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)


Vitamin D example

“All evaluated methods except HPLC demonstrated a more or less considerable deviation of individual 25(OH)D3 values compared with LC-MS/MS.”

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

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Back of the envelope (cont.)

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

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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

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…

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

- 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 \( \text{N}_2 \)
  - 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!