UNCERTAINTY OF MEASUREMENT BUDGET PROCEDURE

This procedure should meet the requirements of ISO 15189 Clauses 5.5.3 (c), and 5.6.2.

To date (Nov. 2005) there is no single document that is universally accepted or sufficiently prescriptive as to provide a procedure that can be generally applied.

Reference was made to the following documents before this Procedure was devised.

TITLE	**Web Address**
CAEAL Policy on the Estimation of Uncertainty of Measurement in Environmental Testing (CAEL = Canadian Association For Environmental Analytical Laboratories)	http://www.caeal.ca/P19_CAEAL_Unce_Pol.pdf
Uncertainty Of Measurement In Biological, Forensic, Medical And Veterinary Testing : NATA Technical Circular #2 : December 2003	http://www.nata.asn.au/publications/downloads/TechCirc2.pdf
Uncertainty of Measurement in Quantitative Medical Testing - A Laboratory Implementation Guide (NATA, AACB, AIMS, RCPA Joint Document)	http://www.aacb.asn.au/pubs/Uncertainty%20of%20measurement.pdf
BIOLOGICAL VARIATION - FROM PRINCIPLES TO PRACTICE (Book by Callum Fraser) 	http://www.aaccdirect.org/ProductCatalog/Product.aspx?ID=1541
Uncertainty of Measurement : RCPA Guideline November 2004.	http://www.rcpa.edu.au/applications/DocumentLibraryManager2/upload/Uncertainty%20of%20measurement.pdf

The sources of variation that become embedded within a pathology laboratory result are many and varied but fall under the following broad headings :

- Biological Variation
- Pre-Analytical Variation
- Analytical Variation

Biological Variation has been quantitated by a number of workers and James Westgard has compiled an exhaustive list on his website http://www.westgard.com/biodatabase1.htm . A very similar database is also viewable at http://www.dgrhoads.com/db2004/bv2004.php which has been compiled by David G Rhoads Associates, Inc..

Pre-Analytical Variation occurs external to the laboratory and is usually mostly outside of the laboratory's control. Suffice it to say that where preanalytical variation can be controlled by appropriate patient preparation advice eg.

- *Fast from midnight before this test ..*
- *This test must be performed on serum samples from antenatal clinic patients who are in their second trimester of pregnancy…..*

then this should be included in the handbook or advice given to Doctors using your Lab's services..

Analytical Variation is well understood by laboratory scientists and is easily expressed as coefficients of variations of an assay at a low and a high concentration eg at the Low and High QC sample levels.

I have elected to apply a procedure based upon the recommendations given by Callum Fraser in his book 'BIOLOGICAL VARIATION - FROM PRINCIPLES TO PRACTICE' (Doc ID# 3076).

> If analytical variation is called SD_A and within-subject biological variation is called SD_I then total variation (SD_T) can be calculated as follows:
>
> $SD_T^2 = SD_A^2 + SD_I^2$ or $SD_T = (SD_A^2 + SD_I^2)^{1/2}$.
>
> If we determine or estimate CV_A at the same level as CV_I, the means of the values will be the same in this case, so the calculation of total variation becomes
>
> $CV_T^2 = CV_A^2 + CV_I^2$
>
> or
>
> $CV_T = (CV_A^2 + CV_I^2)^{1/2}$.

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> - *Desirable performance* is defined by $CV_A < 0.50CV_I$. Quality specifications generated using this formula should be viewed as being generally applicable. This is the original, most widely accepted, and very frequently used quality specification based on biological variation, but we have suggested that, in order to cater to those analytes for which the general quality specifications appear too "loose" or too "stringent," then:
> - *Optimum performance* is defined by $CV_A < 0.25CV_I$. The more-stringent quality specifications generated using this formula should be used for quantities for which desirable performance standards are easily achieved with current technology and methodology.
> - *Minimum performance* is defined by $CV_A < 0.75CV_I$. The less-stringent quality specifications generated using this formula should be used for those quantities for which the desirable performance standards are not attainable with current technology and methodology.

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1. PROCEDURE :

(a) Record the values of the following parameters on each quantitative test

- Analyte Name
- Lower Limit of Normal
- Upper Limit of Normal
- Biological Coefficient of Variation (**CVw** from http://www.westgard.com/biodatabase1.htm)
- Low QC value in concentration units
- CV% observed in this laboratory for 30 or more measurements made on the same batch of this Low QC material
- High QC value in concentration units
- CV% observed in this laboratory for 30 or more measurements made on the same batch of this High QC material

(b) Transcribe these data into the Excel template :

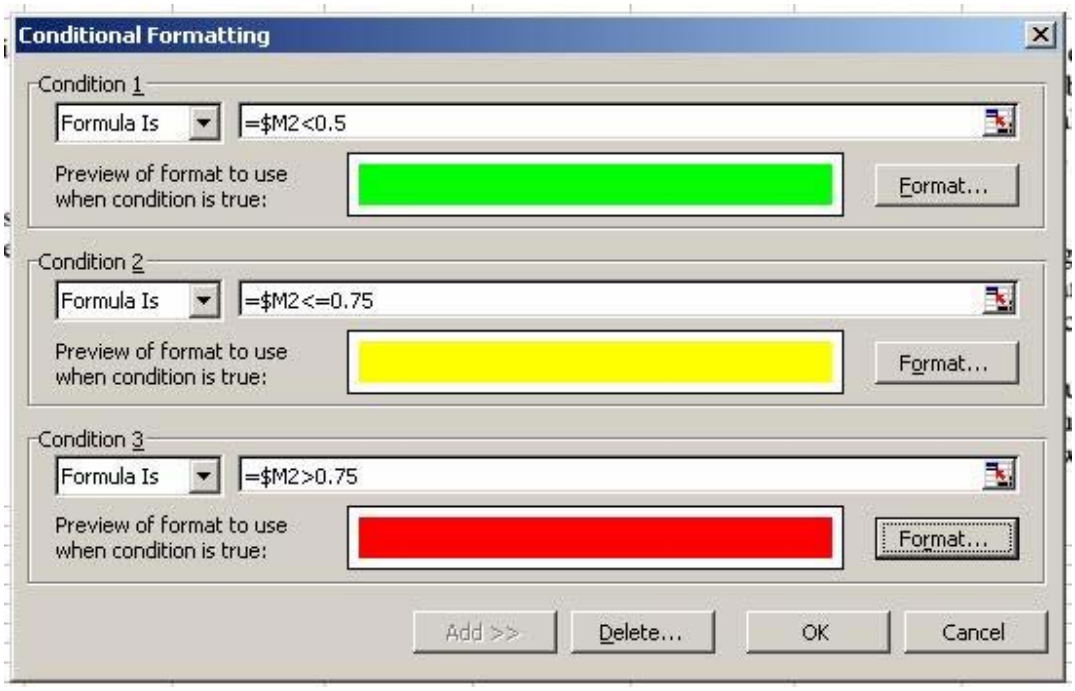
www.medlabstats.com/uncertainty/uncertainty-budget-excel-template.xls

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P
1	ANALYTE	Lower Limit of Normal	Higher Limit of Normal	BIOLOGICAL CV% from http://www.westgard.com/biodatabase1.htm	LOW QC VALUE	LOW QC CV%	HIGH QC VALUE	HIGH QC CV%	UNCERTAINTY (CONC) AT LOW QC VALUE	UNCERTAINTY (CONC) AT HIGH QC VALUE	UNCERTAINTY % AT LOW QC VALUE	UNCERTAINTY % AT HIGH QC VALUE	PERFORMANCE INDEX CVa / CVi at LOW QC LEVEL	PERFORMANCE INDEX CVa / CVi at HIGH QC LEVEL	PERFORMANCE INDEX AT LOW QC LEVEL	PERFORM INDEX AT QC LEVEL
2	ALB	35	50	3.1	26.7	1.95	38.4	1.75	0.98	1.37	3.66	3.56	0.63	0.56		
3	K	3.5	5	4.8	4.2	1.06	6.2	0.86	0.21	0.30	4.92	4.88	0.22	0.18		
4	Cortisol	138	690	20.9	35	7	435	4.5	7.71	93.00	22.04	21.38	0.33	0.22		
5									0.00	0.00	0.00	0.00	#DIV/0!	#DIV/0!		
6									0.00	0.00	0.00	0.00	#DIV/0!	#DIV/0!		
7									0.00	0.00	0.00	0.00	#DIV/0!	#DIV/0!		
8									0.00	0.00	0.00	0.00	#DIV/0!	#DIV/0!		
9									0.00	0.00	0.00	0.00	#DIV/0!	#DIV/0!		
10									0.00	0.00	0.00	0.00	#DIV/0!	#DIV/0!		
11									0.00	0.00	0.00	0.00	#DIV/0!	#DIV/0!		
12									0.00	0.00	0.00	0.00	#DIV/0!	#DIV/0!		
13									0.00	0.00	0.00	0.00	#DIV/0!	#DIV/0!		
14																
15																
16																

These data go into columns **A** to **H (overwrite the data that are in the first three rows of this template which are there only as a guide).** As soon as theses eight items of data have been entered, then the embedded formulae will complete the calculated values for columns **I** to **P.** Columns **O** and **P** have embedded Conditional Formatting statements which turn the respective cells

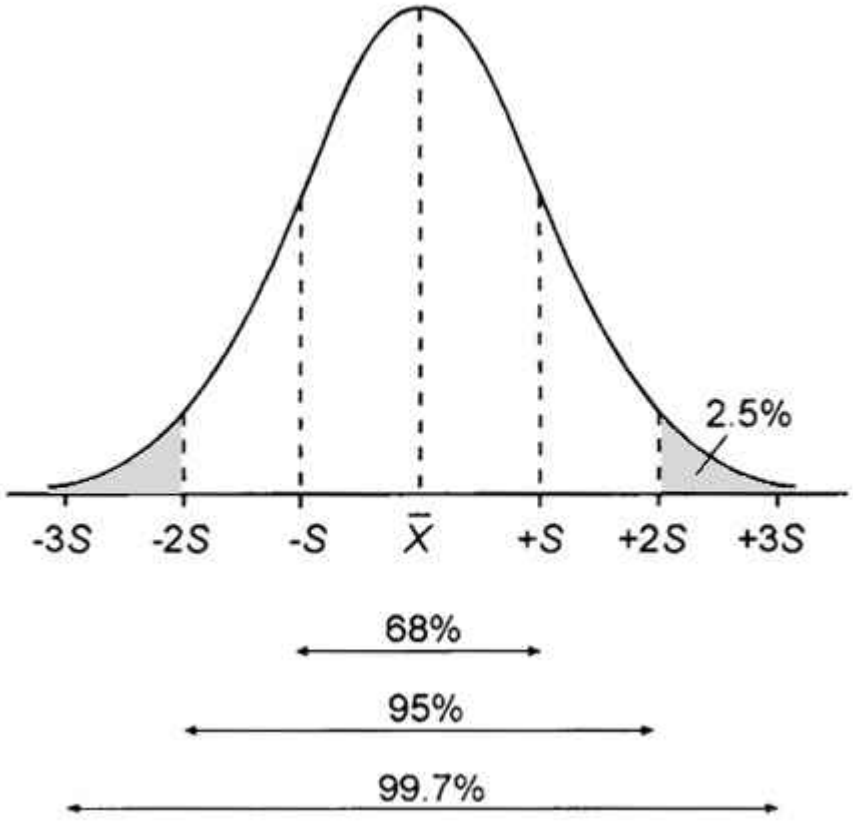
- Green if the Performance Index calculation returns a value is less than 0.5 (Desirable Performance [or better if less than 0.25])
- Yellow if the Performance Index calculation returns a value less than or equal to 0.75 (Minimum Performance)
- Red if the Performance Index calculation returns a value greater than 0.75 (Unsuitable Performance)

(The logic is a cascade and continues until it reaches a condition that is 'True' at which point it halts and the background colour is fixed at that point.)



2. COMMUNICATING WHAT THE RESULTS MEAN.

- A result quoted as +/- CV% or +/- one SD covers only 68% of the range of likely values
- A result quoted as +/- 2*CV% or +/- two SD covers only 95% of the range of likely values



- Two consecutive results are only significantly different at the 95% confidence level if the difference between the two results is equal to or greater than 2.77 * CV% or 2.77 * SD. The coefficient 2.77 is taken from the Table below :

Generation and Application of Data on Biological Variation in Clinical Chemistry

Callum Fraser

Critical Reviews in Clin Lab Sci, Vol 27, #5, 1989, pp409-437

Multipliers for $(CV_A^2 + CV_I^2)^{1/2}$ To Obtain Critical Difference at Different Levels of Probability

Multiplier :	3.64	2.77	2.33	1.81	1.47	1.19	0.95
P value :	0.01	0.05	0.10	0.20	0.30	0.40	0.50

This same article should be referred to if you wish to set up a biological variation study of your own.
