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# Program Life-Cycle Management in LSAF

PHUSE SDE Utrecht 2019

10. October 2019, Nutricia Research

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## Agenda

- Background at Ferring
- Supporting Life Cycle Management in LSAF
- Business Implementation Plans at Ferring
- Tackling Dependencies in LSAF
- Conclusion



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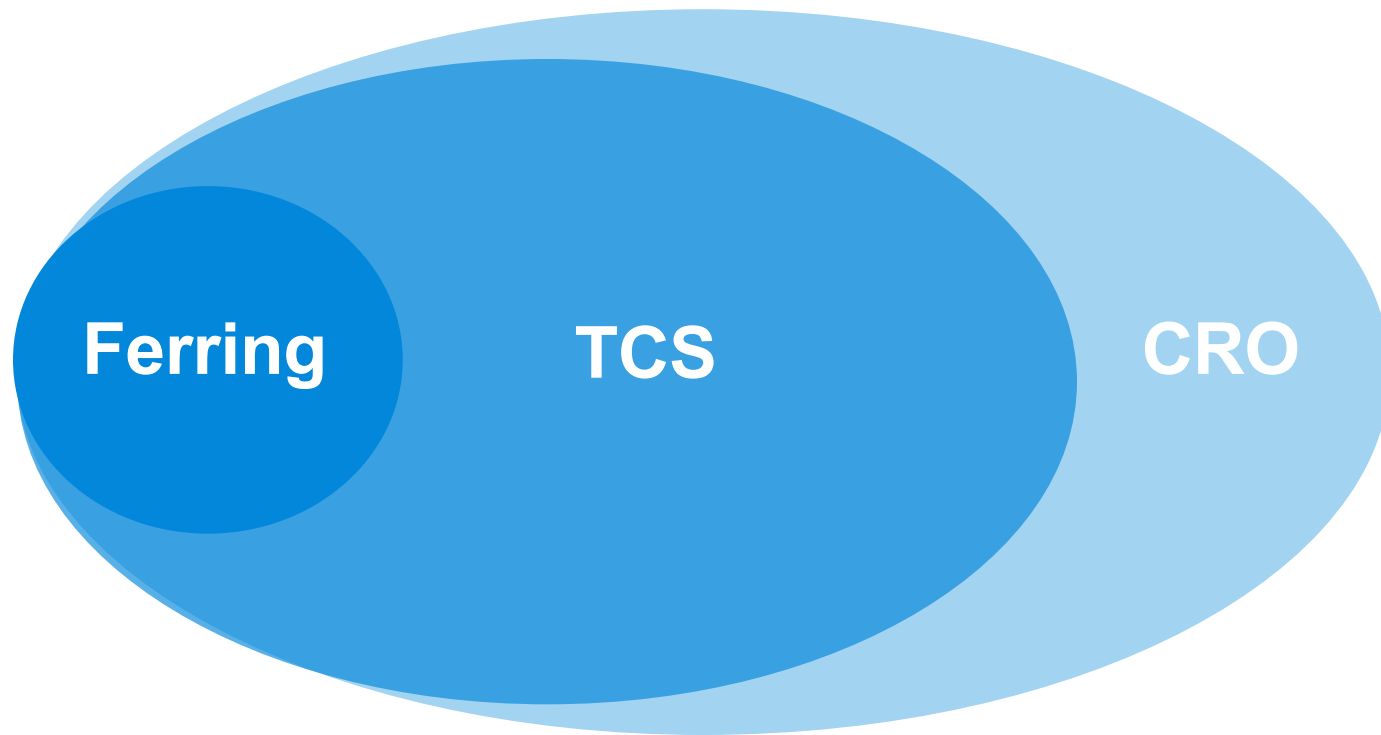
**Presence in all development centres**  
resources, expertise, technology, standards



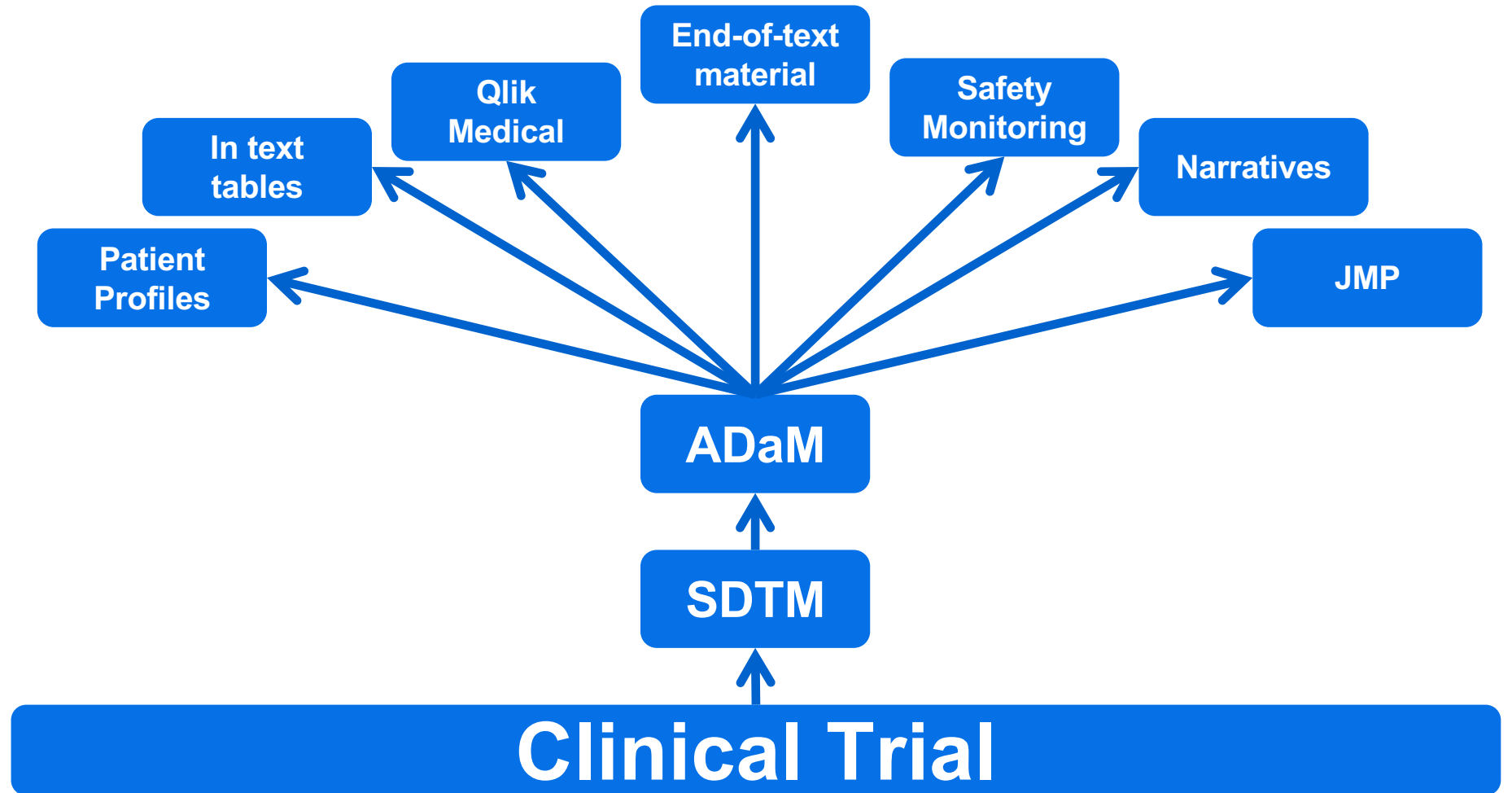
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- **same systems**
- **same processes**
- **communication**
- **continuity**





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## Copy, Run & Lock

### Conduct

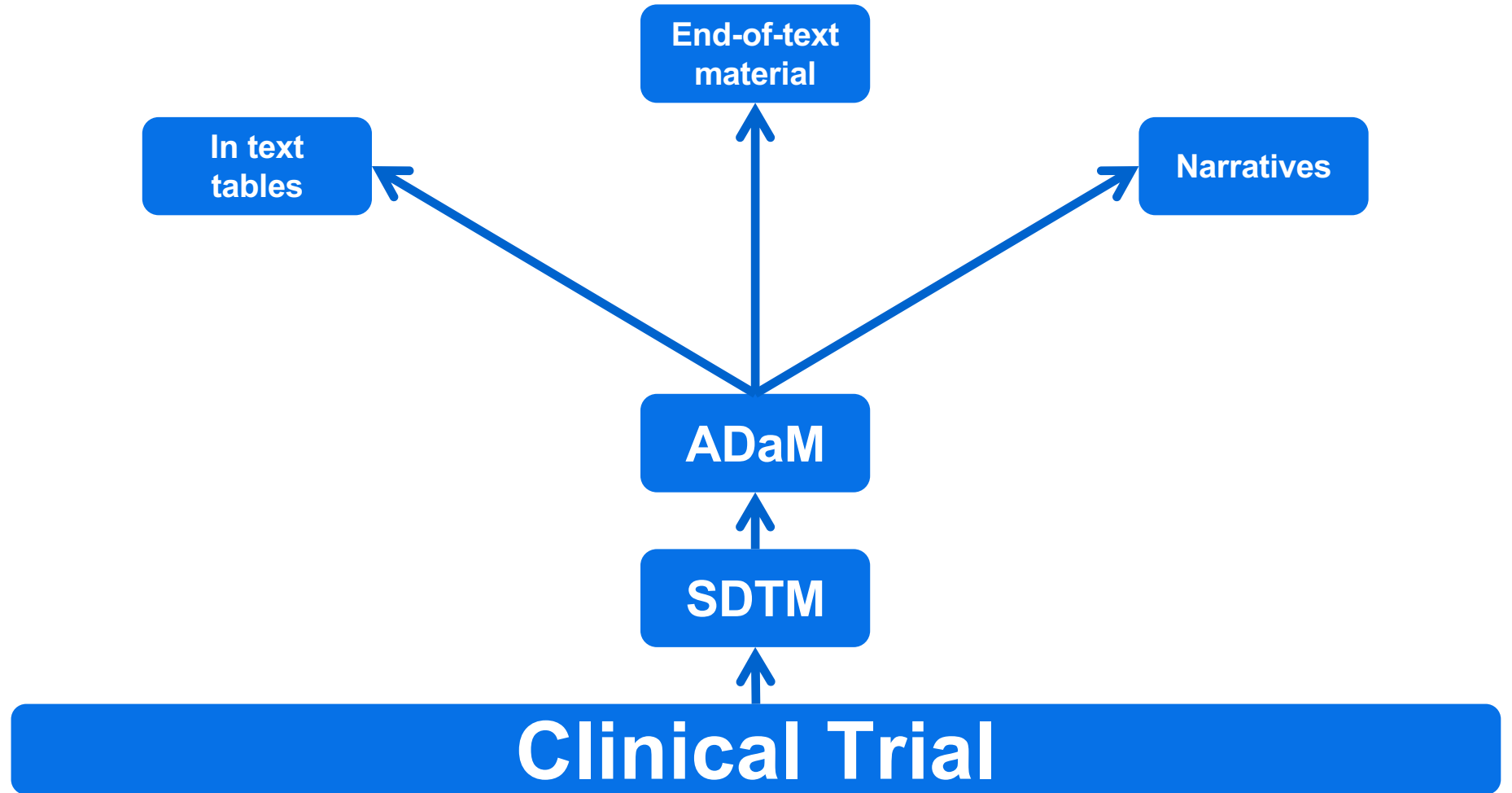
- Datasets
- Programs
- Macros
- Logfiles
- Output

### DBL

- Datasets
- Programs
- Macros
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- Output

### CTR

- Datasets
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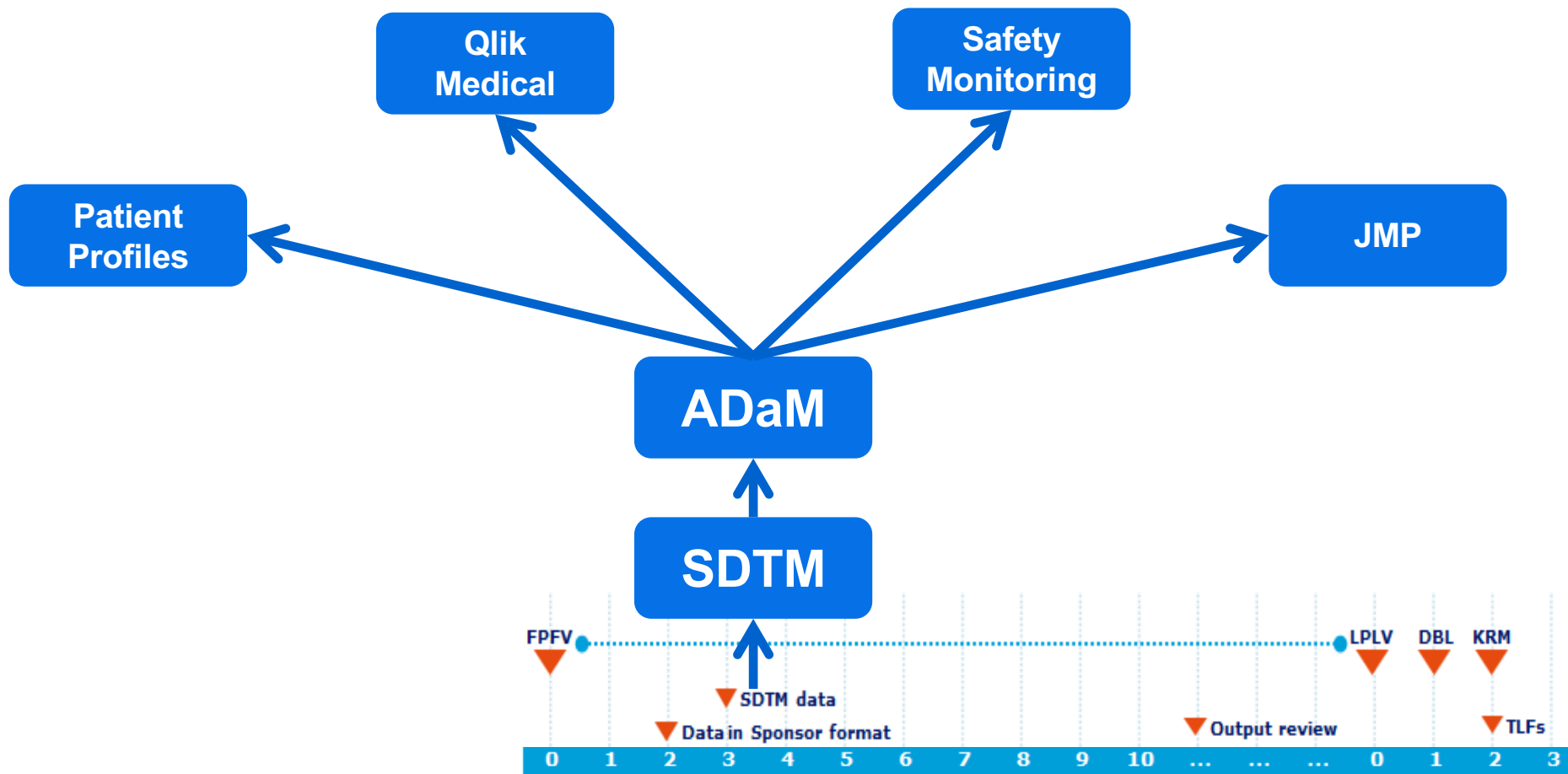
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## Guidance for Industry

### Oversight of Clinical Investigations — A Risk-Based Approach to Monitoring

U.S. Department of Health and Human Services  
Food and Drug Administration  
Center for Drug Evaluation and Research (CDER)  
Center for Biologics Evaluation and Research (CBER)  
Center for Devices and Radiological Health (CDRH)  
Office of Good Clinical Practice (OGCP)  
Office of Regulatory Affairs (ORA)  
August 2013  
Procedural

OMB Control No. 0910-0733  
Expiration Date: 06/30/2019 (Note: Expiration date updated 07/15/2016)  
See additional PRA statement in section VII of this guidance.

---

## V. DOCUMENTING MONITORING ACTIVITIES

Documentation of monitoring activities should generally include the following:

- The date of the activity and the individual(s) conducting and participating in it
- A summary of the data or activities reviewed
- A description of any noncompliance, potential noncompliance, data irregularities, or other deficiencies identified
- A description of any actions taken, to be taken, or recommended, including the person responsible for completing actions and the anticipated date of completion

Documentation of monitoring should include sufficient detail to allow verification that the monitoring plan was followed.

Monitoring documentation should be provided to appropriate management in a timely manner for review and follow-up, as indicated.



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### DBL

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### CTR

- Datasets
- Programs
- Macros
- Logfiles
- Output

The screenshot shows the SAS Workspace interface with a file tree on the left and a data table on the right. The file tree is expanded to show the 'adam' folder under 'Data'. The data table has columns for 'Size', 'Date', 'Repository Version', and 'Workspace Status'. Annotations include green Excel icons above the table, vertical text labels 'Programming Plan', 'Validation Report', and 'Program Header' with red double-headed arrows pointing to specific rows in the table.

Size	Date	Repository Version	Workspace Status
28 KB	Jan 1		

**Programming Plan**

- Name of program
- Programmer
- Date
- Validator
- Validation status

**Validation Report**

- Name of program
- Programmer
- Date
- Validator
- Validation status

**Program Header**

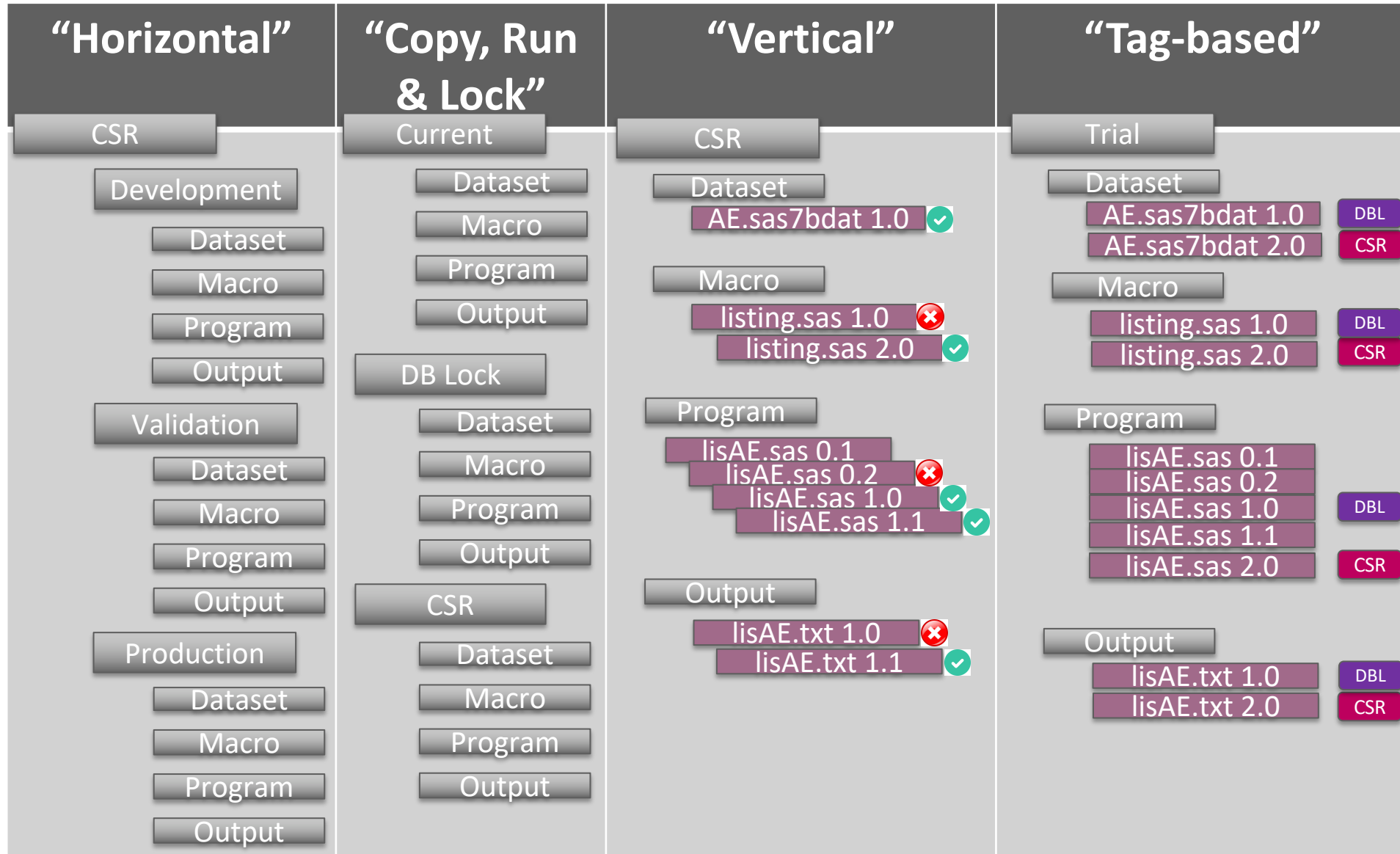
- Name of program
- Programmer
- Date

Action Status

User: Trainer

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Check In Files

Comment: This is the first version

Add: Version type for selected rows: Major

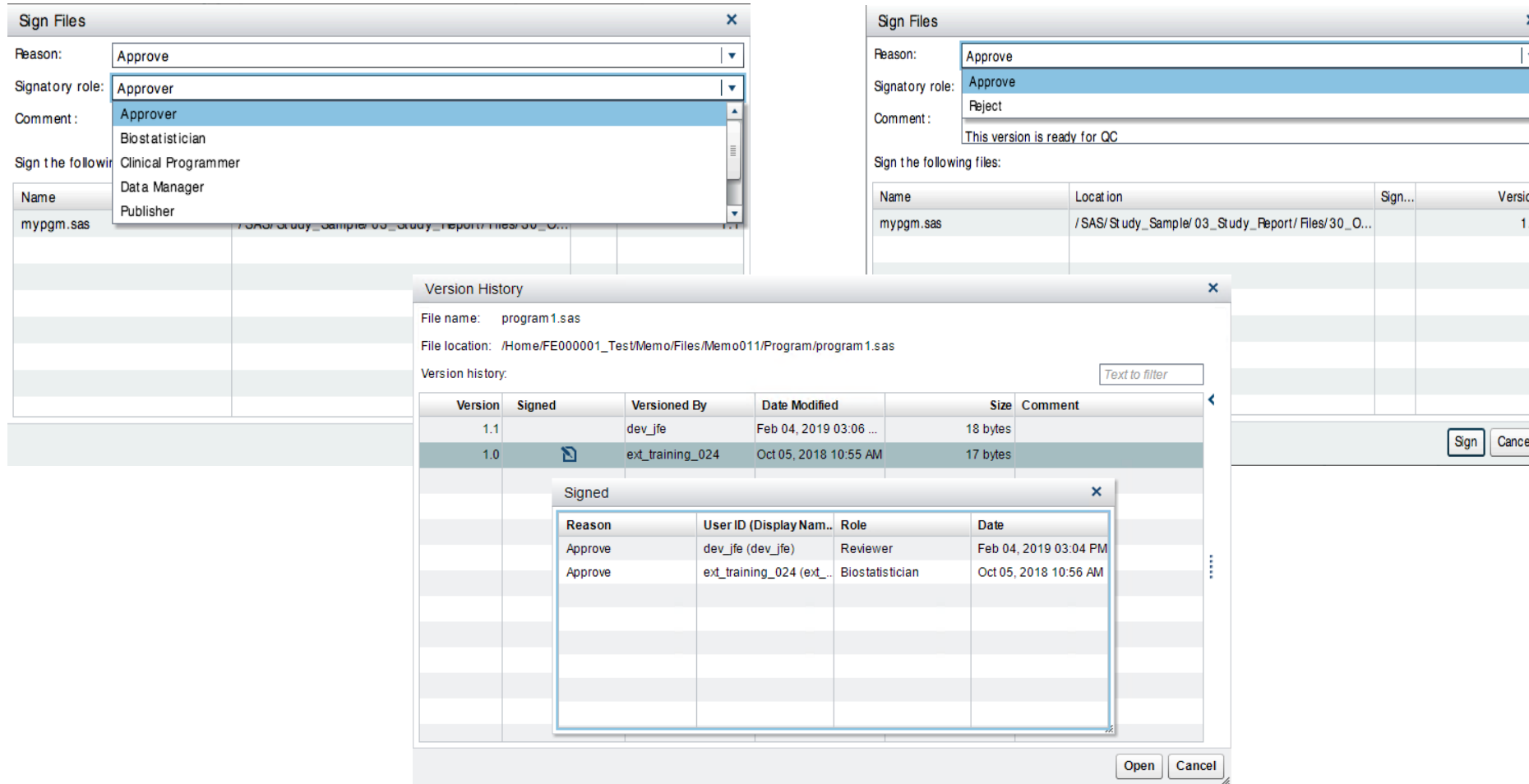
Name	Location	<input checked="" type="checkbox"/> Enable Versioning	Version Type	Version
mypgm.sas	/SAS/Study_Sample/03_Study_Report...	<input checked="" type="checkbox"/>	Major	1.0

Existing: Version type for selected rows: Major

Name	Location	Current ...	Version Type	Version

Check In Cancel

- Possibility to enable and disable versioning
- New versions created at check-in and check-out or when files are overwritten
- Each time a user modifies a program under versioning, a new version is created as next Major, Minor or Custom version.



The screenshot displays the LSAF eSignature interface. It features a 'Sign Files' dialog box with a dropdown for 'Reason' (set to 'Approve'), a dropdown for 'Signatory role' (set to 'Approver'), and a list of roles including 'Approver', 'Biostatistician', 'Clinical Programmer', 'Data Manager', and 'Publisher'. Below this is a table of files to be signed, including 'mypgm.sas'. A 'Version History' window is also open, showing the file 'program1.sas' with its location and a table of versions. The 'Signed' window shows a list of previous signatures with columns for Reason, User ID, Role, and Date.

Version	Signed	Versioned By	Date Modified	Size	Comment
1.1		dev_jfe	Feb 04, 2019 03:06 ...	18 bytes	
1.0		ext_training_024	Oct 05, 2018 10:55 AM	17 bytes	

Reason	User ID (Display Nam..	Role	Date
Approve	dev_jfe (dev_jfe)	Reviewer	Feb 04, 2019 03:04 PM
Approve	ext_training_024 (ext_...	Biostatistician	Oct 05, 2018 10:56 AM

- Versions can be eSigned with different roles and reasons
- Roles and reasons can be customized
- **eSignatures are not carried forward from one version to the next**

### %LSAF\_GETCHILDREN

name	versionLabel	isVersioned	isCheckedOut	is Signed	lastModifiedBy	dateLastModified
program01	1.0	1	0	1	dev_jfe	20AUG18:12:37:25
program02	1.0	1	0	1	dev_jfe	20AUG18:12:37:26
program03	1.0	1	0	1	dev_jfe	20AUG18:12:37:26
program04	1.0	1	0	0	dev_jfe	20AUG18:12:37:26
program05		0	0	0	dev_jfe	20AUG18:12:37:26
program06	1.2	1	0	1	dev_jfe	20AUG18:13:55:45
program07	1.0	1	0	1	dev_jfe	20AUG18:14:17:51

1 row per program

### %LSAF\_GETVERSION

name	versionLabel	isCheckedOut	isLocked	is Signed	createdBy	dateCreated	lastModifiedBy	dateLastModified
program01.sas	1.0	0	0	1	dev_jfe	20AUG18:12:37:25	dev_jfe	20AUG18:12:37:25
program02.sas	1.0	0	0	1	dev_jfe	20AUG18:12:37:26	dev_jfe	20AUG18:12:37:26
program03.sas	1.0	0	0	1	dev_jfe	20AUG18:12:37:26	dev_jfe	20AUG18:12:37:26
program04.sas	1.0	0	0	0	dev_jfe	20AUG18:12:37:26	dev_jfe	20AUG18:12:37:26
program06.sas	1.0	0	0	0	dev_jfe	20AUG18:13:49:25	dev_jfe	20AUG18:13:49:25
program06.sas	1.1	0	0	1	dev_jfe	20AUG18:13:49:25	dev_jfe	20AUG18:13:50:31
program06.sas	1.2	0	0	1	dev_jfe	20AUG18:13:49:25	dev_jfe	20AUG18:13:55:45
program07.sas	1.0	0	0	1	dev_jfe	20AUG18:14:17:51	dev_jfe	20AUG18:14:17:51

1 row per program and version

### %LSAF\_GETSIGNATURES

name	versionLabel	userId	reason	role	date Signed	role 1
program01.sas	1.0	ext_training_016	Approve	Reviewer	20AUG18:12:48:48	Validator
program01.sas	1.0	dev_jfe	Approve	Biostatistician	20AUG18:12:38:27	Programmer
program02.sas	1.0	dev_jfe	Approve	Biostatistician	20AUG18:12:38:27	Programmer
program03.sas	1.0	ext_training_016	Approve	Reviewer	20AUG18:12:49:13	Validator
program03.sas	1.0	dev_jfe	Approve	Biostatistician	20AUG18:13:48:18	Programmer
program06.sas	1.2	ext_training_016	Approve	Reviewer	20AUG18:13:58:18	Validator
program06.sas	1.2	dev_jfe	Approve	Biostatistician	20AUG18:13:56:29	Programmer
program07.sas	1.0	ext_training_016	Reject	Reviewer	20AUG18:14:21:35	Validator
program07.sas	1.0	dev_jfe	Approve	Biostatistician	20AUG18:14:18:12	Programmer

1 row per version and eSign



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# Derive Validation Status

## Program Status

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Status	Versioned	Checked out	Program Author signed	Program Approver signed
Rejected	Yes	No	Approve	Reject
Validated	Yes	No	Approve	Approve



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# Derive Validation Status

## Program Status



Status	Versioned	Checked out	Program Author signed	Program Approver signed
Rejected	Yes	No	Approve	Reject
Validated	Yes	No	Approve	Approve
Not yet started*	NA	NA	NA	NA
Ongoing	Yes / No	Yes	Yes / No	Yes / No
Draft not versioned	No	No	No	No
Draft versioned	Yes	No	No	No
Ready for validation	Yes	No	Approve	No
Signed not versioned	No	No	Yes / No**	Yes / No**

\* Available in Programming Plan but not in LSAF

\*\* At least one has to be yes



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# Derive Validation Status

## Potential Issues

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Issue	Description
1	Program author signed as 'Reject'
2	Program author and program approver is the same
3	Program approver signed before program author
4	Program approver missing in Programming Plan but present in LSAF
5	Program author is missing in Programming Plan but present in LSAF
6	Programmer checked in not signed as Program author
7	Program approver has signed but program author has not signed
8	Programming Plan author is different from actual in LSAF
9	Programming Plan approver is different from actual in LSAF
10	Program not listed in Programming Plan
11	Unknown issue



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# Ferring Study Dashboard

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Program	Title	Current Version	Programmer	Programmer Decision	Programmer e-sign timestamp	Validator	Validator Decision	Validator e-sign timestamp	Validation Date	Total Versions	Status	Last Validated Version
ca0_codelist.sas	Create formats/codellists	1.1	isn	Approve	10Sep2019:09:16:41	scao	Approve	10Sep2019:09:20:59	10Sep2019:09:20:59	2	Validated	1.1
ca0_do_adam.sas	Copy required ADaM datasets from main trial	1.2	isn	Approve	10Sep2019:09:16:41	scao	Approve	10Sep2019:09:20:59	10Sep2019:09:20:59	3	Validated	1.2
ca1_adaefu.sas	Adverse Event	1.1	isn	Approve	05Sep2019:03:11:57	asja	Approve	05Sep2019:11:45:34	05Sep2019:11:45:34	2	Validated	1.1
ca1_addsfu.sas	Disposition	1.1	gags	Approve	05Sep2019:11:19:51	isn	Approve	05Sep2019:12:37:28	05Sep2019:12:37:28	2	Validated	1.1
ca1_adpregfu.sas	Pregnancy	1.1	scao	Approve	05Sep2019:11:17:29	isn	Approve	05Sep2019:12:37:28	05Sep2019:12:37:28	2	Validated	1.1
ca2_adlossfu.sas	Pregnancy Loss	1.1	scao	Approve	05Sep2019:11:17:29	isn	Approve	05Sep2019:12:37:28	05Sep2019:12:37:28	2	Validated	1.1
ca2_adneonat.sas	Neonate	1.1	isn	Approve	05Sep2019:03:11:57	asja	Approve	05Sep2019:11:44:55	05Sep2019:11:44:55	2	Validated	1.1
t_adlossfu.sas	Early pregnancy loss - subjects with positive	1.0	scao	Approve	05Sep2019:12:19:59	rikm	Approve	05Sep2019:13:37:00	05Sep2019:13:37:00	1	Validated	1.0
t_adpregfu.sas	Ongoing pregnancy - Full Analysis Set	1.0	gags	Approve	05Sep2019:12:54:35	rikm	Approve	05Sep2019:13:37:00	05Sep2019:13:37:00	1	Validated	1.0
t_malcong.sas	Malformation/congenital anomaly - Safety An	1.0	scao	Approve	05Sep2019:12:19:59	rikm	Approve	05Sep2019:13:36:59	05Sep2019:13:36:59	1	Validated	1.0
t_neonate_4weeks.sas	Neonate health at 4 weeks after birth - all	1.0	isn	Approve	05Sep2019:12:44:19	aami	Approve	05Sep2019:13:00:29	05Sep2019:13:00:29	1	Validated	1.0
t_neonate_birth.sas	Neonatal characteristics at birth - all neo	1.0	scao	Approve	05Sep2019:12:24:16	rikm	Approve	05Sep2019:13:36:59	05Sep2019:13:36:59	1	Validated	1.0
t_neonate_nolivebirth.sas	Reason for no live birth (fetuses/neonate l	1.0	asja	Approve	05Sep2019:12:37:43	rikm	Approve	05Sep2019:13:37:00	05Sep2019:13:37:00	1	Validated	1.0

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### Conduct

- Datasets
- Programs
- Macros
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The screenshot shows the SAS Workspace interface with a file tree on the left and a data table on the right. The file tree is expanded to show the 'adam' folder under 'Data'. The data table has columns for 'Size', 'Date', 'Repository Version', and 'Workspace Status'. Three green boxes with red arrows point to specific rows in the table, each containing a list of program details.

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28 KB	Jan 1		

**Programming Plan**

- Name of program
- Programmer
- Date
- Validator
- Validation status

**Validation Report**

- Name of program
- Programmer
- Date
- Validator
- Validation status

**Program Header**

- Name of program
- Programmer
- Date

Action Status

User: Trainer



### Sign & Version

#### Datasets

- Not versioned

#### Programs

- Versioning
- Signing

#### Macros

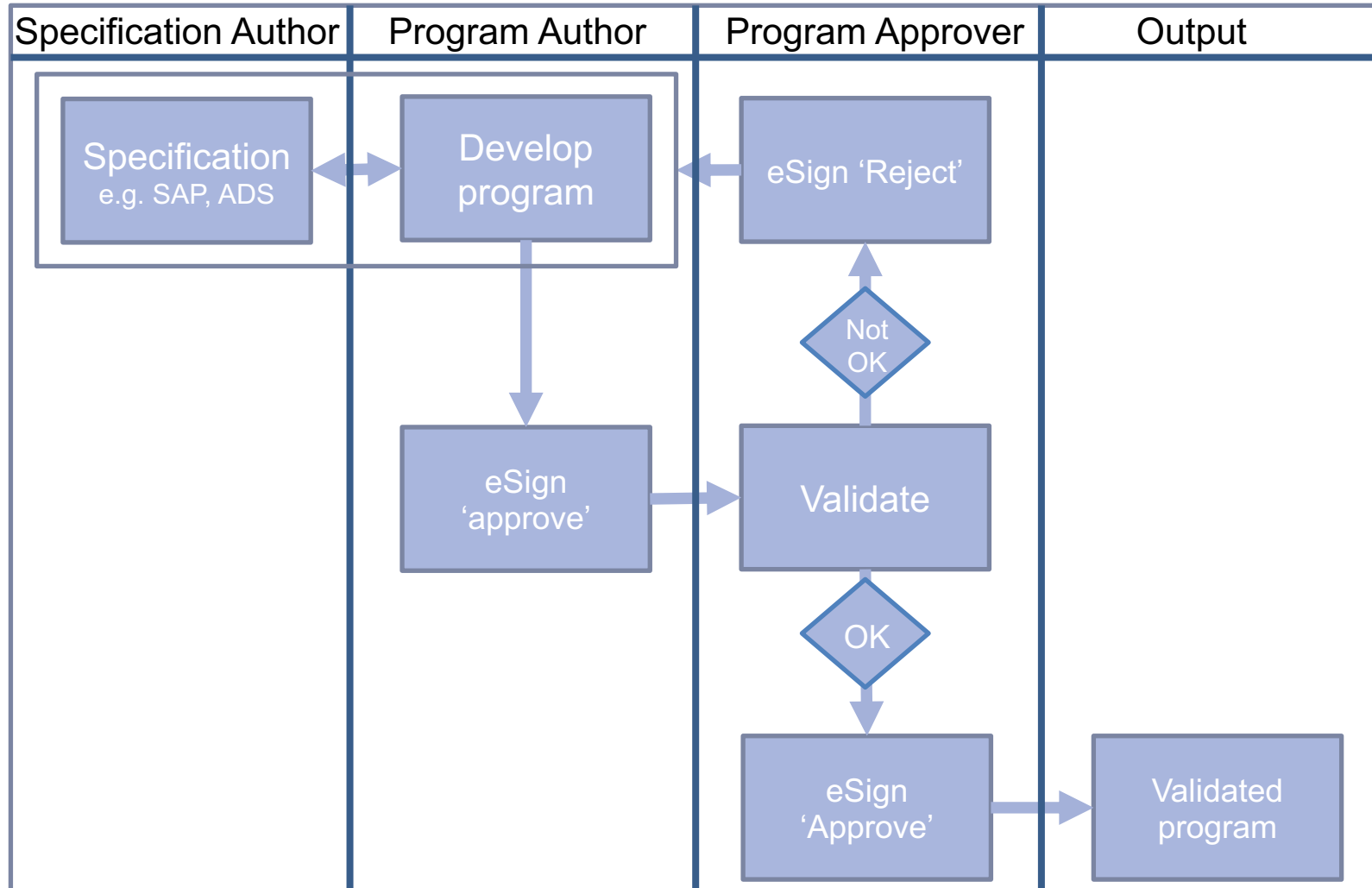
- Versioning
- Signing

#### Logfiles

- Not versioned
- Snapshot at delivery

#### Outputs

- Not versioned
- Packages versioned





## Sign & Version

### Datasets

- Not versioned

### Programs

- Versioning
- Signing

### Macros

- Versioning
- Signing

### Logfiles

- Not versioned
- Snapshot at delivery

### Outputs

- Not versioned
- Packages versioned

Step	Responsible	Action
1	Program Author	Develop the program in the LSAF workspace. Check the program into the LSAF repository and turn on versioning.
2	Program Author	Using the role 'Author' eSign the program indicating 'Approve' including a comment that this is the first version. If the validation level is not available elsewhere it must be included in the comment .
3	Program Approver	Validate according to the specified validation level.  In case of findings continue to step 4.  In case of no findings continue to step 8.
4	Program Approver	Using the role 'Approver' eSign the program indicating 'Reject' including the validation finding(s) as a comment.  If an update to the specification is required then continue to step 5.  If an update to the program is required then continue to step 6.
5	Specification Author	Update the specification according to the validation findings.
6	Program author	Check the program out from the LSAF repository. Update the program according to the validation findings. Check the program back into the LSAF repository.
7	Program author	Using the role 'Author' eSign the program indicating 'Approve' including a comment addressing the validation finding(s). Repeat the process starting from step 3.
8	Program Approver	Using the role 'Approver' eSign the program indicating 'Approve' including a comment that the validation has been completed, e.g. 'No deviation found'.



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## Sign & Version

### Datasets

- Not versioned

### Programs

- Versioning
- Signing

### Macros

- Versioning
- Signing

### Logfiles

- Not versioned
- Snapshot at delivery

### Outputs

- Not versioned
- Packages versioned

The screenshot shows the SAS Workspace interface. On the left is a file tree with the following structure:

- Workspace
  - QAGPharma
    - LSAF Training Examples
      - Files
        - Data
    - PainXD-Study101
      - Efficacy Reports
        - Files
          - Programs
            - Dev
        - Files
          - Data
            - adam
            - sdtm
          - Logs, Listings, Manifests
          - Macros
      - Users

The main table has the following columns: Name, Size, Date, Repository Version, Workspace Status. A row is visible with the value '28 KB' under the Size column and 'Jan 1' under the Date column. Three green callout boxes are overlaid on the table:

- Programming Plan**
  - Name of program
  - Programmer
  - Validator
- Validation Report**
  - Generated from metadata
- Program Header**
  - Name of program

Action Status

User: Trainer



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## Sign & Version

Datasets

- Not versioned

Programs

- Versioning
- Signing

Macros

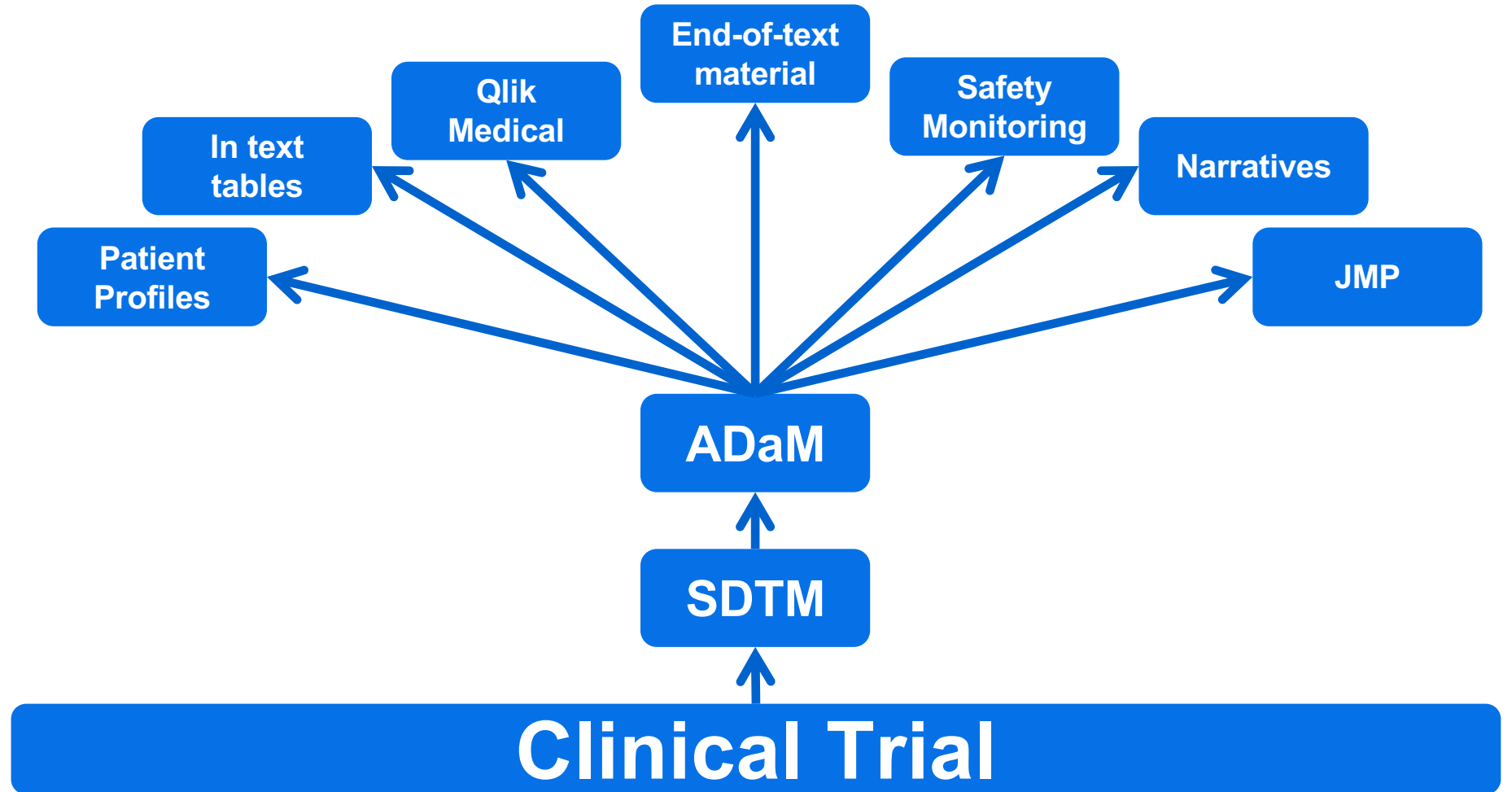
- Versioning
- Signing

Logfiles

- Not versioned
- Snapshot at delivery

Outputs

- Not versioned
- Packages versioned



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# Future Roadmap

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## Program Status Utility

- Can be executed for libraries where we don't have progplans.
- Sync with Validation report for all program entries and their validator credentials.

## Ideas for Related Utilities

- Provide snapshots of artifacts current at a given date (Programs, Jobs, Macros etc.)
- Add version and program status in footnotes for all output
- Extend to a full validation report



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# Validation Report

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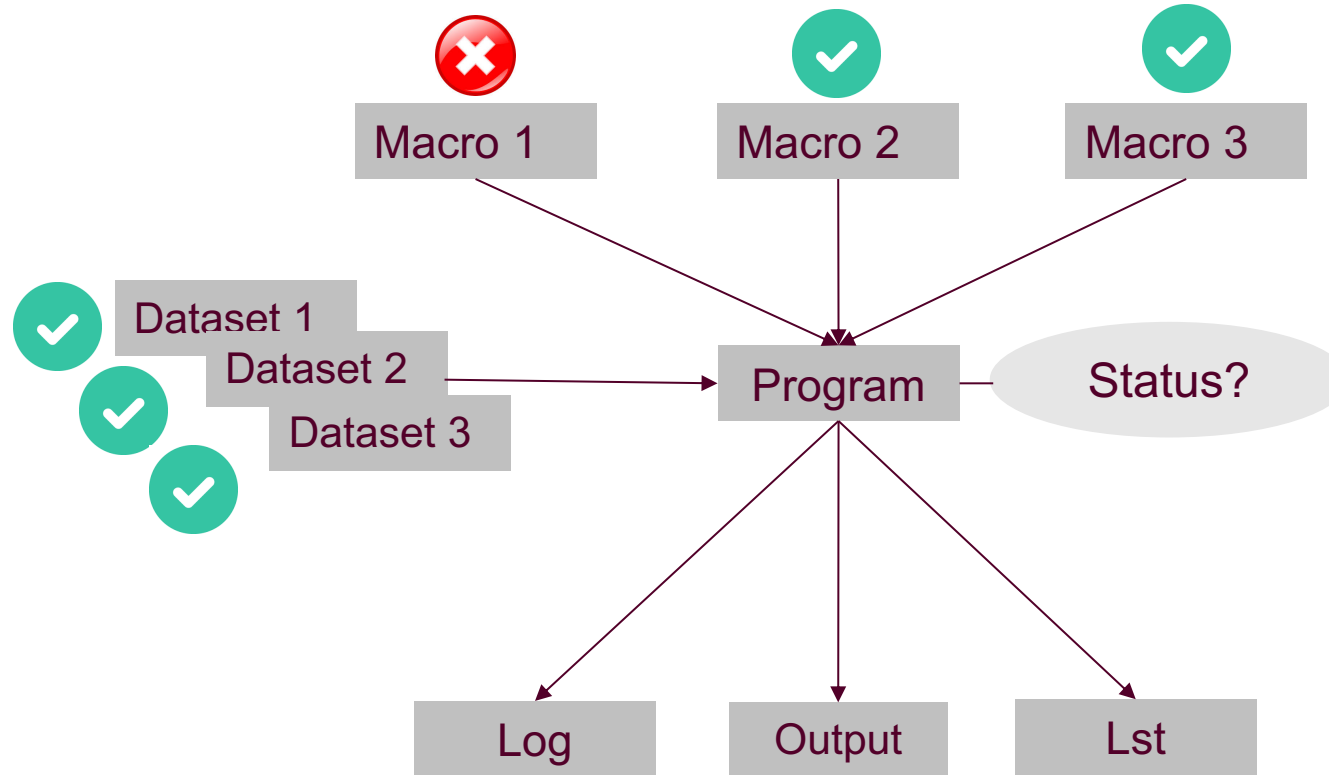
<b>Version</b>	<b>User</b>	<b>Role</b>	<b>Date / time</b>	<b>Decision</b>	<b>Comment</b>
1.00	XXXX	Author	6. jul. 2018 10:00	Approve	Ready for validation
1.00	YYYY	Approver	7. jul 2018 14.16	Reject	Validation finding
1.01	XXXX	Author	8. jul. 2018 11:16	Approve	Finding addressed
1.01	YYYY	Approver	9. jul 2018 11.53	Approve	No deviation found

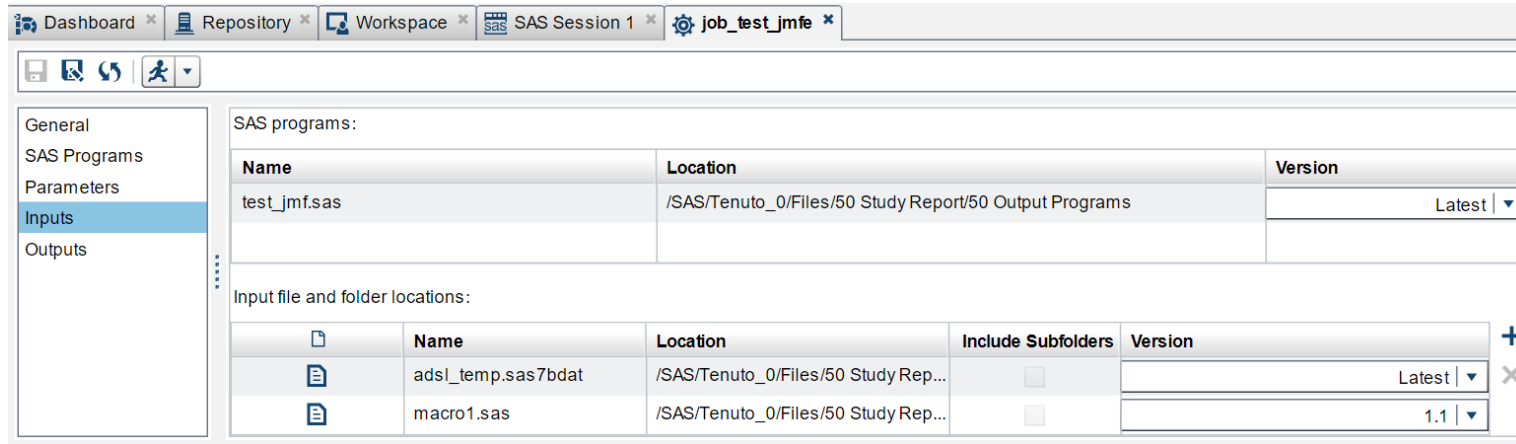
## Agenda

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- Future Plans at Ferring
- **Tackling Dependencies in LSAF**
- Conclusion

# Tackling Dependencies (1)

## How to consider status of dependent artefacts?





Dashboard x Repository x Workspace x SAS Session 1 x job\_test\_jmfe x

General  
SAS Programs  
Parameters  
Inputs  
Outputs

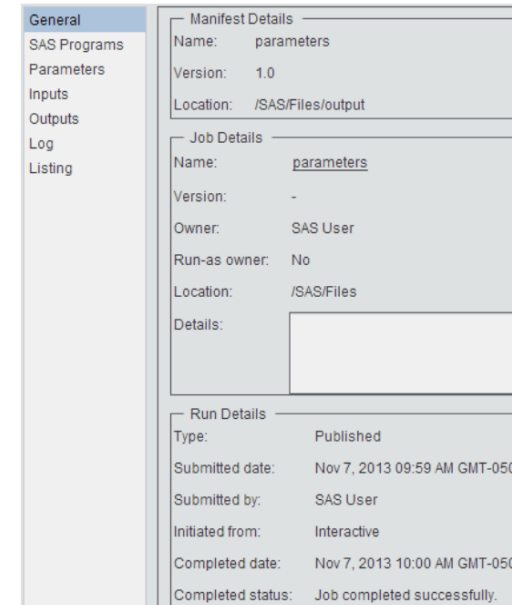
SAS programs:

Name	Location	Version
test_jmf.sas	/SAS/Tenuto_0/Files/50 Study Report/50 Output Programs	Latest   v

Input file and folder locations:

Name	Location	Include Subfolders	Version
adsl_temp.sas7bdat	/SAS/Tenuto_0/Files/50 Study Rep...	<input type="checkbox"/>	Latest   v
macro1.sas	/SAS/Tenuto_0/Files/50 Study Rep...	<input type="checkbox"/>	1.1   v

- Executes SAS programs as a background process
- Represents a single SAS session with a shared WORK library
- Lists all inputs and outputs
- Inputs can be specified as “Latest” or pointing to a specific version
- **Jobs information can be read using LSAF APIs**
- Produce a job manifest with all execution information



General  
SAS Programs  
Parameters  
Inputs  
Outputs  
Log  
Listing

Manifest Details

Name: parameters  
Version: 1.0  
Location: /SAS/Files/output

Job Details

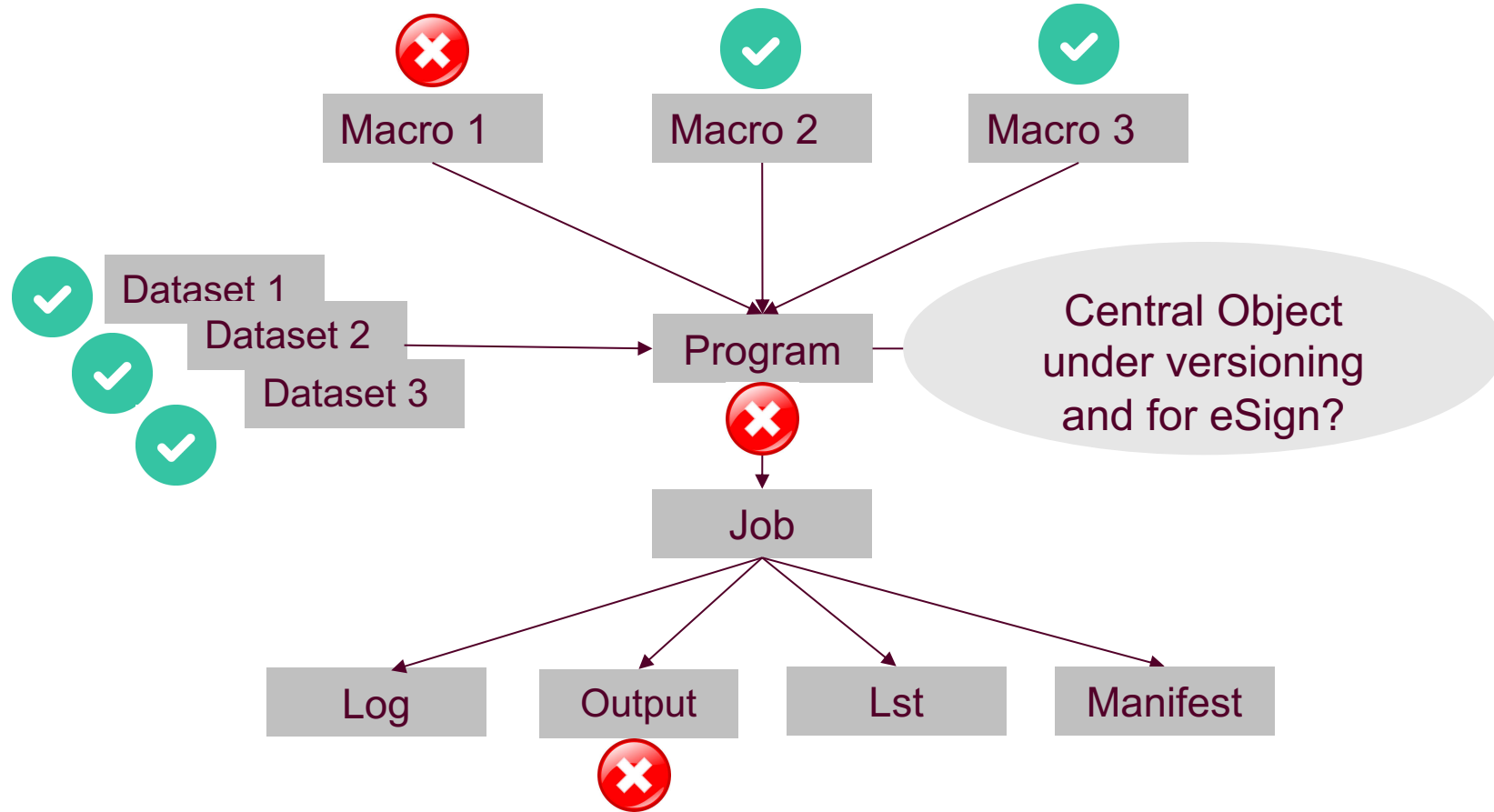
Name: parameters  
Version: -  
Owner: SAS User  
Run-as owner: No  
Location: /SAS/Files  
Details:

Run Details

Type: Published  
Submitted date: Nov 7, 2013 09:59 AM GMT-0500  
Submitted by: SAS User  
Initiated from: Interactive  
Completed date: Nov 7, 2013 10:00 AM GMT-0500  
Completed status: Job completed successfully.

# Tackling Dependencies (3)

## Expand Validation Status to Inputs and Outputs



## Agenda

- Background at Ferring
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- **Conclusion**

**Status information is computed** from programmer and validator eSignatures:

- All operational information is **programmatically retrievable** using LSAF APIs
- **Cannot be out of Sync** with "ProgPlan" by Design!

**Inadvertent changes** will result in a new version with status Draft or the deletion of eSignatures if the program is not under versioning.

**Human errors can easily be tracked** in the system and reported.

Process assumes that **users turn on versioning** at the latest when code is ready for validation.

**Metrics on programming iterations needed** can be captured and provide feedback to management on team performance, standard program needs or training.

Concepts can be extended to **tackle dependencies by analysing jobs** and their manifests