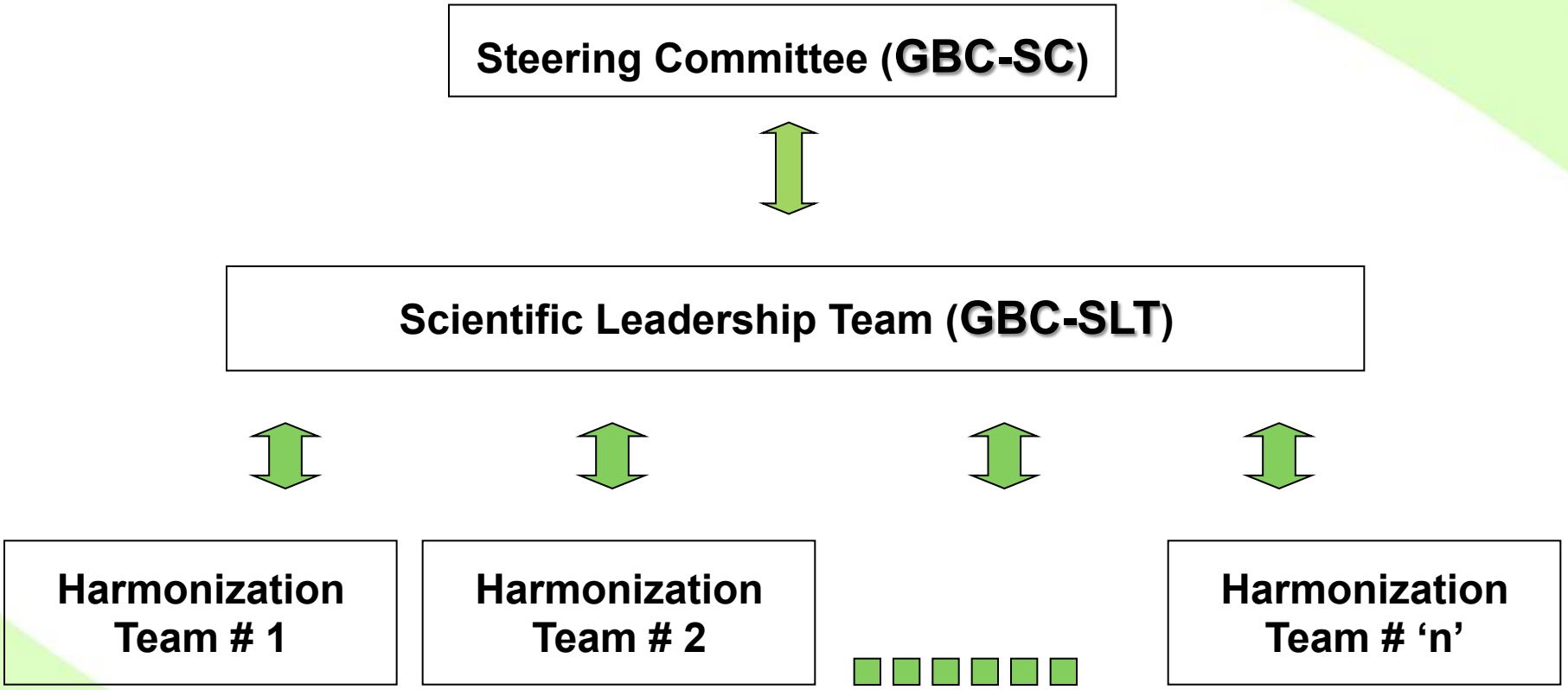
GLOBAL BIOANALYSIS CONSORTIUM

Regulated Bioanalysis
A Proposed Global Harmonization Process

Info for HT-L
Version 29April 2011

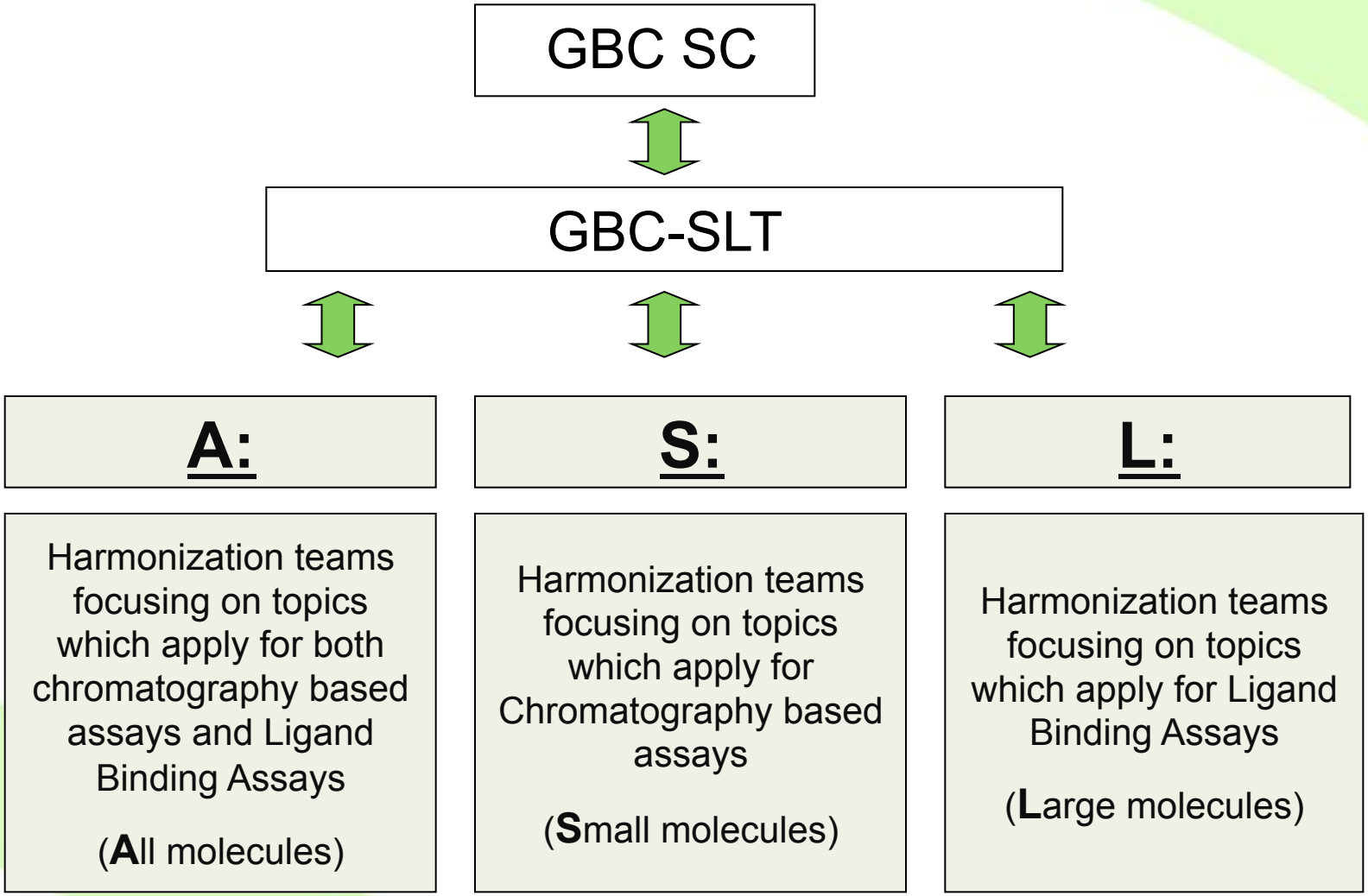
Global Bioanalysis Consortium
On harmonization of bioanalytical guidance

Organization Chart

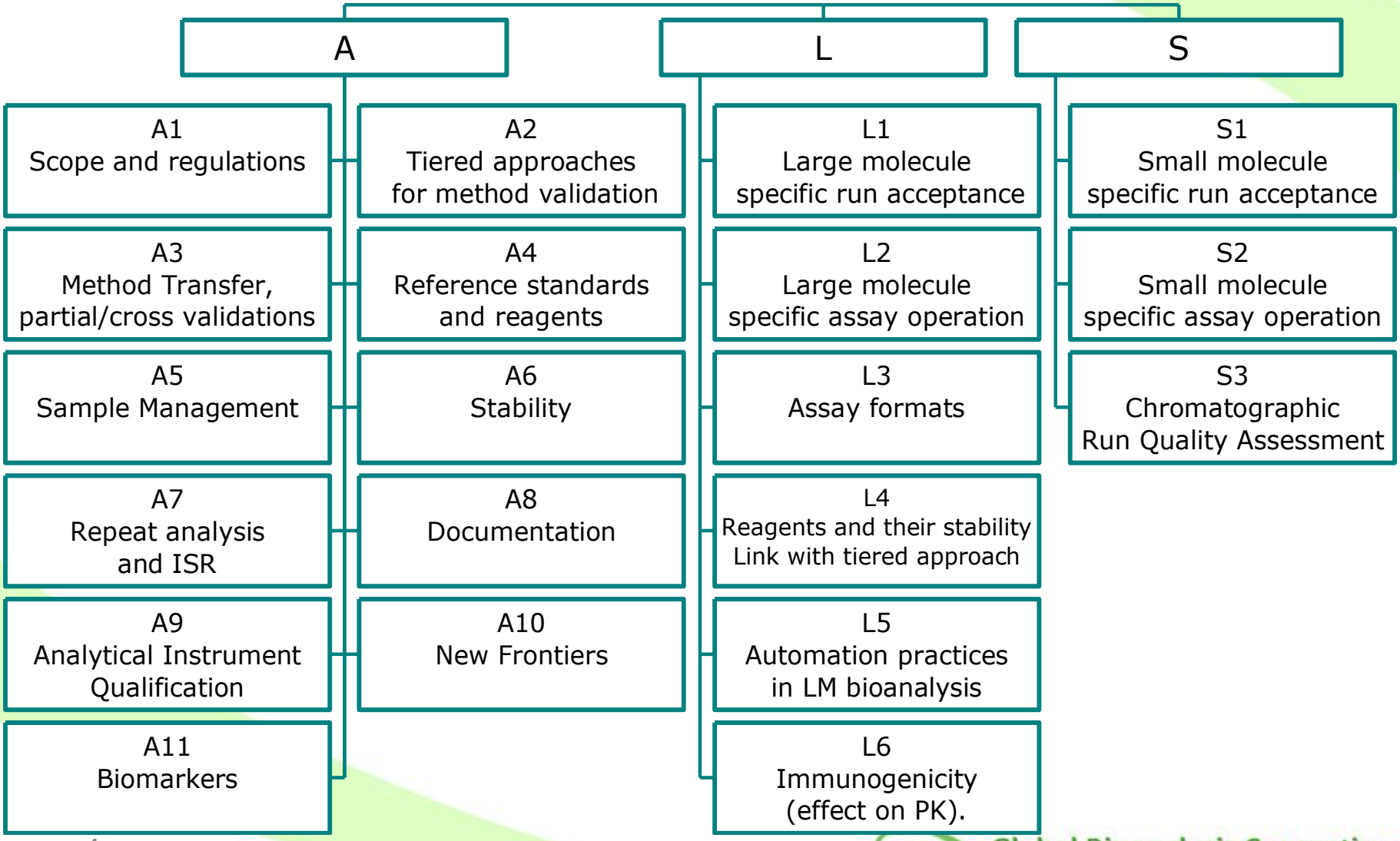


Which Harmonization Teams?

Overview



Which Harmonization Teams ?



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
A8: Tom Verhaeghe
A9: Chad Briscoe
A10: Bob Bethem
A11: Howard Hill

L1: Marian Kelley
L2: Lauren Stevenson
L3: Sherri Dudal
L4: Lindsay King
L5: Han Gunn
L6: Jeff Sailstad

S1: Douglas Fast
S2: Eric Woolf
S3: Stuart Mc Dougall

HT-L / SC sponsors liaison

A1: Surendra Bansal
A2: Steve Lowes
A3: Ray Briggs
A4: Joseph Bower
A5: Mike Redrup
A6: Nico van den Merbel
A7: Eric Fluhler
A8: Tom Verhaeghe
A9: Chad Briscoe
A10: Bob Bethem
A11: Howard Hill

L1: Marian Kelley
L2: Lauren Stevenson
L3: Sherri Dudal
L4: Lindsay King
L5: Han Gunn
L6: Jeff Sailstad

S1: Douglas Fast
S2: Eric Woolf
S3: Stuart Mc Dougall

SC sponsors duo/trio to HT-L:

Philip/Tatsuo/Daniel
Mark/Rafael
Peter/Shrinivas
Michaela/Binodh/Fabio

Operating committees:
3. Harmonization Team Leads (HT-L)

Roles and Responsibilities of HT-L

- **Leads** a specific HT
- **Identifies** team members for his/her team (preferably from multiple regions and recruited via application forms)
- **Responsible** for organizing regular HT meetings (agenda/timing) and ensuring meeting minutes are available.
- **Connects** with GBC-SLT, of which all HT-L are member, to report back on progress or get input.
- **Connects** with other HT-L in case of overlapping discussions

HT-Leads - Objectives

Your 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 e.g. 80% may already have industry-regulatory consensus

HT-Leads – short term goals

Select your team members

- From application list (will be provided)
- From different regions
  - No region > 50% of members
  - No region should be excluded unless the region agrees (SC to provide input)
  - Try to limit to 10 max, for practical reasons
- Individuals may be selected for max. 3 teams
  - HT-L may become member of maximum 2 other HT teams as member
- Look for thought leaders; people who have published, spoken or previously been involved in topic at workshops
- HT-L should be mindful to include experts with LBA experience for 'A' teams as well

Timelines

- Bring proposal back to SC sponsor by May 20th (Japan HT members can be included beyond that date)
- Feedback from SC sponsor by May 31st
- Team to start working from June 1st onwards

HT-Leads – short term goals

Evaluate Scope with team

- 1 slide per HT on high level scope is provided (see BU slides - 1)
  - This '1 slide' is a first guideline on what could be included, it is **not** a fence to work in.
  - Please feel free to include missing topics as you feel appropriate. Being mindful of overlap with other HT
  - Suggest topics to other teams that are generated in your discussions
- Ensure there is clarity within team on Scope

Timelines

- Finalize Scope and meet with GBC SC sponsors and other team leaders to review for completeness and evaluate overlap or points of contact for resolution of individual team by June 15th
- Other topics can be added as discussions in the team evolves

HT Objectives

Have regular meetings with team

- Frequency for you and your team to decide, being mindful of below mentioned timelines
- Inform GBC SC sponsor and other Team leads of progress
- Seek counsel and input as needed
- Keep minutes
  - utilize a team member to record minutes
  - distribute and permit team to comment
  - ensure agreement prior to finalizing

Timelines

- Monthly feedback to SC sponsor (in TC)
- Quarterly SLT TC (LiveMeeting) meetings will be organized to keep connected.

HT activities - 1 of 5

Compile regional information on regulations and practices related to the Teams scope

- Share regulations with other Team
- A lot of prework has been done by various SC members as part of their presentations at international conferences – please check the GBC website.

Evaluate scope list to those that are fully

- agreed to
- generally agreed to
- those with no agreement.

See next slide for details

The GBC SC believes that for many (if not all) topics, 80% of the items will be generally agreed to with only 20% in the latter two categories.

HT activities - 2 of 5

- 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 team leaders for input

Team members should reach back to regional organizations for input

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

HT activities – 3 of 5

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 presentation at international meeting
  - This will be foundation of publications in international journals
  - Note: timing of publications in relation to international meeting tbd by SC
- Where no consensus is achieved, provide arguments on both sides

HT activities - 4 of 5

Likely, SC will plan a SLT face-to-face, approx. 3 months prior to the GBC Global meeting (which we hope to schedule in Q2-2012), to

- discuss current status
- get broader input from all SLT members
- remove hurdles
- consolidate results to date
- prepare for GBC Global meeting

HT activities 5 of 5

Communication of results

- Communication of the outcome of the internal discussions needs approval by SC to prevent inappropriate sharing of premature and insufficiently consolidated thinking

Back up slides – 1

HT 1 slides

Which teams?
details on scope and deliverables

A1: Scope and regulations

Team members:

Team lead

- Surendra Bansal - NA

Other members

- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail

In scope

- Scope and regulations (GxPs) for bioanalytical validation and samples analysis – consider all region/countries , including emerging guidelines
- Other regulations/guidances if applicable e.g.
  - FDA and OECD equivalents
  - Cfr 21part11
  - ICH
  - References to bioanalysis in e.g clinical guidelines
- Glossary

Interdependencies with other teams – if any

Out of scope

A2: Tiered approaches for method validation

Team members:

Team lead

- Steve Lowes - NA

Other members

- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail

In scope

- Definitions of screening, qualification in relation to validation, applicable for
  - Validation/qualification of assays for tissues
  - Tiered approach for metabolites quantification
  - Biomarker assay qualification/validation
- Stability assessment in tiered approach (blood, tissue, urine, metabolites, biomarkers – as applicable..)

Interdependencies with other teams – if any

- A11

Out of scope

A3: Method Transfer, partial and cross validation

Team members:

Team lead

- Ray Briggs - EU

Other members

- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail

In scope

- Life cycle of a method after first full validation or relation with other validated methods.
  - Partial validation
  - Method transfer
  - Cross validation
- Definitions of method transfer, partial and cross validations
- Recommendation on when to perform method transfer, partial and cross validations
- Recommendations of which experiments are desirable for each proposed steps after full validation

Interdependencies with other teams – if any

- A4 (consistency in standards and chemicals)
- A6
- A7 (shared criteria for cross-validation)

Out of scope

A4: Reference standards and reagents

Team members:

Team lead

- Joseph Bower - NA

Other members

- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail

In scope

- Reference standards used for drugs, metabolites and internal standards – Purity certification and COA
- Preparation of stock solutions, calibration standards and QCs

Interdependencies with other teams – if any

- A2

Out of scope

A5: Sample Management

Team members:

Team lead

- Mike Redrup – EU

Other members

- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail

In scope

- All aspects of sample management from collection to disposition - Cold chain management
  - Collection, handling and storage at clinical/ animal lab
  - Storage and shipment from clinical/animal lab to CL or analytical lab
  - Pre analysis storage at analytical lab
  - Post analysis storage or shipment
  - Disposal or archiving/banking
  - Sample management using LIMS / sample management systems

Interdependencies with other teams – if any

- A6
- A3 (incurred samples in cross-validations)
- A7 (?)

Out of scope

A6: Stability

Team members:

Team lead

- Nico van de Merbel - EU

Other members

- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail

In scope

- Stability in relation to validated methods
- Reference standards and reagent stability
- Process stability established during validation
- Stability in matrix
- Co-formulated drugs, co-administered drugs
- Whole blood and tissue stability for validated methods
- Stability at the sample collection - A6
- Degradation vs. stability vs. solubility loss vs. absorptive loss

Interdependencies with other teams – if any

- A2
- A3
- A5

Out of scope

- Stability assessment in tiered approach (blood, tissue, urine, metabolites, biomarkers – as applicable..) – A2

A7: Repeat analysis and ISR

Team members:

Team lead

- Eric Fluhler - NA

Other members

- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
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- Name – region – e-mail
- Name – region – e-mail

In scope

Repeat analysis:

- Repeats for analytical reasons
- PK repeats (Including pre-dose concentrations)
- Incl. recommendation on single analyte repeat in multi-analyte assay
- Reinjection <-> Reanalysis
- Decision trees
- Criteria, Failure and Investigation

ISR:

- Including multiple analytes & endogenous compounds
- Criteria, Failure and Investigation
- Number / percentage of ISR samples
- Types of studies

Interdependencies with other teams – if any

Out of scope

A8: Documentation

Team members:

Team lead

- Tom Verhaeghe - EU

Other members

- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail

In scope

- Definitions of different report types
- Documentation of method development
- Method Validation reports
- Study protocol / plan
- Study reports
- Failure investigation and documentation
- Documentation at analytical site (including data generation, handling and reporting)
- Raw data definitions data (electronic and paper) including notebook records, instrument use and maintenance records
- Archiving

Interdependencies with other teams – if any

- A1

Out of scope

A9: Analytical Instrument Qualification

Team members:

Team lead

- Chad Briscoe – NA

Other members

- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail

In scope

- Software Validation
- Instrument qualification based on instrument categories
- System suitability
- Instrument decommissioning

Interdependencies with other teams – if any

- A1

Out of scope

A10: New Frontiers

Team members:

Team lead

- Bob Bethem – NA

Other members

- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail

In scope

- Understand analogies with established techniques and need for regulatory recommendation vs. need fro increased scientific validation prior to recommending regulations, i.e. new techniques already applied in regulatory context (peptide PK/TK with LC-MS/MS)
- Examples are, but not limited to
  - Micro-sampling (includes DBS)
  - Alternate technologies (AMS, ICPMS)
  - Large molecules analysis by new technologies

Interdependencies with other teams – if any

- A1

Out of scope

A11: Biomarkers

Team members:

Team lead

- Howard Hill – EU

Other members

- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
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- Name – region – e-mail
- Name – region – e-mail

In scope

- Extent of validation linked to phase of development and intended data use
  - Explore related regulations for CLIA and TDM assays

Interdependencies with other teams – if any

- A2

Out of scope

L1: Large molecule specific run acceptance

Team members:

Team lead

- Marian Kelley – NA

Other members

- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail

In scope

- Non Linearity of the standard curves
- Assay range (ELISA vs. MSD)
- Accuracy, precision, total error
- Appropriate calibration curve and QC ranges (during validation and for study specific)
- Selection of regression analysis
- Individual runs and overall run acceptance during validation
- Individual runs acceptance during samples analysis

Interdependencies with other teams – if any

- S1

Out of scope

L2: Large molecule specific assay operation

Team members:

Team lead

- Lauren Stevenson – NA – e-mail

Other members

- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail

In scope

- Testing of ruggedness and robustness
- Setting up a balanced validation design
- Dilution linearity
- Specificity testing
- Selectivity testing
- Parallelism
- Hook effect

Interdependencies with other teams – if any

Out of scope

L3: Assay formats

Team members:

Team lead

- Sherri Dudal – EU

Other members

- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail

In scope

- Possible assay platforms for LBAs – Gyros, Biacore, ELISA (96, 384 etc), MSD
- Acceptance criteria for these new methods
- How to set up the assays – placement of standards and QCs in these new formats
- Pros and cons of using these formats

Interdependencies with other teams – if any

Out of scope

L4: Reagents and their stability - Link with tiered approach

Team members:

Team lead

- Lindsay King – NA– e-mail

Other members

- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail

In scope

- What are the critical reagents
- What to do when you change critical reagents
- Stability of reagents
- Batch to batch variation
- In-house vs. commercial reagents pros and cons
- Specificity testing of the reagents

Interdependencies with other teams – if any

- Link with tiered approach

Out of scope

L5: Automation practices in LM bioanalysis

Team members:

Team lead

- Han Gunn – NA

Other members

- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail

In scope

- Choosing automation
- Full automation vs. modular
- How to conduct validation with an automated instrument as an analyst
- Setting acceptance criteria based on the automated assays
- Validating the instrument vs. the method
- Carry over
- Fixed tips vs. disposable tips

Interdependencies with other teams – if any

- Link with tiered approach

Out of scope

L6: Immunogenicity (Effect on PK)

Team members:

Team lead

- Jeff Sailstad – NA

Other members

- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail

In scope

- How does immunogenicity data affect the pharmacokinetics
- How to assess this parameter during the validation

Interdependencies with other teams – if any

- Link with tiered approach

Out of scope

- Immunogenicity Assessment
- Cut point analysis
- Screening assay
- Confirmatory assay
- Nab assay

S1: Small molecule specific run acceptance

Team members:

Team lead

- Douglas Fast – NA

Other members

- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail

In scope

- Linearity, Accuracy, Precision
- Appropriate calibration curve and QC ranges (during validation and for study specific)
- Selection of regression analysis (linear vs. best fit)
- Individual runs and overall run acceptance during validation
- Individual runs acceptance during samples analysis

Interdependencies with other teams – if any

- L1

Out of scope

S2: Small molecule specific assay operation

Team members:

Team lead

- Eric Woolf – NA

Other members

- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail

In scope

- Carryover and contamination
- Sensitivity
- Specificity - selectivity
- Matrix Effects
- Recovery
- IS evaluation

Interdependencies with other teams – if any

Out of scope

S3: Chromatographic Run Quality Assessment

Team members:

Team lead

- Stuart Mc Dougall – NA

Other members

- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail
- Name – region – e-mail

In scope

- Chromatographic resolution and peak shape
- Noise signal
- Peak integration algorithms and manual integrations
- Other quality parameters potentially needed for recommendation, e.g. :
  - Changes in slopes during study

Interdependencies with other teams – if any

Out of scope

Back up slides – 2

others

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.

Operating committees:
Summary - membership

GBC Steering Committee (GBC-SC)
- Participation with balanced representation from all (4) regions
- Members from organizations which represent the regional BA community
- Balanced membership to cover LBA and chromatographic assays

GBC Scientific Leadership Team (GBC-SLT)
- Participation based on scientific expertise and contribution
- Members = SC + FM + HT-L

  Steering Committee, Founding members (FM) and Harmonization Team Leads (HT-L)

Harmonization teams (HT)
- Participation based on scientific expertise and contribution
- HT = HT-lead + HT-members

Operating committees:
Summary - roles

GBC Steering Committee (GBC-SC)
- Build/coordinate GBC as organization
- Facilitates and coordinates
- Represent GBC in outside world

GBC Scientific Leadership Team (GBC-SLT)
- 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)
- Prepare proposals, blending (emerging) science, existing and emerging guidelines, on a harmonized way forward on all 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

Roles and Responsibilities of the GBC-SC

- **Coordinate** the GBC process of a global BMV harmonization strategy.
- **Organize** and register GBC as an independent entity unless association with reputed existing organization is in the best interest of GBC
- **Financial** responsibility for overseeing finances and filings
- **Oversight** and co-ordinate the GBC-SLT and facilitate conflict resolution
- **Communicate** or facilitate communication of the GBC progress to global community
- **Represent** or facilitate representation of GBC at international and regional meetings.
- **Dialogue** with Health Authorities/regulatory agencies on behalf of GBC
- **Organize** international meetings/conferences for harmonization / globalization
- **Interact** with and appraise other interested BA and related groups having interest in GBC
- **Report back** to GBC-Scientific Leadership Team
- **Sponsor** of selection of HT teams

Operating committees: details

1. GBC SC (cntd)

Notes:

- SC membership aims at balanced representation from all identified regions
- Size of SC will be kept small
- Regions to manage representation in GBC in line with regional expectations

- Currently **4 regions** are identified:
  - North America (NA = US and Canada)
  - Latin America (LA = South America + Mexico)
  - EU (Europe + Africa)
  - Asia-Pacific (APAC)

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)

- Tatsuo Kurokawa (JBDG)
- Shrinivas Savale (APA-India)
- Daniel Tang (SBDG&BBDG)

Europe (Europe + Africa/Middle East)

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

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-blending of HT outcome to ensure consistency and continuity
  - Representation of biologics and small molecule analytical in HT

Operating committees: details
Harmonization teams (HT) - cntd

HT composition - Profile of HT members

- Team consists of a **team lead** and **subject matter experts**, preferably from multiple regions and recruited via application forms
  - 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** (via TC). The team is mindful of time zone challenges, 'difficult hours' rotate equally amongst the team members
  - **No region should be excluded**, unless the regional SC member confirms lack of expertise, the subject 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)
- Will include all technologies during assessment, but may defer some in favor of earlier enacted recommendations for those more broadly used

Operating committees: details
Harmonization teams (HT)

Roles and Responsibilities of HT

- **Engage on discussing** different harmonization topics in preparation of harmonization meeting(s)
  - Discuss - share experience in support of harmonization and best practice.
  - Prepare proposals, blend (emerging) science, existing and emerging guidelines into a harmonized way forward on a specific harmonization topic assigned to the team - propose draft proposals to GBC-SLT
  - By focusing on content in detail, come forward with a **recommendation**, reached by consensus, to be presented at Global Harmonization meeting(s).
  - Present HT subject content at Global Harmonization meeting
  - Each team focuses on the their **defined topics**, but is mindful of potential **overlaps** and will discuss these with HT-L and/or SLT
- **Interact** (via HT-L) with GBC-SC (each HT has a SC sponsor as first point of contact) and SLT on a regulars basis to ensure progress, potential roadblocks or overlap and consistency

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 (ISR)

Fundamentals of what goes into a bioanalytical report

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

Topics Requiring Consensus Building
Examples

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

Operating committees details

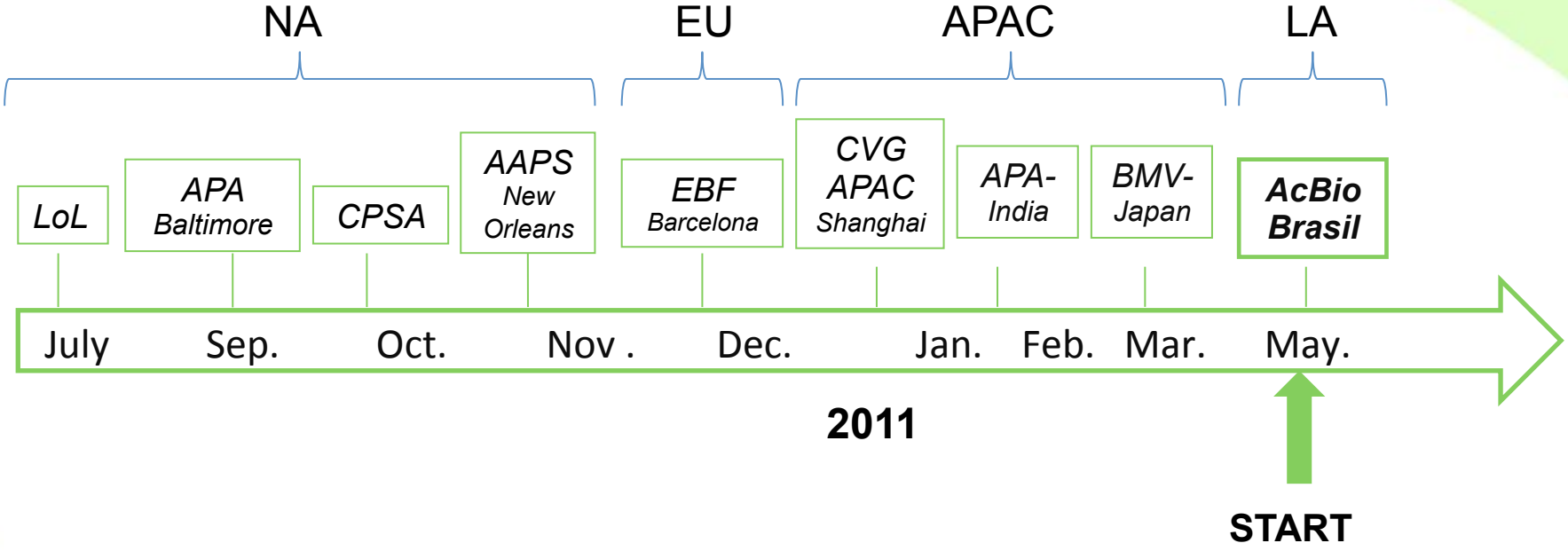
Dynamics of SC – SLT – HT-L interactions

Dynamics of SC – SLT – HT-L interactions

- HT-L feedback and interaction through in SC-sponsorship:
  - Each HT has a SC sponsor as first point of contact
  - Each HT will provide monthly executive summaries (via HT-L, in agreed template format) to facilitate feedback from HT to SC and across teams.
  - Essential part of this feedback is on progress and hurdles identified by the HT.
  - All summaries are shared with full SLT for information purposes
  - Difficult to resolve hurdles are escalate to SC prior to escalation to SLT
- In order to make sure SLT does not become a virtual team, quarterly TCs should be planned. Logistics to be determined
- Plan for a SLT face to face in Q1-2012 for consolidation and joint discussion of all topics, in preparation of 1st Global Meeting

Where are we now?

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

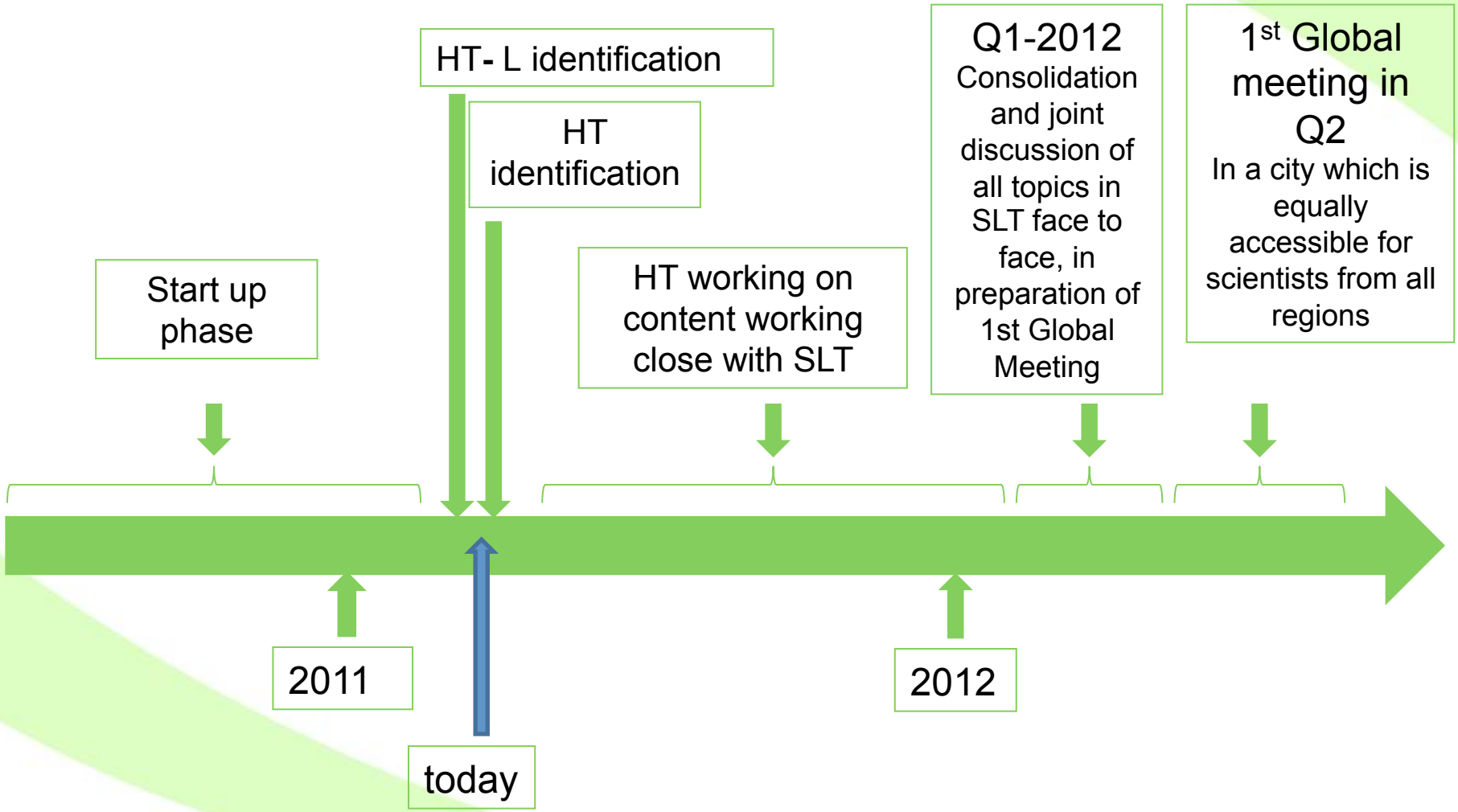


- Engaged **270+ experts** from industry, with participation from all regions
- From these 270+ experts, SC identified **20 Harmonization Team leaders (HT-L)**
- HT-L are currently composing their teams
- Within a few weeks, all harmonization teams will be up and running

What took us so long?

- We made sure **SC was composed with all regions included**
  - With GBC process starting in EU-NA, APAC took a bit longer to identify SC members
  - Consider industry feedback on initial low representation of LBA expertise in SC
- We made sure **all regions were informed**
  - GBC was depending on global meeting calendars
    - With calendars favorable for NA + EU, APAC + LA took longer to engage
  - Make sure all regions had the time to absorb information and mission
  - Allow time for experts from all regions to enroll based on the same information and at their own pace
- **Managed the enrolment of 270+ experts** from industry
- Carefully identified **20 Harmonization Team leaders (HT-L)**

Proposed way forward



Global Bioanalysis Consortium
On harmonization of bioanalytical guidance

Acknowledgment

Founding members and Steering Committee members:

The GBC Steering Committee:

- Mark Arnold (AAPS)
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- Michaela Golob (EBF)
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