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UNIVERSITÀ DEGLI STUDI DI MILANO

HARMONIZATION OF AUTOMATED INTERFERENCE INDEX ASSESSMENT AND USE

Alberto Dolci

UOC Patologia Clinica

ASST Fatebenefratelli Sacco, Milano

12th International Scientific Meeting

STANDARDIZATION IN LABORATORY MEDICINE AND PATIENT SAFETY

AGENDA

- Systematic monitoring of sample quality is a clinical laboratory requirement
- Visual assessment: quo usque tandem?
- Harmonization of HIL assessment:
  - interference substance
  - wavelenght, algorithm and reporting units
  - interference thresholds (TEa)
  - management of unreliable results
- Harmonization of HIL use:
  - where to measure (along the TLA path)
  - IQC
  - EQAS
  - interference on HIL

SAMPLE QUALITY AS CLINICAL LABORATORY REQUIREMENT

5.4.6 Sample reception

The laboratory's procedure for sample reception shall ensure that the following conditions are met.

a) *passim*

b) Laboratory-developed and documented criteria for acceptance or rejection of samples are applied.

c) *passim*

d) *passim*

e) Authorized personnel shall evaluate received samples to ensure that they meet the acceptance criteria relevant for the requested examination(s).

f) *passim*

SAMPLE QUALITY AS CLINICAL LABORATORY REQUIREMENT

Haemolysed sample	Pre-HemV	Percentage of: Number of samples with free hemoglobin (Hb) >0.5 g/L detected by visual inspection/Total number of checked samples for hemolysis
	Pre-HemI	Percentage of: Number of samples with free hemoglobin (Hb) >0.5 g/L detected by automated hemolytic index/Total number of checked samples for hemolysis
	Pre-HemR	Percentage of: Number of samples rejected due to hemolysis/Total number of checked samples for hemolysis

Sciacovelli L. Defining a roadmap for harmonizing quality indicators in Laboratory Medicine: a consensus statement on behalf of the IFCC WG "Laboratory Error and Patient Safety" and EFLM TFG "Performance specifications for the extra-analytical phases". Clin Chem Lab Med 2017;55:1478-88

ISO 14971 Medical Devices – Application of Risk Management to Medical Devices.

VISUAL ASSESSMENT

Table 1. Distribution of Lipemia, Hemolysis, and Icterus in Serum Samples from Hospitalized Patients

Specimen classification	No. of specimens	% of specimens with interferent quantified	Range of results (and mean)
Total	2599	—	—
Total with interferent >1+	838	78	—
Lipemia			
Total >1+	69	81	—
1+	42	83	0.86–15.15 (4.3)[a]
2+	12	67	1.23–9.64 (4.5)
3+	7	71	3.09–12.26 (5.8)
4+	5	100	3.05–8.62 (6.2)
5+	3	100	0.85–31.88 (15.8)
Hemolysis			
Total >1+	244	46	—
1+	103	43	0.16–1.75 (0.48)[b]
2+	80	48	0.10–1.69 (0.64)
3+	43	42	0.17–2.11 (1.10)
4+	18	72	1.08–3.48 (2.28)
5+	0	—	—
Icterus			
Total >1+	525	92	—
1+	181	92	1–120 (19)[c]
2+	137	92	4–370 (52)
3+	86	98	2–264 (65)
4+	72	97	7–301 (85)
5+	49	96	4–328 (87)

[a] Triglycerides, g/L. [b] Hemoglobin, g/L. [c] Bilirubin, mg/L.

Glick MR Clin Chem 1989;35:9373–9

VISUAL ASSESSMENT

Serum samples rate:

8.0% by visual inspection

3,4% by H index

weighted κ coefficient 0,42

EDTA-plasma samples rate:

4,5% by visual inspection

7,9% by H index

weighted κ coefficient 0,35

Table 1. *Comparison between visual grading of haemolysis and measurement of the haemolysis index (H index)*

	Visual grading of haemolysis			
H index (g/L)	Nil	Mild	Moderate	Severe
Serum ($n = 800$)				
Nil (< 1)	730	40	3	0
Mild (1-2·5)	6	1	8	5
Moderate (2·5-5)	0	0	0	5
Severe (> 5)	0	0	0	2
Plasma ($n = 800$)				
Nil (< 1)	722	10	3	2
Mild (1-2·5)	33	4	7	3
Moderate (2·5-5)	7	2	3	0
Severe (> 5)	2	0	0	2

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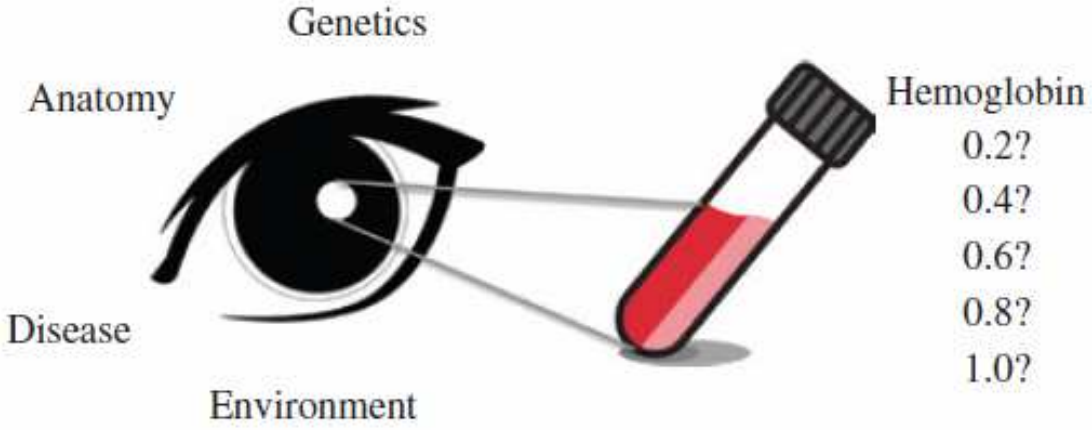
Hawkins R. Ann Clin Biochem 2002;39:521-2

Giuseppe Lippi and Janne Cadamuro

Visual assessment of sample quality: *quo usque tandem?*



- Not sensitive enough
- Inaccurate
- **High inter-observer variability**

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Clin Chem Lab Med 2018;56:513–5

VISUAL ASSESSMENT

L

LIH Olympus reagent	Visual inspection			
	0	1	2	
0	1642	27	0	1669 (97.9%)
1	5	21	7	33 (1.9%)
2	0	1	1	2 (0.1%)
	1647 (96.7%)	49 (2.9%)	8 (0.5%)	1704

I

LIH Olympus reagent	Visual inspection			
	0	1	2	
0 (n)	1586	41	3	1630 (95.7%)
1 (+ and ++)	17	31	11	59 (3.5%)
2 (3+ to 5+)	0	7	8	15 (0.9%)
	1603 (94.1%)	79 (4.6%)	22 (1.3%)	1704

H

LIH Olympus reagent	Visual inspection			
	0	1	2	
0	1529	26	1	1556 (91.3%)
1	27	59	18	104 (6.1%)
2	2	25	17	44 (2.6%)
	1558 (91.4%)	110 (6.5%)	36 (2.1%)	1704

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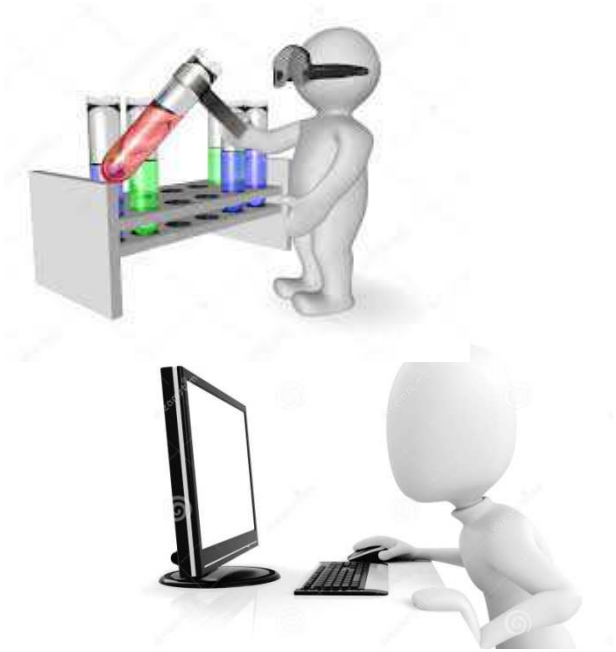
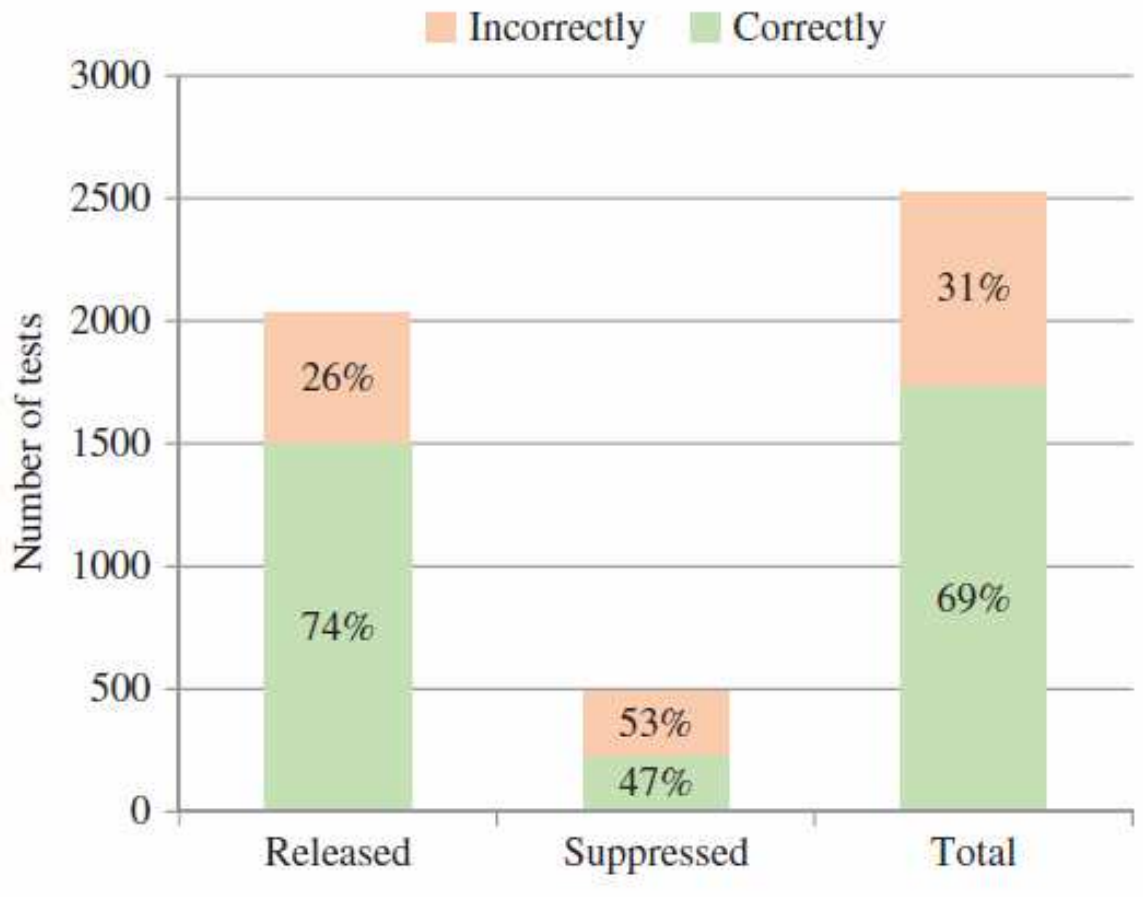
Simundic AM. Clin Chem Lab Med 2009;47:1361-5

HI VISUAL ASSESSMENT & MANUAL HANDLING





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Luksic AH. Clin Chem Lab Med 2018;56:574-81

HI VISUAL ASSESSMENT & MANUAL HANDLING

RISK ASSESSMENT

	S1	S2	S3	S4	S5
O5					TnT
O4	AST, LD		DBil	TBil	K
O3			Amy		
O2		ALT	Ca, Cl	CRP, Crea, Na, Urea	
O1	ALP, GGT		P, Mg, Prot	Alb, CK, EtOH, Lact, Lip	Glu

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Luksic AH. Clin Chem Lab Med 2018;56:574-81

AUTOMATED ASSESSMENT OF INTERFERENCE INDICES (HIL)

- Most clinical chemistry platforms, and even some coagulation analyzers offer the opportunity of automated assessment of the so-called **serum indices** (hemolysis, icterus and lipemia).
- As the impact of analytical interference caused by these substances varies between analytes, instruments and reagents, interference testing needs to be performed by **diagnostic assay manufacturers** according to **current guidelines** and reported to end-users.

Call for more transparency in manufacturers declarations on serum indices: On behalf of the Working Group for Preanalytical Phase (WG-PRE), European Federation of Clinical Chemistry and Laboratory Medicine (EFLM)

Check for updates

Von Meyer A. Clin Chim Acta 2018;484:328-32

HARMONIZATION OF HIL ASSESSMENT

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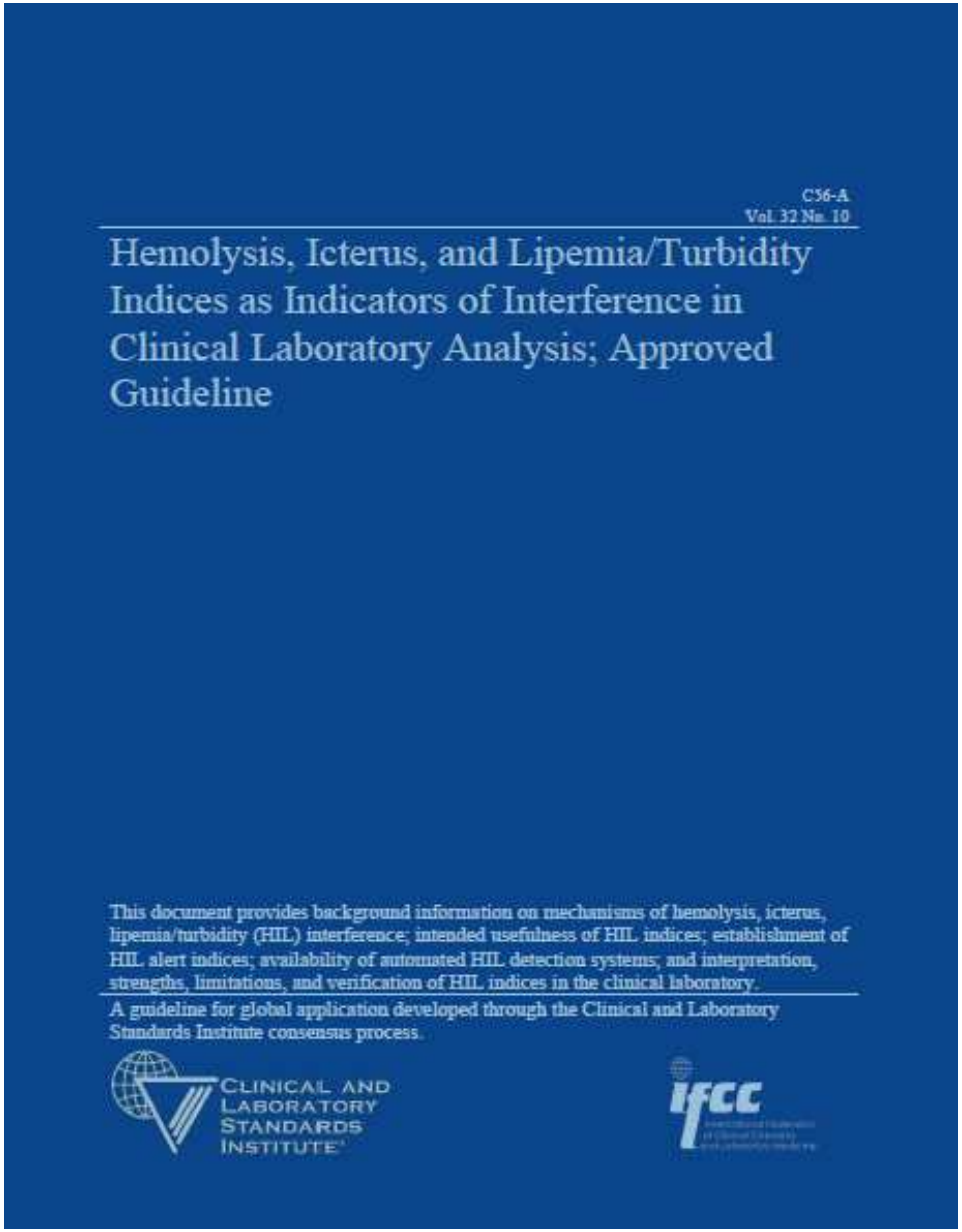
Approved Guideline
July 2012



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C56-A
Vol. 32 No. 10

Hemolysis, Icterus, and Lipemia/Turbidity Indices as Indicators of Interference in Clinical Laboratory Analysis; Approved Guideline

1 Scope

Hemolysis, icterus, and lipemia/turbidity (HIL) indices are often measured on serum and plasma, to assess sample quality. This document offers consensus guidelines for the use of automated HIL indices by laboratories, as an aid to annotating potentially affected results as well as the rejection of a specimen or result.

This guideline is intended for use by:

- Manufacturers responsible for establishing HIL indices and alert indices (cutoff values) for use in the automated HIL detection systems in their clinical laboratory instruments
- Laboratory directors, managers, supervisors and medical technologists for establishing or evaluating HIL indices and making judgments about the acceptability of specimens and test results

Discussion

Call for more transparency in manufacturers declarations on serum indices: On behalf of the Working Group for Preanalytical Phase (WG-PRE), European Federation of Clinical Chemistry and Laboratory Medicine (EFLM)

Alexander von Meyer[a,*], Janne Cadamuro[b], Giuseppe Lippi[c], Ana-Maria Simundic[d]

Some important drawbacks remain in this practice, mainly pertaining the measurement procedure, the approach for reporting interference data, the definition of objective thresholds of interference after which test results may be biased, and the lack of harmonized practices for describing how interference cut-offs have been identified. Therefore, this document aims to discuss these important caveats and propose some reliable solutions that may be adopted by **manufacturers** for increasing worldwide harmonization of serum indices.

Clin Chim Acta 2018;484:328-32

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INTERFERENCE SUBSTANCE

H FRESH ERYTHROCYTE HEMOLYSATE

HIL System	Hemolysis (hemoglobin)
1	Erythrocyte Hemolysate
2	Erythrocyte Hemolysate
3	Erythrocyte Hemolysate
4	Erythrocyte Hemolysate and Patient Samples
5	Erythrocyte Hemolysate
6	Erythrocyte Hemolysate
7	Erythrocyte Hemolysate

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INTERFERENCE SUBSTANCE

H FRESH ERYTHROCYTE HEMOLYSATE

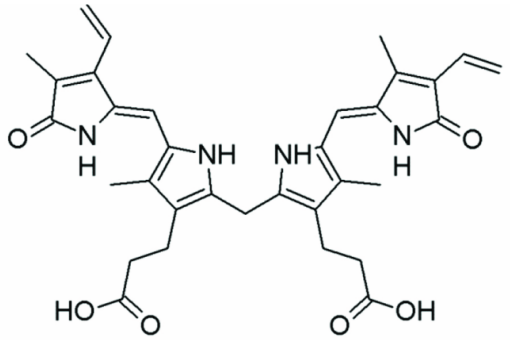
How to prepare RBC lysates?

- **Freezing and thawing the whole blood sample**
- **Lysis of whole blood by distilled (or deionized) water with or without detergents (e.g., saponin or Triton X- 100)**
- Sonication
- **Passing anticoagulated blood through a fine blood collection needle**
- Stirring whole blood with a metallic bar
- Applying the blade of a tissue homogenizer to the sample

Lippi G. Clin Lab 2012;58:351-5

INTERFERENCE SUBSTANCE

BILIRUBIN



HIL System	Icterus (bilirubin)
1	Unconjugated
2	Unconjugated
3	Unconjugated
4	Unconjugated, Conjugated, and Patient Samples
5	Unconjugated
6	Unconjugated, Patient Samples
7	Unconjugated, Conjugated

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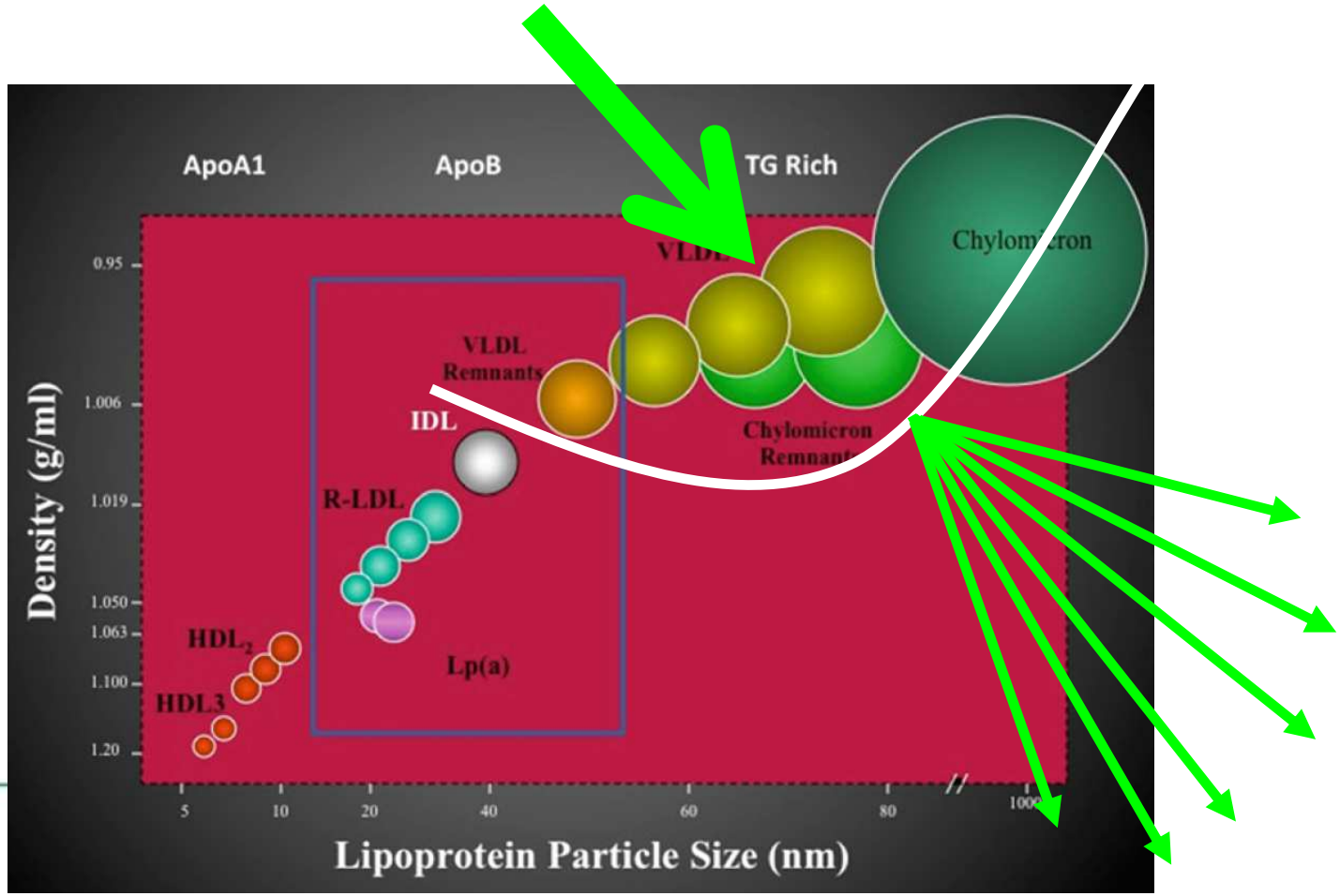
INTERFERENCE SUBSTANCE

L = LIPEMIA/TURBIDITY



INTERFERENCE SUBSTANCE

L 20% INTRALIPID® (or the equivalent)

HIL System	Lipemia/Turbidity
1	20% Intralipid®
2	20% Intralipid®
3	20% Intralipid®
4	20% Intralipid® and Patient Samples
5	20% Intralipid®
6	20% Intralipid®
7	20% Intralipid®

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INTERFERENT TEST CONCENTRATION

H Hemoglobin should be at least 1000 mg/dL

I Bilirubin should be at least 30 mg/dL

L Triglycerides in Intralipid® at least 1000 mg/dL

HIL System	Hemoglobin (mg/dL)	Total bilirubin (mg/dL)	Triglycerides (mg/dL)
1	1000	60	3000
2	525	30	1000
3	2000	60	2000
4	500-1000	20-60	500-800
5	500	40	500
6	500	30	N/A
7	1000	60	2000

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SAMPLE VOLUME REQUIRED FOR HIL

The volume of sample consumed for HIL measurement should be provided by the manufacturer and should be minimized to the lowest volume that will yield an accurate measurement.

SAMPLE DILUTION AND DILUENT

It should be specified if and how samples are diluted and what diluent is used. These are important considerations to avoid precipitation of paraproteins.

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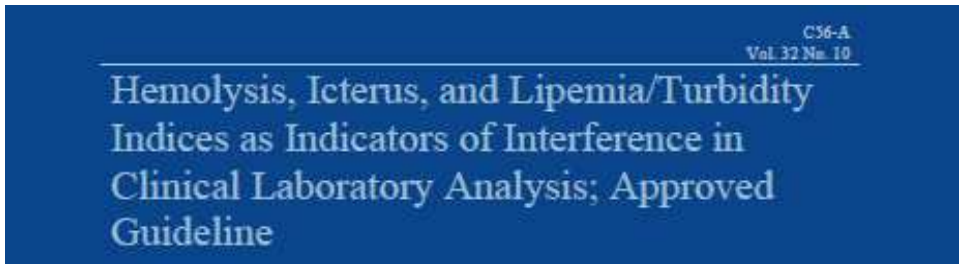
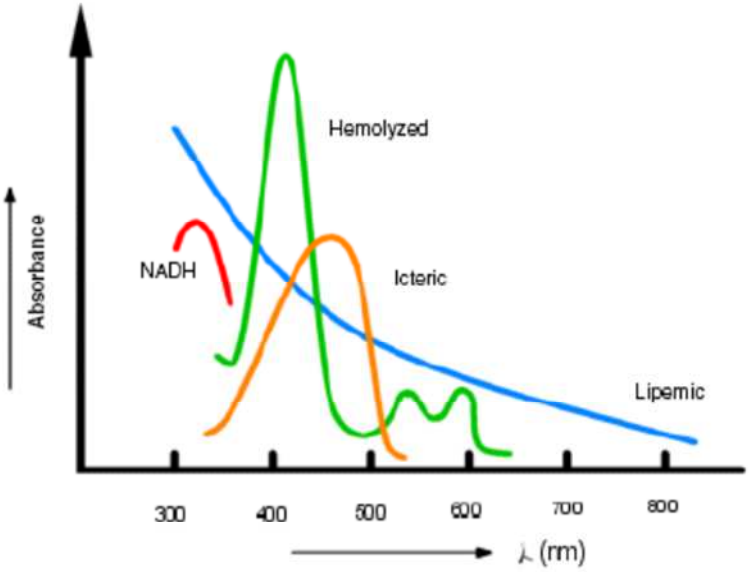


- **WAVELENGTH**
- **ALGORITHM**
- **REPORTING UNIT**



Company	Analyzer	Index	Report	Read wavelength [nm]
Abbott	Architect	Hemolysis	Continuous	572/604;628/660
		Icterus	Continuous	
		Lipemia	Continuous	
Beckman Coulter	AU	Hemolysis	Ordinal (6 level)	410/480;600/800
		Icterus	Ordinal	
		Lipemia	Ordinal	
	Synchron	Hemolysis	Ordinal (11 level)	340;410;470;600;670
		Icterus	Ordinal (21 level)	
		Lipemia	Ordinal (11 level)	
Ortho	Vitros	Hemolysis	Continuous	522/750
		Icterus	Ordinal	
		Lipemia	Ordinal or continuous	
Roche	COBAS	Hemolysis	Continuous	570/600;660/700
		Icterus	Continuous	480/505;570/600; 660/700
		Lipemia	Continuous	660/700
Siemens	ADVIA	Hemolysis	Ordinal (5 level)	571/596
		Icterus	Ordinal or continuous	
		Lipemia	Ordinal	
	Dimension	Hemolysis	Ordinal	405/700
		Icterus		
		Lipemia		

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Von Meyer A. Clin Chim Acta 2018;484:328-32

PROPOSAL FOR ASSESSMENT AND REPORTING OF SERUM INDICES BY MANUFACTURERS

1.3.1. Assessment of indices

a) Wavelengths used for measuring each serum index
b) Calculating formula
c) Sensitivity, linearity and range of measurement
d) Sample volume and type (e.g., serum or plasma)
e) Sample buffer for blank measurement and for sample dilution
f) Traceability of hemolysis and icteric indices to the concentration of free hemoglobin and total bilirubin, respectively
g) A possible correlation between lipemic index and triglycerides concentration should also be made available

1.3.2. Reporting of the indices

a) Manufacturers should report all results of serum indices as continuous values
b) All results should be transferable to the LIS on a separate channel

Call for more transparency in manufacturers declarations on serum indices:
On behalf of the Working Group for Preanalytical Phase (WG-PRE),
European Federation of Clinical Chemistry and Laboratory Medicine (EFLM)

Check for updates

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Von Meyer A. Clin Chim Acta 2018;484:328-32

PROPOSAL FOR THE SETUP OF INTERFERENCE EXPERIMENTS AND INTERFERENCE CUT-OFFS

1.4.1. Set up of interference experiments

Companies should report the full process used for interference experiments in their package inserts. Furthermore, the guideline or rationale used for assessing decisional limits (i.e., cutoffs) and raw data should be made available. The implementation of laboratory-specific thresholds should be supported by the manufacturer according to guidelines. **Harmonization of interference experiments is advisable**, since international guidelines already have provided guidance on this issue.

Call for more transparency in manufacturers declarations on serum indices: On behalf of the Working Group for Preanalytical Phase (WG-PRE), European Federation of Clinical Chemistry and Laboratory Medicine (EFLM)

Von Meyer A. Clin Chim Acta 2018;484:328-32

PROPOSAL FOR THE SETUP OF INTERFERENCE EXPERIMENTS AND INTERFERENCE CUT-OFFS

1.4.1. Reporting of the interference cut-offs

Manufacturers should at least provide the following information about their interference experiments:

a) Analyte concentrations at which interferences were tested (at least two, low and high in the clinical range, preferably close to the clinical decision point)

b) An interferogram both in the package insert and in electronic files for each tested analyte concentration

c) Raw data obtained from the experiments (should be made available upon request)

d) When more than a single cut-off is proposed by the manufacturer, the underlying reasons should be clearly specified.

Call for more transparency in manufacturers declarations on serum indices: On behalf of the Working Group for Preanalytical Phase (WG-PRE), European Federation of Clinical Chemistry and Laboratory Medicine (EFLM)

Von Meyer A. Clin Chim Acta 2018;484:328-32

INTERFERENCE THRESHOLD

2.2 Contributions to Inaccurate Test Results

2.2.1 Medical Relevance

IMPORTANT NOTE:

Medical relevance determines whether an analytical effect is considered interference.

3.1 Acceptance Criteria for Interference Testing

IMPORTANT NOTE:

Acceptance criteria should be defined before evaluating the interference, considering the **medical** use of the test results.

3.1.1 Sources of Information

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ANALYTICAL PERFORMANCE SPECIFICATIONS

- **Model 1: Based on the effect of analytical performance on clinical outcome**

- **Model 2: Based on components of biological variation of the measurand**

- **Model 3: Based on state of the art of the measurement (i.e., the highest level of analytical performance technically achievable)**

Sandberg S. Clin Chem Lab Med 2015;53:833-5

Ferruccio Ceriotti et al. on behalf of the EFLM Task and Finish Group on Allocation of laboratory tests to different models for performance specifications (TFG-DM)

Criteria for assigning laboratory measurands to models for analytical performance specifications defined in the 1st EFLM Strategic Conference

Clin Chem Lab Med 2017;55:189-94

Table 1: Proposal for assignment of some commonly requested laboratory measurands to the three models for analytical performance specifications (APS) as defined in the Milan Consensus.[a]

APS model 1: outcome-based	APS model 2: biological variation	APS model 3: state-of-the-art
P-Cholesterol+ester	P-Sodium ion	U-Sodium ion
P-Cholesterol+ester in LDL	P-Potassium ion	U-Potassium ion
P-Cholesterol+ester in HDL	P-Chloride	U-Chloride
P-Triglycerides	P-Bicarbonate	U-Calcium ion
P-Glucose	P-Calcium ion	U-Magnesium ion
B-Hemoglobin A_{1c}	P-Magnesium ion	U-Phosphate (inorganic)
P-Albumin	P-Phosphate (inorganic)	U-Creatinine
P-Troponin T and P-troponin I	P-Creatinine	U-Urate
P-Thyrotropin	P-Cystatin C	
B-Hemoglobin	P-Urate	
B-Platelets	P-Proteins	
B-Neutrophil leukocytes	B-Erythrocytes	
	B-Erythrocyte volume fraction	
	B-Erythrocyte volume	
	P-Prothrombin time	
	P-activated partial thromboplastin time	

[a]Some of the measurands can also have APS from other models depending on their clinical use. P and B denotes the system blood plasma or whole blood, respectively. Measurements might be performed in different types of sample matrices, such as serum, heparin plasma, citrate plasma, etc., as appropriate for the method.

INTERFERENCE THRESHOLD

8.1 Acceptability Criteria for Evaluating Interference Effects

It is important that the manufacturer uses criteria to define the magnitude of the allowable bias observed between the test pool and the control pool. The manufacturer should review the clinical relevance of the observed bias for each analyte.

In evaluating HIL interferences for each measured analyte, the manufacturer should consider the maximum allowable bias due to hemolysis, icterus, and lipemia/turbidity, which is dependent upon the clinical application of the test. This allowable interference bias should be part of total allowable error that can be derived from biological variation of the analyte and the precision of the analytical method. Fraser defines clinically significant interference when the result in the presence of the interferent differs more than $1.96 \times (CV_a^2 + CV_w^2)^{½}$ from the result without the interferent.[48] (CV_a is the analytical coefficient of variation and CV_w is the within-subject biological variation.)

As an alternative, the consensus of clinical experts could be used to establish interference criteria. Each manufacturer should state the acceptable criteria used to define interference claims in the product labeling.

RCV

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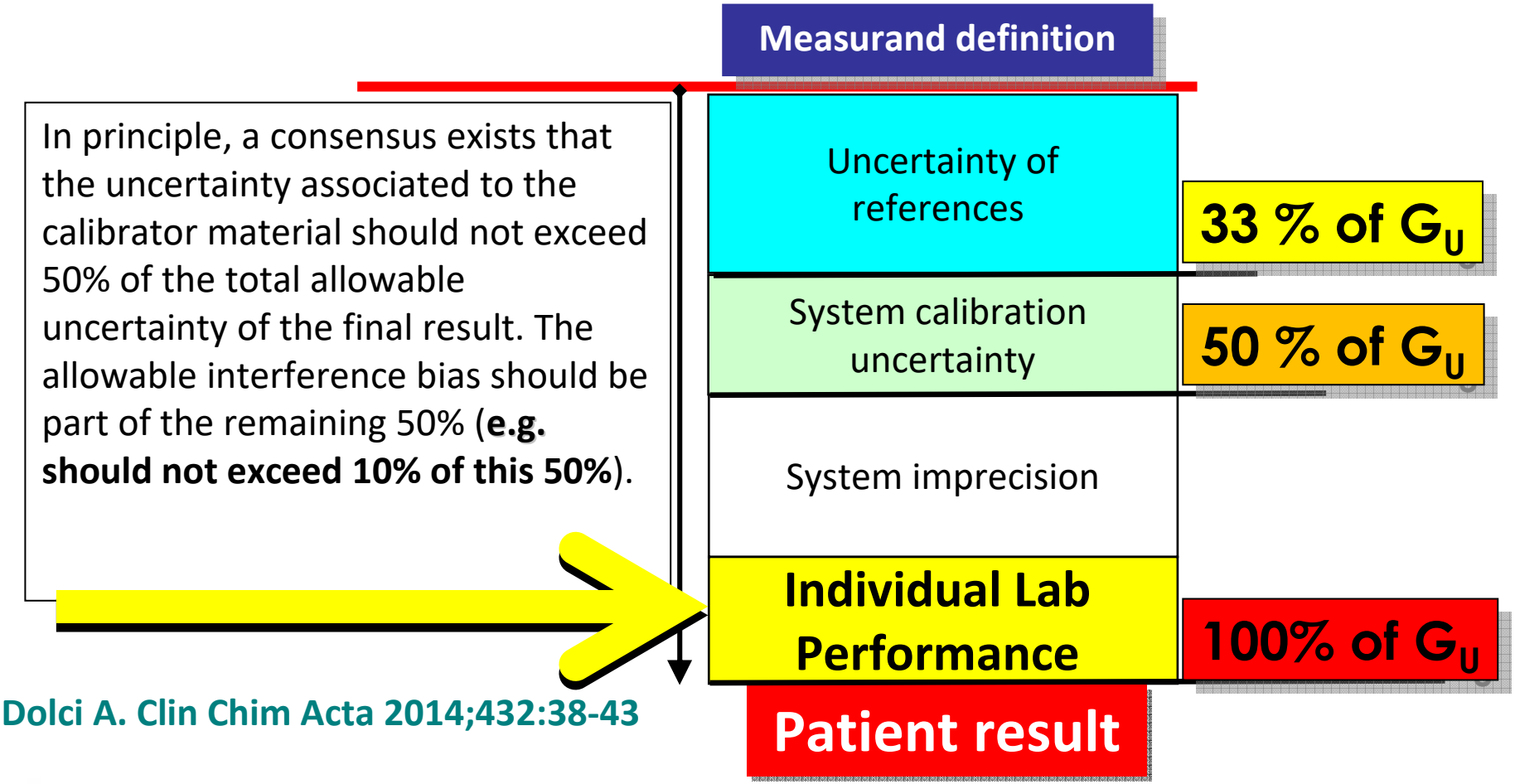
TOTAL MEASUREMENT UNCERTAINTY BUDGET

In principle, a consensus exists that the uncertainty associated to the calibrator material should not exceed 50% of the total allowable uncertainty of the final result. The allowable interference bias should be part of the remaining 50% (**e.g. should not exceed 10% of this 50%**).



Dolci A. Clin Chim Acta 2014;432:38-43

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Braga F. Clin Chem Lab Med 2015;53:905-12
Braga F. Clin Biochem 2018;57:7-11

MANAGING UNRELIABLE SAMPLES

The possible actions may be dichotomized to:
a)reporting the test result with a flag or warning comment to alert the ordering clinician or
b)not reporting the result at all, informing the clinician about the specific interference found, rejecting the sample and asking for a new sample.

The use of corrective formulas is unreliable and misleading, and is strongly discouraged.

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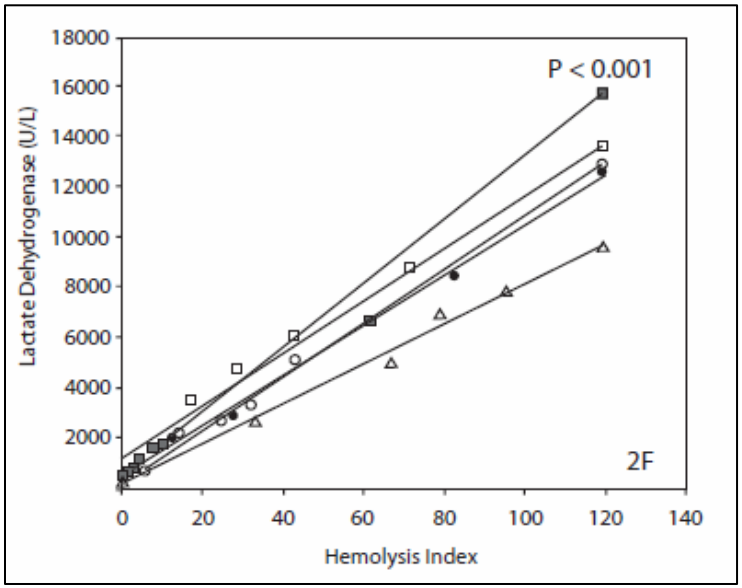
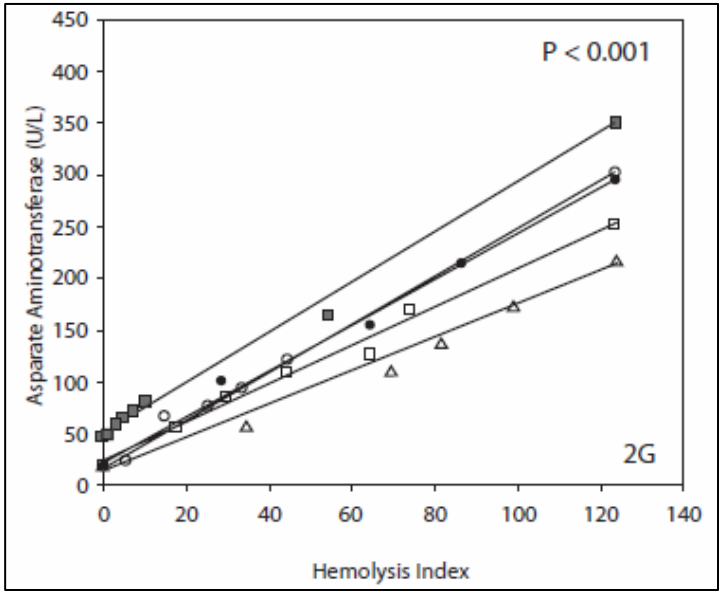
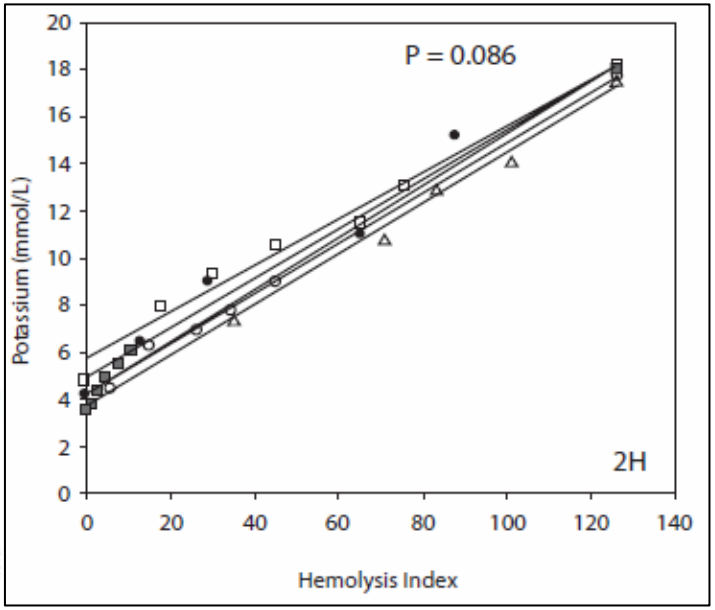
Dolci A. Clin Chim Acta 2014;432:38-43

MECHANICAL INJURY OF BLOOD, AS IT MIGHT ARISE FROM PREANALYTICAL PROBLEMS, OCCURS DISHOMOGENEOU LY, SO THAT **CORRECTIVE FORMULAS ARE UNRELIABLE AND LIKELY MISLEADING**







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Lippi G. Biochem Med 2011;21:297–305

Point

Janne Cadamuro*, Cornelia Mrazek, Elisabeth Haschke-Becher and Sverre Sandberg

To report or not to report: a proposal on how to deal with altered test results in hemolytic samples

A very pragmatic approach using different sample acceptance criteria or actually developing different "personalized" performance specifications depending on the knowledge of a specific test, a specific department or a specific patient.

Clin Chem Lab Med. 2017;55:1109-11

Counterpoint

Giuseppe Lippi*, Gianfranco Cervellin and Mario Plebani

Reporting altered test results in hemolyzed samples: is the cure worse than the disease?

The strategy proposed generates a dogmatic paradox and ultimately poses **serious threats to** many ongoing **harmonization** projects in laboratory medicine.

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Clin Chem Lab Med. 2017;56:1112-4

Giuseppe Lippi*, Janne Cadamuro, Alexander von Meyer and Ana-Maria Simundic, on behalf of the European Federation of Clinical Chemistry and Laboratory Medicine (EFLM) Working Group for Preanalytical Phase (WG-PRE)

Practical recommendations for managing hemolyzed samples in clinical chemistry testing

When the HI is associated with analyte variation exceeding clinically significant bias (i.e. variation exceeds the RCV), **results** of hemolysis-sensitive tests **should be suppressed** and replaced with a comment that **biased results cannot be released because the sample is** preanalytically **compromised** and advising the recollection of another sample.

If HI values reach an even higher critical cut-off (i.e. H corresponding to a cell-free hemoglobin concentration ≥10 g/L), **all laboratory data may be** unreliable and should hence be **suppressed** and replaced with a comment

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Lippi G. Clin Chem Lab Med. 2018;56:718-27

SUPPRESSING ALL TEST RESULTS IN GROSSLY HEMOLYZED SAMPLES: IS THIS APPROACH APPROPRIATE IN EVERY CASE?

We retrieved clinical and laboratory data of all patients who had grossly hemolyzed plasma or serum sample, i.e.
HI ≥1000, corresponding to a **free Hb concentration ≥10 g/L.**
60 patients which accounted to **0.04%** of the 166,752 tested.
The rate was significantly **higher** ($p < 0.0001$)
in plasma samples (HI ≥ 1000 in 0.13% of samples, n = 34) than
in serum samples (HI ≥ 1000 in 0.02% of samples, n = 26)

In vivo hemolysis ruled out after data matching and collegial discussion, n (%)

60 (100%)

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Szőke D. Clin Chem Lab Med. 2018
doi.org/10.1515/cclm-2018-1071

AUTOMATIC ASSESSMENT & REPORTING

The TLA middleware, working as process control and management tool, should also carry out specimen integrity check, and results of the tests interfered, as detected by automated indices, should not be reported as a number, but replaced in the laboratory report during **autoverification process** with specific comments, such as "hemolysed (or icteric or lipemic) specimen", to avoid producing spurious and unreliable results, which may lead to diagnostic errors, cause clinical confusion and worsen patient outcome.

Moreover, the automatic check of poor quality (specimen integrity) of samples, performed by TLA middleware, leads to **immediate report of specific comments** as result of the affected tests, speeding up intralaboratory TAT.

Dolci A. Clin Biochem 2017;50:611-5

AUTOMATED INTERFERENCE INDICES USE

Laboratories should, therefore, implement automatic determination of degree of interference on analyzers into their routine practice, as proposed by CLSI C56A guideline. Values of measured HIL indices can be transferred to a laboratory information system to implement sets of rules for the management of unsuitable samples. This procedure ensures standardized decision making within the laboratory.

Nevertheless, implementing every new method into routine work requires performing verification procedures.

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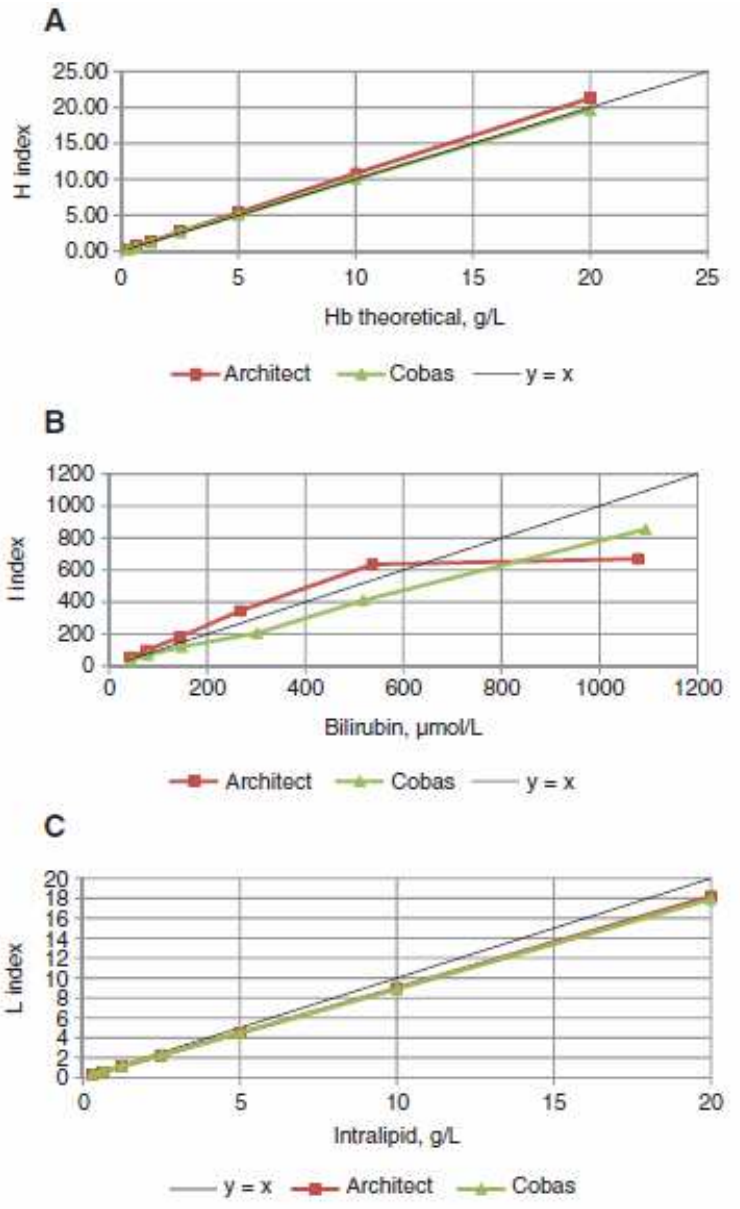
Nikolac Gabaj N. Clin Chem Lab Med 2018;56:776-88

ACCURACY

1.3.1. Assessment of indices

1. Wavelengths used
2. Calculating formula
3. Sensitivity, linearity and range of measurement
4. Sample volume and type
5. Sample buffer
6. Traceability of HI and II to the concentration of free hemoglobin and total bilirubin, respectively
7. A possible correlation between lipemic index and triglycerides concentration should also be made available



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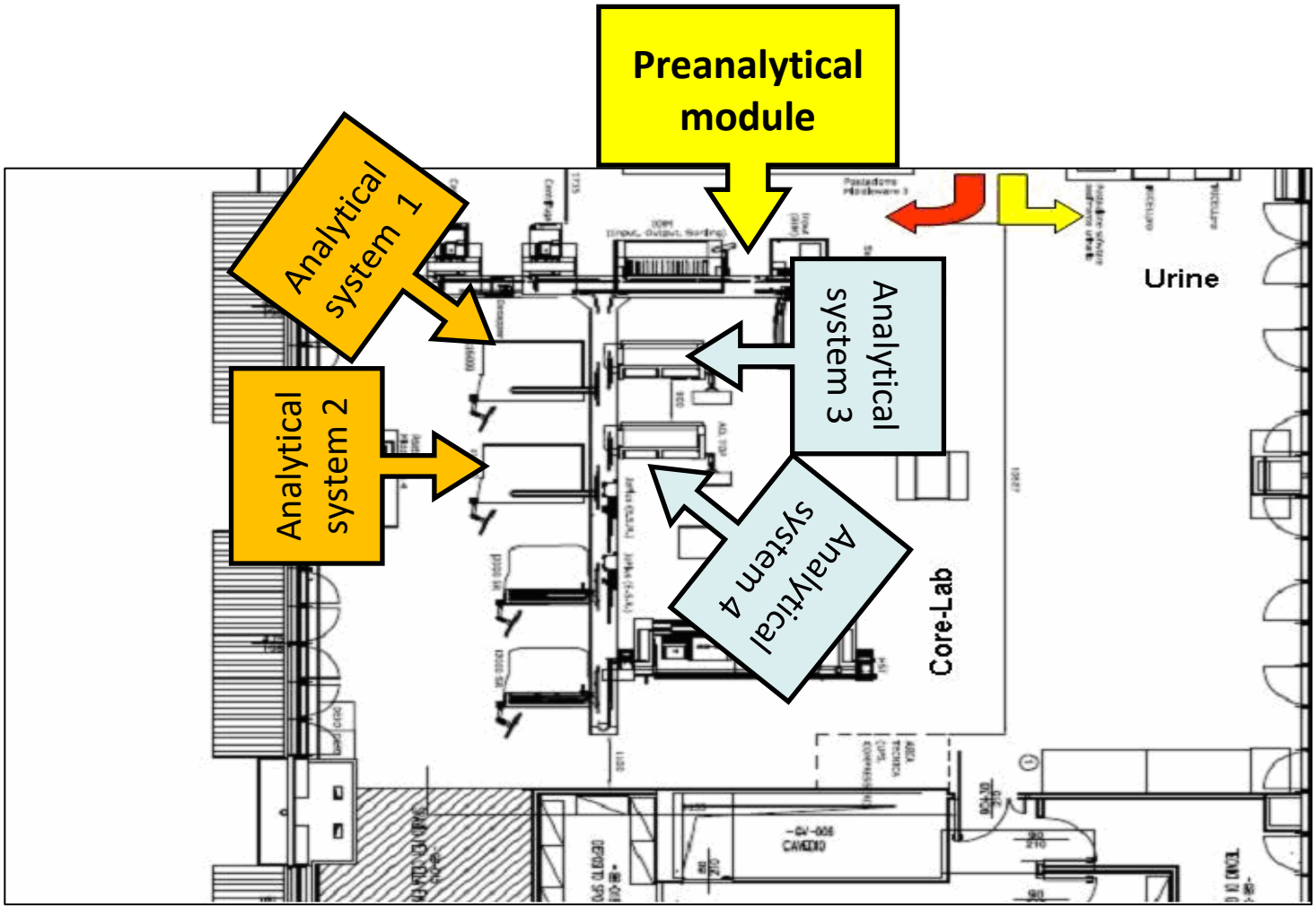
Nikolac Gabaj N. Clin Chem Lab Med 2018;56:776-88

HIL: WHERE TO MEASURE ALONG THE TLA PATH



Local quality assurance of serum or plasma (HIL) indices

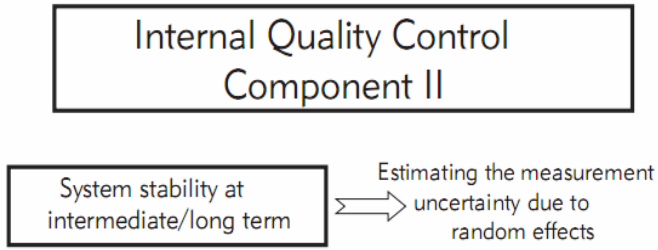
Giuseppe Lippi[a,*], Janne Cadamuro[b], Alexander von Meyer[c], Ana-Maria Simundic[d], , on behalf of the European Federation of Clinical Chemistry, , Laboratory Medicine (EFLM) Working Group, for Preanalytical Phase (WG-PRE)

The **quality of HIL measurement should be assessed as it is for any other diagnostic test**, there is no complete or straightforward guidance on how the quality of this type of testing should be performed.

Quality assurance in laboratory medicine is typically carried out using quality control materials, as part of either internal quality control (**IQC**) or external quality assessment (**EQA**) programs. Whilst EQA is typically performed using materials purchased by commercial manufacturers or independent organizations, **IQC can** also **be** sourced from external suppliers or **prepared by the laboratory**, as endorsed by ISO Guide 80:2014

Clin Biochem 2018;54:112–8

ESTABLISHING AND MAINTAINING IQC MANAGEMENT SYSTEM FOR THE HIL INDICES BASED ON IN-HOUSE PREPARED QC MATERIALS



Materials used to estimate random uncertainty should be **from a third-party source**, independent from the company manufacturing the measuring system, should be **commutable** and should have a **concentration level of the analyte relevant to the clinical application** of the measurement.

We prepared a **serum pool** with an **HI value around 100** (~1 g/L of free Hb), manufactured with anonymized leftover samples from laboratory routine and **stored in 250 µL aliquots at –20 °C.**

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Aloisio E. Clin Biochem 2018;57:62–4

HI RANDOM UNCERTAINTY ESTIMATION

Table 1
Random uncertainty of the photometric measurement of hemolysis index (HI) on Abbott Architect c16000 platforms.

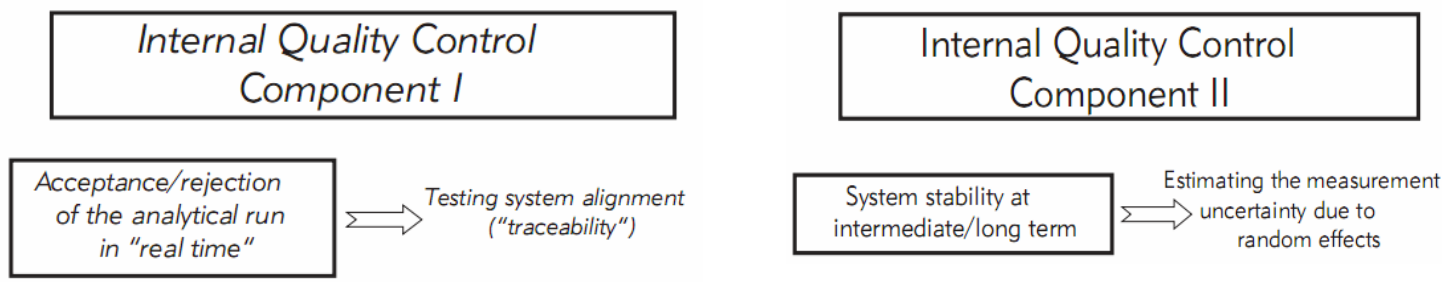
	No. of determinations	Mean HI	Monthly CVs[a]	Cumulative CV[b]	Relative expanded uncertainty[c]
Architect c16000–1	442	101.3	0.7% - 2.7%	1.59%	3.18%
Architect c16000–2	451	103.1	0.8% - 2.5%	1.63%	3.26%
Between platforms	893	101.7	1.2% - 2.7%	1.82%	3.64%

[a] Minimum and maximum values are reported.
[b] Cumulative CV is calculated as the average of monthly CVs obtained in the study period.
[c] By a coverage factor of 2.

The obtained performance could be considered in establishing the **state of the art** of the measurement to be employed for the definition of quality specifications **for HI measurement, by following the model 3** of the European Federation of Clinical Chemistry and Laboratory Medicine Strategic Conference.

Aloisio E. Clin Biochem 2018;57:62–4

IMPLEMENTATION OF AN IQC PROGRAMME FOR THE PHOTOMETRIC DETERMINATION OF ICTERIC INDEX



We use quantitative determination of II as a front-line test for screening blood samples with abnormal total bilirubin (TB) concentrations, i.e. >1.2 mg/dL.

II ≤ 0.8 TB not measured and reported as ≤ 1.2 mg/dL

Necessity of monitoring the analytical quality of II photometric determination, which, performed at the first level of the algorithm, could directly affect patient diagnosis and treatment.

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Aloisio E. J Clin Pathol 2018;71:851–2

IMPLEMENTATION OF AN IQC PROGRAMME FOR THE PHOTOMETRIC DETERMINATION OF ICTERIC INDEX

Internal Quality Control Component I

Acceptance/rejection of the analytical run in "real time" ⟹ *Testing system alignment ("traceability")*

Internal Quality Control Component II

System stability at intermediate/long term ⟹ Estimating the measurement uncertainty due to random effects

- **3 times a day**
- **control material used in our laboratory** to check the alignment of most chemistry tests
- **2** (low and medium) **levels**
- **40** preliminary **II determinations** on both platforms **to define** lot specific **target values** and **acceptability ranges** (±20%)

- **once a day**
- in-house prepared **serum pool**
- **single level**
- **II value around 1,2-1,3**
- optimal **goal for imprecision** derived from **biological variability** data **of TB,** i.e. ≤5.5%

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Aloisio E. J Clin Pathol 2018;71:851–2

IMPLEMENTATION OF AN IQC PROGRAMME FOR THE PHOTOMETRIC DETERMINATION OF ICTERIC INDEX

Internal Quality Control Component I

Acceptance/rejection of the analytical run in "real time" ⇒ *Testing system alignment ("traceability")*

Internal Quality Control Component II

System stability at intermediate/long term ⇒ Estimating the measurement uncertainty due to random effects

Table 1 Results of the IQC for II determination, obtained during the period spanning from June 2016 to September 2017

	IQC component I (testing system alignment)		IQC component II (deriving random uncertainty)					
	Number of determinations	Failed (%)	Number of determinations	Mean II	Cumulative CV (%)	Monthly CV* (%)	Desirable CV (%)	Optimal CV (%)
Architect c16000-1	2562	1.8	323	1.3	2.7	0–5.2	≤10.9	≤5.5
Architect c16000-2	1896	3.4	327	1.2	3.4	0–5.1		

*Minimum and maximum values are reported.
CV, coefficient of variation; II, icteric index; IQC, internal quality control.

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Aloisio E. J Clin Pathol 2018;71:851–2

EQAS

Whilst **EQA** is typically performed using materials purchased by commercial manufacturers or independent organizations.

Regarding the HIL indices, **commercial EQA** and IQC materials **are only now becoming available**, so that providing recommendations about their use with the HIL indices seems premature.

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Local quality assurance of serum or plasma (HIL) indices

Giuseppe Lippi[a,*], Janne Cadamuro[b], Alexander von Meyer[c], Ana-Maria Simundic[d], , on behalf of the European Federation of Clinical Chemistry, , Laboratory Medicine (EFLM) Working Group, for Preanalytical Phase (WG-PRE)

Clin Biochem 2018;54:112–8

INTERFERENCE ON HIL AUTOMATED ASSESSMENT

Like any other spectrophotometric assay, serum indices may be interfered with by either endogenous (e.g. green biliverdin, brown methemalbumin, orange beta-carotenes) or exogenous compounds that may be present in the specimen and overlap one or more wavelengths used for serum index measurement.

Rose bengal

Has a **spectrophotometric peak absorbance at 562 nm**, producing **spuriously elevated HI values** on Roche platforms, but no interference by Beckman Coulter Synchron HI.

Patent Blue V

Has a **spectrophotometric peak absorbance at 640 nm**, producing a **false positive interference of the lipemia/turbidity** index, which in turn induces a **negative interference in both HI and icteric indices** and has a linear dose–response effect.

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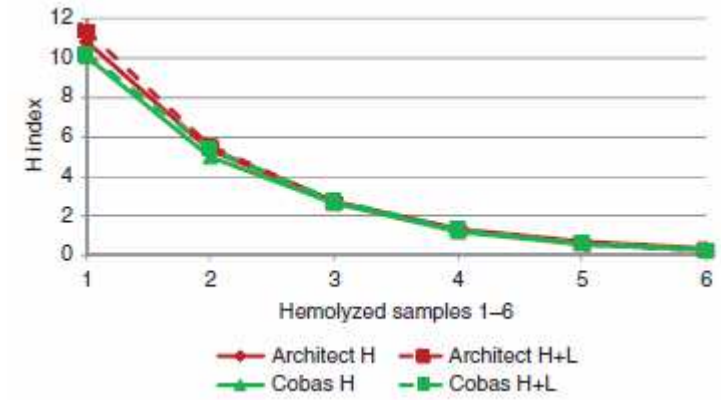
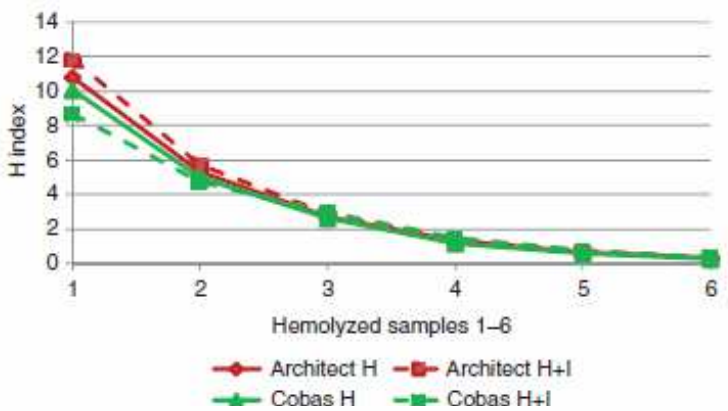
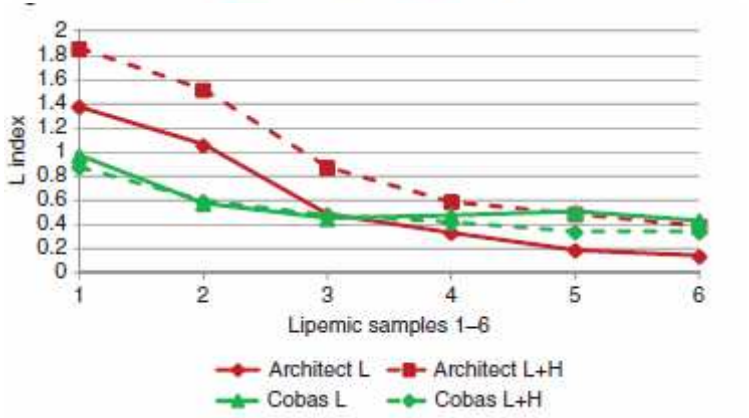
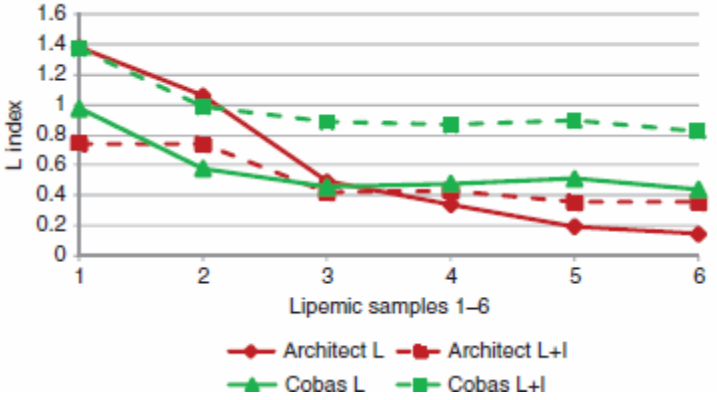
Dolci A. Clin Chim Acta 2014;432:38-43
Dimeski G. Clin Chem 2009;55:1040–1
Darby D. Ann Clin Biochem 2008;45:289–92

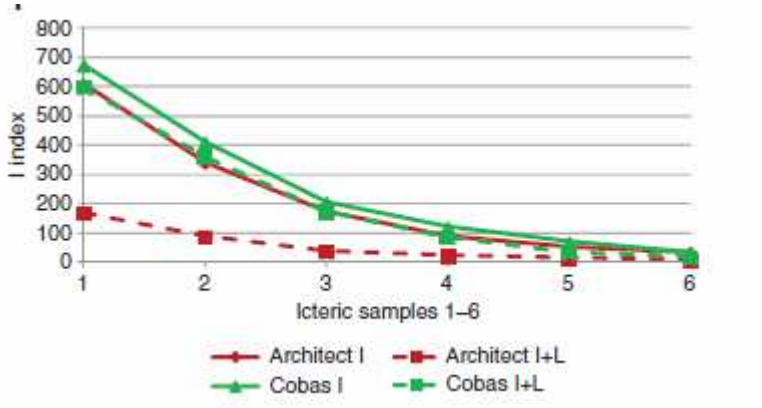
INTERFERENCE ON HIL AUTOMATED ASSESSMENT

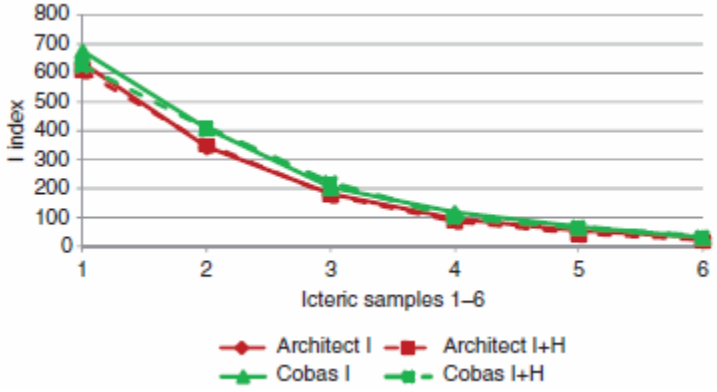












Nikolac Gabaj N. Clin Chem Lab Med 2018;56:776-88

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