GLOBAL BIOANALYSIS CONSORTIUM

Regulated Bioanalysis
A Proposed Global Harmonization Process

presented by Dr. S. Ravisankar for GBC
(replacing Dr. Shrinivas Savale
authorized by GBC Steering Committee)

BABE 2012 - Hyderabad

Global Bioanalysis Consortium
On harmonization of bioanalytical guidance

History

2008-2009:

- Loose discussions in multiple BA communities contemplating on the need and added value of harmonized BA guidelines

Dec. 2009 - EBF Conference (Barcelona, Spain)

- Formal request for harmonization from Bioanalytical community
- Acknowledgement by Regulatory Agencies present (FDA & EMA)
- Discussion among international pharmaceutical scientific organizations with a strong stake in bioanalysis: **AAPS, APA, CVG** and **EBF**
- Request Health Authorities to initiate a harmonization process
  - Offer support to Health Authorities for such a process
  - Letter sent to FDA and EMA in February 2010
- Publication as **Open letter** in April 2010 issue of *Bioanalysis*
- Entertain initial idea of forming a Global Bioanalysis Consortium

GBC: History *(cntd)*

Dec. 2009 - EBF Conference

OPEN LETTER

Request for Global Harmonization of the Guidance for Bioanalytical Method Validation and Sample Analysis

Open letter to the bioanalytical community. Sent to the US FDA/European Medicines Agency in February 2010

Philip Timmerman, MSc
Website: www.european bioanalysisforum.eu/

EBF

Steve Lowes, PhD
Website: www.aaps pharmaceutica.com

aaps

Douglas M Fast, PhD
Website: www.applied pharmaceuticalanalysis.org

APPLIED PHARMACEUTICAL ANALYSIS

Fabio Garofolo, PhD
Website: www.canadianlcms group.com

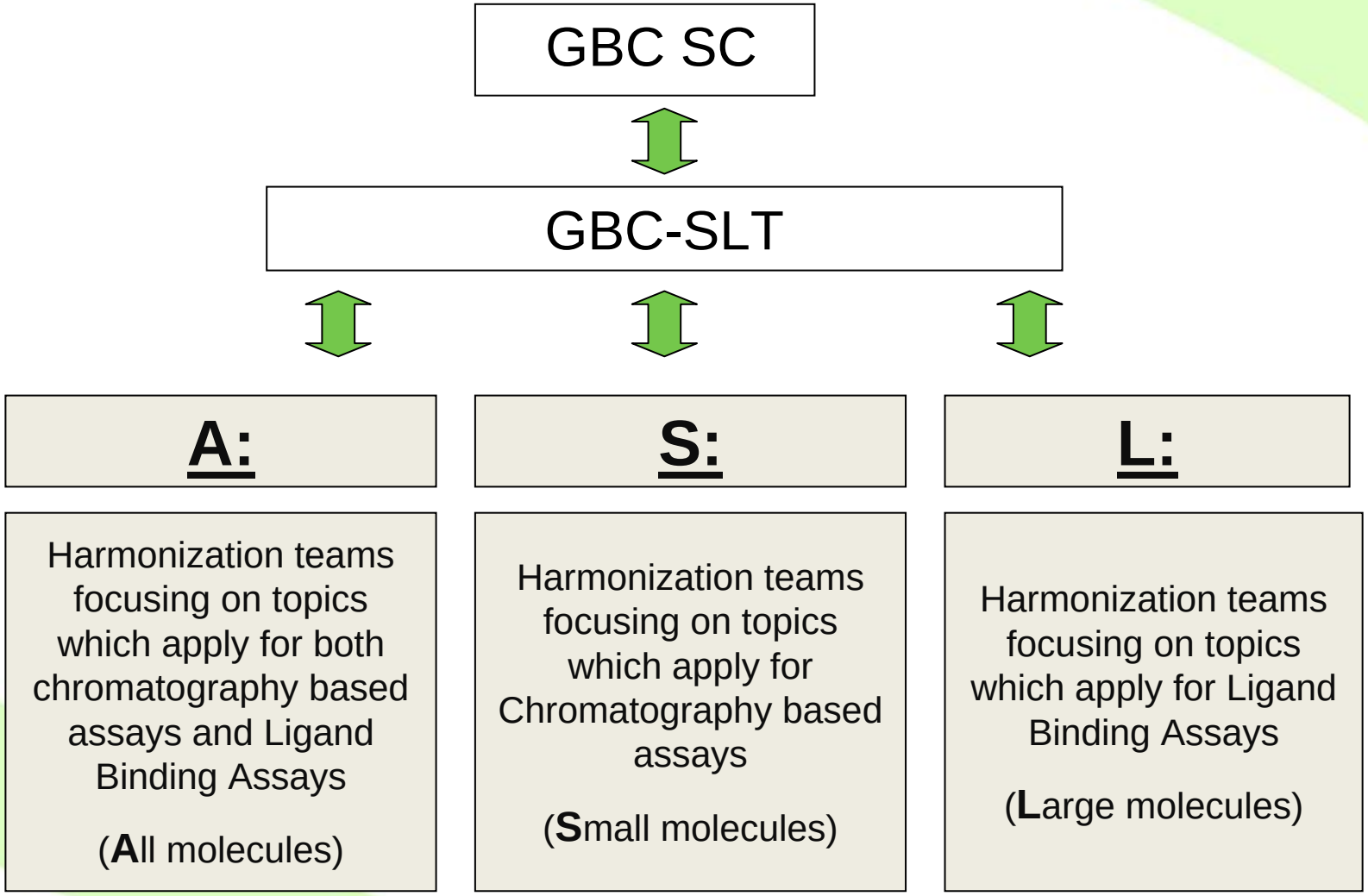
CVG

Apr. 2010 - CVG Workshop (Montreal, Canada)

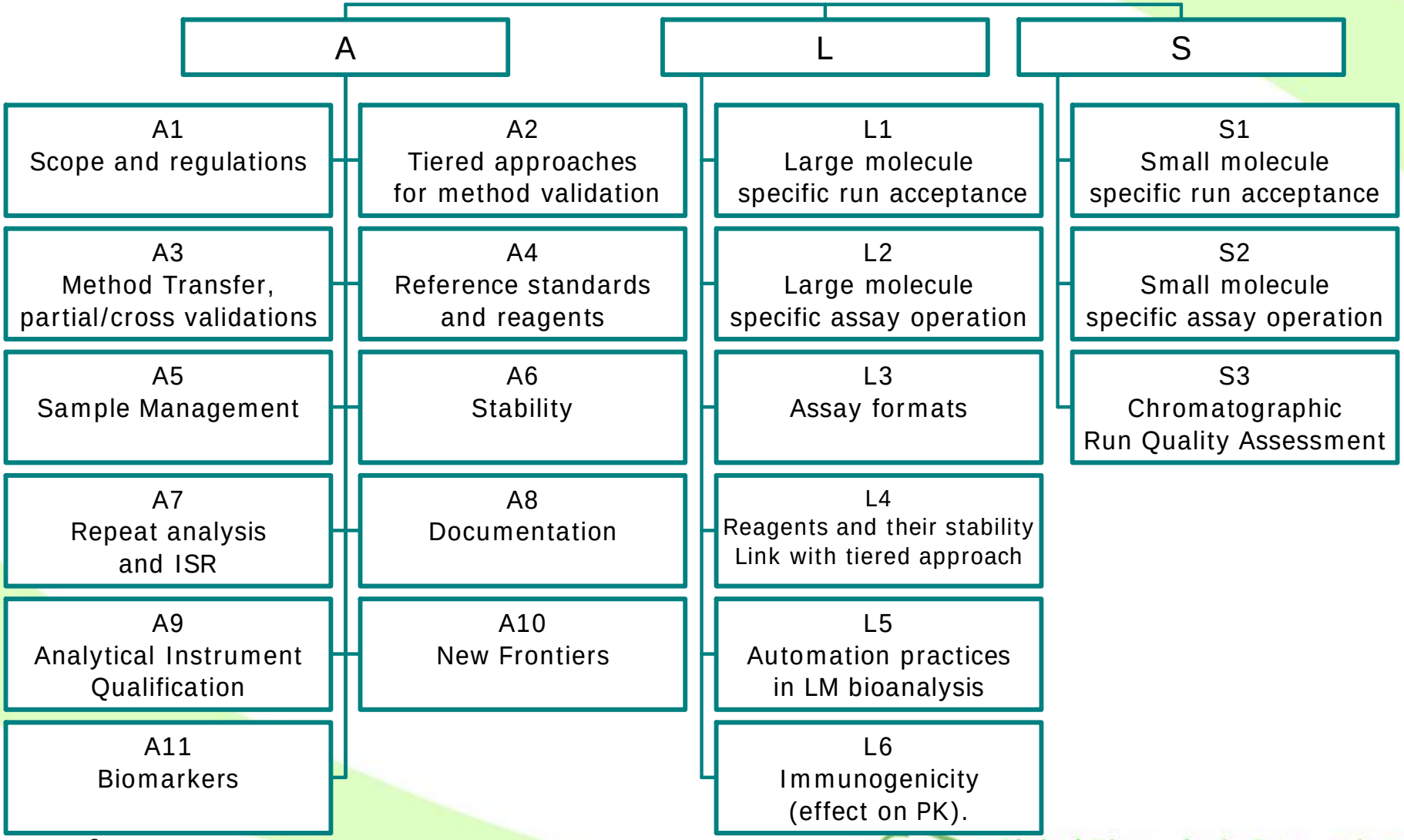
- Consensus reached among panelists, 5 regulatory agencies and international attendees on how to proceed with the Global Harmonization of Bioanalytical Guidances: institution of a **Global Bioanalytical Consortium**
- Agreement on the main characteristic of a **Global Bioanalytical Guidance:**
  - **Should be science driven**
  - **Should include rationale behind each requirement to prevent "box checking"**
  - **Should look at global picture, not local issues**
  - **Should NOT be a prescriptive guidance**
  - **Must get buy-in from all the countries**

Which Harmonization Teams?

Overview



Which Harmonization Teams ?



SC Sponsorship of Harmonization Teams

Team Leaders	SC Sponsor
A1: Surendra Bansal	Philip Timmerman
A2: Steve Lowes	
A4: Joseph Bower	
A6: Nico van den Merbel	Daniel Tang Shinobu Kudoh
A11: Russ Weiner	
A3: Ray Briggs	Peter van Amsterdam
A5: Mike Redrup	
A7: Eric Fluhler	
A8: Tom Verhaeghe	Shrinivas Savale

Team Leaders	SC Sponsor
L1: Marian Kelley	Michaela Golob
L2: Lauren Stevenson	
L3: Sherri Dudal	
L4: Lindsay King	Fabio Garofolo
L5: Scott Davis	Binodh DeSilva
L6: Jeff Sailstad	
A9: Chad Briscoe	Rafael Barrientos
A10: Bob Bethem/ Chad Ray	Mark Arnold
S1: Douglas Fast	
S2: Eric Woolf	
S3: Stuart McDougall	

Operating committees: HT-L

A1: Surendra Bansal

A2: Steve Lowes

A3: Ray Briggs

A4: Joseph Bower

A5: Mike Redrup

A6: Nico van den Merbel

A7: Eric Fluhler

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Harmonization Team Objectives

HT Leaders Objectives

- Remove concepts of company or region from your thinking - you're leading a global effort.
- Facilitate discussion, don't push your personal agenda

Teams are to develop science-based best practices

- Recognize that consensus may not be possible. People with different views will spark vigorous discussion.
- Prevent bullying by the loudest voice. Allow and stimulate less extrovert people to share their opinion and experience
- Recognize that some governments /regions may have regulations that are outdated or inconsistent with a science-based approach. Be prepared to defend proposals that conflict with existing regulations.

80:20 Rule

- Not all items within the Scope of the Team need to be redone, in fact 80% may already have industry-regulatory consensus

HT activities

Compile regional information on regulations and practices related to the Team's scope

- Share regulations with other Team
- A lot of prework has been done

Evaluate scope list to categorize those that:

- Are fully agreed to
- Are generally agreed to
- Have no agreement

HT activities

- For those that are **agreed to** write science-based language as proposed position
- For those that are **generally agreed to**, discuss differences and develop science-based position, write science-based language as proposed position
- For those that are **not generally agreed to**, prioritize the list to enable discussion on those with the greatest impact to the bioanalytical community
  - Have internal team discussions and where possible, develop recommendations
  - Where no consensus is achieved, provide arguments on both sides
  - Utilize GBC SC and other HT leaders for input

Team members should reach back to regional organizations for input

- Query regional organization membership on positions on a topic(s)
- Coordinate across Teams. Regional memberships will lose interest if frequently bombarded with requests.

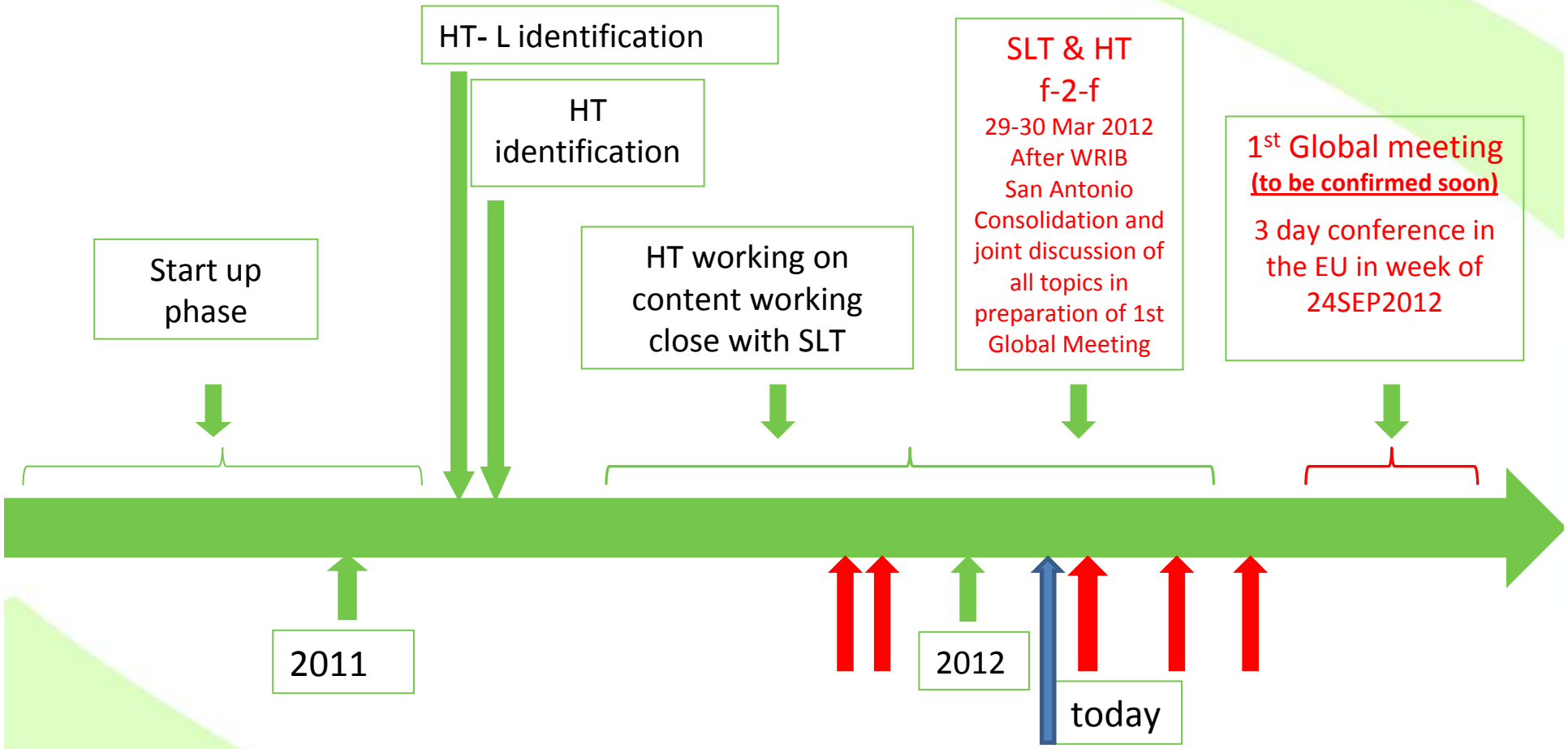
HT activities

Proposals and outcome

- Write proposals in a clear and concise manner that are suitable for publication, include references to existing literature and regulations
  - As noted above, where proposal conflicts with existing regulations, additional details and discussion may be needed

- Create slide deck for communication of proposals that go into greater depth and may contain data. This will be foundation of
  - Presentations at regional meetings
  - Presentation at international meeting
  - Publications in international journals
  - Note: timing of publications in relation to international meeting
    - ***Targeting International meeting in last week of Sept 2012 – venue selection in EU is ongoing***
- Where no consensus is achieved, provide arguments on both sides

Proposed way forward



Identified regional meetings

- Invite 4-5 topics to present the progress of their teams and to share.
- Present high level progress on other topics
- Get input

Global Bioanalysis Consortium
On harmonization of bioanalytical guidance

S1: Small molecule – Specific run acceptance

Team members:

Team lead

- Douglas Fast NA
  Douglas.Fast@covance.com

Other members

- Maristela Andraus LA
- Matt Barfield EU
- Michael Blackburn EU
- Ben Gordon EU
- David Hoffman NA
- Noriko Inoue APAC
- Amy LaPaglia NA
- Richard LeLacheur NA
  Deputy Team Lead
- Gabriel Marcelin Jimenez LA
- Scott Reuschel NA
- Ravi Sankar APAC

In scope:

- **During validation**
  - Linearity, accuracy, precision
  - Calibration curve range and QC placement
  - Selection of regression analysis model (linear, quadratic, weighting)
  - Criteria for individual runs and overall acceptance
  - Validation of plasma blank samples
  - Cross validation of anticoagulants and counterions
- **During samples analysis**
  - Individual run acceptance
  - Internal standard criteria
  - Carryover
  - Positive control or predose samples
  - Anomalous sample results on run acceptance
  - System suitability testing
  - Sample and run reinjection
  - System conditioning

Interdependencies with other teams:

- A2, A7, A8, A9, L1, S2, S3

Out of scope:

S3: Chromatographic Run Quality Assessment

Team members:

Team lead

- Stuart McDougall EU

stuart.mcdougall@covance.com

Other members

- Ravi Kumar Trivedi APAC
- Ravi Sankar APAC
- Chris Holliman NA
- Hollie Barton NA
- John Dunn NA
- Ray Farmen NA
- Katja Heinig EU
- Liz Thomas EU
- Maria Francesca Riccio LA
- Junji Komaba APAC

Interdependencies with other teams

- S1 Small molecule specific run acceptance (Run acceptance, IS acceptance criteria & SST)
- S2 Small molecule specific assay operation (sensitivity, specificity and selectivity)
- A9 - Analytical instrument qualification (calibration and maintenance)
- A1 - Scope and regulations (21CFR11, audit trail, glossary of terms)

In scope

- All analytes giving a quantitative chromatographic response
- Chromatographic approaches (primarily LC)
- Chromatographic detection (primarily MS)
- Calibration and maintenance of chromatographic systems
- Signal to Noise
- Resolution & selectivity
- Peak shape
- SST
- Data sampling
- Peak smoothing & peak filtering
- Internal Standard response criteria
- General integration parameters (not vendor specific)
- Integration process (automated, semi-automated, manual)
- Reintegration (post regression)
- Chromatographic data review
- Audit trail (integration & reintegration)

Out of scope

- Specific integration parameters (vendor)
- Regression slope
- Instrument qualification

Thank You

Acknowledgements

- The GBC Founding Members
- The GBC Steering Committee
- The Harmonization Team leaders and members