

Future of Mass Spectrometry in Clinical Research and Forensic Toxicology

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Agenda

- The “Heritage” of Mass Spec vendors
- Market Conditions
- Regulatory Challenges
- Trends/ Frontiers
 - Screening – Speed and simplicity
 - Ease of Use Improvements
 - Connectivity and Automation
 - New workflows enabled by mass spectrometry
- Future of Mass Spectrometry in Clinical Research

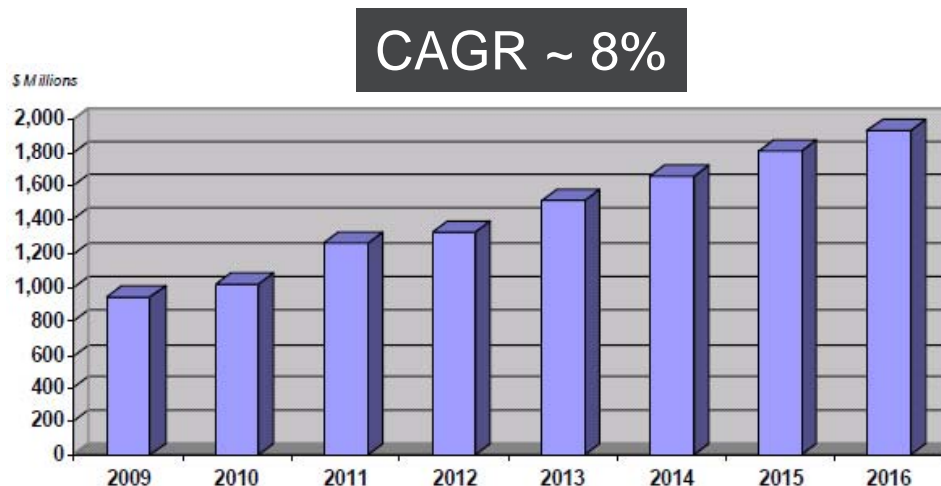
Mass Spec LC-MS Vendor Heritage



MS Revenue Growth – Overall vs Clintox

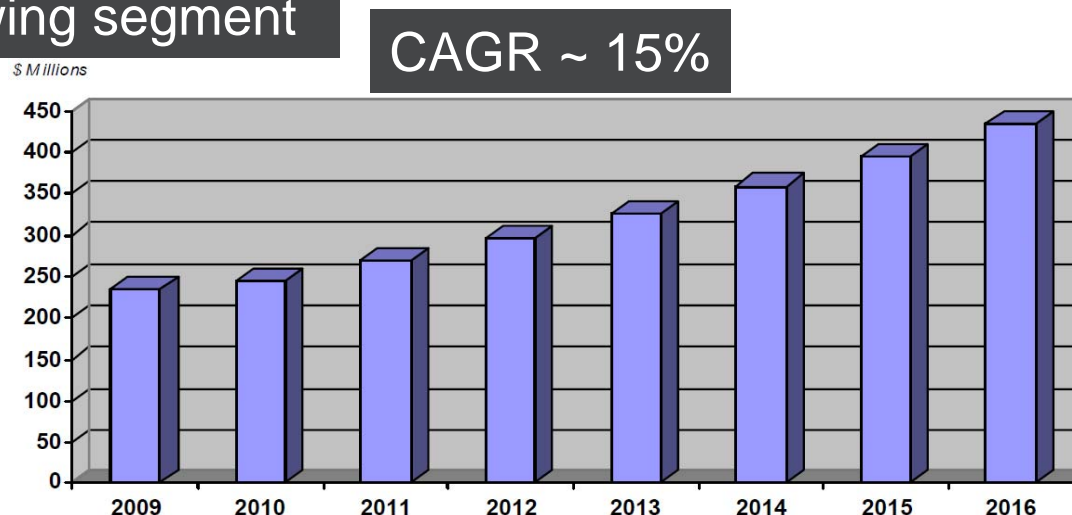
Overall MS

Year	Sales (\$ Millions)
2009	950
2010	1,025
2011	1,266
2012	1,329
2013	1,512
2014	1,654
2015	1,809
2016	1,927



Clintox – Fastest growing segment

Year	Sales (\$ Millions)
2009	234
2010	245
2011	270
2012	296
2013	326
2014	359
2015	395
2016	434



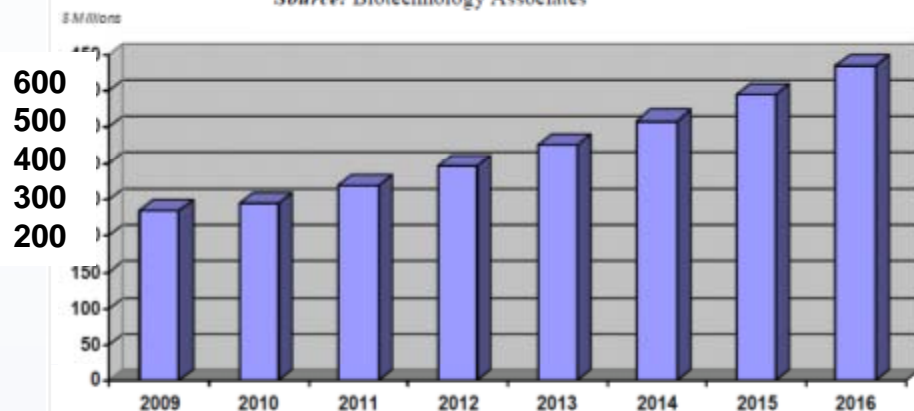
Source: Biotechnology Associates

Global Forecasts Clinical Research Markets

MS Sales

Year	Sales (\$ Millions)
2009	234
2010	260
2011	320
2012	370
2013	420
2014	460
2015	520
2016	600

Source: Biotechnology Associates



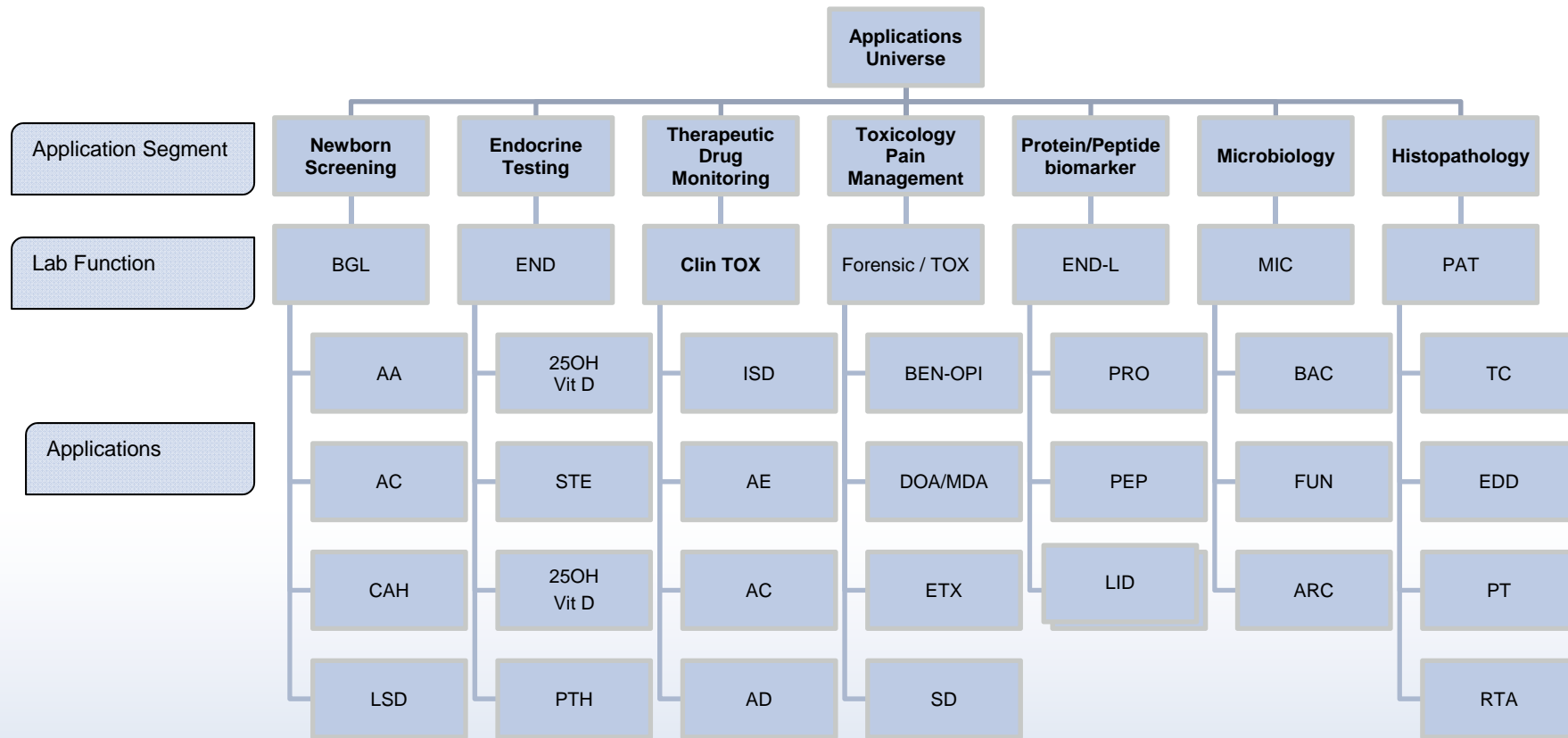
Immunoassay market

BCC Projects the Global Market for Immunoassay Testing to Reach \$21 Billion by 2017

Global demand for immunoassay testing is expected to increase at a five-year compound annual growth rate (CAGR) of 4.7%. Worldwide growth has the potential to expand to nearly \$21 billion by 2017.



Universe of Clinical Research and Forensic Toxicology Applications



BGL – Bio Chemical Genetics; AA – Amino Acids; AC – Acyl Carnitines; CAH – Congenital Adrenal Hyperplasia; LSD – Lys Sto Dis
 END – Endocrine labs: 25OH Vit D, 1,25 Vit D; STE – Steroids; PTH – Parathyroid Hormone
 Clin TOX labs; ISD – Immunosuppressant Drugs; AE – Anti Epileptics; AC – Anti Convulsing; AD – Anti Depressant
 Forensics / TOX; BEN –OPI Benzodiazepines Opiates; ETX – ETG/ETS; DOA/MDA – Medical Drugs of Abuse; Illicit drugs;SD - Sports Doping
 END-L –PRO- Endogenous Proteins; PEP -Endogenous Peptides; LID -Immunoassay displacement (large molecules)
 MIC – Microbiology; BAC – Bacteria; FUN – Fungi; ARC – Archaea
 PAT – Pathology; TC – Tissue Classification; EDD – Early Disease Detect; PT – Pers Therapeutic; RTA – Real Time Assessment

Market Breakdown: Regulatory Challenge



Clinical Research – CLIA regulated but the FDA is involved

Endocrinology (steroids, vitamin D, endogenous peptides/ proteins)

Toxicology (immunosuppressants, therapeutic drugs)

Biochemistry (neo-nate – amino acids, organic acids,)

Clinical Drug Testing/ Pain Management



Forensic Tox / Drugs of Abuse – well established guidelines

- Hazardous Materials I(Compound ID and Regulation - State, County, City)
- Crime Labs (State, County, City)
- Coroner's labs (County, City)
- Federal Agencies (FBI)
- DEA
- Workplace testing (urine, hair, oral fluid, blood)

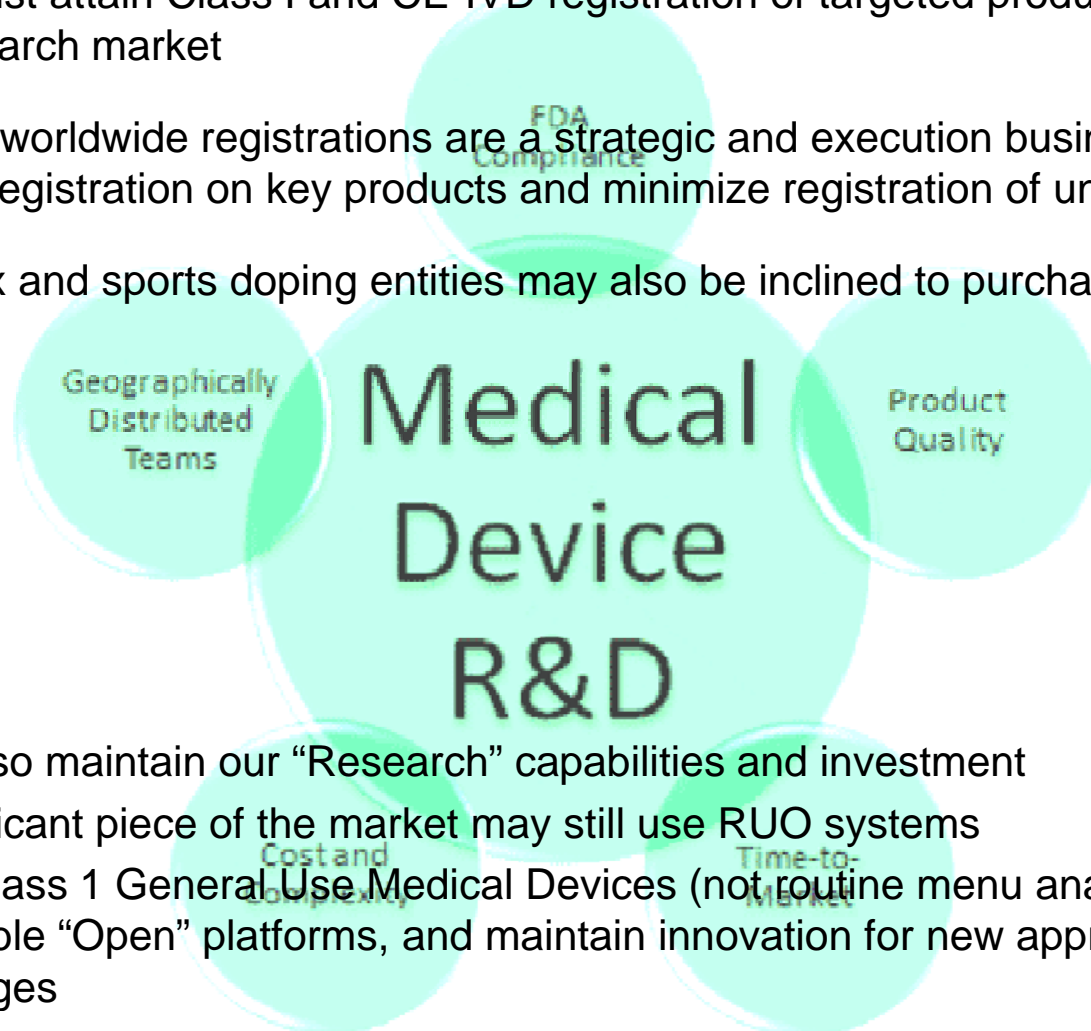


Sports Doping - Well established guidelines

- World Anti-doping Code (WADA)
- USADA – monitors Athletes competing in the U.S.
- Animal racing – self regulated federations
 - Exactive is well accepted in equine testing labs around the world

Market Positioning – A Fine Balance

- Vendors must attain Class I and CE-IVD registration of targeted products to stay in the clinical research market
- Class I and worldwide registrations are a strategic and execution business challenge – must have registration on key products and minimize registration of unnecessary products
- Forensic tox and sports doping entities may also be inclined to purchase of MD listed devices.



- We must also maintain our “Research” capabilities and investment
 - A significant piece of the market may still use RUO systems
 - Offer Class 1 General Use Medical Devices (not routine menu analyzers) – they must be flexible “Open” platforms, and maintain innovation for new approaches to biological challenges
 - Money and time spent on MD listings, threatens innovation budgets.

Trends / Frontiers – Screening: Speed / Simplicity

- Analysis complete in 20 seconds or less
- Minimal chromatography – Desire to “skip” chromatography until the confirmation stage
 - Paperspray
 - RapidFire
 - TurboFire - “Turboflow Only Analysis”
 - LDTD
 - DART
 - DESI

Requirement: Mass Spec must provide More Speed, Selectivity, Robustness, and Simplicity (ex: “universal” ESI ion source)

Ex: – Secondary screen of IA to reduce false confirmations ... May replace the primary screen!

Trends / Frontiers: Ease of use

- Mass spec platforms will continue to incrementally improve in sensitivity and evolve fit for purpose “shortcuts” in operation
- Mass Spec processing software will continue to get easier to use and be designed and sold “for purpose”
- Sample prep and mutiplexing will simplify and continue movement toward “for purpose”
- Chromatography will be miniaturized, minimized and simplified to fit for purpose designs.
- High Resolution Accurate Mass Systems
 - Continuously evolve around resolution, mass accuracy, and sensitivity
 - Will push immunoassay as screening devices
 - Easier to implement than unit resolution systems for specific applications (large molecules, molecules with poor fragmentation characteristics)

Trends / Frontiers – Automation, Spots, Breath, Going Green

- End to end automation / connectivity

- Sample tracking, sample handling, on and off line prep, LIS-LIMS connectivity.
- It's not enough to offer an unconnected piece of the workflow!

- Spots

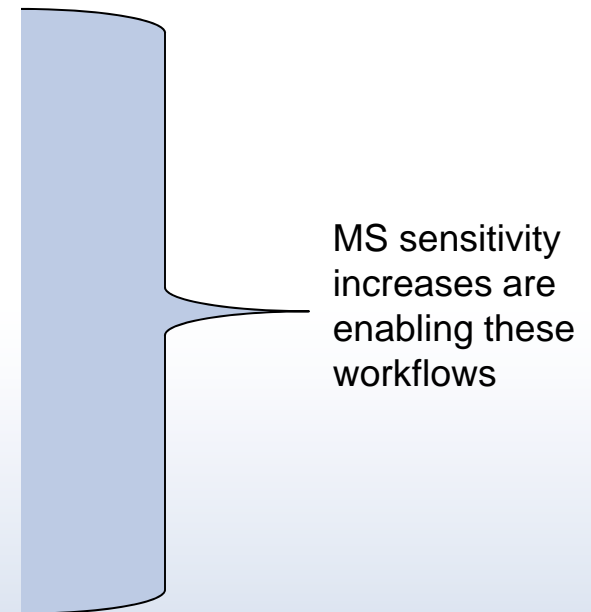
- Blood, Urine, Oral Fluids ... Milk?
- Automation of Guthrie cards for the application universe?
 - Cutting and flow through automation
 - Paperspray
 - Whole Blood Workflow vs. Spot Workflow

- Breath Analysis

- What's old is new again.
- Breath capture membrane generating significant interest
- Requires automation

- Movement towards Low Flow HPLC

- Solvent usage a cost and disposal issues for the labs
- Low flow workflows demonstrate improved sensitivity, solvent saving, robustness, and speed.



Trends / Frontiers – Translational Workflows

- Translational Solutions / Workflows
 - Discover and translate “omics” markers to routine methods
 - Improve throughput (on-line prep, multiplexing)
 - Improve precision.
 - Improve sensitivity
 - Improve robustness
 - Software to go from Discovery to Applied
 - Translate existing immunoassay tests (screening/ confirmatory – Small to large molecules)
 - Match / improve throughput
 - Improve precision
 - Improve sensitivity
 - Reduce workflow costs

Trends / Frontiers – Point of Care Solutions

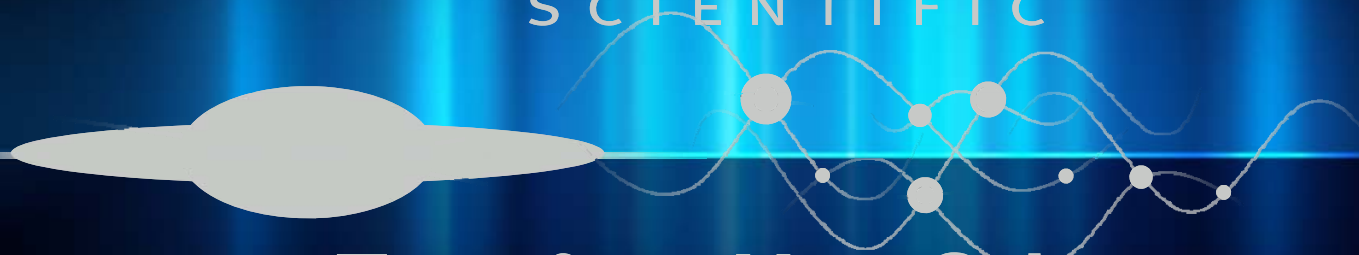
- “Point of Care” Closed Solutions
 - Routine “menu” of tests – small and large molecules
 - Blood Spot / Guthrie Card Analyzers
 - Whole Blood – Cell Disintegrated Blood
 - Bacterial Analyzers – More advances to come.
 - MS Surgery Sniffer

Future of Mass Spectrometry - Conclusion

- The use of LC-MS will continue to expand in Clinical Research
- LC-MS will continue to displace immunoassay for screening
- LC-MS and other mass spec technology will cross the chasm to automated, 510k compliant, fit for purpose medical devices within the next 5 years.



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