



# GLOBAL BIOANALYSIS CONSORTIUM

## Regulated Bioanalysis - A Proposed Global Harmonization Process

presented on behalf of GBC

at

The APA-India Conference  
Feb. 2011 - Hyderabad, India



## Mission Statement

Create an all inclusive **Global Bioanalysis Consortium** (GBC) consisting of represented **scientific associations** with world wide influence to merge existing or emerging bioanalytical guidance to create one, **unified consensus document** that can be presented to the regulatory bodies/health authorities in various countries.

# GBC: Goals and Objectives

- To bring together stakeholders from the pharmaceutical industry, contract research organizations and academia to share **current understanding of bioanalysis guidelines**, identify differences in these guidelines or differences in the interpretation or application thereof to routine regulated bioanalysis.
- To come forward with **recommendations** to Health Authorities and regulatory bodies worldwide on globally agreed best practices for Bioanalytical Method Validation (BMV) and application of such methods/technologies to the analysis of drugs of all molecular sizes in support of clinical and nonclinical studies.

# GBC: Goals and Objectives

- To invite relevant stakeholders, from industry, academia, Health Authorities and regulatory bodies, to jointly discuss the GBC recommendations at a **global conference(s)** in order to achieve globally agreed guidelines on bioanalysis.
- Going forward, to serve as a **pivot point** on the continued harmonized interpretation and/or updates of globally agreed guidelines.

# GBC: History

**Feb. 2010: Letter to FDA and EMA**

**April 2010: Publication as Open Letter**

**Apr. 2010: CVG Workshop – Consensus to start**

## OPEN LETTER

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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.europeanbioanalysisforum.eu/](http://www.europeanbioanalysisforum.eu/)



Steve Lowes, PhD  
Website: [www.aapspharmaceutica.com](http://www.aapspharmaceutica.com)



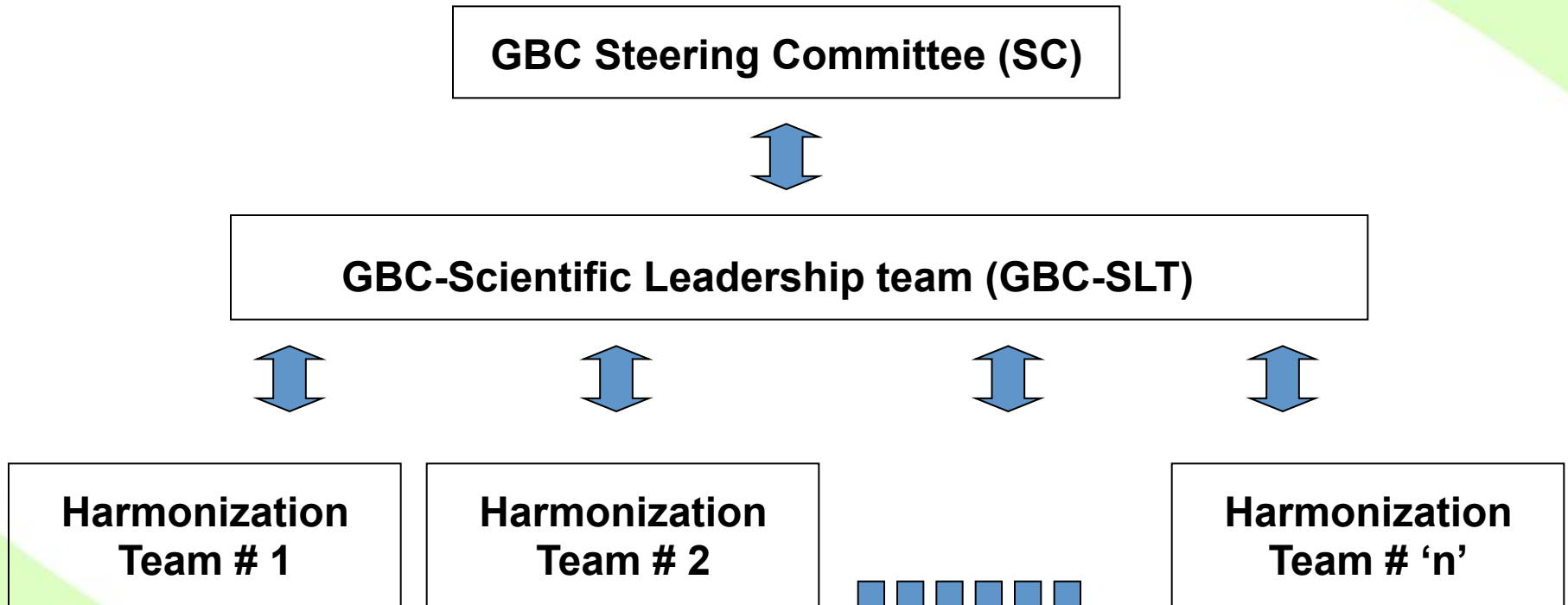
Douglas M Fast, PhD  
Website: [www.appliedpharmaceuticalanalysis.org](http://www.appliedpharmaceuticalanalysis.org)



Fabio Garofolo, PhD  
Website: [www.canadianlcmsgroup.com](http://www.canadianlcmsgroup.com)



# GBC: how to organize?



**Details on next slides**

# Operating committees: Summary

## GBC Steering Committee (GBC-SC)

- Participation: based on balanced representation from all (4) regions
- Role:
  - Build/coordinating GBC as organization (2010: together with founding members)
  - Facilitate and coordinate
  - represent of GBC to outside world

## GBC Scientific Leadership Team (GBC-SLT) = SC+FM+HT-L

- Participation: based on scientific expertise and anticipated contribution
- **Composition: Steering Committee, Founding members (FM) and Harmonization team Leads (HT-L)**
- Role:
  - Coordinate HT interactions and provide input as needed
  - Provide scientific leadership to facilitate progress
  - Ensure HTs work in concert and don't derail

## Harmonization teams (HT)

- Participation: based on scientific expertise and contribution
- Role:
  - Prepare proposals, blending (emerging) science, existing and emerging guidelines, on a harmonized way forward on the specific harmonization topic assigned to the team
  - Propose draft harmonized proposals to GBC-SLT
  - Present harmonized proposal at the GBC conference

# Operating committees: details

## 1. GBC SC (cntd)

### Steering Committee (as per 02-2011)

Updates since 12-2010:

- Optimization of regional representation
- Increase LBA expertise

#### North America (US + Canada)

- Binodh DeSilva (via AAPS)
- Fabio Garofolo (via CVG)
- Mark Arnold (via AAPS)

#### Europe (Europe + Africa/Middle East)

- Peter van Amsterdam (via EBF)
- Philip Timmerman (via EBF)
- SC via EU with LBA focus

#### Asia Pacific (Asia + Pacific area)

- Daniel Tang (via SBDG&BBDG)
- SC member (via APA-India)
- SC member (via Japan)

#### Latin America (South America + Mexico)

- Rafael Barrientos (via AcBio)



# Operating committees: details

## 2. GBC Scientific Leadership Team (GBC-SLT)

### Roles and Responsibilities of GBC-SLT

- **Participation:** The GBC-SLT consists of recognized BA experts who can contribute significantly to the long-term mission of GBC and are committed to devote time and energy in GBC activities
- **Harmonization:** GBC-SLT members should
  - Develop/support harmonization activities in their regional meetings and organizations, speak with one voice and report back to GBC-SC
  - Connect and support the harmonization teams (HT) (via HT lead)
  - Interact with BA community and regulators to achieve GBC mission. However, GBC-SLT members should be mindful of communication to regulators from GBC that should be limited to the SC members.
- **Ensure:**
  - Ensure GBC activities are all inclusive, both on regions and experts
  - Harmonization and blending of HT contents to ensure consistency and continuity
  - Representation of biologics and small molecule analytical in HT

# Operating committees: details

## 3. Harmonization teams (HT)

### Roles and Responsibilities of HT

- **Engage on discussing** different harmonization topics in preparation of harmonization meeting(s)
  - Discuss and share experience in support of harmonization and best practice.
  - Prepare proposals, blending (emerging) science, existing and emerging guidelines, on a harmonized way forward on the specific harmonization topic assigned to the team
  - By focusing on content in detail, will come forward with a **recommendation**, reached by consensus, to be presented at Global Harmonization meeting(s).
  - Propose draft harmonized proposals to GBC-SLT
  - Present HT subject content at Global Harmonization meeting
- **Interact** (via HT Lead) with GBC-SLT on a regular basis to ensure progress and consistency
- Team consists of **a team lead** and subject matter experts, preferably from multiple regions
- Will include all technologies during assessment, but may defer some in favor of earlier enacted recommendations for those more broadly used.

# Operating committees: details

## 3. Harmonization teams (HT) - cntd

### Roles and Responsibilities of HT

- Each team focuses on the their **defined topics**, but is mindful of potential **overlaps** and will discuss these with the other teams (via team lead and GBC-SLT)
- Teams report back on content and progress (via team lead) to GBC-SLT to allow oversight of progress or identify potential roadblocks/contradictions
- Individual membership to more than 1 team can be beneficial and is endorsed, but for practical reasons membership is limited to 3 teams
- Team members are committed to attend HT-meetings (TCs). The team is mindful of time zone challenges, 'difficult hours' rotate equally amongst the team members.

# Operating committees: details

## 3. Harmonization teams (HT)

### Profile of HT members

- Profile of HT members
  - Selected team members should be **experienced in the topic**
  - **No region should be excluded**, unless the region SC confirms lack of expertise, the subject matter is out of scope or insufficient experts volunteer
  - No region should have >50% of team members.
  - Size of teams can vary (advice: 5-10 members, depending on the topic)
  - Selection process: see slides 13/14

# Operating committees: details

## 4. Selection process of HT-Leads and HT members

### HT Leads

- GBC-SC **will propose** the HT leads based on level of expertise the candidates have with the topic of the specific team to the GBC-SC.
- The principle is to be **selective** rather than **restrictive**.
- Candidates for HT leads can make themselves known by submitting the registration form to:
  - [apply@globalbioanalysisconsortium.org](mailto:apply@globalbioanalysisconsortium.org)
  - Identifying the team they volunteer to lead

### HT members

- HT leads will identify their team based on level of expertise the candidates have with the topic of the specific team.
- Candidates for HT membership can make themselves known by submitting the registration form to:
  - [apply@globalbioanalysisconsortium.org](mailto:apply@globalbioanalysisconsortium.org)
  - Identifying the team they volunteer to be a member of

# Operating committees: details

## 4. Selection of HT-Leads and HT members - cntd

Registration Form available from GBC website

- <http://www.globalbioanalysisconsortium.org>

Registration Form seeks input on:

Name

Organization

Region you will represent

Experience on Small vs. Large molecule analysis (or both)

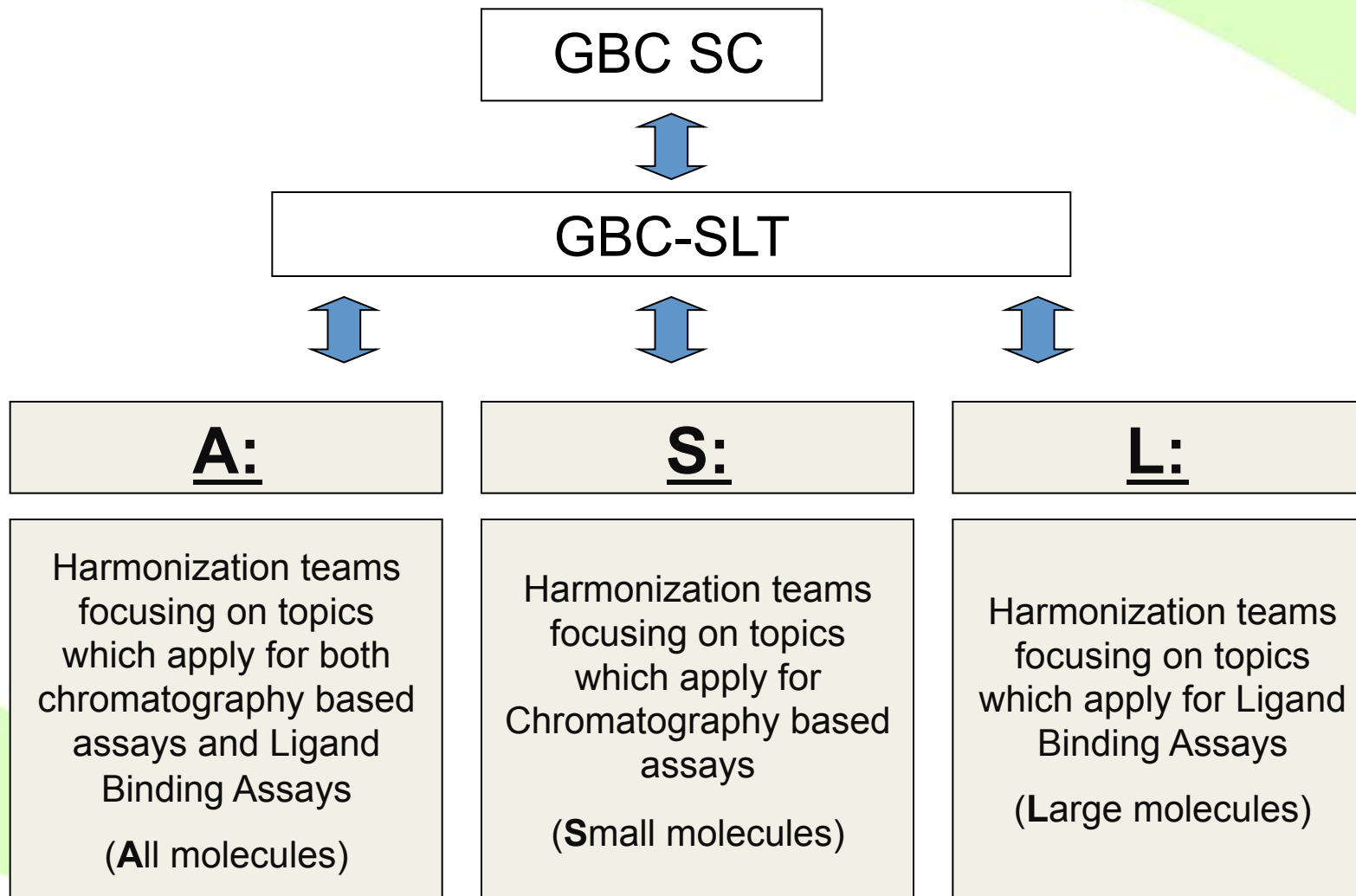
Interest:

- Lead an HT (commit to the time, effort and travel)
- Participate in a HT
- Which teams are you interested in

**Deadline for Registration: 21 February 2011**

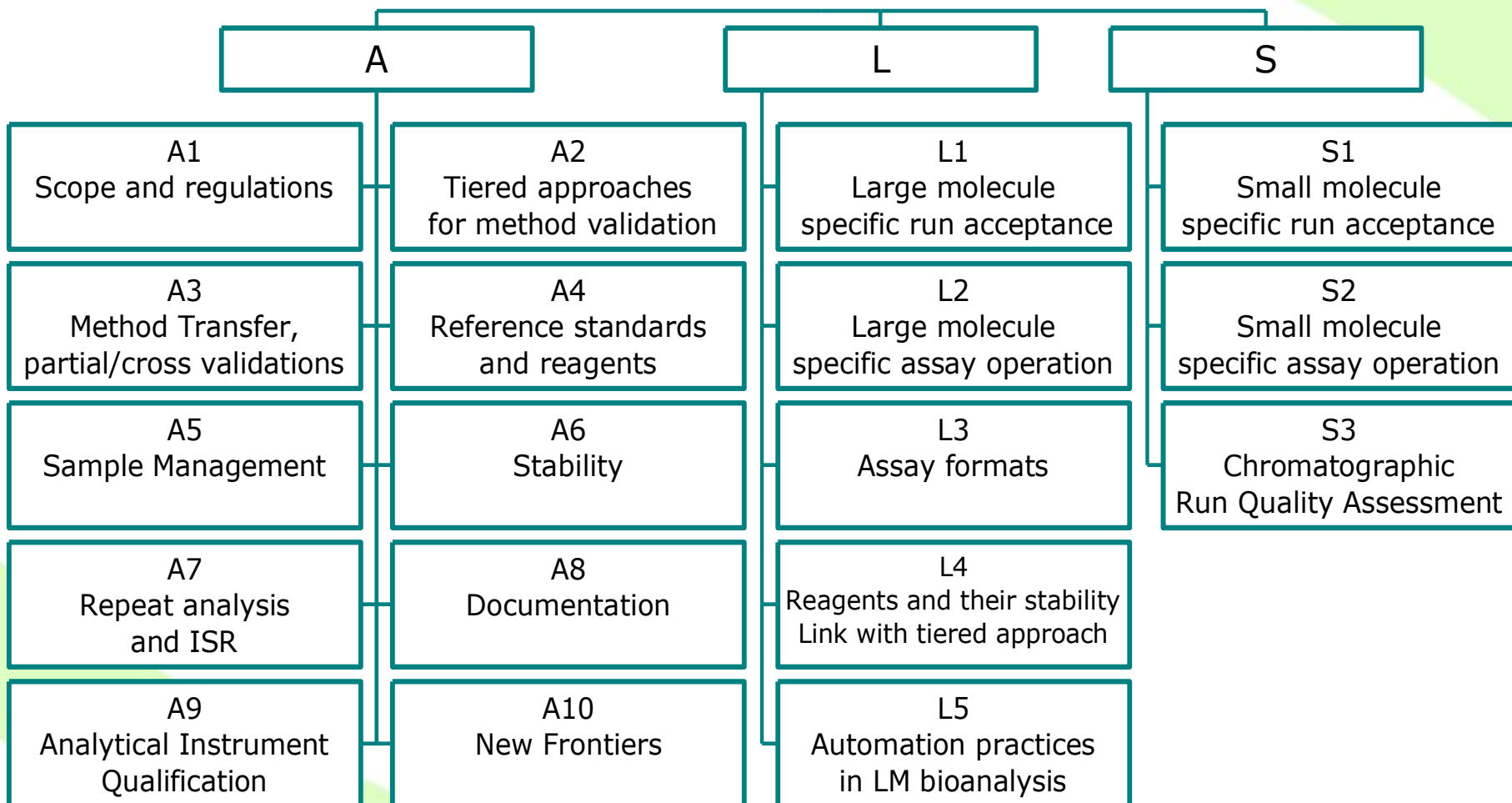
# Which Harmonization Teams?

## Overview



# Which Harmonization Teams ?

## Current Thinking





# Which Harmonization Teams ?

## Example: Harmonization team A6 - Stability

### Scope:

- Reference standards and reagent stability
- Process stability established during validation
- Stability in matrix
- Co-formulated and co-administered drugs
- Whole blood and tissue stability
- Stability at the sample collection time
- Degradation vs. stability vs. solubility loss vs. absorptive loss

### Moving forward:

- Team to have regular TCs
- Team to give feedback to SC/SLT at regular intervals or bioanalytical community as appropriate
- Team to present outcome at GBC conference

### Proposed discussion points:

- Understand and discuss areas of difference in interpretation – provide clarification
- Understand current (global) regulatory environment on assigned topic
    - Consider both Existing guidelines and anticipated or emerging guidelines
  - Acknowledge consensus (probably 80%)
  - Focus on missing, unclear or conflicting guidelines (maybe 20%)

# Examples of Consensus Topics

## Basic 6 principles of Method Validation

- Accuracy, Precision, Sensitivity, Selectivity, Stability and Reproducibility (ISR)
  - Overall design of the validation experiments
  - Run acceptance criteria: 4/6/15(20) or 4/6/20(25) Rules

## Principles of Incurred sample reanalysis

## Fundamentals of what goes into a bioanalytical report

- For MV or sample analysis
- Recent debate around the report generation process and finalization

# Examples of Topics Requiring Consensus Building

## Within current Method Validation guidance

- Tiered approaches to metabolites
- Statistical approaches vs. fixed number (e.g. 4/6/15 rule)
- Analyte stability experiments
- Scientific investigations
- Method transfer and cross-validations
- Internal standard criteria

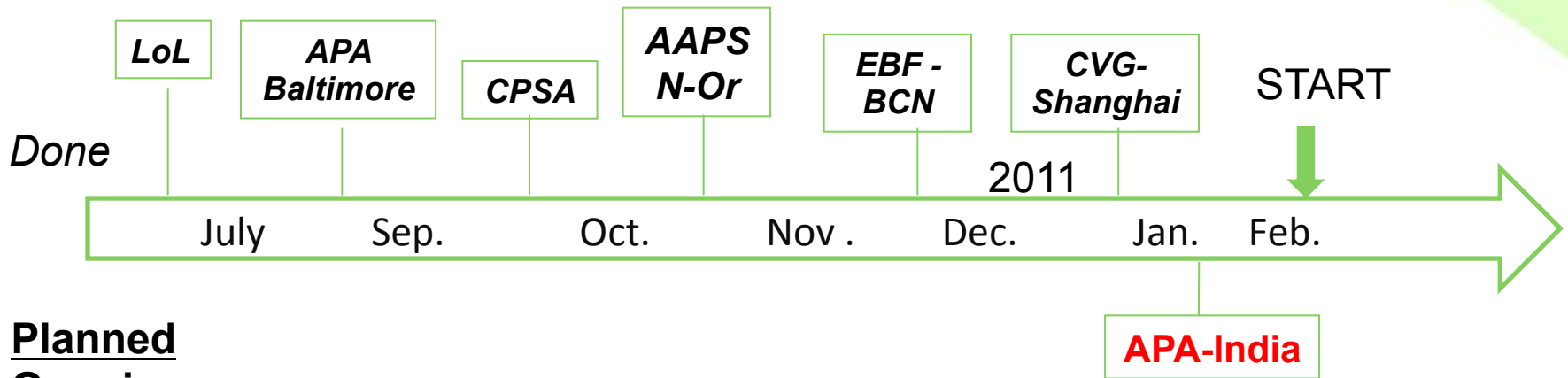
## Other developments

- Challenge of LBA vs. chromatographic assays
- Will regulatory language accommodate emerging technologies? – chromatographic and LBA
- Accommodating biomarker assays
- New technologies or other evolving issues



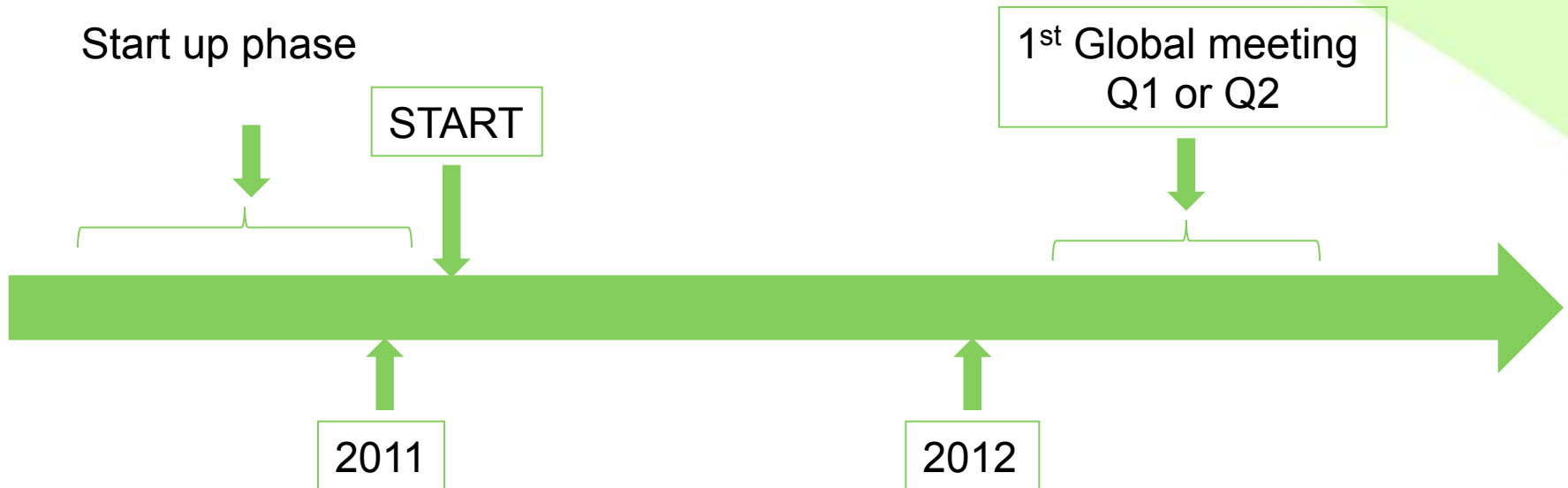
# Proposed way forward

- Create **awareness and get input** at international Bioanalysis meetings in all regions



- Get broader **consensus** on process from industry
- Finalize identification of harmonization team topics (Q1 2011)
- Reach out to **health authorities/regulatory** agencies to create awareness and reach agreement on process

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- Finalize identification of harmonization team topics (Q1 2011)
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# Acknowledgment

GBC Founding Team (FT) members and Steering Committee (SC) members:

- Peter van Amsterdam (FT, SC)
- Mark Arnold (FT, SC)
- Surendra Bansal (FT)
- Rafael Barrientos (SC)
- Binodh DeSilva (SC)
- Douglas Fast (FT)
- Fabio Garofolo (FT, SC)
- Steve Lowes (FT)
- Daniel Tang (SC)
- Philip Timmerman (FT, SC)
- Eric Woolf (FT)