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STATISTICAL TOOLS FOR PROCESS CONTROL AND QUALITY IMPROVEMENT IN THE PHARMACEUTICAL INDUSTRY

P. Wehrlé and A. Stamm.

Laboratoire de Pharmacotechnie
Faculté de Pharmacie de Strasbourg, B.P.24 F67401 Illkirch - France

ABSTRACT

If every batch coming off a production line could flawlessly reproduce the original design, there would be little need for statistical input in quality control. Unfortunately, in the real world of manufacturing, many factors combine to make each unit unique, so that some form of statistical control is necessary for any manufacturing process. Building control chart is the most efficient way to detect non random causes of variation that are easy to remove. Then the process is in a state of statistical control, capabilities studies are helpful to define if the process is meeting the specifications. When a process is stable over time and is found highly capable, the opportunity of applying optimization methods to really improve the products characteristics must not be lost. Multifactorial analyses are used to highlight the fundamental structures of the data above all when numerous variables are collected for a great number of items. Obviously, excellency can not be achieved just by using only one of these methods or by running a single shot approach, quality improvement is a long and exciting way by which the knowledge about the process is built up step by step, from day to day.

INTRODUCTION

In an ideal manufacturing world, any production would turn out perfect products. No quality control would be necessary because every batch of pure drug that came off the production line would contain exactly 100% of drug, every 500 mg tablet would weigh exactly 500 mg and every product would flawlessly reproduce the original design.

Unfortunately, in the real world of manufacturing, many factors combine and interact to make each unit unique. Temperature, humidity, materials used, machine settings all vary and affect the product. The actual items that come out of the production process may be thinner or thicker, longer or shorter, heavier or lighter, different from their ideal dimensions (1).

If each and every item produced could be tested, there would be little need for statistical input in quality control. Those individual dosage units that are found to be unsatisfactory could be discarded and only the good items would be released for further distribution. But mostly 100% sampling is difficult if not impossible and the expense would probably be prohibitive both to manufacturer and consumer (2). The inevitable variation in product quality and the economic bounds and constraints make some form of statistical quality control necessary for any manufacturing process.

The challenge is an economic one for both the producer and the consumer: for the producer who would like to reduce the number of rejected items, for the consumer who expects to receive only products corresponding strictly to his own specifications.

The common interest should not only be the control of the process in order to obtain good products acceptable for both but also the process optimization in order to continuously improve the products characteristics. The use of statistical quality control techniques and optimization methods is the most efficient way to reach this objective.

BASIC CONCEPTS

The first idea we always must keep in our minds is: "there is natural variation in everything" (3). A manufacturing process is mostly affected by the surroundings, materials, methods, machines and also workers. When the variation of a process is the addition of a great number of independent parameters having individually only small influence on the whole variation, this process can be described by the well known normal distribution characterized by

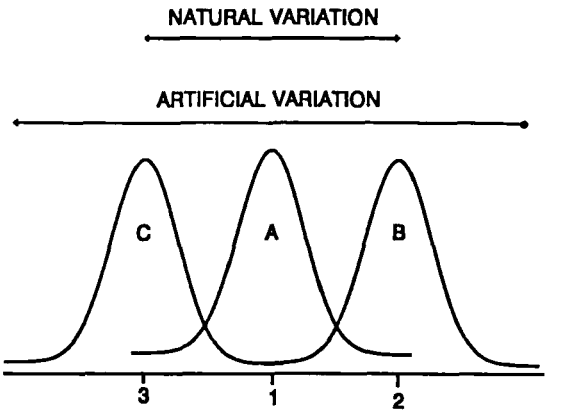


Figure 1. Machine over-setting (4).

the mean and the standard deviation. The independent parameters are called natural, random or inherent causes of variation. Eliminating any one of these minor causes is mostly not cost-effective and often not possible.

When a manufacturing process suddenly breaks down, it is under the influence of isolatable or assignable causes of variation. On the contrary, these causes are generally exterior to the process, easy to locate, easy to remove and therefore cost-effective.

For a manufacturing process, the objective of main importance is to distinguish between the random variables and the assignable causes of variation. Working without having this objective always as a leitmotive would be misleading. Still nowadays, a great error of judgment often done by the management consists in supposing that each process accident or non conformity is due to an assignable cause and this without taking into account the natural variation of the process. The main consequence of this attitude is process or machine over-setting which is firstly time wasting and can lead in the worst case to an artificial increase of the process variation.

Take the example of a product which characteristic during the production is varying in reality like curve A (figure1).

If the operator in charge of the process takes an individual item and measures its characteristic, there is a non nil probability that this measurement is done in position 2. If this operator is not informed about the process variation and is not accustomed with some basic statistics, he will set the machine in order to bring point 2 in position 1 corresponding to the central and target value.

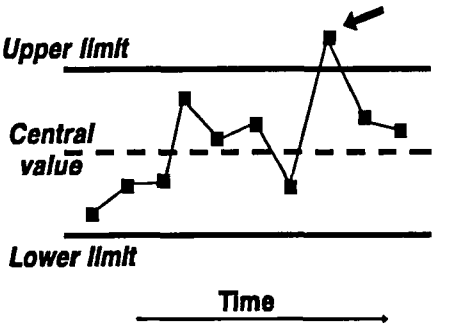


Figure 2. Basic control chart.

Then, the production distribution translates on the left corresponding to curve B. In this situation there is a non nil probability to take an item which characteristic is in position 3. Using always the same reasoning, the worker will set the machine again to the target value in position 1. The new production distribution corresponds to curve C. With the best of intentions, from setting to setting, the operator is increasing the natural process variation. In the worst case it can be twice the initial one.

So it appears a great need of statistical tools allowing firstly to study and then to control the process variation. Building control charts is the most efficient way to define how much of the variability is due to random fluctuations and how much is due to specific causes that you can isolate and correct.

CONTROL CHARTS

A control chart is a simple but powerful tool that provides an immediately useful graphical representation. Every control chart consists of:

- a set of data points chronologically plotted and corresponding to the characteristic of interest during the production,
- a central line representing an estimate of the process mean or process standard deviation or other statistics,
- lower and upper limits by which the data can be evaluated.

If a data falls outside of the limits, the process is said "out of control" because it is under the influence of isolatable causes of variation (figure 2). If all

of the data fall within the limits, the process is said "in control" and only inherent causes are producing the variation in quality from product to product. This is the general characteristics and use of a control chart.

There are numerous different control charts indeed and the choice of a particular chart mainly depends on the process characteristics to be studied and the objectives that one wishes to achieve but also on the way and possibility of sampling (5). The quality characteristics of a given manufactured product can be observed in either two ways:

- the features of the product can be measured on some continuous scale and then the so called control charts for variables or measurement data can be built. This is the case for example when variables such as purity of drugs, tablets hardness, tablets weight, or content uniformity are determined.
- the product also can be classified into one, two or more discrete classes, either conforming or not conforming to some set of criteria. The so called control charts for attributes data is generally used when qualitative variables such as appearance, colour, taste and so on are measured.

Mean and Range charts

In order to apply statistical theories without introducing bias, the most efficient and commonly used way of sampling consists in testing 5 items taken at constant time interval until 20 subgroups are collected.

Chart to control the process mean - Mean chart

When the items are collected the first operation is calculation of the mean for each subgroup and calculation of the mean of the means.

$$\bar{X}_i = (x_1 + x_2 + \ldots + x_{n/N}).(n/N)$$

$$\bar{\bar{X}} = (\bar{X}_1 + \bar{X}_2 + \ldots + \bar{X}_N)/N$$

The mean chart can then be built (figure 3). The central line corresponds to the mean of the means. Upper and lower limits are control limits statistically computed with the obtained data. These limits are statistical indices characteristic of the process. They must clearly be separated from specification limits only based on engineering boundaries giving no statistical information .

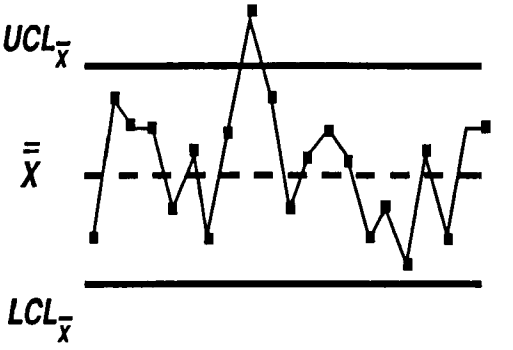


Figure 3. Mean chart

Shewhart who introduced the concept of control chart set these control limits to 3 standard deviations. According to the normal distribution, the probability of observing a value outside these limits is very small: 0.27%. So because of this very low probability, if such a case occurs this means that it is due to an non random cause in other words to a assignable cause of variation that can be isolated and withdrawn.

Charts to control the process variability.

Process variability can be controlled using either a standard deviation chart or a range chart. The range R_i, difference between the highest and the lowest value, can easily be calculated by hand, so that a range control chart can be built directly on the production line by an operator having only poor knowledge about statistics. The range is also a good estimator of the variability when the sample size is small which is often the case.

$$R_i = x_{maxi} - x_{mini}$$

$$\bar{R} = (R_1 + R_2 + \ldots + R_N)/N$$

But for a sample exceeding 10 items, the standard deviation is a better estimator less dependent on normal distribution of the data. Because in the reality, it is not always possible to collect a great number of items, above all in the Pharmaceutical Industry, the range chart will be presented here.

The central line of the range chart is the mean of the ranges calculated for each subgroup. Control limits are the followings. Because the real value of sigma is unknown, estimators must be calculated to set the control limits. This

point will not be developed especially as these values are given on commonly used and standardized tables (6).

Upper control limit UCL_R

$$UCL_R = \bar{R} + 3\sigma_R = D_4\bar{R}$$

Lower control limit LCL_R

$$LCL_R = \bar{R} - 3\sigma_R = D_3\bar{R}$$

D3, D4: In standardized tables

Interpreting of measurements data charts

First of all, a range chart should always be analysed before the mean chart. The reason for this recommendation is that unless the variability of the process is in a state of statistical control, we do not have a stable distribution of measurements with a single fixed mean. It would be misleading to analyse the mean chart at first without any information about the real variability of the process. This precaution taken, the basic analysis consists in detecting any point above upper or lower limits. If such points appear, this means that the distribution has suddenly changed. This can be due to:

- calculation or plotting errors,
- an accident during sampling,
- the stop of a machine,
- the change or mixing of materials,
- the change of the testing machine itself, the new one being more precise pointing out a greater dispersion.

However, 3-sigma control limits are not the only statistical test for determining wether the data plotted on a control chart are following a non-random pattern. Rules for trend analysis exist (7) that are helpful to identify unnatural points inside the 3-sigma limits and are therefore useful for determining problems in a process and this before they cause the process to be shut down. Examples of these rules are the followings (figure 4):

case #1: 8 successive points or 7 successive intervals stabilised or increasing above the central line. The distribution is increasing due for example to:

- a change of operator or an operator being tired,
- a machine out of adjustment,
- an overheating of a machine ....

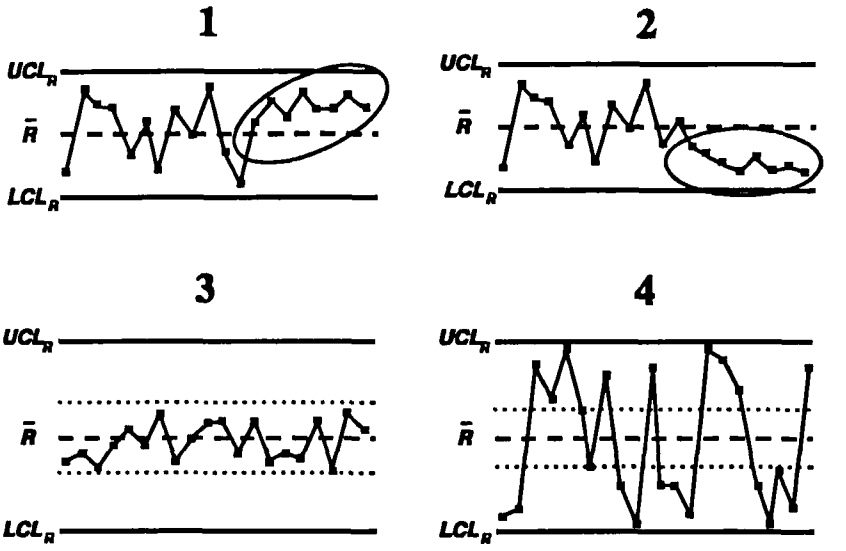


Figure 4. Examples of Trend Analysis.

case #2: 8 successive points or 7 successive intervals stabilised or decreasing below the central line. This situation points out a decrease of the distribution being sharper. In this case one must be able to distinguish between a real improvement of the process or a modification in the system of measurement clogging or being for example more dirty so that the distribution decreases artificially.

case #3: more than two thirds of the points are within the third central part of control interval. This situation can reveal a stratification due to measurements coming from different sources having a different mean range. This is the case for instance when each subgroup contains items from different machines. We must also be careful that an operator afraid to make a bad work is not changing the results so that they are near the central value.

case #4: the points are plotted always near the control limits without fluctuation near the mean. This is characteristic of population resulting of different sub-populations having quite very different dispersions. The sampling method must be modified or each population must be controlled separately.

Whatever the situation, it is necessary to find out the assignable causes and to eliminate them. This is only possible when a detailed journal checking every action is kept up to date. And of course, if the problem has been solved, the

successful action must clearly appear on this journal so that the operator can rapidly take an action if this situation appears again.

Interpreting Mean chart

When the ranges are under statistical control, the dispersion of the studied characteristic is stable over time. Only in this case it is possible to analyse the mean chart in order to see if the position of the characteristic has changed or not. Like for the range chart, same analyses can be performed and quite same attitudes can be taken when the process comes out of control.

Charts: just process barometers or real tools for quality improvement?

Control charts are powerful to point out the presence of an assignable cause. When such an assignable cause is detected all must be done to locate and to remove it. When this operation has successfully been performed, new control limits must be recalculated. This can be realized with the actual data but points out of control being withdrawn. If it is possible, the best way consists in collecting completely new samples, building a completely new chart in order to see if the assignable causes have effectively been removed. Then, new and stronger limits can be defined and extend to future subgroups. So from control chart to control chart the quality of the product can be improved.

Control charts should also be maintained and used regularly because operators become aware of the importance that management is attaching to quality improvement and subsequentely exercise greater care (3).

Other control charts for measurements data

Classical control charts for measurement data can be used only when subgroups can be built. This is not always possible or practical.

This situation occurs for example when items are produced at a very slow rate. If items are produced every hour, it would take 5 hours to form a subgroup, by then the process might already gone out of control.

Other particular case, variables such as temperature, pressure but also purity of drugs could not be charted with soubgrouping since a subgroup of 5 purity analyses made in quick order would likely give virtually the same value (3).

Individual observations chart and moving range chart

As seen previously, in classical range chart, control limits are base on estimators using the subgroups ranges. Obviously, subgroup ranges cannot be used here there are no subgroups. The commonly accepted procedure is to create

ranges by taking differences of successive observations, (second minus first, third minus second, etc...). These particular range values are called the moving ranges MR.

$$MR_I = | X_I - X_{I-1} |$$

Central line: $(0<I\leq n-1)$

$$\overline{MR} = 1/(n-1) \sum MR_I$$

Control limits:

$$UCL_{MR} = D_4 \overline{MR}$$

$$LCL_{MR} = D_3 \overline{MR}$$

The average of these moving ranges corresponds to the central line of the chart. Control limits are calculated using estimators given in standardized tables and depending on the size of the moving range.

A moving range chart complements a X chart similar to the way a range chart complements a mean chart. X chart for individual observations is constituted of a central line which materialize the mean of the individual observations. The average of the moving ranges is then used in the same manner that average range is used in estimating the standard deviation and therefore in estimating the control limits for an mean chart. The moving range chart and the chart for individual observations can be analysed approximately like the classical range and mean charts.

Cumulative sum procedures or CUSUM charts.

In some industries such as electronics, chemical or pharmaceutical industries and above all for continuous processes, it would be of main interest to detect even small variations and this as quickly as possible and with the lower rate of false alarms. The cumulative sum procedure is able to reach this goal. This method consists in accumulating differences between each successive observation and a target value (1,3).

$$\begin{aligned} S_1 &= x_1 - x_0 \\ S_2 &= (x_1 - x_0) + (x_2 - x_0) = S_1 + (x_2 - x_0) \\ S_3 &= S_1 + (x_3 - x_0) \\ S_t &= S_{t-1} + (x_t - x_0) \end{aligned}$$

where x_0 is the target value and x_i each individual observation $(0<i\leq t)$.

By plotting the cumulative sums on a chart, small variations are associated with an increase of the slope. If successive observations are very close to the target value an horizontal line is obtained. To detect a point corresponding to a

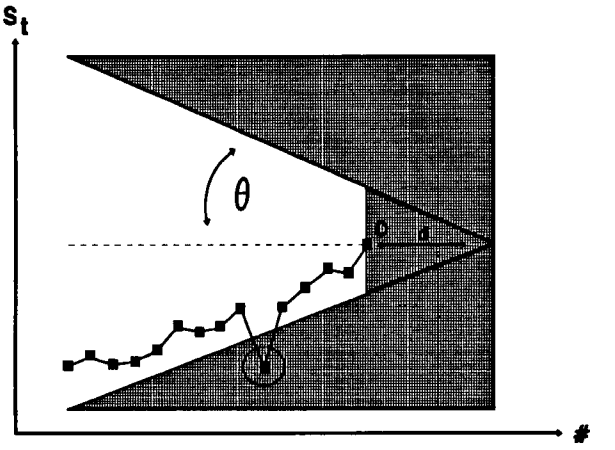


Figure 5. Cusum chart with the V shaped mask.

situation out of control, parallel control limits are no more efficient, a V shaped mask must be superimposed on the chart. The characteristics of this mask are depending particularly on the shift that is to be detected (figure 5).

For detecting large shifts greater than 3 sigma, it is difficult to improve upon the performance of the classical X chart method. But for small shifts, around one sigma, the cusum procedure is much more efficient. For example, if we expect to detect a shift of 0.5 sigma, with a classical Shewart chart we will have to wait that 160 successive items are collected before receiving an out of control signal when only 38 successive items are needed with a CUSUM procedure. Numerous cusum derivatives exist that can be used for either measurements or attributes data, either for subgrouped or individual data, either to control the process mean or the process variability (3).

Control charts for attributes data

Control charts for attributes data are based also on standard distributions such as poisson distribution, binomial distribution or binomial distribution approximated by the normal distribution, so there use is not totally different to the use of measurements data charts.Depending on the objectives to be achieved, a np chart for the number of non conforming units, p chart for the proportion of the non conforming units, c chart for the number of nonconformities or u chart for the number of the nonconformities per unit must be applied.

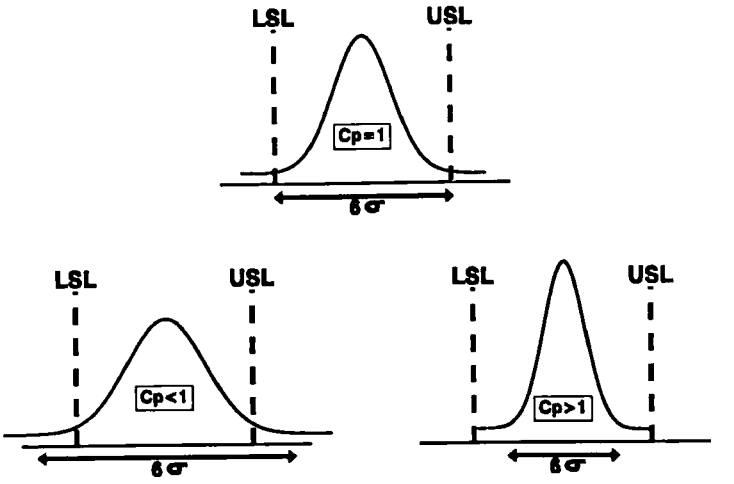


Figure 6. Different Cp values and the corresponding distributions.

PROCESS CAPABILITIES STUDIES

Control limits are statistical indexes calculated with the actual data collected from the process. But it is not a scoop that apart from the control limits there are other limits determined from engineering or consumer specifications. So then the process is in statistical control, other tools helping to define if the process is meeting these specifications are necessary.

To define if the studied process variable is within the specifications limits, different capability indices can be calculated (8). The Cp value is the most commonly used. It corresponds to the ratio between the allowable process spread and the actual process spread, in other words: the upper specification limit (USL) minus the lower one (LSL) divided by the confidence interval (which is usually corresponding to 6 $\sigma_{est.}$).

$$C_p = \frac{\text{ALLOWABLE process spread}}{\text{ACTUAL process spread}}$$

$$C_p = \frac{USL - LSL}{6\sigma_{estim.}}$$

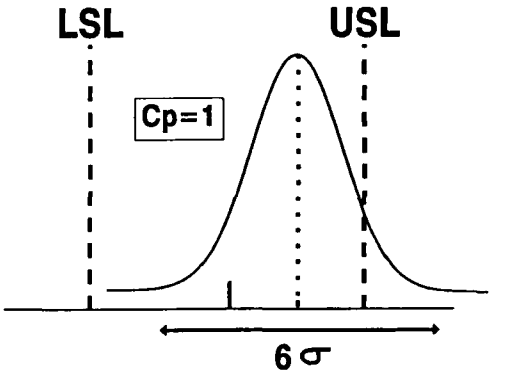


Figure 7: Weakness of the Cp value.

So, a process is within the specifications if Cp is more than 1 (figure 6).

But when the process is not centred, the use of the Cp index could be misleading (figure 7).

This is due to the fact that Cp is not a function of the mean, so that for a same value of sigma, if the process is on target or not, the Cp value would be the same. To avoid this problem an other capability index is defined. This is the Cpk index taking into account the process mean $\mu_{estim.}$.

$$Cpk = \min (Z_{USL}, Z_{LSL}) / 3$$

where: $Z_{USL} = (USL - \mu_{estim.})/\sigma_{estim.}$

and $Z_{LSL} = (\mu_{estim.} - LSL)/\sigma_{estim.}$

If Cpk=1, the process just meets the specifications. Assuming approximately a normal distribution, 6 sigma confidence interval is within the specifications and then the probability of non conforming units is 27 every 10000. More often for industries such as the pharmaceutical industry, the Cpk limit value is fixed to 1.33 corresponding to 8 sigma within the specifications. In this case, only 64 of every one million units would be classified as non conforming.

So, to improve a process there is more to do than just running the process into a state of statistical control. Improvement also entails reducing process variability and the Cpk value is a good index to measure the extent to which this is being achieved. The way to excellency should not only be to try to reach a goal value but also to continuously increase the Cpk index.

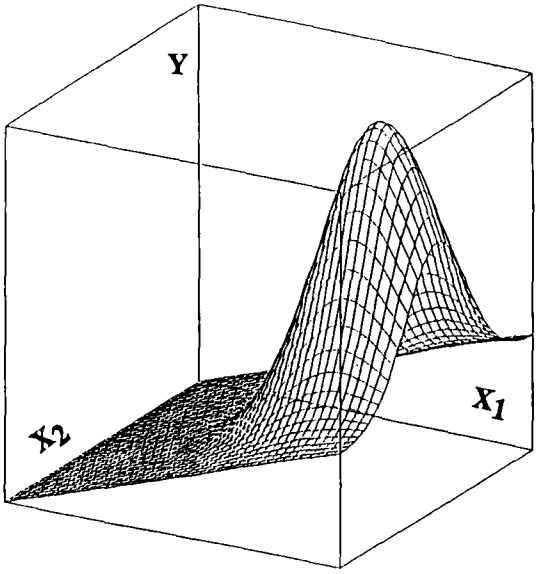


Figure 8: Response Surface.

OPTIMIZATION METHODS

Control charts and capabilities studies are more ore less "listening" or passive statistical tools. More often no attempt is made to see what happens when the process is changed. To really improve the process and reach optimal operating conditions, the use of more conversational or active statistical methods is necessary (3).

Experimental design are helpful to identify the factors that affect the quality of a product. They are efficient and economical methods which allow to collect a maximum of information with a minimum of experiments (9-12). The objective is to define exactly how the variables that can be controlled influence the process which is evaluated by one or more response variables, the final goal being to select the operating conditions leading to optimal levels of response.

For example when the influence of two controlled variables X1 and X2 on a response variable Y is studied, the mathematical function between X1, X2 and Y defines completely the response surface which can be compared with a geographic relief (figure 8). When an optimum exists, it is visualized by the top of a hill. The levels of X1 and X2 leading to the same level of response allow to define isoresponse curves similar to topographic contour lines.

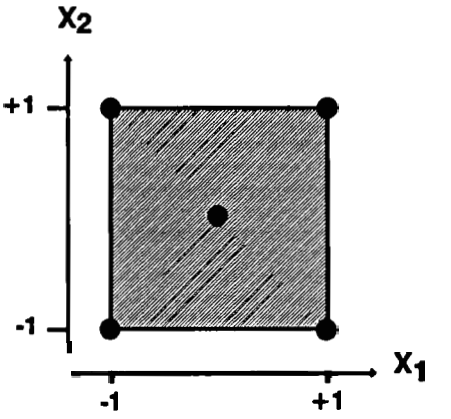


Figure 9. 2^k Experimental Design +1 (k=2).

Far to the optimum, the contour lines are in fact parallel and the response surface quite plane can be described by a first order polynomial including rectangle terms of interactions.

$$Y = a + b.X_1 + c.X_2 + d.X_1.X_2$$

Y : Response Variable
X_1 : First controlled Variable
X_2 : Second controlled Variable
a : Constant
b,c,d : Regression Coefficients

The regression coefficients of such a model can easily be calculated after realization of a 2 power 2 experimental design, in other words by studying each controlled variable at 2 different levels (figure 9). The model is validated is the central experiment gives the same result as the one estimated with the model.

The method of steepest ascent consists in continuing the experimentation on the line perpendicular to the contourlines passing by the centre of the design in the direction of the improvement of the studied property and this until no better response is observed. The last experiment can then constitute the basis of a new design able to adjust the response surface equation. The experimentation stops when a good result is obtained or when the coefficient of the rectangle term corresponding to the interaction is statistically significant. The response surface is no more plane, the important curvature must be defined by an other model.

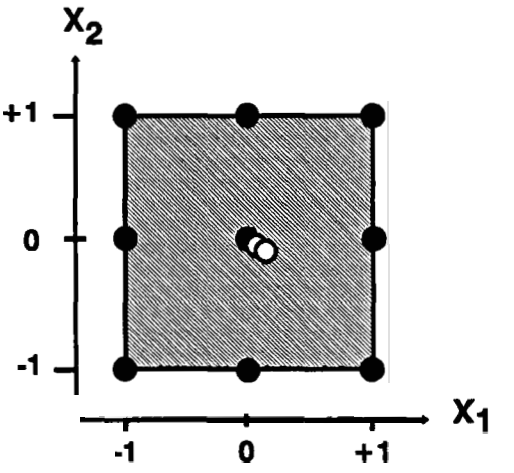


Figure 10. 3^k Experimental Design +2.

Near the region of the optimum, the curvature of the response surface can be described by a second order polynomial which regression coefficients can be computed after setting each controlled variables at 3 different levels, in other words by performing a **3^k experimental design** (figure 10).

$$Y = a + b.X_1 + c.X_2 + d.X_1.X_2 + e.X_1^2 + f.X_2^2$$

Y : Response Variable
X_1 : First controlled Variable
X_2 : Second controlled Variable
a : Constant
b,c,d,e,f : Regression Coefficients

Analysis of variance can then be performed to validate the model and the experimental error can be evaluated by repeating the central experiment.

The main disadvantage of the 3^k experimental design is the great number of experiments to be executed since the number of controlled variables is high. For 5 variables not less than 243 experiments need to be done.

Central Composite Design of Box and Wilson (10, 11) is an economical option to the full 3^k experimental design. This design consists in adding to a central core of 2^k, one central point and 2k outer points at a distance $\pm\alpha$ to the centre. The alpha value corresponds to orthogonality and isovariance by rotativity criteria (figure 11).

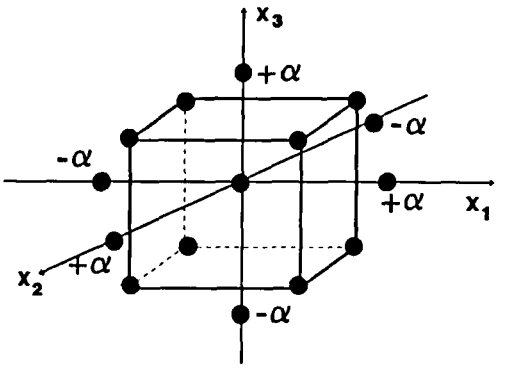


Figure 11. Central Composite Design 2^k+2k+1.

The number of experiments significantly decreases, for 5 variables 243 experiments are needed for the 3^5 design when only 43 experiments are required for the corresponding central composite design.

This rapid presentation of the experimental design methodology would not be complete if the problem of mixture optimization well known to the pharmacist responsible for formulation is not evoked. In this particular case, the experimental field is no more a square, a cube or an hypercub but a triangle, a tetrahedron or a hypertetrahedron. In fact, here, controlled variables are proportions of components whose sum is always equal to one or 100%. Scheffé (13) was the first to propose a design adapted to this kind of problem by realization of experiments corresponding to pure compounds. Needless to say that these experiments are mostly not realistic and even not feasible. In order to palliate this inconvenience, Mac Lean and Anderson (14) developed an other type of design taking into account formulation constraints (figure 12).

All these experimental designs are based on a clearly postulated mathematical model describing completely the response surface. Other methods exists that do not need any calculations and the use of a computer. They just cover the response surface without creating it leading step by step to the optimum. They belong to the so called EVOP or evolutionary operations.

The Box-Evop method (3, 10, 11) consists in building a classical 2^k experimental design. This initial plan is then translated in the direction of the improvement of the process and this without any mathematical modelization, only basic statistics are needed. The translation is performed with only small

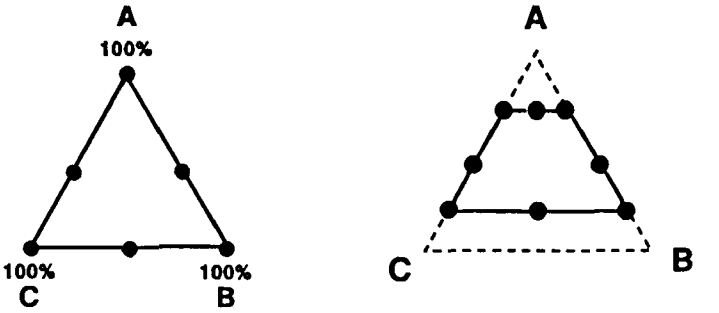


Figure 12. Sheffé and Mac Lean experimental designs.

changes in the settings of the process variables so that the process is not disrupted.

Because of its great easiness of use and also because it can be applied when there are more than few process variables to be varied, the **Simplex Evolutionary Operation** of Spendley Hext and Himsworth (15) is one of the most interesting alternatives to Box-Evop method. For k variables a simplex is constituted of k+1 experiments. In a 2 dimension space, the simplex is a triangle, each vertex corresponding to an experiment. These experiments are performed and compared. The experimental point giving the worst result is then reflected by the centre of gravity of the 2 remaining. The experiment represented by this reflected point is also tested, the 3 last responses are compared and so on until k+1 simplices give the same best point (figure 13).

MULTIFACTORIAL ANALYSES

Multifactorial analyses are nowadays very interesting and ought to be used more often. Since a great number of process controls can be set because of the development of automatic recording systems, it is very easy to collect, above all in industry, a lot of data. But at the end of the operations the experimenter is in front of a mountain of check lists which does constitute a real obstacle for a rapid and complete understanding of the informations included in this great number of values. The use of mathematical methods called factorial or multifactorial analyses is helpful.

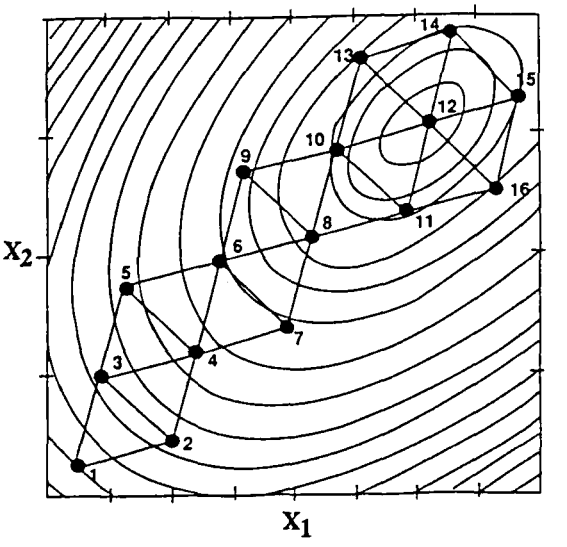


Figure 13. Simplex Evolutionary Operation.

Theory of these method was already presented in details (16, 17, 18). To simplify, the basis of these methods can be approximately compared with the principle of a camera. In fact, a camera permits to pass from a 3 dimensions space the one of in which we live to a 2 dimensions space the one of the photograph. But the quality of the collected information still depends if the photograph is taken from one angle of view or from another (figure 14).

Factorial Analyses are helpful to select a minimum of "angles of view" called factors but efficient to collect the maximum of information.

Principal Component Analysis which belongs to these methods is efficient to treat great tables of data crossing individual trials or experiments and quantitative variables corresponding to these experiments. With this method, it is possible to pass from a multifactorial space very complicated to understand to a space of three or even two dimensions and this with the minimum lost of information. It is then easy to produce simple graphs in which the fundamental structures of the data are recapitulated (17). Relations between the studied variables can be brought to light and characteristics of the items regrouped into sub-populations can be pointed out (figures 15, 16). This method proved useful to study the lubrication of a water soluble tablet (19).

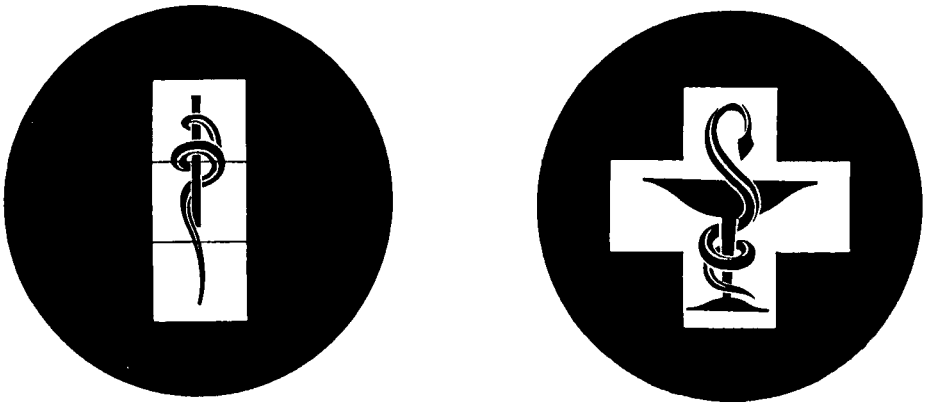


Figure 14. Importance of the angle of view.

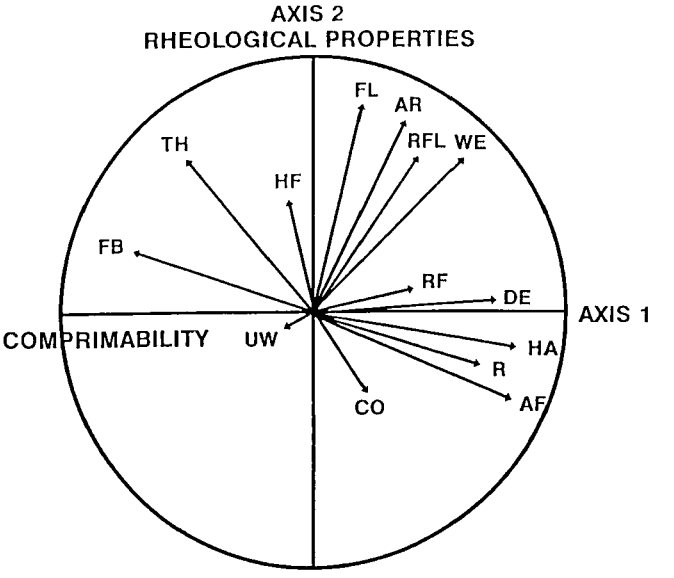


Figure 15. Circle of correlations between variables.

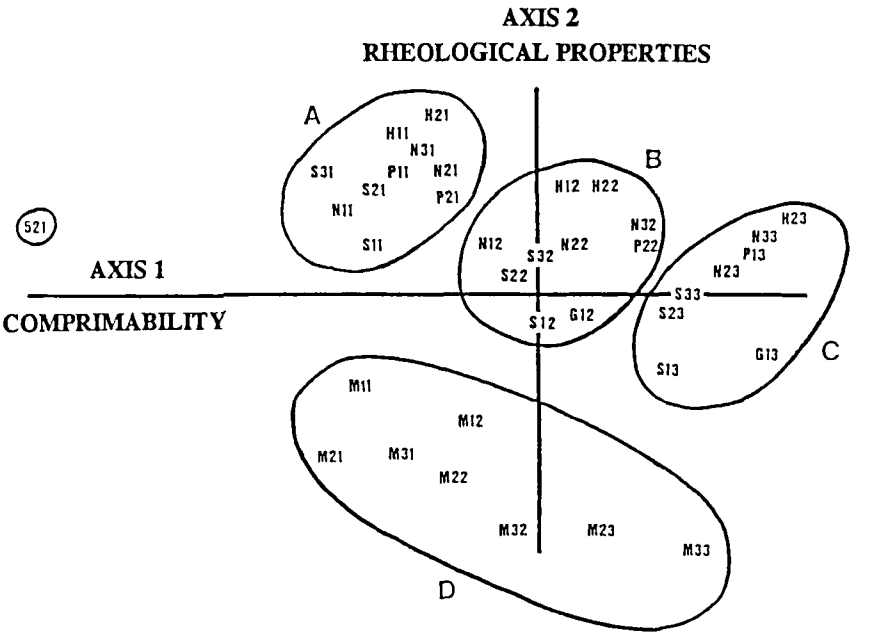


Figure 16. Representation of individual items on the principal axes.

When the experiments can be regrouped in different homogeneous populations, the Factorial Discriminant Analysis is particularly efficient. Using this method, simple graphics can be obtained. By projection, each experiment of a population is as close as possible to the mean of this population and the mean of each population as far as possible from one group to an other. The main interesting consequence is that variables able to separate the populations at best can be brought to light. Classification of an additional unidentified experiment is a second interest of this factorial method. Scaling up of wet granulation was studied using this factorial analysis (20).

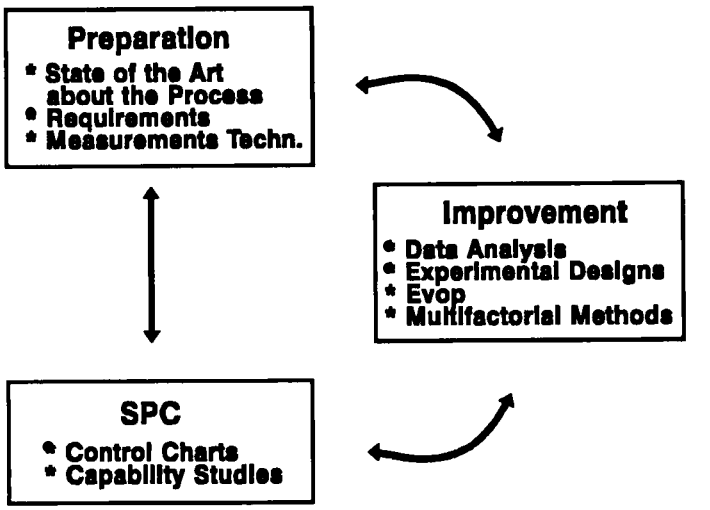
The correspondence analysis is particularly interesting when data are collected in a table of contengency crossing variables organized in modalities. This method is able to treat either quantitative or qualitative variables. For example, it was used to study the effectiveness of different drugs to ease pain. The drugs were given to hospital patients and tested using a five points scale: poor, fair, good, very good, excellent. The correspondence analysis pointed out the most efficient drug (21). This method is also helpful to treat the results

obtained for different formulations of pharmaceutical dosage forms by a jury testing their appearance, taste, ...

CONCLUSION

All the methods presented above have their own places in quality improvement and are strongly interconnected.

The first step of quality improvement consists in collecting all the informations concerning the studied process. Using an Ishikawa diagram also called fishbone chart is useful to define the parameters having an influence on the process or product characteristics when the Pareto diagram is efficient to classify them in order of their frequency of occurrence. The state of the art about the process being precisely defined, measurements technics being validated, requirements and specifications limits can then be set.



The first time control charts are used the assignable causes responsible of the process being out of statistical controlto must be identified and removed. Then the process is stabilized, applying control charts with stronger limits is the best way to have a strict control of it. In this situation, capabilities studies must be performed in order to define how the process is meeting the engineering specifications. When the process is in a state of statistical control and above all if it is found highly capable the opportunity of improving its characteristics by using data analyses in conjunction with optimization methods must not be lost.

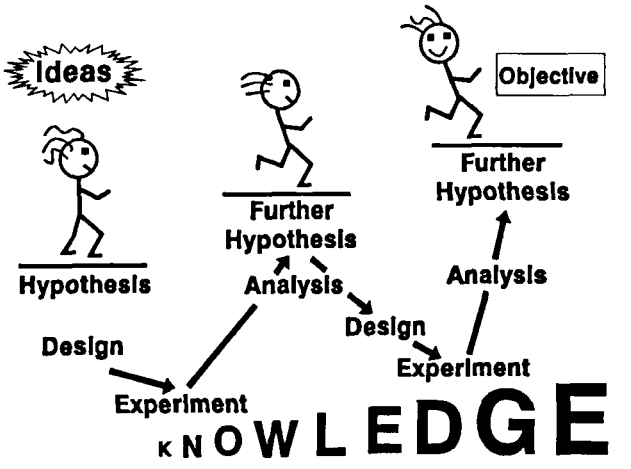


Figure 17. The Way to Excellency (22).

Adopting this philosophy will lead not only to control but also to progressively improve the process, new requirements and objectives being day to day adjusted.

There are no easy paths to quality improvement, you can not use a single experiment or a one shot approach and be finished with it (22). Quality improvement is a long and step by step way by which your knowledge about the process or the product is continuously improved (figure 17).

Excellency can finally be achieved only if everyone, worker and manager, is convince of the efficiency of this general statistical process control methodology and is really involved in this exciting way to quality control and quality progress.

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