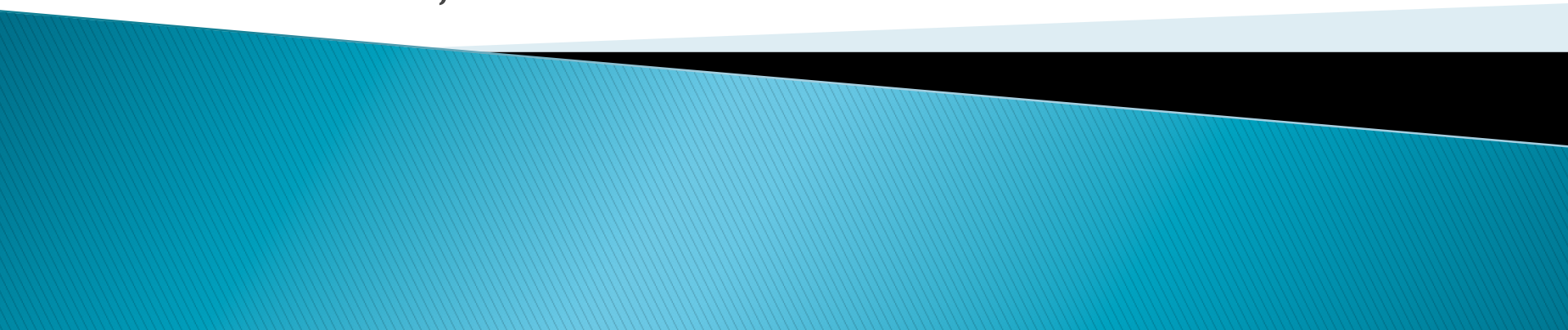


Managing 21 CFR Part 11 Compliance: Using Checksums on Open Systems

Carey Smoak, Roche Molecular Systems, Inc.,
Pleasanton, CA



Overview

- ▶ Checksum History
- ▶ Usage in Healthcare
 - eCTD
 - SAS Installation
 - Data transfers
- ▶ Conclusion



Definitions

- ▶ Cipher
 - Put (a message) into secret writing; encode
 - Not necessarily computer-related
- ▶ Checksum
 - A count of the number of bits in a transmission unit
 - Computer-related

Definitions

- ▶ MD5
 - Message-Digest Algorithm
- ▶ SHA1
 - Secure Hashing Algorithm
 - SHA1 more secure than MD5
 - SHA1 was created because of practical attacks on MD5
 - NSA (National Security Administration) develops SHA algorithms



A Bit of History: Ciphers

- ▶ 1860 AD, Wheatstone disc was used to create polyalphabetic ciphers
- ▶ WWII – German U-boats used Enigma machine
- ▶ 1960's (my childhood) – Decoder Rings





Message Delivery

▶ Correctness

- Data transmission is considered correct when the contents which are transferred and the contents which are received; that both are identical



Message Delivery

- ▶ Childhood Game: Telephone
 - Aka: operator, grapevine, broken telephone, etc.
 - One person whispers a message to another, which is passed through a line of people until the last player announces the message to the entire group.
 - The statement announced by the last player usually differs significantly from the original message.
 - Reasons for changes include anxiousness or impatience, erroneous corrections and deliberate alterations.

Message Delivery

- ▶ Error Detection of Transmitted Message
 - Unintentional modification of the message
 - Example: file becomes corrupted during transmission via the internet
 - *In scope for this presentation*
 - Intentional (malicious) modification of the message
 - *Out of scope for this presentation*

Message Delivery

- ▶ Example of MD5 checksum using FCIV (Windows PC):
 - 86fa7014d5c52f166c907d3777d30c61
- ▶ FCIV can be downloaded from the Internet
 - <http://www.microsoft.com/en-us/download/details.aspx?id=11533>
 - FCIV = File Checksum Integrity Verifier
- ▶ Example
 - At command prompt, type:
 - fciv demog.csv -sha1 -> list.txt
 - fciv can also be run within SAS programs using the “x” command

Practical Uses of Checksums

- ▶ Check digits in Social Security Numbers
- ▶ ISBN book numbers
- ▶ International Bank Account Numbers
- ▶ International Standard Serial Number
- ▶ International Standard Music Number
- ▶ UPC
- ▶ Encoding passwords

Uses of Checksum in Healthcare

- ▶ eCTD
- ▶ Software Installation
- ▶ Data Transfers



Uses of Checksum in Healthcare: eCTD

The eCTD FDA guidance specifically states the addition checksum files:

“The eCTD submission should contain checksums for each individual file including a checksum file for the eCTD XML instance. Initially, the MD5 Message-Digest Algorithm (MD5) should be used for this purpose.”



Uses of Checksum in Healthcare: Software Installation

- ▶ Ensure that the installation files were copied correctly
 - Verify proper installation of software products (e.g., SAS)

Uses of Checksum in Healthcare: Software Installation

Additional Fonts

18:57 Monday, January 25, 2010

Dest. Path	File Name	Status	Expected Checksum \ Actual Checksum	Option
core\resource	saswalb.ttf	Pass	66212b8ede10692139c00882e1d564c7 \ 66212b8ede10692139c00882e1d564c7	ttfontsmva1-Required files
core\resource	saswalbi.ttf	Pass	f748ef73854576a74d763648468f7a6a \ f748ef73854576a74d763648468f7a6a	ttfontsmva1-Required files
core\resource	saswali.ttf	Pass	5c3b9214ca1b381b06e0a08e324b2dfc \ 5c3b9214ca1b381b06e0a08e324b2dfc	ttfontsmva1-Required files
core\resource	saswalr.ttf	Pass	fceb61362e93faabda2616786dbb7f6 \ fceb61362e93faabda2616786dbb7f6	ttfontsmva1-Required files
core\resource	saswcub.ttf	Pass	640db57933a9b42ab8cec42aa4a9ba6d \ 640db57933a9b42ab8cec42aa4a9ba6d	ttfontsmva1-Required files
core\resource	saswcubi.ttf	Pass	43434a18329cab3f0396b6b8f5d3a2bd \ 43434a18329cab3f0396b6b8f5d3a2bd	ttfontsmva1-Required files
core\resource	saswcu.ttf	Pass	c5136492fddd00432702013d8fefeb2a \ c5136492fddd00432702013d8fefeb2a	ttfontsmva1-Required files
core\resource	saswcur.ttf	Pass	4bb026b93e1348e4d89bf144f3eae0fa \ 4bb026b93e1348e4d89bf144f3eae0fa	ttfontsmva1-Required files
core\resource	saswthb.ttf	Pass	eed447c461454369814af8452b6aae78 \ eed447c461454369814af8452b6aae78	ttfontsmva1-Required files
core\resource	saswthbi.ttf	Pass	fcf0a4e163433fa54a9c16c4ae174dc4 \ fcf0a4e163433fa54a9c16c4ae174dc4	ttfontsmva1-Required files
core\resource	saswthi.ttf	Pass	57c95b6121f00d4ac81135344cb2c1fc \ 57c95b6121f00d4ac81135344cb2c1fc	ttfontsmva1-Required files
core\resource	saswthr.ttf	Pass	3817f7a18c5ee7de55d8fafbc4472d61 \ 3817f7a18c5ee7de55d8fafbc4472d61	ttfontsmva1-Required files
core\resource	simhei.ttf	Pass	a2f5fc4709b4d1403f60c710b529d902 \ a2f5fc4709b4d1403f60c710b529d902	ttfontsmva1-Required files
core\resource	simsun.ttc	Pass	291e2c2fc40b685487cc8563ec0c0802 \ 291e2c2fc40b685487cc8563ec0c0802	ttfontsmva1-Required files

Uses of Checksum in Healthcare: Open versus Closed System

- ▶ ***Closed system*** means an environment in which system access is controlled by persons who are responsible for the content of electronic records that are on the system.
- ▶ ***Open system*** means an environment in which system access is ***not*** controlled by persons who are responsible for the content of electronic records that are on the system.

Uses of Checksum in Healthcare: Control

- ▶ Closed systems are controlled environments
 - For example, clinical database
- ▶ Open systems need the following to be compliant
 - Record authenticity
 - Integrity
 - Confidentiality
- ▶ See Code of Federal Regulations – Part 11
Electronic Records; Electronic Signatures
 - <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm?CFRPart=11&showFR=1> – revised April 1, 2012

Uses of Checksum in Healthcare: Regulatory Compliance

▶ Three Criteria:

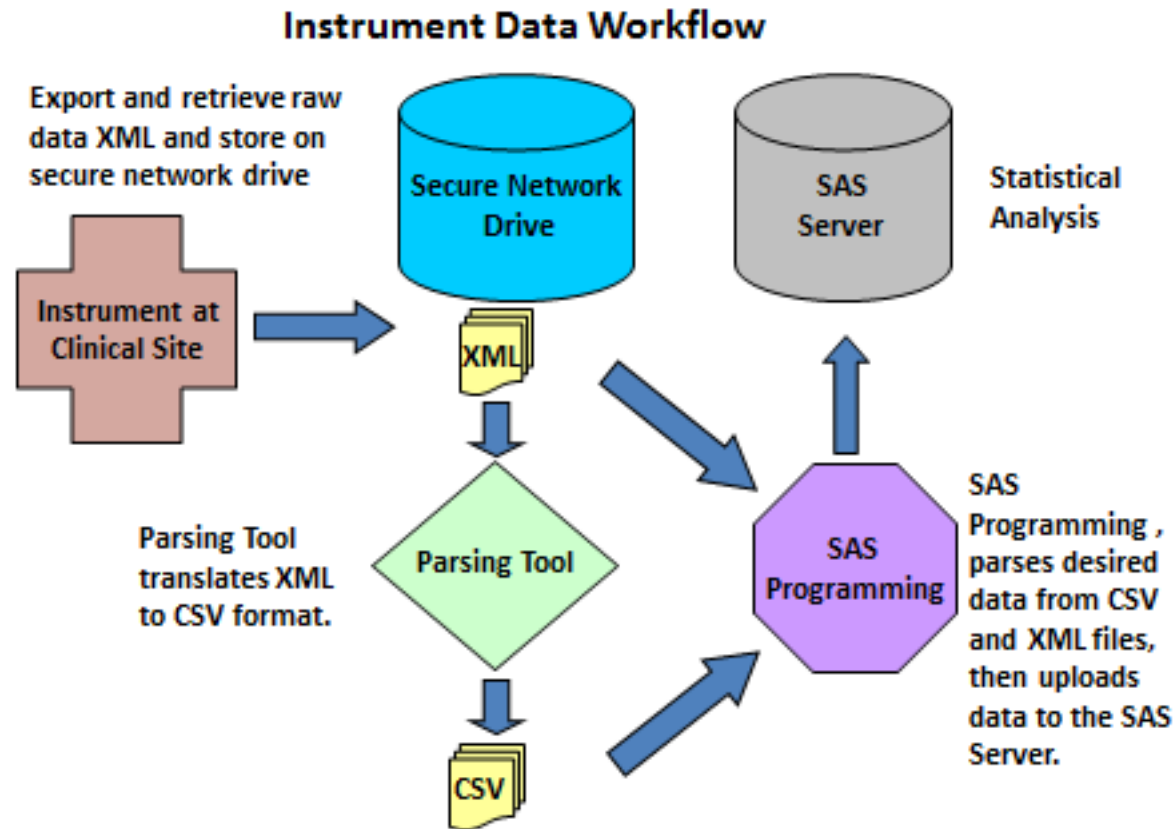
- Demonstrate staff qualification (training).
- Demonstrate activity conducted according to regulatory requirements (SOPs).
- Documents and records generated during the activity to provide assurances and/or evidence to clarify and to support the auditor's assessment.
 - *In scope for this presentation.*
- See Pharmaceutical Programming 3:5–7, 2010.

Uses of Checksum in Healthcare: Case Studies

- ▶ # 1 – open system without checksums
- ▶ # 2 – open system with checksums

Case Study # 1: Open System

What are the risks?

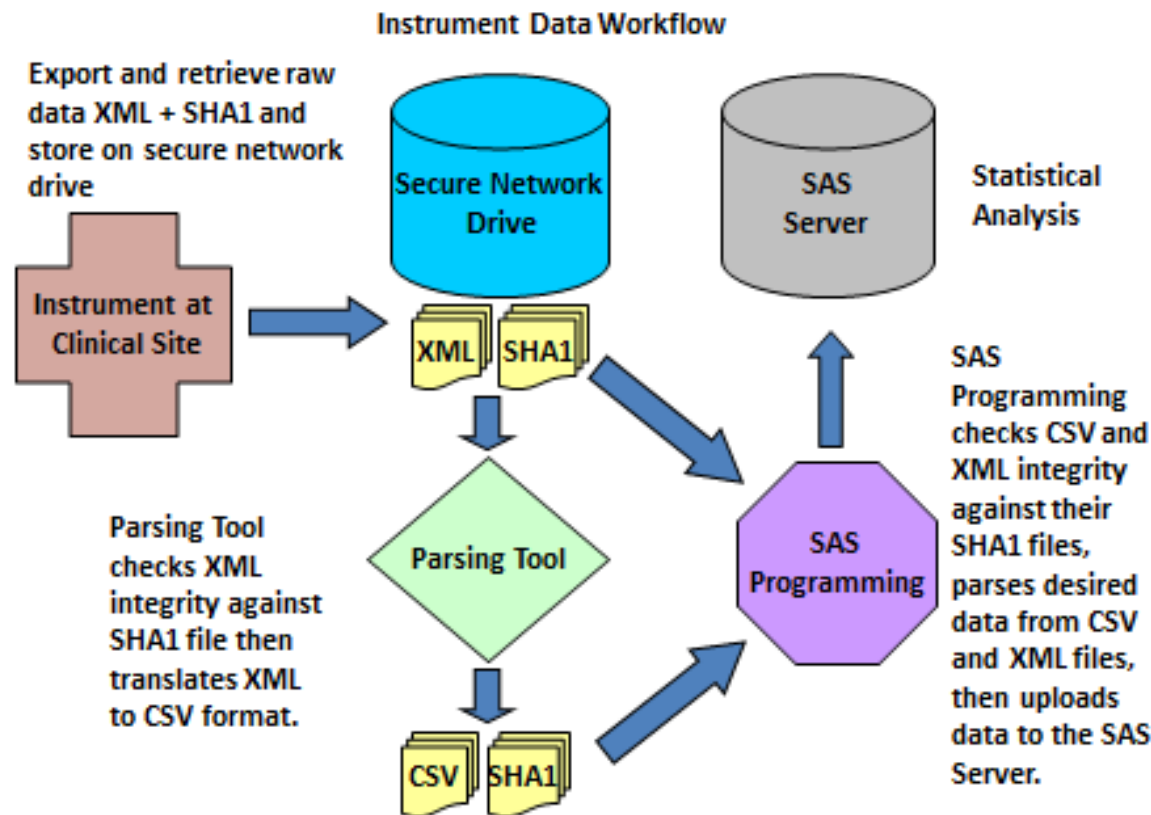


Case Study #1: Open Systems

What are the risks?

- ▶ Data reception step does not ensure transfer correctness, e.g., file modification during transmission is not detected
- ▶ Parsing step does not verify that the input is the correct data
- ▶ SAS programming step (even if validated) cannot verify that the input is the correct data

Case Study # 2: Open System Solution – Use of Checksums



Case Study # 2: Open System

Solution – Use of Checksums

- ▶ Data reception step uses checksum (SHA1) to ensure transfer correctness, e.g., file modification during transmission will be detected
- ▶ Parsing step uses checksum (SHA1) to verify that the input is the correct data
- ▶ SAS programming uses checksum (SHA1) step to verify that the input is the correct data

Case Study # 2: Open System Solution – Use of Checksums

- ▶ Does the open system described in # 2 meet the spirit of 21 CFR Part 11 compliance?
 - Secure environment with limited access
 - Not addressed by checksums, met by login practices
 - Correct transmission of data
 - Addressed by checksums
 - Confidentiality was not a consideration in this system

Conclusions

- ▶ Open systems can be perfectly compliant!
- ▶ Sponsors are responsible for ensuring that they satisfy all of the criteria:
 - Integrity
 - Record authenticity
 - Confidentiality
- ▶ Checksums can help to ensure data integrity



Conclusions

- ▶ The core concepts of checksums began many centuries ago
 - Ciphers and Cryptography
- ▶ This is a testament to the relevance and effectiveness of checksums

References

- ▶ The use of checksums to ensure data integrity in the healthcare industry. Pharmaceutical Programming 5:38–41, 2012
- ▶ Checksum Please: A Way to Ensure Data Integrity –
<http://www.lexjansen.com/pharmasug/2012/TA/PharmaSUG-2012-TA01.pdf>
- ▶ Managing 21 CFR Part 11 Compliance: Using Checksum on Opens Systems –
<http://www.lexjansen.com/pharmasug/2013/MS/PharmaSUG-2013-MS06.pdf>

Contact Information

- ▶ Carey Smoak
 - carey.smoak@roche.com