EUROPEAN HARMONISATION INITIATIVES

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EFLM WG-Harmonisation of total testing process

EQALM

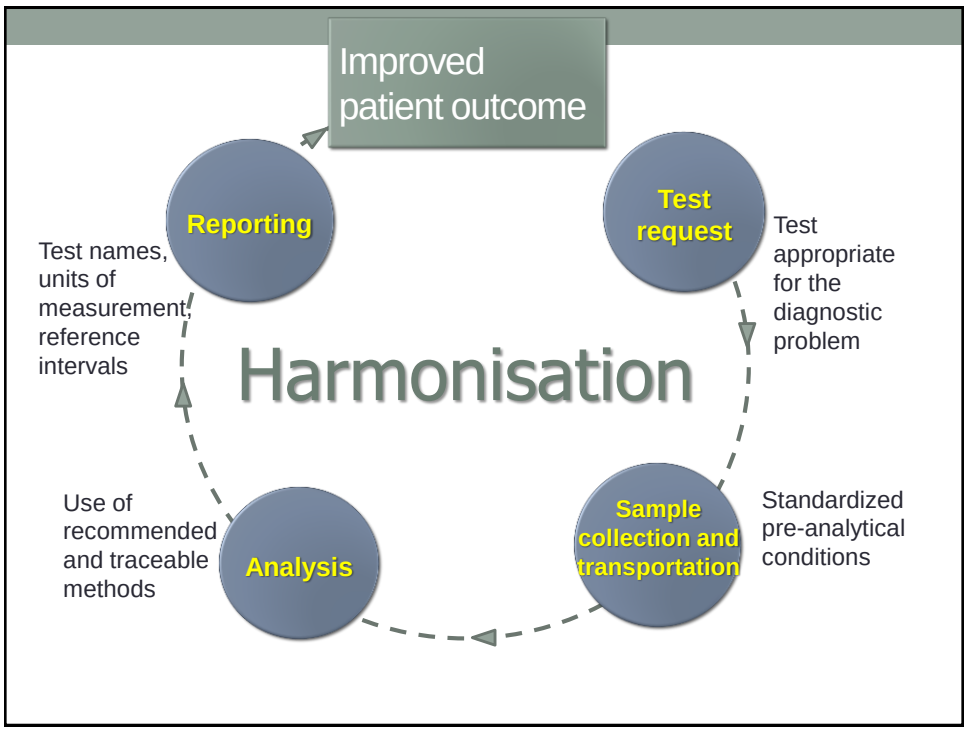
EQALM symposium 2015
8-9 October, Bergen, Norway

Why harmonisation?

- **Improved patient service**
  - The right test, correctly performed, on the right material, reported and commented on adequately = substantial contribution to an improved patient outcome.
- **Improved patient safety**
  - Different names for the same test , different units of measurement, different reference intervals may lead to erroneous interpretations of the laboratory test results by the clinician.
- **Improved data comparability among laboratories and with time**
  - Patients mobility, patient empowerment, electronic patient records
  - Application of clinical guidelines, common reference intervals or decision limits
  - Data collection in clinical trials

Why harmonisation?

- **Savings**
  - Many tests repetitions are caused by the poor comparability among laboratories.
  - Costs of further referrals and investigations for tests (i.e. tumor markers) which may have been requested unnecessarily in the first instance and produce false positive results.
- **Credibility and reliability of the clinical laboratories**
  - Non homogeneous pre-analytical instructions, poor comparability of results, different reporting way challenge the quality of our service.
- **Accreditation programs**



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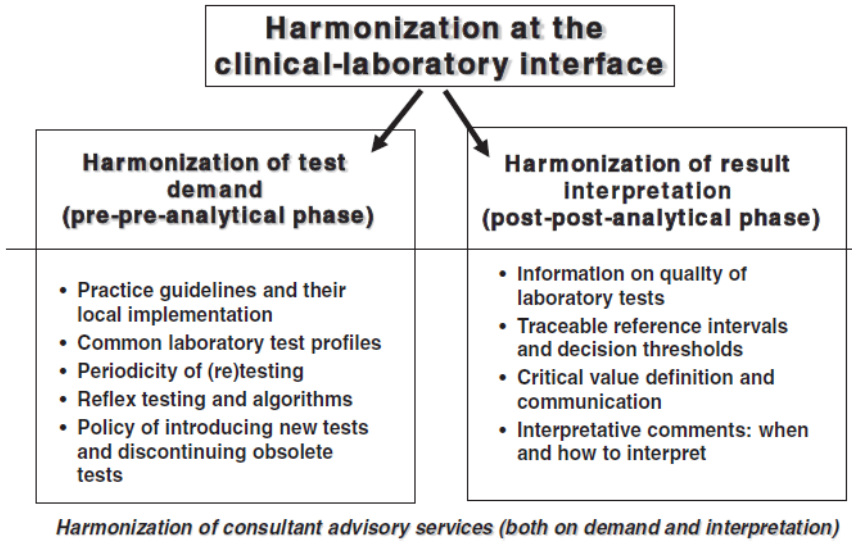

Plebani M, Panteghini M. Clin Chim Acta 2014;432:15-21

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Working Group: Harmonisation of Total Testing Process

Terms of reference

- Survey and summarize National European and Pan European harmonization initiatives.
- Promote and coordinate the diffusion of at least two especially promising harmonization initiatives among the EFLM member societies.
- Take initiatives to harmonize nomenclature, units and reference intervals on a European level.

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Plan of action for the first two years

- The WG will act as a **collector of the harmonisation initiatives** arising from other WGs or Task and Finish Groups of EFLM and from National Member Societies active in the field, and will **disseminate** them to all the EFLM Member Societies attempting to **monitor** their application and effects.
- The WG will survey and promote the use of harmonised **nomenclature** for measurands and promote the use of **amount of substance units** in the European countries.
- The WG will **promote the implementation of common reference intervals** for the measurands where this approach is feasible.

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EFLM survey on Harmonisation in Total Testing Process

- Covered the 3 main phases of the process: pre-analytical (8 questions), analytical (5 questions) and post-analytical (8 questions).
- The questionnaire was distributed in 2 phases: 1st, end of March (complete version, 21 questions) sent to the National representatives of the 40 Nations of EFLM. **Received 22 replies** (+ Kazakhstan); 2nd, a reduced version (9 questions) to focalize on the most relevant aspects of the pre- and post-analytical phases, sent in July only to the remaining 18 countries. **Received 14 replies, so only 4 countries are missing.**

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Questions of the pre-analytical phase

1. Is it common practice in your country to use “profiles” (e.g. liver function, electrolytes, etc.) for test requesting?
   - 20 Yes
   - 17 No
2. If YES, did/does your society produce some document on harmonization of test requesting profiles?
   - 7 Yes, but only 3 sent documents (Russia, Kazakhstan, The Netherland) all not readable (language!)

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Questions of the pre-analytical phase

3. Did/Does your society, alone or in collaboration with clinical societies, elaborate guidelines for diagnostic approaches to specific diseases? (e.g. myocardial infarction, coeliac disease, etc.)
   - 18 Yes
   - 19 No

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Existing guidelines

- Gestational Diabetes
- Diabetes
- CKD
- Tumor markers
- Thyroid disease
- Thyroid disease in pregnancy
- Autoimmune disease
- proteinuria
- Coeliac disease
- Ref val of lipoproteins
- dyslipidemia
- Myocardial infarction

- Very heterogeneous material
- Most of the documents in national languages
- Several topics covered in multiple countries (AMI, CKD, diabetes, tumor markers)

Should we try to prepare European guidelines to avoid 40 times repetition of the same efforts?

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pre-analytical phase

4. Did/Does your society publish indications for optimal timing for test repetition or minimal retesting intervals
   - 30 No
   - 6 Yes, but only 1 available document from UK
5. Did/Does your society produce a document on quality of the diagnostic samples or have some activity currently on this topic?
   - 22 No
   - 15 Yes

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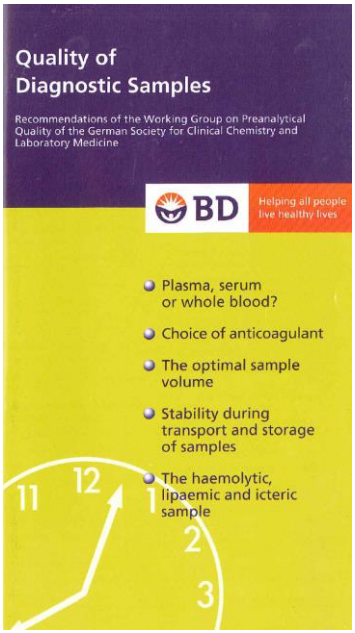

- **Sample collection an transportation**
  - An example of document from the German Society, EFLM WG-Pre-analytical has some analogous document in preparation

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Questions present only in the first survey

- Did/Does your society validate and promote any sort of reflex testing?
  - 7 YES (out of 22 replies), but no documents.
- Has your society officially declared the obsolescence of any laboratory test?
  - Only 2 YES, but no documents

Other pre-analytical harmonization activities

- Documents regarding how to perform phlebotomy or collection of other samples (urine, CSF etc.)

Croatia	http://www.biochemia-medica.com/2013/23/242
Slovenia	Venous blood, capillary blood, urine collection , CSF
Italy	Blood sampling / Urine collection
Norway	Blood sampling instructions
The Netherland	Correct way of carrying out phlebotomy

DE GRUYTER Clin Chem Lab Med 2015; 53(3): 357–370

Opinion Paper

Giuseppe Lippi[a,*], Giuseppe Banfi, Stephen Church[a], Michael Cornes[a], Gabriella De Carli, Kjell Grankvist[a], Gunn B. Kristensen[a], Mercedes Ibarz[a], Mauro Panteghini, Mario Plebani, Mads Nybo[a], Stuart Smellie, Martina Zaninotto and Ana-Maria Simundic[a] on behalf of the European Federation for Clinical Chemistry and Laboratory Medicine Working Group for Preanalytical Phase

Preanalytical quality improvement. In pursuit of harmony, on behalf of European Federation for Clinical Chemistry and Laboratory Medicine (EFLM) Working group for Preanalytical Phase (WG-PRE)

- Simundic AM, Cornes M, Grankvist K, et al. Standardization of collection requirements for fasting samples: for the Working Group on Preanalytical Phase (WG-PA) of the European Federation of Clinical Chemistry and Laboratory Medicine (EFLM). Clin Chim Acta 2014;432:33-7.
- Simundic AM, Cornes MP, Grankvist K, et al. Colour coding for blood collection tube closures - a call for harmonisation. Clin Chem Lab Med 2015;53:371-6

Harmonisation of blood sampling

- Effective implementation of EU Directive on needlestick injury prevention (2010/32/EU)
  - Use of safety-engineered devices (SED)
- Patient preparation
  - Definition of fasting requirements
  - Requirements for physical activity
  - Order of draw
  - Colour codes of the test tubes

Colour coding for blood collection tube closures

EFLM TFG chaired by A. Simundic

Table 2 Standard colours or manufacturers' core tube closure colours currently provided by several major tube manufacturers.

	Additive	1	2	3	4	5	6	7
Serum (clotting activator)	Clot activator	White	Red	Red	Red/Black ring	Brown	Red	Red
Serum-gel (clotting activator)	Gel, clot activator	Brown	Brown	Gold	Red with Yellow ring	Red Gold	Yellow	Gold
Plasma	Heparin	Orange	Green	Dark green	Green with black ring	Dark green	Dark green	Green
Plasma gel	Heparin	Orange/Brown	Green/Brown	Mint green	Green with yellow ring	Light green	Green	Green
Plasma	Citrate	Green	Blue	Blue	Blue with black ring	Pale blue	Blue	Blue
Whole blood	Citrate	Purple	Black	Black	Blue with yellow ring	Black	Black	Black
Whole blood	EDTA	Red	Purple	Purple	Purple with black ring	Purple	Light lavender Lavender	Lavender
Plasma gel	EDTA	Red	Purple/Brown	White	Purple with yellow ring		White	
Glucose (fluoride)	Glycolytic inhibitor	Yellow	Grey	Grey	Grey with black ring	Grey	Grey	Grey
Trace element tube	EDTA	Orange	Orange	Dark blue	Dark Blue with black ring			
Source		Catalogue	Catalogue	Catalogue	Website	Catalogue	Website	Catalogue

Road map

- All stakeholders, including all manufacturers working in the field, have been invited to join a dialogue to establish a universally acceptable colour coding standard for blood collection tube closures;
- Standard writing bodies (ISO, CLSI) should add the colour coding standard agreed on to the existing recommendations;
- Manufacturers should implement the agreed colour coding standard.

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Harmonisation / standardisation of the analytical phase

- Creation of reference measurement systems: IFCC task
- Quality goals: EFLM Task Force on Performance Specifications in Laboratory Medicine

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Post-analytical phase

1. Did/Does your society make documents or guidelines on use or definition of autovalidation rules?
   - 6 Yes, but only 1 document from Switzerland
2. Rules for reporting “critical values”
   - EFLM has a Task and Finish Group on Critical Results (TFG-CR) that will soon release a paper
3. Do you have any data on the diffusion of the use of SI unit (amount of substance units, e.g. mmol/L) in your country?
4. Did/Does your society promote officially the use of SI units?
5. Would your society be in favour of initiatives devoted to the introduction of SI units (mmol/L)?

	Nation	Use of SI units	Intention to promote SI
1	Albania	<10%	NO
2	Austria		
3	Belgium	50 – 80%	Yes
4	Bosnia Herzegovina	100%	Yes
5	Bulgaria	100%	NO
6	Croatia	>80%	Yes
7	Cyprus	<10%	NO
8	Czech Republic	>80%	NO
9	Denmark	>80%	Yes
10	Estonia	50 – 80%	Yes
11	Finland	>80%	Yes
12	France	100%	Yes
13	Germany	25 – 50%	Yes
14	Greece	<10%	Yes
15	Hungary	>80%	NO
16	Iceland	>80%	Yes
17	Ireland	<10%	Yes
18	Israel	<10%	Yes
19	Italy	<10%	Yes
20	Kosovo		
21	Latvia		
22	Lithuania	>80%	Yes
23	Luxembourg		
24	Macedonia	>80%	Yes
25	Montenegro	>80%	Yes
26	Norway	>80%	Yes
27	Poland	50 - 80%	Yes
28	Portugal	10 – 25%	NO
29	Romania	10 – 25%	Yes
30	Russia	100%	Yes
31	Serbia	100%	Yes
32	Slovak Republic	>80%	Yes
33	Slovenia	100%	Yes
34	Spain	<10%	Yes
35	Sweden	>80%	Yes
36	Switzerland	>80%	Yes
37	The Netherland	>80%	Yes
38	Turkey	<10%	Yes
39	Ukraine	100%	Yes
40	UK	>80%	Yes

Units of measurement

- In 8 European countries less than 10% of the results are reported in SI units.
- Six societies do not promote officially the use of SI units: Belgian, Czech, Italian, Greek, Macedonian and Norwegian, but only in 2 of them (Italy and Greece) the use of SI unit is <10%.
- 3 societies (Albania, Cyprus and Portugal) declare to be against a campaign for their implementation
- **Use of katal**. Only in 5 countries: Czech republic, Slovenia, Slovakia, Sweden and Ukraine. Should we suggest to abandon it?
- WG-H will start a campaign within the EFLM members for:
  - **Moving to SI units for all the electrolytes**
  - **Using only Liter (L) as denominator for all the measures where SI units are not available (proteins)**

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Considerations on the results of the survey

- Not harmonised harmonisation activities!!
- Several initiatives, but difficult to spread among countries also for the problems related to different languages
- Reference interval problem not yet touched

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Harmonisation as a three-level process

- **International**: standardization and among methods harmonization, definition of best practice standards, preparation of clinical practice guidelines for test requesting and result interpretation;
- **National**: Diffusion of internationally developed guidelines; release of laboratory practices for standardization and harmonization of all TTP steps, including communication of test results and critical values;
- **Local**: Adoption of international and national recommendations; implementation of measurement units, reference intervals, decision limits and Standard Operating Procedures for the pre- and post-analytical phases.

Modified from **Plebani M**. Harmonization in laboratory medicine: the complete picture. Clin Chem Lab Med 2013;51:741-51.


Thanks for
your attention!