GLOBAL BIOANALYSIS CONSORTIUM

Regulated Bioanalysis - A Proposed Global Harmonization Process

General Slides – March 2011

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.

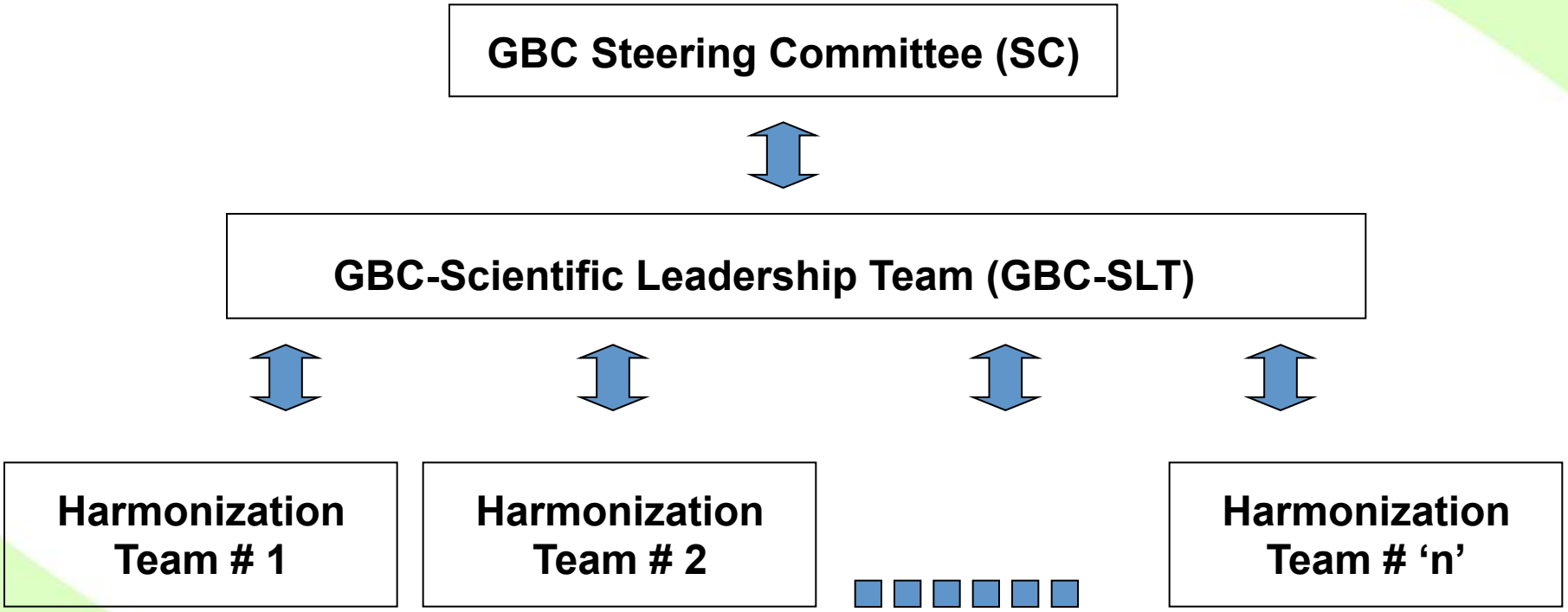
- To come forward with **recommendations** to Health Authorities and regulatory bodies worldwide on globally agreed best practices for Bioanalytical Method Validation (BMV) and application of such methods/technologies to the analysis of drugs of all molecular sizes in support of clinical and nonclinical 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: how to organize?



Details on next slides

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 + HL-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
GBC-SC: members

Updates since January - 2011:

- **Optimization of regional representation by addition of India and Japan SC**
- **Increase LBA expertise: add SC with LBA focus**

North America (US + Canada)

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

Latin America (South America + Mexico)

- Rafael Barrientos (AcBio)

Asia Pacific (Asia + Pacific area)

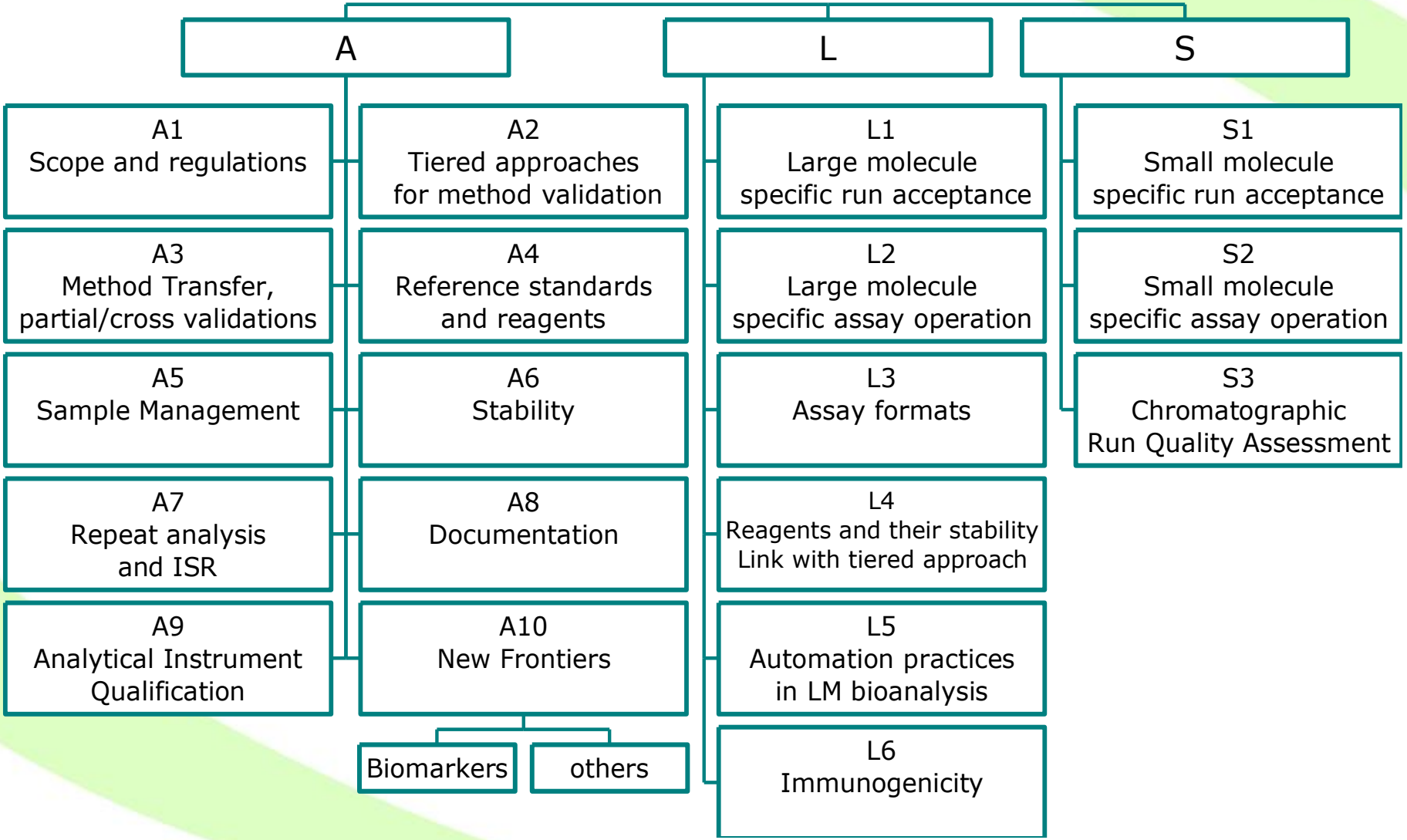
- Daniel Tang (SBDG&BBDG)
- Shrinivas Savale (APA-India)
- Tatsuo Kurokawa (Japan)

Europe (Europe + Africa/Middle East)

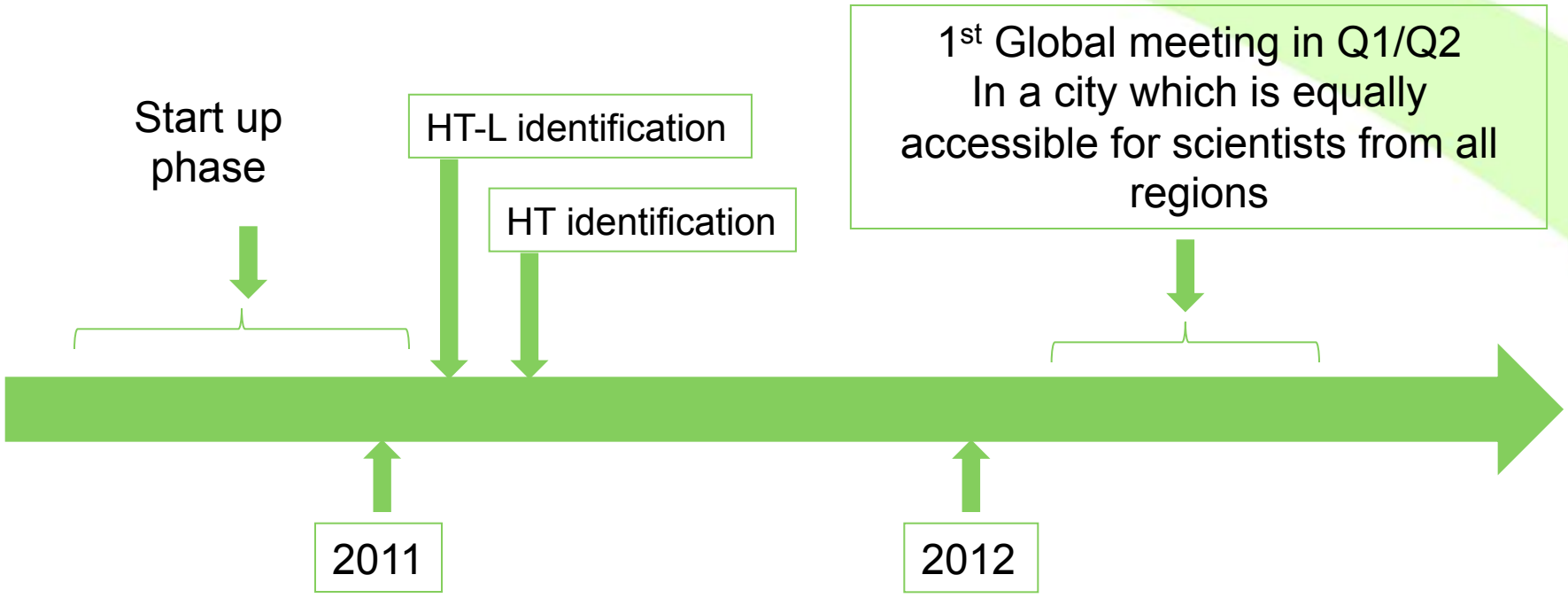
- Peter van Amsterdam (EBF)
- Philip Timmerman (EBF)
- Michaela Golob (EBF)

I'll add team leader names to boxes

Which Harmonization Teams ?



Proposed way forward



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

Acknowledgment

Founding members and Steering Committee members:

The GBC Steering Committee:

- Mark Arnold (AAPS)
- Rafael Barrientos (AcBio)
- Daniel Tang (SBDG&BBDG)
- Shrinivas Savale (APA-India)
- Tatsuo Kurokawa (Japan)
- Peter van Amsterdam (EBF)
- Philip Timmerman (EBF)
- Michaela Golob (EBF)
- Binodh DeSilva (AAPS)
- Fabio Garofolo (CVG)

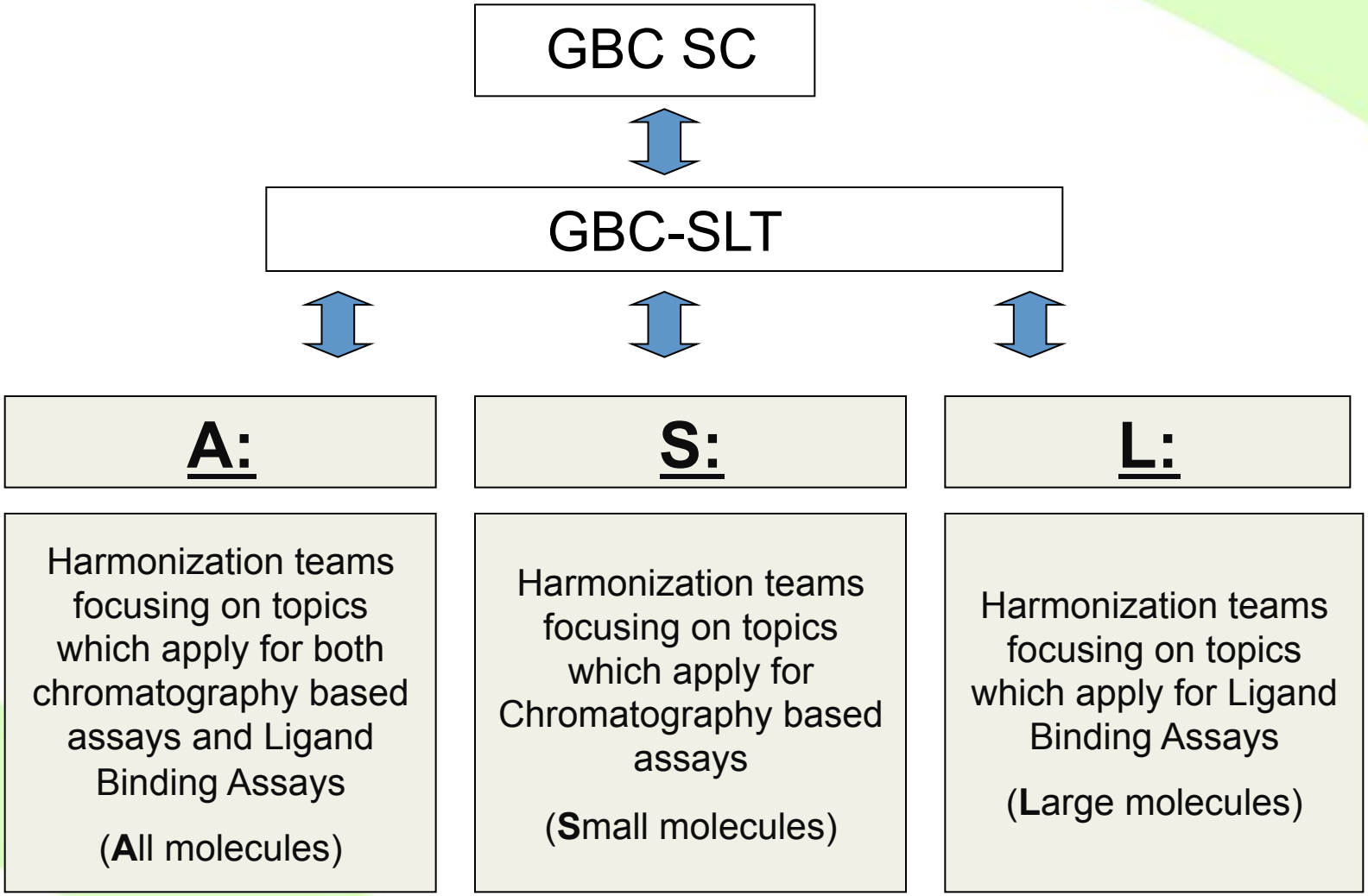
and

- Surendra Bansal (AAPS)
- Douglas Fast (BSAT)
- Steve Lowes (AAPS)
- Eric Woolf (BSAT)

Back up slides

Which Harmonization Teams?

Overview



Harmonization team activities?

An 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

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 of conflicting guidelines (maybe 20%)

Moving forward:

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

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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

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

Back up slides – details on teams

- GBC History
- Operating committee details
  1. GBC-SC
  2. GBC-SLT
  3. HT-L and HT
  4. Team activities
  5. Dynamics of SC-SLT-HT-L interactions
  6. Selection process HT-L and HT
- Which teams? details on scope and deliverables

GBC: 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)

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**

GBC: History

Feb. 2010: Letter to FDA and EMA

April 2010: Publication as Open Letter

Apr. 2010: CVG Workshop – Consensus to start

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

Operating committees details

1. GBC SC

Operating committees: details
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
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 details

2. GBC SLT

Operating committees: details
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

3. GBC HT and HT-L

Operating committees: details
Harmonization teams (HT) - cntd

Profile of HT members – team composition

- 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 (TCs). 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 Team Leads (HT-L)

Roles and Responsibilities of HT-L

- Leads the 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 to report back on progress or get input.
- Connects with other HT leads in case of overlapping discussions

Operating committees: details
Objective of the HT Lead

Objective of HT-L

- Remove concepts of company or region from thinking - you're leading a global effort
- Facilitate discussion, don't push 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.
- Recognize that some governments 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

Operating committees: details
Role of HT-L

Select team members

- from application list
- from different regions
- look for thought leaders; people who have published, spoken or previously been involved in topic at workshops

Evaluate Scope with team

- Is everything presented appropriate to team?
- Is anything missing?
- Ensure there is clarity within team on Scope
- Finalize Scope and meet with GBC EC and other team leaders to review and evaluate overlap or points of contact for resolution of individual team

Inform GBC SC and other Team leads of progress

- seek counsel and input as needed

Operating committees: details
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, 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-SLT on a regulars basis to ensure progress, potential roadblocks or overlap and consistency

Operating committees details

4. Team activities

Team activities 1/3

Keep minutes

- utilize a team member to record minutes
- distribute and permit team to comment
- ensure agreement prior to finalizing

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

- Share regulations with other Team leaders/Teams

Team activities 2/3

Based on commonality, filter scope list to those that are fully agreed to, generally agreed to, and those with no agreement. The GBC EC 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.

- 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 EC 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.

Team activities 3/3

Proposals

- 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*
- Where no consensus is achieved, provide arguments on both sides

Operating committees details

5. Dynamics of SC-SLT-HT-L interactions

Dynamics of SLT – SC – HT-L interactions

- HT-L feedback and interaction through in SC-sponsorship:
  - SC members will become sponsors of HT
  - A team of 2 SC members will become the sponsor for 3-4 HT
  - 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

Operating committees details

6. Selection process HT-L and HT

Operating committees: details
Selection process of HT-L and HT members

HT-L

GBC-SC will propose the HT-L 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-L can make themselves known by submitting the registration form to:
  - apply@globalbioanalysisconsortium.org
  - Identifying the team they volunteer **to lead**

HT members

- HT-L 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
  - Identifying the team they volunteer **to join**

Operating committees: details
Selection of HT-L and HT members - cntd

Registration Form can be found on GBC website

http://www.globalbioanalysisconsortium.org

Registration Form seeks input on:

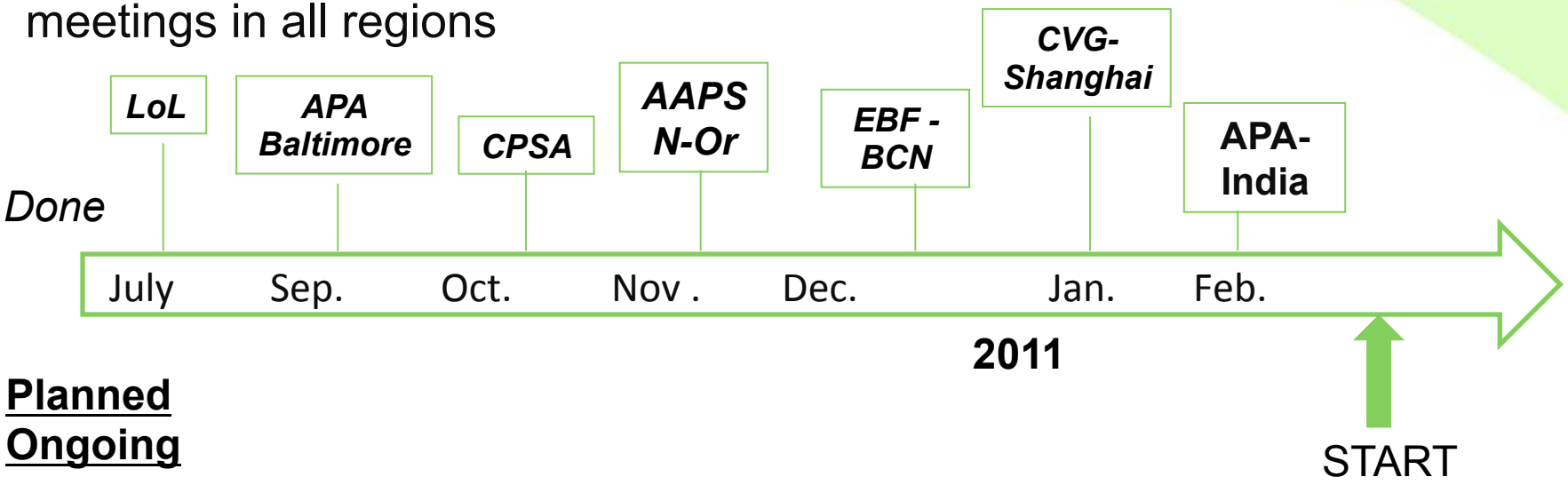
Name
Organization
Region you will represent
Experience on Small *vs.* Large molecule analysis (or both)
Interest:

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

Registration ended : 21 February 2011

Where are we now – March 2011

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



Planned
Ongoing

- 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

Which teams?
details on scope and deliverables

A1: Scope and regulations

Team members:

Team lead

- Name – region – e-mail

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

In scope

- Scope and regulations (GxPs) for bioanalytical validation and samples analysis
- Glossary

Interdependencies with other teams – if any

- Scope and regulations (GxPs) for bioanalytical validation and samples analysis
- Glossary

Out of scope

- Scope and regulations (GxPs) for bioanalytical validation and samples analysis
- Glossary

A2: Tiered approaches for method validation

Team members:

Team lead

- Name – region – 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

- 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

Out of scope

A3 Method Transfer, partial and cross validation

Team members:

Team lead

- Name – region – 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

- 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

- A6

Out of scope

A4: Reference standards and reagents

Team members:

Team lead

- Name – region – e-mail

Other members

- 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

- 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

- Name – region – e-mail

Other members

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

Interdependencies with other teams – if any

- A6

Out of scope

A6: Stability

Team members:

Team lead

- Name – region – e-mail

Other members

- 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
- 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..) – A3

A7: Repeat analysis and ISR

Team members:

Team lead

- Name – region – 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

- Repeats for analytical reasons
- PK repeats
- ISR
- Incl. recommendation onsingle analyte repeat in multi-analyte assay

Interdependencies with other teams – if any

Out of scope

A8: Documentation

Team members:

Team lead

- Name – region – 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

- Definitions of different report types
- Documentation of method development
- Method Validation reports
- Study reports
- Failure investigation and documentation
- Documentation at analytical site
- 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

- Name – region – e-mail

Other members

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

- Name – region – e-mail

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

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

A10: New Frontiers – biomarkers?

Team members:

Team lead

- Name – region – 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

Interdependencies with other teams – if any

– A1

Out of scope

A10: New Frontiers – others?

Team members:

Team lead

- Name – region – e-mail

Other members

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

In scope

Interdependencies with other teams – if any

– A1

Out of scope

L1: Large molecule specific run acceptance

Team members:

Team lead

- Name – region – e-mail

Other members

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

In scope

- Linearity, 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

- Name – region – 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

Interdependencies with other teams – if any

Out of scope

L3: Assay formats

Team members:

Team lead

- Name – region – 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

Interdependencies with other teams – if any

Out of scope

L4: Reagents and their stability - Link with tiered approach

Team members:

Team lead

- Name – region – 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

Interdependencies with other teams – if any

Link with tiered approach

Out of scope

L5: Automation practices in LM bioanalysis

Team members:

Team lead

- Name – region – 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

Interdependencies with other teams – if any

Link with tiered approach

Out of scope

L6: Immunogenicity

Team members:

Team lead

- Name – region – 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

Interdependencies with other teams – if any

Link with tiered approach

Out of scope

S1: Small molecule specific run acceptance

Team members:

Team lead

- Name – region – 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

- 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

S1: Small molecule specific assay operation

Team members:

Team lead

- Name – region – 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

- 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

- Name – region – 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

- 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