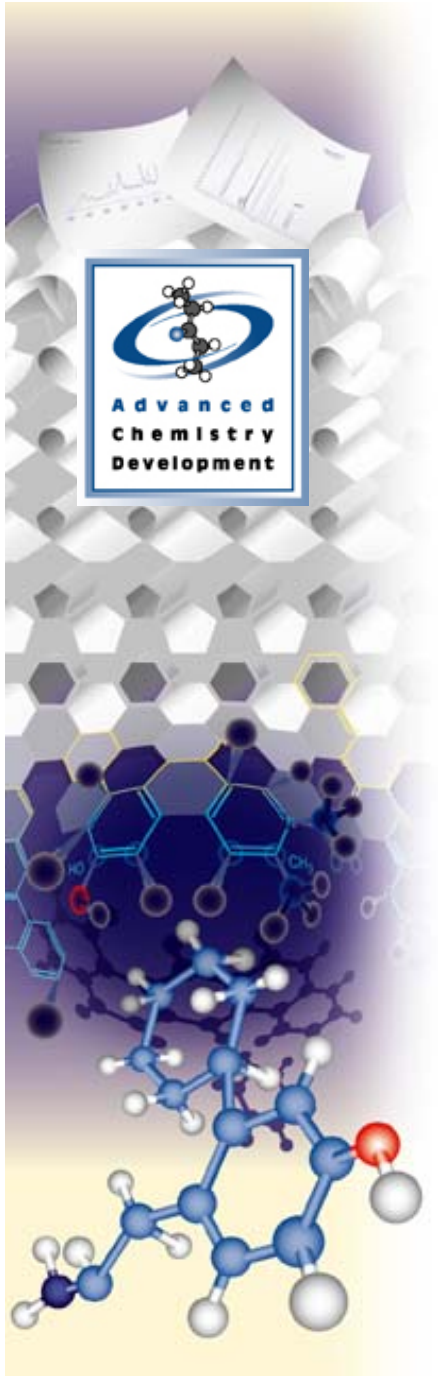


A Complete Solution for Structure Identification

Ryan Sasaki
NMR Technical Marketing Specialist

ACD/Labs' ENC Seminar,
Providence, RI
April 10th, 2005

Advanced Chemistry Development, Inc. (ACD/Labs)

Visionary Software for Scientists

State of the Industry

- Structure identification is not what it used to be
  - Open Access
  - New NMR experiments
  - Electronic databases
- Today's Chemists and Spectroscopists need help!
  - Data bottlenecks exist here

New Options

- Software can open up these bottlenecks
  - Organization, routing and storage of data
  - Easing data interpretation
- Measurable impact on the bottom line!

Verification for Structure Confirmation

- Definition:
  - A measurement of how well a particular structure corresponds to an NMR spectrum
  - This is a very different challenge from Elucidation

Verification Value

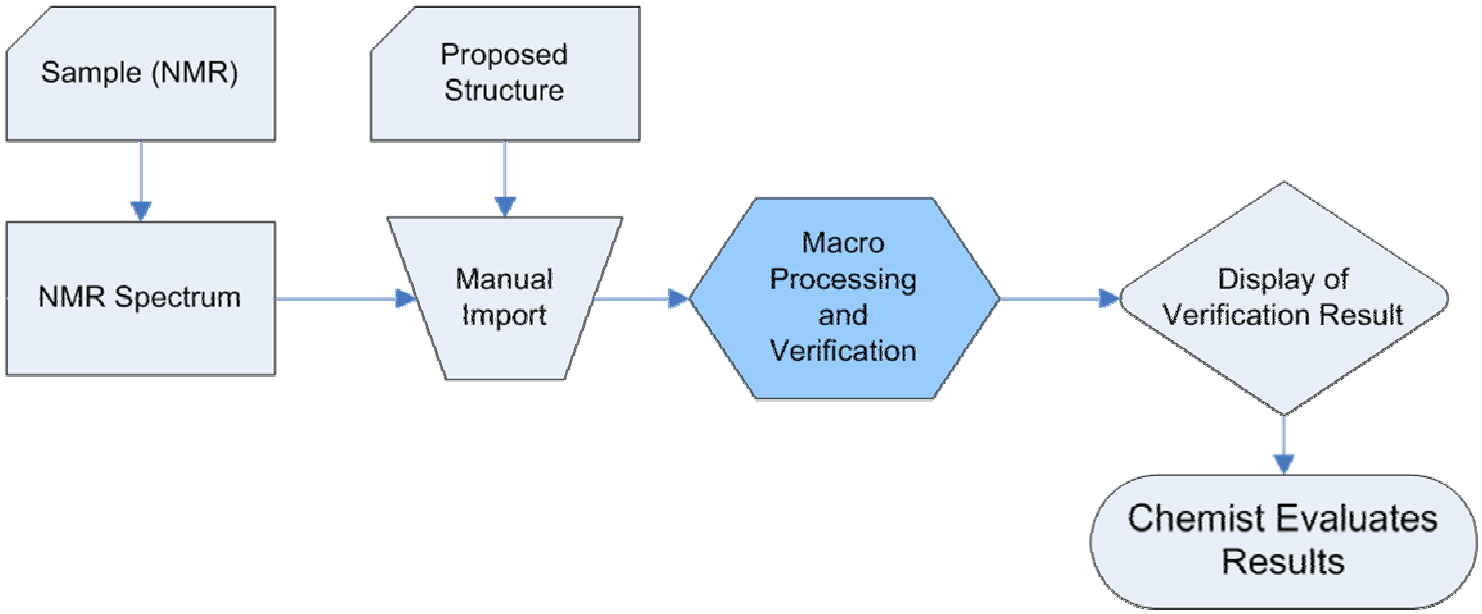
- Assisted spectral verification:
  - Time savings per sample for the Chemist or Spectroscopist
  - Increased accuracy and confidence of assignment
  - Unbiased validation of expert opinion

3 Verification Workflows

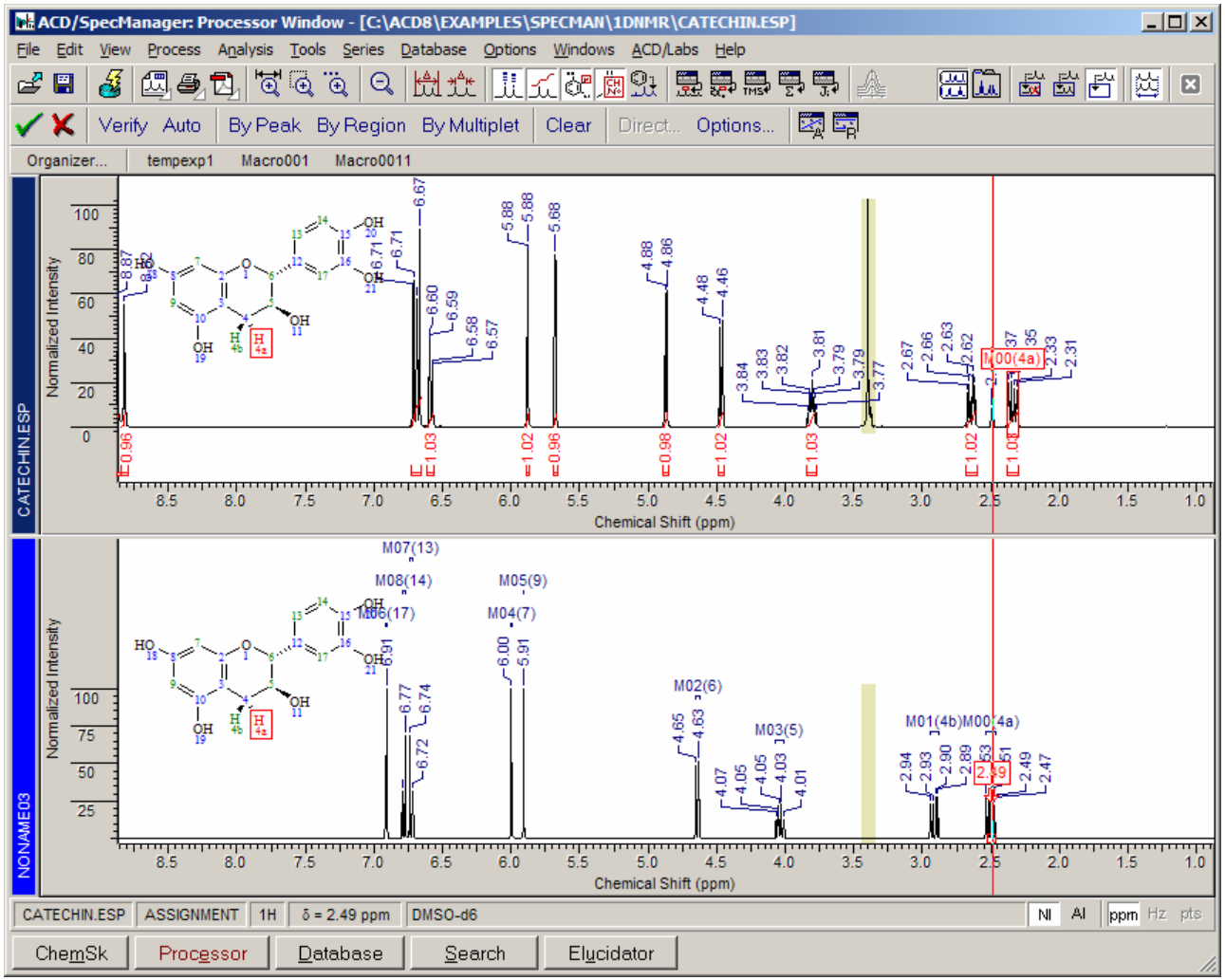
- Desktop Verification
  - For individual Chemists and Spectroscopists
- Batch Verification
  - For Spectroscopists
- Automated Verification
  - For walk-up NMR instruments

Desktop Verification

- One at a time
- Interactive procedure



Assignment Help



Visionary Software for Scientists

Spectroscopy • Chromatography • PhysChem • Chemical Naming • Drawing • Databasing • Enterprise Solutions

Desktop Verification

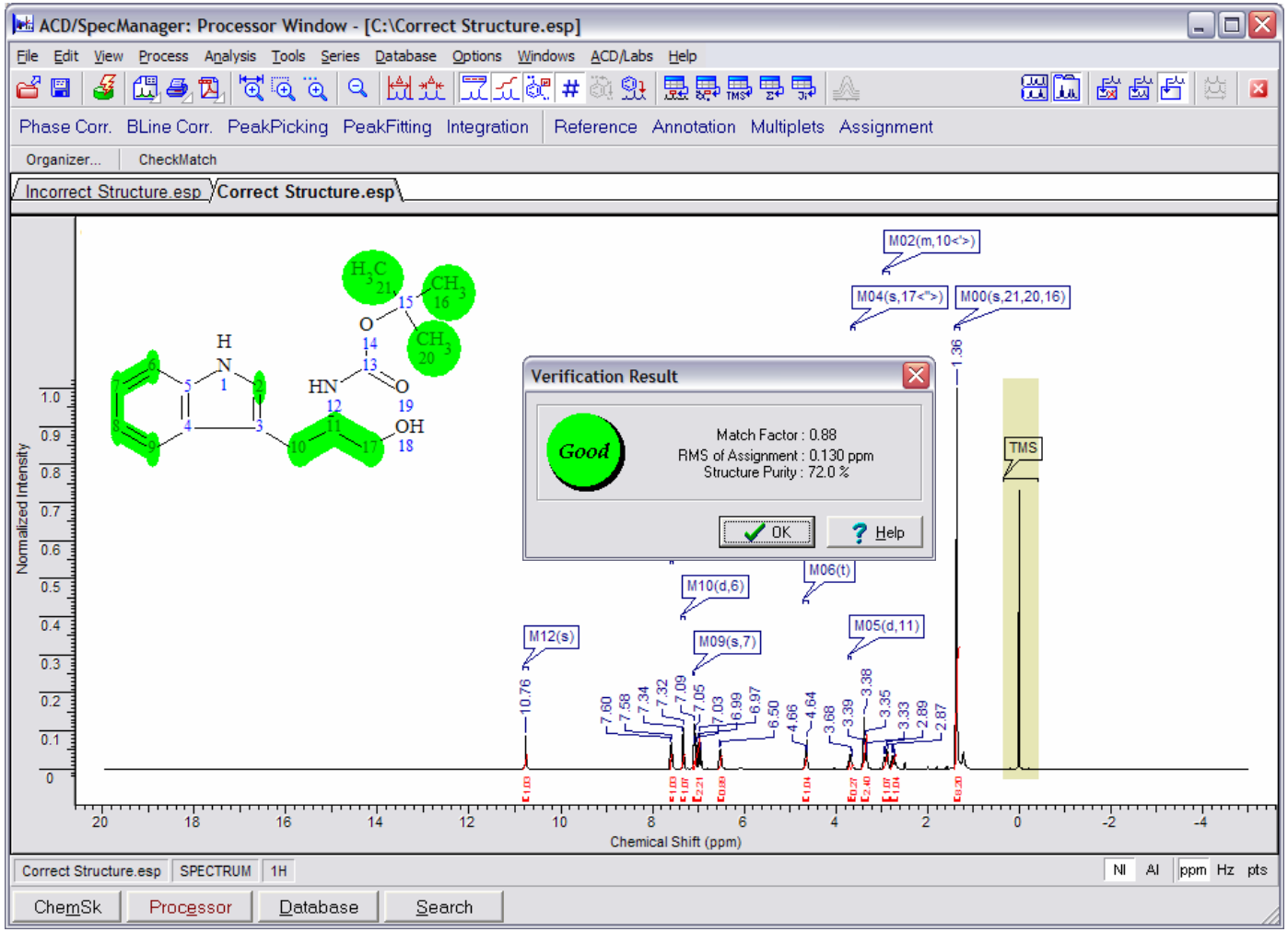
Verification Introduction

Workflows
- Desktop
- Batch
- Walk-up

Validation

Elucidation

Summary



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2D NMR Overlay

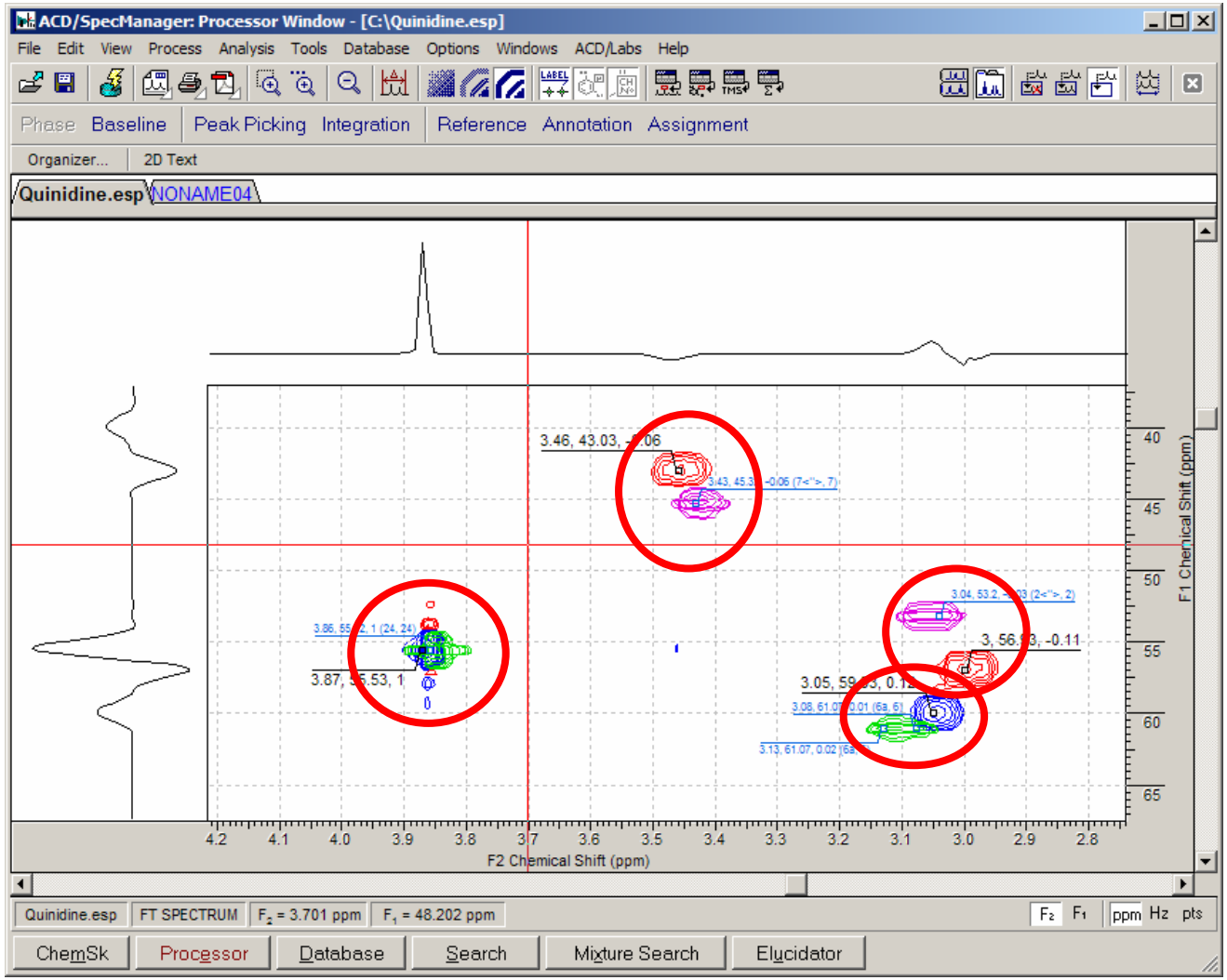
Verification Introduction

Workflows
- Desktop
- Batch
- Walk-up

Validation

Elucidation

Summary



Visionary Software for Scientists

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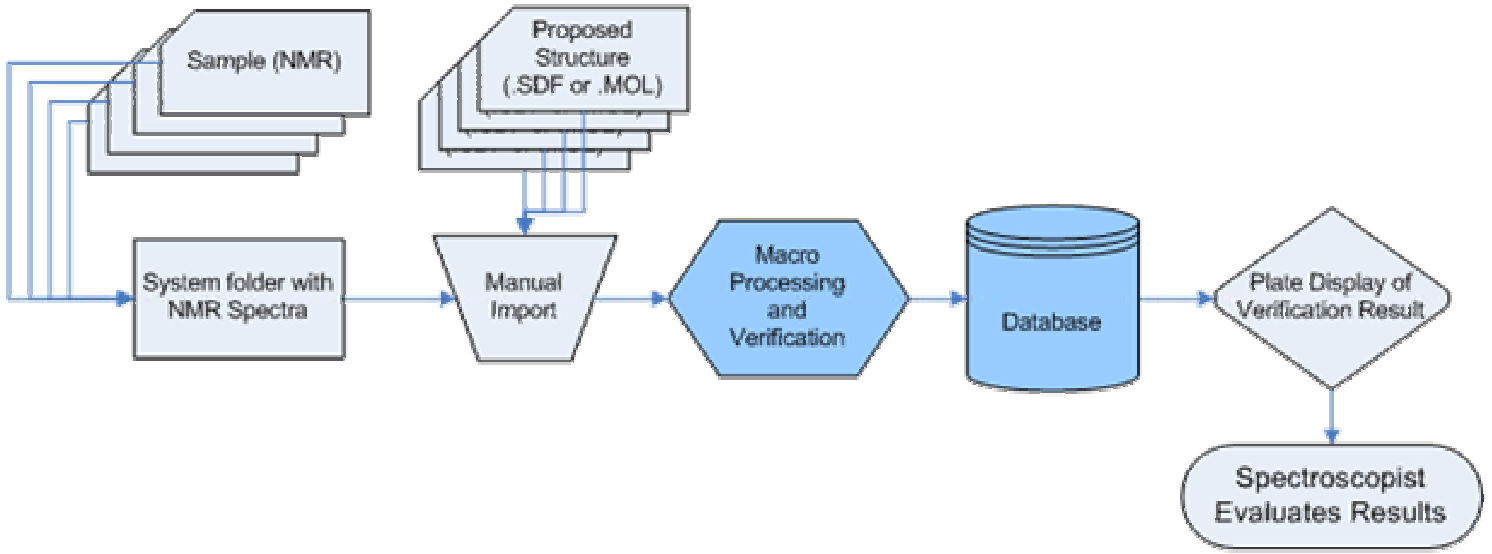
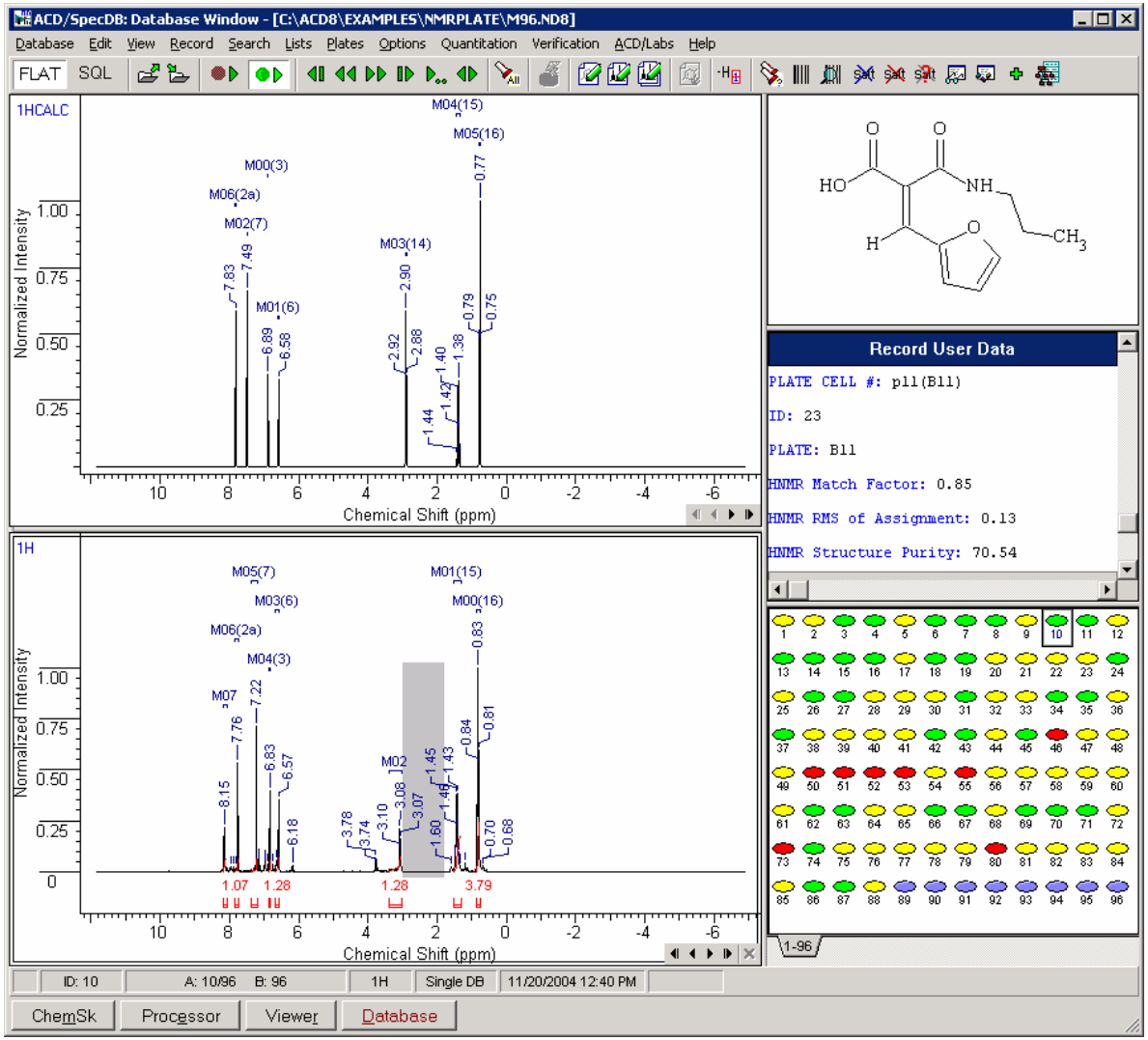
Batch Verification



- Plates of data
  - Related or Non-related structures
- Interactive Batch workflow
  - High-throughput processing
  - High-throughput evaluation

Batch Verification

- Verification Introduction
- Workflows
  - Desktop
  - Batch
  - Walk-up
- Validation
- Elucidation
- Summary



Visionary Software for Scientists

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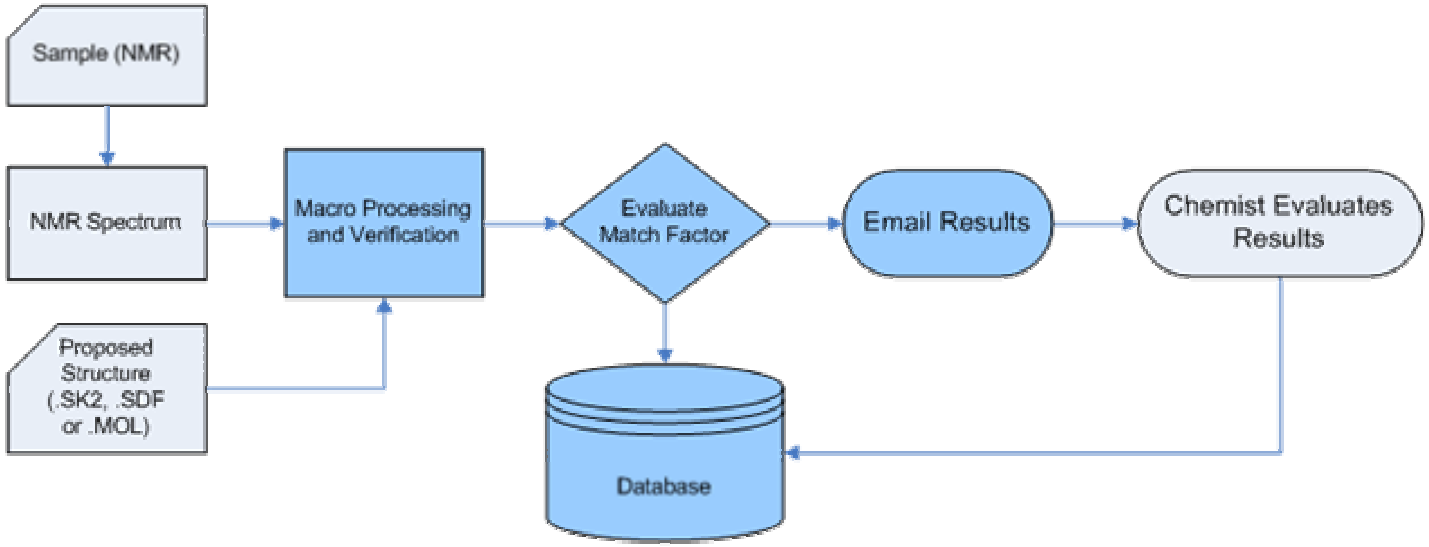
Automated Verification

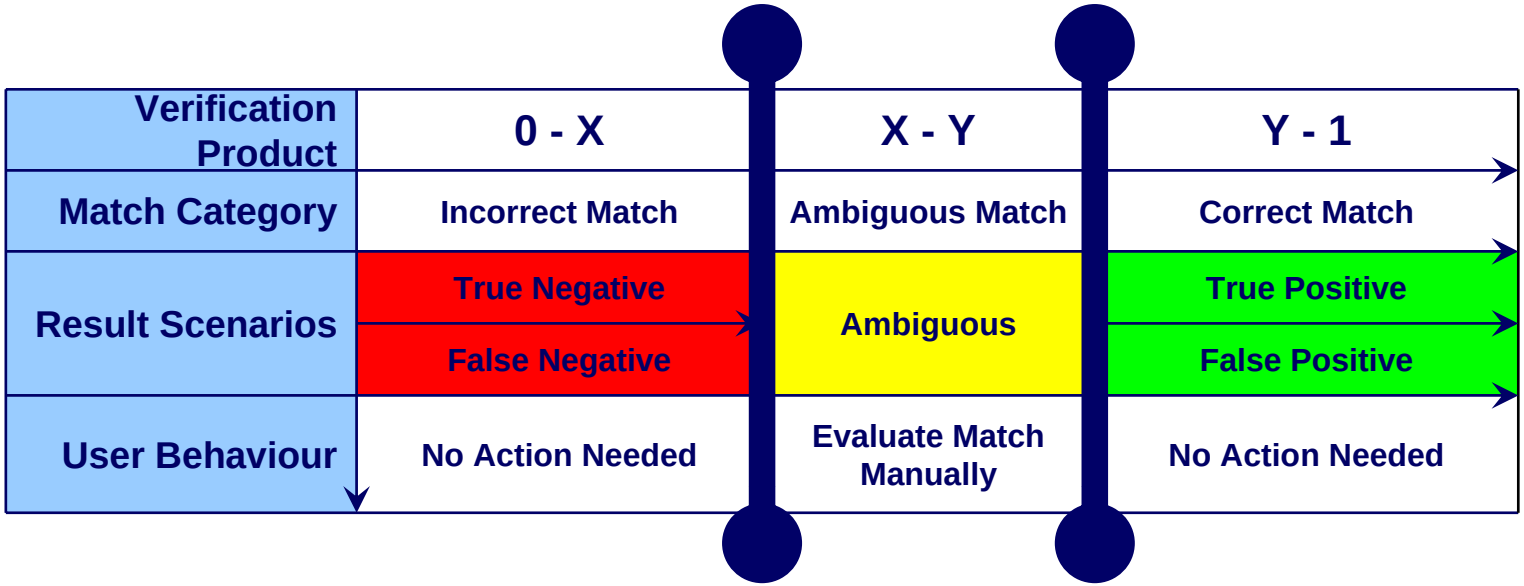


- Automatic spectrum retrieval
- Automatic spectrum preparation
- Automatic spectrum evaluation
- Automatic result output

Verification Validation

- Extensive testing has been done
  - On all different types of data
  - 1D and 2D
  - Large and small datasets
  - Correct and incorrect matches

Performance Metrics

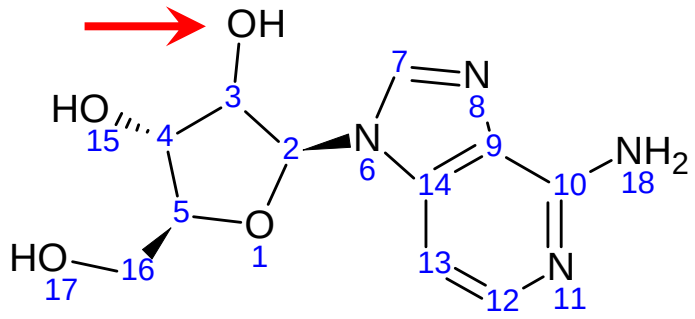
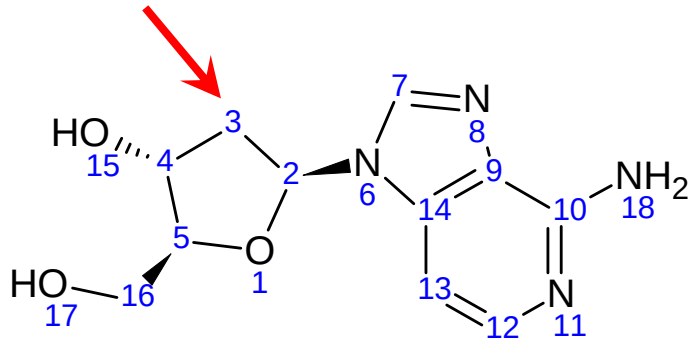


- 3 match categories
- 5 result scenarios
  - Only ‘Ambiguous’ results need manual evaluation

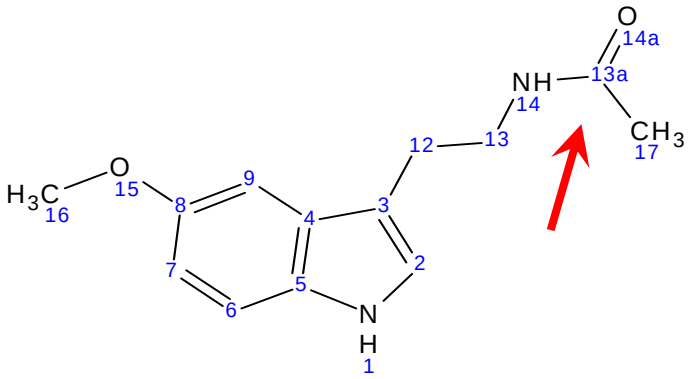
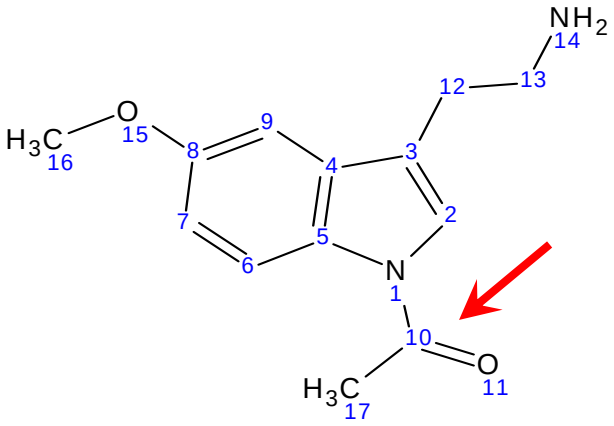
Test Validation

- Set of structures purposely incorrect
  - ‘Blind’ to validation team
  - Substituted for structures that are similar but distinguishable

Test Structures

Structure	Correct	Match Factor	Structure Purity	RMS, ppm
	Yes	0.93	62%	0.08
	No	0.41	69%	0.58

Test Structures

Structure	Correct	Match Factor	Structure Purity	RMS, ppm
	Yes	0.97	90%	0.09
	No	0.74	71%	0.17

Combining 1D and 2D Verification

- More than the sum of the parts
  - 1D is used as a filter
    - If VP>85, match is correct
  - 2D is used as a filter
    - If carbon match<0.3, match is incorrect
  - Combination of both is also used in evaluation
    - Average of both matches

Test Results

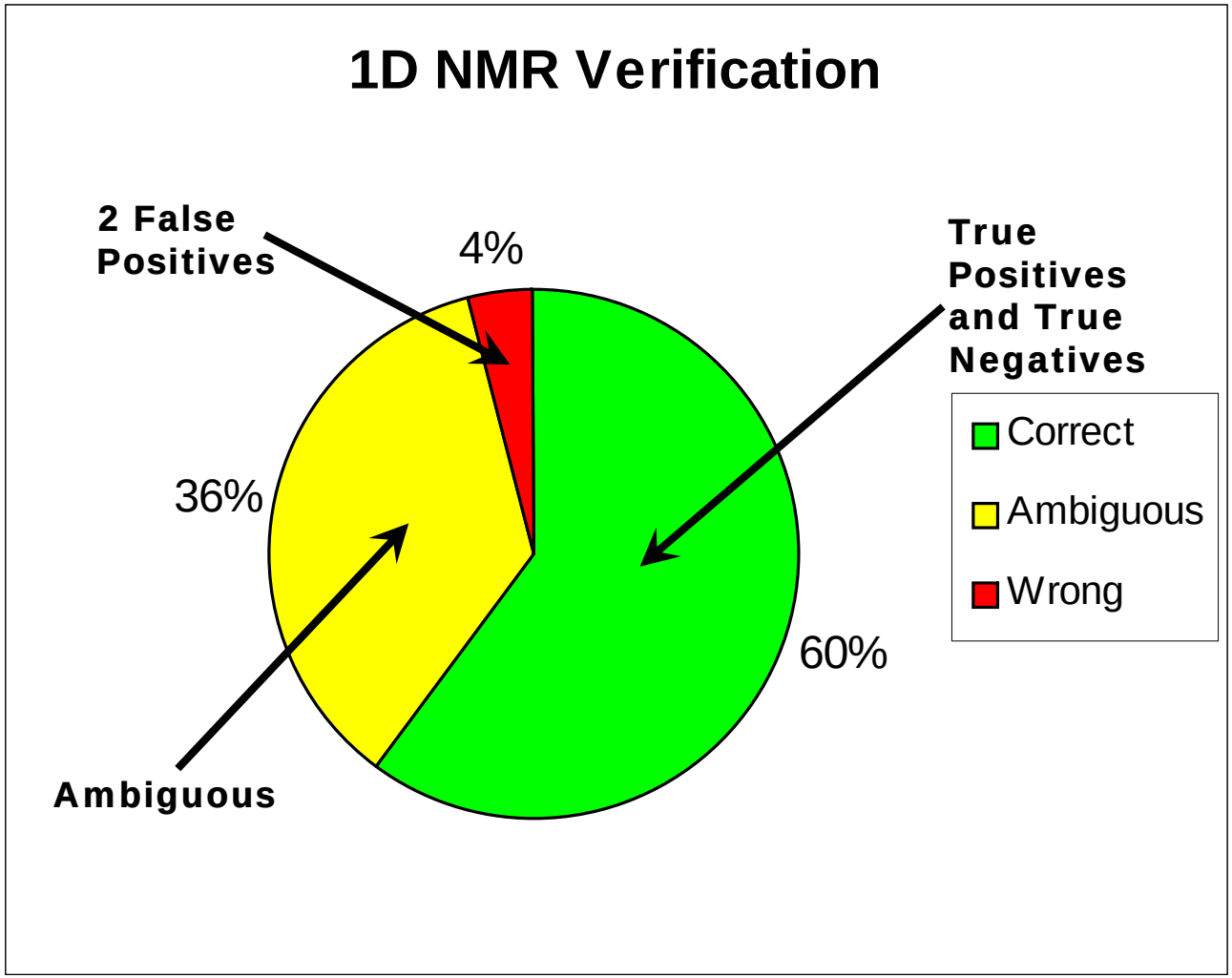
	1D Verification Result				2D Verification Result				Combination Result		
#	HNMR RMS of Assignment	HNMR Match Factor	HNMR Structure Purity	VP	Spectrum MF (1H, F2)	Structure MF (1H, F2)	Spectrum MF (13C, F1)	Structure MF (13C, F1)	Average 1H Match	Average 13C Match	Complex Match
3	0.09	0.93	95.4	88.7	0.42	0.76	0.46	0.46	0.59	0.46	0.89
7	0.10	0.93	91.3	84.9	0.23	0.94	0.58	0.88	0.58	0.73	0.85
14	0.12	0.85	90.3	76.7	0.15	0.84	0.52	0.67	0.50	0.59	0.77
22	0.19	0.84	90.0	75.6	0.19	0.64	0.64	0.64	0.41	0.64	0.68
10	0.14	0.90	89.3	80.4	0.16	0.32	0.61	0.32	0.24	0.46	0.80
6	0.12	0.89	96.0	85.5	0.69	0.92	0.89	0.89	0.81	0.89	0.85
12	0.18	0.81	96.9	78.5	0.30	0.51	0.77	0.57	0.41	0.67	0.79
9	0.16	0.88	93.0	81.8	0.16	0.27	0.59	0.29	0.21	0.44	0.82
1	0.14	0.93	99.3	92.4	0.52	0.86	0.88	0.88	0.69	0.88	0.92
17	0.16	0.81	90.0	72.9	0.23	0.00	0.79	0.11	0.12	0.45	0.54
20	0.18	0.76	88.3	67.1	0.19	0.55	0.72	0.64	0.37	0.68	0.68
13	0.19	0.81								0.83	0.77
8	0.13	0.88								0.74	0.85
18	0.11	0.76								0.80	0.77
16	0.18	0.77								0.70	0.71
25	0.37	0.56								0.40	0.43
24	0.40	0.55	88.8	48.8	0.24	0.00	0.17	0.00	0.12	0.09	0.22
26	0.32	0.59	78.8	46.5	0.27	0.54	0.76	0.65	0.41	0.71	0.63
11	0.18	0.83	95.9	79.6	0.14	0.49	0.51	0.41	0.32	0.46	0.80
5	0.14	0.88	98.2	86.4	0.15	0.51	0.63	0.63	0.33	0.63	0.86
15	0.24	0.80	93.7	74.9	0.36	0.81	0.48	0.48	0.59	0.48	0.57
4	0.09	0.97	90.0	87.3	0.20	0.92	0.64	0.86	0.56	0.75	0.87
21	0.29	0.68	89.0	60.5	0.28	0.74	0.36	0.36	0.51	0.36	0.44
23	0.39	0.55	96.7	53.2	0.26	0.00	0.92	0.00	0.13	0.46	0.48
19	0.27	0.75	94.5	70.9	0.26	0.48	0.79	0.57	0.37	0.68	0.69

CORRECT MATCHES

	1D Verification Result				2D Verification Result				Combination Result		
#	HNMR RMS of Assignment	HNMR Match Factor	HNMR Structure Purity	VP	Spectrum MF (1H, F2)	Structure MF (1H, F2)	Spectrum MF (13C, F1)	Structure MF (13C, F1)	Average 1H Match	Average 13C Match	Complex Match
20	0.58	0.40	69.0	27.6	0.23	0.46	0.58	0.28	0.34	0.43	0.38
21	0.43	0.54	78.4	42.3	0.05	0.15	0.02	0.02	0.10	0.02	0.16
23	0.21	0.61	66.7	40.7	0.05	0.31	0.11	0.49	0.18	0.30	0.34
13	0.18	0.86	96.4	82.9	0.23	0.64	0.36	0.36	0.44	0.36	0.83
2	0.17	0.81	60.5	49.0	0.19	0.10	0.44	0.08	0.14	0.26	0.34
4	0.91	0.34	96.0	32.6	0.46	0.48	0.50	0.23	0.47	0.37	0.35
17	0.31	0.67	96.9	64.9	0.40	0.52	0.42	0.21	0.46	0.31	0.43
18	0.48	0.42	85.7	36.0	0.03	0.08	0.12	0.09	0.05	0.11	0.19
26	0.28	0.79	99.3	78.5	0.32	0.79	0.64	0.64	0.55	0.64	0.78
19	0.29	0.47	83.3	39.1	0.18	0.12	0.40	0.02	0.15	0.21	0.27
22	0.42	0.39								0.35	0.33
7	0.23	0.74								0.43	0.50
1	0.81	0.21								0.47	0.36
24	1.01	0.10								0.42	0.28
5	0.72	0.37								0.25	0.28
3	0.72	0.41								0.10	0.19
11	0.75	0.31	88.8	27.5	0.07	0.00	0.49	0.00	0.04	0.25	0.26
6	0.48	0.47	96.5	45.4	0.19	0.00	0.58	0.00	0.10	0.29	0.34
15	0.19	0.63	41.3	26.0	0.09	0.11	0.26	0.05	0.10	0.16	0.19
9	0.45	0.47	89.3	42.0	0.10	0.32	0.16	0.37	0.21	0.27	0.32
10	0.32	0.73	88.2	64.4	0.34	0.77	0.56	0.74	0.56	0.65	0.65
14	0.31	0.64	89.8	57.5	0.10	0.34	0.39	0.39	0.22	0.39	0.45
25	0.30	0.66	82.6	54.5	0.16	0.47	0.18	0.18	0.32	0.18	0.30
12	0.79	0.64	96.7	61.9	0.31	0.00	0.77	0.00	0.15	0.39	0.46
16	0.25	0.68	94.5	64.3	0.18	0.22	0.53	0.28	0.20	0.41	0.49

INCORRECT MATCHES

Test Summary



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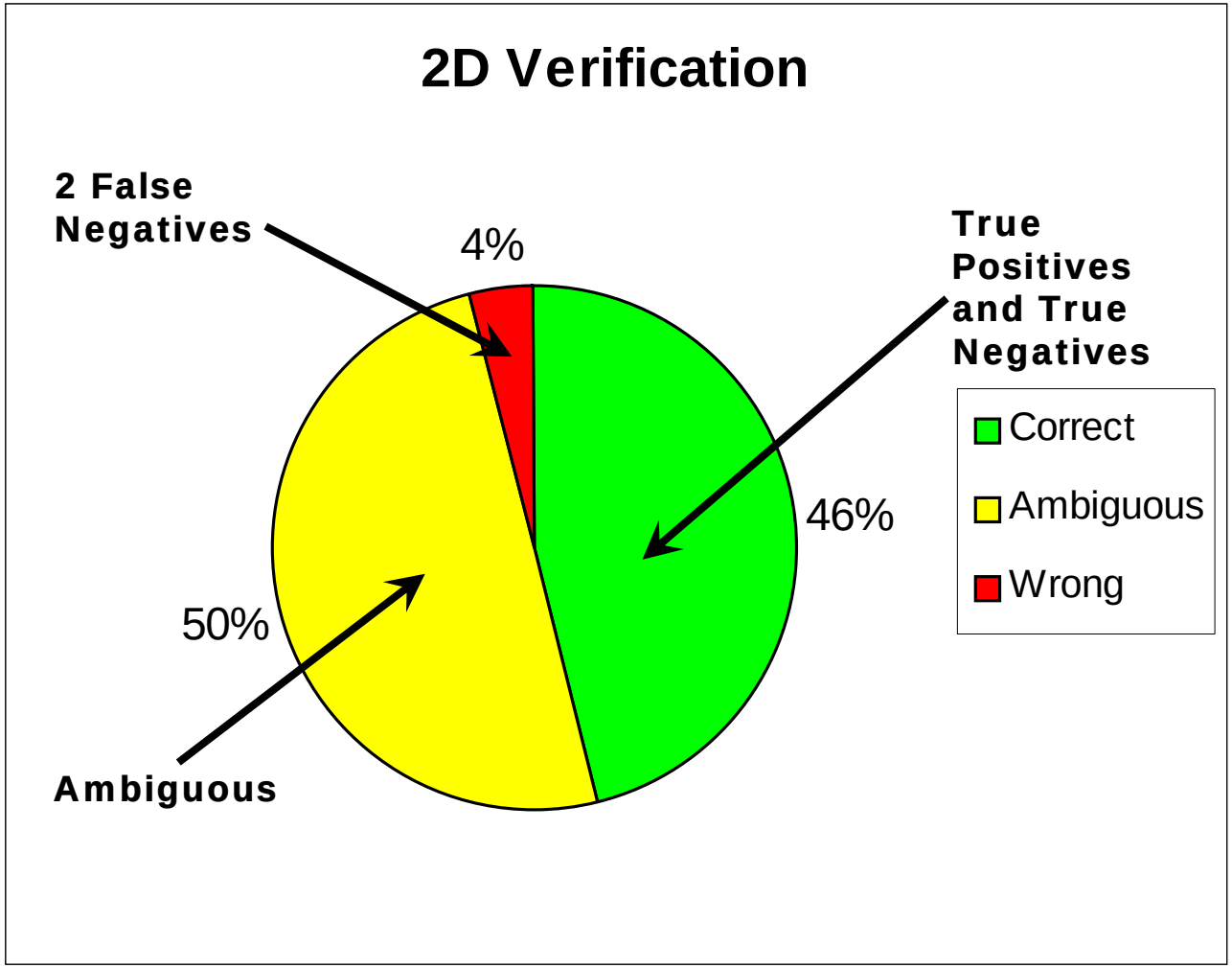


Test Summary

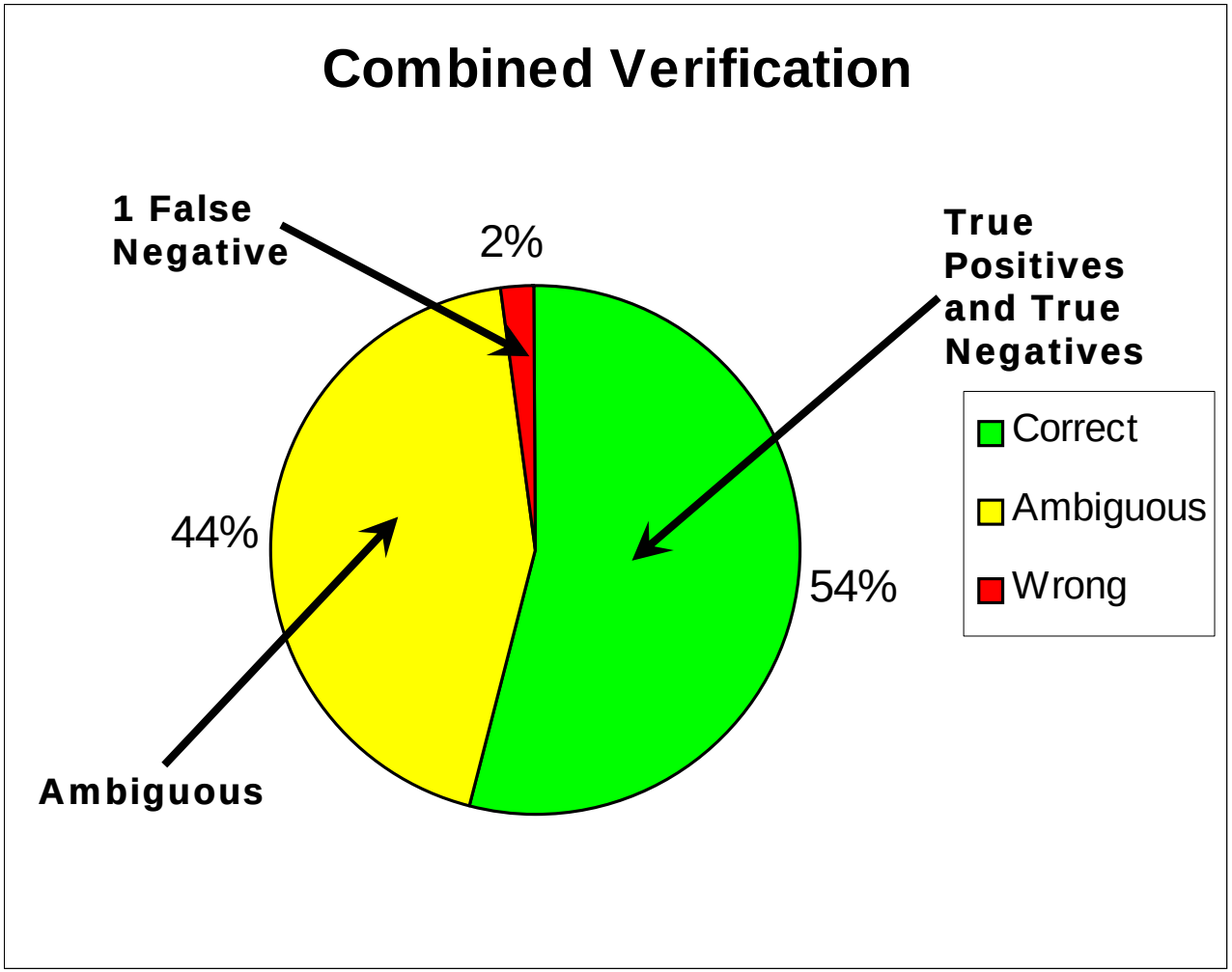
Verification Introduction

Workflows
- Desktop
- Batch
- Walk-up

Validation

Elucidation

Summary



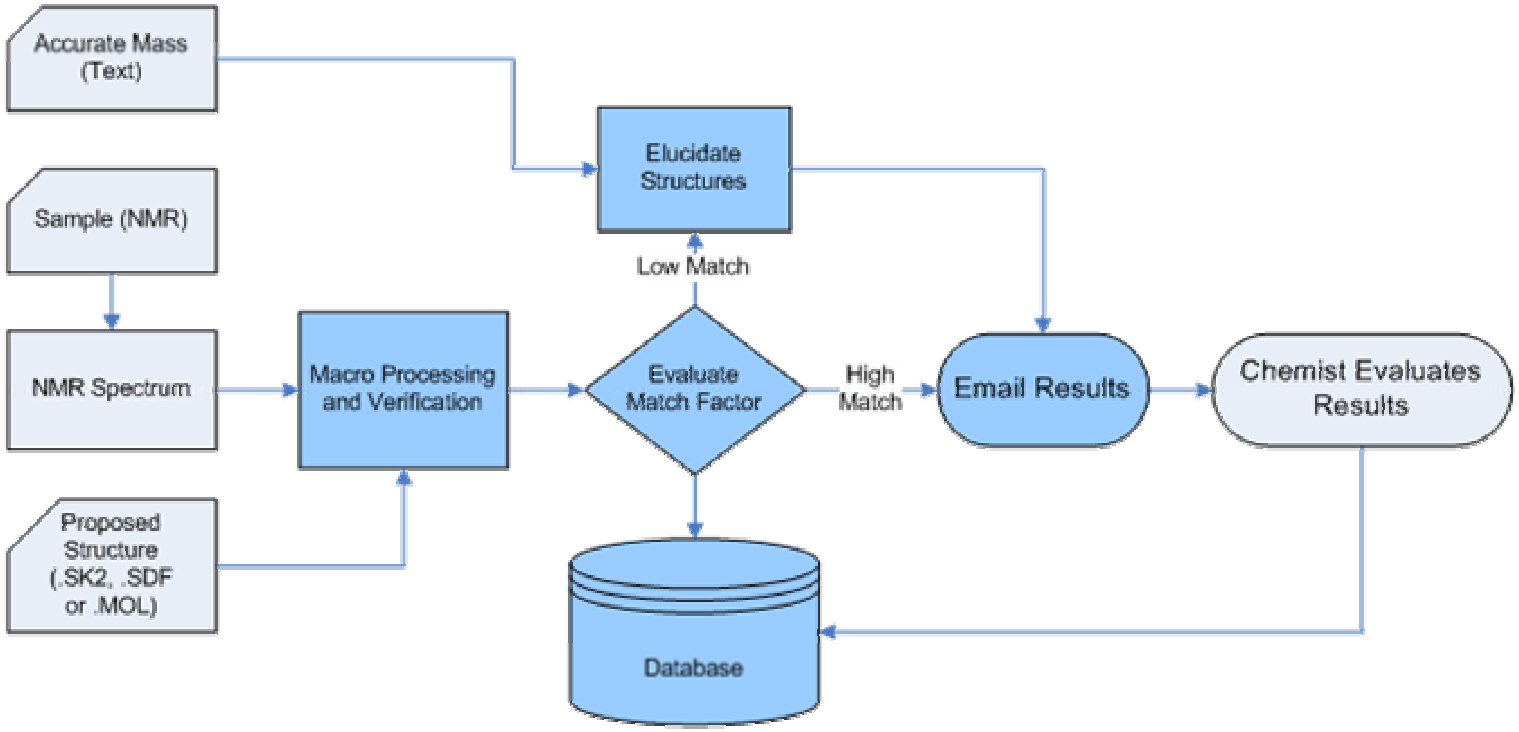
Summary Results

- When using 1D and 2D NMR
  - At least 54% of all spectrum structure matches can be automatically evaluated
  - Minimum 54% time savings

Verification: The First Step

- What next?
  - If correct: move on
  - If incorrect: evaluate manually
    - Can the software still help?
      - Absolutely
- After evaluation, elucidation is a logical next step
  - Can be executed automatically based on verification result

Verification and Elucidation Workflow



- Elucidation is automated just like Verification

Summary

- Verification is flexible, accurate and automated
- Accuracy has been validated
- Verification is not the end:
  - Results communication
  - Automated evaluation
  - Elucidation

Acknowledgements

- Tim Spitzer, GSK
- Sergey Golotvin, ACD/Labs
- Tony Williams, ACD/Labs
- Brent Lefebvre, ACD/Labs
- Arvin Moser, ACD/Labs