LabNetAnalysis – An instrument for the analysis of data from laboratory networks based on RExcel

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Outline

- IFCC[1] HbA1c[2] standardization network
- Statistical analysis
- Implementation
- References

[1]International Federation of Clinical Chemistry
[2]beta-n terminal glycated hemoglobin A

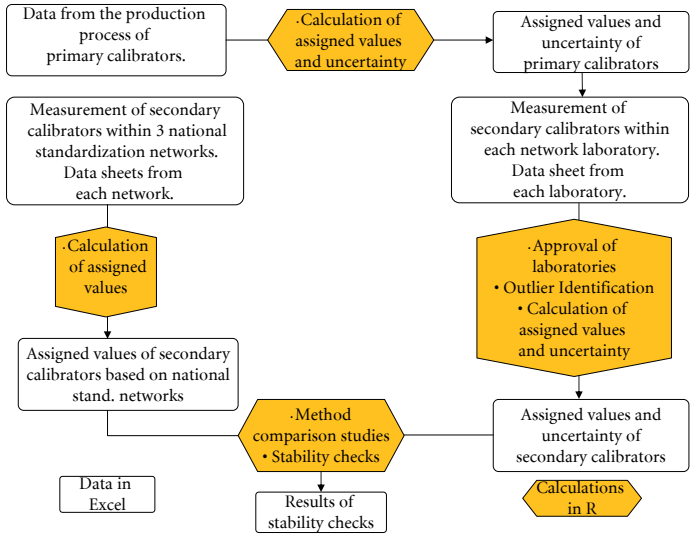
HbA1c

- HbA0 - Hemoglobin, HbA1c – glycated hemoglobin
- Most important biochemical marker for the monitoring of the glychemic status of patients with diabetes mellitus.
- Measurements are based on national standards, e.g. in USA, Japan, Europe. Differences in the specificity of the reference methods lead to different HbA1c levels. (5 USA-HbA1c% are about 3 Europe – HbA1c %).
- Changes of 0.5% HbA1c may lead to changes in therapy.

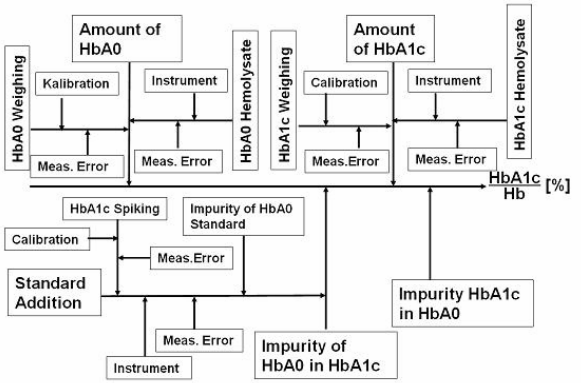
IFCC HbA1c standardization network

- Working group of the IFCC to develop a worldwide standard, to which all HbA1c assays are traceable.
- Development of a very specific reference measurement method for the determination of HbA1c, value assignment to HbA1c standards.
- Installation of a worldwide network of reference laboratories. HbA1c standards are measured in each laboratory, reported values are combined to assigned value of the standard.
- Need for a software for the automatic analysis of the data of this laboratory network.

Analysis Flow

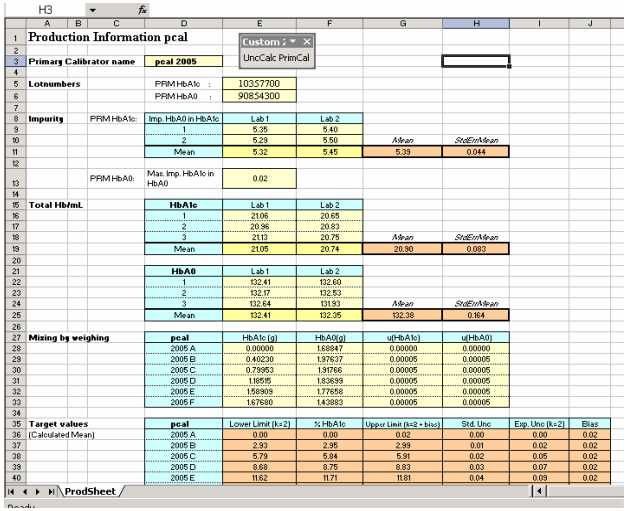


Production of primary calibrators



- Identification of mayor uncertainty sources.
- Different data sources and formats.
- Standardization of data input.

Standardized input and output sheet



Production Information pcal

Primary Calibrator name: pcal 2005

Custom ; UncCalc PrimCal

Lotnumbers: PRM HbA1c : 10357700; PRM HbA0 : 90854300

Impurity	PRM HbA1c:	Imp. HbA0 in HbA1c	Lab 1	Lab 2		
		1	5.35	5.40		
		2	5.29	5.50	Mean	StdErrMean
		Mean	5.32	5.45	5.39	0.044
	PRM HbA0:	Max. Imp. HbA1c in HbA0	0.02			

Total Hb/mL	HbA1c	Lab 1	Lab 2		
	1	21.06	20.85		
	2	20.96	20.83		
	3	21.13	20.75	Mean	StdErrMean
	Mean	21.05	20.74	20.90	0.083

	HbA0	Lab 1	Lab 2		
	1	132.41	132.60		
	2	132.17	132.53		
	3	132.64	131.93	Mean	StdErrMean
	Mean	132.41	132.35	132.38	0.164

Mixing by weighing	pcal	HbA1c (g)	HbA0(g)	u(HbA1c)	u(HbA0)
	2005 A	0.00000	1.68847	0.00000	0.00000
	2005 B	0.40230	1.97637	0.00005	0.00005
	2005 C	0.79953	1.91766	0.00005	0.00005
	2005 D	1.18535	1.83639	0.00005	0.00005
	2005 E	1.58909	1.77658	0.00005	0.00005
	2005 F	1.67680	1.43883	0.00005	0.00005

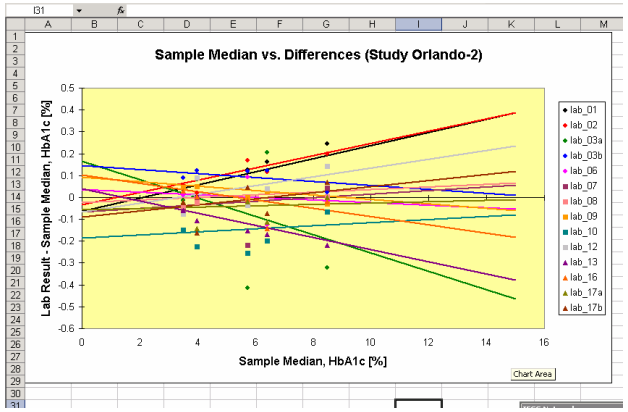
Target values (Calculated Mean)	pcal	Lower Limit (k=2)	% HbA1c	Upper Limit (k=2 + bias)	Std. Unc	Exp. Unc (k=2)	Bias
	2005 A	0.00	0.00	0.02	0.00	0.00	0.02
	2005 B	2.93	2.95	2.99	0.01	0.02	0.02
	2005 C	5.79	5.84	5.91	0.02	0.05	0.02
	2005 D	8.68	8.75	8.83	0.03	0.07	0.02
	2005 E	11.62	11.71	11.81	0.04	0.09	0.02

ProdSheet

Approval of laboratories

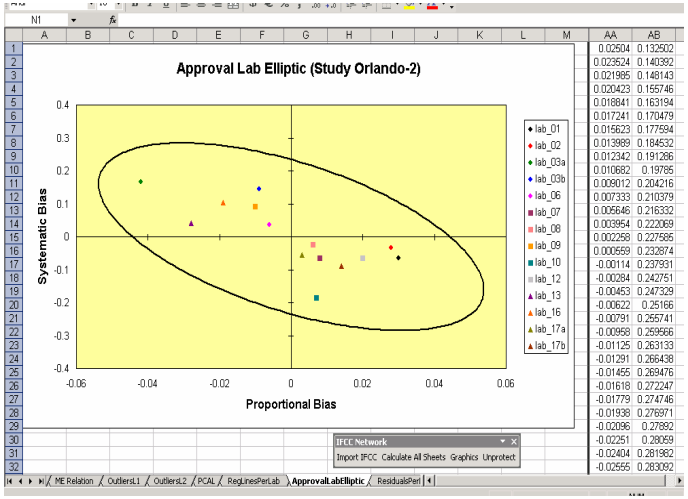
- Laboratories, being members of the network need to be controlled, candidate laboratories need to be approved.
- Comparison of the measured values of the respective laboratory of multiple samples with the values of the other laboratories.
- Random coefficient model, based on the lab-specific values, versus the overall median of each sample. Estimation of lab-specific intercept and slope.
- Estimated lab-specific intercept and slopes will naturally differ in a certain range, differences above this threshold are not accepted.

Approval of laboratories



- Based on historical data, a confidence ellipse, representing the natural variation of intercept and slope was derived. Laboratories outside this ellipse are not approved.

Approval of laboratories

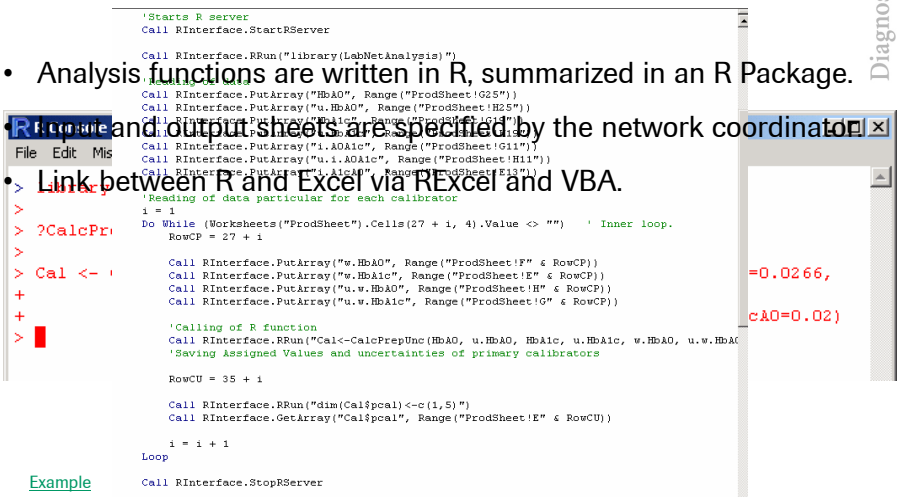


Creation of Graphics in Excel

Calculation of Coordinates in R

Implementation

- Analysis functions are written in R, summarized in an R Package.
- Input and output sheets are specified by the network coordinator.
- Link between R and Excel via RExcel and VBA.



Example

Master data handling

- For some parts of the analysis master data is needed, e.g. data derived from previous studies.
  - For example the shape of the ellipse for laboratory approval
- Input of this data over Excel sheet, saving of the data in .RData files in specified folder.
- During the analysis this data is imported by R.

User handling

- Specification of folders with
  - Data of the primary calibrators
  - Data of the IFCC laboratories
  - Data of the DCM laboratories
  - Master data files
- On one click the whole analysis is carried out.
- Excel sheets with results and graphics are inserted in the respective file.

Conclusions

- The connection between R and Excel, by RExcel, provides a good interface to meet the requirements of end-user and statistician for routine-fashioned data analysis.
- Standardized data-handling, data-flow and reporting.
- User-friendly handling.
- Full repertoire of statistical methods, easy adaption of “development” function in R, to “production” functions.

References

- Konnert A., Berding C., Arends S., et.al., Statistical rules for laboratory networks, JTEV, 32, 2006
- Konnert A., Arends S., Schubert S., et.al., Uncertainty calculation for calibrators of the IFCC HbA1c standardization network, Accred.Qual.Ass., 2006
- http://www.cran.r-project.org/
- http://www.cran.r-project.org/ -> Others -> R DCOM

Thank you.
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