The Metabolomics Quality Assurance and Quality Control Consortium (mQACC): A Community-led Initiative to Develop and Promote Quality Assurance and Quality Control in Untargeted Metabolomics Research

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November 16, 2019

Quality Assurance (QA) & Quality Control (QC)

QA and QC processes are hugely important to ensure that the data acquired and reported in scientific publications and housed in data repositories are of high quality and are analytically reproducible.

Quality Assurance

- Processes related to the procedures applied in **preparation for data acquisition**
- Includes staff training, standard operating procedures, instrument maintenance and calibration

Quality Control

- Processes related to the procedures applied **during and after data acquisition**
- Includes use of measured data from standard/certified reference materials and quality control samples to address the veracity of experimental data

Without well-defined QA and QC procedures for untargeted metabolomics, harmonization across laboratories and multi-laboratory studies become nearly impossible.

Metabolomics Society 2015 Questionnaire

Metabolomics (2017) 13:50
DOI 10.1007/s11306-017-1188-9

CrossMark

SHORT COMMUNICATION

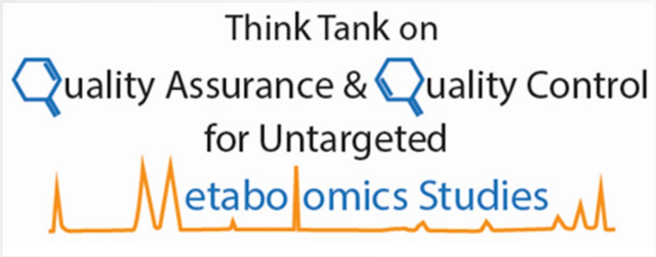
Quality assurance and quality control processes: summary of a metabolomics community questionnaire

Warwick B. Dunn[1] · David I. Broadhurst[2] · Arthur Edison[3] · Claude Guillou[4] · Mark R. Viant[1] · Daniel W. Bearden[5] · Richard D. Beger[6]

Four Recommendations

- Appropriate agencies and the Metabolomics Society should provide guidance on quality assurance processes and their review and develop consensus processes through specialist meetings and reports
- To provide education to the metabolomics community, with an emphasis on early career scientists, on usage of quality materials, and to provide continuing education to ensure these good practices continue
- To communicate with the metabolomics community to define the types and volumes of Standard Reference Materials required
- Recognizing the need to provide further incentive for laboratories to improve overall QA/QC practices, expert panels should be convened to develop workable, practical QA/QC recommendations and guidelines

Think Tank on Quality Assurance & Quality Control for Untargeted Metabolomics Studies



October 2017

1. Identify the most useful metrics for assessing study and data quality for untargeted metabolomic studies.
2. Identify and prioritize processes to ensure appropriate reporting of QA/QC data.
3. Identify and prioritize the types of test materials that are needed in the field of metabolomics for QA/QC in untargeted studies.

How did we intend to meet this objectives?

- Think Tank = Working Meeting
- Bring stakeholders together to identify key points that are actionable
  - High-level discussion
  - Implementation - next steps
- Prioritize ideas
- Develop a plan of action for continued collaboration to address key priorities

Objective #1

Identify the most useful metrics for assessing study and data quality for untargeted metabolomic studies

World Café Focus

What are the current gaps that should be addressed to establish widespread best practices for QA in untargeted metabolomics?

- Document complete experimental processes and reporting from study design to data analysis
- Define the best practices and those that should be avoided in sample collection, processing and storage

What are the current gaps that should be addressed to establish widespread best practices for QC protocols in untargeted metabolomics?

- Obtain buy in from scientific journals, companies, software developers, database developers, and funders
- Educate community about QC procedures

Objective #2

Identify and prioritize processes to ensure appropriate reporting of QA/QC data

World Café Focus

What is needed to establish QC acceptance criteria reporting across the wider community?

- Establish minimum acceptance criteria, including creating a broad-based scoring system [For example, one QC scoring scheme could include: (i.e., 0 = none, 1 = pooled, 2 = pooled and SRM)]
- Create reporting standards/SOPs for the entire analytical process

What should be the minimum QA and QC reporting standards for publications and databases?

- Define acceptance criteria [e.g., scoring system (or explain why criteria were not met)]
- QC metadata should be reported (e.g., sample order, QC sample reference material used) and define elements under each category with adequate details for reproducibility

Objective #3

Identify and prioritize the types of test materials that are needed in the field of metabolomics for QA/QC in untargeted studies

World Café Focus

What are the key characteristics of high-availability test material sample types for metabolomics?

- Develop test materials for inter-laboratory comparisons
- Inexpensive materials
- Same sample for all technologies—must cover wide range of characteristics

What best use practices should be established for test material samples by the community?

- Define best practices
- Need consensus, including when you run the test material and timing of use, to allow for data harmonization
- Use for lab qualification, instrument qualification, training

Think Tank Priorities & Action Plan

1. ***Publish a workshop report*** to communicate the meeting proceedings to the metabolomics community and allow new members to join the consortium.
2. ***Publish a white paper*** which could include: (1) metabolomics practices with a focus on QA/QC procedures; (2) an emphasis on the use of QC samples as best practices and give examples of current use; (3) a discussion of metabolomics QA/QC being a developing principle, the need to develop standards, and the need for the wider community to be involved in the process; and (4) a description of the QC procedures performed in experienced labs to begin a community dialogue on the topic.
3. ***Engage scientific journals*** to report that the community believes that good, documented QC practices, including analysis of QC samples, should be part of the acceptance criteria for publication.
4. ***Document and subsequently publish the complete experimental procedure for metabolomics***, including the QC practices
5. ***Establish a community forum*** to discuss the development of reference standards, and interlaboratory comparison exercises.
6. ***Engage the community to identify key reference materials that need to be developed***.
7. ***Form a steering committee and larger scientific advisory board***.
8. ***Identify funding opportunities*** to hold meetings and continue the group discussion and planning.
9. ***Organize workshop(s)*** on QA/QC at the Metabolomics Society meeting to promote community engagement in these efforts.

Think Tank Priorities & Action Plan

Completed:

Workshop on QA/QC at Metabolomics Society 2018

QA and QC in Untargeted Metabolomics

Speakers: Clary Clish, Annie Evans, Ping-Ching Hsu, Jonathan Mosley, and Krista Zanetti

Workshop on QA/QC at Metabolomics Society 2019

The Importance of Quality Assurance and Quality Control in Untargeted Metabolomics

Speakers: Warwick Dunn, Claire O'Donovan, Christina Jones

Interactive Forum on QA/QC Best Practices at MANA 2019

Establishing QA/QC Best Practices in LC-MS-Based Untargeted Metabolomics

Speakers: Krista Zanetti, Jonathan Mosley

Think Tank Priorities & Action Plan

Completed:

Think Tank Report

Metabolomics (2019) 15:4
https://doi.org/10.1007/s11306-018-1460-7

SHORT COMMUNICATION

Towards quality assurance and quality control in untargeted metabolomics studies

Richard D. Beger[1] · Warwick B. Dunn[2] · Abbas Bandukwala[3] · Bianca Bethan[4] · David Broadhurst[5] · Clary B. Clish[6] · Surendra Dasari[7] · Leslie Derr[8] · Annie Evans[9] · Steve Fischer[10] · Thomas Flynn[3] · Thomas Hartung[11] · David Herrington[12] · Richard Higashi[13] · Ping-Ching Hsu[14] · Christina Jones[15] · Maureen Kachman[16] · Helen Karuso[17] · Gary Kruppa[18] · Katrice Lippa[15] · Padma Maruvada[19] · Jonathan Mosley[20] · Ioanna Ntai[21] · Claire O'Donovan[22] · Mary Playdon[23] · Daniel Raftery[24] · Daniel Shaughnessy[25] · Amanda Souza[21] · Timothy Spaeder[9] · Barbara Spalholz[23] · Fariba Tayyari[26] · Baljit Ubhi[27] · Mukesh Verma[23] · Tilman Walk[4] · Ian Wilson[28] · Keren Witkin[23] · Daniel W. Bearden[29,30] · Krista A. Zanetti[23]

Received: 15 October 2018 / Accepted: 5 December 2018 / Published online: 3 January 2019

Abstract
We describe here the agreed upon first development steps and priority objectives of a community engagement effort to address current challenges in quality assurance (QA) and quality control (QC) in untargeted metabolomic studies. This has included (1) a QA and QC questionnaire responded to by the metabolomics community in 2015 which recommended education of the metabolomics community, development of appropriate standard reference materials and providing incentives for laboratories to apply QA and QC; (2) a 2-day 'Think Tank on Quality Assurance and Quality Control for Untargeted Metabolomic Studies' held at the National Cancer Institute's Shady Grove Campus and (3) establishment of the Metabolomics Quality Assurance and Quality Control Consortium (mQACC) to drive forward developments in a coordinated manner.

Keywords Quality assurance (QA) · Quality control (QC) · Community engagement · Test materials · Reporting metrics

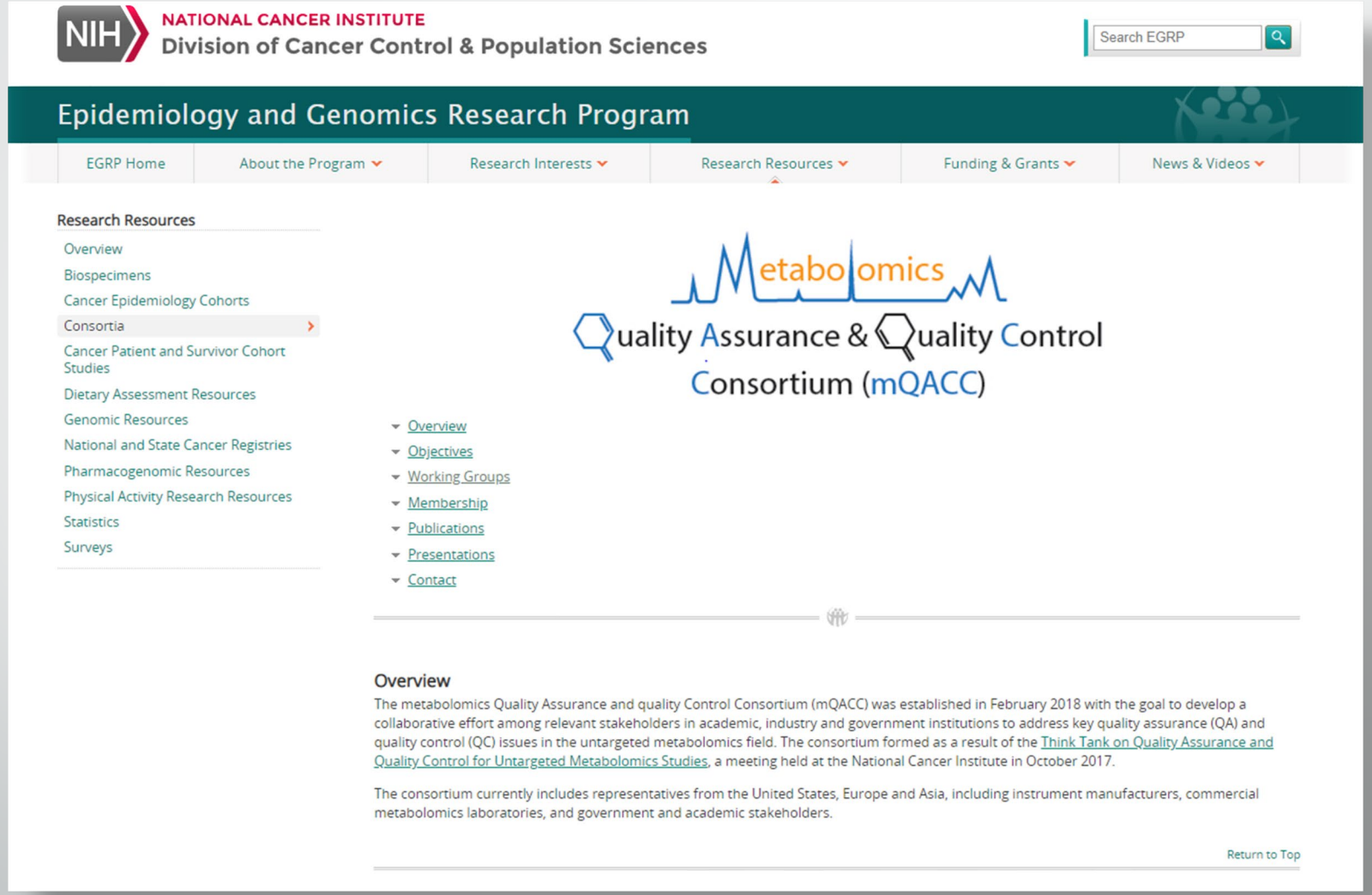
Think Tank Priorities & Action Plan

In Progress:

- **Manuscript** documenting the complete experimental procedure for untargeted metabolomics and the QC practices of Think Tank participants
  - Leads
    - Annie Evans, Metabolon
    - Claire O'Donovan, European Bioinformatics Institute

- **Identify 2-3 reference materials** that need to quickly move forward
  - Leads
    - Katrice Lippa, NIST
    - Christina Jones, NIST

Formalized Collaboration



https://epi.grants.cancer.gov/Consortia/mQACC/

Metabolomics Quality Assurance & Quality Control Consortium (mQACC)

Mission

To engage the metabolomics community to communicate and promote the development, dissemination and harmonization of best QA/QC practices in untargeted metabolomics

Objectives

- To identify, catalog, harmonize and disseminate QA/QC best practices for untargeted metabolomics
- To establish mechanisms to enable the metabolomics community to adopt QA/QC best practices
- To promote and support systematic training in QA/QC best practices for the metabolomics community
- To encourage the prioritization and development of reference materials applicable to metabolomics research

mQACC Working Groups

Experimental Processes

Anne M. Evans
Metabolon

Claire O'Donovan
European Bioinformatics Institute

The Experimental Processes Working Group was formed to describe the QA and QC protocols that have been established within consortium participants' laboratories.

- Share these practices with the broader metabolomics community as a platform for future QA/QC workflow development
- Summarize these QA/QC protocols and disseminate them through publications and conference presentations.

mQACC Working Groups

Reference & Test Materials

Katrice A. Lippa
NIST

Christina M. Jones
NIST

The Reference & Test Materials Working Group was established to encourage the prioritization and development of reference materials applicable to metabolomics research.

- Working to develop measurement designs and prototype materials that can be utilized across most, if not all, instrumentation platforms and employed for interlaboratory comparisons
- Defining the measurement challenges that different types of reference and test materials have the potential to address, as well as establishing best use practices for test and reference materials

mQACC Working Groups

Best Practices

Jonathan Mosley
US EPA

Ioanna Ntai
Thermo Fisher Scientific

The Best Practices Working Group was established to identify, catalog, harmonize, and disseminate QA/QC best practices, as well as to document experimental processes, for untargeted metabolomics.

- Actively identifying areas of common agreement among mQACC's member laboratories for defining best QA/QC practices for LC-MS based untargeted metabolomics
- Developing surveys to extend the catalog of identified QA/QC best practices to GC-MS and NMR platforms

mQACC Working Groups

Reporting Standards

Ian Wilson
Imperial College London

Jennifer Kirwan
Max Delbrück Center for Molecular Medicine in the Helmholtz Association

The Reporting Standards Working Group was formed to develop and promote consistent, meaningful and pragmatic community reporting standards in publications (and other documents) describing untargeted metabolomics studies (metabolic phenotyping/metabonomics) that detail the advisable quality assurance (QA) and quality control (QC) measures. This represents part of a strategy to educate the research community about the importance of QA and QC in untargeted metabolomics and promote good practices.

Membership

67 members across North America, South America, Europe, and Australia.

Eligibility Requirements:

- mQACC members should have an interest in QA/QC for untargeted metabolomics and be affiliated with/represent industry, government or academic institutions, or contract research organizations.
- Members should have or have held a position within the last five years at the postdoctoral level or higher.
- To maintain mQACC membership, active participation in at least one working group and attendance for at least three teleconference and/or face-to-face meetings every year is necessary.

Membership Types:

- **Affiliate Member**: Member with practical experience in untargeted metabolomics, including quality assurance and quality control practices.
- **Non-affiliate Member**: Member who does not have practical experience in the field of metabolomics, but in a related field (e.g., proteomics). A non-affiliate member must have an interest in the field, including an interest in QA/QC.

https://epi.grants.cancer.gov/Consortia/mQACC/

Metabolomics Quality Assurance & Quality Control Consortium (mQACC)

Coordinating Committee:

- Warwick Dunn (Chair)
- Christina M. Jones
- Richard Beger

Fadi Abdi
Abbas Bandukwala
Aiko Barsch
Dan Bearden
Richard Beger
Chris Beecher
Bianca Bethan
John Bowden
David Broadhurst
Corey Broeckling
Clary Clish
Surendara Dasari
Leslie Derr
Suraj Dhungana
Warwick Dunn
Tim Ebbels
Annie Evans
Steve Fischer
Roberto Flores
Thomas Flynn
Charles Grieser
Amy Harms
Thomas Hartung
Majda Haznadar
David Herrington
Rick Higashi
Ping-Ching Hsu
Tao Huan
Christina Jones
Judith Jans
Maureen Kachman
Michael Kiebish
Jennifer Kirwan
Andre Kleensang
Julia Kuligowski
Matthew Lewis
Katrice Lippa
Padma Maruvada
Sven Meyer
María Eugenía Monge
Jonathan Mosley
Laura Moussa
Ioanna Ntai
Claire O'Donovan
George Papanicolaou
Rui Pinto
Mary Playdon
Dan Raftery
Sharon Ross
Michael Schmidt
Tracey Schock
Stacey Sherrod
Amanda Souza
Jinchun Sun
Fariba Tayyari
Alpesh Thakker
Georgios Theodoridis
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