Data Integrity
with Varian Star Workstation

by:

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Computers have become mainstays in the analytical laboratory, especially with chromatographic instruments. They have become data collectors, report generators, system controllers and error monitors. These beneficial tools allow final analytical results to be generated from the detector signal, they permit complete control of the experimental conditions and they can monitor overall system performance. Improved productivity, faster sample turnarounds, better accuracies for results, and easier, more foolproof operations are all gains made over old manual approaches.

However, without some criteria set for monitoring the quality and integrity of the final result, improper use of these computers can yield very inaccurate answers. And without adequate safeguards, opportunities can exist for possible mischief, such as altering sample labeling and archived notes, and even loss of raw data files from accidental overwriting.

The US Food and Drug Administration has been very aggressive in establishing controls to maintain integrity of laboratory data. They have outlined requirements in several sections of the *US Code of Federal Regulations (CFR)*, 4-1-00 Edition (available on-line at *www.access. gpo.gov/nara/cfr*), including Food and Drug Administration Department of Health and Human Services Title 21, Chapter I, Part 11, Subpart B, and Title 21, Chapter I, Part 58, Subpart G. A summation is provided in CFR, Title 21, Part 11 Subpart B, § 11.10 –

> *"**Persons who use closed systems** [environment in which system access is controlled by persons who are responsible for the content of electronic records] **to create, modify, maintain, or transmit electronic records shall employ procedures and controls designed to ensure… that the signer cannot readily repudiate the signed record as not genuine."***

Computers can generate results very quickly and very massively; many numbers can be generated that can overwhelm the abilities of the operator to make assure their accuracies and pertinence. Employing a workstation that possesses built-in quality checks can quickly validate this massive data. And ensuring the proper allocations of areas with easy-to-understand algorithms eliminates a tedious manual review of chromatograms and the manual reassignment of areas.

Over the generations of data systems and workstations from Varian (including the CDS111, Vista 401, DS654 and currently Star), Varian has always made strong efforts to protect the integrity of generated results. Varian Star Workstation Version 5.5 is a culmination of those historical efforts and adaptations of new protocols from federal and industry standards, including GLP and ISO9000. The following outlines several of the features in the Varian Star Workstation manifested toward the lofty goal of maintaining data integrity.

This monograph merely lists features available in the Star Workstation and does not include how to accomplish the deeds. The operator is presumed to be knowledgeable enough with the Star Workstation or is willing to explore menus and help screens within the Star Workstation to locate the features from the hints and displays provided.

CFR, Title 21, Part 58 Subpart G, § 58.130 (e) –

"Any change in automated data entries shall be made so as not to obscure the original entry…"

1. **No** Overwriting of Data Files. Incremented extension XXX is automatically added to yield a unique label if the new file name matches a previous file. The original file cannot be obscured.

| Name	Size	Type	Modified
default sample	16KB	Star Workstation Data File	11/9/1999 10:33 AM
default sample001	17KB	Star Workstation Data File	11/9/1999 10:35 AM
default sample002	17KB	Star Workstation Data File	11/9/1999 10:36 AM
default sample003	17KB	Star Workstation Data File	11/9/1999 10:38 AM
default sample004	15KB	Star Workstation Data File	11/9/1999 10:39 AM

2. **Cannot** Change Sample ID. Once ID is assigned at original data collection, it cannot be altered later and, therefore, cannot be obscured.

```
Title       : Test Run
Run File    : C:\SaturnWS\GCExamples\Cal_3.run
Method File : C:\star\examples\Is_examp.mth
Sample ID   : 80.0 NP

Injection Date: 12/25/1992 3:58 AM    Calculation Date: 3/26/1998 12:13 PM
```

3. **Cannot** Change Date/Time of Injection. Once the Injection Date/Time are recorded, they cannot be altered later and, therefore, cannot be obscured.

4. **Cannot** Alter Log Files. Message, Configuration, Fraction (LC), Run, Revision, Stream Selector (SSV) and Error Logs are automatically generated by Star to document operations within the Workstation. These files can be printed, but cannot be altered later; therefore, they cannot be obscured.
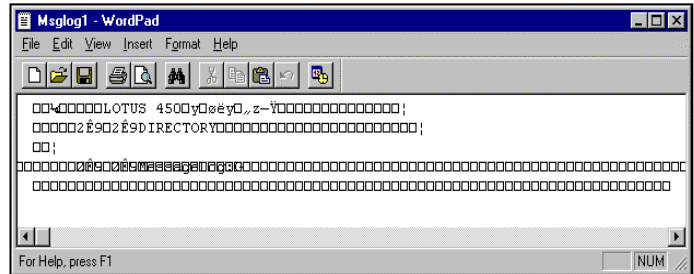

5. **Cannot** Change Sample Notes - in data file after run is performed; they can be appended with Recalc Notes.

CFR, Title 21, Part 58 Subpart G, § 58.63 (c) –

"Written records shall be maintained of all inspection, maintenance, testing, calibrating, and/or standardizing operations"

6. **All Calibration Data Is Archived With Every Raw Data File.** Details on each standard can be recovered from the data file <u>without</u> an undocumented link to a separate computation method that could have been altered since the original run.
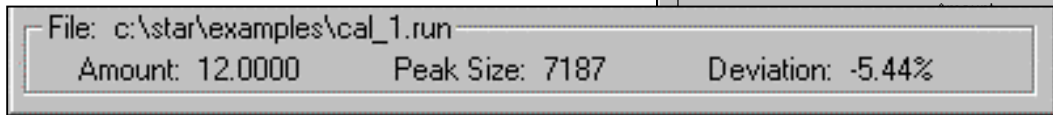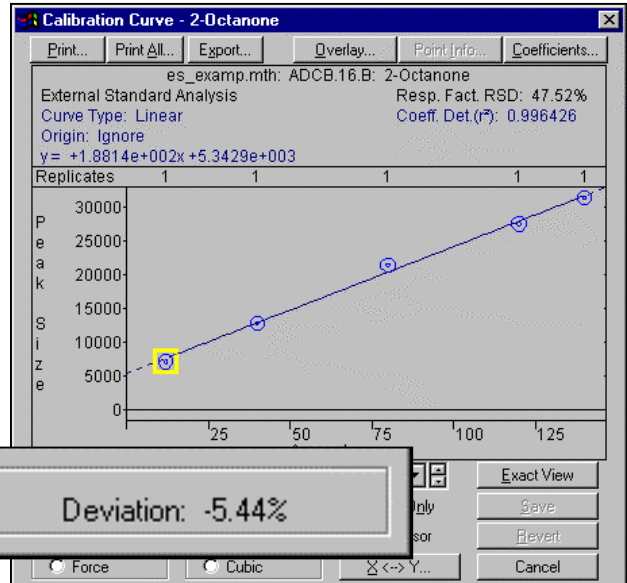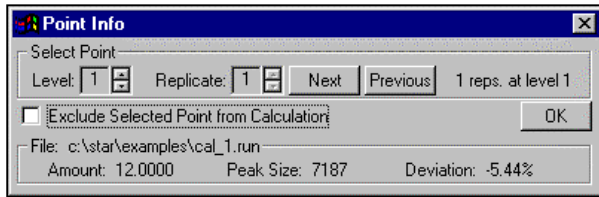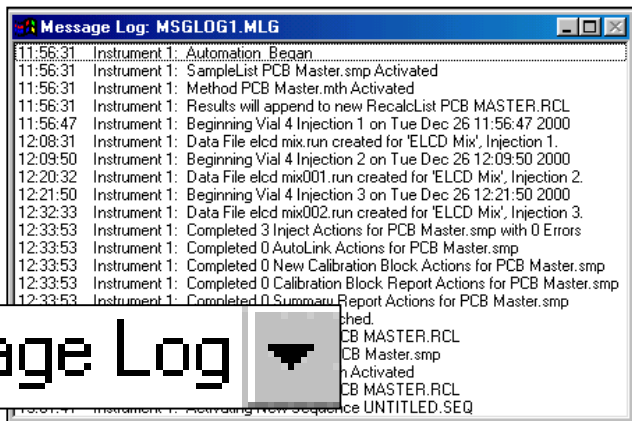

7. **Instrument Maintenance and Repairs Can Be Documented Within Module Notes**. These user-entered notes are saved with every raw data file and cannot be altered later.
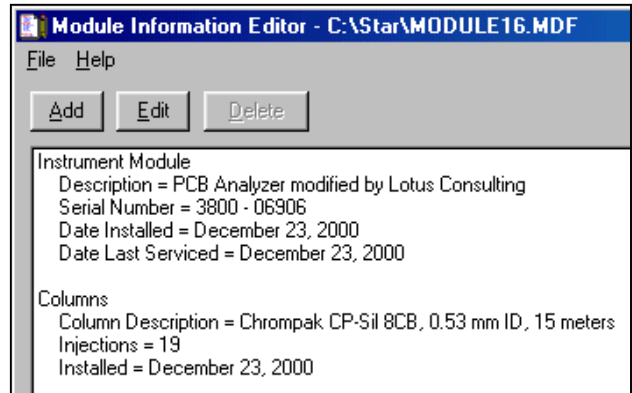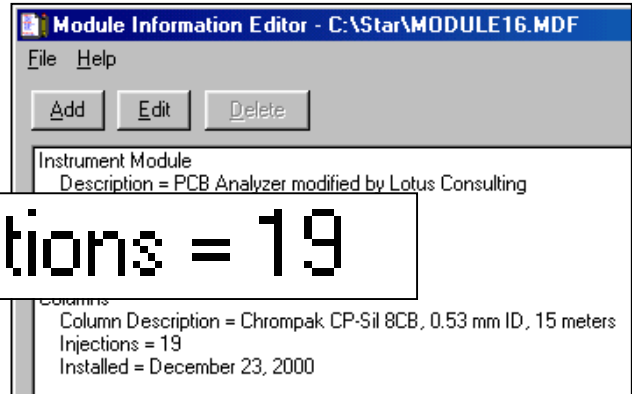

8. **Message Log Contains Complete Listing Of System Operations**, including calibration sequence and sample runs. This log can be printed automatically at completion of sequence operations.

9. **Injection Counter in Module Notes** provides automatic notification for routine maintenance – for example, septum replacement or column regeneration or column replacement

Module Information Editor - C:\Star\MODULE16.MDF

File Help

[Add] [Edit] [Delete]

Instrument Module
    Description = PCB Analyzer modified by Lotus Consulting

Injections = 19

Columns
    Column Description = Chrompak CP-Sil 8CB, 0.53 mm ID, 15 meters
    Injections = 19
    Installed = December 23, 2000

10. **Instrument Run Log Documents Instrument Operating Conditions**, even changes made during run – a great assistance in method development. Example run was originally made in 1992, and all GC conditions employed then can be recovered today. Conditions employed to generate data can be verified for compliance with standard operating procedures for the laboratory.
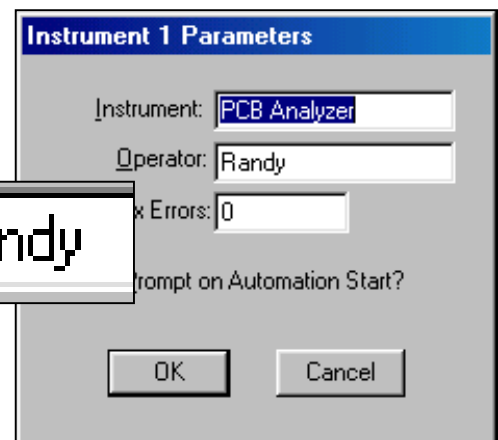
```
3400 GC Event Log:
    0.00   Change in Run Status : INJECT
    0.00   Initial Detector B Type : FID
    0.00   Initial Detector B Attenuation : 8
    0.00   Initial Detector B Range : 11
    0.00   Initial Detector B Autozero : YES
    0.00   Initial Column Temperature (degrees C) : 70
    0.00   Initial Injector Temperature (degrees C) : 250
    0.00   Initial Detector Temperature (degrees C) : 250
    0.00   Initial Auxiliary Temperature (degrees C) : 250
    0.01   Initial Pressure A (psi) : 15.5
    0.01   Initial Flow A (ml/minute) : 3.7
    0.04   AutoSampler Volume (ul) : 2.0
    0.04   Start Column Temperature Ramp (degrees C/minute) : 10.0
    0.13   Injection Residence Time (minutes) : 0.10
   13.01   End Column Temperature Ramp (degrees C) : 200
   15.00   Change in Run Status : END
```

CFR, Title 21, Part 58 Subpart G, § 58.130 (e) –

"In automated data systems, the individual responsible for direct data input shall be identified at the time of data input"

11. **Automatic Prompt for Operator Name at Start of Data Collection.** Entry for "Operator" is documented on every report in that sequence.

Instrument 1 Parameters

Instrument: PCB Analyzer

Operator: Randy

x Errors: 0

Operator: Randy

Prompt on Automation Start?

[OK] [Cancel]

```
Method File : C:\My Documents\Brochure
Sample ID   : ELCD Mix

Injection Date: 12/26/2000 1:36 PM     Calculation Date: 1/5/

Operator    : Randy              Detector Type: ADCB (1 V
Workstation:                     Bus Address  : 16
Instrument : PCB Analyzer        Sample Rate  : 10.00 Hz
Channel    : A = ELCD A          Run Time     : 3.198 min
```

CFR, Title 21, Part 58 Subpart G, § 58.190 (b) –

"Raw data… may be retained elsewhere provided that the archives have special reference to those other locations."

12. **StarFinder Documents Location of Archived Files**. When data is transferred off to a storage device, its location can be recorded in StarFinder.
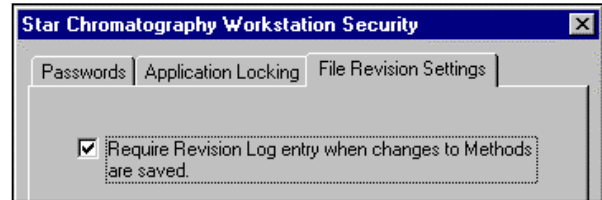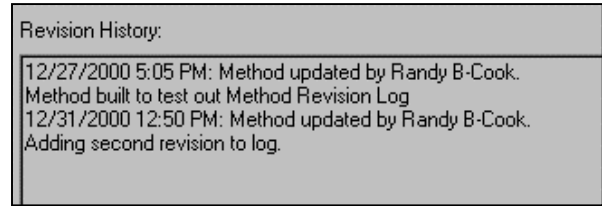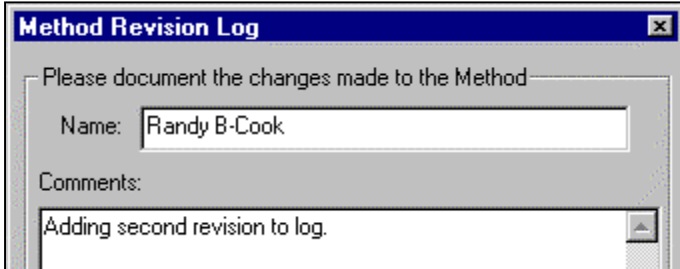

CFR, Title 21, Part 58 Subpart G, § 58.81 (a) –

"A testing facility shall have standard operating procedures in writing setting forth nonclinical laboratory study methods… All deviations...shall be authorized by the study director and shall be documented in the raw data.

13. **Methods Can Be Set to Require a Password Prior to Saving –** to prohibit unauthorized changes to methods.
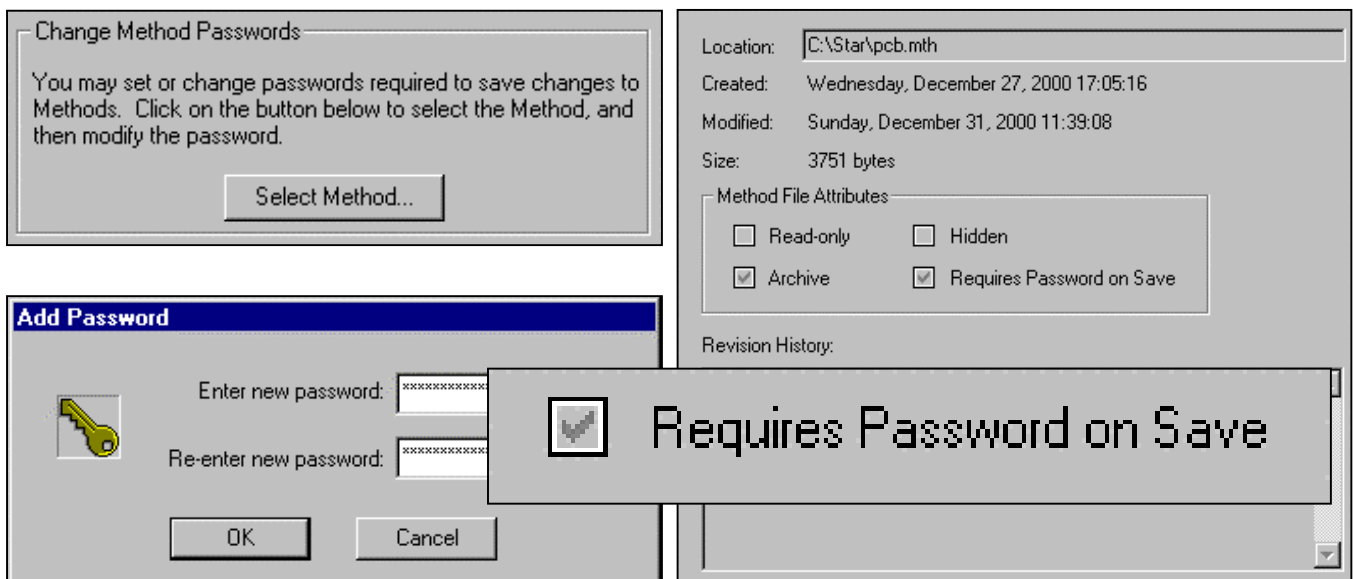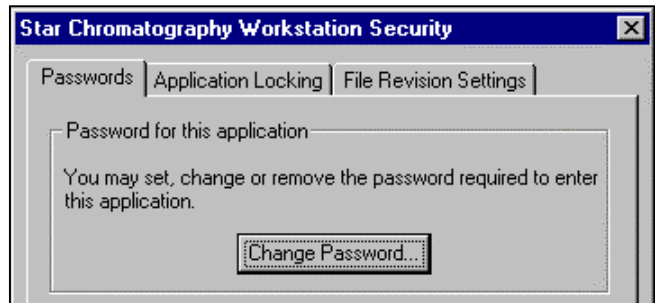
14. **To Document Changes in a Method, an Automatic Prompt Can Be Set Up to Add Comments to Revision History -** maintained with the method and with every data file using that method.
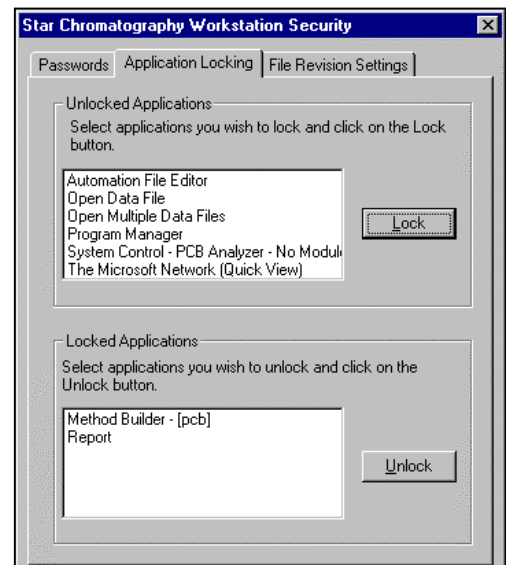
Revision History:

12/27/2000 5:05 PM: Method updated by Randy B-Cook.
Method built to test out Method Revision Log
12/31/2000 12:50 PM: Method updated by Randy B-Cook.
Adding second revision to log.

Method Revision Log ✕

Please document the changes made to the Method

Name: Randy B-Cook

Comments:

Adding second revision to log.

Star Chromatography Workstation Security ✕

Passwords | Application Locking | File Revision Settings

☑ Require Revision Log entry when changes to Methods are saved.

CFR, Title 21, Part 11 Subpart B, § 11.10 –

"Procedures and controls shall include…(d) limiting access to authorized individuals."

15. **Access to Star Security application is password controlled -** limiting access to changes in security procedures and passwords.

Star Chromatography Workstation Security ✕

Passwords | Application Locking | File Revision Settings

Password for this application

You may set, change or remove the password required to enter this application.
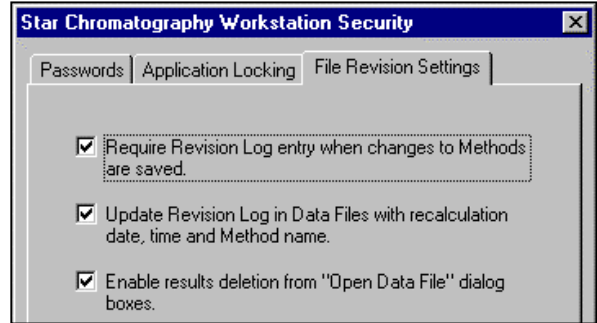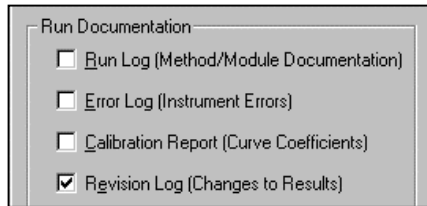
Change Password...

16. **Even Specific Applications in Star, such as Interactive Graphics or Standard Reports, Can Be Limited.** When an application is locked, access to it is not permitted. Only after it is unlocked with a password is access allowed.

Star Chromatography Workstation Security ✕

Passwords | Application Locking | File Revision Settings

Unlocked Applications

Select applications you wish to lock and click on the Lock button.

Automation File Editor
Open Data File
Open Multiple Data Files
Program Manager
System Control - PCB Analyzer - No Module
The Microsoft Network (Quick View)

Lock

Locked Applications

Select applications you wish to unlock and click on the Unlock button.

Method Builder - [pcb]
Report

Unlock

CFR, Title 21, Part 11 Subpart B, § 11.10 –

"Procedures and controls shall include…(e) use of secure, computer-generated, time-stamped audit trails to independently record time and date of operator entries and actions that create, modify, or delete electronic records."

17. **Revision Log for Results** - After both checking the box for "Update Revision Log" and enabling the Revision Log in Run Documentation, time and date of operator revisions are independently recorded. This log can be printed as part of every report of results.

Star Chromatography Workstation Security

Passwords | Application Locking | File Revision Settings

☑ Require Revision Log entry when changes to Methods are saved.

☑ Update Revision Log in Data Files with recalculation date, time and Method name.

☑ Enable results deletion from "Open Data File" dialog boxes.

Run Documentation
- ☐ Run Log (Method/Module Documentation)
- ☐ Error Log (Instrument Errors)
- ☐ Calibration Report (Curve Coefficients)
- ☑ Revision Log (Changes to Results)

```
Revision Log:

12/27/2000 4:59 PM: Calculated results from channel A using method:
    'c:\my documents\brochures\data integrity with star workstation\12-26-00 1:37:00 pm elcd mix-b.mth'
12/27/2000 6:20 PM: Calculated results from channel A using method:
    'c:\my documents\brochures\data integrity with star workstation\12-26-00 1:37:00 pm elcd mix-b.mth'
12/31/2000 1:40 PM: Calculated results from channel A using method:
    'c:\my documents\brochures\data integrity with star workstation\12-26-00 1:37:00 pm elcd mix-b.mth'
```

```
Revision Log:

12/31/2000 2:09 PM: Deleted results calculated on 12/26/2000 9:45 PM
    from channel B of ADCB at address 16.
```

Del Results...

CFR, Title 21, Part 11 Subpart B, § 11.10 –

"Procedures and controls shall include… (a) validation of systems to ensure accuracy, reliability, consistent intended performance, and the ability to discern invalid or altered records."

18. **Validation of System Software Can Be Accomplished Through "Help…About System Control…Validate System Files".** This test reports that the checksums of the installed applications are identical to those recorded at the factory. Also reported is the software installation history. Separately, the Star Regulatory Compliance Manual, provided on CD, provides detailed procedures for validating computations and report generation.

Help
- Help Topics
- Product Support Web Site
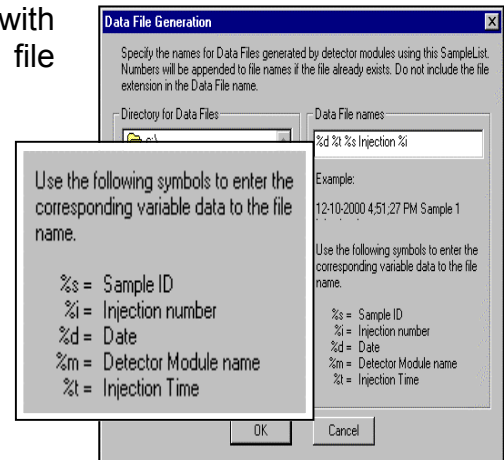- About System Control...

Validate Installed Files
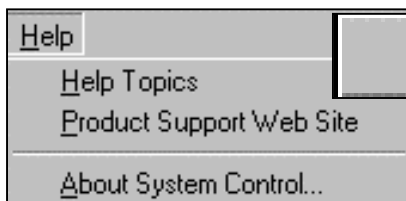
```
FILE SYSTEM VALIDATION REPORT

File System: Star Workstation 5.51
Workstation: OEMCOMPUTER

Directory: c:\star

Source file: c:\star\star.val

Test Results:
    53 files tested
    53 files OK
    *** File System OK ***

Installation History:

---------- Sun Dec 24 10:08:40 2000
Star Chromatography Workstation 5.50

---------- Sun Dec 24 10:08:42 2000
Installed: Star Chromatography Workstation 5.50 GC Module Drivers

---------- Sun Dec 24 10:08:44 2000
Installed: Advanced Applications 5.50

---------- Sun Dec 24 10:10:50 2000
Installed: StarWS 5.50 Update#1   Core Files
Description updated to:
    Star Workstation 5.51

---------- Sun Dec 24 10:10:52 2000
Installed: StarWS 5.50 Update#1 Control Files

---------- Sun Dec 24 10:10:52 2000
Installed: StarWS 5.50 Update#1   GC Files

Report Prepared on Sun Dec 31 13:58:46 2000 by _____

Approved: _____
```

Other Features in Star to Assure Data Integrity:

19. **File Names Can Be Assigned Variables** - (mixed with operator-chosen fixed alpha-numerics) for easier file recovery.


20. **Files Names Can Be 255 Characters Long**, limited by Microsoft Windows, for clearer labeling and easier recovery of data.

21. **Single Data File Contains Everything Employed To Generate That Data**, including: a) raw data for all data channels, b) computed results for all data channels, c) reports for each data channel, d) method used, e) error log, f) run log, g) baseline used in background subtraction, h) snippet of baseline noise monitor, i) calibration data, and j) calibration curves for all data channels. This grouping makes full recovery of data easy and trouble-free and it assures that the original computations can be accurately reenacted later.

22. **Single Method Contains Parameters for Full Instrument Control, Data Collection, Computations, Report Generation, Custom Report, and Printing.** Mistakes in operations are greatly reduced when all parameters are maintained together.
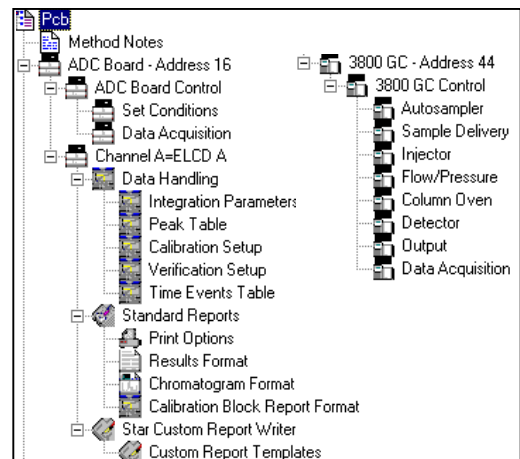
23. **Full Instrument Control from Workstation** – minimizes operating errors when all conditions, including temperatures, flows, AutoSamplers and valves actuations, are combined together in one method.
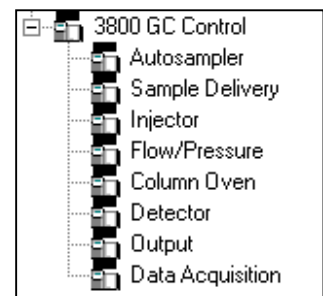
24. **Auto Start at Specific Time** – For example, the instrument can be set to perform a complete calibration sequence before work shift begins. Calibrations can be performed more often and still keep productivity up.

	Sample Name	Sample Type	Cal. level	Inj.	AutoLink	Rack
1		Autolink ▼			WAIT 3:	
2	Aroclor 122		1	1	none	1
3	Aroclor 101		1	1	none	1
4	Aroclor 123		1	1	none	1
5	Aroclor 124		1	1	none	1
6	Aroclor 124		1	1	none	1

AutoLink Parameters

Command

WAIT 3:

25. **+1000 Volts to –1000 Volts Electrometer Range on Varian 3800 -** No cutoff when signal drifts negatively, or is very large; applicable to FID, TSD, PID, PDD. Range can be set to most sensitive scale and still very large peaks can be measured – over the complete range of most detectors. Eliminates errors when wrong range is chosen.

FID/TSD Detector Full Scale

Front: 1000 V

Middle: 1000 V

Rear: 1000 V

26. **Noise Monitor – Diagnostic for Potential Detector Problems.** Monitor occurs just prior to start of every run. Value is employed in peak detection.

```
Multiplier: 1          Divisor: 1          Unidentified

Baseline Offset: 6248 microVolts

Noise (used): 35 microVolts - monitored before this run
```

27. **Peak Detection Based on Meaningful Parameters – Peakwidth and Signal-to-Noise**, not arbitrary setting of "slope sensitivity". Peakwidths can be obtained from the sample report and S/N is determined from "noise monitor". Peak areas are computed more accurately and with much less effort when expected peakwidths closely match the actual widths.

Peak Detection

☐ Subtract Blank Baseline

Initial S/N Ratio: 5

Initial Peakwidth: 4 sec

Initial Tangent Height %: 10

Initial S/N Ratio: 5

Initial Peakwidth: 4 sec

```
              Width
  Area    Sep.  1/2
(counts)  Code (sec)
--------- ---- -----
 5273082   BV   5.4
 2215177   VV   4.7
 2089208   VB   3.2
========= ---- -----
 9577467
```

28. **Display of Detector Bunch Points in Graphics –** provides visual indication for adequate number of points to define the peak. Twenty points across the peak normally define the peak properly and yield the best allocation of its area**.**

Detector Bunch Rate: 8 points (5.0 Hz)
Noise Monitor Length: 64 bunched points (12.8 sec)

Detector Bunch Rate: 8

FID/TSD Detector Full Scale
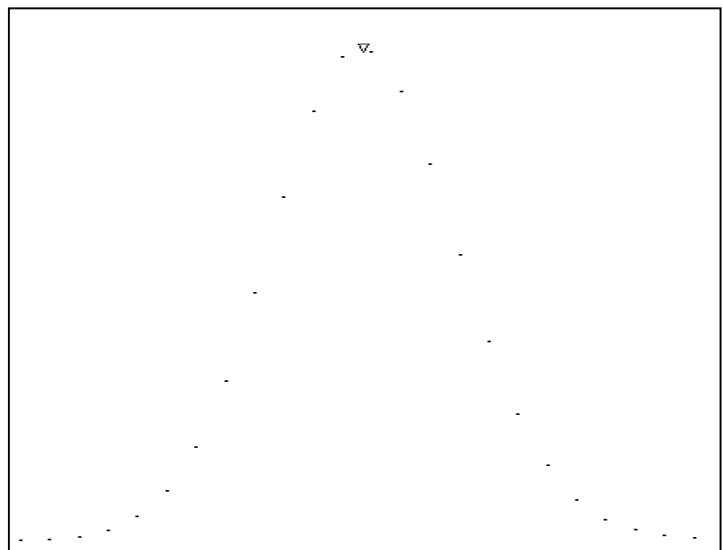
Front: 1000 V

Middle: 1000 V

Rear: 1000 V

Interactive Graphics

Layout | Trace Settings | Offsets | Colors

● Point

Plot Type
○ Line ○ Outline ● Point   ○ Line

OK   Cancel   Use Defaults   Help

29. **Automatic Tan% Judgement** – Overlapping peaks are problematic when attempting to accurately apportion areas. If the peaks are similar in size, a perpendicular drop to baseline between the peaks is a reasonable estimation. However, when one peak is much smaller than the other, a better guess is to tangent skim. The Tan% parameter allows an automatic judgement based on the relative height of the rider peak to the height of the major peak; less manual intervention in area allocations is then required.
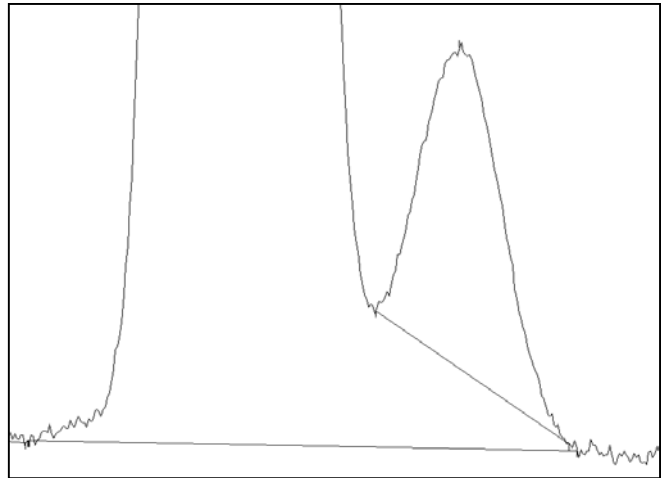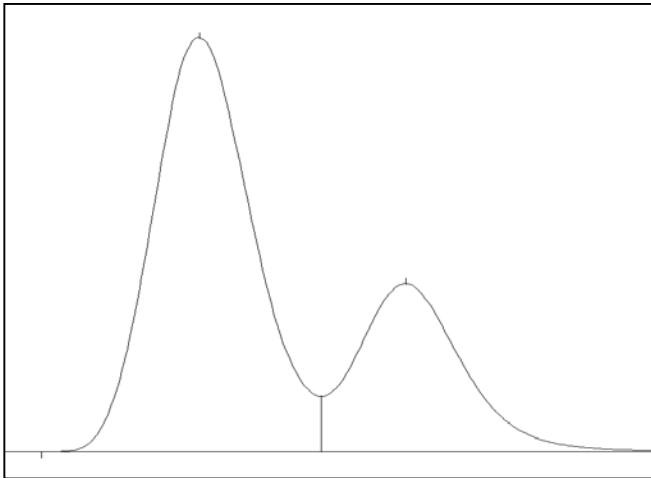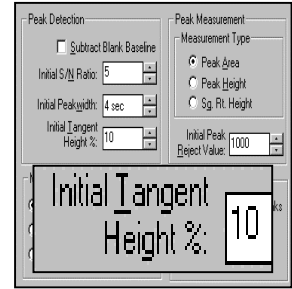
30. **Multiple Reference Peaks** – allow automatic adjustment of peak table for subtle shifts in retention times normally expected in chromatography. If a sizeable change occurs (a shift outside the defined window), a missing reference peak generates an error that can effect a halt in system operations.
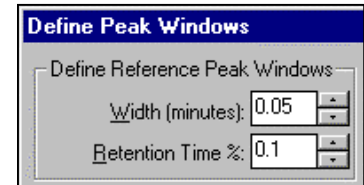
31. **Replicate Standard Tolerance –** permits a quality check when multiple standards are employed to generate a calibration curve. If replicates are not consistent (within the defined range), an error is generated that can effect a halt in system operations.
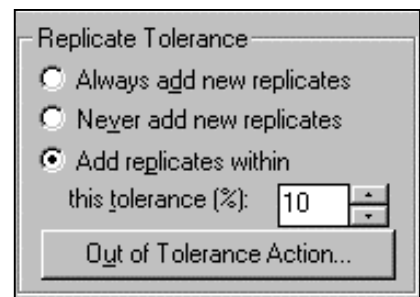
32. **Verification Sample –** After a calibration sequence is performed, one (or more) of the standards can be reexamined as a "verification" sample to provide assurance that the calibration is proper. If a result is outside the tolerance, an error is generated that can effect a halt in system operations.

	Sample Name	Sample Type	Cal. level
1	Control Sample 3	Verification ▼	4
2	Sx 52417281	Analysis ▼	
3		▼	
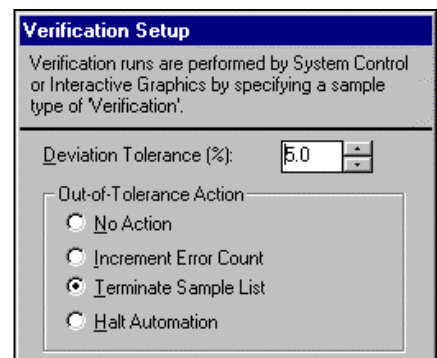
33. **Calibration Overrange –** Sample concentration for an unknown exceeding the highest standard by the tolerance specified will generate an error. This error can effect a halt in system operations.

Calibration Range Tolerance
Peaks outside the range + tolerance generate calibration range errors.

Range Tolerance (%): 10.0

Out of Tolerance Action...
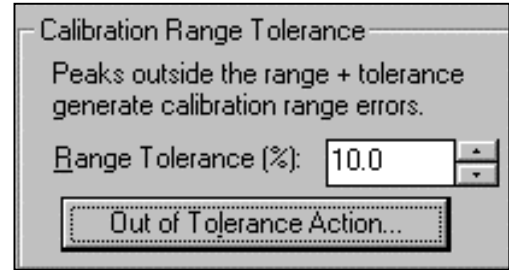
34. **Error Monitoring** – "Fatal" errors will cause an immediate halt to system operations and a message will be added to the Message Log. "Fatal" errors include: Maximum Non-Fatal Errors Achieved, GC Flameout, Coolant Timeout, Temp Probe Failure, Data Loss Due to Workstation Disconnection, AutoSampler Fault and Gas Saver Timeout. "Non-Fatal errors a) can be documented but ignored, b) can increment an error counter, c) can terminate the sample list and proceed with the next line in the sequence, or d) can halt system operations immediately – options selected by the operator. This group of errors includes: Reference Peak Missing, Internal Standard Peak Missing, Factors Out of Tolerance, Replicate Standard Tolerance, Calibration Range Tolerance, and Verification Sample Tolerance. The operator can choose the maximum number of consecutive faulty runs of the same type that can occur before a fatal error is triggered and operations are halted.

Calibration Range Tolerance

Out-of-Tolerance Action
- ○ No Action
- ◉ Increment Error Count
- ○ Terminate Sample List
- ○ Halt Automation

Save   Cancel

Instrument 1 Parameters

Instrument: PCB Analyzer
Operator: R B-Cook
Max Errors: 3

Max Errors: 3