The APT Report Library: A Tool for Clinical Trials Analysis

The challenges of clinical trials analysis:

Most clinical data analyses are highly customized statistical reports. Time pressure to produce these reports is usually intense. But despite the time pressure, the quality of the work can't be compromised.

Standardized processes are critical to ensuring timely and accurate work. However, the unique design of many studies makes standardizing difficult.

Meeting the challenge:

A well-defined, well-validated 'tool' library can help satisfy the pressure to produce reliable, customized reports in minimum time.

A macro library separates the complex, generic components of processing from the ones that are specific to a particular analysis. The application program is short and to the point. The code in the application program contains only the details that are relevant to that analysis.

Validating and documenting an application program using the macro library is correspondingly short and to the point. The validation and documentation need only deal with the analysis-specific details.

The complex details of processing are handled by the macro library. These details are described – and proven correct – in one place. The macro documentation and validation is provided with the macro library and applies to all analyses done under that version of the macro library.

A General Approach to Analysis Reports

How can we possibly come up with a general approach to the huge variety of analysis reports that are needed for a typical clinical trial? With APT, we have approached it by creating a conceptual 'map' of the report page. A typical report has labeling information for the analysis variables and the statistics on the left side of the page, and one or more columns of statistical results on the left.

Often, but not always, the columns are defined by the treatment group. In the body of the report, we may need to produce a variety of statistic types on a variety of variables.

We may also need to generate repeated groups of statistics by category variables such as investigator site, laboratory test code, or time points. These categories may need to be presented as sections within a page, or as separate pages.

Each statistics macro call adds lines to the report by generating the statistics on a specific macro variable, with specific formatting requirements, and fitting the results into the generic structure.

	APT Example Table				*Title Area*
Page-by Variables	**Investigator Site: Jones Memorial Hospital**		*(User Can Define 'Spanned' Column Headers)*		*Header labels*
			Drug A (N=32)	**Placebo (N=38)**	
	Study Completion Status				*Segment label*
		Completed Study	**30 (94%)**	**38 (100%)**	*Statistics*
		Early Termination	**2 (6%)**	**0 (0%)**	
	Subject Age by Sex				*Segment label*
	Female	**N**	**14**	**18**	*Statistics*
		Mean (SD)	**25.0 (6.4)**	**22.1 (6.8)**	
	Male	**N**	**18**	**20**	
		Mean (SD)	**28.4 (8.2)**	**29.2 (7.9)**	
	Break Variables	*Line Label Area*	*Statistics*		

In the example below, the first ‘segment’ counts the number of subjects who have any lab data per study week (a ‘subject count’ summary). The second ‘segment’ summarizes the baseline labs using both descriptive statistics and comparative statistics. This section is broken out by the lab test identifier. The p-values can be generated overall (all three groups) or for selected pairs of groups.

APT can generate separate pages per category with count of subjects. Any number of category variables can be used.

Column heading text can span columns. Up to 4 levels of spanned heading can be defined.

A Generic APT© Report

Treatment Groups

Subject Sex: Female (N=24)

		Placebo (N=8)	Treated: Low Dose (N=8)	Treated: High Dose (N=8)	Total (N=24)	Overall P-value
Subjects with Lab Result per Study Week						
	WEEK 1	8(100.0)	8(100.0)	8(100.0)	24(100.0)	
	WEEK 2	8(100.0)	6 (75.0)	4 (50.0)	18(75.0)	
	WEEK 3	8(100.0)	6 (75.0)	4 (50.0)	18(75.0)	
Summary of Baseline Lab Results						
Hematocrit (%)	N	8	8	8	24	
	Mean (SD)	41.9(4.6)	43.5(3.4)	42.6(3.1)	42.7(3.7)	0.721
	P-value vs. Placebo		0.426	0.740		
RBC (10^6/MM^2)	N	8	8	8	24	
	Mean (SD)	5.0(0.5)	4.6(0.4)	4.6(0.6)	4.7(0.5)	0.244
	P-value vs. Placebo		0.143	0.152		

Each statistic segment can independently control the type of statistics, formatting, breakout variables, and other characteristics

Statistics can be printed with any format, and arranged vertically or horizontally.

Statistics can be centered or decimal aligned.

P-values can be generated for selected pairs of groups.

Comparative statistics can display in a separate column or on a separate line

P-values can be generated over all groups.

Comparative statistics can be done differently for different segments

What if APT doesn't do exactly what I want?

APT has a wide variety of statistical and formatting capabilities. Still, no general set of routines can possibly cover 100% of all imaginable analyses. However, the modular design of APT allows a user to customize the statistics dataset in between statistics macro calls, or prior to printing. The structure of the statistics dataset is fully described in the user manual – enabling a 'power user' to accomplish an almost unlimited variety of reports.

What is included with the APT Library?

A program package is not complete without a comprehensive software development and support process behind it.

Validation is crucial in a regulated environment. Users must have documented evidence that the package fulfills its requirements. The effort of producing this documentation is a substantial part of the development effort, and one that few biostatistics departments can afford to do in-house.

- The APT Library includes a fully executed and reviewed validation suite.

Training is essential for efficient, accurate use of any set of programming tools. Users need to know the quickest way to get correct results. Training is an ongoing need, as new people are incorporated, as experienced people encounter new or complex requirements, and as improved features become available.

- The APT Library includes a complete training program.

Documentation is necessary for effective use of the system. Users must have reference materials available.

- The APT Library includes a complete user manual.

Support is mandatory for any software product. Users must have answers about questions about usage, identification of software issues, and prompt response to reported bugs.

- The APT Library includes telephone, email, and on-site support (by arrangement).