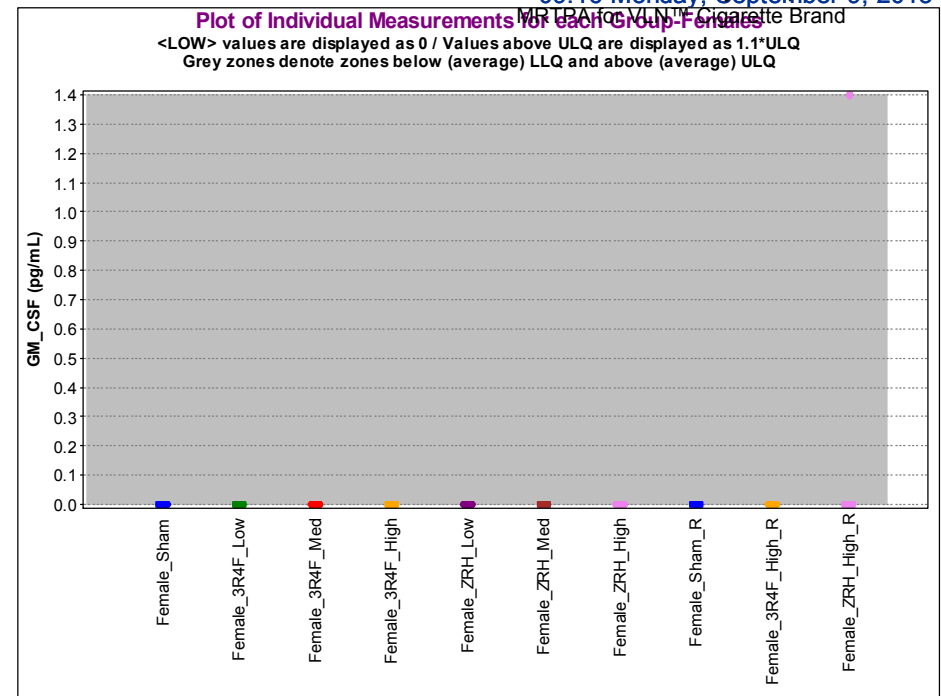
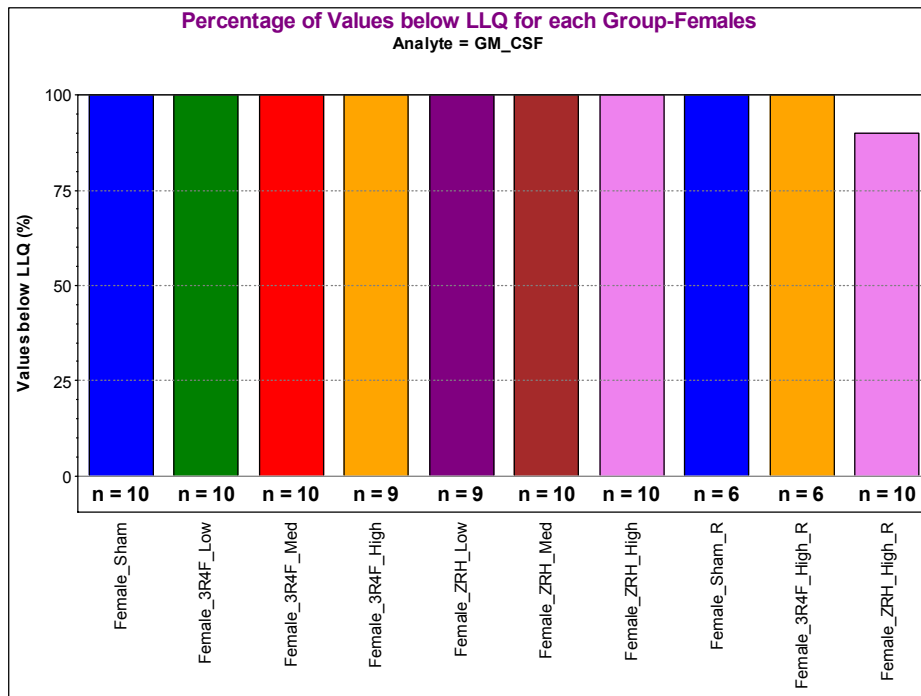
Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	10	0	0	1.4	.
Male	3	3R4F Low	10	10	10	0	0	1.4	.
Male	3	3R4F Medium	10	10	10	0	0	1.4	.
Male	3	3R4F High	10	10	10	0	0	1.4	.
Male	3	ZRH Low	10	10	10	0	0	1.4	.
Male	3	ZRH Medium	10	10	9	1	0	1.4	.
Male	3	ZRH High	10	10	10	0	0	1.4	.
Male	4.5	Sham Recovery	6	6	6	0	0	1.4	.
Male	4.5	3R4F High Recovery	5	5	5	0	0	1.4	.
Male	4.5	ZRH High Recovery	10	10	10	0	0	1.4	.
Female	3	Sham	10	10	10	0	0	1.4	.
Female	3	3R4F Low	10	10	10	0	0	1.4	.
Female	3	3R4F Medium	10	10	10	0	0	1.4	.
Female	3	3R4F High	9	9	9	0	0	1.4	.
Female	3	ZRH Low	9	9	9	0	0	1.4	.
Female	3	ZRH Medium	10	10	10	0	0	1.4	.
Female	3	ZRH High	10	10	10	0	0	1.4	.
Female	4.5	Sham Recovery	6	6	6	0	0	1.4	.
Female	4.5	3R4F High Recovery	6	6	6	0	0	1.4	.
Female	4.5	ZRH High Recovery	10	10	9	1	0	1.4	.

Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = GM_CSF

Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	0.700	0.700	0.700	0.700	0.700	0.700	0.000	0.000	0.0	.	.	1.4	.
Male	3	3R4F Low	0.700	0.700	0.700	0.700	0.700	0.700	0.000	0.000	0.0	.	.	1.4	.
Male	3	3R4F Medium	0.700	0.700	0.700	0.700	0.700	0.700	0.000	0.000	0.0	.	.	1.4	.
Male	3	3R4F High	0.700	0.700	0.700	0.700	0.700	0.700	0.000	0.000	0.0	.	.	1.4	.
Male	3	ZRH Low	0.700	0.700	0.700	0.700	0.700	0.700	0.000	0.000	0.0	.	.	1.4	.
Male	3	ZRH Medium	0.700	0.700	0.700	0.700	6.900	1.320	1.961	0.620	148.5	3.162	10.000	1.4	.
Male	3	ZRH High	0.700	0.700	0.700	0.700	0.700	0.700	0.000	0.000	0.0	.	.	1.4	.
Male	4.5	Sham Recovery	0.700	0.700	0.700	0.700	0.700	0.700	0.000	0.000	0.0	.	.	1.4	.
Male	4.5	3R4F High Recovery	0.700	0.700	0.700	0.700	0.700	0.700	0.000	0.000	0.0	.	.	1.4	.
Male	4.5	ZRH High Recovery	0.700	0.700	0.700	0.700	0.700	0.700	0.000	0.000	0.0	.	.	1.4	.
Female	3	Sham	0.700	0.700	0.700	0.700	0.700	0.700	0.000	0.000	0.0	.	.	1.4	.
Female	3	3R4F Low	0.700	0.700	0.700	0.700	0.700	0.700	0.000	0.000	0.0	.	.	1.4	.
Female	3	3R4F Medium	0.700	0.700	0.700	0.700	0.700	0.700	0.000	0.000	0.0	.	.	1.4	.
Female	3	3R4F High	0.700	0.700	0.700	0.700	0.700	0.700	0.000	0.000	0.0	.	.	1.4	.
Female	3	ZRH Low	0.700	0.700	0.700	0.700	0.700	0.700	0.000	0.000	0.0	.	.	1.4	.
Female	3	ZRH Medium	0.700	0.700	0.700	0.700	0.700	0.700	0.000	0.000	0.0	.	.	1.4	.
Female	3	ZRH High	0.700	0.700	0.700	0.700	0.700	0.700	0.000	0.000	0.0	.	.	1.4	.
Female	4.5	Sham Recovery	0.700	0.700	0.700	0.700	0.700	0.700	0.000	0.000	0.0	.	.	1.4	.
Female	4.5	3R4F High Recovery	0.700	0.700	0.700	0.700	0.700	0.700	0.000	0.000	0.0	.	.	1.4	.
Female	4.5	ZRH High Recovery	0.700	0.700	0.700	0.700	1.400	0.770	0.221	0.070	28.7	3.162	10.000	1.4	.





Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = GM_CSF

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	1.000000
---- Sham vs. 3R4F Medium for Male	1.000000
---- Sham vs. 3R4F High for Male	1.000000
---- Sham vs. ZRH Low for Male	1.000000
---- Sham vs. ZRH Medium for Male	0.317311
---- Sham vs. ZRH High for Male	1.000000
---- ZRH Low vs. 3R4F Medium for Male	1.000000
---- ZRH Medium vs. 3R4F High for Male	0.317311
---- ZRH High vs. 3R4F High for Male	1.000000
---- Sham Recovery vs. 3R4F High Recovery for Male	1.000000
---- Sham Recovery vs. ZRH High Recovery for Male	1.000000
---- Sham vs. Sham Recovery for Male	1.000000
---- 3R4F High vs. 3R4F High Recovery for Male	1.000000
---- ZRH High vs. ZRH High Recovery for Male	1.000000
---- 3R4F High Recovery vs. ZRH High Recovery for Male	1.000000
---- Sham vs. 3R4F Low for Female	1.000000
---- Sham vs. 3R4F Medium for Female	1.000000
---- Sham vs. 3R4F High for Female	1.000000
---- Sham vs. ZRH Low for Female	1.000000
---- Sham vs. ZRH Medium for Female	1.000000
---- Sham vs. ZRH High for Female	1.000000
---- ZRH Low vs. 3R4F Medium for Female	1.000000
---- ZRH Medium vs. 3R4F High for Female	1.000000
---- ZRH High vs. 3R4F High for Female	1.000000
---- Sham Recovery vs. 3R4F High Recovery for Female	1.000000
---- Sham Recovery vs. ZRH High Recovery for Female	0.438578
---- Sham vs. Sham Recovery for Female	1.000000

Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = GM_CSF

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	1.000000
---- ZRH High vs. ZRH High Recovery for Female	0.317311
---- 3R4F High Recovery vs. ZRH High Recovery for Female	0.438578

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 15

Haptoglobin

Unit = ug/mL

Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = Haptoglobin

Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	0	10	0	2.4	.
Male	3	3R4F Low	10	10	0	10	0	2.4	.
Male	3	3R4F Medium	10	10	0	10	0	2.4	.
Male	3	3R4F High	10	10	0	10	0	2.4	.
Male	3	ZRH Low	10	10	0	10	0	2.4	.
Male	3	ZRH Medium	10	10	0	10	0	2.4	.
Male	3	ZRH High	10	10	0	10	0	2.4	.
Male	4.5	Sham Recovery	6	6	0	6	0	2.4	.
Male	4.5	3R4F High Recovery	5	5	0	5	0	2.4	.
Male	4.5	ZRH High Recovery	10	10	1	9	0	2.4	.
Female	3	Sham	10	10	0	10	0	2.4	.
Female	3	3R4F Low	10	10	1	9	0	2.4	.
Female	3	3R4F Medium	10	10	0	10	0	2.4	.
Female	3	3R4F High	9	9	0	9	0	2.4	.
Female	3	ZRH Low	9	9	0	9	0	2.4	.
Female	3	ZRH Medium	10	10	0	10	0	2.4	.
Female	3	ZRH High	10	10	0	10	0	2.4	.
Female	4.5	Sham Recovery	6	6	0	6	0	2.4	.
Female	4.5	3R4F High Recovery	6	6	0	6	0	2.4	.
Female	4.5	ZRH High Recovery	10	10	0	10	0	2.4	.

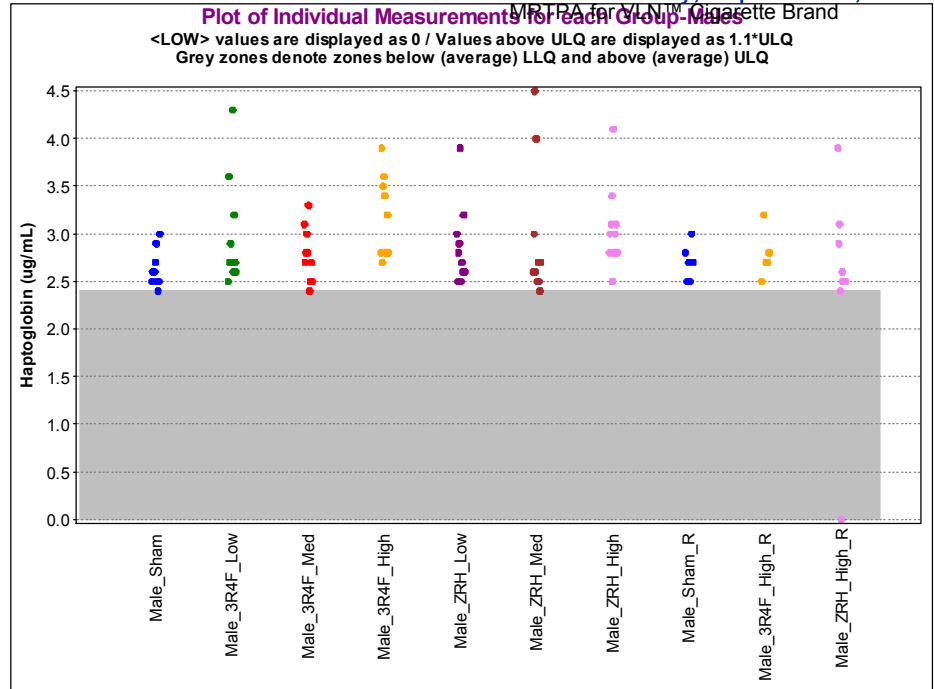
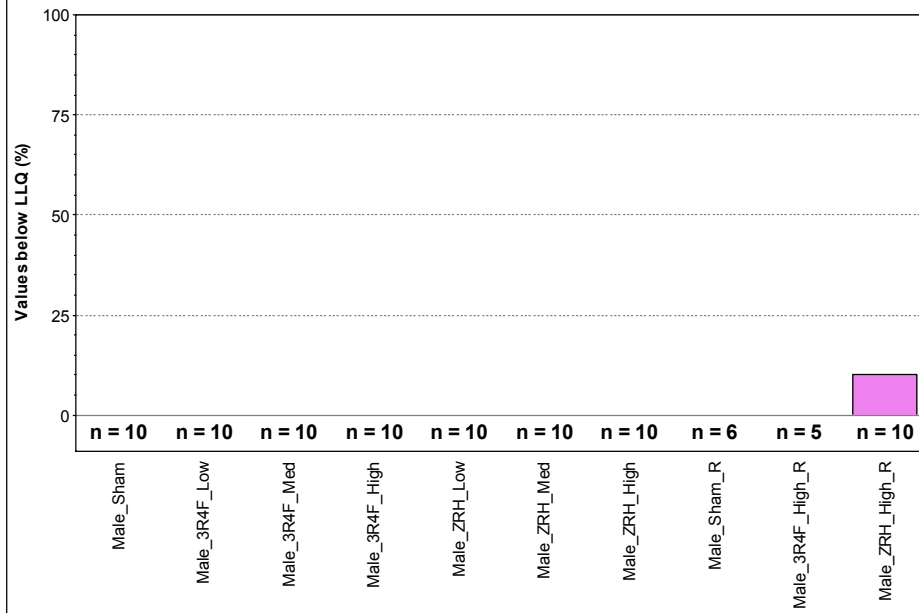
Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = Haptoglobin

Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	2.400	2.500	2.600	2.700	3.000	2.630	0.189	0.060	7.2	1.069	0.420	2.4	.
Male	3	3R4F Low	2.500	2.600	2.700	3.200	4.300	2.980	0.571	0.181	19.2	1.686	2.427	2.4	.
Male	3	3R4F Medium	2.400	2.500	2.750	3.000	3.300	2.780	0.286	0.090	10.3	0.500	-0.450	2.4	.
Male	3	3R4F High	2.700	2.800	3.000	3.500	3.900	3.150	0.428	0.135	13.6	0.549	-1.221	2.4	.
Male	3	ZRH Low	2.500	2.600	2.750	3.000	3.900	2.870	0.427	0.135	14.9	1.757	3.451	2.4	.
Male	3	ZRH Medium	2.400	2.500	2.650	3.000	4.500	2.950	0.714	0.226	24.2	1.687	1.715	2.4	.
Male	3	ZRH High	2.500	2.800	3.000	3.100	4.100	3.060	0.438	0.138	14.3	1.550	3.365	2.4	.
Male	4.5	Sham Recovery	2.500	2.500	2.700	2.800	3.000	2.700	0.190	0.077	7.0	0.527	-0.093	2.4	.
Male	4.5	3R4F High Recovery	2.500	2.700	2.700	2.800	3.200	2.780	0.259	0.116	9.3	1.228	2.399	2.4	.
Male	4.5	ZRH High Recovery	1.200	2.500	2.500	2.900	3.900	2.610	0.672	0.213	25.8	-0.242	2.910	2.4	.
Female	3	Sham	2.400	2.500	2.700	2.900	6.300	3.050	1.161	0.367	38.1	2.978	9.129	2.4	.
Female	3	3R4F Low	1.200	2.500	2.550	2.700	3.500	2.520	0.557	0.176	22.1	-1.081	4.617	2.4	.
Female	3	3R4F Medium	2.500	2.700	2.750	2.900	4.800	2.950	0.665	0.210	22.6	2.896	8.777	2.4	.
Female	3	3R4F High	2.500	2.600	2.600	2.900	3.700	2.789	0.376	0.125	13.5	2.094	4.941	2.4	.
Female	3	ZRH Low	2.600	2.600	2.800	3.300	4.300	3.089	0.645	0.215	20.9	1.259	0.139	2.4	.
Female	3	ZRH Medium	2.500	2.500	2.700	3.200	4.100	2.900	0.506	0.160	17.4	1.651	2.956	2.4	.
Female	3	ZRH High	2.600	2.800	3.050	3.400	3.700	3.120	0.368	0.116	11.8	0.120	-1.214	2.4	.
Female	4.5	Sham Recovery	2.500	2.600	2.600	2.700	3.500	2.750	0.373	0.152	13.6	2.292	5.410	2.4	.
Female	4.5	3R4F High Recovery	2.500	2.500	2.650	2.700	3.900	2.817	0.538	0.220	19.1	2.299	5.430	2.4	.
Female	4.5	ZRH High Recovery	2.600	2.600	2.750	3.000	3.600	2.850	0.321	0.101	11.2	1.581	2.623	2.4	.

Percentage of Values below LLQ for each Group-Males

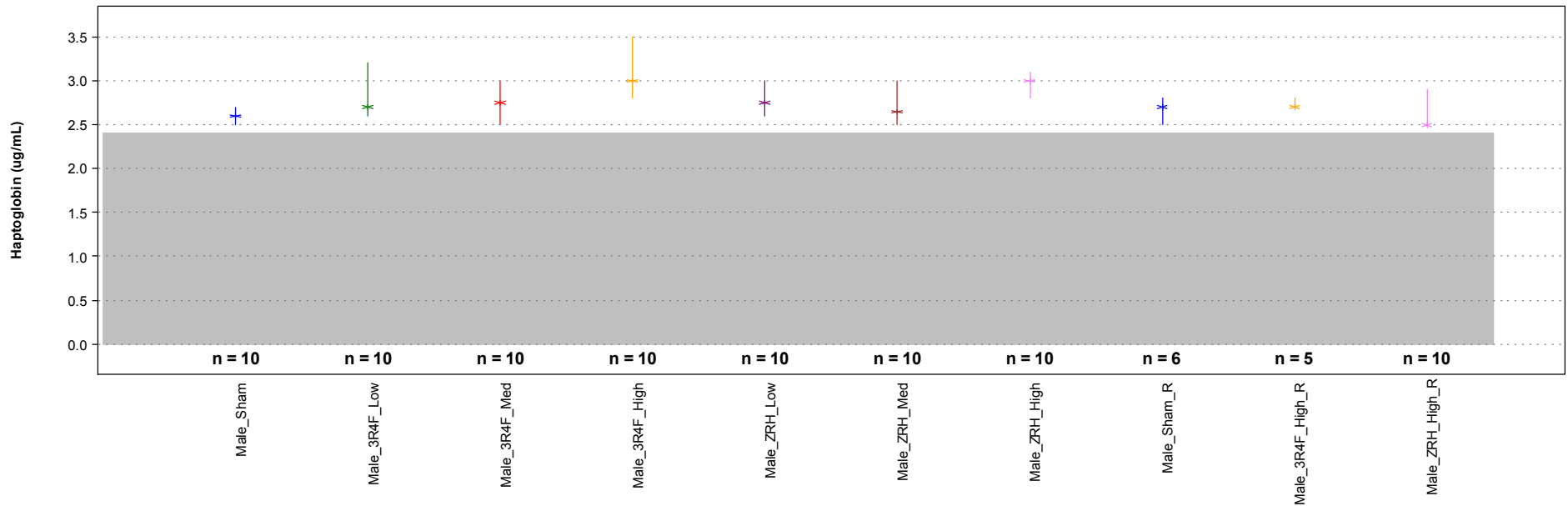
Analyte = Haptoglobin



Plot of Descriptive Robust Statistics-Males

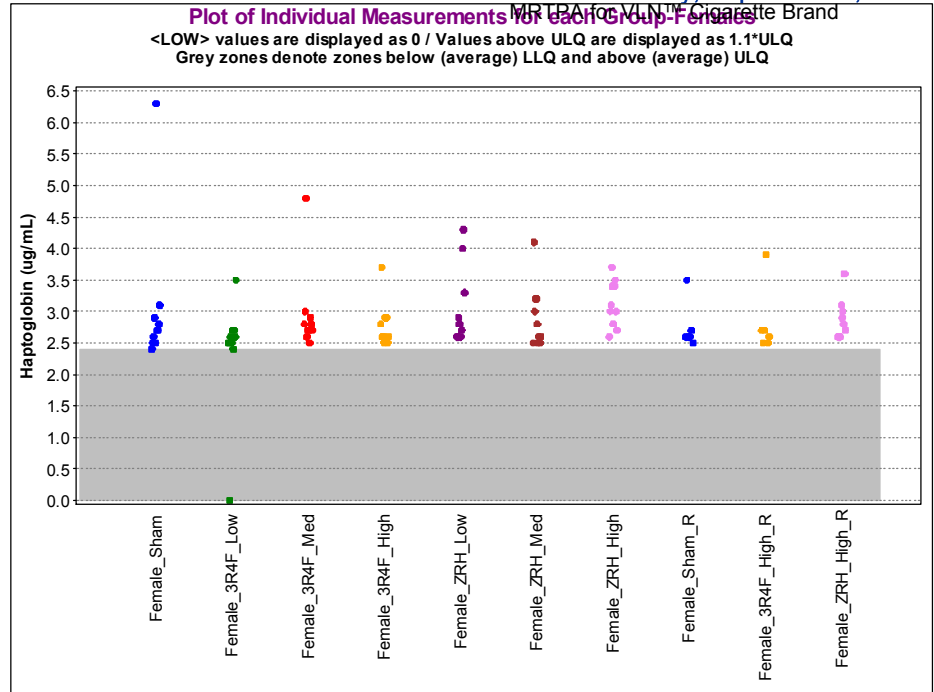
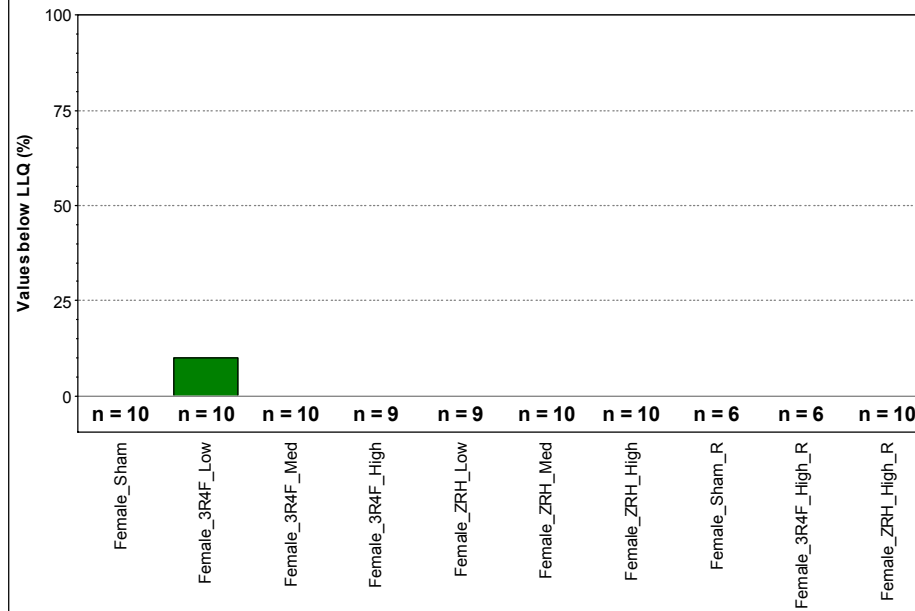
Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



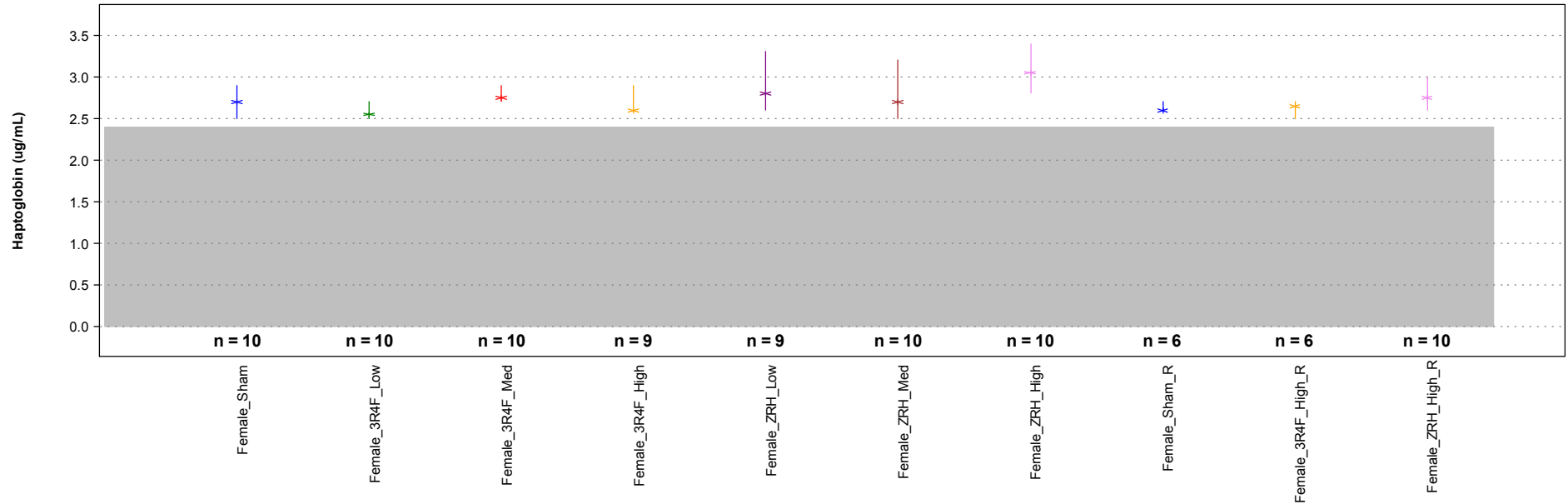
Percentage of Values below LLQ for each Group-Females

Analyte = Haptoglobin

**Plot of Descriptive Robust Statistics-Females**

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = Haptoglobin

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	0.059938
---- Sham vs. 3R4F Medium for Male	0.221015
---- Sham vs. 3R4F High for Male	0.002634
---- Sham vs. ZRH Low for Male	0.134008
---- Sham vs. ZRH Medium for Male	0.397393
---- Sham vs. ZRH High for Male	0.006788
---- ZRH Low vs. 3R4F Medium for Male	0.789787
---- ZRH Medium vs. 3R4F High for Male	0.067965
---- ZRH High vs. 3R4F High for Male	0.727860
---- Sham Recovery vs. 3R4F High Recovery for Male	0.636328
---- Sham Recovery vs. ZRH High Recovery for Male	0.435279
---- Sham vs. Sham Recovery for Male	0.405741
---- 3R4F High vs. 3R4F High Recovery for Male	0.052113
---- ZRH High vs. ZRH High Recovery for Male	0.039053
---- 3R4F High Recovery vs. ZRH High Recovery for Male	0.261209
---- Sham vs. 3R4F Low for Female	0.180040
---- Sham vs. 3R4F Medium for Female	0.540749
---- Sham vs. 3R4F High for Female	1.000000
---- Sham vs. ZRH Low for Female	0.344122
---- Sham vs. ZRH Medium for Female	0.731091
---- Sham vs. ZRH High for Female	0.053002
---- ZRH Low vs. 3R4F Medium for Female	0.772612
---- ZRH Medium vs. 3R4F High for Female	0.770806
---- ZRH High vs. 3R4F High for Female	0.036008
---- Sham Recovery vs. 3R4F High Recovery for Female	0.934083
---- Sham Recovery vs. ZRH High Recovery for Female	0.234107
---- Sham vs. Sham Recovery for Female	0.700419

Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = Haptoglobin

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	0.763726
---- ZRH High vs. ZRH High Recovery for Female	0.085609
---- 3R4F High Recovery vs. ZRH High Recovery for Female	0.319910

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 18

Interferon gamma (IFN-gamma)

Unit = pg/mL

Descriptive Statistics by Exposure Duration and Treatment Type

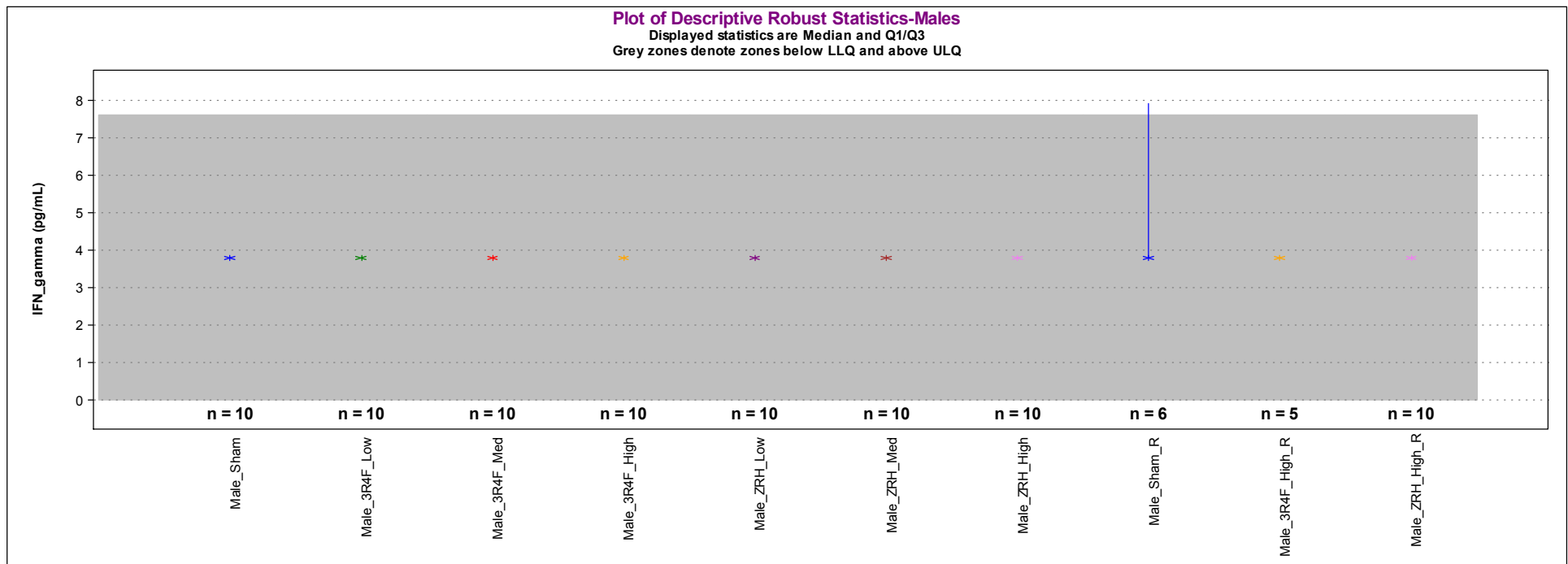
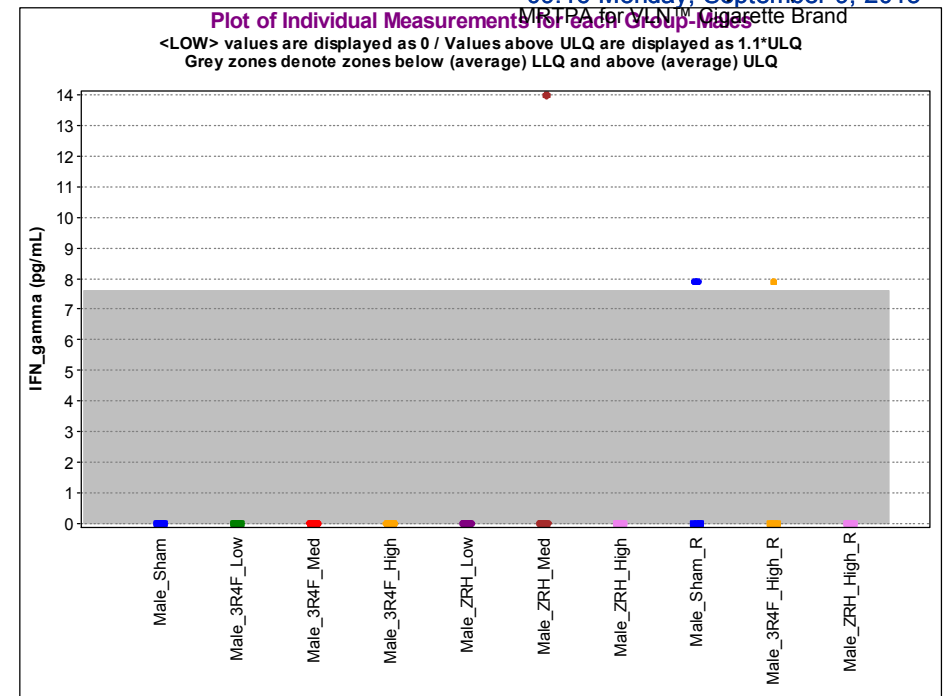
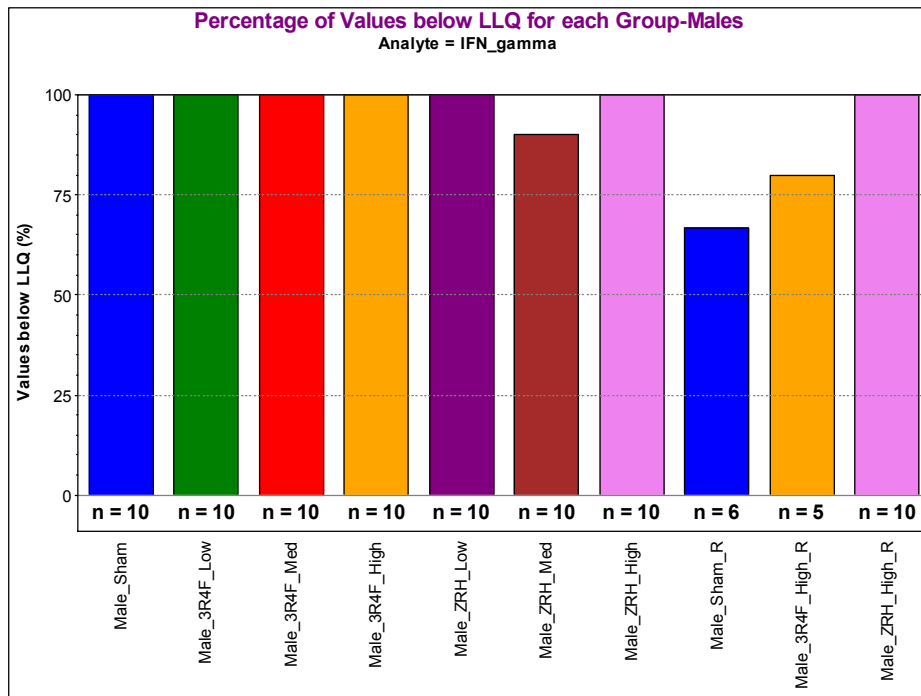
Analyte = IFN_gamma

Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	10	0	0	7.6	.
Male	3	3R4F Low	10	10	10	0	0	7.6	.
Male	3	3R4F Medium	10	10	10	0	0	7.6	.
Male	3	3R4F High	10	10	10	0	0	7.6	.
Male	3	ZRH Low	10	10	10	0	0	7.6	.
Male	3	ZRH Medium	10	10	9	1	0	7.6	.
Male	3	ZRH High	10	10	10	0	0	7.6	.
Male	4.5	Sham Recovery	6	6	4	2	0	7.6	.
Male	4.5	3R4F High Recovery	5	5	4	1	0	7.6	.
Male	4.5	ZRH High Recovery	10	10	10	0	0	7.6	.
Female	3	Sham	10	10	10	0	0	7.6	.
Female	3	3R4F Low	10	10	10	0	0	7.6	.
Female	3	3R4F Medium	10	10	10	0	0	7.6	.
Female	3	3R4F High	9	9	9	0	0	7.6	.
Female	3	ZRH Low	9	9	9	0	0	7.6	.
Female	3	ZRH Medium	10	10	10	0	0	7.6	.
Female	3	ZRH High	10	10	10	0	0	7.6	.
Female	4.5	Sham Recovery	6	6	3	3	0	7.6	.
Female	4.5	3R4F High Recovery	6	6	4	2	0	7.6	.
Female	4.5	ZRH High Recovery	10	10	7	3	0	7.6	.

Descriptive Statistics by Exposure Duration and Treatment Type

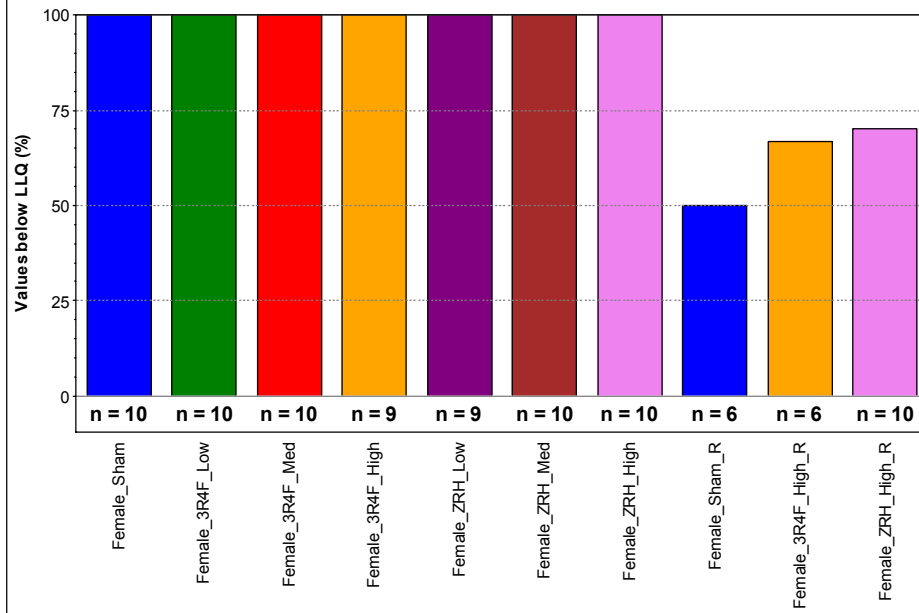
Analyte = IFN_gamma

Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	3.800	3.800	3.800	3.800	3.800	3.800	0.000	0.000	0.0	.	.	7.6	.
Male	3	3R4F Low	3.800	3.800	3.800	3.800	3.800	3.800	0.000	0.000	0.0	.	.	7.6	.
Male	3	3R4F Medium	3.800	3.800	3.800	3.800	3.800	3.800	0.000	0.000	0.0	.	.	7.6	.
Male	3	3R4F High	3.800	3.800	3.800	3.800	3.800	3.800	0.000	0.000	0.0	.	.	7.6	.
Male	3	ZRH Low	3.800	3.800	3.800	3.800	3.800	3.800	0.000	0.000	0.0	.	.	7.6	.
Male	3	ZRH Medium	3.800	3.800	3.800	3.800	14.000	4.820	3.226	1.020	66.9	3.162	10.000	7.6	.
Male	3	ZRH High	3.800	3.800	3.800	3.800	3.800	3.800	0.000	0.000	0.0	.	.	7.6	.
Male	4.5	Sham Recovery	3.800	3.800	3.800	7.900	7.900	5.167	2.117	0.864	41.0	0.968	-1.875	7.6	.
Male	4.5	3R4F High Recovery	3.800	3.800	3.800	3.800	7.900	4.620	1.834	0.820	39.7	2.236	5.000	7.6	.
Male	4.5	ZRH High Recovery	3.800	3.800	3.800	3.800	3.800	3.800	0.000	0.000	0.0	.	.	7.6	.
Female	3	Sham	3.800	3.800	3.800	3.800	3.800	3.800	0.000	0.000	0.0	.	.	7.6	.
Female	3	3R4F Low	3.800	3.800	3.800	3.800	3.800	3.800	0.000	0.000	0.0	.	.	7.6	.
Female	3	3R4F Medium	3.800	3.800	3.800	3.800	3.800	3.800	0.000	0.000	0.0	.	.	7.6	.
Female	3	3R4F High	3.800	3.800	3.800	3.800	3.800	3.800	0.000	0.000	0.0	.	.	7.6	.
Female	3	ZRH Low	3.800	3.800	3.800	3.800	3.800	3.800	0.000	0.000	0.0	.	.	7.6	.
Female	3	ZRH Medium	3.800	3.800	3.800	3.800	3.800	3.800	0.000	0.000	0.0	.	.	7.6	.
Female	3	ZRH High	3.800	3.800	3.800	3.800	3.800	3.800	0.000	0.000	0.0	.	.	7.6	.
Female	4.5	Sham Recovery	3.800	3.800	5.850	7.900	8.000	5.867	2.264	0.924	38.6	0.001	-3.330	7.6	.
Female	4.5	3R4F High Recovery	3.800	3.800	3.800	7.900	7.900	5.167	2.117	0.864	41.0	0.968	-1.875	7.6	.
Female	4.5	ZRH High Recovery	3.800	3.800	3.800	8.000	14.000	5.760	3.501	1.107	60.8	1.787	2.706	7.6	.

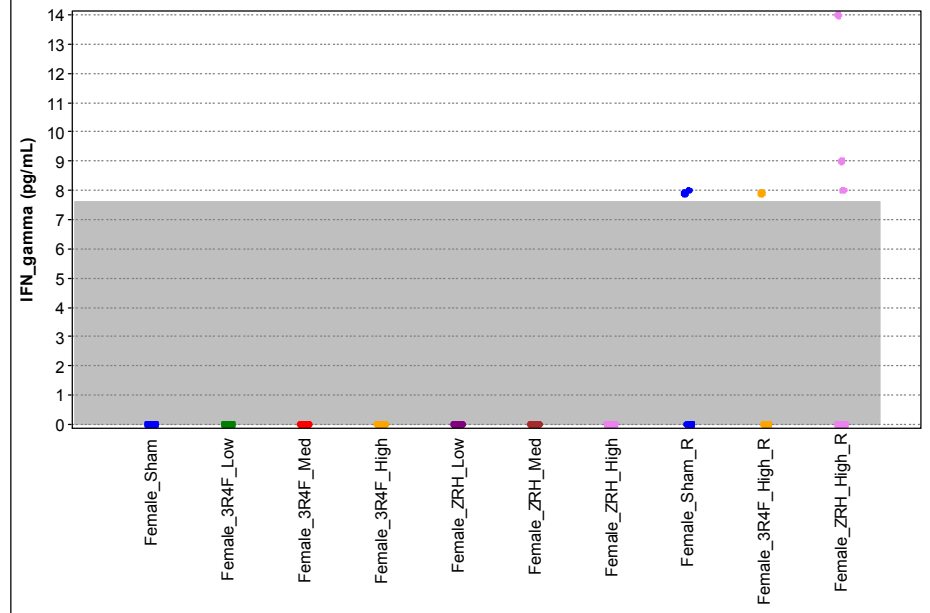


Percentage of Values below LLQ for each Group-Females

Analyte = IFN_gamma

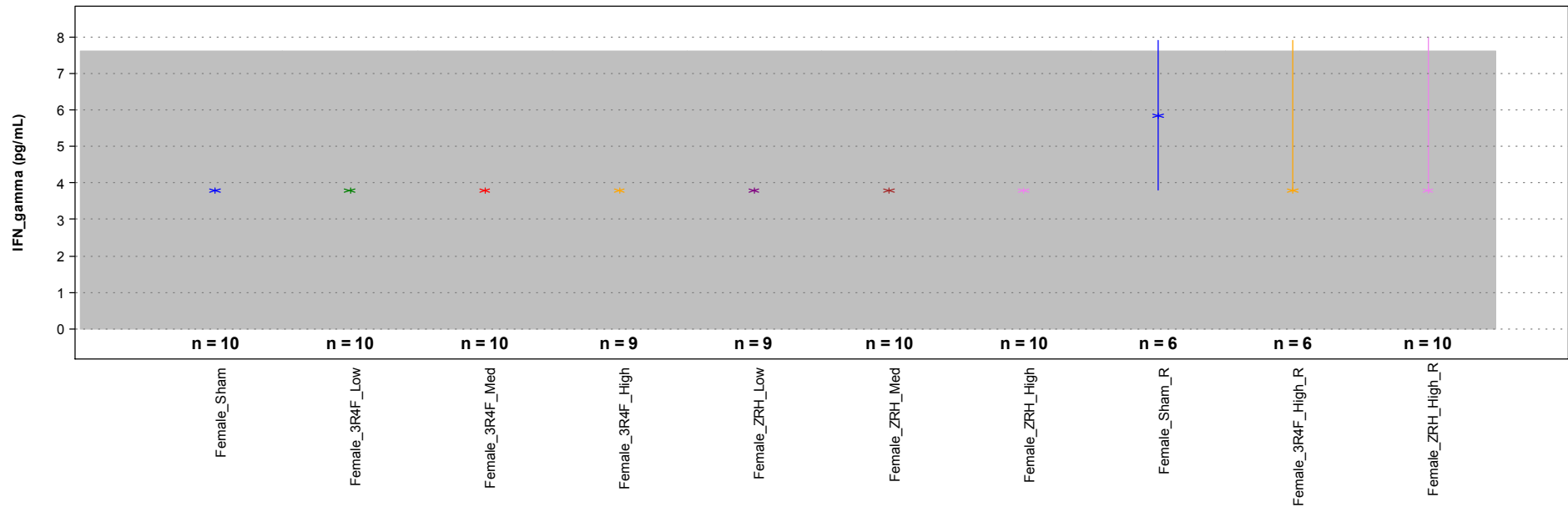
**Plot of Individual Measurements for IFN_gamma - Females**

<LOW> values are displayed as 0 / Values above ULQ are displayed as 1.1*ULQ
 Grey zones denote zones below (average) LLQ and above (average) ULQ

**Plot of Descriptive Robust Statistics-Females**

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = IFN_{gamma}

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	1.000000
---- Sham vs. 3R4F Medium for Male	1.000000
---- Sham vs. 3R4F High for Male	1.000000
---- Sham vs. ZRH Low for Male	1.000000
---- Sham vs. ZRH Medium for Male	0.317311
---- Sham vs. ZRH High for Male	1.000000
---- ZRH Low vs. 3R4F Medium for Male	1.000000
---- ZRH Medium vs. 3R4F High for Male	0.317311
---- ZRH High vs. 3R4F High for Male	1.000000
---- Sham Recovery vs. 3R4F High Recovery for Male	0.637352
---- Sham Recovery vs. ZRH High Recovery for Male	0.058782
---- Sham vs. Sham Recovery for Male	0.058782
---- 3R4F High vs. 3R4F High Recovery for Male	0.157299
---- ZRH High vs. ZRH High Recovery for Male	1.000000
---- 3R4F High Recovery vs. ZRH High Recovery for Male	0.157299
---- Sham vs. 3R4F Low for Female	1.000000
---- Sham vs. 3R4F Medium for Female	1.000000
---- Sham vs. 3R4F High for Female	1.000000
---- Sham vs. ZRH Low for Female	1.000000
---- Sham vs. ZRH Medium for Female	1.000000
---- Sham vs. ZRH High for Female	1.000000
---- ZRH Low vs. 3R4F Medium for Female	1.000000
---- ZRH Medium vs. 3R4F High for Female	1.000000
---- ZRH High vs. 3R4F High for Female	1.000000
---- Sham Recovery vs. 3R4F High Recovery for Female	0.465209
---- Sham Recovery vs. ZRH High Recovery for Female	0.802776
---- Sham vs. Sham Recovery for Female	0.016827

Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = IFN_gamma

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	0.072267
---- ZRH High vs. ZRH High Recovery for Female	0.068157
---- 3R4F High Recovery vs. ZRH High Recovery for Female	0.791750

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 28

Interleukin-10 (IL-10)

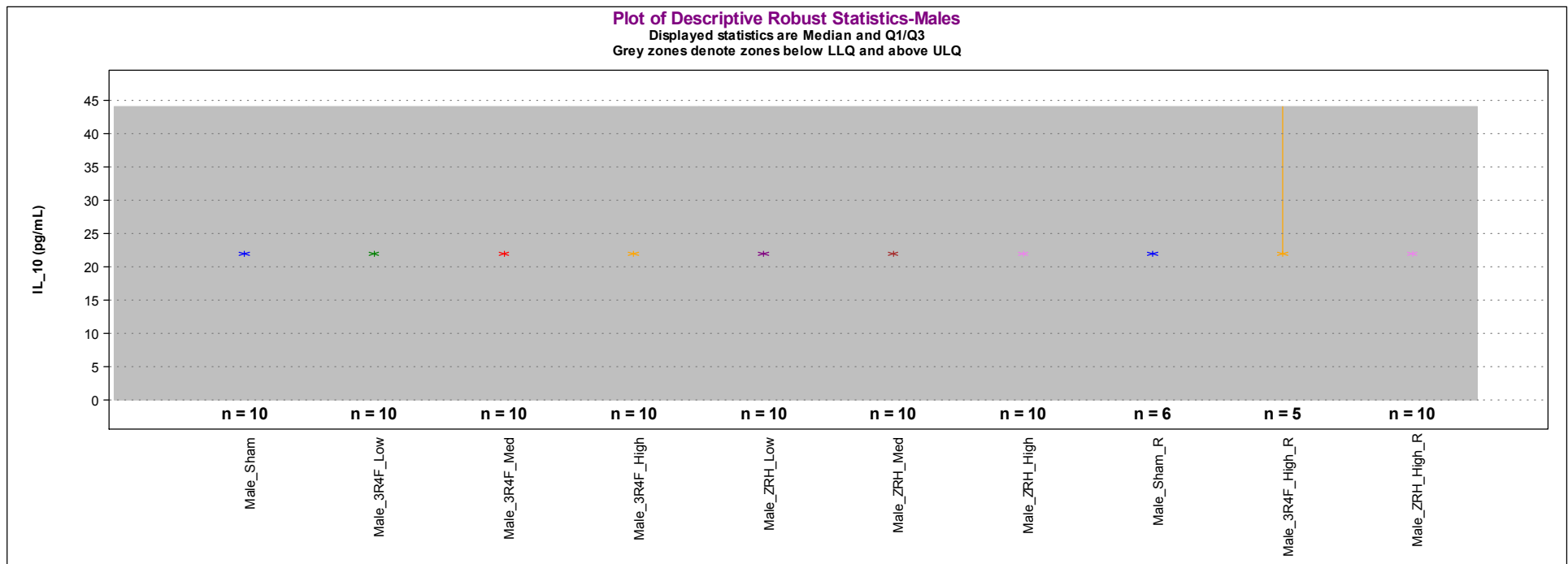
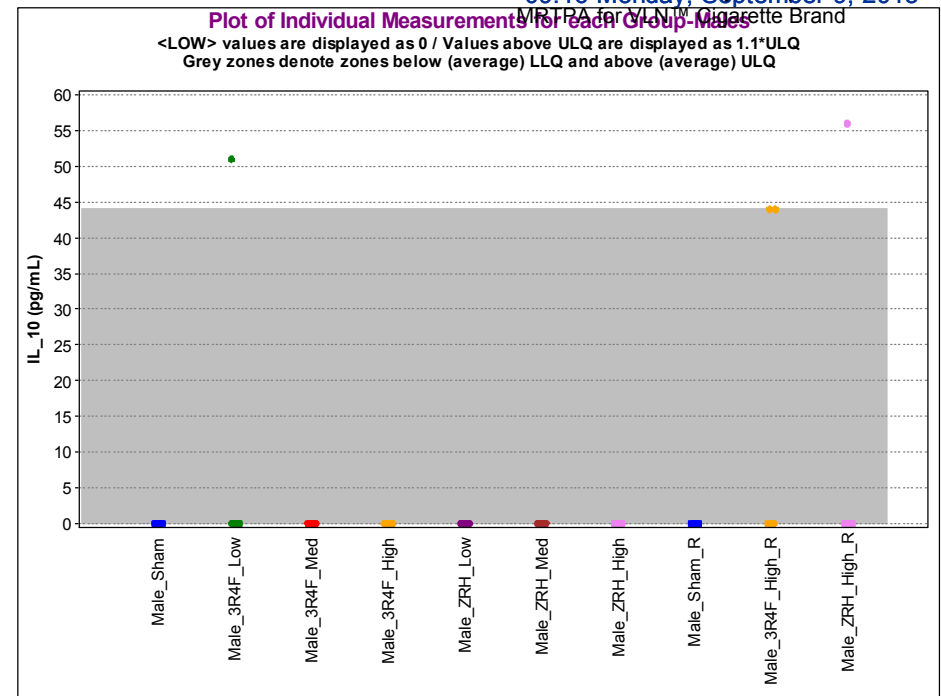
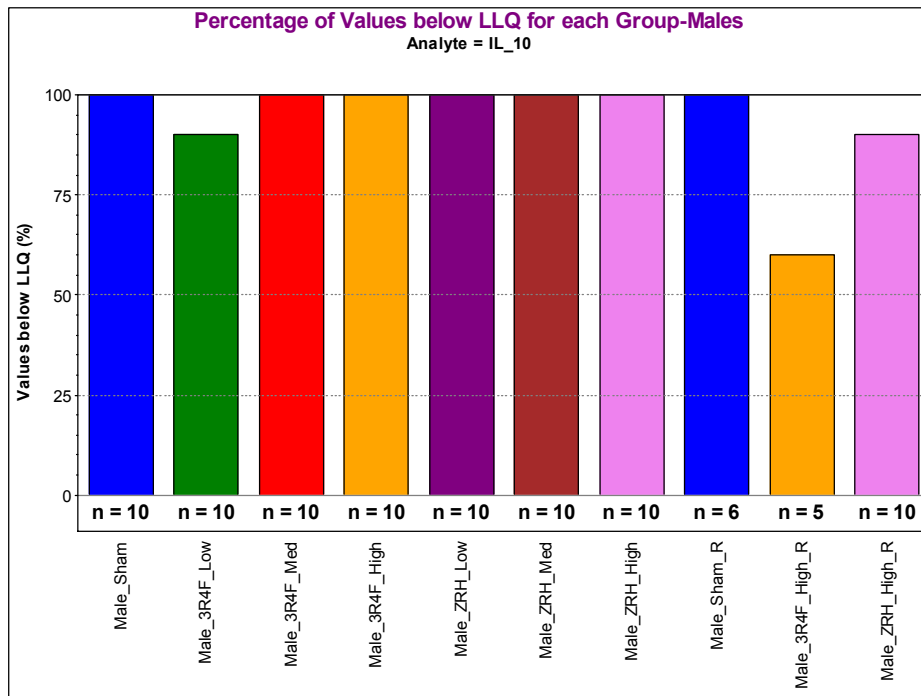
Unit = pg/mL

Descriptive Statistics by Exposure Duration and Treatment Type**Analyte = IL₁₀**

Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	10	0	0	44	.
Male	3	3R4F Low	10	10	9	1	0	44	.
Male	3	3R4F Medium	10	10	10	0	0	44	.
Male	3	3R4F High	10	10	10	0	0	44	.
Male	3	ZRH Low	10	10	10	0	0	44	.
Male	3	ZRH Medium	10	10	10	0	0	44	.
Male	3	ZRH High	10	10	10	0	0	44	.
Male	4.5	Sham Recovery	6	6	6	0	0	44	.
Male	4.5	3R4F High Recovery	5	5	3	2	0	44	.
Male	4.5	ZRH High Recovery	10	10	9	1	0	44	.
Female	3	Sham	10	10	10	0	0	44	.
Female	3	3R4F Low	10	10	10	0	0	44	.
Female	3	3R4F Medium	10	10	9	1	0	44	.
Female	3	3R4F High	9	9	8	1	0	44	.
Female	3	ZRH Low	9	9	9	0	0	44	.
Female	3	ZRH Medium	10	10	10	0	0	44	.
Female	3	ZRH High	10	10	9	1	0	44	.
Female	4.5	Sham Recovery	6	6	3	3	0	44	.
Female	4.5	3R4F High Recovery	6	6	6	0	0	44	.
Female	4.5	ZRH High Recovery	10	10	9	1	0	44	.

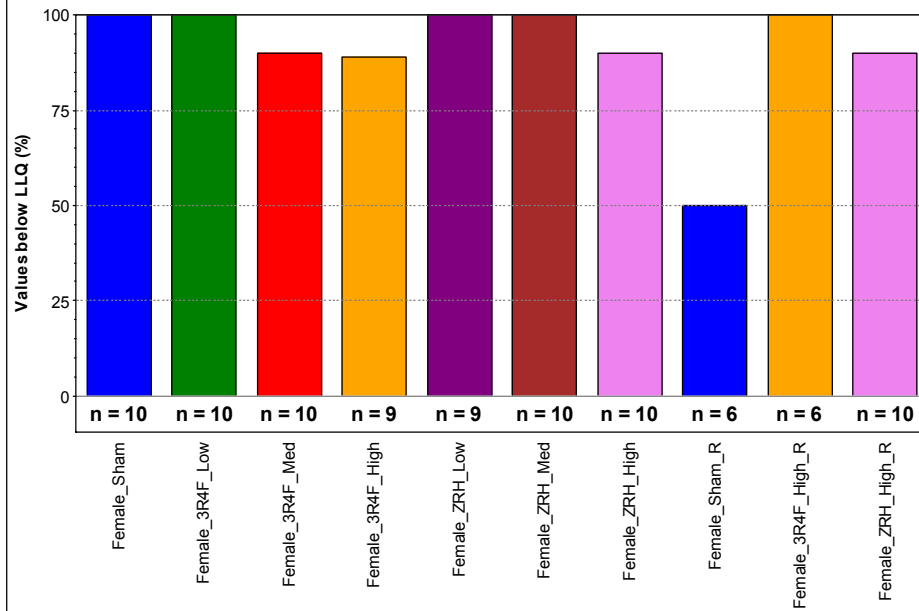
Descriptive Statistics by Exposure Duration and Treatment Type**Analyte = IL₁₀**

Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	22.000	22.000	22.000	22.000	22.000	22.000	0.000	0.000	0.0	.	.	44	.
Male	3	3R4F Low	22.000	22.000	22.000	22.000	51.000	24.900	9.171	2.900	36.8	3.162	10.000	44	.
Male	3	3R4F Medium	22.000	22.000	22.000	22.000	22.000	22.000	0.000	0.000	0.0	.	.	44	.
Male	3	3R4F High	22.000	22.000	22.000	22.000	22.000	22.000	0.000	0.000	0.0	.	.	44	.
Male	3	ZRH Low	22.000	22.000	22.000	22.000	22.000	22.000	0.000	0.000	0.0	.	.	44	.
Male	3	ZRH Medium	22.000	22.000	22.000	22.000	22.000	22.000	0.000	0.000	0.0	.	.	44	.
Male	3	ZRH High	22.000	22.000	22.000	22.000	22.000	22.000	0.000	0.000	0.0	.	.	44	.
Male	4.5	Sham Recovery	22.000	22.000	22.000	22.000	22.000	22.000	0.000	0.000	0.0	.	.	44	.
Male	4.5	3R4F High Recovery	22.000	22.000	22.000	44.000	44.000	30.800	12.050	5.389	39.1	0.609	-3.333	44	.
Male	4.5	ZRH High Recovery	22.000	22.000	22.000	22.000	56.000	25.400	10.752	3.400	42.3	3.162	10.000	44	.
Female	3	Sham	22.000	22.000	22.000	22.000	22.000	22.000	0.000	0.000	0.0	.	.	44	.
Female	3	3R4F Low	22.000	22.000	22.000	22.000	22.000	22.000	0.000	0.000	0.0	.	.	44	.
Female	3	3R4F Medium	22.000	22.000	22.000	22.000	49.000	24.700	8.538	2.700	34.6	3.162	10.000	44	.
Female	3	3R4F High	22.000	22.000	22.000	22.000	72.000	27.556	16.667	5.556	60.5	3.000	9.000	44	.
Female	3	ZRH Low	22.000	22.000	22.000	22.000	22.000	22.000	0.000	0.000	0.0	.	.	44	.
Female	3	ZRH Medium	22.000	22.000	22.000	22.000	22.000	22.000	0.000	0.000	0.0	.	.	44	.
Female	3	ZRH High	22.000	22.000	22.000	22.000	46.000	24.400	7.589	2.400	31.1	3.162	10.000	44	.
Female	4.5	Sham Recovery	22.000	22.000	33.000	44.000	56.000	35.000	14.900	6.083	42.6	0.374	-2.084	44	.
Female	4.5	3R4F High Recovery	22.000	22.000	22.000	22.000	22.000	22.000	0.000	0.000	0.0	.	.	44	.
Female	4.5	ZRH High Recovery	22.000	22.000	22.000	22.000	51.000	24.900	9.171	2.900	36.8	3.162	10.000	44	.

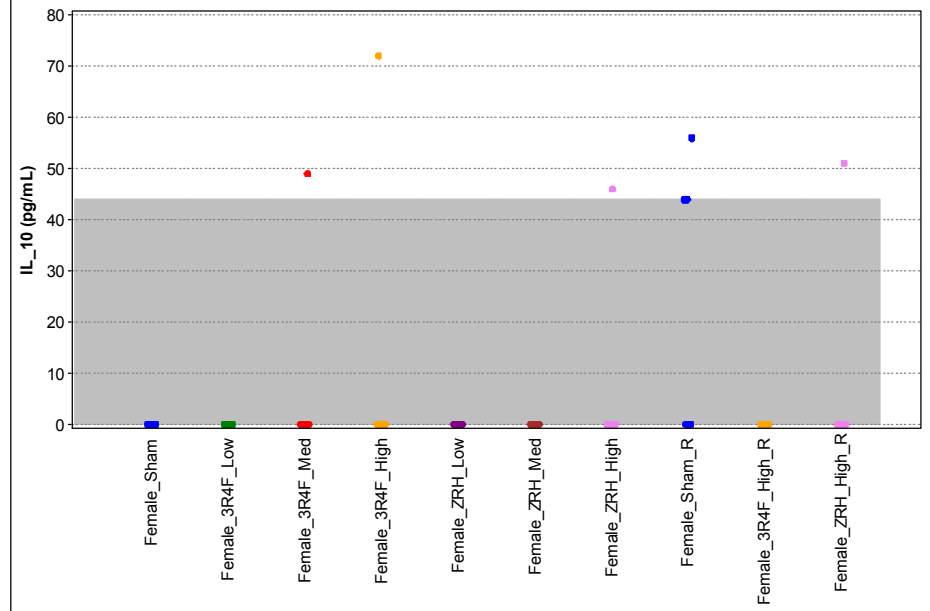


Percentage of Values below LLQ for each Group-Females

Analyte = IL_10

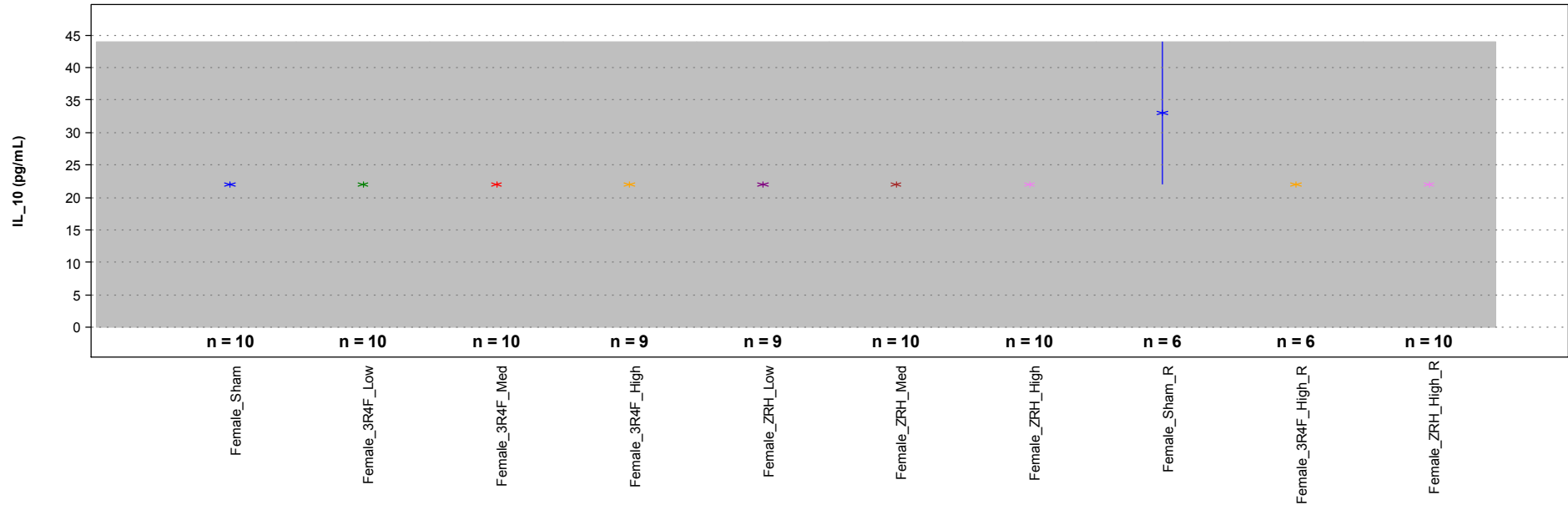
**Plot of Individual Measurements for IL_10 - Females**

<LOW> values are displayed as 0 / Values above ULQ are displayed as 1.1*ULQ
 Grey zones denote zones below (average) LLQ and above (average) ULQ

**Plot of Descriptive Robust Statistics-Females**

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = IL₁₀

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	0.317311
---- Sham vs. 3R4F Medium for Male	1.000000
---- Sham vs. 3R4F High for Male	1.000000
---- Sham vs. ZRH Low for Male	1.000000
---- Sham vs. ZRH Medium for Male	1.000000
---- Sham vs. ZRH High for Male	1.000000
---- ZRH Low vs. 3R4F Medium for Male	1.000000
---- ZRH Medium vs. 3R4F High for Male	1.000000
---- ZRH High vs. 3R4F High for Male	1.000000
---- Sham Recovery vs. 3R4F High Recovery for Male	0.102470
---- Sham Recovery vs. ZRH High Recovery for Male	0.438578
---- Sham vs. Sham Recovery for Male	1.000000
---- 3R4F High vs. 3R4F High Recovery for Male	0.037940
---- ZRH High vs. ZRH High Recovery for Male	0.317311
---- 3R4F High Recovery vs. ZRH High Recovery for Male	0.254213
---- Sham vs. 3R4F Low for Female	1.000000
---- Sham vs. 3R4F Medium for Female	0.317311
---- Sham vs. 3R4F High for Female	0.291841
---- Sham vs. ZRH Low for Female	1.000000
---- Sham vs. ZRH Medium for Female	1.000000
---- Sham vs. ZRH High for Female	0.317311
---- ZRH Low vs. 3R4F Medium for Female	0.342782
---- ZRH Medium vs. 3R4F High for Female	0.291841
---- ZRH High vs. 3R4F High for Female	0.878275
---- Sham Recovery vs. 3R4F High Recovery for Female	0.057780
---- Sham Recovery vs. ZRH High Recovery for Female	0.100846
---- Sham vs. Sham Recovery for Female	0.016827

Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = IL_10

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	0.414216
---- ZRH High vs. ZRH High Recovery for Female	0.942166
---- 3R4F High Recovery vs. ZRH High Recovery for Female	0.438578

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 29

Interleukin-11 (IL-11)

Unit = pg/mL

Descriptive Statistics by Exposure Duration and Treatment Type**Analyte = IL_11**

Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	6	4	0	14	.
Male	3	3R4F Low	10	10	5	5	0	14	.
Male	3	3R4F Medium	10	10	4	6	0	14	.
Male	3	3R4F High	10	10	4	6	0	14	.
Male	3	ZRH Low	10	10	5	5	0	14	.
Male	3	ZRH Medium	10	10	3	7	0	14	.
Male	3	ZRH High	10	10	4	6	0	14	.
Male	4.5	Sham Recovery	6	6	1	5	0	14	.
Male	4.5	3R4F High Recovery	5	5	0	5	0	14	.
Male	4.5	ZRH High Recovery	10	10	4	6	0	14	.
Female	3	Sham	10	10	3	7	0	14	.
Female	3	3R4F Low	10	10	0	10	0	14	.
Female	3	3R4F Medium	10	10	2	8	0	14	.
Female	3	3R4F High	9	9	1	8	0	14	.
Female	3	ZRH Low	9	9	2	7	0	14	.
Female	3	ZRH Medium	10	10	0	10	0	14	.
Female	3	ZRH High	10	10	3	7	0	14	.
Female	4.5	Sham Recovery	6	6	0	6	0	14	.
Female	4.5	3R4F High Recovery	6	6	0	6	0	14	.
Female	4.5	ZRH High Recovery	10	10	0	10	0	14	.

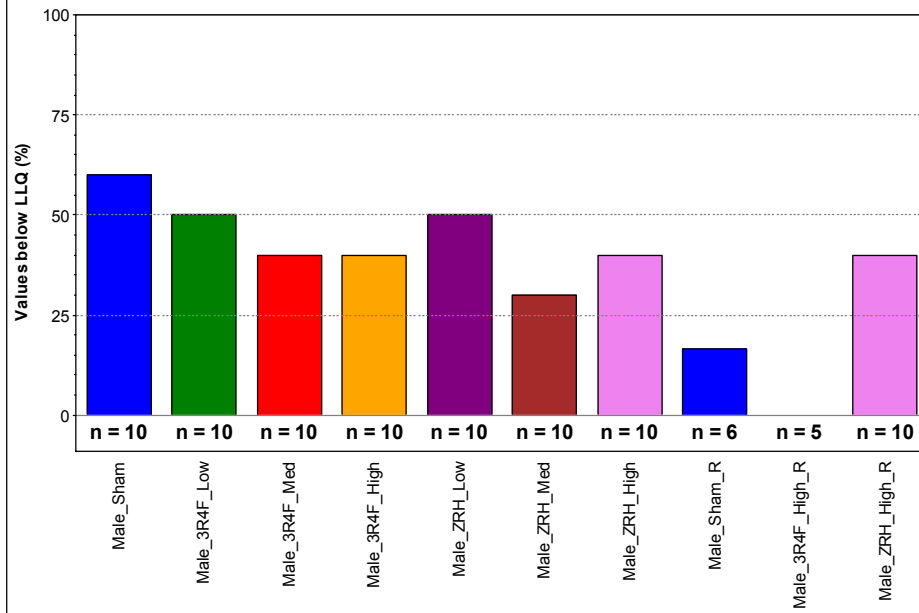
Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = IL₁₁

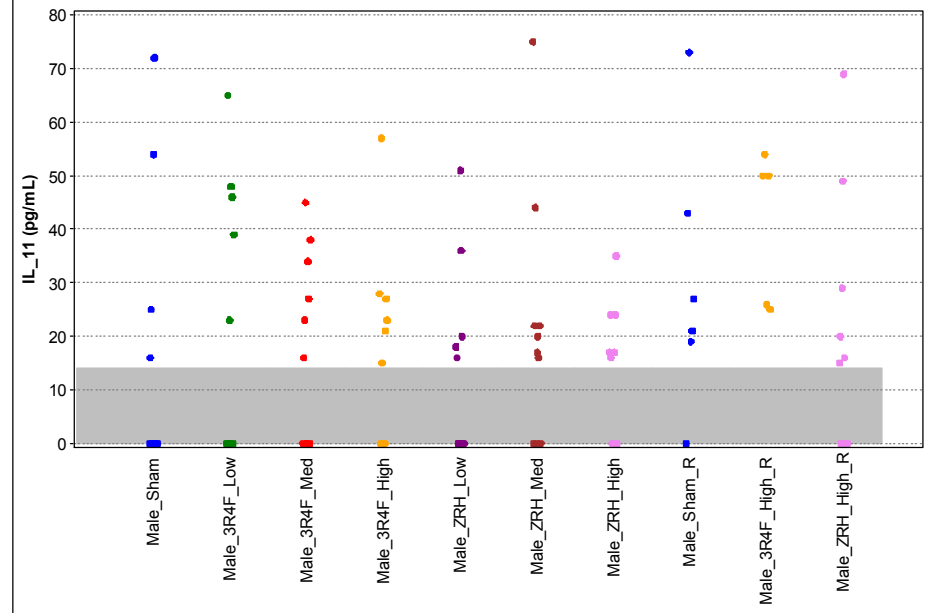
Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	7.000	7.000	7.000	25.000	72.000	20.900	23.350	7.384	111.7	1.675	1.713	14	.
Male	3	3R4F Low	7.000	7.000	15.000	46.000	65.000	25.600	22.077	6.981	86.2	0.660	-1.155	14	.
Male	3	3R4F Medium	7.000	7.000	19.500	34.000	45.000	21.100	14.464	4.574	68.6	0.436	-1.370	14	.
Male	3	3R4F High	7.000	7.000	18.000	27.000	57.000	19.900	15.609	4.936	78.4	1.581	3.060	14	.
Male	3	ZRH Low	7.000	7.000	11.500	20.000	51.000	17.600	14.998	4.743	85.2	1.546	1.796	14	.
Male	3	ZRH Medium	7.000	7.000	18.500	22.000	75.000	23.700	21.093	6.670	89.0	1.903	3.748	14	.
Male	3	ZRH High	7.000	7.000	16.500	24.000	35.000	16.100	9.515	3.009	59.1	0.762	-0.005	14	.
Male	4.5	Sham Recovery	7.000	19.000	24.000	43.000	73.000	31.667	23.415	9.559	73.9	1.255	1.539	14	.
Male	4.5	3R4F High Recovery	25.000	26.000	50.000	50.000	54.000	41.000	14.248	6.372	34.8	-0.550	-3.212	14	.
Male	4.5	ZRH High Recovery	7.000	7.000	15.500	29.000	69.000	22.600	21.009	6.644	93.0	1.537	1.671	14	.
Female	3	Sham	7.000	7.000	19.500	37.000	47.000	22.600	14.653	4.634	64.8	0.440	-1.245	14	.
Female	3	3R4F Low	14.000	17.000	21.000	34.000	41.000	24.300	9.776	3.091	40.2	0.845	-0.920	14	.
Female	3	3R4F Medium	7.000	18.000	19.000	24.000	64.000	22.300	15.882	5.022	71.2	2.260	6.412	14	.
Female	3	3R4F High	7.000	17.000	19.000	22.000	41.000	20.778	9.271	3.090	44.6	1.151	2.883	14	.
Female	3	ZRH Low	7.000	16.000	18.000	20.000	31.000	18.000	8.062	2.687	44.8	0.164	-0.268	14	.
Female	3	ZRH Medium	15.000	19.000	20.500	25.000	71.000	25.900	16.435	5.197	63.5	2.770	8.129	14	.
Female	3	ZRH High	7.000	7.000	16.500	18.000	38.000	16.000	9.055	2.864	56.6	1.586	3.904	14	.
Female	4.5	Sham Recovery	17.000	21.000	25.000	30.000	85.000	33.833	25.514	10.416	75.4	2.261	5.284	14	.
Female	4.5	3R4F High Recovery	19.000	26.000	31.500	36.000	50.000	32.333	10.443	4.264	32.3	0.773	1.448	14	.
Female	4.5	ZRH High Recovery	14.000	19.000	26.000	61.000	93.000	38.100	27.767	8.781	72.9	1.179	0.025	14	.

Percentage of Values below LLQ for each Group-Males

Analyte = IL_11

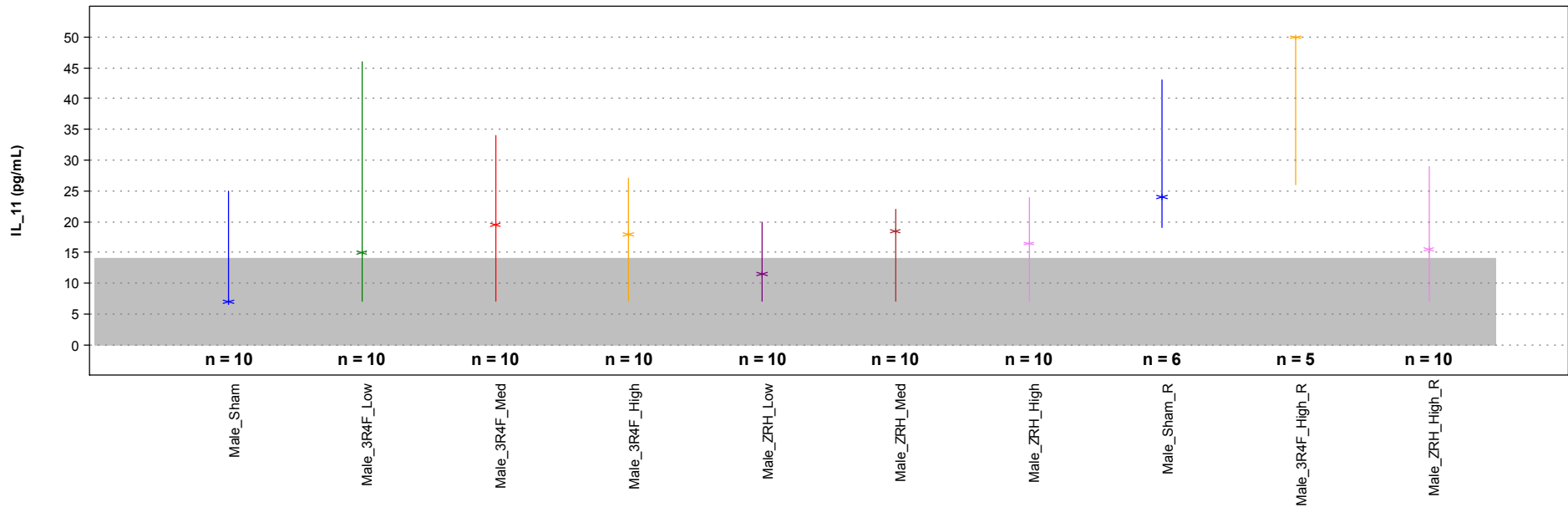
**Plot of Individual Measurements for each Group-Males**

<LOW> values are displayed as 0 / Values above ULQ are displayed as 1.1*ULQ
 Grey zones denote zones below (average) LLQ and above (average) ULQ

**Plot of Descriptive Robust Statistics-Males**

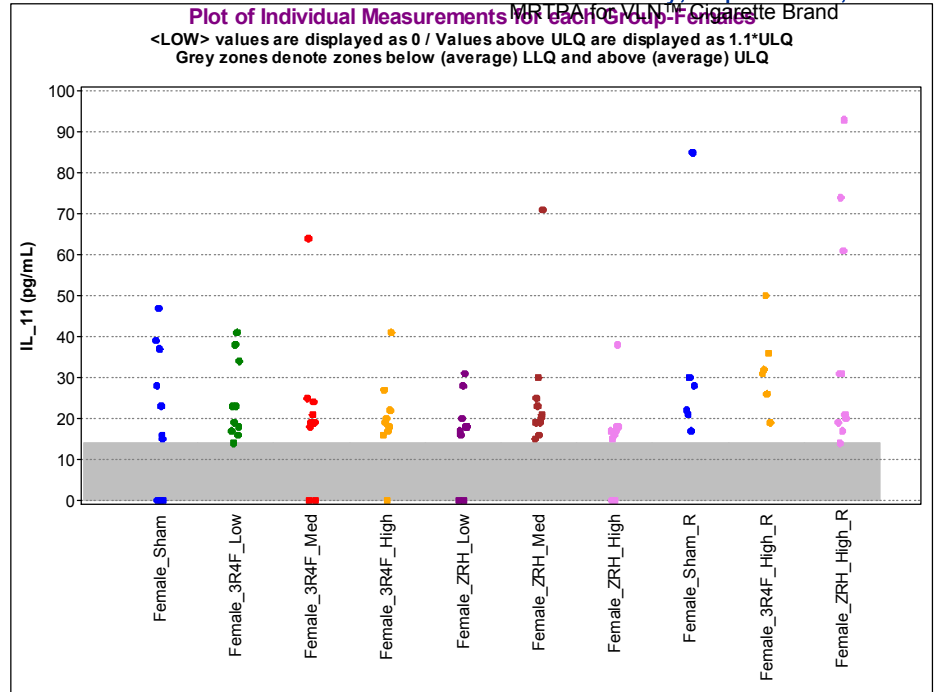
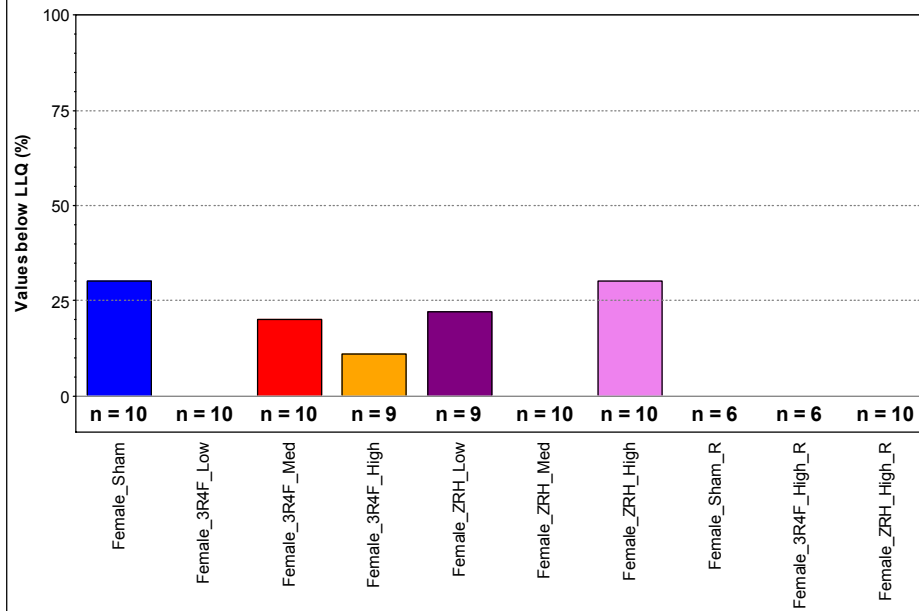
Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



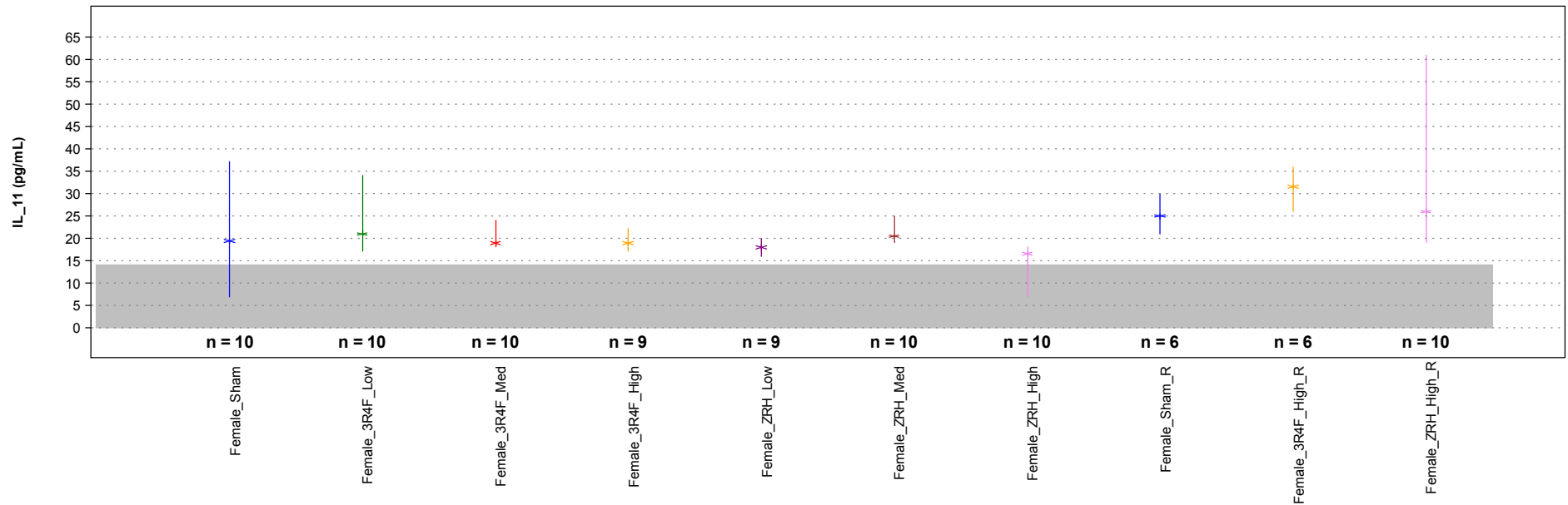
Percentage of Values below LLQ for each Group-Females

Analyte = IL_11

**Plot of Descriptive Robust Statistics-Females**

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = IL_11

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	0.679073
---- Sham vs. 3R4F Medium for Male	0.544497
---- Sham vs. 3R4F High for Male	0.571814
---- Sham vs. ZRH Low for Male	0.901177
---- Sham vs. ZRH Medium for Male	0.361684
---- Sham vs. ZRH High for Male	0.715911
---- ZRH Low vs. 3R4F Medium for Male	0.552083
---- ZRH Medium vs. 3R4F High for Male	0.877189
---- ZRH High vs. 3R4F High for Male	0.754548
---- Sham Recovery vs. 3R4F High Recovery for Male	0.272229
---- Sham Recovery vs. ZRH High Recovery for Male	0.270912
---- Sham vs. Sham Recovery for Male	0.141032
---- 3R4F High vs. 3R4F High Recovery for Male	0.047802
---- ZRH High vs. ZRH High Recovery for Male	0.845014
---- 3R4F High Recovery vs. ZRH High Recovery for Male	0.047802
---- Sham vs. 3R4F Low for Female	0.569441
---- Sham vs. 3R4F Medium for Female	1.000000
---- Sham vs. 3R4F High for Female	0.934610
---- Sham vs. ZRH Low for Female	0.741442
---- Sham vs. ZRH Medium for Female	0.622127
---- Sham vs. ZRH High for Female	0.466064
---- ZRH Low vs. 3R4F Medium for Female	0.410497
---- ZRH Medium vs. 3R4F High for Female	0.461251
---- ZRH High vs. 3R4F High for Female	0.083789
---- Sham Recovery vs. 3R4F High Recovery for Female	0.336668
---- Sham Recovery vs. ZRH High Recovery for Female	1.000000
---- Sham vs. Sham Recovery for Female	0.354777

Unadjusted P-values Obtained by Kruskal-Wallis Test
Analyte = IL_11

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	0.038995
---- ZRH High vs. ZRH High Recovery for Female	0.009884
---- 3R4F High Recovery vs. ZRH High Recovery for Female	0.624206

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 30

Interleukin-12 Subunit p70 (IL-12p70)

Unit = ng/mL

Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = IL₁₂p70

Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	10	0	0	0.027	.
Male	3	3R4F Low	10	10	10	0	0	0.027	.
Male	3	3R4F Medium	10	10	10	0	0	0.027	.
Male	3	3R4F High	10	10	10	0	0	0.027	.
Male	3	ZRH Low	10	10	10	0	0	0.027	.
Male	3	ZRH Medium	10	10	10	0	0	0.027	.
Male	3	ZRH High	10	10	10	0	0	0.027	.
Male	4.5	Sham Recovery	6	6	2	4	0	0.027	.
Male	4.5	3R4F High Recovery	5	5	3	2	0	0.027	.
Male	4.5	ZRH High Recovery	10	10	6	4	0	0.027	.
Female	3	Sham	10	10	10	0	0	0.027	.
Female	3	3R4F Low	10	10	10	0	0	0.027	.
Female	3	3R4F Medium	10	10	9	1	0	0.027	.
Female	3	3R4F High	9	9	9	0	0	0.027	.
Female	3	ZRH Low	9	9	9	0	0	0.027	.
Female	3	ZRH Medium	10	10	10	0	0	0.027	.
Female	3	ZRH High	10	10	10	0	0	0.027	.
Female	4.5	Sham Recovery	6	6	5	1	0	0.027	.
Female	4.5	3R4F High Recovery	6	6	3	3	0	0.027	.
Female	4.5	ZRH High Recovery	10	10	10	0	0	0.027	.

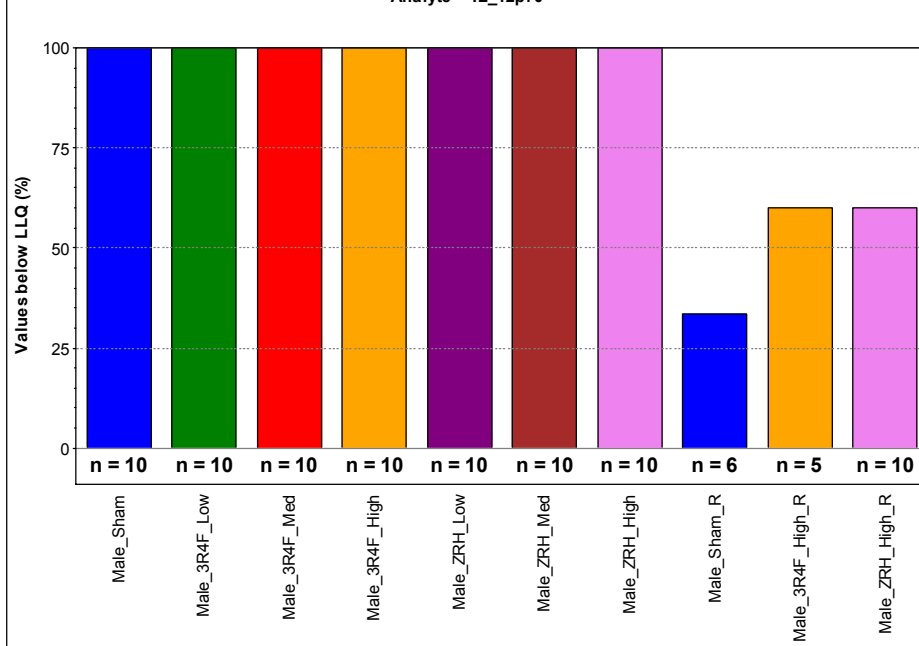
Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = IL₁₂p70

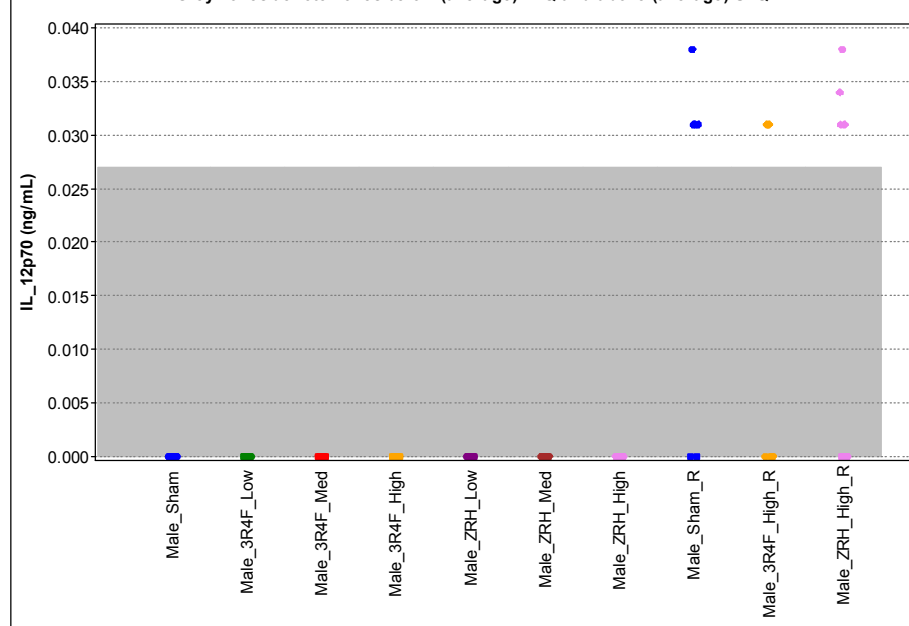
Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	0.014	0.014	0.014	0.014	0.014	0.014	0.000	0.000	0.0	.	.	0.027	.
Male	3	3R4F Low	0.014	0.014	0.014	0.014	0.014	0.014	0.000	0.000	0.0	.	.	0.027	.
Male	3	3R4F Medium	0.014	0.014	0.014	0.014	0.014	0.014	0.000	0.000	0.0	.	.	0.027	.
Male	3	3R4F High	0.014	0.014	0.014	0.014	0.014	0.014	0.000	0.000	0.0	.	.	0.027	.
Male	3	ZRH Low	0.014	0.014	0.014	0.014	0.014	0.014	0.000	0.000	0.0	.	.	0.027	.
Male	3	ZRH Medium	0.014	0.014	0.014	0.014	0.014	0.014	0.000	0.000	0.0	.	.	0.027	.
Male	3	ZRH High	0.014	0.014	0.014	0.014	0.014	0.014	0.000	0.000	0.0	.	.	0.027	.
Male	4.5	Sham Recovery	0.014	0.014	0.031	0.031	0.038	0.026	0.010	0.004	39.1	-0.640	-1.642	0.027	.
Male	4.5	3R4F High Recovery	0.014	0.014	0.014	0.031	0.031	0.021	0.010	0.004	46.8	0.609	-3.333	0.027	.
Male	4.5	ZRH High Recovery	0.014	0.014	0.014	0.031	0.038	0.022	0.011	0.003	48.9	0.610	-1.840	0.027	.
Female	3	Sham	0.014	0.014	0.014	0.014	0.014	0.014	0.000	0.000	0.0	.	.	0.027	.
Female	3	3R4F Low	0.014	0.014	0.014	0.014	0.014	0.014	0.000	0.000	0.0	.	.	0.027	.
Female	3	3R4F Medium	0.014	0.014	0.014	0.014	0.032	0.015	0.006	0.002	38.1	3.162	10.000	0.027	.
Female	3	3R4F High	0.014	0.014	0.014	0.014	0.014	0.014	0.000	0.000	0.0	.	.	0.027	.
Female	3	ZRH Low	0.014	0.014	0.014	0.014	0.014	0.014	0.000	0.000	0.0	.	.	0.027	.
Female	3	ZRH Medium	0.014	0.014	0.014	0.014	0.014	0.014	0.000	0.000	0.0	.	.	0.027	.
Female	3	ZRH High	0.014	0.014	0.014	0.014	0.014	0.014	0.000	0.000	0.0	.	.	0.027	.
Female	4.5	Sham Recovery	0.014	0.014	0.014	0.014	0.031	0.016	0.007	0.003	43.5	2.449	6.000	0.027	.
Female	4.5	3R4F High Recovery	0.014	0.014	0.022	0.031	0.038	0.023	0.011	0.005	47.7	0.226	-2.601	0.027	.
Female	4.5	ZRH High Recovery	0.014	0.014	0.014	0.014	0.014	0.014	0.000	0.000	0.0	.	.	0.027	.

Percentage of Values below LLQ for each Group-Males

Analyte = IL_12p70

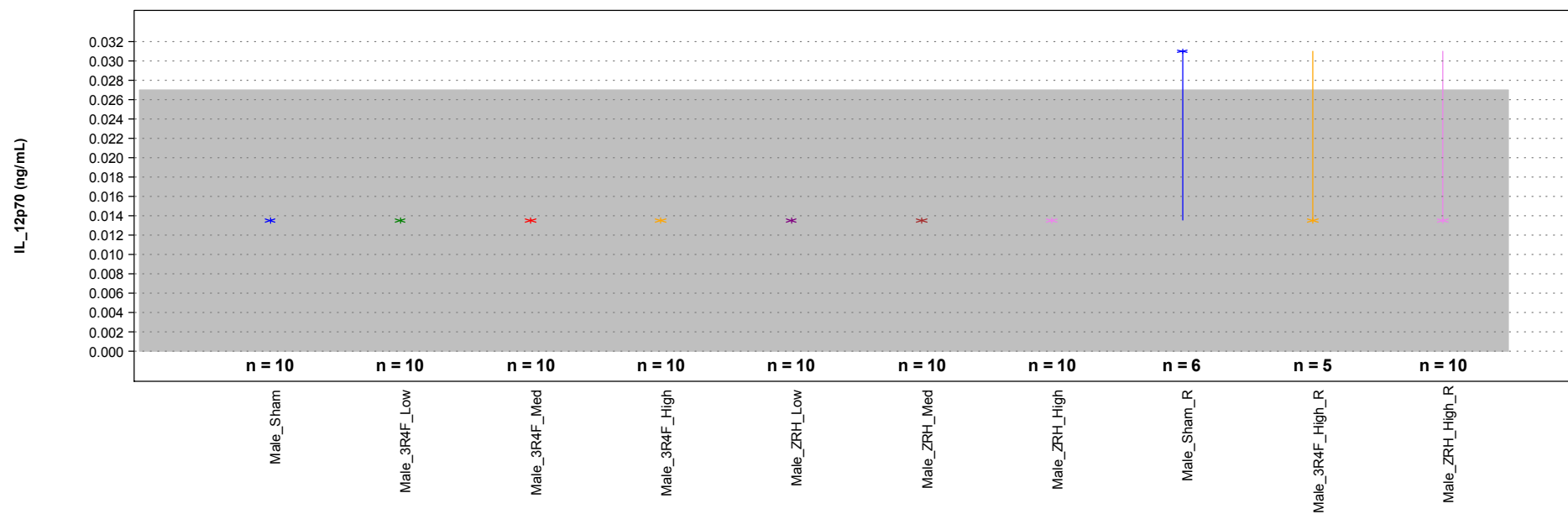
**Plot of Individual Measurements for Each Group-Males**

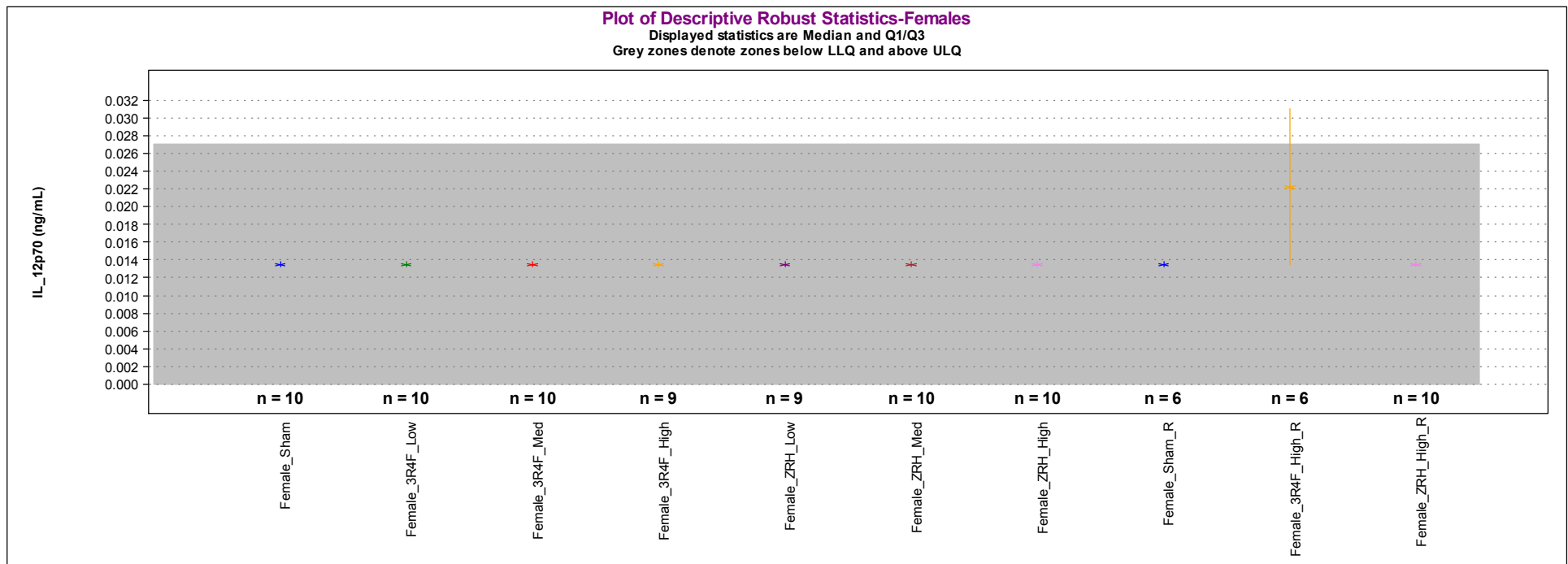
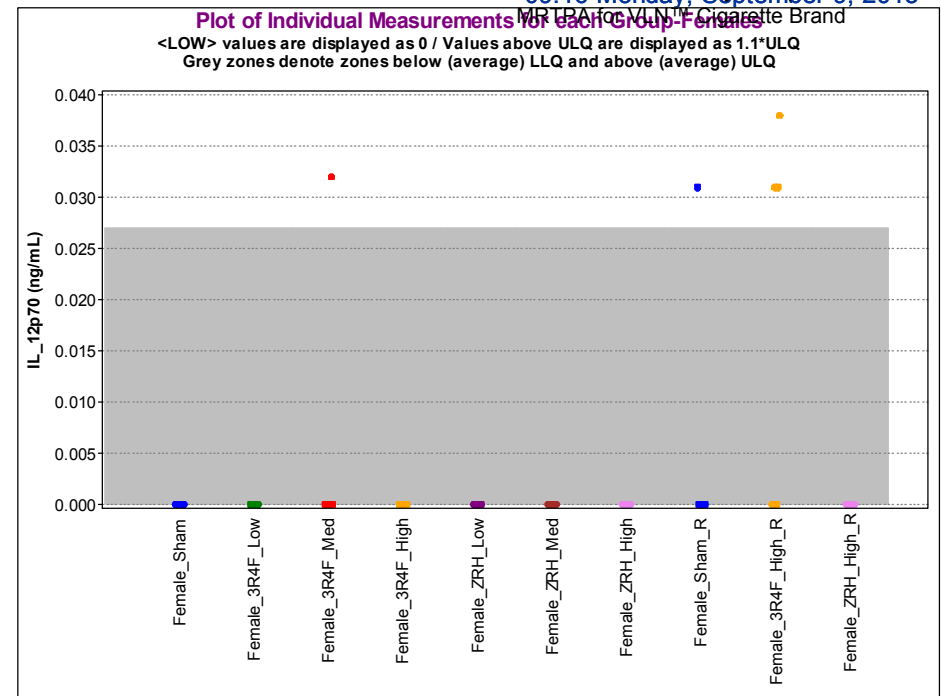
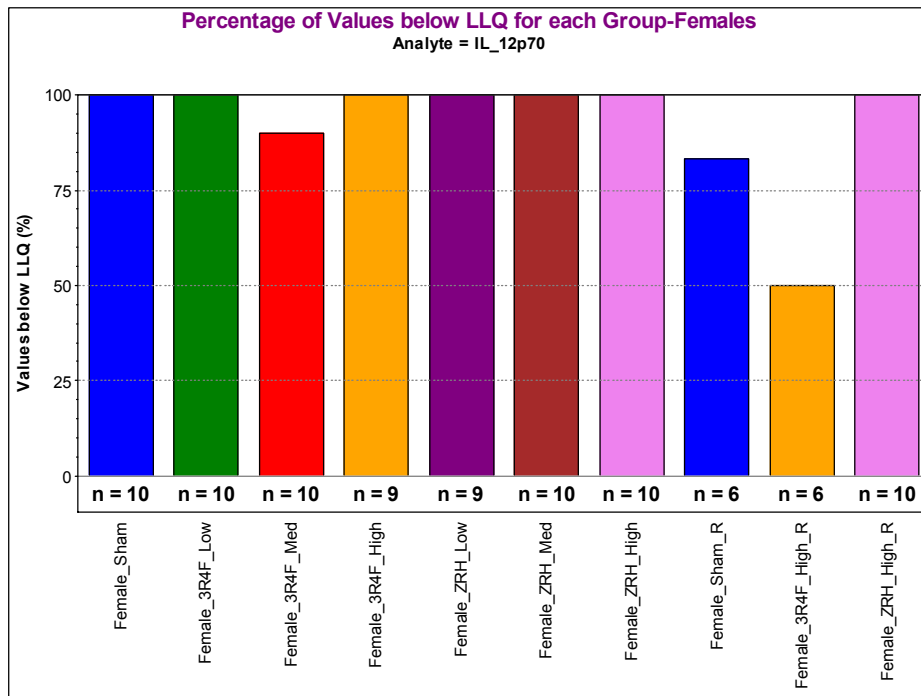
<LOW> values are displayed as 0 / Values above ULQ are displayed as 1.1*ULQ
 Grey zones denote zones below (average) LLQ and above (average) ULQ

**Plot of Descriptive Robust Statistics-Males**

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ





Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = IL₁₂p70

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	1.000000
---- Sham vs. 3R4F Medium for Male	1.000000
---- Sham vs. 3R4F High for Male	1.000000
---- Sham vs. ZRH Low for Male	1.000000
---- Sham vs. ZRH Medium for Male	1.000000
---- Sham vs. ZRH High for Male	1.000000
---- ZRH Low vs. 3R4F Medium for Male	1.000000
---- ZRH Medium vs. 3R4F High for Male	1.000000
---- ZRH High vs. 3R4F High for Male	1.000000
---- Sham Recovery vs. 3R4F High Recovery for Male	0.312871
---- Sham Recovery vs. ZRH High Recovery for Male	0.443261
---- Sham vs. Sham Recovery for Male	0.004177
---- 3R4F High vs. 3R4F High Recovery for Male	0.037940
---- ZRH High vs. ZRH High Recovery for Male	0.030442
---- 3R4F High Recovery vs. ZRH High Recovery for Male	0.779835
---- Sham vs. 3R4F Low for Female	1.000000
---- Sham vs. 3R4F Medium for Female	0.317311
---- Sham vs. 3R4F High for Female	1.000000
---- Sham vs. ZRH Low for Female	1.000000
---- Sham vs. ZRH Medium for Female	1.000000
---- Sham vs. ZRH High for Female	1.000000
---- ZRH Low vs. 3R4F Medium for Female	0.342782
---- ZRH Medium vs. 3R4F High for Female	1.000000
---- ZRH High vs. 3R4F High for Female	1.000000
---- Sham Recovery vs. 3R4F High Recovery for Female	0.210962
---- Sham Recovery vs. ZRH High Recovery for Female	0.196706
---- Sham vs. Sham Recovery for Female	0.196706

Unadjusted P-values Obtained by Kruskal-Wallis Test
Analyte = IL_12p70

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	0.022687
---- ZRH High vs. ZRH High Recovery for Female	1.000000
---- 3R4F High Recovery vs. ZRH High Recovery for Female	0.016827

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 31

Interleukin-17A (IL-17A)

Unit = ng/mL

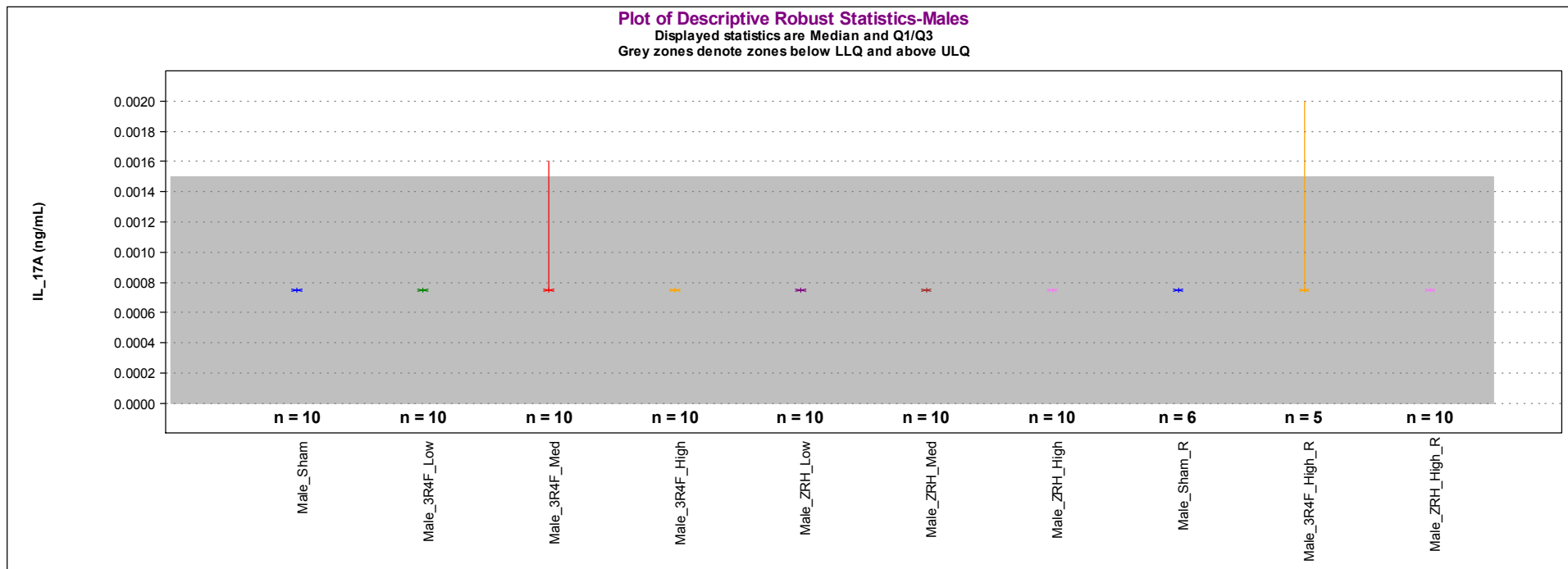
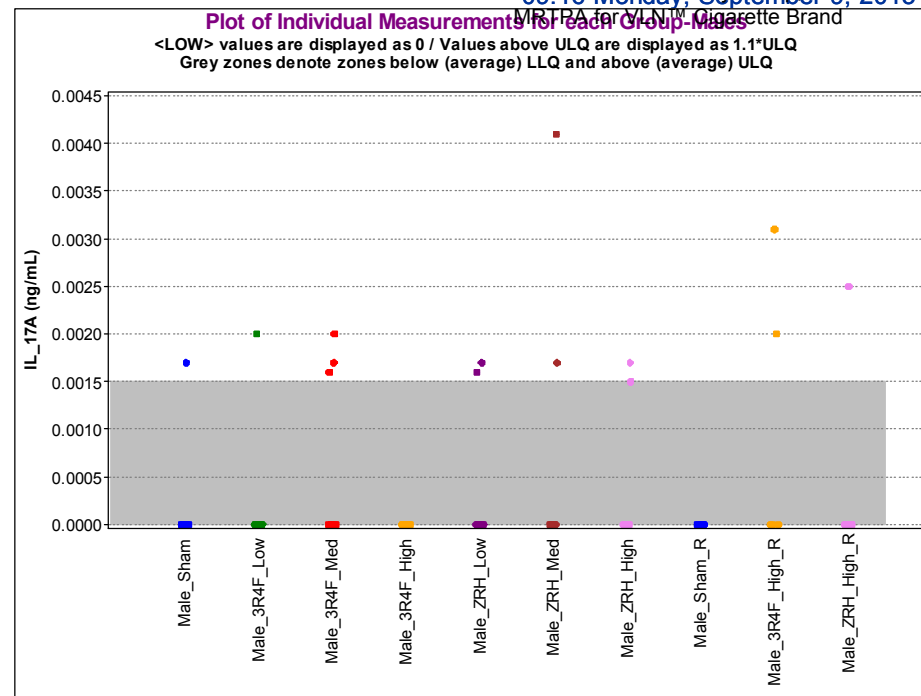
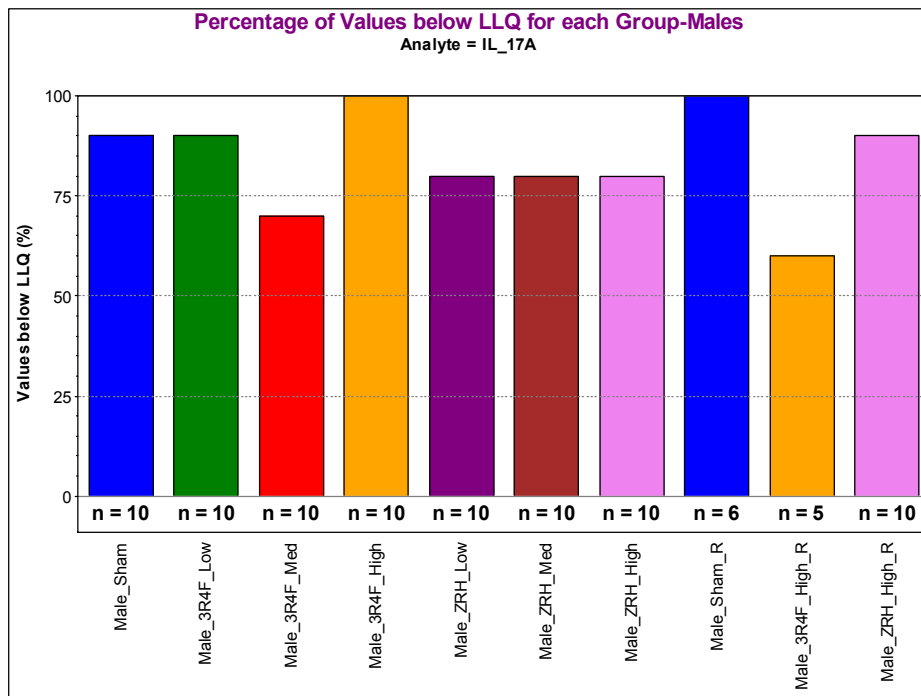
Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = IL₁₇A

Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	9	1	0	0.002	.
Male	3	3R4F Low	10	10	9	1	0	0.002	.
Male	3	3R4F Medium	10	10	7	3	0	0.002	.
Male	3	3R4F High	10	10	10	0	0	0.002	.
Male	3	ZRH Low	10	10	8	2	0	0.002	.
Male	3	ZRH Medium	10	10	8	2	0	0.002	.
Male	3	ZRH High	10	10	8	2	0	0.002	.
Male	4.5	Sham Recovery	6	6	6	0	0	0.002	.
Male	4.5	3R4F High Recovery	5	5	3	2	0	0.002	.
Male	4.5	ZRH High Recovery	10	10	9	1	0	0.002	.
Female	3	Sham	10	10	10	0	0	0.002	.
Female	3	3R4F Low	10	10	9	1	0	0.002	.
Female	3	3R4F Medium	10	10	8	2	0	0.002	.
Female	3	3R4F High	9	9	9	0	0	0.002	.
Female	3	ZRH Low	9	9	9	0	0	0.002	.
Female	3	ZRH Medium	10	10	8	2	0	0.002	.
Female	3	ZRH High	10	10	10	0	0	0.002	.
Female	4.5	Sham Recovery	6	6	4	2	0	0.002	.
Female	4.5	3R4F High Recovery	6	6	5	1	0	0.002	.
Female	4.5	ZRH High Recovery	10	10	7	3	0	0.002	.

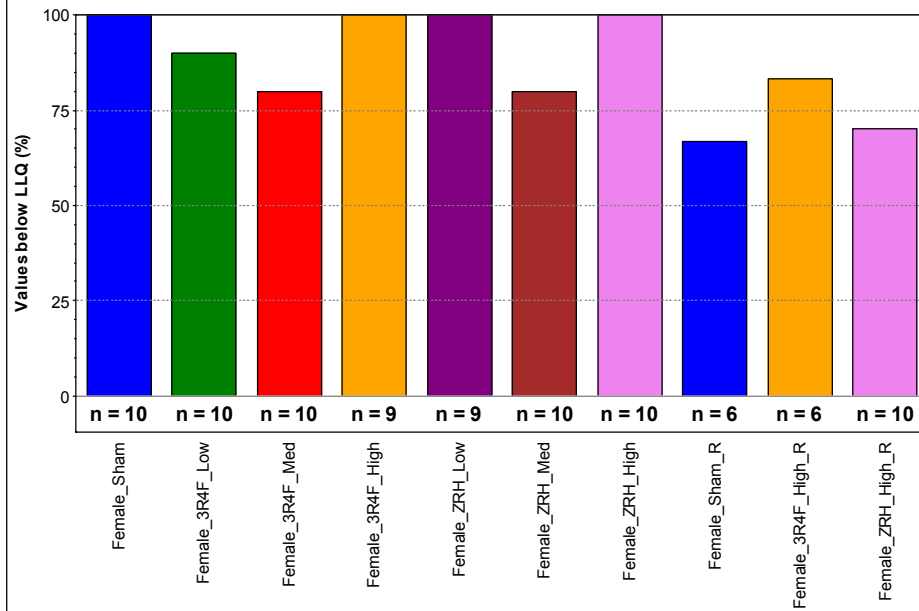
Descriptive Statistics by Exposure Duration and Treatment Type**Analyte = IL_17A**

Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	0.001	0.001	0.001	0.001	0.002	0.001	0.000	0.000	35.6	3.162	10.000	0.002	.
Male	3	3R4F Low	0.001	0.001	0.001	0.001	0.002	0.001	0.000	0.000	45.2	3.162	10.000	0.002	.
Male	3	3R4F Medium	0.001	0.001	0.001	0.002	0.002	0.001	0.001	0.000	47.5	1.189	-0.455	0.002	.
Male	3	3R4F High	0.001	0.001	0.001	0.001	0.001	0.001	0.000	0.000	0.0	.	.	0.002	.
Male	3	ZRH Low	0.001	0.001	0.001	0.001	0.002	0.001	0.000	0.000	40.9	1.796	1.525	0.002	.
Male	3	ZRH Medium	0.001	0.001	0.001	0.001	0.004	0.001	0.001	0.000	90.6	2.778	7.890	0.002	.
Male	3	ZRH High	0.001	0.001	0.001	0.001	0.002	0.001	0.000	0.000	39.3	1.854	1.924	0.002	.
Male	4.5	Sham Recovery	0.001	0.001	0.001	0.001	0.001	0.001	0.000	0.000	0.0	.	.	0.002	.
Male	4.5	3R4F High Recovery	0.001	0.001	0.001	0.002	0.003	0.001	0.001	0.000	72.1	1.176	-0.129	0.002	.
Male	4.5	ZRH High Recovery	0.001	0.001	0.001	0.001	0.003	0.001	0.001	0.000	59.8	3.162	10.000	0.002	.
Female	3	Sham	0.001	0.001	0.001	0.001	0.001	0.001	0.000	0.000	0.0	.	.	0.002	.
Female	3	3R4F Low	0.001	0.001	0.001	0.001	0.002	0.001	0.000	0.000	45.2	3.162	10.000	0.002	.
Female	3	3R4F Medium	0.001	0.001	0.001	0.001	0.002	0.001	0.000	0.000	42.6	1.779	1.406	0.002	.
Female	3	3R4F High	0.001	0.001	0.001	0.001	0.001	0.001	0.000	0.000	0.0	.	.	0.002	.
Female	3	ZRH Low	0.001	0.001	0.001	0.001	0.001	0.001	0.000	0.000	0.0	.	.	0.002	.
Female	3	ZRH Medium	0.001	0.001	0.001	0.001	0.002	0.001	0.000	0.000	39.0	1.779	1.406	0.002	.
Female	3	ZRH High	0.001	0.001	0.001	0.001	0.001	0.001	0.000	0.000	0.0	.	.	0.002	.
Female	4.5	Sham Recovery	0.001	0.001	0.001	0.002	0.002	0.001	0.001	0.000	50.6	1.186	-0.578	0.002	.
Female	4.5	3R4F High Recovery	0.001	0.001	0.001	0.001	0.003	0.001	0.001	0.000	68.6	2.449	6.000	0.002	.
Female	4.5	ZRH High Recovery	0.001	0.001	0.001	0.002	0.004	0.001	0.001	0.000	77.1	2.168	4.729	0.002	.

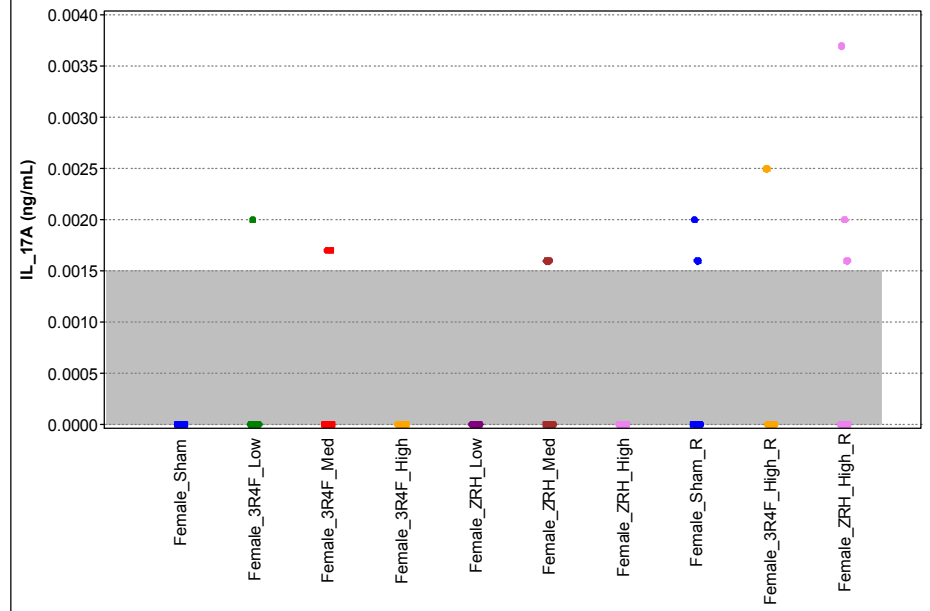


Percentage of Values below LLQ for each Group-Females

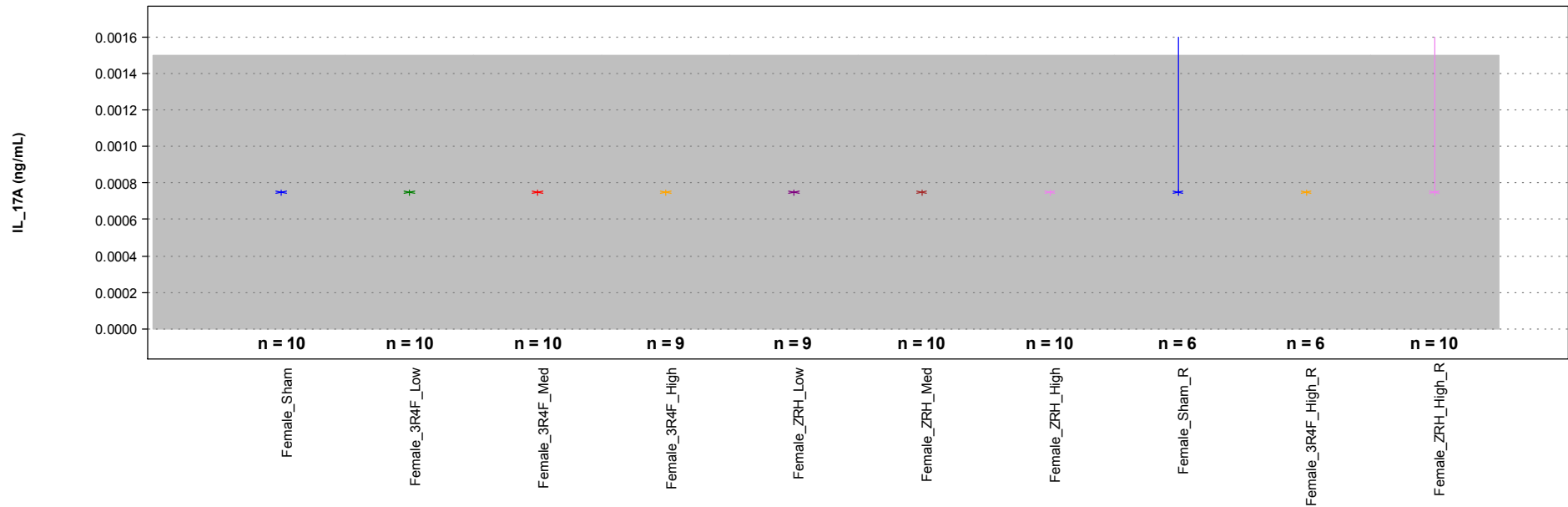
Analyte = IL_17A

**Plot of Individual Measurements for IL_17A - Females**

<LOW> values are displayed as 0 / Values above ULQ are displayed as 1.1*ULQ
 Grey zones denote zones below (average) LLQ and above (average) ULQ

**Plot of Descriptive Robust Statistics-Females**

Displayed statistics are Median and Q1/Q3
 Grey zones denote zones below LLQ and above ULQ



Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = IL_17A

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	0.942166
---- Sham vs. 3R4F Medium for Male	0.279189
---- Sham vs. 3R4F High for Male	0.317311
---- Sham vs. ZRH Low for Male	0.583882
---- Sham vs. ZRH Medium for Male	0.503216
---- Sham vs. ZRH High for Male	0.583882
---- ZRH Low vs. 3R4F Medium for Male	0.550596
---- ZRH Medium vs. 3R4F High for Male	0.146793
---- ZRH High vs. 3R4F High for Male	0.146793
---- Sham Recovery vs. 3R4F High Recovery for Male	0.104204
---- Sham Recovery vs. ZRH High Recovery for Male	0.438578
---- Sham vs. Sham Recovery for Male	0.438578
---- 3R4F High vs. 3R4F High Recovery for Male	0.038434
---- ZRH High vs. ZRH High Recovery for Male	0.626690
---- 3R4F High Recovery vs. ZRH High Recovery for Male	0.189121
---- Sham vs. 3R4F Low for Female	0.317311
---- Sham vs. 3R4F Medium for Female	0.146233
---- Sham vs. 3R4F High for Female	1.000000
---- Sham vs. ZRH Low for Female	1.000000
---- Sham vs. ZRH Medium for Female	0.146233
---- Sham vs. ZRH High for Female	1.000000
---- ZRH Low vs. 3R4F Medium for Female	0.167421
---- ZRH Medium vs. 3R4F High for Female	0.167421
---- ZRH High vs. 3R4F High for Female	1.000000
---- Sham Recovery vs. 3R4F High Recovery for Female	0.674219
---- Sham Recovery vs. ZRH High Recovery for Female	1.000000
---- Sham vs. Sham Recovery for Female	0.059346

Unadjusted P-values Obtained by Kruskal-Wallis Test
Analyte = IL_17A

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	0.220671
---- ZRH High vs. ZRH High Recovery for Female	0.068157
---- 3R4F High Recovery vs. ZRH High Recovery for Female	0.617970

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 32

Interleukin-18 (IL-18)

Unit = ng/mL

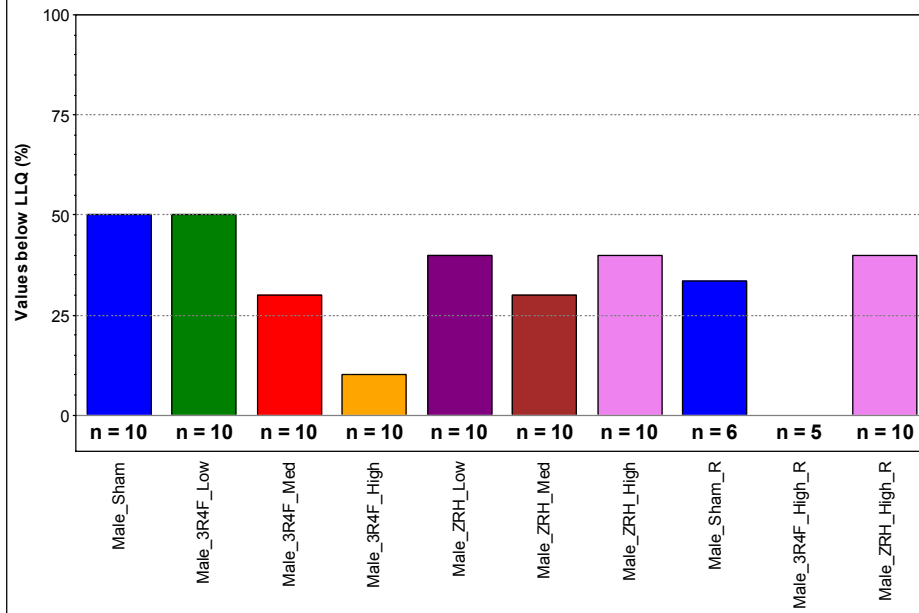
Descriptive Statistics by Exposure Duration and Treatment Type**Analyte = IL₁₈**

Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	5	5	0	1.6	.
Male	3	3R4F Low	10	10	5	5	0	1.6	.
Male	3	3R4F Medium	10	10	3	7	0	1.6	.
Male	3	3R4F High	10	10	1	9	0	1.6	.
Male	3	ZRH Low	10	10	4	6	0	1.6	.
Male	3	ZRH Medium	10	10	3	7	0	1.6	.
Male	3	ZRH High	10	10	4	6	0	1.6	.
Male	4.5	Sham Recovery	6	6	2	4	0	1.6	.
Male	4.5	3R4F High Recovery	5	5	0	5	0	1.6	.
Male	4.5	ZRH High Recovery	10	10	4	6	0	1.6	.
Female	3	Sham	10	10	0	10	0	1.6	.
Female	3	3R4F Low	10	10	2	8	0	1.6	.
Female	3	3R4F Medium	10	10	2	8	0	1.6	.
Female	3	3R4F High	9	9	2	7	0	1.6	.
Female	3	ZRH Low	9	9	2	7	0	1.6	.
Female	3	ZRH Medium	10	10	3	7	0	1.6	.
Female	3	ZRH High	10	10	2	8	0	1.6	.
Female	4.5	Sham Recovery	6	6	0	6	0	1.6	.
Female	4.5	3R4F High Recovery	6	6	1	5	0	1.6	.
Female	4.5	ZRH High Recovery	10	10	5	5	0	1.6	.

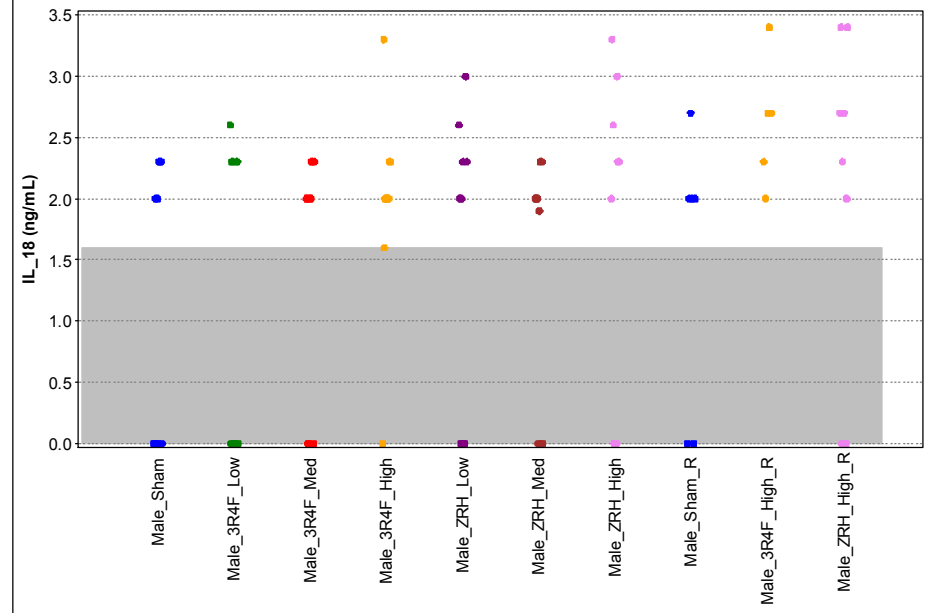
Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = IL₁₈

Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	0.800	0.800	1.400	2.300	2.300	1.490	0.736	0.233	49.4	0.076	-2.430	1.6	.
Male	3	3R4F Low	0.800	0.800	1.550	2.300	2.600	1.580	0.827	0.262	52.3	0.045	-2.469	1.6	.
Male	3	3R4F Medium	0.800	0.800	2.000	2.300	2.300	1.730	0.655	0.207	37.9	-0.879	-1.277	1.6	.
Male	3	3R4F High	0.800	2.000	2.000	2.300	3.300	2.030	0.620	0.196	30.5	0.086	2.944	1.6	.
Male	3	ZRH Low	0.800	0.800	2.000	2.300	3.000	1.740	0.858	0.271	49.3	-0.066	-1.762	1.6	.
Male	3	ZRH Medium	0.800	0.800	2.000	2.000	2.300	1.690	0.628	0.199	37.2	-0.860	-1.254	1.6	.
Male	3	ZRH High	0.800	0.800	2.150	2.600	3.300	1.870	0.990	0.313	52.9	0.002	-1.747	1.6	.
Male	4.5	Sham Recovery	0.800	0.800	2.000	2.000	2.700	1.717	0.760	0.310	44.3	-0.356	-1.286	1.6	.
Male	4.5	3R4F High Recovery	2.000	2.300	2.700	2.700	3.400	2.620	0.526	0.235	20.1	0.584	0.610	1.6	.
Male	4.5	ZRH High Recovery	0.800	0.800	2.150	2.700	3.400	1.970	1.092	0.345	55.5	0.027	-1.820	1.6	.
Female	3	Sham	1.600	1.600	2.100	2.100	2.600	2.040	0.353	0.112	17.3	0.058	-0.762	1.6	.
Female	3	3R4F Low	0.800	1.600	1.600	2.100	3.300	1.800	0.751	0.238	41.7	0.570	0.679	1.6	.
Female	3	3R4F Medium	0.800	1.600	1.600	2.100	2.500	1.680	0.555	0.176	33.1	-0.479	-0.336	1.6	.
Female	3	3R4F High	0.800	1.600	1.600	2.300	3.300	1.800	0.814	0.271	45.2	0.590	0.031	1.6	.
Female	3	ZRH Low	0.800	1.600	1.900	2.100	2.100	1.678	0.538	0.179	32.1	-1.075	-0.361	1.6	.
Female	3	ZRH Medium	0.800	0.800	1.600	2.500	2.600	1.720	0.748	0.237	43.5	-0.131	-1.758	1.6	.
Female	3	ZRH High	0.800	1.600	1.850	2.600	3.100	1.890	0.759	0.240	40.2	-0.050	-0.728	1.6	.
Female	4.5	Sham Recovery	2.000	2.000	2.350	2.900	3.400	2.500	0.593	0.242	23.7	0.612	-1.330	1.6	.
Female	4.5	3R4F High Recovery	0.800	2.000	2.000	2.000	2.700	1.917	0.615	0.251	32.1	-1.176	3.230	1.6	.
Female	4.5	ZRH High Recovery	0.800	0.800	1.550	2.700	3.100	1.750	1.023	0.324	58.5	0.148	-2.276	1.6	.

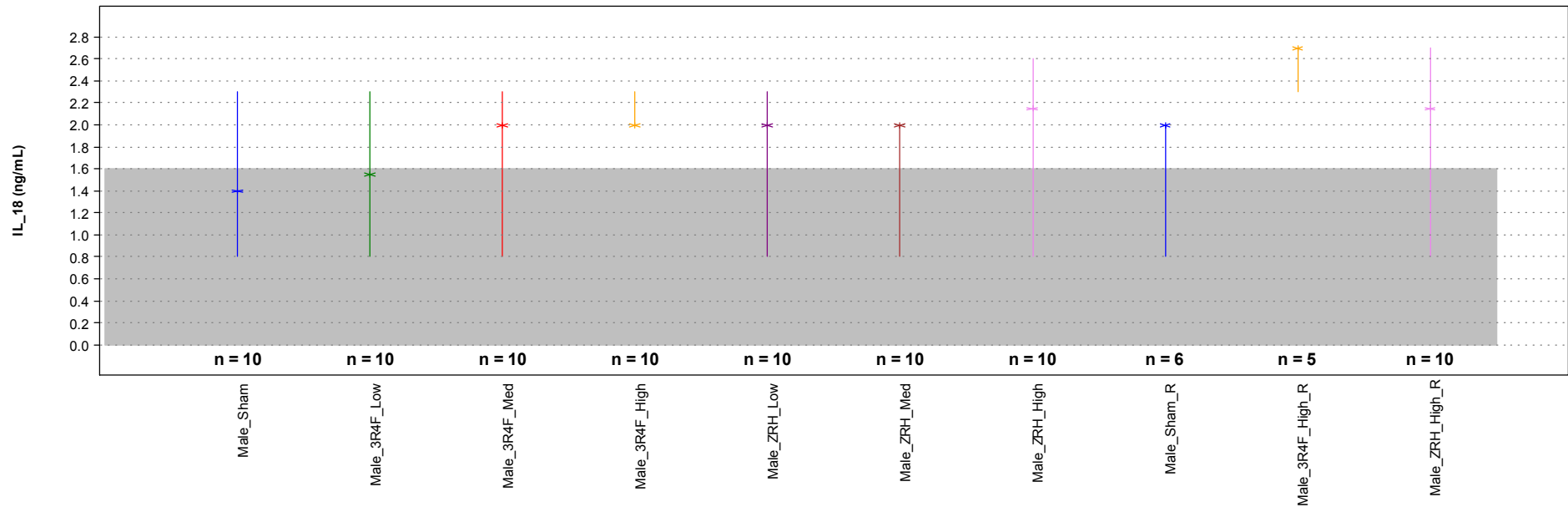
Percentage of Values below LLQ for each Group-MalesAnalyte = IL₁₈**Plot of Individual Measurements for Each Group-Males**

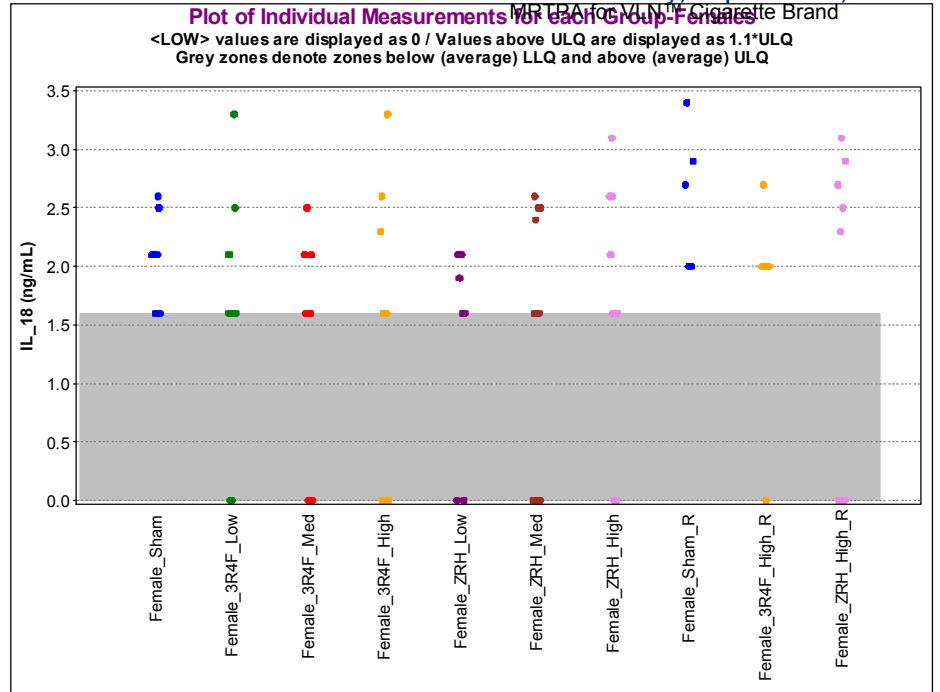
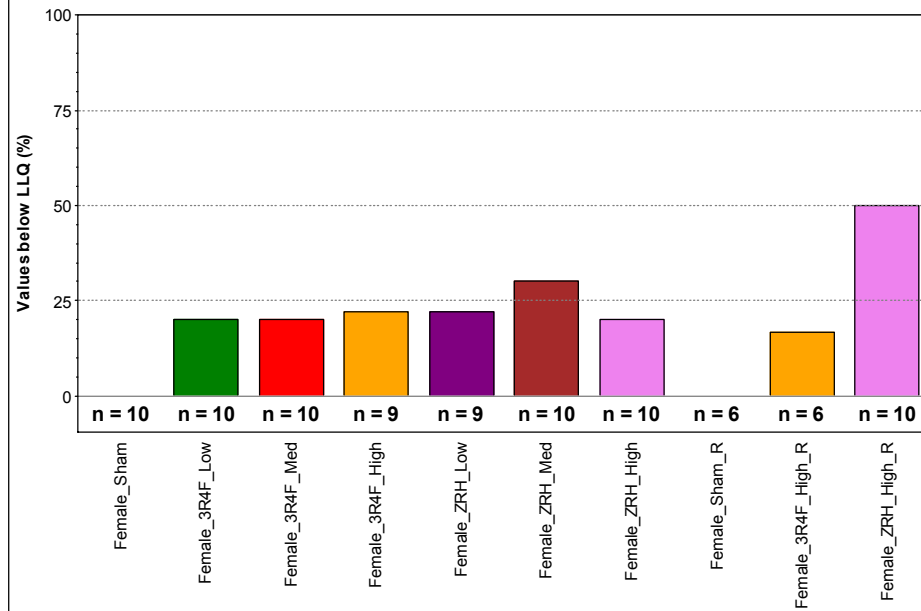
<LOW> values are displayed as 0 / Values above ULQ are displayed as 1.1*ULQ
 Grey zones denote zones below (average) LLQ and above (average) ULQ

**Plot of Descriptive Robust Statistics-Males**

Displayed statistics are Median and Q1/Q3

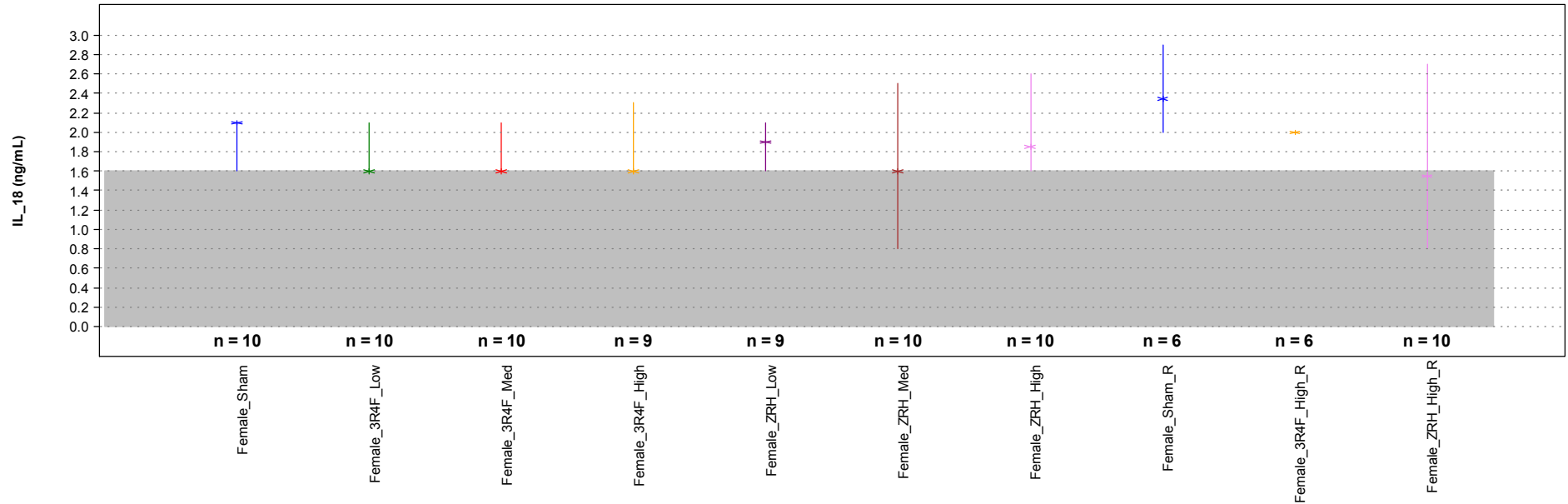
Grey zones denote zones below LLQ and above ULQ



Percentage of Values below LLQ for each Group-FemalesAnalyte = IL₁₈**Plot of Descriptive Robust Statistics-Females**

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = IL₁₈

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	0.590348
---- Sham vs. 3R4F Medium for Male	0.573618
---- Sham vs. 3R4F High for Male	0.252245
---- Sham vs. ZRH Low for Male	0.470120
---- Sham vs. ZRH Medium for Male	0.779793
---- Sham vs. ZRH High for Male	0.298035
---- ZRH Low vs. 3R4F Medium for Male	0.812751
---- ZRH Medium vs. 3R4F High for Male	0.317819
---- ZRH High vs. 3R4F High for Male	1.000000
---- Sham Recovery vs. 3R4F High Recovery for Male	0.047042
---- Sham Recovery vs. ZRH High Recovery for Male	0.535403
---- Sham vs. Sham Recovery for Male	0.729034
---- 3R4F High vs. 3R4F High Recovery for Male	0.048837
---- ZRH High vs. ZRH High Recovery for Male	0.724509
---- 3R4F High Recovery vs. ZRH High Recovery for Male	0.315685
---- Sham vs. 3R4F Low for Female	0.251660
---- Sham vs. 3R4F Medium for Female	0.128591
---- Sham vs. 3R4F High for Female	0.330632
---- Sham vs. ZRH Low for Female	0.138136
---- Sham vs. ZRH Medium for Female	0.394058
---- Sham vs. ZRH High for Female	0.666010
---- ZRH Low vs. 3R4F Medium for Female	0.931843
---- ZRH Medium vs. 3R4F High for Female	0.899026
---- ZRH High vs. 3R4F High for Female	0.735913
---- Sham Recovery vs. 3R4F High Recovery for Female	0.128240
---- Sham Recovery vs. ZRH High Recovery for Female	0.223755
---- Sham vs. Sham Recovery for Female	0.318800

Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = IL_18

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	0.469825
---- ZRH High vs. ZRH High Recovery for Female	0.786335
---- 3R4F High Recovery vs. ZRH High Recovery for Female	1.000000

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 20

Interleukin-1 alpha (IL-1 alpha)

Unit = pg/mL

Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = IL_1_alpha

Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	9	1	0	26	.
Male	3	3R4F Low	10	10	9	1	0	26	.
Male	3	3R4F Medium	10	10	9	1	0	26	.
Male	3	3R4F High	10	10	8	2	0	26	.
Male	3	ZRH Low	10	10	10	0	0	26	.
Male	3	ZRH Medium	10	10	10	0	0	26	.
Male	3	ZRH High	10	10	9	1	0	26	.
Male	4.5	Sham Recovery	6	6	6	0	0	26	.
Male	4.5	3R4F High Recovery	5	5	3	2	0	26	.
Male	4.5	ZRH High Recovery	10	10	9	1	0	26	.
Female	3	Sham	10	10	9	1	0	26	.
Female	3	3R4F Low	10	10	8	2	0	26	.
Female	3	3R4F Medium	10	10	7	3	0	26	.
Female	3	3R4F High	9	9	7	2	0	26	.
Female	3	ZRH Low	9	9	8	1	0	26	.
Female	3	ZRH Medium	10	10	9	1	0	26	.
Female	3	ZRH High	10	10	8	2	0	26	.
Female	4.5	Sham Recovery	6	6	5	1	0	26	.
Female	4.5	3R4F High Recovery	6	6	6	0	0	26	.
Female	4.5	ZRH High Recovery	10	10	10	0	0	26	.

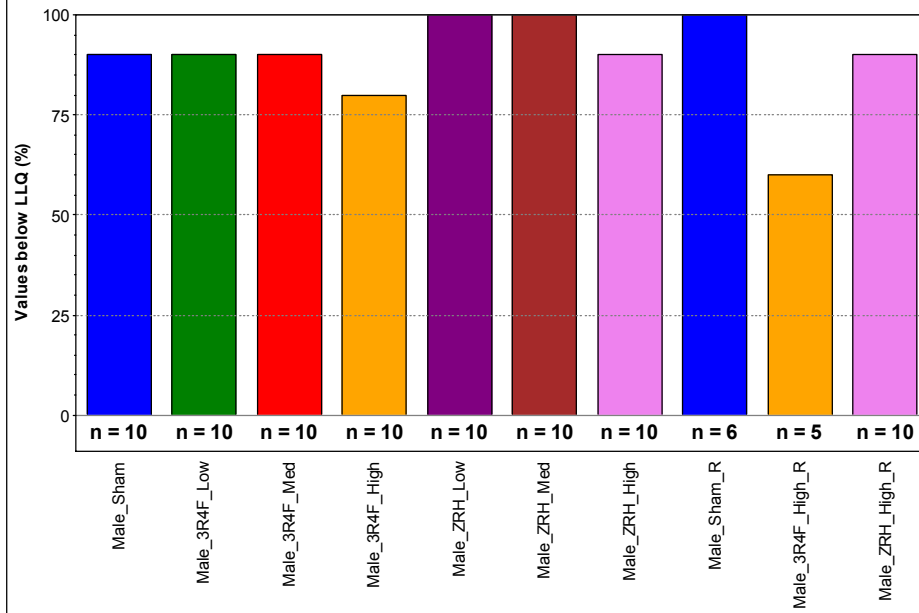
Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = IL_1_alpha

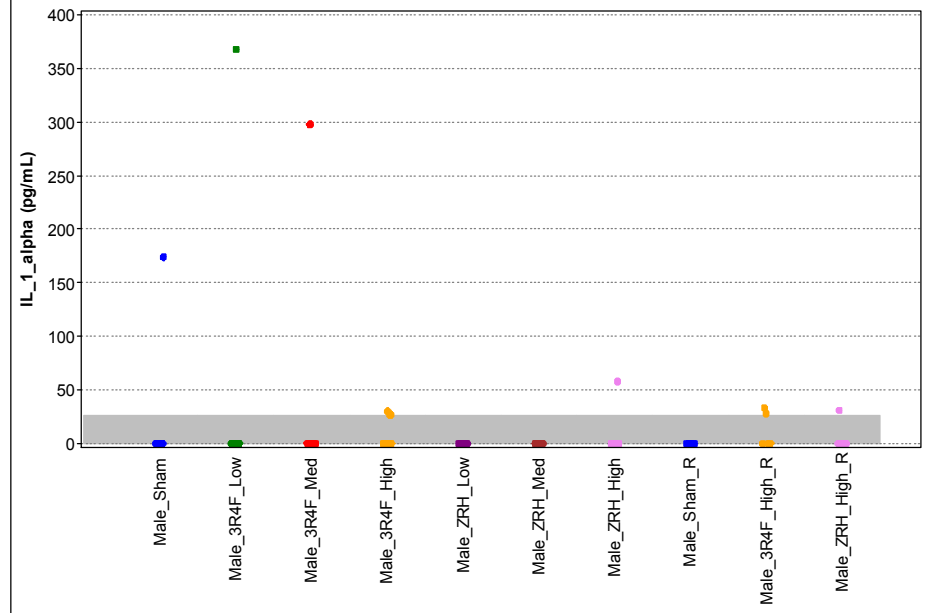
Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	13.000	13.000	13.000	13.000	174.000	29.100	50.913	16.100	175.0	3.162	10.000	26	.
Male	3	3R4F Low	13.000	13.000	13.000	13.000	368.000	48.500	112.261	35.500	231.5	3.162	10.000	26	.
Male	3	3R4F Medium	13.000	13.000	13.000	13.000	298.000	41.500	90.125	28.500	217.2	3.162	10.000	26	.
Male	3	3R4F High	13.000	13.000	13.000	13.000	30.000	16.100	6.574	2.079	40.8	1.830	1.761	26	.
Male	3	ZRH Low	13.000	13.000	13.000	13.000	13.000	13.000	0.000	0.000	0.0	.	.	26	.
Male	3	ZRH Medium	13.000	13.000	13.000	13.000	13.000	13.000	0.000	0.000	0.0	.	.	26	.
Male	3	ZRH High	13.000	13.000	13.000	13.000	58.000	17.500	14.230	4.500	81.3	3.162	10.000	26	.
Male	4.5	Sham Recovery	13.000	13.000	13.000	13.000	13.000	13.000	0.000	0.000	0.0	.	.	26	.
Male	4.5	3R4F High Recovery	13.000	13.000	13.000	28.000	33.000	20.000	9.747	4.359	48.7	0.756	-2.479	26	.
Male	4.5	ZRH High Recovery	13.000	13.000	13.000	13.000	31.000	14.800	5.692	1.800	38.5	3.162	10.000	26	.
Female	3	Sham	13.000	13.000	13.000	13.000	67.000	18.400	17.076	5.400	92.8	3.162	10.000	26	.
Female	3	3R4F Low	13.000	13.000	13.000	13.000	34.000	16.500	7.561	2.391	45.8	1.984	2.816	26	.
Female	3	3R4F Medium	13.000	13.000	13.000	30.000	520.000	67.100	159.290	50.372	237.4	3.151	9.946	26	.
Female	3	3R4F High	13.000	13.000	13.000	13.000	46.000	20.000	13.910	4.637	69.6	1.633	0.820	26	.
Female	3	ZRH Low	13.000	13.000	13.000	13.000	30.000	14.889	5.667	1.889	38.1	3.000	9.000	26	.
Female	3	ZRH Medium	13.000	13.000	13.000	13.000	54.000	17.100	12.965	4.100	75.8	3.162	10.000	26	.
Female	3	ZRH High	13.000	13.000	13.000	13.000	28.000	15.900	6.118	1.935	38.5	1.785	1.452	26	.
Female	4.5	Sham Recovery	13.000	13.000	13.000	13.000	28.000	15.500	6.124	2.500	39.5	2.449	6.000	26	.
Female	4.5	3R4F High Recovery	13.000	13.000	13.000	13.000	13.000	13.000	0.000	0.000	0.0	.	.	26	.
Female	4.5	ZRH High Recovery	13.000	13.000	13.000	13.000	13.000	13.000	0.000	0.000	0.0	.	.	26	.

Percentage of Values below LLQ for each Group-Males

Analyte = IL_1_alpha

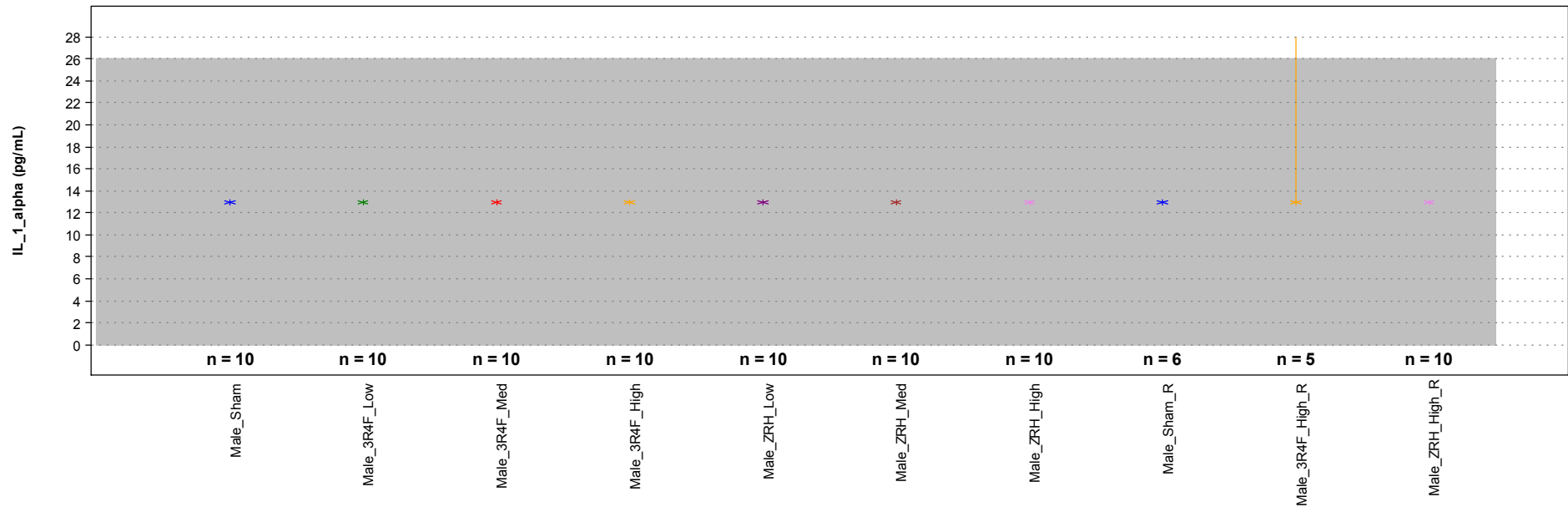
**Plot of Individual Measurements for Each Group-Males**

<LOW> values are displayed as 0 / Values above ULQ are displayed as 1.1*ULQ
 Grey zones denote zones below (average) LLQ and above (average) ULQ

**Plot of Descriptive Robust Statistics-Males**

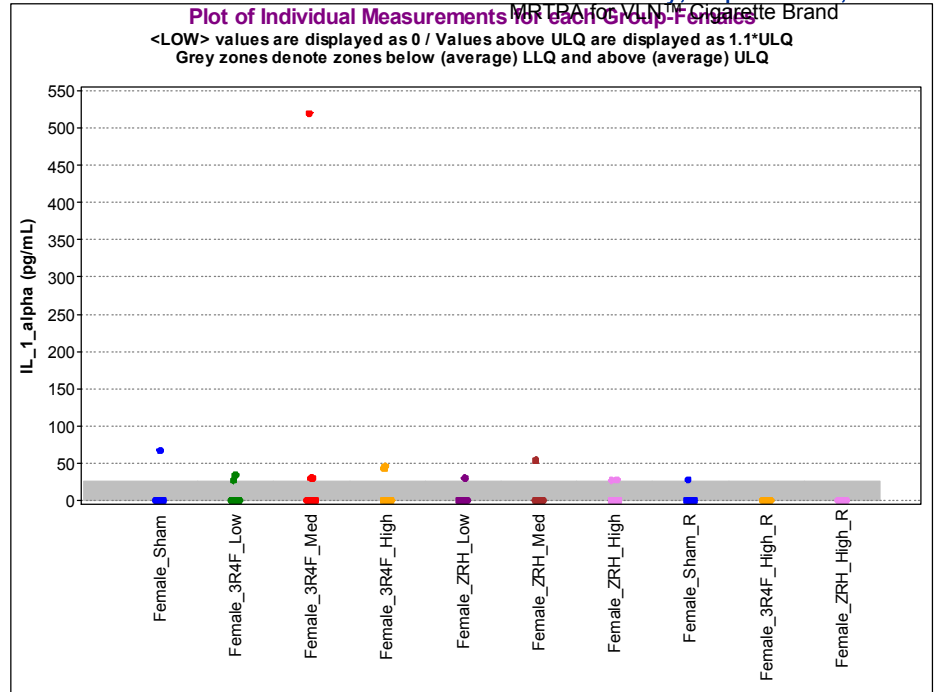
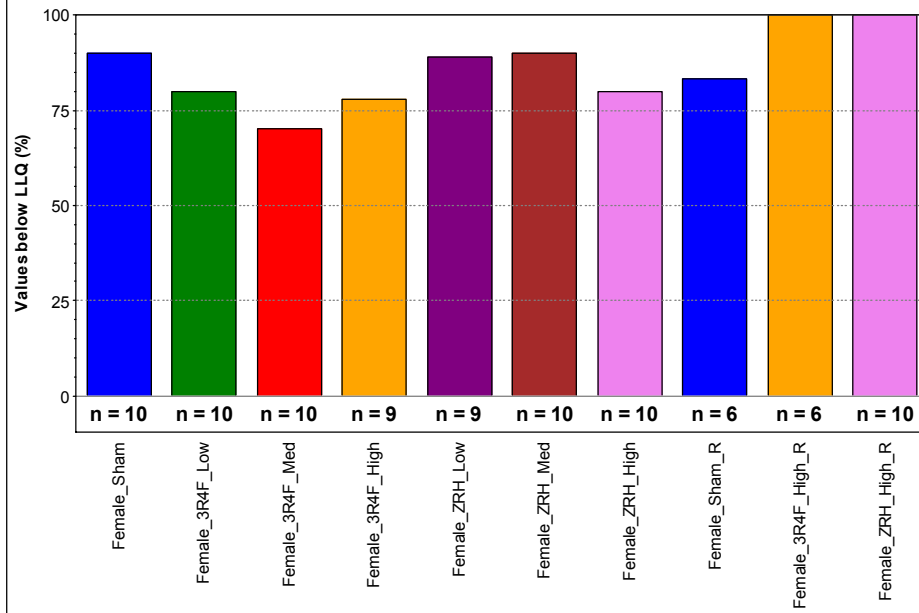
Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



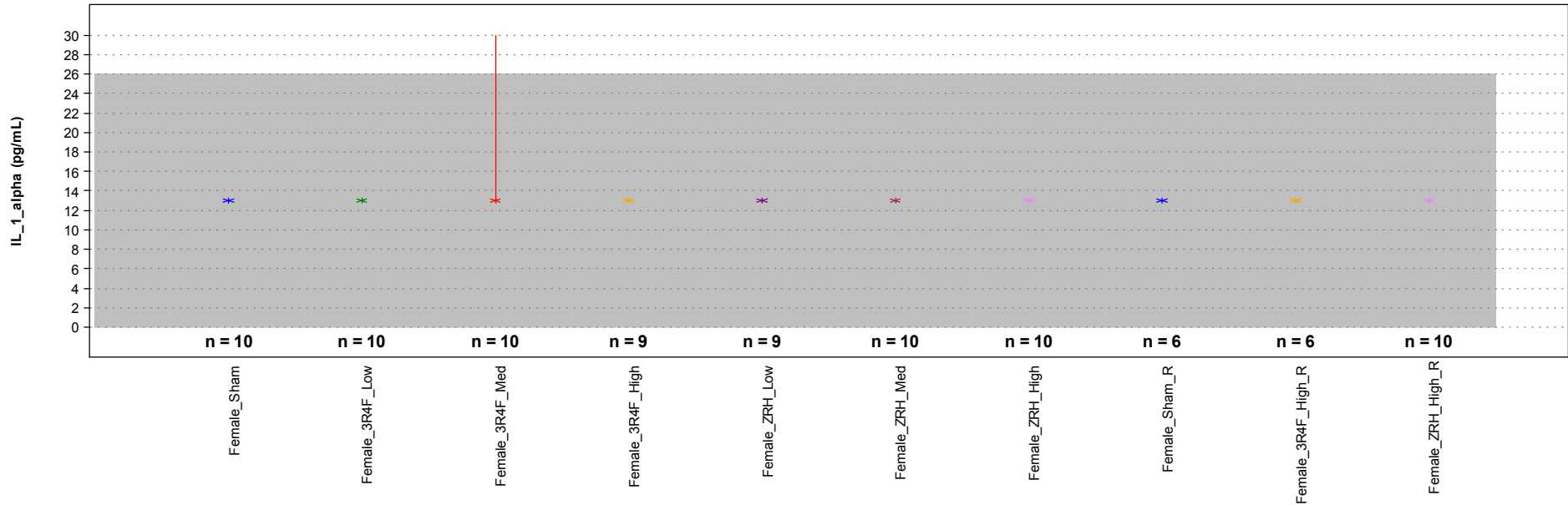
Percentage of Values below LLQ for each Group-Females

Analyte = IL_1_alpha

**Plot of Descriptive Robust Statistics-Females**

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = IL_1_alpha

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	0.942166
---- Sham vs. 3R4F Medium for Male	0.942166
---- Sham vs. 3R4F High for Male	0.626690
---- Sham vs. ZRH Low for Male	0.317311
---- Sham vs. ZRH Medium for Male	0.317311
---- Sham vs. ZRH High for Male	0.942166
---- ZRH Low vs. 3R4F Medium for Male	0.317311
---- ZRH Medium vs. 3R4F High for Male	0.146793
---- ZRH High vs. 3R4F High for Male	0.626690
---- Sham Recovery vs. 3R4F High Recovery for Male	0.104204
---- Sham Recovery vs. ZRH High Recovery for Male	0.438578
---- Sham vs. Sham Recovery for Male	0.438578
---- 3R4F High vs. 3R4F High Recovery for Male	0.345637
---- ZRH High vs. ZRH High Recovery for Male	0.942166
---- 3R4F High Recovery vs. ZRH High Recovery for Male	0.189121
---- Sham vs. 3R4F Low for Female	0.626690
---- Sham vs. 3R4F Medium for Female	0.303933
---- Sham vs. 3R4F High for Female	0.562983
---- Sham vs. ZRH Low for Female	1.000000
---- Sham vs. ZRH Medium for Female	0.942166
---- Sham vs. ZRH High for Female	0.626690
---- ZRH Low vs. 3R4F Medium for Female	0.301228
---- ZRH Medium vs. 3R4F High for Female	0.562983
---- ZRH High vs. 3R4F High for Female	0.731289
---- Sham Recovery vs. 3R4F High Recovery for Female	0.317311
---- Sham Recovery vs. ZRH High Recovery for Female	0.196706
---- Sham vs. Sham Recovery for Female	0.777297

Unadjusted P-values Obtained by Kruskal-Wallis Test
Analyte = IL_1_alpha

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	0.231998
---- ZRH High vs. ZRH High Recovery for Female	0.146793
---- 3R4F High Recovery vs. ZRH High Recovery for Female	1.000000

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 21

Interleukin-1 beta (IL-1 beta)

Unit = ng/mL

Descriptive Statistics by Exposure Duration and Treatment Type**Analyte = IL_1_beta**

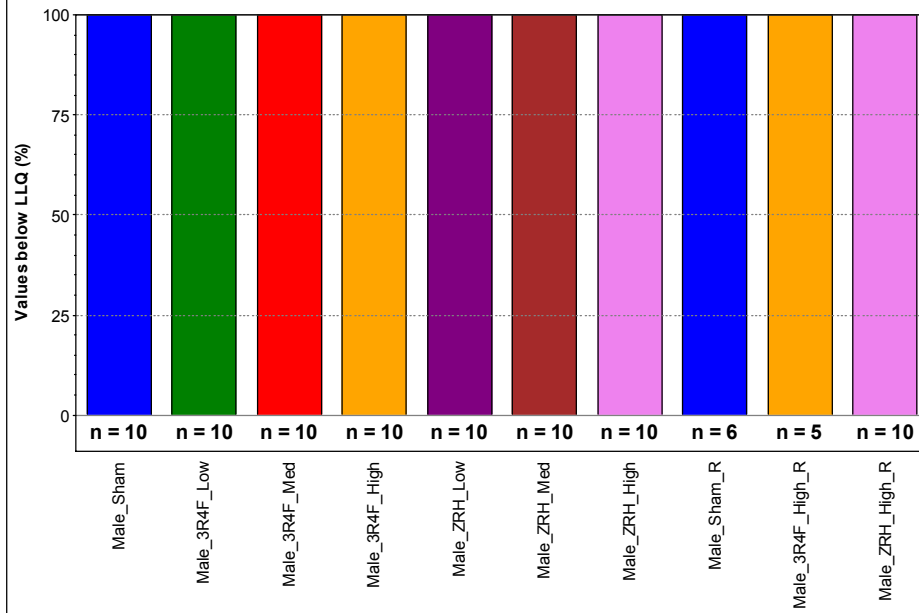
Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	10	0	0	1.3	.
Male	3	3R4F Low	10	10	10	0	0	1.3	.
Male	3	3R4F Medium	10	10	10	0	0	1.3	.
Male	3	3R4F High	10	10	10	0	0	1.3	.
Male	3	ZRH Low	10	10	10	0	0	1.3	.
Male	3	ZRH Medium	10	10	10	0	0	1.3	.
Male	3	ZRH High	10	10	10	0	0	1.3	.
Male	4.5	Sham Recovery	6	6	6	0	0	1.3	.
Male	4.5	3R4F High Recovery	5	5	5	0	0	1.3	.
Male	4.5	ZRH High Recovery	10	10	10	0	0	1.3	.
Female	3	Sham	10	10	10	0	0	1.3	.
Female	3	3R4F Low	10	10	10	0	0	1.3	.
Female	3	3R4F Medium	10	10	10	0	0	1.3	.
Female	3	3R4F High	9	9	9	0	0	1.3	.
Female	3	ZRH Low	9	9	9	0	0	1.3	.
Female	3	ZRH Medium	10	10	10	0	0	1.3	.
Female	3	ZRH High	10	10	10	0	0	1.3	.
Female	4.5	Sham Recovery	6	6	6	0	0	1.3	.
Female	4.5	3R4F High Recovery	6	6	6	0	0	1.3	.
Female	4.5	ZRH High Recovery	10	10	10	0	0	1.3	.

Descriptive Statistics by Exposure Duration and Treatment Type**Analyte = IL_1_beta**

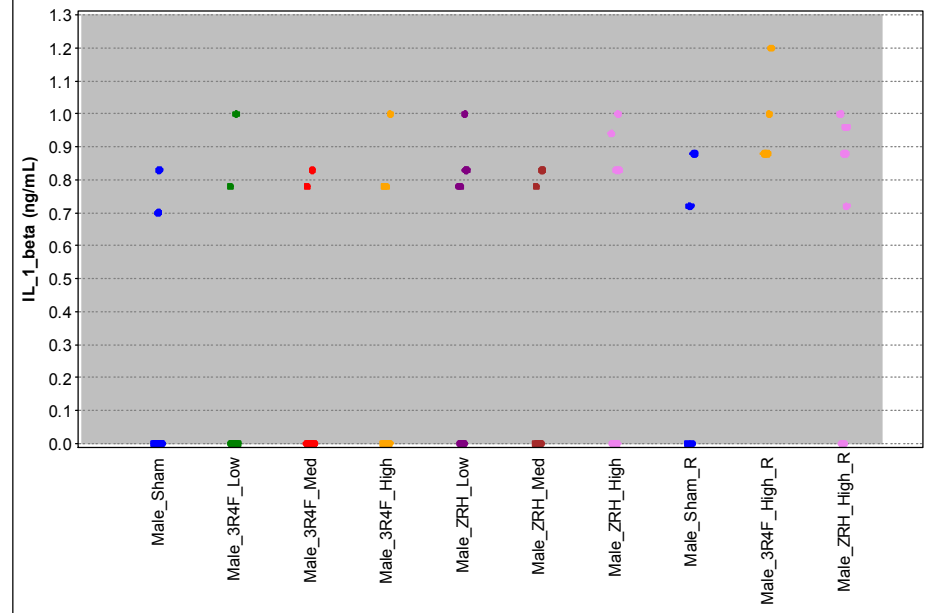
Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	0.650	0.650	0.650	0.650	0.650	0.650	0.000	0.000	0.0	.	.	1.3	.
Male	3	3R4F Low	0.650	0.650	0.650	0.650	0.650	0.650	0.000	0.000	0.0	.	.	1.3	.
Male	3	3R4F Medium	0.650	0.650	0.650	0.650	0.650	0.650	0.000	0.000	0.0	.	.	1.3	.
Male	3	3R4F High	0.650	0.650	0.650	0.650	0.650	0.650	0.000	0.000	0.0	.	.	1.3	.
Male	3	ZRH Low	0.650	0.650	0.650	0.650	0.650	0.650	0.000	0.000	0.0	.	.	1.3	.
Male	3	ZRH Medium	0.650	0.650	0.650	0.650	0.650	0.650	0.000	0.000	0.0	.	.	1.3	.
Male	3	ZRH High	0.650	0.650	0.650	0.650	0.650	0.650	0.000	0.000	0.0	.	.	1.3	.
Male	4.5	Sham Recovery	0.650	0.650	0.650	0.650	0.650	0.650	0.000	0.000	0.0	.	.	1.3	.
Male	4.5	3R4F High Recovery	0.650	0.650	0.650	0.650	0.650	0.650	0.000	0.000	0.0	.	.	1.3	.
Male	4.5	ZRH High Recovery	0.650	0.650	0.650	0.650	0.650	0.650	0.000	0.000	0.0	.	.	1.3	.
Female	3	Sham	0.650	0.650	0.650	0.650	0.650	0.650	0.000	0.000	0.0	.	.	1.3	.
Female	3	3R4F Low	0.650	0.650	0.650	0.650	0.650	0.650	0.000	0.000	0.0	.	.	1.3	.
Female	3	3R4F Medium	0.650	0.650	0.650	0.650	0.650	0.650	0.000	0.000	0.0	.	.	1.3	.
Female	3	3R4F High	0.650	0.650	0.650	0.650	0.650	0.650	0.000	0.000	0.0	.	.	1.3	.
Female	3	ZRH Low	0.650	0.650	0.650	0.650	0.650	0.650	0.000	0.000	0.0	.	.	1.3	.
Female	3	ZRH Medium	0.650	0.650	0.650	0.650	0.650	0.650	0.000	0.000	0.0	.	.	1.3	.
Female	3	ZRH High	0.650	0.650	0.650	0.650	0.650	0.650	0.000	0.000	0.0	.	.	1.3	.
Female	4.5	Sham Recovery	0.650	0.650	0.650	0.650	0.650	0.650	0.000	0.000	0.0	.	.	1.3	.
Female	4.5	3R4F High Recovery	0.650	0.650	0.650	0.650	0.650	0.650	0.000	0.000	0.0	.	.	1.3	.
Female	4.5	ZRH High Recovery	0.650	0.650	0.650	0.650	0.650	0.650	0.000	0.000	0.0	.	.	1.3	.

Percentage of Values below LLQ for each Group-Males

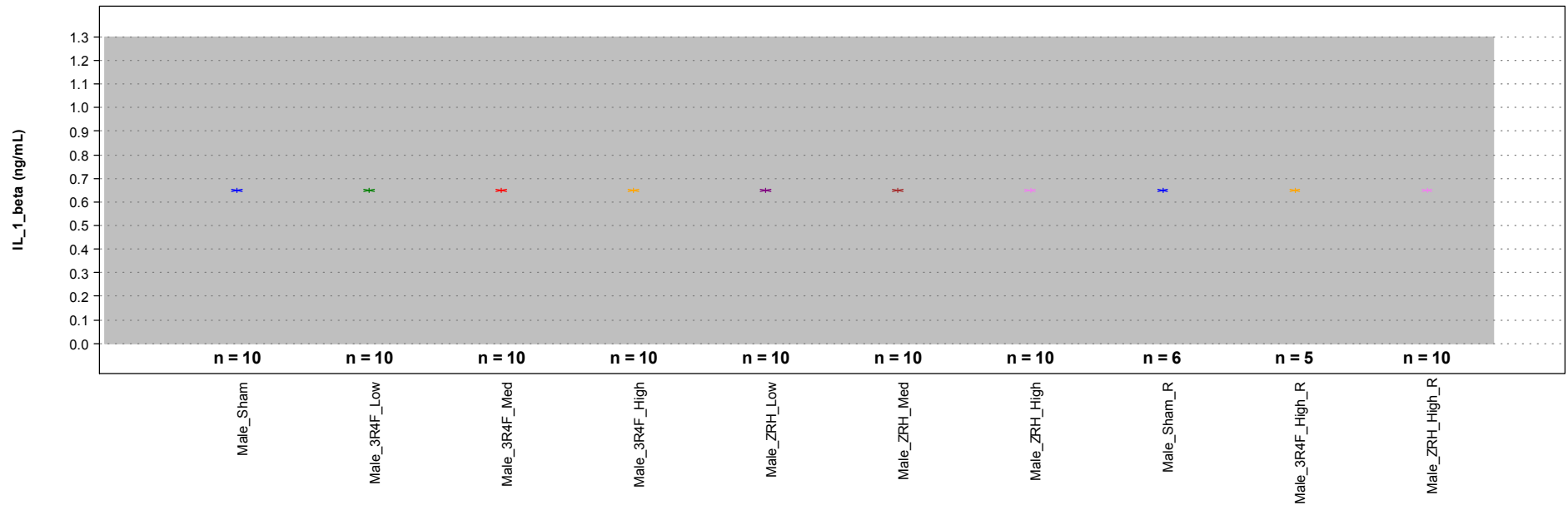
Analyte = IL_1_beta

**Plot of Individual Measurements for Each Group-Males**

<LOW> values are displayed as 0 / Values above ULQ are displayed as 1.1*ULQ
 Grey zones denote zones below (average) LLQ and above (average) ULQ

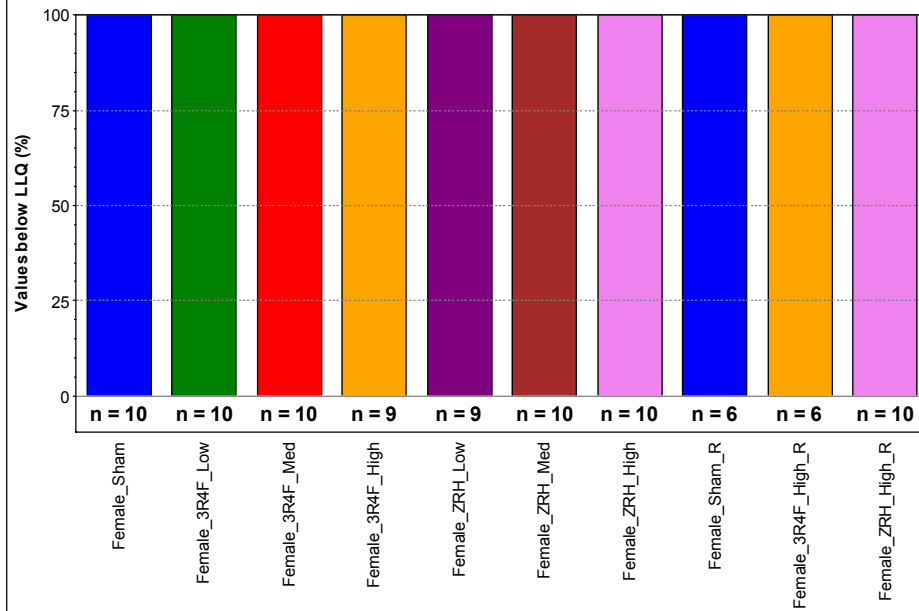
**Plot of Descriptive Robust Statistics-Males**

Displayed statistics are Median and Q1/Q3
 Grey zones denote zones below LLQ and above ULQ

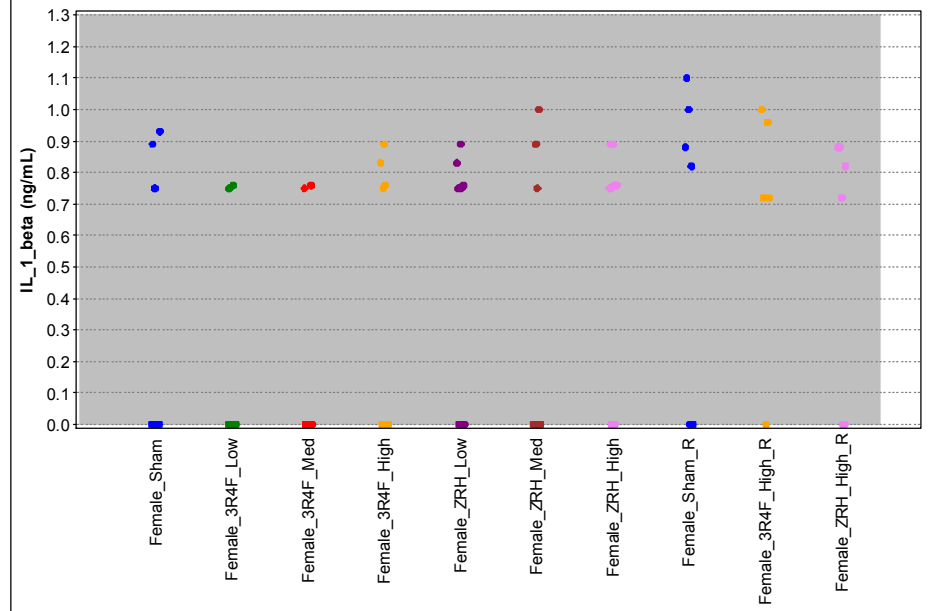


Percentage of Values below LLQ for each Group-Females

Analyte = IL_1_beta

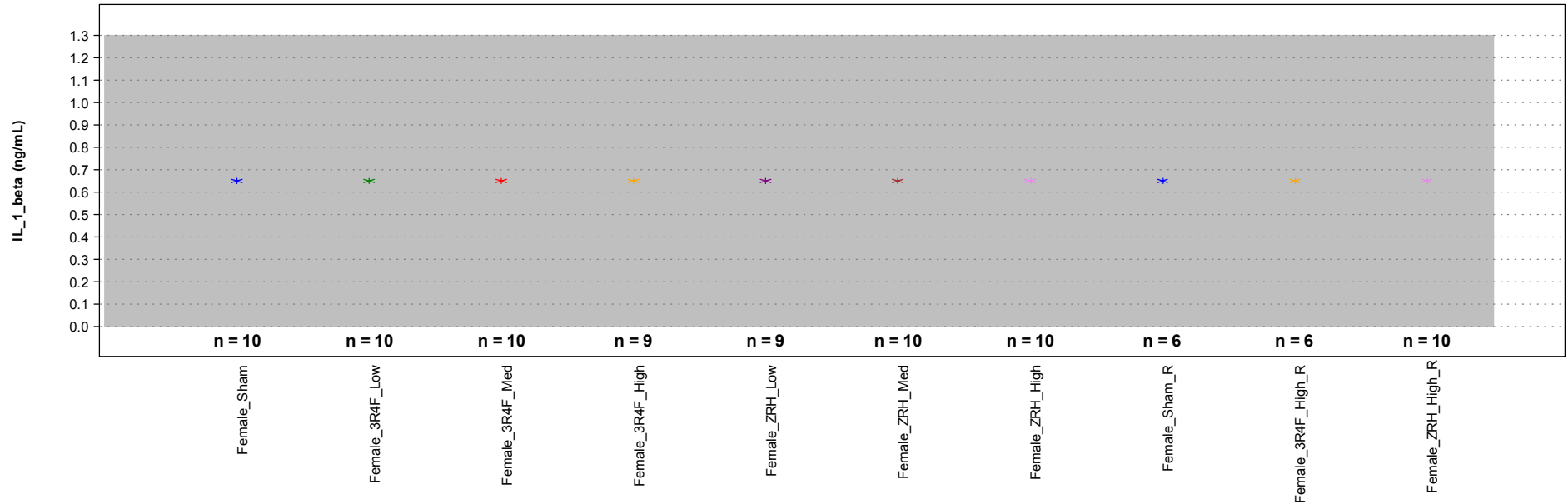
**Plot of Individual Measurements of IL_1_beta for each Group-Females**

<LOW> values are displayed as 0 / Values above ULQ are displayed as 1.1*ULQ
 Grey zones denote zones below (average) LLQ and above (average) ULQ

**Plot of Descriptive Robust Statistics-Females**

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = IL_1_beta

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	1.000000
---- Sham vs. 3R4F Medium for Male	1.000000
---- Sham vs. 3R4F High for Male	1.000000
---- Sham vs. ZRH Low for Male	1.000000
---- Sham vs. ZRH Medium for Male	1.000000
---- Sham vs. ZRH High for Male	1.000000
---- ZRH Low vs. 3R4F Medium for Male	1.000000
---- ZRH Medium vs. 3R4F High for Male	1.000000
---- ZRH High vs. 3R4F High for Male	1.000000
---- Sham Recovery vs. 3R4F High Recovery for Male	1.000000
---- Sham Recovery vs. ZRH High Recovery for Male	1.000000
---- Sham vs. Sham Recovery for Male	1.000000
---- 3R4F High vs. 3R4F High Recovery for Male	1.000000
---- ZRH High vs. ZRH High Recovery for Male	1.000000
---- 3R4F High Recovery vs. ZRH High Recovery for Male	1.000000
---- Sham vs. 3R4F Low for Female	1.000000
---- Sham vs. 3R4F Medium for Female	1.000000
---- Sham vs. 3R4F High for Female	1.000000
---- Sham vs. ZRH Low for Female	1.000000
---- Sham vs. ZRH Medium for Female	1.000000
---- Sham vs. ZRH High for Female	1.000000
---- ZRH Low vs. 3R4F Medium for Female	1.000000
---- ZRH Medium vs. 3R4F High for Female	1.000000
---- ZRH High vs. 3R4F High for Female	1.000000
---- Sham Recovery vs. 3R4F High Recovery for Female	1.000000
---- Sham Recovery vs. ZRH High Recovery for Female	1.000000
---- Sham vs. Sham Recovery for Female	1.000000

Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = IL_1_beta

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	1.000000
---- ZRH High vs. ZRH High Recovery for Female	1.000000
---- 3R4F High Recovery vs. ZRH High Recovery for Female	1.000000

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 22

Interleukin-2 (IL-2)

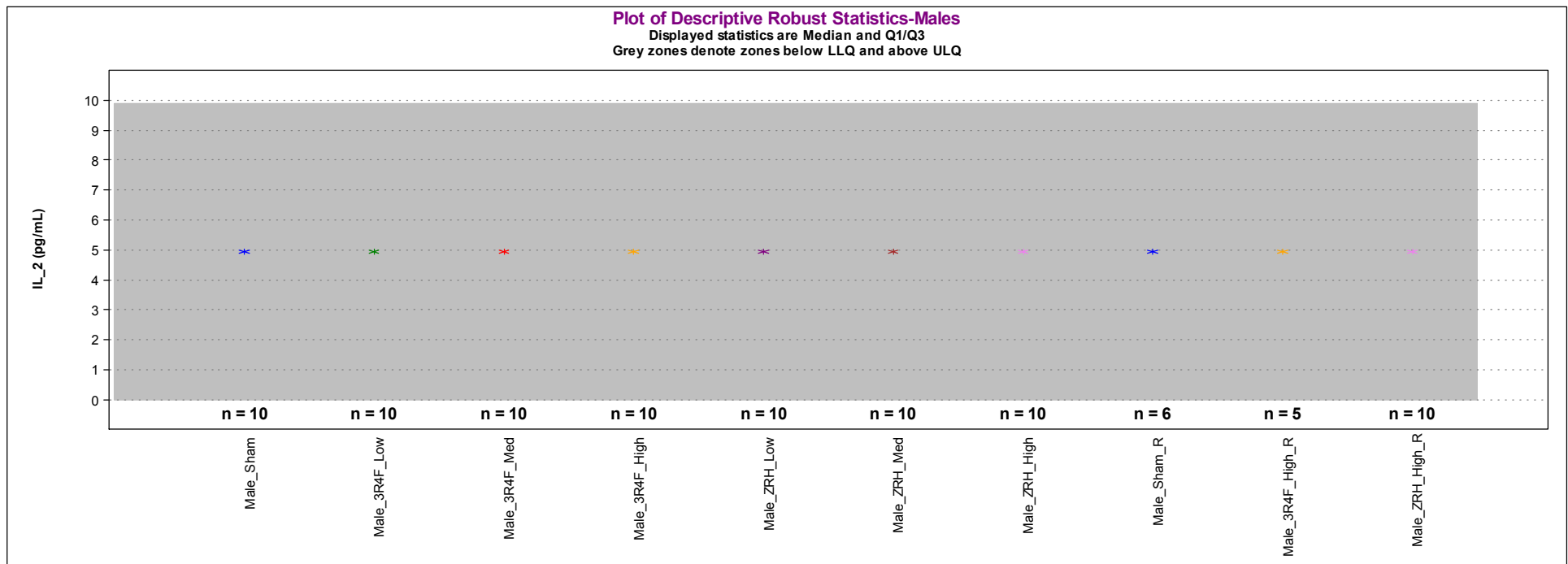
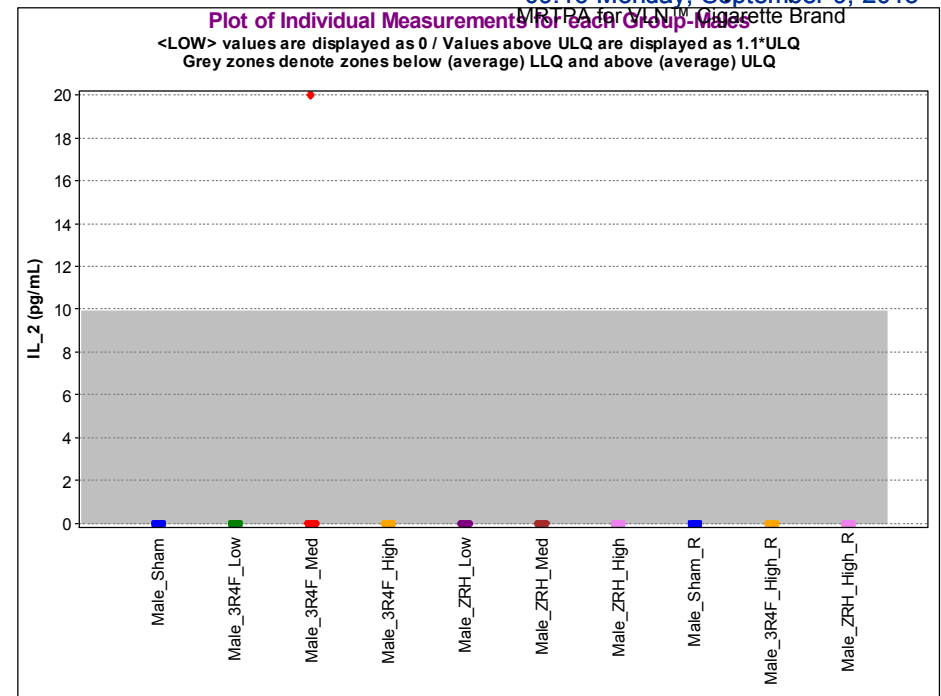
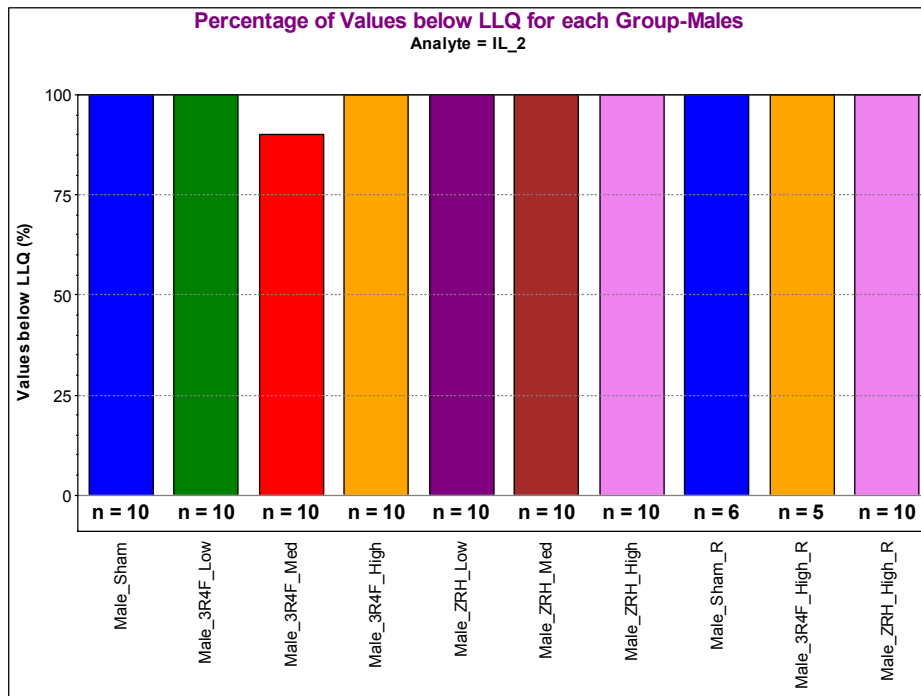
Unit = pg/mL

Descriptive Statistics by Exposure Duration and Treatment Type**Analyte = IL_2**

Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	10	0	0	9.9	.
Male	3	3R4F Low	10	10	10	0	0	9.9	.
Male	3	3R4F Medium	10	10	9	1	0	9.9	.
Male	3	3R4F High	10	10	10	0	0	9.9	.
Male	3	ZRH Low	10	10	10	0	0	9.9	.
Male	3	ZRH Medium	10	10	10	0	0	9.9	.
Male	3	ZRH High	10	10	10	0	0	9.9	.
Male	4.5	Sham Recovery	6	6	6	0	0	9.9	.
Male	4.5	3R4F High Recovery	5	5	5	0	0	9.9	.
Male	4.5	ZRH High Recovery	10	10	10	0	0	9.9	.
Female	3	Sham	10	10	10	0	0	9.9	.
Female	3	3R4F Low	10	10	10	0	0	9.9	.
Female	3	3R4F Medium	10	10	9	1	0	9.9	.
Female	3	3R4F High	9	9	9	0	0	9.9	.
Female	3	ZRH Low	9	9	9	0	0	9.9	.
Female	3	ZRH Medium	10	10	10	0	0	9.9	.
Female	3	ZRH High	10	10	10	0	0	9.9	.
Female	4.5	Sham Recovery	6	6	6	0	0	9.9	.
Female	4.5	3R4F High Recovery	6	6	6	0	0	9.9	.
Female	4.5	ZRH High Recovery	10	10	10	0	0	9.9	.

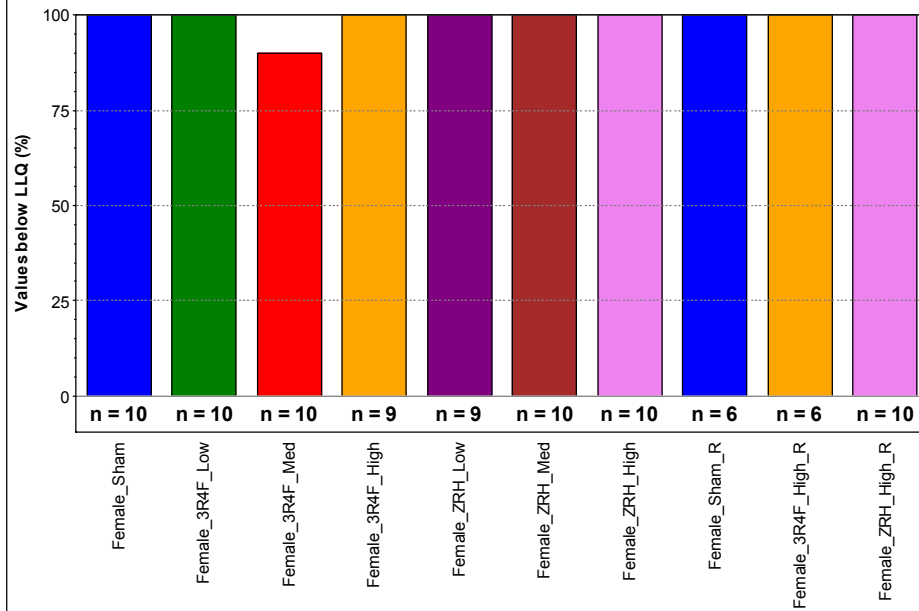
Descriptive Statistics by Exposure Duration and Treatment Type**Analyte = IL_2**

Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	4.950	4.950	4.950	4.950	4.950	4.950	0.000	0.000	0.0	.	.	9.9	.
Male	3	3R4F Low	4.950	4.950	4.950	4.950	4.950	4.950	0.000	0.000	0.0	.	.	9.9	.
Male	3	3R4F Medium	4.950	4.950	4.950	4.950	20.000	6.455	4.759	1.505	73.7	3.162	10.000	9.9	.
Male	3	3R4F High	4.950	4.950	4.950	4.950	4.950	4.950	0.000	0.000	0.0	.	.	9.9	.
Male	3	ZRH Low	4.950	4.950	4.950	4.950	4.950	4.950	0.000	0.000	0.0	.	.	9.9	.
Male	3	ZRH Medium	4.950	4.950	4.950	4.950	4.950	4.950	0.000	0.000	0.0	.	.	9.9	.
Male	3	ZRH High	4.950	4.950	4.950	4.950	4.950	4.950	0.000	0.000	0.0	.	.	9.9	.
Male	4.5	Sham Recovery	4.950	4.950	4.950	4.950	4.950	4.950	0.000	0.000	0.0	.	.	9.9	.
Male	4.5	3R4F High Recovery	4.950	4.950	4.950	4.950	4.950	4.950	0.000	0.000	0.0	.	.	9.9	.
Male	4.5	ZRH High Recovery	4.950	4.950	4.950	4.950	4.950	4.950	0.000	0.000	0.0	.	.	9.9	.
Female	3	Sham	4.950	4.950	4.950	4.950	4.950	4.950	0.000	0.000	0.0	.	.	9.9	.
Female	3	3R4F Low	4.950	4.950	4.950	4.950	4.950	4.950	0.000	0.000	0.0	.	.	9.9	.
Female	3	3R4F Medium	4.950	4.950	4.950	4.950	21.000	6.555	5.075	1.605	77.4	3.162	10.000	9.9	.
Female	3	3R4F High	4.950	4.950	4.950	4.950	4.950	4.950	0.000	0.000	0.0	.	.	9.9	.
Female	3	ZRH Low	4.950	4.950	4.950	4.950	4.950	4.950	0.000	0.000	0.0	.	.	9.9	.
Female	3	ZRH Medium	4.950	4.950	4.950	4.950	4.950	4.950	0.000	0.000	0.0	.	.	9.9	.
Female	3	ZRH High	4.950	4.950	4.950	4.950	4.950	4.950	0.000	0.000	0.0	.	.	9.9	.
Female	4.5	Sham Recovery	4.950	4.950	4.950	4.950	4.950	4.950	0.000	0.000	0.0	.	.	9.9	.
Female	4.5	3R4F High Recovery	4.950	4.950	4.950	4.950	4.950	4.950	0.000	0.000	0.0	.	.	9.9	.
Female	4.5	ZRH High Recovery	4.950	4.950	4.950	4.950	4.950	4.950	0.000	0.000	0.0	.	.	9.9	.

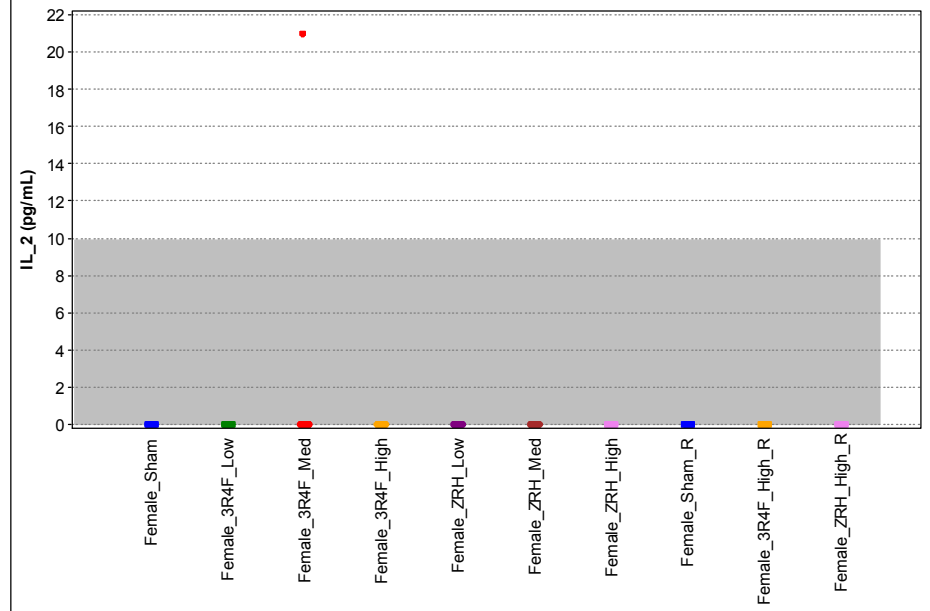


Percentage of Values below LLQ for each Group-Females

Analyte = IL_2

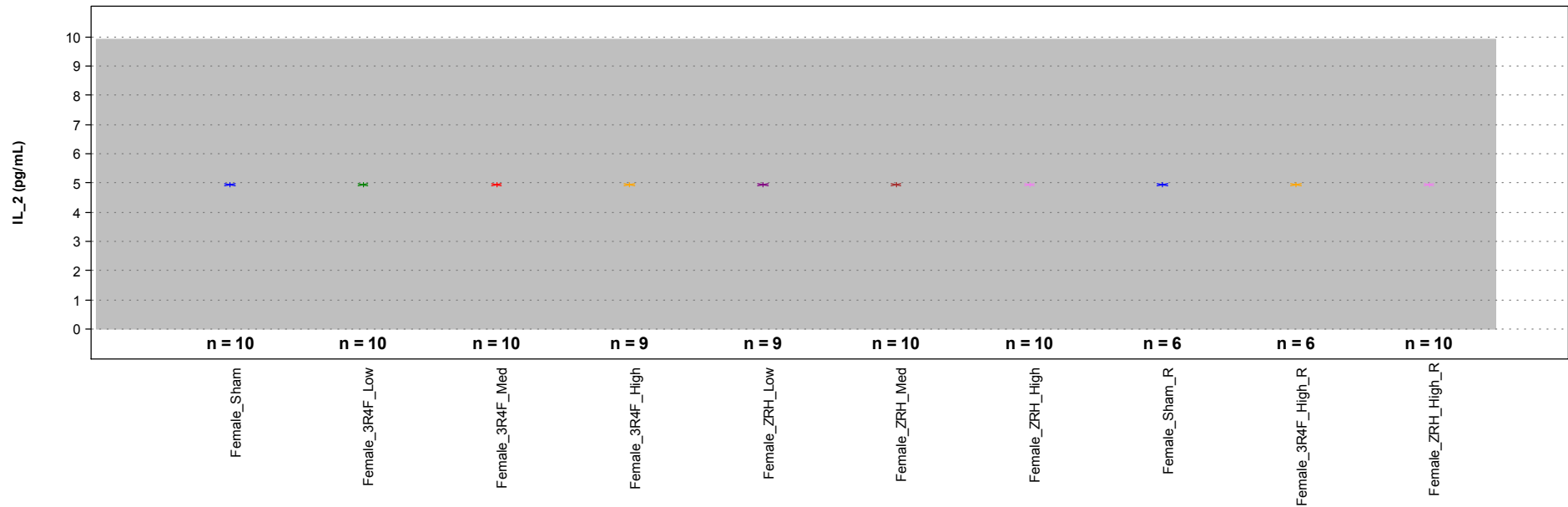


Plot of Individual Measurements for IL_2 in Females
 <LOW> values are displayed as 0 / Values above ULQ are displayed as 1.1*ULQ
 Grey zones denote zones below (average) LLQ and above (average) ULQ

**Plot of Descriptive Robust Statistics-Females**

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = IL_2

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	1.000000
---- Sham vs. 3R4F Medium for Male	0.317311
---- Sham vs. 3R4F High for Male	1.000000
---- Sham vs. ZRH Low for Male	1.000000
---- Sham vs. ZRH Medium for Male	1.000000
---- Sham vs. ZRH High for Male	1.000000
---- ZRH Low vs. 3R4F Medium for Male	0.317311
---- ZRH Medium vs. 3R4F High for Male	1.000000
---- ZRH High vs. 3R4F High for Male	1.000000
---- Sham Recovery vs. 3R4F High Recovery for Male	1.000000
---- Sham Recovery vs. ZRH High Recovery for Male	1.000000
---- Sham vs. Sham Recovery for Male	1.000000
---- 3R4F High vs. 3R4F High Recovery for Male	1.000000
---- ZRH High vs. ZRH High Recovery for Male	1.000000
---- 3R4F High Recovery vs. ZRH High Recovery for Male	1.000000
---- Sham vs. 3R4F Low for Female	1.000000
---- Sham vs. 3R4F Medium for Female	0.317311
---- Sham vs. 3R4F High for Female	1.000000
---- Sham vs. ZRH Low for Female	1.000000
---- Sham vs. ZRH Medium for Female	1.000000
---- Sham vs. ZRH High for Female	1.000000
---- ZRH Low vs. 3R4F Medium for Female	0.342782
---- ZRH Medium vs. 3R4F High for Female	1.000000
---- ZRH High vs. 3R4F High for Female	1.000000
---- Sham Recovery vs. 3R4F High Recovery for Female	1.000000
---- Sham Recovery vs. ZRH High Recovery for Female	1.000000
---- Sham vs. Sham Recovery for Female	1.000000

Unadjusted P-values Obtained by Kruskal-Wallis Test
Analyte = IL_2

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	1.000000
---- ZRH High vs. ZRH High Recovery for Female	1.000000
---- 3R4F High Recovery vs. ZRH High Recovery for Female	1.000000

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 23

Interleukin-3 (IL-3)

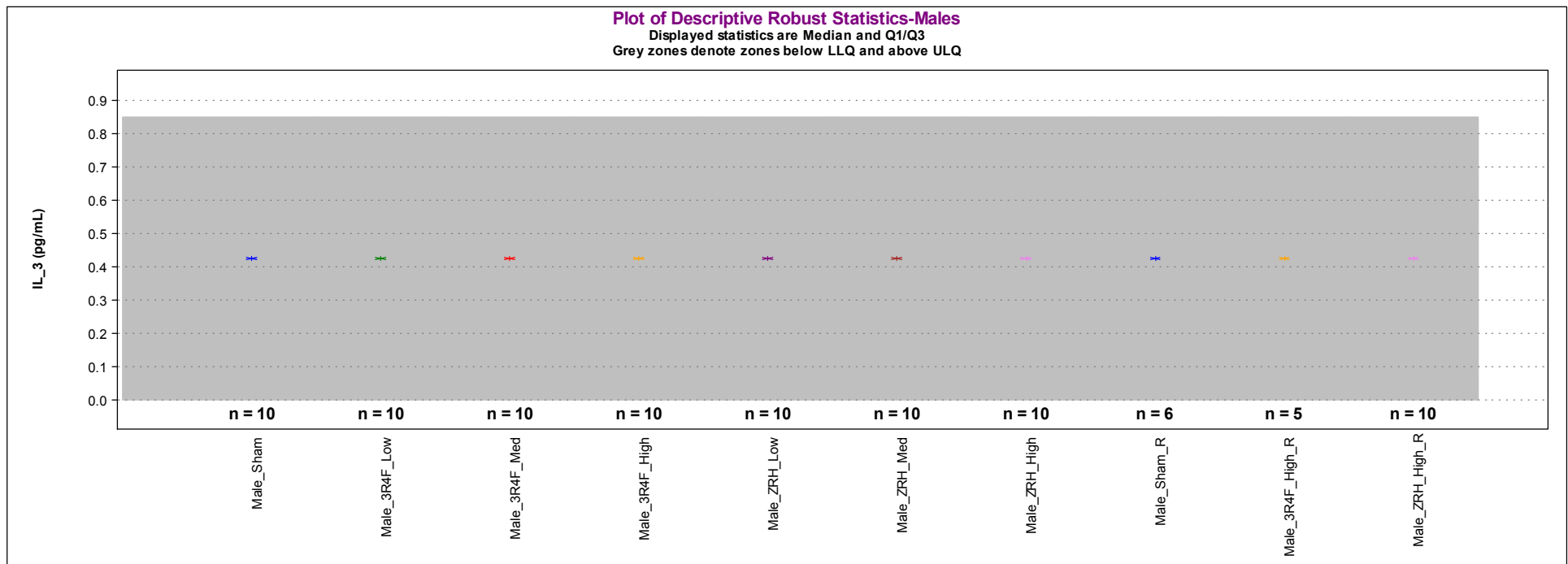
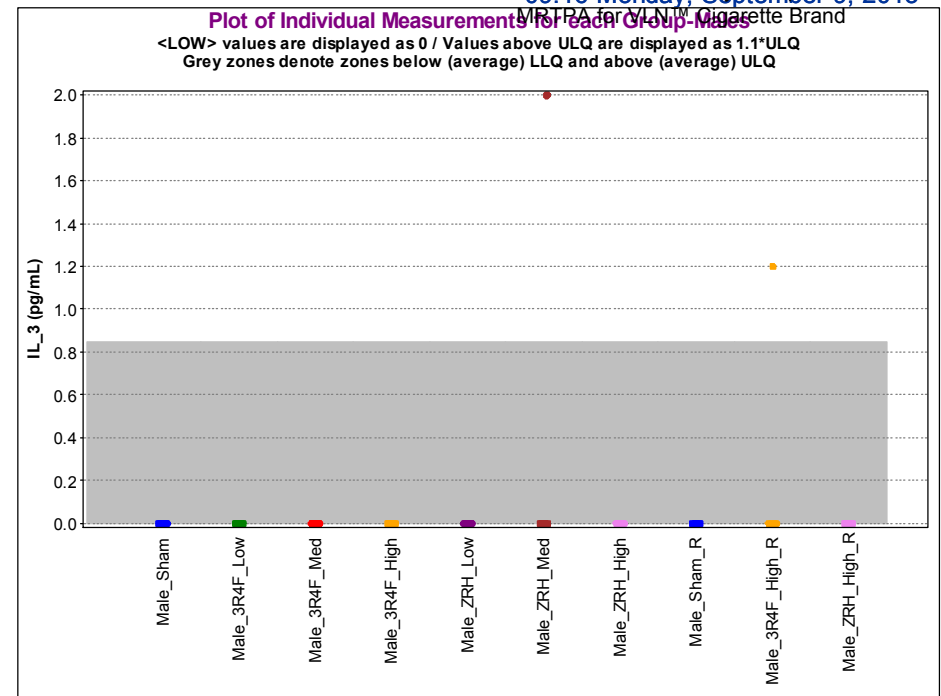
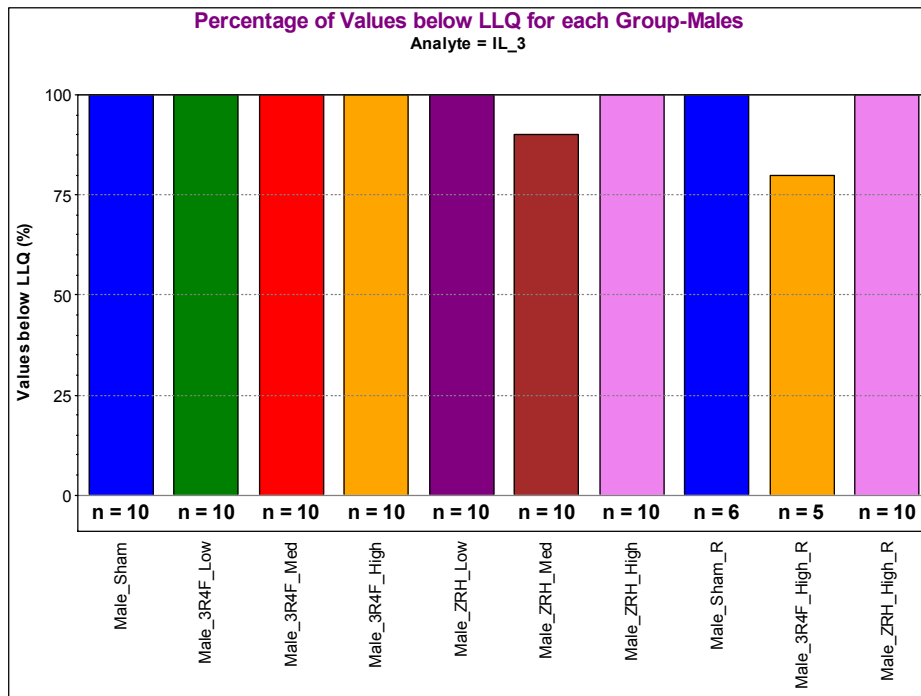
Unit = pg/mL

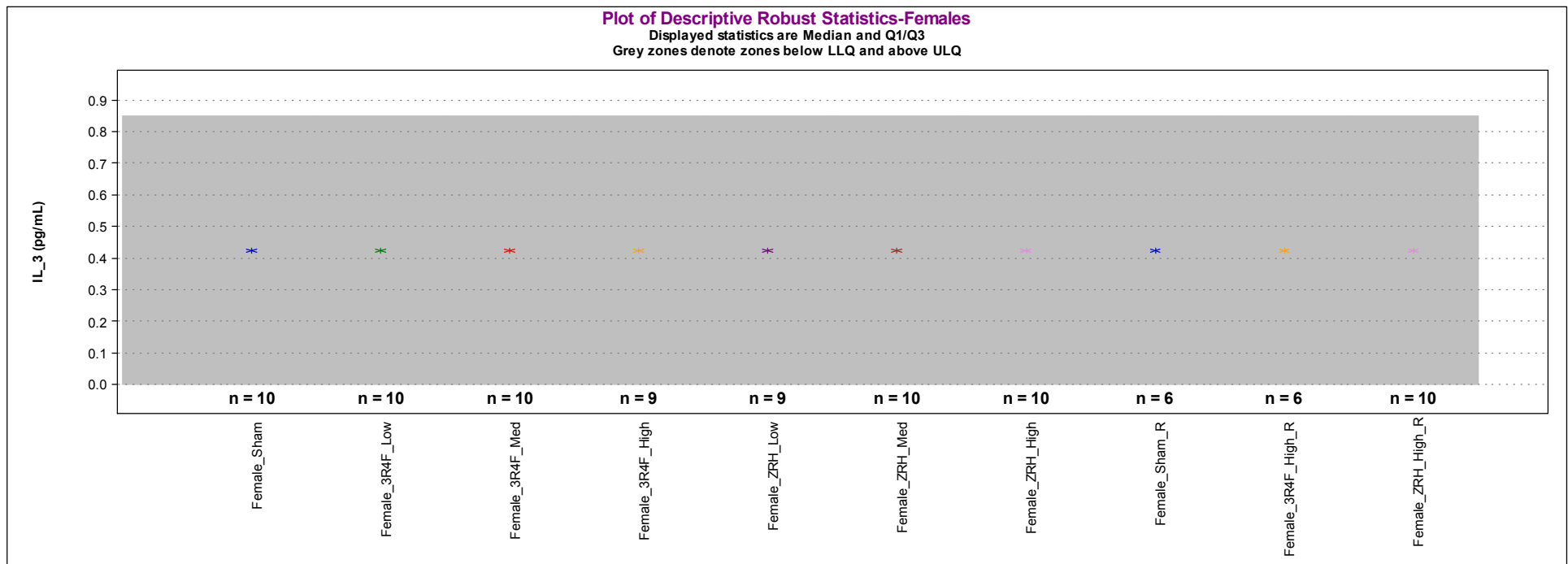
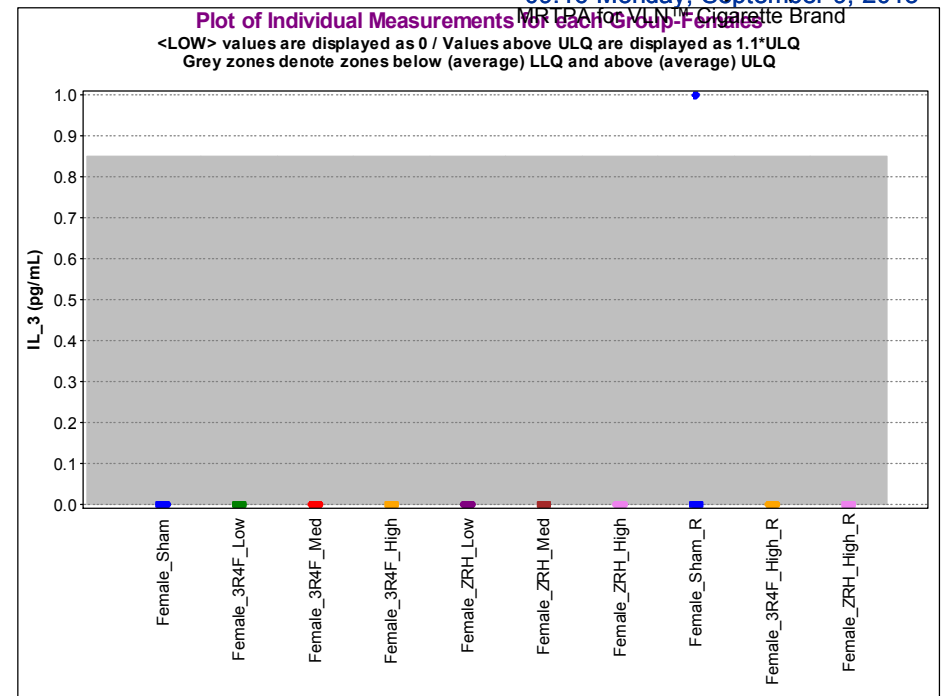
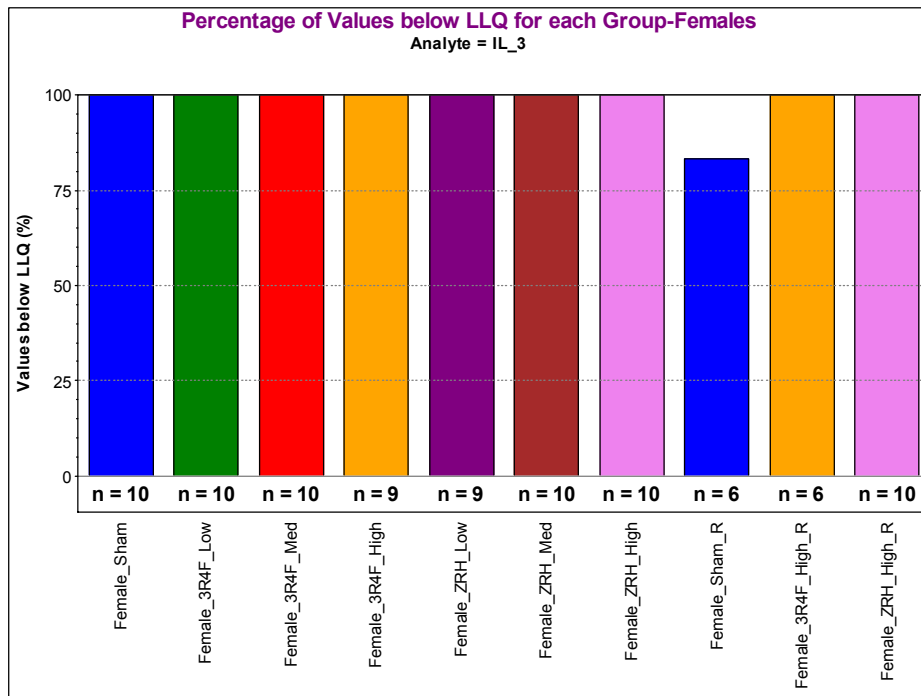
Descriptive Statistics by Exposure Duration and Treatment Type**Analyte = IL_3**

Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	10	0	0	0.85	.
Male	3	3R4F Low	10	10	10	0	0	0.85	.
Male	3	3R4F Medium	10	10	10	0	0	0.85	.
Male	3	3R4F High	10	10	10	0	0	0.85	.
Male	3	ZRH Low	10	10	10	0	0	0.85	.
Male	3	ZRH Medium	10	10	9	1	0	0.85	.
Male	3	ZRH High	10	10	10	0	0	0.85	.
Male	4.5	Sham Recovery	6	6	6	0	0	0.85	.
Male	4.5	3R4F High Recovery	5	5	4	1	0	0.85	.
Male	4.5	ZRH High Recovery	10	10	10	0	0	0.85	.
Female	3	Sham	10	10	10	0	0	0.85	.
Female	3	3R4F Low	10	10	10	0	0	0.85	.
Female	3	3R4F Medium	10	10	10	0	0	0.85	.
Female	3	3R4F High	9	9	9	0	0	0.85	.
Female	3	ZRH Low	9	9	9	0	0	0.85	.
Female	3	ZRH Medium	10	10	10	0	0	0.85	.
Female	3	ZRH High	10	10	10	0	0	0.85	.
Female	4.5	Sham Recovery	6	6	5	1	0	0.85	.
Female	4.5	3R4F High Recovery	6	6	6	0	0	0.85	.
Female	4.5	ZRH High Recovery	10	10	10	0	0	0.85	.

Descriptive Statistics by Exposure Duration and Treatment Type**Analyte = IL_3**

Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	0.425	0.425	0.425	0.425	0.425	0.425	0.000	0.000	0.0	.	.	0.85	.
Male	3	3R4F Low	0.425	0.425	0.425	0.425	0.425	0.425	0.000	0.000	0.0	.	.	0.85	.
Male	3	3R4F Medium	0.425	0.425	0.425	0.425	0.425	0.425	0.000	0.000	0.0	.	.	0.85	.
Male	3	3R4F High	0.425	0.425	0.425	0.425	0.425	0.425	0.000	0.000	0.0	.	.	0.85	.
Male	3	ZRH Low	0.425	0.425	0.425	0.425	0.425	0.425	0.000	0.000	0.0	.	.	0.85	.
Male	3	ZRH Medium	0.425	0.425	0.425	0.425	2.000	0.582	0.498	0.158	85.5	3.162	10.000	0.85	.
Male	3	ZRH High	0.425	0.425	0.425	0.425	0.425	0.425	0.000	0.000	0.0	.	.	0.85	.
Male	4.5	Sham Recovery	0.425	0.425	0.425	0.425	0.425	0.425	0.000	0.000	0.0	.	.	0.85	.
Male	4.5	3R4F High Recovery	0.425	0.425	0.425	0.425	1.200	0.580	0.347	0.155	59.8	2.236	5.000	0.85	.
Male	4.5	ZRH High Recovery	0.425	0.425	0.425	0.425	0.425	0.425	0.000	0.000	0.0	.	.	0.85	.
Female	3	Sham	0.425	0.425	0.425	0.425	0.425	0.425	0.000	0.000	0.0	.	.	0.85	.
Female	3	3R4F Low	0.425	0.425	0.425	0.425	0.425	0.425	0.000	0.000	0.0	.	.	0.85	.
Female	3	3R4F Medium	0.425	0.425	0.425	0.425	0.425	0.425	0.000	0.000	0.0	.	.	0.85	.
Female	3	3R4F High	0.425	0.425	0.425	0.425	0.425	0.425	0.000	0.000	0.0	.	.	0.85	.
Female	3	ZRH Low	0.425	0.425	0.425	0.425	0.425	0.425	0.000	0.000	0.0	.	.	0.85	.
Female	3	ZRH Medium	0.425	0.425	0.425	0.425	0.425	0.425	0.000	0.000	0.0	.	.	0.85	.
Female	3	ZRH High	0.425	0.425	0.425	0.425	0.425	0.425	0.000	0.000	0.0	.	.	0.85	.
Female	4.5	Sham Recovery	0.425	0.425	0.425	0.425	1.000	0.521	0.235	0.096	45.1	2.449	6.000	0.85	.
Female	4.5	3R4F High Recovery	0.425	0.425	0.425	0.425	0.425	0.425	0.000	0.000	0.0	.	.	0.85	.
Female	4.5	ZRH High Recovery	0.425	0.425	0.425	0.425	0.425	0.425	0.000	0.000	0.0	.	.	0.85	.





Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = IL_3

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	1.000000
---- Sham vs. 3R4F Medium for Male	1.000000
---- Sham vs. 3R4F High for Male	1.000000
---- Sham vs. ZRH Low for Male	1.000000
---- Sham vs. ZRH Medium for Male	0.317311
---- Sham vs. ZRH High for Male	1.000000
---- ZRH Low vs. 3R4F Medium for Male	1.000000
---- ZRH Medium vs. 3R4F High for Male	0.317311
---- ZRH High vs. 3R4F High for Male	1.000000
---- Sham Recovery vs. 3R4F High Recovery for Male	0.273322
---- Sham Recovery vs. ZRH High Recovery for Male	1.000000
---- Sham vs. Sham Recovery for Male	1.000000
---- 3R4F High vs. 3R4F High Recovery for Male	0.157299
---- ZRH High vs. ZRH High Recovery for Male	1.000000
---- 3R4F High Recovery vs. ZRH High Recovery for Male	0.157299
---- Sham vs. 3R4F Low for Female	1.000000
---- Sham vs. 3R4F Medium for Female	1.000000
---- Sham vs. 3R4F High for Female	1.000000
---- Sham vs. ZRH Low for Female	1.000000
---- Sham vs. ZRH Medium for Female	1.000000
---- Sham vs. ZRH High for Female	1.000000
---- ZRH Low vs. 3R4F Medium for Female	1.000000
---- ZRH Medium vs. 3R4F High for Female	1.000000
---- ZRH High vs. 3R4F High for Female	1.000000
---- Sham Recovery vs. 3R4F High Recovery for Female	0.317311
---- Sham Recovery vs. ZRH High Recovery for Female	0.196706
---- Sham vs. Sham Recovery for Female	0.196706

Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = IL_3

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	1.000000
---- ZRH High vs. ZRH High Recovery for Female	1.000000
---- 3R4F High Recovery vs. ZRH High Recovery for Female	1.000000

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 24

Interleukin-4 (IL-4)

Unit = pg/mL

Descriptive Statistics by Exposure Duration and Treatment Type**Analyte = IL_4**

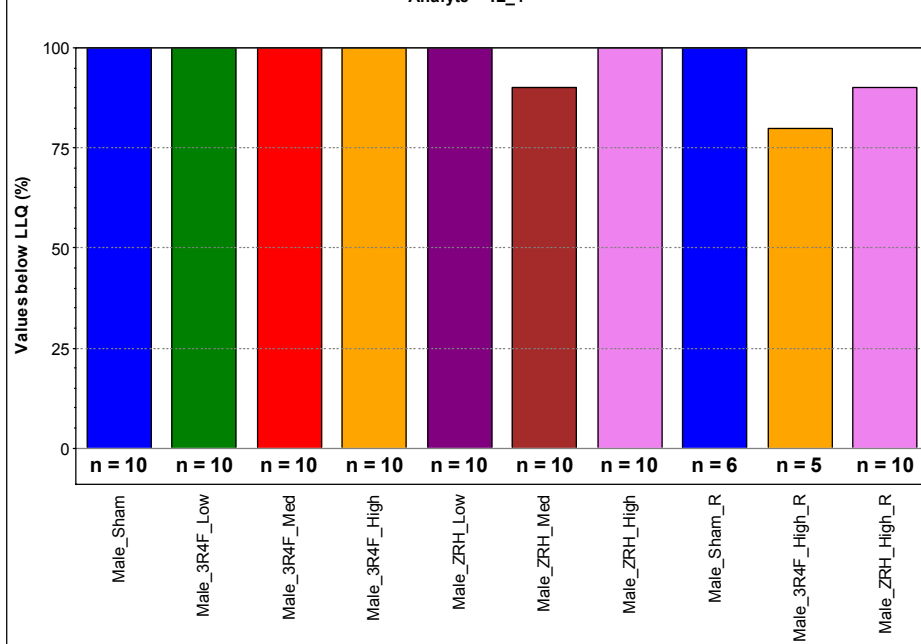
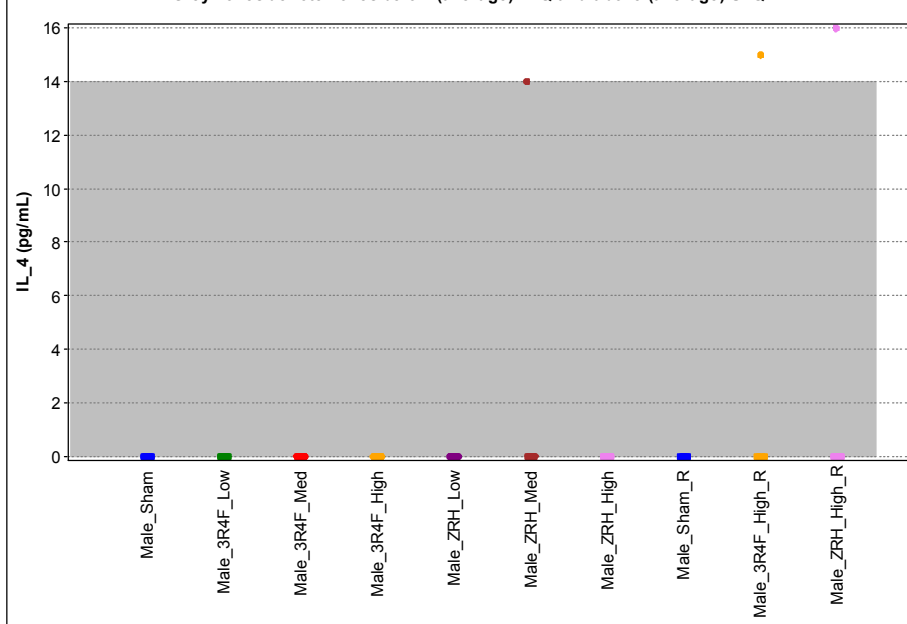
Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	10	0	0	14	.
Male	3	3R4F Low	10	10	10	0	0	14	.
Male	3	3R4F Medium	10	10	10	0	0	14	.
Male	3	3R4F High	10	10	10	0	0	14	.
Male	3	ZRH Low	10	10	10	0	0	14	.
Male	3	ZRH Medium	10	10	9	1	0	14	.
Male	3	ZRH High	10	10	10	0	0	14	.
Male	4.5	Sham Recovery	6	6	6	0	0	14	.
Male	4.5	3R4F High Recovery	5	5	4	1	0	14	.
Male	4.5	ZRH High Recovery	10	10	9	1	0	14	.
Female	3	Sham	10	10	10	0	0	14	.
Female	3	3R4F Low	10	10	10	0	0	14	.
Female	3	3R4F Medium	10	10	10	0	0	14	.
Female	3	3R4F High	9	9	8	1	0	14	.
Female	3	ZRH Low	9	9	9	0	0	14	.
Female	3	ZRH Medium	10	10	9	1	0	14	.
Female	3	ZRH High	10	10	10	0	0	14	.
Female	4.5	Sham Recovery	6	6	5	1	0	14	.
Female	4.5	3R4F High Recovery	6	6	6	0	0	14	.
Female	4.5	ZRH High Recovery	10	10	10	0	0	14	.

Descriptive Statistics by Exposure Duration and Treatment Type**Analyte = IL_4**

Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	7.000	7.000	7.000	7.000	7.000	7.000	0.000	0.000	0.0	.	.	14	.
Male	3	3R4F Low	7.000	7.000	7.000	7.000	7.000	7.000	0.000	0.000	0.0	.	.	14	.
Male	3	3R4F Medium	7.000	7.000	7.000	7.000	7.000	7.000	0.000	0.000	0.0	.	.	14	.
Male	3	3R4F High	7.000	7.000	7.000	7.000	7.000	7.000	0.000	0.000	0.0	.	.	14	.
Male	3	ZRH Low	7.000	7.000	7.000	7.000	7.000	7.000	0.000	0.000	0.0	.	.	14	.
Male	3	ZRH Medium	7.000	7.000	7.000	7.000	14.000	7.700	2.214	0.700	28.7	3.162	10.000	14	.
Male	3	ZRH High	7.000	7.000	7.000	7.000	7.000	7.000	0.000	0.000	0.0	.	.	14	.
Male	4.5	Sham Recovery	7.000	7.000	7.000	7.000	7.000	7.000	0.000	0.000	0.0	.	.	14	.
Male	4.5	3R4F High Recovery	7.000	7.000	7.000	7.000	15.000	8.600	3.578	1.600	41.6	2.236	5.000	14	.
Male	4.5	ZRH High Recovery	7.000	7.000	7.000	7.000	16.000	7.900	2.846	0.900	36.0	3.162	10.000	14	.
Female	3	Sham	7.000	7.000	7.000	7.000	7.000	7.000	0.000	0.000	0.0	.	.	14	.
Female	3	3R4F Low	7.000	7.000	7.000	7.000	7.000	7.000	0.000	0.000	0.0	.	.	14	.
Female	3	3R4F Medium	7.000	7.000	7.000	7.000	7.000	7.000	0.000	0.000	0.0	.	.	14	.
Female	3	3R4F High	7.000	7.000	7.000	7.000	18.000	8.222	3.667	1.222	44.6	3.000	9.000	14	.
Female	3	ZRH Low	7.000	7.000	7.000	7.000	7.000	7.000	0.000	0.000	0.0	.	.	14	.
Female	3	ZRH Medium	7.000	7.000	7.000	7.000	15.000	7.800	2.530	0.800	32.4	3.162	10.000	14	.
Female	3	ZRH High	7.000	7.000	7.000	7.000	7.000	7.000	0.000	0.000	0.0	.	.	14	.
Female	4.5	Sham Recovery	7.000	7.000	7.000	7.000	14.000	8.167	2.858	1.167	35.0	2.449	6.000	14	.
Female	4.5	3R4F High Recovery	7.000	7.000	7.000	7.000	7.000	7.000	0.000	0.000	0.0	.	.	14	.
Female	4.5	ZRH High Recovery	7.000	7.000	7.000	7.000	7.000	7.000	0.000	0.000	0.0	.	.	14	.

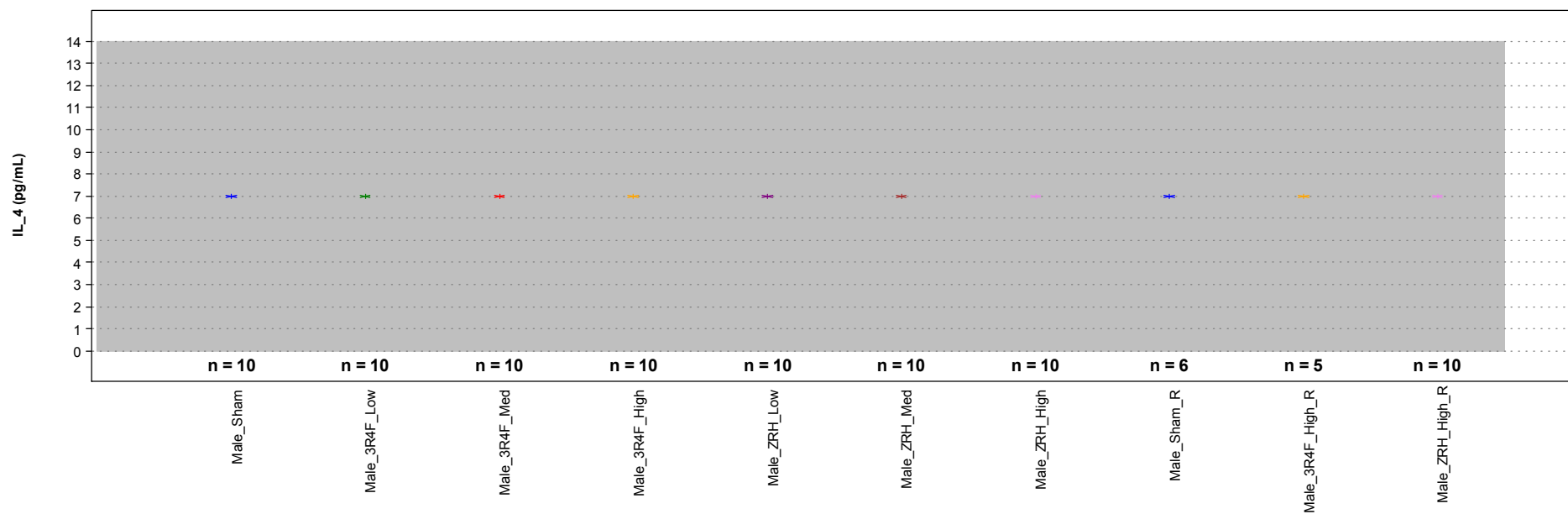
Percentage of Values below LLQ for each Group-Males

Analyte = IL_4

**Plot of Individual Measurements for IL_4 - Males****Plot of Descriptive Robust Statistics-Males**

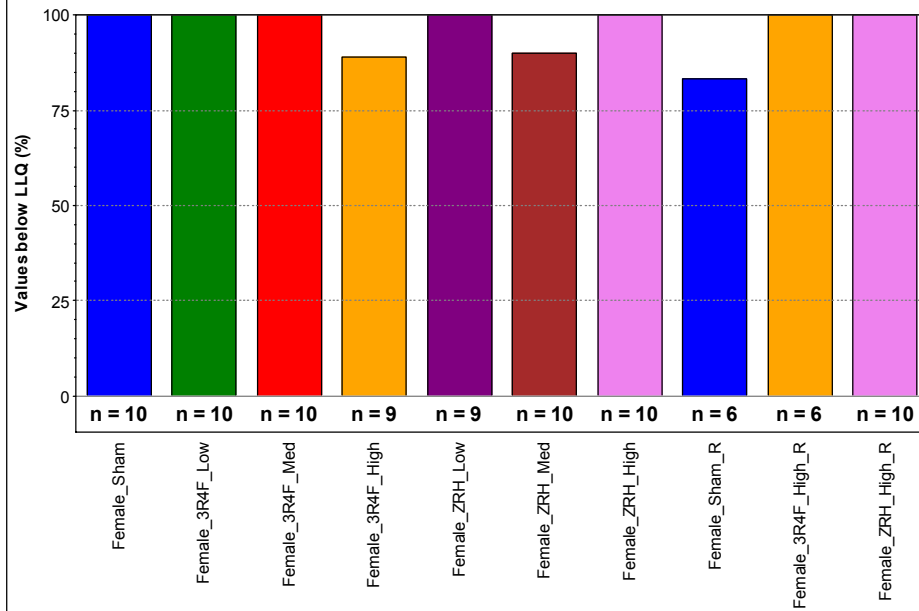
Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ

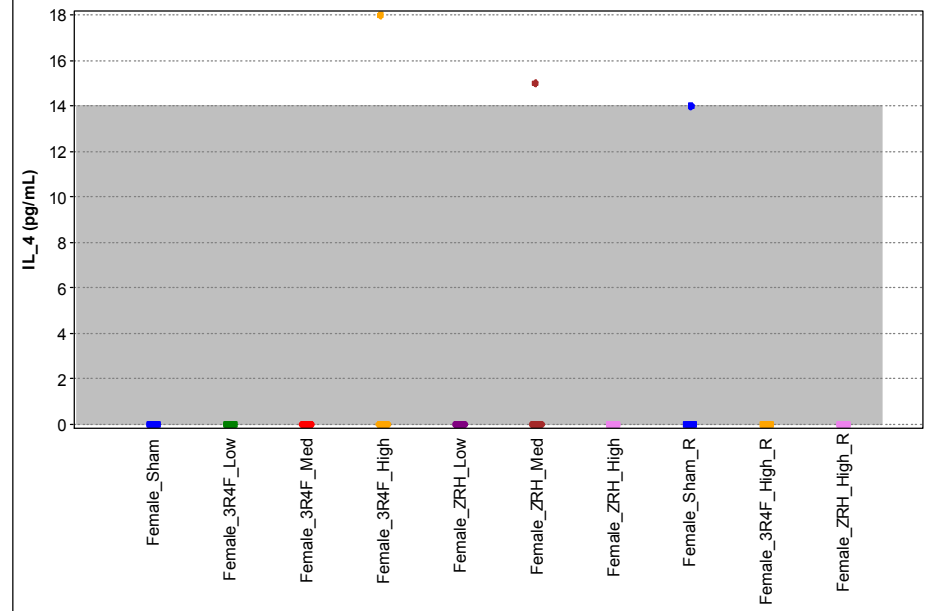


Percentage of Values below LLQ for each Group-Females

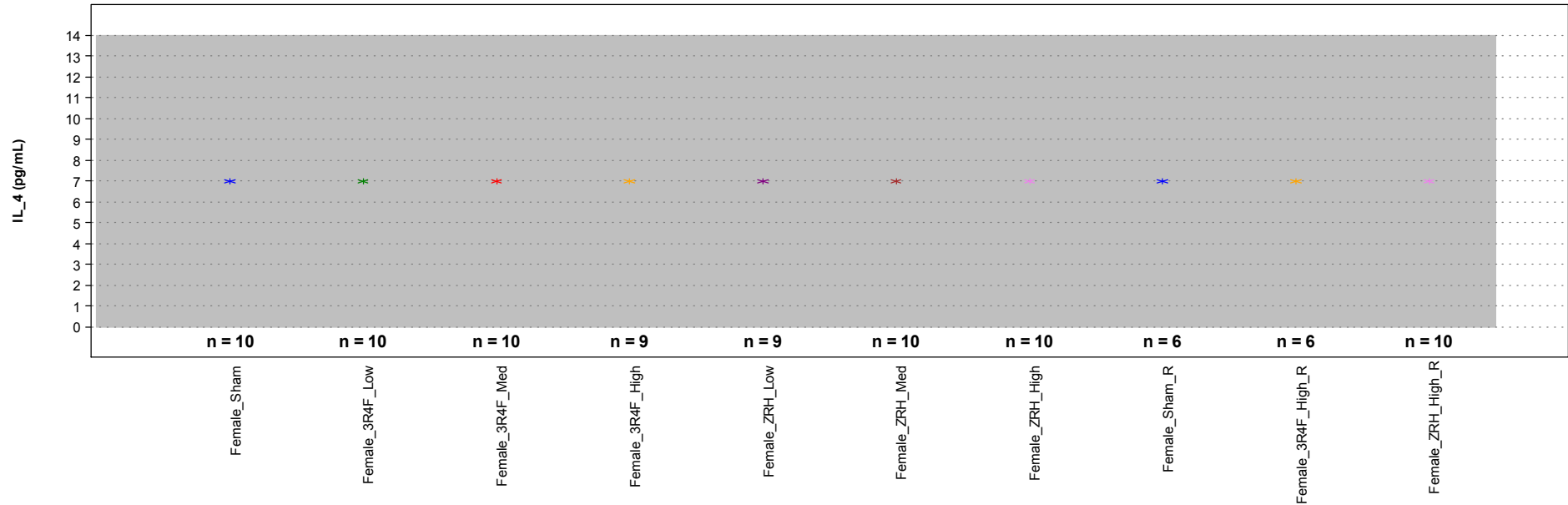
Analyte = IL_4

**Plot of Individual Measurements for IL_4 in Females**

<LOW> values are displayed as 0 / Values above ULQ are displayed as 1.1*ULQ
 Grey zones denote zones below (average) LLQ and above (average) ULQ

**Plot of Descriptive Robust Statistics-Females**

Displayed statistics are Median and Q1/Q3
 Grey zones denote zones below LLQ and above ULQ



Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = IL_4

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	1.000000
---- Sham vs. 3R4F Medium for Male	1.000000
---- Sham vs. 3R4F High for Male	1.000000
---- Sham vs. ZRH Low for Male	1.000000
---- Sham vs. ZRH Medium for Male	0.317311
---- Sham vs. ZRH High for Male	1.000000
---- ZRH Low vs. 3R4F Medium for Male	1.000000
---- ZRH Medium vs. 3R4F High for Male	0.317311
---- ZRH High vs. 3R4F High for Male	1.000000
---- Sham Recovery vs. 3R4F High Recovery for Male	0.273322
---- Sham Recovery vs. ZRH High Recovery for Male	0.438578
---- Sham vs. Sham Recovery for Male	1.000000
---- 3R4F High vs. 3R4F High Recovery for Male	0.157299
---- ZRH High vs. ZRH High Recovery for Male	0.317311
---- 3R4F High Recovery vs. ZRH High Recovery for Male	0.678845
---- Sham vs. 3R4F Low for Female	1.000000
---- Sham vs. 3R4F Medium for Female	1.000000
---- Sham vs. 3R4F High for Female	0.291841
---- Sham vs. ZRH Low for Female	1.000000
---- Sham vs. ZRH Medium for Female	0.317311
---- Sham vs. ZRH High for Female	1.000000
---- ZRH Low vs. 3R4F Medium for Female	1.000000
---- ZRH Medium vs. 3R4F High for Female	0.878275
---- ZRH High vs. 3R4F High for Female	0.291841
---- Sham Recovery vs. 3R4F High Recovery for Female	0.317311
---- Sham Recovery vs. ZRH High Recovery for Female	0.196706
---- Sham vs. Sham Recovery for Female	0.196706

Unadjusted P-values Obtained by Kruskal-Wallis Test
Analyte = IL_4

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	0.414216
---- ZRH High vs. ZRH High Recovery for Female	1.000000
---- 3R4F High Recovery vs. ZRH High Recovery for Female	1.000000

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 25

Interleukin-5 (IL-5)

Unit = ng/mL

Descriptive Statistics by Exposure Duration and Treatment Type**Analyte = IL_5**

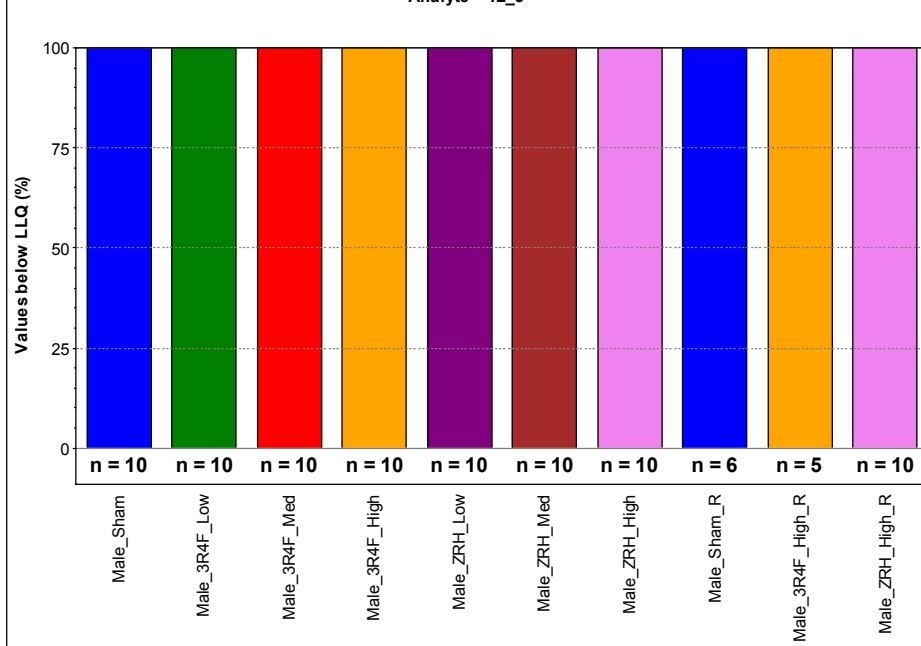
Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	10	0	0	0.15	.
Male	3	3R4F Low	10	10	10	0	0	0.15	.
Male	3	3R4F Medium	10	10	10	0	0	0.15	.
Male	3	3R4F High	10	10	10	0	0	0.15	.
Male	3	ZRH Low	10	10	10	0	0	0.15	.
Male	3	ZRH Medium	10	10	10	0	0	0.15	.
Male	3	ZRH High	10	10	10	0	0	0.15	.
Male	4.5	Sham Recovery	6	6	6	0	0	0.15	.
Male	4.5	3R4F High Recovery	5	5	5	0	0	0.15	.
Male	4.5	ZRH High Recovery	10	10	10	0	0	0.15	.
Female	3	Sham	10	10	10	0	0	0.15	.
Female	3	3R4F Low	10	10	10	0	0	0.15	.
Female	3	3R4F Medium	10	10	10	0	0	0.15	.
Female	3	3R4F High	9	9	9	0	0	0.15	.
Female	3	ZRH Low	9	9	9	0	0	0.15	.
Female	3	ZRH Medium	10	10	10	0	0	0.15	.
Female	3	ZRH High	10	10	10	0	0	0.15	.
Female	4.5	Sham Recovery	6	6	6	0	0	0.15	.
Female	4.5	3R4F High Recovery	6	6	6	0	0	0.15	.
Female	4.5	ZRH High Recovery	10	10	10	0	0	0.15	.

Descriptive Statistics by Exposure Duration and Treatment Type**Analyte = IL_5**

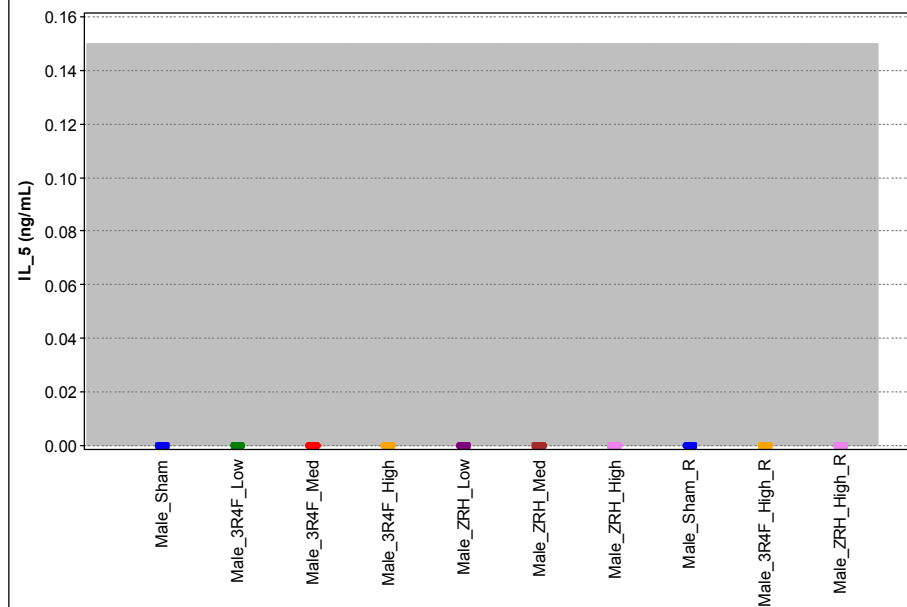
Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	0.075	0.075	0.075	0.075	0.075	0.075	0.000	0.000	0.0	.	.	0.15	.
Male	3	3R4F Low	0.075	0.075	0.075	0.075	0.075	0.075	0.000	0.000	0.0	.	.	0.15	.
Male	3	3R4F Medium	0.075	0.075	0.075	0.075	0.075	0.075	0.000	0.000	0.0	.	.	0.15	.
Male	3	3R4F High	0.075	0.075	0.075	0.075	0.075	0.075	0.000	0.000	0.0	.	.	0.15	.
Male	3	ZRH Low	0.075	0.075	0.075	0.075	0.075	0.075	0.000	0.000	0.0	.	.	0.15	.
Male	3	ZRH Medium	0.075	0.075	0.075	0.075	0.075	0.075	0.000	0.000	0.0	.	.	0.15	.
Male	3	ZRH High	0.075	0.075	0.075	0.075	0.075	0.075	0.000	0.000	0.0	.	.	0.15	.
Male	4.5	Sham Recovery	0.075	0.075	0.075	0.075	0.075	0.075	0.000	0.000	0.0	.	.	0.15	.
Male	4.5	3R4F High Recovery	0.075	0.075	0.075	0.075	0.075	0.075	0.000	0.000	0.0	.	.	0.15	.
Male	4.5	ZRH High Recovery	0.075	0.075	0.075	0.075	0.075	0.075	0.000	0.000	0.0	.	.	0.15	.
Female	3	Sham	0.075	0.075	0.075	0.075	0.075	0.075	0.000	0.000	0.0	.	.	0.15	.
Female	3	3R4F Low	0.075	0.075	0.075	0.075	0.075	0.075	0.000	0.000	0.0	.	.	0.15	.
Female	3	3R4F Medium	0.075	0.075	0.075	0.075	0.075	0.075	0.000	0.000	0.0	.	.	0.15	.
Female	3	3R4F High	0.075	0.075	0.075	0.075	0.075	0.075	0.000	0.000	0.0	.	.	0.15	.
Female	3	ZRH Low	0.075	0.075	0.075	0.075	0.075	0.075	0.000	0.000	0.0	.	.	0.15	.
Female	3	ZRH Medium	0.075	0.075	0.075	0.075	0.075	0.075	0.000	0.000	0.0	.	.	0.15	.
Female	3	ZRH High	0.075	0.075	0.075	0.075	0.075	0.075	0.000	0.000	0.0	.	.	0.15	.
Female	4.5	Sham Recovery	0.075	0.075	0.075	0.075	0.075	0.075	0.000	0.000	0.0	.	.	0.15	.
Female	4.5	3R4F High Recovery	0.075	0.075	0.075	0.075	0.075	0.075	0.000	0.000	0.0	.	.	0.15	.
Female	4.5	ZRH High Recovery	0.075	0.075	0.075	0.075	0.075	0.075	0.000	0.000	0.0	.	.	0.15	.

Percentage of Values below LLQ for each Group-Males

Analyte = IL_5

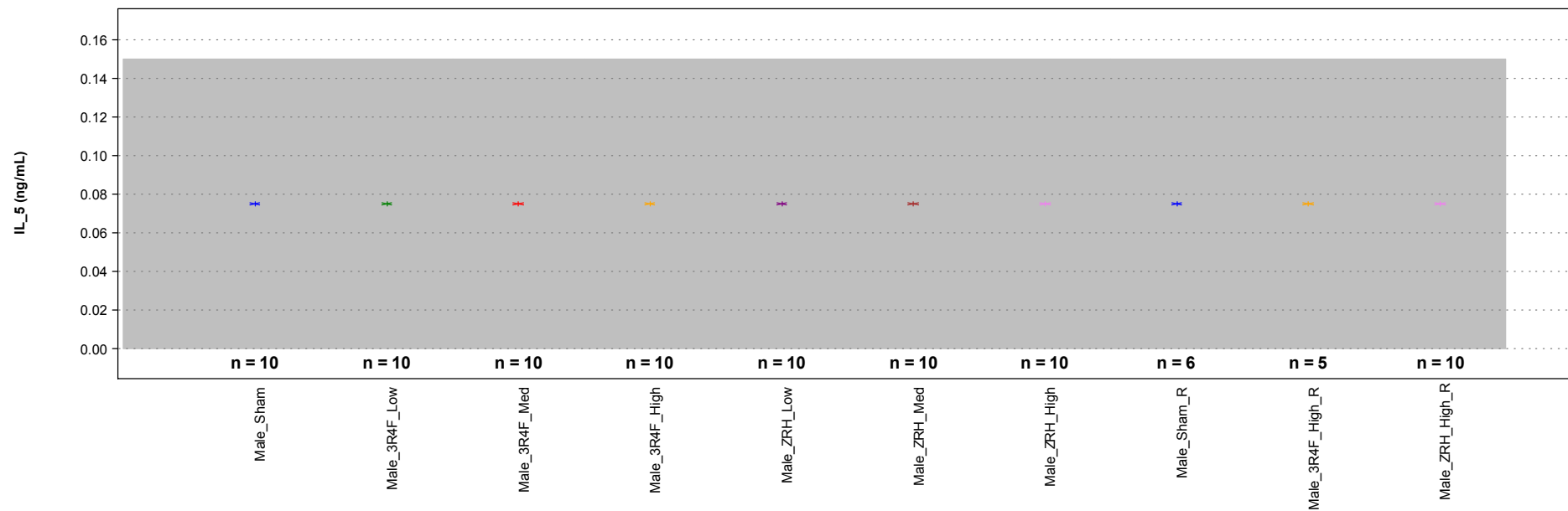
**Plot of Individual Measurements for Each Group-Males**

<LOW> values are displayed as 0 / Values above ULQ are displayed as 1.1*ULQ
 Grey zones denote zones below (average) LLQ and above (average) ULQ

**Plot of Descriptive Robust Statistics-Males**

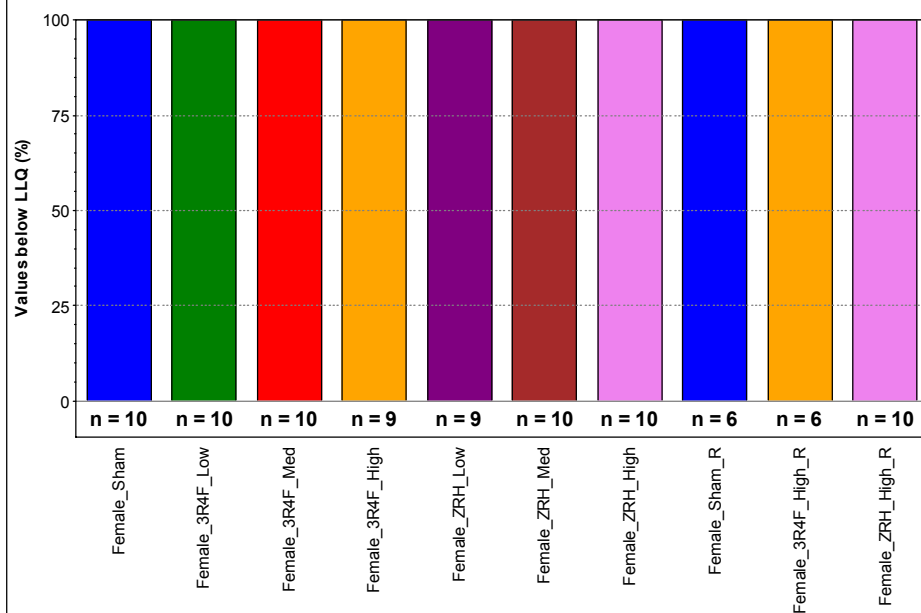
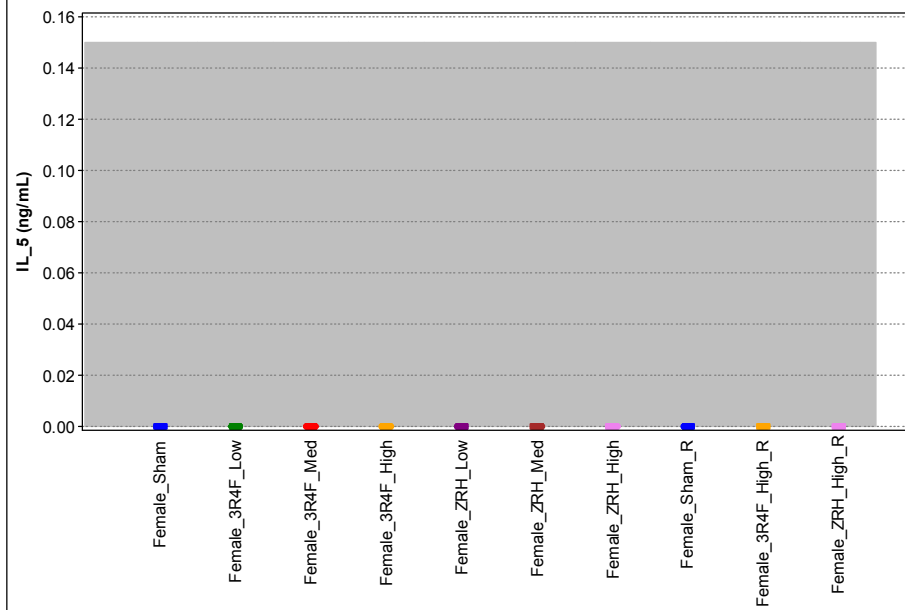
Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



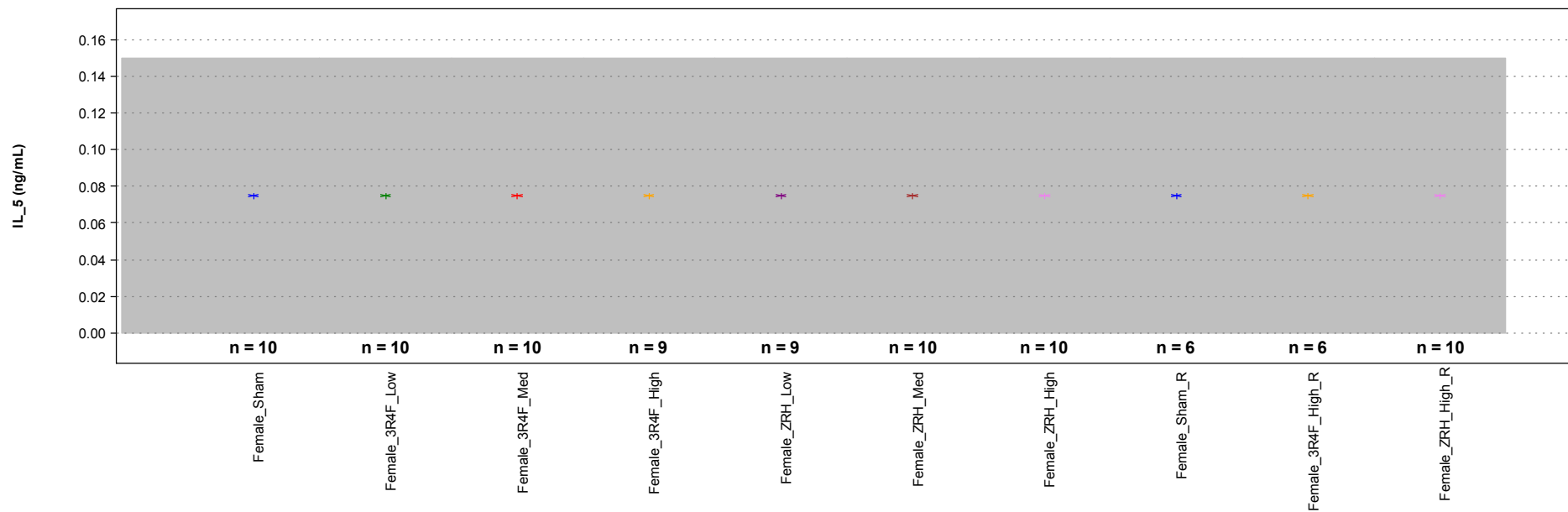
Percentage of Values below LLQ for each Group-Females

Analyte = IL_5


Plot of Individual Measurements
 <LOW> values are displayed as 0 / Values above ULQ are displayed as 1.1*ULQ
 Grey zones denote zones below (average) LLQ and above (average) ULQ
**Plot of Descriptive Robust Statistics-Females**

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = IL_5

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	1.000000
---- Sham vs. 3R4F Medium for Male	1.000000
---- Sham vs. 3R4F High for Male	1.000000
---- Sham vs. ZRH Low for Male	1.000000
---- Sham vs. ZRH Medium for Male	1.000000
---- Sham vs. ZRH High for Male	1.000000
---- ZRH Low vs. 3R4F Medium for Male	1.000000
---- ZRH Medium vs. 3R4F High for Male	1.000000
---- ZRH High vs. 3R4F High for Male	1.000000
---- Sham Recovery vs. 3R4F High Recovery for Male	1.000000
---- Sham Recovery vs. ZRH High Recovery for Male	1.000000
---- Sham vs. Sham Recovery for Male	1.000000
---- 3R4F High vs. 3R4F High Recovery for Male	1.000000
---- ZRH High vs. ZRH High Recovery for Male	1.000000
---- 3R4F High Recovery vs. ZRH High Recovery for Male	1.000000
---- Sham vs. 3R4F Low for Female	1.000000
---- Sham vs. 3R4F Medium for Female	1.000000
---- Sham vs. 3R4F High for Female	1.000000
---- Sham vs. ZRH Low for Female	1.000000
---- Sham vs. ZRH Medium for Female	1.000000
---- Sham vs. ZRH High for Female	1.000000
---- ZRH Low vs. 3R4F Medium for Female	1.000000
---- ZRH Medium vs. 3R4F High for Female	1.000000
---- ZRH High vs. 3R4F High for Female	1.000000
---- Sham Recovery vs. 3R4F High Recovery for Female	1.000000
---- Sham Recovery vs. ZRH High Recovery for Female	1.000000
---- Sham vs. Sham Recovery for Female	1.000000

Unadjusted P-values Obtained by Kruskal-Wallis Test
Analyte = IL_5

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	1.000000
---- ZRH High vs. ZRH High Recovery for Female	1.000000
---- 3R4F High Recovery vs. ZRH High Recovery for Female	1.000000

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 26

Interleukin-6 (IL-6)

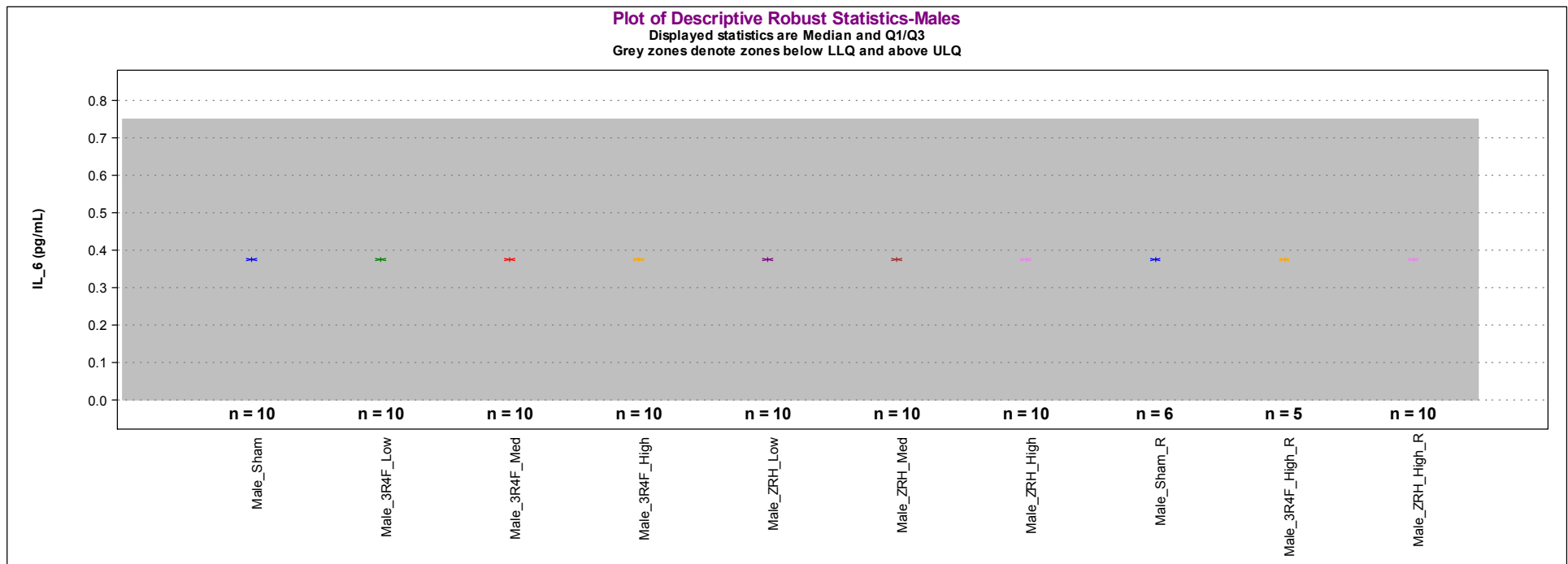
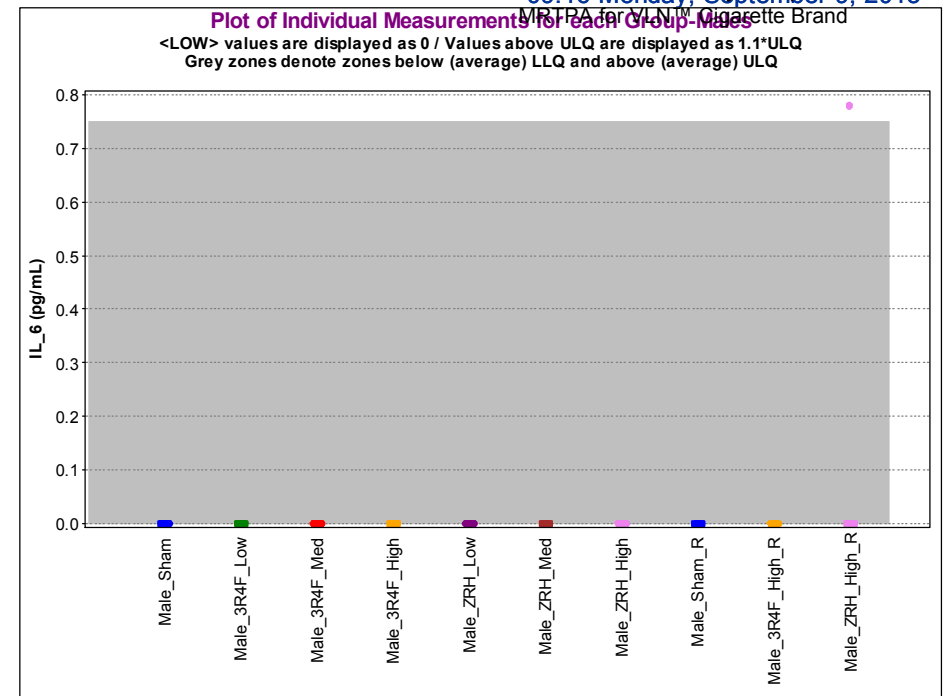
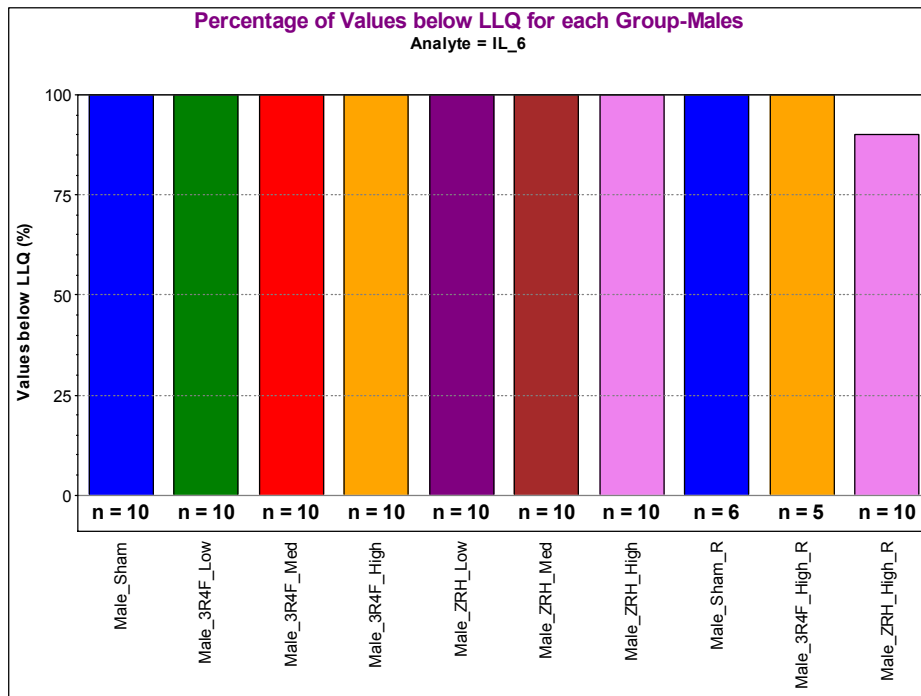
Unit = pg/mL

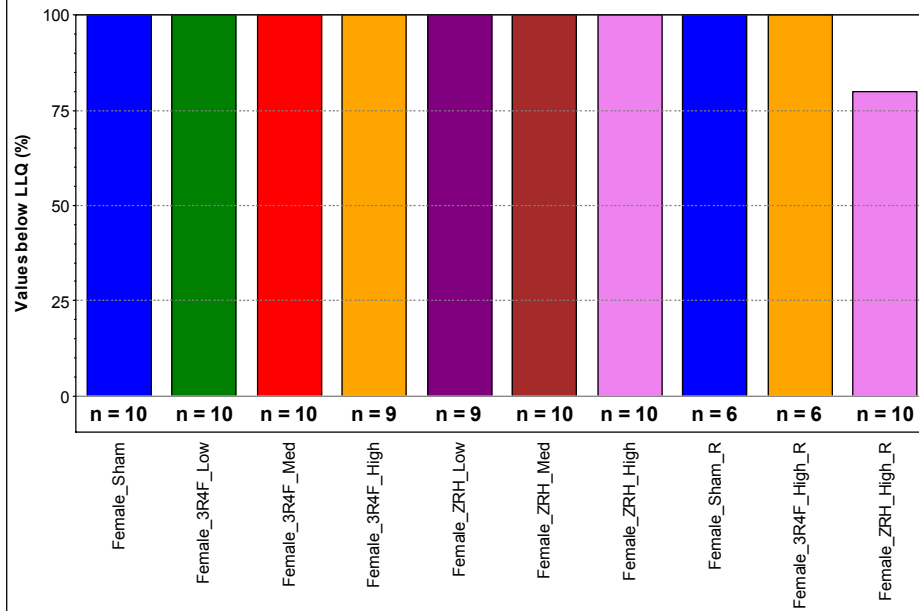
Descriptive Statistics by Exposure Duration and Treatment Type**Analyte = IL_6**

Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	10	0	0	0.75	.
Male	3	3R4F Low	10	10	10	0	0	0.75	.
Male	3	3R4F Medium	10	10	10	0	0	0.75	.
Male	3	3R4F High	10	10	10	0	0	0.75	.
Male	3	ZRH Low	10	10	10	0	0	0.75	.
Male	3	ZRH Medium	10	10	10	0	0	0.75	.
Male	3	ZRH High	10	10	10	0	0	0.75	.
Male	4.5	Sham Recovery	6	6	6	0	0	0.75	.
Male	4.5	3R4F High Recovery	5	5	5	0	0	0.75	.
Male	4.5	ZRH High Recovery	10	10	9	1	0	0.75	.
Female	3	Sham	10	10	10	0	0	0.75	.
Female	3	3R4F Low	10	10	10	0	0	0.75	.
Female	3	3R4F Medium	10	10	10	0	0	0.75	.
Female	3	3R4F High	9	9	9	0	0	0.75	.
Female	3	ZRH Low	9	9	9	0	0	0.75	.
Female	3	ZRH Medium	10	10	10	0	0	0.75	.
Female	3	ZRH High	10	10	10	0	0	0.75	.
Female	4.5	Sham Recovery	6	6	6	0	0	0.75	.
Female	4.5	3R4F High Recovery	6	6	6	0	0	0.75	.
Female	4.5	ZRH High Recovery	10	10	8	2	0	0.75	.

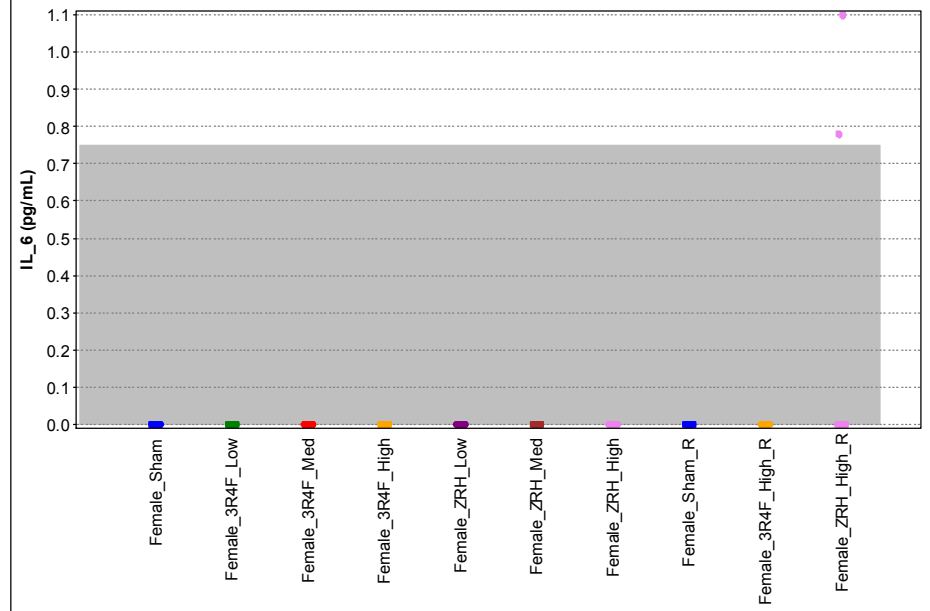
Descriptive Statistics by Exposure Duration and Treatment Type**Analyte = IL_6**

Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	0.375	0.375	0.375	0.375	0.375	0.375	0.000	0.000	0.0	.	.	0.75	.
Male	3	3R4F Low	0.375	0.375	0.375	0.375	0.375	0.375	0.000	0.000	0.0	.	.	0.75	.
Male	3	3R4F Medium	0.375	0.375	0.375	0.375	0.375	0.375	0.000	0.000	0.0	.	.	0.75	.
Male	3	3R4F High	0.375	0.375	0.375	0.375	0.375	0.375	0.000	0.000	0.0	.	.	0.75	.
Male	3	ZRH Low	0.375	0.375	0.375	0.375	0.375	0.375	0.000	0.000	0.0	.	.	0.75	.
Male	3	ZRH Medium	0.375	0.375	0.375	0.375	0.375	0.375	0.000	0.000	0.0	.	.	0.75	.
Male	3	ZRH High	0.375	0.375	0.375	0.375	0.375	0.375	0.000	0.000	0.0	.	.	0.75	.
Male	4.5	Sham Recovery	0.375	0.375	0.375	0.375	0.375	0.375	0.000	0.000	0.0	.	.	0.75	.
Male	4.5	3R4F High Recovery	0.375	0.375	0.375	0.375	0.375	0.375	0.000	0.000	0.0	.	.	0.75	.
Male	4.5	ZRH High Recovery	0.375	0.375	0.375	0.375	0.780	0.416	0.128	0.041	30.8	3.162	10.000	0.75	.
Female	3	Sham	0.375	0.375	0.375	0.375	0.375	0.375	0.000	0.000	0.0	.	.	0.75	.
Female	3	3R4F Low	0.375	0.375	0.375	0.375	0.375	0.375	0.000	0.000	0.0	.	.	0.75	.
Female	3	3R4F Medium	0.375	0.375	0.375	0.375	0.375	0.375	0.000	0.000	0.0	.	.	0.75	.
Female	3	3R4F High	0.375	0.375	0.375	0.375	0.375	0.375	0.000	0.000	0.0	.	.	0.75	.
Female	3	ZRH Low	0.375	0.375	0.375	0.375	0.375	0.375	0.000	0.000	0.0	.	.	0.75	.
Female	3	ZRH Medium	0.375	0.375	0.375	0.375	0.375	0.375	0.000	0.000	0.0	.	.	0.75	.
Female	3	ZRH High	0.375	0.375	0.375	0.375	0.375	0.375	0.000	0.000	0.0	.	.	0.75	.
Female	4.5	Sham Recovery	0.375	0.375	0.375	0.375	0.375	0.375	0.000	0.000	0.0	.	.	0.75	.
Female	4.5	3R4F High Recovery	0.375	0.375	0.375	0.375	0.375	0.375	0.000	0.000	0.0	.	.	0.75	.
Female	4.5	ZRH High Recovery	0.375	0.375	0.375	0.375	1.100	0.488	0.250	0.079	51.2	2.159	3.994	0.75	.



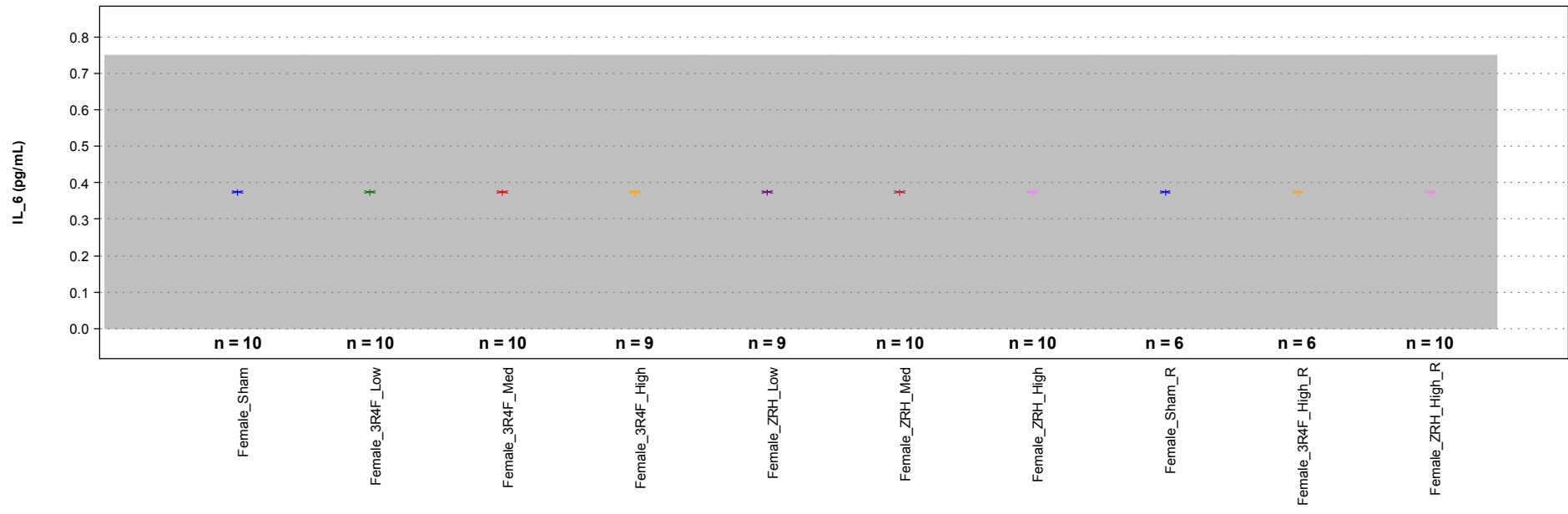
Percentage of Values below LLQ for each Group-FemalesAnalyte = IL₆**Plot of Individual Measurements for IL₆ in Females**

<LOW> values are displayed as 0 / Values above ULQ are displayed as 1.1*ULQ
 Grey zones denote zones below (average) LLQ and above (average) ULQ

**Plot of Descriptive Robust Statistics-Females**

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = IL_6

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	1.000000
---- Sham vs. 3R4F Medium for Male	1.000000
---- Sham vs. 3R4F High for Male	1.000000
---- Sham vs. ZRH Low for Male	1.000000
---- Sham vs. ZRH Medium for Male	1.000000
---- Sham vs. ZRH High for Male	1.000000
---- ZRH Low vs. 3R4F Medium for Male	1.000000
---- ZRH Medium vs. 3R4F High for Male	1.000000
---- ZRH High vs. 3R4F High for Male	1.000000
---- Sham Recovery vs. 3R4F High Recovery for Male	1.000000
---- Sham Recovery vs. ZRH High Recovery for Male	0.438578
---- Sham vs. Sham Recovery for Male	1.000000
---- 3R4F High vs. 3R4F High Recovery for Male	1.000000
---- ZRH High vs. ZRH High Recovery for Male	0.317311
---- 3R4F High Recovery vs. ZRH High Recovery for Male	0.479500
---- Sham vs. 3R4F Low for Female	1.000000
---- Sham vs. 3R4F Medium for Female	1.000000
---- Sham vs. 3R4F High for Female	1.000000
---- Sham vs. ZRH Low for Female	1.000000
---- Sham vs. ZRH Medium for Female	1.000000
---- Sham vs. ZRH High for Female	1.000000
---- ZRH Low vs. 3R4F Medium for Female	1.000000
---- ZRH Medium vs. 3R4F High for Female	1.000000
---- ZRH High vs. 3R4F High for Female	1.000000
---- Sham Recovery vs. 3R4F High Recovery for Female	1.000000
---- Sham Recovery vs. ZRH High Recovery for Female	0.257899
---- Sham vs. Sham Recovery for Female	1.000000

Unadjusted P-values Obtained by Kruskal-Wallis Test
Analyte = IL_6

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	1.000000
---- ZRH High vs. ZRH High Recovery for Female	0.146793
---- 3R4F High Recovery vs. ZRH High Recovery for Female	0.257899

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 27

Interleukin-7 (IL-7)

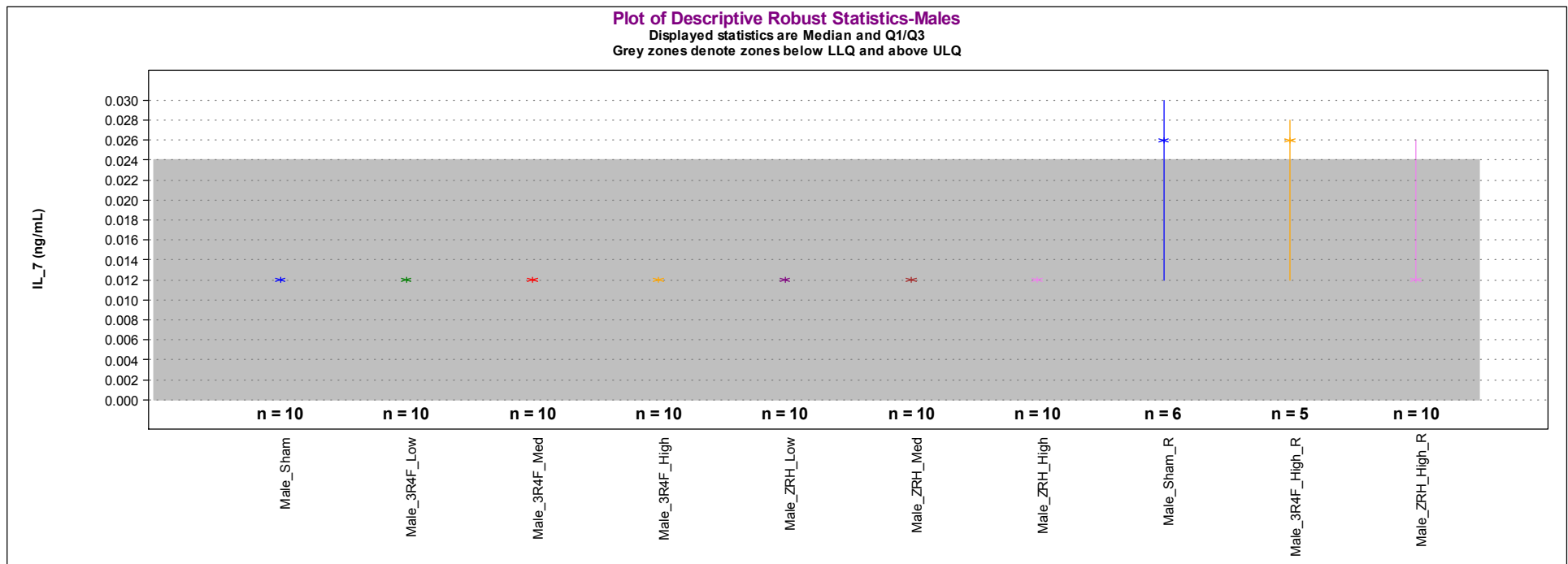
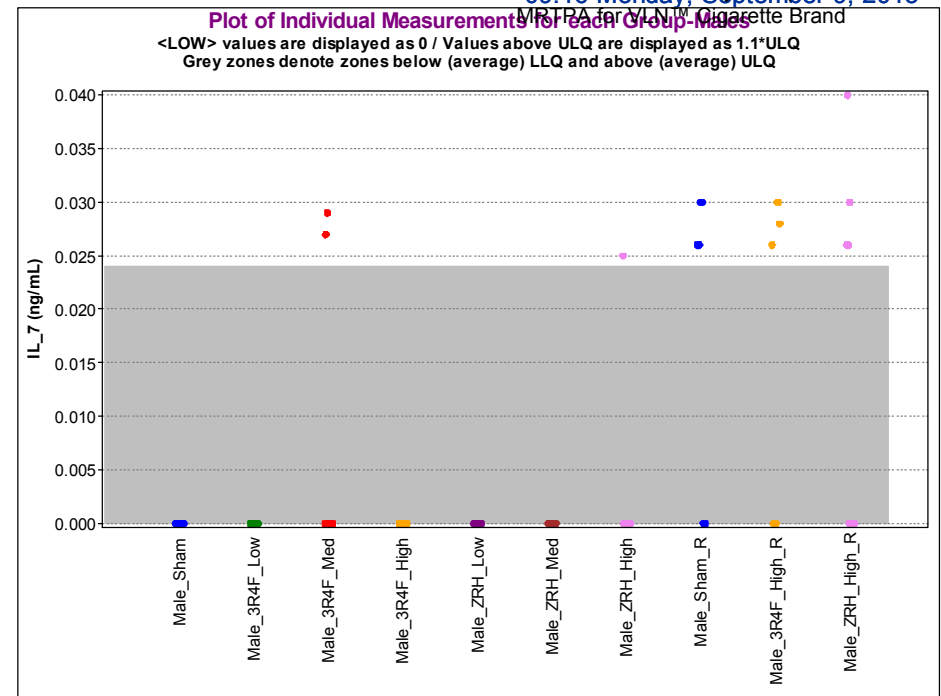
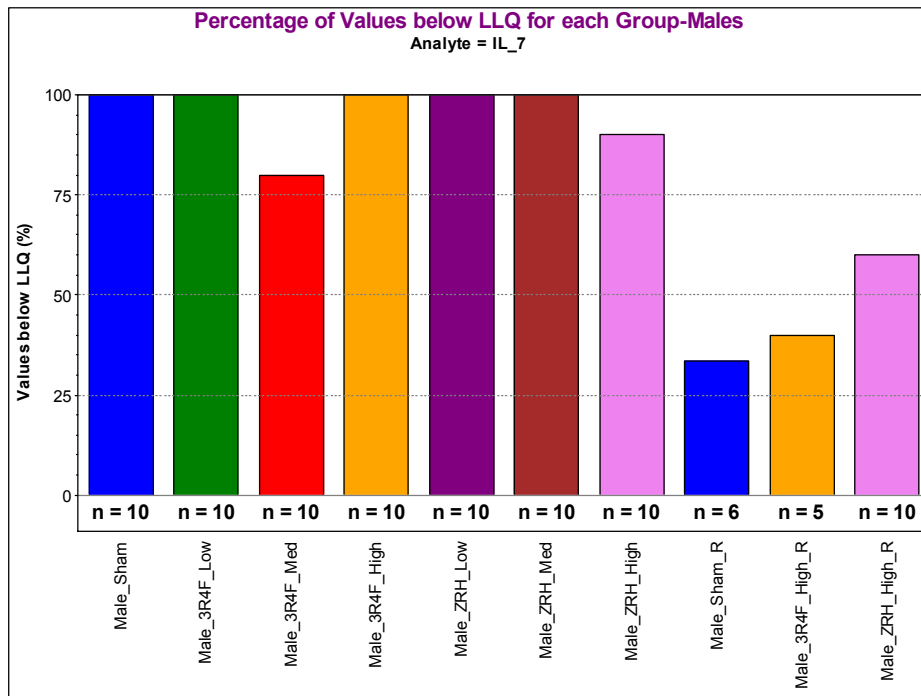
Unit = ng/mL

Descriptive Statistics by Exposure Duration and Treatment Type**Analyte = IL_7**

Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	10	0	0	0.024	.
Male	3	3R4F Low	10	10	10	0	0	0.024	.
Male	3	3R4F Medium	10	10	8	2	0	0.024	.
Male	3	3R4F High	10	10	10	0	0	0.024	.
Male	3	ZRH Low	10	10	10	0	0	0.024	.
Male	3	ZRH Medium	10	10	10	0	0	0.024	.
Male	3	ZRH High	10	10	9	1	0	0.024	.
Male	4.5	Sham Recovery	6	6	2	4	0	0.024	.
Male	4.5	3R4F High Recovery	5	5	2	3	0	0.024	.
Male	4.5	ZRH High Recovery	10	10	6	4	0	0.024	.
Female	3	Sham	10	10	10	0	0	0.024	.
Female	3	3R4F Low	10	10	9	1	0	0.024	.
Female	3	3R4F Medium	10	10	5	5	0	0.024	.
Female	3	3R4F High	9	9	7	2	0	0.024	.
Female	3	ZRH Low	9	9	8	1	0	0.024	.
Female	3	ZRH Medium	10	10	9	1	0	0.024	.
Female	3	ZRH High	10	10	10	0	0	0.024	.
Female	4.5	Sham Recovery	6	6	2	4	0	0.024	.
Female	4.5	3R4F High Recovery	6	6	3	3	0	0.024	.
Female	4.5	ZRH High Recovery	10	10	7	3	0	0.024	.

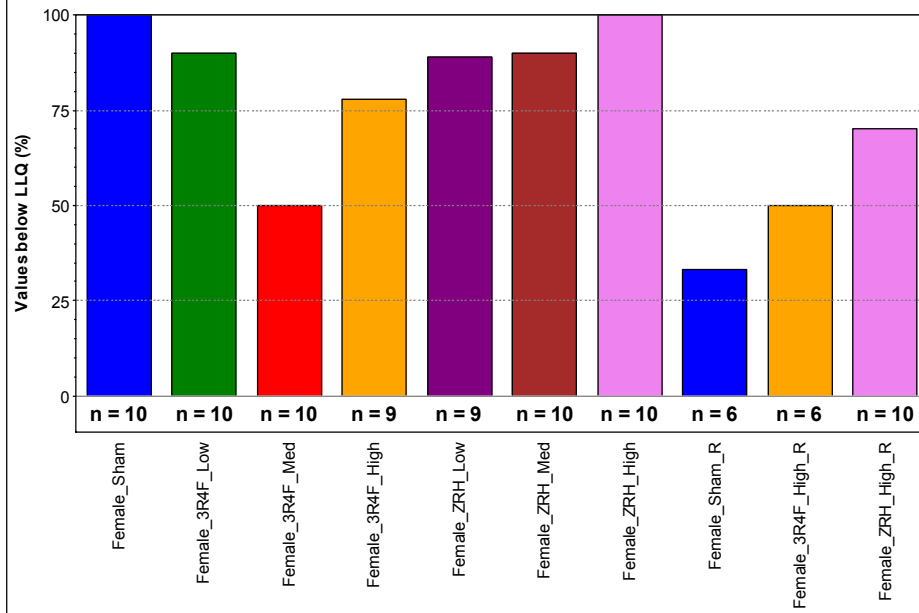
Descriptive Statistics by Exposure Duration and Treatment Type**Analyte = IL_7**

Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	0.012	0.012	0.012	0.012	0.012	0.012	0.000	0.000	0.0	.	.	0.024	.
Male	3	3R4F Low	0.012	0.012	0.012	0.012	0.012	0.012	0.000	0.000	0.0	.	.	0.024	.
Male	3	3R4F Medium	0.012	0.012	0.012	0.012	0.029	0.015	0.007	0.002	44.5	1.800	1.556	0.024	.
Male	3	3R4F High	0.012	0.012	0.012	0.012	0.012	0.012	0.000	0.000	0.0	.	.	0.024	.
Male	3	ZRH Low	0.012	0.012	0.012	0.012	0.012	0.012	0.000	0.000	0.0	.	.	0.024	.
Male	3	ZRH Medium	0.012	0.012	0.012	0.012	0.012	0.012	0.000	0.000	0.0	.	.	0.024	.
Male	3	ZRH High	0.012	0.012	0.012	0.012	0.025	0.013	0.004	0.001	30.9	3.162	10.000	0.024	.
Male	4.5	Sham Recovery	0.012	0.012	0.026	0.030	0.030	0.023	0.008	0.003	37.3	-0.777	-1.875	0.024	.
Male	4.5	3R4F High Recovery	0.012	0.012	0.026	0.028	0.030	0.022	0.009	0.004	41.1	-0.494	-3.165	0.024	.
Male	4.5	ZRH High Recovery	0.012	0.012	0.012	0.026	0.040	0.019	0.010	0.003	53.0	1.030	-0.159	0.024	.
Female	3	Sham	0.012	0.012	0.012	0.012	0.012	0.012	0.000	0.000	0.0	.	.	0.024	.
Female	3	3R4F Low	0.012	0.012	0.012	0.012	0.027	0.014	0.005	0.002	35.1	3.162	10.000	0.024	.
Female	3	3R4F Medium	0.012	0.012	0.019	0.027	0.038	0.020	0.010	0.003	46.6	0.556	-0.955	0.024	.
Female	3	3R4F High	0.012	0.012	0.012	0.012	0.027	0.015	0.006	0.002	41.0	1.648	0.925	0.024	.
Female	3	ZRH Low	0.012	0.012	0.012	0.012	0.024	0.013	0.004	0.001	30.0	3.000	9.000	0.024	.
Female	3	ZRH Medium	0.012	0.012	0.012	0.012	0.024	0.013	0.004	0.001	28.7	3.162	10.000	0.024	.
Female	3	ZRH High	0.012	0.012	0.012	0.012	0.012	0.012	0.000	0.000	0.0	.	.	0.024	.
Female	4.5	Sham Recovery	0.012	0.012	0.027	0.029	0.031	0.023	0.009	0.003	37.5	-0.792	-1.849	0.024	.
Female	4.5	3R4F High Recovery	0.012	0.012	0.024	0.040	0.042	0.026	0.015	0.006	58.7	0.091	-3.093	0.024	.
Female	4.5	ZRH High Recovery	0.012	0.012	0.012	0.031	0.042	0.019	0.012	0.004	61.9	1.226	-0.286	0.024	.

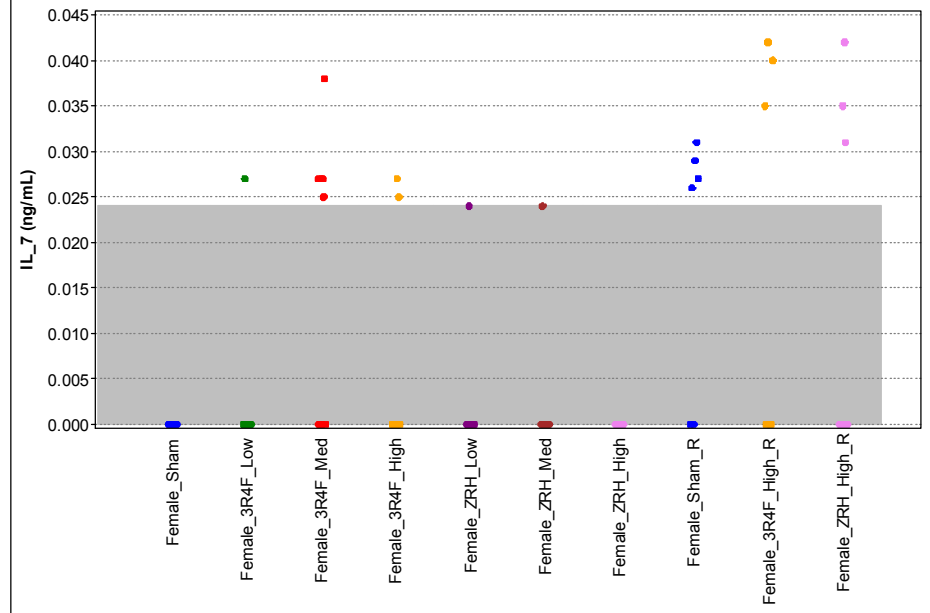


Percentage of Values below LLQ for each Group-Females

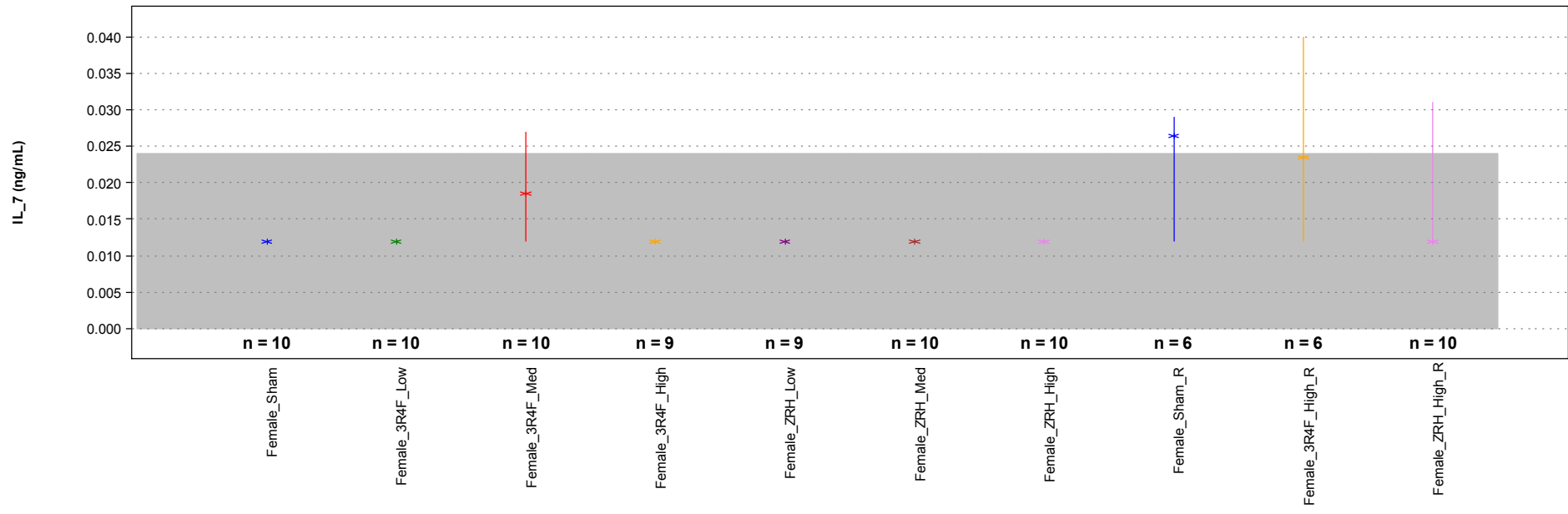
Analyte = IL_7

**Plot of Individual Measurements**

<LOW> values are displayed as 0 / Values above ULQ are displayed as 1.1*ULQ
 Grey zones denote zones below (average) LLQ and above (average) ULQ

**Plot of Descriptive Robust Statistics-Females**

Displayed statistics are Median and Q1/Q3
 Grey zones denote zones below LLQ and above ULQ



Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = IL_7

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	1.000000
---- Sham vs. 3R4F Medium for Male	0.146793
---- Sham vs. 3R4F High for Male	1.000000
---- Sham vs. ZRH Low for Male	1.000000
---- Sham vs. ZRH Medium for Male	1.000000
---- Sham vs. ZRH High for Male	0.317311
---- ZRH Low vs. 3R4F Medium for Male	0.146793
---- ZRH Medium vs. 3R4F High for Male	1.000000
---- ZRH High vs. 3R4F High for Male	0.317311
---- Sham Recovery vs. 3R4F High Recovery for Male	0.848890
---- Sham Recovery vs. ZRH High Recovery for Male	0.411820
---- Sham vs. Sham Recovery for Male	0.004275
---- 3R4F High vs. 3R4F High Recovery for Male	0.008630
---- ZRH High vs. ZRH High Recovery for Male	0.091024
---- 3R4F High Recovery vs. ZRH High Recovery for Male	0.547870
---- Sham vs. 3R4F Low for Female	0.317311
---- Sham vs. 3R4F Medium for Female	0.012767
---- Sham vs. 3R4F High for Female	0.125631
---- Sham vs. ZRH Low for Female	0.291841
---- Sham vs. ZRH Medium for Female	0.317311
---- Sham vs. ZRH High for Female	1.000000
---- ZRH Low vs. 3R4F Medium for Female	0.047212
---- ZRH Medium vs. 3R4F High for Female	0.403442
---- ZRH High vs. 3R4F High for Female	0.125631
---- Sham Recovery vs. 3R4F High Recovery for Female	0.618402
---- Sham Recovery vs. ZRH High Recovery for Female	0.510562
---- Sham vs. Sham Recovery for Female	0.004374

Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = IL_7

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	0.140645
---- ZRH High vs. ZRH High Recovery for Female	0.068157
---- 3R4F High Recovery vs. ZRH High Recovery for Female	0.348972

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 19

Interferon gamma Induced Protein 10 (IP-10)

Unit = pg/mL

Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = IP₁₀

Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	4	6	0	1.4	.
Male	3	3R4F Low	10	10	1	9	0	1.4	.
Male	3	3R4F Medium	10	10	0	10	0	1.4	.
Male	3	3R4F High	10	10	2	8	0	1.4	.
Male	3	ZRH Low	10	10	2	8	0	1.4	.
Male	3	ZRH Medium	10	10	2	8	0	1.4	.
Male	3	ZRH High	10	10	2	8	0	1.4	.
Male	4.5	Sham Recovery	6	6	0	6	0	1.4	.
Male	4.5	3R4F High Recovery	5	5	0	5	0	1.4	.
Male	4.5	ZRH High Recovery	10	10	0	10	0	1.4	.
Female	3	Sham	10	10	4	6	0	1.4	.
Female	3	3R4F Low	10	10	0	10	0	1.4	.
Female	3	3R4F Medium	10	10	0	10	0	1.4	.
Female	3	3R4F High	9	9	0	9	0	1.4	.
Female	3	ZRH Low	9	9	2	7	0	1.4	.
Female	3	ZRH Medium	10	10	2	8	0	1.4	.
Female	3	ZRH High	10	10	0	10	0	1.4	.
Female	4.5	Sham Recovery	6	6	0	6	0	1.4	.
Female	4.5	3R4F High Recovery	6	6	0	6	0	1.4	.
Female	4.5	ZRH High Recovery	10	10	0	10	0	1.4	.

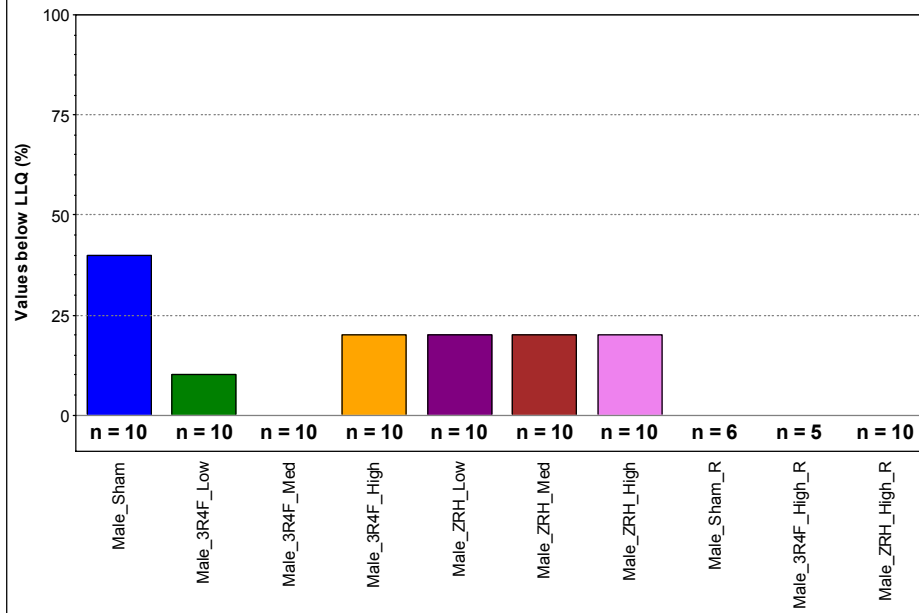
Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = IP₁₀

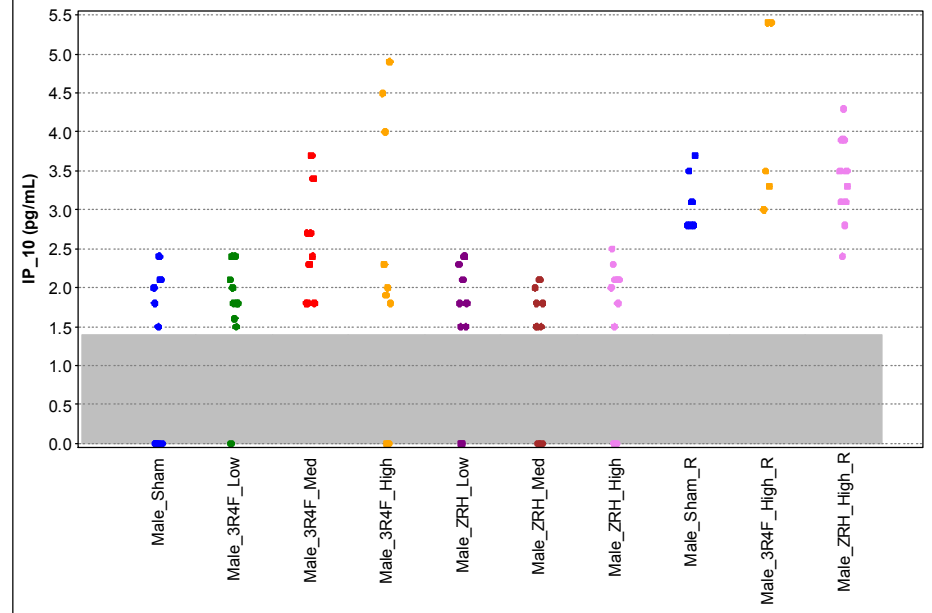
Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	0.700	0.700	1.650	2.100	2.400	1.470	0.701	0.222	47.7	-0.136	-2.024	1.4	.
Male	3	3R4F Low	0.700	1.600	1.800	2.100	2.400	1.810	0.493	0.156	27.2	-1.117	2.228	1.4	.
Male	3	3R4F Medium	1.800	1.800	2.350	2.700	3.700	2.490	0.657	0.208	26.4	0.755	-0.230	1.4	.
Male	3	3R4F High	0.700	1.800	2.150	4.000	4.900	2.510	1.478	0.467	58.9	0.526	-0.904	1.4	.
Male	3	ZRH Low	0.700	1.500	1.800	2.300	2.400	1.720	0.632	0.200	36.8	-0.695	-0.605	1.4	.
Male	3	ZRH Medium	0.700	1.500	1.650	2.000	2.100	1.570	0.514	0.163	32.8	-0.935	-0.150	1.4	.
Male	3	ZRH High	0.700	1.500	2.050	2.100	2.500	1.780	0.629	0.199	35.3	-1.073	-0.001	1.4	.
Male	4.5	Sham Recovery	2.800	2.800	2.950	3.500	3.700	3.117	0.397	0.162	12.7	0.765	-1.532	1.4	.
Male	4.5	3R4F High Recovery	3.000	3.300	3.500	5.400	5.400	4.120	1.182	0.529	28.7	0.505	-3.169	1.4	.
Male	4.5	ZRH High Recovery	2.400	3.100	3.400	3.900	4.300	3.380	0.565	0.179	16.7	-0.090	-0.255	1.4	.
Female	3	Sham	0.700	0.700	1.700	2.000	2.600	1.540	0.785	0.248	51.0	0.061	-1.689	1.4	.
Female	3	3R4F Low	1.700	1.800	2.350	2.500	2.900	2.250	0.392	0.124	17.4	-0.028	-0.907	1.4	.
Female	3	3R4F Medium	2.000	2.600	2.600	3.500	4.400	2.970	0.810	0.256	27.3	0.721	-0.569	1.4	.
Female	3	3R4F High	1.700	2.000	2.500	3.200	4.400	2.700	0.889	0.296	32.9	0.781	0.042	1.4	.
Female	3	ZRH Low	0.700	1.500	1.700	1.800	2.600	1.656	0.646	0.215	39.0	-0.290	-0.318	1.4	.
Female	3	ZRH Medium	0.700	1.800	2.100	2.300	2.400	1.840	0.635	0.201	34.5	-1.356	0.507	1.4	.
Female	3	ZRH High	1.500	1.700	1.950	2.100	3.100	2.000	0.490	0.155	24.5	1.361	1.981	1.4	.
Female	4.5	Sham Recovery	2.400	2.800	3.000	3.100	3.500	2.967	0.367	0.150	12.4	-0.185	0.908	1.4	.
Female	4.5	3R4F High Recovery	3.000	3.500	3.800	4.300	4.700	3.850	0.599	0.245	15.6	0.063	-0.273	1.4	.
Female	4.5	ZRH High Recovery	2.400	3.000	3.100	3.500	4.100	3.200	0.564	0.178	17.6	0.065	-0.589	1.4	.

Percentage of Values below LLQ for each Group-Males

Analyte = IP_10

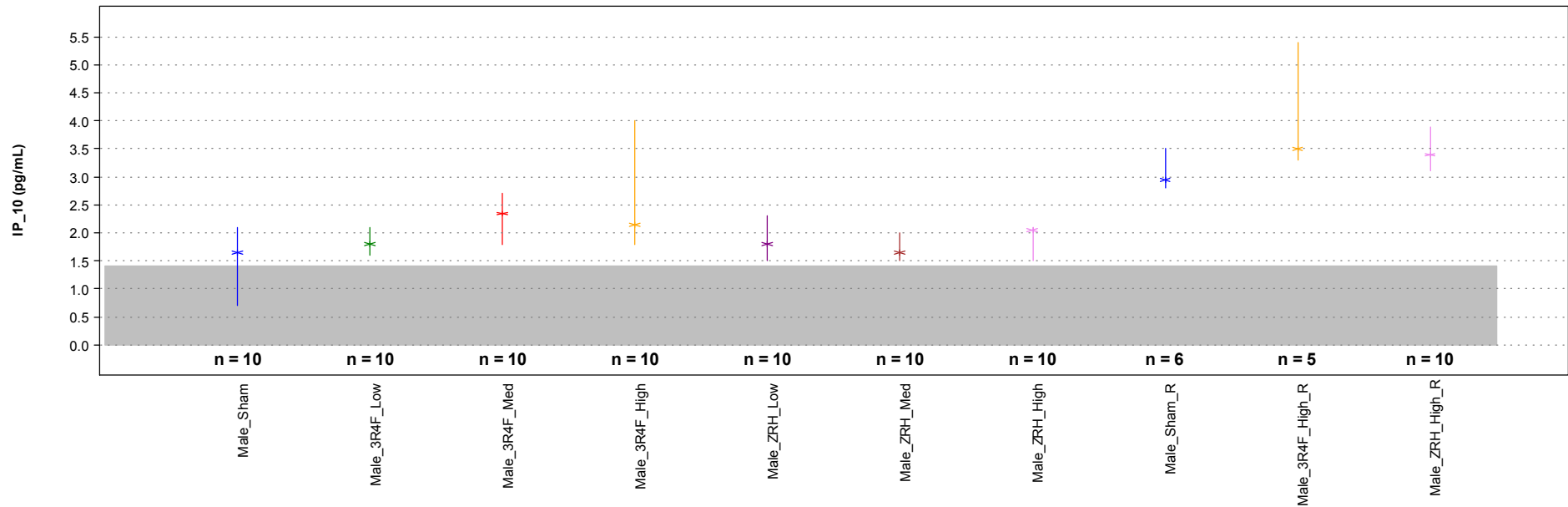
**Plot of Individual Measurements for each Group-Males**

<LOW> values are displayed as 0 / Values above ULQ are displayed as 1.1*ULQ
 Grey zones denote zones below (average) LLQ and above (average) ULQ

**Plot of Descriptive Robust Statistics-Males**

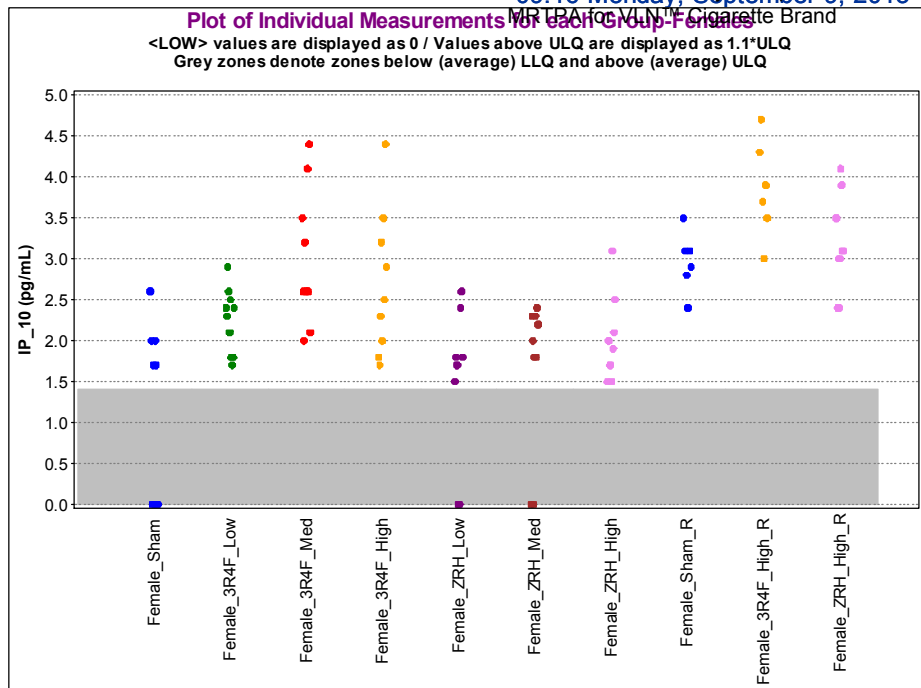
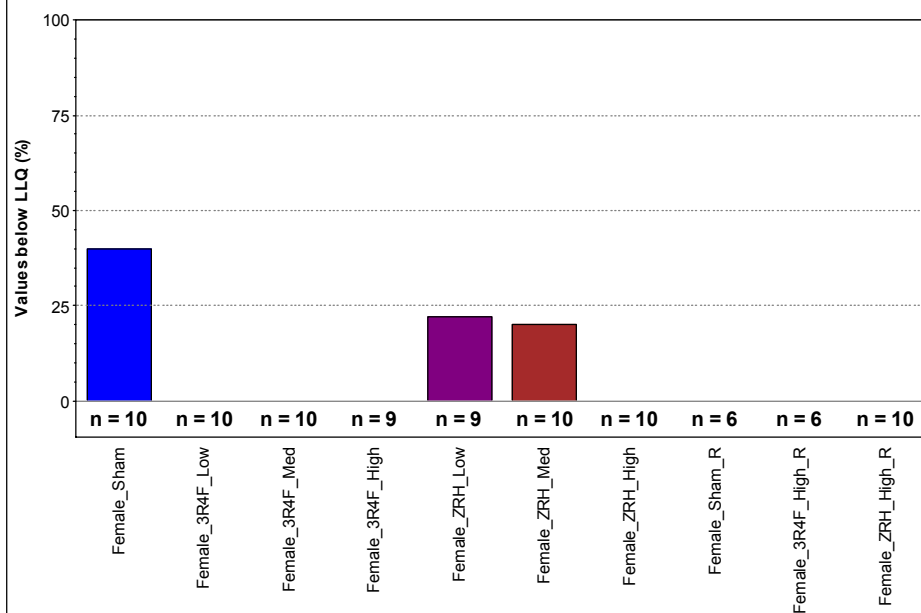
Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



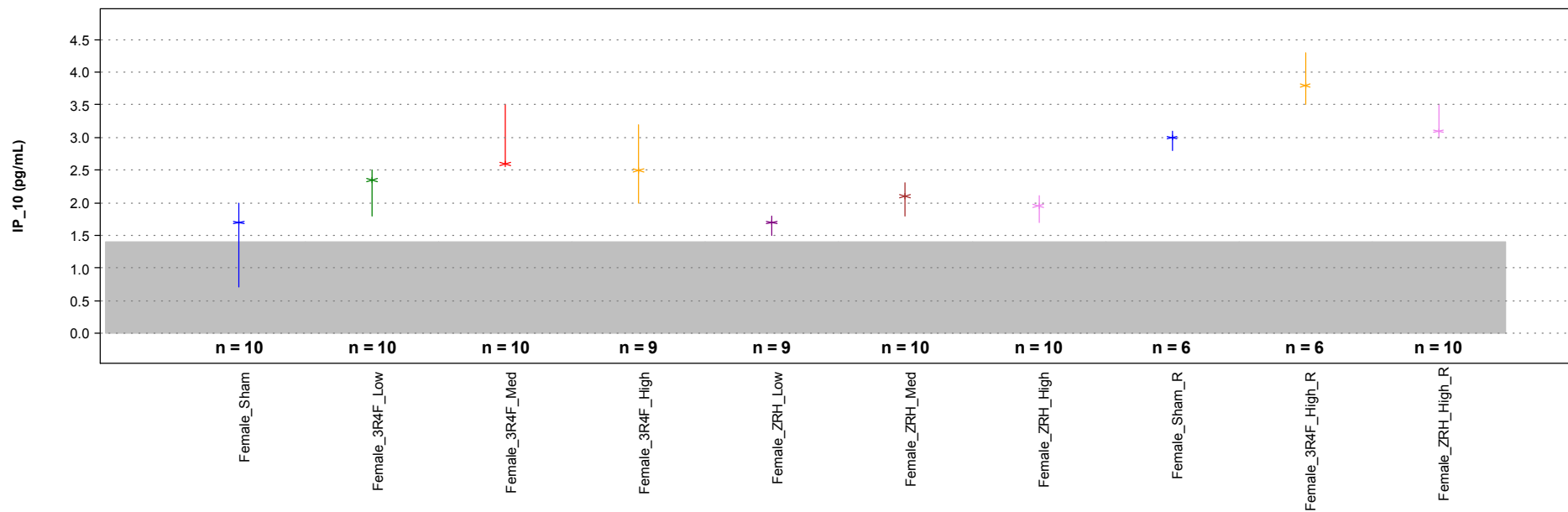
Percentage of Values below LLQ for each Group-Females

Analyte = IP_10

**Plot of Descriptive Robust Statistics-Females**

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = IP_10

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	0.377402
---- Sham vs. 3R4F Medium for Male	0.009496
---- Sham vs. 3R4F High for Male	0.124901
---- Sham vs. ZRH Low for Male	0.440794
---- Sham vs. ZRH Medium for Male	0.938339
---- Sham vs. ZRH High for Male	0.296712
---- ZRH Low vs. 3R4F Medium for Male	0.026541
---- ZRH Medium vs. 3R4F High for Male	0.086450
---- ZRH High vs. 3R4F High for Male	0.402118
---- Sham Recovery vs. 3R4F High Recovery for Male	0.115606
---- Sham Recovery vs. ZRH High Recovery for Male	0.295966
---- Sham vs. Sham Recovery for Male	0.001000
---- 3R4F High vs. 3R4F High Recovery for Male	0.049430
---- ZRH High vs. ZRH High Recovery for Male	0.000203
---- 3R4F High Recovery vs. ZRH High Recovery for Male	0.354867
---- Sham vs. 3R4F Low for Female	0.047578
---- Sham vs. 3R4F Medium for Female	0.001582
---- Sham vs. 3R4F High for Female	0.016949
---- Sham vs. ZRH Low for Female	0.867308
---- Sham vs. ZRH Medium for Female	0.317612
---- Sham vs. ZRH High for Female	0.284050
---- ZRH Low vs. 3R4F Medium for Female	0.001296
---- ZRH Medium vs. 3R4F High for Female	0.064886
---- ZRH High vs. 3R4F High for Female	0.053950
---- Sham Recovery vs. 3R4F High Recovery for Female	0.019805
---- Sham Recovery vs. ZRH High Recovery for Female	0.378803
---- Sham vs. Sham Recovery for Female	0.002149

Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = IP_10

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	0.021440
---- ZRH High vs. ZRH High Recovery for Female	0.001103
---- 3R4F High Recovery vs. ZRH High Recovery for Female	0.071180

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 16

Immunoglobulin A (IgA)

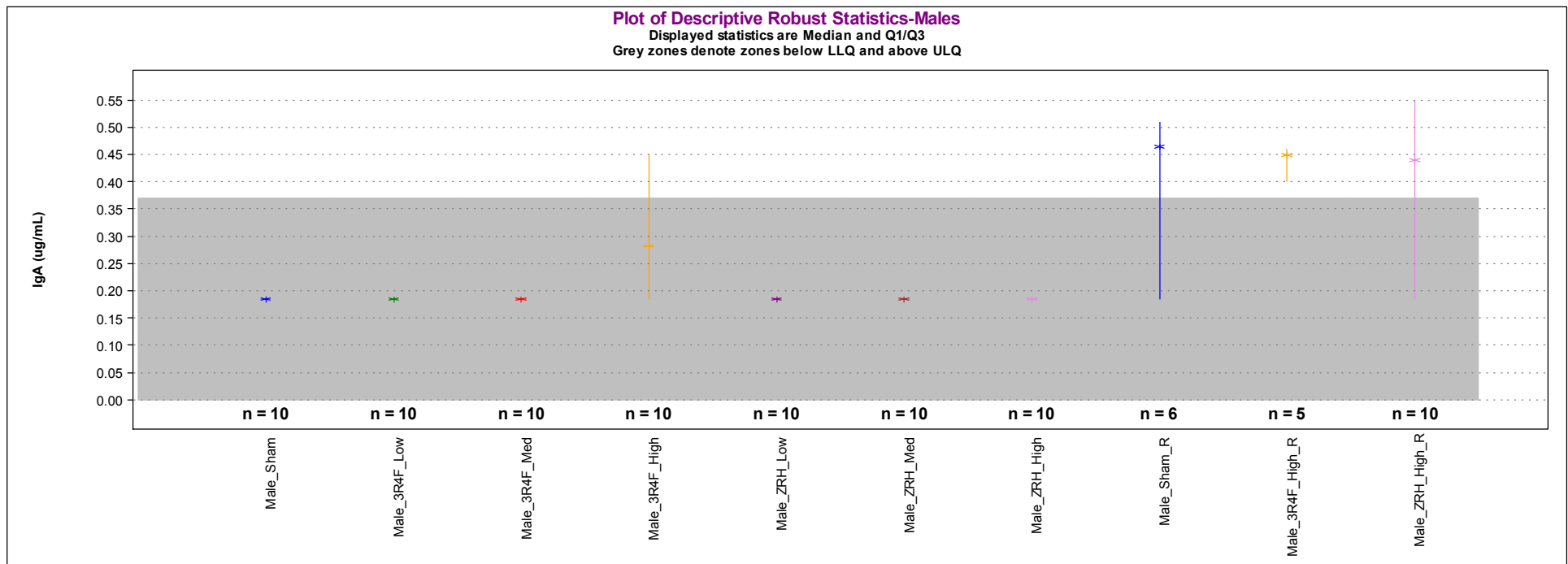
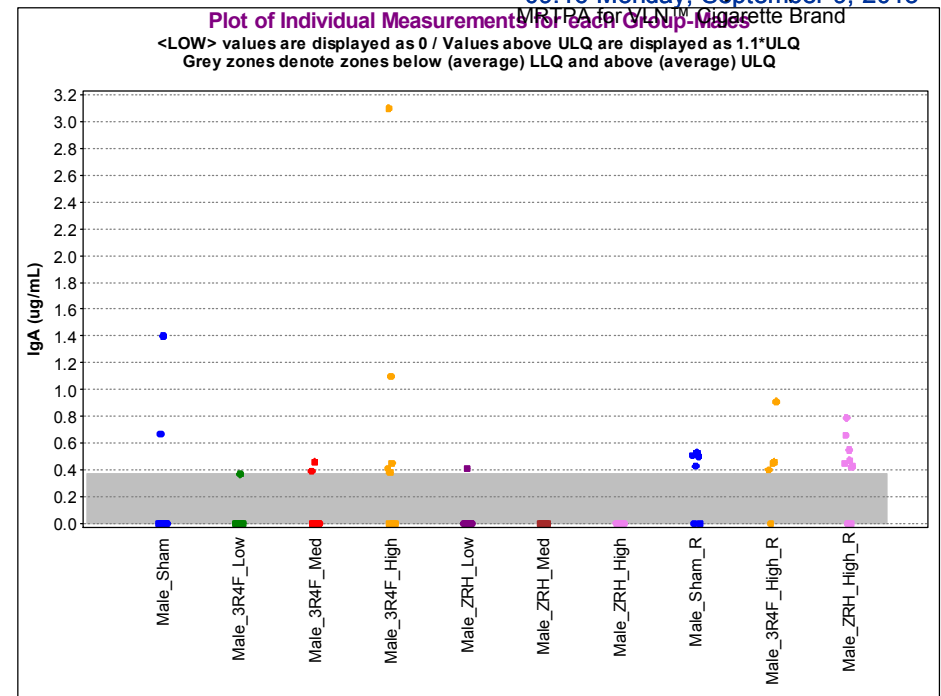
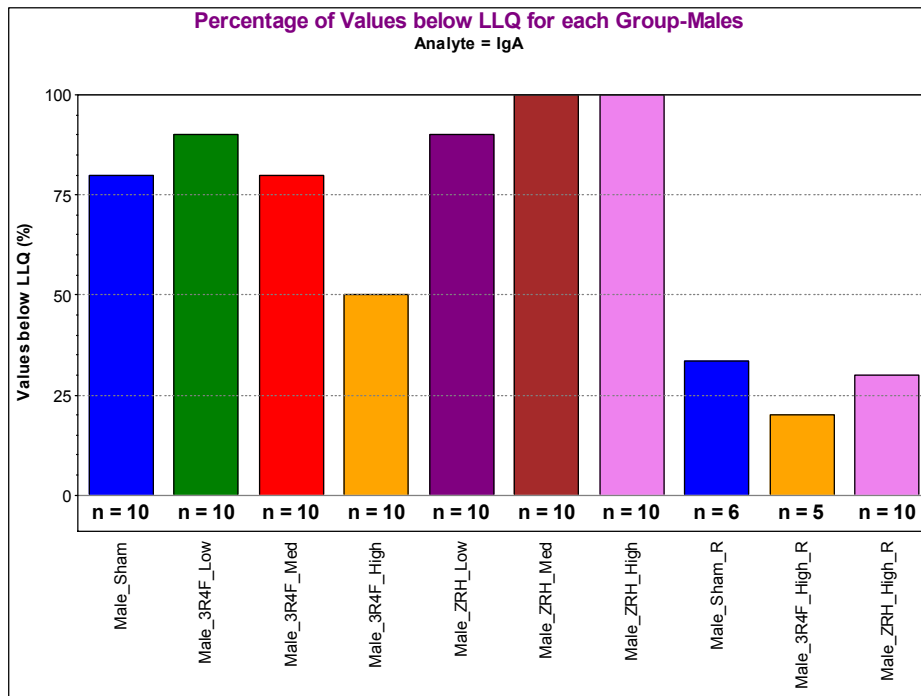
Unit = ug/mL

Descriptive Statistics by Exposure Duration and Treatment Type**Analyte = IgA**

Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	8	2	0	0.37	.
Male	3	3R4F Low	10	10	9	1	0	0.37	.
Male	3	3R4F Medium	10	10	8	2	0	0.37	.
Male	3	3R4F High	10	10	5	5	0	0.37	.
Male	3	ZRH Low	10	10	9	1	0	0.37	.
Male	3	ZRH Medium	10	10	10	0	0	0.37	.
Male	3	ZRH High	10	10	10	0	0	0.37	.
Male	4.5	Sham Recovery	6	6	2	4	0	0.37	.
Male	4.5	3R4F High Recovery	5	5	1	4	0	0.37	.
Male	4.5	ZRH High Recovery	10	10	3	7	0	0.37	.
Female	3	Sham	10	10	9	1	0	0.37	.
Female	3	3R4F Low	10	10	8	2	0	0.37	.
Female	3	3R4F Medium	10	10	6	4	0	0.37	.
Female	3	3R4F High	9	9	7	2	0	0.37	.
Female	3	ZRH Low	9	9	7	2	0	0.37	.
Female	3	ZRH Medium	10	10	6	4	0	0.37	.
Female	3	ZRH High	10	10	6	4	0	0.37	.
Female	4.5	Sham Recovery	6	6	5	1	0	0.37	.
Female	4.5	3R4F High Recovery	6	6	4	2	0	0.37	.
Female	4.5	ZRH High Recovery	10	10	4	6	0	0.37	.

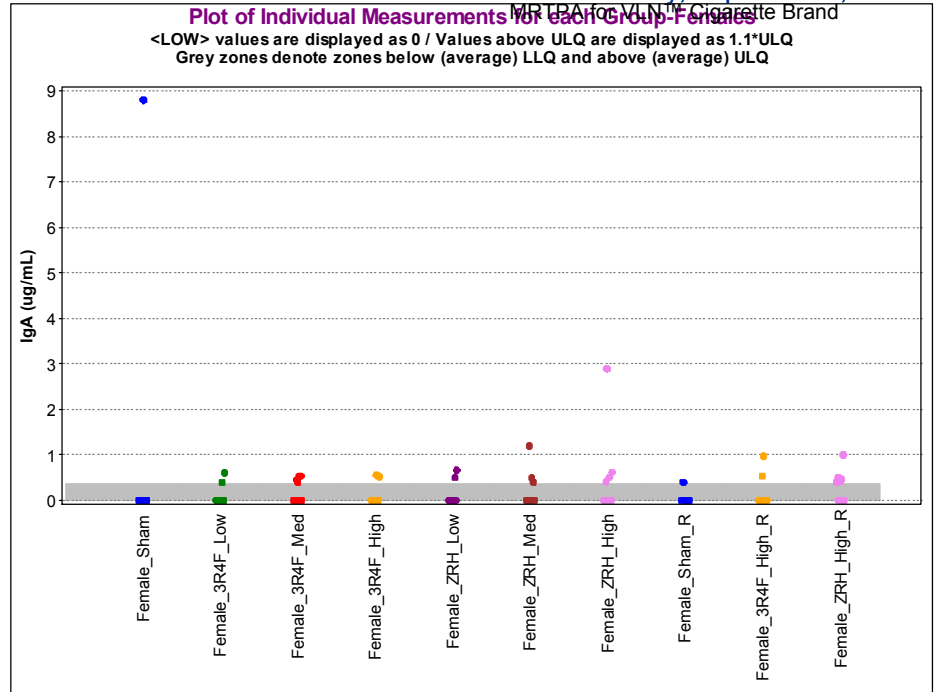
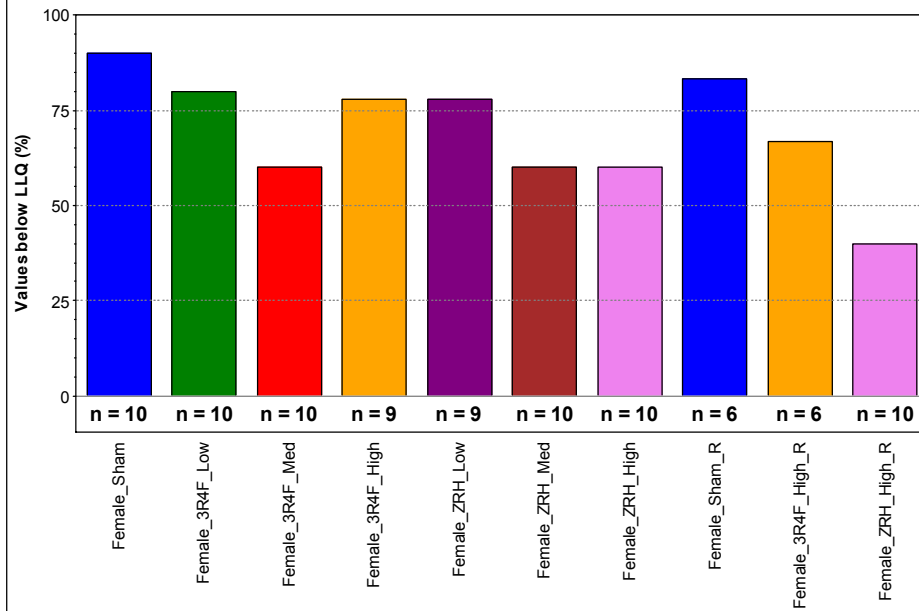
Descriptive Statistics by Exposure Duration and Treatment Type**Analyte = IgA**

Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	0.185	0.185	0.185	0.185	1.400	0.355	0.398	0.126	112.0	2.505	6.224	0.37	.
Male	3	3R4F Low	0.185	0.185	0.185	0.185	0.370	0.204	0.059	0.019	28.7	3.162	10.000	0.37	.
Male	3	3R4F Medium	0.185	0.185	0.185	0.185	0.460	0.233	0.103	0.032	44.0	1.892	2.189	0.37	.
Male	3	3R4F High	0.185	0.185	0.283	0.450	3.100	0.637	0.910	0.288	143.0	2.682	7.460	0.37	.
Male	3	ZRH Low	0.185	0.185	0.185	0.185	0.410	0.208	0.071	0.023	34.3	3.162	10.000	0.37	.
Male	3	ZRH Medium	0.185	0.185	0.185	0.185	0.185	0.185	0.000	0.000	0.0	.	.	0.37	.
Male	3	ZRH High	0.185	0.185	0.185	0.185	0.185	0.185	0.000	0.000	0.0	.	.	0.37	.
Male	4.5	Sham Recovery	0.185	0.185	0.465	0.510	0.530	0.390	0.162	0.066	41.6	-0.797	-1.942	0.37	.
Male	4.5	3R4F High Recovery	0.185	0.400	0.450	0.460	0.910	0.481	0.264	0.118	55.0	1.182	2.639	0.37	.
Male	4.5	ZRH High Recovery	0.185	0.185	0.440	0.550	0.790	0.433	0.205	0.065	47.4	0.220	-0.590	0.37	.
Female	3	Sham	0.185	0.185	0.185	0.185	8.800	1.047	2.724	0.862	260.3	3.162	10.000	0.37	.
Female	3	3R4F Low	0.185	0.185	0.185	0.185	0.610	0.248	0.143	0.045	57.5	2.314	5.011	0.37	.
Female	3	3R4F Medium	0.185	0.185	0.185	0.460	0.540	0.305	0.160	0.051	52.4	0.686	-1.663	0.37	.
Female	3	3R4F High	0.185	0.185	0.185	0.185	0.560	0.265	0.159	0.053	60.0	1.630	0.800	0.37	.
Female	3	ZRH Low	0.185	0.185	0.185	0.185	0.660	0.274	0.180	0.060	65.8	1.804	1.957	0.37	.
Female	3	ZRH Medium	0.185	0.185	0.185	0.420	1.200	0.362	0.319	0.101	88.0	2.397	6.243	0.37	.
Female	3	ZRH High	0.185	0.185	0.185	0.510	2.900	0.555	0.840	0.266	151.3	2.952	8.978	0.37	.
Female	4.5	Sham Recovery	0.185	0.185	0.185	0.185	0.400	0.221	0.088	0.036	39.7	2.449	6.000	0.37	.
Female	4.5	3R4F High Recovery	0.185	0.185	0.185	0.540	0.970	0.375	0.324	0.132	86.5	1.652	2.065	0.37	.
Female	4.5	ZRH High Recovery	0.185	0.185	0.415	0.500	1.000	0.404	0.252	0.080	62.3	1.495	3.023	0.37	.



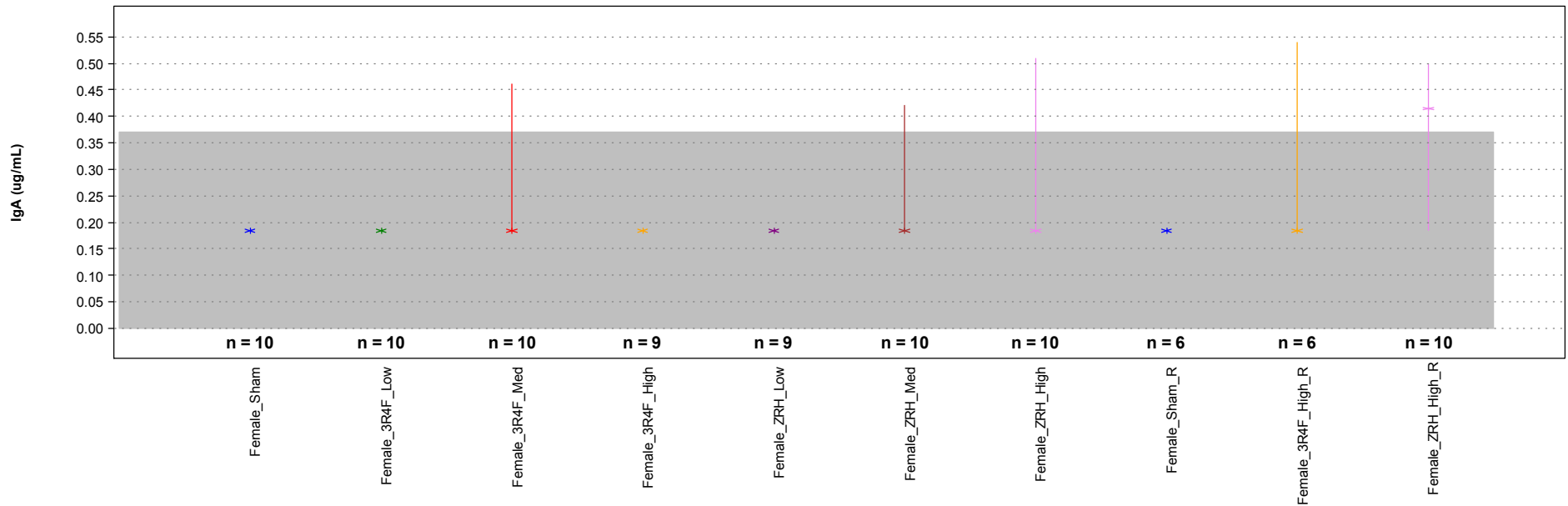
Percentage of Values below LLQ for each Group-Females

Analyte = IgA

**Plot of Descriptive Robust Statistics-Females**

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = IgA

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	0.465643
---- Sham vs. 3R4F Medium for Male	0.828784
---- Sham vs. 3R4F High for Male	0.248875
---- Sham vs. ZRH Low for Male	0.465643
---- Sham vs. ZRH Medium for Male	0.146793
---- Sham vs. ZRH High for Male	0.146793
---- ZRH Low vs. 3R4F Medium for Male	0.543195
---- ZRH Medium vs. 3R4F High for Male	0.013002
---- ZRH High vs. 3R4F High for Male	0.013002
---- Sham Recovery vs. 3R4F High Recovery for Male	1.000000
---- Sham Recovery vs. ZRH High Recovery for Male	0.868732
---- Sham vs. Sham Recovery for Male	0.212634
---- 3R4F High vs. 3R4F High Recovery for Male	0.375465
---- ZRH High vs. ZRH High Recovery for Male	0.001906
---- 3R4F High Recovery vs. ZRH High Recovery for Male	0.901556
---- Sham vs. 3R4F Low for Female	0.626690
---- Sham vs. 3R4F Medium for Female	0.196229
---- Sham vs. 3R4F High for Female	0.562983
---- Sham vs. ZRH Low for Female	0.562983
---- Sham vs. ZRH Medium for Female	0.196520
---- Sham vs. ZRH High for Female	0.196520
---- ZRH Low vs. 3R4F Medium for Female	0.552402
---- ZRH Medium vs. 3R4F High for Female	0.552658
---- ZRH High vs. 3R4F High for Female	0.428530
---- Sham Recovery vs. 3R4F High Recovery for Female	0.400499
---- Sham Recovery vs. ZRH High Recovery for Female	0.063465
---- Sham vs. Sham Recovery for Female	0.777297

Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = IgA

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	0.545186
---- ZRH High vs. ZRH High Recovery for Female	0.686200
---- 3R4F High Recovery vs. ZRH High Recovery for Female	0.642779

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 17

Insulin

Unit = uIU/mL

Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = Insulin

Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	1	9	0	1.3	.
Male	3	3R4F Low	10	10	1	9	0	1.3	.
Male	3	3R4F Medium	10	10	1	9	0	1.3	.
Male	3	3R4F High	10	10	2	8	0	1.3	.
Male	3	ZRH Low	10	10	1	9	0	1.3	.
Male	3	ZRH Medium	10	10	0	10	0	1.3	.
Male	3	ZRH High	10	10	0	10	0	1.3	.
Male	4.5	Sham Recovery	6	6	0	6	0	1.3	.
Male	4.5	3R4F High Recovery	5	5	0	5	0	1.3	.
Male	4.5	ZRH High Recovery	10	10	0	10	0	1.3	.
Female	3	Sham	10	10	4	6	0	1.3	.
Female	3	3R4F Low	10	10	0	10	0	1.3	.
Female	3	3R4F Medium	10	10	2	8	0	1.3	.
Female	3	3R4F High	9	9	3	6	0	1.3	.
Female	3	ZRH Low	9	9	1	8	0	1.3	.
Female	3	ZRH Medium	10	10	4	6	0	1.3	.
Female	3	ZRH High	10	10	3	7	0	1.3	.
Female	4.5	Sham Recovery	6	6	0	6	0	1.3	.
Female	4.5	3R4F High Recovery	6	6	0	6	0	1.3	.
Female	4.5	ZRH High Recovery	10	10	0	10	0	1.3	.

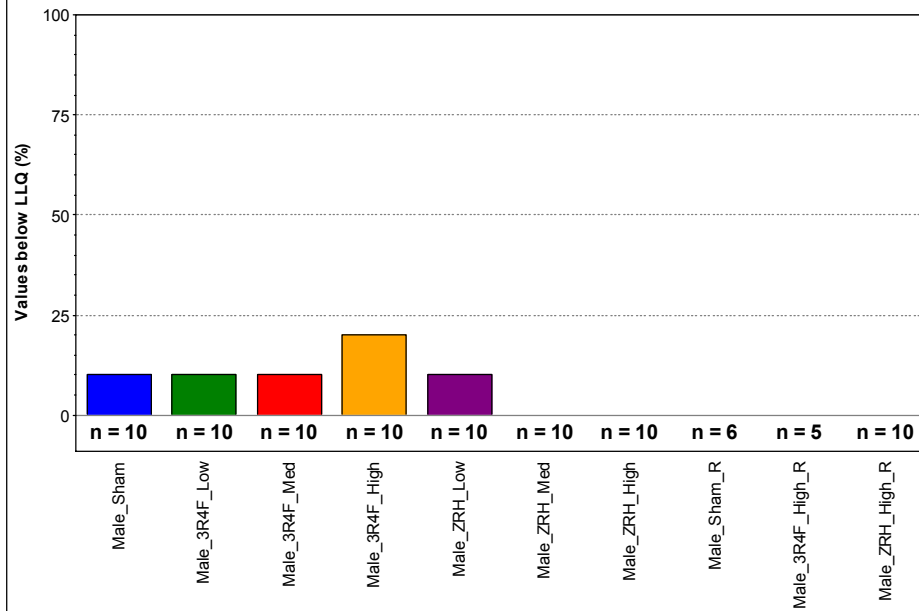
Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = Insulin

Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	0.650	1.400	1.550	2.100	3.700	1.875	0.879	0.278	46.9	1.090	1.176	1.3	.
Male	3	3R4F Low	0.650	2.100	2.500	2.900	3.100	2.345	0.743	0.235	31.7	-1.476	2.230	1.3	.
Male	3	3R4F Medium	0.650	1.700	2.150	3.100	3.400	2.255	0.846	0.268	37.5	-0.447	-0.150	1.3	.
Male	3	3R4F High	0.650	1.500	2.100	2.300	3.500	1.960	0.894	0.283	45.6	-0.012	-0.122	1.3	.
Male	3	ZRH Low	0.650	1.900	2.000	2.200	2.700	1.915	0.554	0.175	28.9	-1.300	2.716	1.3	.
Male	3	ZRH Medium	1.600	1.700	2.350	2.900	4.200	2.400	0.806	0.255	33.6	1.264	1.730	1.3	.
Male	3	ZRH High	1.500	1.700	2.200	2.400	2.800	2.100	0.411	0.130	19.6	0.084	-0.908	1.3	.
Male	4.5	Sham Recovery	1.800	2.200	2.250	2.600	3.700	2.467	0.656	0.268	26.6	1.634	3.270	1.3	.
Male	4.5	3R4F High Recovery	1.800	2.200	3.000	3.000	3.200	2.640	0.607	0.271	23.0	-0.763	-1.841	1.3	.
Male	4.5	ZRH High Recovery	1.700	2.400	2.500	2.700	3.200	2.460	0.425	0.134	17.3	-0.284	0.678	1.3	.
Female	3	Sham	0.650	0.650	1.300	1.400	1.700	1.110	0.414	0.131	37.3	-0.157	-1.843	1.3	.
Female	3	3R4F Low	1.300	1.400	1.500	1.600	1.900	1.540	0.171	0.054	11.1	0.876	1.132	1.3	.
Female	3	3R4F Medium	0.650	1.500	1.600	1.700	1.800	1.440	0.424	0.134	29.5	-1.616	1.107	1.3	.
Female	3	3R4F High	0.650	0.650	1.500	1.600	2.200	1.317	0.549	0.183	41.7	-0.104	-0.951	1.3	.
Female	3	ZRH Low	0.650	1.300	1.500	1.600	2.600	1.517	0.515	0.172	33.9	0.733	2.876	1.3	.
Female	3	ZRH Medium	0.650	0.650	1.400	1.500	1.700	1.160	0.449	0.142	38.7	-0.318	-2.102	1.3	.
Female	3	ZRH High	0.650	0.650	1.400	1.700	1.900	1.295	0.480	0.152	37.1	-0.518	-1.400	1.3	.
Female	4.5	Sham Recovery	1.900	2.100	2.400	2.700	2.800	2.383	0.349	0.142	14.6	-0.216	-1.453	1.3	.
Female	4.5	3R4F High Recovery	1.500	1.800	1.900	2.100	2.600	1.967	0.367	0.150	18.7	0.908	1.834	1.3	.
Female	4.5	ZRH High Recovery	1.800	2.200	2.700	3.000	3.300	2.550	0.521	0.165	20.4	-0.297	-1.186	1.3	.

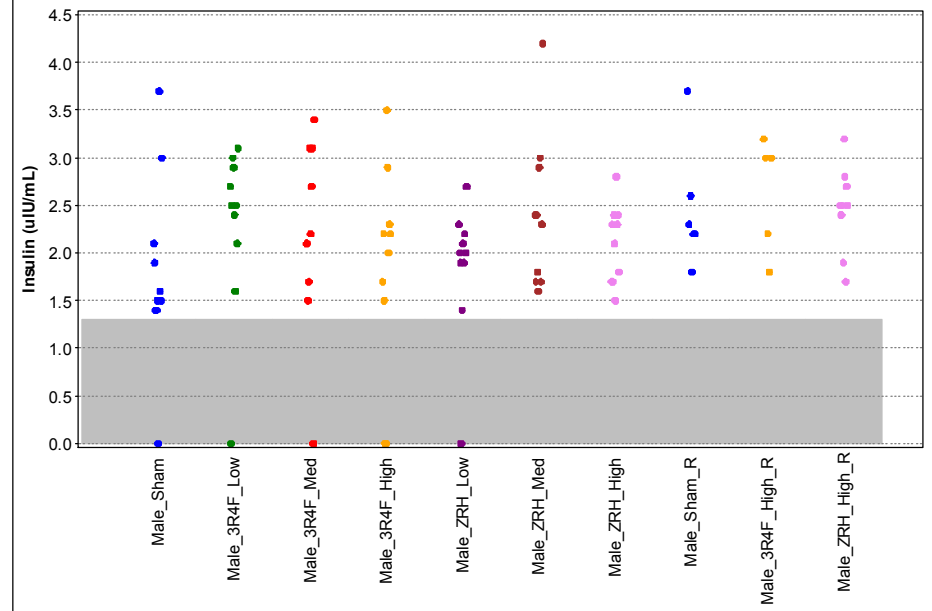
Percentage of Values below LLQ for each Group-Males

Analyte = Insulin



Plot of Individual Measurements for each Group-Males

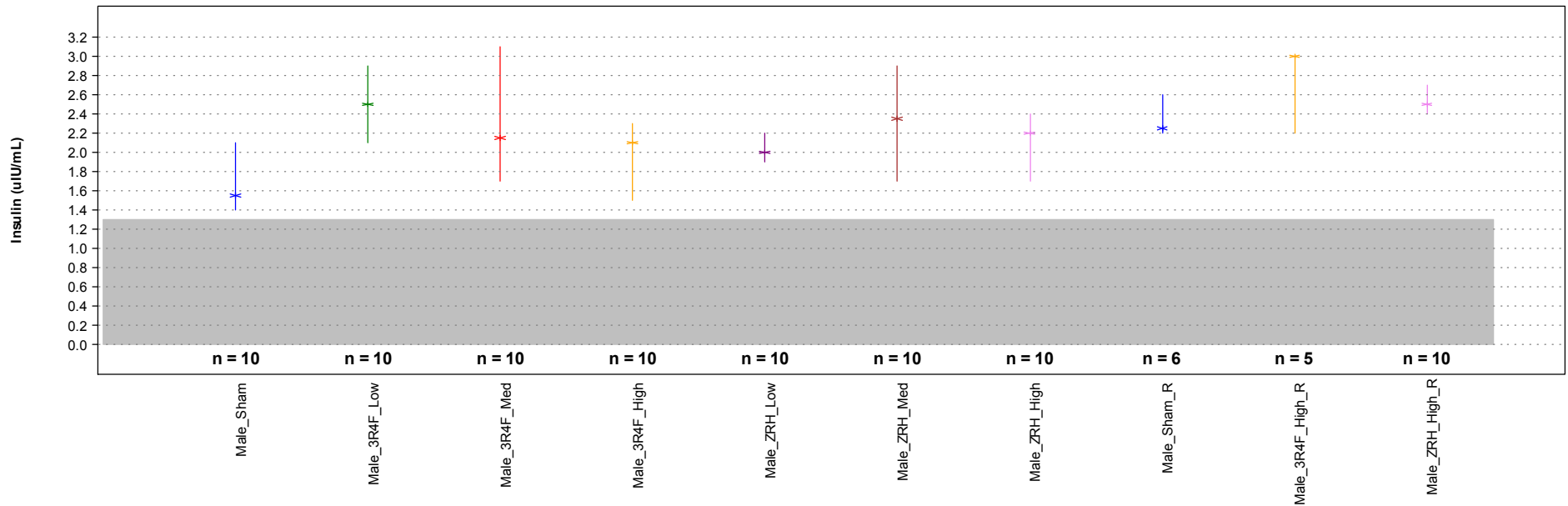
<LOW> values are displayed as 0 / Values above ULQ are displayed as 1.1*ULQ
 Grey zones denote zones below (average) LLQ and above (average) ULQ



Plot of Descriptive Robust Statistics-Males

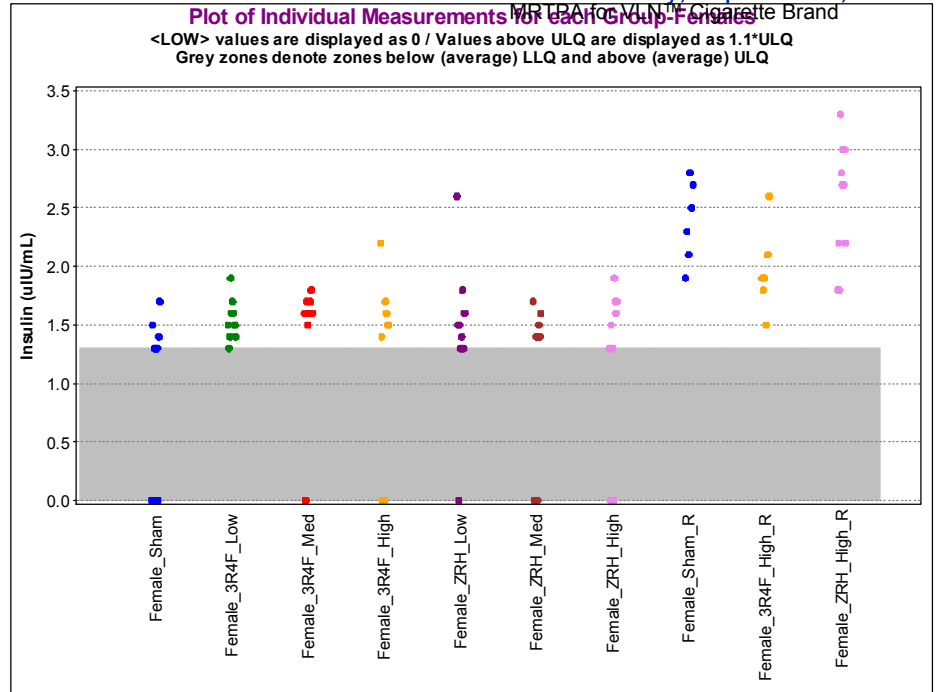
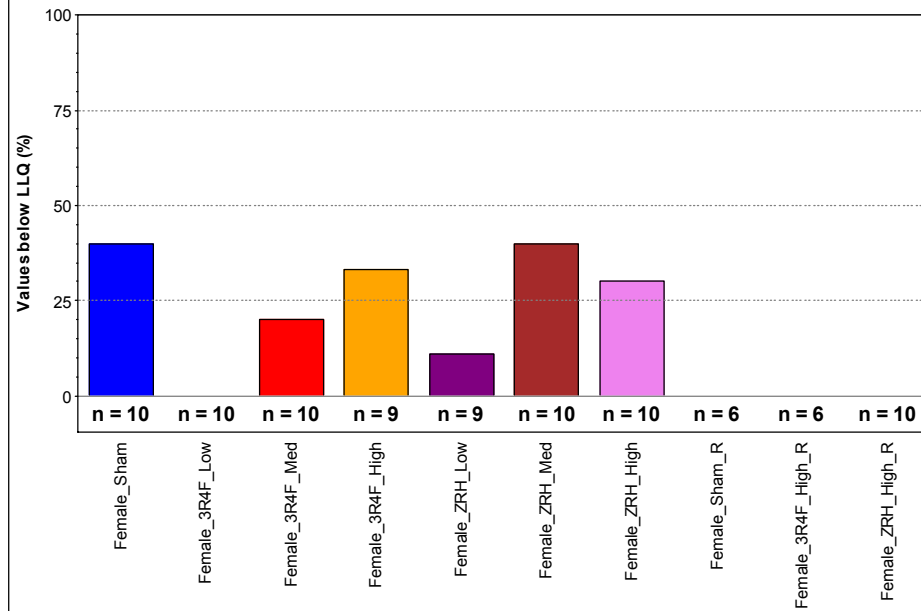
Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



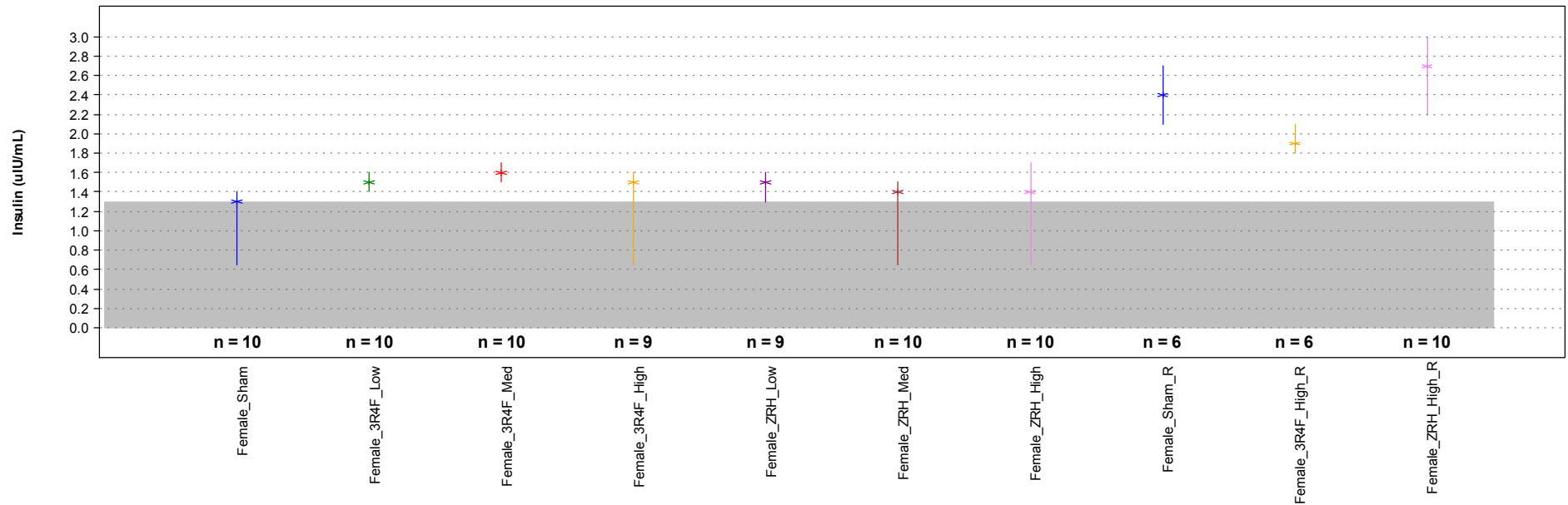
Percentage of Values below LLQ for each Group-Females

Analyte = Insulin

**Plot of Descriptive Robust Statistics-Females**

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = Insulin

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	0.111465
---- Sham vs. 3R4F Medium for Male	0.160233
---- Sham vs. 3R4F High for Male	0.494665
---- Sham vs. ZRH Low for Male	0.403550
---- Sham vs. ZRH Medium for Male	0.069013
---- Sham vs. ZRH High for Male	0.139120
---- ZRH Low vs. 3R4F Medium for Male	0.271227
---- ZRH Medium vs. 3R4F High for Male	0.255225
---- ZRH High vs. 3R4F High for Male	0.569002
---- Sham Recovery vs. 3R4F High Recovery for Male	0.643515
---- Sham Recovery vs. ZRH High Recovery for Male	0.513317
---- Sham vs. Sham Recovery for Male	0.056943
---- 3R4F High vs. 3R4F High Recovery for Male	0.139507
---- ZRH High vs. ZRH High Recovery for Male	0.036205
---- 3R4F High Recovery vs. ZRH High Recovery for Male	0.497861
---- Sham vs. 3R4F Low for Female	0.010248
---- Sham vs. 3R4F Medium for Female	0.033810
---- Sham vs. 3R4F High for Female	0.238918
---- Sham vs. ZRH Low for Female	0.073265
---- Sham vs. ZRH Medium for Female	0.555497
---- Sham vs. ZRH High for Female	0.292307
---- ZRH Low vs. 3R4F Medium for Female	0.481647
---- ZRH Medium vs. 3R4F High for Female	0.422905
---- ZRH High vs. 3R4F High for Female	1.000000
---- Sham Recovery vs. 3R4F High Recovery for Female	0.063200
---- Sham Recovery vs. ZRH High Recovery for Female	0.478195
---- Sham vs. Sham Recovery for Female	0.001009

Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = Insulin

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	0.023984
---- ZRH High vs. ZRH High Recovery for Female	0.000270
---- 3R4F High Recovery vs. ZRH High Recovery for Female	0.038166

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 14

Growth-Regulated Alpha Protein (KC/GRO)

Unit = ng/mL

Descriptive Statistics by Exposure Duration and Treatment Type

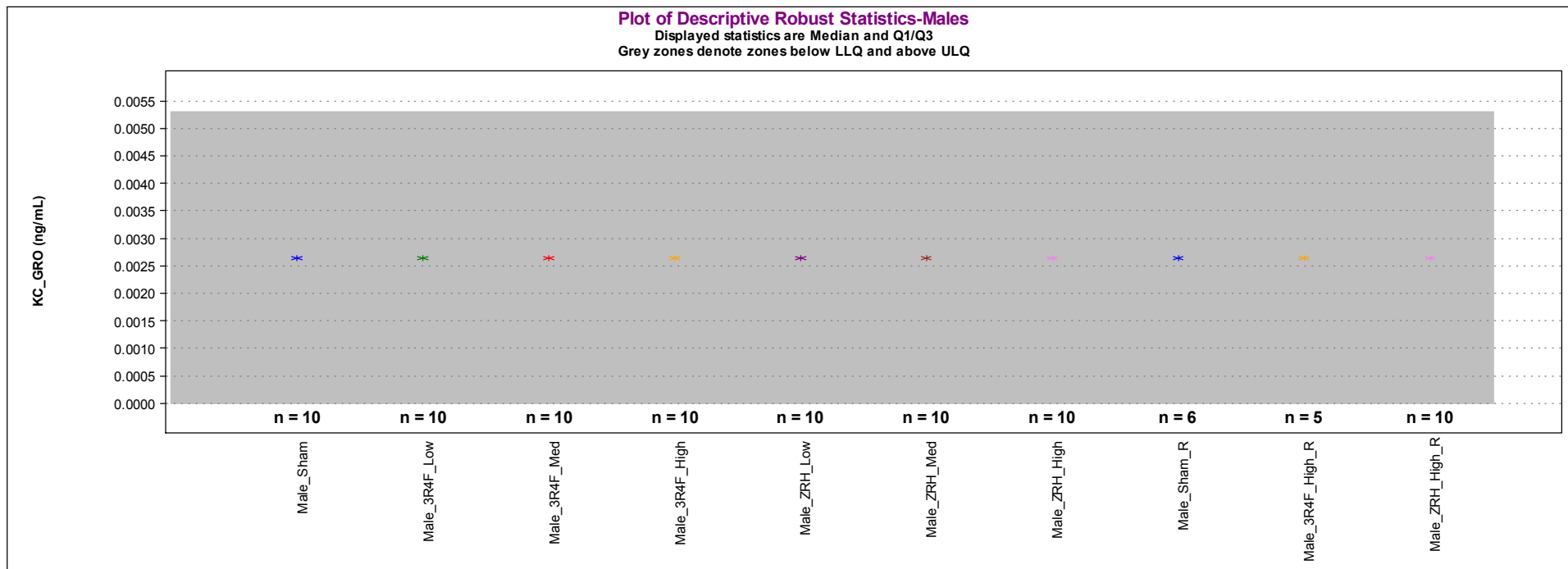
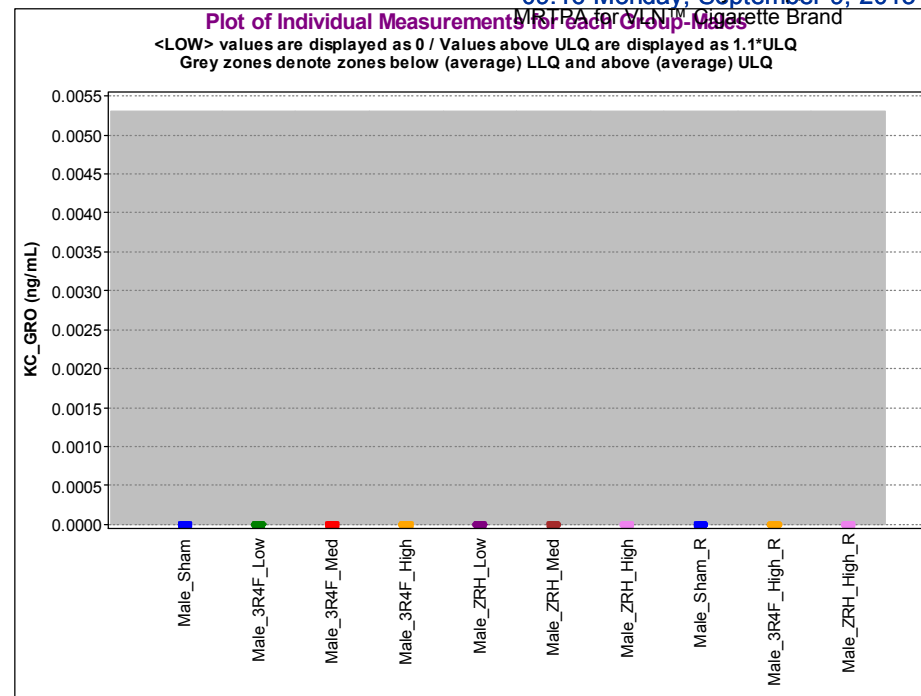
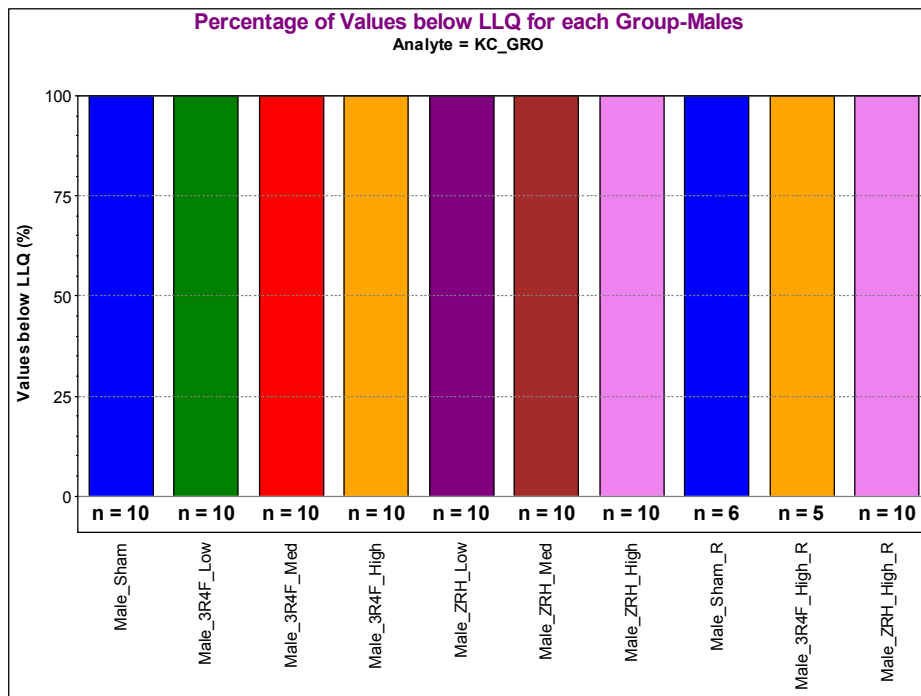
Analyte = KC_GRO

Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	10	0	0	0.005	.
Male	3	3R4F Low	10	10	10	0	0	0.005	.
Male	3	3R4F Medium	10	10	10	0	0	0.005	.
Male	3	3R4F High	10	10	10	0	0	0.005	.
Male	3	ZRH Low	10	10	10	0	0	0.005	.
Male	3	ZRH Medium	10	10	10	0	0	0.005	.
Male	3	ZRH High	10	10	10	0	0	0.005	.
Male	4.5	Sham Recovery	6	6	6	0	0	0.005	.
Male	4.5	3R4F High Recovery	5	5	5	0	0	0.005	.
Male	4.5	ZRH High Recovery	10	10	10	0	0	0.005	.
Female	3	Sham	10	10	10	0	0	0.005	.
Female	3	3R4F Low	10	10	10	0	0	0.005	.
Female	3	3R4F Medium	10	10	10	0	0	0.005	.
Female	3	3R4F High	9	9	9	0	0	0.005	.
Female	3	ZRH Low	9	9	9	0	0	0.005	.
Female	3	ZRH Medium	10	10	10	0	0	0.005	.
Female	3	ZRH High	10	10	10	0	0	0.005	.
Female	4.5	Sham Recovery	6	6	6	0	0	0.005	.
Female	4.5	3R4F High Recovery	6	6	6	0	0	0.005	.
Female	4.5	ZRH High Recovery	10	10	10	0	0	0.005	.

Descriptive Statistics by Exposure Duration and Treatment Type

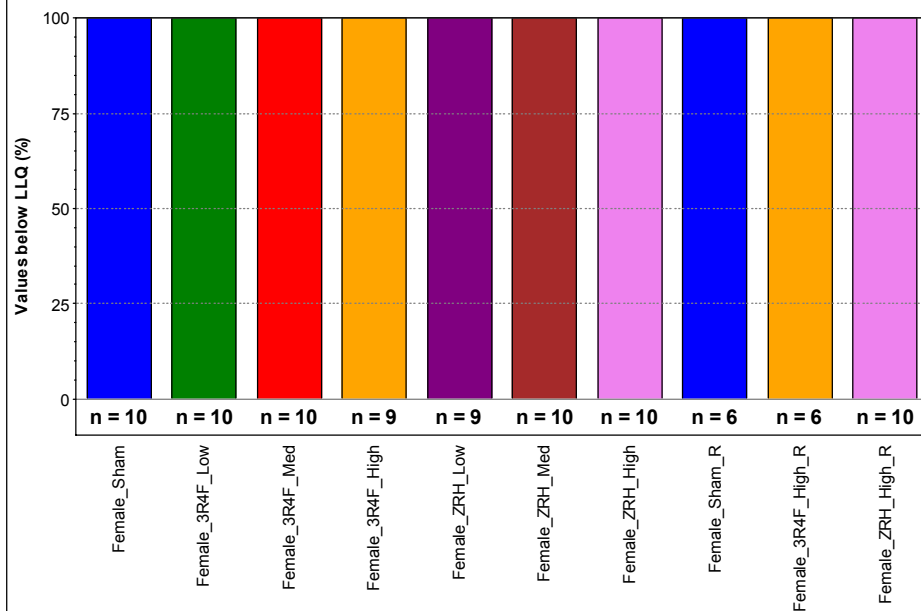
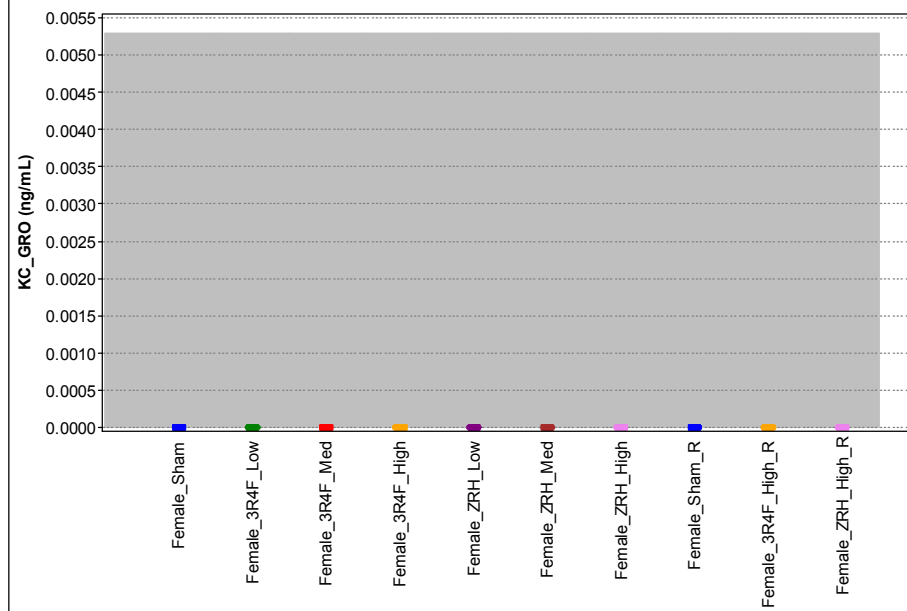
Analyte = KC_GRO

Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	0.003	0.003	0.003	0.003	0.003	0.003	0.000	0.000	0.0	.	.	0.005	.
Male	3	3R4F Low	0.003	0.003	0.003	0.003	0.003	0.003	0.000	0.000	0.0	.	.	0.005	.
Male	3	3R4F Medium	0.003	0.003	0.003	0.003	0.003	0.003	0.000	0.000	0.0	.	.	0.005	.
Male	3	3R4F High	0.003	0.003	0.003	0.003	0.003	0.003	0.000	0.000	0.0	.	.	0.005	.
Male	3	ZRH Low	0.003	0.003	0.003	0.003	0.003	0.003	0.000	0.000	0.0	.	.	0.005	.
Male	3	ZRH Medium	0.003	0.003	0.003	0.003	0.003	0.003	0.000	0.000	0.0	.	.	0.005	.
Male	3	ZRH High	0.003	0.003	0.003	0.003	0.003	0.003	0.000	0.000	0.0	.	.	0.005	.
Male	4.5	Sham Recovery	0.003	0.003	0.003	0.003	0.003	0.003	0.000	0.000	0.0	.	.	0.005	.
Male	4.5	3R4F High Recovery	0.003	0.003	0.003	0.003	0.003	0.003	0.000	0.000	0.0	.	.	0.005	.
Male	4.5	ZRH High Recovery	0.003	0.003	0.003	0.003	0.003	0.003	0.000	0.000	0.0	.	.	0.005	.
Female	3	Sham	0.003	0.003	0.003	0.003	0.003	0.003	0.000	0.000	0.0	.	.	0.005	.
Female	3	3R4F Low	0.003	0.003	0.003	0.003	0.003	0.003	0.000	0.000	0.0	.	.	0.005	.
Female	3	3R4F Medium	0.003	0.003	0.003	0.003	0.003	0.003	0.000	0.000	0.0	.	.	0.005	.
Female	3	3R4F High	0.003	0.003	0.003	0.003	0.003	0.003	0.000	0.000	0.0	.	.	0.005	.
Female	3	ZRH Low	0.003	0.003	0.003	0.003	0.003	0.003	0.000	0.000	0.0	.	.	0.005	.
Female	3	ZRH Medium	0.003	0.003	0.003	0.003	0.003	0.003	0.000	0.000	0.0	.	.	0.005	.
Female	3	ZRH High	0.003	0.003	0.003	0.003	0.003	0.003	0.000	0.000	0.0	.	.	0.005	.
Female	4.5	Sham Recovery	0.003	0.003	0.003	0.003	0.003	0.003	0.000	0.000	0.0	.	.	0.005	.
Female	4.5	3R4F High Recovery	0.003	0.003	0.003	0.003	0.003	0.003	0.000	0.000	0.0	.	.	0.005	.
Female	4.5	ZRH High Recovery	0.003	0.003	0.003	0.003	0.003	0.003	0.000	0.000	0.0	.	.	0.005	.



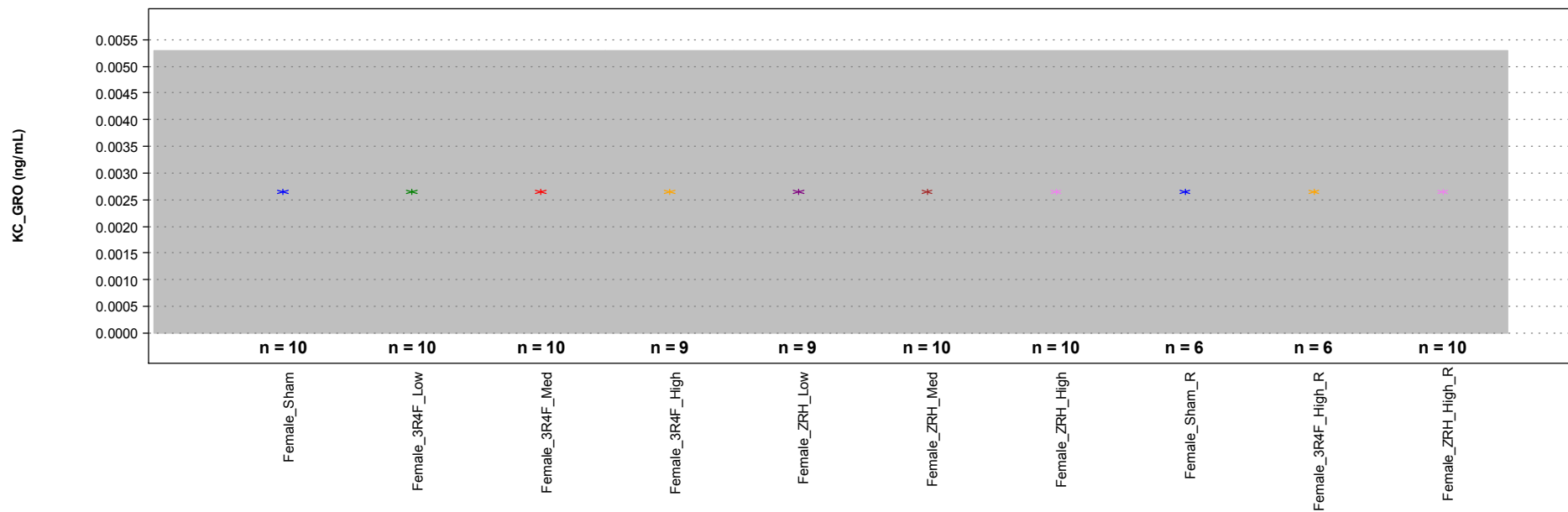
Percentage of Values below LLQ for each Group-Females

Analyte = KC_GRO

**Plot of Individual Measurements for each Group-Females**
<LOW> values are displayed as 0 / Values above ULQ are displayed as 1.1*ULQ
Grey zones denote zones below (average) LLQ and above (average) ULQ**Plot of Descriptive Robust Statistics-Females**

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = KC_GRO

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	1.000000
---- Sham vs. 3R4F Medium for Male	1.000000
---- Sham vs. 3R4F High for Male	1.000000
---- Sham vs. ZRH Low for Male	1.000000
---- Sham vs. ZRH Medium for Male	1.000000
---- Sham vs. ZRH High for Male	1.000000
---- ZRH Low vs. 3R4F Medium for Male	1.000000
---- ZRH Medium vs. 3R4F High for Male	1.000000
---- ZRH High vs. 3R4F High for Male	1.000000
---- Sham Recovery vs. 3R4F High Recovery for Male	1.000000
---- Sham Recovery vs. ZRH High Recovery for Male	1.000000
---- Sham vs. Sham Recovery for Male	1.000000
---- 3R4F High vs. 3R4F High Recovery for Male	1.000000
---- ZRH High vs. ZRH High Recovery for Male	1.000000
---- 3R4F High Recovery vs. ZRH High Recovery for Male	1.000000
---- Sham vs. 3R4F Low for Female	1.000000
---- Sham vs. 3R4F Medium for Female	1.000000
---- Sham vs. 3R4F High for Female	1.000000
---- Sham vs. ZRH Low for Female	1.000000
---- Sham vs. ZRH Medium for Female	1.000000
---- Sham vs. ZRH High for Female	1.000000
---- ZRH Low vs. 3R4F Medium for Female	1.000000
---- ZRH Medium vs. 3R4F High for Female	1.000000
---- ZRH High vs. 3R4F High for Female	1.000000
---- Sham Recovery vs. 3R4F High Recovery for Female	1.000000
---- Sham Recovery vs. ZRH High Recovery for Female	1.000000
---- Sham vs. Sham Recovery for Female	1.000000

Unadjusted P-values Obtained by Kruskal-Wallis Test
Analyte = KC_GRO

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	1.000000
---- ZRH High vs. ZRH High Recovery for Female	1.000000
---- 3R4F High Recovery vs. ZRH High Recovery for Female	1.000000

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 34

Leukemia Inhibitory Factor (LIF)

Unit = pg/mL

Descriptive Statistics by Exposure Duration and Treatment Type**Analyte = LIF**

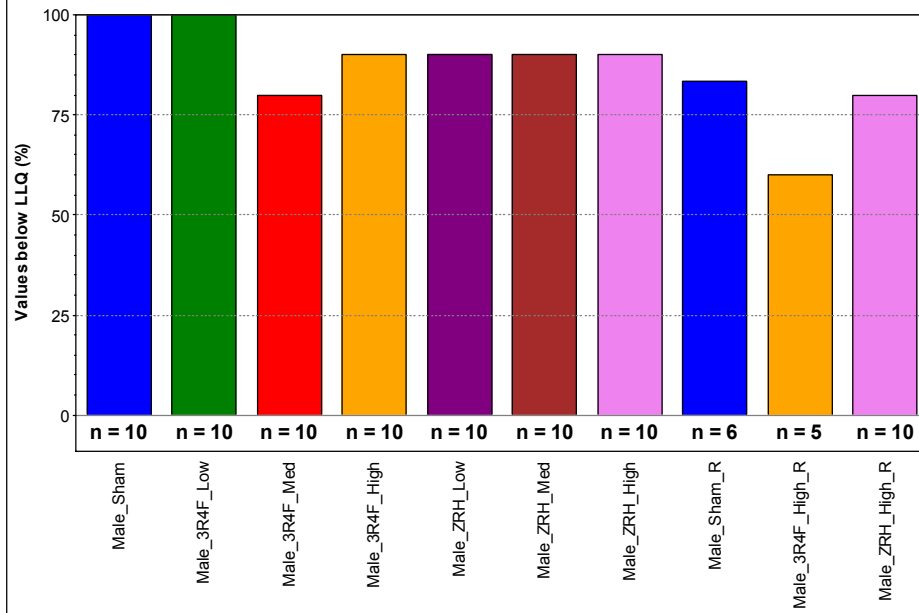
Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	10	0	0	93	.
Male	3	3R4F Low	10	10	10	0	0	93	.
Male	3	3R4F Medium	10	10	8	2	0	93	.
Male	3	3R4F High	10	10	9	1	0	93	.
Male	3	ZRH Low	10	10	9	1	0	93	.
Male	3	ZRH Medium	10	10	9	1	0	93	.
Male	3	ZRH High	10	10	9	1	0	93	.
Male	4.5	Sham Recovery	6	6	5	1	0	93	.
Male	4.5	3R4F High Recovery	5	5	3	2	0	93	.
Male	4.5	ZRH High Recovery	10	10	8	2	0	93	.
Female	3	Sham	10	10	6	4	0	93	.
Female	3	3R4F Low	10	10	9	1	0	93	.
Female	3	3R4F Medium	10	10	10	0	0	93	.
Female	3	3R4F High	9	9	6	3	0	93	.
Female	3	ZRH Low	9	9	6	3	0	93	.
Female	3	ZRH Medium	10	10	8	2	0	93	.
Female	3	ZRH High	10	10	8	2	0	93	.
Female	4.5	Sham Recovery	6	6	4	2	0	93	.
Female	4.5	3R4F High Recovery	6	6	5	1	0	93	.
Female	4.5	ZRH High Recovery	10	10	6	4	0	93	.

Descriptive Statistics by Exposure Duration and Treatment Type**Analyte = LIF**

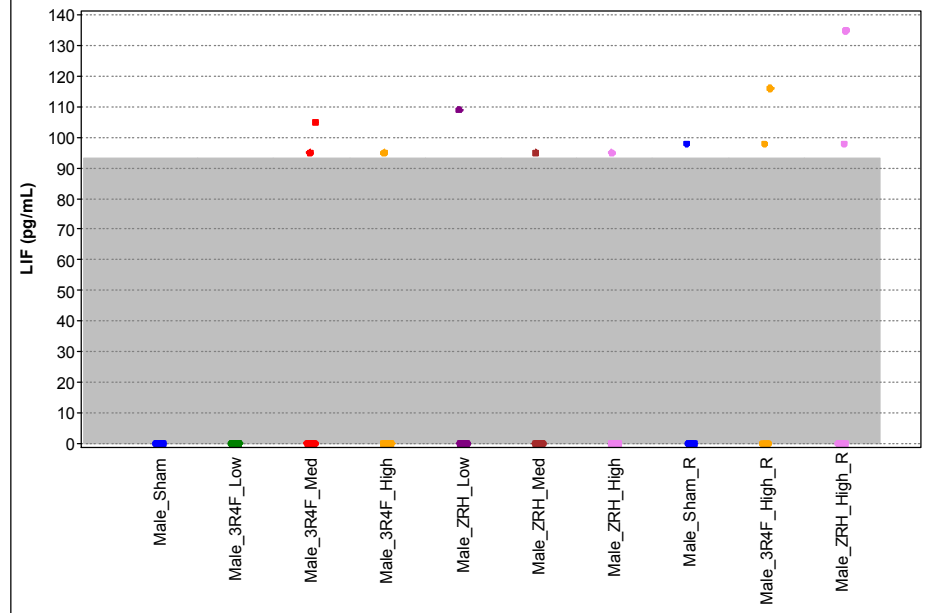
Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	46.500	46.500	46.500	46.500	46.500	46.500	0.000	0.000	0.0	.	.	93	.
Male	3	3R4F Low	46.500	46.500	46.500	46.500	46.500	46.500	0.000	0.000	0.0	.	.	93	.
Male	3	3R4F Medium	46.500	46.500	46.500	46.500	105.000	57.200	22.680	7.172	39.7	1.826	1.737	93	.
Male	3	3R4F High	46.500	46.500	46.500	46.500	95.000	51.350	15.337	4.850	29.9	3.162	10.000	93	.
Male	3	ZRH Low	46.500	46.500	46.500	46.500	109.000	52.750	19.764	6.250	37.5	3.162	10.000	93	.
Male	3	ZRH Medium	46.500	46.500	46.500	46.500	95.000	51.350	15.337	4.850	29.9	3.162	10.000	93	.
Male	3	ZRH High	46.500	46.500	46.500	46.500	95.000	51.350	15.337	4.850	29.9	3.162	10.000	93	.
Male	4.5	Sham Recovery	46.500	46.500	46.500	46.500	98.000	55.083	21.025	8.583	38.2	2.449	6.000	93	.
Male	4.5	3R4F High Recovery	46.500	46.500	46.500	98.000	116.000	70.700	33.743	15.090	47.7	0.768	-2.412	93	.
Male	4.5	ZRH High Recovery	46.500	46.500	46.500	46.500	135.000	60.500	30.776	9.732	50.9	2.117	3.711	93	.
Female	3	Sham	46.500	46.500	46.500	99.000	116.000	69.200	29.714	9.396	42.9	0.591	-1.888	93	.
Female	3	3R4F Low	46.500	46.500	46.500	46.500	99.000	51.750	16.602	5.250	32.1	3.162	10.000	93	.
Female	3	3R4F Medium	46.500	46.500	46.500	46.500	46.500	46.500	0.000	0.000	0.0	.	.	93	.
Female	3	3R4F High	46.500	46.500	46.500	99.000	116.000	67.778	32.292	10.764	47.6	0.940	-1.370	93	.
Female	3	ZRH Low	46.500	46.500	46.500	99.000	133.000	67.778	33.392	11.131	49.3	1.211	0.002	93	.
Female	3	ZRH Medium	46.500	46.500	46.500	46.500	133.000	60.400	30.380	9.607	50.3	2.074	3.424	93	.
Female	3	ZRH High	46.500	46.500	46.500	46.500	99.000	57.000	22.136	7.000	38.8	1.779	1.406	93	.
Female	4.5	Sham Recovery	46.500	46.500	46.500	98.000	116.000	66.667	31.756	12.964	47.6	1.106	-1.054	93	.
Female	4.5	3R4F High Recovery	46.500	46.500	46.500	46.500	98.000	55.083	21.025	8.583	38.2	2.449	6.000	93	.
Female	4.5	ZRH High Recovery	46.500	46.500	46.500	104.000	135.000	72.000	34.310	10.850	47.7	0.804	-1.056	93	.

Percentage of Values below LLQ for each Group-Males

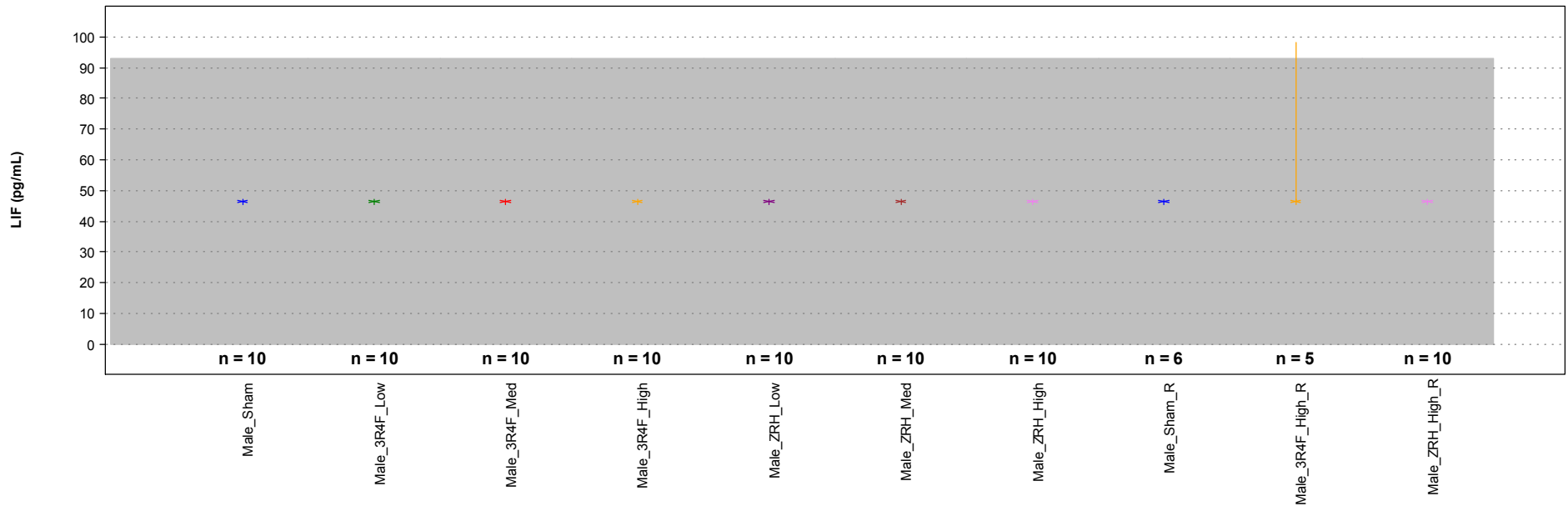
Analyte = LIF

**Plot of Individual Measurements for each Group-Males**

<LOW> values are displayed as 0 / Values above ULQ are displayed as 1.1*ULQ
 Grey zones denote zones below (average) LLQ and above (average) ULQ

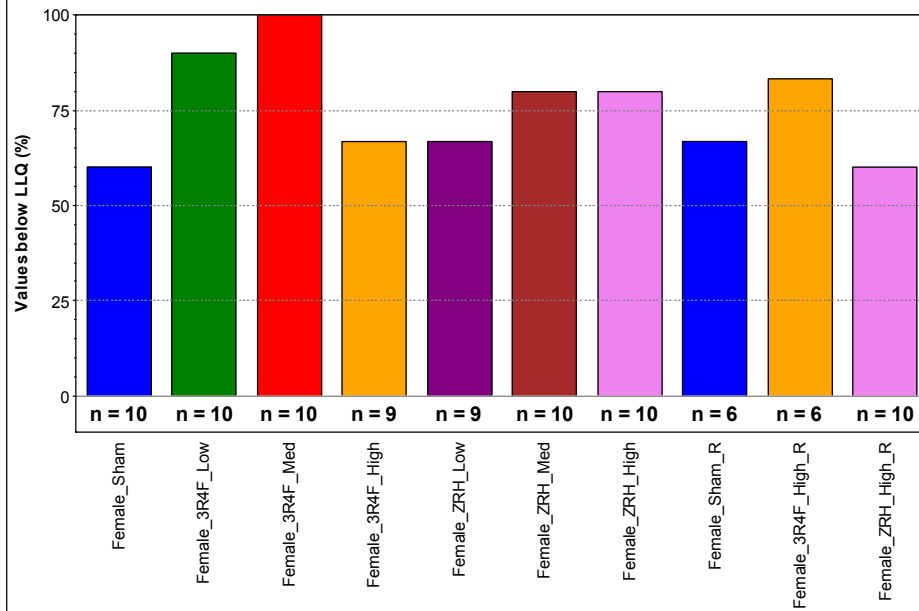
**Plot of Descriptive Robust Statistics-Males**

Displayed statistics are Median and Q1/Q3
 Grey zones denote zones below LLQ and above ULQ

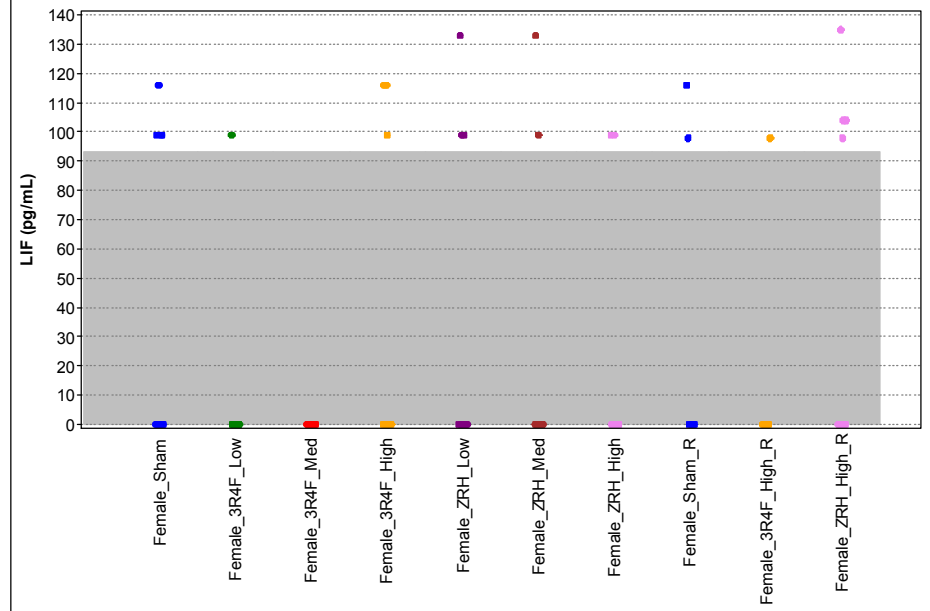


Percentage of Values below LLQ for each Group-Females

Analyte = LIF

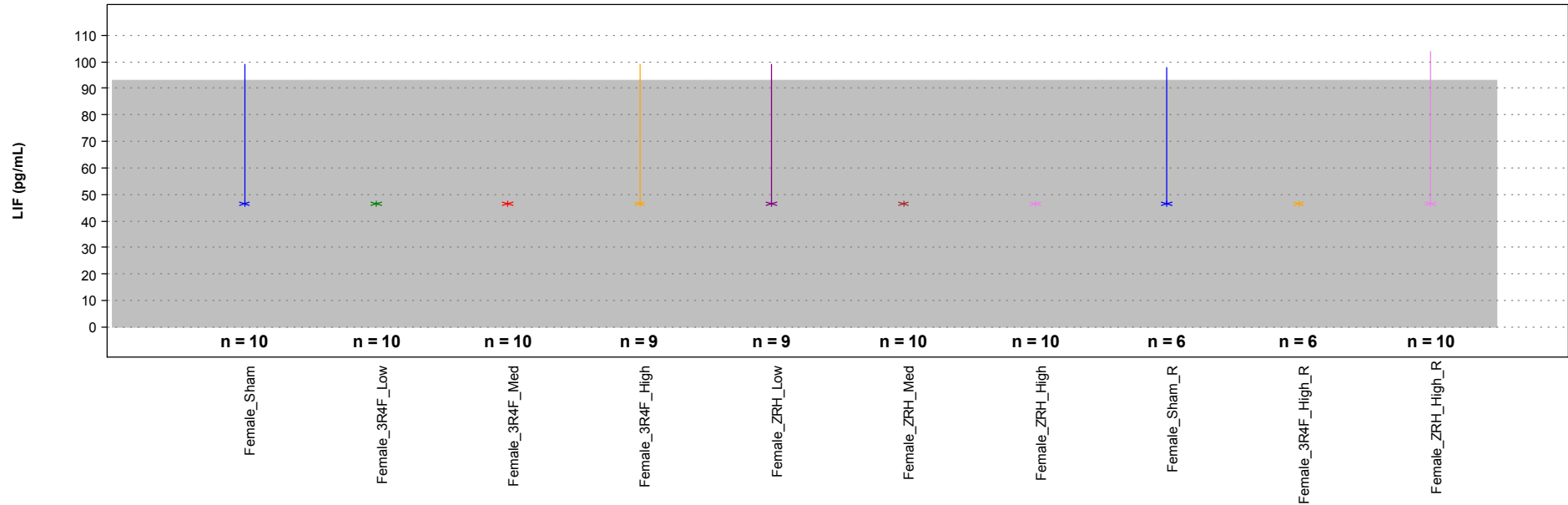
**Plot of Individual Measurements for each Group-Females**

<LOW> values are displayed as 0 / Values above ULQ are displayed as 1.1*ULQ
 Grey zones denote zones below (average) LLQ and above (average) ULQ

**Plot of Descriptive Robust Statistics-Females**

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = LIF

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	1.000000
---- Sham vs. 3R4F Medium for Male	0.146793
---- Sham vs. 3R4F High for Male	0.317311
---- Sham vs. ZRH Low for Male	0.317311
---- Sham vs. ZRH Medium for Male	0.317311
---- Sham vs. ZRH High for Male	0.317311
---- ZRH Low vs. 3R4F Medium for Male	0.626690
---- ZRH Medium vs. 3R4F High for Male	1.000000
---- ZRH High vs. 3R4F High for Male	1.000000
---- Sham Recovery vs. 3R4F High Recovery for Male	0.351195
---- Sham Recovery vs. ZRH High Recovery for Male	0.811070
---- Sham vs. Sham Recovery for Male	0.196706
---- 3R4F High vs. 3R4F High Recovery for Male	0.136678
---- ZRH High vs. ZRH High Recovery for Male	0.465643
---- 3R4F High Recovery vs. ZRH High Recovery for Male	0.478723
---- Sham vs. 3R4F Low for Female	0.121142
---- Sham vs. 3R4F Medium for Female	0.030060
---- Sham vs. 3R4F High for Female	0.962067
---- Sham vs. ZRH Low for Female	0.848587
---- Sham vs. ZRH Medium for Female	0.425601
---- Sham vs. ZRH High for Female	0.299694
---- ZRH Low vs. 3R4F Medium for Female	0.053588
---- ZRH Medium vs. 3R4F High for Female	0.561797
---- ZRH High vs. 3R4F High for Female	0.397692
---- Sham Recovery vs. 3R4F High Recovery for Female	0.460597
---- Sham Recovery vs. ZRH High Recovery for Female	0.754892
---- Sham vs. Sham Recovery for Female	0.754195

Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = LIF

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	0.363444
---- ZRH High vs. ZRH High Recovery for Female	0.262864
---- 3R4F High Recovery vs. ZRH High Recovery for Female	0.261271

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 33

Leptin

Unit = ng/mL

Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = Leptin

Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	0	10	0	0.011	.
Male	3	3R4F Low	10	10	0	10	0	0.011	.
Male	3	3R4F Medium	10	10	0	10	0	0.011	.
Male	3	3R4F High	10	10	0	10	0	0.011	.
Male	3	ZRH Low	10	10	0	10	0	0.011	.
Male	3	ZRH Medium	10	10	0	10	0	0.011	.
Male	3	ZRH High	10	10	0	10	0	0.011	.
Male	4.5	Sham Recovery	6	6	0	6	0	0.011	.
Male	4.5	3R4F High Recovery	5	5	0	5	0	0.011	.
Male	4.5	ZRH High Recovery	10	10	0	10	0	0.011	.
Female	3	Sham	10	10	0	10	0	0.011	.
Female	3	3R4F Low	10	10	0	10	0	0.011	.
Female	3	3R4F Medium	10	10	0	10	0	0.011	.
Female	3	3R4F High	9	9	0	9	0	0.011	.
Female	3	ZRH Low	9	9	0	9	0	0.011	.
Female	3	ZRH Medium	10	10	0	10	0	0.011	.
Female	3	ZRH High	10	10	0	10	0	0.011	.
Female	4.5	Sham Recovery	6	6	0	6	0	0.011	.
Female	4.5	3R4F High Recovery	6	6	0	6	0	0.011	.
Female	4.5	ZRH High Recovery	10	10	0	10	0	0.011	.

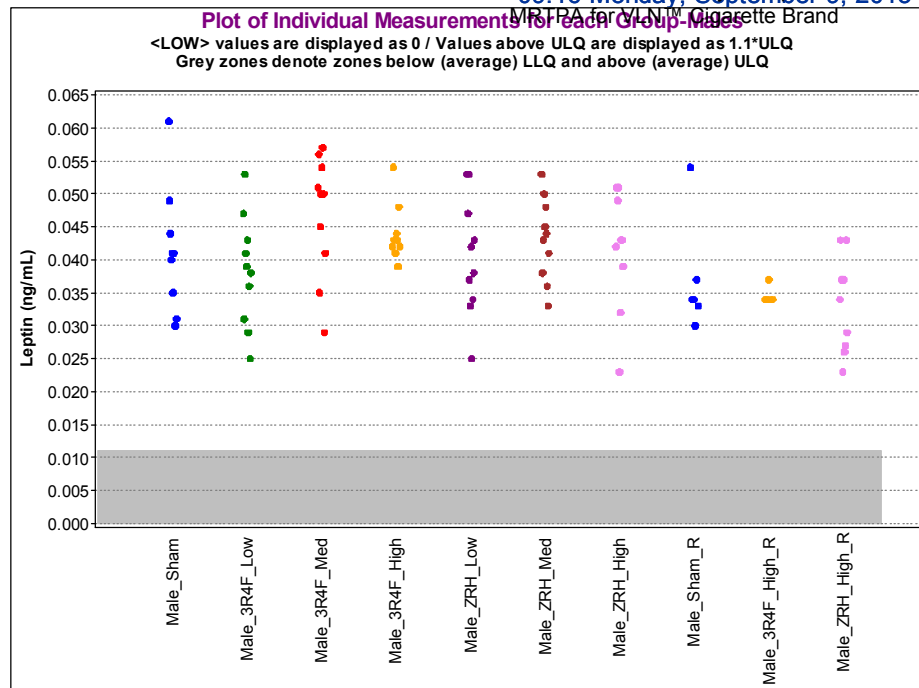
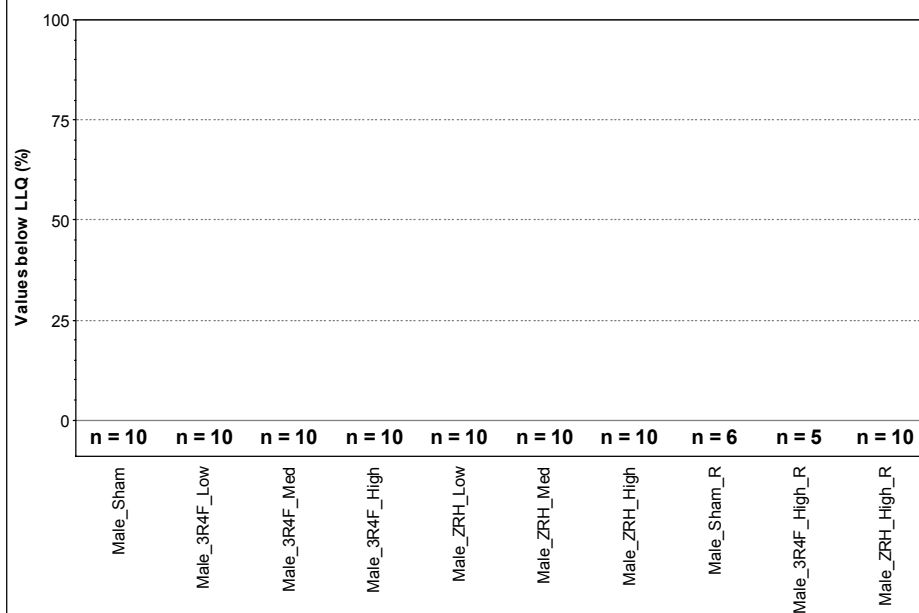
Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = Leptin

Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	0.030	0.031	0.041	0.044	0.061	0.040	0.010	0.003	24.1	1.021	1.172	0.011	.
Male	3	3R4F Low	0.025	0.031	0.039	0.043	0.053	0.038	0.008	0.003	22.1	0.136	-0.293	0.011	.
Male	3	3R4F Medium	0.029	0.041	0.050	0.054	0.057	0.047	0.009	0.003	19.8	-0.898	-0.119	0.011	.
Male	3	3R4F High	0.039	0.041	0.043	0.044	0.054	0.044	0.004	0.001	9.9	1.753	3.299	0.011	.
Male	3	ZRH Low	0.025	0.034	0.040	0.047	0.053	0.041	0.009	0.003	22.1	-0.054	-0.474	0.011	.
Male	3	ZRH Medium	0.033	0.038	0.044	0.048	0.053	0.043	0.006	0.002	14.6	-0.059	-0.716	0.011	.
Male	3	ZRH High	0.023	0.039	0.043	0.049	0.051	0.041	0.009	0.003	21.2	-0.932	0.892	0.011	.
Male	4.5	Sham Recovery	0.030	0.033	0.034	0.037	0.054	0.037	0.009	0.004	23.3	2.081	4.669	0.011	.
Male	4.5	3R4F High Recovery	0.034	0.034	0.034	0.034	0.037	0.035	0.001	0.001	3.9	2.236	5.000	0.011	.
Male	4.5	ZRH High Recovery	0.023	0.027	0.036	0.037	0.043	0.034	0.007	0.002	21.0	-0.094	-1.294	0.011	.
Female	3	Sham	0.028	0.029	0.033	0.037	0.041	0.033	0.004	0.001	13.4	0.405	-0.893	0.011	.
Female	3	3R4F Low	0.030	0.031	0.033	0.035	0.042	0.033	0.004	0.001	11.0	1.558	2.807	0.011	.
Female	3	3R4F Medium	0.025	0.026	0.031	0.036	0.048	0.032	0.007	0.002	21.6	1.212	1.934	0.011	.
Female	3	3R4F High	0.024	0.032	0.034	0.035	0.047	0.034	0.006	0.002	18.2	0.612	2.036	0.011	.
Female	3	ZRH Low	0.024	0.029	0.030	0.034	0.037	0.031	0.005	0.002	14.6	-0.113	-0.946	0.011	.
Female	3	ZRH Medium	0.024	0.030	0.031	0.037	0.045	0.033	0.006	0.002	18.2	0.862	0.845	0.011	.
Female	3	ZRH High	0.027	0.030	0.034	0.036	0.042	0.034	0.005	0.001	14.0	0.339	-0.332	0.011	.
Female	4.5	Sham Recovery	0.026	0.029	0.037	0.040	0.048	0.036	0.008	0.003	21.9	0.277	-0.169	0.011	.
Female	4.5	3R4F High Recovery	0.023	0.025	0.029	0.034	0.037	0.030	0.005	0.002	18.4	0.253	-1.574	0.011	.
Female	4.5	ZRH High Recovery	0.026	0.029	0.033	0.044	0.056	0.037	0.011	0.004	29.9	1.055	-0.333	0.011	.

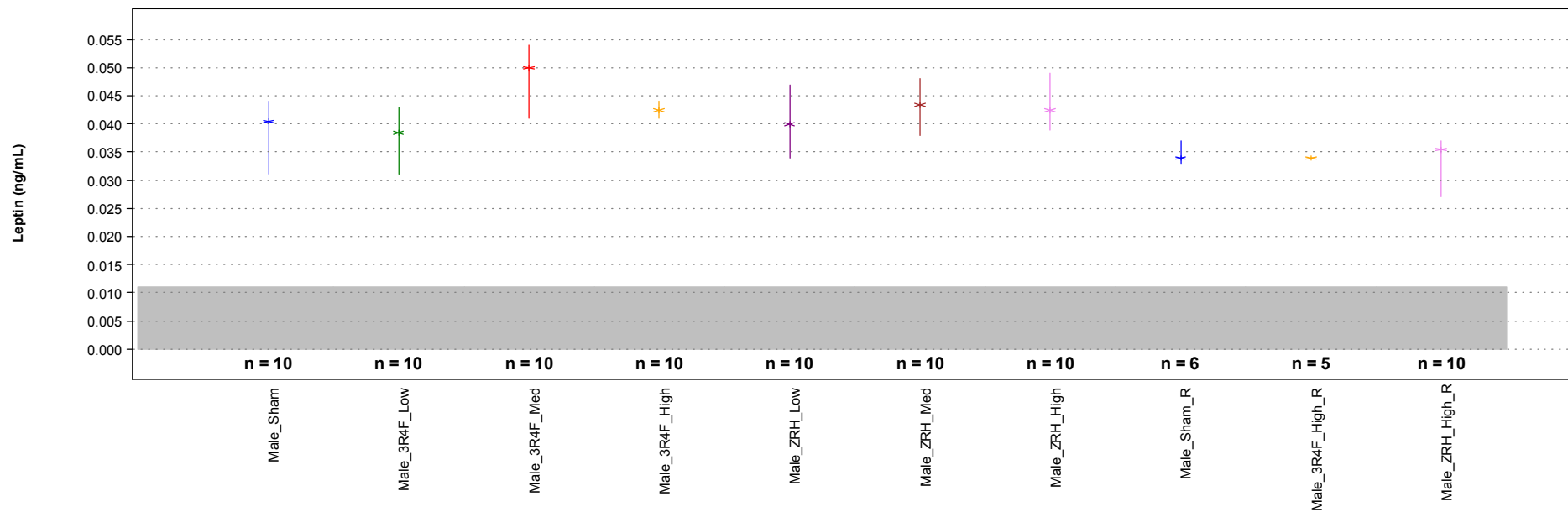
Percentage of Values below LLQ for each Group-Males

Analyte = Leptin

**Plot of Descriptive Robust Statistics-Males**

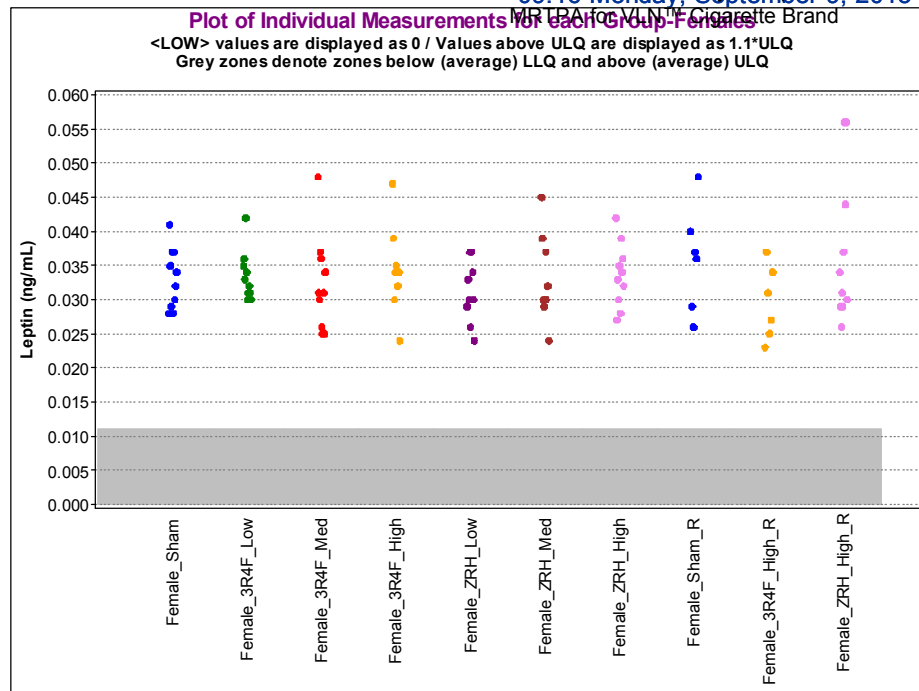
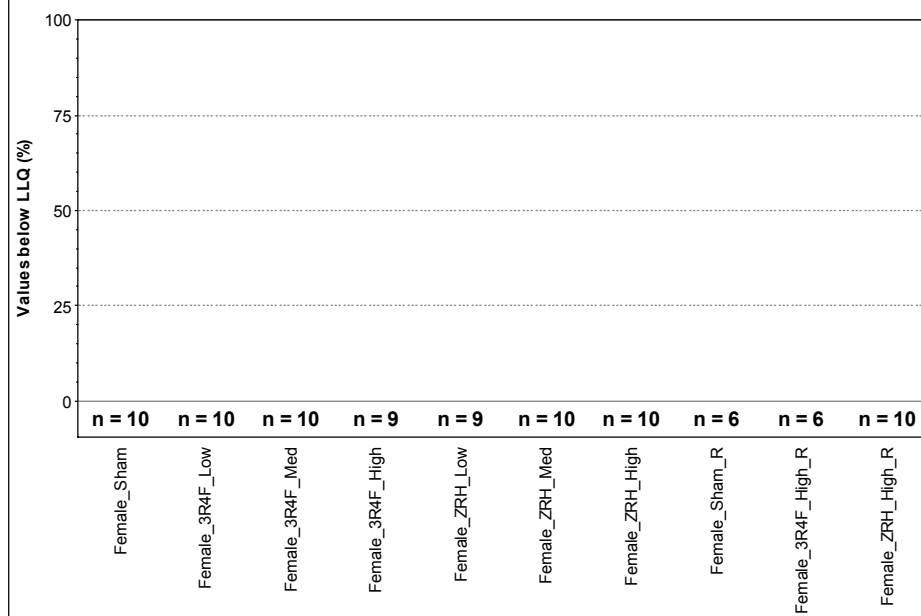
Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



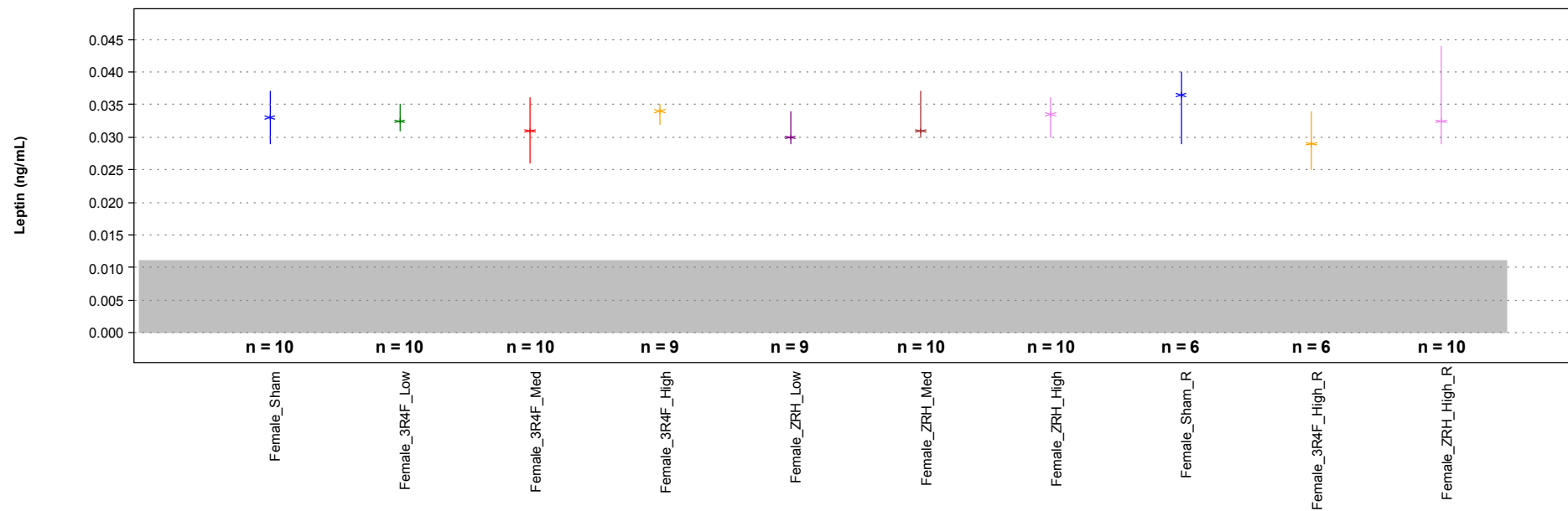
Percentage of Values below LLQ for each Group-Females

Analyte = Leptin

**Plot of Descriptive Robust Statistics-Females**

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = Leptin

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	0.676896
---- Sham vs. 3R4F Medium for Male	0.103199
---- Sham vs. 3R4F High for Male	0.159758
---- Sham vs. ZRH Low for Male	0.762108
---- Sham vs. ZRH Medium for Male	0.240258
---- Sham vs. ZRH High for Male	0.519579
---- ZRH Low vs. 3R4F Medium for Male	0.130281
---- ZRH Medium vs. 3R4F High for Male	1.000000
---- ZRH High vs. 3R4F High for Male	0.647666
---- Sham Recovery vs. 3R4F High Recovery for Male	0.764592
---- Sham Recovery vs. ZRH High Recovery for Male	0.701063
---- Sham vs. Sham Recovery for Male	0.445685
---- 3R4F High vs. 3R4F High Recovery for Male	0.001948
---- ZRH High vs. ZRH High Recovery for Male	0.043786
---- 3R4F High Recovery vs. ZRH High Recovery for Male	0.949762
---- Sham vs. 3R4F Low for Female	0.790566
---- Sham vs. 3R4F Medium for Female	0.543984
---- Sham vs. 3R4F High for Female	0.681101
---- Sham vs. ZRH Low for Female	0.459065
---- Sham vs. ZRH Medium for Female	0.939286
---- Sham vs. ZRH High for Female	0.879424
---- ZRH Low vs. 3R4F Medium for Female	0.805490
---- ZRH Medium vs. 3R4F High for Female	0.343477
---- ZRH High vs. 3R4F High for Female	0.837268
---- Sham Recovery vs. 3R4F High Recovery for Female	0.127538
---- Sham Recovery vs. ZRH High Recovery for Female	1.000000
---- Sham vs. Sham Recovery for Female	0.478849

Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = Leptin

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	0.171452
---- ZRH High vs. ZRH High Recovery for Female	0.820330
---- 3R4F High Recovery vs. ZRH High Recovery for Female	0.173568

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 35

Lymphotactin

Unit = pg/mL

Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = Lymphotactin

Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	5	5	0	4.3	.
Male	3	3R4F Low	10	10	5	5	0	4.3	.
Male	3	3R4F Medium	10	10	4	6	0	4.3	.
Male	3	3R4F High	10	10	3	7	0	4.3	.
Male	3	ZRH Low	10	10	5	5	0	4.3	.
Male	3	ZRH Medium	10	10	3	7	0	4.3	.
Male	3	ZRH High	10	10	6	4	0	4.3	.
Male	4.5	Sham Recovery	6	6	0	6	0	4.3	.
Male	4.5	3R4F High Recovery	5	5	0	5	0	4.3	.
Male	4.5	ZRH High Recovery	10	10	0	10	0	4.3	.
Female	3	Sham	10	10	2	8	0	4.3	.
Female	3	3R4F Low	10	10	1	9	0	4.3	.
Female	3	3R4F Medium	10	10	1	9	0	4.3	.
Female	3	3R4F High	9	9	0	9	0	4.3	.
Female	3	ZRH Low	9	9	3	6	0	4.3	.
Female	3	ZRH Medium	10	10	1	9	0	4.3	.
Female	3	ZRH High	10	10	3	7	0	4.3	.
Female	4.5	Sham Recovery	6	6	0	6	0	4.3	.
Female	4.5	3R4F High Recovery	6	6	0	6	0	4.3	.
Female	4.5	ZRH High Recovery	10	10	0	10	0	4.3	.

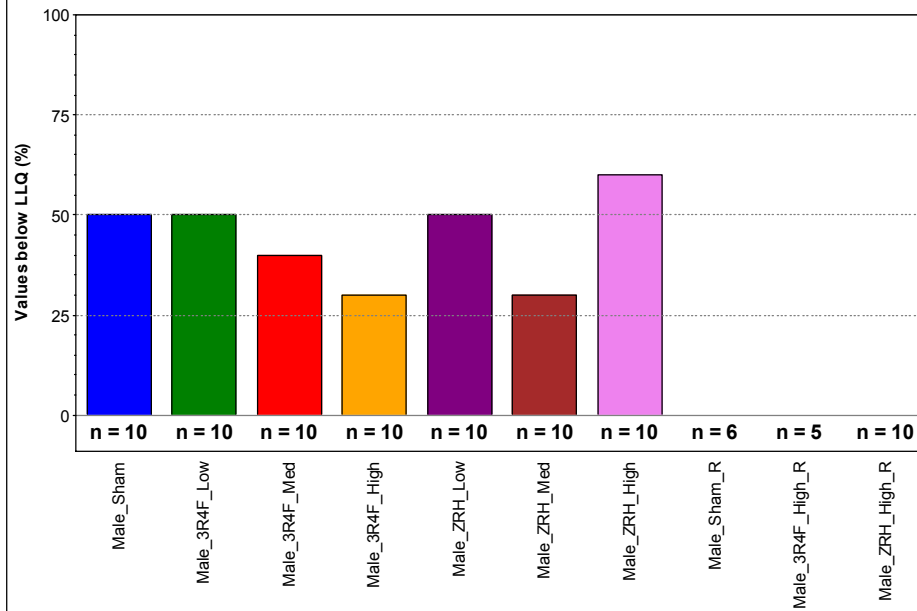
Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = Lymphotactin

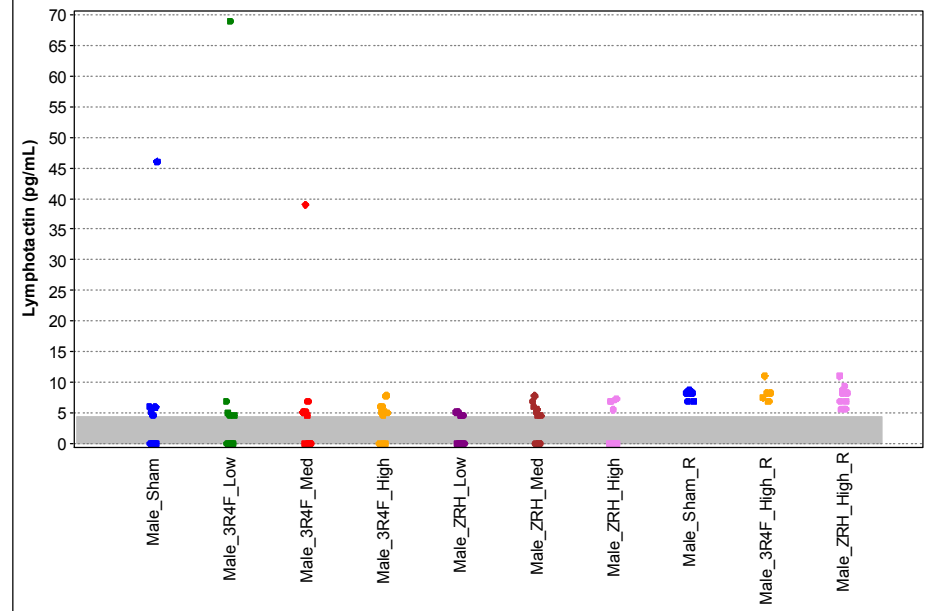
Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	2.150	2.150	3.375	5.900	46.000	7.835	13.512	4.273	172.5	3.074	9.587	4.3	.
Male	3	3R4F Low	2.150	2.150	3.375	5.000	69.000	10.085	20.768	6.568	205.9	3.124	9.820	4.3	.
Male	3	3R4F Medium	2.150	2.150	4.850	5.100	39.000	7.440	11.219	3.548	150.8	3.028	9.375	4.3	.
Male	3	3R4F High	2.150	2.150	5.050	6.000	7.800	4.605	1.910	0.604	41.5	-0.120	-0.715	4.3	.
Male	3	ZRH Low	2.150	2.150	3.375	4.600	5.100	3.475	1.409	0.445	40.5	0.061	-2.445	4.3	.
Male	3	ZRH Medium	2.150	2.150	4.850	6.000	7.800	4.695	2.013	0.637	42.9	-0.102	-1.072	4.3	.
Male	3	ZRH High	2.150	2.150	2.150	6.900	7.300	3.950	2.368	0.749	60.0	0.603	-1.937	4.3	.
Male	4.5	Sham Recovery	6.900	6.900	8.200	8.200	8.800	7.867	0.784	0.320	10.0	-0.549	-1.540	4.3	.
Male	4.5	3R4F High Recovery	6.900	7.500	8.200	8.200	11.000	8.360	1.573	0.703	18.8	1.569	2.969	4.3	.
Male	4.5	ZRH High Recovery	5.600	5.600	7.550	8.800	11.000	7.620	1.824	0.577	23.9	0.477	-0.528	4.3	.
Female	3	Sham	2.150	4.700	5.200	5.200	7.300	4.830	1.589	0.502	32.9	-0.733	0.562	4.3	.
Female	3	3R4F Low	2.150	5.600	6.250	6.900	7.300	5.825	1.523	0.482	26.2	-1.824	3.529	4.3	.
Female	3	3R4F Medium	2.150	5.600	7.100	9.100	115.000	17.495	34.322	10.854	196.2	3.141	9.901	4.3	.
Female	3	3R4F High	4.400	5.200	5.600	6.400	7.300	5.689	0.994	0.331	17.5	0.433	-0.892	4.3	.
Female	3	ZRH Low	2.150	2.150	5.200	6.500	7.800	4.850	2.214	0.738	45.6	-0.271	-1.642	4.3	.
Female	3	ZRH Medium	2.150	4.400	5.000	5.600	5.600	4.805	1.058	0.335	22.0	-1.968	4.611	4.3	.
Female	3	ZRH High	2.150	2.150	4.550	5.200	6.400	4.285	1.610	0.509	37.6	-0.405	-1.262	4.3	.
Female	4.5	Sham Recovery	5.600	7.100	7.650	9.700	11.000	8.117	1.961	0.801	24.2	0.394	-0.681	4.3	.
Female	4.5	3R4F High Recovery	5.600	6.900	7.550	9.400	11.000	8.000	1.959	0.800	24.5	0.530	-0.496	4.3	.
Female	4.5	ZRH High Recovery	5.600	7.800	9.550	11.000	13.000	9.400	2.130	0.673	22.7	-0.231	0.162	4.3	.

Percentage of Values below LLQ for each Group-Males

Analyte = Lymphotactin

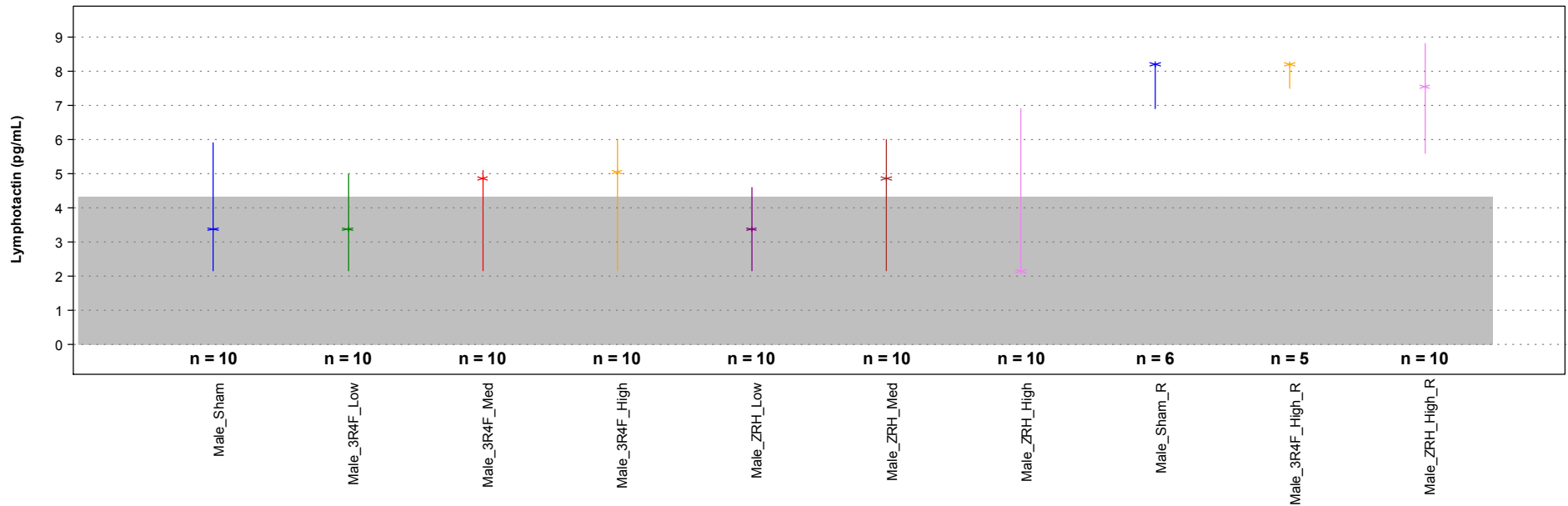
**Plot of Individual Measurements for each Group-Males**

<LOW> values are displayed as 0 / Values above ULQ are displayed as 1.1*ULQ
 Grey zones denote zones below (average) LLQ and above (average) ULQ

**Plot of Descriptive Robust Statistics-Males**

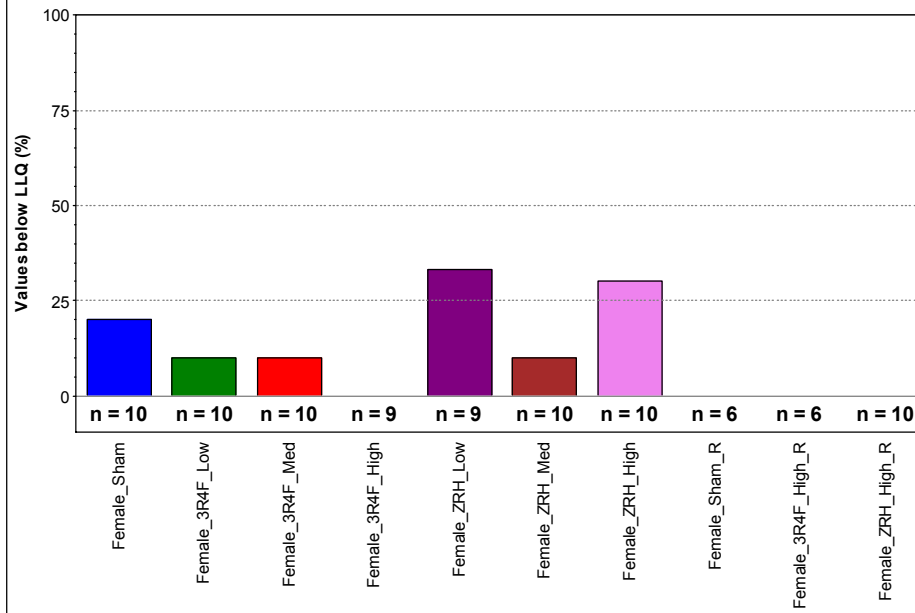
Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ

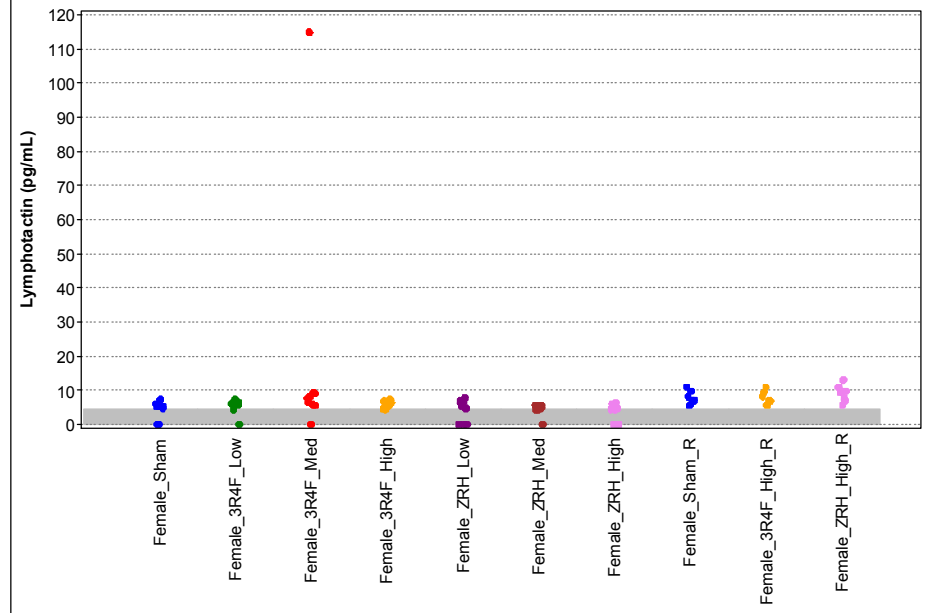


Percentage of Values below LLQ for each Group-Females

Analyte = Lymphotactin

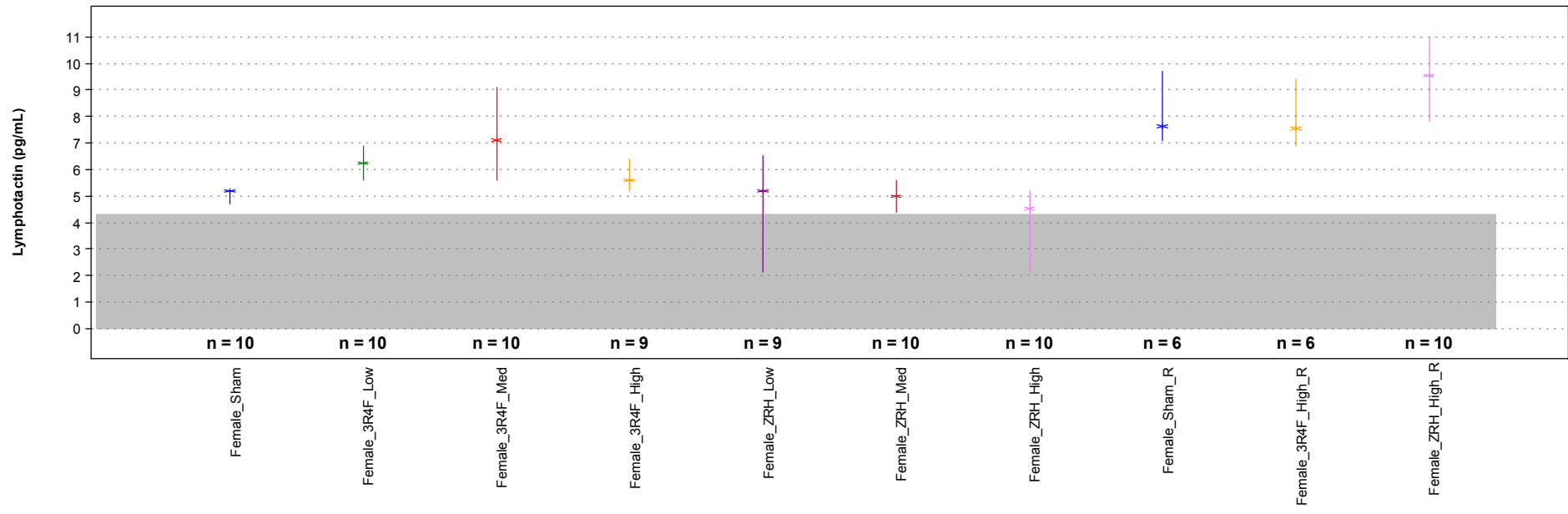
**Plot of Individual Measurements**

<LOW> values are displayed as 0 / Values above ULQ are displayed as 1.1*ULQ
 Grey zones denote zones below (average) LLQ and above (average) ULQ

**Plot of Descriptive Robust Statistics-Females**

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Unadjusted P-values Obtained by Kruskal-Wallis Test **Analyte = Lymphotactin**

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	0.903404
---- Sham vs. 3R4F Medium for Male	0.811225
---- Sham vs. 3R4F High for Male	0.530617
---- Sham vs. ZRH Low for Male	0.515648
---- Sham vs. ZRH Medium for Male	0.505763
---- Sham vs. ZRH High for Male	0.934024
---- ZRH Low vs. 3R4F Medium for Male	0.278619
---- ZRH Medium vs. 3R4F High for Male	0.938627
---- ZRH High vs. 3R4F High for Male	0.578581
---- Sham Recovery vs. 3R4F High Recovery for Male	0.846623
---- Sham Recovery vs. ZRH High Recovery for Male	0.696690
---- Sham vs. Sham Recovery for Male	0.007993
---- 3R4F High vs. 3R4F High Recovery for Male	0.004587
---- ZRH High vs. ZRH High Recovery for Male	0.004358
---- 3R4F High Recovery vs. ZRH High Recovery for Male	0.493132
---- Sham vs. 3R4F Low for Female	0.073353
---- Sham vs. 3R4F Medium for Female	0.009716
---- Sham vs. 3R4F High for Female	0.228528
---- Sham vs. ZRH Low for Female	0.802905
---- Sham vs. ZRH Medium for Female	0.908480
---- Sham vs. ZRH High for Female	0.395176
---- ZRH Low vs. 3R4F Medium for Female	0.070821
---- ZRH Medium vs. 3R4F High for Female	0.157072
---- ZRH High vs. 3R4F High for Female	0.052889
---- Sham Recovery vs. 3R4F High Recovery for Female	0.686311
---- Sham Recovery vs. ZRH High Recovery for Female	0.274160
---- Sham vs. Sham Recovery for Female	0.004437

Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = Lymphotactin

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	0.017492
---- ZRH High vs. ZRH High Recovery for Female	0.000273
---- 3R4F High Recovery vs. ZRH High Recovery for Female	0.171972

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 44

Monocyte Chemotactic Protein 1 (MCP-1)

Unit = pg/mL

Descriptive Statistics by Exposure Duration and Treatment Type

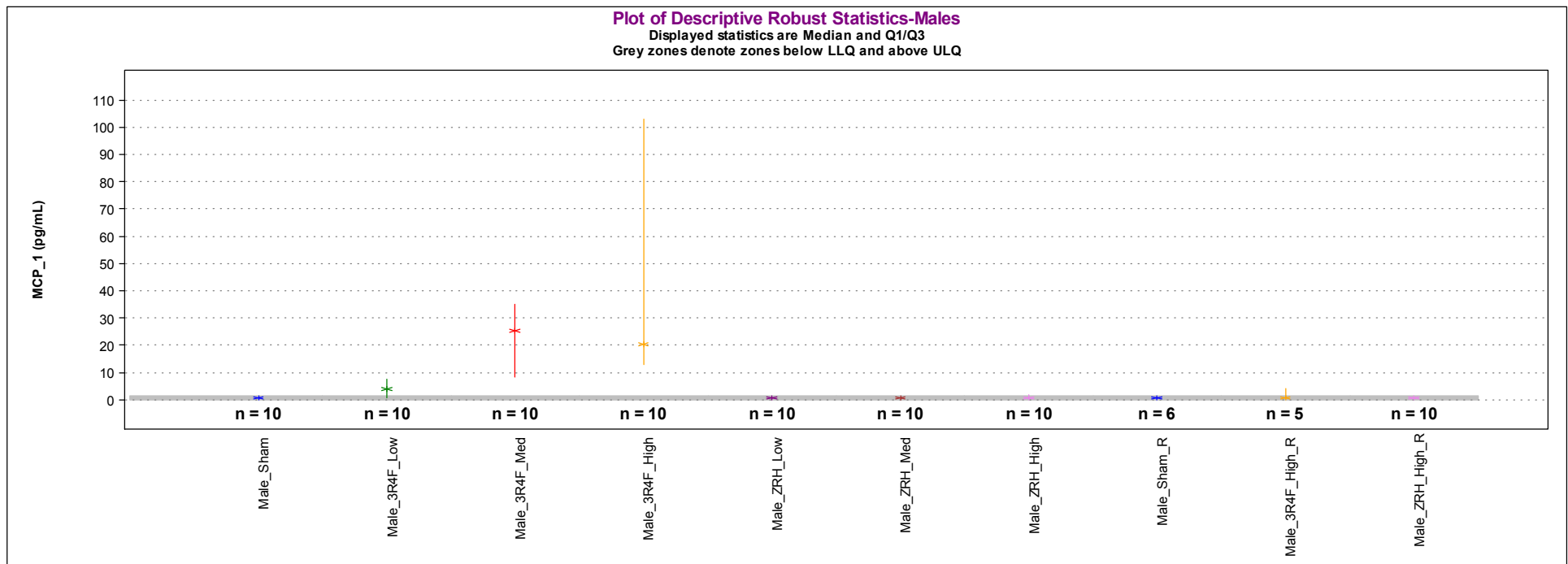
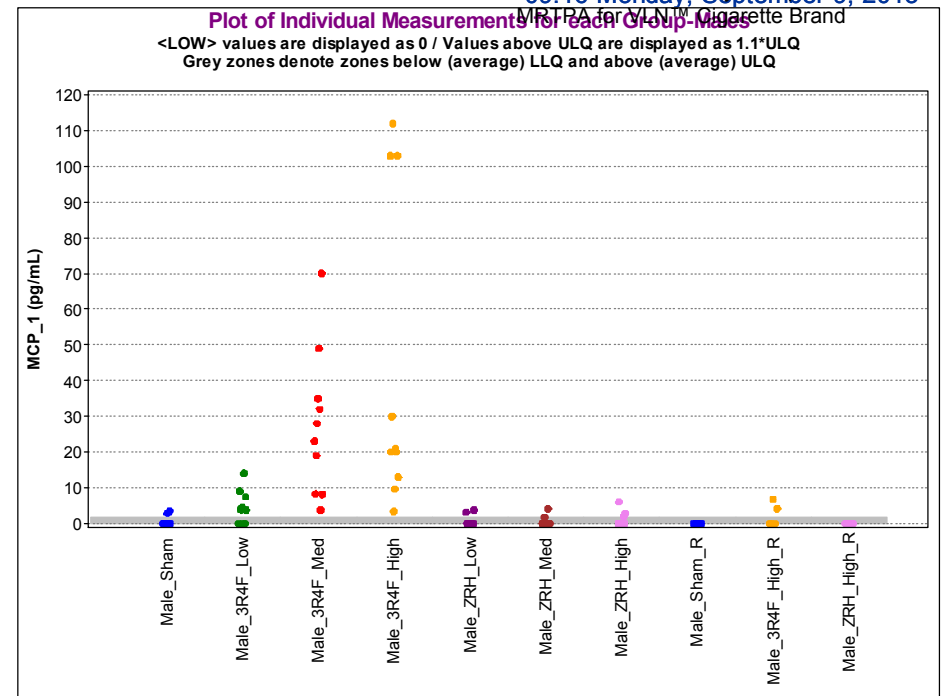
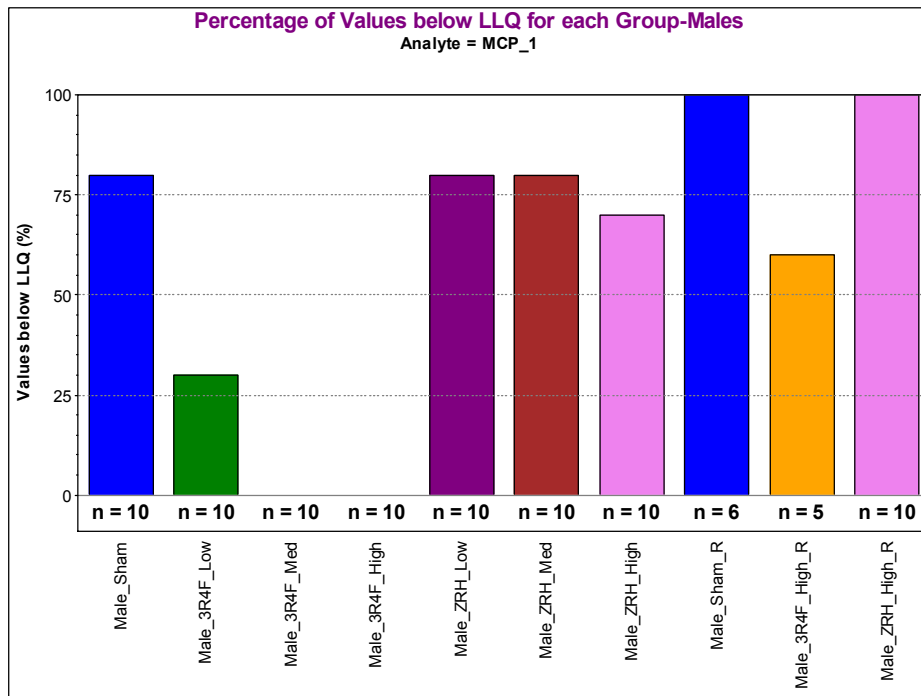
Analyte = MCP_1

Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	8	2	0	1.6	.
Male	3	3R4F Low	10	10	3	7	0	1.6	.
Male	3	3R4F Medium	10	10	0	10	0	1.6	.
Male	3	3R4F High	10	10	0	10	0	1.6	.
Male	3	ZRH Low	10	10	8	2	0	1.6	.
Male	3	ZRH Medium	10	10	8	2	0	1.6	.
Male	3	ZRH High	10	10	7	3	0	1.6	.
Male	4.5	Sham Recovery	6	6	6	0	0	1.6	.
Male	4.5	3R4F High Recovery	5	5	3	2	0	1.6	.
Male	4.5	ZRH High Recovery	10	10	10	0	0	1.6	.
Female	3	Sham	10	10	10	0	0	1.6	.
Female	3	3R4F Low	10	10	2	8	0	1.6	.
Female	3	3R4F Medium	10	10	0	10	0	1.6	.
Female	3	3R4F High	9	9	0	9	0	1.6	.
Female	3	ZRH Low	9	9	8	1	0	1.6	.
Female	3	ZRH Medium	10	10	7	3	0	1.6	.
Female	3	ZRH High	10	10	7	3	0	1.6	.
Female	4.5	Sham Recovery	6	6	6	0	0	1.6	.
Female	4.5	3R4F High Recovery	6	6	2	4	0	1.6	.
Female	4.5	ZRH High Recovery	10	10	10	0	0	1.6	.

Descriptive Statistics by Exposure Duration and Treatment Type

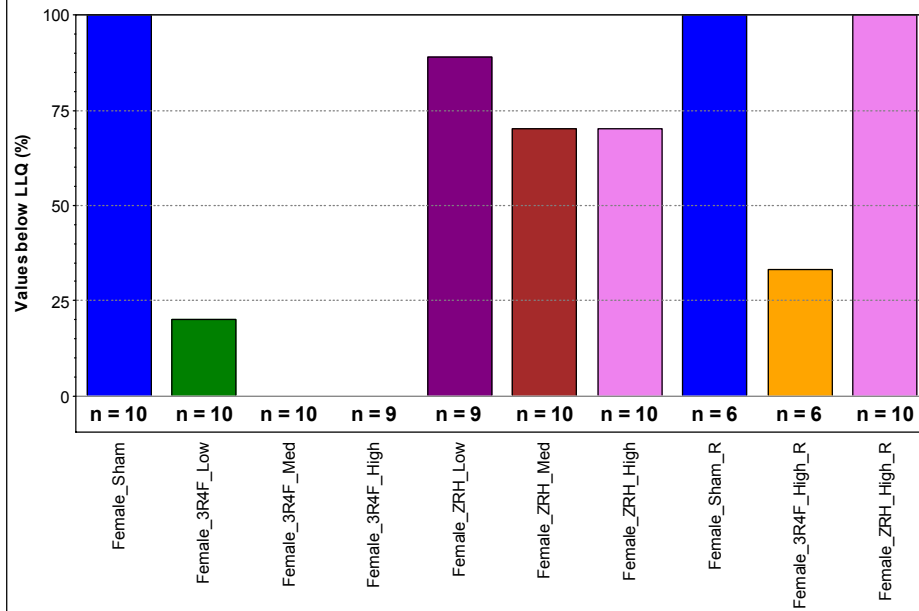
Analyte = MCP_1

Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	0.800	0.800	0.800	0.800	3.500	1.280	1.022	0.323	79.8	1.863	1.989	1.6	.
Male	3	3R4F Low	0.800	0.800	3.950	7.400	14.000	4.900	4.210	1.331	85.9	1.170	1.242	1.6	.
Male	3	3R4F Medium	3.800	8.300	25.500	35.000	70.000	27.630	20.386	6.447	73.8	0.942	0.772	1.6	.
Male	3	3R4F High	3.400	13.000	20.500	103.000	112.000	43.500	43.784	13.846	100.7	0.945	-1.206	1.6	.
Male	3	ZRH Low	0.800	0.800	0.800	0.800	3.800	1.340	1.147	0.363	85.6	1.846	1.870	1.6	.
Male	3	ZRH Medium	0.800	0.800	0.800	0.800	4.100	1.220	1.051	0.332	86.1	2.802	8.034	1.6	.
Male	3	ZRH High	0.800	0.800	0.800	1.900	6.000	1.630	1.679	0.531	103.0	2.380	5.828	1.6	.
Male	4.5	Sham Recovery	0.800	0.800	0.800	0.800	0.800	0.800	0.000	0.000	0.0	.	.	1.6	.
Male	4.5	3R4F High Recovery	0.800	0.800	0.800	4.200	6.800	2.680	2.733	1.222	102.0	1.092	-0.590	1.6	.
Male	4.5	ZRH High Recovery	0.800	0.800	0.800	0.800	0.800	0.800	0.000	0.000	0.0	.	.	1.6	.
Female	3	Sham	0.800	0.800	0.800	0.800	0.800	0.800	0.000	0.000	0.0	.	.	1.6	.
Female	3	3R4F Low	0.800	2.400	4.500	11.000	13.000	5.770	4.502	1.424	78.0	0.525	-1.323	1.6	.
Female	3	3R4F Medium	19.000	26.000	35.000	41.000	88.000	40.100	22.078	6.982	55.1	1.440	1.526	1.6	.
Female	3	3R4F High	16.000	41.000	68.000	89.000	110.000	65.444	32.520	10.840	49.7	-0.083	-1.339	1.6	.
Female	3	ZRH Low	0.800	0.800	0.800	0.800	3.400	1.089	0.867	0.289	79.6	3.000	9.000	1.6	.
Female	3	ZRH Medium	0.800	0.800	0.800	2.200	6.200	1.700	1.759	0.556	103.5	2.253	5.172	1.6	.
Female	3	ZRH High	0.800	0.800	0.800	1.600	6.700	1.670	1.882	0.595	112.7	2.585	6.893	1.6	.
Female	4.5	Sham Recovery	0.800	0.800	0.800	0.800	0.800	0.800	0.000	0.000	0.0	.	.	1.6	.
Female	4.5	3R4F High Recovery	0.800	0.800	3.050	3.600	19.000	5.050	6.940	2.833	137.4	2.281	5.384	1.6	.
Female	4.5	ZRH High Recovery	0.800	0.800	0.800	0.800	0.800	0.800	0.000	0.000	0.0	.	.	1.6	.

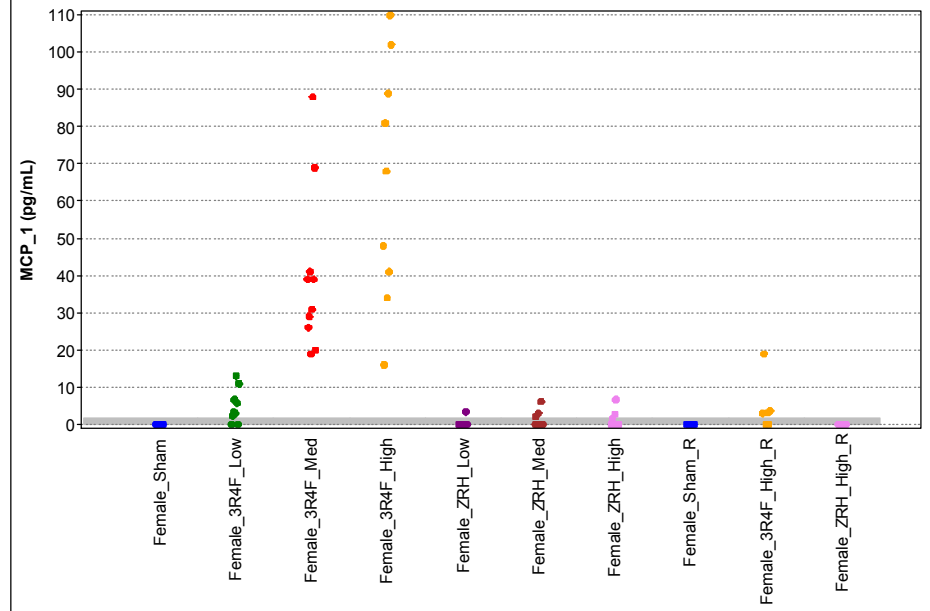


Percentage of Values below LLQ for each Group-Females

Analyte = MCP_1

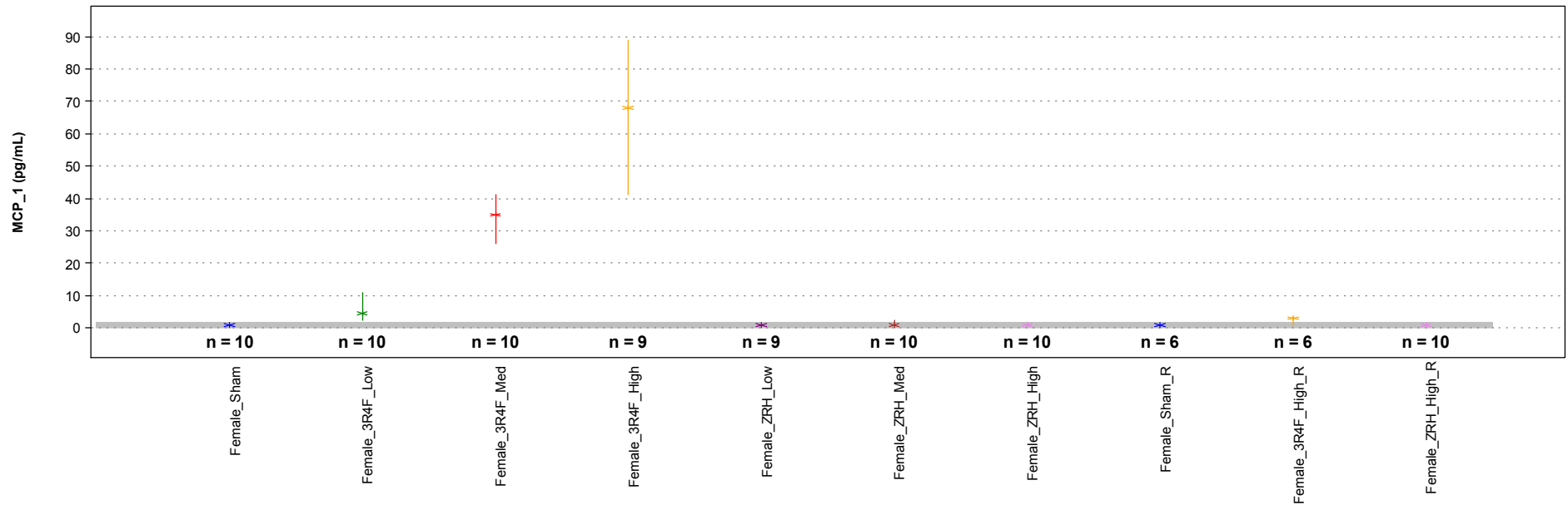
**Plot of Individual Measurements**

<LOW> values are displayed as 0 / Values above ULQ are displayed as 1.1*ULQ
 Grey zones denote zones below (average) LLQ and above (average) ULQ

**Plot of Descriptive Robust Statistics-Females**

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = MCP_1

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	0.008100
---- Sham vs. 3R4F Medium for Male	0.000094237
---- Sham vs. 3R4F High for Male	0.000128
---- Sham vs. ZRH Low for Male	0.913892
---- Sham vs. ZRH Medium for Male	1.000000
---- Sham vs. ZRH High for Male	0.691077
---- ZRH Low vs. 3R4F Medium for Male	0.000110
---- ZRH Medium vs. 3R4F High for Male	0.000128
---- ZRH High vs. 3R4F High for Male	0.000152
---- Sham Recovery vs. 3R4F High Recovery for Male	0.104204
---- Sham Recovery vs. ZRH High Recovery for Male	1.000000
---- Sham vs. Sham Recovery for Male	0.257899
---- 3R4F High vs. 3R4F High Recovery for Male	0.004624
---- ZRH High vs. ZRH High Recovery for Male	0.068157
---- 3R4F High Recovery vs. ZRH High Recovery for Male	0.038434
---- Sham vs. 3R4F Low for Female	0.000639
---- Sham vs. 3R4F Medium for Female	0.000053411
---- Sham vs. 3R4F High for Female	0.000070977
---- Sham vs. ZRH Low for Female	0.291841
---- Sham vs. ZRH Medium for Female	0.068157
---- Sham vs. ZRH High for Female	0.068157
---- ZRH Low vs. 3R4F Medium for Female	0.000134
---- ZRH Medium vs. 3R4F High for Female	0.000165
---- ZRH High vs. 3R4F High for Female	0.000165
---- Sham Recovery vs. 3R4F High Recovery for Female	0.022230
---- Sham Recovery vs. ZRH High Recovery for Female	1.000000
---- Sham vs. Sham Recovery for Female	1.000000

Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = MCP_1

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	0.002163
---- ZRH High vs. ZRH High Recovery for Female	0.068157
---- 3R4F High Recovery vs. ZRH High Recovery for Female	0.004374

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 45

Monocyte Chemotactic Protein 3 (MCP-3)

Unit = pg/mL

Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = MCP_3

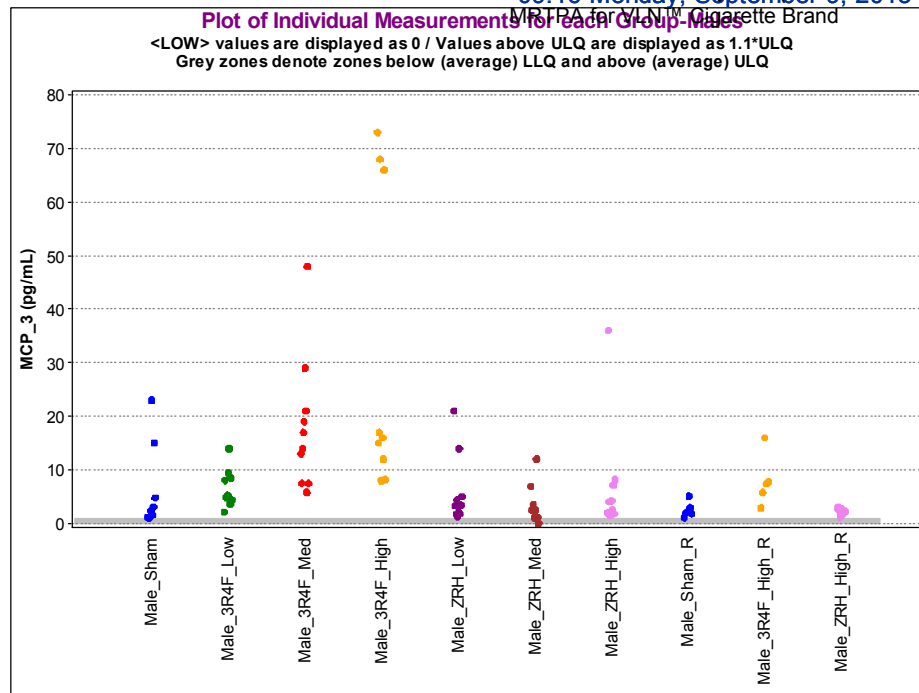
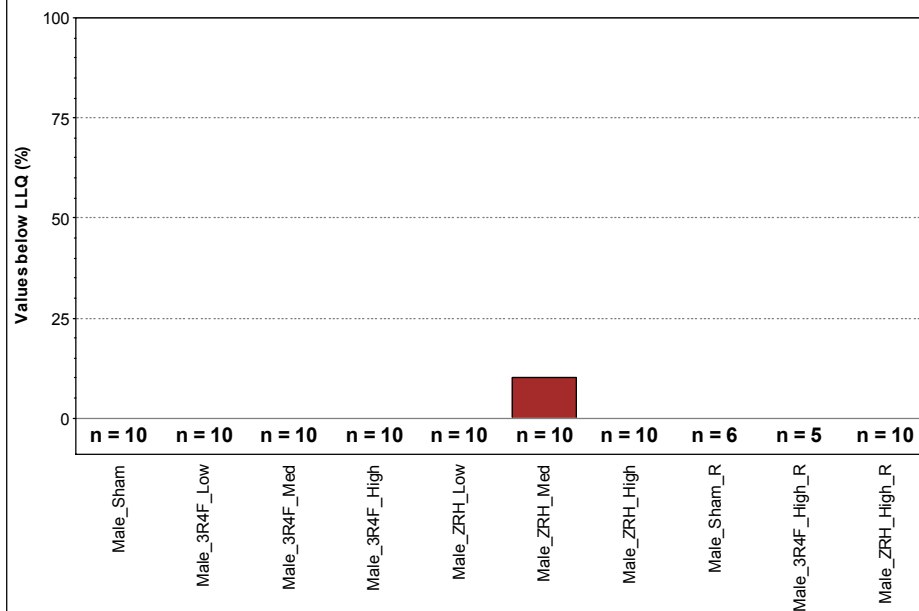
Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	0	10	0	0.88	.
Male	3	3R4F Low	10	10	0	10	0	0.88	.
Male	3	3R4F Medium	10	10	0	10	0	0.88	.
Male	3	3R4F High	10	10	0	10	0	0.88	.
Male	3	ZRH Low	10	10	0	10	0	0.88	.
Male	3	ZRH Medium	10	10	1	9	0	0.88	.
Male	3	ZRH High	10	10	0	10	0	0.88	.
Male	4.5	Sham Recovery	6	6	0	6	0	0.88	.
Male	4.5	3R4F High Recovery	5	5	0	5	0	0.88	.
Male	4.5	ZRH High Recovery	10	10	0	10	0	0.88	.
Female	3	Sham	10	10	0	10	0	0.88	.
Female	3	3R4F Low	10	10	0	10	0	0.88	.
Female	3	3R4F Medium	10	10	0	10	0	0.88	.
Female	3	3R4F High	9	9	0	9	0	0.88	.
Female	3	ZRH Low	9	9	0	9	0	0.88	.
Female	3	ZRH Medium	10	10	0	10	0	0.88	.
Female	3	ZRH High	10	10	0	10	0	0.88	.
Female	4.5	Sham Recovery	6	6	0	6	0	0.88	.
Female	4.5	3R4F High Recovery	6	6	0	6	0	0.88	.
Female	4.5	ZRH High Recovery	10	10	0	10	0	0.88	.

Descriptive Statistics by Exposure Duration and Treatment Type**Analyte = MCP_3**

Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	0.980	1.100	2.000	4.800	23.000	5.438	7.486	2.367	137.7	1.944	2.974	0.88	.
Male	3	3R4F Low	2.100	4.400	5.100	8.500	14.000	6.500	3.506	1.109	53.9	1.056	1.064	0.88	.
Male	3	3R4F Medium	5.800	7.500	15.500	21.000	48.000	18.180	12.658	4.003	69.6	1.593	2.930	0.88	.
Male	3	3R4F High	8.000	8.200	15.500	66.000	73.000	29.130	27.757	8.778	95.3	0.997	-1.178	0.88	.
Male	3	ZRH Low	1.300	1.800	3.350	5.000	21.000	5.810	6.489	2.052	111.7	1.906	2.919	0.88	.
Male	3	ZRH Medium	0.440	1.100	2.450	3.500	12.000	3.364	3.548	1.122	105.5	1.948	3.749	0.88	.
Male	3	ZRH High	1.400	2.000	3.250	7.100	36.000	6.950	10.462	3.308	150.5	2.893	8.696	0.88	.
Male	4.5	Sham Recovery	1.100	1.800	2.100	2.900	5.100	2.517	1.393	0.569	55.4	1.543	2.835	0.88	.
Male	4.5	3R4F High Recovery	2.900	5.800	7.400	7.800	16.000	7.980	4.880	2.182	61.1	1.342	2.639	0.88	.
Male	4.5	ZRH High Recovery	1.100	2.000	2.300	2.700	3.000	2.280	0.588	0.186	25.8	-0.753	0.282	0.88	.
Female	3	Sham	1.000	1.300	1.600	2.000	2.400	1.620	0.457	0.144	28.2	0.294	-0.888	0.88	.
Female	3	3R4F Low	2.700	5.400	5.950	8.400	12.000	6.890	2.937	0.929	42.6	0.572	-0.369	0.88	.
Female	3	3R4F Medium	8.200	16.000	22.500	28.000	43.000	22.820	10.602	3.353	46.5	0.692	0.083	0.88	.
Female	3	3R4F High	12.000	20.000	34.000	43.000	47.000	32.000	13.491	4.497	42.2	-0.441	-1.595	0.88	.
Female	3	ZRH Low	1.300	1.500	2.000	3.100	12.000	4.089	4.253	1.418	104.0	1.548	0.674	0.88	.
Female	3	ZRH Medium	1.200	1.500	1.600	8.800	14.000	4.890	5.315	1.681	108.7	1.226	-0.279	0.88	.
Female	3	ZRH High	1.800	2.100	3.400	5.300	18.000	4.950	4.849	1.533	98.0	2.569	7.236	0.88	.
Female	4.5	Sham Recovery	1.400	1.600	2.000	2.200	2.900	2.017	0.523	0.214	25.9	0.814	1.084	0.88	.
Female	4.5	3R4F High Recovery	3.200	4.200	5.600	7.100	21.000	7.783	6.619	2.702	85.0	2.216	5.124	0.88	.
Female	4.5	ZRH High Recovery	1.100	1.600	2.050	2.400	4.700	2.210	0.992	0.314	44.9	1.911	4.825	0.88	.

Percentage of Values below LLQ for each Group-Males

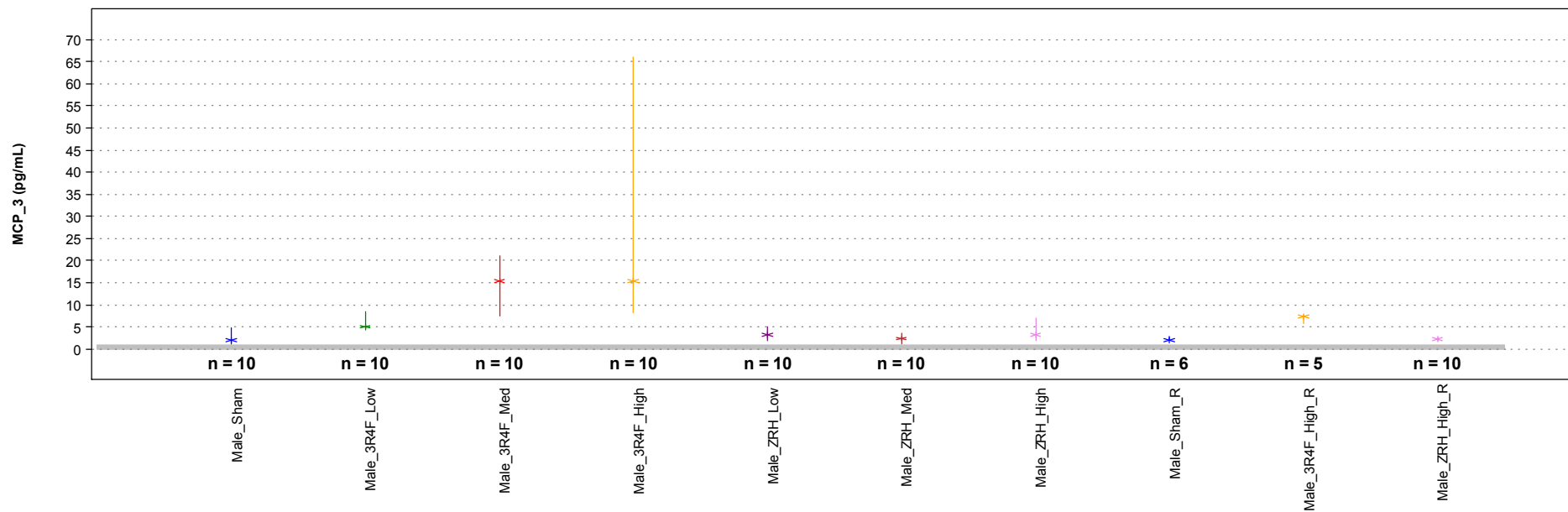
Analyte = MCP_3



Plot of Descriptive Robust Statistics-Males

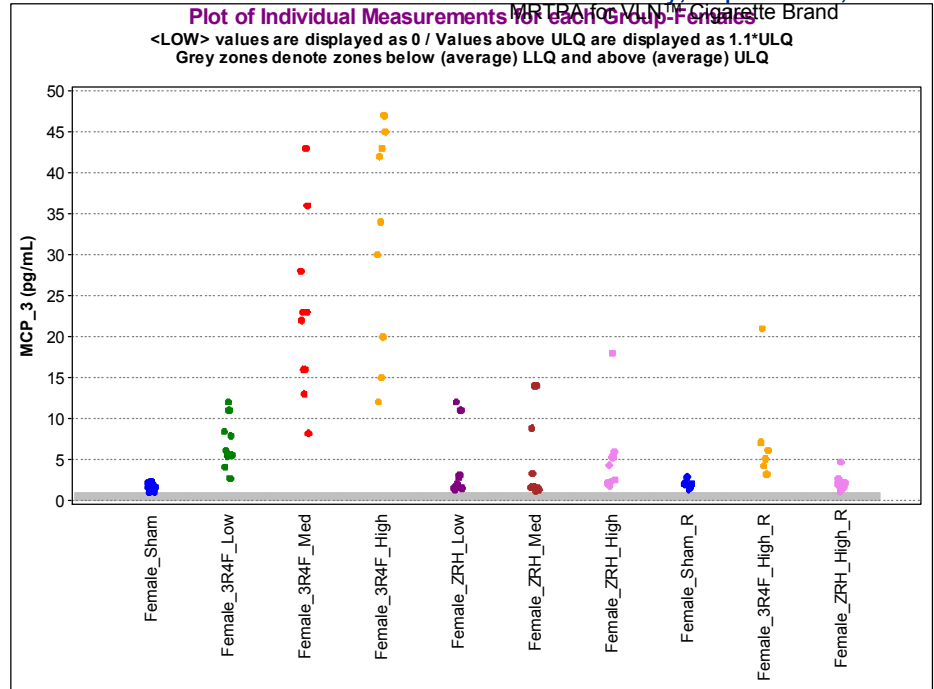
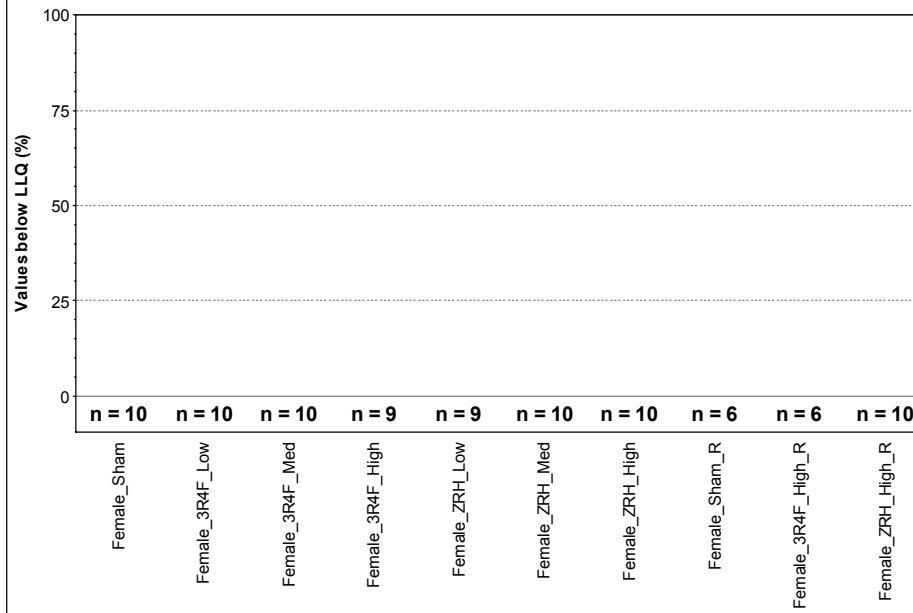
Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Percentage of Values below LLQ for each Group-Females

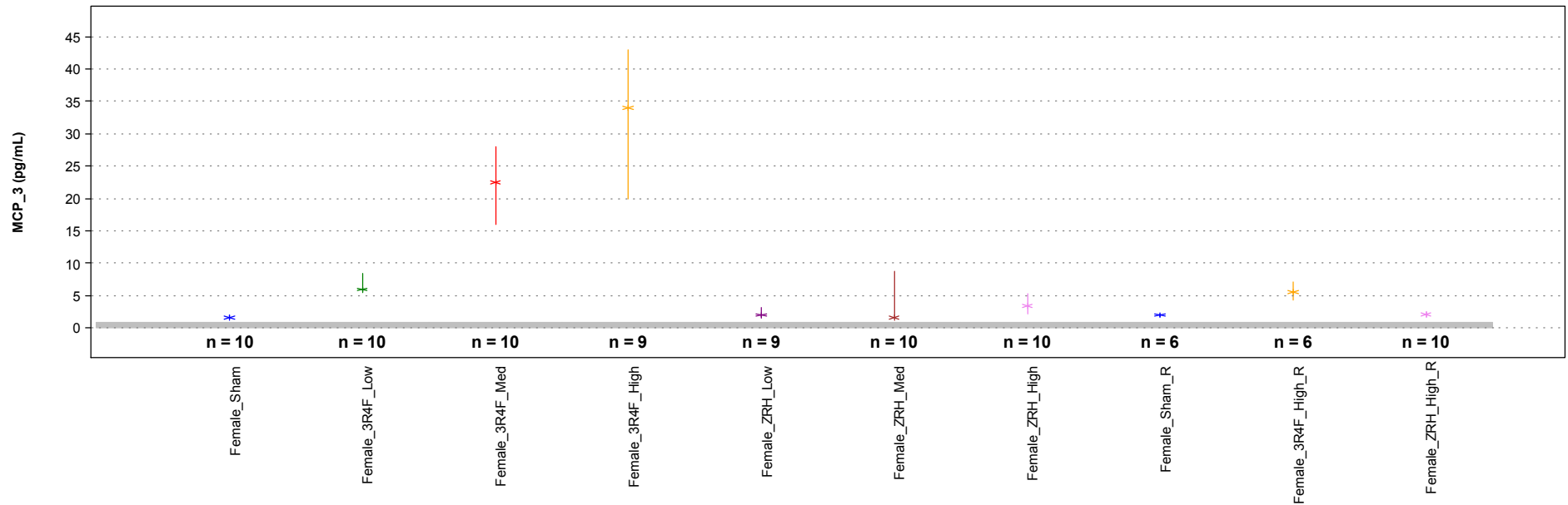
Analyte = MCP_3



Plot of Descriptive Robust Statistics-Females

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = MCP_3

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	0.069537
---- Sham vs. 3R4F Medium for Male	0.005125
---- Sham vs. 3R4F High for Male	0.003585
---- Sham vs. ZRH Low for Male	0.272675
---- Sham vs. ZRH Medium for Male	0.789709
---- Sham vs. ZRH High for Male	0.256660
---- ZRH Low vs. 3R4F Medium for Male	0.004030
---- ZRH Medium vs. 3R4F High for Male	0.000429
---- ZRH High vs. 3R4F High for Male	0.002194
---- Sham Recovery vs. 3R4F High Recovery for Male	0.013497
---- Sham Recovery vs. ZRH High Recovery for Male	0.827638
---- Sham vs. Sham Recovery for Male	0.913372
---- 3R4F High vs. 3R4F High Recovery for Male	0.016831
---- ZRH High vs. ZRH High Recovery for Male	0.211950
---- 3R4F High Recovery vs. ZRH High Recovery for Male	0.003935
---- Sham vs. 3R4F Low for Female	0.000155
---- Sham vs. 3R4F Medium for Female	0.000153
---- Sham vs. 3R4F High for Female	0.000236
---- Sham vs. ZRH Low for Female	0.129219
---- Sham vs. ZRH Medium for Female	0.285345
---- Sham vs. ZRH High for Female	0.001665
---- ZRH Low vs. 3R4F Medium for Female	0.000439
---- ZRH Medium vs. 3R4F High for Female	0.000434
---- ZRH High vs. 3R4F High for Female	0.000444
---- Sham Recovery vs. 3R4F High Recovery for Female	0.003885
---- Sham Recovery vs. ZRH High Recovery for Female	0.826623
---- Sham vs. Sham Recovery for Female	0.155761

Unadjusted P-values Obtained by Kruskal-Wallis Test
Analyte = MCP_3

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	0.004678
---- ZRH High vs. ZRH High Recovery for Female	0.040565
---- 3R4F High Recovery vs. ZRH High Recovery for Female	0.002354

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 46

Monocyte Chemotactic Protein-5 (MCP-5)

Unit = pg/mL

Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = MCP_5

Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	10	0	0	0.47	.
Male	3	3R4F Low	10	10	10	0	0	0.47	.
Male	3	3R4F Medium	10	10	10	0	0	0.47	.
Male	3	3R4F High	10	10	10	0	0	0.47	.
Male	3	ZRH Low	10	10	10	0	0	0.47	.
Male	3	ZRH Medium	10	10	9	1	0	0.47	.
Male	3	ZRH High	10	10	10	0	0	0.47	.
Male	4.5	Sham Recovery	6	6	6	0	0	0.47	.
Male	4.5	3R4F High Recovery	5	5	5	0	0	0.47	.
Male	4.5	ZRH High Recovery	10	10	10	0	0	0.47	.
Female	3	Sham	10	10	10	0	0	0.47	.
Female	3	3R4F Low	10	10	10	0	0	0.47	.
Female	3	3R4F Medium	10	10	10	0	0	0.47	.
Female	3	3R4F High	9	9	9	0	0	0.47	.
Female	3	ZRH Low	9	9	9	0	0	0.47	.
Female	3	ZRH Medium	10	10	10	0	0	0.47	.
Female	3	ZRH High	10	10	10	0	0	0.47	.
Female	4.5	Sham Recovery	6	6	6	0	0	0.47	.
Female	4.5	3R4F High Recovery	6	6	6	0	0	0.47	.
Female	4.5	ZRH High Recovery	10	10	10	0	0	0.47	.

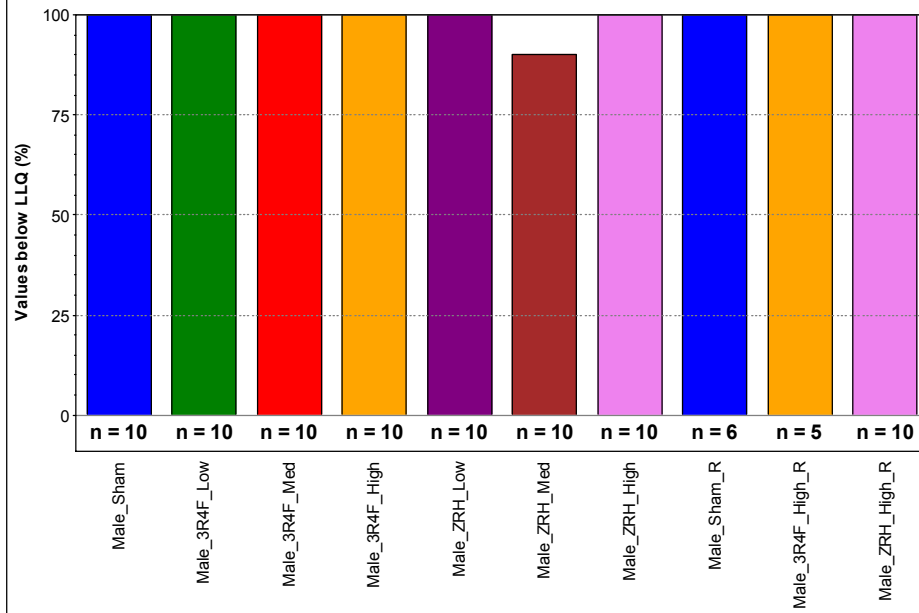
Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = MCP_5

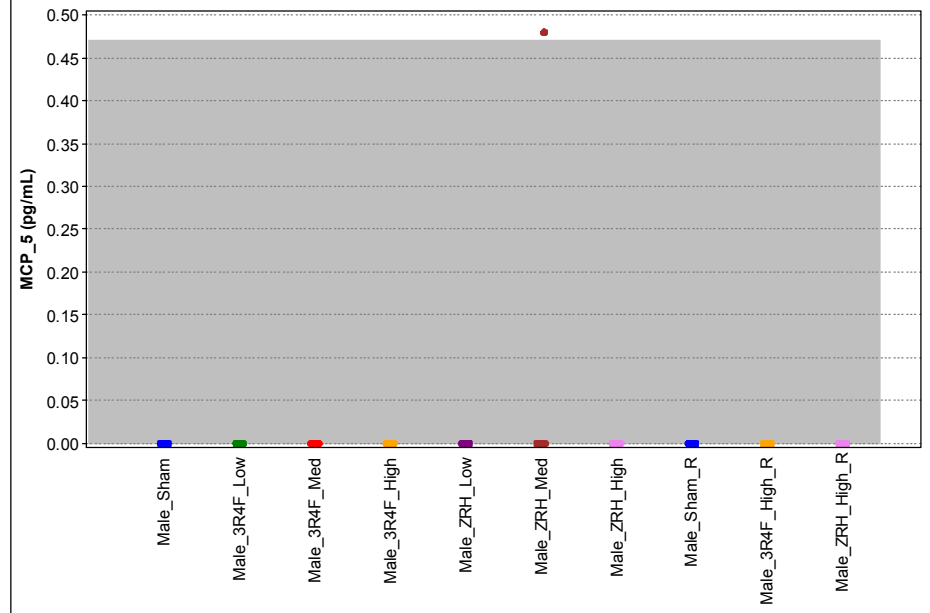
Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	0.235	0.235	0.235	0.235	0.235	0.235	0.000	0.000	0.0	.	.	0.47	.
Male	3	3R4F Low	0.235	0.235	0.235	0.235	0.235	0.235	0.000	0.000	0.0	.	.	0.47	.
Male	3	3R4F Medium	0.235	0.235	0.235	0.235	0.235	0.235	0.000	0.000	0.0	.	.	0.47	.
Male	3	3R4F High	0.235	0.235	0.235	0.235	0.235	0.235	0.000	0.000	0.0	.	.	0.47	.
Male	3	ZRH Low	0.235	0.235	0.235	0.235	0.235	0.235	0.000	0.000	0.0	.	.	0.47	.
Male	3	ZRH Medium	0.235	0.235	0.235	0.235	0.480	0.260	0.077	0.025	29.9	3.162	10.000	0.47	.
Male	3	ZRH High	0.235	0.235	0.235	0.235	0.235	0.235	0.000	0.000	0.0	.	.	0.47	.
Male	4.5	Sham Recovery	0.235	0.235	0.235	0.235	0.235	0.235	0.000	0.000	0.0	.	.	0.47	.
Male	4.5	3R4F High Recovery	0.235	0.235	0.235	0.235	0.235	0.235	0.000	0.000	0.0	.	.	0.47	.
Male	4.5	ZRH High Recovery	0.235	0.235	0.235	0.235	0.235	0.235	0.000	0.000	0.0	.	.	0.47	.
Female	3	Sham	0.235	0.235	0.235	0.235	0.235	0.235	0.000	0.000	0.0	.	.	0.47	.
Female	3	3R4F Low	0.235	0.235	0.235	0.235	0.235	0.235	0.000	0.000	0.0	.	.	0.47	.
Female	3	3R4F Medium	0.235	0.235	0.235	0.235	0.235	0.235	0.000	0.000	0.0	.	.	0.47	.
Female	3	3R4F High	0.235	0.235	0.235	0.235	0.235	0.235	0.000	0.000	0.0	.	.	0.47	.
Female	3	ZRH Low	0.235	0.235	0.235	0.235	0.235	0.235	0.000	0.000	0.0	.	.	0.47	.
Female	3	ZRH Medium	0.235	0.235	0.235	0.235	0.235	0.235	0.000	0.000	0.0	.	.	0.47	.
Female	3	ZRH High	0.235	0.235	0.235	0.235	0.235	0.235	0.000	0.000	0.0	.	.	0.47	.
Female	4.5	Sham Recovery	0.235	0.235	0.235	0.235	0.235	0.235	0.000	0.000	0.0	.	.	0.47	.
Female	4.5	3R4F High Recovery	0.235	0.235	0.235	0.235	0.235	0.235	0.000	0.000	0.0	.	.	0.47	.
Female	4.5	ZRH High Recovery	0.235	0.235	0.235	0.235	0.235	0.235	0.000	0.000	0.0	.	.	0.47	.

Percentage of Values below LLQ for each Group-Males

Analyte = MCP_5

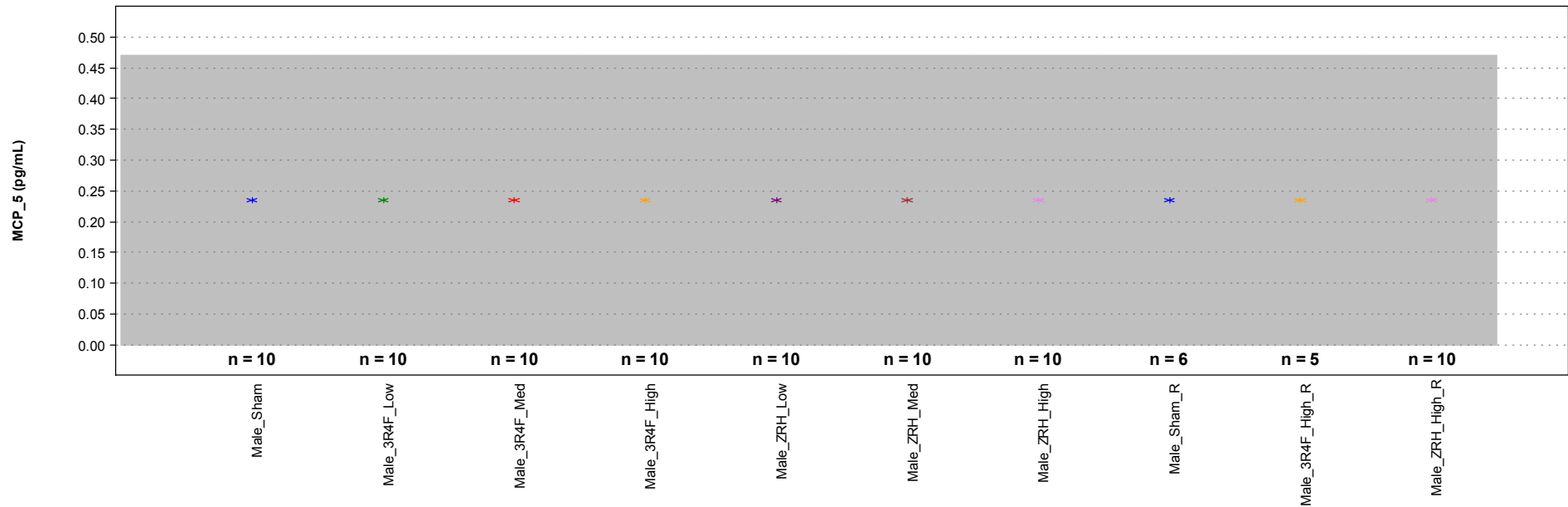
**Plot of Individual Measurements for each Group-Males**

<LOW> values are displayed as 0 / Values above ULQ are displayed as 1.1*ULQ
 Grey zones denote zones below (average) LLQ and above (average) ULQ

**Plot of Descriptive Robust Statistics-Males**

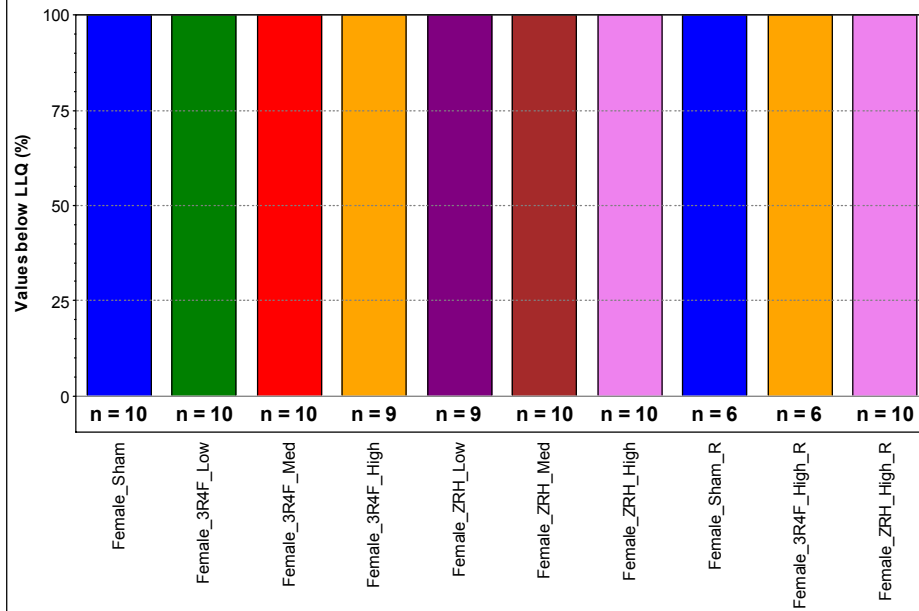
Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ

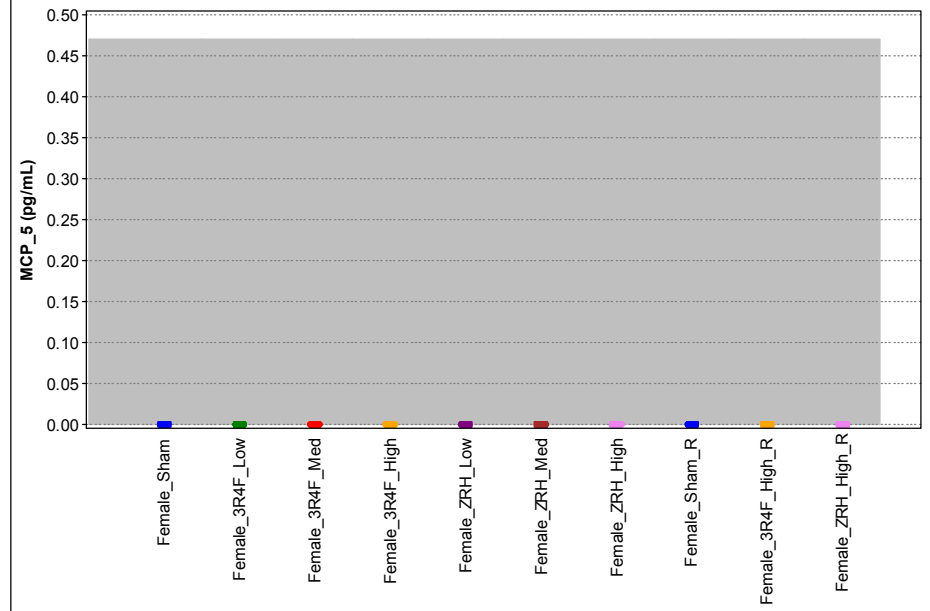


Percentage of Values below LLQ for each Group-Females

Analyte = MCP_5

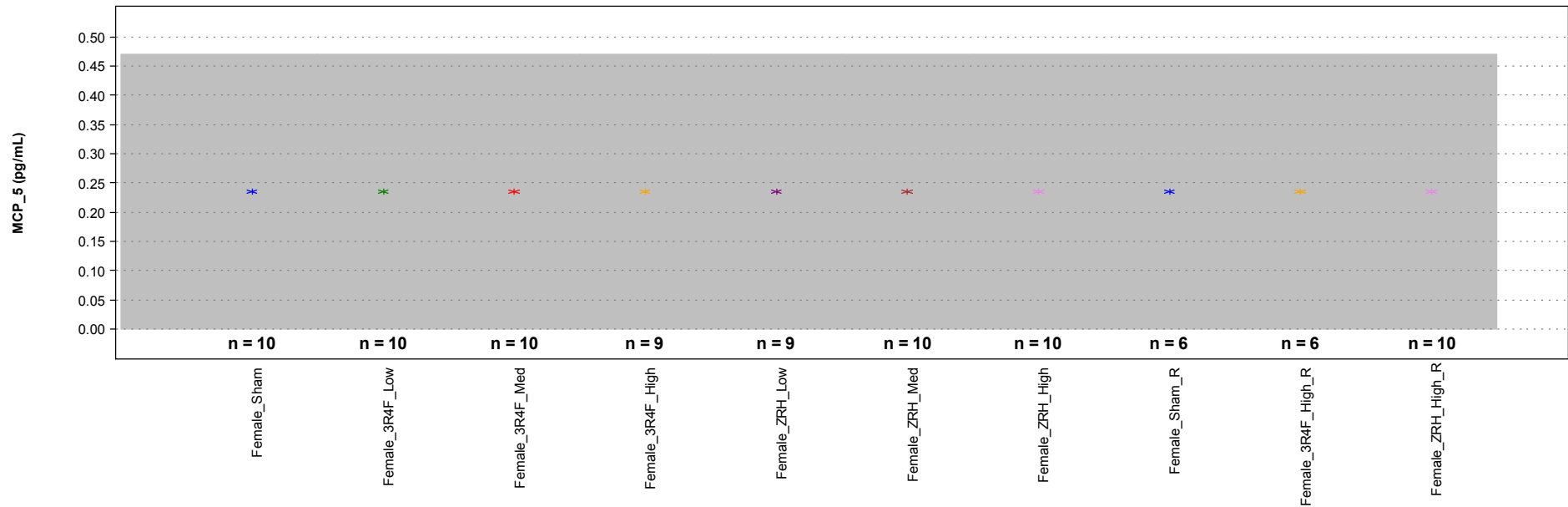
**Plot of Individual Measurements MCP_5 (pg/mL) - Females**

<LOW> values are displayed as 0 / Values above ULQ are displayed as 1.1*ULQ
 Grey zones denote zones below (average) LLQ and above (average) ULQ

**Plot of Descriptive Robust Statistics-Females**

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Unadjusted P-values Obtained by Kruskal-Wallis Test **Analyte = MCP_5**

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	1.000000
---- Sham vs. 3R4F Medium for Male	1.000000
---- Sham vs. 3R4F High for Male	1.000000
---- Sham vs. ZRH Low for Male	1.000000
---- Sham vs. ZRH Medium for Male	0.317311
---- Sham vs. ZRH High for Male	1.000000
---- ZRH Low vs. 3R4F Medium for Male	1.000000
---- ZRH Medium vs. 3R4F High for Male	0.317311
---- ZRH High vs. 3R4F High for Male	1.000000
---- Sham Recovery vs. 3R4F High Recovery for Male	1.000000
---- Sham Recovery vs. ZRH High Recovery for Male	1.000000
---- Sham vs. Sham Recovery for Male	1.000000
---- 3R4F High vs. 3R4F High Recovery for Male	1.000000
---- ZRH High vs. ZRH High Recovery for Male	1.000000
---- 3R4F High Recovery vs. ZRH High Recovery for Male	1.000000
---- Sham vs. 3R4F Low for Female	1.000000
---- Sham vs. 3R4F Medium for Female	1.000000
---- Sham vs. 3R4F High for Female	1.000000
---- Sham vs. ZRH Low for Female	1.000000
---- Sham vs. ZRH Medium for Female	1.000000
---- Sham vs. ZRH High for Female	1.000000
---- ZRH Low vs. 3R4F Medium for Female	1.000000
---- ZRH Medium vs. 3R4F High for Female	1.000000
---- ZRH High vs. 3R4F High for Female	1.000000
---- Sham Recovery vs. 3R4F High Recovery for Female	1.000000
---- Sham Recovery vs. ZRH High Recovery for Female	1.000000
---- Sham vs. Sham Recovery for Female	1.000000

Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = MCP_5

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	1.000000
---- ZRH High vs. ZRH High Recovery for Female	1.000000
---- 3R4F High Recovery vs. ZRH High Recovery for Female	1.000000

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 37

Macrophage-Derived Chemokine (MDC)

Unit = pg/mL

Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = MDC

Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	6	4	0	11	.
Male	3	3R4F Low	10	10	0	10	0	11	.
Male	3	3R4F Medium	10	10	0	10	0	11	.
Male	3	3R4F High	10	10	0	10	0	11	.
Male	3	ZRH Low	10	10	3	7	0	11	.
Male	3	ZRH Medium	10	10	4	6	0	11	.
Male	3	ZRH High	10	10	3	7	0	11	.
Male	4.5	Sham Recovery	6	6	1	5	0	11	.
Male	4.5	3R4F High Recovery	5	5	1	4	0	11	.
Male	4.5	ZRH High Recovery	10	10	3	7	0	11	.
Female	3	Sham	10	10	3	7	0	11	.
Female	3	3R4F Low	10	10	0	10	0	11	.
Female	3	3R4F Medium	10	10	0	10	0	11	.
Female	3	3R4F High	9	9	0	9	0	11	.
Female	3	ZRH Low	9	9	4	5	0	11	.
Female	3	ZRH Medium	10	10	1	9	0	11	.
Female	3	ZRH High	10	10	3	7	0	11	.
Female	4.5	Sham Recovery	6	6	2	4	0	11	.
Female	4.5	3R4F High Recovery	6	6	0	6	0	11	.
Female	4.5	ZRH High Recovery	10	10	5	5	0	11	.

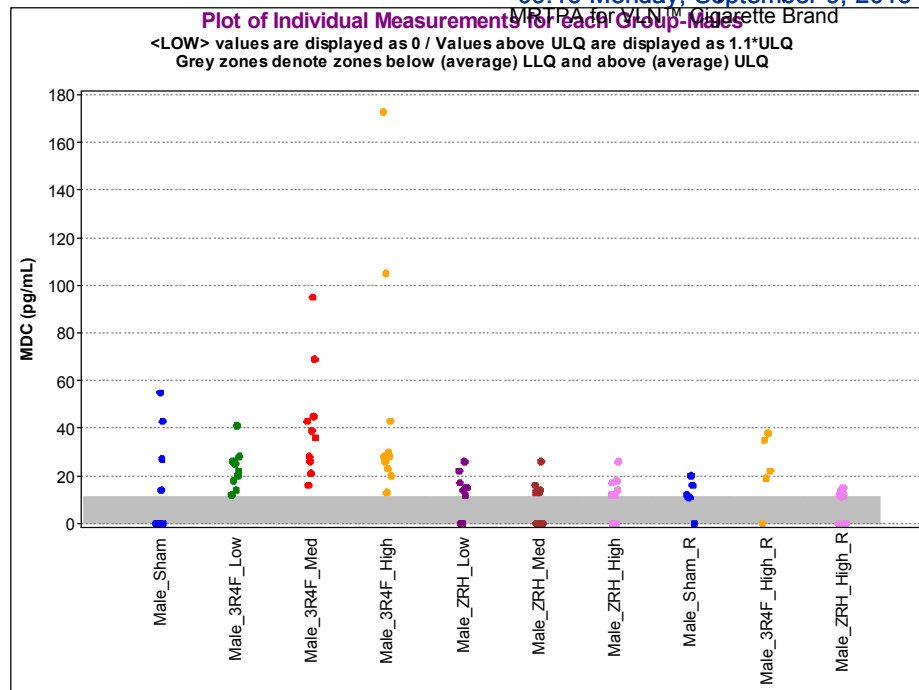
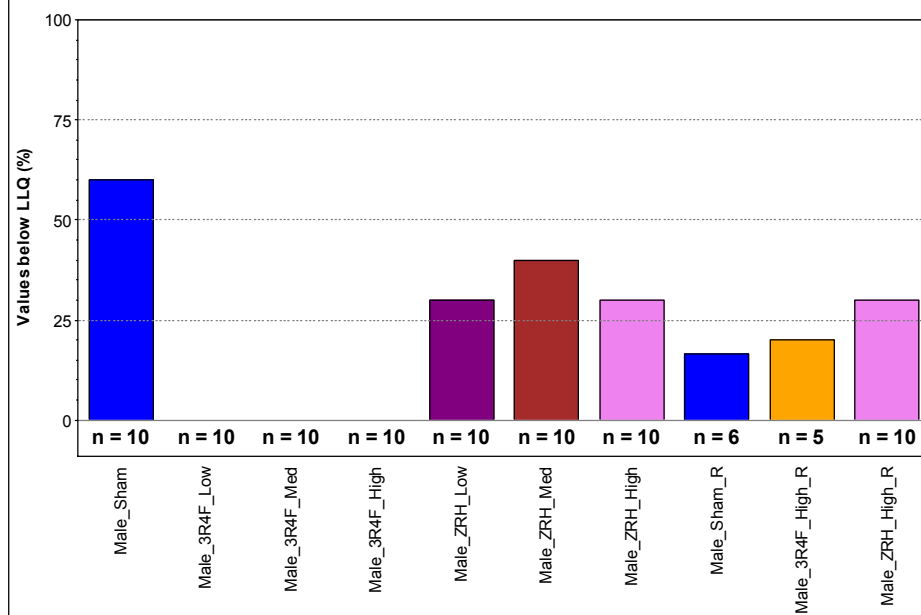
Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = MDC

Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	5.500	5.500	5.500	27.000	55.000	17.200	18.325	5.795	106.5	1.410	0.706	11	.
Male	3	3R4F Low	12.000	18.000	23.500	26.000	41.000	23.200	8.217	2.598	35.4	0.862	1.636	11	.
Male	3	3R4F Medium	16.000	26.000	37.500	45.000	95.000	41.800	23.948	7.573	57.3	1.393	1.824	11	.
Male	3	3R4F High	13.000	23.000	28.000	43.000	173.000	48.900	50.698	16.032	103.7	2.092	3.942	11	.
Male	3	ZRH Low	5.500	5.500	14.500	17.000	26.000	13.750	6.985	2.209	50.8	0.305	-0.564	11	.
Male	3	ZRH Medium	5.500	5.500	13.000	14.000	26.000	11.800	6.588	2.083	55.8	0.953	1.144	11	.
Male	3	ZRH High	5.500	5.500	12.000	17.000	26.000	12.750	6.516	2.061	51.1	0.705	0.528	11	.
Male	4.5	Sham Recovery	5.500	11.000	11.500	16.000	20.000	12.583	4.944	2.018	39.3	0.209	0.420	11	.
Male	4.5	3R4F High Recovery	5.500	19.000	22.000	35.000	38.000	23.900	13.117	5.866	54.9	-0.403	-0.825	11	.
Male	4.5	ZRH High Recovery	5.500	5.500	12.000	13.000	15.000	10.550	3.662	1.158	34.7	-0.659	-1.265	11	.
Female	3	Sham	5.500	5.500	12.500	14.000	14.000	10.750	3.744	1.184	34.8	-0.811	-1.375	11	.
Female	3	3R4F Low	14.000	18.000	22.000	31.000	47.000	25.700	11.422	3.612	44.4	1.029	0.003	11	.
Female	3	3R4F Medium	17.000	24.000	35.000	40.000	67.000	35.600	14.539	4.598	40.8	1.024	1.418	11	.
Female	3	3R4F High	16.000	31.000	33.000	48.000	72.000	37.667	17.292	5.764	45.9	0.826	0.758	11	.
Female	3	ZRH Low	5.500	5.500	11.000	14.000	22.000	10.778	5.794	1.931	53.8	0.765	0.013	11	.
Female	3	ZRH Medium	5.500	12.000	13.500	17.000	26.000	14.850	5.637	1.783	38.0	0.558	1.033	11	.
Female	3	ZRH High	5.500	5.500	14.000	16.000	19.000	12.350	5.061	1.600	41.0	-0.552	-1.309	11	.
Female	4.5	Sham Recovery	5.500	5.500	12.500	13.000	14.000	10.500	3.924	1.602	37.4	-0.856	-1.872	11	.
Female	4.5	3R4F High Recovery	17.000	17.000	21.000	25.000	53.000	25.667	13.779	5.625	53.7	2.156	4.847	11	.
Female	4.5	ZRH High Recovery	5.500	5.500	8.750	13.000	16.000	9.550	4.438	1.403	46.5	0.268	-1.991	11	.

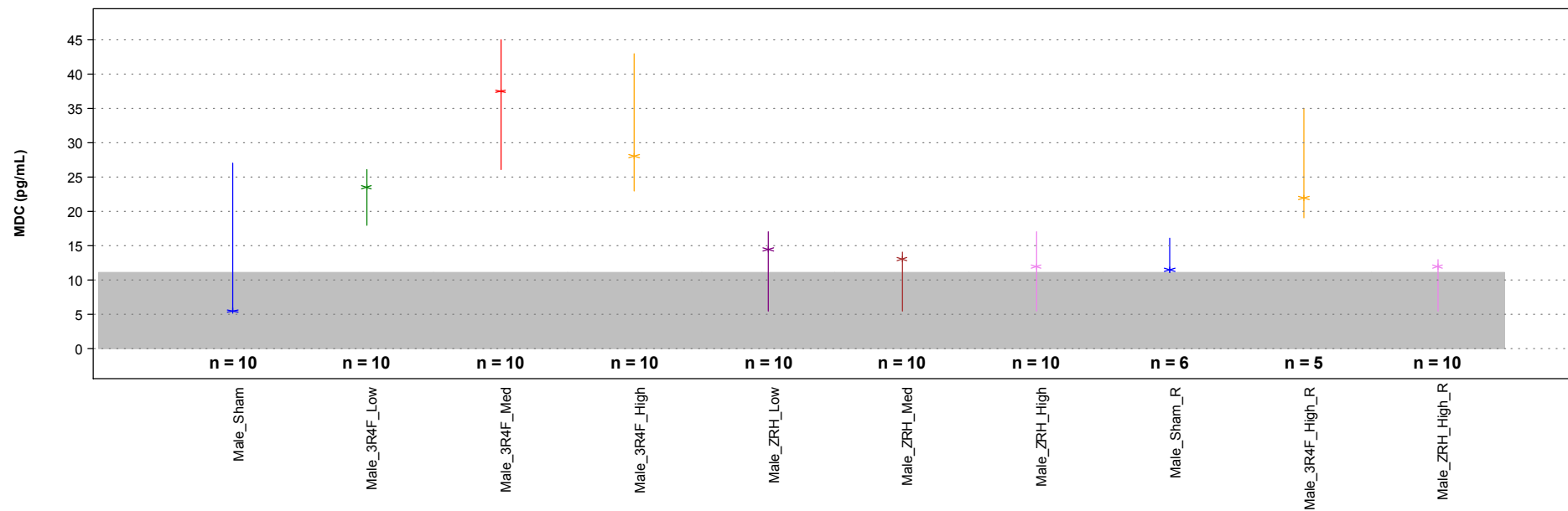
Percentage of Values below LLQ for each Group-Males

Analyte = MDC

**Plot of Descriptive Robust Statistics-Males**

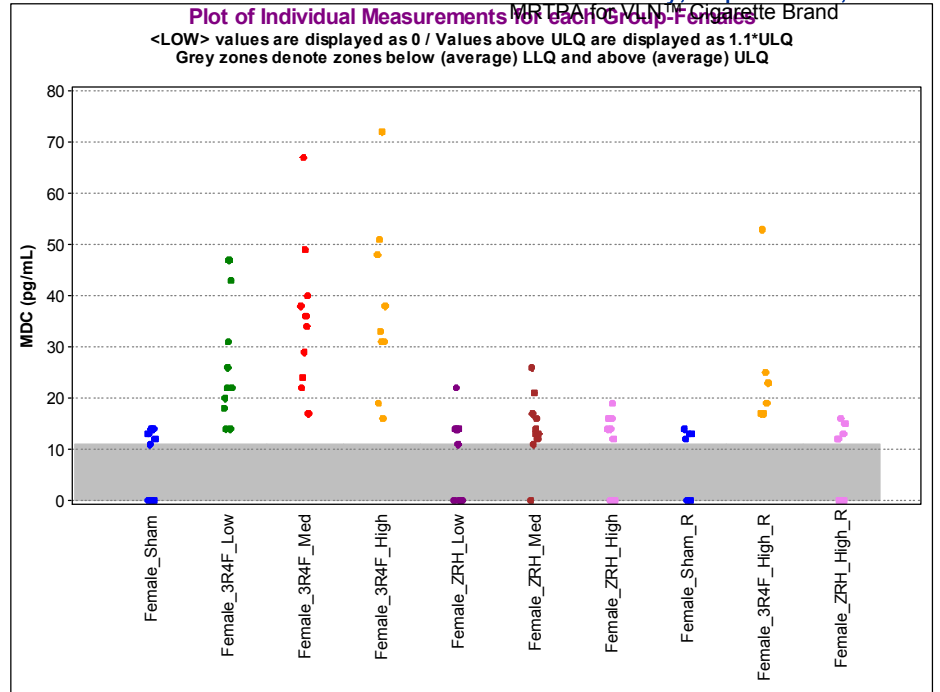
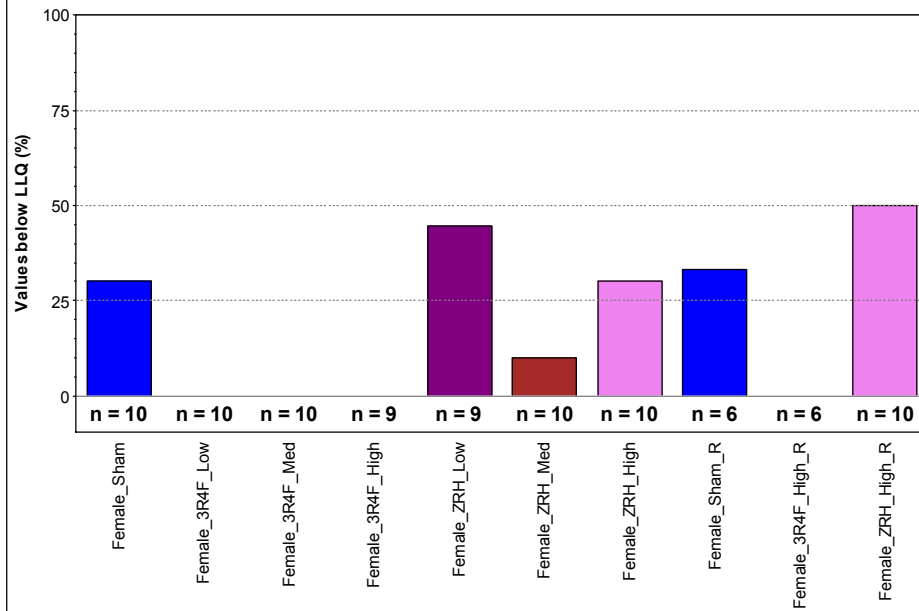
Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



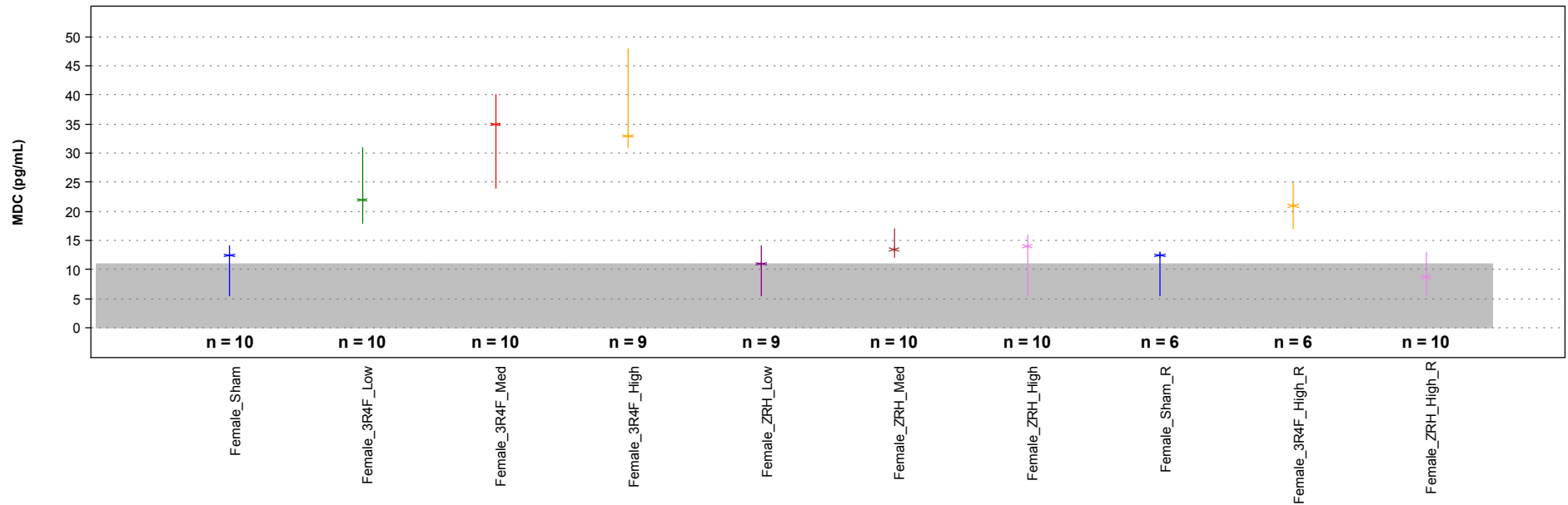
Percentage of Values below LLQ for each Group-Females

Analyte = MDC

**Plot of Descriptive Robust Statistics-Females**

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = MDC

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	0.116027
---- Sham vs. 3R4F Medium for Male	0.012749
---- Sham vs. 3R4F High for Male	0.023718
---- Sham vs. ZRH Low for Male	0.606156
---- Sham vs. ZRH Medium for Male	0.935488
---- Sham vs. ZRH High for Male	0.720810
---- ZRH Low vs. 3R4F Medium for Male	0.000748
---- ZRH Medium vs. 3R4F High for Male	0.001223
---- ZRH High vs. 3R4F High for Male	0.000964
---- Sham Recovery vs. 3R4F High Recovery for Male	0.119000
---- Sham Recovery vs. ZRH High Recovery for Male	0.658687
---- Sham vs. Sham Recovery for Male	0.570991
---- 3R4F High vs. 3R4F High Recovery for Male	0.326755
---- ZRH High vs. ZRH High Recovery for Male	0.460451
---- 3R4F High Recovery vs. ZRH High Recovery for Male	0.040700
---- Sham vs. 3R4F Low for Female	0.000333
---- Sham vs. 3R4F Medium for Female	0.000149
---- Sham vs. 3R4F High for Female	0.000224
---- Sham vs. ZRH Low for Female	1.000000
---- Sham vs. ZRH Medium for Female	0.125923
---- Sham vs. ZRH High for Female	0.215636
---- ZRH Low vs. 3R4F Medium for Female	0.000350
---- ZRH Medium vs. 3R4F High for Female	0.001240
---- ZRH High vs. 3R4F High for Female	0.000550
---- Sham Recovery vs. 3R4F High Recovery for Female	0.003761
---- Sham Recovery vs. ZRH High Recovery for Female	0.648503
---- Sham vs. Sham Recovery for Female	0.822927

Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = MDC

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	0.174168
---- ZRH High vs. ZRH High Recovery for Female	0.157265
---- 3R4F High Recovery vs. ZRH High Recovery for Female	0.000940

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 38

Macrophage Inflammatory Protein-1alpha (MIP-1 alpha)

Unit = ng/mL

Descriptive Statistics by Exposure Duration and Treatment Type

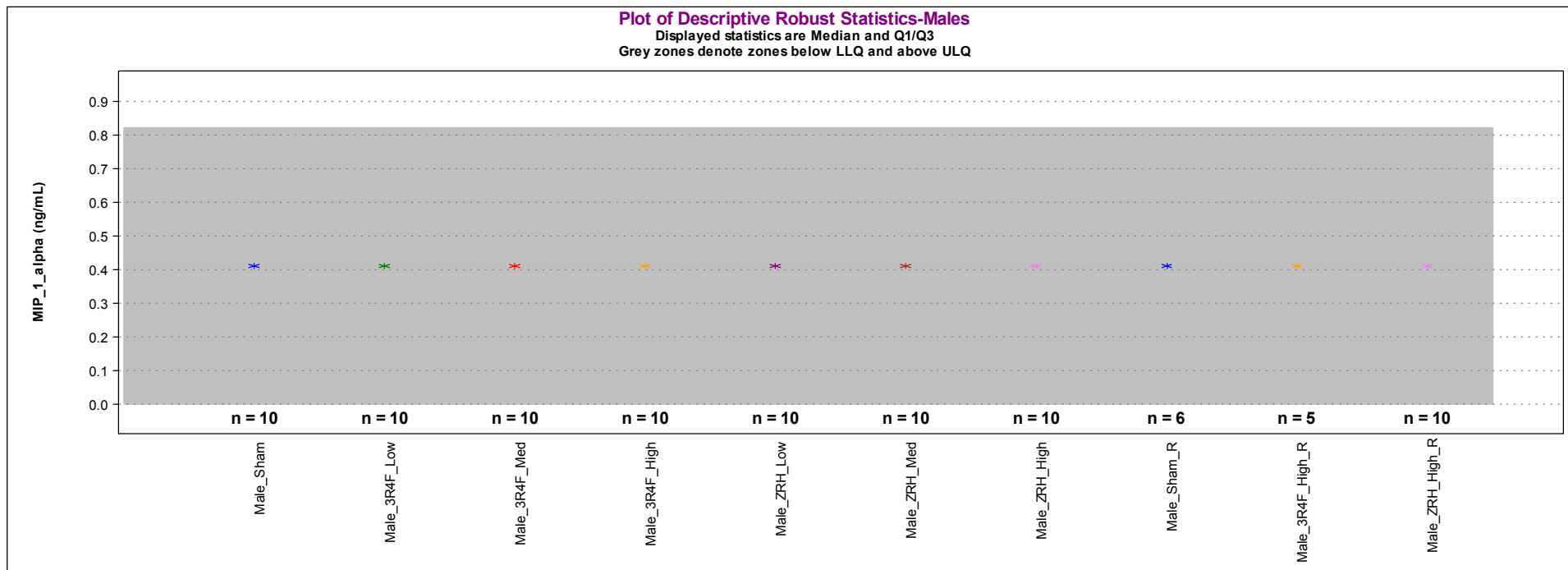
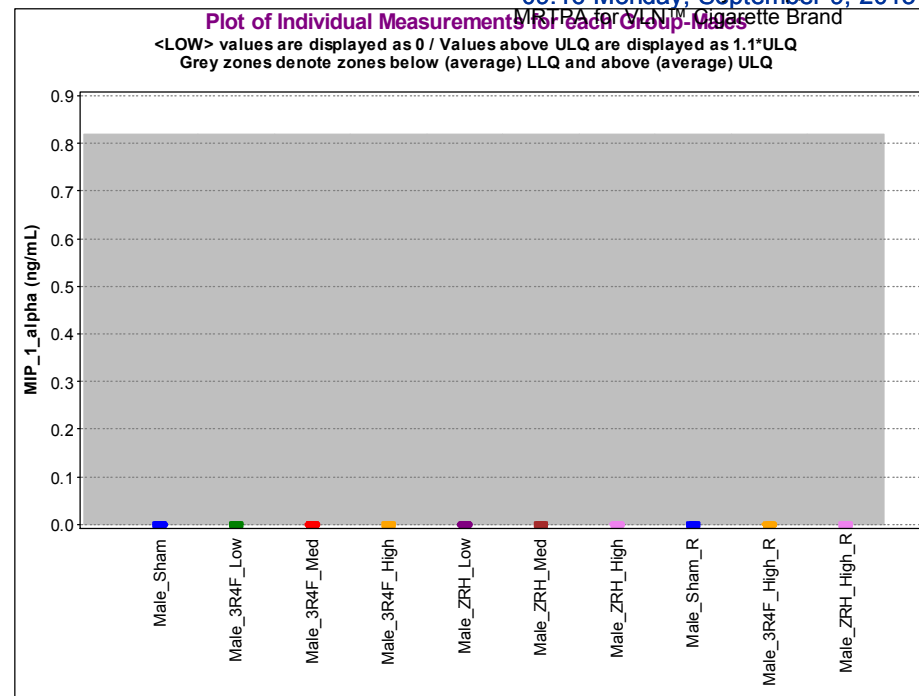
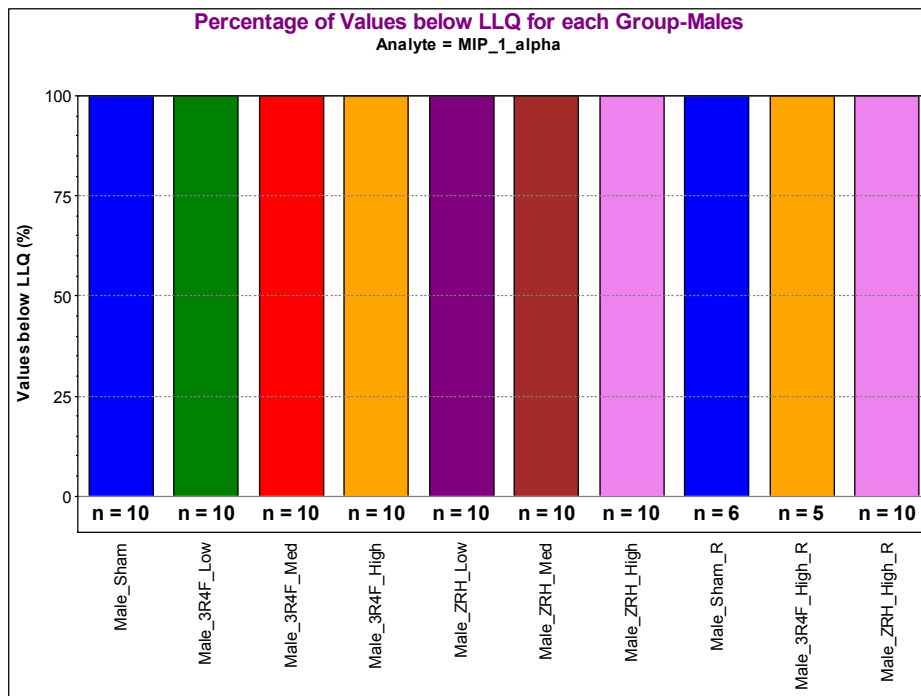
Analyte = MIP_1_alpha

Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	10	0	0	0.82	.
Male	3	3R4F Low	10	10	10	0	0	0.82	.
Male	3	3R4F Medium	10	10	10	0	0	0.82	.
Male	3	3R4F High	10	10	10	0	0	0.82	.
Male	3	ZRH Low	10	10	10	0	0	0.82	.
Male	3	ZRH Medium	10	10	10	0	0	0.82	.
Male	3	ZRH High	10	10	10	0	0	0.82	.
Male	4.5	Sham Recovery	6	6	6	0	0	0.82	.
Male	4.5	3R4F High Recovery	5	5	5	0	0	0.82	.
Male	4.5	ZRH High Recovery	10	10	10	0	0	0.82	.
Female	3	Sham	10	10	10	0	0	0.82	.
Female	3	3R4F Low	10	10	10	0	0	0.82	.
Female	3	3R4F Medium	10	10	10	0	0	0.82	.
Female	3	3R4F High	9	9	9	0	0	0.82	.
Female	3	ZRH Low	9	9	9	0	0	0.82	.
Female	3	ZRH Medium	10	10	10	0	0	0.82	.
Female	3	ZRH High	10	10	10	0	0	0.82	.
Female	4.5	Sham Recovery	6	6	6	0	0	0.82	.
Female	4.5	3R4F High Recovery	6	6	6	0	0	0.82	.
Female	4.5	ZRH High Recovery	10	10	10	0	0	0.82	.

Descriptive Statistics by Exposure Duration and Treatment Type

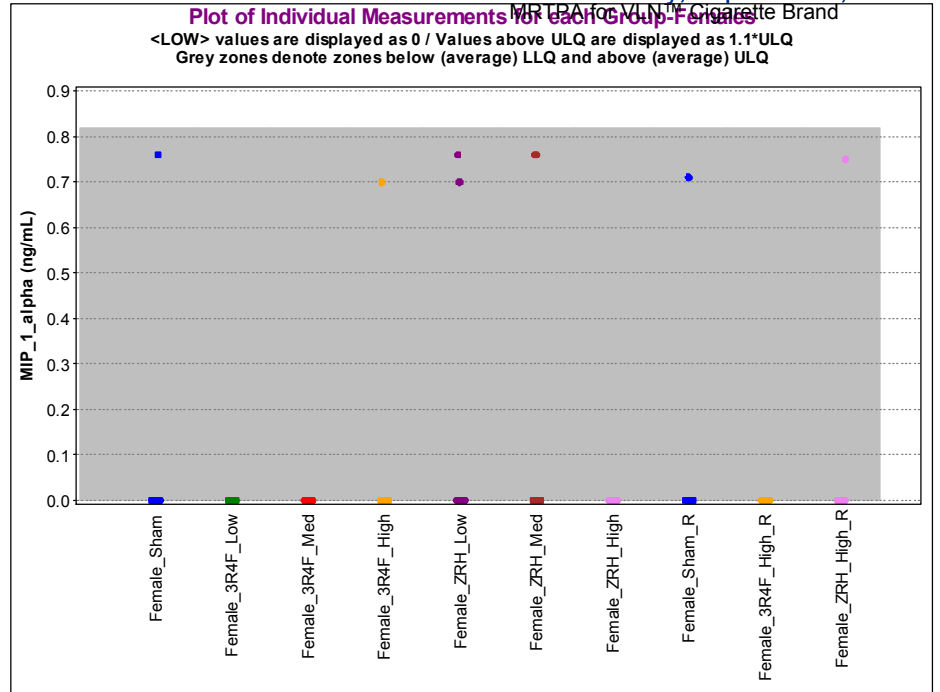
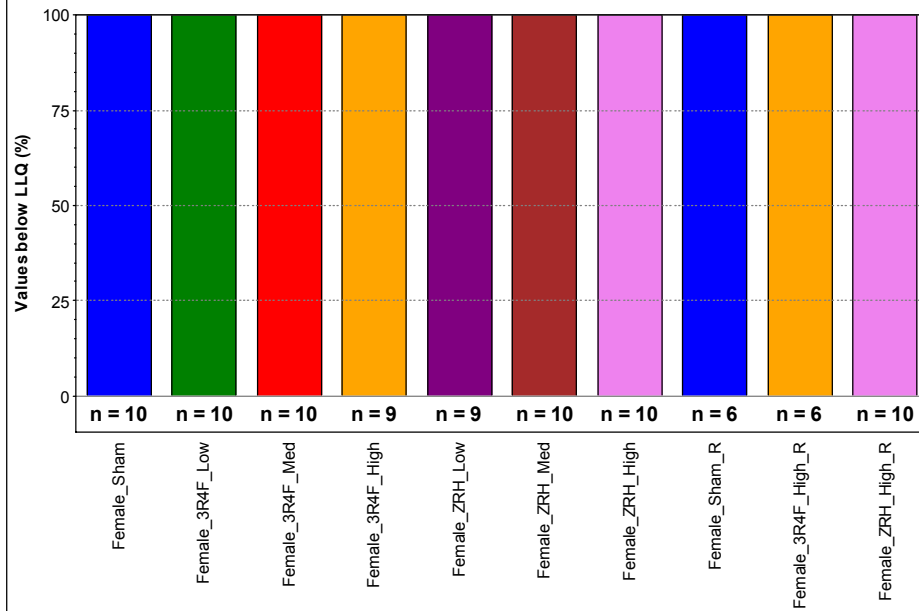
Analyte = MIP_1_alpha

Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	0.410	0.410	0.410	0.410	0.410	0.410	0.000	0.000	0.0	.	.	0.82	.
Male	3	3R4F Low	0.410	0.410	0.410	0.410	0.410	0.410	0.000	0.000	0.0	.	.	0.82	.
Male	3	3R4F Medium	0.410	0.410	0.410	0.410	0.410	0.410	0.000	0.000	0.0	.	.	0.82	.
Male	3	3R4F High	0.410	0.410	0.410	0.410	0.410	0.410	0.000	0.000	0.0	.	.	0.82	.
Male	3	ZRH Low	0.410	0.410	0.410	0.410	0.410	0.410	0.000	0.000	0.0	.	.	0.82	.
Male	3	ZRH Medium	0.410	0.410	0.410	0.410	0.410	0.410	0.000	0.000	0.0	.	.	0.82	.
Male	3	ZRH High	0.410	0.410	0.410	0.410	0.410	0.410	0.000	0.000	0.0	.	.	0.82	.
Male	4.5	Sham Recovery	0.410	0.410	0.410	0.410	0.410	0.410	0.000	0.000	0.0	.	.	0.82	.
Male	4.5	3R4F High Recovery	0.410	0.410	0.410	0.410	0.410	0.410	0.000	0.000	0.0	.	.	0.82	.
Male	4.5	ZRH High Recovery	0.410	0.410	0.410	0.410	0.410	0.410	0.000	0.000	0.0	.	.	0.82	.
Female	3	Sham	0.410	0.410	0.410	0.410	0.410	0.410	0.000	0.000	0.0	.	.	0.82	.
Female	3	3R4F Low	0.410	0.410	0.410	0.410	0.410	0.410	0.000	0.000	0.0	.	.	0.82	.
Female	3	3R4F Medium	0.410	0.410	0.410	0.410	0.410	0.410	0.000	0.000	0.0	.	.	0.82	.
Female	3	3R4F High	0.410	0.410	0.410	0.410	0.410	0.410	0.000	0.000	0.0	.	.	0.82	.
Female	3	ZRH Low	0.410	0.410	0.410	0.410	0.410	0.410	0.000	0.000	0.0	.	.	0.82	.
Female	3	ZRH Medium	0.410	0.410	0.410	0.410	0.410	0.410	0.000	0.000	0.0	.	.	0.82	.
Female	3	ZRH High	0.410	0.410	0.410	0.410	0.410	0.410	0.000	0.000	0.0	.	.	0.82	.
Female	4.5	Sham Recovery	0.410	0.410	0.410	0.410	0.410	0.410	0.000	0.000	0.0	.	.	0.82	.
Female	4.5	3R4F High Recovery	0.410	0.410	0.410	0.410	0.410	0.410	0.000	0.000	0.0	.	.	0.82	.
Female	4.5	ZRH High Recovery	0.410	0.410	0.410	0.410	0.410	0.410	0.000	0.000	0.0	.	.	0.82	.



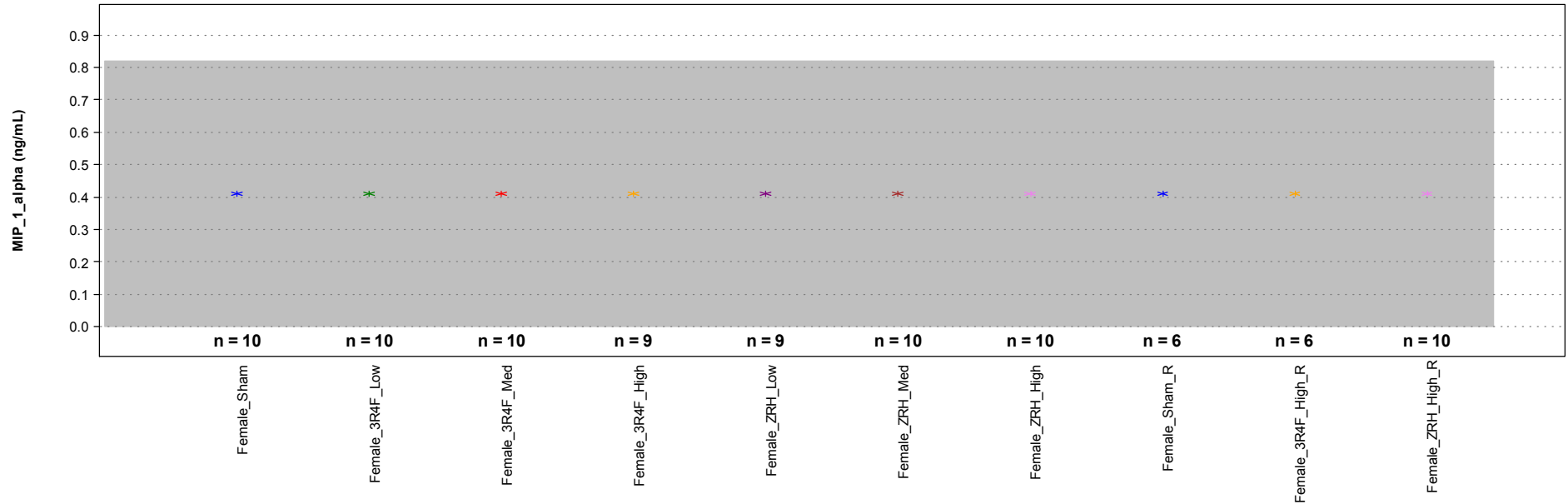
Percentage of Values below LLQ for each Group-Females

Analyte = MIP_1_alpha

**Plot of Descriptive Robust Statistics-Females**

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = MIP_1_alpha

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	1.000000
---- Sham vs. 3R4F Medium for Male	1.000000
---- Sham vs. 3R4F High for Male	1.000000
---- Sham vs. ZRH Low for Male	1.000000
---- Sham vs. ZRH Medium for Male	1.000000
---- Sham vs. ZRH High for Male	1.000000
---- ZRH Low vs. 3R4F Medium for Male	1.000000
---- ZRH Medium vs. 3R4F High for Male	1.000000
---- ZRH High vs. 3R4F High for Male	1.000000
---- Sham Recovery vs. 3R4F High Recovery for Male	1.000000
---- Sham Recovery vs. ZRH High Recovery for Male	1.000000
---- Sham vs. Sham Recovery for Male	1.000000
---- 3R4F High vs. 3R4F High Recovery for Male	1.000000
---- ZRH High vs. ZRH High Recovery for Male	1.000000
---- 3R4F High Recovery vs. ZRH High Recovery for Male	1.000000
---- Sham vs. 3R4F Low for Female	1.000000
---- Sham vs. 3R4F Medium for Female	1.000000
---- Sham vs. 3R4F High for Female	1.000000
---- Sham vs. ZRH Low for Female	1.000000
---- Sham vs. ZRH Medium for Female	1.000000
---- Sham vs. ZRH High for Female	1.000000
---- ZRH Low vs. 3R4F Medium for Female	1.000000
---- ZRH Medium vs. 3R4F High for Female	1.000000
---- ZRH High vs. 3R4F High for Female	1.000000
---- Sham Recovery vs. 3R4F High Recovery for Female	1.000000
---- Sham Recovery vs. ZRH High Recovery for Female	1.000000
---- Sham vs. Sham Recovery for Female	1.000000

Unadjusted P-values Obtained by Kruskal-Wallis Test
Analyte = MIP_1_alpha

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	1.000000
---- ZRH High vs. ZRH High Recovery for Female	1.000000
---- 3R4F High Recovery vs. ZRH High Recovery for Female	1.000000

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 39

Macrophage Inflammatory Protein-1 beta (MIP-1 beta)

Unit = pg/mL

Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = MIP_1_beta

Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	2	8	0	11	.
Male	3	3R4F Low	10	10	0	10	0	11	.
Male	3	3R4F Medium	10	10	0	10	0	11	.
Male	3	3R4F High	10	10	0	10	0	11	.
Male	3	ZRH Low	10	10	1	9	0	11	.
Male	3	ZRH Medium	10	10	0	10	0	11	.
Male	3	ZRH High	10	10	0	10	0	11	.
Male	4.5	Sham Recovery	6	6	0	6	0	11	.
Male	4.5	3R4F High Recovery	5	5	0	5	0	11	.
Male	4.5	ZRH High Recovery	10	10	0	10	0	11	.
Female	3	Sham	10	10	0	10	0	11	.
Female	3	3R4F Low	10	10	0	10	0	11	.
Female	3	3R4F Medium	10	10	0	10	0	11	.
Female	3	3R4F High	9	9	0	9	0	11	.
Female	3	ZRH Low	9	9	0	9	0	11	.
Female	3	ZRH Medium	10	10	0	10	0	11	.
Female	3	ZRH High	10	10	0	10	0	11	.
Female	4.5	Sham Recovery	6	6	0	6	0	11	.
Female	4.5	3R4F High Recovery	6	6	0	6	0	11	.
Female	4.5	ZRH High Recovery	10	10	0	10	0	11	.

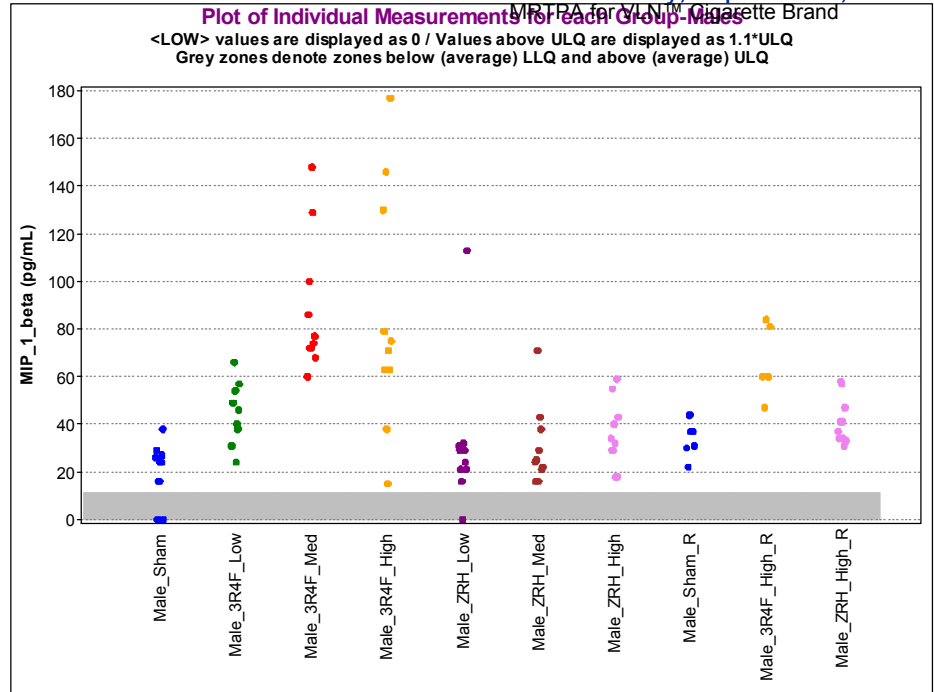
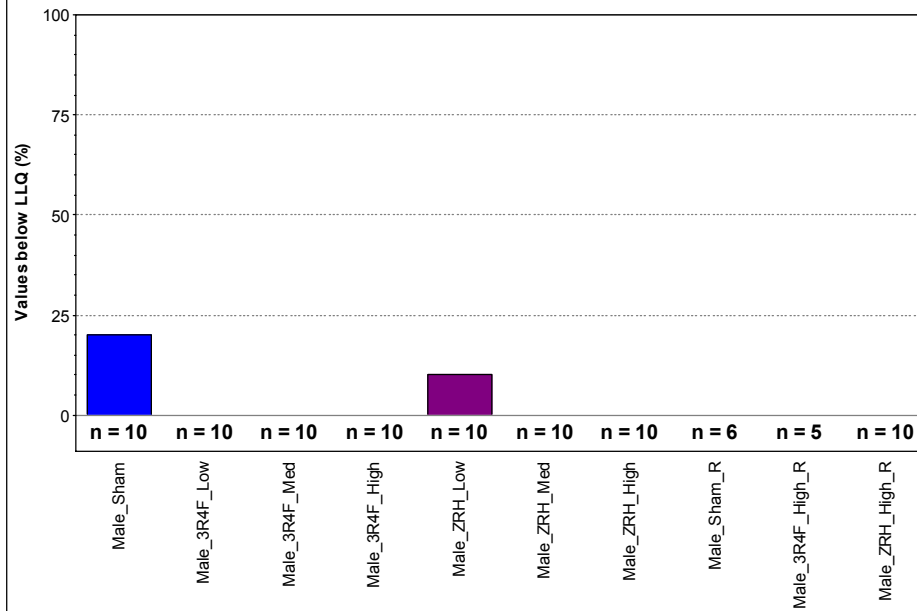
Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = MIP_1_beta

Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	5.500	16.000	24.000	27.000	38.000	21.100	10.341	3.270	49.0	-0.272	-0.384	11	.
Male	3	3R4F Low	24.000	38.000	47.500	54.000	66.000	45.400	12.510	3.956	27.6	-0.164	-0.235	11	.
Male	3	3R4F Medium	60.000	72.000	75.500	100.000	148.000	88.600	28.749	9.091	32.4	1.350	0.835	11	.
Male	3	3R4F High	15.000	63.000	73.000	130.000	177.000	85.700	50.127	15.851	58.5	0.637	-0.284	11	.
Male	3	ZRH Low	5.500	21.000	26.500	31.000	113.000	32.150	29.522	9.336	91.8	2.710	8.112	11	.
Male	3	ZRH Medium	16.000	21.000	24.500	38.000	71.000	30.500	16.702	5.282	54.8	1.812	3.578	11	.
Male	3	ZRH High	18.000	29.000	33.000	43.000	59.000	35.700	13.825	4.372	38.7	0.450	-0.532	11	.
Male	4.5	Sham Recovery	22.000	30.000	34.000	37.000	44.000	33.500	7.556	3.085	22.6	-0.234	0.220	11	.
Male	4.5	3R4F High Recovery	47.000	60.000	60.000	81.000	84.000	66.400	15.662	7.004	23.6	0.080	-2.051	11	.
Male	4.5	ZRH High Recovery	31.000	34.000	39.000	47.000	58.000	41.300	9.764	3.088	23.6	0.924	-0.459	11	.
Female	3	Sham	13.000	21.000	22.000	26.000	32.000	22.600	5.481	1.733	24.3	-0.124	0.301	11	.
Female	3	3R4F Low	30.000	36.000	48.000	53.000	94.000	48.700	18.409	5.822	37.8	1.754	4.152	11	.
Female	3	3R4F Medium	50.000	62.000	87.000	125.000	155.000	94.200	35.339	11.175	37.5	0.538	-0.782	11	.
Female	3	3R4F High	55.000	82.000	105.000	129.000	178.000	108.778	36.796	12.265	33.8	0.516	0.346	11	.
Female	3	ZRH Low	21.000	24.000	26.000	28.000	34.000	26.333	3.905	1.302	14.8	0.617	0.847	11	.
Female	3	ZRH Medium	16.000	20.000	22.500	33.000	41.000	26.100	8.556	2.706	32.8	0.771	-0.802	11	.
Female	3	ZRH High	25.000	28.000	38.500	50.000	94.000	42.900	20.453	6.468	47.7	1.965	4.482	11	.
Female	4.5	Sham Recovery	30.000	33.000	40.000	41.000	44.000	38.000	5.367	2.191	14.1	-0.710	-1.034	11	.
Female	4.5	3R4F High Recovery	53.000	63.000	75.000	76.000	115.000	76.167	21.075	8.604	27.7	1.405	2.948	11	.
Female	4.5	ZRH High Recovery	25.000	31.000	38.500	41.000	45.000	36.600	6.653	2.104	18.2	-0.645	-0.829	11	.

Percentage of Values below LLQ for each Group-Males

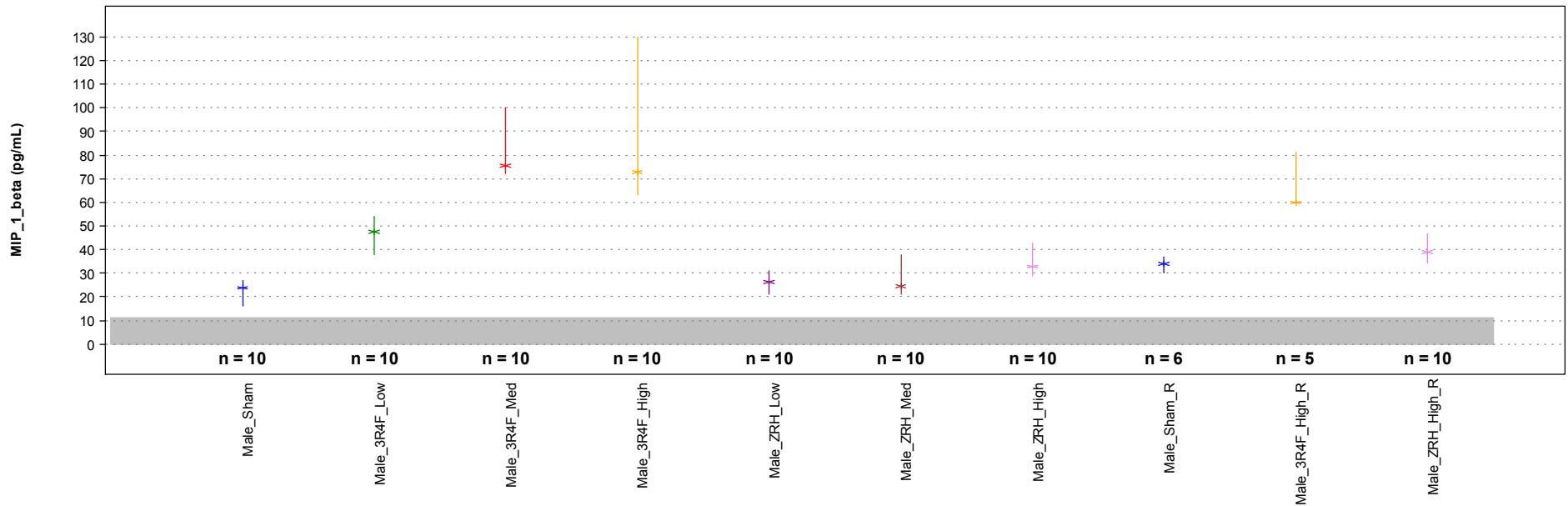
Analyte = MIP_1_beta



Plot of Descriptive Robust Statistics-Males

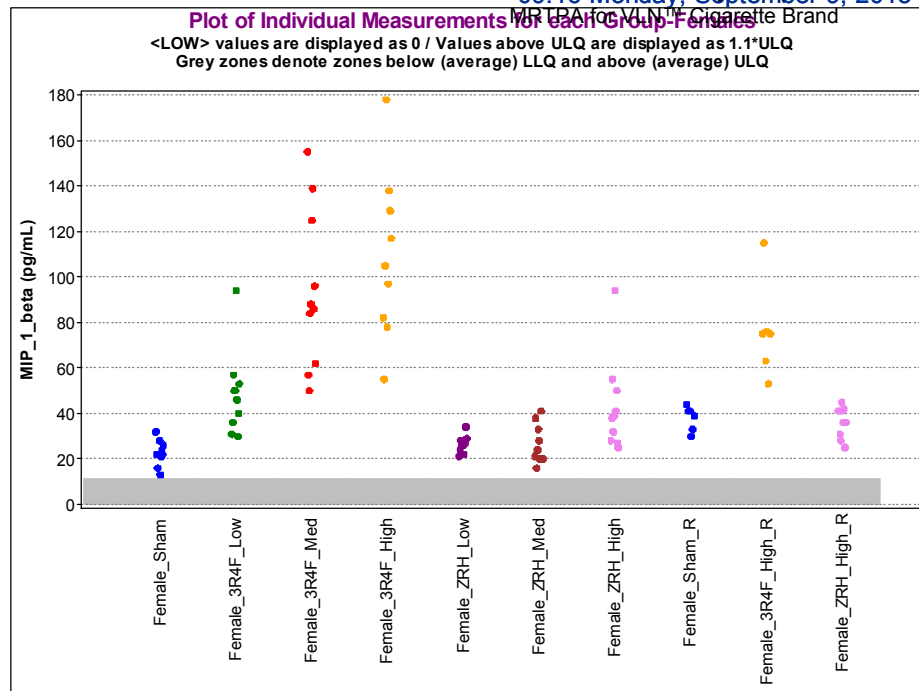
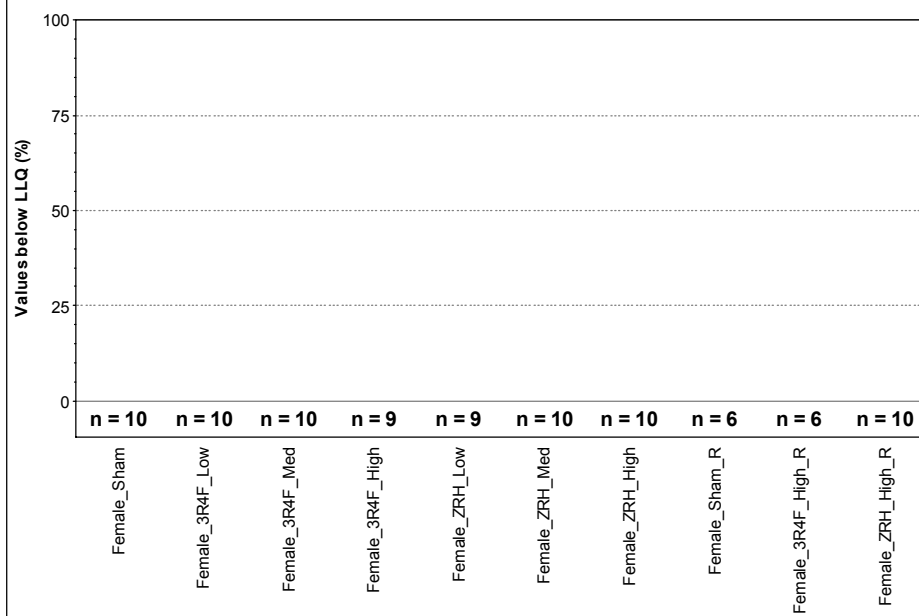
Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Percentage of Values below LLQ for each Group-Females

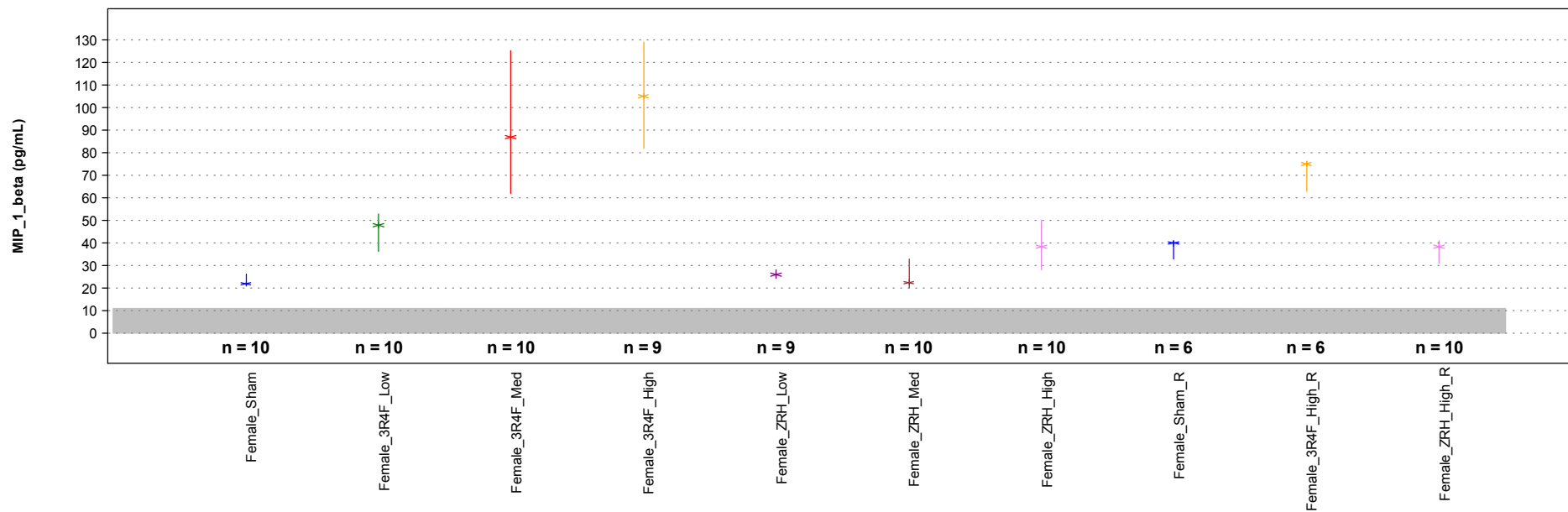
Analyte = MIP_1_beta



Plot of Descriptive Robust Statistics-Females

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = MIP_1_beta

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	0.000973
---- Sham vs. 3R4F Medium for Male	0.000153
---- Sham vs. 3R4F High for Male	0.001672
---- Sham vs. ZRH Low for Male	0.361259
---- Sham vs. ZRH Medium for Male	0.322639
---- Sham vs. ZRH High for Male	0.012346
---- ZRH Low vs. 3R4F Medium for Male	0.001480
---- ZRH Medium vs. 3R4F High for Male	0.008055
---- ZRH High vs. 3R4F High for Male	0.006441
---- Sham Recovery vs. 3R4F High Recovery for Male	0.005939
---- Sham Recovery vs. ZRH High Recovery for Male	0.141054
---- Sham vs. Sham Recovery for Male	0.029577
---- 3R4F High vs. 3R4F High Recovery for Male	0.539566
---- ZRH High vs. ZRH High Recovery for Male	0.225252
---- 3R4F High Recovery vs. ZRH High Recovery for Male	0.005682
---- Sham vs. 3R4F Low for Female	0.000278
---- Sham vs. 3R4F Medium for Female	0.000153
---- Sham vs. 3R4F High for Female	0.000233
---- Sham vs. ZRH Low for Female	0.118043
---- Sham vs. ZRH Medium for Female	0.704182
---- Sham vs. ZRH High for Female	0.001123
---- ZRH Low vs. 3R4F Medium for Female	0.000237
---- ZRH Medium vs. 3R4F High for Female	0.000233
---- ZRH High vs. 3R4F High for Female	0.000699
---- Sham Recovery vs. 3R4F High Recovery for Female	0.003823
---- Sham Recovery vs. ZRH High Recovery for Female	0.825591
---- Sham vs. Sham Recovery for Female	0.001593

Unadjusted P-values Obtained by Kruskal-Wallis Test
Analyte = MIP_1_beta

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	0.033736
---- ZRH High vs. ZRH High Recovery for Female	0.849378
---- 3R4F High Recovery vs. ZRH High Recovery for Female	0.001082

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 40

Macrophage Inflammatory Protein-1 gamma Rat (MIP-1 gamma Rat)

Unit = ng/mL

Descriptive Statistics by Exposure Duration and Treatment Type**Analyte = MIP_1_gamma_Rat**

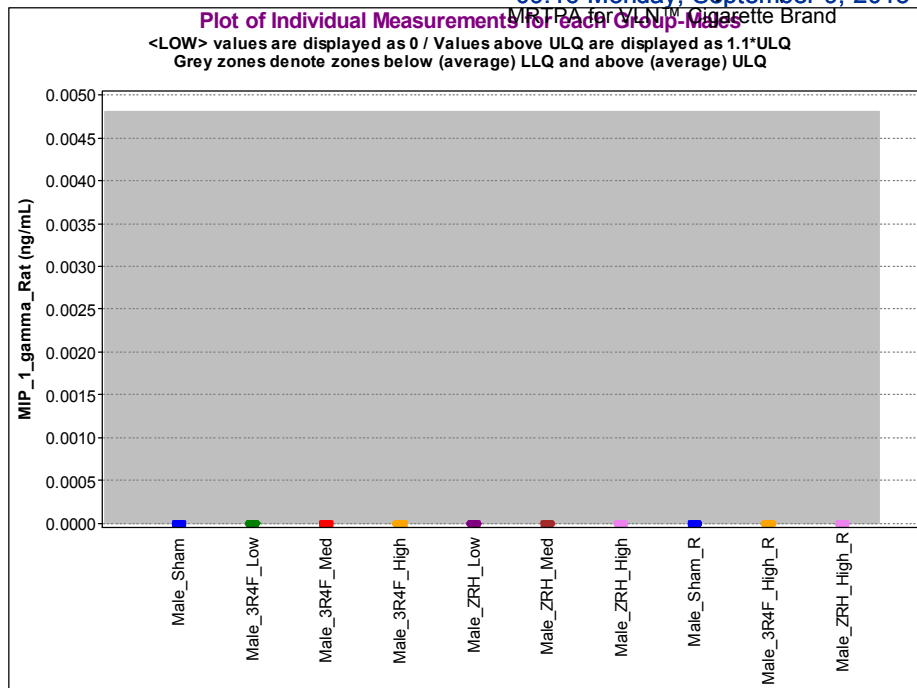
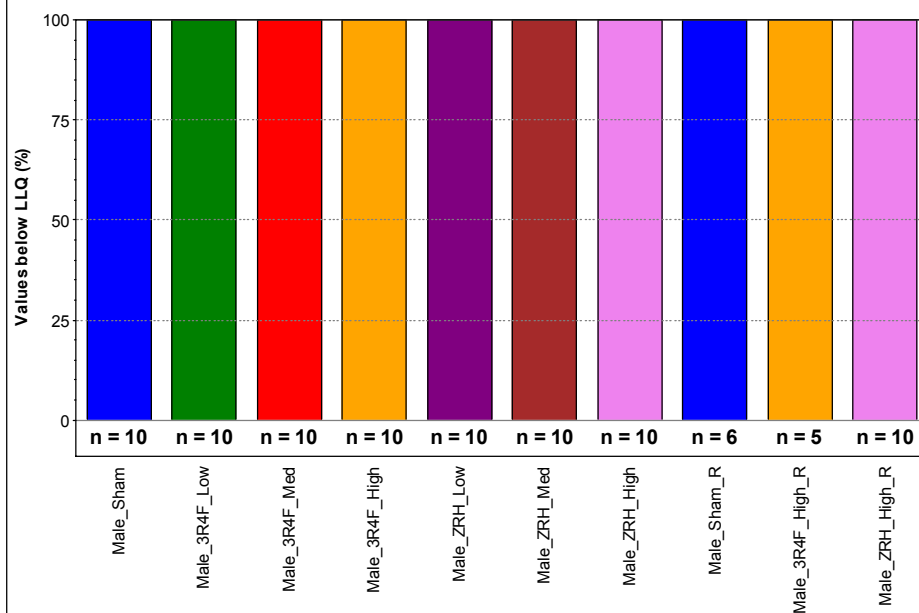
Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	10	0	0	0.005	.
Male	3	3R4F Low	10	10	10	0	0	0.005	.
Male	3	3R4F Medium	10	10	10	0	0	0.005	.
Male	3	3R4F High	10	10	10	0	0	0.005	.
Male	3	ZRH Low	10	10	10	0	0	0.005	.
Male	3	ZRH Medium	10	10	10	0	0	0.005	.
Male	3	ZRH High	10	10	10	0	0	0.005	.
Male	4.5	Sham Recovery	6	6	6	0	0	0.005	.
Male	4.5	3R4F High Recovery	5	5	5	0	0	0.005	.
Male	4.5	ZRH High Recovery	10	10	10	0	0	0.005	.
Female	3	Sham	10	10	10	0	0	0.005	.
Female	3	3R4F Low	10	10	10	0	0	0.005	.
Female	3	3R4F Medium	10	10	10	0	0	0.005	.
Female	3	3R4F High	9	9	9	0	0	0.005	.
Female	3	ZRH Low	9	9	9	0	0	0.005	.
Female	3	ZRH Medium	10	10	10	0	0	0.005	.
Female	3	ZRH High	10	10	10	0	0	0.005	.
Female	4.5	Sham Recovery	6	6	6	0	0	0.005	.
Female	4.5	3R4F High Recovery	6	6	6	0	0	0.005	.
Female	4.5	ZRH High Recovery	10	10	10	0	0	0.005	.

Descriptive Statistics by Exposure Duration and Treatment Type**Analyte = MIP_1_gamma_Rat**

Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	0.002	0.002	0.002	0.002	0.002	0.002	0.000	0.000	0.0	.	.	0.005	.
Male	3	3R4F Low	0.002	0.002	0.002	0.002	0.002	0.002	0.000	0.000	0.0	.	.	0.005	.
Male	3	3R4F Medium	0.002	0.002	0.002	0.002	0.002	0.002	0.000	0.000	0.0	.	.	0.005	.
Male	3	3R4F High	0.002	0.002	0.002	0.002	0.002	0.002	0.000	0.000	0.0	.	.	0.005	.
Male	3	ZRH Low	0.002	0.002	0.002	0.002	0.002	0.002	0.000	0.000	0.0	.	.	0.005	.
Male	3	ZRH Medium	0.002	0.002	0.002	0.002	0.002	0.002	0.000	0.000	0.0	.	.	0.005	.
Male	3	ZRH High	0.002	0.002	0.002	0.002	0.002	0.002	0.000	0.000	0.0	.	.	0.005	.
Male	4.5	Sham Recovery	0.002	0.002	0.002	0.002	0.002	0.002	0.000	0.000	0.0	.	.	0.005	.
Male	4.5	3R4F High Recovery	0.002	0.002	0.002	0.002	0.002	0.002	0.000	0.000	0.0	.	.	0.005	.
Male	4.5	ZRH High Recovery	0.002	0.002	0.002	0.002	0.002	0.002	0.000	0.000	0.0	.	.	0.005	.
Female	3	Sham	0.002	0.002	0.002	0.002	0.002	0.002	0.000	0.000	0.0	.	.	0.005	.
Female	3	3R4F Low	0.002	0.002	0.002	0.002	0.002	0.002	0.000	0.000	0.0	.	.	0.005	.
Female	3	3R4F Medium	0.002	0.002	0.002	0.002	0.002	0.002	0.000	0.000	0.0	.	.	0.005	.
Female	3	3R4F High	0.002	0.002	0.002	0.002	0.002	0.002	0.000	0.000	0.0	.	.	0.005	.
Female	3	ZRH Low	0.002	0.002	0.002	0.002	0.002	0.002	0.000	0.000	0.0	.	.	0.005	.
Female	3	ZRH Medium	0.002	0.002	0.002	0.002	0.002	0.002	0.000	0.000	0.0	.	.	0.005	.
Female	3	ZRH High	0.002	0.002	0.002	0.002	0.002	0.002	0.000	0.000	0.0	.	.	0.005	.
Female	4.5	Sham Recovery	0.002	0.002	0.002	0.002	0.002	0.002	0.000	0.000	0.0	.	.	0.005	.
Female	4.5	3R4F High Recovery	0.002	0.002	0.002	0.002	0.002	0.002	0.000	0.000	0.0	.	.	0.005	.
Female	4.5	ZRH High Recovery	0.002	0.002	0.002	0.002	0.002	0.002	0.000	0.000	0.0	.	.	0.005	.

Percentage of Values below LLQ for each Group-Males

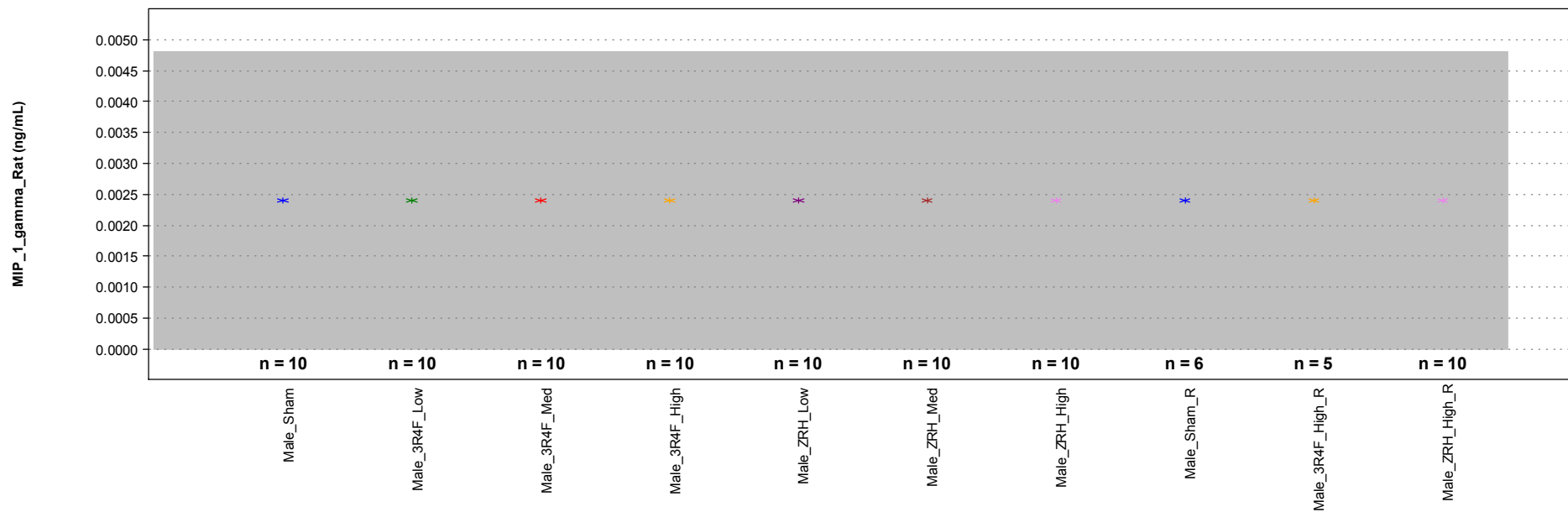
Analyte = MIP_1_gamma_Rat



Plot of Descriptive Robust Statistics-Males

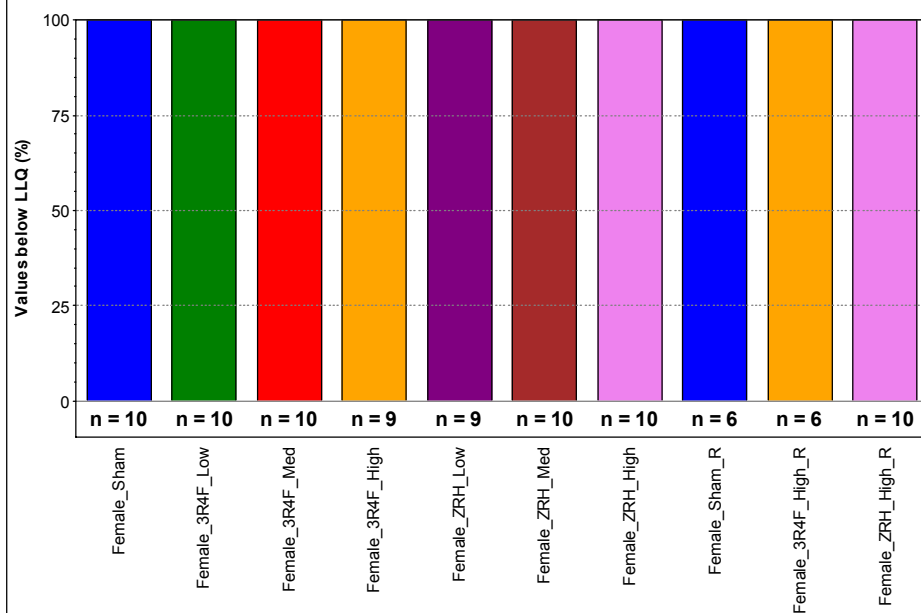
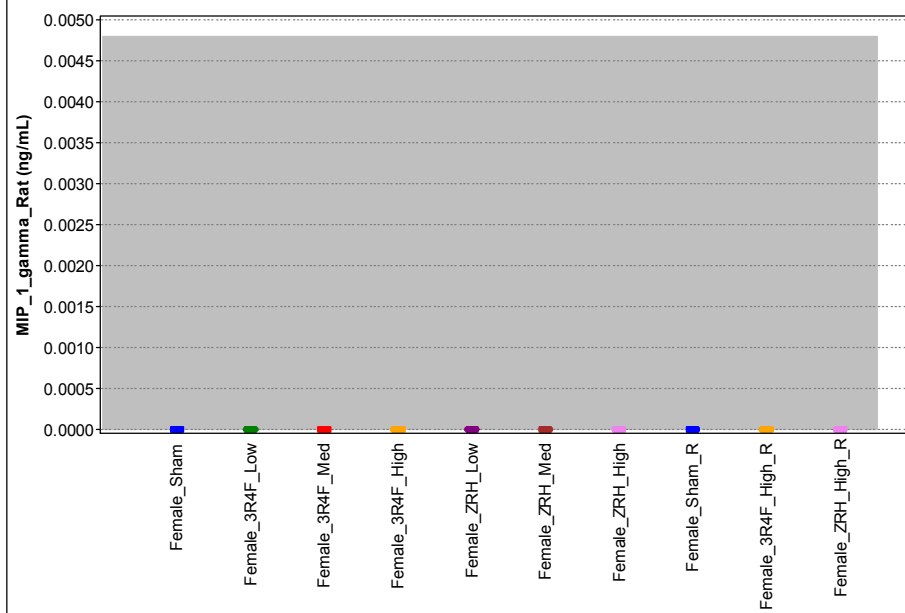
Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



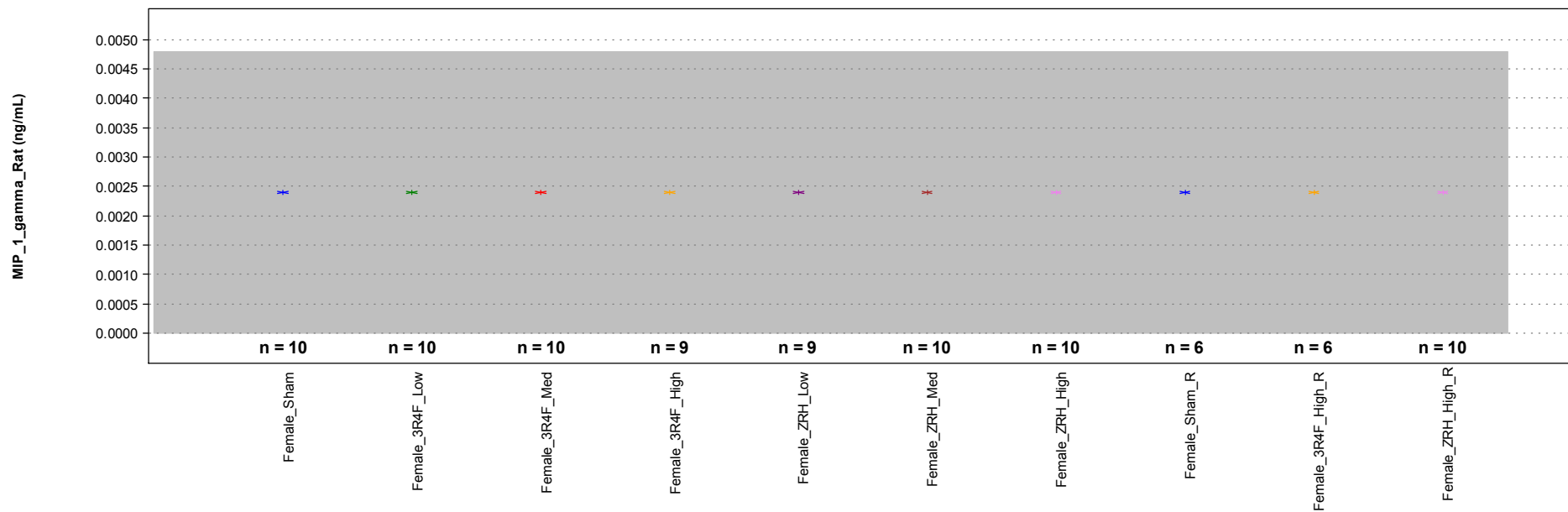
Percentage of Values below LLQ for each Group-Females

Analyte = MIP_1_gamma_Rat

**Plot of Individual Measurements**<LOW> values are displayed as 0 / Values above ULQ are displayed as 1.1*ULQ
Grey zones denote zones below (average) LLQ and above (average) ULQ**Plot of Descriptive Robust Statistics-Females**

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = MIP_1_gamma_Rat

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	1.000000
---- Sham vs. 3R4F Medium for Male	1.000000
---- Sham vs. 3R4F High for Male	1.000000
---- Sham vs. ZRH Low for Male	1.000000
---- Sham vs. ZRH Medium for Male	1.000000
---- Sham vs. ZRH High for Male	1.000000
---- ZRH Low vs. 3R4F Medium for Male	1.000000
---- ZRH Medium vs. 3R4F High for Male	1.000000
---- ZRH High vs. 3R4F High for Male	1.000000
---- Sham Recovery vs. 3R4F High Recovery for Male	1.000000
---- Sham Recovery vs. ZRH High Recovery for Male	1.000000
---- Sham vs. Sham Recovery for Male	1.000000
---- 3R4F High vs. 3R4F High Recovery for Male	1.000000
---- ZRH High vs. ZRH High Recovery for Male	1.000000
---- 3R4F High Recovery vs. ZRH High Recovery for Male	1.000000
---- Sham vs. 3R4F Low for Female	1.000000
---- Sham vs. 3R4F Medium for Female	1.000000
---- Sham vs. 3R4F High for Female	1.000000
---- Sham vs. ZRH Low for Female	1.000000
---- Sham vs. ZRH Medium for Female	1.000000
---- Sham vs. ZRH High for Female	1.000000
---- ZRH Low vs. 3R4F Medium for Female	1.000000
---- ZRH Medium vs. 3R4F High for Female	1.000000
---- ZRH High vs. 3R4F High for Female	1.000000
---- Sham Recovery vs. 3R4F High Recovery for Female	1.000000
---- Sham Recovery vs. ZRH High Recovery for Female	1.000000
---- Sham vs. Sham Recovery for Female	1.000000

Unadjusted P-values Obtained by Kruskal-Wallis Test
Analyte = MIP_1_gamma_Rat

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	1.000000
---- ZRH High vs. ZRH High Recovery for Female	1.000000
---- 3R4F High Recovery vs. ZRH High Recovery for Female	1.000000

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 41

Macrophage Inflammatory Protein-2 (MIP-2)

Unit = pg/mL

Descriptive Statistics by Exposure Duration and Treatment Type**Analyte = MIP_2**

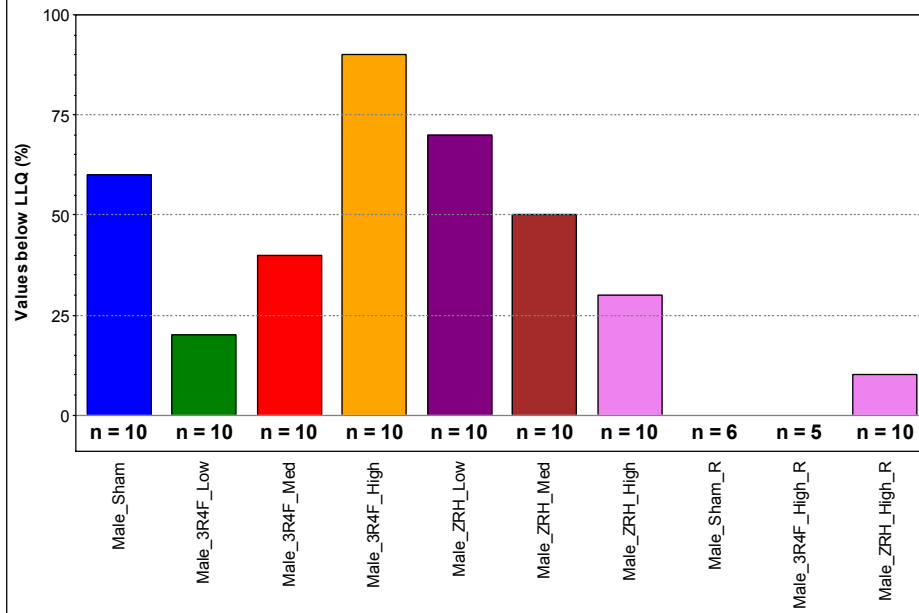
Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	6	4	0	2.2	.
Male	3	3R4F Low	10	10	2	8	0	2.2	.
Male	3	3R4F Medium	10	10	4	6	0	2.2	.
Male	3	3R4F High	10	10	9	1	0	2.2	.
Male	3	ZRH Low	10	10	7	3	0	2.2	.
Male	3	ZRH Medium	10	10	5	5	0	2.2	.
Male	3	ZRH High	10	10	3	7	0	2.2	.
Male	4.5	Sham Recovery	6	6	0	6	0	2.2	.
Male	4.5	3R4F High Recovery	5	5	0	5	0	2.2	.
Male	4.5	ZRH High Recovery	10	10	1	9	0	2.2	.
Female	3	Sham	10	10	3	7	0	2.2	.
Female	3	3R4F Low	10	10	1	9	0	2.2	.
Female	3	3R4F Medium	10	10	4	6	0	2.2	.
Female	3	3R4F High	9	9	4	5	0	2.2	.
Female	3	ZRH Low	9	9	1	8	0	2.2	.
Female	3	ZRH Medium	10	10	1	9	0	2.2	.
Female	3	ZRH High	10	10	0	10	0	2.2	.
Female	4.5	Sham Recovery	6	6	1	5	0	2.2	.
Female	4.5	3R4F High Recovery	6	6	0	6	0	2.2	.
Female	4.5	ZRH High Recovery	10	10	1	9	0	2.2	.

Descriptive Statistics by Exposure Duration and Treatment Type**Analyte = MIP_2**

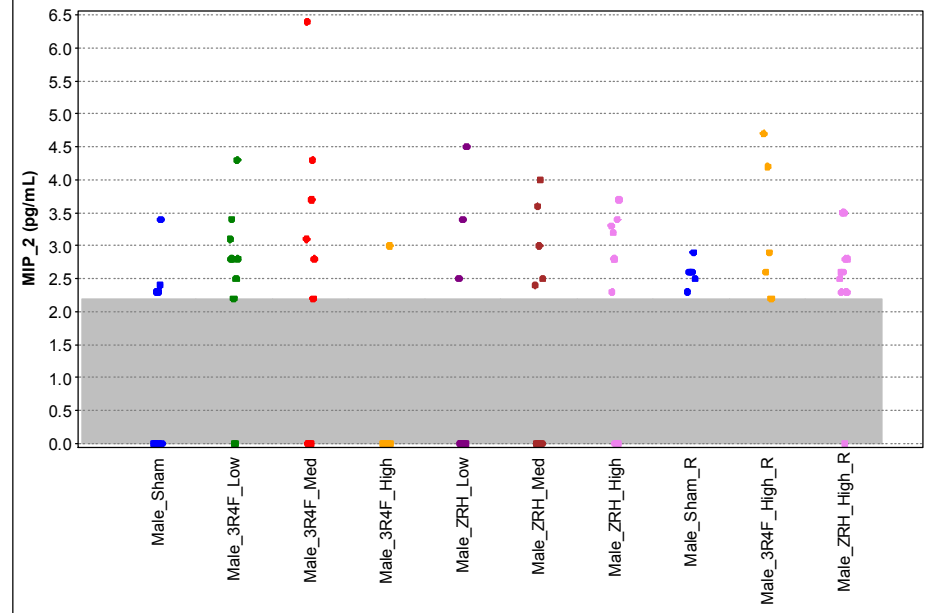
Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	1.100	1.100	1.100	2.300	3.400	1.700	0.834	0.264	49.1	1.052	0.005	2.2	.
Male	3	3R4F Low	1.100	2.200	2.800	3.100	4.300	2.610	0.976	0.309	37.4	-0.224	0.243	2.2	.
Male	3	3R4F Medium	1.100	1.100	2.500	3.700	6.400	2.690	1.761	0.557	65.5	1.021	0.719	2.2	.
Male	3	3R4F High	1.100	1.100	1.100	1.100	3.000	1.290	0.601	0.190	46.6	3.162	10.000	2.2	.
Male	3	ZRH Low	1.100	1.100	1.100	2.500	4.500	1.810	1.237	0.391	68.3	1.564	1.326	2.2	.
Male	3	ZRH Medium	1.100	1.100	1.750	3.000	4.000	2.100	1.151	0.364	54.8	0.552	-1.380	2.2	.
Male	3	ZRH High	1.100	1.100	2.800	3.300	3.700	2.480	1.026	0.324	41.4	-0.553	-1.474	2.2	.
Male	4.5	Sham Recovery	2.300	2.500	2.600	2.600	2.900	2.583	0.194	0.079	7.5	0.347	1.915	2.2	.
Male	4.5	3R4F High Recovery	2.200	2.600	2.900	4.200	4.700	3.320	1.076	0.481	32.4	0.488	-2.304	2.2	.
Male	4.5	ZRH High Recovery	1.100	2.300	2.600	2.800	3.500	2.600	0.678	0.214	26.1	-0.871	2.256	2.2	.
Female	3	Sham	1.100	1.100	2.250	2.600	3.700	2.160	0.846	0.268	39.2	0.094	-0.264	2.2	.
Female	3	3R4F Low	1.100	2.700	2.950	3.500	4.300	2.960	0.864	0.273	29.2	-0.804	1.760	2.2	.
Female	3	3R4F Medium	1.100	1.100	2.300	3.400	3.700	2.200	1.070	0.338	48.6	0.226	-1.698	2.2	.
Female	3	3R4F High	1.100	1.100	2.200	2.600	3.100	1.922	0.820	0.273	42.6	0.078	-1.987	2.2	.
Female	3	ZRH Low	1.100	2.500	2.700	3.100	4.600	2.811	0.947	0.316	33.7	0.132	1.799	2.2	.
Female	3	ZRH Medium	1.100	2.300	2.450	3.000	3.700	2.560	0.690	0.218	27.0	-0.601	1.817	2.2	.
Female	3	ZRH High	2.300	2.300	3.000	3.700	4.300	3.150	0.729	0.231	23.1	0.193	-1.273	2.2	.
Female	4.5	Sham Recovery	1.100	2.600	3.050	3.900	4.100	2.967	1.080	0.441	36.4	-1.017	1.244	2.2	.
Female	4.5	3R4F High Recovery	2.600	3.200	4.100	4.700	4.700	3.900	0.899	0.367	23.0	-0.496	-1.786	2.2	.
Female	4.5	ZRH High Recovery	1.100	2.900	3.400	4.100	6.300	3.560	1.353	0.428	38.0	0.399	1.911	2.2	.

Percentage of Values below LLQ for each Group-Males

Analyte = MIP_2

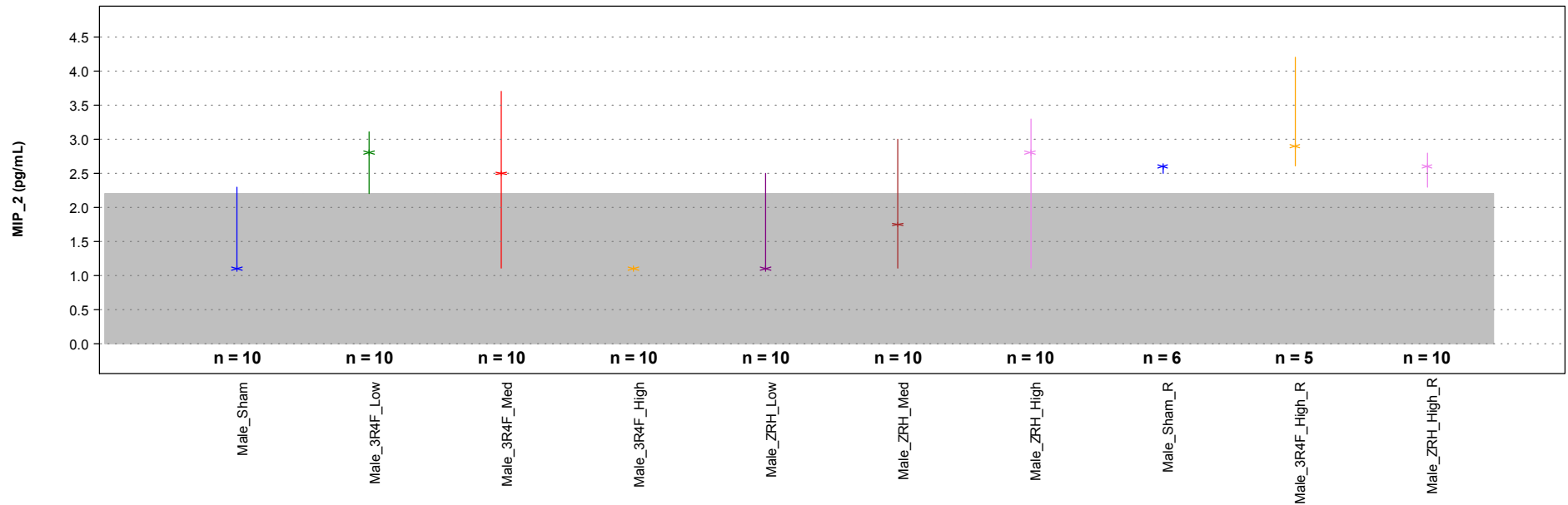
**Plot of Individual Measurements for each Group-Males**

<LOW> values are displayed as 0 / Values above ULQ are displayed as 1.1*ULQ
 Grey zones denote zones below (average) LLQ and above (average) ULQ

**Plot of Descriptive Robust Statistics-Males**

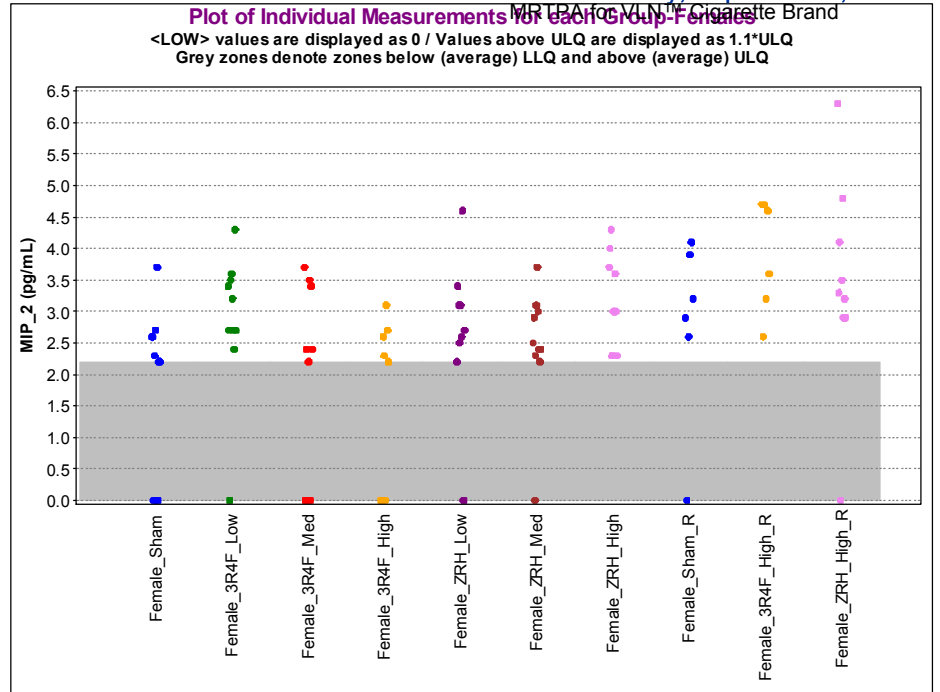
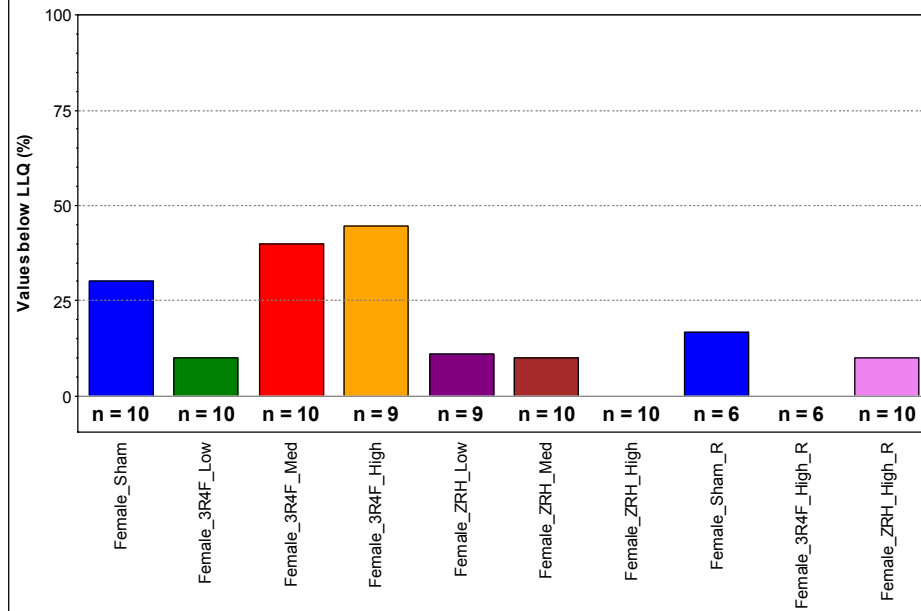
Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



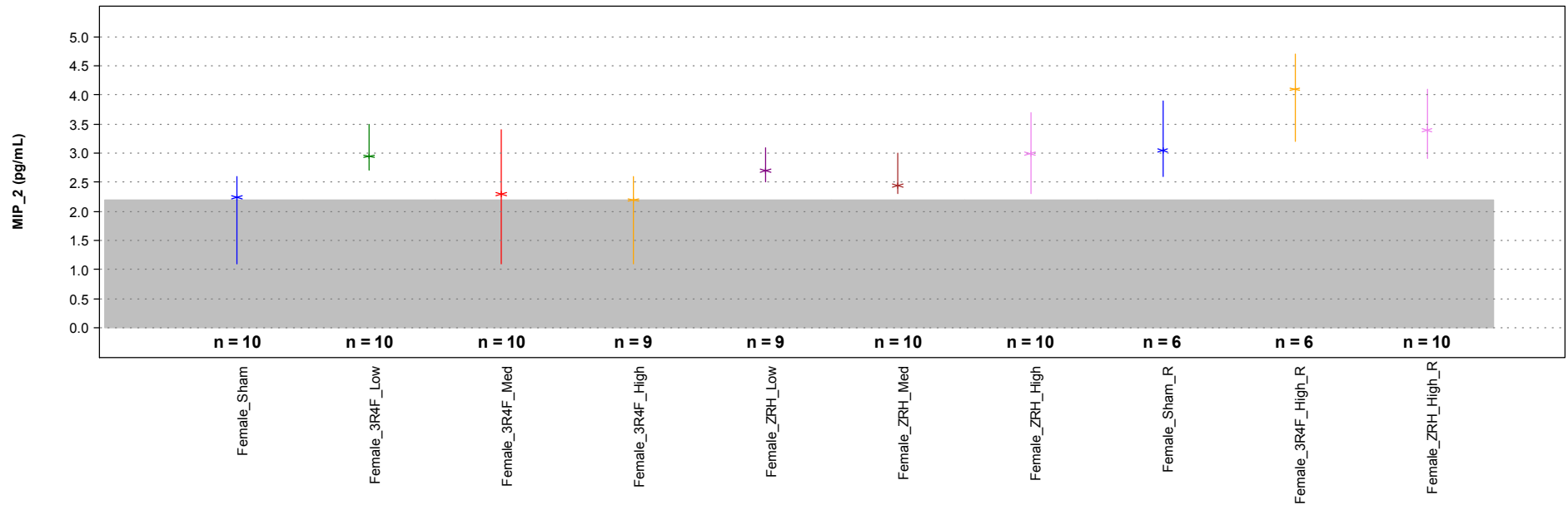
Percentage of Values below LLQ for each Group-Females

Analyte = MIP_2

**Plot of Descriptive Robust Statistics-Females**

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = MIP_2

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	0.038020
---- Sham vs. 3R4F Medium for Male	0.196061
---- Sham vs. 3R4F High for Male	0.163988
---- Sham vs. ZRH Low for Male	0.964589
---- Sham vs. ZRH Medium for Male	0.340877
---- Sham vs. ZRH High for Male	0.087604
---- ZRH Low vs. 3R4F Medium for Male	0.214537
---- ZRH Medium vs. 3R4F High for Male	0.062180
---- ZRH High vs. 3R4F High for Male	0.009227
---- Sham Recovery vs. 3R4F High Recovery for Male	0.261054
---- Sham Recovery vs. ZRH High Recovery for Male	0.868135
---- Sham vs. Sham Recovery for Male	0.013684
---- 3R4F High vs. 3R4F High Recovery for Male	0.002368
---- ZRH High vs. ZRH High Recovery for Male	0.908830
---- 3R4F High Recovery vs. ZRH High Recovery for Male	0.267333
---- Sham vs. 3R4F Low for Female	0.027067
---- Sham vs. 3R4F Medium for Female	0.969110
---- Sham vs. 3R4F High for Female	0.674043
---- Sham vs. ZRH Low for Female	0.117552
---- Sham vs. ZRH Medium for Female	0.238120
---- Sham vs. ZRH High for Female	0.014757
---- ZRH Low vs. 3R4F Medium for Female	0.247959
---- ZRH Medium vs. 3R4F High for Female	0.126842
---- ZRH High vs. 3R4F High for Female	0.009337
---- Sham Recovery vs. 3R4F High Recovery for Female	0.147401
---- Sham Recovery vs. ZRH High Recovery for Female	0.353705
---- Sham vs. Sham Recovery for Female	0.070335

Unadjusted P-values Obtained by Kruskal-Wallis Test
Analyte = MIP_2

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	0.003514
---- ZRH High vs. ZRH High Recovery for Female	0.494665
---- 3R4F High Recovery vs. ZRH High Recovery for Female	0.549626

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 42

Macrophage Inflammatory Protein-3 beta (MIP-3 beta)

Unit = ng/mL

Descriptive Statistics by Exposure Duration and Treatment Type

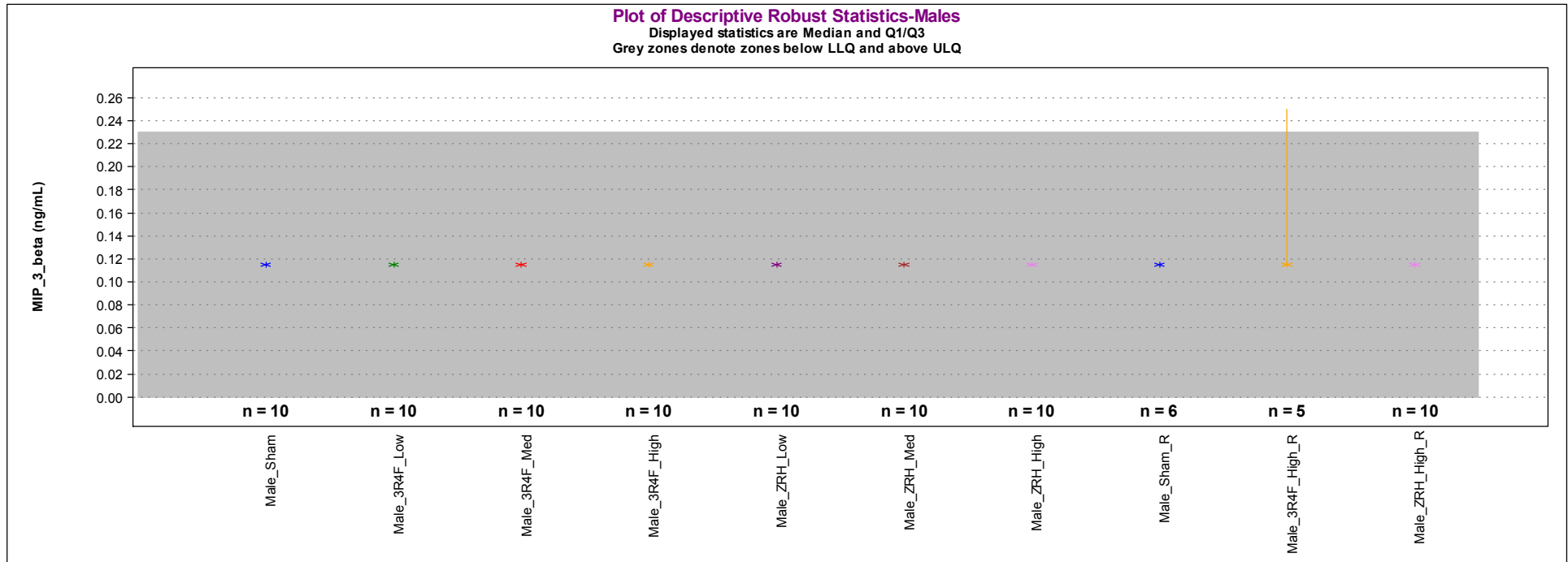
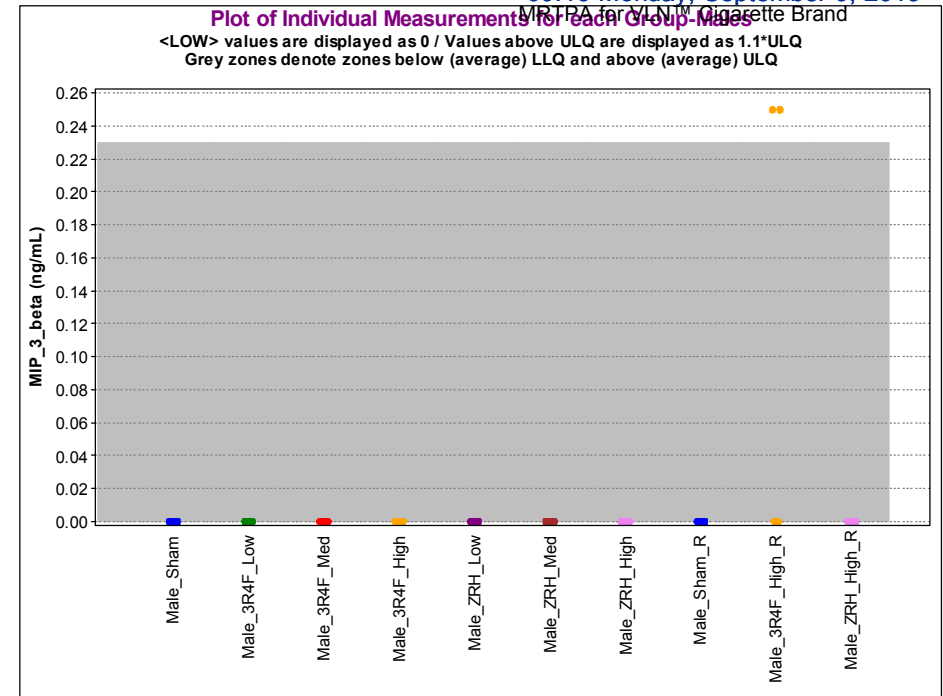
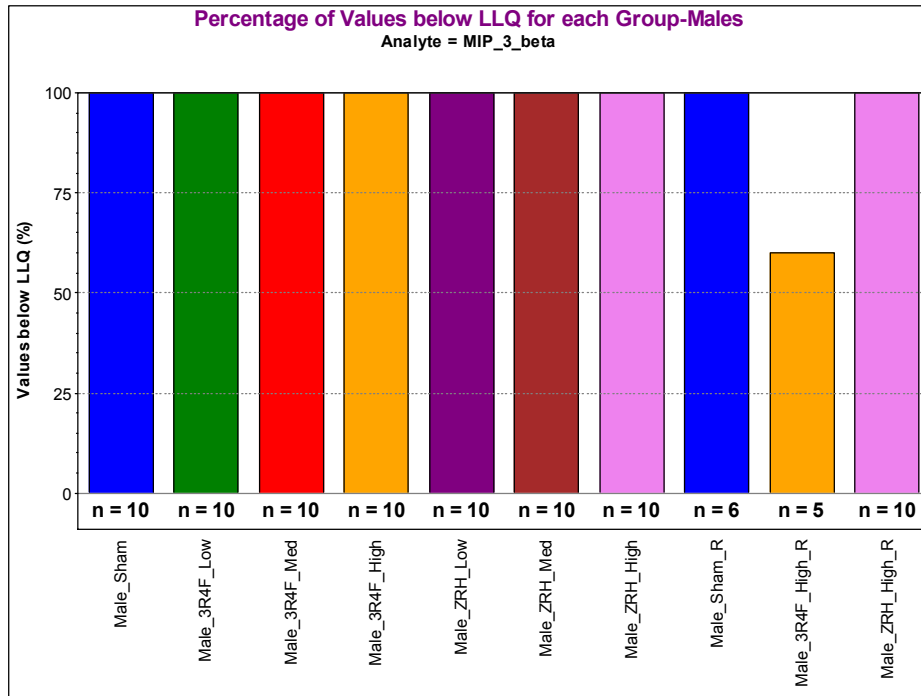
Analyte = MIP_3_beta

Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	10	0	0	0.23	.
Male	3	3R4F Low	10	10	10	0	0	0.23	.
Male	3	3R4F Medium	10	10	10	0	0	0.23	.
Male	3	3R4F High	10	10	10	0	0	0.23	.
Male	3	ZRH Low	10	10	10	0	0	0.23	.
Male	3	ZRH Medium	10	10	10	0	0	0.23	.
Male	3	ZRH High	10	10	10	0	0	0.23	.
Male	4.5	Sham Recovery	6	6	6	0	0	0.23	.
Male	4.5	3R4F High Recovery	5	5	3	2	0	0.23	.
Male	4.5	ZRH High Recovery	10	10	10	0	0	0.23	.
Female	3	Sham	10	10	10	0	0	0.23	.
Female	3	3R4F Low	10	10	10	0	0	0.23	.
Female	3	3R4F Medium	10	10	10	0	0	0.23	.
Female	3	3R4F High	9	9	9	0	0	0.23	.
Female	3	ZRH Low	9	9	9	0	0	0.23	.
Female	3	ZRH Medium	10	10	10	0	0	0.23	.
Female	3	ZRH High	10	10	10	0	0	0.23	.
Female	4.5	Sham Recovery	6	6	6	0	0	0.23	.
Female	4.5	3R4F High Recovery	6	6	6	0	0	0.23	.
Female	4.5	ZRH High Recovery	10	10	10	0	0	0.23	.

Descriptive Statistics by Exposure Duration and Treatment Type

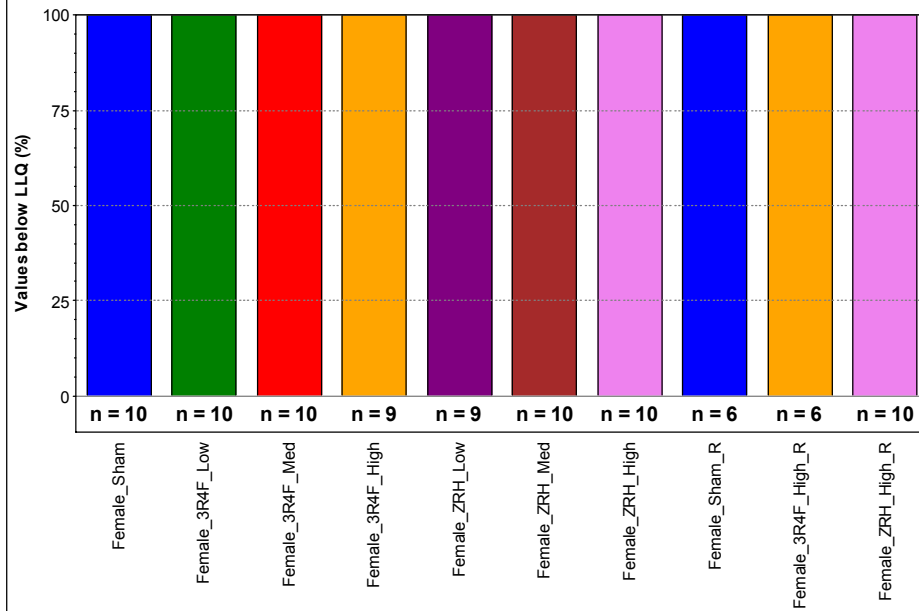
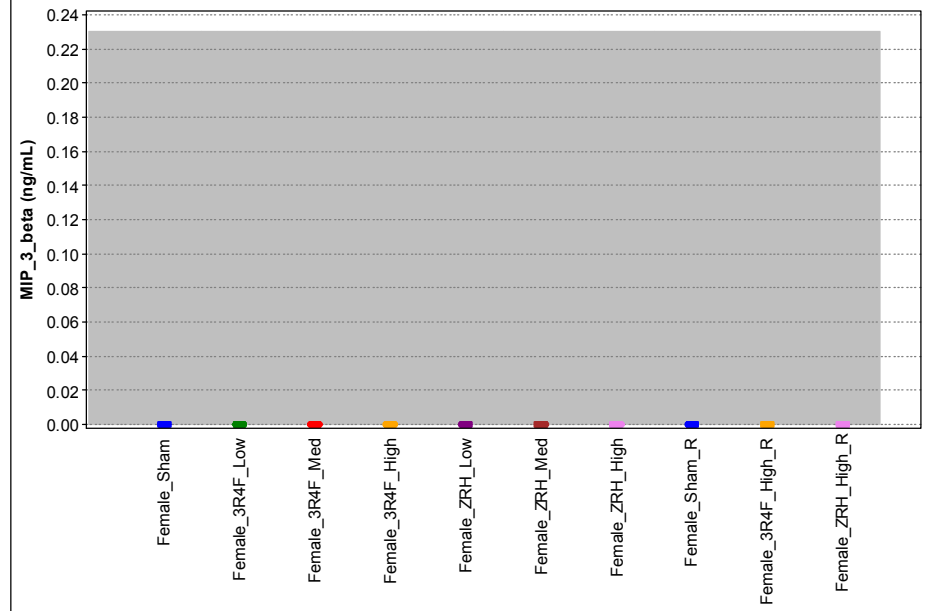
Analyte = MIP_3_beta

Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	0.115	0.115	0.115	0.115	0.115	0.115	0.000	0.000	0.0	.	.	0.23	.
Male	3	3R4F Low	0.115	0.115	0.115	0.115	0.115	0.115	0.000	0.000	0.0	.	.	0.23	.
Male	3	3R4F Medium	0.115	0.115	0.115	0.115	0.115	0.115	0.000	0.000	0.0	.	.	0.23	.
Male	3	3R4F High	0.115	0.115	0.115	0.115	0.115	0.115	0.000	0.000	0.0	.	.	0.23	.
Male	3	ZRH Low	0.115	0.115	0.115	0.115	0.115	0.115	0.000	0.000	0.0	.	.	0.23	.
Male	3	ZRH Medium	0.115	0.115	0.115	0.115	0.115	0.115	0.000	0.000	0.0	.	.	0.23	.
Male	3	ZRH High	0.115	0.115	0.115	0.115	0.115	0.115	0.000	0.000	0.0	.	.	0.23	.
Male	4.5	Sham Recovery	0.115	0.115	0.115	0.115	0.115	0.115	0.000	0.000	0.0	.	.	0.23	.
Male	4.5	3R4F High Recovery	0.115	0.115	0.115	0.250	0.250	0.169	0.074	0.033	43.8	0.609	-3.333	0.23	.
Male	4.5	ZRH High Recovery	0.115	0.115	0.115	0.115	0.115	0.115	0.000	0.000	0.0	.	.	0.23	.
Female	3	Sham	0.115	0.115	0.115	0.115	0.115	0.115	0.000	0.000	0.0	.	.	0.23	.
Female	3	3R4F Low	0.115	0.115	0.115	0.115	0.115	0.115	0.000	0.000	0.0	.	.	0.23	.
Female	3	3R4F Medium	0.115	0.115	0.115	0.115	0.115	0.115	0.000	0.000	0.0	.	.	0.23	.
Female	3	3R4F High	0.115	0.115	0.115	0.115	0.115	0.115	0.000	0.000	0.0	.	.	0.23	.
Female	3	ZRH Low	0.115	0.115	0.115	0.115	0.115	0.115	0.000	0.000	0.0	.	.	0.23	.
Female	3	ZRH Medium	0.115	0.115	0.115	0.115	0.115	0.115	0.000	0.000	0.0	.	.	0.23	.
Female	3	ZRH High	0.115	0.115	0.115	0.115	0.115	0.115	0.000	0.000	0.0	.	.	0.23	.
Female	4.5	Sham Recovery	0.115	0.115	0.115	0.115	0.115	0.115	0.000	0.000	0.0	.	.	0.23	.
Female	4.5	3R4F High Recovery	0.115	0.115	0.115	0.115	0.115	0.115	0.000	0.000	0.0	.	.	0.23	.
Female	4.5	ZRH High Recovery	0.115	0.115	0.115	0.115	0.115	0.115	0.000	0.000	0.0	.	.	0.23	.



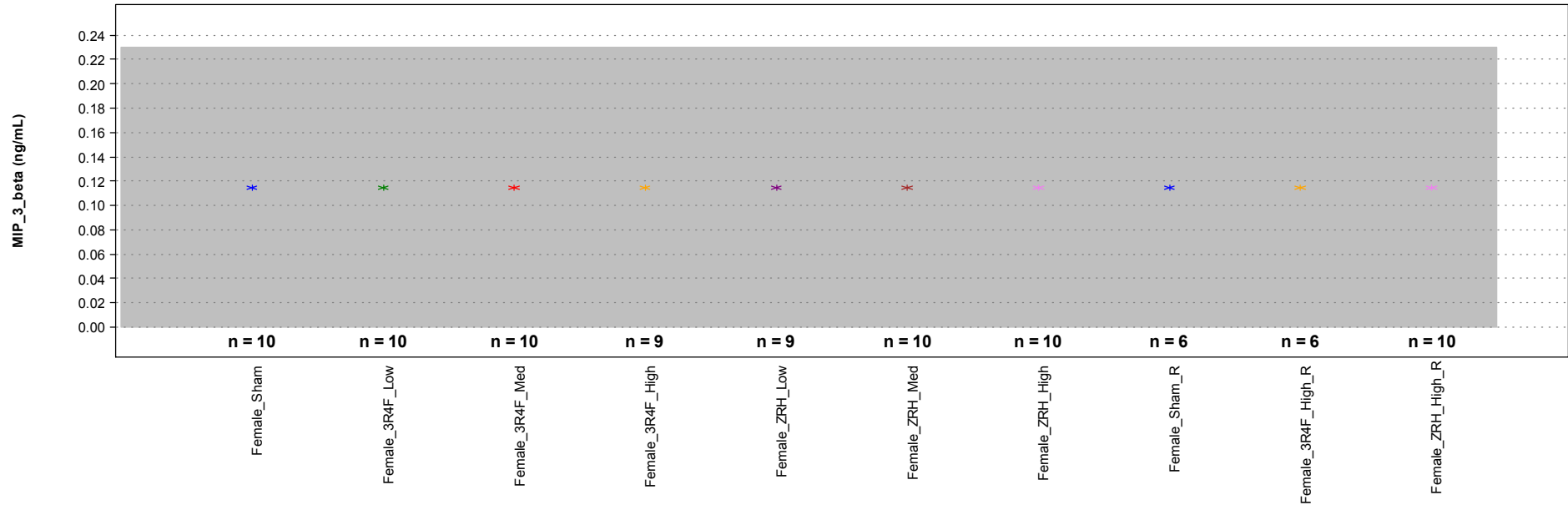
Percentage of Values below LLQ for each Group-Females

Analyte = MIP_3_beta

**Plot of Individual Measurements**<LOW> values are displayed as 0 / Values above ULQ are displayed as 1.1*ULQ
Grey zones denote zones below (average) LLQ and above (average) ULQ**Plot of Descriptive Robust Statistics-Females**

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = MIP_3_beta

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	1.000000
---- Sham vs. 3R4F Medium for Male	1.000000
---- Sham vs. 3R4F High for Male	1.000000
---- Sham vs. ZRH Low for Male	1.000000
---- Sham vs. ZRH Medium for Male	1.000000
---- Sham vs. ZRH High for Male	1.000000
---- ZRH Low vs. 3R4F Medium for Male	1.000000
---- ZRH Medium vs. 3R4F High for Male	1.000000
---- ZRH High vs. 3R4F High for Male	1.000000
---- Sham Recovery vs. 3R4F High Recovery for Male	0.102470
---- Sham Recovery vs. ZRH High Recovery for Male	1.000000
---- Sham vs. Sham Recovery for Male	1.000000
---- 3R4F High vs. 3R4F High Recovery for Male	0.037940
---- ZRH High vs. ZRH High Recovery for Male	1.000000
---- 3R4F High Recovery vs. ZRH High Recovery for Male	0.037940
---- Sham vs. 3R4F Low for Female	1.000000
---- Sham vs. 3R4F Medium for Female	1.000000
---- Sham vs. 3R4F High for Female	1.000000
---- Sham vs. ZRH Low for Female	1.000000
---- Sham vs. ZRH Medium for Female	1.000000
---- Sham vs. ZRH High for Female	1.000000
---- ZRH Low vs. 3R4F Medium for Female	1.000000
---- ZRH Medium vs. 3R4F High for Female	1.000000
---- ZRH High vs. 3R4F High for Female	1.000000
---- Sham Recovery vs. 3R4F High Recovery for Female	1.000000
---- Sham Recovery vs. ZRH High Recovery for Female	1.000000
---- Sham vs. Sham Recovery for Female	1.000000

Unadjusted P-values Obtained by Kruskal-Wallis Test
Analyte = MIP_3_beta

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	1.000000
---- ZRH High vs. ZRH High Recovery for Female	1.000000
---- 3R4F High Recovery vs. ZRH High Recovery for Female	1.000000

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 43

Matrix Metalloproteinase-9 (MMP-9)

Unit = ng/mL

Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = MMP_9

Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	9	1	0	0.14	.
Male	3	3R4F Low	10	10	10	0	0	0.14	.
Male	3	3R4F Medium	10	10	10	0	0	0.14	.
Male	3	3R4F High	10	10	9	1	0	0.14	.
Male	3	ZRH Low	10	10	10	0	0	0.14	.
Male	3	ZRH Medium	10	10	10	0	0	0.14	.
Male	3	ZRH High	10	10	10	0	0	0.14	.
Male	4.5	Sham Recovery	6	6	6	0	0	0.14	.
Male	4.5	3R4F High Recovery	5	5	5	0	0	0.14	.
Male	4.5	ZRH High Recovery	10	10	10	0	0	0.14	.
Female	3	Sham	10	10	10	0	0	0.14	.
Female	3	3R4F Low	10	10	10	0	0	0.14	.
Female	3	3R4F Medium	10	10	10	0	0	0.14	.
Female	3	3R4F High	9	9	9	0	0	0.14	.
Female	3	ZRH Low	9	9	9	0	0	0.14	.
Female	3	ZRH Medium	10	10	10	0	0	0.14	.
Female	3	ZRH High	10	10	10	0	0	0.14	.
Female	4.5	Sham Recovery	6	6	5	1	0	0.14	.
Female	4.5	3R4F High Recovery	6	6	6	0	0	0.14	.
Female	4.5	ZRH High Recovery	10	10	10	0	0	0.14	.

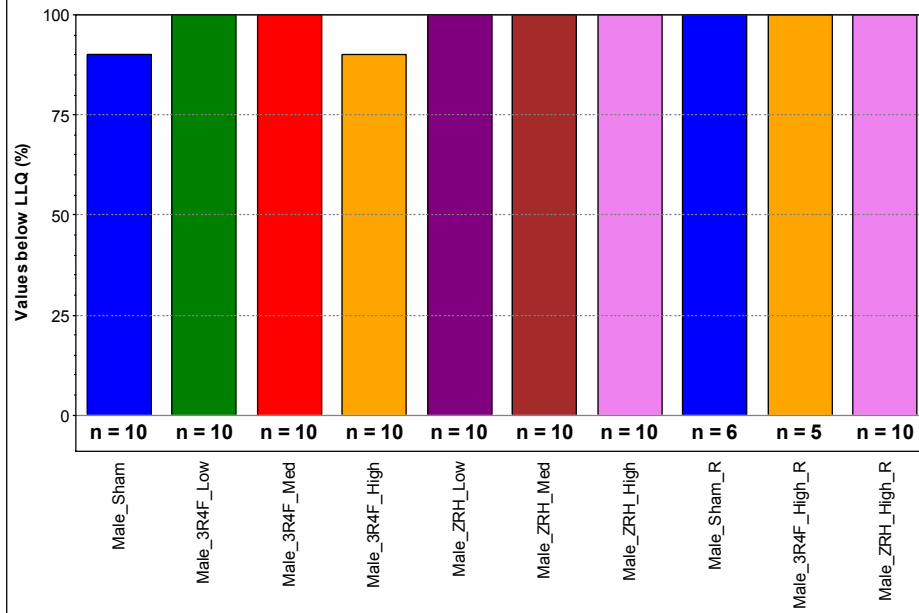
Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = MMP_9

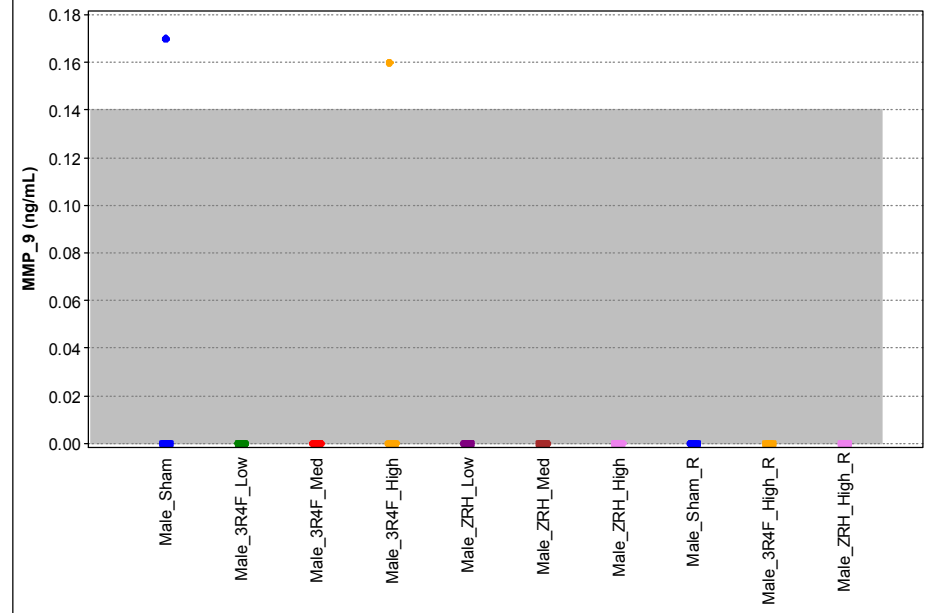
Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	0.070	0.070	0.070	0.070	0.170	0.080	0.032	0.010	39.5	3.162	10.000	0.14	.
Male	3	3R4F Low	0.070	0.070	0.070	0.070	0.070	0.070	0.000	0.000	0.0	.	.	0.14	.
Male	3	3R4F Medium	0.070	0.070	0.070	0.070	0.070	0.070	0.000	0.000	0.0	.	.	0.14	.
Male	3	3R4F High	0.070	0.070	0.070	0.070	0.160	0.079	0.028	0.009	36.0	3.162	10.000	0.14	.
Male	3	ZRH Low	0.070	0.070	0.070	0.070	0.070	0.070	0.000	0.000	0.0	.	.	0.14	.
Male	3	ZRH Medium	0.070	0.070	0.070	0.070	0.070	0.070	0.000	0.000	0.0	.	.	0.14	.
Male	3	ZRH High	0.070	0.070	0.070	0.070	0.070	0.070	0.000	0.000	0.0	.	.	0.14	.
Male	4.5	Sham Recovery	0.070	0.070	0.070	0.070	0.070	0.070	0.000	0.000	0.0	.	.	0.14	.
Male	4.5	3R4F High Recovery	0.070	0.070	0.070	0.070	0.070	0.070	0.000	0.000	0.0	.	.	0.14	.
Male	4.5	ZRH High Recovery	0.070	0.070	0.070	0.070	0.070	0.070	0.000	0.000	0.0	.	.	0.14	.
Female	3	Sham	0.070	0.070	0.070	0.070	0.070	0.070	0.000	0.000	0.0	.	.	0.14	.
Female	3	3R4F Low	0.070	0.070	0.070	0.070	0.070	0.070	0.000	0.000	0.0	.	.	0.14	.
Female	3	3R4F Medium	0.070	0.070	0.070	0.070	0.070	0.070	0.000	0.000	0.0	.	.	0.14	.
Female	3	3R4F High	0.070	0.070	0.070	0.070	0.070	0.070	0.000	0.000	0.0	.	.	0.14	.
Female	3	ZRH Low	0.070	0.070	0.070	0.070	0.070	0.070	0.000	0.000	0.0	.	.	0.14	.
Female	3	ZRH Medium	0.070	0.070	0.070	0.070	0.070	0.070	0.000	0.000	0.0	.	.	0.14	.
Female	3	ZRH High	0.070	0.070	0.070	0.070	0.070	0.070	0.000	0.000	0.0	.	.	0.14	.
Female	4.5	Sham Recovery	0.070	0.070	0.070	0.070	0.150	0.083	0.033	0.013	39.2	2.449	6.000	0.14	.
Female	4.5	3R4F High Recovery	0.070	0.070	0.070	0.070	0.070	0.070	0.000	0.000	0.0	.	.	0.14	.
Female	4.5	ZRH High Recovery	0.070	0.070	0.070	0.070	0.070	0.070	0.000	0.000	0.0	.	.	0.14	.

Percentage of Values below LLQ for each Group-Males

Analyte = MMP_9

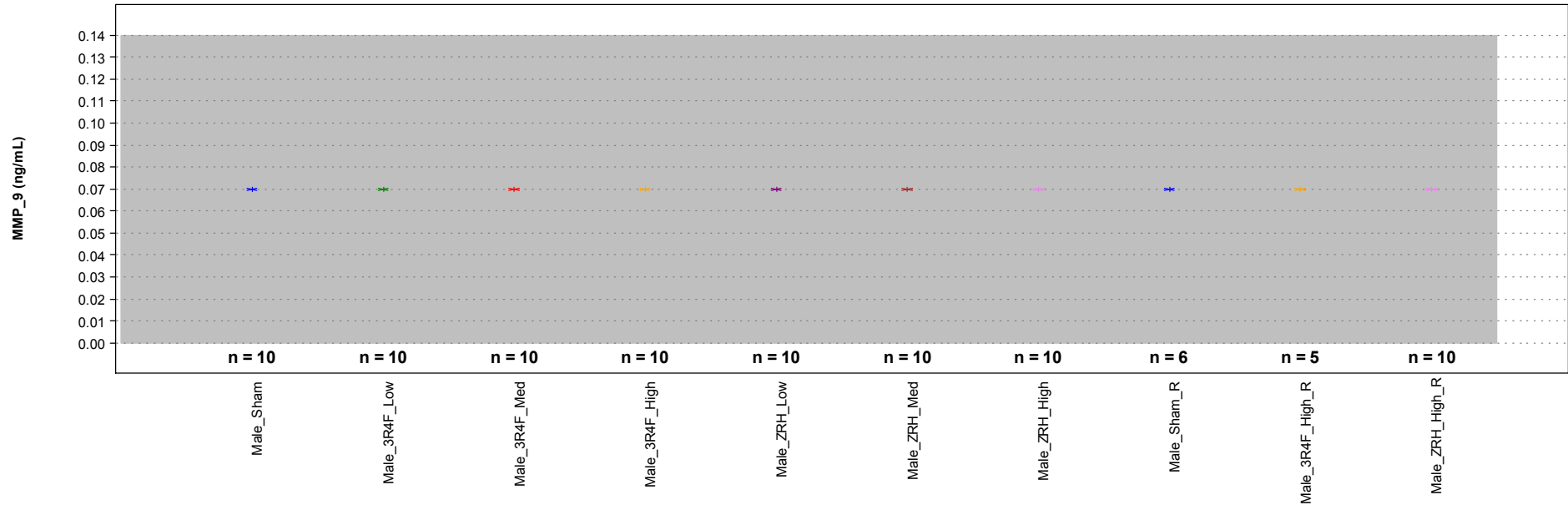
**Plot of Individual Measurements for each Group-Males**

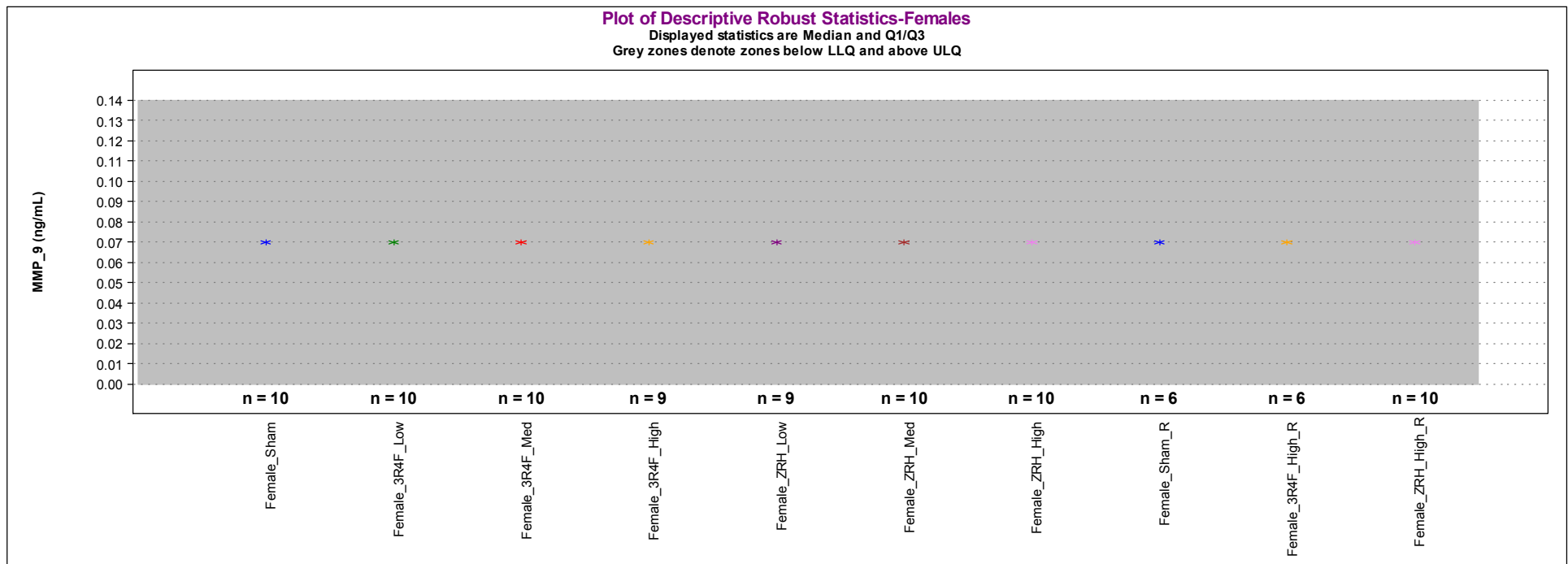
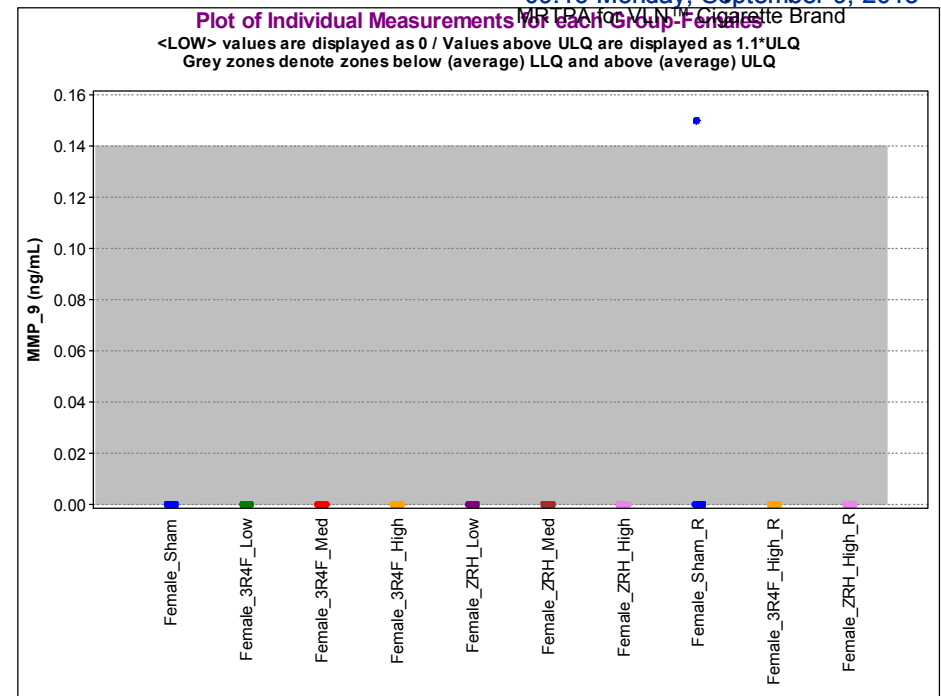
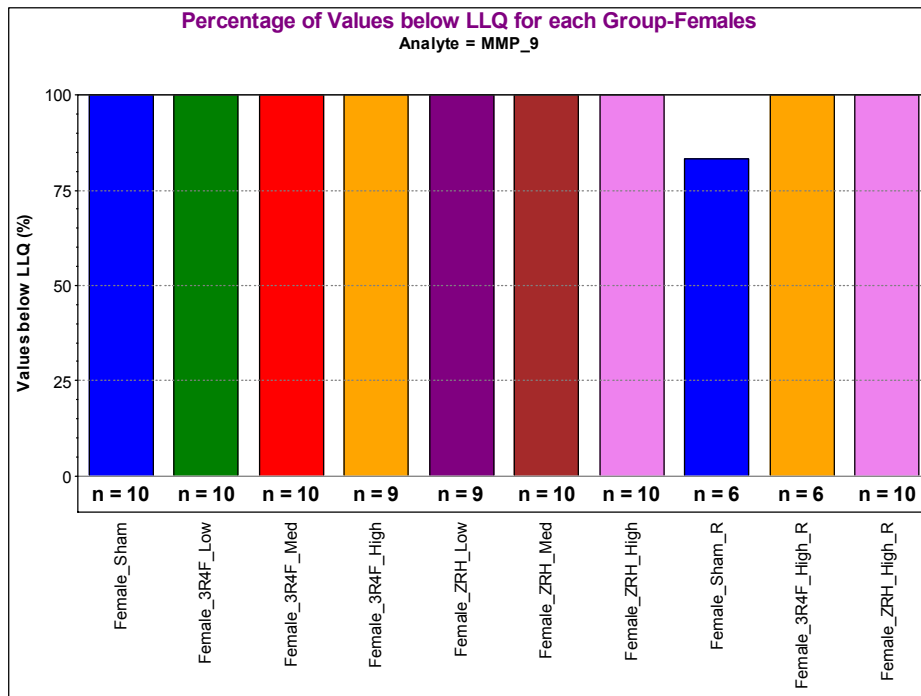
<LOW> values are displayed as 0 / Values above ULQ are displayed as 1.1*ULQ
 Grey zones denote zones below (average) LLQ and above (average) ULQ

**Plot of Descriptive Robust Statistics-Males**

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ





Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = MMP_9

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	0.317311
---- Sham vs. 3R4F Medium for Male	0.317311
---- Sham vs. 3R4F High for Male	0.942166
---- Sham vs. ZRH Low for Male	0.317311
---- Sham vs. ZRH Medium for Male	0.317311
---- Sham vs. ZRH High for Male	0.317311
---- ZRH Low vs. 3R4F Medium for Male	1.000000
---- ZRH Medium vs. 3R4F High for Male	0.317311
---- ZRH High vs. 3R4F High for Male	0.317311
---- Sham Recovery vs. 3R4F High Recovery for Male	1.000000
---- Sham Recovery vs. ZRH High Recovery for Male	1.000000
---- Sham vs. Sham Recovery for Male	0.438578
---- 3R4F High vs. 3R4F High Recovery for Male	0.479500
---- ZRH High vs. ZRH High Recovery for Male	1.000000
---- 3R4F High Recovery vs. ZRH High Recovery for Male	1.000000
---- Sham vs. 3R4F Low for Female	1.000000
---- Sham vs. 3R4F Medium for Female	1.000000
---- Sham vs. 3R4F High for Female	1.000000
---- Sham vs. ZRH Low for Female	1.000000
---- Sham vs. ZRH Medium for Female	1.000000
---- Sham vs. ZRH High for Female	1.000000
---- ZRH Low vs. 3R4F Medium for Female	1.000000
---- ZRH Medium vs. 3R4F High for Female	1.000000
---- ZRH High vs. 3R4F High for Female	1.000000
---- Sham Recovery vs. 3R4F High Recovery for Female	0.317311
---- Sham Recovery vs. ZRH High Recovery for Female	0.196706
---- Sham vs. Sham Recovery for Female	0.196706

Unadjusted P-values Obtained by Kruskal-Wallis Test
Analyte = MMP_9

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	1.000000
---- ZRH High vs. ZRH High Recovery for Female	1.000000
---- 3R4F High Recovery vs. ZRH High Recovery for Female	1.000000

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 47

Myeloperoxidase (MPO)

Unit = ng/mL

Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = MPO

Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	1	9	0	0.13	.
Male	3	3R4F Low	10	10	0	10	0	0.13	.
Male	3	3R4F Medium	10	10	0	10	0	0.13	.
Male	3	3R4F High	10	10	0	10	0	0.13	.
Male	3	ZRH Low	10	10	0	10	0	0.13	.
Male	3	ZRH Medium	10	10	0	10	0	0.13	.
Male	3	ZRH High	10	10	0	10	0	0.13	.
Male	4.5	Sham Recovery	6	6	0	6	0	0.13	.
Male	4.5	3R4F High Recovery	5	5	0	5	0	0.13	.
Male	4.5	ZRH High Recovery	10	10	0	10	0	0.13	.
Female	3	Sham	10	10	0	10	0	0.13	.
Female	3	3R4F Low	10	10	0	10	0	0.13	.
Female	3	3R4F Medium	10	10	0	10	0	0.13	.
Female	3	3R4F High	9	9	0	9	0	0.13	.
Female	3	ZRH Low	9	9	0	9	0	0.13	.
Female	3	ZRH Medium	10	10	0	10	0	0.13	.
Female	3	ZRH High	10	10	0	10	0	0.13	.
Female	4.5	Sham Recovery	6	6	1	5	0	0.13	.
Female	4.5	3R4F High Recovery	6	6	0	6	0	0.13	.
Female	4.5	ZRH High Recovery	10	10	1	9	0	0.13	.

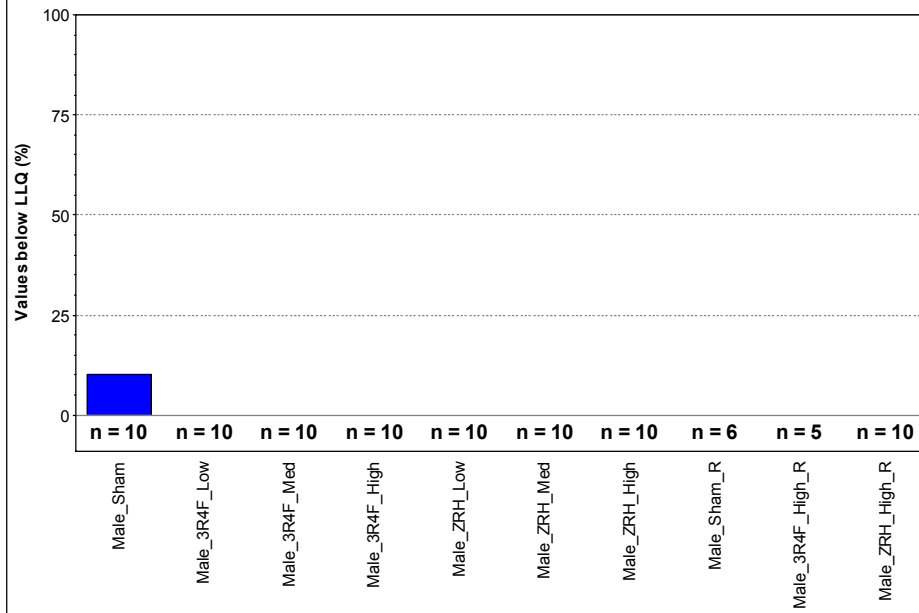
Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = MPO

Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	0.065	0.280	1.195	3.100	7.800	2.012	2.418	0.765	120.2	1.706	3.184	0.13	.
Male	3	3R4F Low	1.800	3.300	5.900	7.400	18.000	6.470	4.561	1.442	70.5	1.981	4.947	0.13	.
Male	3	3R4F Medium	7.700	14.000	14.500	20.000	27.000	16.070	5.476	1.732	34.1	0.628	0.693	0.13	.
Male	3	3R4F High	11.000	14.000	20.500	26.000	36.000	21.600	8.605	2.721	39.8	0.579	-0.822	0.13	.
Male	3	ZRH Low	0.750	1.200	1.500	2.500	5.000	2.035	1.305	0.413	64.1	1.582	2.137	0.13	.
Male	3	ZRH Medium	0.230	0.490	1.300	2.100	5.100	1.663	1.493	0.472	89.8	1.515	2.393	0.13	.
Male	3	ZRH High	0.650	0.850	1.750	3.400	7.100	2.368	1.980	0.626	83.6	1.679	3.163	0.13	.
Male	4.5	Sham Recovery	0.280	0.490	0.700	1.800	4.900	1.478	1.762	0.719	119.2	1.988	4.000	0.13	.
Male	4.5	3R4F High Recovery	5.200	6.500	9.200	9.800	12.000	8.540	2.707	1.211	31.7	-0.043	-1.301	0.13	.
Male	4.5	ZRH High Recovery	0.160	0.310	0.525	0.980	1.400	0.646	0.445	0.141	68.9	0.750	-0.814	0.13	.
Female	3	Sham	0.240	0.760	0.835	0.980	1.100	0.785	0.261	0.082	33.2	-1.201	1.122	0.13	.
Female	3	3R4F Low	3.300	4.700	5.700	11.000	13.000	7.210	3.610	1.142	50.1	0.617	-1.267	0.13	.
Female	3	3R4F Medium	13.000	19.000	23.000	26.000	31.000	22.300	5.716	1.808	25.6	-0.409	-0.468	0.13	.
Female	3	3R4F High	18.000	32.000	36.000	37.000	42.000	32.222	8.348	2.783	25.9	-1.062	-0.013	0.13	.
Female	3	ZRH Low	0.550	0.820	1.100	2.700	4.200	1.711	1.361	0.454	79.6	1.049	-0.491	0.13	.
Female	3	ZRH Medium	0.270	0.560	1.200	3.600	5.100	1.974	1.839	0.582	93.2	1.051	-0.632	0.13	.
Female	3	ZRH High	0.800	1.100	1.700	2.900	6.300	2.280	1.636	0.517	71.7	1.861	3.954	0.13	.
Female	4.5	Sham Recovery	0.065	0.270	0.510	0.660	1.000	0.503	0.324	0.132	64.5	0.272	0.190	0.13	.
Female	4.5	3R4F High Recovery	3.500	5.000	9.500	12.000	13.000	8.750	3.896	1.590	44.5	-0.383	-1.930	0.13	.
Female	4.5	ZRH High Recovery	0.065	0.620	0.690	1.200	3.600	1.097	1.009	0.319	92.0	1.960	4.319	0.13	.

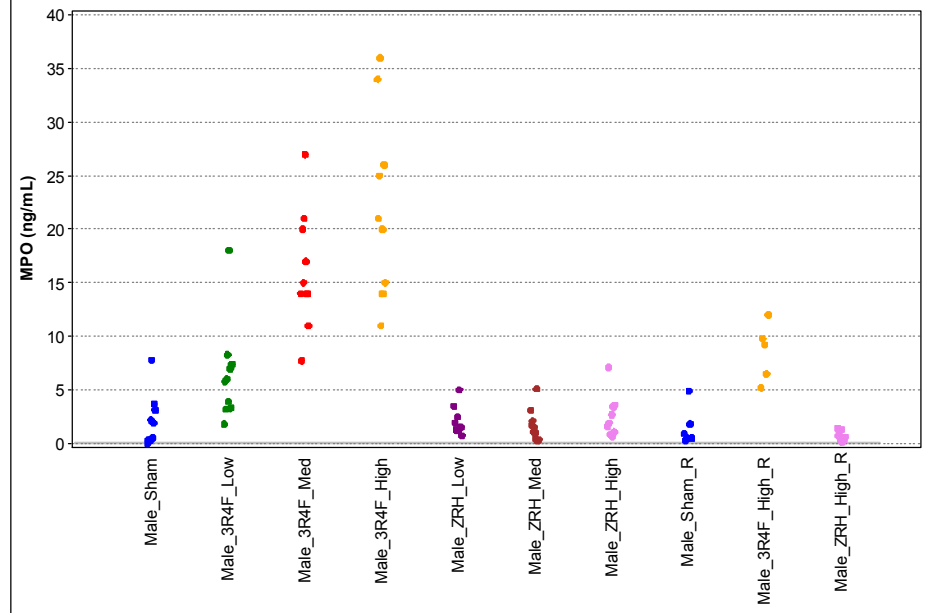
Percentage of Values below LLQ for each Group-Males

Analyte = MPO



Plot of Individual Measurements for Each Group-Males

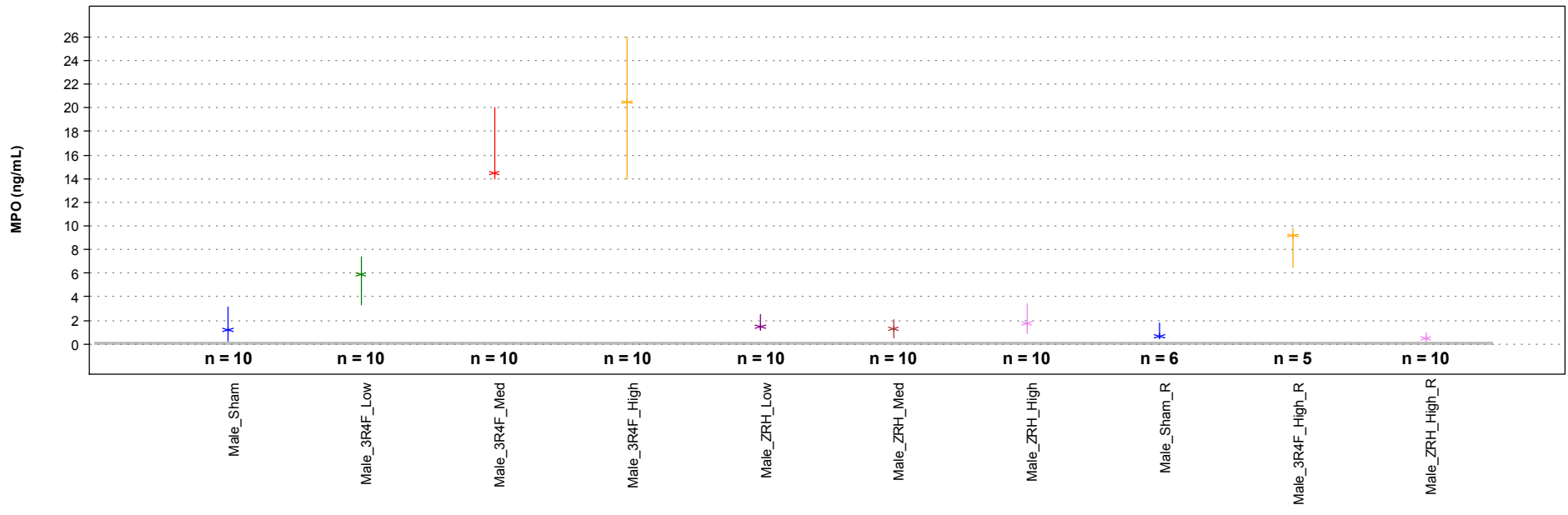
<LOW> values are displayed as 0 / Values above ULQ are displayed as 1.1*ULQ
 Grey zones denote zones below (average) LLQ and above (average) ULQ



Plot of Descriptive Robust Statistics-Males

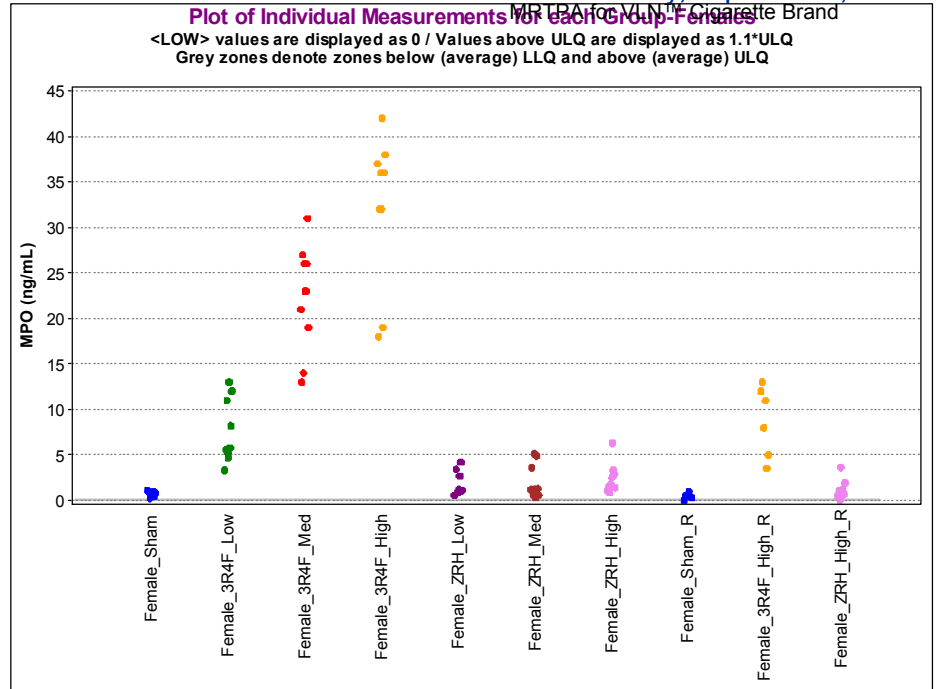
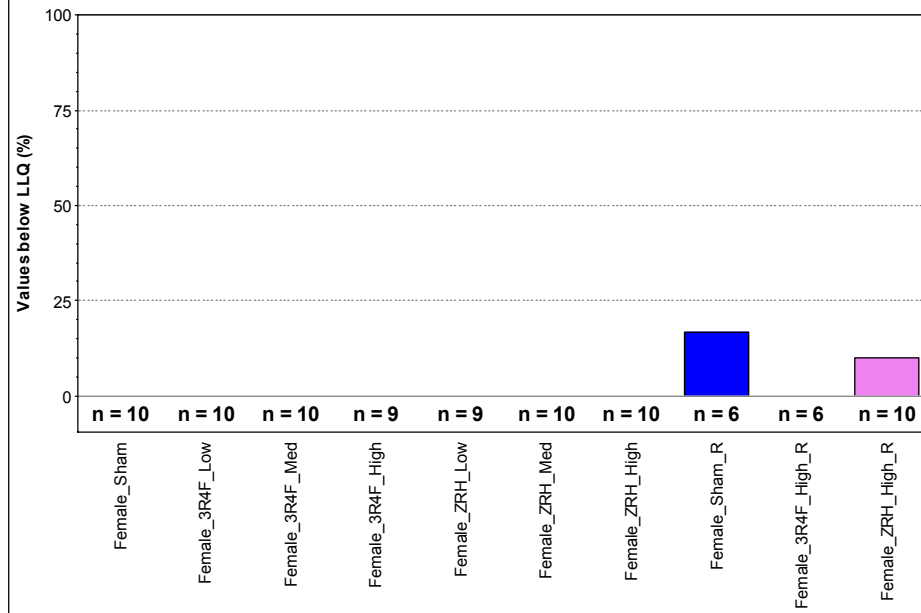
Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



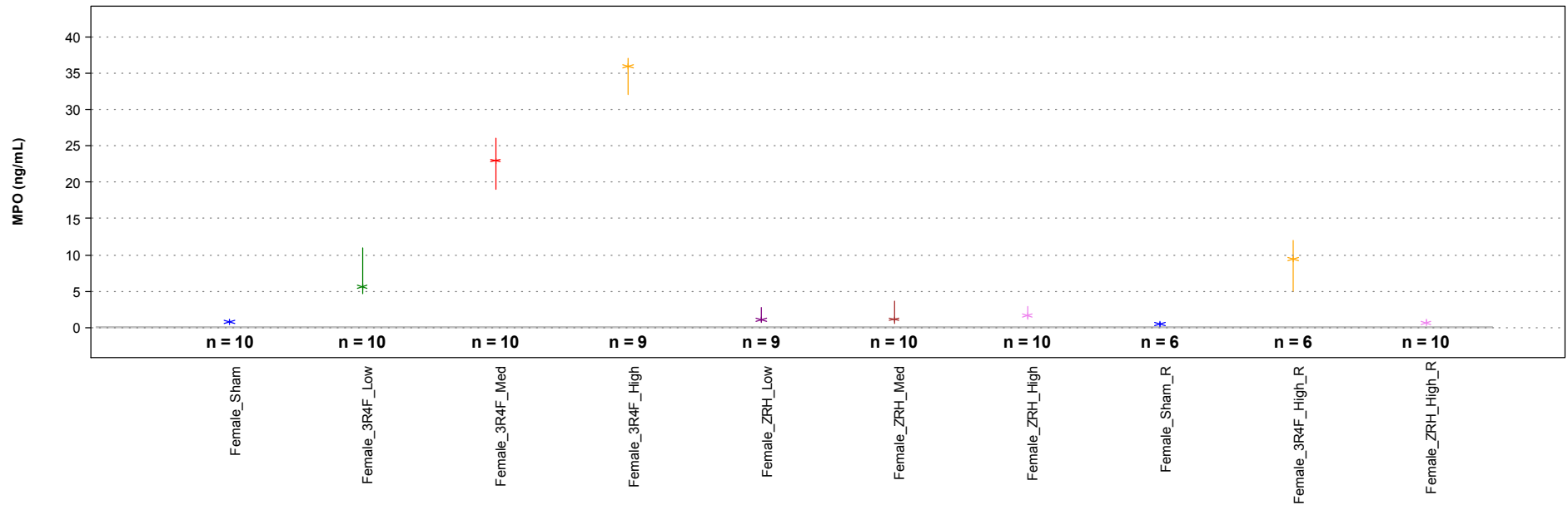
Percentage of Values below LLQ for each Group-Females

Analyte = MPO

**Plot of Descriptive Robust Statistics-Females**

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = MPO

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	0.006502
---- Sham vs. 3R4F Medium for Male	0.000208
---- Sham vs. 3R4F High for Male	0.000156
---- Sham vs. ZRH Low for Male	0.472176
---- Sham vs. ZRH Medium for Male	0.879649
---- Sham vs. ZRH High for Male	0.344523
---- ZRH Low vs. 3R4F Medium for Male	0.000152
---- ZRH Medium vs. 3R4F High for Male	0.000156
---- ZRH High vs. 3R4F High for Male	0.000156
---- Sham Recovery vs. 3R4F High Recovery for Male	0.006054
---- Sham Recovery vs. ZRH High Recovery for Male	0.328616
---- Sham vs. Sham Recovery for Male	0.956590
---- 3R4F High vs. 3R4F High Recovery for Male	0.003261
---- ZRH High vs. ZRH High Recovery for Male	0.004072
---- 3R4F High Recovery vs. ZRH High Recovery for Male	0.002200
---- Sham vs. 3R4F Low for Female	0.000156
---- Sham vs. 3R4F Medium for Female	0.000155
---- Sham vs. 3R4F High for Female	0.000236
---- Sham vs. ZRH Low for Female	0.130742
---- Sham vs. ZRH Medium for Female	0.063822
---- Sham vs. ZRH High for Female	0.001132
---- ZRH Low vs. 3R4F Medium for Female	0.000236
---- ZRH Medium vs. 3R4F High for Female	0.000234
---- ZRH High vs. 3R4F High for Female	0.000234
---- Sham Recovery vs. 3R4F High Recovery for Female	0.003948
---- Sham Recovery vs. ZRH High Recovery for Female	0.103233
---- Sham vs. Sham Recovery for Female	0.115510

Unadjusted P-values Obtained by Kruskal-Wallis Test
Analyte = MPO

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	0.001434
---- ZRH High vs. ZRH High Recovery for Female	0.023135
---- 3R4F High Recovery vs. ZRH High Recovery for Female	0.001658

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 36

Macrophage Colony-Stimulating Factor-1 (M-CSF-1)

Unit = ng/mL

Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = M_CSF_1

Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	0	10	0	0.01	.
Male	3	3R4F Low	10	10	0	10	0	0.01	.
Male	3	3R4F Medium	10	10	0	10	0	0.01	.
Male	3	3R4F High	10	10	0	10	0	0.01	.
Male	3	ZRH Low	10	10	0	10	0	0.01	.
Male	3	ZRH Medium	10	10	0	10	0	0.01	.
Male	3	ZRH High	10	10	0	10	0	0.01	.
Male	4.5	Sham Recovery	6	6	0	6	0	0.01	.
Male	4.5	3R4F High Recovery	5	5	0	5	0	0.01	.
Male	4.5	ZRH High Recovery	10	10	0	10	0	0.01	.
Female	3	Sham	10	10	0	10	0	0.01	.
Female	3	3R4F Low	10	10	0	10	0	0.01	.
Female	3	3R4F Medium	10	10	0	10	0	0.01	.
Female	3	3R4F High	9	9	0	9	0	0.01	.
Female	3	ZRH Low	9	9	0	9	0	0.01	.
Female	3	ZRH Medium	10	10	0	10	0	0.01	.
Female	3	ZRH High	10	10	0	10	0	0.01	.
Female	4.5	Sham Recovery	6	6	0	6	0	0.01	.
Female	4.5	3R4F High Recovery	6	6	0	6	0	0.01	.
Female	4.5	ZRH High Recovery	10	10	0	10	0	0.01	.

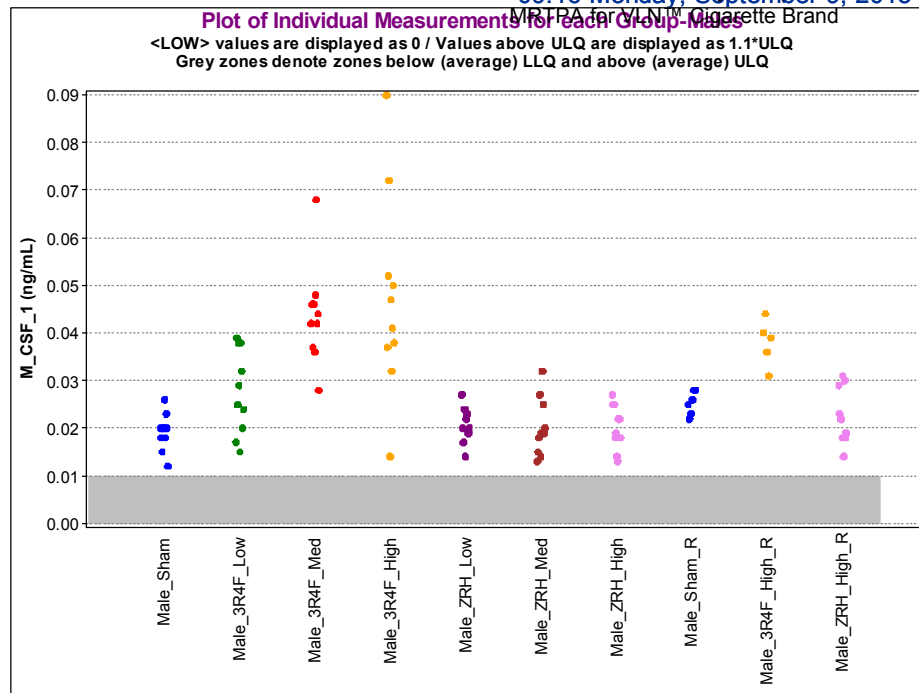
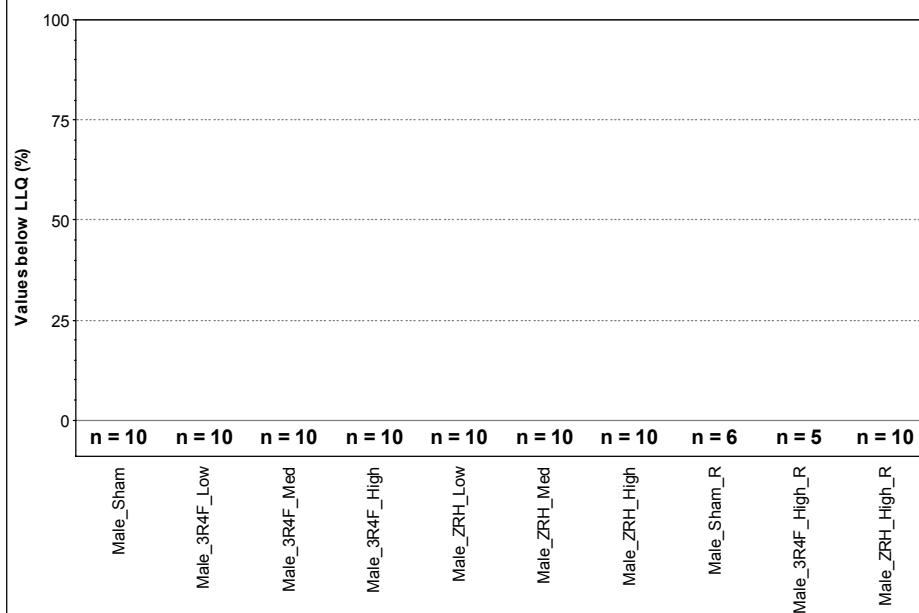
Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = M_CSF_1

Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	0.012	0.018	0.020	0.020	0.026	0.019	0.004	0.001	20.2	-0.189	0.805	0.01	.
Male	3	3R4F Low	0.015	0.020	0.027	0.038	0.039	0.028	0.009	0.003	32.2	-0.018	-1.511	0.01	.
Male	3	3R4F Medium	0.028	0.037	0.043	0.046	0.068	0.044	0.010	0.003	23.8	1.207	3.368	0.01	.
Male	3	3R4F High	0.014	0.037	0.044	0.052	0.090	0.047	0.021	0.007	44.8	0.736	1.084	0.01	.
Male	3	ZRH Low	0.014	0.019	0.020	0.023	0.027	0.021	0.004	0.001	18.0	0.033	0.284	0.01	.
Male	3	ZRH Medium	0.013	0.015	0.019	0.025	0.032	0.020	0.006	0.002	30.1	0.801	-0.053	0.01	.
Male	3	ZRH High	0.013	0.018	0.021	0.025	0.027	0.020	0.005	0.001	23.2	-0.195	-1.036	0.01	.
Male	4.5	Sham Recovery	0.022	0.023	0.026	0.028	0.028	0.025	0.003	0.001	9.9	-0.221	-1.715	0.01	.
Male	4.5	3R4F High Recovery	0.031	0.036	0.039	0.040	0.044	0.038	0.005	0.002	12.8	-0.461	0.443	0.01	.
Male	4.5	ZRH High Recovery	0.014	0.018	0.022	0.029	0.031	0.023	0.006	0.002	25.4	0.281	-1.082	0.01	.
Female	3	Sham	0.014	0.015	0.019	0.020	0.030	0.019	0.005	0.001	24.4	1.677	3.898	0.01	.
Female	3	3R4F Low	0.023	0.029	0.031	0.042	0.050	0.034	0.009	0.003	26.0	0.788	-0.245	0.01	.
Female	3	3R4F Medium	0.029	0.032	0.043	0.049	0.060	0.043	0.011	0.003	25.7	0.206	-1.263	0.01	.
Female	3	3R4F High	0.029	0.053	0.056	0.057	0.074	0.052	0.014	0.005	27.3	-0.690	0.375	0.01	.
Female	3	ZRH Low	0.015	0.019	0.021	0.022	0.026	0.021	0.004	0.001	17.2	0.103	-0.480	0.01	.
Female	3	ZRH Medium	0.015	0.020	0.022	0.025	0.026	0.022	0.003	0.001	15.8	-0.516	-0.040	0.01	.
Female	3	ZRH High	0.013	0.020	0.022	0.025	0.028	0.022	0.004	0.001	19.3	-0.733	1.137	0.01	.
Female	4.5	Sham Recovery	0.015	0.018	0.025	0.027	0.031	0.023	0.006	0.002	26.1	-0.244	-1.435	0.01	.
Female	4.5	3R4F High Recovery	0.022	0.028	0.039	0.040	0.044	0.035	0.008	0.003	23.9	-0.875	-0.644	0.01	.
Female	4.5	ZRH High Recovery	0.016	0.020	0.023	0.024	0.028	0.022	0.004	0.001	15.9	-0.220	0.117	0.01	.

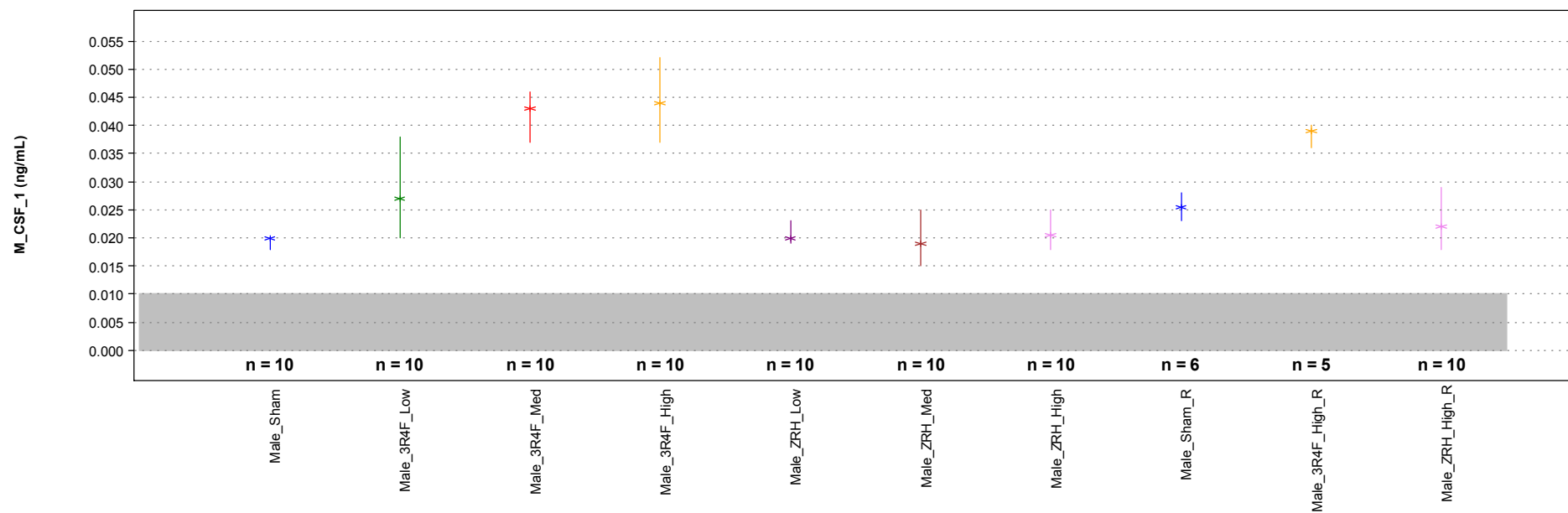
Percentage of Values below LLQ for each Group-Males

Analyte = M_CSF_1

**Plot of Descriptive Robust Statistics-Males**

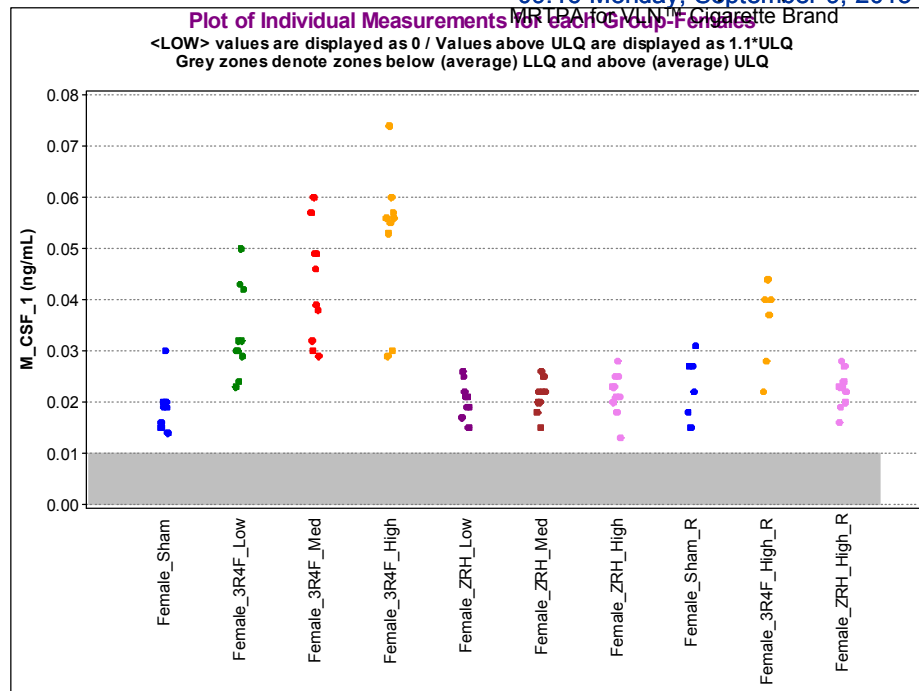
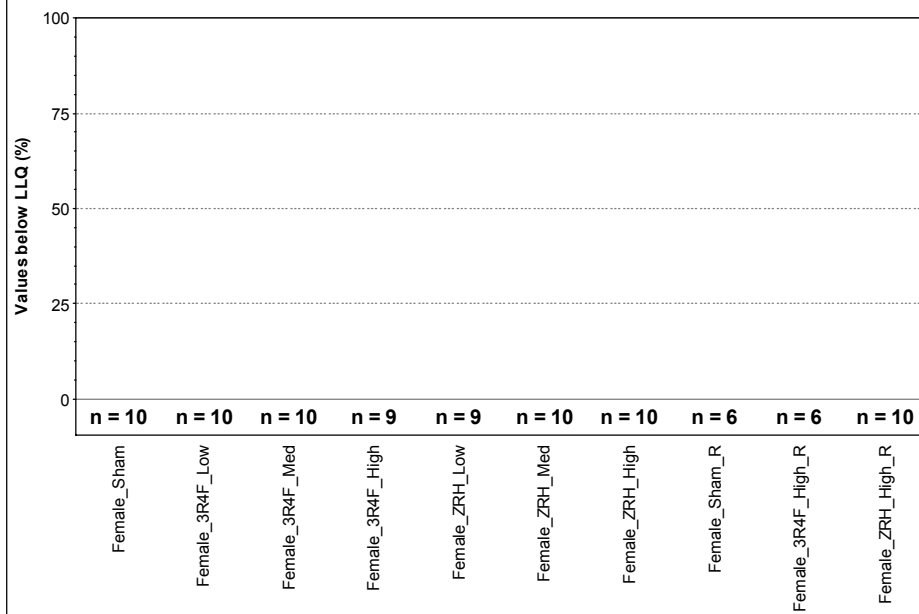
Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



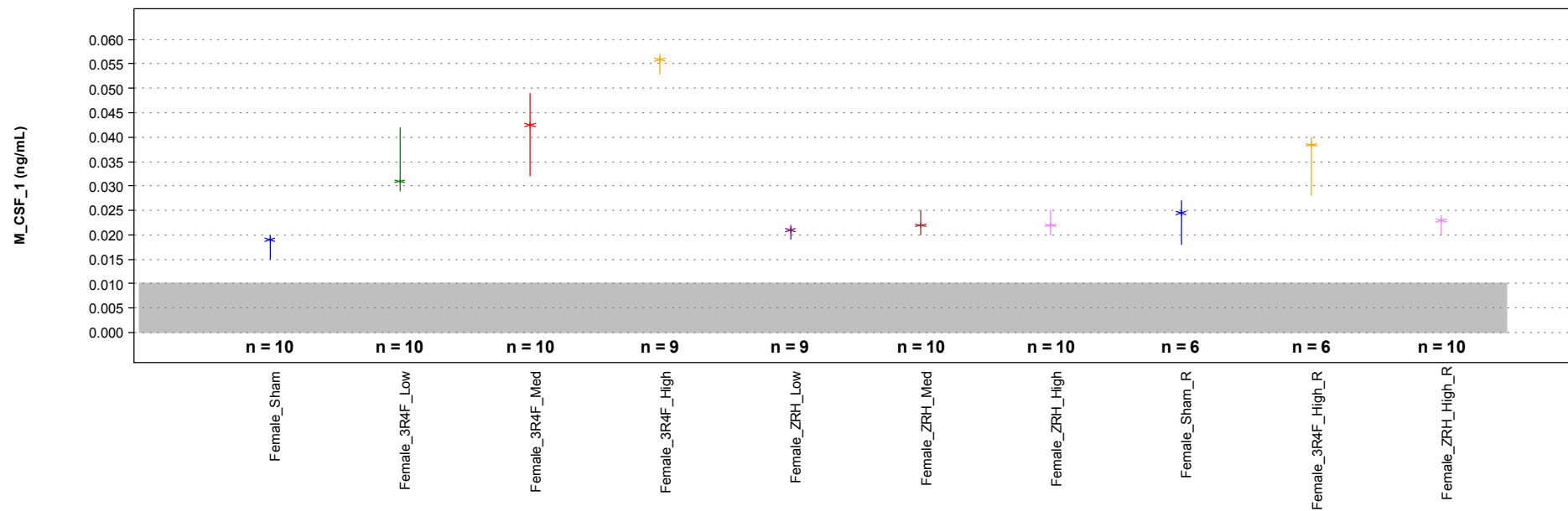
Percentage of Values below LLQ for each Group-Females

Analyte = M_CSF_1

**Plot of Descriptive Robust Statistics-Females**

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = M_CSF_1

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	0.035992
---- Sham vs. 3R4F Medium for Male	0.000146
---- Sham vs. 3R4F High for Male	0.001857
---- Sham vs. ZRH Low for Male	0.514453
---- Sham vs. ZRH Medium for Male	0.969551
---- Sham vs. ZRH High for Male	0.647415
---- ZRH Low vs. 3R4F Medium for Male	0.000153
---- ZRH Medium vs. 3R4F High for Male	0.001917
---- ZRH High vs. 3R4F High for Male	0.001679
---- Sham Recovery vs. 3R4F High Recovery for Male	0.006054
---- Sham Recovery vs. ZRH High Recovery for Male	0.300312
---- Sham vs. Sham Recovery for Male	0.006144
---- 3R4F High vs. 3R4F High Recovery for Male	0.270344
---- ZRH High vs. ZRH High Recovery for Male	0.401578
---- 3R4F High Recovery vs. ZRH High Recovery for Male	0.002624
---- Sham vs. 3R4F Low for Female	0.000480
---- Sham vs. 3R4F Medium for Female	0.000236
---- Sham vs. 3R4F High for Female	0.000365
---- Sham vs. ZRH Low for Female	0.187698
---- Sham vs. ZRH Medium for Female	0.055940
---- Sham vs. ZRH High for Female	0.062524
---- ZRH Low vs. 3R4F Medium for Female	0.000234
---- ZRH Medium vs. 3R4F High for Female	0.000228
---- ZRH High vs. 3R4F High for Female	0.000233
---- Sham Recovery vs. 3R4F High Recovery for Female	0.029768
---- Sham Recovery vs. ZRH High Recovery for Female	0.869900
---- Sham vs. Sham Recovery for Female	0.155453

Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = M_CSF_1

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	0.024885
---- ZRH High vs. ZRH High Recovery for Female	0.760262
---- 3R4F High Recovery vs. ZRH High Recovery for Female	0.012154

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 48

Myoglobin

Unit = ng/mL

Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = Myoglobin

Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	0	10	0	0.06	.
Male	3	3R4F Low	10	10	0	10	0	0.06	.
Male	3	3R4F Medium	10	10	0	10	0	0.06	.
Male	3	3R4F High	10	10	0	10	0	0.06	.
Male	3	ZRH Low	10	10	0	10	0	0.06	.
Male	3	ZRH Medium	10	10	0	10	0	0.06	.
Male	3	ZRH High	10	10	0	10	0	0.06	.
Male	4.5	Sham Recovery	6	6	0	6	0	0.06	.
Male	4.5	3R4F High Recovery	5	5	0	5	0	0.06	.
Male	4.5	ZRH High Recovery	10	10	0	10	0	0.06	.
Female	3	Sham	10	10	0	10	0	0.06	.
Female	3	3R4F Low	10	10	0	10	0	0.06	.
Female	3	3R4F Medium	10	10	0	10	0	0.06	.
Female	3	3R4F High	9	9	0	9	0	0.06	.
Female	3	ZRH Low	9	9	0	9	0	0.06	.
Female	3	ZRH Medium	10	10	0	10	0	0.06	.
Female	3	ZRH High	10	10	0	10	0	0.06	.
Female	4.5	Sham Recovery	6	6	0	6	0	0.06	.
Female	4.5	3R4F High Recovery	6	6	0	6	0	0.06	.
Female	4.5	ZRH High Recovery	10	10	0	10	0	0.06	.

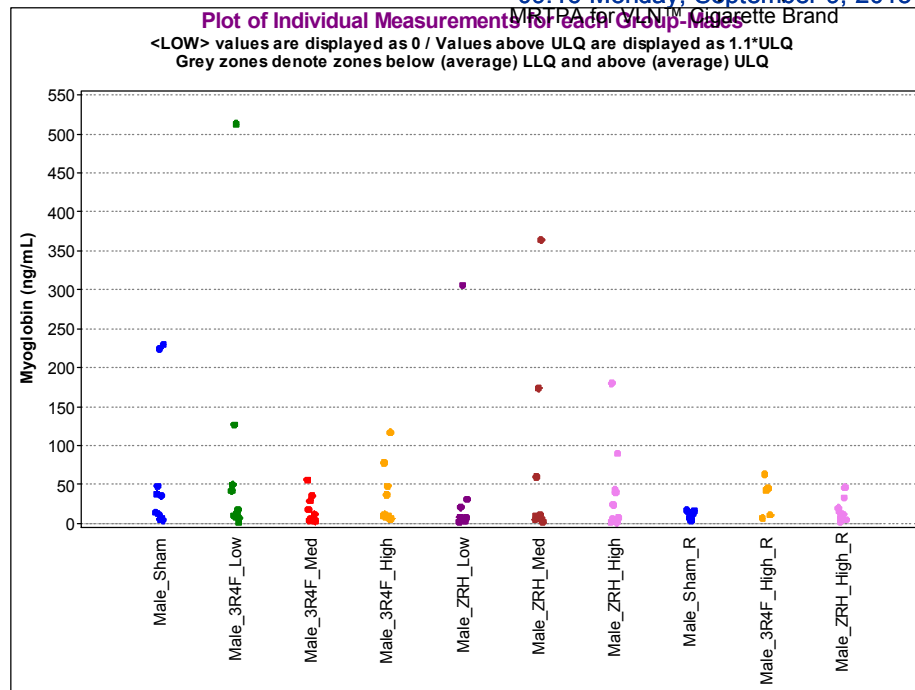
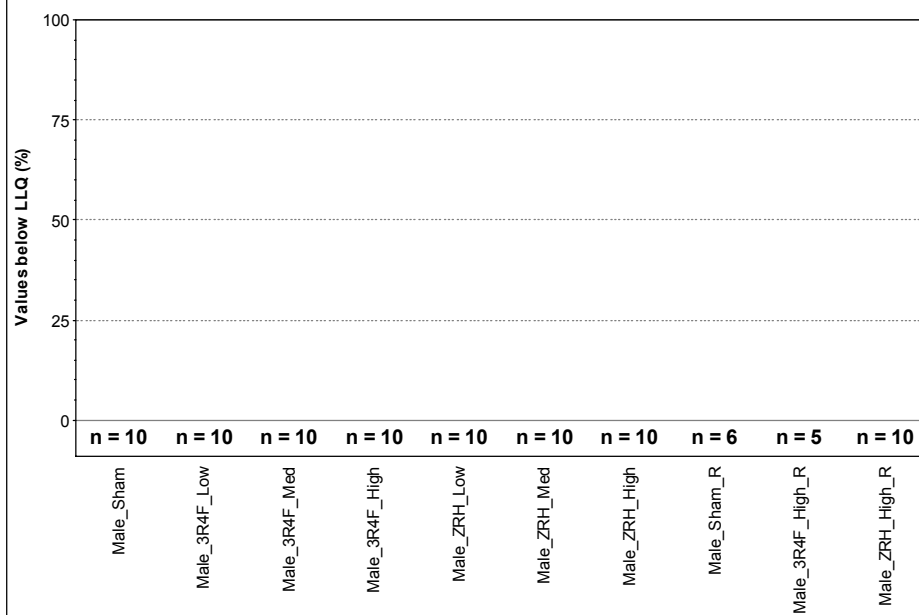
Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = Myoglobin

Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	4.300	6.200	25.000	48.000	230.000	61.750	88.450	27.970	143.2	1.651	1.142	0.06	.
Male	3	3R4F Low	2.100	8.800	16.000	50.000	513.000	79.140	156.941	49.629	198.3	2.863	8.462	0.06	.
Male	3	3R4F Medium	2.900	4.100	9.200	29.000	56.000	17.340	17.769	5.619	102.5	1.357	1.173	0.06	.
Male	3	3R4F High	5.900	7.700	11.000	48.000	117.000	33.150	37.902	11.986	114.3	1.510	1.564	0.06	.
Male	3	ZRH Low	2.100	3.900	7.100	21.000	306.000	39.410	94.119	29.763	238.8	3.108	9.737	0.06	.
Male	3	ZRH Medium	2.000	4.800	8.550	60.000	364.000	64.410	117.968	37.305	183.2	2.271	4.991	0.06	.
Male	3	ZRH High	1.300	3.300	15.550	43.000	180.000	39.570	56.727	17.939	143.4	2.025	4.173	0.06	.
Male	4.5	Sham Recovery	3.600	7.100	13.500	16.000	17.000	11.783	5.372	2.193	45.6	-0.775	-1.098	0.06	.
Male	4.5	3R4F High Recovery	6.800	11.000	43.000	45.000	63.000	33.760	24.039	10.751	71.2	-0.125	-2.195	0.06	.
Male	4.5	ZRH High Recovery	2.400	4.900	11.500	20.000	46.000	15.780	13.936	4.407	88.3	1.390	1.376	0.06	.
Female	3	Sham	6.700	8.800	12.500	27.000	157.000	29.480	45.705	14.453	155.0	2.942	8.940	0.06	.
Female	3	3R4F Low	1.800	7.500	16.000	20.000	83.000	20.390	22.996	7.272	112.8	2.664	7.803	0.06	.
Female	3	3R4F Medium	1.200	8.500	9.550	12.000	232.000	34.570	70.550	22.310	204.1	2.984	9.084	0.06	.
Female	3	3R4F High	6.000	9.100	13.000	26.000	208.000	41.189	66.009	22.003	160.3	2.511	6.450	0.06	.
Female	3	ZRH Low	1.400	8.000	12.000	20.000	402.000	60.200	129.738	43.246	215.5	2.872	8.377	0.06	.
Female	3	ZRH Medium	2.500	5.000	7.650	63.000	329.000	52.700	101.265	32.023	192.2	2.735	7.826	0.06	.
Female	3	ZRH High	2.500	10.000	17.000	35.000	138.000	29.590	39.824	12.594	134.6	2.688	7.750	0.06	.
Female	4.5	Sham Recovery	5.500	8.800	23.500	47.000	326.000	72.383	125.141	51.089	172.9	2.373	5.698	0.06	.
Female	4.5	3R4F High Recovery	6.300	7.100	15.500	65.000	100.000	34.900	38.854	15.862	111.3	1.228	0.038	0.06	.
Female	4.5	ZRH High Recovery	4.700	6.400	15.500	21.000	37.000	16.970	10.871	3.438	64.1	0.748	-0.206	0.06	.

Percentage of Values below LLQ for each Group-Males

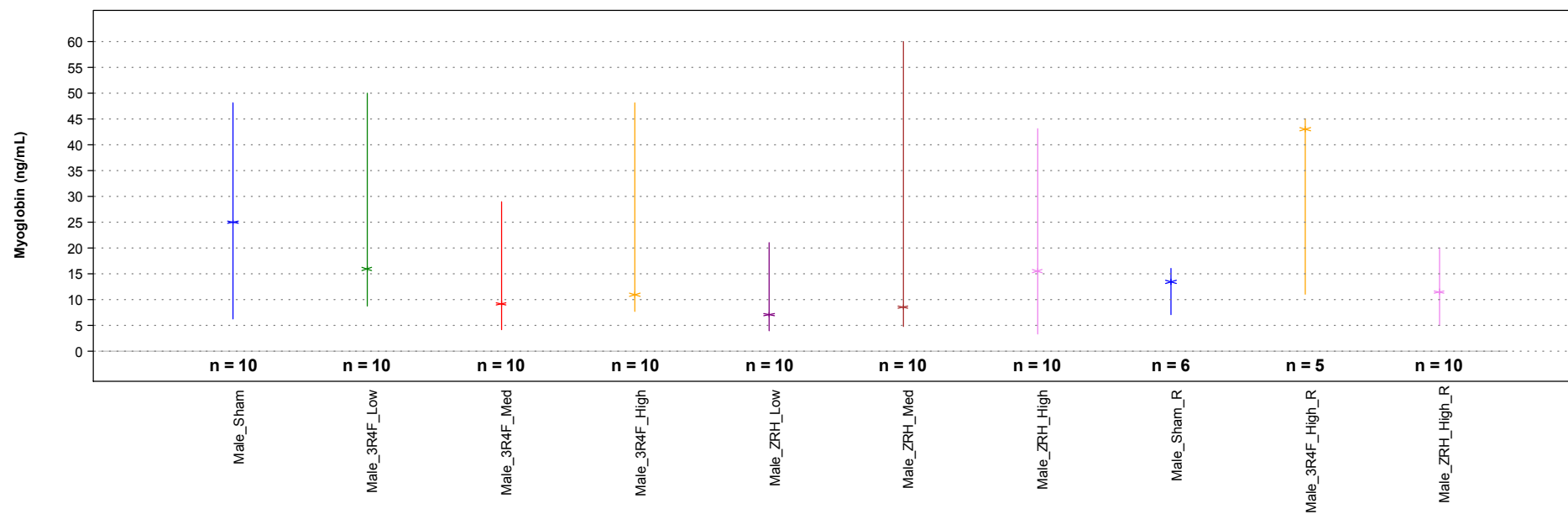
Analyte = Myoglobin



Plot of Descriptive Robust Statistics-Males

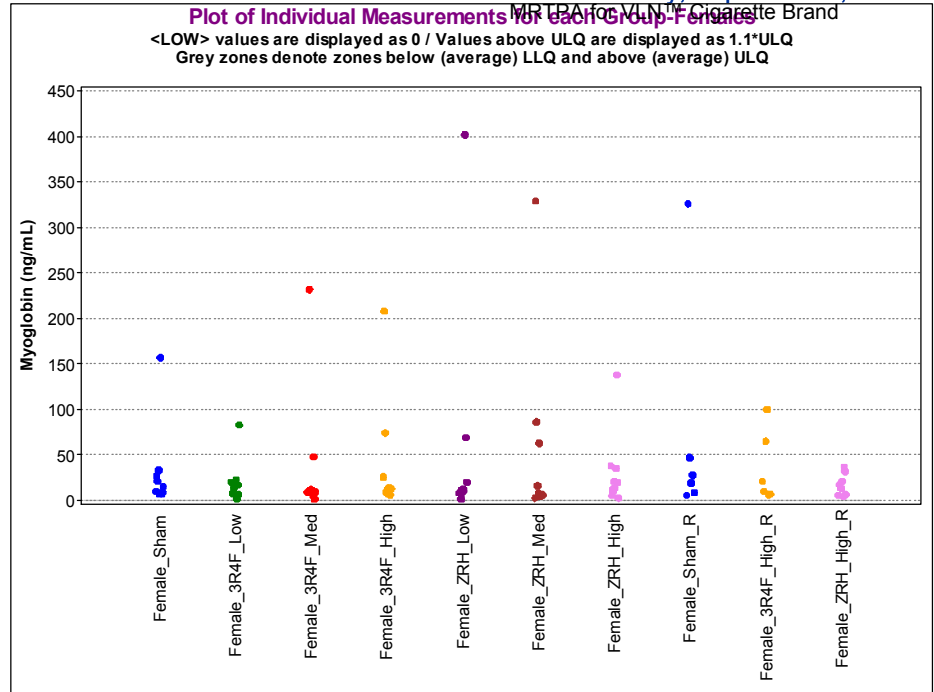
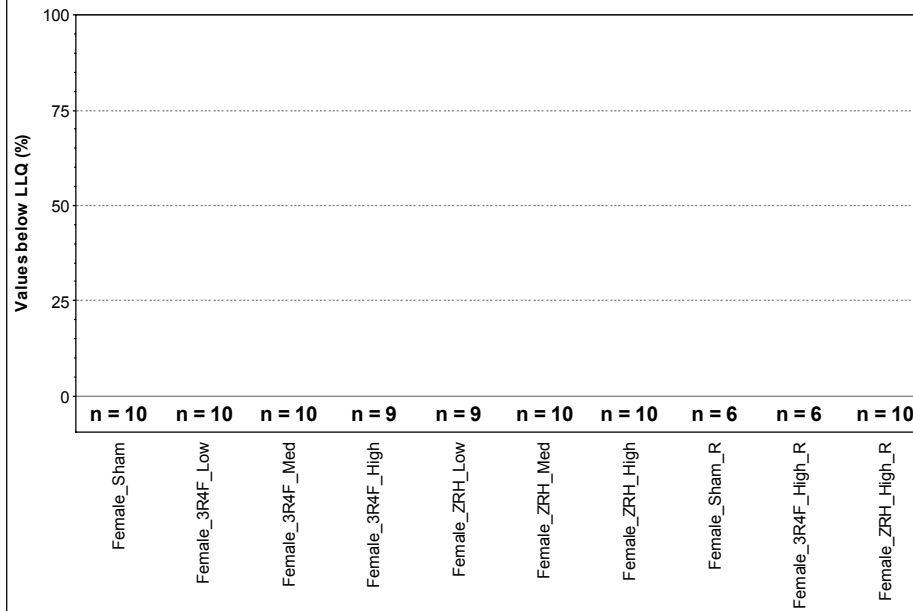
Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



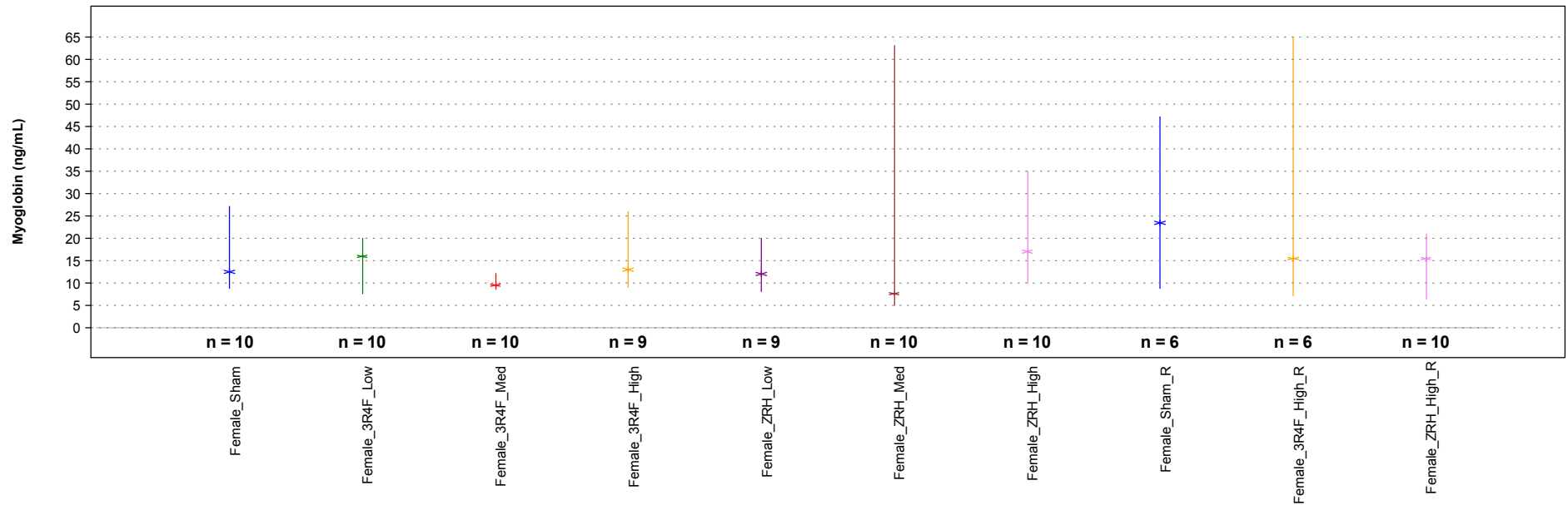
Percentage of Values below LLQ for each Group-Females

Analyte = Myoglobin

**Plot of Descriptive Robust Statistics-Females**

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = Myoglobin

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	0.909688
---- Sham vs. 3R4F Medium for Male	0.173294
---- Sham vs. 3R4F High for Male	0.762195
---- Sham vs. ZRH Low for Male	0.130570
---- Sham vs. ZRH Medium for Male	0.449521
---- Sham vs. ZRH High for Male	0.449692
---- ZRH Low vs. 3R4F Medium for Male	0.733634
---- ZRH Medium vs. 3R4F High for Male	0.520209
---- ZRH High vs. 3R4F High for Male	0.496292
---- Sham Recovery vs. 3R4F High Recovery for Male	0.273322
---- Sham Recovery vs. ZRH High Recovery for Male	0.913500
---- Sham vs. Sham Recovery for Male	0.356198
---- 3R4F High vs. 3R4F High Recovery for Male	0.624206
---- ZRH High vs. ZRH High Recovery for Male	0.820596
---- 3R4F High Recovery vs. ZRH High Recovery for Male	0.198048
---- Sham vs. 3R4F Low for Female	0.791260
---- Sham vs. 3R4F Medium for Female	0.545047
---- Sham vs. 3R4F High for Female	0.934897
---- Sham vs. ZRH Low for Female	0.870226
---- Sham vs. ZRH Medium for Female	0.364346
---- Sham vs. ZRH High for Female	0.762195
---- ZRH Low vs. 3R4F Medium for Female	0.512889
---- ZRH Medium vs. 3R4F High for Female	0.326975
---- ZRH High vs. 3R4F High for Female	0.967407
---- Sham Recovery vs. 3R4F High Recovery for Female	0.872780
---- Sham Recovery vs. ZRH High Recovery for Female	0.356198
---- Sham vs. Sham Recovery for Female	0.550509

Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = Myoglobin

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	0.906102
---- ZRH High vs. ZRH High Recovery for Female	0.705246
---- 3R4F High Recovery vs. ZRH High Recovery for Female	0.550509

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 49

Oncostatin-M (OSM)

Unit = ng/mL

Descriptive Statistics by Exposure Duration and Treatment Type

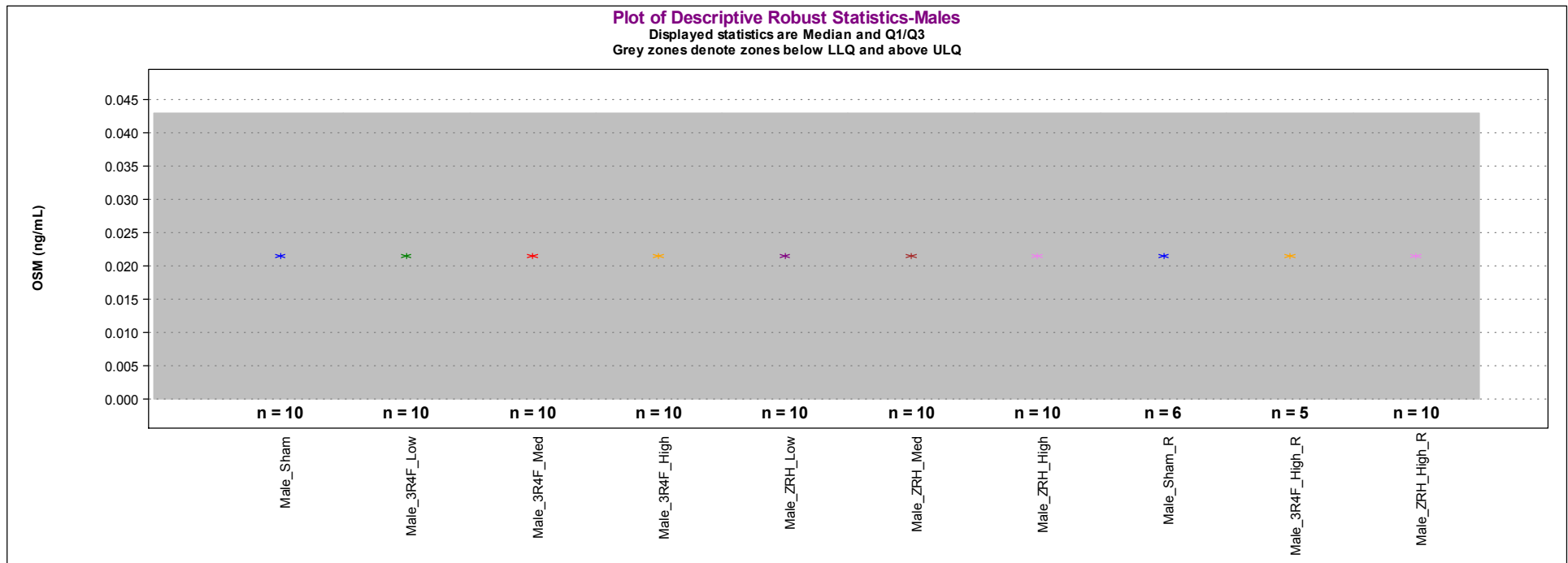
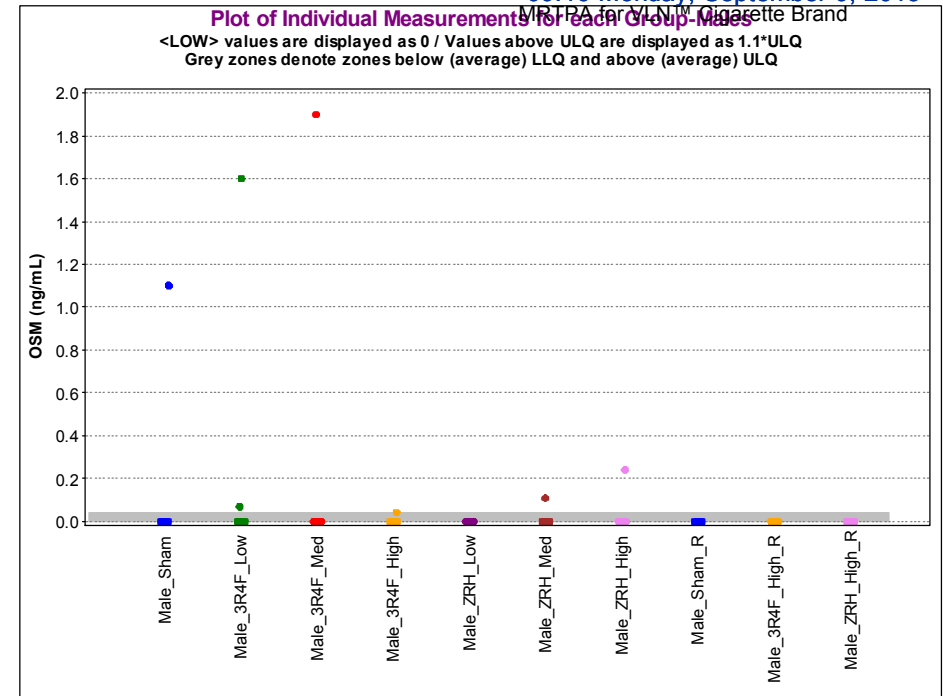
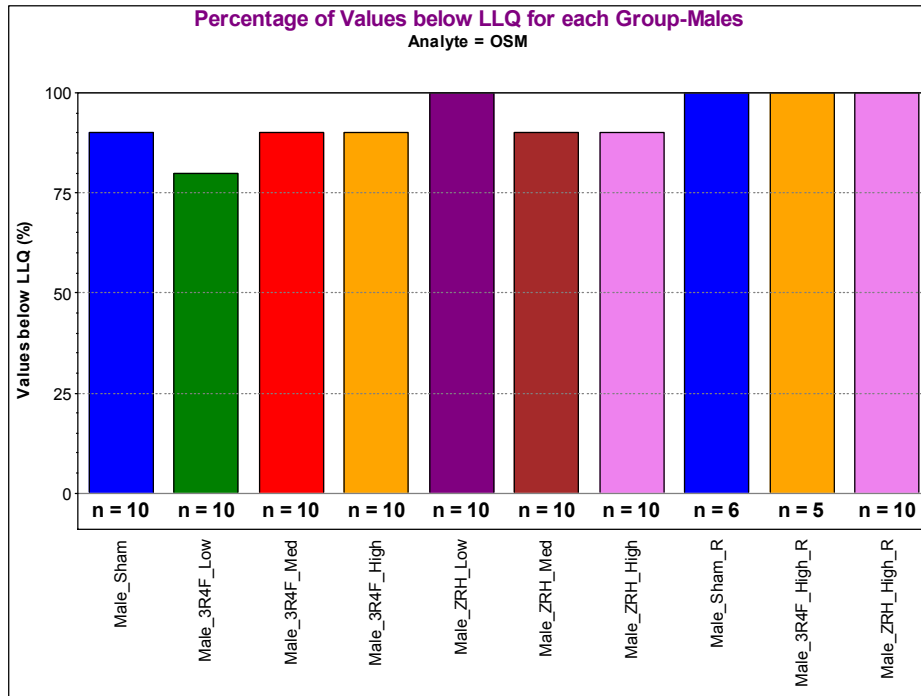
Analyte = OSM

Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	9	1	0	0.043	.
Male	3	3R4F Low	10	10	8	2	0	0.043	.
Male	3	3R4F Medium	10	10	9	1	0	0.043	.
Male	3	3R4F High	10	10	9	1	0	0.043	.
Male	3	ZRH Low	10	10	10	0	0	0.043	.
Male	3	ZRH Medium	10	10	9	1	0	0.043	.
Male	3	ZRH High	10	10	9	1	0	0.043	.
Male	4.5	Sham Recovery	6	6	6	0	0	0.043	.
Male	4.5	3R4F High Recovery	5	5	5	0	0	0.043	.
Male	4.5	ZRH High Recovery	10	10	10	0	0	0.043	.
Female	3	Sham	10	10	9	1	0	0.043	.
Female	3	3R4F Low	10	10	9	1	0	0.043	.
Female	3	3R4F Medium	10	10	9	1	0	0.043	.
Female	3	3R4F High	9	9	7	2	0	0.043	.
Female	3	ZRH Low	9	9	8	1	0	0.043	.
Female	3	ZRH Medium	10	10	9	1	0	0.043	.
Female	3	ZRH High	10	10	9	1	0	0.043	.
Female	4.5	Sham Recovery	6	6	4	2	0	0.043	.
Female	4.5	3R4F High Recovery	6	6	5	1	0	0.043	.
Female	4.5	ZRH High Recovery	10	10	10	0	0	0.043	.

Descriptive Statistics by Exposure Duration and Treatment Type

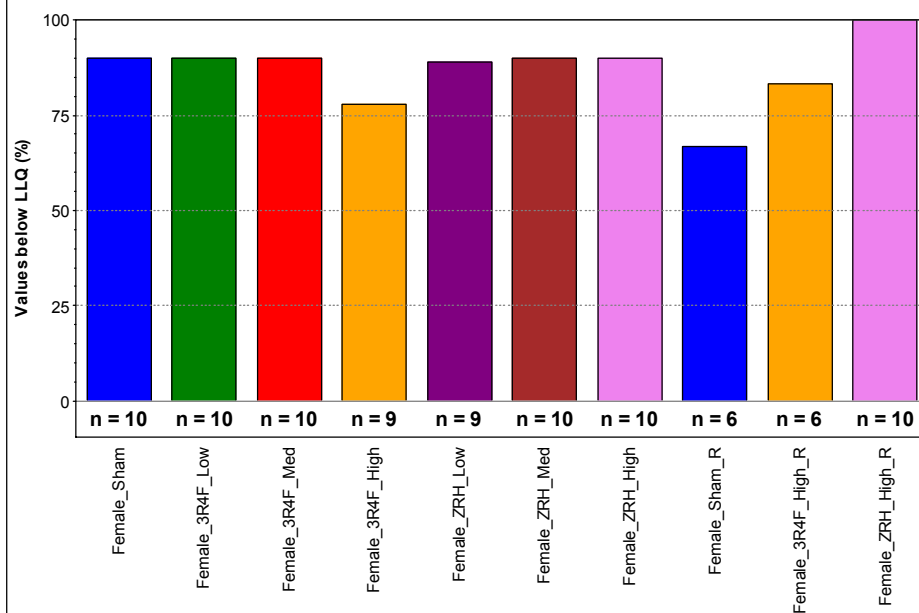
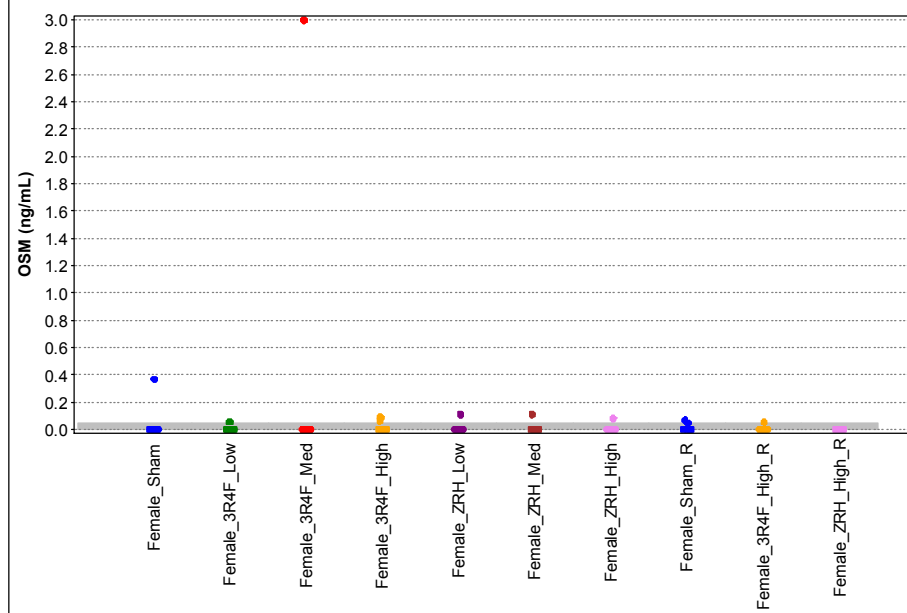
Analyte = OSM

Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	0.022	0.022	0.022	0.022	1.100	0.129	0.341	0.108	263.7	3.162	10.000	0.043	.
Male	3	3R4F Low	0.022	0.022	0.022	0.022	1.600	0.184	0.498	0.157	270.2	3.157	9.974	0.043	.
Male	3	3R4F Medium	0.022	0.022	0.022	0.022	1.900	0.209	0.594	0.188	283.8	3.162	10.000	0.043	.
Male	3	3R4F High	0.022	0.022	0.022	0.022	0.043	0.024	0.007	0.002	28.7	3.162	10.000	0.043	.
Male	3	ZRH Low	0.022	0.022	0.022	0.022	0.022	0.021	0.000	0.000	0.0	.	.	0.043	.
Male	3	ZRH Medium	0.022	0.022	0.022	0.022	0.110	0.030	0.028	0.009	92.2	3.162	10.000	0.043	.
Male	3	ZRH High	0.022	0.022	0.022	0.022	0.240	0.043	0.069	0.022	159.4	3.162	10.000	0.043	.
Male	4.5	Sham Recovery	0.022	0.022	0.022	0.022	0.022	0.021	0.000	0.000	0.0	.	.	0.043	.
Male	4.5	3R4F High Recovery	0.022	0.022	0.022	0.022	0.022	0.022	0.000	0.000	0.0	.	.	0.043	.
Male	4.5	ZRH High Recovery	0.022	0.022	0.022	0.022	0.022	0.021	0.000	0.000	0.0	.	.	0.043	.
Female	3	Sham	0.022	0.022	0.022	0.022	0.370	0.056	0.110	0.035	195.6	3.162	10.000	0.043	.
Female	3	3R4F Low	0.022	0.022	0.022	0.022	0.055	0.025	0.011	0.003	42.6	3.162	10.000	0.043	.
Female	3	3R4F Medium	0.022	0.022	0.022	0.022	3.000	0.319	0.942	0.298	294.9	3.162	10.000	0.043	.
Female	3	3R4F High	0.022	0.022	0.022	0.022	0.089	0.034	0.025	0.008	74.5	1.859	2.317	0.043	.
Female	3	ZRH Low	0.022	0.022	0.022	0.022	0.110	0.031	0.030	0.010	94.1	3.000	9.000	0.043	.
Female	3	ZRH Medium	0.022	0.022	0.022	0.022	0.110	0.030	0.028	0.009	92.2	3.162	10.000	0.043	.
Female	3	ZRH High	0.022	0.022	0.022	0.022	0.080	0.027	0.018	0.006	67.6	3.162	10.000	0.043	.
Female	4.5	Sham Recovery	0.022	0.022	0.022	0.047	0.069	0.034	0.020	0.008	59.7	1.453	0.958	0.043	.
Female	4.5	3R4F High Recovery	0.022	0.022	0.022	0.022	0.052	0.027	0.012	0.005	46.8	2.449	6.000	0.043	.
Female	4.5	ZRH High Recovery	0.022	0.022	0.022	0.022	0.022	0.021	0.000	0.000	0.0	.	.	0.043	.



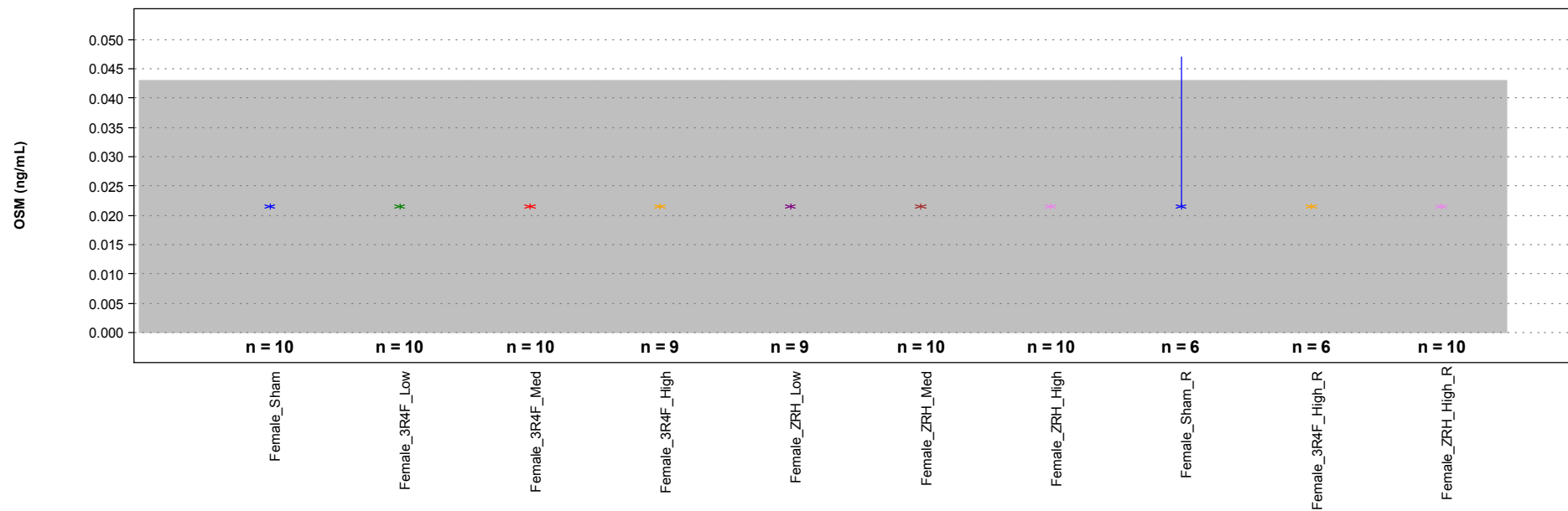
Percentage of Values below LLQ for each Group-Females

Analyte = OSM

**Plot of Individual Measurements for each Group-Females**
 <LOW> values are displayed as 0 / Values above ULQ are displayed as 1.1*ULQ
 Grey zones denote zones below (average) LLQ and above (average) ULQ**Plot of Descriptive Robust Statistics-Females**

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = OSM

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	0.543195
---- Sham vs. 3R4F Medium for Male	0.942166
---- Sham vs. 3R4F High for Male	0.942166
---- Sham vs. ZRH Low for Male	0.317311
---- Sham vs. ZRH Medium for Male	0.942166
---- Sham vs. ZRH High for Male	0.942166
---- ZRH Low vs. 3R4F Medium for Male	0.317311
---- ZRH Medium vs. 3R4F High for Male	0.942166
---- ZRH High vs. 3R4F High for Male	0.942166
---- Sham Recovery vs. 3R4F High Recovery for Male	1.000000
---- Sham Recovery vs. ZRH High Recovery for Male	1.000000
---- Sham vs. Sham Recovery for Male	0.438578
---- 3R4F High vs. 3R4F High Recovery for Male	0.479500
---- ZRH High vs. ZRH High Recovery for Male	0.317311
---- 3R4F High Recovery vs. ZRH High Recovery for Male	1.000000
---- Sham vs. 3R4F Low for Female	0.942166
---- Sham vs. 3R4F Medium for Female	0.942166
---- Sham vs. 3R4F High for Female	0.562983
---- Sham vs. ZRH Low for Female	1.000000
---- Sham vs. ZRH Medium for Female	0.942166
---- Sham vs. ZRH High for Female	0.942166
---- ZRH Low vs. 3R4F Medium for Female	1.000000
---- ZRH Medium vs. 3R4F High for Female	0.562983
---- ZRH High vs. 3R4F High for Female	0.479596
---- Sham Recovery vs. 3R4F High Recovery for Female	0.528336
---- Sham Recovery vs. ZRH High Recovery for Female	0.059346
---- Sham vs. Sham Recovery for Female	0.339745

Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = OSM

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	0.673606
---- ZRH High vs. ZRH High Recovery for Female	0.317311
---- 3R4F High Recovery vs. ZRH High Recovery for Female	0.196706

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 50

Plasminogen Activator Inhibitor 1 (PAI-1)

Unit = ng/mL

Descriptive Statistics by Exposure Duration and Treatment Type**Analyte = PAI_1**

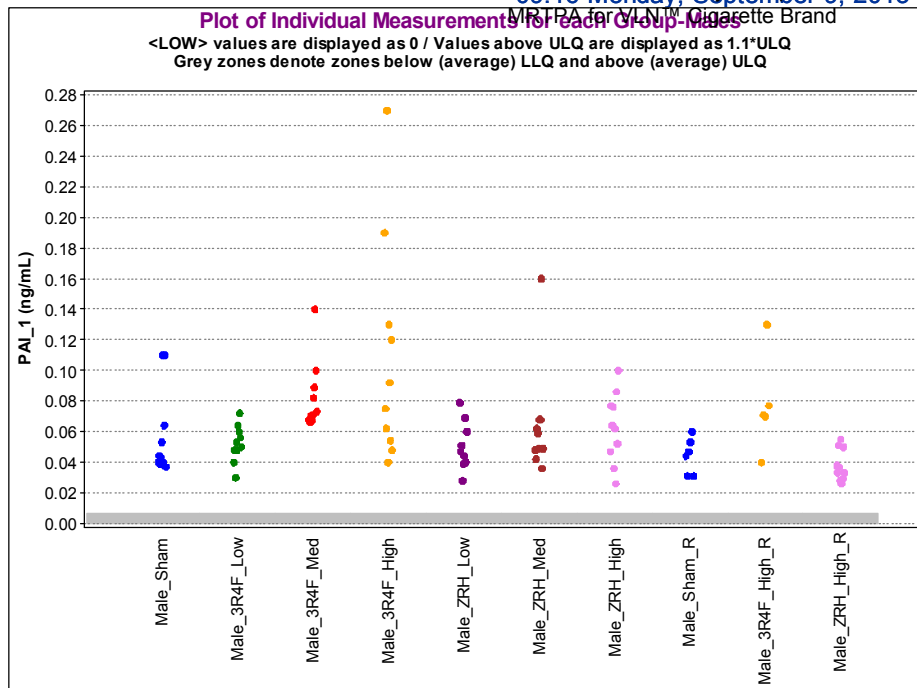
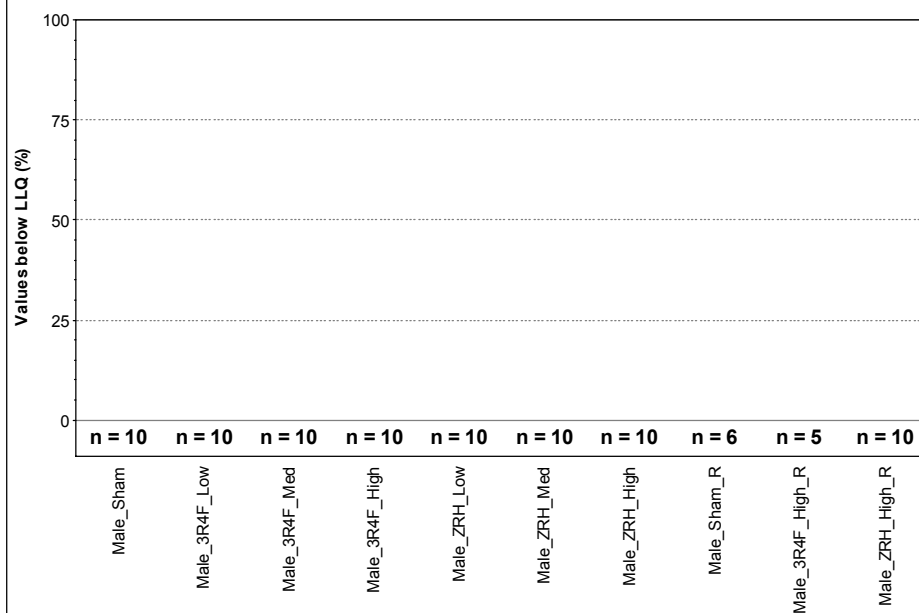
Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	0	10	0	0.007	.
Male	3	3R4F Low	10	10	0	10	0	0.007	.
Male	3	3R4F Medium	10	10	0	10	0	0.007	.
Male	3	3R4F High	10	10	0	10	0	0.007	.
Male	3	ZRH Low	10	10	0	10	0	0.007	.
Male	3	ZRH Medium	10	10	0	10	0	0.007	.
Male	3	ZRH High	10	10	0	10	0	0.007	.
Male	4.5	Sham Recovery	6	6	0	6	0	0.007	.
Male	4.5	3R4F High Recovery	5	5	0	5	0	0.007	.
Male	4.5	ZRH High Recovery	10	10	0	10	0	0.007	.
Female	3	Sham	10	10	0	10	0	0.007	.
Female	3	3R4F Low	10	10	0	10	0	0.007	.
Female	3	3R4F Medium	10	10	0	10	0	0.007	.
Female	3	3R4F High	9	9	0	9	0	0.007	.
Female	3	ZRH Low	9	9	0	9	0	0.007	.
Female	3	ZRH Medium	10	10	0	10	0	0.007	.
Female	3	ZRH High	10	10	0	10	0	0.007	.
Female	4.5	Sham Recovery	6	6	0	6	0	0.007	.
Female	4.5	3R4F High Recovery	6	6	0	6	0	0.007	.
Female	4.5	ZRH High Recovery	10	10	0	10	0	0.007	.

Descriptive Statistics by Exposure Duration and Treatment Type**Analyte = PAI_1**

Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	0.037	0.040	0.044	0.064	0.110	0.058	0.029	0.009	49.2	1.475	0.664	0.007	.
Male	3	3R4F Low	0.030	0.048	0.052	0.060	0.072	0.052	0.012	0.004	23.0	-0.210	0.360	0.007	.
Male	3	3R4F Medium	0.066	0.068	0.072	0.089	0.140	0.083	0.023	0.007	27.8	2.043	4.398	0.007	.
Male	3	3R4F High	0.040	0.054	0.084	0.130	0.270	0.108	0.073	0.023	67.7	1.409	1.606	0.007	.
Male	3	ZRH Low	0.028	0.040	0.049	0.060	0.079	0.052	0.015	0.005	29.7	0.350	-0.347	0.007	.
Male	3	ZRH Medium	0.036	0.048	0.054	0.068	0.160	0.064	0.035	0.011	55.2	2.633	7.618	0.007	.
Male	3	ZRH High	0.026	0.047	0.063	0.077	0.100	0.063	0.023	0.007	36.7	-0.027	-0.640	0.007	.
Male	4.5	Sham Recovery	0.031	0.031	0.046	0.053	0.060	0.044	0.012	0.005	26.4	-0.042	-1.410	0.007	.
Male	4.5	3R4F High Recovery	0.040	0.070	0.071	0.077	0.130	0.078	0.033	0.015	42.1	1.078	2.511	0.007	.
Male	4.5	ZRH High Recovery	0.026	0.029	0.035	0.050	0.055	0.038	0.010	0.003	27.4	0.629	-1.172	0.007	.
Female	3	Sham	0.026	0.028	0.029	0.037	0.047	0.033	0.007	0.002	20.9	1.172	0.557	0.007	.
Female	3	3R4F Low	0.028	0.036	0.049	0.057	0.078	0.049	0.015	0.005	30.6	0.558	0.332	0.007	.
Female	3	3R4F Medium	0.029	0.053	0.067	0.074	0.098	0.065	0.020	0.006	30.3	-0.061	0.381	0.007	.
Female	3	3R4F High	0.042	0.084	0.096	0.110	0.120	0.089	0.026	0.009	29.4	-0.867	-0.183	0.007	.
Female	3	ZRH Low	0.025	0.039	0.044	0.063	0.095	0.050	0.022	0.007	42.8	1.148	1.195	0.007	.
Female	3	ZRH Medium	0.024	0.032	0.039	0.048	0.100	0.049	0.028	0.009	56.5	1.516	0.898	0.007	.
Female	3	ZRH High	0.033	0.045	0.047	0.068	0.100	0.056	0.019	0.006	34.6	1.459	2.436	0.007	.
Female	4.5	Sham Recovery	0.025	0.025	0.029	0.035	0.036	0.030	0.005	0.002	16.5	0.472	-2.051	0.007	.
Female	4.5	3R4F High Recovery	0.061	0.062	0.071	0.085	0.150	0.083	0.034	0.014	40.7	2.073	4.476	0.007	.
Female	4.5	ZRH High Recovery	0.023	0.035	0.050	0.061	0.075	0.048	0.016	0.005	33.3	0.120	-0.632	0.007	.

Percentage of Values below LLQ for each Group-Males

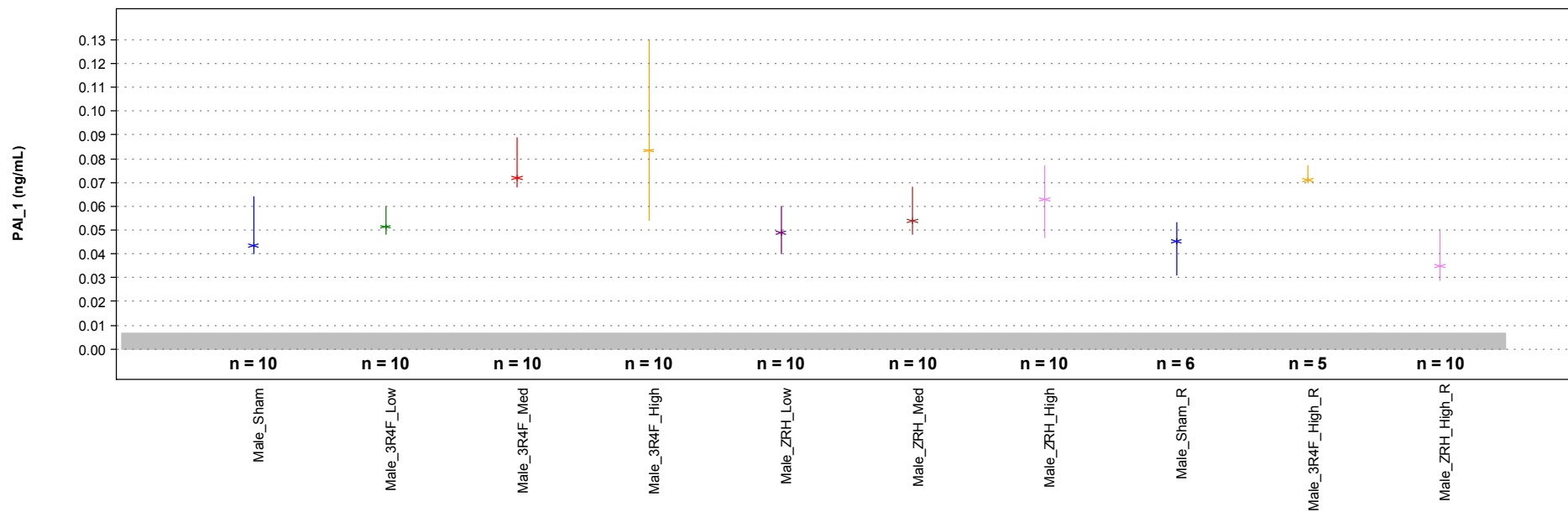
Analyte = PAI_1



Plot of Descriptive Robust Statistics-Males

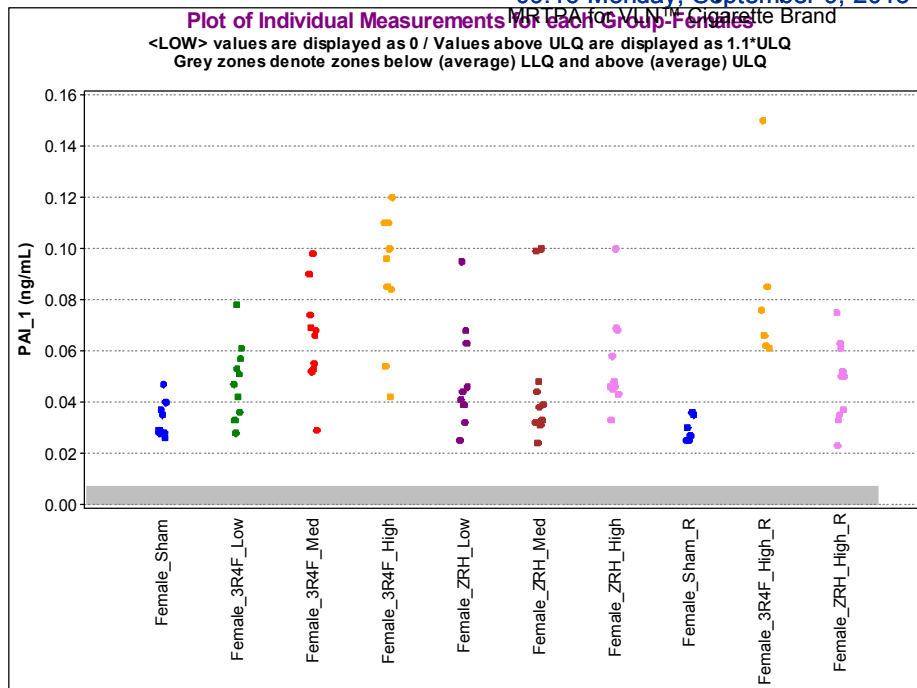
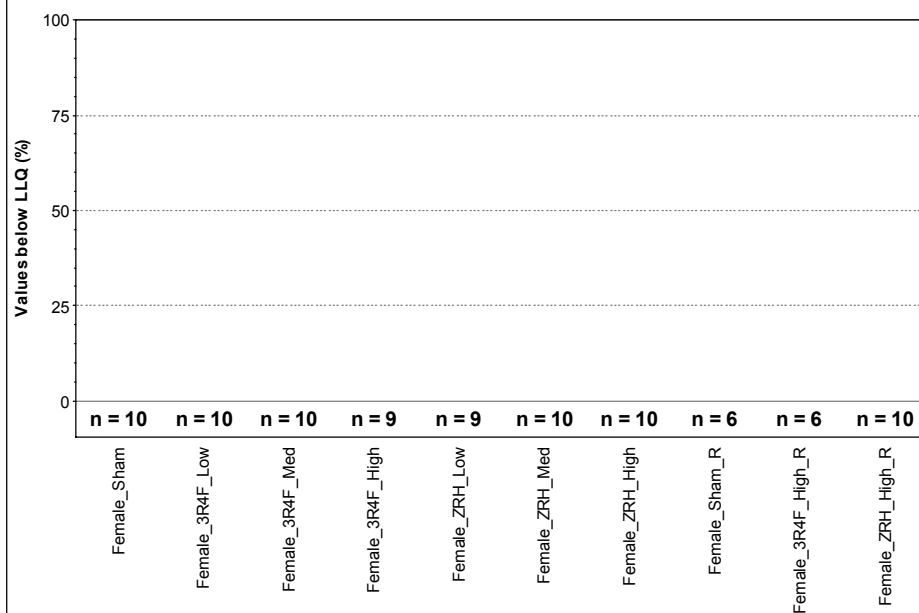
Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



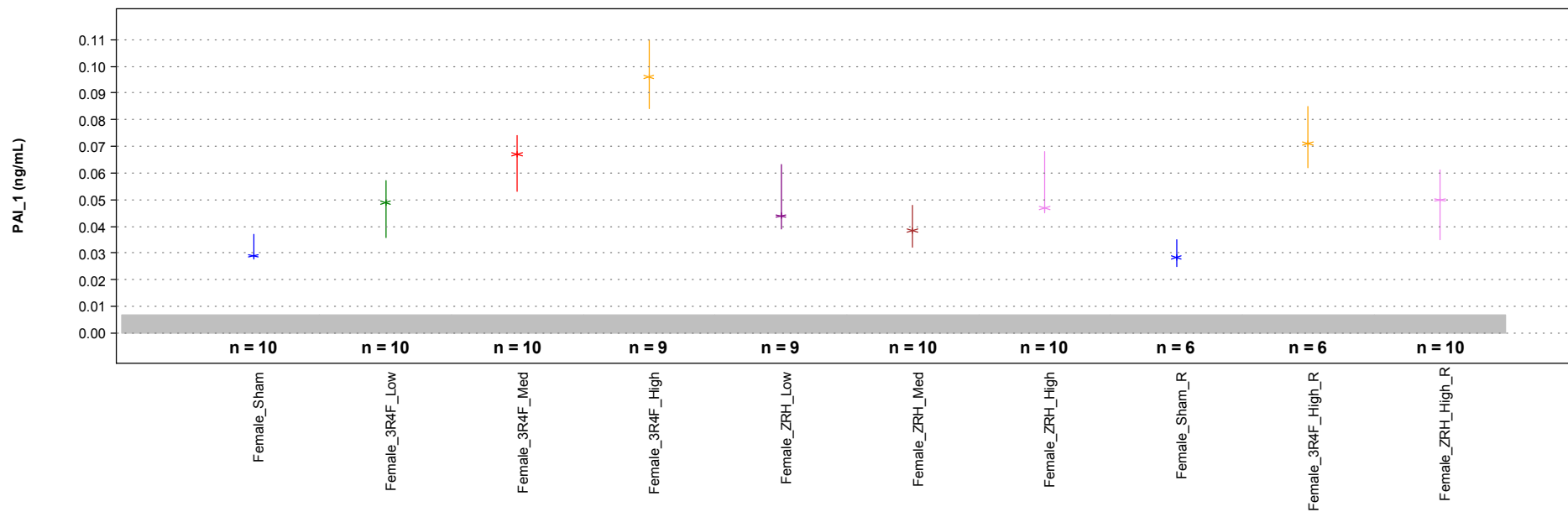
Percentage of Values below LLQ for each Group-Females

Analyte = PAI_1

**Plot of Descriptive Robust Statistics-Females**

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = PAI_1

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	0.595593
---- Sham vs. 3R4F Medium for Male	0.015487
---- Sham vs. 3R4F High for Male	0.028069
---- Sham vs. ZRH Low for Male	0.879469
---- Sham vs. ZRH Medium for Male	0.363624
---- Sham vs. ZRH High for Male	0.520052
---- ZRH Low vs. 3R4F Medium for Male	0.001932
---- ZRH Medium vs. 3R4F High for Male	0.111870
---- ZRH High vs. 3R4F High for Male	0.161815
---- Sham Recovery vs. 3R4F High Recovery for Male	0.044126
---- Sham Recovery vs. ZRH High Recovery for Male	0.328259
---- Sham vs. Sham Recovery for Male	0.586214
---- 3R4F High vs. 3R4F High Recovery for Male	0.623586
---- ZRH High vs. ZRH High Recovery for Male	0.017174
---- 3R4F High Recovery vs. ZRH High Recovery for Male	0.007000
---- Sham vs. 3R4F Low for Female	0.009828
---- Sham vs. 3R4F Medium for Female	0.000645
---- Sham vs. 3R4F High for Female	0.000316
---- Sham vs. ZRH Low for Female	0.033373
---- Sham vs. ZRH Medium for Female	0.081524
---- Sham vs. ZRH High for Female	0.001462
---- ZRH Low vs. 3R4F Medium for Female	0.079048
---- ZRH Medium vs. 3R4F High for Female	0.007909
---- ZRH High vs. 3R4F High for Female	0.019802
---- Sham Recovery vs. 3R4F High Recovery for Female	0.003885
---- Sham Recovery vs. ZRH High Recovery for Female	0.025850
---- Sham vs. Sham Recovery for Female	0.300312

Unadjusted P-values Obtained by Kruskal-Wallis Test
Analyte = PAI_1

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	0.442841
---- ZRH High vs. ZRH High Recovery for Female	0.622784
---- 3R4F High Recovery vs. ZRH High Recovery for Female	0.007784

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 54

T-Cell-Specific Protein RANTES (RANTES)

Unit = pg/mL

Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = RANTES

Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	9	1	0	0.006	.
Male	3	3R4F Low	10	10	9	1	0	0.006	.
Male	3	3R4F Medium	10	10	9	1	0	0.006	.
Male	3	3R4F High	10	10	10	0	0	0.006	.
Male	3	ZRH Low	10	10	10	0	0	0.006	.
Male	3	ZRH Medium	10	10	10	0	0	0.006	.
Male	3	ZRH High	10	10	9	1	0	0.006	.
Male	4.5	Sham Recovery	6	6	6	0	0	0.006	.
Male	4.5	3R4F High Recovery	5	5	5	0	0	0.006	.
Male	4.5	ZRH High Recovery	10	10	10	0	0	0.006	.
Female	3	Sham	10	10	9	1	0	0.006	.
Female	3	3R4F Low	10	10	10	0	0	0.006	.
Female	3	3R4F Medium	10	10	9	1	0	0.006	.
Female	3	3R4F High	9	9	8	1	0	0.006	.
Female	3	ZRH Low	9	9	9	0	0	0.006	.
Female	3	ZRH Medium	10	10	10	0	0	0.006	.
Female	3	ZRH High	10	10	10	0	0	0.006	.
Female	4.5	Sham Recovery	6	6	6	0	0	0.006	.
Female	4.5	3R4F High Recovery	6	6	6	0	0	0.006	.
Female	4.5	ZRH High Recovery	10	10	10	0	0	0.006	.

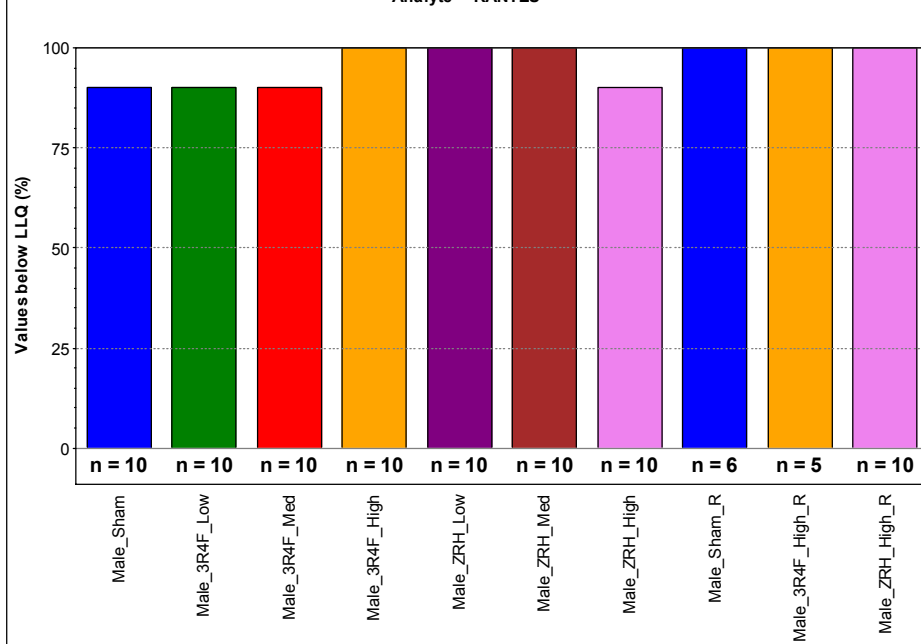
Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = RANTES

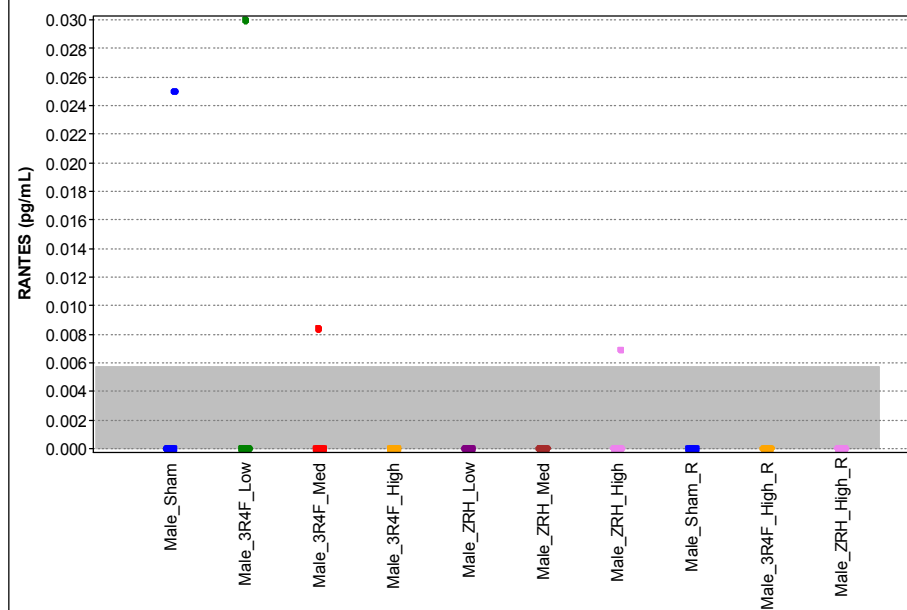
Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	0.003	0.003	0.003	0.003	0.025	0.005	0.007	0.002	138.3	3.162	10.000	0.006	.
Male	3	3R4F Low	0.003	0.003	0.003	0.003	0.030	0.006	0.009	0.003	154.3	3.162	10.000	0.006	.
Male	3	3R4F Medium	0.003	0.003	0.003	0.003	0.008	0.003	0.002	0.001	51.5	3.162	10.000	0.006	.
Male	3	3R4F High	0.003	0.003	0.003	0.003	0.003	0.003	0.000	0.000	0.0	.	.	0.006	.
Male	3	ZRH Low	0.003	0.003	0.003	0.003	0.003	0.003	0.000	0.000	0.0	.	.	0.006	.
Male	3	ZRH Medium	0.003	0.003	0.003	0.003	0.003	0.003	0.000	0.000	0.0	.	.	0.006	.
Male	3	ZRH High	0.003	0.003	0.003	0.003	0.007	0.003	0.001	0.000	39.3	3.162	10.000	0.006	.
Male	4.5	Sham Recovery	0.003	0.003	0.003	0.003	0.003	0.003	0.000	0.000	0.0	.	.	0.006	.
Male	4.5	3R4F High Recovery	0.003	0.003	0.003	0.003	0.003	0.003	0.000	0.000	0.0	.	.	0.006	.
Male	4.5	ZRH High Recovery	0.003	0.003	0.003	0.003	0.003	0.003	0.000	0.000	0.0	.	.	0.006	.
Female	3	Sham	0.003	0.003	0.003	0.003	0.009	0.003	0.002	0.001	55.4	3.162	10.000	0.006	.
Female	3	3R4F Low	0.003	0.003	0.003	0.003	0.003	0.003	0.000	0.000	0.0	.	.	0.006	.
Female	3	3R4F Medium	0.003	0.003	0.003	0.003	0.046	0.007	0.014	0.004	190.4	3.162	10.000	0.006	.
Female	3	3R4F High	0.003	0.003	0.003	0.003	0.006	0.003	0.001	0.000	32.8	3.000	9.000	0.006	.
Female	3	ZRH Low	0.003	0.003	0.003	0.003	0.003	0.003	0.000	0.000	0.0	.	.	0.006	.
Female	3	ZRH Medium	0.003	0.003	0.003	0.003	0.003	0.003	0.000	0.000	0.0	.	.	0.006	.
Female	3	ZRH High	0.003	0.003	0.003	0.003	0.003	0.003	0.000	0.000	0.0	.	.	0.006	.
Female	4.5	Sham Recovery	0.003	0.003	0.003	0.003	0.003	0.003	0.000	0.000	0.0	.	.	0.006	.
Female	4.5	3R4F High Recovery	0.003	0.003	0.003	0.003	0.003	0.003	0.000	0.000	0.0	.	.	0.006	.
Female	4.5	ZRH High Recovery	0.003	0.003	0.003	0.003	0.003	0.003	0.000	0.000	0.0	.	.	0.006	.

Percentage of Values below LLQ for each Group-Males

Analyte = RANTES

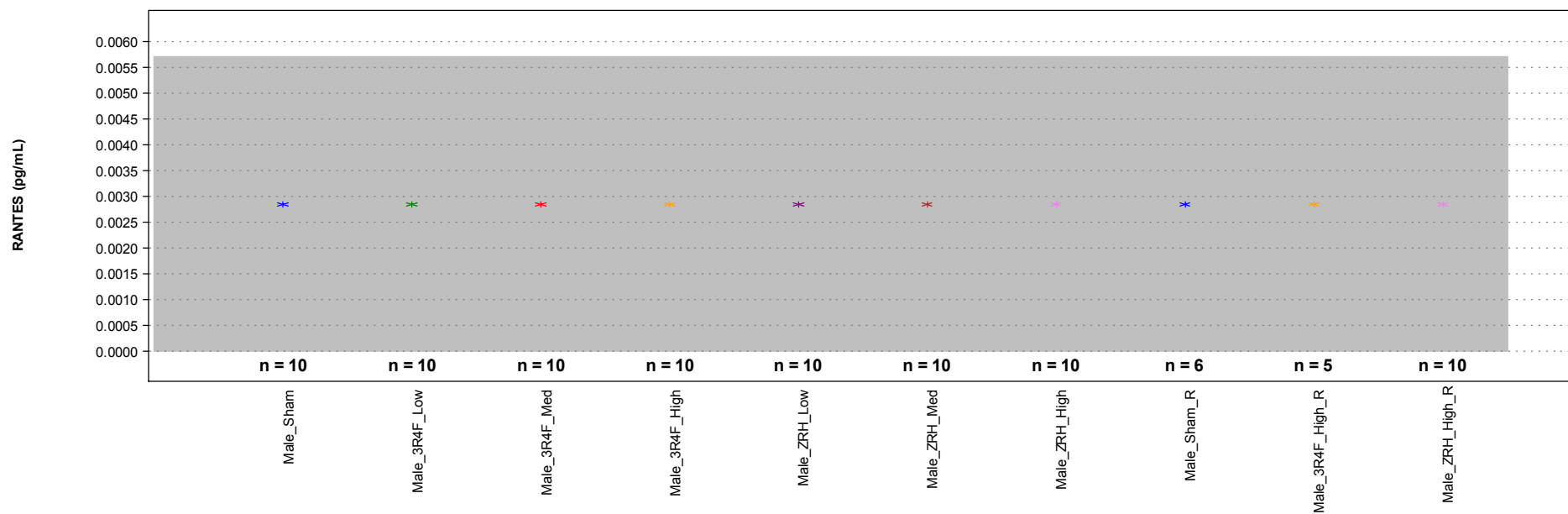
**Plot of Individual Measurements for each Group-Males**

<LOW> values are displayed as 0 / Values above ULQ are displayed as 1.1*ULQ
 Grey zones denote zones below (average) LLQ and above (average) ULQ

**Plot of Descriptive Robust Statistics-Males**

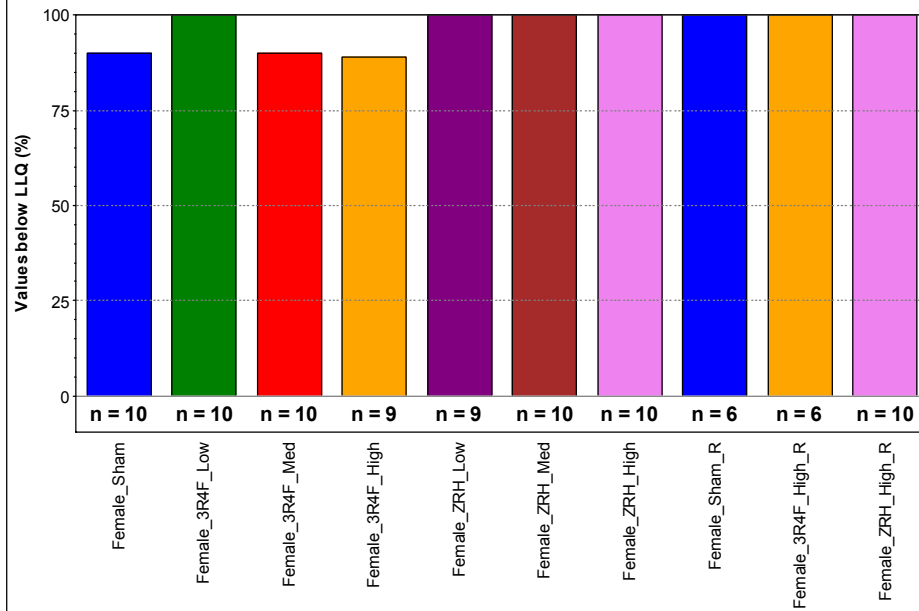
Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ

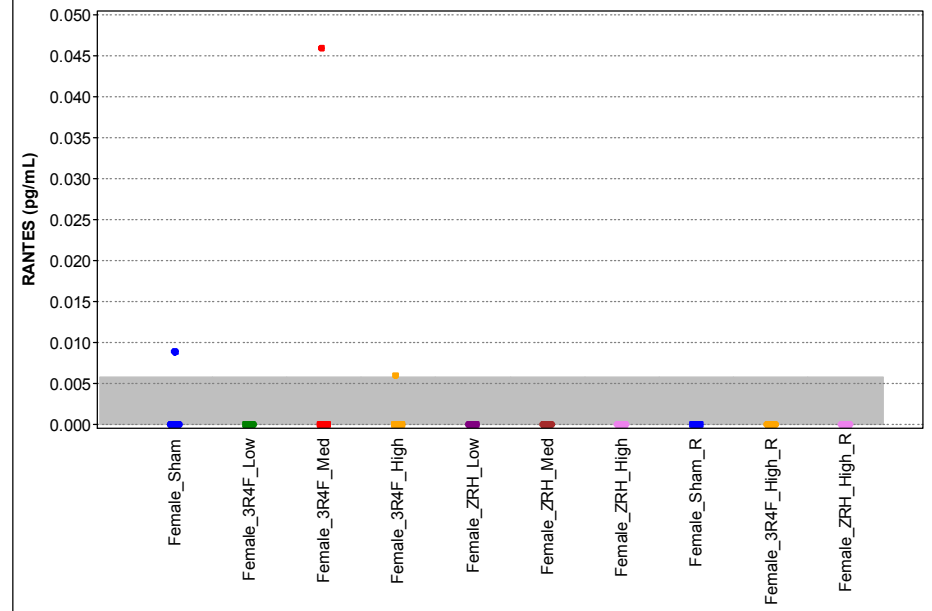


Percentage of Values below LLQ for each Group-Females

Analyte = RANTES

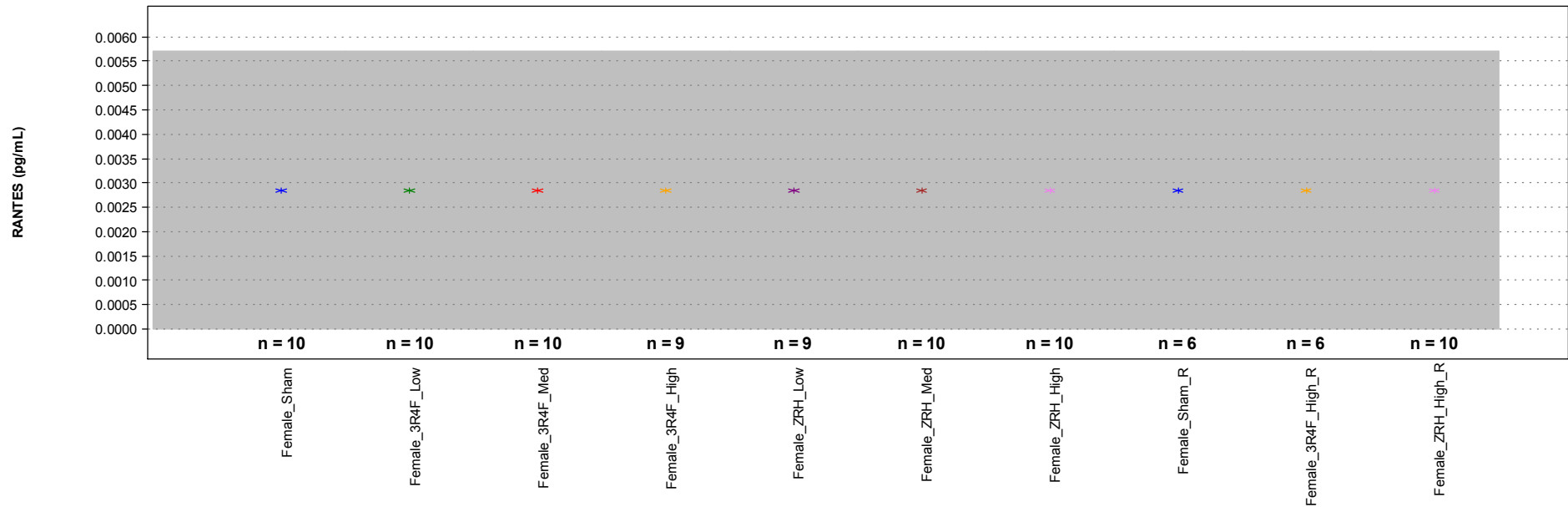
**Plot of Individual Measurements for RANTES in Females**

<LOW> values are displayed as 0 / Values above ULQ are displayed as 1.1*ULQ
 Grey zones denote zones below (average) LLQ and above (average) ULQ

**Plot of Descriptive Robust Statistics-Females**

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = RANTES

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	0.942166
---- Sham vs. 3R4F Medium for Male	0.942166
---- Sham vs. 3R4F High for Male	0.317311
---- Sham vs. ZRH Low for Male	0.317311
---- Sham vs. ZRH Medium for Male	0.317311
---- Sham vs. ZRH High for Male	0.942166
---- ZRH Low vs. 3R4F Medium for Male	0.317311
---- ZRH Medium vs. 3R4F High for Male	1.000000
---- ZRH High vs. 3R4F High for Male	0.317311
---- Sham Recovery vs. 3R4F High Recovery for Male	1.000000
---- Sham Recovery vs. ZRH High Recovery for Male	1.000000
---- Sham vs. Sham Recovery for Male	0.438578
---- 3R4F High vs. 3R4F High Recovery for Male	1.000000
---- ZRH High vs. ZRH High Recovery for Male	0.317311
---- 3R4F High Recovery vs. ZRH High Recovery for Male	1.000000
---- Sham vs. 3R4F Low for Female	0.317311
---- Sham vs. 3R4F Medium for Female	0.942166
---- Sham vs. 3R4F High for Female	1.000000
---- Sham vs. ZRH Low for Female	0.342782
---- Sham vs. ZRH Medium for Female	0.317311
---- Sham vs. ZRH High for Female	0.317311
---- ZRH Low vs. 3R4F Medium for Female	0.342782
---- ZRH Medium vs. 3R4F High for Female	0.291841
---- ZRH High vs. 3R4F High for Female	0.291841
---- Sham Recovery vs. 3R4F High Recovery for Female	1.000000
---- Sham Recovery vs. ZRH High Recovery for Female	1.000000
---- Sham vs. Sham Recovery for Female	0.438578

Unadjusted P-values Obtained by Kruskal-Wallis Test
Analyte = RANTES

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	0.414216
---- ZRH High vs. ZRH High Recovery for Female	1.000000
---- 3R4F High Recovery vs. ZRH High Recovery for Female	1.000000

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 51

Resistin

Unit = ng/mL

Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = Resistin

Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	0	10	0	0.008	.
Male	3	3R4F Low	10	10	0	10	0	0.008	.
Male	3	3R4F Medium	10	10	0	10	0	0.008	.
Male	3	3R4F High	10	10	0	10	0	0.008	.
Male	3	ZRH Low	10	10	0	10	0	0.008	.
Male	3	ZRH Medium	10	10	0	10	0	0.008	.
Male	3	ZRH High	10	10	0	10	0	0.008	.
Male	4.5	Sham Recovery	6	6	0	6	0	0.008	.
Male	4.5	3R4F High Recovery	5	5	0	5	0	0.008	.
Male	4.5	ZRH High Recovery	10	10	0	10	0	0.008	.
Female	3	Sham	10	10	0	10	0	0.008	.
Female	3	3R4F Low	10	10	0	10	0	0.008	.
Female	3	3R4F Medium	10	10	0	10	0	0.008	.
Female	3	3R4F High	9	9	0	9	0	0.008	.
Female	3	ZRH Low	9	9	0	9	0	0.008	.
Female	3	ZRH Medium	10	10	0	10	0	0.008	.
Female	3	ZRH High	10	10	0	10	0	0.008	.
Female	4.5	Sham Recovery	6	6	0	6	0	0.008	.
Female	4.5	3R4F High Recovery	6	6	0	6	0	0.008	.
Female	4.5	ZRH High Recovery	10	10	0	10	0	0.008	.

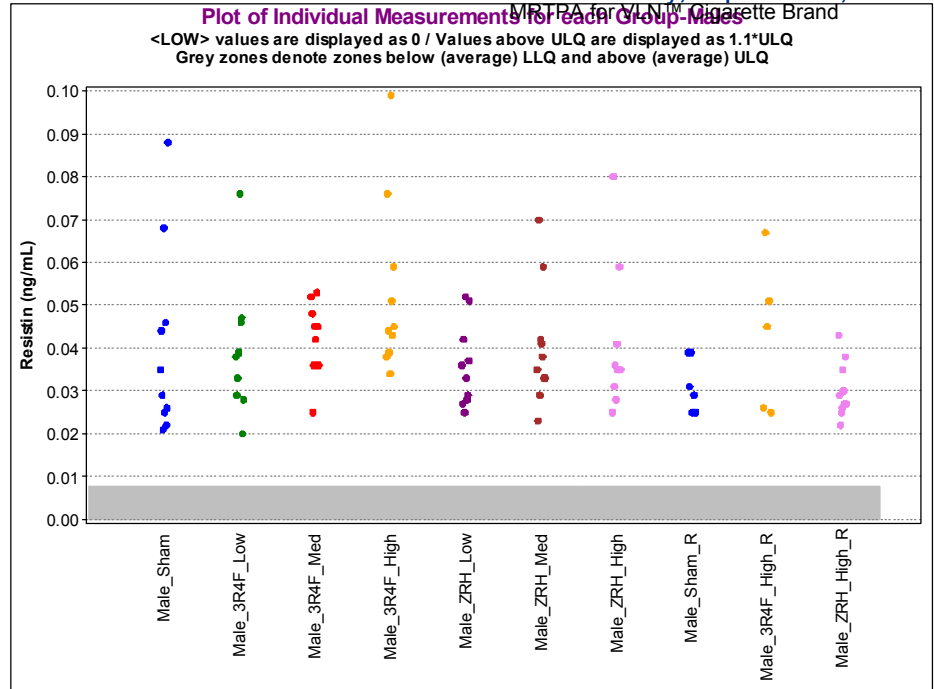
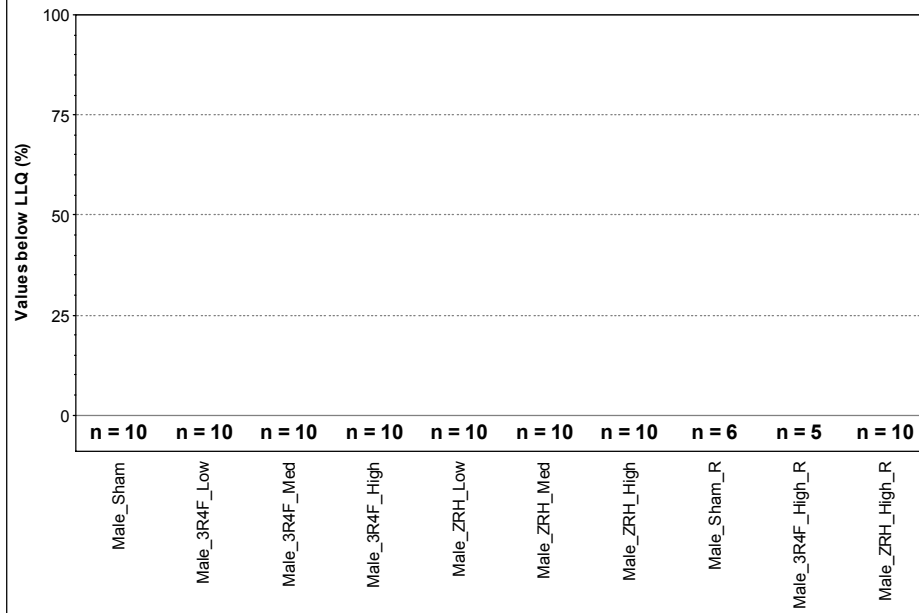
Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = Resistin

Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	0.021	0.025	0.032	0.046	0.088	0.040	0.022	0.007	54.7	1.383	1.245	0.008	.
Male	3	3R4F Low	0.020	0.029	0.039	0.046	0.076	0.040	0.015	0.005	38.7	1.519	3.512	0.008	.
Male	3	3R4F Medium	0.025	0.036	0.044	0.048	0.053	0.042	0.009	0.003	20.7	-0.551	0.023	0.008	.
Male	3	3R4F High	0.034	0.039	0.045	0.059	0.099	0.053	0.020	0.006	38.5	1.604	2.174	0.008	.
Male	3	ZRH Low	0.025	0.028	0.035	0.042	0.052	0.036	0.010	0.003	26.9	0.728	-0.718	0.008	.
Male	3	ZRH Medium	0.023	0.033	0.037	0.042	0.070	0.040	0.014	0.004	35.1	1.234	1.174	0.008	.
Male	3	ZRH High	0.025	0.031	0.035	0.041	0.080	0.041	0.017	0.005	41.2	1.825	3.139	0.008	.
Male	4.5	Sham Recovery	0.025	0.025	0.030	0.039	0.039	0.031	0.006	0.003	20.4	0.440	-1.951	0.008	.
Male	4.5	3R4F High Recovery	0.025	0.026	0.045	0.051	0.067	0.043	0.018	0.008	41.4	0.326	-1.320	0.008	.
Male	4.5	ZRH High Recovery	0.022	0.026	0.028	0.035	0.043	0.030	0.007	0.002	21.6	0.930	0.135	0.008	.
Female	3	Sham	0.014	0.015	0.017	0.021	0.022	0.018	0.003	0.001	17.5	0.304	-1.632	0.008	.
Female	3	3R4F Low	0.019	0.021	0.024	0.028	0.035	0.025	0.005	0.002	20.1	1.059	0.603	0.008	.
Female	3	3R4F Medium	0.021	0.021	0.027	0.034	0.047	0.029	0.009	0.003	29.9	0.959	0.223	0.008	.
Female	3	3R4F High	0.019	0.021	0.023	0.031	0.100	0.033	0.026	0.009	78.3	2.621	7.145	0.008	.
Female	3	ZRH Low	0.014	0.019	0.022	0.031	0.033	0.024	0.007	0.002	29.1	0.226	-1.420	0.008	.
Female	3	ZRH Medium	0.014	0.017	0.024	0.026	0.050	0.024	0.010	0.003	42.0	2.001	5.151	0.008	.
Female	3	ZRH High	0.019	0.022	0.024	0.035	0.041	0.027	0.008	0.002	28.0	0.772	-0.936	0.008	.
Female	4.5	Sham Recovery	0.015	0.020	0.027	0.029	0.080	0.033	0.024	0.010	71.7	2.156	4.967	0.008	.
Female	4.5	3R4F High Recovery	0.020	0.020	0.026	0.030	0.051	0.029	0.012	0.005	40.1	1.841	3.740	0.008	.
Female	4.5	ZRH High Recovery	0.018	0.020	0.024	0.032	0.045	0.027	0.009	0.003	32.1	0.983	0.203	0.008	.

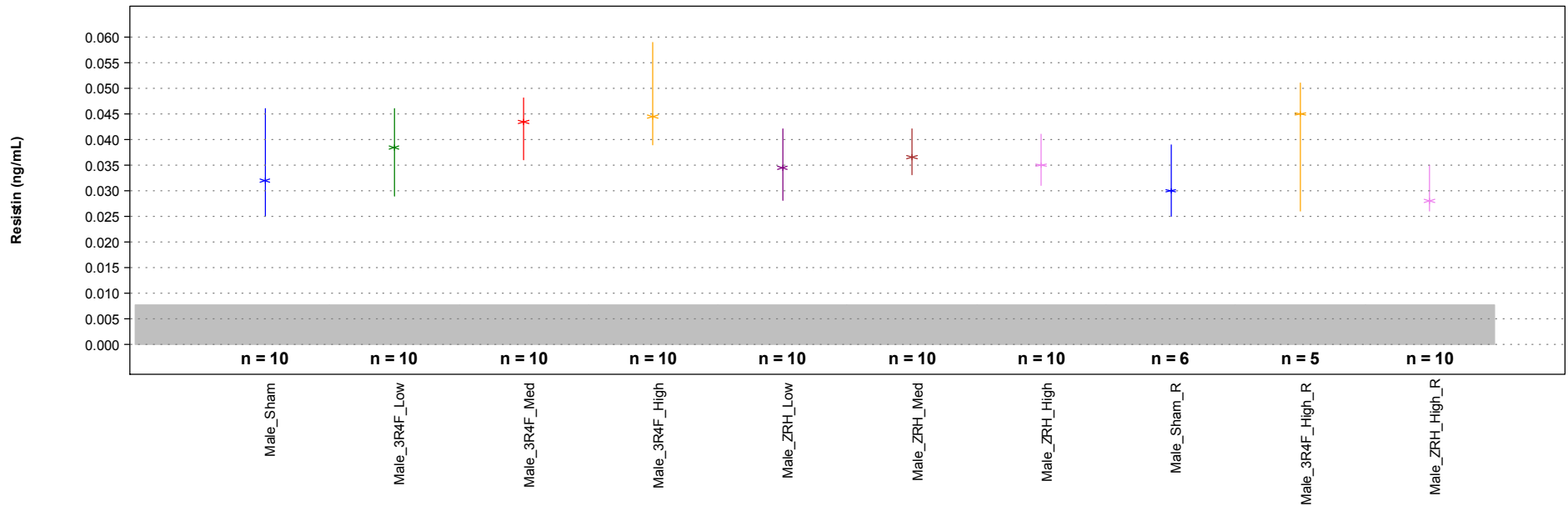
Percentage of Values below LLQ for each Group-Males

Analyte = Resistin

**Plot of Descriptive Robust Statistics-Males**

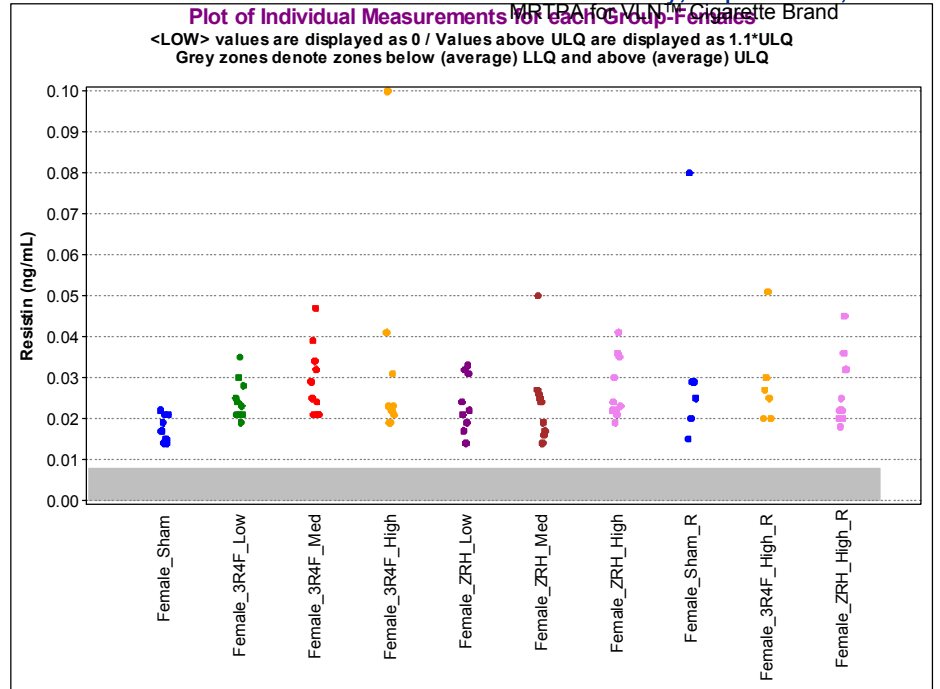
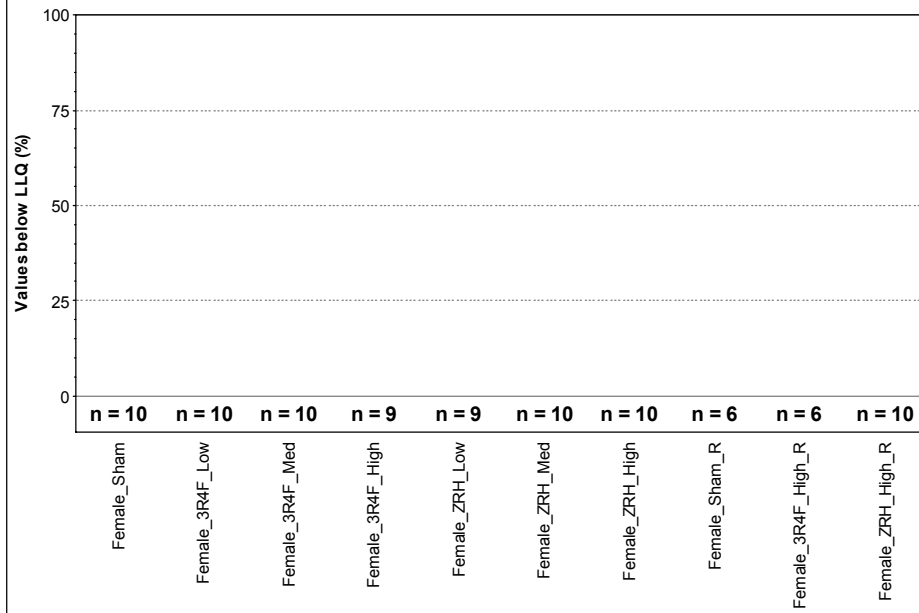
Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



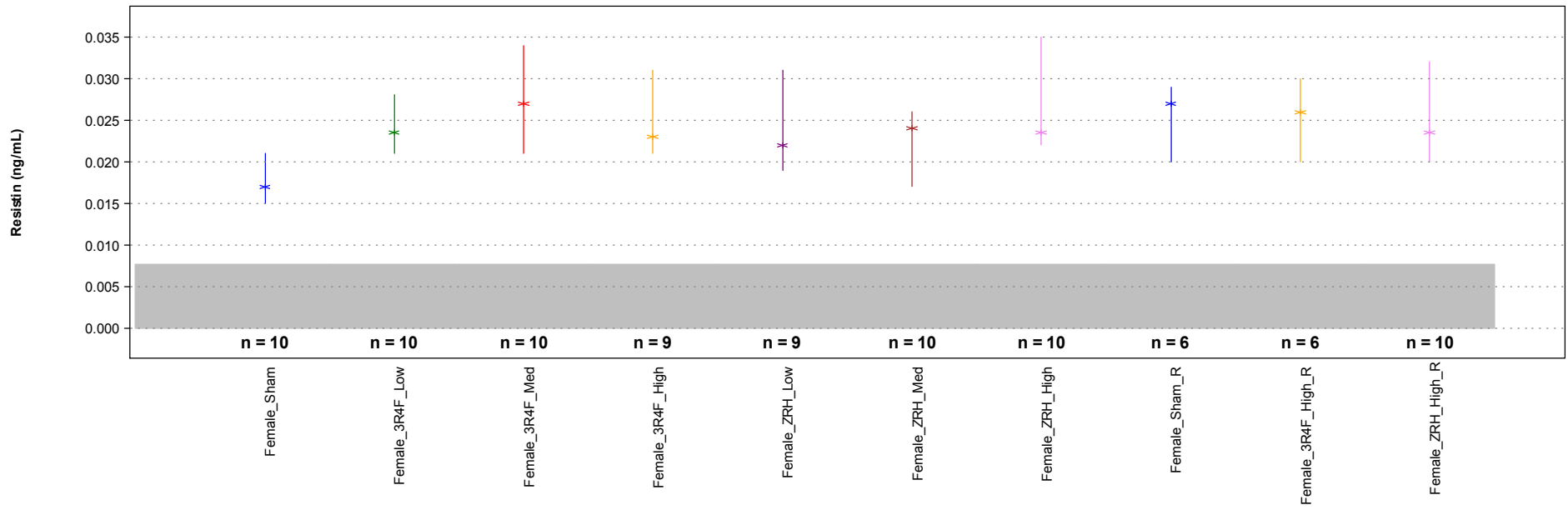
Percentage of Values below LLQ for each Group-Females

Analyte = Resistin

**Plot of Descriptive Robust Statistics-Females**

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = Resistin

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	0.649779
---- Sham vs. 3R4F Medium for Male	0.271952
---- Sham vs. 3R4F High for Male	0.103980
---- Sham vs. ZRH Low for Male	0.762195
---- Sham vs. ZRH Medium for Male	0.596287
---- Sham vs. ZRH High for Male	0.595175
---- ZRH Low vs. 3R4F Medium for Male	0.171346
---- ZRH Medium vs. 3R4F High for Male	0.049110
---- ZRH High vs. 3R4F High for Male	0.044751
---- Sham Recovery vs. 3R4F High Recovery for Male	0.267814
---- Sham Recovery vs. ZRH High Recovery for Male	0.702760
---- Sham vs. Sham Recovery for Male	0.702970
---- 3R4F High vs. 3R4F High Recovery for Male	0.539566
---- ZRH High vs. ZRH High Recovery for Male	0.080718
---- 3R4F High Recovery vs. ZRH High Recovery for Male	0.269058
---- Sham vs. 3R4F Low for Female	0.002005
---- Sham vs. 3R4F Medium for Female	0.000793
---- Sham vs. 3R4F High for Female	0.003554
---- Sham vs. ZRH Low for Female	0.039898
---- Sham vs. ZRH Medium for Female	0.044187
---- Sham vs. ZRH High for Female	0.000956
---- ZRH Low vs. 3R4F Medium for Female	0.150875
---- ZRH Medium vs. 3R4F High for Female	0.623290
---- ZRH High vs. 3R4F High for Female	0.742441
---- Sham Recovery vs. 3R4F High Recovery for Female	0.935508
---- Sham Recovery vs. ZRH High Recovery for Female	0.956493
---- Sham vs. Sham Recovery for Female	0.029096

Unadjusted P-values Obtained by Kruskal-Wallis Test
Analyte = Resistin

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	0.722961
---- ZRH High vs. ZRH High Recovery for Female	0.790333
---- 3R4F High Recovery vs. ZRH High Recovery for Female	0.869514

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 52

Serum Amyloid P-Component (SAP)

Unit = ug/mL

Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = SAP

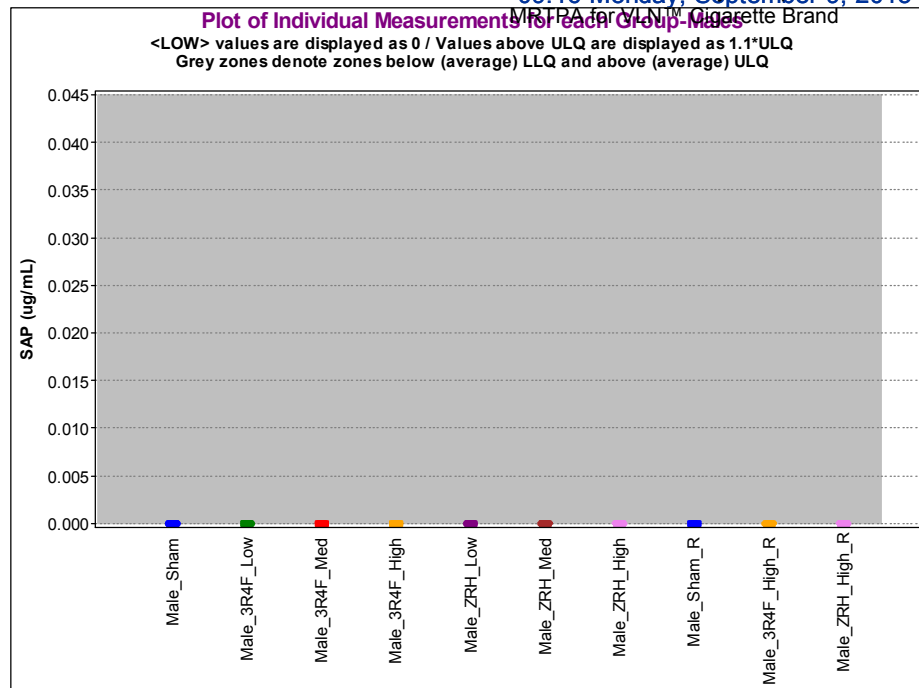
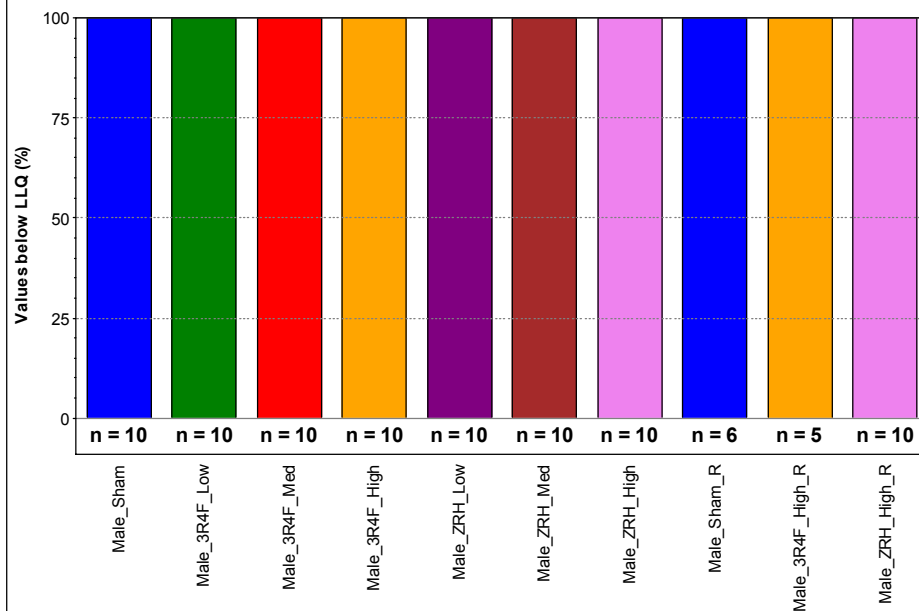
Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	10	0	0	0.045	.
Male	3	3R4F Low	10	10	10	0	0	0.045	.
Male	3	3R4F Medium	10	10	10	0	0	0.045	.
Male	3	3R4F High	10	10	10	0	0	0.045	.
Male	3	ZRH Low	10	10	10	0	0	0.045	.
Male	3	ZRH Medium	10	10	10	0	0	0.045	.
Male	3	ZRH High	10	10	10	0	0	0.045	.
Male	4.5	Sham Recovery	6	6	6	0	0	0.045	.
Male	4.5	3R4F High Recovery	5	5	5	0	0	0.045	.
Male	4.5	ZRH High Recovery	10	10	10	0	0	0.045	.
Female	3	Sham	10	10	10	0	0	0.045	.
Female	3	3R4F Low	10	10	7	3	0	0.045	.
Female	3	3R4F Medium	10	10	9	1	0	0.045	.
Female	3	3R4F High	9	9	7	2	0	0.045	.
Female	3	ZRH Low	9	9	9	0	0	0.045	.
Female	3	ZRH Medium	10	10	6	4	0	0.045	.
Female	3	ZRH High	10	10	9	1	0	0.045	.
Female	4.5	Sham Recovery	6	6	6	0	0	0.045	.
Female	4.5	3R4F High Recovery	6	6	6	0	0	0.045	.
Female	4.5	ZRH High Recovery	10	10	10	0	0	0.045	.

Descriptive Statistics by Exposure Duration and Treatment Type**Analyte = SAP**

Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	0.023	0.023	0.023	0.023	0.023	0.022	0.000	0.000	0.0	.	.	0.045	.
Male	3	3R4F Low	0.023	0.023	0.023	0.023	0.023	0.022	0.000	0.000	0.0	.	.	0.045	.
Male	3	3R4F Medium	0.023	0.023	0.023	0.023	0.023	0.022	0.000	0.000	0.0	.	.	0.045	.
Male	3	3R4F High	0.023	0.023	0.023	0.023	0.023	0.022	0.000	0.000	0.0	.	.	0.045	.
Male	3	ZRH Low	0.023	0.023	0.023	0.023	0.023	0.022	0.000	0.000	0.0	.	.	0.045	.
Male	3	ZRH Medium	0.023	0.023	0.023	0.023	0.023	0.022	0.000	0.000	0.0	.	.	0.045	.
Male	3	ZRH High	0.023	0.023	0.023	0.023	0.023	0.022	0.000	0.000	0.0	.	.	0.045	.
Male	4.5	Sham Recovery	0.023	0.023	0.023	0.023	0.023	0.022	0.000	0.000	0.0	.	.	0.045	.
Male	4.5	3R4F High Recovery	0.023	0.023	0.023	0.023	0.023	0.023	0.000	0.000	0.0	.	.	0.045	.
Male	4.5	ZRH High Recovery	0.023	0.023	0.023	0.023	0.023	0.022	0.000	0.000	0.0	.	.	0.045	.
Female	3	Sham	0.023	0.023	0.023	0.023	0.023	0.022	0.000	0.000	0.0	.	.	0.045	.
Female	3	3R4F Low	0.023	0.023	0.023	0.049	0.100	0.036	0.025	0.008	70.8	2.209	5.028	0.045	.
Female	3	3R4F Medium	0.023	0.023	0.023	0.023	0.045	0.025	0.007	0.002	28.7	3.162	10.000	0.045	.
Female	3	3R4F High	0.023	0.023	0.023	0.023	0.052	0.028	0.012	0.004	41.5	1.690	1.204	0.045	.
Female	3	ZRH Low	0.023	0.023	0.023	0.023	0.023	0.022	0.000	0.000	0.0	.	.	0.045	.
Female	3	ZRH Medium	0.023	0.023	0.023	0.053	0.059	0.035	0.017	0.005	47.7	0.572	-2.001	0.045	.
Female	3	ZRH High	0.023	0.023	0.023	0.023	0.048	0.025	0.008	0.003	32.2	3.162	10.000	0.045	.
Female	4.5	Sham Recovery	0.023	0.023	0.023	0.023	0.023	0.022	0.000	0.000	0.0	.	.	0.045	.
Female	4.5	3R4F High Recovery	0.023	0.023	0.023	0.023	0.023	0.022	0.000	0.000	0.0	.	.	0.045	.
Female	4.5	ZRH High Recovery	0.023	0.023	0.023	0.023	0.023	0.022	0.000	0.000	0.0	.	.	0.045	.

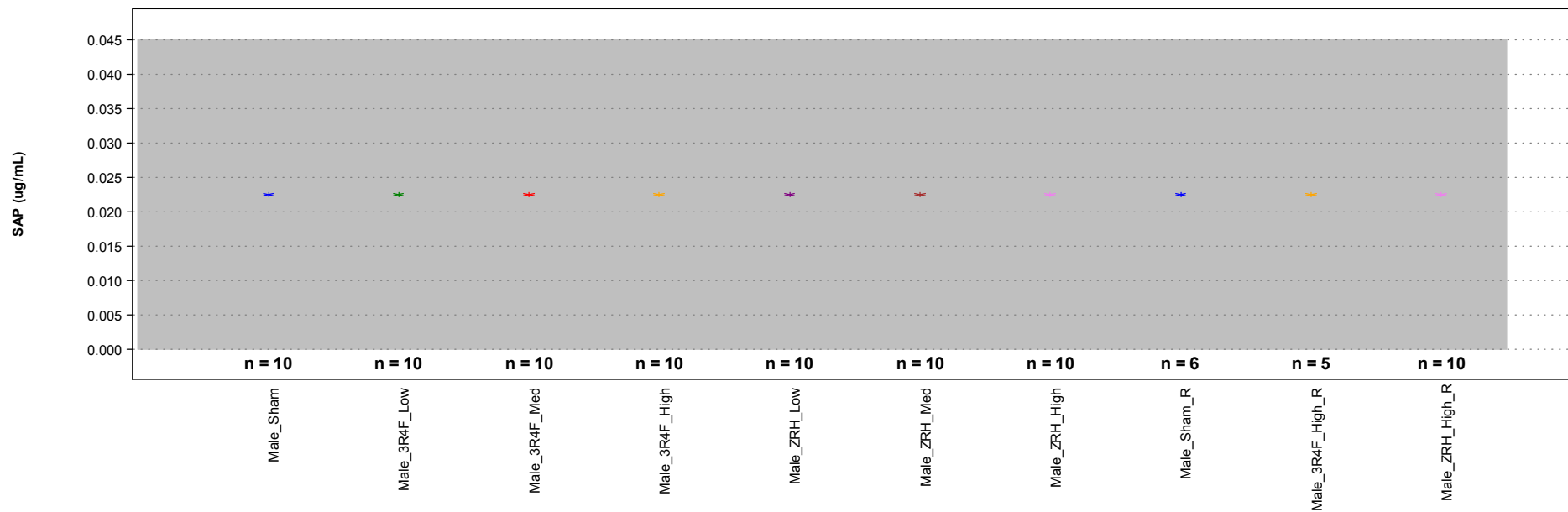
Percentage of Values below LLQ for each Group-Males

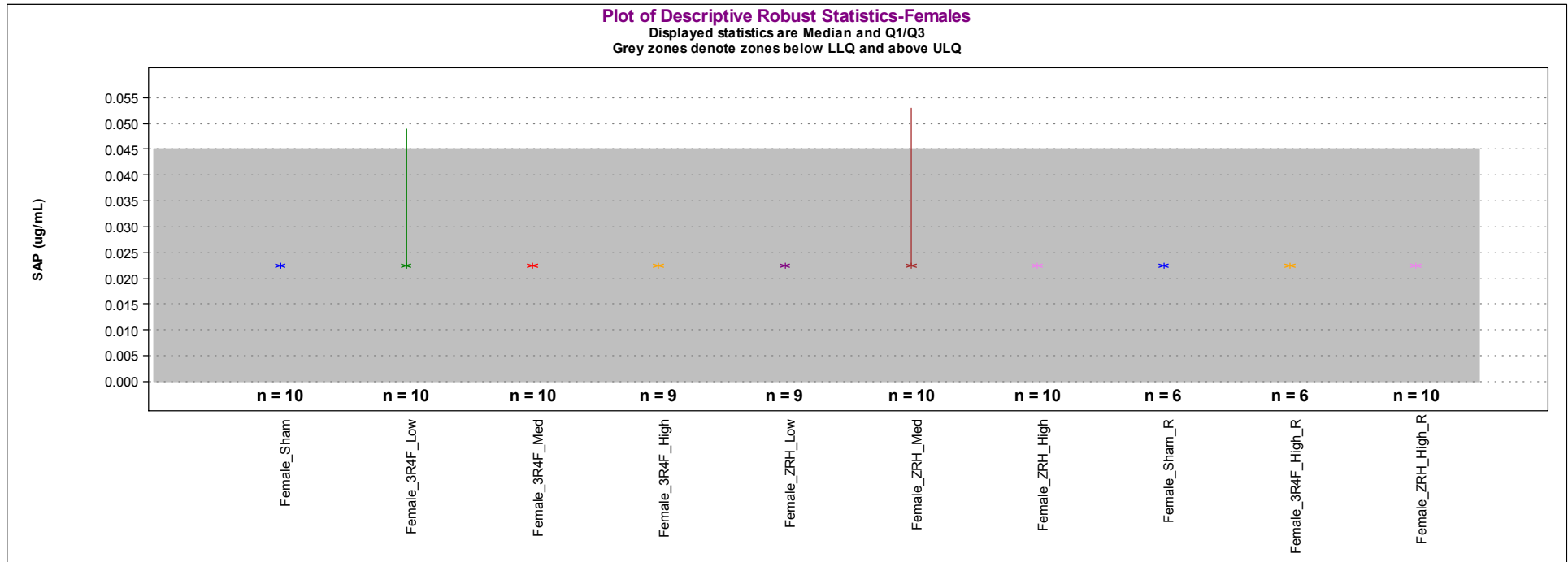
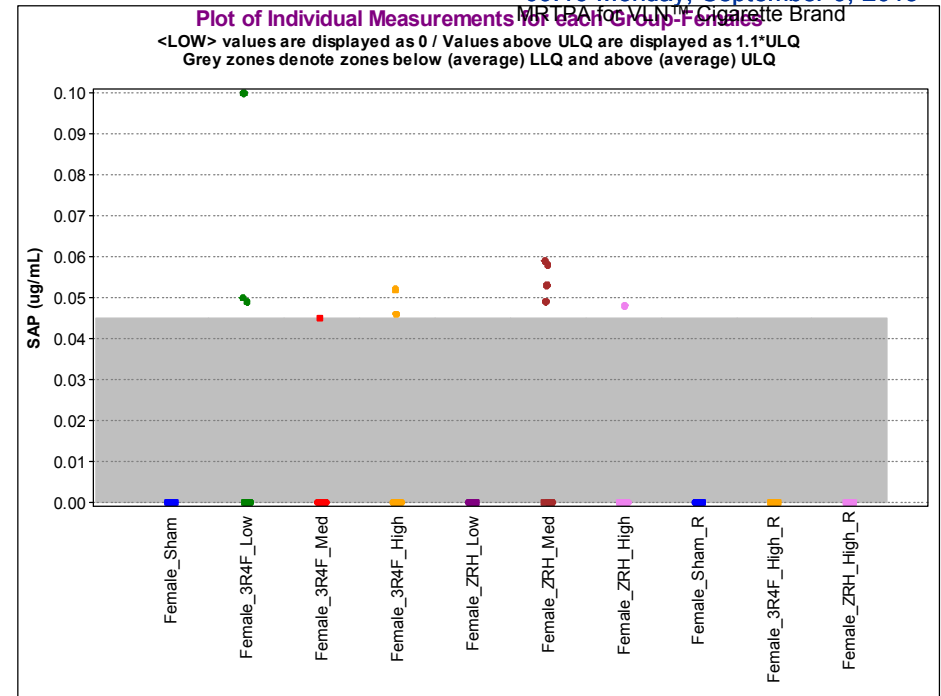
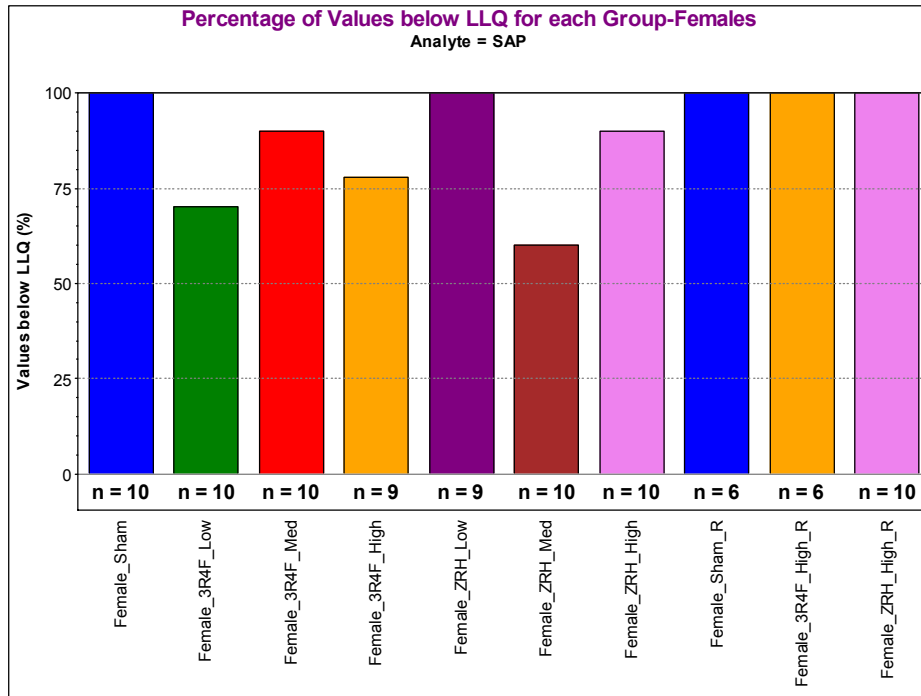
Analyte = SAP

**Plot of Descriptive Robust Statistics-Males**

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ





Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = SAP

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	1.000000
---- Sham vs. 3R4F Medium for Male	1.000000
---- Sham vs. 3R4F High for Male	1.000000
---- Sham vs. ZRH Low for Male	1.000000
---- Sham vs. ZRH Medium for Male	1.000000
---- Sham vs. ZRH High for Male	1.000000
---- ZRH Low vs. 3R4F Medium for Male	1.000000
---- ZRH Medium vs. 3R4F High for Male	1.000000
---- ZRH High vs. 3R4F High for Male	1.000000
---- Sham Recovery vs. 3R4F High Recovery for Male	1.000000
---- Sham Recovery vs. ZRH High Recovery for Male	1.000000
---- Sham vs. Sham Recovery for Male	1.000000
---- 3R4F High vs. 3R4F High Recovery for Male	1.000000
---- ZRH High vs. ZRH High Recovery for Male	1.000000
---- 3R4F High Recovery vs. ZRH High Recovery for Male	1.000000
---- Sham vs. 3R4F Low for Female	0.068157
---- Sham vs. 3R4F Medium for Female	0.317311
---- Sham vs. 3R4F High for Female	0.125631
---- Sham vs. ZRH Low for Female	1.000000
---- Sham vs. ZRH Medium for Female	0.030570
---- Sham vs. ZRH High for Female	0.317311
---- ZRH Low vs. 3R4F Medium for Female	0.342782
---- ZRH Medium vs. 3R4F High for Female	0.276330
---- ZRH High vs. 3R4F High for Female	0.479596
---- Sham Recovery vs. 3R4F High Recovery for Female	1.000000
---- Sham Recovery vs. ZRH High Recovery for Female	1.000000
---- Sham vs. Sham Recovery for Female	1.000000

Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = SAP

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	0.231998
---- ZRH High vs. ZRH High Recovery for Female	0.317311
---- 3R4F High Recovery vs. ZRH High Recovery for Female	1.000000

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 53

Stem Cell Factor (SCF)

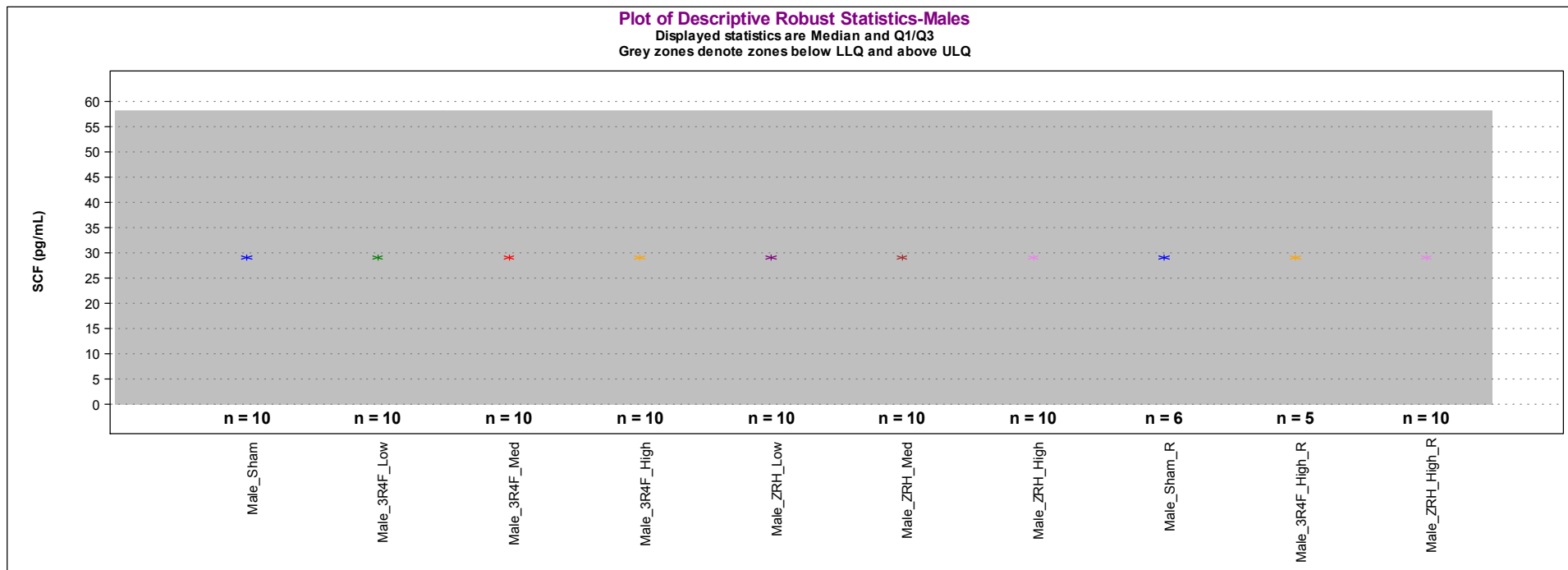
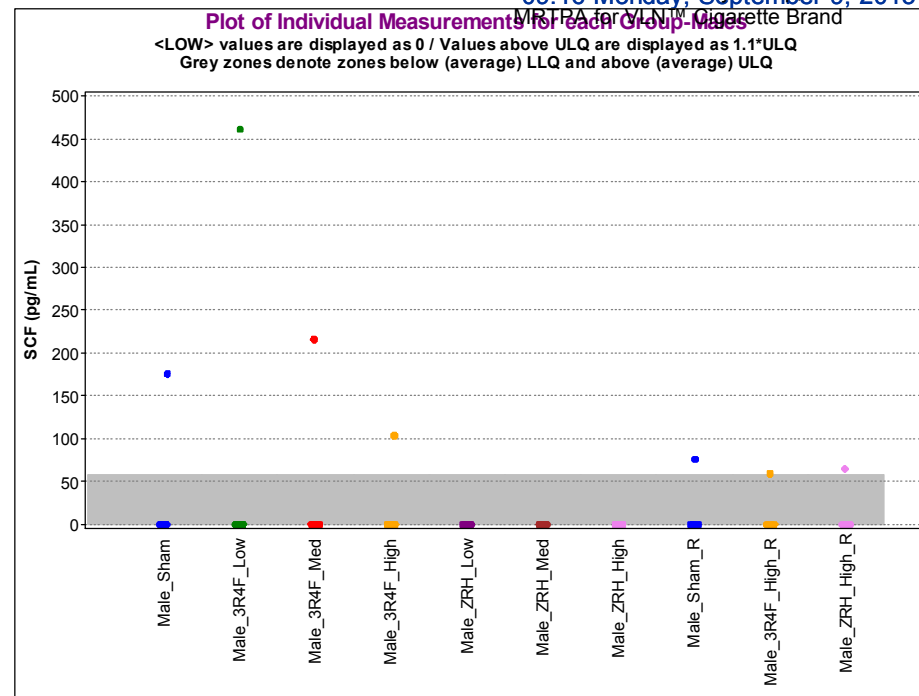
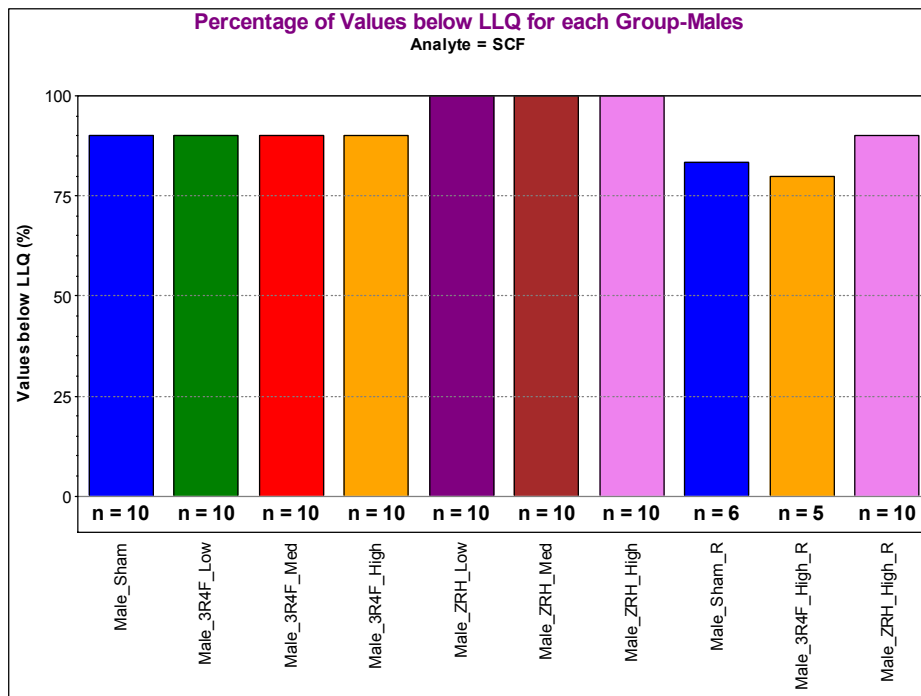
Unit = pg/mL

Descriptive Statistics by Exposure Duration and Treatment Type**Analyte = SCF**

Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	9	1	0	58	.
Male	3	3R4F Low	10	10	9	1	0	58	.
Male	3	3R4F Medium	10	10	9	1	0	58	.
Male	3	3R4F High	10	10	9	1	0	58	.
Male	3	ZRH Low	10	10	10	0	0	58	.
Male	3	ZRH Medium	10	10	10	0	0	58	.
Male	3	ZRH High	10	10	10	0	0	58	.
Male	4.5	Sham Recovery	6	6	5	1	0	58	.
Male	4.5	3R4F High Recovery	5	5	4	1	0	58	.
Male	4.5	ZRH High Recovery	10	10	9	1	0	58	.
Female	3	Sham	10	10	10	0	0	58	.
Female	3	3R4F Low	10	10	10	0	0	58	.
Female	3	3R4F Medium	10	10	7	3	0	58	.
Female	3	3R4F High	9	9	7	2	0	58	.
Female	3	ZRH Low	9	9	9	0	0	58	.
Female	3	ZRH Medium	10	10	10	0	0	58	.
Female	3	ZRH High	10	10	10	0	0	58	.
Female	4.5	Sham Recovery	6	6	4	2	0	58	.
Female	4.5	3R4F High Recovery	6	6	5	1	0	58	.
Female	4.5	ZRH High Recovery	10	10	8	2	0	58	.

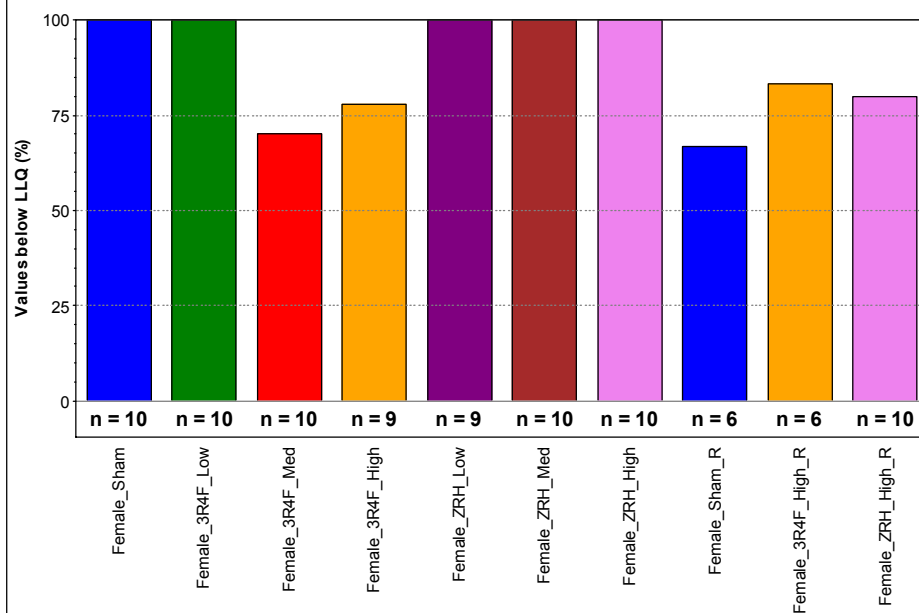
Descriptive Statistics by Exposure Duration and Treatment Type**Analyte = SCF**

Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	29.000	29.000	29.000	29.000	176.000	43.700	46.485	14.700	106.4	3.162	10.000	58	.
Male	3	3R4F Low	29.000	29.000	29.000	29.000	461.000	72.200	136.610	43.200	189.2	3.162	10.000	58	.
Male	3	3R4F Medium	29.000	29.000	29.000	29.000	216.000	47.700	59.135	18.700	124.0	3.162	10.000	58	.
Male	3	3R4F High	29.000	29.000	29.000	29.000	104.000	36.500	23.717	7.500	65.0	3.162	10.000	58	.
Male	3	ZRH Low	29.000	29.000	29.000	29.000	29.000	29.000	0.000	0.000	0.0	.	.	58	.
Male	3	ZRH Medium	29.000	29.000	29.000	29.000	29.000	29.000	0.000	0.000	0.0	.	.	58	.
Male	3	ZRH High	29.000	29.000	29.000	29.000	29.000	29.000	0.000	0.000	0.0	.	.	58	.
Male	4.5	Sham Recovery	29.000	29.000	29.000	29.000	76.000	36.833	19.188	7.833	52.1	2.449	6.000	58	.
Male	4.5	3R4F High Recovery	29.000	29.000	29.000	29.000	59.000	35.000	13.416	6.000	38.3	2.236	5.000	58	.
Male	4.5	ZRH High Recovery	29.000	29.000	29.000	29.000	65.000	32.600	11.384	3.600	34.9	3.162	10.000	58	.
Female	3	Sham	29.000	29.000	29.000	29.000	29.000	29.000	0.000	0.000	0.0	.	.	58	.
Female	3	3R4F Low	29.000	29.000	29.000	29.000	29.000	29.000	0.000	0.000	0.0	.	.	58	.
Female	3	3R4F Medium	29.000	29.000	29.000	61.000	471.000	79.900	138.124	43.679	172.9	3.104	9.718	58	.
Female	3	3R4F High	29.000	29.000	29.000	29.000	65.000	36.556	15.026	5.009	41.1	1.639	0.864	58	.
Female	3	ZRH Low	29.000	29.000	29.000	29.000	29.000	29.000	0.000	0.000	0.0	.	.	58	.
Female	3	ZRH Medium	29.000	29.000	29.000	29.000	29.000	29.000	0.000	0.000	0.0	.	.	58	.
Female	3	ZRH High	29.000	29.000	29.000	29.000	29.000	29.000	0.000	0.000	0.0	.	.	58	.
Female	4.5	Sham Recovery	29.000	29.000	29.000	65.000	65.000	41.000	18.590	7.589	45.3	0.968	-1.875	58	.
Female	4.5	3R4F High Recovery	29.000	29.000	29.000	29.000	65.000	35.000	14.697	6.000	42.0	2.449	6.000	58	.
Female	4.5	ZRH High Recovery	29.000	29.000	29.000	29.000	61.000	35.400	13.492	4.267	38.1	1.779	1.406	58	.

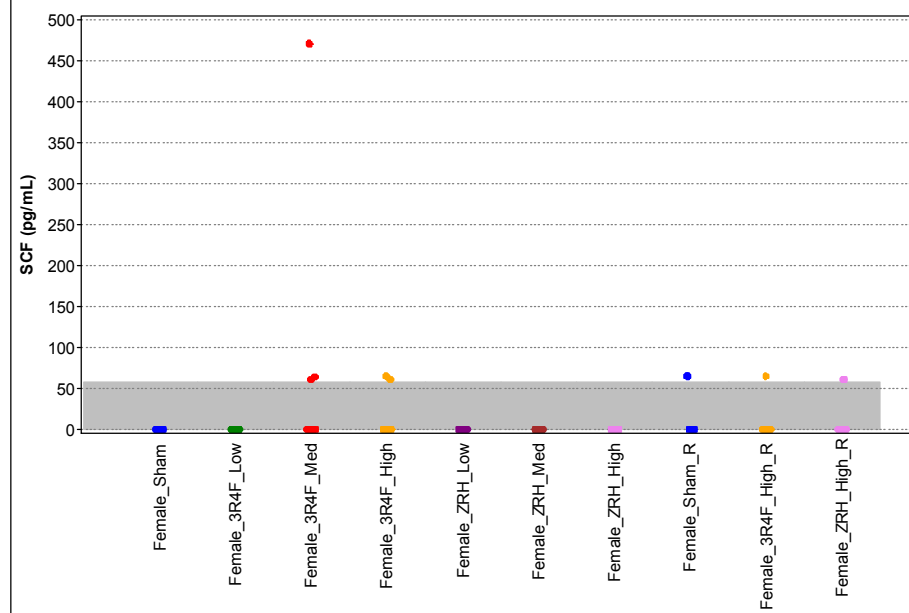


Percentage of Values below LLQ for each Group-Females

Analyte = SCF

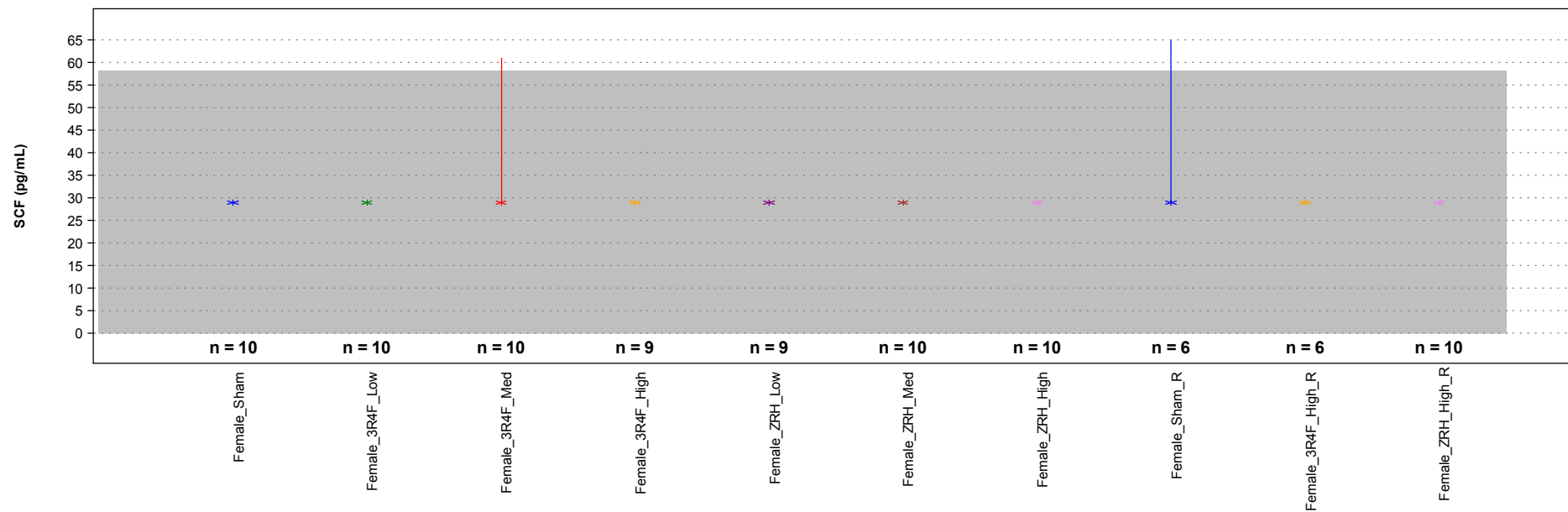
**Plot of Individual Measurements for each Group-Females**

<LOW> values are displayed as 0 / Values above ULQ are displayed as 1.1*ULQ
 Grey zones denote zones below (average) LLQ and above (average) ULQ

**Plot of Descriptive Robust Statistics-Females**

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = SCF

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	0.942166
---- Sham vs. 3R4F Medium for Male	0.942166
---- Sham vs. 3R4F High for Male	0.942166
---- Sham vs. ZRH Low for Male	0.317311
---- Sham vs. ZRH Medium for Male	0.317311
---- Sham vs. ZRH High for Male	0.317311
---- ZRH Low vs. 3R4F Medium for Male	0.317311
---- ZRH Medium vs. 3R4F High for Male	0.317311
---- ZRH High vs. 3R4F High for Male	0.317311
---- Sham Recovery vs. 3R4F High Recovery for Male	1.000000
---- Sham Recovery vs. ZRH High Recovery for Male	0.637352
---- Sham vs. Sham Recovery for Male	0.777297
---- 3R4F High vs. 3R4F High Recovery for Male	0.678845
---- ZRH High vs. ZRH High Recovery for Male	0.317311
---- 3R4F High Recovery vs. ZRH High Recovery for Male	0.678845
---- Sham vs. 3R4F Low for Female	1.000000
---- Sham vs. 3R4F Medium for Female	0.068157
---- Sham vs. 3R4F High for Female	0.125631
---- Sham vs. ZRH Low for Female	1.000000
---- Sham vs. ZRH Medium for Female	1.000000
---- Sham vs. ZRH High for Female	1.000000
---- ZRH Low vs. 3R4F Medium for Female	0.082697
---- ZRH Medium vs. 3R4F High for Female	0.125631
---- ZRH High vs. 3R4F High for Female	0.125631
---- Sham Recovery vs. 3R4F High Recovery for Female	0.523288
---- Sham Recovery vs. ZRH High Recovery for Female	0.391366
---- Sham vs. Sham Recovery for Female	0.058782

Unadjusted P-values Obtained by Kruskal-Wallis Test
Analyte = SCF

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	0.865962
---- ZRH High vs. ZRH High Recovery for Female	0.146233
---- 3R4F High Recovery vs. ZRH High Recovery for Female	1.000000

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 56

Tissue Inhibitor of Metalloproteinases 1 Mouse (TIMP-1 Mouse)

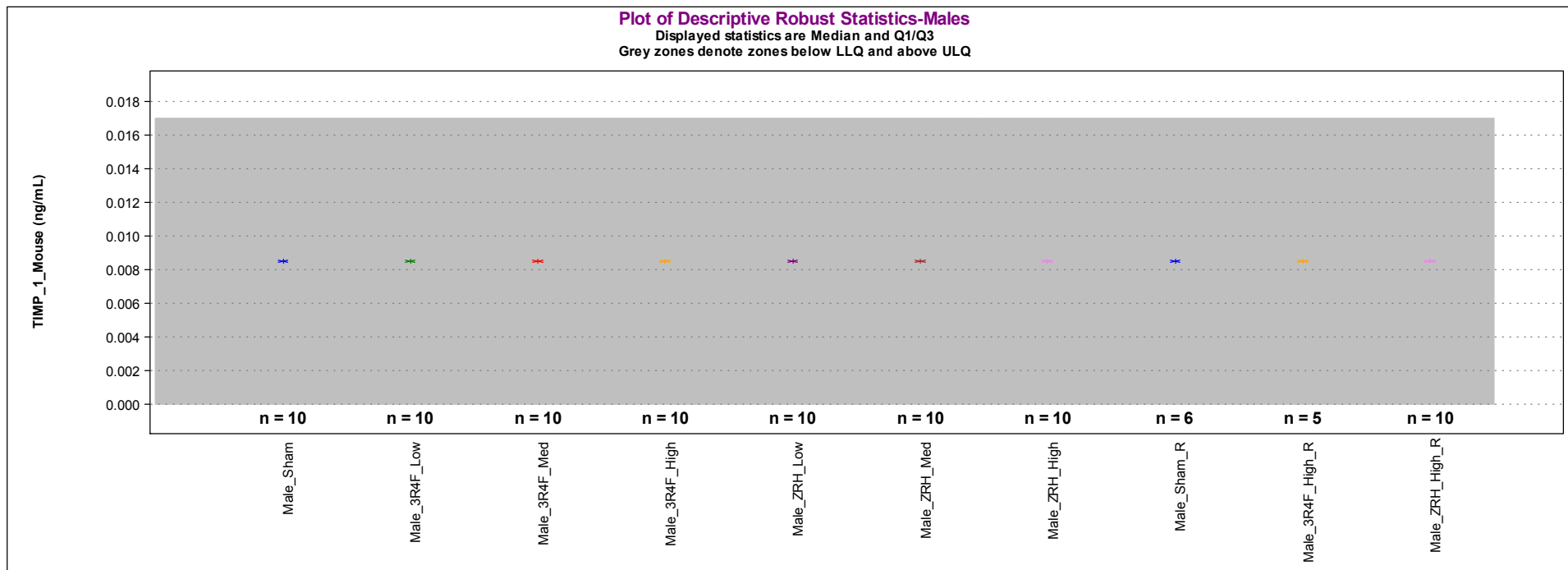
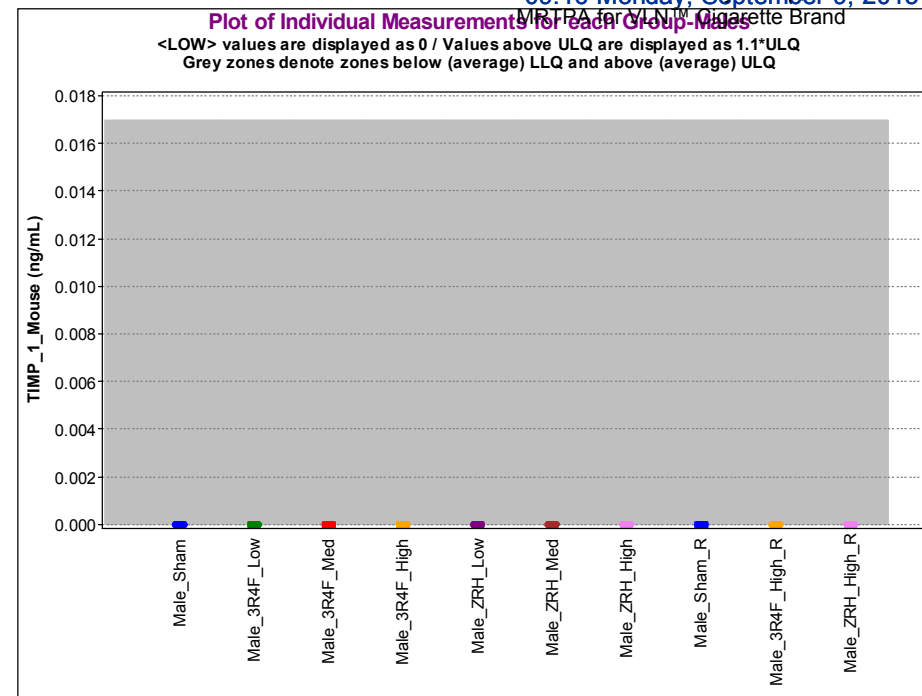
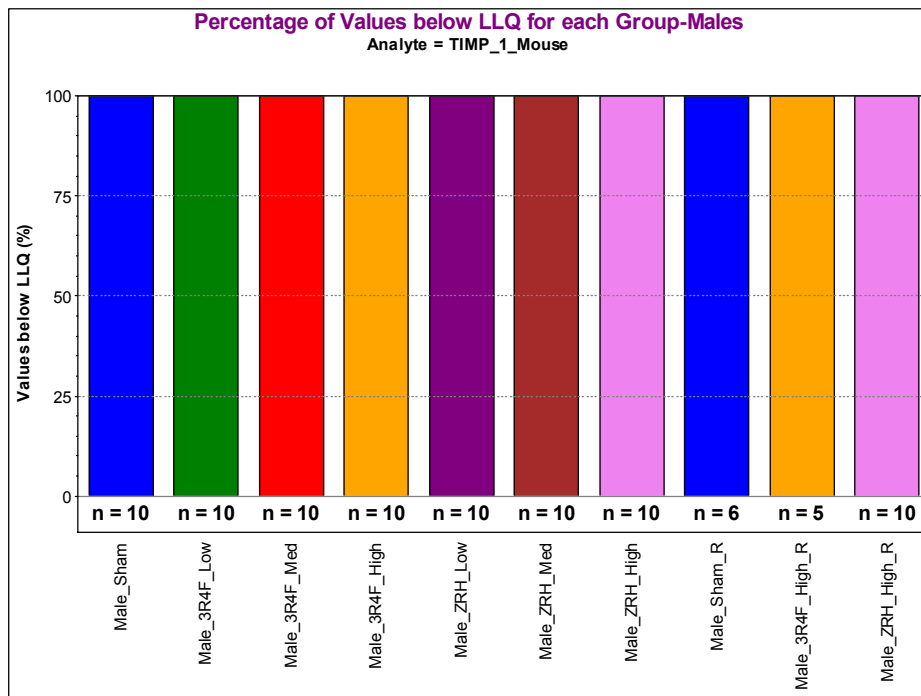
Unit = ng/mL

Descriptive Statistics by Exposure Duration and Treatment Type**Analyte = TIMP_1_Mouse**

Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	10	0	0	0.017	.
Male	3	3R4F Low	10	10	10	0	0	0.017	.
Male	3	3R4F Medium	10	10	10	0	0	0.017	.
Male	3	3R4F High	10	10	10	0	0	0.017	.
Male	3	ZRH Low	10	10	10	0	0	0.017	.
Male	3	ZRH Medium	10	10	10	0	0	0.017	.
Male	3	ZRH High	10	10	10	0	0	0.017	.
Male	4.5	Sham Recovery	6	6	6	0	0	0.017	.
Male	4.5	3R4F High Recovery	5	5	5	0	0	0.017	.
Male	4.5	ZRH High Recovery	10	10	10	0	0	0.017	.
Female	3	Sham	10	10	10	0	0	0.017	.
Female	3	3R4F Low	10	10	10	0	0	0.017	.
Female	3	3R4F Medium	10	10	9	1	0	0.017	.
Female	3	3R4F High	9	9	9	0	0	0.017	.
Female	3	ZRH Low	9	9	9	0	0	0.017	.
Female	3	ZRH Medium	10	10	10	0	0	0.017	.
Female	3	ZRH High	10	10	10	0	0	0.017	.
Female	4.5	Sham Recovery	6	6	6	0	0	0.017	.
Female	4.5	3R4F High Recovery	6	6	6	0	0	0.017	.
Female	4.5	ZRH High Recovery	10	10	10	0	0	0.017	.

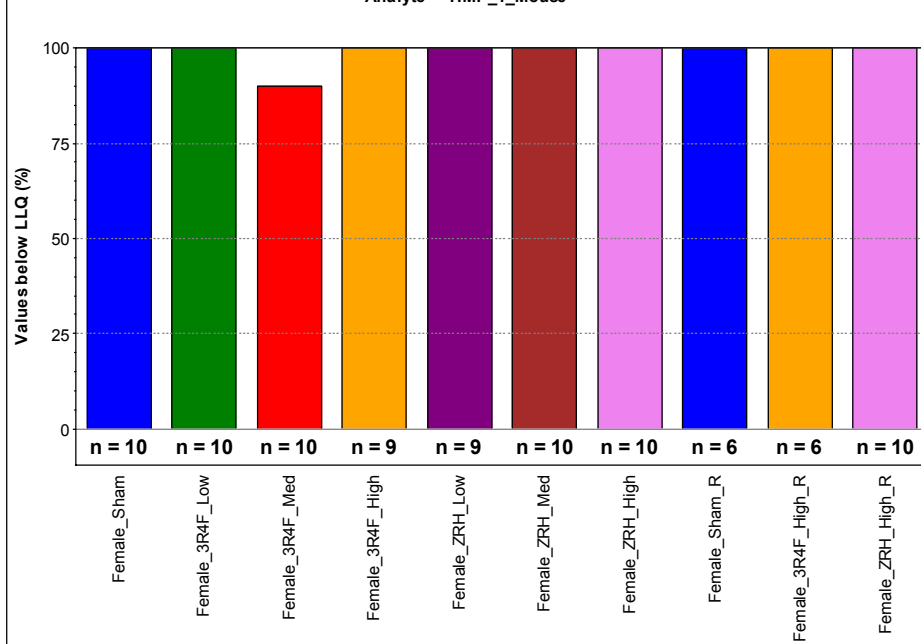
Descriptive Statistics by Exposure Duration and Treatment Type**Analyte = TIMP_1_Mouse**

Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	0.009	0.009	0.009	0.009	0.009	0.009	0.000	0.000	0.0	.	.	0.017	.
Male	3	3R4F Low	0.009	0.009	0.009	0.009	0.009	0.009	0.000	0.000	0.0	.	.	0.017	.
Male	3	3R4F Medium	0.009	0.009	0.009	0.009	0.009	0.009	0.000	0.000	0.0	.	.	0.017	.
Male	3	3R4F High	0.009	0.009	0.009	0.009	0.009	0.009	0.000	0.000	0.0	.	.	0.017	.
Male	3	ZRH Low	0.009	0.009	0.009	0.009	0.009	0.009	0.000	0.000	0.0	.	.	0.017	.
Male	3	ZRH Medium	0.009	0.009	0.009	0.009	0.009	0.009	0.000	0.000	0.0	.	.	0.017	.
Male	3	ZRH High	0.009	0.009	0.009	0.009	0.009	0.009	0.000	0.000	0.0	.	.	0.017	.
Male	4.5	Sham Recovery	0.009	0.009	0.009	0.009	0.009	0.009	0.000	0.000	0.0	.	.	0.017	.
Male	4.5	3R4F High Recovery	0.009	0.009	0.009	0.009	0.009	0.009	0.000	0.000	0.0	.	.	0.017	.
Male	4.5	ZRH High Recovery	0.009	0.009	0.009	0.009	0.009	0.009	0.000	0.000	0.0	.	.	0.017	.
Female	3	Sham	0.009	0.009	0.009	0.009	0.009	0.009	0.000	0.000	0.0	.	.	0.017	.
Female	3	3R4F Low	0.009	0.009	0.009	0.009	0.009	0.009	0.000	0.000	0.0	.	.	0.017	.
Female	3	3R4F Medium	0.009	0.009	0.009	0.009	0.021	0.010	0.004	0.001	40.5	3.162	10.000	0.017	.
Female	3	3R4F High	0.009	0.009	0.009	0.009	0.009	0.009	0.000	0.000	0.0	.	.	0.017	.
Female	3	ZRH Low	0.009	0.009	0.009	0.009	0.009	0.009	0.000	0.000	0.0	.	.	0.017	.
Female	3	ZRH Medium	0.009	0.009	0.009	0.009	0.009	0.009	0.000	0.000	0.0	.	.	0.017	.
Female	3	ZRH High	0.009	0.009	0.009	0.009	0.009	0.009	0.000	0.000	0.0	.	.	0.017	.
Female	4.5	Sham Recovery	0.009	0.009	0.009	0.009	0.009	0.009	0.000	0.000	0.0	.	.	0.017	.
Female	4.5	3R4F High Recovery	0.009	0.009	0.009	0.009	0.009	0.009	0.000	0.000	0.0	.	.	0.017	.
Female	4.5	ZRH High Recovery	0.009	0.009	0.009	0.009	0.009	0.009	0.000	0.000	0.0	.	.	0.017	.

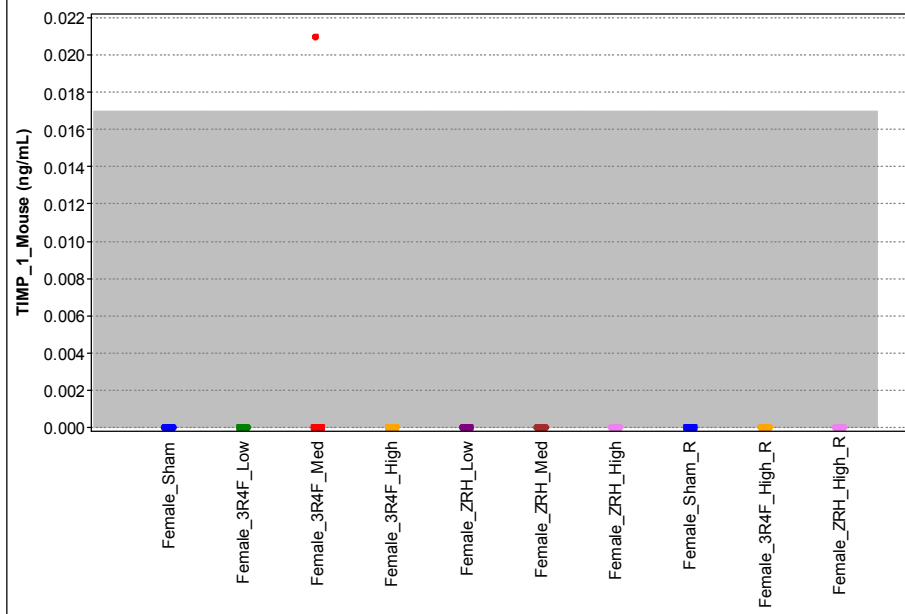


Percentage of Values below LLQ for each Group-Females

Analyte = TIMP_1_Mouse

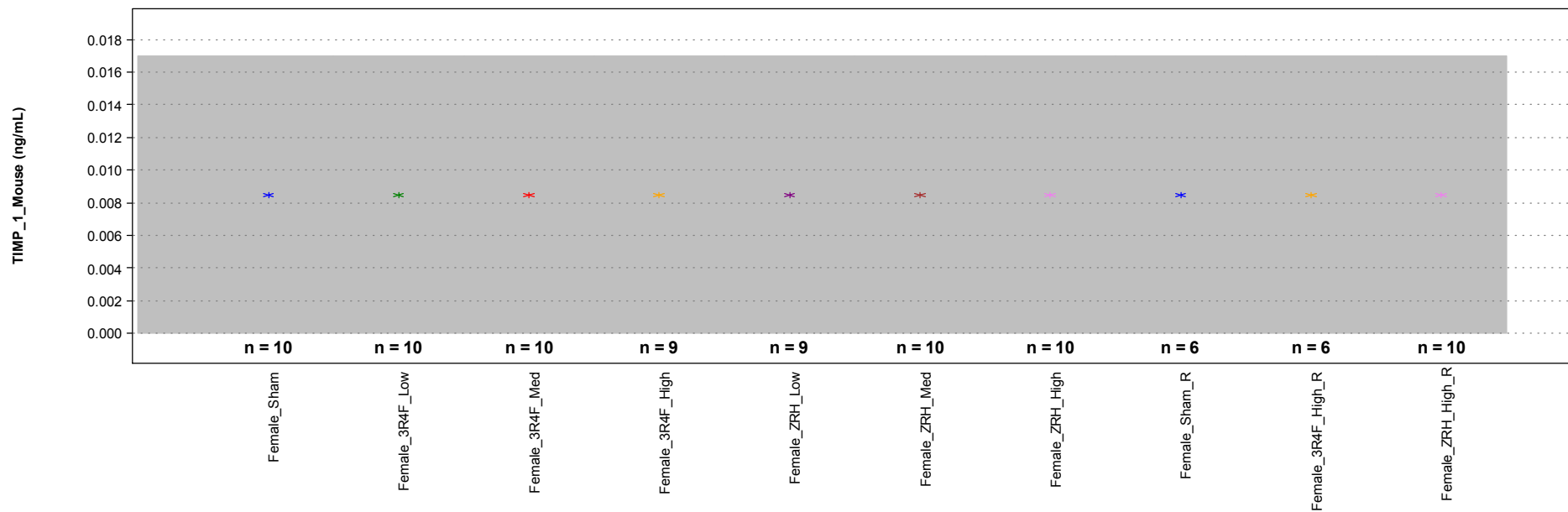
**Plot of Individual Measurements for each Group-Females**

<LOW> values are displayed as 0 / Values above ULQ are displayed as 1.1*ULQ
Grey zones denote zones below (average) LLQ and above (average) ULQ

**Plot of Descriptive Robust Statistics-Females**

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = TIMP_1_Mouse

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	1.000000
---- Sham vs. 3R4F Medium for Male	1.000000
---- Sham vs. 3R4F High for Male	1.000000
---- Sham vs. ZRH Low for Male	1.000000
---- Sham vs. ZRH Medium for Male	1.000000
---- Sham vs. ZRH High for Male	1.000000
---- ZRH Low vs. 3R4F Medium for Male	1.000000
---- ZRH Medium vs. 3R4F High for Male	1.000000
---- ZRH High vs. 3R4F High for Male	1.000000
---- Sham Recovery vs. 3R4F High Recovery for Male	1.000000
---- Sham Recovery vs. ZRH High Recovery for Male	1.000000
---- Sham vs. Sham Recovery for Male	1.000000
---- 3R4F High vs. 3R4F High Recovery for Male	1.000000
---- ZRH High vs. ZRH High Recovery for Male	1.000000
---- 3R4F High Recovery vs. ZRH High Recovery for Male	1.000000
---- Sham vs. 3R4F Low for Female	1.000000
---- Sham vs. 3R4F Medium for Female	0.317311
---- Sham vs. 3R4F High for Female	1.000000
---- Sham vs. ZRH Low for Female	1.000000
---- Sham vs. ZRH Medium for Female	1.000000
---- Sham vs. ZRH High for Female	1.000000
---- ZRH Low vs. 3R4F Medium for Female	0.342782
---- ZRH Medium vs. 3R4F High for Female	1.000000
---- ZRH High vs. 3R4F High for Female	1.000000
---- Sham Recovery vs. 3R4F High Recovery for Female	1.000000
---- Sham Recovery vs. ZRH High Recovery for Female	1.000000
---- Sham vs. Sham Recovery for Female	1.000000

Unadjusted P-values Obtained by Kruskal-Wallis Test
Analyte = TIMP_1_Mouse

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	1.000000
---- ZRH High vs. ZRH High Recovery for Female	1.000000
---- 3R4F High Recovery vs. ZRH High Recovery for Female	1.000000

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 57

Tumor Necrosis Factor alpha (TNF-alpha)

Unit = ng/mL

Descriptive Statistics by Exposure Duration and Treatment Type

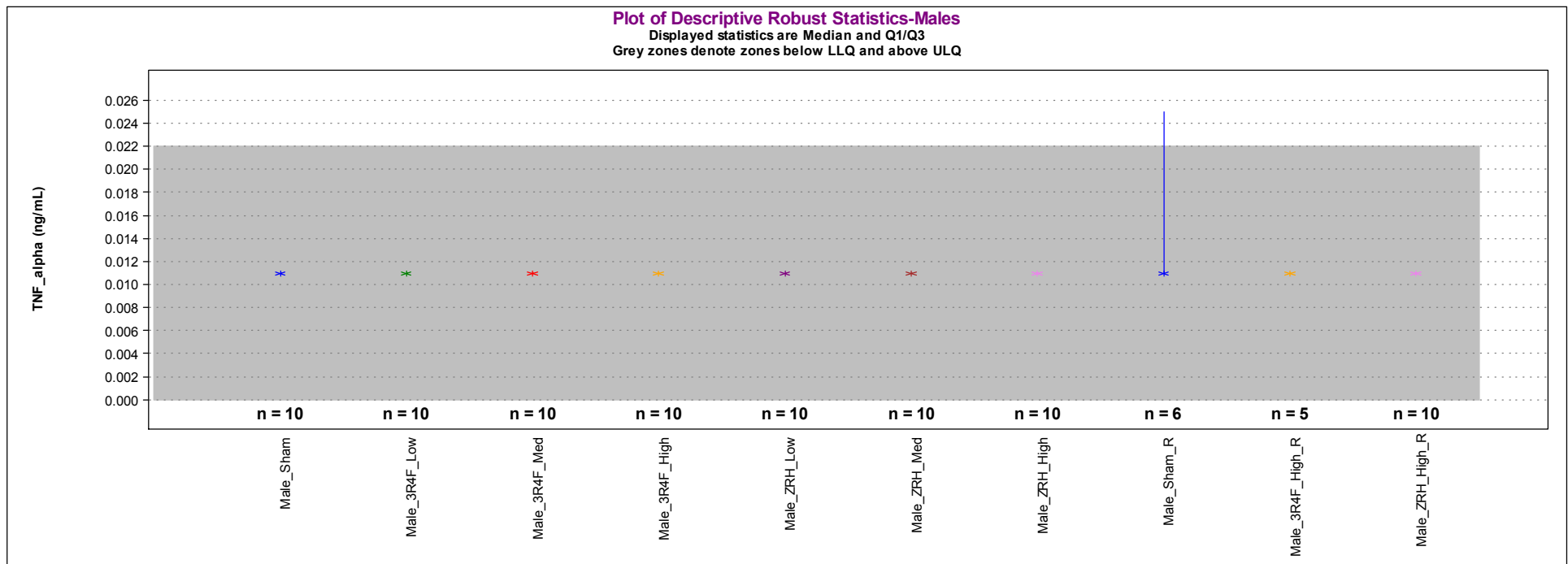
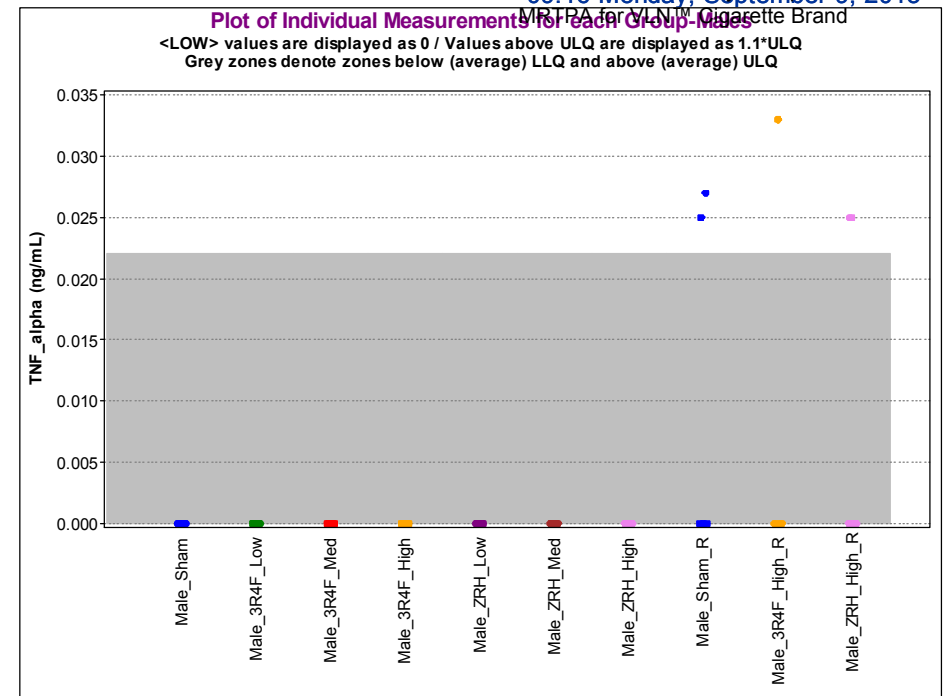
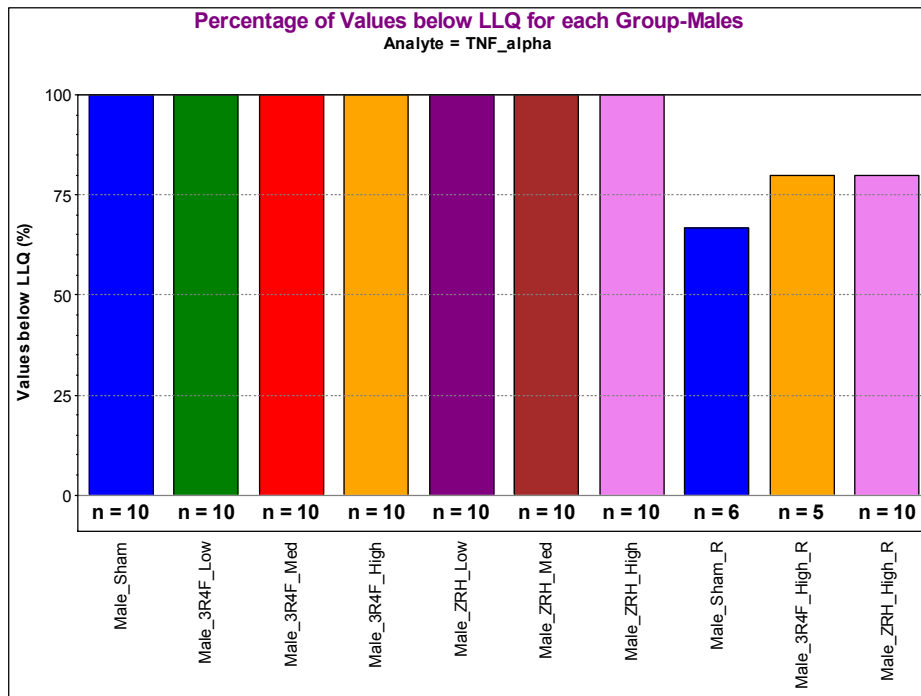
Analyte = TNF_alpha

Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	10	0	0	0.022	.
Male	3	3R4F Low	10	10	10	0	0	0.022	.
Male	3	3R4F Medium	10	10	10	0	0	0.022	.
Male	3	3R4F High	10	10	10	0	0	0.022	.
Male	3	ZRH Low	10	10	10	0	0	0.022	.
Male	3	ZRH Medium	10	10	10	0	0	0.022	.
Male	3	ZRH High	10	10	10	0	0	0.022	.
Male	4.5	Sham Recovery	6	6	4	2	0	0.022	.
Male	4.5	3R4F High Recovery	5	5	4	1	0	0.022	.
Male	4.5	ZRH High Recovery	10	10	8	2	0	0.022	.
Female	3	Sham	10	10	10	0	0	0.022	.
Female	3	3R4F Low	10	10	10	0	0	0.022	.
Female	3	3R4F Medium	10	10	10	0	0	0.022	.
Female	3	3R4F High	9	9	9	0	0	0.022	.
Female	3	ZRH Low	9	9	9	0	0	0.022	.
Female	3	ZRH Medium	10	10	10	0	0	0.022	.
Female	3	ZRH High	10	10	10	0	0	0.022	.
Female	4.5	Sham Recovery	6	6	5	1	0	0.022	.
Female	4.5	3R4F High Recovery	6	6	6	0	0	0.022	.
Female	4.5	ZRH High Recovery	10	10	7	3	0	0.022	.

Descriptive Statistics by Exposure Duration and Treatment Type

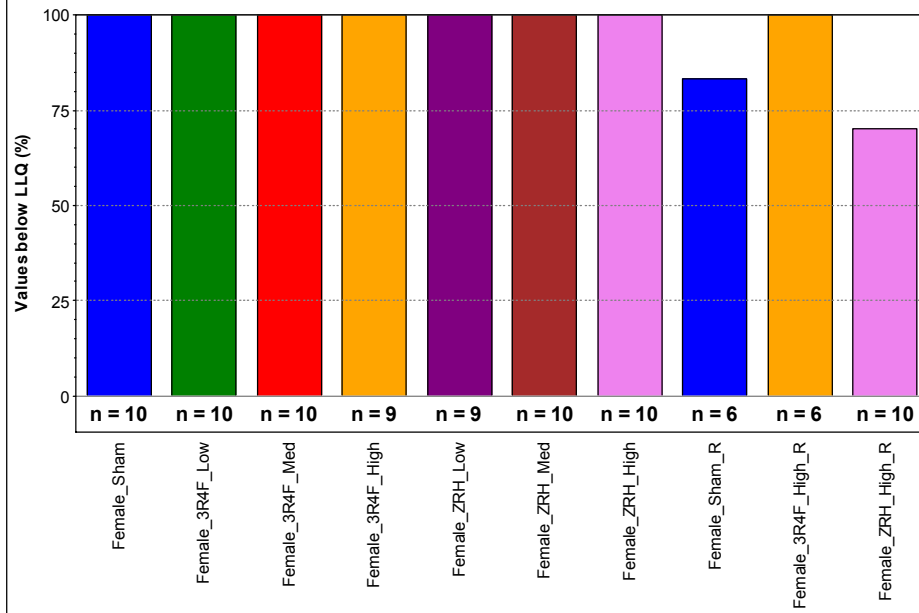
Analyte = TNF_alpha

Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	0.011	0.011	0.011	0.011	0.011	0.011	0.000	0.000	0.0	.	.	0.022	.
Male	3	3R4F Low	0.011	0.011	0.011	0.011	0.011	0.011	0.000	0.000	0.0	.	.	0.022	.
Male	3	3R4F Medium	0.011	0.011	0.011	0.011	0.011	0.011	0.000	0.000	0.0	.	.	0.022	.
Male	3	3R4F High	0.011	0.011	0.011	0.011	0.011	0.011	0.000	0.000	0.0	.	.	0.022	.
Male	3	ZRH Low	0.011	0.011	0.011	0.011	0.011	0.011	0.000	0.000	0.0	.	.	0.022	.
Male	3	ZRH Medium	0.011	0.011	0.011	0.011	0.011	0.011	0.000	0.000	0.0	.	.	0.022	.
Male	3	ZRH High	0.011	0.011	0.011	0.011	0.011	0.011	0.000	0.000	0.0	.	.	0.022	.
Male	4.5	Sham Recovery	0.011	0.011	0.011	0.025	0.027	0.016	0.008	0.003	48.6	0.997	-1.702	0.022	.
Male	4.5	3R4F High Recovery	0.011	0.011	0.011	0.011	0.033	0.015	0.010	0.004	63.9	2.236	5.000	0.022	.
Male	4.5	ZRH High Recovery	0.011	0.011	0.011	0.011	0.025	0.014	0.006	0.002	42.8	1.779	1.406	0.022	.
Female	3	Sham	0.011	0.011	0.011	0.011	0.011	0.011	0.000	0.000	0.0	.	.	0.022	.
Female	3	3R4F Low	0.011	0.011	0.011	0.011	0.011	0.011	0.000	0.000	0.0	.	.	0.022	.
Female	3	3R4F Medium	0.011	0.011	0.011	0.011	0.011	0.011	0.000	0.000	0.0	.	.	0.022	.
Female	3	3R4F High	0.011	0.011	0.011	0.011	0.011	0.011	0.000	0.000	0.0	.	.	0.022	.
Female	3	ZRH Low	0.011	0.011	0.011	0.011	0.011	0.011	0.000	0.000	0.0	.	.	0.022	.
Female	3	ZRH Medium	0.011	0.011	0.011	0.011	0.011	0.011	0.000	0.000	0.0	.	.	0.022	.
Female	3	ZRH High	0.011	0.011	0.011	0.011	0.011	0.011	0.000	0.000	0.0	.	.	0.022	.
Female	4.5	Sham Recovery	0.011	0.011	0.011	0.011	0.025	0.013	0.006	0.002	42.9	2.449	6.000	0.022	.
Female	4.5	3R4F High Recovery	0.011	0.011	0.011	0.011	0.011	0.011	0.000	0.000	0.0	.	.	0.022	.
Female	4.5	ZRH High Recovery	0.011	0.011	0.011	0.023	0.031	0.016	0.008	0.002	49.1	1.299	0.105	0.022	.

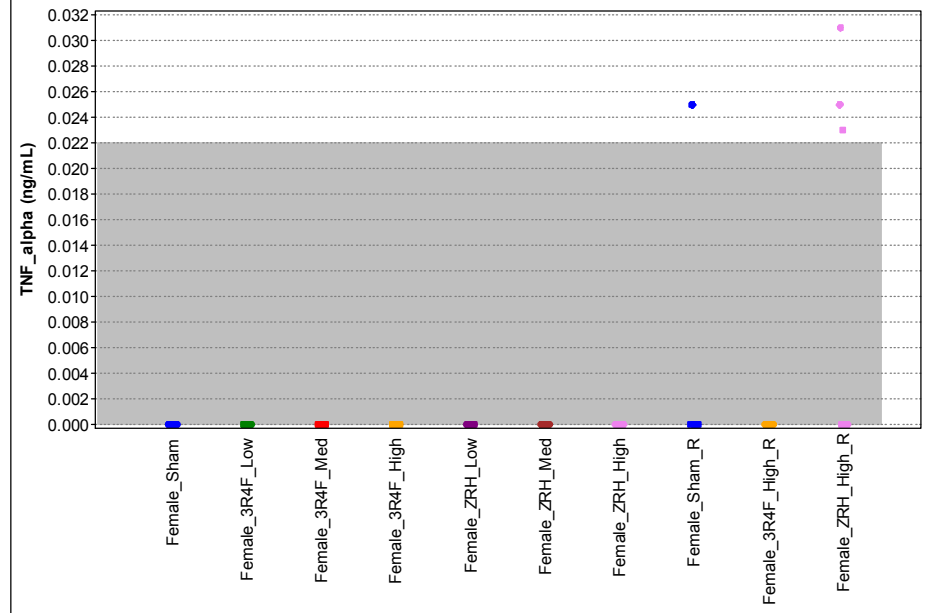


Percentage of Values below LLQ for each Group-Females

Analyte = TNF_alpha

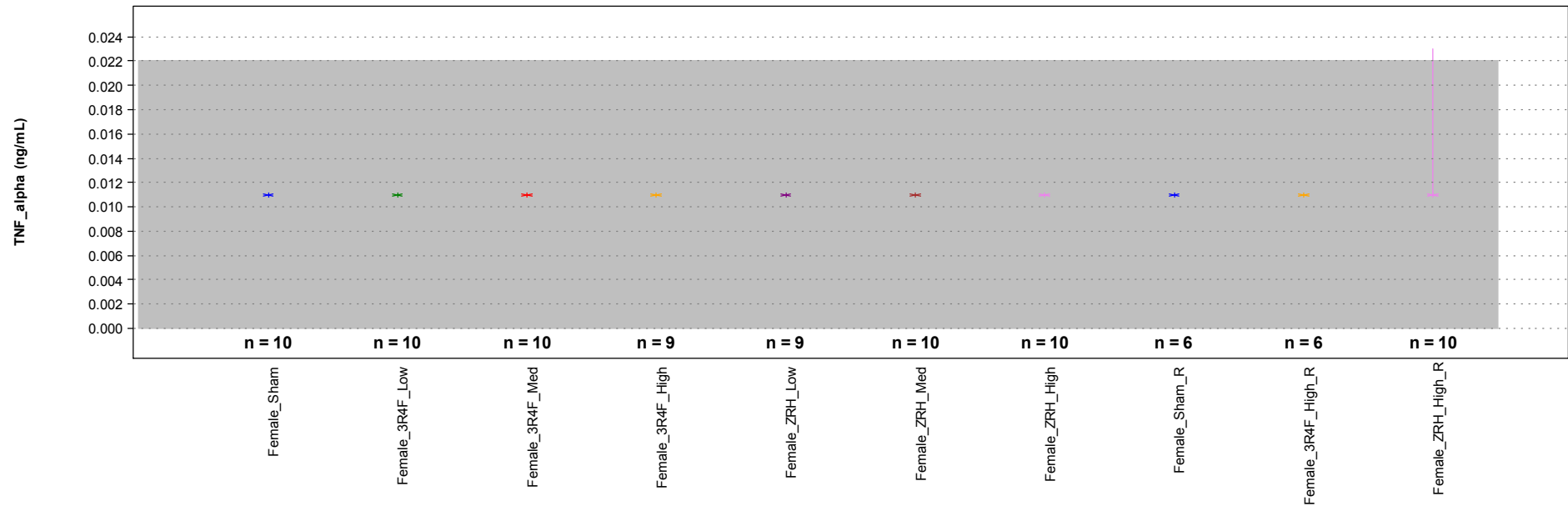
**Plot of Individual Measurements**

<LOW> values are displayed as 0 / Values above ULQ are displayed as 1.1*ULQ
 Grey zones denote zones below (average) LLQ and above (average) ULQ

**Plot of Descriptive Robust Statistics-Females**

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Unadjusted P-values Obtained by Kruskal-Wallis Test **Analyte = TNF_alpha**

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	1.000000
---- Sham vs. 3R4F Medium for Male	1.000000
---- Sham vs. 3R4F High for Male	1.000000
---- Sham vs. ZRH Low for Male	1.000000
---- Sham vs. ZRH Medium for Male	1.000000
---- Sham vs. ZRH High for Male	1.000000
---- ZRH Low vs. 3R4F Medium for Male	1.000000
---- ZRH Medium vs. 3R4F High for Male	1.000000
---- ZRH High vs. 3R4F High for Male	1.000000
---- Sham Recovery vs. 3R4F High Recovery for Male	0.816375
---- Sham Recovery vs. ZRH High Recovery for Male	0.473920
---- Sham vs. Sham Recovery for Male	0.059346
---- 3R4F High vs. 3R4F High Recovery for Male	0.157299
---- ZRH High vs. ZRH High Recovery for Male	0.146233
---- 3R4F High Recovery vs. ZRH High Recovery for Male	0.860756
---- Sham vs. 3R4F Low for Female	1.000000
---- Sham vs. 3R4F Medium for Female	1.000000
---- Sham vs. 3R4F High for Female	1.000000
---- Sham vs. ZRH Low for Female	1.000000
---- Sham vs. ZRH Medium for Female	1.000000
---- Sham vs. ZRH High for Female	1.000000
---- ZRH Low vs. 3R4F Medium for Female	1.000000
---- ZRH Medium vs. 3R4F High for Female	1.000000
---- ZRH High vs. 3R4F High for Female	1.000000
---- Sham Recovery vs. 3R4F High Recovery for Female	0.317311
---- Sham Recovery vs. ZRH High Recovery for Female	0.568202
---- Sham vs. Sham Recovery for Female	0.196706

Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = TNF_alpha

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	1.000000
---- ZRH High vs. ZRH High Recovery for Female	0.068157
---- 3R4F High Recovery vs. ZRH High Recovery for Female	0.152143

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 55

Thrombopoietin

Unit = ng/mL

Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = Thrombopoietin

Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	10	0	0	12	.
Male	3	3R4F Low	10	10	10	0	0	12	.
Male	3	3R4F Medium	10	10	10	0	0	12	.
Male	3	3R4F High	10	10	10	0	0	12	.
Male	3	ZRH Low	10	10	10	0	0	12	.
Male	3	ZRH Medium	10	10	10	0	0	12	.
Male	3	ZRH High	10	10	10	0	0	12	.
Male	4.5	Sham Recovery	6	6	6	0	0	12	.
Male	4.5	3R4F High Recovery	5	5	5	0	0	12	.
Male	4.5	ZRH High Recovery	10	10	10	0	0	12	.
Female	3	Sham	10	10	10	0	0	12	.
Female	3	3R4F Low	10	10	10	0	0	12	.
Female	3	3R4F Medium	10	10	10	0	0	12	.
Female	3	3R4F High	9	9	9	0	0	12	.
Female	3	ZRH Low	9	9	9	0	0	12	.
Female	3	ZRH Medium	10	10	10	0	0	12	.
Female	3	ZRH High	10	10	10	0	0	12	.
Female	4.5	Sham Recovery	6	6	6	0	0	12	.
Female	4.5	3R4F High Recovery	6	6	6	0	0	12	.
Female	4.5	ZRH High Recovery	10	10	10	0	0	12	.

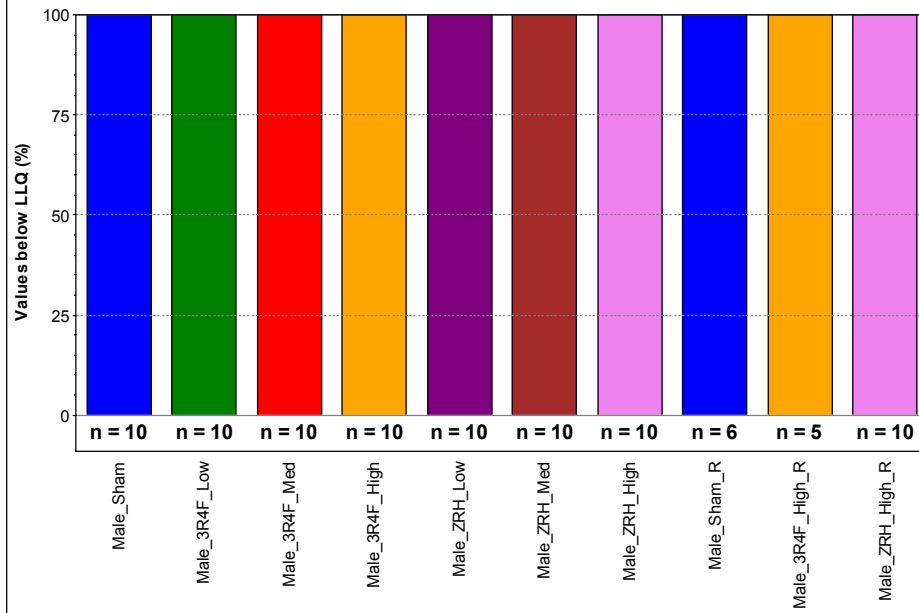
Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = Thrombopoietin

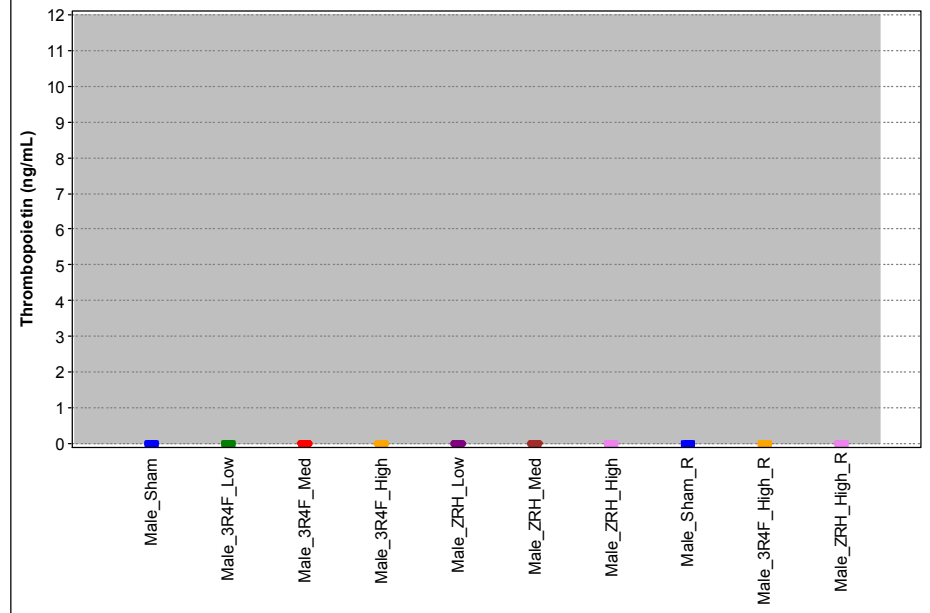
Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	6.000	6.000	6.000	6.000	6.000	6.000	0.000	0.000	0.0	.	.	12	.
Male	3	3R4F Low	6.000	6.000	6.000	6.000	6.000	6.000	0.000	0.000	0.0	.	.	12	.
Male	3	3R4F Medium	6.000	6.000	6.000	6.000	6.000	6.000	0.000	0.000	0.0	.	.	12	.
Male	3	3R4F High	6.000	6.000	6.000	6.000	6.000	6.000	0.000	0.000	0.0	.	.	12	.
Male	3	ZRH Low	6.000	6.000	6.000	6.000	6.000	6.000	0.000	0.000	0.0	.	.	12	.
Male	3	ZRH Medium	6.000	6.000	6.000	6.000	6.000	6.000	0.000	0.000	0.0	.	.	12	.
Male	3	ZRH High	6.000	6.000	6.000	6.000	6.000	6.000	0.000	0.000	0.0	.	.	12	.
Male	4.5	Sham Recovery	6.000	6.000	6.000	6.000	6.000	6.000	0.000	0.000	0.0	.	.	12	.
Male	4.5	3R4F High Recovery	6.000	6.000	6.000	6.000	6.000	6.000	0.000	0.000	0.0	.	.	12	.
Male	4.5	ZRH High Recovery	6.000	6.000	6.000	6.000	6.000	6.000	0.000	0.000	0.0	.	.	12	.
Female	3	Sham	6.000	6.000	6.000	6.000	6.000	6.000	0.000	0.000	0.0	.	.	12	.
Female	3	3R4F Low	6.000	6.000	6.000	6.000	6.000	6.000	0.000	0.000	0.0	.	.	12	.
Female	3	3R4F Medium	6.000	6.000	6.000	6.000	6.000	6.000	0.000	0.000	0.0	.	.	12	.
Female	3	3R4F High	6.000	6.000	6.000	6.000	6.000	6.000	0.000	0.000	0.0	.	.	12	.
Female	3	ZRH Low	6.000	6.000	6.000	6.000	6.000	6.000	0.000	0.000	0.0	.	.	12	.
Female	3	ZRH Medium	6.000	6.000	6.000	6.000	6.000	6.000	0.000	0.000	0.0	.	.	12	.
Female	3	ZRH High	6.000	6.000	6.000	6.000	6.000	6.000	0.000	0.000	0.0	.	.	12	.
Female	4.5	Sham Recovery	6.000	6.000	6.000	6.000	6.000	6.000	0.000	0.000	0.0	.	.	12	.
Female	4.5	3R4F High Recovery	6.000	6.000	6.000	6.000	6.000	6.000	0.000	0.000	0.0	.	.	12	.
Female	4.5	ZRH High Recovery	6.000	6.000	6.000	6.000	6.000	6.000	0.000	0.000	0.0	.	.	12	.

Percentage of Values below LLQ for each Group-Males

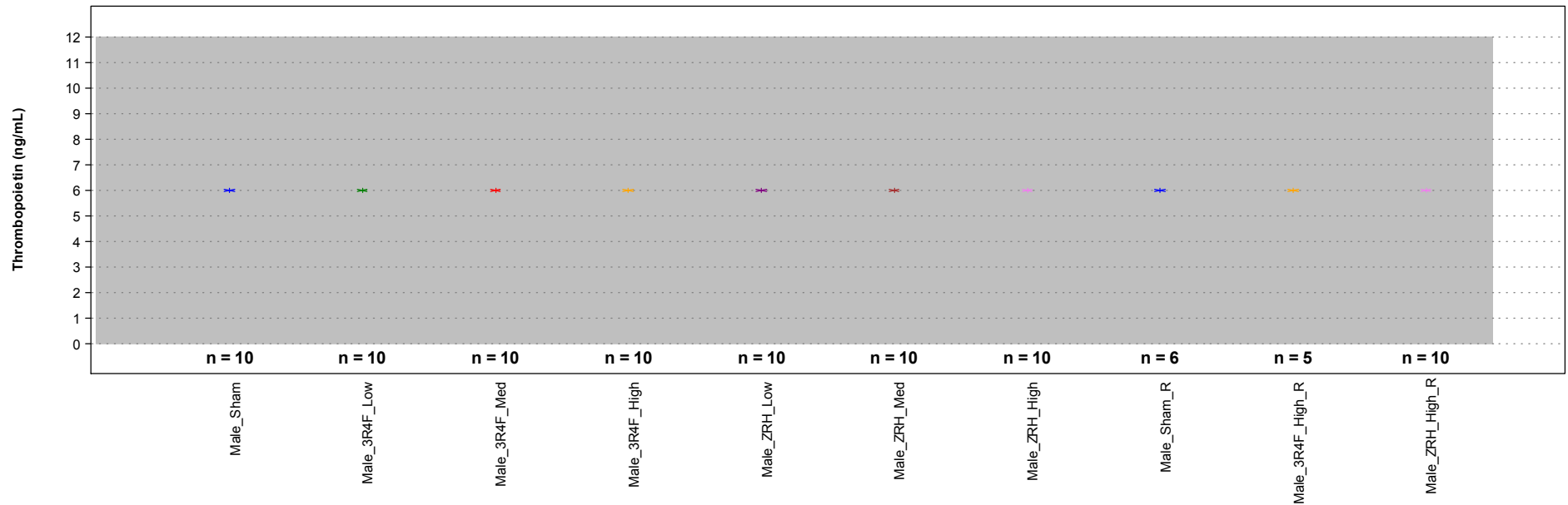
Analyte = Thrombopoietin

**Plot of Individual Measurements for each Group-Males**

<LOW> values are displayed as 0 / Values above ULQ are displayed as 1.1*ULQ
Grey zones denote zones below (average) LLQ and above (average) ULQ

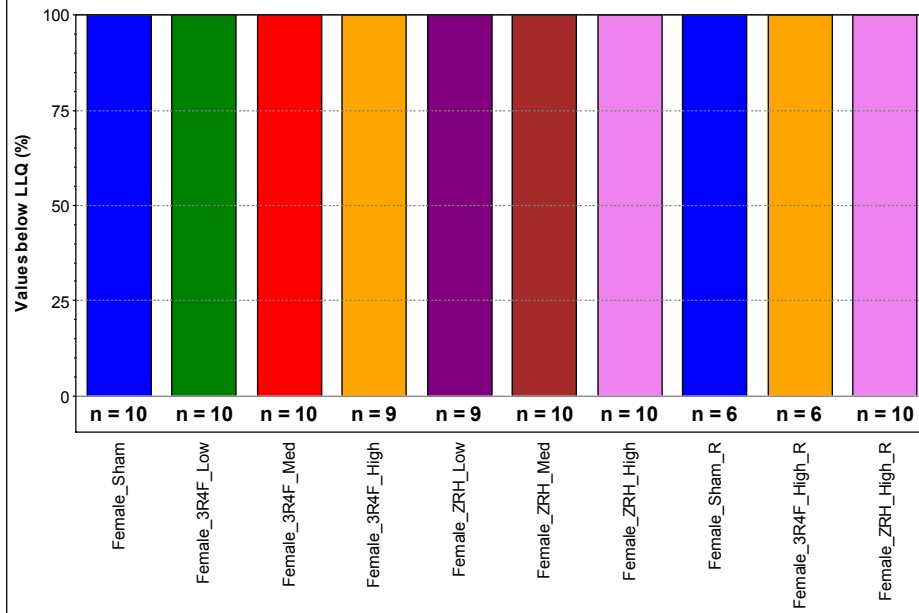
**Plot of Descriptive Robust Statistics-Males**

Displayed statistics are Median and Q1/Q3
Grey zones denote zones below LLQ and above ULQ

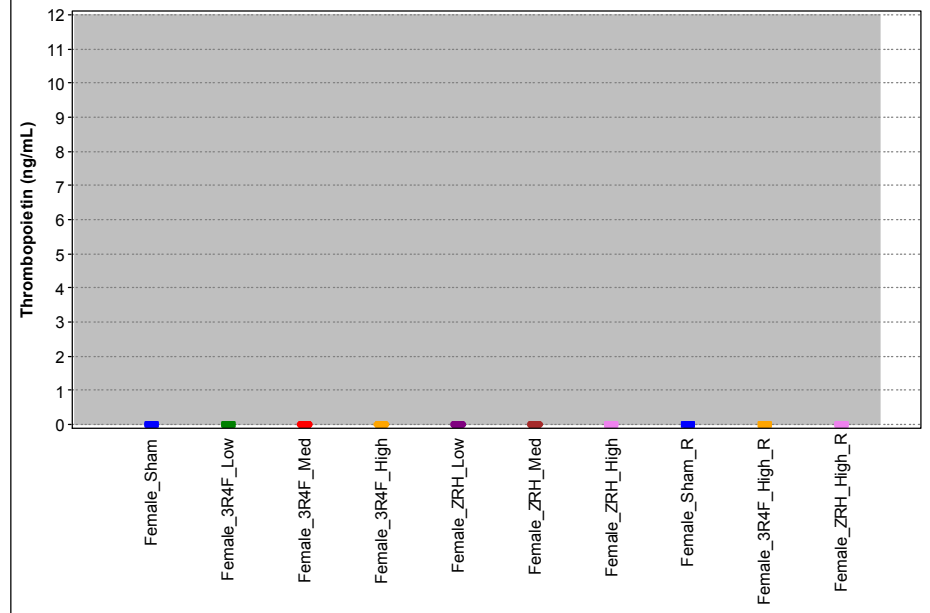


Percentage of Values below LLQ for each Group-Females

Analyte = Thrombopoietin

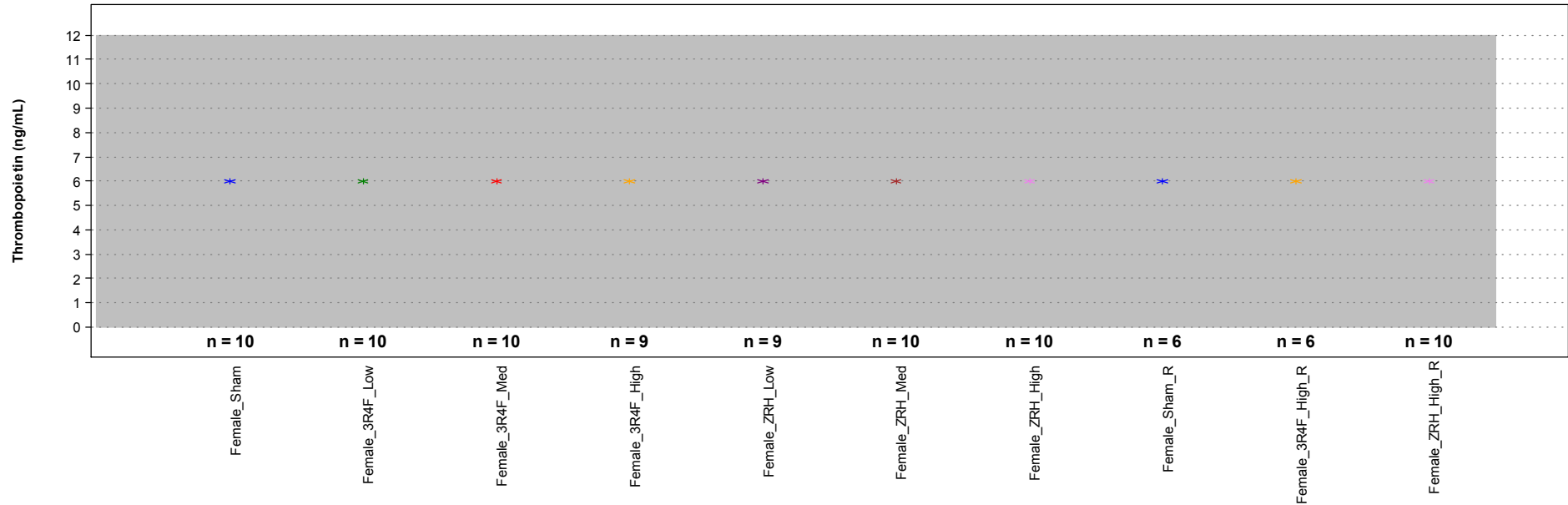
**Plot of Individual Measurements**

<LOW> values are displayed as 0 / Values above ULQ are displayed as 1.1*ULQ
Grey zones denote zones below (average) LLQ and above (average) ULQ

**Plot of Descriptive Robust Statistics-Females**

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Unadjusted P-values Obtained by Kruskal-Wallis Test **Analyte = Thrombopoietin**

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	1.000000
---- Sham vs. 3R4F Medium for Male	1.000000
---- Sham vs. 3R4F High for Male	1.000000
---- Sham vs. ZRH Low for Male	1.000000
---- Sham vs. ZRH Medium for Male	1.000000
---- Sham vs. ZRH High for Male	1.000000
---- ZRH Low vs. 3R4F Medium for Male	1.000000
---- ZRH Medium vs. 3R4F High for Male	1.000000
---- ZRH High vs. 3R4F High for Male	1.000000
---- Sham Recovery vs. 3R4F High Recovery for Male	1.000000
---- Sham Recovery vs. ZRH High Recovery for Male	1.000000
---- Sham vs. Sham Recovery for Male	1.000000
---- 3R4F High vs. 3R4F High Recovery for Male	1.000000
---- ZRH High vs. ZRH High Recovery for Male	1.000000
---- 3R4F High Recovery vs. ZRH High Recovery for Male	1.000000
---- Sham vs. 3R4F Low for Female	1.000000
---- Sham vs. 3R4F Medium for Female	1.000000
---- Sham vs. 3R4F High for Female	1.000000
---- Sham vs. ZRH Low for Female	1.000000
---- Sham vs. ZRH Medium for Female	1.000000
---- Sham vs. ZRH High for Female	1.000000
---- ZRH Low vs. 3R4F Medium for Female	1.000000
---- ZRH Medium vs. 3R4F High for Female	1.000000
---- ZRH High vs. 3R4F High for Female	1.000000
---- Sham Recovery vs. 3R4F High Recovery for Female	1.000000
---- Sham Recovery vs. ZRH High Recovery for Female	1.000000
---- Sham vs. Sham Recovery for Female	1.000000

Unadjusted P-values Obtained by Kruskal-Wallis Test
Analyte = Thrombopoietin

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	1.000000
---- ZRH High vs. ZRH High Recovery for Female	1.000000
---- 3R4F High Recovery vs. ZRH High Recovery for Female	1.000000

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 58

Vascular Cell Adhesion Molecule-1 (VCAM-1)

Unit = ng/mL

Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = VCAM_1

Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	1	9	0	0.054	.
Male	3	3R4F Low	10	10	0	10	0	0.054	.
Male	3	3R4F Medium	10	10	0	10	0	0.054	.
Male	3	3R4F High	10	10	0	10	0	0.054	.
Male	3	ZRH Low	10	10	2	8	0	0.054	.
Male	3	ZRH Medium	10	10	2	8	0	0.054	.
Male	3	ZRH High	10	10	3	7	0	0.054	.
Male	4.5	Sham Recovery	6	6	0	6	0	0.054	.
Male	4.5	3R4F High Recovery	5	5	0	5	0	0.054	.
Male	4.5	ZRH High Recovery	10	10	1	9	0	0.054	.
Female	3	Sham	10	10	3	7	0	0.054	.
Female	3	3R4F Low	10	10	0	10	0	0.054	.
Female	3	3R4F Medium	10	10	0	10	0	0.054	.
Female	3	3R4F High	9	9	0	9	0	0.054	.
Female	3	ZRH Low	9	9	3	6	0	0.054	.
Female	3	ZRH Medium	10	10	3	7	0	0.054	.
Female	3	ZRH High	10	10	1	9	0	0.054	.
Female	4.5	Sham Recovery	6	6	1	5	0	0.054	.
Female	4.5	3R4F High Recovery	6	6	1	5	0	0.054	.
Female	4.5	ZRH High Recovery	10	10	5	5	0	0.054	.

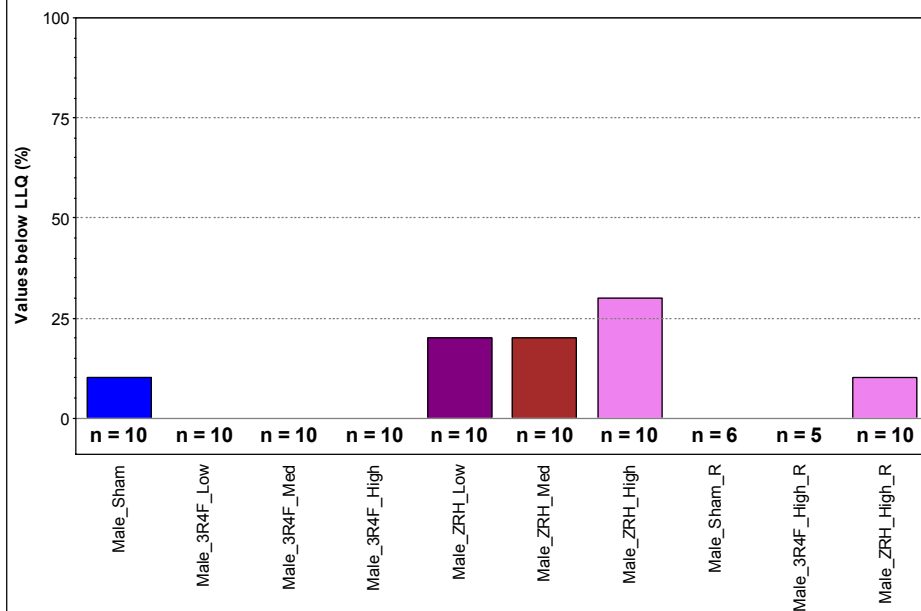
Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = VCAM_1

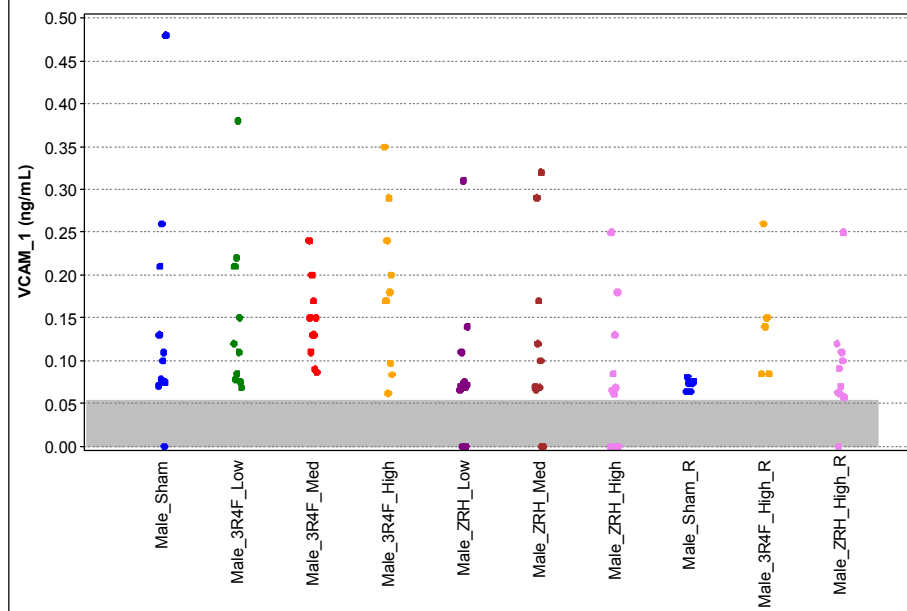
Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	0.027	0.075	0.105	0.210	0.480	0.154	0.134	0.042	86.8	1.865	3.704	0.054	.
Male	3	3R4F Low	0.069	0.078	0.115	0.210	0.380	0.150	0.097	0.031	65.1	1.667	2.848	0.054	.
Male	3	3R4F Medium	0.087	0.110	0.140	0.170	0.240	0.146	0.048	0.015	33.0	0.732	0.218	0.054	.
Male	3	3R4F High	0.062	0.097	0.175	0.240	0.350	0.184	0.091	0.029	49.5	0.437	-0.348	0.054	.
Male	3	ZRH Low	0.027	0.066	0.071	0.110	0.310	0.097	0.082	0.026	85.1	2.262	5.843	0.054	.
Male	3	ZRH Medium	0.027	0.066	0.085	0.170	0.320	0.126	0.104	0.033	82.4	1.157	0.141	0.054	.
Male	3	ZRH High	0.027	0.027	0.068	0.130	0.250	0.092	0.074	0.023	80.1	1.301	1.081	0.054	.
Male	4.5	Sham Recovery	0.064	0.064	0.074	0.076	0.081	0.072	0.007	0.003	9.5	-0.313	-1.336	0.054	.
Male	4.5	3R4F High Recovery	0.085	0.085	0.140	0.150	0.260	0.144	0.072	0.032	49.7	1.309	1.799	0.054	.
Male	4.5	ZRH High Recovery	0.027	0.061	0.081	0.110	0.250	0.095	0.061	0.019	64.6	1.990	5.032	0.054	.
Female	3	Sham	0.027	0.027	0.058	0.082	0.180	0.069	0.047	0.015	68.8	1.646	3.034	0.054	.
Female	3	3R4F Low	0.059	0.065	0.090	0.130	0.170	0.101	0.043	0.014	42.6	0.782	-0.822	0.054	.
Female	3	3R4F Medium	0.065	0.077	0.097	0.130	0.220	0.111	0.048	0.015	43.5	1.477	2.048	0.054	.
Female	3	3R4F High	0.061	0.085	0.100	0.180	0.320	0.141	0.086	0.029	61.2	1.385	1.172	0.054	.
Female	3	ZRH Low	0.027	0.027	0.077	0.079	0.210	0.083	0.063	0.021	76.5	1.255	0.864	0.054	.
Female	3	ZRH Medium	0.027	0.027	0.087	0.110	0.240	0.093	0.069	0.022	73.4	1.165	1.181	0.054	.
Female	3	ZRH High	0.027	0.059	0.082	0.110	0.220	0.094	0.057	0.018	60.2	1.394	1.834	0.054	.
Female	4.5	Sham Recovery	0.027	0.056	0.072	0.110	0.210	0.091	0.065	0.026	70.9	1.517	2.619	0.054	.
Female	4.5	3R4F High Recovery	0.027	0.055	0.120	0.160	0.230	0.119	0.073	0.030	61.7	0.324	-0.298	0.054	.
Female	4.5	ZRH High Recovery	0.027	0.027	0.044	0.081	0.180	0.064	0.050	0.016	78.4	1.509	2.202	0.054	.

Percentage of Values below LLQ for each Group-Males

Analyte = VCAM_1

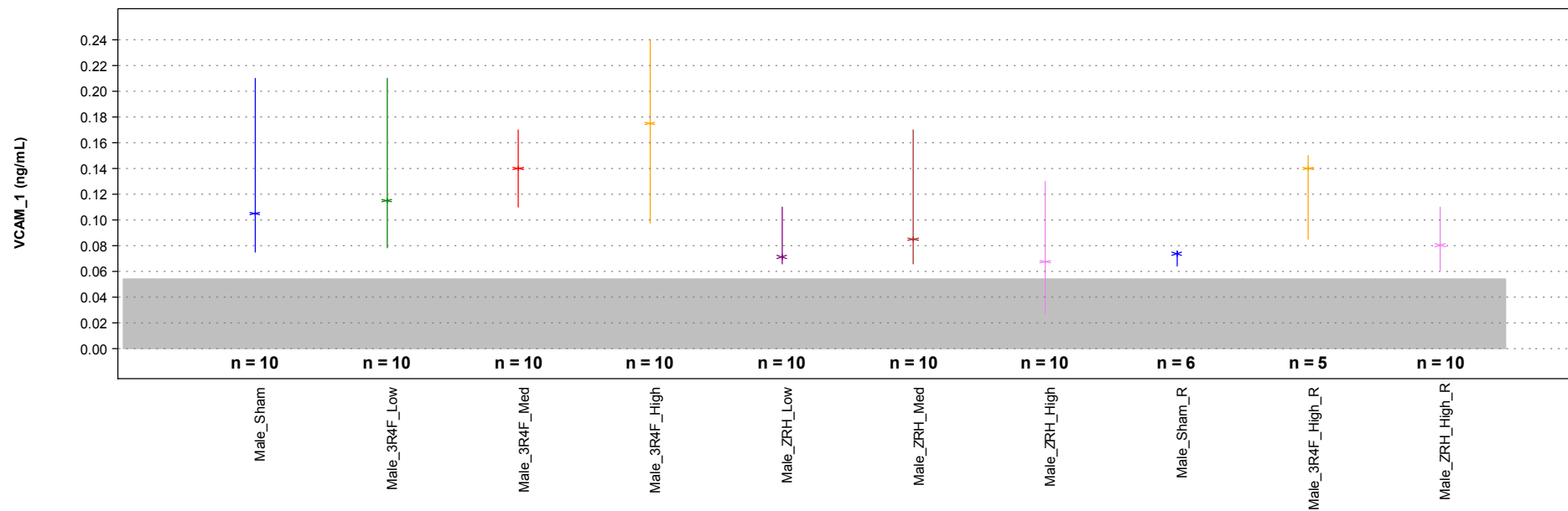
**Plot of Individual Measurements for each Group-Males**

<LOW> values are displayed as 0 / Values above ULQ are displayed as 1.1*ULQ
 Grey zones denote zones below (average) LLQ and above (average) ULQ

**Plot of Descriptive Robust Statistics-Males**

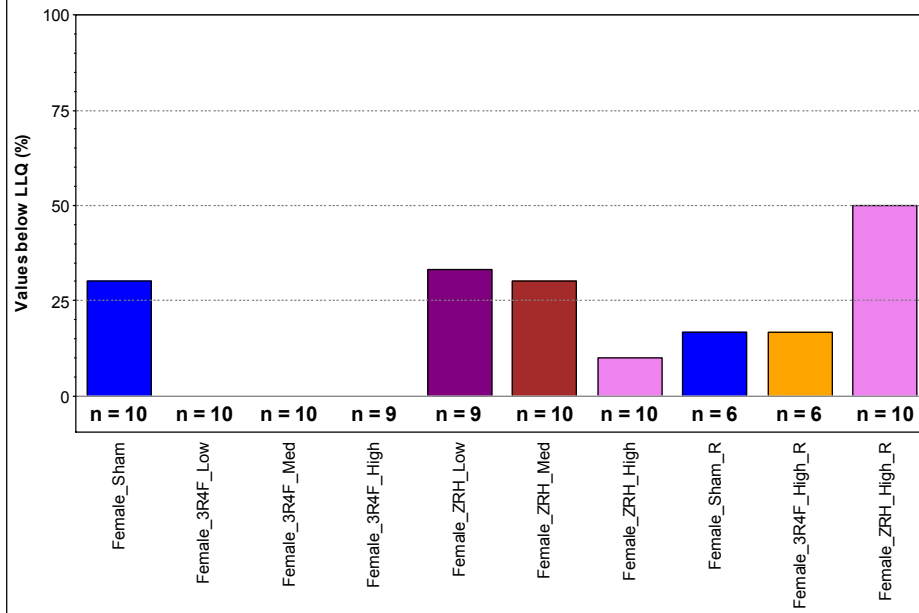
Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ

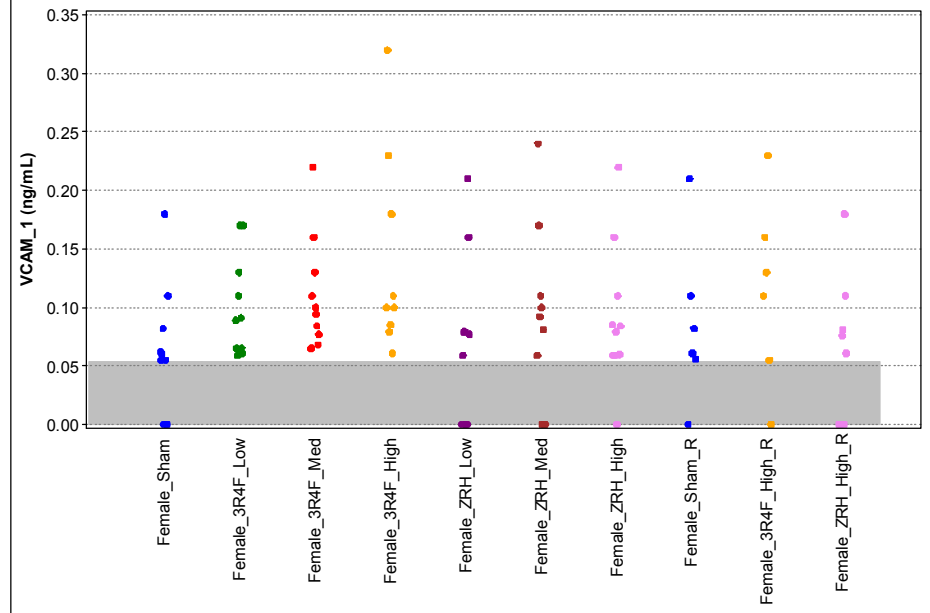


Percentage of Values below LLQ for each Group-Females

Analyte = VCAM_1

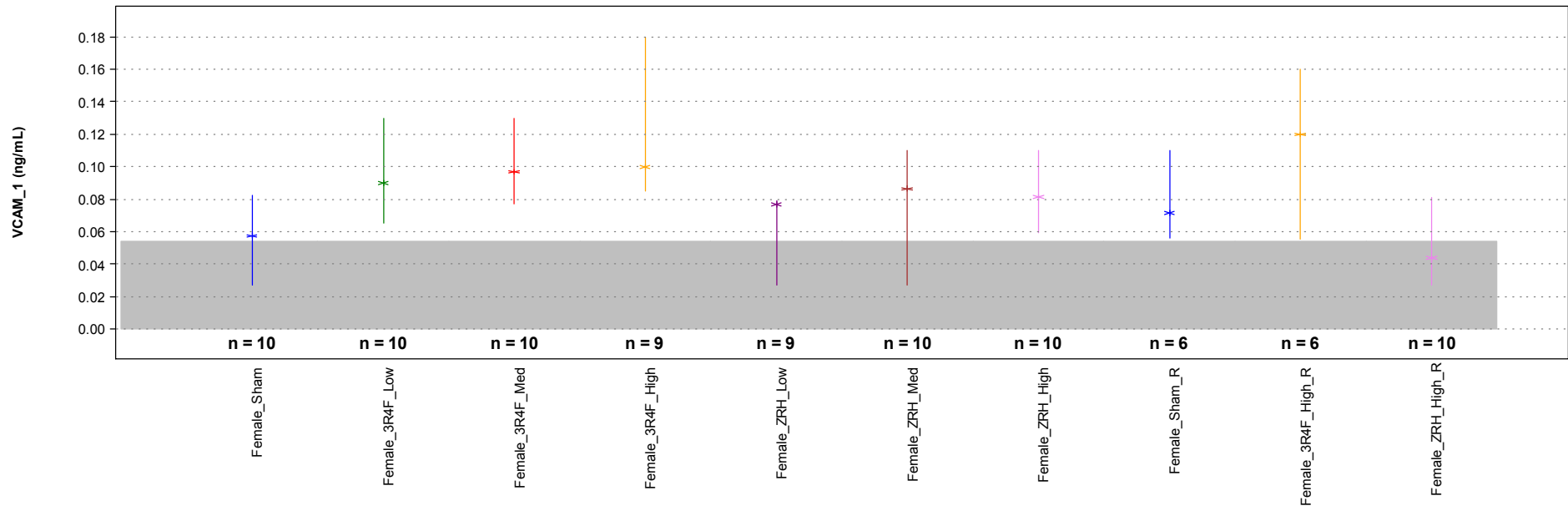
**Plot of Individual Measurements**

<LOW> values are displayed as 0 / Values above ULQ are displayed as 1.1*ULQ
 Grey zones denote zones below (average) LLQ and above (average) ULQ

**Plot of Descriptive Robust Statistics-Females**

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = VCAM_1

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	0.762021
---- Sham vs. 3R4F Medium for Male	0.343613
---- Sham vs. 3R4F High for Male	0.325569
---- Sham vs. ZRH Low for Male	0.129702
---- Sham vs. ZRH Medium for Male	0.426485
---- Sham vs. ZRH High for Male	0.128977
---- ZRH Low vs. 3R4F Medium for Male	0.013875
---- ZRH Medium vs. 3R4F High for Male	0.139569
---- ZRH High vs. 3R4F High for Male	0.025415
---- Sham Recovery vs. 3R4F High Recovery for Male	0.005825
---- Sham Recovery vs. ZRH High Recovery for Male	0.828013
---- Sham vs. Sham Recovery for Male	0.064801
---- 3R4F High vs. 3R4F High Recovery for Male	0.390420
---- ZRH High vs. ZRH High Recovery for Male	0.676204
---- 3R4F High Recovery vs. ZRH High Recovery for Male	0.111027
---- Sham vs. 3R4F Low for Female	0.044509
---- Sham vs. 3R4F Medium for Female	0.017007
---- Sham vs. 3R4F High for Female	0.013966
---- Sham vs. ZRH Low for Female	0.708750
---- Sham vs. ZRH Medium for Female	0.443279
---- Sham vs. ZRH High for Female	0.183553
---- ZRH Low vs. 3R4F Medium for Female	0.119678
---- ZRH Medium vs. 3R4F High for Female	0.176193
---- ZRH High vs. 3R4F High for Female	0.093445
---- Sham Recovery vs. 3R4F High Recovery for Female	0.520377
---- Sham Recovery vs. ZRH High Recovery for Female	0.289303
---- Sham vs. Sham Recovery for Female	0.351908

Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = VCAM_1

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	0.813172
---- ZRH High vs. ZRH High Recovery for Female	0.167586
---- 3R4F High Recovery vs. ZRH High Recovery for Female	0.118670

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 59

Vascular Endothelial Growth Factor A (VEGF-A)

Unit = pg/mL

Descriptive Statistics by Exposure Duration and Treatment Type**Analyte = VEGF_A**

Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	0	10	0	44	.
Male	3	3R4F Low	10	10	0	10	0	44	.
Male	3	3R4F Medium	10	10	0	10	0	44	.
Male	3	3R4F High	10	10	0	10	0	44	.
Male	3	ZRH Low	10	10	0	10	0	44	.
Male	3	ZRH Medium	10	10	0	10	0	44	.
Male	3	ZRH High	10	10	0	10	0	44	.
Male	4.5	Sham Recovery	6	6	0	6	0	44	.
Male	4.5	3R4F High Recovery	5	5	0	5	0	44	.
Male	4.5	ZRH High Recovery	10	10	0	10	0	44	.
Female	3	Sham	10	10	0	10	0	44	.
Female	3	3R4F Low	10	10	0	10	0	44	.
Female	3	3R4F Medium	10	10	0	10	0	44	.
Female	3	3R4F High	9	9	0	9	0	44	.
Female	3	ZRH Low	9	9	0	9	0	44	.
Female	3	ZRH Medium	10	10	0	10	0	44	.
Female	3	ZRH High	10	10	0	10	0	44	.
Female	4.5	Sham Recovery	6	6	0	6	0	44	.
Female	4.5	3R4F High Recovery	6	6	0	6	0	44	.
Female	4.5	ZRH High Recovery	10	10	0	10	0	44	.

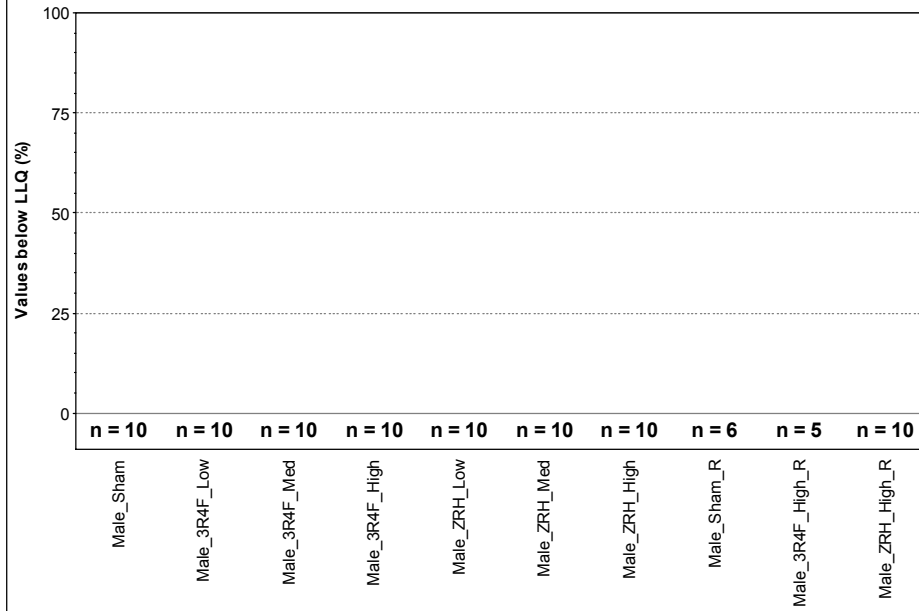
Descriptive Statistics by Exposure Duration and Treatment Type

Analyte = VEGF_A

Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	211.000	590.000	708.500	1130.000	1980.000	855.000	520.790	164.688	60.9	1.063	1.400	44	.
Male	3	3R4F Low	235.000	586.000	759.000	1070.000	1370.000	803.800	340.730	107.748	42.4	0.166	-0.224	44	.
Male	3	3R4F Medium	755.000	882.000	916.000	987.000	1050.000	917.800	83.959	26.550	9.1	-0.367	0.522	44	.
Male	3	3R4F High	152.000	535.000	759.000	1390.000	1880.000	890.400	525.150	166.067	59.0	0.632	-0.175	44	.
Male	3	ZRH Low	319.000	512.000	678.500	748.000	1690.000	734.300	374.014	118.274	50.9	2.065	5.390	44	.
Male	3	ZRH Medium	311.000	400.000	671.000	860.000	1490.000	719.800	365.452	115.566	50.8	1.042	0.942	44	.
Male	3	ZRH High	219.000	437.000	552.500	831.000	968.000	591.100	251.567	79.553	42.6	0.112	-1.216	44	.
Male	4.5	Sham Recovery	530.000	652.000	755.000	1210.000	1230.000	855.333	297.043	121.267	34.7	0.573	-1.832	44	.
Male	4.5	3R4F High Recovery	555.000	608.000	661.000	943.000	1200.000	793.400	272.232	121.746	34.3	0.998	-0.592	44	.
Male	4.5	ZRH High Recovery	430.000	652.000	1065.000	1320.000	1380.000	997.200	368.213	116.439	36.9	-0.691	-1.044	44	.
Female	3	Sham	304.000	470.000	617.000	759.000	962.000	615.500	205.605	65.018	33.4	0.111	-0.723	44	.
Female	3	3R4F Low	438.000	498.000	580.000	723.000	950.000	616.200	159.596	50.469	25.9	0.998	0.659	44	.
Female	3	3R4F Medium	553.000	697.000	817.500	967.000	1940.000	979.200	452.352	143.046	46.2	1.557	1.432	44	.
Female	3	3R4F High	347.000	817.000	991.000	1100.000	1370.000	922.111	304.222	101.407	33.0	-0.660	0.554	44	.
Female	3	ZRH Low	267.000	328.000	409.000	655.000	997.000	509.778	250.875	83.625	49.2	1.040	0.128	44	.
Female	3	ZRH Medium	362.000	477.000	587.000	777.000	837.000	603.300	168.687	53.344	28.0	0.073	-1.545	44	.
Female	3	ZRH High	303.000	412.000	480.000	817.000	1320.000	628.700	321.366	101.625	51.1	1.191	0.957	44	.
Female	4.5	Sham Recovery	397.000	599.000	901.000	970.000	1840.000	934.667	494.981	202.075	53.0	1.357	2.707	44	.
Female	4.5	3R4F High Recovery	300.000	685.000	737.000	907.000	939.000	717.500	228.641	93.342	31.9	-1.383	2.480	44	.
Female	4.5	ZRH High Recovery	397.000	501.000	689.000	830.000	1940.000	815.100	458.910	145.120	56.3	1.910	3.963	44	.

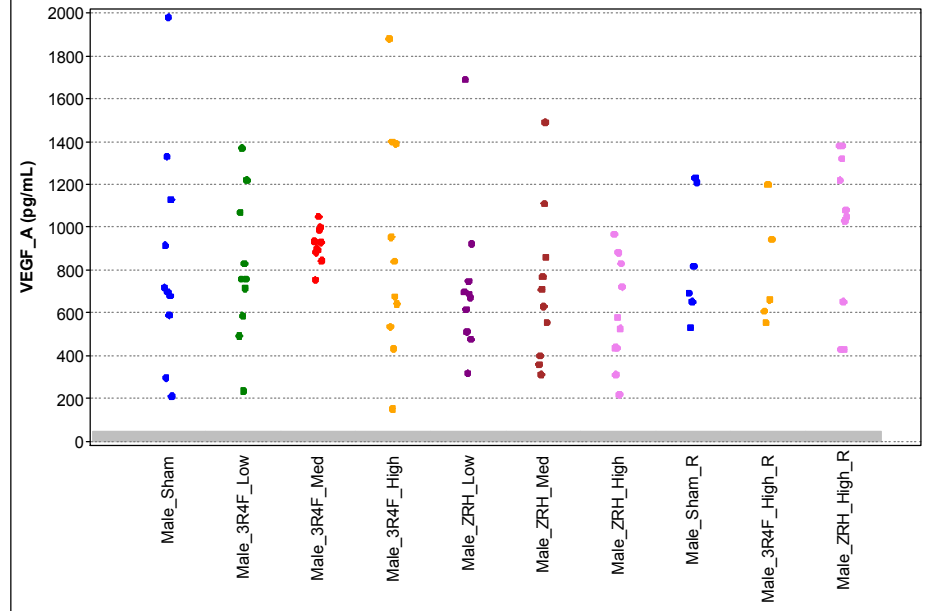
Percentage of Values below LLQ for each Group-Males

Analyte = VEGF_A



Plot of Individual Measurements for each Group-Males

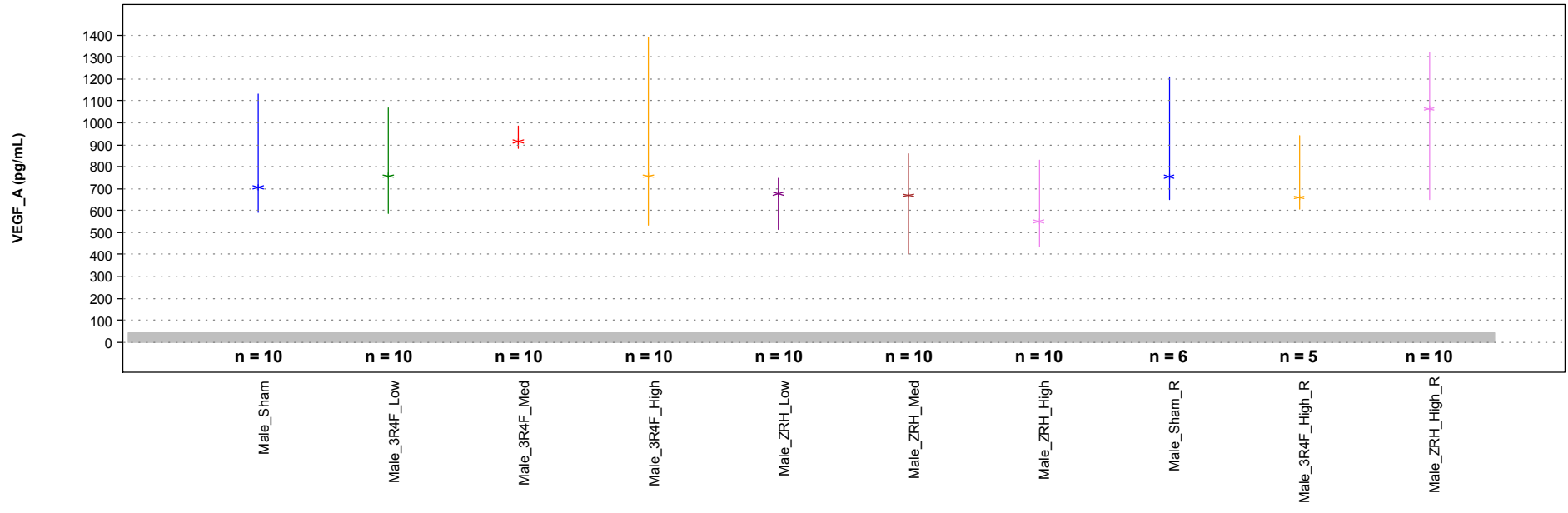
<LOW> values are displayed as 0 / Values above ULQ are displayed as 1.1*ULQ
 Grey zones denote zones below (average) LLQ and above (average) ULQ



Plot of Descriptive Robust Statistics-Males

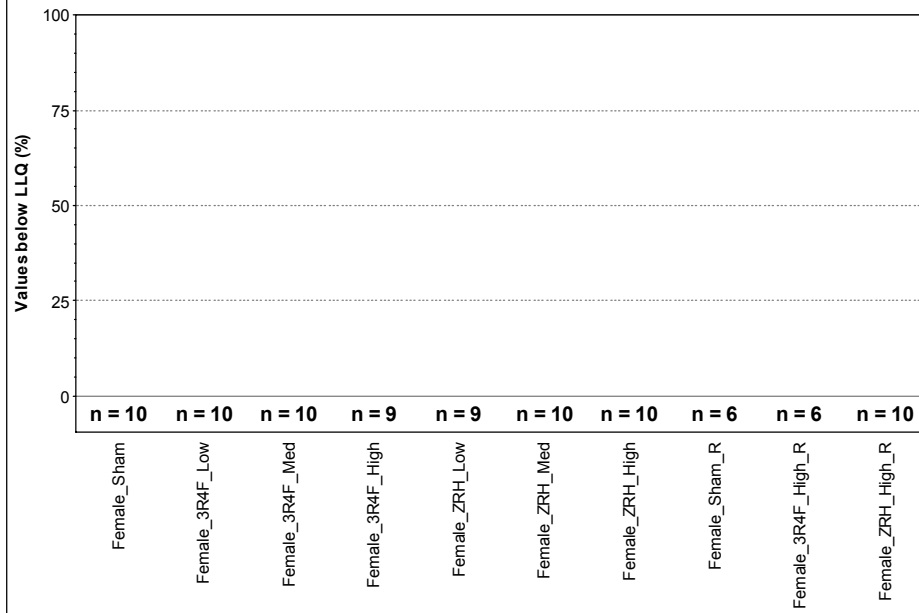
Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ

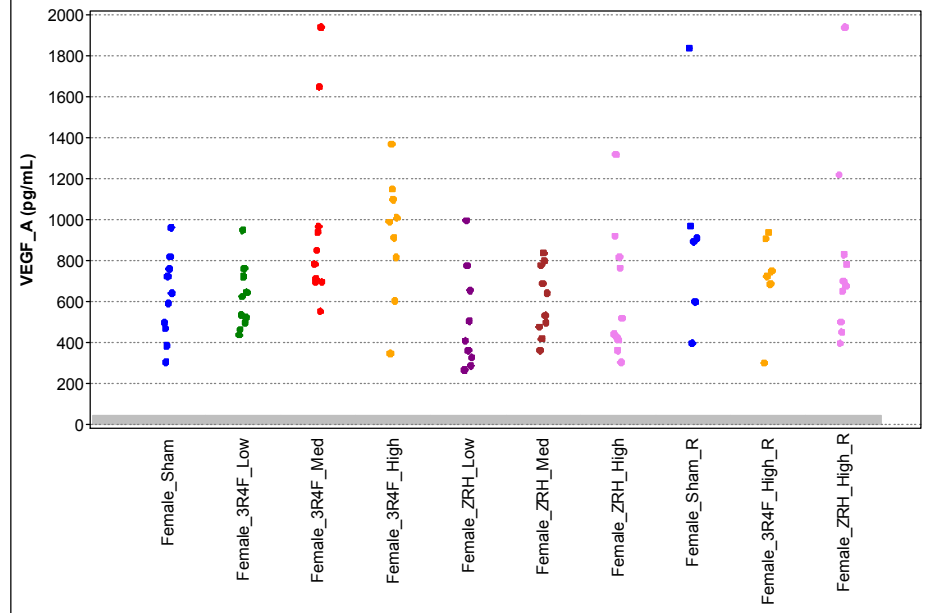


Percentage of Values below LLQ for each Group-Females

Analyte = VEGF_A

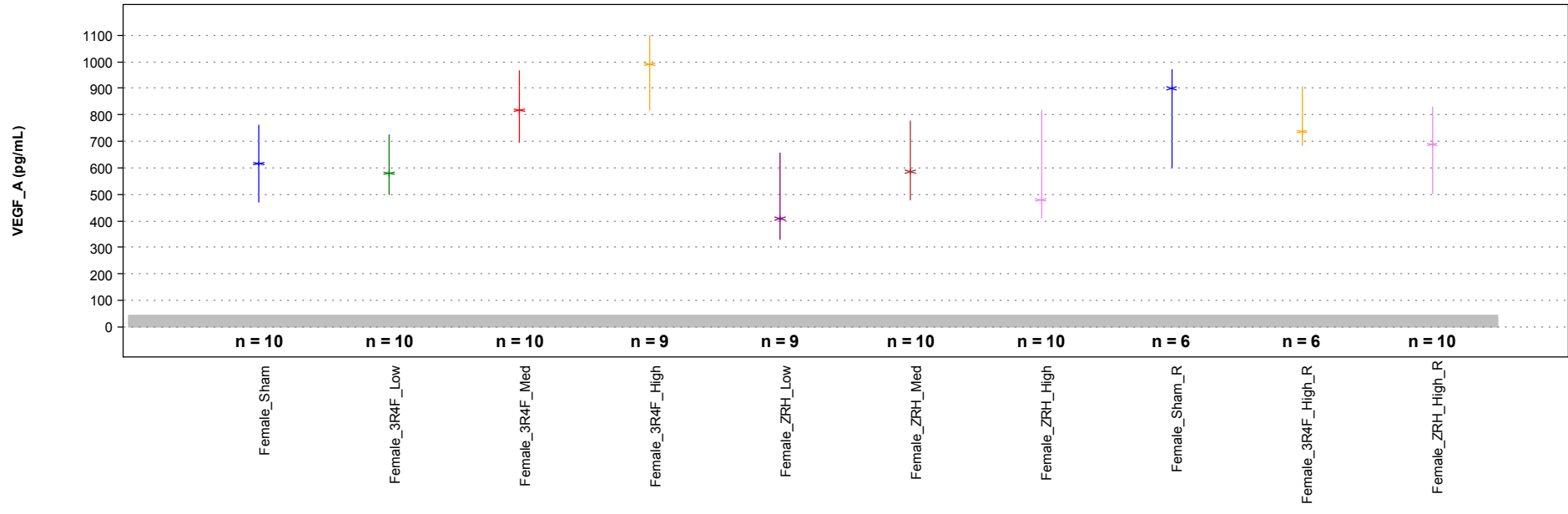
**Plot of Individual Measurements**

<LOW> values are displayed as 0 / Values above ULQ are displayed as 1.1*ULQ
 Grey zones denote zones below (average) LLQ and above (average) ULQ

**Plot of Descriptive Robust Statistics-Females**

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = VEGF_A

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	0.879784
---- Sham vs. 3R4F Medium for Male	0.256839
---- Sham vs. 3R4F High for Male	1.000000
---- Sham vs. ZRH Low for Male	0.570606
---- Sham vs. ZRH Medium for Male	0.650147
---- Sham vs. ZRH High for Male	0.289737
---- ZRH Low vs. 3R4F Medium for Male	0.008151
---- ZRH Medium vs. 3R4F High for Male	0.496292
---- ZRH High vs. 3R4F High for Male	0.226301
---- Sham Recovery vs. 3R4F High Recovery for Male	0.583882
---- Sham Recovery vs. ZRH High Recovery for Male	0.479825
---- Sham vs. Sham Recovery for Male	0.913627
---- 3R4F High vs. 3R4F High Recovery for Male	0.806496
---- ZRH High vs. ZRH High Recovery for Male	0.023186
---- 3R4F High Recovery vs. ZRH High Recovery for Male	0.269487
---- Sham vs. 3R4F Low for Female	0.939743
---- Sham vs. 3R4F Medium for Female	0.034294
---- Sham vs. 3R4F High for Female	0.022243
---- Sham vs. ZRH Low for Female	0.288487
---- Sham vs. ZRH Medium for Female	0.969839
---- Sham vs. ZRH High for Female	0.762369
---- ZRH Low vs. 3R4F Medium for Female	0.008981
---- ZRH Medium vs. 3R4F High for Female	0.017892
---- ZRH High vs. 3R4F High for Female	0.054907
---- Sham Recovery vs. 3R4F High Recovery for Female	0.423340
---- Sham Recovery vs. ZRH High Recovery for Female	0.480472
---- Sham vs. Sham Recovery for Female	0.103742

Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = VEGF_A

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	0.098960
---- ZRH High vs. ZRH High Recovery for Female	0.289918
---- 3R4F High Recovery vs. ZRH High Recovery for Female	0.744882

OECD ZRH 90-days Study (P15006)

Statistical Analysis of MAP Data in BALF

Analyte no 60

von Willebrand factor (vWF)

Unit = ng/mL

Descriptive Statistics by Exposure Duration and Treatment Type

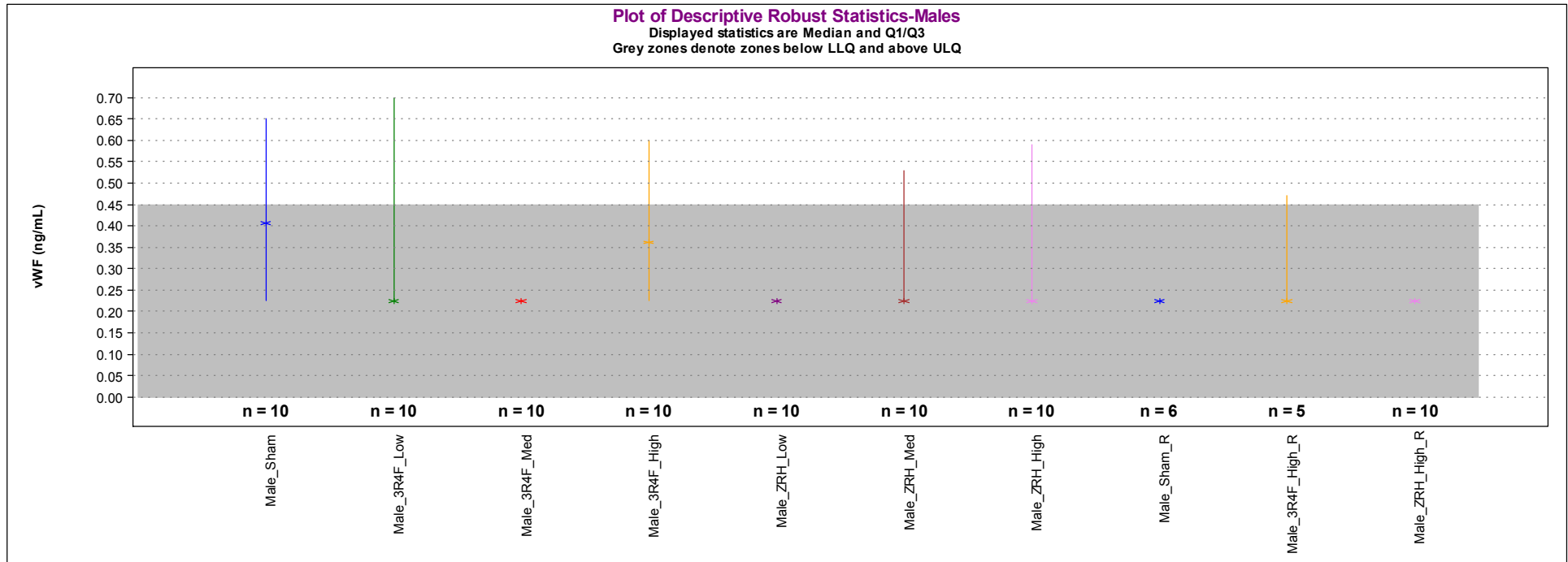
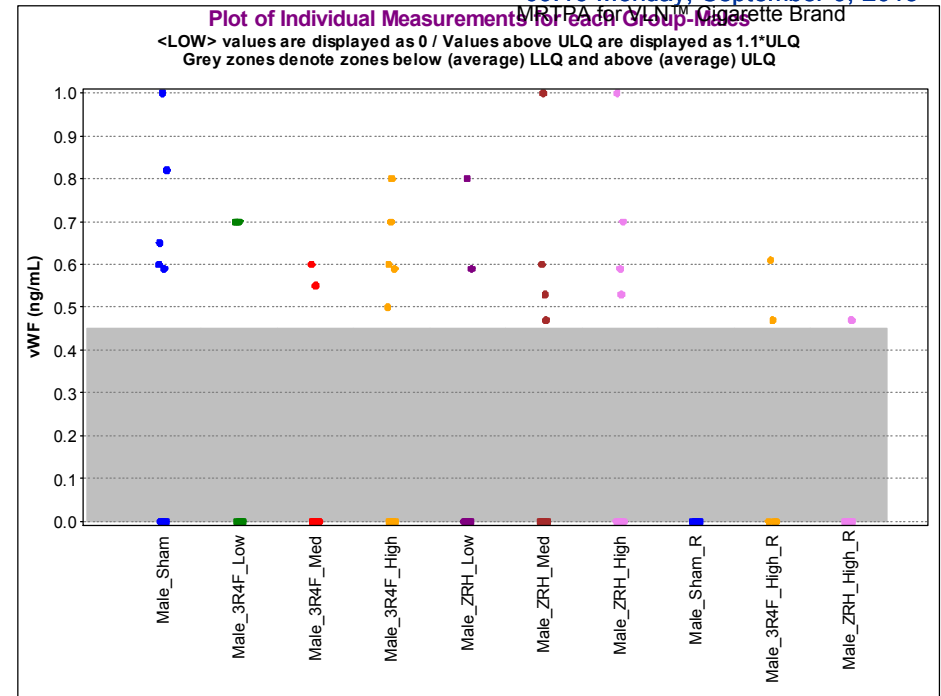
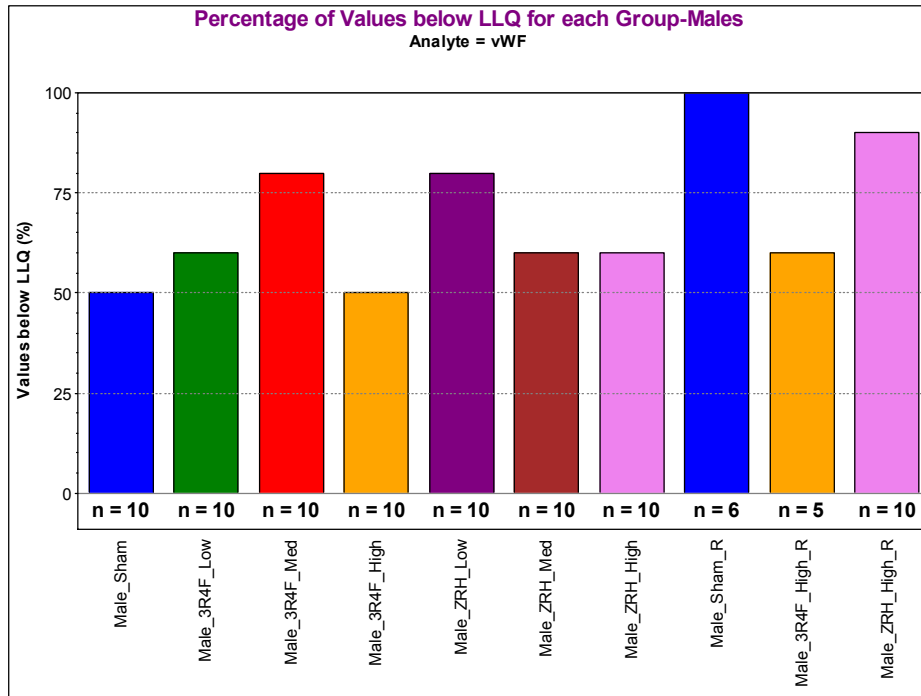
Analyte = vWF

Gender	Duration (months)	Treatment Type	Planned Size	Measured Size	Below LLQ	Valid Size	Above ULQ	LLQ	ULQ
Male	3	Sham	10	10	5	5	0	0.45	.
Male	3	3R4F Low	10	10	6	4	0	0.45	.
Male	3	3R4F Medium	10	10	8	2	0	0.45	.
Male	3	3R4F High	10	10	5	5	0	0.45	.
Male	3	ZRH Low	10	10	8	2	0	0.45	.
Male	3	ZRH Medium	10	10	6	4	0	0.45	.
Male	3	ZRH High	10	10	6	4	0	0.45	.
Male	4.5	Sham Recovery	6	6	6	0	0	0.45	.
Male	4.5	3R4F High Recovery	5	5	3	2	0	0.45	.
Male	4.5	ZRH High Recovery	10	10	9	1	0	0.45	.
Female	3	Sham	10	10	8	2	0	0.45	.
Female	3	3R4F Low	10	10	8	2	0	0.45	.
Female	3	3R4F Medium	10	10	8	2	0	0.45	.
Female	3	3R4F High	9	9	7	2	0	0.45	.
Female	3	ZRH Low	9	9	8	1	0	0.45	.
Female	3	ZRH Medium	10	10	7	3	0	0.45	.
Female	3	ZRH High	10	10	9	1	0	0.45	.
Female	4.5	Sham Recovery	6	6	4	2	0	0.45	.
Female	4.5	3R4F High Recovery	6	6	4	2	0	0.45	.
Female	4.5	ZRH High Recovery	10	10	10	0	0	0.45	.

Descriptive Statistics by Exposure Duration and Treatment Type

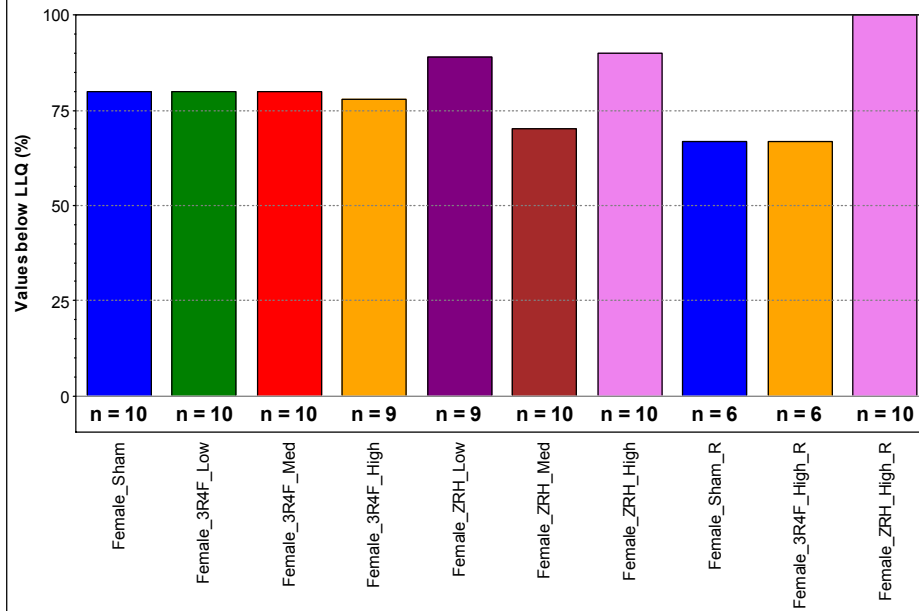
Analyte = vWF

Gender	Duration (months)	Treatment Type	MIN	Q1	MED	Q3	MAX	Mean	STD	SEM	CV	SKEW	KURT	LLQ	ULQ
Male	3	Sham	0.225	0.225	0.408	0.650	1.000	0.479	0.292	0.092	61.0	0.606	-1.046	0.45	.
Male	3	3R4F Low	0.225	0.225	0.225	0.700	0.700	0.415	0.245	0.078	59.1	0.484	-2.277	0.45	.
Male	3	3R4F Medium	0.225	0.225	0.225	0.225	0.600	0.295	0.148	0.047	50.2	1.807	1.601	0.45	.
Male	3	3R4F High	0.225	0.225	0.363	0.600	0.800	0.432	0.231	0.073	53.5	0.389	-1.708	0.45	.
Male	3	ZRH Low	0.225	0.225	0.225	0.225	0.800	0.319	0.204	0.065	64.0	2.030	3.127	0.45	.
Male	3	ZRH Medium	0.225	0.225	0.225	0.530	1.000	0.395	0.259	0.082	65.7	1.620	2.470	0.45	.
Male	3	ZRH High	0.225	0.225	0.225	0.590	1.000	0.417	0.276	0.087	66.1	1.227	0.618	0.45	.
Male	4.5	Sham Recovery	0.225	0.225	0.225	0.225	0.225	0.225	0.000	0.000	0.0	.	.	0.45	.
Male	4.5	3R4F High Recovery	0.225	0.225	0.225	0.470	0.610	0.351	0.179	0.080	51.1	0.941	-1.429	0.45	.
Male	4.5	ZRH High Recovery	0.225	0.225	0.225	0.225	0.470	0.250	0.077	0.025	31.1	3.162	10.000	0.45	.
Female	3	Sham	0.225	0.225	0.225	0.225	0.920	0.321	0.226	0.072	70.5	2.547	6.490	0.45	.
Female	3	3R4F Low	0.225	0.225	0.225	0.225	0.540	0.282	0.121	0.038	42.9	1.839	1.824	0.45	.
Female	3	3R4F Medium	0.225	0.225	0.225	0.225	0.860	0.320	0.214	0.068	66.9	2.285	4.819	0.45	.
Female	3	3R4F High	0.225	0.225	0.225	0.225	0.860	0.349	0.250	0.083	71.5	1.717	1.384	0.45	.
Female	3	ZRH Low	0.225	0.225	0.225	0.225	0.540	0.260	0.105	0.035	40.4	3.000	9.000	0.45	.
Female	3	ZRH Medium	0.225	0.225	0.225	0.710	0.920	0.392	0.274	0.087	70.0	1.213	-0.320	0.45	.
Female	3	ZRH High	0.225	0.225	0.225	0.225	0.540	0.257	0.100	0.032	38.8	3.162	10.000	0.45	.
Female	4.5	Sham Recovery	0.225	0.225	0.225	0.470	0.810	0.363	0.240	0.098	66.0	1.736	2.519	0.45	.
Female	4.5	3R4F High Recovery	0.225	0.225	0.225	0.470	0.470	0.307	0.127	0.052	41.3	0.968	-1.875	0.45	.
Female	4.5	ZRH High Recovery	0.225	0.225	0.225	0.225	0.225	0.225	0.000	0.000	0.0	.	.	0.45	.

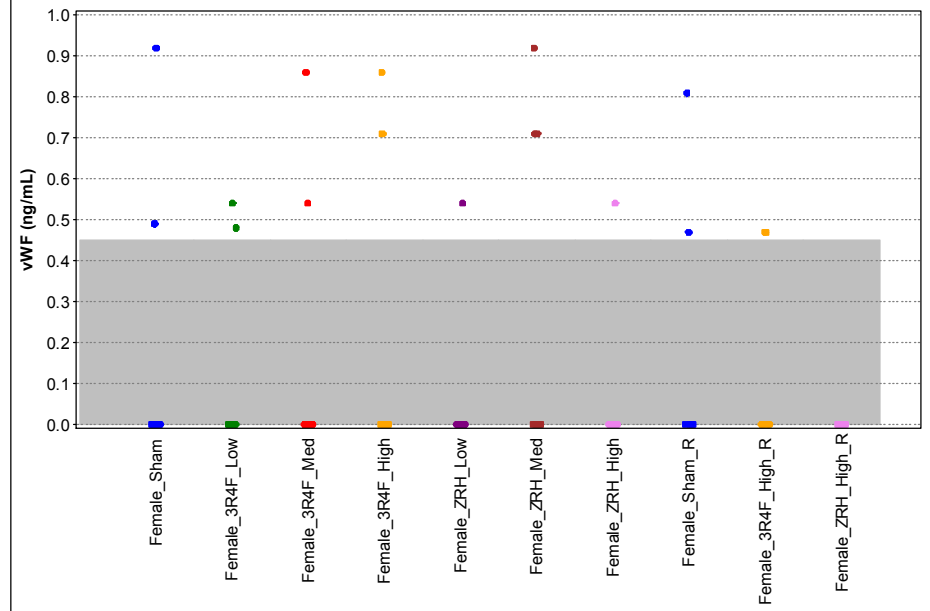


Percentage of Values below LLQ for each Group-Females

Analyte = vWF

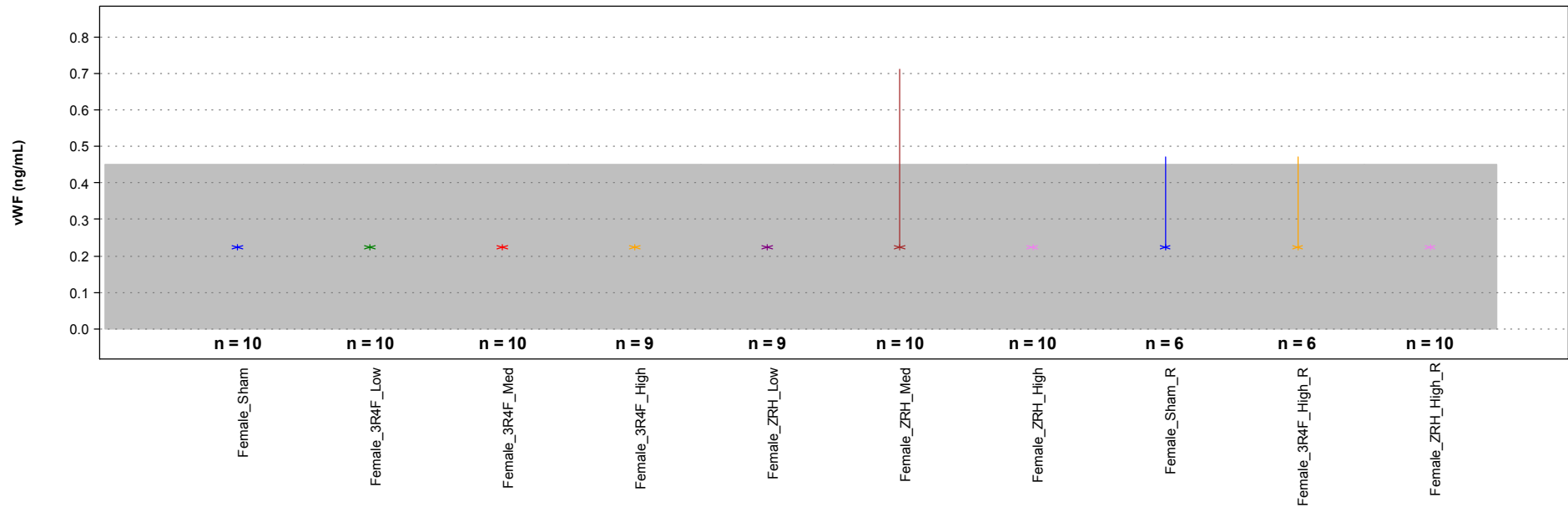
**Plot of Individual Measurements**

<LOW> values are displayed as 0 / Values above ULQ are displayed as 1.1*ULQ
 Grey zones denote zones below (average) LLQ and above (average) ULQ

**Plot of Descriptive Robust Statistics-Females**

Displayed statistics are Median and Q1/Q3

Grey zones denote zones below LLQ and above ULQ



Unadjusted P-values Obtained by Kruskal-Wallis Test

Analyte = vWF

Comparison Type	Unadjusted p-value
---- Sham vs. 3R4F Low for Male	0.803080
---- Sham vs. 3R4F Medium for Male	0.100636
---- Sham vs. 3R4F High for Male	0.716028
---- Sham vs. ZRH Low for Male	0.143115
---- Sham vs. ZRH Medium for Male	0.456040
---- Sham vs. ZRH High for Male	0.562088
---- ZRH Low vs. 3R4F Medium for Male	0.913892
---- ZRH Medium vs. 3R4F High for Male	0.590515
---- ZRH High vs. 3R4F High for Male	0.740432
---- Sham Recovery vs. 3R4F High Recovery for Male	0.104204
---- Sham Recovery vs. ZRH High Recovery for Male	0.438578
---- Sham vs. Sham Recovery for Male	0.047913
---- 3R4F High vs. 3R4F High Recovery for Male	0.549980
---- ZRH High vs. ZRH High Recovery for Male	0.091234
---- 3R4F High Recovery vs. ZRH High Recovery for Male	0.160530
---- Sham vs. 3R4F Low for Female	0.913892
---- Sham vs. 3R4F Medium for Female	1.000000
---- Sham vs. 3R4F High for Female	0.908865
---- Sham vs. ZRH Low for Female	0.607149
---- Sham vs. ZRH Medium for Female	0.584291
---- Sham vs. ZRH High for Female	0.543195
---- ZRH Low vs. 3R4F Medium for Female	0.562558
---- ZRH Medium vs. 3R4F High for Female	0.711573
---- ZRH High vs. 3R4F High for Female	0.403442
---- Sham Recovery vs. 3R4F High Recovery for Female	0.847390
---- Sham Recovery vs. ZRH High Recovery for Female	0.059346
---- Sham vs. Sham Recovery for Female	0.669028

Unadjusted P-values Obtained by Kruskal-Wallis Test
Analyte = vWF

Comparison Type	Unadjusted p-value
---- 3R4F High vs. 3R4F High Recovery for Female	0.879605
---- ZRH High vs. ZRH High Recovery for Female	0.317311
---- 3R4F High Recovery vs. ZRH High Recovery for Female	0.058782