



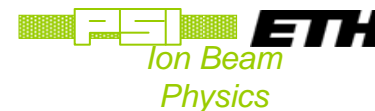
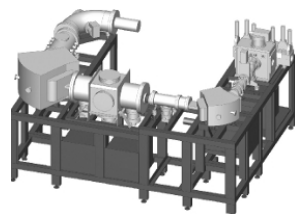
Building understanding through early human metabolism™

Innovation for the pharmacokinetics and metabolism of drug candidates in clinical and non-clinical studies

An Accelerator Mass Spectrometry Contract Research Organization

BioMICADAS

The next generation AMS for pharmaceutical analyses



Please contact us for more information www.vitaleascience.com

530.341.0200 (U.S.)

We strive to develop long-term relationships with our clientele by providing advanced clinical drug development solutions on time and on budget

Quality

On Time

Industry Standard Operations and Reporting

Problem Solving

Data Interpretation



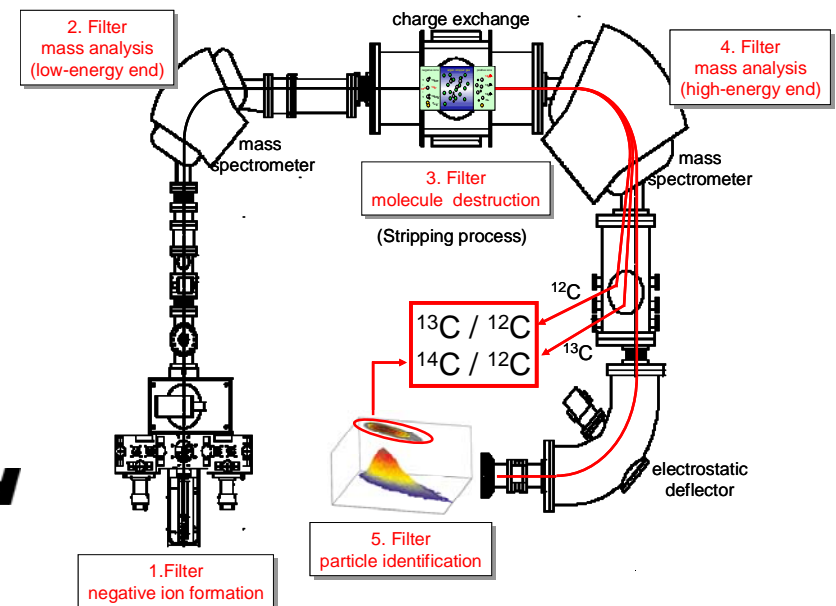
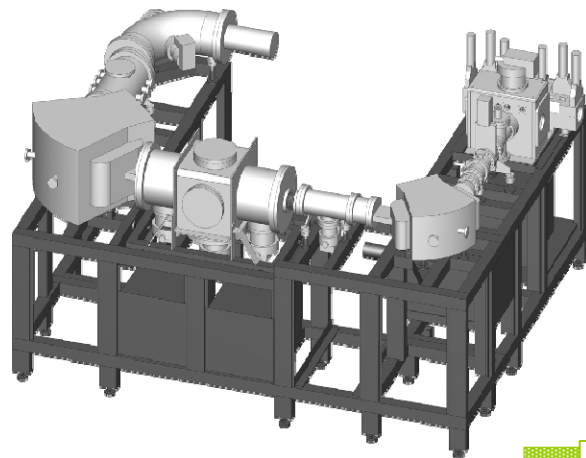
Vitalea Science: Emphasis on human ADME using Accelerator Mass Spectrometry and trace radiolabel

Human ADME data is attained from the ability to measure changing drug concentrations in fluids, tissues, and excreta: usually requires a radiolabeled form of drug

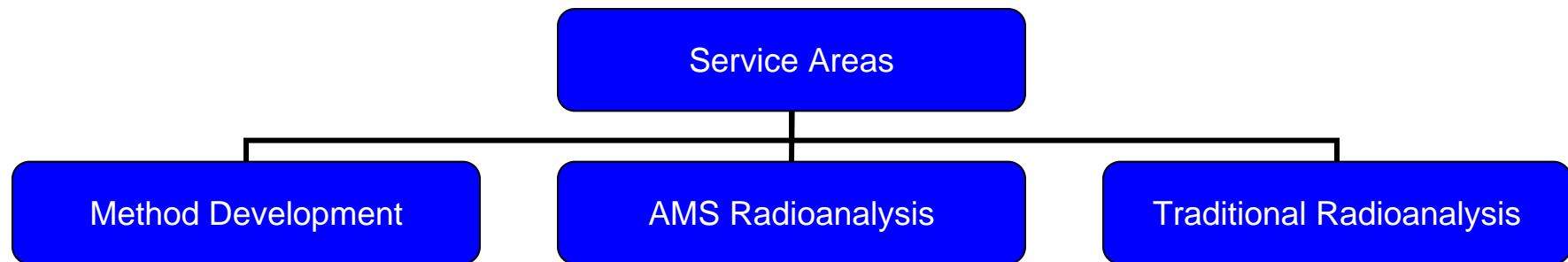
Accelerator Mass Spectrometry with ^{14}C labeled drugs: analytical tool that empowers early drug development with trace radiation

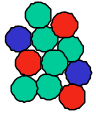
- Absorption
- Distribution
- Metabolism
- Elimination

- Reduced radioactive burden (nanoCurie human doses)
- Attomole quantitation without matrix interferences
- Safe and ethical approach to human ADME



We support ADME at any radiological dose level




Biological Sample
(¹⁴C, ¹³C, ¹²C atoms)

Liquid Scintillation Counting

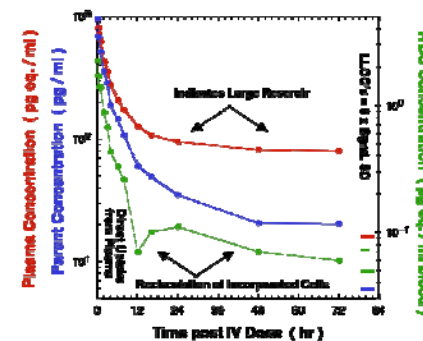
- Measures b-decay of ¹⁴C atom
- Detected as photons of light

Accelerator Mass Spectrometry

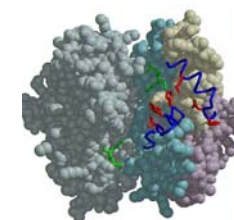
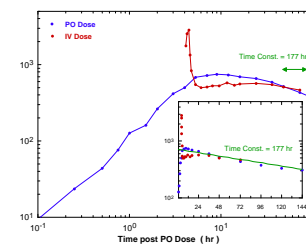
- Counts individual atoms
- ¹⁴C, ¹³C, ¹²C atoms separated by differences in mass, charge, and energy

Clinical study designs our technology supports

- **Microdosing (^{14}C)**
 - Candidate selection based upon HUMAN data under an exploratory IND application (<100 ug/100 nCi)
- **Microtracing – Low radiation Human A(D)ME**
 - Mass balance and metabolism (A(D)ME) at therapeutic doses using “microtrace” ^{14}C (~ 100 – 500 nCi)
- **Absolute Bioavailability (single study design)**
 - Microtracer IV given at T_{max} of cold therapeutic oral dose
- **Highly potent and distributed drugs**
 - Highly sensitive quantitation of total drug material and analytes to attomole levels
- **Biologics PK/Biodistribution**
 - Bypass Elisa development. Weeks from labeling to PK/biodistribution determinations



We have defined AMS appropriate Validation Packages



GLP Facility

- Purpose-built lab– Davis, California – July 2008
- GLP Quality system with independent QA unit
- ULT freezers with 24/7 continuous monitoring
- Emergency backup generators
- Archive room
- GLP equipment on 3 to 6 month calibration services
- Containment room with for traditional radioanalysis
- Expansion space



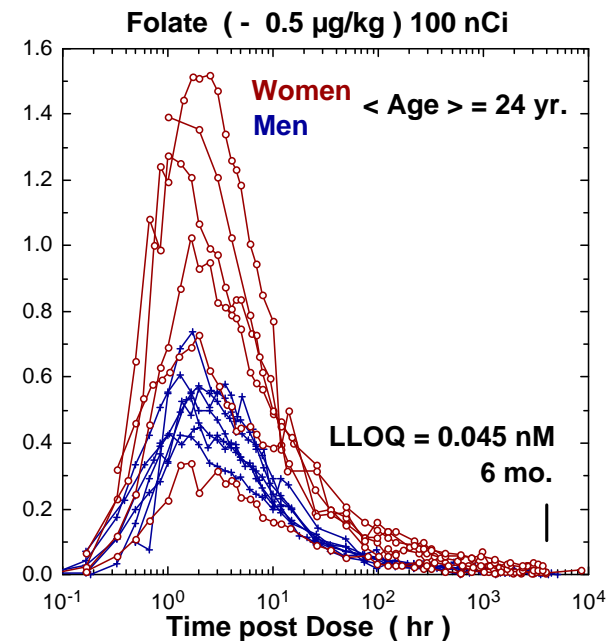
Quality Assurance – Organization/Regulatory reference

- Organization – defined to meet GLP requirements
- Personnel/Training
- Document Control
- Quality Control
- Independent Quality Assurance Unit
- Facilities
- Equipment & Computerized Systems (including Part 11)
- Study Conduct
- Reporting
- Archiving
- 21 CFR Part 58 GLP, OECD GLP
- 21 CFR Part 11 E-Records & E-Signatures
- ICH E6 Guideline for Good Clinical Practice
- Good Clinical Practice (GCLP) Guidance Document (BARQA)
- Other regulations or guidances where applicable

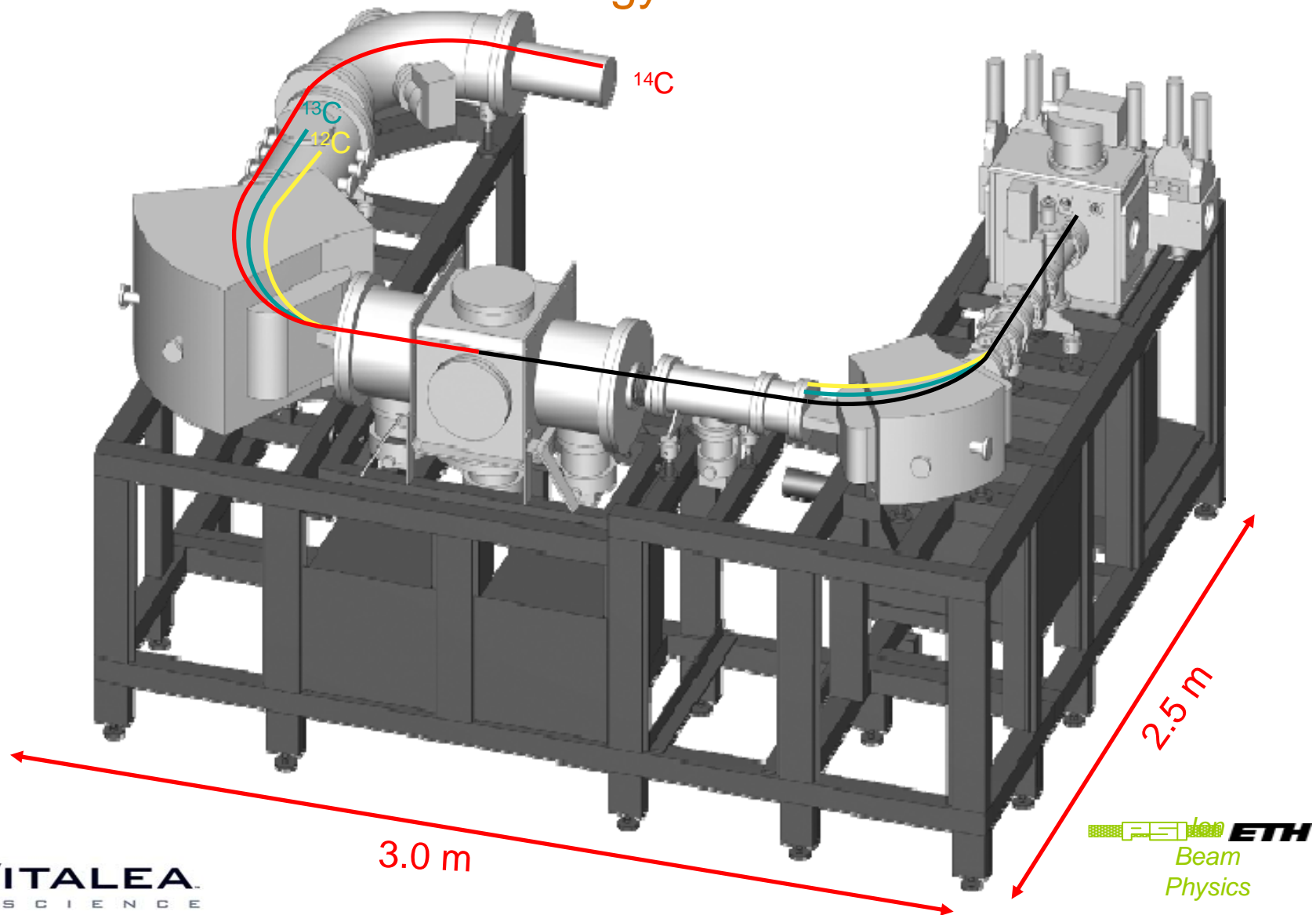
List of SOPs available on request

Why Vitalea is selected

- Quality
- Meeting aggressive timelines
- Scientific team
- Trusted CRO management
- Global clinical network
- We will assist with
 - Clinical protocol development
 - Radiosynthesis outsourcing
 - Clinical placement
 - Human dosimetry approvals
 - Defense of submission with regulatory bodies
- More than data: An experienced partner!
- References available

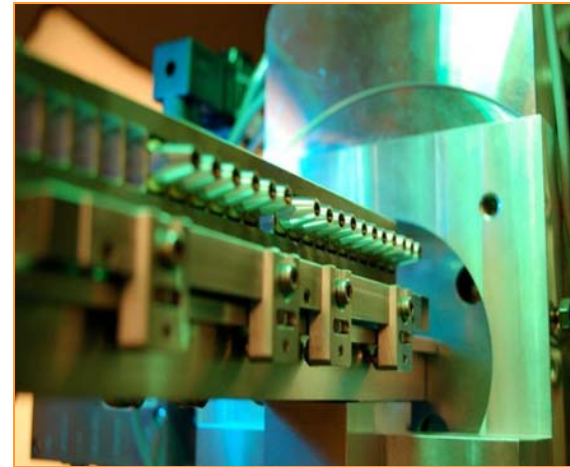


AMS technology: BioMICADAS: developed at the Swiss Federal Institute of Technology



Only 24/7 AMS Spectrometer

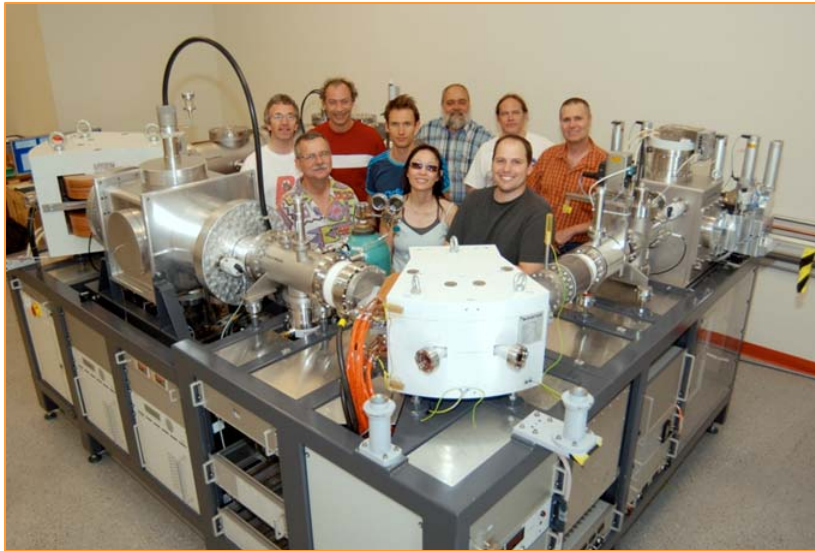
- Full validation package
- 21 CFR part 11 assessment
- Only AMS capable of uninterrupted operation (no venting)
- Constructed using “off the shelf” components
- Unparalleled robustness
- Expanded dynamic range – single instrument ADME studies with microcurie-sized doses
- Gas-fed interface
- LC interface under development
- Exclusive to Vitalea



Validated Spectrometer Performance	
Specificity	1:10 ¹⁴
Robustness	2.5%
Reproducibility	<1% single sample
Precision	1.5% multiple samples
Stability	<3% over 1 year
LLOQ	0.01 Modern
ULOQ	300 Modern
Accuracy/linearity	0.99/0.01
Throughput	200 samples/day
GLP System Suitability	1 per week

Multiple spectrometers

California
(GLP)



ETH Switzerland



- Proven equivalency

Metabolite Platform - throughput of UPLC-AMS clinical analysis



Validated Waters
Accuity™ UPLC with
fraction collectors



3 traces per
hour
60 specimens
per day



3 species per
trace
180 samples
per day



Septa-seal carbon
reduction

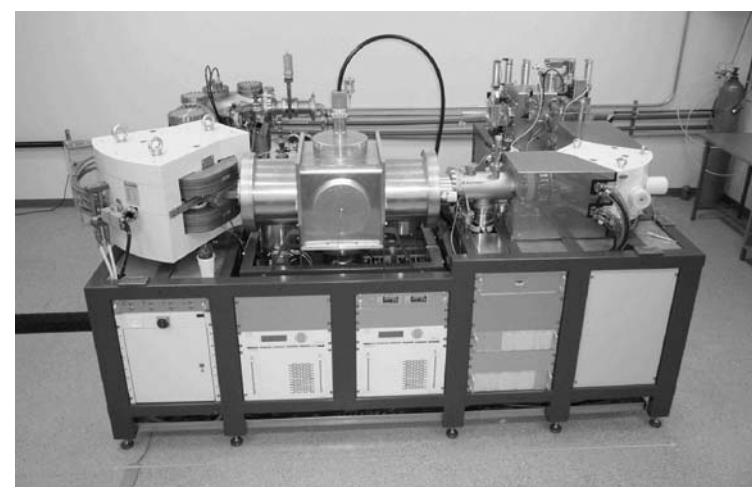


>200 samples per day



BioMICADAS AMS spectrometer

- Validated UPLC/HPLC system (10 min run times)
- Our founders developed state-of-the art graphitization methods
- 24/7 AMS
- = **SPEED and REPRODUCIBILITY**

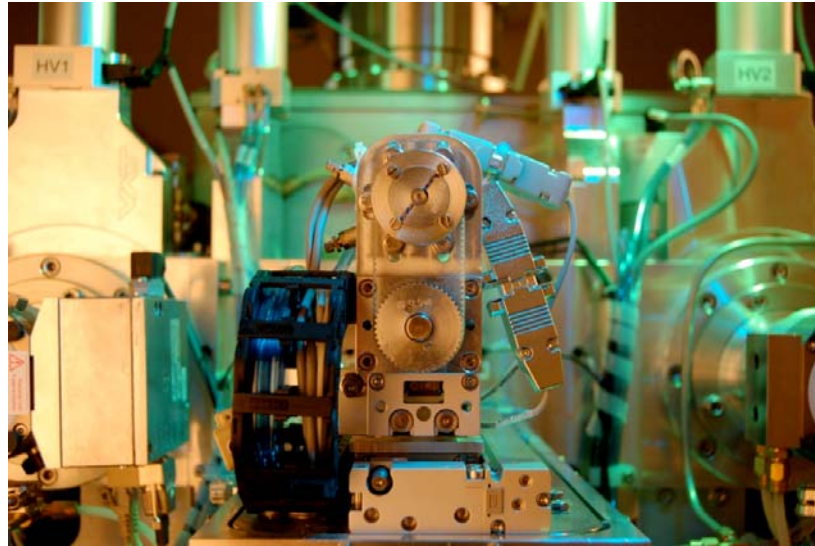


Scientific leadership

- Stephen Dueker, Ph.D, – Founder and CSO: Pioneered first human microdosing studies in 1996 at University of California.
- Robert Bethem - Founder of Alta Analytical CRO and co-author of the book *Trace Quantitative Analysis by Mass Spectrometry*, published in 2009.
- John Vogel, Ph.D. – Science Director: Founder of bio-AMS when at National Labs. Owns all the basic patents on bio-AMS and Sample preparation.
- Robert Ings, Ph.D. – Science Advisor: Internationally recognized leader in quantitative bioanalysis while at Pharmacia and Amgen
- Pete Lohstroh – Ph.D. in Pharmacology. Organization Principal Scientist
- Jason Giacomo – Ph.D. Physics. Hardware/electronics expert. Advancing operational efficiency of AMS.

Recent Publications

- Vogel JS, Lohstroh PN, Keck BD, and Dueker SR (In Press) Quantitative drug metabolism with accelerator mass spectrometry in Lee MS and Zhu M, eds., *Mass spectrometry in drug metabolism and disposition: basic principles and applications*. (John Wiley & Sons: New York)
- Dueker SR, Lohstroh PN, Giacomo JA, Keck BD, and Vogel JS Early Human ADME using microdoses and microtracers: Bioanalytical considerations. *Bioanalysis* (2010) 2(3), 441-454
- Keck BD, Ognibene T & Vogel JS Analytical Validation of Accelerator Mass Spectrometry for Pharmaceutical Development: *Bioanalysis* (2010) 2(3), 469-485
- Vogel JS, Giacomo JA, Schulze-Konig T, Keck BD, Lohstroh PN, Dueker SR Accelerator mass spectrometry best practices for accuracy and precision in bioanalytical ^{14}C measurements. *Bioanalysis* (2010) 2(3), 455-468



Thank you
contact

Stephen.Dueker@vitaleascience.com

