DEVELOPING A TRAINING CURRICULUM FOR LC-MS/MS LABS

Practical Training Track Interactive Workshop

Facilitator: Shannon Haymond, PhD

Conflict of Interest Disclosures

- Grant/Research Support: None
- Salary/Consultant Fees: None
- Stocks/Bonds: None
- Intellectual Property/Royalty Income: None
- Honoraria, expenses: *MSACL, AACC, NCI*
- Scientific Committee: *MSACL, AACC*

Objectives for the next hour

- Given the topic and associated learning objectives, each group will
  - (a) describe the training activities or resources,
  - (b) identify methods/media that would serve as training content, and
  - (c) develop ideas for competency assessment.

Outline for the next hour

- 20 min – Background
  - Faye Vicente – Developing a Training Curriculum for LC-MS/MS
  - Dr. Judy Stone – Using Online Resources for LC-MS/MS Training

- 25 min – Interactive session with group work
- 15 min – Group summaries and wrap up

DEVELOPING A TRAINING CURRICULUM FOR LC-MS/MS

Faye Vicente C(ASCP)^{CM}

Manager, Clinical Mass Spectrometry

Ann & Robert H. Lurie Children's Hospital of Chicago

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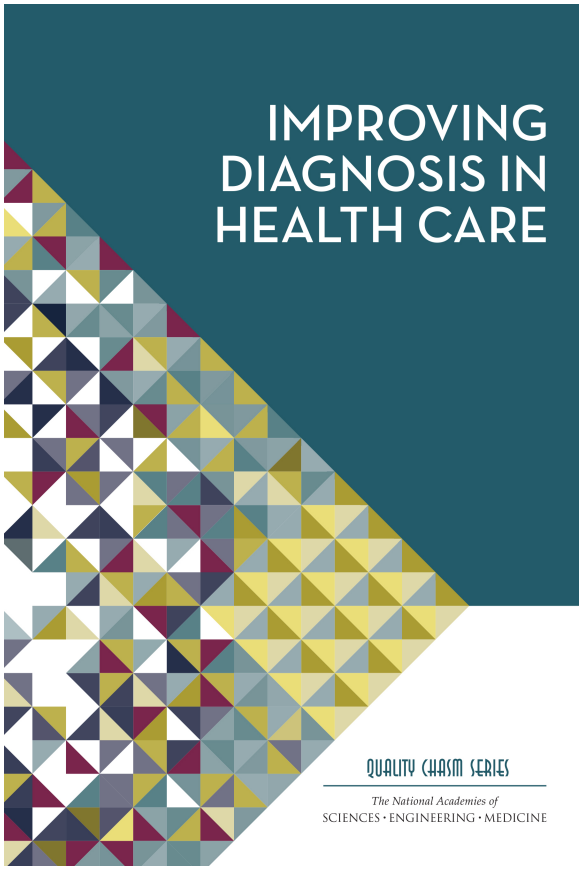
Training - a frequent regulatory problem!

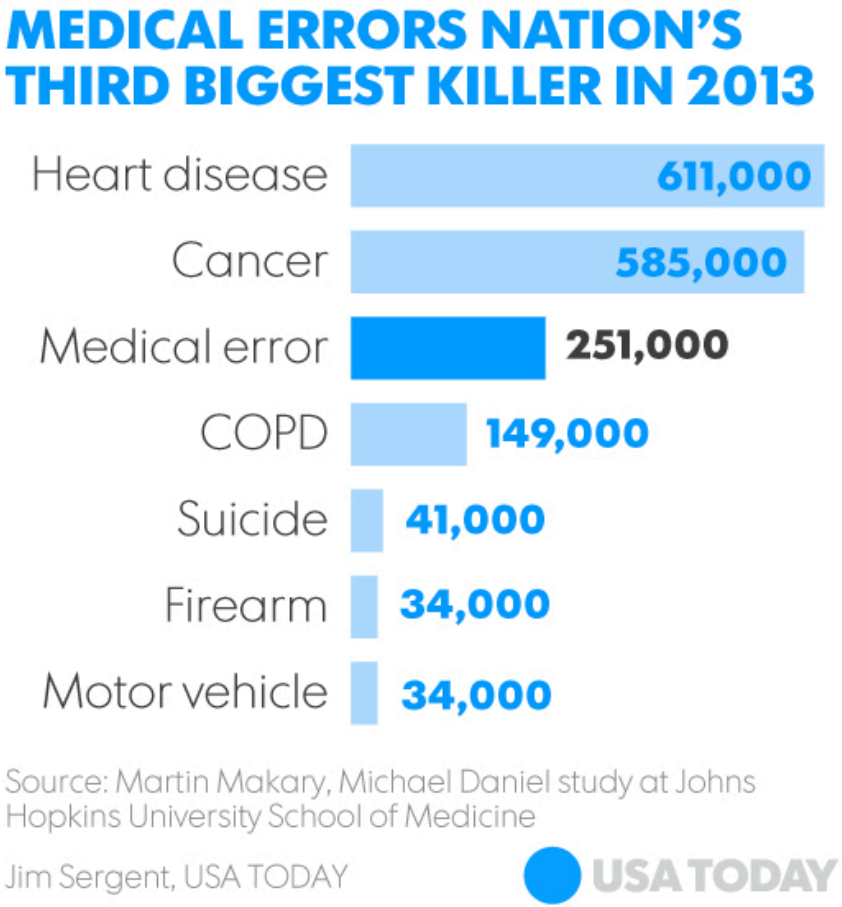
Deficiencies related to staff competency among major accrediting bodies in 2015:

- CAP #1 category of deficiencies
- COLA #1 category of deficiencies
- Joint Commission #2 category of deficiencies

http://www.mlo-online.com/clia-and-regulatory-readiness-how-can-your-lab-always-be-ready
June 22, 2016

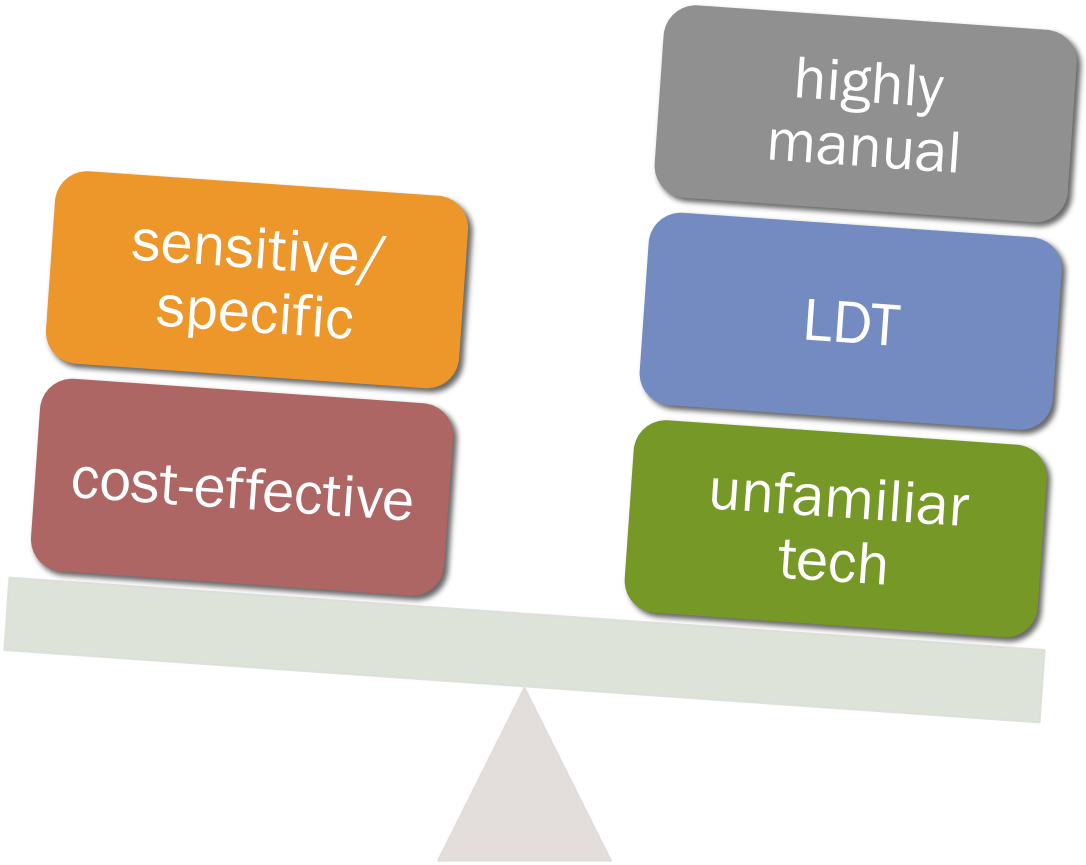
Increasing news about medical error

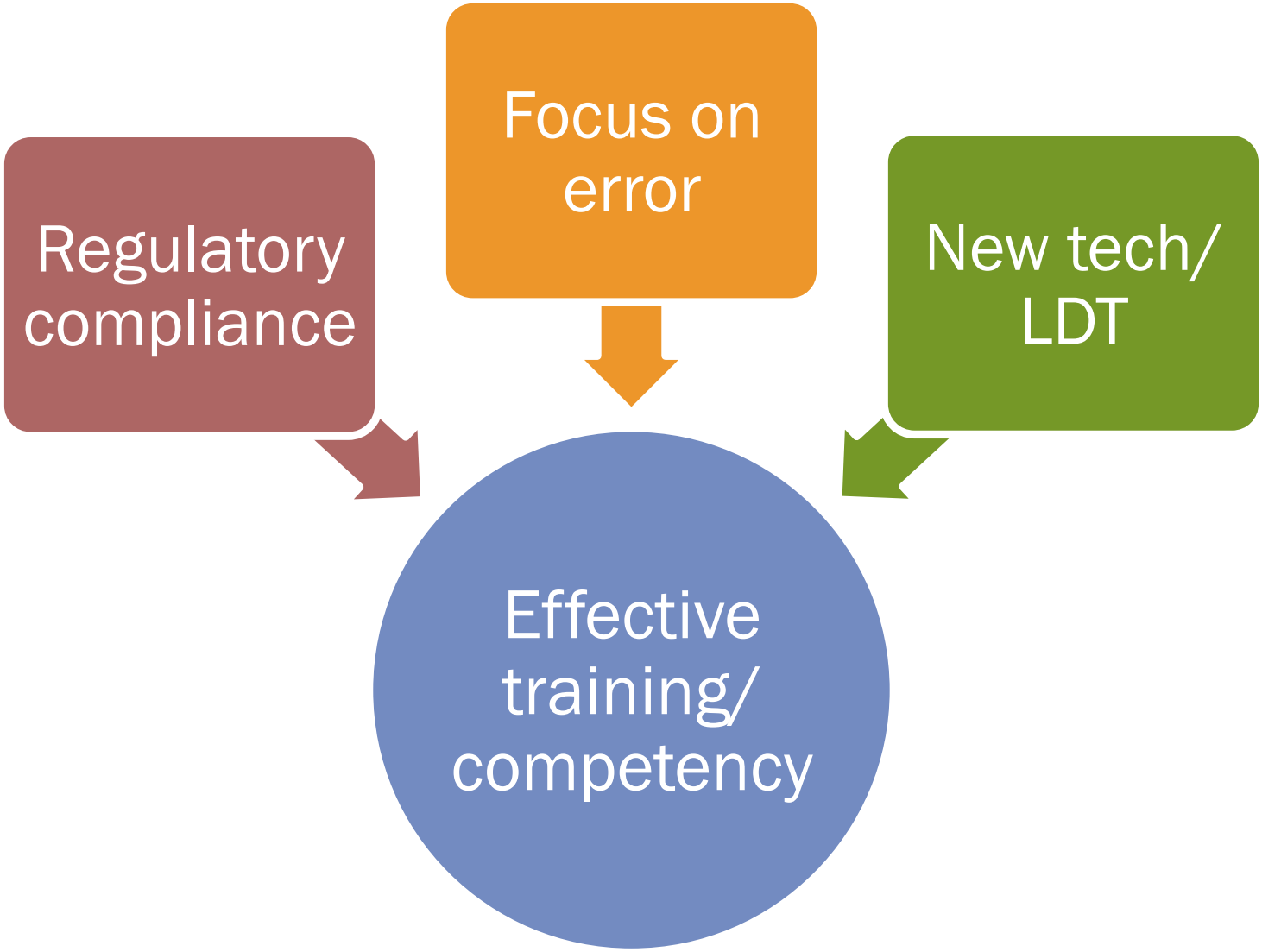




~12M diagnostic errors per year in US
~1 in every 20 adults

MS in clinical labs – at increased risk?

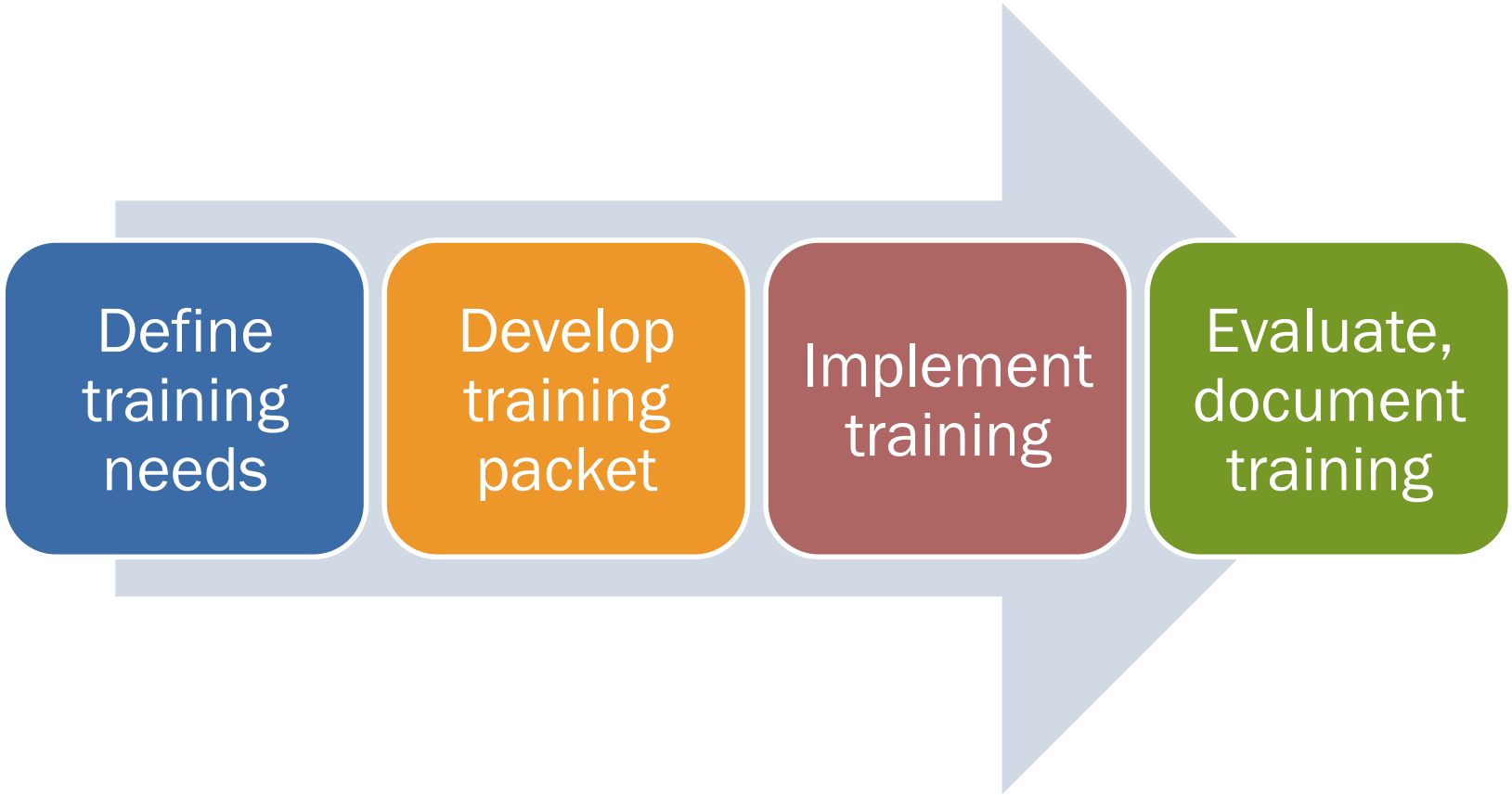



Regulatory compliance
Focus on error
New tech/ LDT
Effective training/ competency

Is there any regulatory guidance?

There is a CLSI guideline

CLSI QMS03-A3: Four Stages of Training



Clinical and Laboratory Standards Institute (CLSI). Training and competence assessment—FourthEdition. CLSI document QMS03-A3 2016.

What's in a training packet?

Competence Assessment Plan

- Overview of learning objectives with an explanation of how each will be assessed

Training Checklists

- Guides trainers and trainees, sets sequence, resources, and standardizes the training experience

Direct Observation Checklist

- Used by trainee for self-evaluation and by trainer to note progress of the training

Competency Assessment

- Assesses learner's knowledge using several methods

Training Evaluation

- Used by trainee to evaluate trainer(s) and training process

There are specific CAP checklist items

- Laboratory General Checklist – All Personnel
  - GEN.55450 Personnel Training
    - Records showing that lab personnel have satisfactorily completed training on all tasks performed prior to starting patient testing and prior to reporting patient results
  - GEN.55500 Competence Assessment – Nonwaived Testing
    - Competency of lab personnel performing nonwaived testing is assessed at the required frequency
    - Records must include all six elements for each test system

Six elements of competency assessment

- Direct observation of routine patient test processes and procedures
- Monitoring the recording and reporting of test results
- Review of intermediate test results or worksheets, QC records, PT results, and PM records
- Direct observation of performance of instrument maintenance and function checks
- Assessment of performance through testing previously analyzed specimens, blind test samples or PT samples
- Assessment of problem solving skills

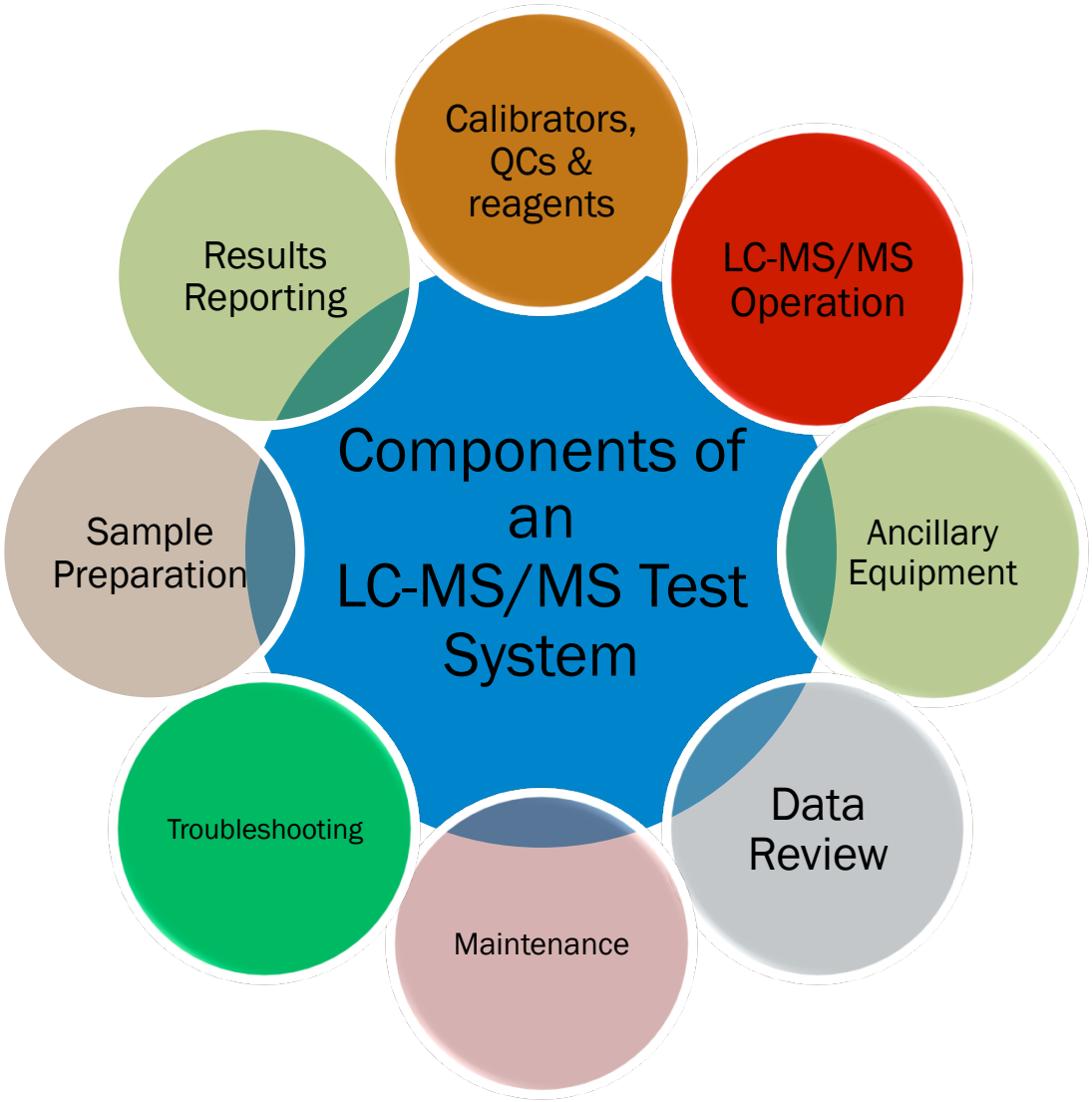
Early on, define your test system

- Define instrument or assay as test systems
- Includes pre-analytic, analytic and post-analytic steps used to produce a test result or set of results
- LC-MS/MS assay method is a test system
  - Single analyte methods
  - Multiplexed assays such as immunosuppressant drugs and steroid panels

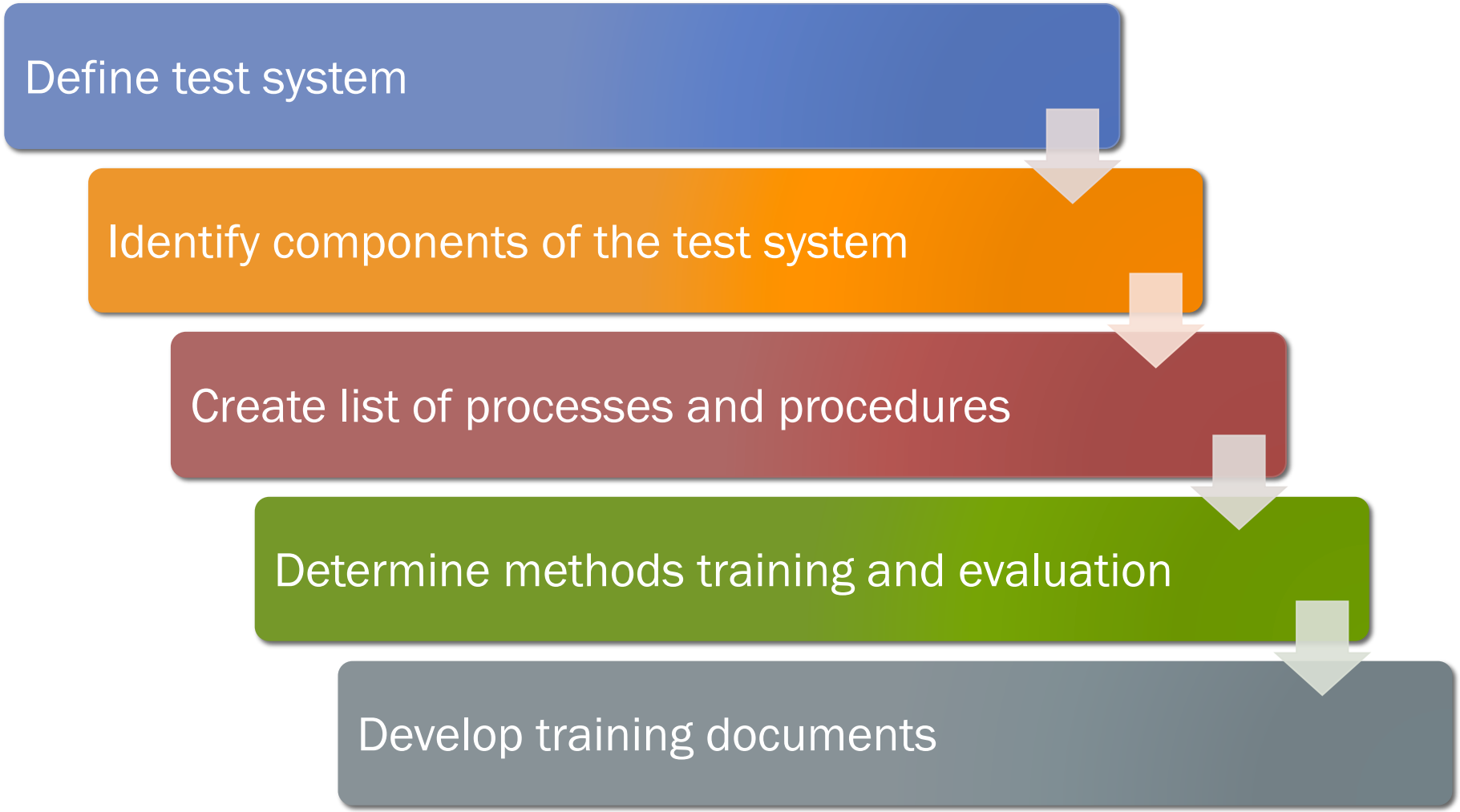
I. Equipment and Consumables:

A. Waters Xevo TQ MS triple-quadrupole mass spectrometer operated in the electrospray positive ionization mode coupled to Waters IVD ACQUITY UPLC system equipped with a column heater, MassLynx V4.1 and TargetLynx Application Manager, Intellistart application
B. Peak Scientific nitrogen generator NM120L
C. High purity argon gas, 99.9%
D. Phenomenex C18 (ODS, Octadecyl) 4 x 3.0mm ID
E. Phenomenex SecurityGuard Guard Holder
F. Eppendorf Microcentrifuge 5424, 21,130 rcf (15,000 rpm)
G. Fisher Scientific Fixed Speed Touch Mini Vortexer
H. Analytical Balance (0.00000 g)

- Analysis of Cyclosporine A, Tacrolimus (FK506) and Sirolimus (Rapamycin) in Whole Blood by UPLC-MS/MS
- Daily Operation of the Waters Xevo TQ MS Acquity UPLC System
- Maintenance of the UPLC/MS
- Optimization and Monitoring the Performance of the Xevo TQ Mass Spectrometer
- Calibrating the Mass Range of the Xevo TQ Mass Spectrometer Using Positive Electrospray Ionization
- Preparation of New UPLC Columns for Clinical and Research Use
- Monitoring HPLC/UPLC Column Performance
- Maintenance of Centrifuges
- Maintenance of Analytical and Top Loading Balances in the Mass Spectrometry Laboratory


Components of an LC-MS/MS Test System
Calibrators, QCs & reagents
LC-MS/MS Operation
Ancillary Equipment
Data Review
Maintenance
Troubleshooting
Sample Preparation
Results Reporting

Test system drives training



How do we ensure consistency and comprehensiveness of the training?

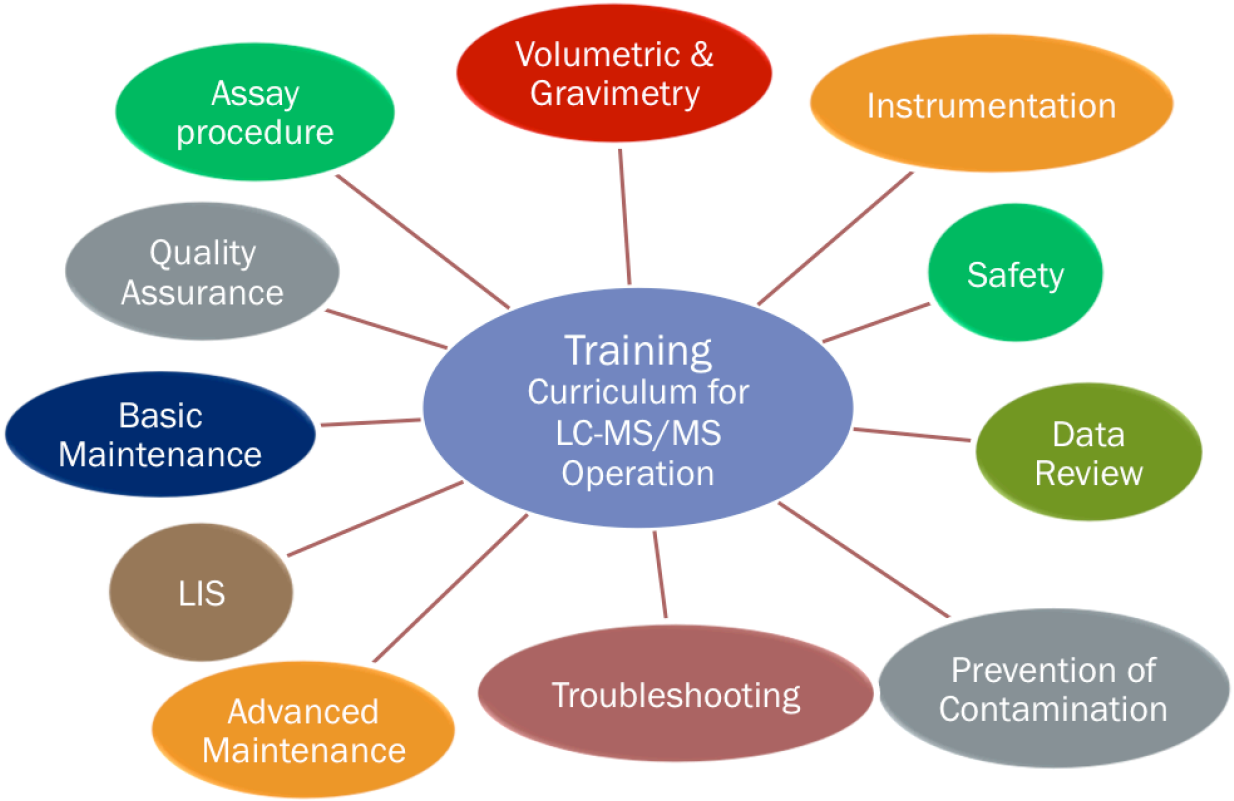
We'll need a training curriculum

- The total package of learning activities designed for trainees to acquire the specific knowledge and skills (competencies) they need to do their jobs.

- Three primary components:
  - the content or information to be transmitted
  - the organization (structure and format) of the curriculum
  - the training and competency methods used

Training content

The specific information, facts, attitudes, and skills to be transmitted by the training program. These are formalized in the competency statements.



Structure and format

- Refers to the construction of individual sections, and the organizations of the parts of the curriculum into an integrated whole to meet the objectives
  - providing a broad overview of the content and how it is organized
- Sections and activities are sequenced in a way that makes sense and facilitates learning and generalization of the content
  - from simple to complex, from the universal to the exception, and from fundamental to more specialized applications
- Repeating key concepts in different contexts and relating sections of a curriculum helps with retention and deeper understanding

Training and competency methods

- The strategies used to transmit the content, promote learning and retention and conduct assessment

- Present the same concepts using a variety of learning strategies
  - Examples: observance of demonstrations (live or video); simulation or practice under supervision; independent testing or identification of specially provided samples; lectures; use of computer-based exercises; self-study

- Use multiple methods of assessment – align with 6 elements defined by CAP

In summary

- Inadequate training and competency programs may contribute to diagnostic errors and result in regulatory non-compliance issues.
- CLSI QMS03-A3 and CAP checklist items provide a regulatory framework for developing a training and competency program.
- A training curriculum can facilitate comprehensive and consistent training and competency, if the right content, structure/format, and methods are included.

Using online resources for LC-MS/MS Training

Judy Stone, MT(ASCP), Ph.D., DABCC
Univ. of Calif., San Diego Health System

Conflict of Interest Disclosures

- **Grant/Research Support: None**
- **Salary/Consultant Fees: None**
- **Stocks/Bonds: None**
- **Intellectual Property/Royalty Income: None**

- **Extraction media, LC columns and/or R&D instruments at no charge from:** ***Agilent, Biotage, Phenomenex, SCIEX, Sigma-Aldrich, Tecan, Waters***

- **Honoraria, expenses** – ***MSACL, AACC***
- **Scientific Committee** – ***MSACL***

Value Hierarchies for Operator Training

Frequency & Duration – best to worst

1. **Initial intense, then continuing: weekly, refresher, as needed**
2. Initial intense
3. Continuing – as needed
4. Continuing – refresher, weekly, monthly

Location – best to worst

1. **Onsite**
2. Online
3. Requiring travel

Content – best to worst

1. **Hands-on + practical and theory lectures, comprehensive & topical**
2. Hands-on
3. Practical lectures, topical
4. Theory lectures, comprehensive

Format, Media – best to worst

1. **Multiple – case based, live lecture, short & long video on-demand, interactive, scheduled & self-paced**
2. Case based, interactive
3. Self-paced, on demand
4. Scheduled short & long video
5. Scheduled live lecture

What about comprehensive hands-on bench training?

- Included in any standard CLS generalist courses? Not to my knowledge
- **Clinical** versus non-clinical
- Short courses with a hands-on component (North America)

Clinical Comprehensive Hands-on Training

- Michigan State University certificate program (online + one week summer laboratory onsite)
- Emory/CDC Center for Clinical Mass Spectrometry & Advanced Technologies, 4.5 day course (Jim Ritchie, Julie Botelho, Hubert Vesper)
- Wakefield University summer course (Steve Wong)
- Virginia Commonwealth University summer course – 12 lectures, 36 lab hours (Lorin Bachmann)

Non-clinical Hands-on Training

- Mass Spec Training.com – University of the Pacific – 5 day summer course (none listed for summer 2018, Singapore course Oct 2017)

- Mass Spec vendor courses (some have clinical emphasis)

Online & Live w/o Hands-on

1. Comprehensive short courses & certificate programs ($)
   - Clinical: AACC online, MSACL meetings, ASMS meetings
   - Non-clinical: ASMS meetings, ACS meetings, Pittcon meetings, LC Resources (Jupille, Snyder, Dolan), LCMS Limited (Voyksner), LC-MS Online Training (Henion), LC-GCs Chromacademy, Separation Sciences – ***see lists at "The LC/MS Homepage" and LC Resources/Resources***

2. A la carte (topical) LC-MS content (open source)
   - Clinical – ***MSACL online & Practical Training tracks***
   - Non-clinical – see next slides

Open source, a la carte (topical) options

1. MSACL
2. Mass Spectrometry & LC Vendors
3. Sample preparation & Column Vendors
4. LC tubing & fittings Vendors
5. Chromacademy (Lite no charge, Premium $)
6. Ionsource^{sm}
7. Youtube

- LC Resources\Resources – useful links
- The LC/MS Homepage – lots of lists

Categorizing content - *examples*

- **Lecture videos (20-60 min)**

  System Suitability Testing, Michael Wright (60 min)
  MSACL Practical Training website/Learning Center/Content

- **Bite-size videos (<10 min)**

  Introduction to Ultra High Performance Liquid Chromatography Whiteboard –ThermoFisher Video (3.18 min) https://www.youtube.com/watch?v=Qf6060arkqM

- **PDFs**

  Controlling Contamination in UltraPerformance LC®/MS and HPLC/MS Systems, Waters
  http://www.waters.com/webassets/cms/support/docs/715001307d_cntrl_cntm.pdf

- **Self-paced tutorial links**

  Reverse Phase HPLC Basics for LC/MS – IonSource℠
  http://www.ionsource.com/tutorial/chromatography/rphplc.htm#The%20HPLC

Example: Troubleshooting-1

Topic	Description	Objectives	Method/ Medium	Assessment

TOPIC: Basics of LC-MS/MS Troubleshooting

DESCRIPTION: This section contains discussion of:

- common LC-MS/MS problems
- a structured approach to troubleshooting
- selected troubleshooting techniques and case examples
- resources for additional learning, future reference

Example: Troubleshooting-2

OBJECTIVES (competency goals):

1. List 3 common LC problems and their source(s)
2. Demonstrate how to evaluate a system-suitability test against acceptance criteria
3. Identify the symptoms of a bad LC connection (images)
4. Show you can make a good LC PEEK connection
5. Recognize bad chromatography due to an aged column or guard column (images)
6. Show you can correctly change & then record the information needed for a new column/guard column
7. Demonstrate finding an LC leak or LC over-pressure

Example: Troubleshooting-3

METHOD/MEDIUM:

1. Training checklist
2. 60 min videos on Troubleshooting

- MSACL Learning Center/Content/Video Library/Practical Training/ Troubleshooting - LC-MSMS Troubleshooting 101: Tips and Tricks for Getting Started : PART 1 J. Will Thompson, *Duke University School of Medicine*
- MSACL Learning Center/Content/Video Library/Series:LC-MS Troubleshooting - The Basics of LC-MSMS Troubleshooting: Tools, Strategy, Cases, Judy Stone, Univ. of Calif., San Diego/CALM

3. <10 min videos on Troubleshooting

- LC-GCs CHROMacademy Lite/Troubleshooting Videos/ - HPLC troubleshooting video guide to high pump backpressure

Example: Troubleshooting-4

4. PDF

- Waters website - Acquity UPLC Troubleshooting, Tips and Tricks - http://www.waters.com/webassets/cms/library/docs/local_seminar_presentations/FI_NUT2011_F1_F4_ACQUITY_%20UPLC_Tips_and_Tricks.pdf

5. Self-paced links

- Upchurch/IDEX Health & Science website - Fittings Primer - https://www.idex-hs.com/education-and-tools/educational-materials/fittings-primer

ASSESSMENT:

1. Quiz
2. Observation
3. Supervised troubleshooting

Speaker and Presentation Evaluations for Haymond/Vicente/ Stone Survey Monkey

https://www.surveymonkey.com/r/7STNWBR

Please let us know what training resources you need

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