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HANDLING STABILITY DATA VIA THE COMPUTER

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17.1 Introduction

The computer is rapidly becomming an indispensible tool to all involved in the pharmaceutical stability process. In many facilities it is an integral part of data acquisition, storage, analysis and reporting. Its versatility and efficiency have brought a new dimension to handling stability data, providing the means for the pharmaceutical manufacturers to keep pace with the rapidly advancing scientific and regulatory aspects of our industry. Historically, this evolution can be attributed to many events, some computer related and others stemming from significant changes in philosophy within the pharmaceutical industry.

The computer has changed drastically since the first commercial models came upon the scene in the 1940's. Improvements in size, speed, capacity and price have done much to entice pharmaceutical scientists to rely more heavily upon computerized systems. Very recently the tremendous improvements in micro circuits have increased memory capacity and decreased its relative cost to the point where any laboratory can have at its disposal what used to be termed a larger computer. Also, many software companies have taken advantage of cheaper memory by developing higher level systems which are more "user friendly".

These changes in computer technology, important as they are, probably are not the key reason for the rapid evolution evident today within pharma-

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ceutical stability. The key instead lies in a fundamental change in philosophy within the industry and more specifically within those units specifically concerned with stability. Only recently have we seen a concerted effort to deal with data from the position that it is a sample from a much larger distribution. And only by understanding and defining this underlying distribution can we make accurate statements concerning measured product variables. Dealing with pharmaceutical products and processes from a mathematical or statistical point of view is not revolutionary, but its widespread application and acceptance in industry and the regulatory agencies is something quite recent. Further, this concept is the key necessary to bridge the gap and provide modern computer technology with a usable framework to efficiently handle pharmaceutical stability data.

17.2 Data Acquisition and Retention

17.2.1 File Content

Pharmaceutical scientists working in stability deal with many types of data stemming from many sources. Determining which data is important enough to be amintained in on-line computer files is not as easy a job as it sounds. Consideration must be given to the type of data, our ability to capture it, the volume of data, the purpose for which it will be used and how frequently it will be referenced. It is important to remember that just because a computer is available and capable of holding data, one should not automatically store data in it. It takes resources to develop the data systems, enter the data and maintain accurate files. A proper return on this investment of time and effort must be ensured prior to taking on the task.

Well then, just what type of data should be placed in computer files to maintain an effective stability system? Obviously there is no universally applicable answer to this question, but the following is an outline of types of data to be considered:

a. Stability protocols (number of batches, test stations, test performed, etc.).

b. Batches on stability (batch number, type of batch, date of manufacture, date on stability, type of container and closure,

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condition of storage, tests performed, units of measure, and results found.

c. Sample storage location.

d. Product history information (equipment, process, and formulation changes).

e. Batch history information (rework information, minor manufacturing or process changes).

f. Stability trend data and investigation results.

g. Expiration dating periods (date determined, method of determination, limiting variable).

h. Laboratory instrument and personnel tracking data.

17.2.2 Data Capture

It is obvious from the above list that stability technicians must obtain data from a number of functions, i.e., Production, Packaging, Pharmaceutical Services, Quality Assurance Laboratories, Regulatory Compliance, etc. Efficiently acquiring this array of information through automated means is a complex task. Collection systems which work well for one type of data may be less efficient for another type. The requirements and needs of each data source must be carefully examined before deciding upon the proper mode of acquisition.

In areas where the speed of entry is not critical due to low volumes of data or a lack of time constraints, manual data entry may be perfectly suitable. In stability, we find these situations in dealing with scheduling information, formulation data and protocol requirements. In each of these situations we are quite likely to have all of the information available some time in advance to the system needing it.

a. Product scheduling is usually performed on a weekly or monthly basis. Products placed on stability can be chosen and the necessary information entered at that time.

b. According to current Good Manufacturing Practices, product formulations must be established and approved prior to their

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use. Any minor changes to the process or product can be entered as the information is available.

c. Stability protocols must be established some time prior to product manufacture and usually fall into one of a small number of established general protocols.

Also in each of these cases, the amount of information to be entered is relatively small.

In direct contrast, there are situations in stability where data acquisition through a minicomputer or a microcomputer is a necessity due to the volume of data and the speed at which it is accumulated. A prime example of this is seen in laboratory data acquisition from HPLC, GC, IR and UV instrumentation. Readings must be taken from these instruments several times per second so that peak heights or areas under the curve can be determined, and subsequent calculations made. Manual transfer of this raw data would be close to impossible but, electronic capture through some "intelligent" device ensures accuracy and efficiency with minimal intervention.

In certain instances a compromise might be necessary; one might favor automation with some additional manual input. Gathering sample and instrument tracking data is an ideal example of this situation. The important factors here are the low volume of information, infrequent entries, yet the need for complete and timely data. Other examples of this boderline case can be found in lab data for physical tests, wet chemistry analysis and descriptive information. There are portions of these tests which generate sufficient data to warrant automatic capture, e.g., titration endpoints, hardness measurements, weight variation, etc. In general though, it is difficult to justify the cost of total automation almost any data input, but few of us are striving for reduced manual involvement regardless of cost. Therefore, prudence should lead us to a proper marriage of automated and manual data input.

17.2.3 Accuracy Check

Checking new data to ensure that it conforms to all known expectations is of utmost importance if the computer is to serve a useful purpose. The only

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way we can hope to get accurate answers from the computer is to give it good data. Put more succinctly, "garbage in - garbage out". Also, it should not be assumed that these checks only apply to manually entered data. Electronic problems (signal noise, malfunctioning components, etc.), as well as man made problems (poor connections, inappropriate parameter settings, etc.), can cause direct outputs from instruments or equipment to be incorrect, or at least different from the norm.

Initial data checks should determine whether or not the incoming information is of the proper type - alpha or numeric. Some additional checks which can be specifically programmed into each system are:

Alpha Data

a. Are specific words or strings required in this field so that subsequent sorts can be properly performed?
b. Are all expected data fields filled? Is the entry sequence complete?
c. Are any characters included which could cause problems with other routines or programs?

Numeric Data

a. Does the data fit within the expected range of numbers? The range can be established based upon past history or by determining an appropriate statistical confidence interval using a target value and the associated standard deviation. ($X \pm 1.96S$ = 95% confidence interval).
b. Does the data contain the proper number of significant digits?
c. Are all expected data fields filled?
d. Is the check digit correct for the incoming number or data? A check digit is an additional number entered with the data as a separate check for all other digits in the data sequence. It is determined by an algorithm capable of generating a unique digit based upon the preceeding sequence of numbers. (Simplified Example: 548735 Check Digit = 5 + 4 - 8 + 7 - 3 = 5). A check

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digit is normally used when dealing with established codes or identification numbers.

If aberrant data is detected, the computer should indicate to the operator that a problem exists. At this point a check can be initiated to ensure that the proper information was entered or transmitted to the computer. Alternatively, a bypass instruction can be given so that the data flow is not interrupted and an investigation can be started later. In either event, inappropriate data must be screened and kept from the files to maintain maximum accuracy.

17.2.4 File Security

As more data goes on the computer and is accessed by an increasing number of personnel, it becomes important to secure the files against inadvertant change and inappropriate access. Many levels of security can be established and indeed, the entire process can be made extremely complex, but it soon becomes apparent that a few basic precautions are all that is required in most online stability systems. These approaches are effective without causing the security system to become a nightmare for the system designer and user alike.

The first precaution involves limiting who can get into the system and how that person can interact with the system. Interaction with the computer files can be controlled by assigning access codes or passwords to personnel. The system should be programmed to recognize these codes and limit the type of operations available to each user. They may allow personnel to a) look at files, but not copy or alter them, b) input data, but not make any changes, c) complete file access or d) no file access.

Secondly, it is important that all transactions with the system and its files be recorded through an audit trail. This ensures that we are able to reconstruct any file as it was at any point in time. It also allows us to trace other changes within the system by knowing who performed the operation, what the operation was, when it was performed and what effect it had upon the system.

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A third precaution which can be taken is file back up. All data files should be periodically copied onto a permanent storage device such as magnetic tape which is in turn stored in a remote location. This might be done daily, weekly or even monthly depending upon the system size, complexity and activity. Maintenance of these back up tapes ensures that if the system crashes or is severely damaged in some way, it can be brought back up as it was at some previous point without having to undergo a complete file reconstruction.

Finally, it is important we ensure that critical areas within the system are functioning properly. This can be accomplished through periodic tests with check data. Basically, check data is an input which should trigger a known output or change in the system. With a little planning and thought, data can be constructed so that it tests critical limits and areas within the system to ensure that no inadvertant changes have occurred. An example of this might be a previously recorded instrument signal input coupled with established manual inputs which should yield a given assay value or analytical result after a series of calculations.

17.3 Data Analysis

Stability systems, much the same as many other systems, are not designed to generate data files as an end in itself. Instead, our efforts are bent upon building an effective decision making tool. This requires two basic ingredients: 1) accurate and comprehensive data and 2) meaningful data analysis. In the previous sections we laid the ground work for building data files and now we will look at some approaches to data analysis.

17.3.1 General Comparisons

Just because stability data is collected in an automated fashion and stored in a computer, again one should not jump to the conclusion that all data analysis must be totally automated. The ability of the human eye and brain to detect unusual patterns or trends is excellent. It is important that any comprehensive data analysis system include adequate provisions for data sorting and display so that it may be subjected to such "eyeball" analysis.

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A general approach to this might be to use the computer to sort data by product, container/closure, formula revision, date of manufacture and test. Following this the data should be displayed in tabular or graphic form and "eyeballed" in an attempt to detect changes in test level, variation or any other reoccurring patterns. In this manner, stability analysts could in many instances detect changes or trends and make a decision as to whether or not a stability problem exists. This manual or human approach eliminates to a large extent the expense of generating the formal programs or routines to perform these operations in an automated fashion. You can well appreciate the complexity of such a task if we were to take into account all of the many and varied possibilities for trends and changes.

17.3.2 Linear Regression

In direct contrast, there are areas of stability data analysis where the computer plays the primary role, i.e., determining appropriate predictive models. In recent years, the model which has been generally accepted in stability is least squares linear regression. The acceptance of this model within the industry has not been arbitrary, but is based instead upon some fundamental mathematical concepts.

Most drug products which undergo degradation follow a zero or a first order reaction rate. That is, the measured amount of active ingredient or some other test value changes in a linear fashion or a log linear fashion with time. If the measured variable is defined as Y and the elapsed time is defined as X, then the mathematical formulas associated with these two reaction orders are:

$$\text{Zero Order} : \quad Y = a + bx$$

$$\text{First Order} : \quad \text{Log } Y = a + bx$$

Where: $a = Y$ Intercept

$b =$ Slope

Armed with these basic concepts and the capability of modern computer technology, an analyst can make some fairly precise statements concerning the stability of a drug product.

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The acutal mechanics of determining the best fit equation can be approached from several directions. Statistical packages such as SAS (available through SAS Institute, Inc., Cary, N.C.) and APL Statistics Package (available through International Business Machines Corp., Data Processing Division, White Plains, N.Y.) include subroutines to determine the least squares best fit for the linear regression given a set of Y and X pairs (stability results). Alternatively, the calculations for this operation can be programmed as part of a complete stability system. If this approach is taken, reference can be made to a general statistical test (1). With either approach, the speed and accuracy of the computer becomes the central factor in determining a good stability model for the respective product and test.

Example

Select data for a given product and test from the stability data base (file) and subject it to linear regression analysis. (Note: In most instances it is not necessary to determine whether the component degrades according to a zero order or a first order reaction because over the area of interest both models can be approximated by a straight line. See Figure 1). The computer would supply a report listing the best fit equation $Y = a + bx$, the predicted values from the equation, the 95% confidence interval for line of best fit, and a plot of the data. (See Tables I and II and Figure 2). Using the regression line or the 95% confidence interval for the regression line, the analyst would make a prediction of how long the product would remain within specification.

Depending upon the computer resources available, additional tests could be run to determine the appropriateness of the model selection and whether the data was properly pooled. Most statistical packages offer several tests for determining proper model fit as part of the regression report. Alternatively, a separate analysis of variance may be performed, (2) residuals may be subjected to nonparametric test (3) or the data may be plotted and examined visually. Also, tests may be performed upon regression lines calculated from subsets of the pooled data to determine if there are significant differences between slopes, intercepts and variability about the line (4).

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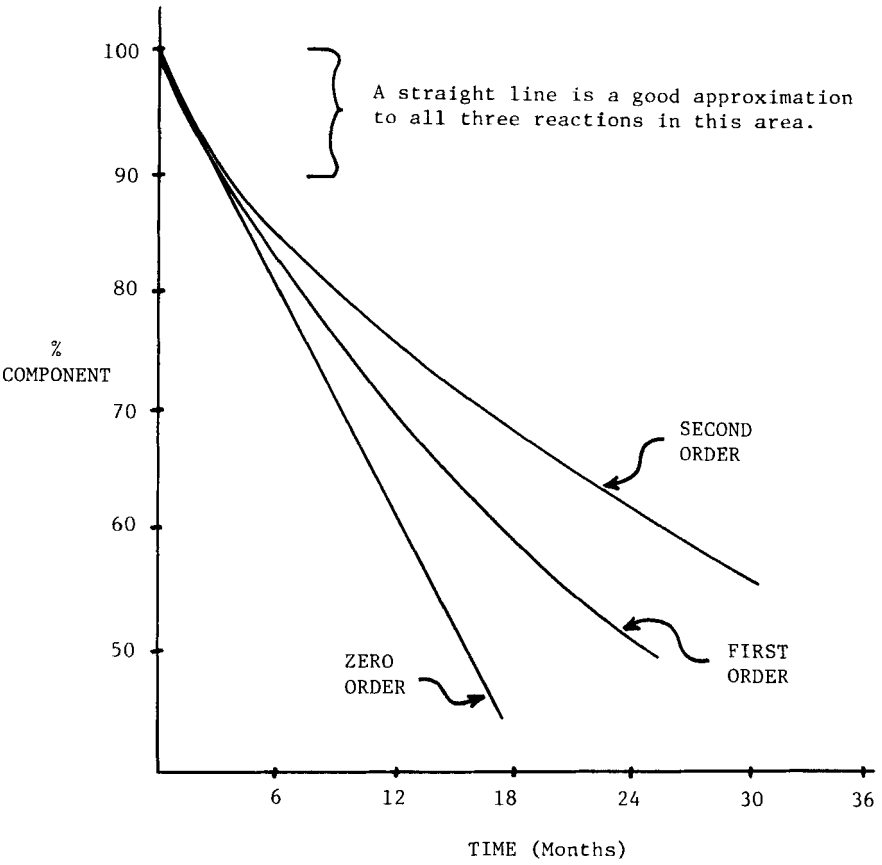

FIGURE 1

TABLE I

Room Temperature Stability Data
Vitamin Capsule (HDPE Bottle)
Calcium Pantothenate (Units/Cap)

Size	Control	0 M	6 M	12 M	18 M	24 M	36 M	48 M
50	QVL	32.7	22.0	20.0	16.5	14.1	12.0	10.1
100	GKM	31.3	23.0	27.0	18.9			
100	TES	30.9	26.9	24.4	18.7			
50	TGZ	27.4		22.0				
50	DHE	33.0	27.4					

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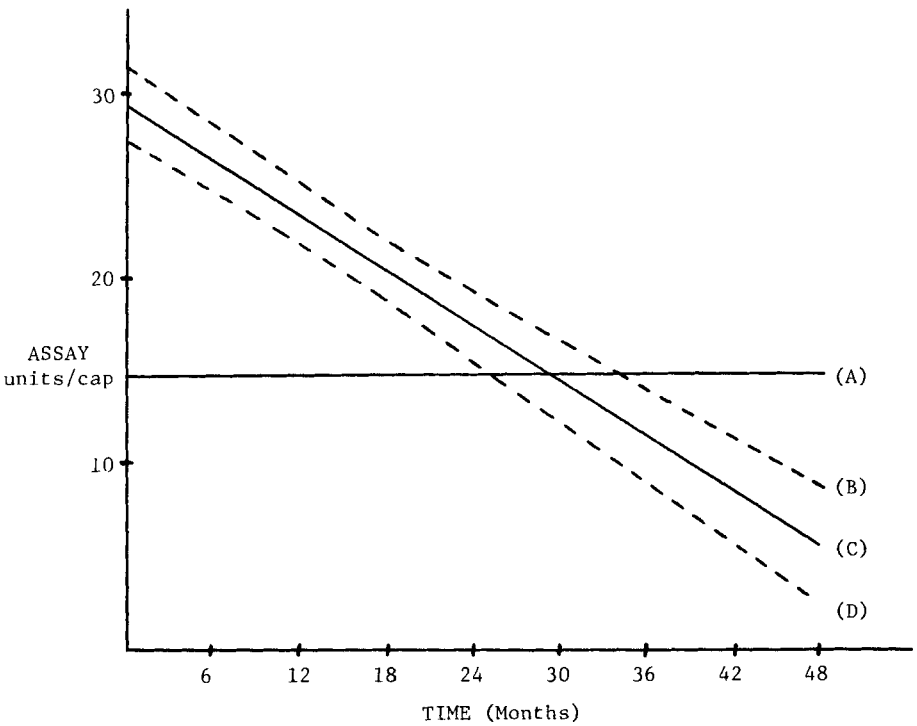
TABLE II

Linear Equation: Y = 29.0587 - 0.4864X

	Initial	6 M	12 M	18 M	24 M	36 M	48 M
95% Confidence	30.70	27.45	24.39	21.59	18.98	14.05	9.24
Predicted Value	29.06	26.14	23.22	20.30	17.39	11.55	5.71
95% Confidence	27.42	24.83	22.05	19.02	15.79	9.05	2.18



(A) Lower Product Specification
(B) Upper 95% Confidence Limit
(C) Line of Best Fit
(D) Lower 95% Confidence Limit

FIGURE 2

Room Temperature Stability Data
Vitamin Capsule (Calcium Pantothenate)

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This would indicate whether or not the data was drawn from several significantly different processes.

17.3.3 Other Models

Even though today linear regression is the most widely accepted model for predicting drug stability, one should not preclude the use of other models. The speed and versatility of the computer provides us with the opportunity to try other relationships in an attempt to find the most useful predictive tool. Among the possibilities are the Arrhenius relationship and the Weibull distribution. The basic mathematical calculations used in each of these alternative models are available in most statistical packages, and can be combined in an overall program to generate the respective stability model (5,6).

17.3.4 Reports

Although reports are not in the strictest sense a form of data analysis, they are so closely tied to it that it is difficult to review one without the other. Reports are the media through which we show the logic behind our data analysis and the ultimate conclusions reached. The formatting and compiling of reports is another area where the computer and automation in general proves to be indispensible.

The simplest type of report associated with stability is a data printout, with or without a special sort. The ability to go into the data files and retrieve information to make decisions is a very important aspect of a computerized stability system. The programs necessary to achieve this are usually part of any good editor routine included in major operating systems. Previously mentioned systems such as SAS and APL (in the ADRS subsystem) have all of the software necessary to sort data according to specific variables and print subsequent reports. Alternatively, a user can write the necessary routines to sort and print the data within their own automated stability system.

A more complex form of report routinely used within stability is the regression analysis report. This would typically include specific information

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on the regression line, i.e., slope, intercept, 95% confidence interval on the line, etc., as well as statistical data regarding goodness of fit of the regression, i.e., analysis of variance, t test for slope and intercept, listing of residuals, etc. (See Figure 3 for an example from SAS). These reports are generally produced as part of the statistical package analysis. Of course this does assume that the data is subjected to analysis by some package such as SAS Regression or APL Regression. In conjunction with the written reports produced with regression analysis, it is usually very informative to have a plot of the regression either using a printer or a plotter. (See Figure 4 for an example from SAS using a printer).

Analyzing data may lead to indication of change in product stability for individual batches or even groups of batches. Therefore, a formal method of trend notification must be a part of any stability system. These trend notice reports can be composed and issued by the computer. Any information gathered from investigations of the trend can be stored in the computer using key words or phrases so that it can be quickly scanned to check any subsequent similar trends. Also, the computer can be used as a follow-up device to ensure that all trend notices are brought to some appropriate conclusion.

Finally, one should not overlook the utility of the computer in the day to day operation of the stability system. Data files usually contain all of the information necessary to prepare work schedules and list work loads expected over a period of time. Effective utilization of this information through management reports is a necessity in today's expense conscience world.

17.4 Different Approaches

All that we have discussed so far indicates the computer is a useful tool for the stability function, but exactly how can it be accomplished? What types of hardware and software (programs) are needed? The answer to these questions starts out with that terrible phrase, "it depends". It depends upon the size of the operation we are dealing with, i.e., how big the company is; how many stability samples are in the program; what type of computer facilities are already in-house? There are many options depending upon the answers to these questions and a host of other variables.

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FIGURE 3

VITAMIN CAPSULE (CALCIUM PANTOTHENATE) 11:18 THURSDAY, NOVEMBER 11, 1982 1

GENERAL LINEAR MODELS PROCEDURE

DEPENDENT VARIABLE: Y

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F VALUE	PR > F	R-SQUARE	C.V.
MODEL	1	706.43736608	706.43736608	82.30	0.0001	0.828801	12.7005
ERROR	17	145.92368655	8.58374627		STD DEV		Y MEAN
CORRECTED TOTAL	18	852.36105263			2.92980311		23.06842105

SOURCE	DF	TYPE I SS	F VALUE	PR > F	DF	TYPE IV SS	F VALUE	PR > F
X	1	706.43736608	82.30	0.0001	1	706.43736608	82.30	0.0001

PARAMETER	ESTIMATE	T FOR HO: PARAMETER=0	PR > |T|	STD ERROR OF ESTIMATE
INTERCEPT	29.05869289	30.84	0.0001	0.94222393
X	-0.48638959	-9.07	0.0001	0.05361495

OBSERVATION	OBSERVED VALUE	PREDICTED VALUE	RESIDUAL	LOWER 95% CL FOR MEAN	UPPER 95% CL FOR MEAN
1	32.70000000	29.05869289	3.64130711	27.07078679	31.04659900
2	31.30000000	29.05869289	2.24130711	27.07078679	31.04659900
3	30.90000000	29.05869289	1.84130711	27.07078679	31.04659900
4	27.40000000	29.05869289	-1.65869289	27.07078679	31.04659900
5	33.00000000	29.05869289	3.94130711	27.07078679	31.04659900
6	22.00000000	26.14035533	-4.14035533	24.55247147	27.72823919
7	23.00000000	26.14035533	-3.14035533	24.55247147	27.72823919
8	26.90000000	26.14035533	0.75964467	24.55247147	27.72823919
9	27.40000000	26.14035533	1.25964467	24.55247147	27.72823919
10	20.00000000	23.22201777	-3.22201777	21.80347932	24.64055621
11	27.00000000	23.22201777	3.77798223	21.80347932	24.64055621
12	24.40000000	23.22201777	1.17798223	21.80347932	24.64055621
13	22.00000000	23.22201777	-1.22201777	21.80347932	24.64055621
14	16.50000000	20.30368020	-3.80368020	18.74663197	21.86072843
15	18.90000000	20.30368020	-1.40368020	18.74663197	21.86072843
16	18.70000000	20.30368020	-1.60368020	18.74663197	21.86072843
17	14.10000000	17.38534264	-3.28534264	15.44683323	19.32385205
18	12.00000000	11.54866751	0.45133249	8.51741811	14.57991691
19	10.10000000	5.71199239	4.38800761	1.43364997	9.99033481

SUM OF RESIDUALS	0.00000000
SUM OF SQUARED RESIDUALS	145.92368655
SUM OF SQUARED RESIDUALS - ERROR SS	-0.00000000
PRESS STATISTIC	220.08061809
FIRST ORDER AUTOCORRELATION	0.01874938
DURBIN-WATSON D	1.73968801

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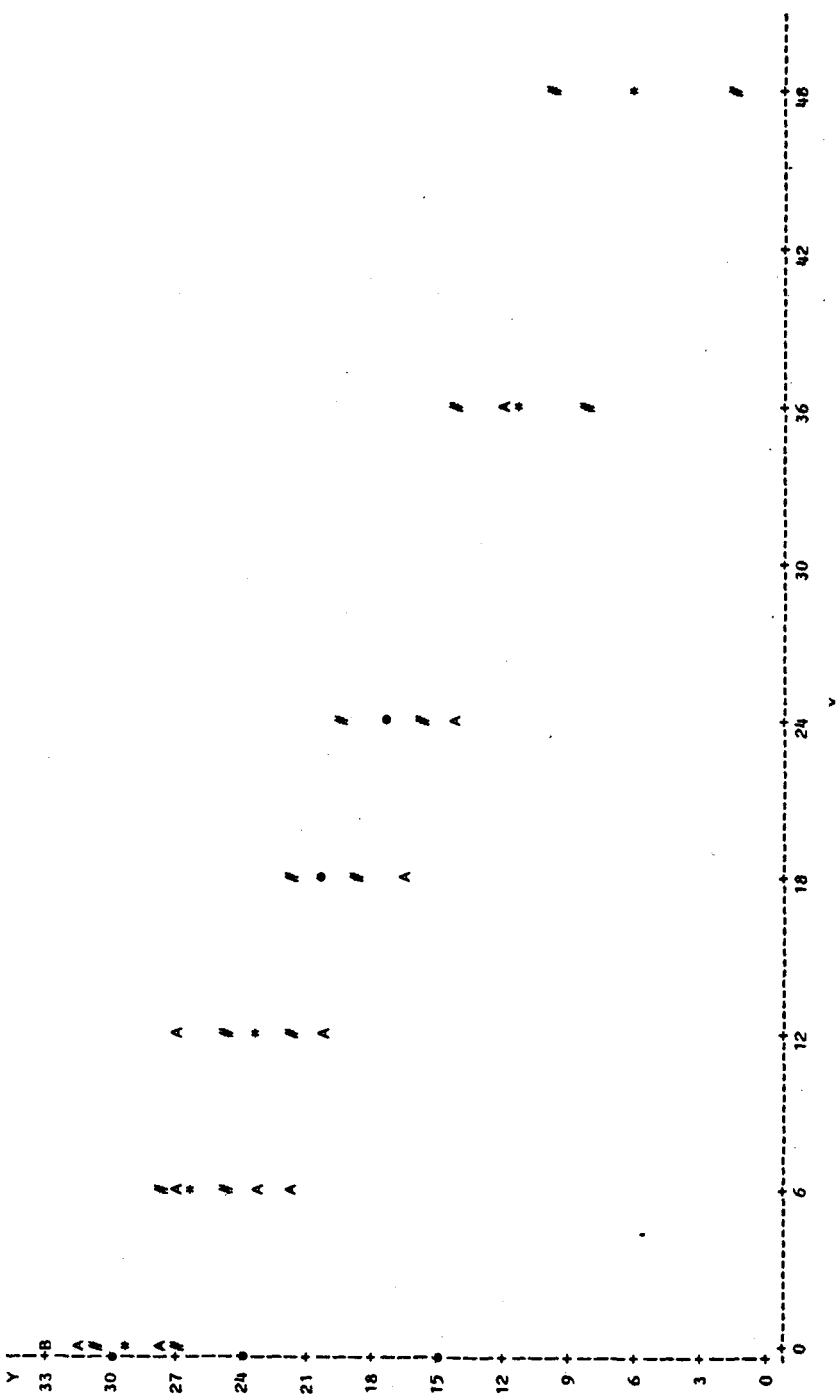
FIGURE 4



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17.4.1 Interim Systems

The first set of options are what can be termed interim systems. These approaches are ideal for small companies or young stability programs with undefined growth patterns. In general, they provide for storage of stability data and the means to perform the calculations necessary to determine expiration dating periods and stability trends. With a little imagination and work they might even provide some rudimentary scheduling functions.

The most basic system capable of performing stability functions at this level would be a large programmable calculator or a micro computer. These machines would be expected to conform to the following minimum specifications:

a. 48K bytes random access memory
b. 250 K bytes on line storage
c. Support a scientific language
d. Provide printed output
e. Support some sort of statistical package

Due to the price and general application of this type of computing device, finding preprogrammed stability packages for them would be difficult. Most programming for stability systems would have to be performed in-house. At best, some use could be made of preprogrammed statistics or report writing packages.

The second type of system in this category would make use of a large mini computer or a central computer already in-house and being used by some other function like accounting, marketing or warehousing. With a minimum of programming work, the capability of this type of computer can be used to perform many functions required by stability. The approach would be as follows:

a. Build data files using the on-line editor system available with most machines of this size.
b. Purchase or lease an appropriate statistical package to perform regression analyses and other required statistical calculations. Some systems capable of performing these

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calculations are SAS, APL Statistics Package, and RS-1. (RS-1 is available through Bolt, Beranck and Newman, Inc., Moulton Street, Cambridge, Mass.).

c. Write software to edit and modify the data files as required by the respective statistical package.

d. Utilize available printing hardware and software for producing reports.

Admittedly, these interim systems do not produce the polished product that a more formal system would. They lack security, ease of data entry and manipulation, but they do provide the computing power necessary to comply with the basic requirements of the government and current industry standards for drug product stability. Further, their use provides a period of training for stability personnel which should ensure a better definition of the design requirements for any formal stability system to be used later.

17.4.2 Formal Systems

Systems designed specifically for handling stability programs may be purchased or programmed in-house. In either case, the required computer will generally be a large mini or a main frame computer. The method of obtaining the software will depend upon the specific circumstances of the company involved. Generally the two most critical variables in the decision process will be the staff available in the data processing department and the amount of time alloted to complete the job.

Many stability people involved in this type of decision are opting to purchase a preprogrammed (canned) package. This has many benefits, but the most important of these is reduced lag time to completion of the system. Deciding to buy from an outside concern does not eliminate many of the preliminary planning steps and does not totally eliminate programming. (Often many modifications of the system are necessary to ensure that the specialized needs of the individual company are met.) It does ensure thousands of man hours of designing, programming and debugging can go into the stability system

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without actually taking months or years to implement it. Another very significant benefit is that it usually has a price tag which is less than the total cost to develop a comparable system in-house.

If the option to design and program a stability system in-house is your choice there are some aids available. The American Society for Testing and Materials has prepared a number of reports through their Committee E-31 which will give some helpful hints regarding laboratory automation and lab systems in general. (Refer to ASTM Standard Guidelines E622, E623, E624, E626, E672, E730, E731 available through American Society for Testing Materials, Race Street, Philadelphia, PA). There are texts available which deal with defining and developing management information systems (7). International Business Machines Corporation markets an independent study program entitled, "Managing the Application Development Process: Project Reviews" (IBM Corporation, DPD Educaion - Publishing/Media Support, Education Center, South Road, Poughkeepsie, N.Y.). In general though, these will only serve as guidelines; the most important input will come from the stability scientist based upon his understanding of the needs and requirements of a pharmaceutical stability program.

17.5 Advantages Achieved

Until this point we have dealt to a greater or lesser degree with the mechanics of computerized stability systems. This is all very interesting, but what do we really gain from computerized systems? How can this approach to stability be sold to management? Thoroughly answering these questions could result in a complete book in itself and will not be attempted here. Instead, a list of the more important improvements achieved through computerization will be offered as a starting point upon which you can build.

17.5.1 Improved Scheduling

Greater laboratory efficiency can be achieved through computer assisted scheduling of laboratory testing. Readily accessible stability data allows for long- and short-term checks into the numbers and types of stability samples

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coming up for test. With this information supervisors can properly platoon the samples to make the best use of available personnel and instrumentation. Also, analysis of peaks and valleys in the overall laboratory work load allows for proper selection of new batches for stability so that a more constant workload is maintained in the future. Maximum utilization of personnel and instrumentation is a very important factor in reducing total costs and improving the return of your investment for stability testing.

17.5.2 Reduced Laboratory Retests

The power of the computer can be used to effectively reduce one of the most important contributors to stability costs - laboratory retests. The 95% confidence interval for the points about the regression line may be used to screen individual data points to determine the probability of their being members of the population defined by the regression model. (See Figure 5). If an individual point exceeds these limits, then and only then, is it retested. This ensures the expense for retesting is only incurred when absolutely necessary to make a decision. A further benefit is gained in that these decisions are consistant and statistically valid as required by the current Good Manufacturing Practices.

17.5.3 Improved Decision Making Capability

Having stability data readily available on-line encourages its more effective use throughout the company. Instead of a file being the personal property of one individual or group, it becomes the property of the entire company, available to research, international, formulations improvement, etc., for their daily decision making processes. Each time the data is used to make a decision, the effective cost of generating it is reduced. A system of accessible data tends to eliminate redundant experiments and increases the corporate ability to make timely decisions based upon facts, not conjecture.

17.5.4 Efficient Data Handling

On-line stability data files remove the drudgery and expense of entering and reentering data each time a new calculation is performed or a report is

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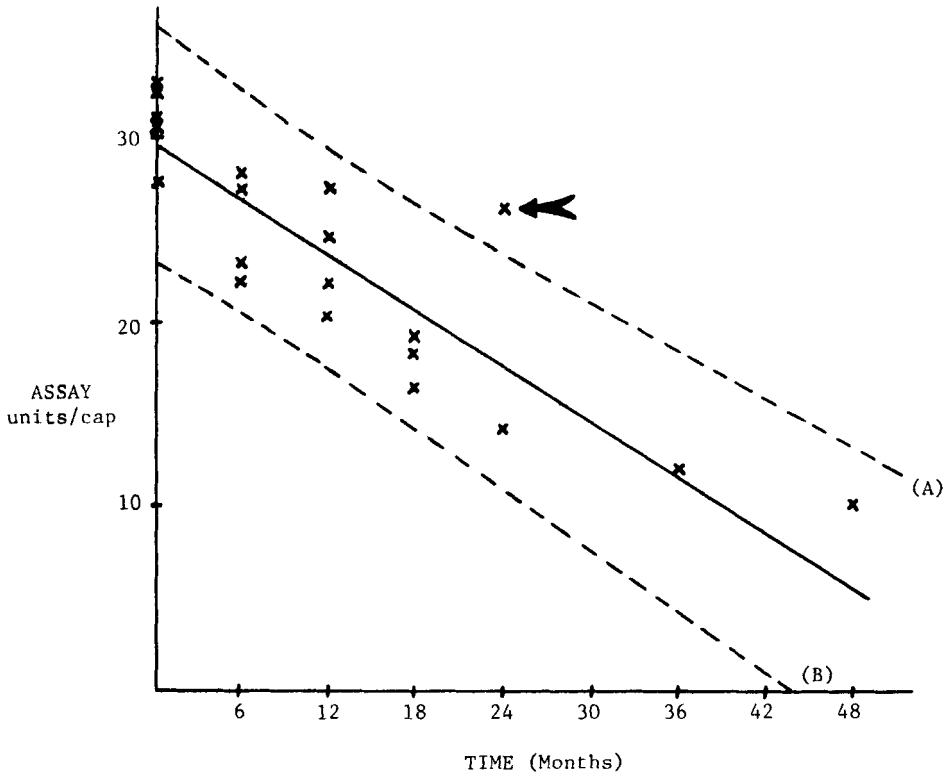

(A) Upper 95% Confidence Limit for Individual Points
(B) Lower 95% Confidence Limit for Individual Points

FIGURE 5

Room Temperature Stability Data
Vitamin Capsule (Calcium Pantothenate).

generated. A few simple commands are all that is necessary to properly sort the data and prepare reports to meet specific requests, such as:

a. Periodic NDA or ANDA updates
b. Data necessary to register products in foreign countries
c. Analyses of data to investigate trends
d. Data requested for marketing purposes
e. Stability information requested by pharmacies or hospitals
f. Data required by state agencies

The ability to actively work with the stability data files to meet these demands results in significant time savings which in turn translates

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into dollar savings. Also, there are situations where time is of the essence. In these instances, rapid data retrieval enables quicker reviews and decisions.

17.6 Summary

The computer certainly is not a panacea for stability, but it does seem to provide help in many significant areas. It efficiently and accurately acquires data which can be stored in a manner which is accessable yet can be made secure. It is capable of performing many complex and repetitive mathematical analyses in a consistent and rapid fashion. It can contribute significantly in scheduling and managing laboratory operations. In general, the effort expended to design and implement a computerized stability system is usually recovered many fold. Its return on investment is real and justifiable.

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