Updates on the Progress of the Global Bioanalytical Consortium Harmonization Teams (GBC-HT) for Small & Large Molecules

Dr. Fabio Garofolo for GBC

AAPS Annual Meeting

October 2011 - Washington DC - USA

Global Bioanalysis Consortium

On harmonization of bioanalytical guidance

Agenda

- Brief History
- Review GBC structure
- Harmonization Teams Activities
- New insights developed at GBC-SC meetings

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

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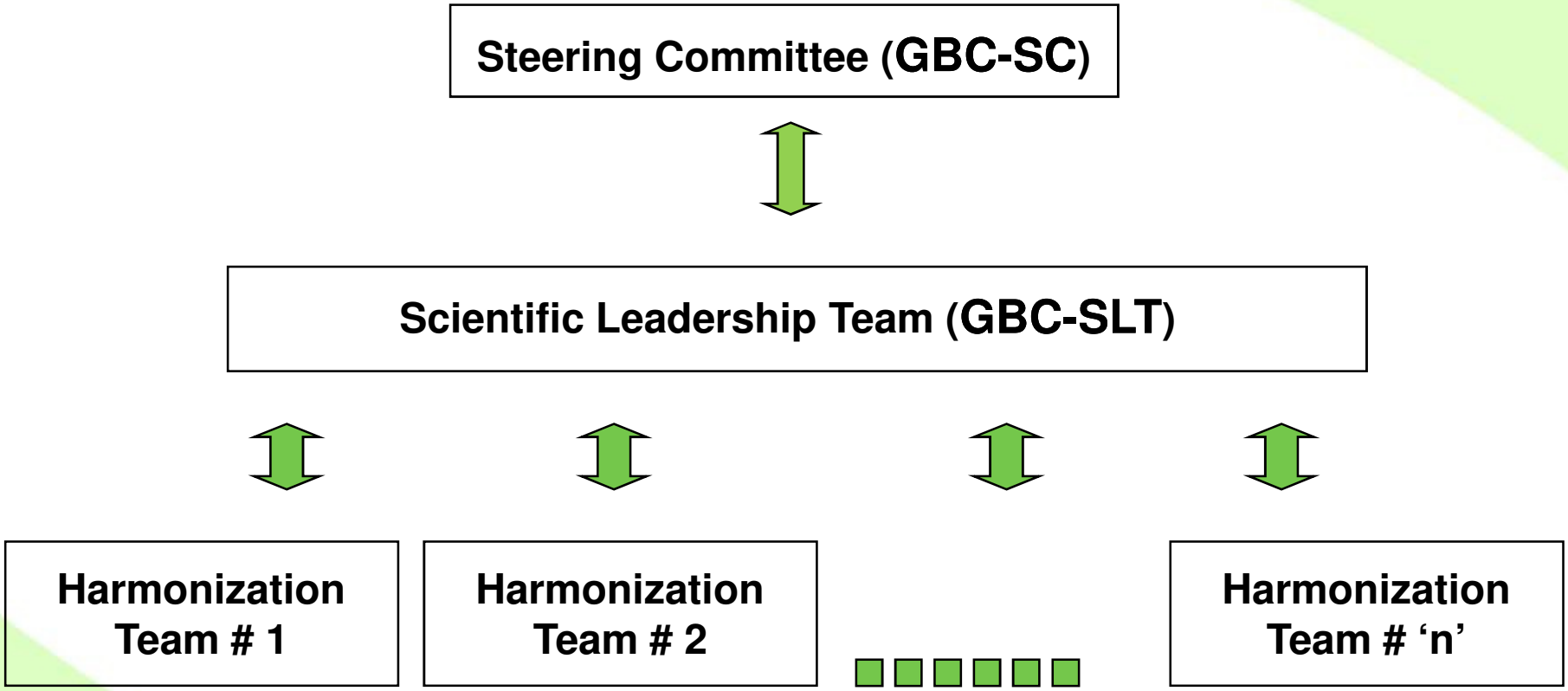
History

Apr. 2010 – 4th 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**

Organization Chart



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Operating committees: GBC-SC

North America (US + Canada)

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

Latin America (South America + Mexico)

- Rafael Barrientos (**AcBio**)

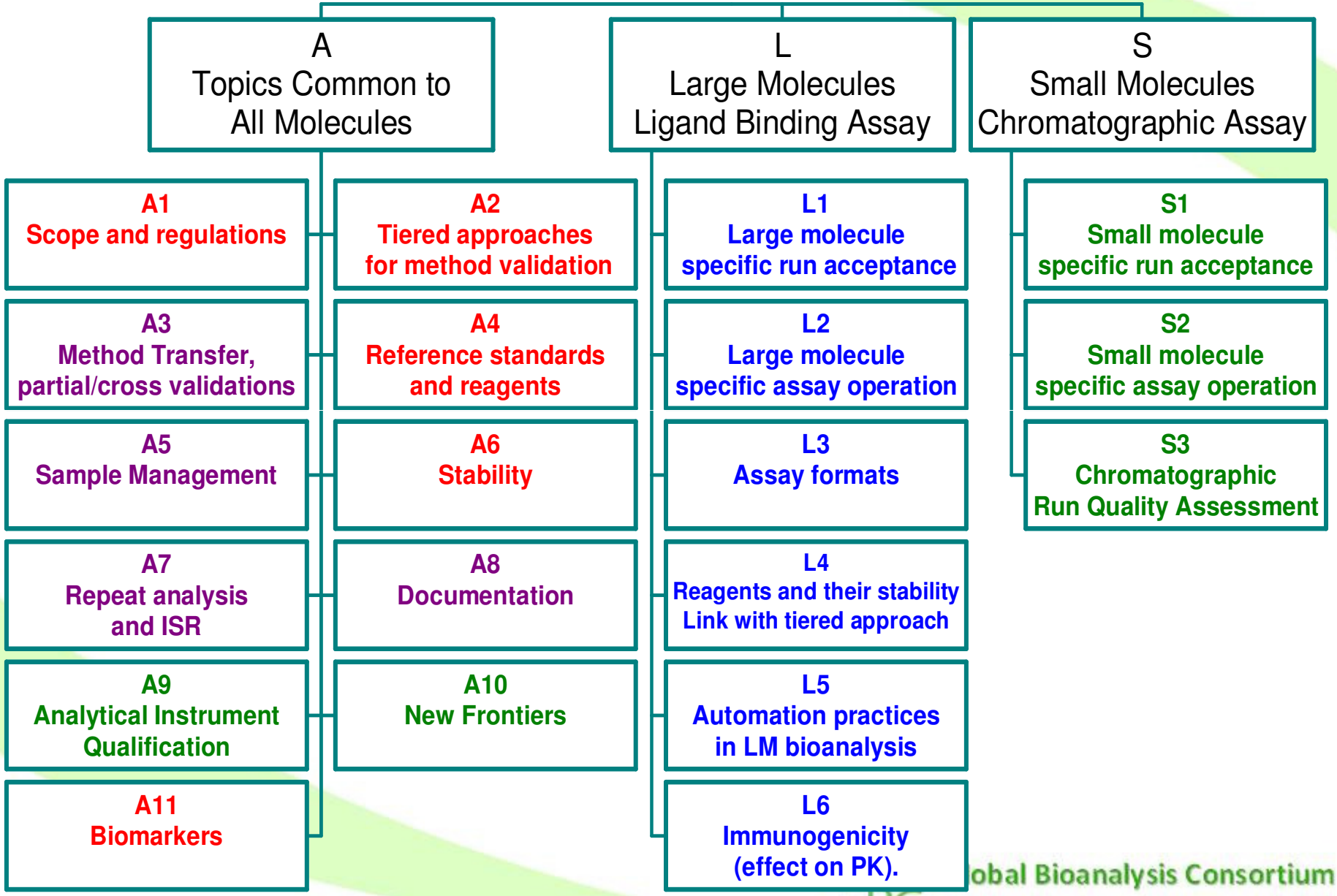
Asia Pacific (Asia + Pacific area)

- Shinobu Kudoh (**JBF**)
- Shrinivas Savale (**APA-India**)
- Daniel Tang (**SBDG&BBDG**)

Europe (Europe + Africa/Middle East)

- Peter van Amsterdam (**EBF**)
- Michaela Golob (**EBF**)
- Philip Timmerman (**EBF**)

Harmonization Teams



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Harmonization Teams

Team Leaders	SC Sponsor	Team Leaders	SC Sponsor
A1: Surendra Bansal A2: Steve Lowes A4: Joseph Bower A6: Nico van de Merbel A11: TBD	Philip Timmerman Daniel Tang Shinobu Kudoh	L1: Marian Kelley L2: Lauren Stevenson L3: Sherri Dudal L4: Lindsay King L5: Scott Davis L6: Jeff Sailstad	Michaela Golob Fabio Garofolo Binodh DeSilva
A3: Ray Briggs A5: Mike Redrup A7: Eric Fluhler A8: Tom Verhaeghe	Peter van Amsterdam Shrinivas Savale	A9: Chad Briscoe A10: Bob Bethem S1: Douglas Fast S2: Eric Woolf S3: Stuart McDougall	Rafael Barrientos Mark Arnold

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S2: Small Molecule Specific Assay Operation

Team members:

Team lead

- Eric Woolf – NA – woolf@merck.com

Other members

- Abhishek Sharma– APAC
- Barbara Duncan – NA
- Berthold Lausecker– EU
- Gabriel Marcelín – LA
- Kazutaka Togashi– APAC
- Miguel Vago- LA
- Pat Bennett– NA
- Ravi Kumar Trivedi – APAC
- Roger Hayes– NA
- Steve White- EU

Interdependencies with other teams:

Team A6 (re: stability)

- Sample reinjection
- API Salt / Counter-ion changes

Team A9 (re: system suitability)

- System Equilibration –

In scope

- Carryover and contamination
  - methodology to assess
  - acceptance criteria
  - impact of sample analysis sequence
- Sensitivity
  - "One off" std. curve range changes
- Specificity - selectivity
  - impact of co. meds/metabolites
- Matrix Effects
  - assessment methodology
  - effect of hemolyzed/hyperlipidemic plasma
- Recovery
  - assessment methodology & acceptance criteria
- IS evaluation
  - addition methodology
  - response variability assessment & acceptance criteria
- System equilibration
  - use of study samples
- Sample reinjections
- Reporting of failed runs
- Impact of salt form/counter ion changes of analyte
- Preparation of calibrators – organic solvent content

Out of scope

- stability criteria

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L1: Large Molecule Specific Run Acceptance

Team members:

Team lead

- Marian Kelley – NA – mmk48@comcast.net

Other members

- Paula Kaminski, NA
- Daniella Stollner, EU
- Ross Bamford, EU
- Muruganandam Arumugam, APAC
- Ravi Trivedi, APAC
- Samantha Little, EU
- Lauren Stevenson, NA
- Dongbei Li, APAC
- Chris Beaver, NA

In scope:

- Non-Linearity, of standard curve
- Makeup of standard curve
- Standard Curve editing
- Selection of "best" curve fit
- Quality Controls
- Assay range definition
- Accuracy, precision, total error
- Individual runs and overall run acceptance during validation
- Individual runs acceptance during samples analysis

Inter-dependencies with other teams

- S1 Small Molecule Run Acceptance
- L2 Specific LBA Operation

Out of scope:

- Stability of QCs long term during sample analysis: If it fails what do you compare to? Nominal, fresh? Two fold question: technical vs. stability. *Will be addressed in L2 team*

NEW insights developed at GBC-SC meetings

Desire for **increased engagement**, input and contribution from the different regions

- The current team dynamics and composition may not sufficiently engage current non contributors in the broader scientific community
- Open discussion

Desire to provide opportunity for **regular updates** on GBC progress in an open format

- The current process may lead to a significant period of 'radio silence'
- Prevent that all GBC-proposals come as one avalanche at the global meeting, which may be too much to manage if not previewed
- Provide regulators a chance to get better understanding of activities of GBC

Proposal - How?

Shift **GBC Global Meeting** from Q2 to **Q3 2012**.

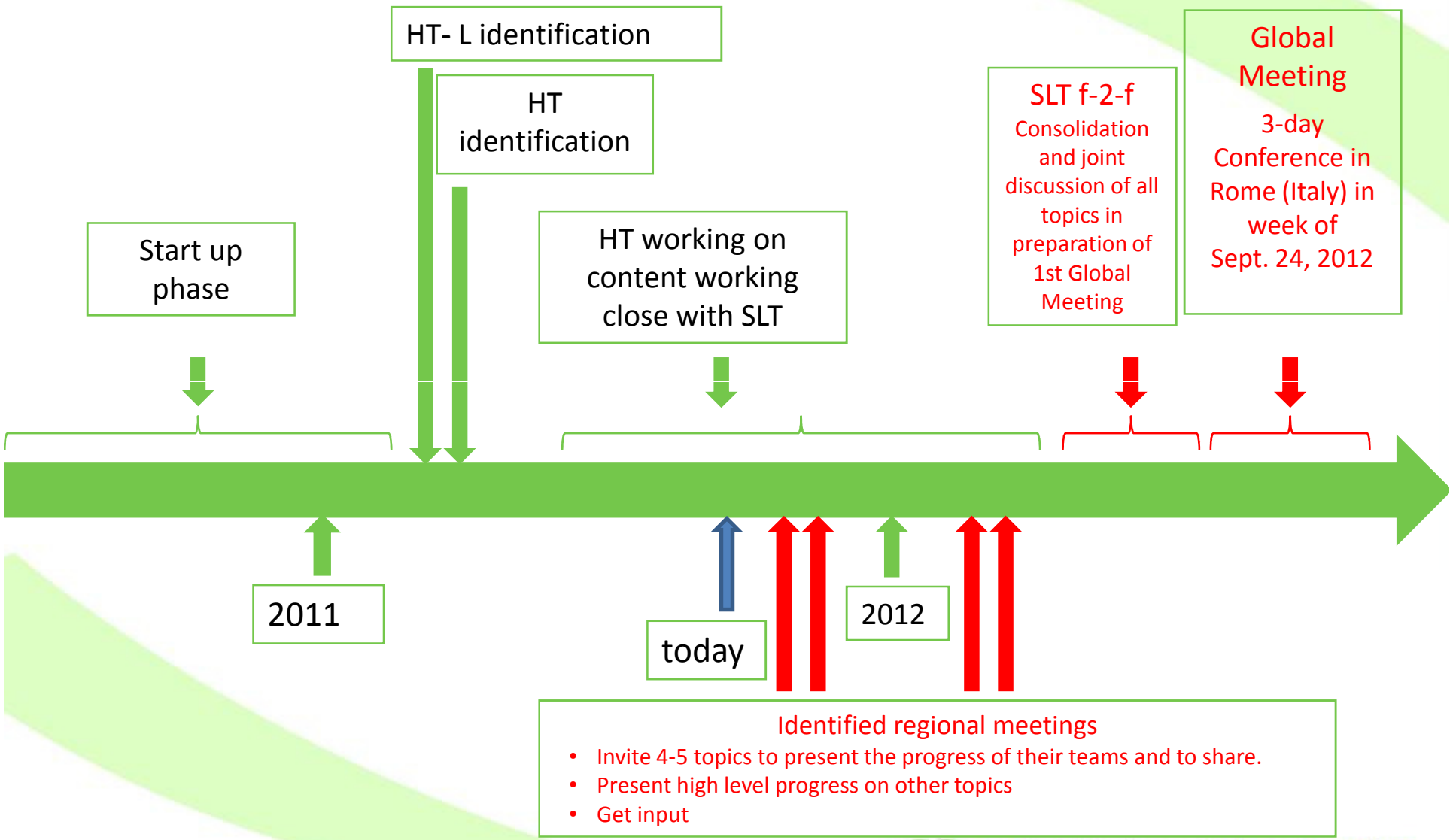
Use appropriate **2011-2012 regional meetings** in all 4 regions (best attended and most affordable in each region, >1x region) to give a flavor of the progress we are making.

- If the regional meeting can accommodate, include a **GBC session** in those meetings to provide update and allow input
- Invite **4-5 topic HT-L** (or a regional representative from those teams) to present the progress of their teams and to share.
- Stimulate HT-SC(s) to present **high level progress** on other topics, with input from other HT
- Engage with meeting organizers how to optimize **GBC visibility** during the meeting
- **Publish** outcome as a rapid communication to ensure all regions connect **(GBC website or "Bioanalysis")**
- Inviting organizations to provide travel assistance

Potential win-win

- **Connect** GBC better with the regions
  - Reconnection with supporting organizations as our day to day supporters
  - All regions get expanded opportunity to be involved
- **Engage** and inform a broader scientific community in advance of the global meeting
  - Allow BA community to comment within the comfort zone of their region
  - Allow BA community to comment to their regional organizations
- Provide the opportunity to **publish** a summary of thinking in advance of the global meeting
  - Allow participants to know what's coming
  - Be more engaged in the global meeting and not be caught by surprise
- Create visibility, recognition and connectivity in regions
  - for HT-L and HT members
  - for SC members
- Create flexibility to present on topics in need of **influencing current thinking** of regulators or on emerging guidelines

Proposed way forward



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In practice

With AAPS meeting being too soon on the calendar after our strategy update, 4th EBF meeting Barcelona (16-18 November) is first meeting where we will put this strategy in practice

Session Global Harmonization on day 1:

- 4 teams volunteered to give update on progress and get input
  - **A1**
  - **A6**
  - **L6**
  - **S1**
- In addition, session includes round table, moderated by SC members from all 4 regions

From then onwards, other meetings to follow depending on their ability to include GBC sessions (see next slide for meetings potentially qualifying)

In practice

Identified meetings qualifying for inclusion GBC session

- Fit with respect to timing (*italics= post GBC meeting*)
- Fit with respect to willingness of organizers to include GBC session
- Meetings potentially qualifying – further discussion with meeting organizers needed
  - **NA**:
    - Mar. 2012: **6th WRIB** (CVG) – San Antonio, USA
    - May 2012: **NBC** (AAPS) - San Diego, USA
    - May 2012: **ASMS** – Vancouver, Canada
    - Jul. 2012: **Land O'Lakes** - Wisconsin, USA
    - Sep. 2012: **APA USA** (BSAT) – Boston, USA
    - Other regional meetings (e.g., DVDMG)
  - **EU**:
    - Nov. 2011: **4th EBF Open Symposium**– Barcelona, Spain
    - Jun. 2012: **EBF Focus meeting** – Brussels, Belgium
    - *Nov. 2012: **5th EBF Open Symposium**– Barcelona, Spain*
    - Other regional meetings (e.g., Fabian, French GLP,..)
  - **APAC**:
    - Feb 2012: **APA India** (BSAT) – Ahmedabad, India
    - Mar. 2012: **JBF**, Tokyo Japan
    - *Nov. 2012:- **2nd APBC** (CVG) - Shanghai, China*
    - Other regional meetings
  - **LA**:
    - May 2012 – **ACBio** – Sao Paulo, Brazil
    - Other regional meetings

Acknowledgment

- Mark Arnold (AAPS) – SC & FM
- Surendra Bansal (AAPS) - FM
- Rafael Barrientos (AcBio) - SC
- Binodh DeSilva (AAPS) - SC
- Douglas Fast (BSAT) - FM
- Fabio Garofolo (CVG) – SC & FM
- Michaela Golob (EBF) – SC
- Shinobu Kudoh (JBF) – SC
- Steve Lowes (AAPS) - FM
- Shrinivas Savale (APA-India) - SC
- Daniel Tang (SBDG&BBDG) - SC
- Philip Timmerman (EBF) – SC & FM
- Peter van Amsterdam (EBF) – SC & FM
- Eric Woolf (BSAT) – FM

SC = *Steering Committee*
FM = *Founding Member*

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