Justification, Instrument Selection, and Due Diligence for Successful Implementation of MS

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Objectives

- Create a clinical justification
- Create a cost justification
- Create a request for proposal (RFP)
- Perform necessary due diligence
- Describe room modifications required
- Describe differences between method development and method validation
Clinical Justification

• Accuracy and precision of patient results
• Decrease turn-around time for results
• Expand laboratory testing menu
• Medical necessity of mass spectrometry
Testosterone example (worst case)

Testosterone example (best case)

"All evaluated methods except HPLC demonstrated a more or less considerable deviation of individual 25(OH)D₃ values compared with LC-MS/MS"
Immunoassays for Testosterone in Women: Better than a Guess?

Editorial: Serum Testosterone Assays—Accuracy Matters

Requirement for Mass Spectrometry Sex Steroid Assays in the Journal of Clinical Endocrinology and Metabolism
Cost Analysis

• Review send out test menu

• Identify high cost send out items

• Can they be brought “in house” with MS?

• Calculate ROI (none are the same…)
Back of the envelope (3 year ROI)

- Need staffing 2 CLS (57K + 25%) = $142,500/y
- Need technical lead (65K +25%) = $81,250/y
- Need consumables = $100,000/y
- Need service contracts = $60,000/y (1st free)
- HVAC = $15,000/y
- Need two mass spectrometers = $600,000 one time
Back of the envelope (cont.)

- 15,000 Vit D sent out at cost of $25 per test = $375,000/y

- 25% recovery = $93,000 ($282,000/y)

- Lab costs for send out $7 per sample = $105,000/y

- Lab can bill for in house tests $125 per test = $1.9 x 10^9

- Recover about 25% of billable cost = $475,000
Back of the envelope (cont.)

- Three year salary/consumable = $1 \times 10^6$
- Capital costs and service = $720,000$
- Total 3 year cost = $1.72 \times 10^6$
- Total recovered by lab in 3 years = $2.58 \times 10^6$
- Three year ROI = $875,000$
- Don’t give up—often takes several tries to get funding
Request for proposal: background

- Define goals

- Details are important

- The UCSD Mass spectrometry lab will perform…

- To increase speed of results to treating physicians…

- To improve accuracy and precision of results.
Request for Proposals (RFP)

- Plan for about 6 months to work with vendors and purchasing

- Great opportunity to learn about new innovations from various vendors

- UCSD RFP had 112 questions

- Include specific expectations
RFP Should address:

- Space
- Software
- Hardware
- HVAC requirements
- Interface
- Training
- Method development
- Nitrogen supply
- UPS
- LC
- Autosampler
- Service
- Mean time between failures
- Etc.
Developing an RFP

• Talk with Vendors
• Ask about “lock out specs”
• Work with colleagues
• Obtain copies of RFPs previously used
Examples of information in RFP

• Specify the instruments mass range in AMUs:
• Specify the method(s) of ionization of incoming compounds.
• Specify the instruments scan rate (in AMU/second).
• Specify the minimum dwell time for MRM acquisition (in milliseconds)
• Specify the inter-scan delay (in milliseconds)
• What are the dimensions of the equipment? Specify Length x Width x Height in inches.
• What is the speed of positive/negative polarity switches (specify in milliseconds)?
Due Diligence Sample Preparation

- All vendors got exactly the same shipment of samples
- Prepared samples for testosterone, Vit D and drugs of abuse
- Provided clear instructions on goals
- Provided clear instructions for analysis
- Provided methanolic standards and biological samples
- Data formed the basis for site visits
Due Diligence (Vit D example)

- Serum based calibrators with concentrations were provided
- Serum based QC without concentrations were provided
- Methanolic internal standards were provided
- Pooled patient specimens were provided (no target concentrations)
- Pooled patient specimens covered range of interest
- All were packaged and shipped to vendors
Site Visits and Vendor Selection

Data review, sample processing…

Where discoveries are delivered.SM
Site Visits

• Review data generated on samples submitted
• Perform daily instrument set up.
• Evaluate how many samples will fit into A/S
• How much sample clean up required?
• Develop data acquisition method
• Develop data processing method
• Don’t try to see everything!
Vendor Selection

• Compare results from due diligence
• Develop rating system consistent with RFP
• Rate based on
  – performance,
  – reliability,
  – availability of service,
  – Price,
  – Responsiveness,
  – willingness to help with method development
• Probably the hardest decision of setting up MS
Setting up MS lab

Instrument space, HVAC, electrical, gas supply, installation

Where discoveries are delivered.SM

UC San Diego
Health System
Setting up MS lab

• Begin planning on space early in the process
• Get site planning guides from several vendors
• Make sure that your HVAC will handle heat
  – Consult with building engineer
  – Consider “snorkel” vents
• Cannot have too many electrical connections
  – Close attention required
  – UPS requirements different than MS requirements
• Plan out sources of gases
• Instrument placement (workflow, connections, bench?)
Sources of gases

- Source gas is high volume, high purity nitrogen
- Three choices for N₂
  - Nitrogen generator (uses room air)
  - Nitrogen filter (requires 110 psi clean air)
  - Liquid nitrogen (Dewars vs External source)
- Collision gas is low volume, high purity
  - Some use nitrogen
  - If Ar, consider purchasing tank as it lasts forever
- Nice to have source of N₂ for cleaning instrument parts
**Instrument installation**

- Mass spectrometers are heavy!
- Lead tech shadows engineer during installation
- Instrument should pass specs easily
- IQ (instrument qualification)
- OQ (operational qualification)
- PQ (performance qualification)
Method development vs method validation

- Method development-vendor can help
- Many vendors claim to have “validated methods”
- Method validation-clinical lab responsibility
- Accuracy, precision, carryover, linearity, reportable range, method comparison, robustness, interface, supplies, tube validation, storage requirements, stability, matrix effects, extraction efficiency, staff training, competency documentation, back up plan, etc…
Challenges moving forward

• LDT regulation is coming
• Consensus groups will determine utility?
• Laboratory consolidation
Opportunities moving forward

• Physicians requiring accuracy and precision
• PATH (Partnership for Accurate Testing of Hormones)
• Leading standardization efforts
• Defining reference ranges
• Setting criteria for accuracy and precision
• Establishing commutable assays
Thanks for your attention!