

Simple Safety Monitoring with Signal Detection

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Topics

- Introduction
- Case Profile
- Patient Profiles
- Safety Surveillance
- Signal Detection
- Signals Framework
- Summary

Case Profile

- Pharmacovigilance request for review listings
- 2 studies
- 4 Listings
- 600 subjects
- 3600 + pages
- 3 Zip-files due to e-mail system restrictions



- Expecting 1000 subjects
- Expecting 8600+ pages
- ... and then they wanted graphs

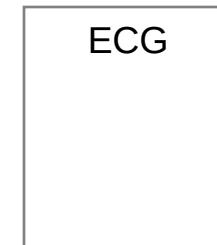
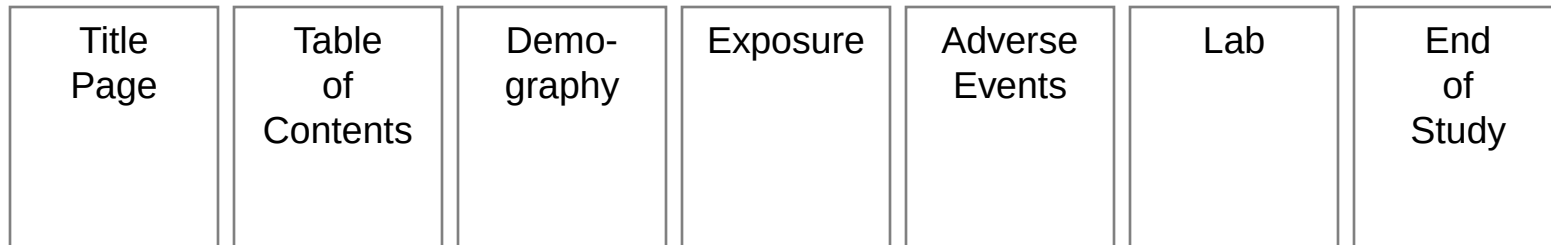
Change of Requirements

- ✓ An individual case report that contains all the necessary information for a subject
 - Display correlation of information and events for a subject
 - Rapid initiation and delivery
- ✓ Dissemination of information such that a subject profile is easily distributable



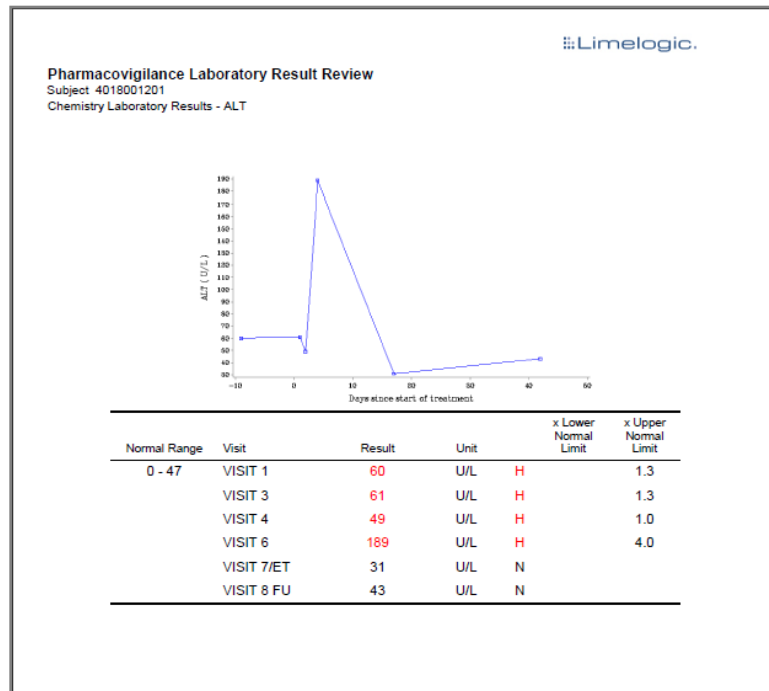
Patient Profiles

Display Panels



- ✓ Standard displays
- ✓ Configurable
- ✓ Customisable
- ✓ Flexible

Patient Review Book



- Standard displays
- Provide both a trend and the observed values
- Color highlighting
 - ✓ Out of Range values
 - ✓ New data
 - ✓ Unscheduled assessments

600 subjects = 600 outputs
Average 10 pages per output

Safety Surveillance

- Evolving joint effort within the study teams
- Part of overall operational conduct of all studies
- More than "a quick look at the data"



- Process and Systematic
- Many different viewpoints
- Evolving knowledge



Identify cases that may exemplify potential safety issues and warrant review

Safety Surveillance – Next Step

- Highlight cases that may exemplify potential safety issues
- Not a priority list / Not a filter
- Arrange cases “worst case first”



Rank subjects according to a set of rules

Safety Rule

Not all rules can be compared directly

Safety Rule
Groups

Different team members would rank subjects
in a different way

Rank Sets

Navigation Lists

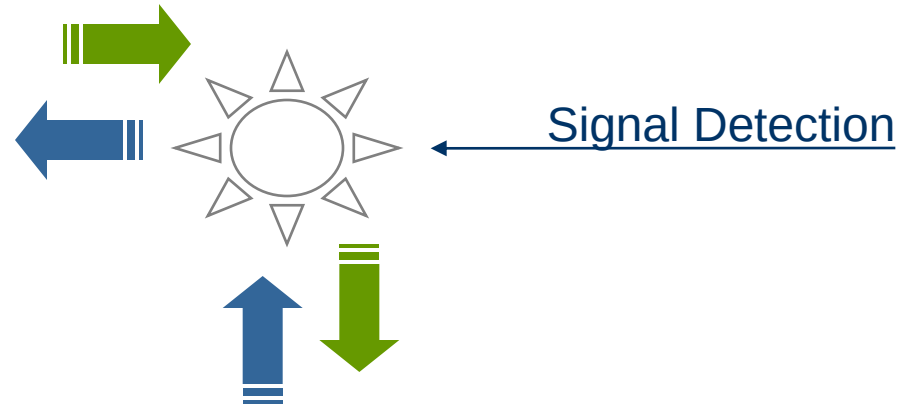
Subject Ranking by Laboratory Results Below or Above Specified Normal Range.

Rank	Unique Subject Identifier	Previous Rank ¹	Laboratory Parameter Group 1					Laboratory Parameter Group 2						
			ALT	AST	Alkaline Phosphatase	Gamma GT	Total Bilirubin	Creatinine	Creatinine Kinase	HCT	HGB	Platelets	Urea (BUN)	WBC
1	406-0021403	-	2.4	2.6	2.4	25.7	.	.	.	.	1.0	1.1	0.1	.
2	406-0021403	-	3.5	8.2	1.9	10.0	.	.	1.4	0.0	0.0	.	0.1	1.0
3	406-0021403	-	1.7	1.4	.	16.0	.	.	1.3	0.2	0.1	.	.	.
4	406-0021403	-	2.9	4.7	1.8	18.3	1.4	.	1.7	0.1	0.0	1.1	0.1	1.4
5	406-0021403	-	8.2	18.3	.	3.8	.	.	.	0.2	0.1	1.4	.	.
6	406-0021403	-	1.3	1.9	3.0	12.2	.	.	.	0.1	0.1	.	.	.
7	406-0021403	-	.	1.2	1.1	11.6	.	.	12.2	0.2	0.0	1.6	.	1.2

- ✓ Highlight cases “worst case first”
- ✓ Overview of safety index results
- ✓ Different scenarios, contexts and areas of interested
- ✓ Single subject level output, e.g. the Patient Review Books
- ✓ Easy navigation to PRBs

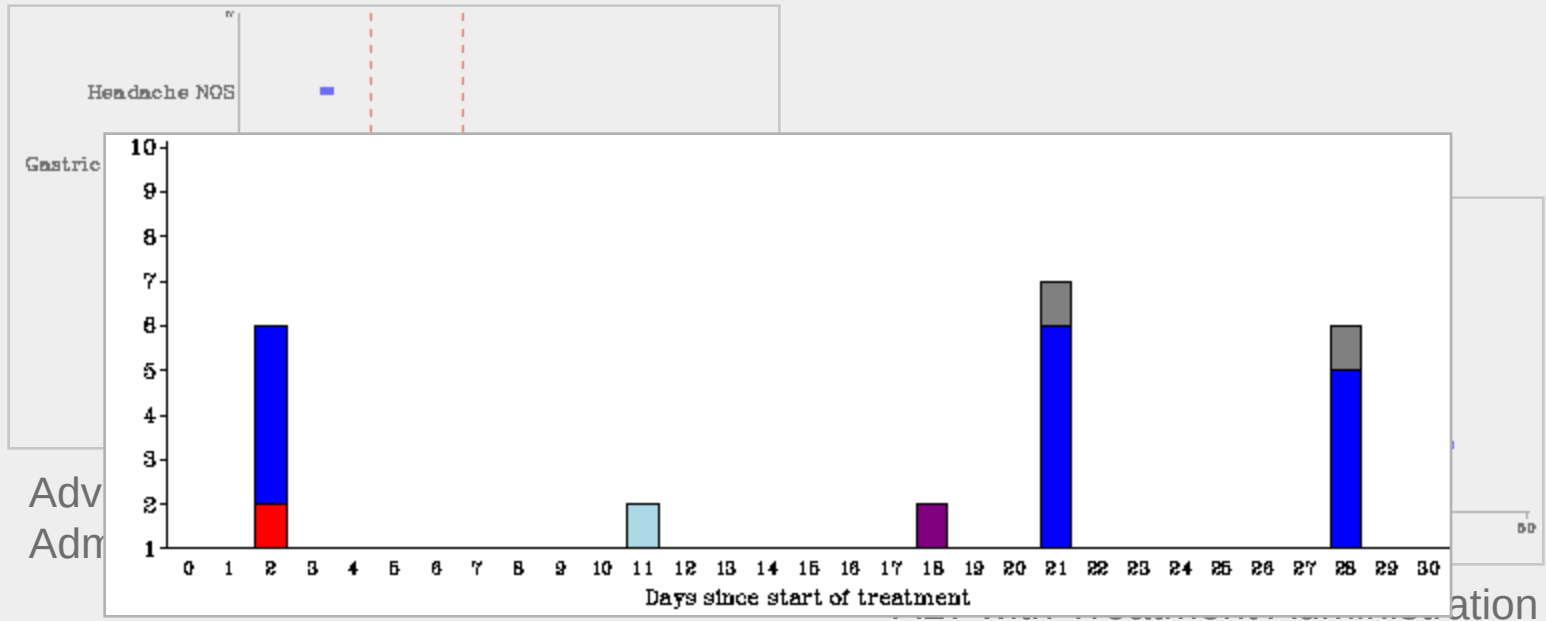
Additional Information

- ✓ Severity Index
- Severity Grade
- Time point
 - Nominal Visit
 - Study Day
- Any other information



- Correlations
 - Events
 - Timing
 - Grade
 - Any combination of *things*
- Associations

Correlations



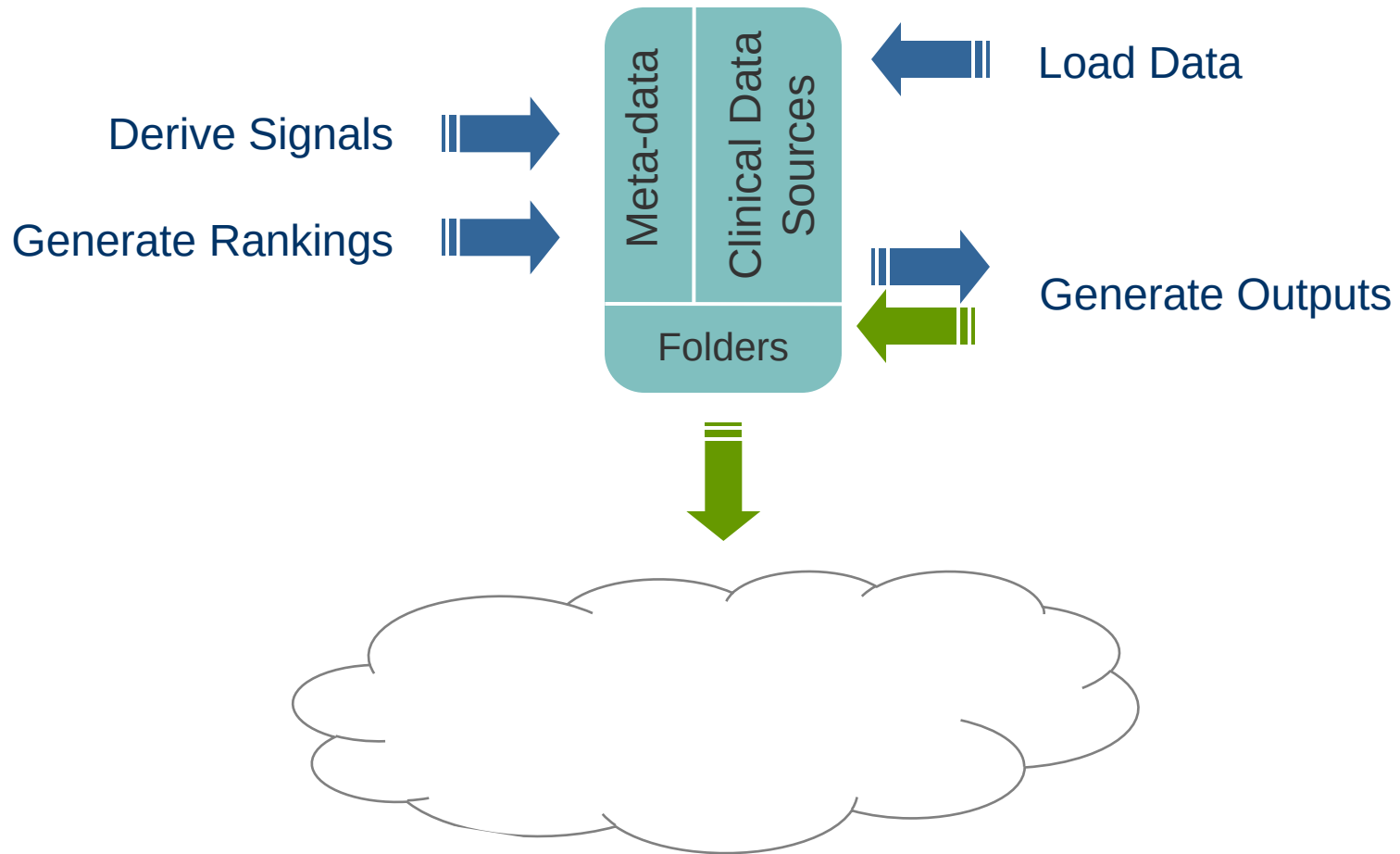
Progress

- ✓ An individual case report that contains all the necessary information for a subject
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Signals Framework

Process



Creating the Database

- Create and initialize Signals database

```
%sgl_db_create( path = /path/to/my/database ) ;
```

- Use another Signals database as a template

```
%sgl_db_connect( path = /path/to/my/database ) ;
```

```
%sgl_db_clone( source=/path/to/other/database ) ;
```



Load Data

- Create a clinical data source snapshot

```
%sgl_db_snapshot( reference = 21oct2009 ) ;
```

- Load clinical data sources

```
%sgl_db_load( snapshot = 21oct2009,
              library = RAW,
              select = DC EX LB EC AE VS,
              accept = all,
              strict = Yes );
```

- Create a clinical data source snapshot

```
%sgl_db_snapshot( reference = 21oct2009,
                  lock = Y ) ;
```



Generate Signals

```
%sgl_connect( path = /path/to/my/database );

%sgl_use( snapshot = 21oct2009 );

< add your SAS code here >

%sgl_signal_save( reference = myrule,
                  data = work.myresults,
                  subject = USUBJID,
                  timepoints = ( nominal = AVISIT,
                                day = ADY ),
                  index = SEVIDX,
                  grade = SEV );

%sgl_disconnect ;
```

Meta-data

Clinical Data
Sources

Folders

Generate Rankings

➤ All ranking sets

```
%sgl_connect( path = /path/to/my/database
              snapshot = 21oct2009 );

%sgl_signal_rank( set = );

%sgl_disconnect ;
```



➤ Only the PV_ONC ranking sets

```
%sgl_connect( path = /path/to/my/database
              snapshot = 21oct2009 );

%sgl_signal_rank( set = PV_ONC );

%sgl_disconnect ;
```

Generate Outputs

➤ Patient Review Books for all subjects in the snapshot

```
%sgl_connect( path = /path/to/my/database,
              snapshot = 21oct2009 );

%sgl_report_pvr( subject = );

%sgl_disconnect ;
```



➤ Navigation Lists for all ranking sets

```
%sgl_connect( path = /path/to/my/database
              snapshot = 21oct2009 );

%sgl_report_nal( view = );

%sgl_disconnect ;
```

Configuring Things

```
%sgl_connect( path = /path/to/my/database );

%sg_signal_define( reference = hyslaw,
                  label = %str( Hys law),

                  %sgl_connect( path = /path/to/my/database );

                  %sgl_signal_define( cntlin = work.mysignals_definition );

%sg_signal_define( reference = 3xALT_2xpd,
                  label = %str( 2 Consecutive 3x UNL ALT Post-dose),
                  description = %str(Two consecutive ALT results
                                     after first treatment
                                     administration that are above
                                     3xULN)
                  );

%sgl_signal_define( cntlin = work.mysignals_definition );
```

Summary

Signals Framework



- ✓ An individual case report that contains all the necessary information for a subject
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Questions & Comments

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THE END