

Better Science = Better Business: Impact of Automated Compound Tuning in a Global DMPK Environment

Advion Users Meeting
57th ASMS Conference
Philadelphia, PA
May 31st, 2009

Progress Since 2007

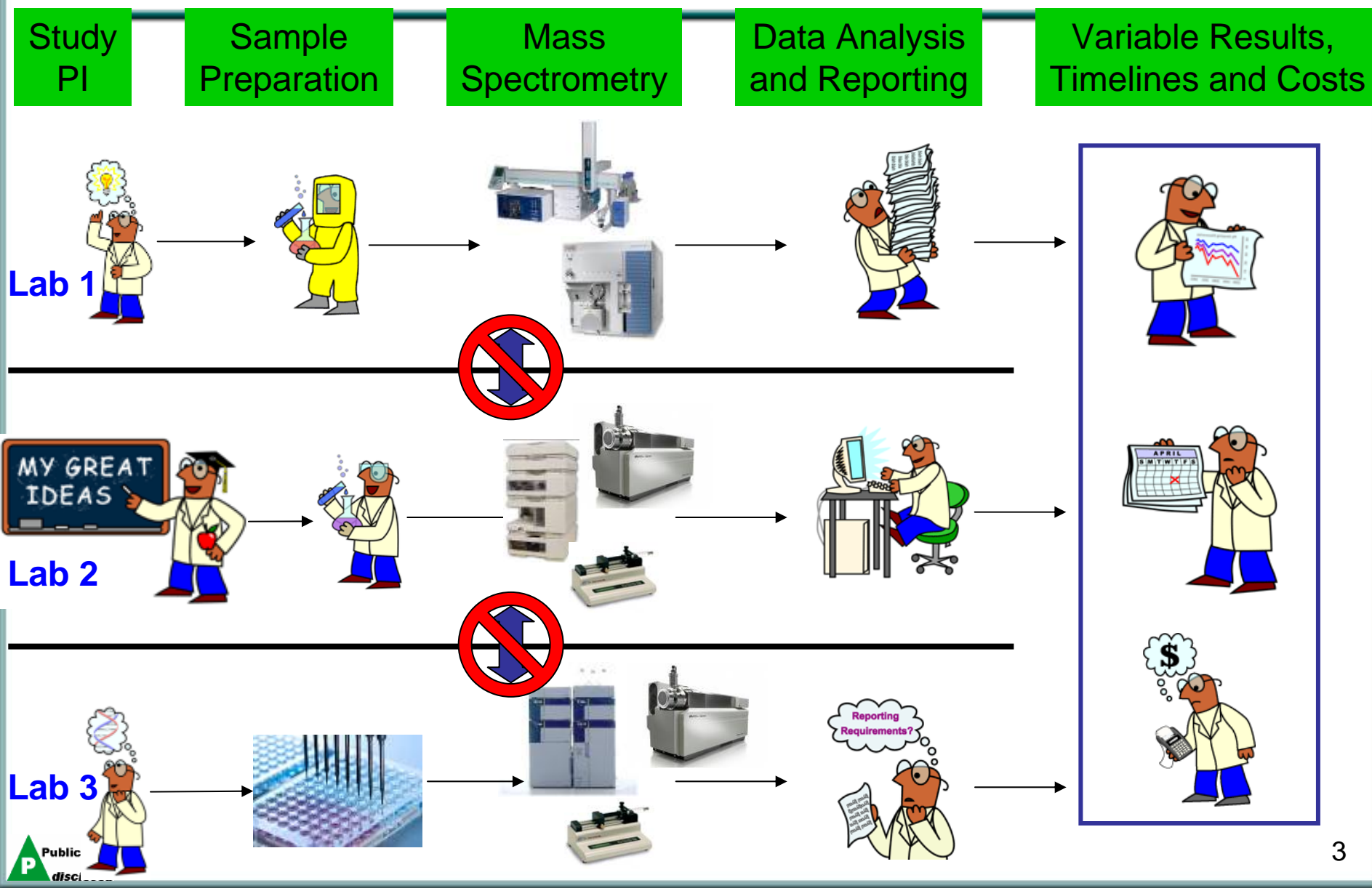


Automated Compound Optimization

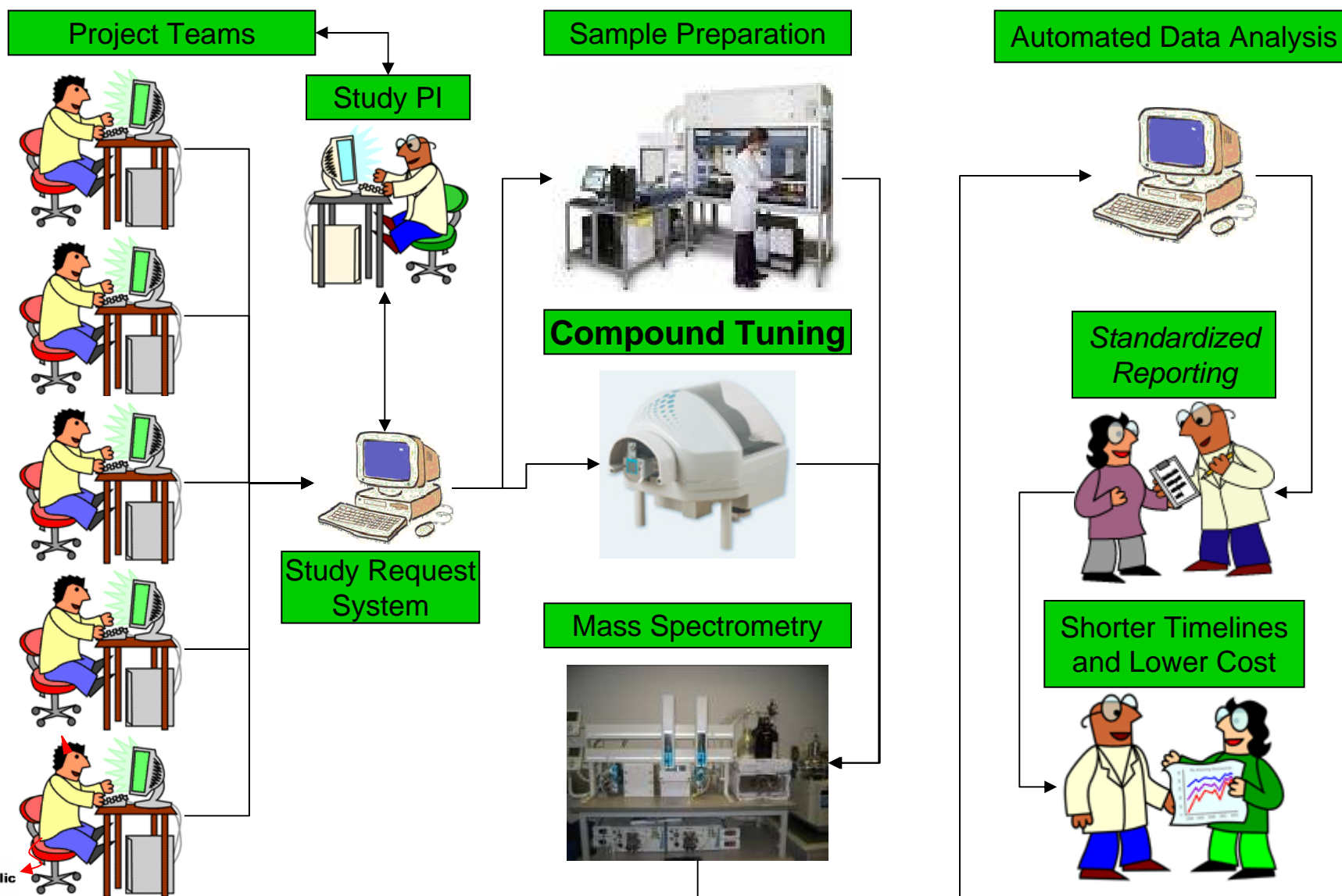
Advion Users Meeting
55th ASMS Conference
Indianapolis, IN
June 3, 2007

Original Concept Presented by Rick King

Past State: No Coordination Across Labs



Current/Future State



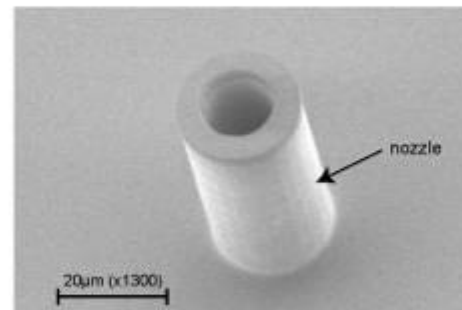
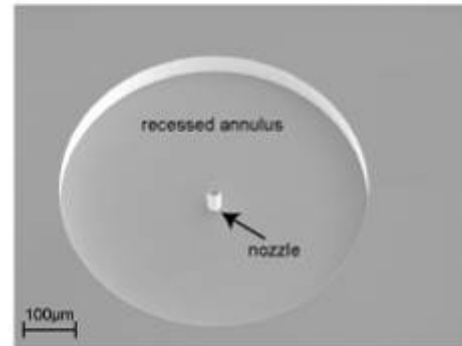
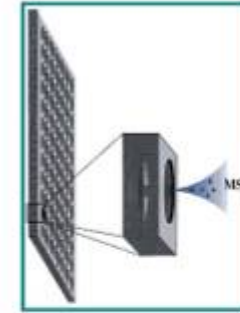
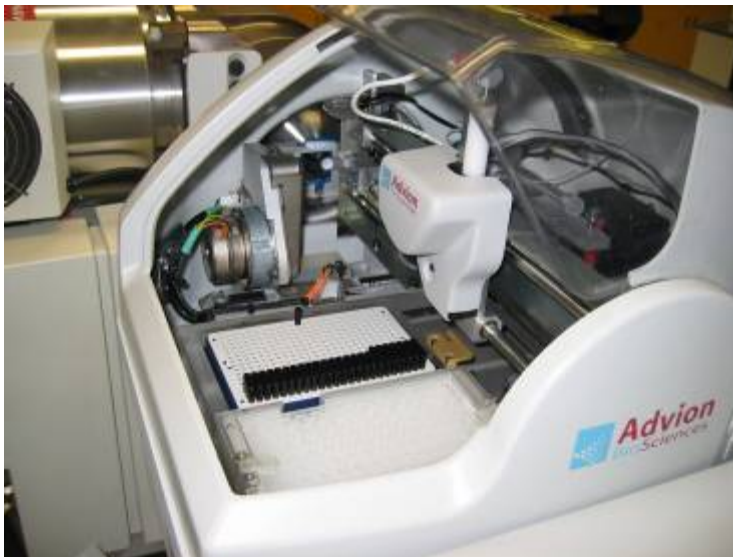
Compound Tuning

- MS/MS conditions for each compound must be optimized prior to quantitative analysis.
- Standard approach is to use syringe pump to infuse compound and tune mass spectrometer.
 - Each successive compound requires manual intervention to clean, reload the syringe and start the acquisition.
- With hundreds of compounds this takes a lot of time.
- Same compound gets “re-tuned” multiple times because information is not shared across assays/sites.

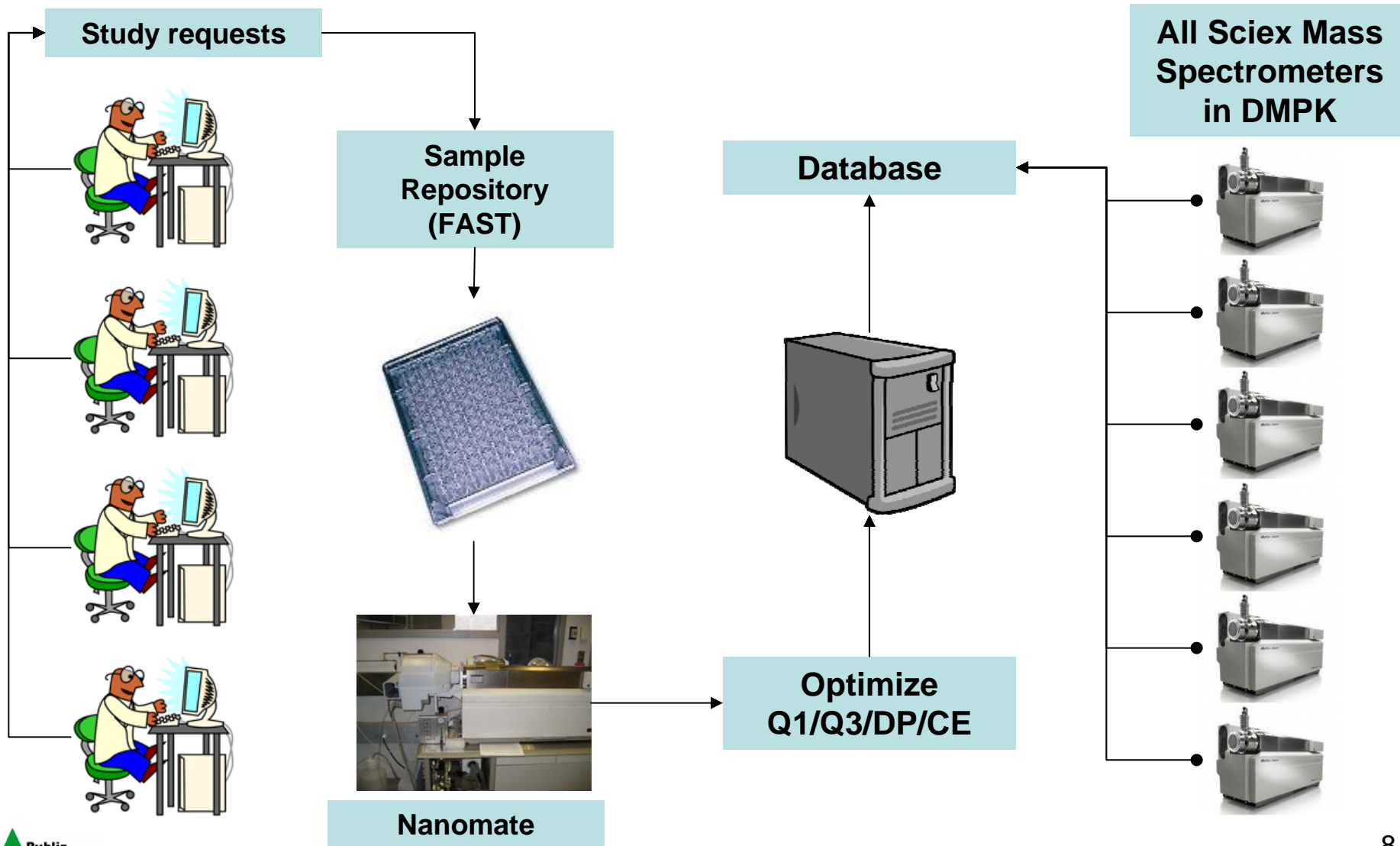
Advion™ Nanomate

- Chip based nano-electrospray device containing 400 individual nozzles. Disposable.
 - Eliminates carryover (one time use for each nozzle)
 - Stable spray, low nL/min flow-rate ideal for infusion experiments
 - Samples are introduced in 96/384 well plate format
- Automaton
 - Sciex software that automates optimization of MRM conditions
 - Q1 m/z, Q3 m/z, declustering potential & collision energy
 - Accepts text-file compound lists
 - Data is saved on a server and shared across instruments

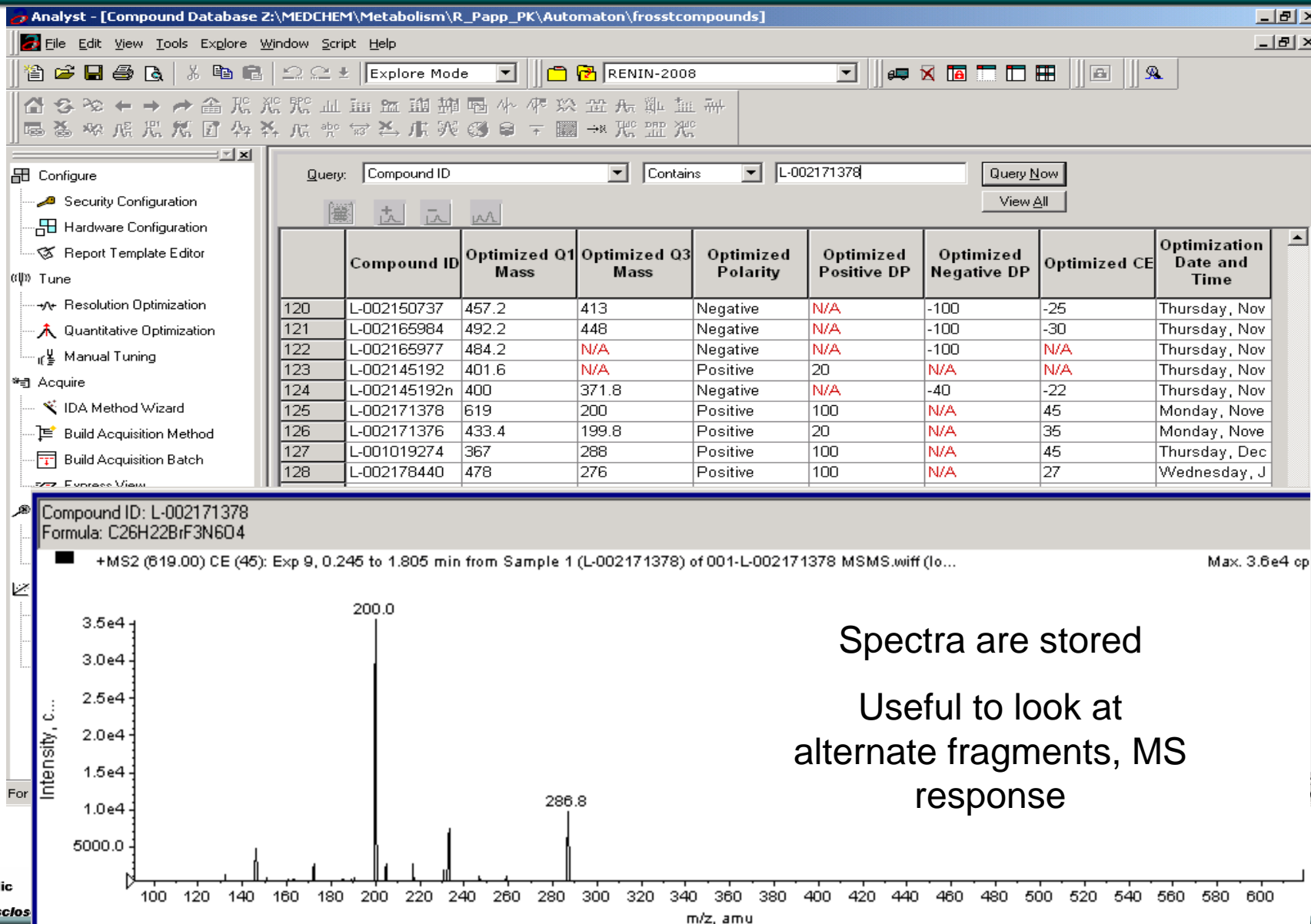
Advion™ Nanomate



Compound Optimization Workflow



MS Compound Library



Spectra are stored
Useful to look at
alternate fragments, MS
response

MRM Architect

MRM Architect v2.0 [Connection: FrosstCompounds.mdb]

Settings Help

compound database

Double-click on a compound below to COPY it into your method

	CompoundID	OptDate	Polarity_Po	Q1Mass	Q3Mass	DF
1	L-000877998-1-002	05/27/09	True	578.10	246.10	
2	Labetalolneg	05/25/09	False	327.60	176.20	
3	Labetalol	05/25/09	True	329.40	162.20	
4	L-002374602-000P	05/25/09	True	643.40	623.30	
5	L-002376072-000S	05/25/09	True	673.60	254.10	
6	L-000644128-000U	05/22/09	True	419.50	199.20	
7	L-002378376-000V	05/22/09	True	411.40	121.00	
8	L-000642957-001D	05/21/09	True	359.30	97.10	
9	L-000638596-001D	05/21/09	True	300.40	98.00	
10	L-002370070-000W	05/21/09	True	411.20		

Compound Name Filter (type an expression then press ENTER):

Compound Property Filter:

Show all compounds

Exclude compounds with:

- Positive polarity
- Negative polarity
- No Q1 Mass
- No DP
- No Q3 Mass
- No CE
- No CXP

Quick Pick Get From List

my method

Double-click on a compound below to REMOVE it from your method

Where there is no CXP value, use this value instead: 15.0

Dwell time (millisec): Xtra Xitions: No

Export all transitions as a single method Use naming rule

Export transitions as separate methods Specify file name

Keep MRM transitions in template method

Do not keep MRM transitions in template method

Choose template method:
 Choose a file

Choose output file:
 Choose a file

Enable Help No methods created yet

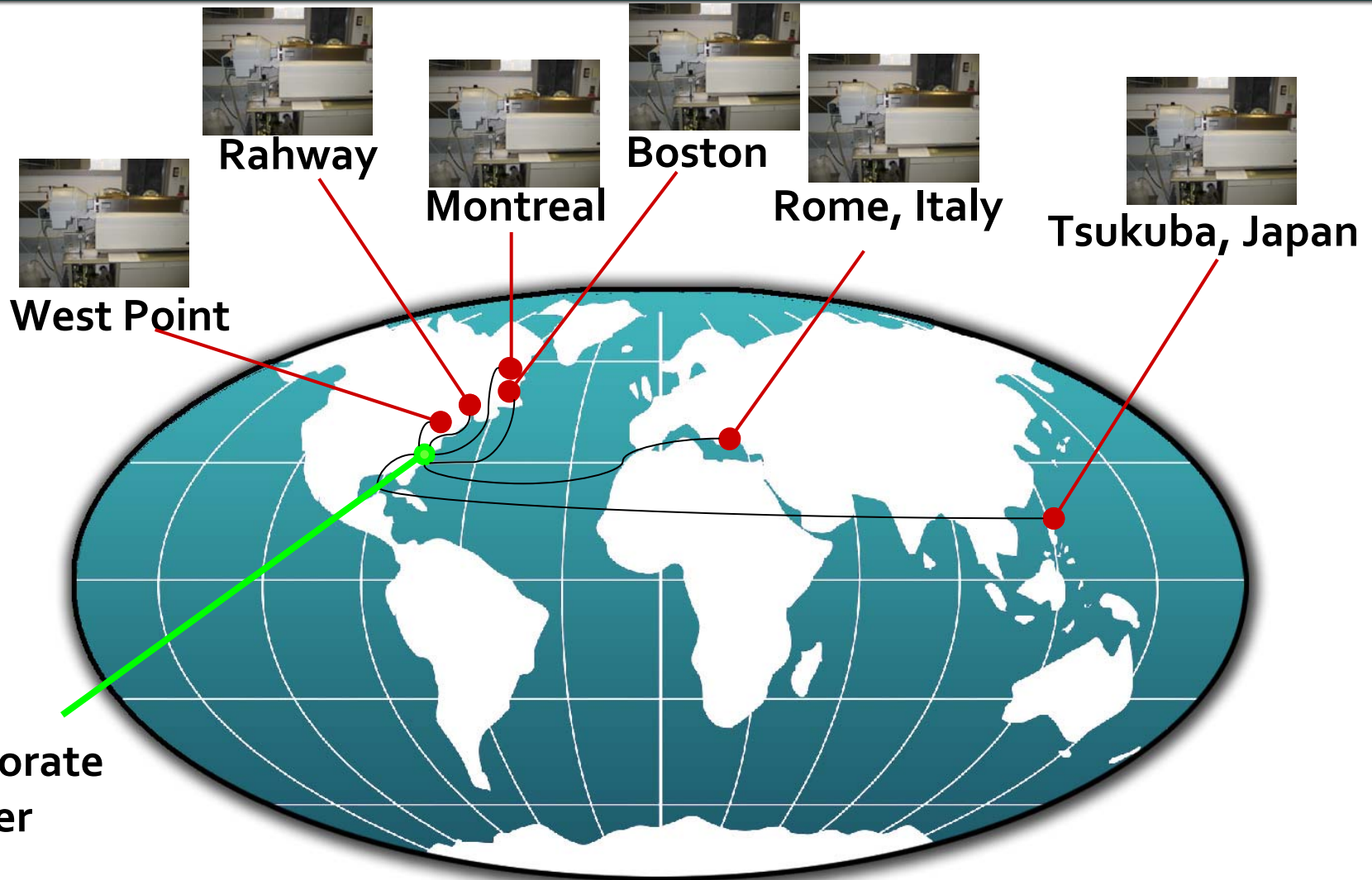
Overall Benefits

- Large numbers of compounds can be optimized using this “walk away” system.
- MS conditions for all compounds are stored in a easy accessible database.
- Very little compound is required to complete each experiment.
- Efficiency Gains:
 - Fewer FTEs required for routine work
 - Better use of “production” systems
 - Elimination of repeat optimizations

Improved Efficiency

- 3 assays in three different groups
 - PK, microsomal stability, pgp
 - Compound gets optimized three times for three different mass spectrometers
 - 15 minutes per optimization for MS parameters
 - 15 minutes to check HPLC condition
 - 15 minutes to make solutions, check instruments, fill solvents, etc.
 - >2 hrs for the same compound
 - 20 compounds a week = 50 hrs or almost 2 FTES
- Consolidated Bioanalysis
 - Compounds get optimized once using an automated system – 5 minutes
 - Samples are prepared in FAST group or compound management groups
 - Generic HPLC methods get optimized once – 10 minutes
 - 20 minutes per compound
 - 100 compounds a week = 33 hrs or less than 1 FTE to do 5x the work

Starting this year...global connectivity



Future Plans

- Global database to come online this year using DiscoveryQuant software from Sciex.
- Next step to look at accurate mass MSMS data collection for metabolite identification studies
 - Collect and assign MSMS spectra of parent compounds before metabolite identification experiments are done
 - Use automated software tools for assignment of fragment ions