

**Productivity Tools  
for Clinical Data  
Analysis**

**Strategic Benefits:**

- A standards-based approach
- Facilitates efficient Part 11 compliance
- Support for good programming practices

**User Benefits:**

- Faster report generation
- Reliability
- Consistency
- Easy validation

## The APT™ Analysis Library Tools for Clinical Trials Report Creation

A key component of the clinical trials process is the accurate and timely programming of statistical results. We believe this is best accomplished using reusable reporting software modules as part of a validated statistical computing environment. The APT™ (Analysis Programming Tools) software provide a foundation for productivity and quality of statistical reports. Validation, an essential component of 21 CFR Part 11 can be streamlined. The software gives the programmer the flexibility to create many of the reports recommended in ICH E3: *Structure and Content of Clinical Study Reports*.

The reporting process benefits in the following ways:

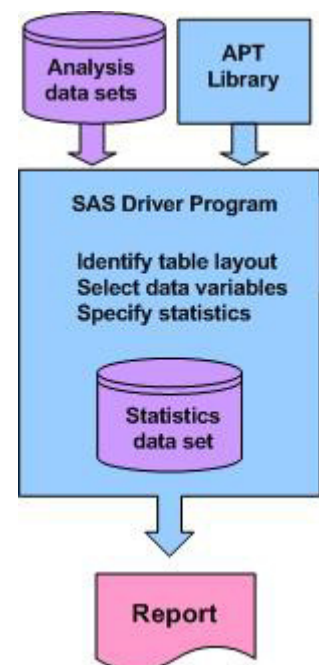
- Enhanced productivity by statistical analysts
- Creation of standard validated SAS reporting programs
- Greater reliability and confidence in reported results
- Consistency of look and appearance
- Publication ready output tables in rtf, html, pdf, or ASCII

APT is a suite of SAS® macros. The APT software runs under SAS® Versions 6.12, 8.x and 9 on Windows and Unix. SAS/BASE and SAS/STAT are required. The statistics are derived directly from SAS statistical procedures. The software is designed to be used by SAS programmers and statisticians at all levels of experience.

### How APT Works

The data input for the reporting software are statistical analysis files. These files are usually derived by transforming raw data from the clinical study database into an analysis-ready format. These files typically include important patient characteristics and derived analysis variables. They are constructed so that statistics can be generated by a simple invocation of a SAS statistical procedure. The analysis file may be in one of several types:

- One record per subject
- One record per subject per visit
- One record per subject per incident



Each file is supplemented by common information like demographic and baseline variables. The data can be analyzed by APT software in any one of these formats.

As depicted in the Figure, an APT report program starts with a macro call that defines all report characteristics. Then one or more statistics-generating macro calls derive summary statistics and accumulate them in a statistics data set. Attributes of the statistics can be controlled individually for each variable analyzed, or they can be carried over by default from one macro call to the next.

When all the statistics have been generated, a final macro call prints the report according to user format specifications. A sample output is displayed below.

### Sample Report 1: Categorical and Numeric Descriptive Statistics

Site: Community Hospital				Comparison of Groups		
		Treated (N=3)	Placebo (N=2)	P-Value	Difference	95% Confidence Limits for Difference
Subject Gender						
	Women	1 (33%)	1 (50%)	1.000	-17	[-100.0 , 70.7]
	Men	2 (67%)	1 (50%)			
	Missing	0	0			
	- Total -	3	2			
Subject Age						
Women	N	1	1			
	Mean (STD)	24.0	62.0			
	Min to Max	24.0 to 24.0	62.0 to 62.0			
Men	N	2	1	0.463		
	Mean (STD)	43.5 (13.4)	25.0			
	Min to Max	34.0 to 53.0	25.0 to 25.0			

This report contains summary statistics on the variables SEX and AGE, with a separate column for each value of the treatment group variable. Additional columns contain statistics comparing the two groups (pvalues, difference in mean, confidence interval for the difference in mean). Each value of the investigator variable is printed on a separate page, with the investigator label printed on the left side of the heading area. The statistics for age are further stratified by sex ('break' variables).

This report illustrates a number of features of the macro library:

- A wide variety of statistics is available (frequency counts, descriptive statistics, p-values, confidence interval for difference in mean, and others)
- Statistics can be displayed using any SAS format or user-defined format. Statistics may be printed on individual lines or grouped on a line together. Literals ("to") may be used.
- The statistics generated, formatting, labeling, and use of stratification variables can be assigned individually for each analysis variable
- Categorical variables that use a format to define all possible categories (such as SEX) may be expanded to show all the defined values, whether they exist in the data or not
- Any analysis variable may be broken out by one or more category variables (such as AGE, which is broken out by SEX)
- Column headings may include the subject count for the population summarized

- The user may define column headings that span more than one statistics column (“Compare Groups”). Up to four levels of spanned headings may be defined
- The macro will attach an caret (^) to p-values that are unreliable due to low cell sizes.

### Sample APT Report 2: Subject Count Statistics

							P-Values	
	Treated Dose 1 (N=12)	Treated Dose 2 (N=16)	Placebo (N=10)	Overall	Dose 1 vs. Placebo			
Totals By Body System And Relation To Drug								
Cardiovascular	0	0	0					
Body as a Whole	8	8	0					
Headache	8	4	0	0.002^	0.001^			
Related	8	4	0	66.7%	25.0%			
Not Related	0	0	0	0.0%	0.0%			
Pain Abdominal	0	4	0	0.046^				
Related	0	4	0	25.0%				
Not Related	0	0	0	0.0%				
Metabolic and Nutritional	3	7	6					
Anorexia	1	3	3	0.426^	0.189^			
Related	0	0	0	0.0%	0.0%			
Not Related	1	3	3	8.3%	18.8%	30.0%		
Diabetes	2	0	0	0.101^	0.175^			
Related	2	0	0	16.7%				
Not Related	0	0	0	0.0%				
Hypoglycemia	0	4	3	0.131^	0.041^			
Related	0	4	3	25.0%	30.0%			
Not Related	0	0	0	0.0%	0.0%			

This is an example of an adverse event report, which summarizes the number of unique subject identifiers per adverse event category. This report summarizes at three levels: the body system, the preferred term, and the severity of the event.

Report features shown in this example include:

- Subject counts can be summarized in one or more nested categories.
- Percentages are based (by default) on the number of subjects in the column group. Other denominators may be specified.
- Categories may be expanded to show all values in the format assigned to the variable. In this case, the body system and severity show all defined categories, whether they appear in the data or not.
- Categories may be sorted by:
  - Frequency order (body system – based on total count in all column groups)
  - Reverse frequency order (not shown)
  - Alphabetic order (preferred term)
  - Internal or unformatted order (severity – unformatted values are 1,2,3,4).
- Characteristics of each level of summarization are independent of the other levels. These characteristics include: the statistics generated, statistic formatting, sort order, and use of format expansion.
- P-values can be generated to compare incidence rates between groups. For each category, the macro

compares the number of subjects in the category (i.e., the number of subjects having the event) with the number of subjects NOT in the category (i.e., the number of subjects at risk who did not have the event), between column groups. This may be done for the whole population or for selected pairs or columns. It may also be done at any level (in this case, at the preferred term level).

### **Documentation, Training and Support**

A detailed user manual is included with examples demonstrating every aspect of the software. PharmaStat can provide on-site training for a fast start.

Also included is a comprehensive validation solution for the APT tools. A comprehensive set of documentation is provided (validation plan, IQ, OQ, PQ, traceability matrix, and validation report).

Support is available by e-mail and telephone. Maintenance and upgrades are provided periodically.

### **Summary**

APT is a flexible standard SAS macro library for statistical reporting, and a vital part of an efficient and validated Statistical Computing Environment. APT is an essential foundation for

- utilizing and enforcing programming and data standards,
- simplifying the development, validation and testing required for “one-off” analysis programs,
- creating standard validated SAS reporting applications, and
- achieving Part 11 compliance while improving programmer efficiency.

Along with onsite installation, qualification and training, PharmaStat offers services to enhance your implementation of APT, including:

- creation of program templates customized to your reporting conventions,
- consulting on programming and data standards, and
- design of efficient Part 11 compliant statistical analysis and reporting processes.

### **About PharmaStat**

PharmaStat’s mission is to provide drug development consulting and services to integrate science, technology and operations for successful implementation of drug development programs.

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## **Software**

### ***Productivity Tools for Clinical Data Analysis***

#### **Report Types**

- **Descriptive and inferential statistics for categorical and continuous variables**
- **Subject count reports e.g. adverse events**
- **Point estimates and confidence intervals**
- **Survival analysis**

#### **Library includes:**

- **Software**
- **User manual**
- **Installation**
- **Training**
- **Support**
- **Validation**

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