Pharmaceuticals

Integrating SAS with Open Source Software

Jeremy Fletcher

Informatics Specialist

Pharma Global Informatics

F. Hoffmann-La Roche

F. Hoffmann – La Roche
A Global Healthcare Leader

Pharmaceuticals

- One of the leading research-intensive healthcare groups
- Core businesses are pharmaceuticals and diagnostics
- A world leader in Diagnostics
- The leading supplier of medicines for cancer and transplantation and a market leader in virology
- Employs roughly 65,000 people in 150 countries
- Has R&D agreements and strategic alliances with numerous partners, including majority ownership interests in Genentech and Chugai

Overview

Pharmaceuticals

1. Objectives
2. Solution and Architecture
3. SAS Reporting Module
4. Development Environment and Processes
5. Summary

Objectives
- Existing Solution

Pharmaceuticals

- Main requirement was to re-develop an existing reporting solution for Periodic Safety Update Reports.
- Existing solution was
  - Manually driven
  - Based on a monolithic SAS program
  - Reliant on a dedicated support person

Objectives
- Proposed Solution

- Proposed solution needed to be
  - Fully validated
  - Documented and supported by an IT function
  - Transitioned from Business to IT
  - Fully automated
  - Integrated with existing IT infrastructure
  - Extended to cater for new functionality

Objectives
- Business Benefits

Roche

Pharmaceuticals

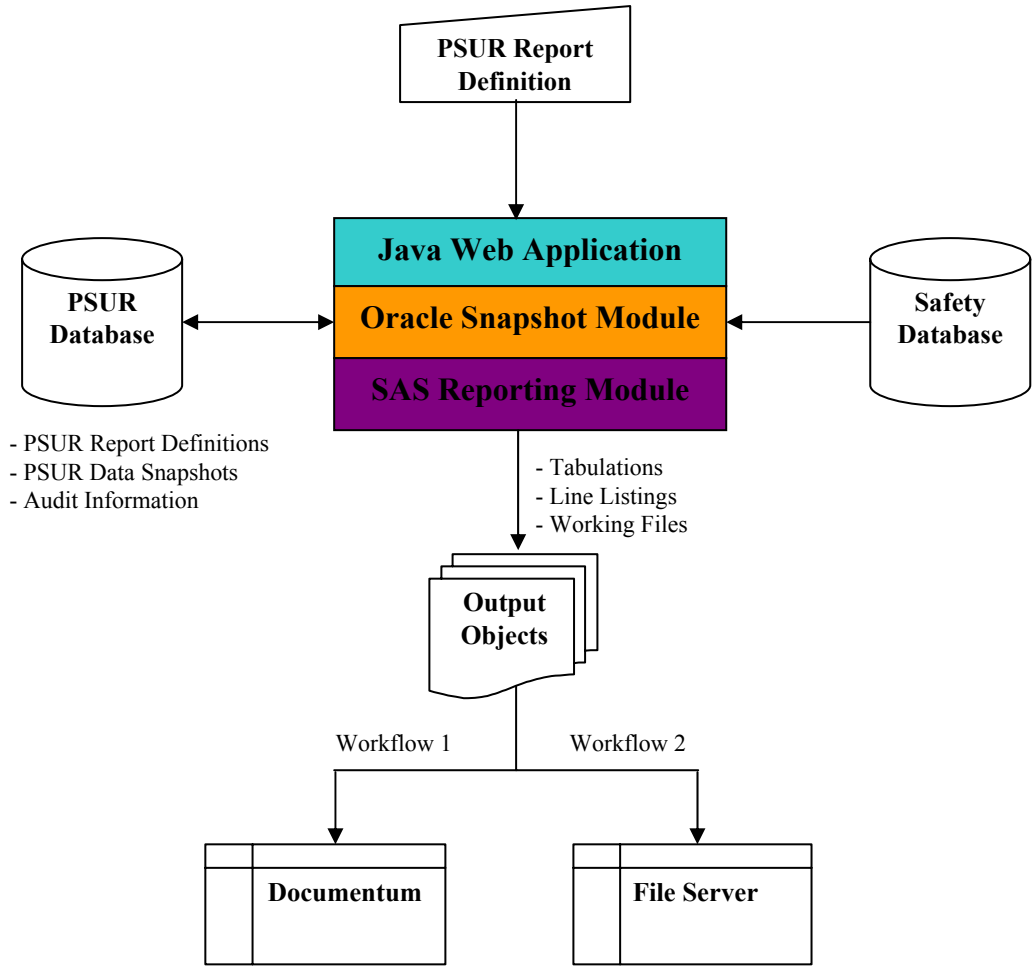
- Standardisation of PSUR publications
  - One common reporting standard
  - Fully validated
- Review of PSUR Guidelines
- Creation of a new accompanying business process, backed up by supporting SOPs
- Switch the authoring from Product Specialists to Medical Writers
- Improved efficiencies

Objectives
- Requirements

Pharmaceuticals

- Reproducibility of reporting outputs
- Automated interfaces to external services
- Different workflows for different user groups
- Large number of reporting outputs
  - Complex line listing
  - Variety of summarisations
  - Combining and splitting output objects

Solution and Architecture - Overview



Pharmaceuticals

Solution and Architecture - Main components

Pharmaceuticals

- Java web application
  - J2EE, Struts, Hibernate
  - Parameter definition
  - Submission of output requests
- Oracle
  - Coding of all business rules and data transformations
  - Creation of data snapshots for report reproducibility
- SAS
  - Report generation
  - Workflow control
  - Email notification

Solution and Architecture - Internal Interfaces

Pharmaceuticals

- Very thin interfaces between all components
- Java to SAS
  - Java submits a SAS executable in batch and immediately releases control
- Java to Oracle
  - Setting parameters to the application database using the Hibernate framework
- SAS to Oracle
  - Executes the Oracle stored procedure to generate a data snapshot
  - Retrieves application parameters and resulting data snapshot

Solution and Architecture
- External Interfaces

- Integration with the existing Drug Safety Portal
- Authentication and authorisation via an existing security mechanism
- Automated publishing of the resulting output files to the Documentum system
- Automated Email notification

Solution and Architecture - Platforms

Roche

Pharmaceuticals

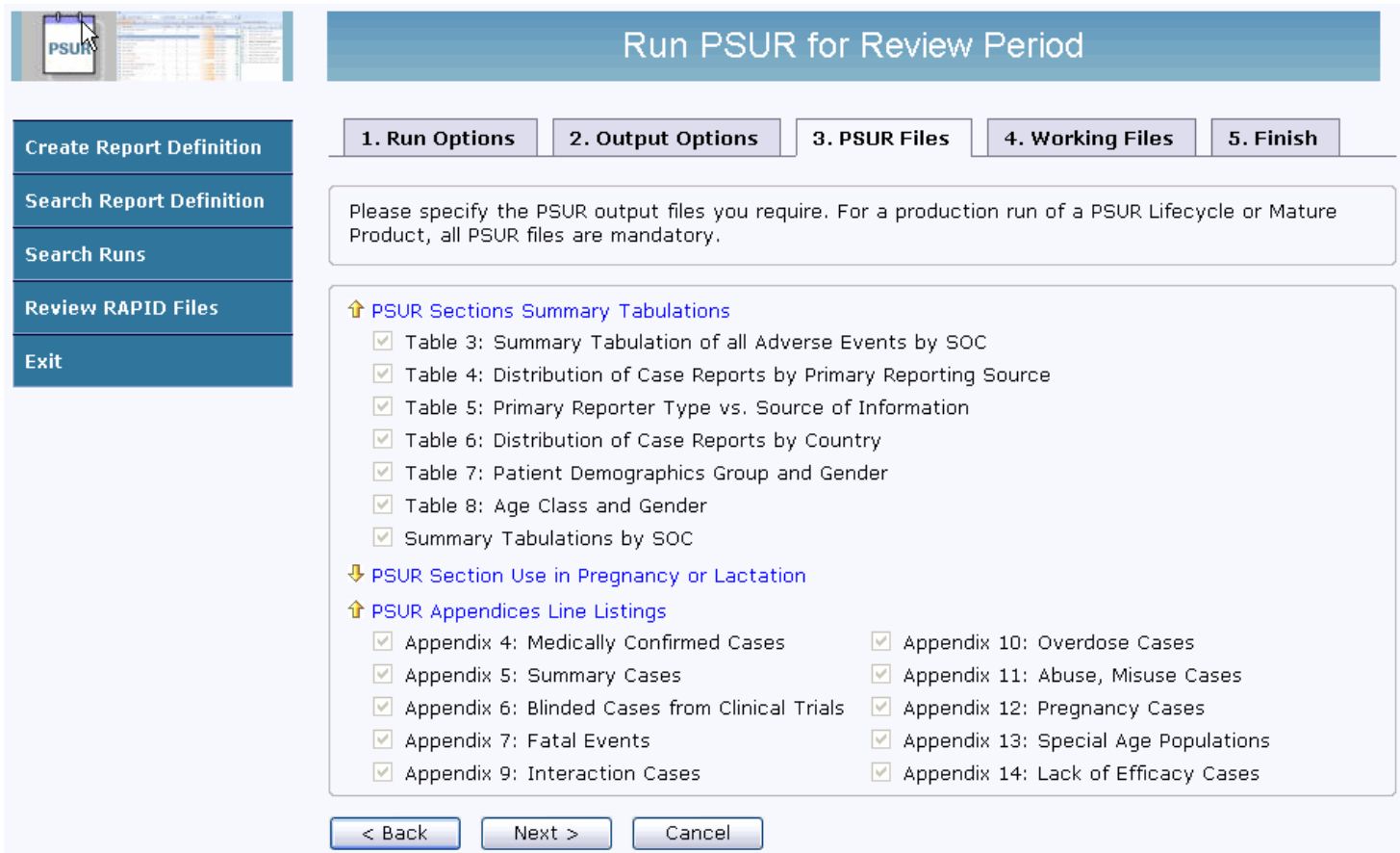
Complete platform independence from the combination of SAS and Java

- Windows development environment
- UNIX integration, testing and production environments

Solution and Architecture - Java Web Application

Pharmaceuticals

Wizard-based report definition

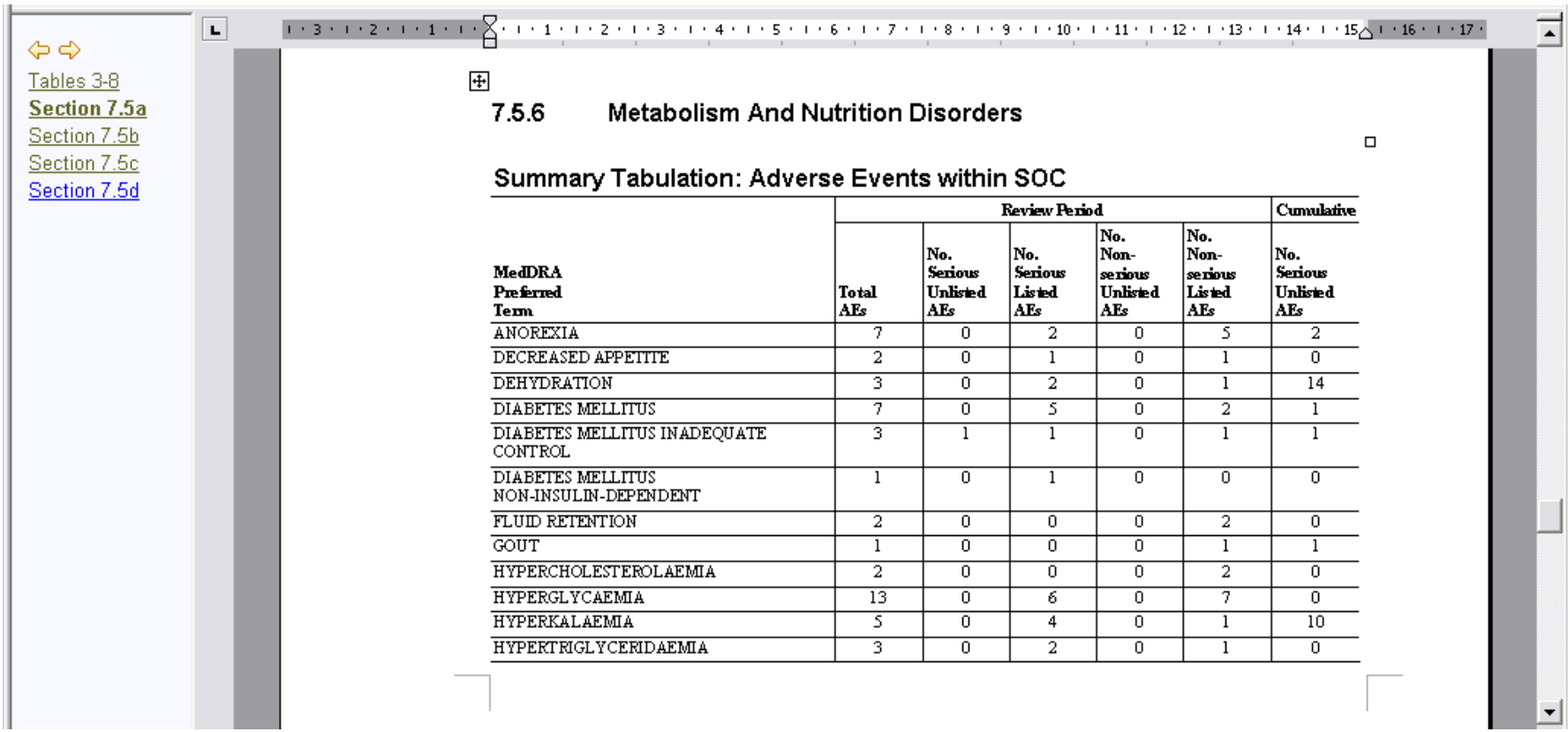


Solution and Architecture
- Java Web Application

Roche

Pharmaceuticals

File Preview



7.5.6 Metabolism And Nutrition Disorders

Summary Tabulation: Adverse Events within SOC

MedDRA Preferred Term	Review Period					Cumulative
	Total AEs	No. Serious Unlisted AEs	No. Serious Listed AEs	No. Non-serious Unlisted AEs	No. Non-serious Listed AEs	No. Serious Unlisted AEs
ANOREXIA	7	0	2	0	5	2
DECREASED APPETITE	2	0	1	0	1	0
DEHYDRATION	3	0	2	0	1	14
DIABETES MELLITUS	7	0	5	0	2	1
DIABETES MELLITUS INADEQUATE CONTROL	3	1	1	0	1	1
DIABETES MELLITUS NON-INSULIN-DEPENDENT	1	0	1	0	0	0
FLUID RETENTION	2	0	0	0	2	0
GOUT	1	0	0	0	1	1
HYPERCHOLESTEROLAEMIA	2	0	0	0	2	0
HYPERGLYCAEMIA	13	0	6	0	7	0
HYPERKALAEMIA	5	0	4	0	1	10
HYPERTRIGLYCERIDAEMIA	3	0	2	0	1	0

SAS Reporting Module - Introduction

Pharmaceuticals

- Metadata
- Output Driver
- Output Programs
- ODS Styles and Templates
- Error Handling

SAS Reporting Module - Introduction

Pharmaceuticals

- Approximately 20 different report types
  - Complex line listing with multiple outputs, indenting, linked wrapping columns, stacked columns, complex pagination requirements.
  - Multiple summarisations, some basic, some more involved.
- Approximately 30 data result sets each containing a standard superset of columns
- Approximately 100 output files from different combinations of report types and result sets.

SAS Reporting Module - Metadata

Roche

Pharmaceuticals

- Metadata driven
  - Links all required combinations of report types and result sets
  - Definition of all text strings within every output
  - Definition of column requirements for each report type
  - Email settings including body text
  - FTP settings

SAS Reporting Module - Metadata

Roche

Pharmaceuticals

- Advantages to using metadata
  - Changes to any text string requires a simple change to a metadata table

	PARAMETER_NAME	PARAMETER_VALUE	CONTEXT	SCOPE
3	header	Medically Confirmed Case Reports	line_listing_medconf	OUTPUT_OBJECT
4	ll_related_mcn_header	Other MCNs for this Patient:	line_listing	PGM
5	ll_date_header	Date:	line_listing	PGM
6	ll_pagenum_header	Page	line_listing	PGM
7	ll_estimate_header	^ = an estimate, see glossary for details	line_listing	PGM
8	ll_related_mcn_continued	Other MCNs for this Patient (continued):	line_listing	PGM
9	no_data_text	No Case Reports Received	_global	GLOBAL
10	ll_column_case	MCN!Country!Age!Sex!Source	line_listing	PGM
11	ll_column_ind_medhist	Indication!- Medical History	line_listing	PGM

SAS Reporting Module - Metadata

Roche

Pharmaceuticals

- Advantages to using metadata
  - Changes to existing combinations of report types and result sets controlled within a metadata table. No programmatic changes required

	OUTPUT_OBJECT	RESULT_SET	RESULT_SET_REFERENCE	CREATED_BY
73	esr_alp_fup_cur_per	alp_follow_up_p	result_set	QM_PSUR
74	esr_alp_fup_prev_per	alp_follow_up_b	result_set	QM_PSUR
75	line_listing_alp_new_preg_cases	alp_preg_initial	result_set	QM_PSUR
76	mcn_1_alp_medconf	alp_initial	result_set	QM_PSUR
77	soc_tables_medconf	cu_med_confirmed	result_set_cu	QM_PSUR

SAS Reporting Module - Metadata

Roche

Pharmaceuticals

- Advantages to using metadata
  - Addition of new outputs based on existing result sets and existing programs also only requires a change to the metadata table

	OUTPUT_OBJECT	OUTPUT_PGM	RUN_ORDER	PSUR_WF_CODE	SPLIT_FLAG
10	line_listing_study_verum_unrel	line_listing	350	WF	N
11	esr_nonmedconf	esr	380	WF	N
12	esr_serious_unlisted	esr_serious_unlisted	410	WF	Y
13	line_listing_summary_cum	line_listing	440	WF	N
14	esr_summary	esr	470	WF	N

SAS Reporting Module - Metadata

Roche

Pharmaceuticals

- Advantages to using metadata
  - Efficiency in only retrieving the columns required for a given result set

	OUTPUT_PGM	RESULT_SET_REFERENCE	VARS
3	esr_special_age	result_set_a	case_id case_report_id
4	esr_serious_unlisted	result_set	case_id case_report_id event_seriousness_flag event_listed_flag case_soc_no_cur
5	summary_gender_age	result_set	case_id gender_code age_at_onset_years
6	line_listing	result_set	case_id adverse_event_id drug_id case_main_drug_id rtsn drsn aesn patient_group_id patient_first_case_id case_soc_abbrev_cur case_soc_no_cur prim_rr_country_code age_at_onset_with_est gender_code origin_code indicat_pt_cur dosage_route received_inn_generic_name onset_dt onset_dt_reported latency pt_cur event_outcome event_seriousness_flag suspect_flag cum_dosage

SAS Reporting Module
- Output Driver

Pharmaceuticals

- Entirely driven by the metadata
- Picks up which programs to run against which result sets and in the pre-defined order
- Picks up and sets the appropriate parameters from the metadata, e.g. result set, column labels
- Controls the destination of the outputs based on the workflow
- Prepares the FTP command files for execution

SAS Reporting Module
- Output Programs

Roche

Pharmaceuticals

- Each output program links directly to a specific report type
- Each may be run with a number of different cuts of the data
- Each has its own defined interface of expected macro parameters and expected source data items and is independent from the application as a whole

SAS Reporting Module
- ODS Styles and Templates

Pharmaceuticals

- All ODS style and ODS template definitions are defined independently from the output programs
- All ODS styles (i.e. fonts, alignment) are stored independently from the ODS templates (i.e. column definitions)
- Use of inheritance to factor out commonalities

SAS Reporting Module
- ODS Styles and Templates

Pharmaceuticals

- Example template

```
define table psur_param_dpn.table;
   style=param_table;
   mvar lb_param_dpn_header;
   column drug_pref_name;
   define header param_header1;
      text lb_param_dpn_header;
   end;
   define column drug_pref_name;
      parent=psur_param_off.column_parent;
      style=param_data_bold;
   end;
end;
```

SAS Reporting Module - Error Handling

Roche

Pharmaceuticals

- Error handling at each data step and procedure boundary
- Email facility
  - Different groups of users
  - All metadata driven
  - Additional notification to the support team in the event of an error

Development Environment & Processes - Overview

Pharmaceuticals

- Developed across 2 sites
  - Java development at one site
  - SAS and Oracle development at a second site
- Multiple developers per component
- Multiple environments
  - Local development
  - Integration
  - System Test
  - UAT
  - Production

Development Environment & Processes - Overview

Pharmaceuticals

The multi-developer, multi-site, multi-environment set-up meant a clear need for **Configuration Management**

Solution

- Use of **CVS** (Concurrent Versioning System) as a mechanism for configuration management
- Use of **Ant** for deployment purposes
- Use of **Eclipse** as a development environment where all program code could be brought together

Development Environment & Processes - CVS

Pharmaceuticals

- History of all development changes
- History of all versions of each individual program file
- Ability to tag/label a release of the application as a whole, i.e. create a snapshot of the application containing all current versions of the individual programs.
- Ability to check in and check out from the central repository
- Ability to compare differences between versions of the programs

Development Environment & Processes - Ant

Pharmaceuticals

- XML-based script for deployment of applications
- Provides a platform-independent and environment-independent deployment
- One build script for deployment of the Java and SAS components
- Some features of Ant
  - File and directory handling
  - Execute and report on unit tests
  - Kick off external processes, for example a SAS executable
  - Compile Java code and deploy onto a remote application server

Development Environment & Processes - Ant

Pharmaceuticals

Example code snippet

- First delete the existing directory containing source programs
- Next make a new directory
- Copy all files from the checked out CVS repository to the source directory
- Add execute permissions on a script file

```
<target name="psur-sas" depends="init" description="Creates and configures SAS directories">
        <delete dir="${psur-sas.src.sas.dir}" />
        <mkdir dir="${psur-sas.src.sas.dir}" />
        <copy todir="${psur-sas.src.sas.dir}">
                <fileset dir="${src.sas.dir}" />
        </copy>
        <chmod file="${psur-sas.sasstart.dir}/${app.script.run.name}" perm="774" />
</target>
```

Development Environment & Processes - Ant

Pharmaceuticals

Once the build script has been created, it can be executed together with a target

```
ant <target>

ant psur-sas
```

This will run the psur-sas target within the ant script which in turn can specify dependencies on other targets within the script.

Development Environment & Processes - Eclipse

Pharmaceuticals

- Richly functional Java IDE
  - Also suitable for SAS-related Java development
- Tight integration with CVS
- Tight integration with Ant
- Editing features (not available within SAS)
  - Search and replace for the application as a whole
  - Version history
  - Compare files
  - Compare different versions of the same file

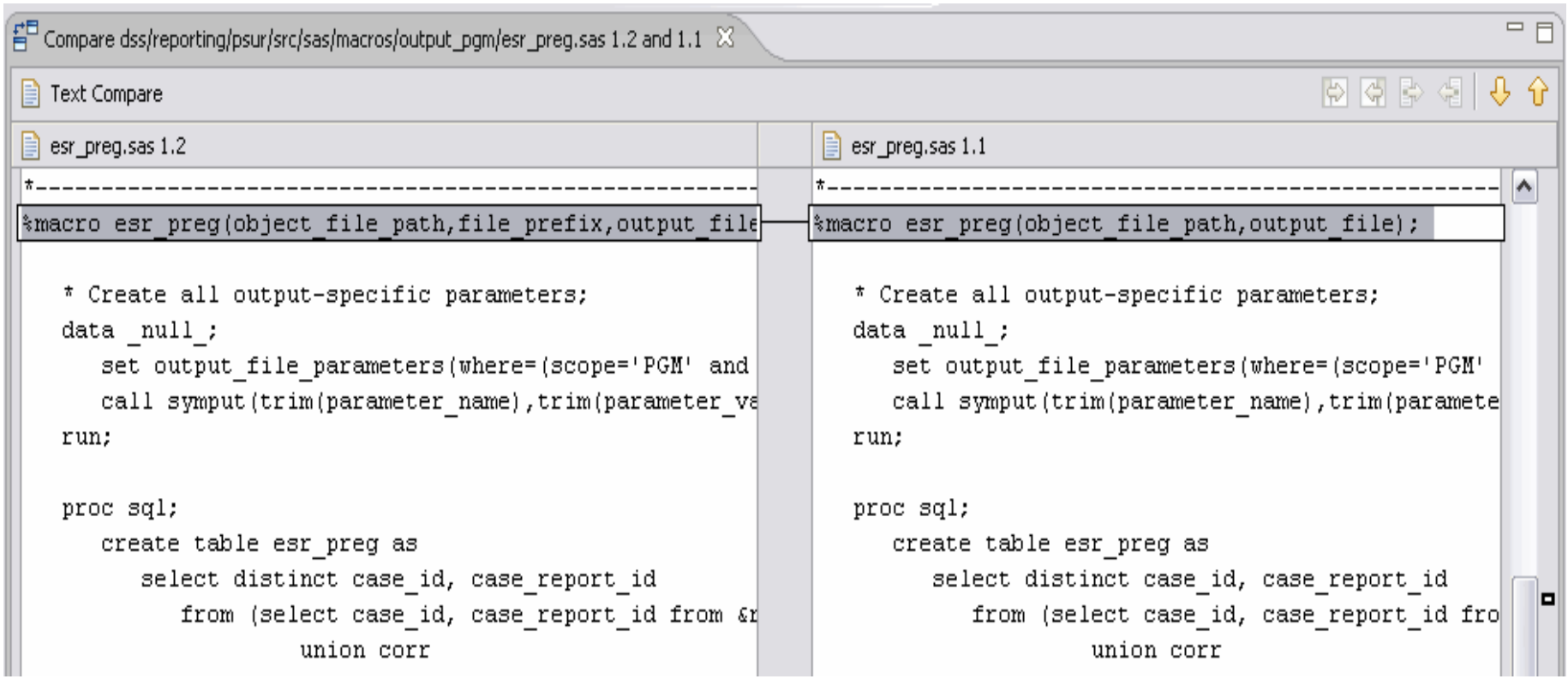
Development Environment & Processes - Eclipse

Pharmaceuticals

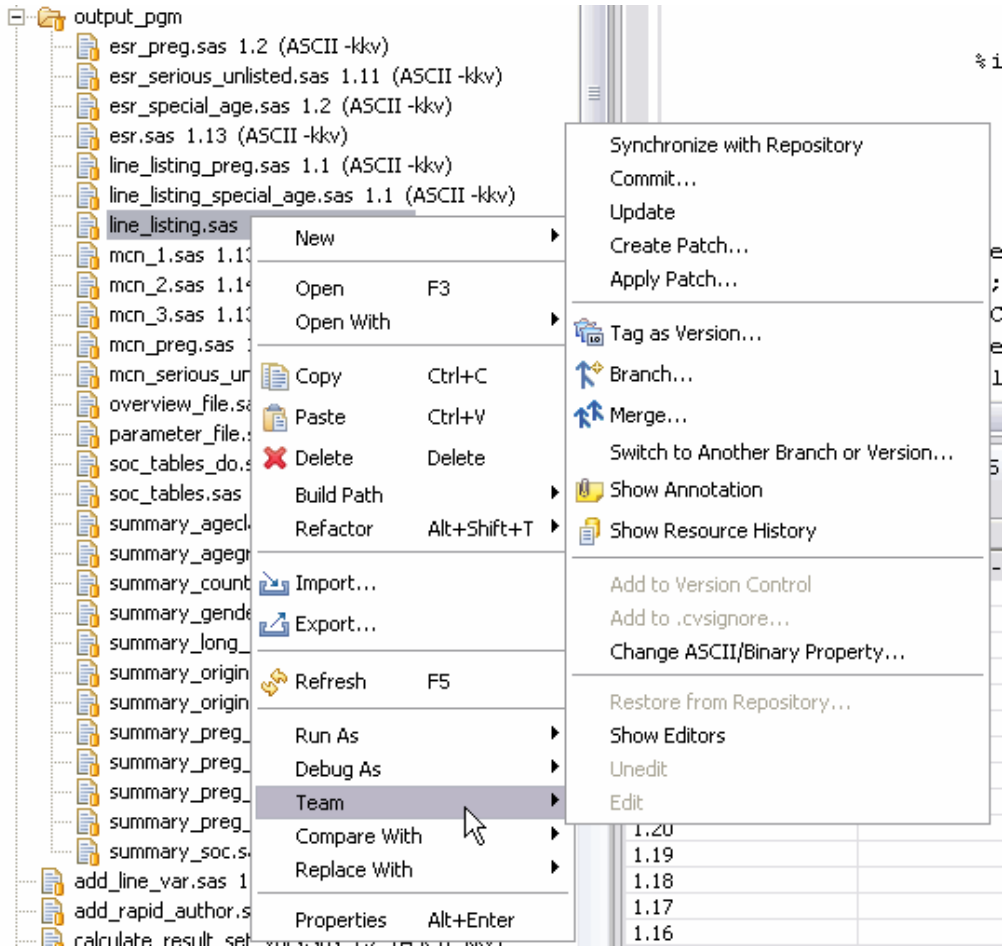
- Synchronise with the CVS repository
  - Incoming changes
  - Outgoing changes
  - Conflicting changes
    - Identification of each specific conflict
    - Visual resolution of each conflict
    - Ability to merge changes

Development Environment & Processes - Eclipse File Compare

Pharmaceuticals



Development Environment & Processes - Eclipse CVS Integration



Pharmaceuticals

Development Environment & Processes - Eclipse Version History

Pharmaceuticals

Problems | Javadoc | Declaration | CVS Resource History | Search

line_listing.sas

Revision	Tags	Date	Author	Comment
***1.30**	**PSUR-REL-1-0-1, ...**	**27.09.05 16:32**	**fletchj1**	**Make the drug therapies section match the spec fr**
1.29		26.09.05 17:02	fletchj1	Changes following dry run of unit testing:[...]
1.28		16.09.05 13:43	fletchj1	Pick the print date up from a macro so that the unit tests c.
1.27		15.09.05 17:29	fletchj1	Ensure the working file header appears for all Mature and ..
1.26		14.09.05 16:50	fletchj1	Remove warning when using soctxt format[...]
1.25		09.09.05 12:48	fletchj1	Remove the drop of onset_dt as it isn't kept
1.24		09.09.05 12:28	fletchj1	Put in &syserr checks around every data step and proc
1.23		08.09.05 11:30	fletchj1	Use onset_dt_reported from the result set instead of onse.
1.22		26.08.05 16:56	fletchj1	Add counts for patient and case to the line listing
1.21		25.08.05 18:03	fletchj1	Use printed end date in the title
1.20		15.08.05 12:30	fletchj1	Use full text for gender[...]
1.19		11.08.05 11:22	fletchj1	Fix a problem with creation of num_pages macro
1.18		10.08.05 13:54	fletchj1	Modified drug title line
1.17		09.08.05 16:28	fletchj1	Make the medhist and drug therapy tables parameter driver
1.16		09.08.05 09:07	fletchj1	Change age at onset to use the new variable with the esti..
1.15		05.08.05 17:13	fletchj1	Removed call to create_table macros - now elsewhere. Als.

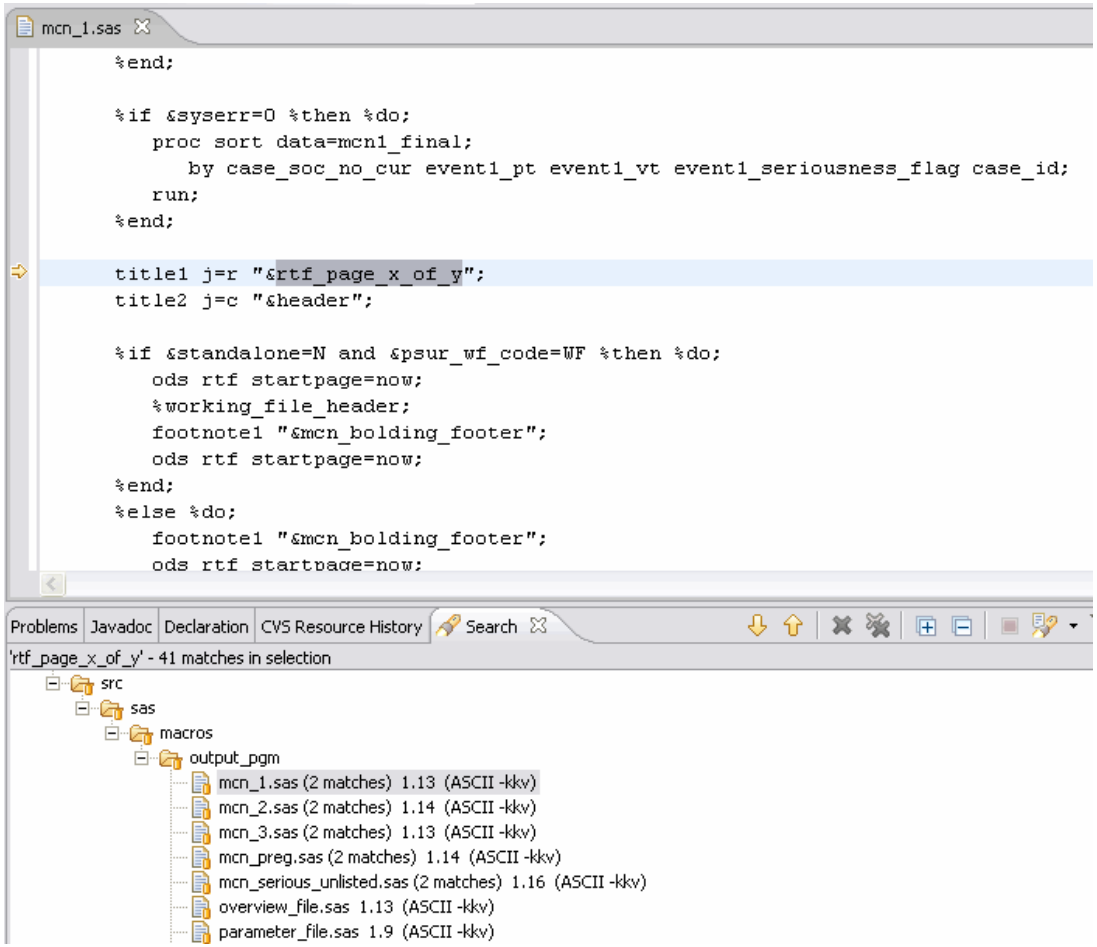
PSUR-DEV-1-1-0
PSUR-REL-1-0-0
PSUR-REL-1-0-1
PSUR-REL-1-0-X

Make the drug therapies section match the spec from teh SDS, to pick up thera

Development Environment & Processes - Eclipse File Searching

Roche

Pharmaceuticals



Development Environment & Processes - Unit Testing

Pharmaceuticals

Reasons for Unit Testing

- Due to the large number of output files, automated SAS unit testing was a crucial development goal
  - Reduce the testing burden
  - Pay-off with repeat testing within the normal testing cycle
  - Pay-off also with future changes where the test suite will highlight any problems when maintenance is performed

Development Environment & Processes - Unit Testing

Pharmaceuticals

Methodology

- Principles of JUnit testing from the Java world were adopted within SAS
- Unit testing integrated into the deployment process with Ant
  - Whenever the application is deployed the Java and SAS unit tests will be run and any problems automatically highlighted

Development Environment & Processes - Unit Testing

Roche

Pharmaceuticals

Example Unit Test Program

```
%macro test_line_listing_for(psur_wf_code,report_type,standalone,empty=N);

    %inc "&unit_test_path/setup_working_file_header.sas";
    %inc "&unit_test_path/setup_line_listing.sas";
    %inc "&unit_test_path/setup_line_listing_data.sas";
    %inc "&unit_test_path/setup_post_process.sas";

    %let output_file=line_listing_%lowcase(&psur_wf_code._&report_type._&standalone);
    %let result_set=ll_unit_test;

    options orientation=&orientation;

    ods rtf body="&object_file_path/&output_file..rtf" style=&pgm_style startpage=no;

    %line_listing;

    ods _all_ close;;

    %rtf_post_process(&object_file_path,&output_file..rtf);

    %inc "&unit_test_path/teardown_working_file_header.sas";
    %inc "&unit_test_path/teardown_line_listing.sas";
    %inc "&unit_test_path/teardown_line_listing_data.sas";
    %inc "&unit_test_path/teardown_post_process.sas";

%mend;
```

Development Environment & Processes - Unit Testing

Roche

Pharmaceuticals

Execution of Scenarios for 1 Unit Test Program

```
%test_line_listing_for(psur_wf_code=WF,   report_type=MP, standalone=Y);
%test_line_listing_for(psur_wf_code=WF,   report_type=QE, standalone=N);
%test_line_listing_for(psur_wf_code=WF,   report_type=QE, standalone=Y);
%test_line_listing_for(psur_wf_code=PSUR, report_type=LP, standalone=N);
%test_line_listing_for(psur_wf_code=PSUR, report_type=LP, standalone=Y);
```

Unit Test Driver

```
%inc "&unit_test_path/test_summary_tables_psur.sas";
%inc "&unit_test_path/test_summary_tables_preg.sas";
%inc "&unit_test_path/test_summary_tables_wf.sas";
%inc "&unit_test_path/test_soc_tables.sas";
%inc "&unit_test_path/test_line_listing.sas";
%inc "&unit_test_path/test_mcn_1.sas";
%inc "&unit_test_path/test_mcn_2.sas";
%inc "&unit_test_path/test_mcn_3.sas";
%inc "&unit_test_path/test_mcn_preg.sas";
%inc "&unit_test_path/test_mcn_serious_unlisted.sas";
%inc "&unit_test_path/test_parameter_file.sas";
```

Development Environment & Processes - Unit Testing

Roche

Pharmaceuticals

Ant Deployment Target

```
<target name="sas-unit-test.execute" depends="sas-unit-test.init" description="Execute SAS Unit Test">
    <exec executable="/opt/SAS/product/v82/sas" dir="${basedir}" failonerror="true">
        <arg line="-autoexec ${sas-unit-test.autoexec.file}" />
        <arg line="-config ${sas-unit-test.config.file}" />
        <arg line="-sysin ${sas-unit-test.src.dir}/psur-unit-test-driver.sas" />
        <arg line="-log ${sas-unit-test.log.file}" />
        <arg line="-work ${sas-unit-test.work.dir}" />
        <arg line="-print '/dev/null'" />
        <env key="sas-unit-test.log.file" value="${sas-unit-test.log.file}" />
        <env key="sas-unit-test.output.dir" value="${sas-unit-test.output.dir}" />
        <env key="sas-unit-test.src.dir" value="${sas-unit-test.src.dir}" />
        <env key="src.sas.dir" value="${src.sas.dir}" />
    </exec>
</target>
```

Development Environment & Processes - Unit Testing

Pharmaceuticals

Ant Execution

```
init:
     [echo] ============================================================
     [echo]           psur: 05-Oct-2005 20:32:34
     [echo] ============================================================


sas-unit-test.init:
   [delete] Deleting: /home/sas/qmuser/systemtest/dss/reporting/PSUR-REL-1-0-1/sas-unit-test/psur-unit-test-config.cfg
   [delete] Deleting: /home/sas/qmuser/systemtest/dss/reporting/PSUR-REL-1-0-1/sas-unit-test/psur-unit-test-autoexec.sas
   [delete] Deleting: /home/sas/qmuser/systemtest/dss/reporting/PSUR-REL-1-0-1/sas-unit-test/psur-unit-test.log
   [delete] Deleting: /home/sas/qmuser/systemtest/dss/reporting/PSUR-REL-1-0-1/sas-unit-test/diff.log
   [delete] Deleting: /home/sas/qmuser/systemtest/dss/reporting/PSUR-REL-1-0-1/sas-unit-test/grep.log
   [delete] Deleting directory /home/sas/qmuser/systemtest/dss/reporting/PSUR-REL-1-0-1/sas-unit-test/work
   [delete] Deleting directory /home/sas/qmuser/systemtest/dss/reporting/PSUR-REL-1-0-1/sas-unit-test/output
   [delete] Deleting directory /home/sas/qmuser/systemtest/dss/reporting/PSUR-REL-1-0-1/sas-unit-test/compare
    [mkdir] Created dir: /home/sas/qmuser/systemtest/dss/reporting/PSUR-REL-1-0-1/sas-unit-test/work
    [mkdir] Created dir: /home/sas/qmuser/systemtest/dss/reporting/PSUR-REL-1-0-1/sas-unit-test/output
    [mkdir] Created dir: /home/sas/qmuser/systemtest/dss/reporting/PSUR-REL-1-0-1/sas-unit-test/compare
     [copy] Copying 2 files to /home/sas/qmuser/systemtest/dss/reporting/PSUR-REL-1-0-1/sas-unit-test
     [copy] Copying 159 files to /home/sas/qmuser/systemtest/dss/reporting/PSUR-REL-1-0-1/sas-unit-test/compare

sas-unit-test.execute:
sas-unit-test:
     [exec] Result: 1
     [exec] Result: 1

BUILD SUCCESSFUL
Total time: 2 minutes 31 seconds
```

Development Environment & Processes - Validation

Roche

Pharmaceuticals

- Up-front validation plan detailing all formal deliverables for the project
- Clearly defined project milestones with full documentation at each step
  - System Delivery Specification
  - Technical System Design
  - Test Plan
  - Test Scripts

Summary

Pharmaceuticals

- Ant, Eclipse and CVS are simply tools to aid the development and deployment process
- Once the application is checked out and deployed, it is purely Java, Oracle and SAS
- They assist in the automation of certain validation steps without impacting formal validation requirements

Summary

Pharmaceuticals

- The combination of Eclipse, CVS and Ant greatly enhance the development process
  - Improve cohesion
  - Simplify configuration management
  - Give structure to the testing process
  - Simplify the deployment and maintenance processes
- These tools are not in standard use within the SAS community but can greatly contribute both in terms of the software and also in terms of the good practices that they embody.

Roche

Pharmaceuticals

Thank you for your attention.

jeremy.fletcher@roche.com