# GLOBAL BIOANALYSIS CONSORTIUM

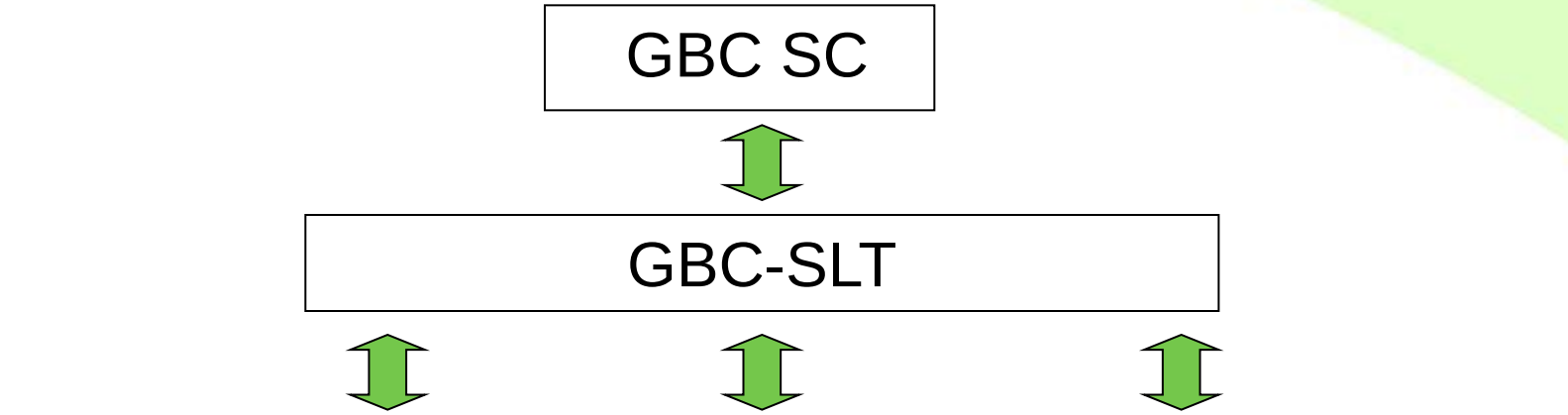
## S1: Small molecule specific run acceptance

Ben Gordon
On behalf of HT S1

EBF Symposium
Barcelona 2011

# Which Harmonization Teams?

## Overview




| **A:** | **S:** | **L:** |
|---|---|---|
| Harmonization teams focusing on topics which apply for both chromatography based assays and Ligand Binding Assays<br><br>(**A**ll molecules) | **Harmonization teams focusing on topics which apply for Chromatography based assays**<br><br>**(Small molecules)** | Harmonization teams focusing on topics which apply for Ligand Binding Assays<br><br>(**L**arge molecules) |

# GBC Harmonizing Team-S1

## Team Members

### North America (US + Canada)

**Team lead**

- **Douglas Fast** – NA – douglas.fast@covance.com

- Amy LaPaglia – NA – Amy.LaPaglia@proteabio.com
- David Hoffman – NA – david.hoffman@sanofi-aventis.com
- Richard LeLacheur – NA – RichLeLacheur@gmail.com
- Scott Reuschel – NA – scott.reuschel@labcorp.com

N=5

### Latin America (South America + Mexico)

- Gabriel Marcelin Jimenez – LA – gabmarcelin@pharmometrica.com.mx
- Maristela Andraus – LA – maristela.andraus@chromanalysis.com.br

N=2

### Asia Pacific (Asia + Pacific area)

- Noriko Inoue – APAC – n.inoue@jclbio.com
- Ravi Sankar – APAC – ravi.sankar@gvkbio.com

N=2

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

- Ben Gordon – EU – Ben.Gordon@uk.netgrs.com
- Matt Barfield – EU – Matthew.Barfield@gsk.com
- Michael Blackburn – EU – Michael.Blackburn@covance.com

N=3

# S1: Small molecule specific run acceptance

**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
- A8?

**Out of scope**

# Validation Run Acceptance

1. Linearity, Accuracy, Precision
2. Appropriate calibration curve range and QC placement across range for certain study types
   - Considerations for ascending dose/FIH studies
     - When, How to change calibration range
     - How to address sample results in limited/low portion of range only (linearity issues, number of calibrant points, QC placement)
   - Other study designs: repeat dose (steady-state results vs. PK results), high dose tox, etc.
3. Criteria on selection of regression analysis model (linear, quadratic, weighting)
4. Criteria for individual runs and overall acceptance during validation
   - IS response acceptance criteria, variability permitted (individual samples or groups of samples)
   - Minimum levels of IS response needed
     - S2 team interaction
   - How to address, report failed validation runs
     - Inclusion, exclusion from summary and statistics
5. Validation of plasma blank samples
   - Stability of blank samples
   - Use of predose samples for calibrators and controls from subjects
     - How long can they be used?
6. Cross validation of anticoagulants and counterions: requirements to perform, acceptance criteria when performed

# Sample Analysis Run Acceptance

1. Individual run acceptance during sample analysis
   - Single analyte vs. Multiple analyte with mixed pass/fail outcomes
2. Internal standard criteria: acceptance criteria, variability permitted
   - Minimum levels of IS response needed
   - Decisions on anomalous IS response: anomaly in individual sample or between groups of samples (i.e., QCs/Calibrants vs. dosed samples)
3. Carryover: acceptance criteria, role of standard (double) blank and standard zero
   - Determination of and criteria for contamination vs. carryover
   - Carryover decisions based on sample-to-sample results rather than just carryover samples
   - Interaction with S2 Team
4. Implications of positive control or predose samples
   - Limits for acceptance of sample results and entire run results
   - Impact on carryover/contamination considerations
   - Guidance on actions/remediation to be taken
5. Implications of anomalous sample results on run acceptance (contamination, sample switch issue?)
6. System suitability testing
   - Purpose of and criteria for suitability testing (approve or not approve a run start or entire run itself)
   - Consider multiple plates and unattended operation: suitability review done at run start or after run completion
   - Is suitability testing only considered at run start or also during run?
7. Sample and run reinjection: when, how to perform reinjection; how to address results
8. System conditioning with matrix samples: guidance on when required, how to perform

# Additional Topics Considered for Inclusion

1. Is S1 Team about molecule size ("small molecule) or detection technique?
   - Inclusion of all analytes determined by LC/MS techniques: anitbodies, proteins, oligos, small molecules
   - Use of small molecule criteria for all LC-MS determinations?
2. Metabolite screening: flexible acceptance criteria, fit for purpose criteria
   - Addressed by A2 Team?
3. Determination of dosed endogenous materials (e.g. steroids)
   - Role of small molecule criteria, biomarker criteria
4. ISR Guidance
   - Actions if ISR fails: implications for entire analytical run
   - Discussion for A7 team?

# HT S1: Source

- GBC will focus on a harmonised science-based approach

- 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 small molecules in support of clinical and nonclinical studies.

- Regulatory Documents [FDA (2001), EMA (2011), Crystall City, EBF and others]

# 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.

# Acknowledgment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