



**GLP**

***Zero to GLP***

***Compliance Issues Facing Today's Bioanalytical Scientists.***

***Incurred Sample Reproducibility: Part 1***



# Why investigate Incurred Sample Reproducibility?



# Why investigate Incurred Sample Reproducibility?

We want to **demonstrate** that using our validated, for intended use, analytical method, that we can **reliably measure analytes(s) of interest** In **both** biological matrices, to which we **have added known concentrations of analyte**, and incurred samples, which represent **analyte which has**, to some extent, **undergone adsorption, distribution, metabolism and elimination within a biological system.**



# How do we investigate Incurred Sample Reproducibility?

- Perform ISR as early as possible
- Select between 5 and 10 % of study samples for reanalysis
- Select samples from as many individuals as is practical
- Select samples > LLOQ which can be quantified without dilution, ideally from both adsorption and elimination phases
- Calculations

$$\left( \frac{(\text{Result}_2 - \text{Result}_1)}{(\text{Average}_{\text{Result 1 and 2}})} \right) \times 100 = \% \text{ Difference}$$

**Incurred sample reproducibility is acceptable  
when % Diff are within  $\pm 20$  ( $\pm 30$  for LBA)  
in 2/3 of samples**

**Review data for any indication of bias**



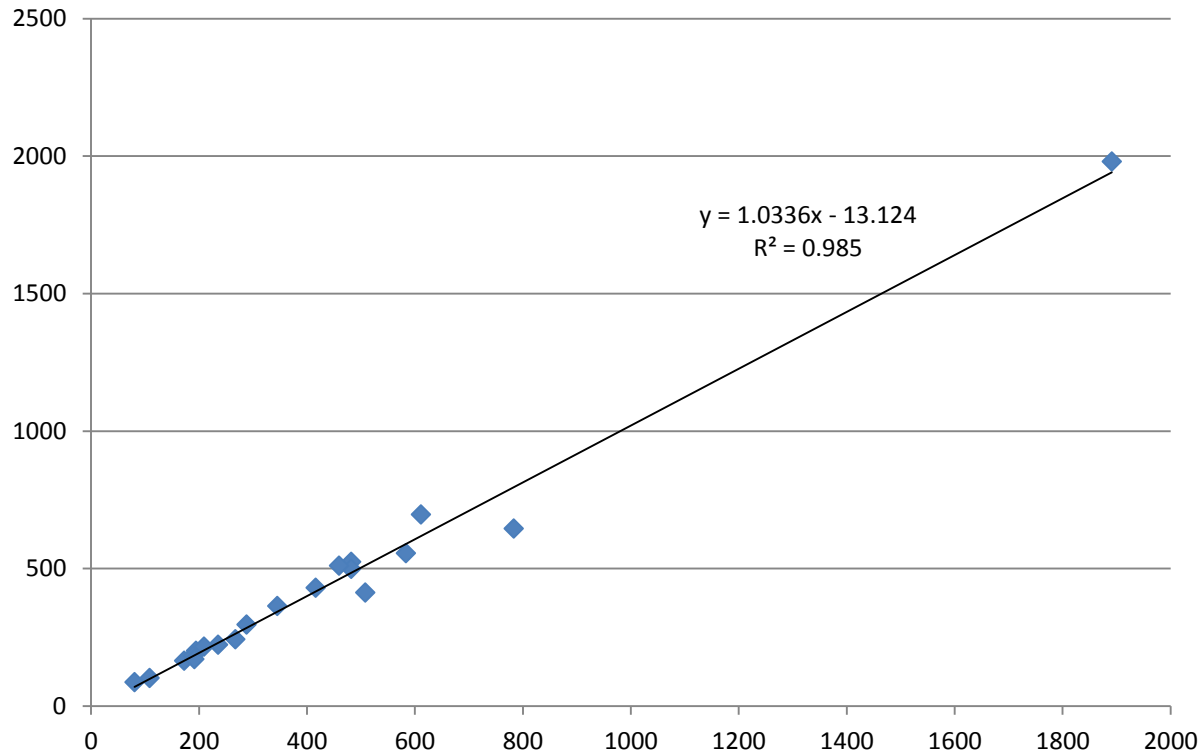
# How do we investigate Incurred Sample Reproducibility?

R1	R2	R2 - R1	Mean R1 and R2	% Diff	% Diff Relative to R1
80.1	87.6	7.50	83.85	8.9	9.4
1891	1981	90.00	1936	4.6	4.8
194	201	7.00	197.5	3.5	3.6
288	297	9.00	292.5	3.1	3.1
416	431	15.00	423.5	3.5	3.6
108	103	-5.00	105.5	-4.7	-4.6
172	165	-7.00	168.5	-4.2	-4.1
482	525	43.00	503.5	8.5	8.9
267	243	-24.00	255	-9.4	-9.0
611	697	86.00	654	13.1	14.1
482	499	17.00	490.5	3.5	3.5
345	365	20.00	355	5.6	5.8
459	511	52.00	485	10.7	11.3
189	183	-6.00	186	-3.2	-3.2
783	646	-137.00	714.5	-19.2	-17.5
191	171	-20.00	181	-11.0	-10.5
508	413	-95.00	460.5	-20.6	-18.7
235	224	-11.00	229.5	-4.8	-4.7
583	556	-27.00	569.5	-4.7	-4.6
209	217	8.00	213	3.8	3.8

Data from: Mario L. Rocci, Jr. , Viswanath Devanarayan , David B. Haughey , and Paula Jardieu , “Confir matory Reanalysis of Incurred Bioanalytical Samples”



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	<i>Coefficients</i>	<i>Standard Error</i>	<i>t Stat</i>	<i>P-value</i>	<i>Lower 95%</i>	<i>Upper 95%</i>
Intercept	-13.12389884	17.17538859	-0.764110738	0.45470188	-49.20805122	22.96025353
X Variable 1	1.033554059	0.030039266	34.40676835	7.08111E-18	0.970443903	1.096664214

