Working with CRO's on Product Metabolism-a more efficient process

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Syngenta Business

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Bringing plant potential to life.

We sell our products in over 120 countries touching almost 95% of the world's population.


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Grant's


kumato


sweet & seedless pepper
Nominated for
FRUIT LOGISTICA
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Syngenta Database-Jealotts Hill

- Server Database.
- Currently Windows XP Platform.
- Chemfolder Enterprise.
- Spectral Database- MS Manager/NMR workbook and Chrom Manager.

Advanced Chemistry Development

ACD/Labs

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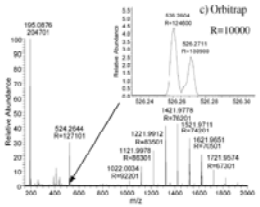
What Data ?

Product Safety – Global Product Metabolism
CRO support
Regulatory / Registration Support
Product life Cycle Management
Met ID / Characterisation
Metabolism problem solving

Early Metabolism – Non radiolabelled

Investigative Toxicology



ADME (Liver heptocytes, Culture metabolism, Stage I)

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Purpose

To provide business efficiency to enable capturing of Syngenta data from our CRO partner(s).

Pilot Project

- Selecting our CRO partner.
- Choosing the options.
- Mapping our workflows for data capture.
- Data Criteria?

CHARLES RIVER
LABORATORIES

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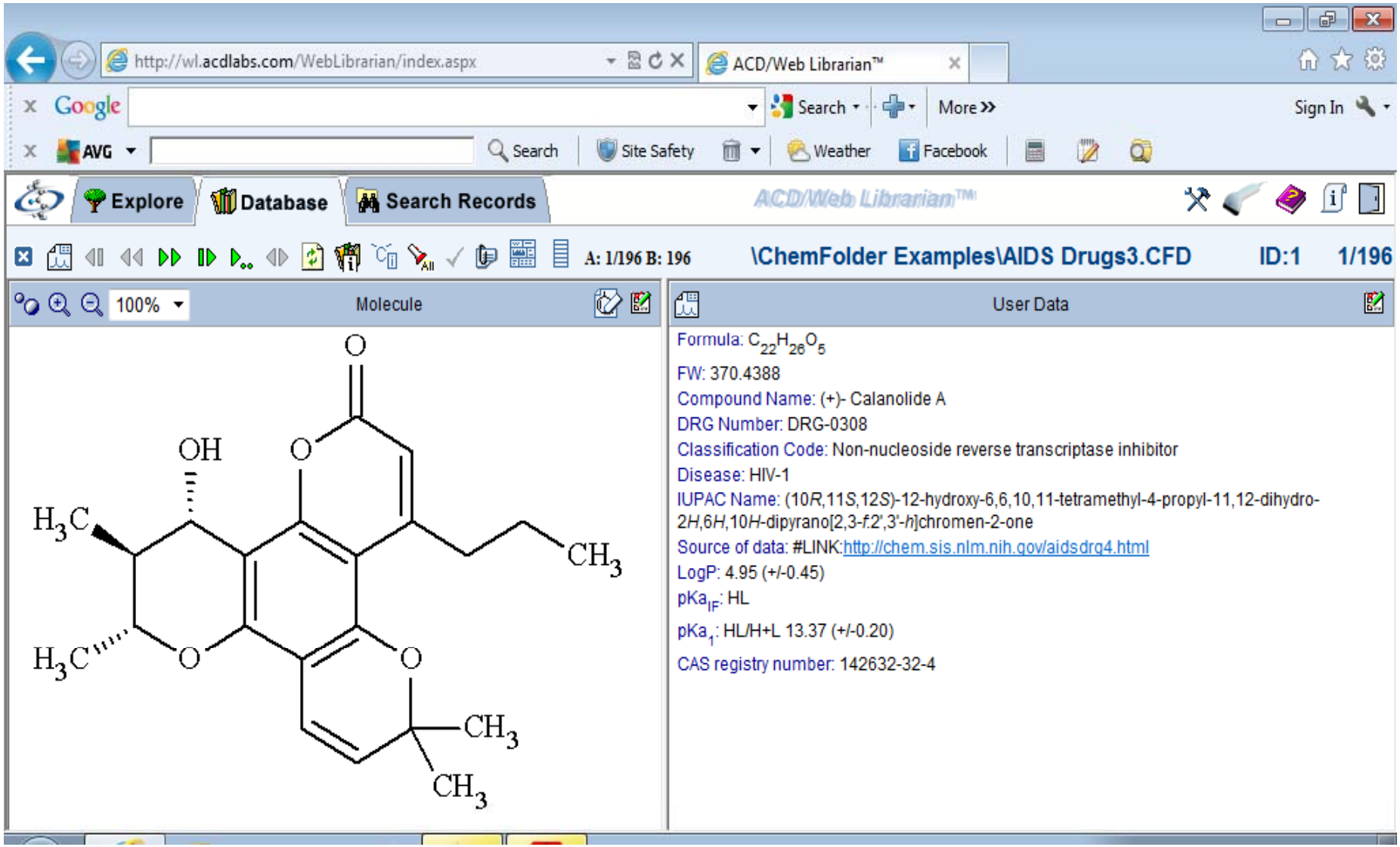
Options Web Librarian

- CRO has access to Syngenta database via web server.
- CRO submit spectra, mass chromatograms and structures via web librarian although we prefer to upload to a review database for us to curate before upload to the master database.
- This configuration, the CRO requirement is web browser and internet access
- IT department do not support this option due to security issues.

Web Librarian



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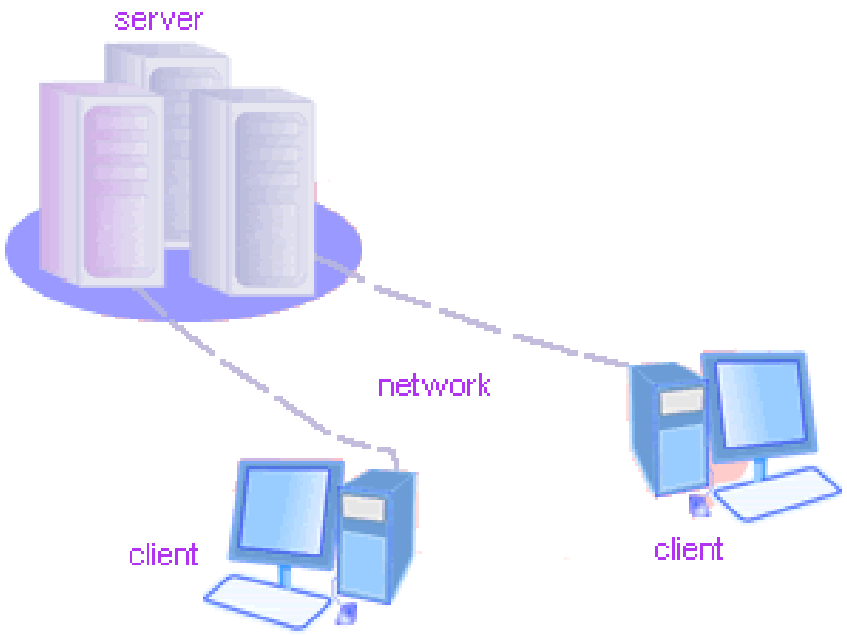
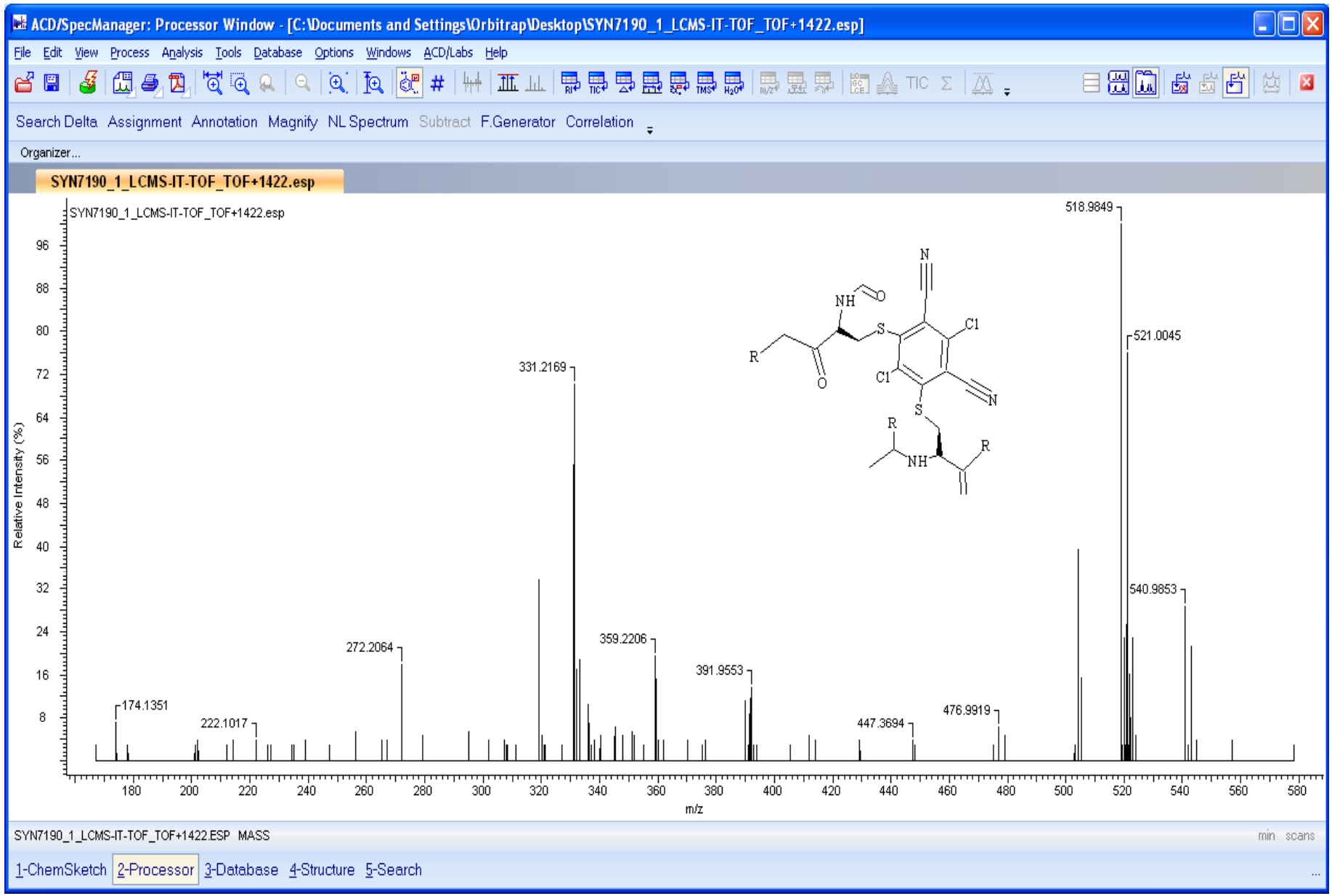
Further Options

- Licensed Software route
- ChemFolder and MS manager software, local.
- CRO to supply nd9 file for MS and MS/MS spectra, CFD files for the structures + biotransformation maps.
- Via Syngenta Teamspace.

Database

Upload of data via Team space

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File Edit View Process Analysis Tools Database Options Windows ACD/Labs Help
Search Delta Assignment Annotation Magnify NL Spectrum Subtract F.Generator Correlation
Organizer...
SYN7190_1_LCMS-IT-TOF_TOF+1422.esp
SYN7190_1_LCMS-IT-TOF_TOF+1422.esp
Relative Intensity (%)
m/z
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521.0045
540.9853
331.2169
272.2064
359.2206
391.9553
174.1351
222.1017
447.3694
476.9919
SYN7190_1_LCMS-IT-TOF_TOF+1422.ESP MASS
min scans
1-ChemSketch 2-Processor 3-Database 4-Structure 5-Search

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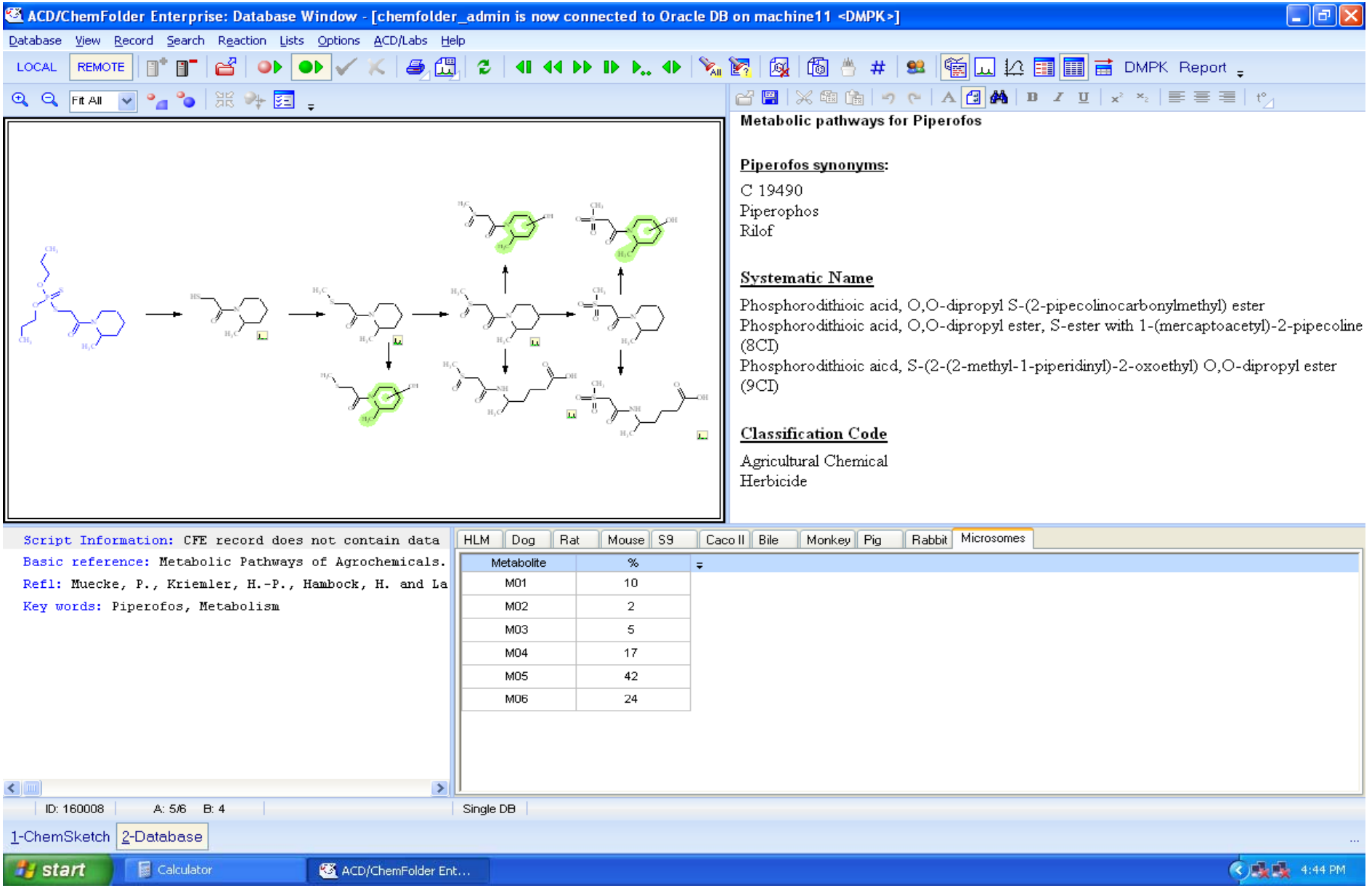
Increasing Efficiency with CROs

- If CROs purchase ChemFolder / SpecDB local (soon Spectrus), then Syngenta would be able to load nd9 and cfe files directly into the database complete with links to metabolites.
- ACD/Labs can arrange this on subscription for CROs.
- Will provide a live searchable database with minimal effort
- Provide Sustainability.
- Save CROs reporting time?

Success Criteria

- Quality of Information .
- Do we capture our spectral data?
- Upload of Biotransformation maps and associated species pathways?
- Roll out with more CRO partners.


ACD/ChemFolder Enterprise: Database Window - [chemfolder_admin is now connected to Oracle DB on machine11 <DMPK>]
Database View Record Search Reaction Lists Options ACD/Labs Help
LOCAL REMOTE
DMPK Report
Fit All
Metabolic pathways for Piperofos
Piperofos synonyms:
C 19490
Piperophos
Rilof
Systematic Name
Phosphorodithioic acid, O,O-dipropyl S-(2-pipecolinocarbonylmethyl) ester
Phosphorodithioic acid, O,O-dipropyl ester, S-ester with 1-(mercaptoacetyl)-2-pipecoline (8CI)
Phosphorodithioic aicd, S-(2-(2-methyl-1-piperidinyl)-2-oxoethyl) O,O-dipropyl ester (9CI)
Classification Code
Agricultural Chemical
Herbicide
Script Information: CFE record does not contain data
Basic reference: Metabolic Pathways of Agrochemicals.
Refl: Muecke, P., Kriemler, H.-P., Hambock, H. and La
Key words: Piperofos, Metabolism
HLM Dog Rat Mouse S9 Caco II Bile Monkey Pig Rabbit Microsomes
Metabolite % M01 10 M02 2 M03 5 M04 17 M05 42 M06 24
ID: 160008 A: 5/6 B: 4 Single DB
1-ChemSketch 2-Database
start Calculator ACD/ChemFolder Ent... 4:44 PM

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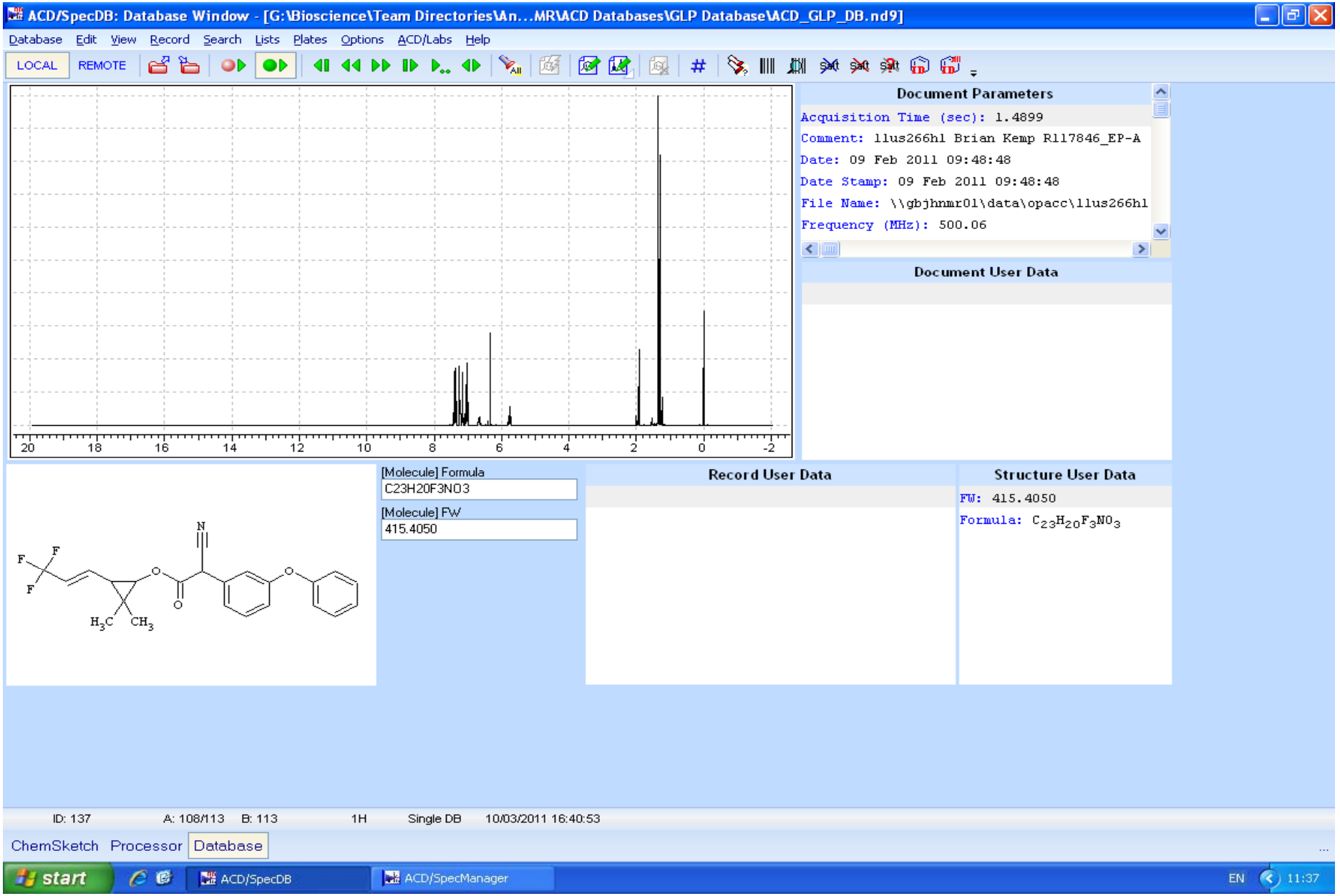
ACD/SpecDB: Database Window - [G:\Bioscience\Team Directories\An...MR\ACD Databases\GLP Database\ACD_GLP_DB.nd9]
Database Edit View Record Search Lists Plates Options ACD/Labs Help
LOCAL REMOTE
20 18 16 14 12 10 8 6 4 2 0 -2
Document Parameters
Acquisition Time (sec): 1.4899
Comment: llus266hl Brian Kemp R117846_EP-A
Date: 09 Feb 2011 09:48:48
Date Stamp: 09 Feb 2011 09:48:48
File Name: \\gbjhnmr01\data\opacc\llus266hl
Frequency (MHz): 500.06
Document User Data
[Molecule] Formula
C23H20F3NO3
[Molecule] FW
415.4050
Record User Data
Structure User Data
FW: 415.4050
Formula: C23H20F3NO3
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ChemSketch Processor Database
start ACD/SpecDB ACD/SpecManager EN 11:37

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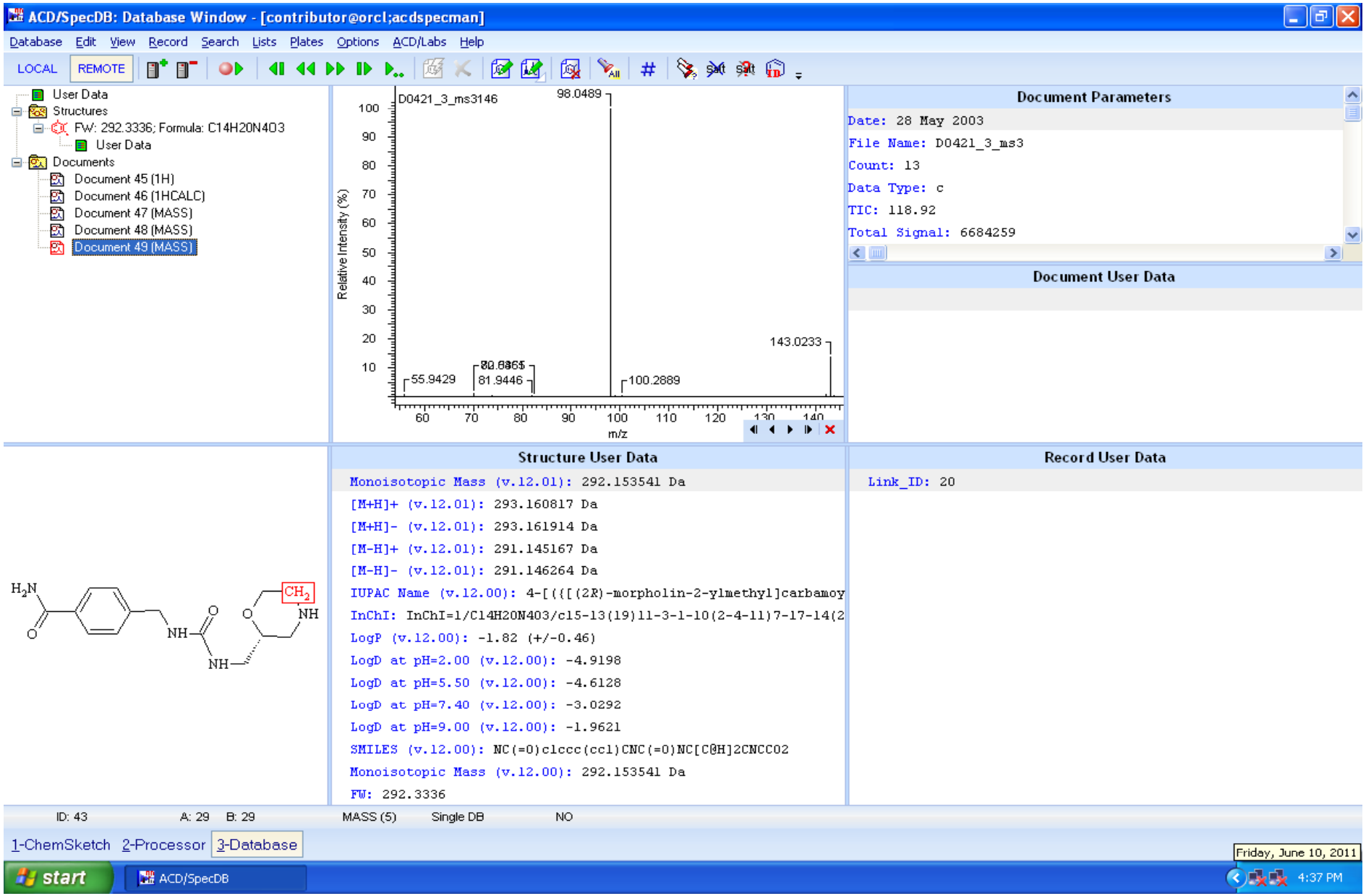
ACD/SpecDB: Database Window - [contributor@orcl;acdspecman]
Database Edit View Record Search Lists Plates Options ACD/Labs Help
LOCAL REMOTE
User Data
Structures
FW: 292.3336; Formula: C14H20N4O3
User Data
Documents
Document 45 (1H)
Document 46 (1HCALC)
Document 47 (MASS)
Document 48 (MASS)
Document 49 (MASS)
D0421_3_ms3146
98.0489
143.0233
55.9429
81.9446
100.2889
Relative Intensity (%)
m/z
Document Parameters
Date: 28 May 2003
File Name: D0421_3_ms3
Count: 13
Data Type: c
TIC: 118.92
Total Signal: 6684259
Document User Data
Structure User Data
Monoisotopic Mass (v.12.01): 292.153541 Da
[M+H]+ (v.12.01): 293.160817 Da
[M+H]- (v.12.01): 293.161914 Da
[M-H]+ (v.12.01): 291.145167 Da
[M-H]- (v.12.01): 291.146264 Da
IUPAC Name (v.12.00): 4-[({[(2R)-morpholin-2-ylmethyl]carbamoy
InChI: InChI=1/C14H20N4O3/c15-13(19)11-3-1-10(2-4-11)7-17-14(2
LogP (v.12.00): -1.82 (+/-0.46)
LogD at pH=2.00 (v.12.00): -4.9198
LogD at pH=5.50 (v.12.00): -4.6128
LogD at pH=7.40 (v.12.00): -3.0292
LogD at pH=9.00 (v.12.00): -1.9621
SMILES (v.12.00): NC(=O)c1ccc(cc1)CNC(=O)NC[C@H]2CNCCO2
Monoisotopic Mass (v.12.00): 292.153541 Da
FW: 292.3336
Record User Data
Link_ID: 20
ID: 43 A: 29 B: 29 MASS (5) Single DB NO
1-ChemSketch 2-Processor 3-Database
Friday, June 10, 2011
start
ACD/SpecDB
4:37 PM

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Data Management Challenges

- Increasing data volumes - storage-extraction of information.
- Data storage over long time.
- Use of data in a multi-location organisation .
- Finding and collating relevant information from multiple sources - NMR, MS, Reports, Spreadsheets.
- Reuse of data- i.e. reprocessing.
- Sharing of data with external partners (CRO's).
- Data Input from CRO's and Syngenta.

Thanks and Acknowledgements

- Syngenta
  - Steve Hadfield - Head of Global Product Metabolism and Analytical Sciences (Sponsor).
  - Norman Sampson - IT incl server support.

- Charles River Laboratories.
  - Rory Mumford
  - Martha Green
  - David MacPherson

- ACD Labs.
  - Peter Russell - Account Manager
  - Ian Peirson Senior Applications Specialist

Bringing plant potential to life