Quality Standards for regulated and non-regulated biomedical research laboratories.

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My interests:

- voluntary adoption of research QA (RQA) best practices/standards into non-regulated research environments
- Support infrastructure for RQA in non-regulated research environments
- integration of RQA into scientist training programs
Quality Assurance Management Systems are designed to:

Improve and maintain the precision and accuracy of a product and establish routine performance.
The products we produce are research data.
Quality Assurance support is rarely found in academic basic research settings
Research Quality Systems

DEVELOPMENTAL PIPELINE

Basic Research  Disease Discovery  Drug Discovery  Preclinical Development  Clinical Trials I, II, III  Manufacturing

Not Regulated

GLP  GCP  GMP

21 CFR Part 11

Voluntary ‘Good Research Practices’?

Study Based  Mentor Based

Process Based- Control consistency required

Flexibility needed for innovation and creative exploration

Slide adapted from one created by Melissa Eitzen, UTMB
How sound scientific principles and good quality practices contribute to the credibility of results


<table>
<thead>
<tr>
<th>Study</th>
<th>Sound Scientific Principles</th>
<th>Good Quality Practices</th>
<th>Credibility of Results</th>
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</thead>
<tbody>
<tr>
<td>Study 1</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Study 2</td>
<td>No</td>
<td>Yes</td>
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<tr>
<td>Study 3</td>
<td>Yes</td>
<td>No</td>
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<tr>
<td>Study 4</td>
<td>Yes</td>
<td>Yes</td>
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Research Quality Assurance is a reasonable strategy for safeguarding research data quality and integrity throughout the research life cycle.
Voluntary RQA Resources Exist
Questions from the Committee
Cost, infrastructure, and resource needs of implementing a RQMS?

**Cost**
- Gap Assessment
- Equipment + Monitoring, Service and Calibration
- Salaries for QA roles and responsibilities
- Quality Control and Proficiency Testing
- Reagent traceability
- Method and Process Validation and Verification
- Accreditation or Certification Costs

**Infrastructure**
- Quality Policy
- RQMS [Address the Total Testing Process]
- Quality Manual
- QMS Software
- Monitoring Program
- Management Review
- Facilities and environment that meet the RQMS and Safety requirements
- Training Program and Continuing Education
- Secure Information, data management and archive
- Biorepository

**Resources**
- Management
- Quality Documents
- Time
- Trained and Competent Personnel
- Recurrent and secure QMS Funding
- Equipment
Specific minimum performance characteristics to be met by a research laboratory?

WHO/CLSI/CDC
12 ‘Quality System Essentials’


http://www.who.int/ihr/training/laboratory_quality/introduction/en/
What are the control processes that **ensure** research results are accurate?

<table>
<thead>
<tr>
<th>Demonstrate that data are accurate, reliable and fit for their intended use. <strong>Quality Assurance</strong></th>
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<tr>
<td><strong>Biospecimens:</strong> Total testing process control (pre-analytical, analytical and post-analytical processes).</td>
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<tr>
<td>Understand measurement uncertainty: analytical and biological variability</td>
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<tr>
<td><strong>QA and QC:</strong> Assure/Monitor the quality of the testing and reporting process:</td>
</tr>
<tr>
<td>1. Define intended use</td>
</tr>
<tr>
<td>2. Validate that methods/procedures fulfill requirements for intended use</td>
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<tr>
<td>3. Design QC to confirm that the requirements have been met</td>
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Can voluntary quality standard adequately protect research participants and would external verification process be required?

Must define or assess:

What adequate means
The risks
The value of disclosure/disclaimer/forewarning of quality limits that may exist in a research environment.

A Voluntary Quality Standard has the advantage of establishing what quality means through its requirements. The important deliverable is to ‘say what you do, and do what you say’. This may provide flexibility.

External verification reduces risk.
How typical is it for an institution to have detailed knowledge or infrastructure appropriate for the oversight of routine and QA practices in the research laboratory?

Typical: QA units within regulated research [GLP, GCP, GMP]

RARE: Non-regulated research

Notes: Overlap should not be assumed
Regulated research does not ensure the presence of a full QMS
Benefits and detriments of requiring CLIA certification for research laboratories?
Opposing Forces

LACK OF

- Resources/Support
- Infrastructure
- Buy-In
- Knowledge
- Training
- Uniform Guidelines
- Monitoring

Need For

- Credible evidence of research rigor, reliability, reconstruction
- Continuous improvement
- Competitive edge (investment in research accountability)
- Changes in research culture and mentoring
Would clinical labs using a research designation circumvent the requirements (and associated costs) of CLIA when performing tests?

Yes I think so, unless the infrastructure, funds and other critical resources are available to meet the requirements.

Labs must have what they need to succeed. An unfunded mandate will not meet that requirement.
Scientists need a research infrastructure that provides science-centered and risk-based ways to maintain and demonstrate the quality of their work.

Reproducible and accurate research data
Helpful resources

1. WHO: Laboratory Quality Management System (LQMS)
   Annex 1: Comparison of CLSI quality management system model to ISO 9001 and ISO 15189.
   http://www.who.int/ihr/training/laboratory_quality/introduction/en/

   Discussion of all ISO 15189, CLIA General Laboratory System Regulations, WHO/CDC/CLSI guidelines
   Practical guide to the CLSI guidelines, ISO standards, CLIA Final Rules as well as Accreditation