A Punch and Die Control Program and Its Contribution to Tableting Technology

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The necessity for a comprehensive quality control program for tableting tools is discussed and the establishment of tool specifications and inspection facilities are described. Several experiments are presented leading to the evaluation of steels, tool shapes, tolerances, granulations, and tool maintenance on the effective life span of the tableting tools.

IN RECENT years tablets have become the most widely employed mode of administering drugs orally. As a result, the techniques involved in their preparation have been under the intensive scrutiny of pharmaceutical researchers to a continually greater degree. The spirit of criticism and inquiry which has developed in this important area of technology has produced many new innovations in techniques and equipment for tableting operations. The latter developments have included multilayer and compression coating machinery as well as increasingly higher speed presses equipped with induced or forced feeders.

Although these more complex devices have undergone considerable study, the important area of tableting tools has been left relatively untouched by both the tablet machinery manufacturers and the industries which employ them. An awareness of this deficit has recently been referred to in two articles published by the tableting tool industry. Gaskell (1) has stated that "the quality of the finished product depends in no small measure on the quality of the tools which actually compress the powders." It is not difficult to realize that with machines with outputs of 3000 to 6000 tablets/min., many tooling difficulties never previously encountered could be anticipated. Heavy losses in productivity resulting from poor quality punches and concurrent frequent tool replacement certainly must be avoided. If the critical variables cannot be adequately controlled, the utility of the high-speed machinery is seriously hampered. Bobbitt (2) has further noted that "mechanical perfection as well as selection of the proper tooling materials are both necessary precursors to permit modern presses to deliver the precision performance and large volume output that has been engineered into them."

Despite commentary such as the above from punch and die manufacturers indicating the need for exacting and reproducible tool quality, experiences at Ciba disclosed a definite need for the initiation of a routine quality control program for incoming tableting tools. To substantiate this, a few specific examples might be of value.

Aside from the normal processing errors that were encountered in dealing with suppliers, numerous problems have developed of which the following are representative: oversized and undersized punch heads, shank diameter irregularities, oversized punch tips, improper punch face finish including surface polish, monogram irregularities, nonuniformity of steel hardness throughout tool, overall punch length variations, and nonconcentricity of die bore and punch tip.

Prior to the initiation of an inspection program, our concept of the causes of the tooling problems which beset us was limited. However, inspection of incoming punches and dies revealed a vast array of nonconformance to specifications set up by the tool suppliers themselves. Certainly no comment is required relevant to the potential difficulties which would be encountered when using unsatisfactory tooling as described above.

It might be advantageous to dwell in greater depth on the subject of punch face characteristics. An example of an unsatisfactory finish on a punch face can be observed in Fig. 1, the obvious irregularities being readily apparent. It takes little imagination to appreciate what effect a punch finish such as this would have on the tablets compressed from it. The results obtained when these punches were returned to the manufacturer for corrective action can be seen in Fig. 2. The faces have been overbuffed and, although the buffing considerably improved the appearance of

Received February 6, 1962, from the Research Dept., Ciba Pharmaceutical Co., Summit, N. J.
Accepted for publication May 11, 1962.
Presented in part to the First Annual Eastern Regional Meeting of the A.PH.A. Industrial Pharmacy Section, New York, N. Y., November 13, 1961.
The authors gratefully wish to acknowledge the contributions made by Messrs. Walter Steinert and George Kessler of the Ciba Plant Service Division.
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Fig. 1.—Punch tip showing surface irregularities.

the face of the punch, it also removed a significant amount of the embossed monogram, particularly the letter A. These punches were rejected a second time. Unfortunately, the above was not an isolated example of unsatisfactory tools obtained from the punch and die manufacturers.

In the pharmaceutical industry controls are established over all aspects of manufacturing procedures. Since tooling is one of the major factors governing the quality of finished tablets, a program of inspection must be considered to be in the category of other necessary incoming material inspections, such as packages and chemicals. Since machine problems often cause considerable production delays as well as postponement of product introductions, we felt that it was important to initiate a more comprehensive quality control program for our tableting tools. As a result, studies were undertaken to develop a standardized program for tool purchase and control.

DESIGN OF THE CONTROL PROGRAM

The objective of a control program for punches and dies, as in any other quality control program, was to define clearly and precisely the tooling desired and subsequently to maintain this high quality of tooling through careful inspection. The first step toward our objective involved the establishment of tool specifications and tolerances for all punches and dies acceptable both to Ciba and the tool suppliers.

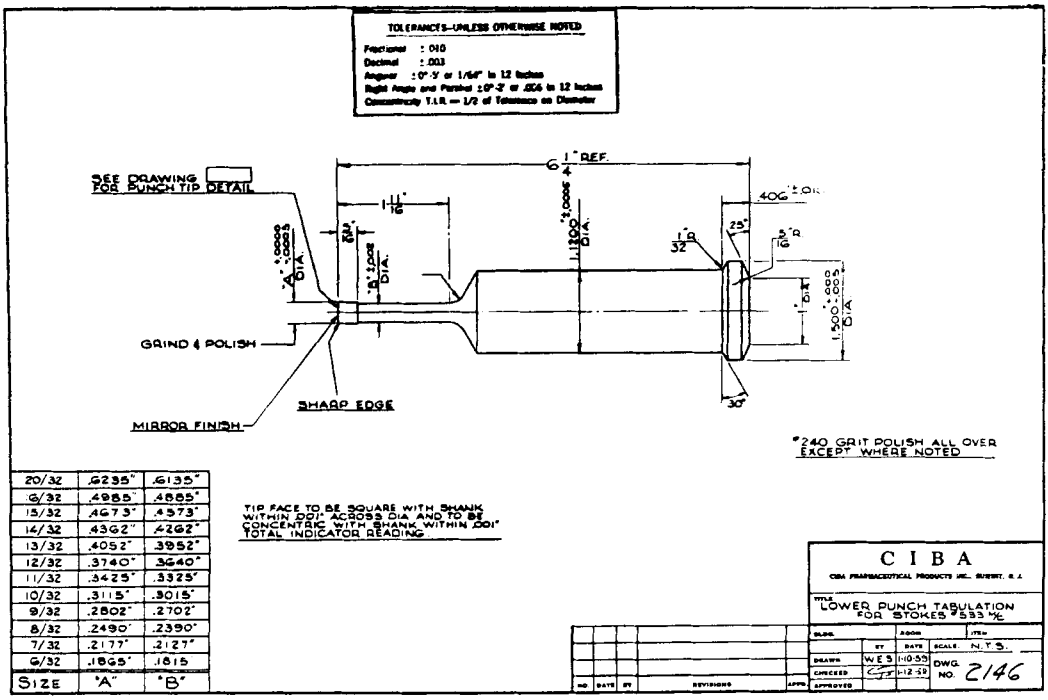
Development of Specifications.—The development of satisfactory tool specifications required the combined efforts of several divisions, including Pharmaceutical Manufacturing, Plant Engineering, Purchasing and Pharmacy Research, as well as the cooperation of the tool manufacturer. The specifications established were based upon the requirements of the machines used, the products being manufactured, and the working tolerances of the tool manufacturers. To obtain maximum flexibility, a system of drawings was developed encompassing monograms, punch blanks, punch tips, dies, and special shaped punch and die sets.

Preliminary drawings of all tools used were developed and eventually assumed the form seen in Fig. 3. This representative example is a typical punch body drawing with carefully evaluated tolerances on all critical dimensions. All specification drawings include tooling size ranges from $^{6}/_{32}$ to $^{20}/_{32}$ inch by the use of appropriate tabulations. Separate punch tip detail drawings define tip shape, depth of concavity, types of monogram, and the length of the tools. In order to reproduce the quality of the punch face it was necessary to control the quality of the hobs being used by the manufacturer. This required the preparation of monogram drawings which defined tolerances for every facet of the monogram, including spacing, depth, and overall length of each of the letters. Further, in consideration of recent tablet counterfeiting attempts, it is evident that the development of such precisely controlled monograms would facilitate the detection of these criminal acts.

Fig. 2.—Punch tip after buffing.

Inspection Program.—The establishment of specifications as described above did not, in itself, solve the problem of tool control. The initiation of a 100% inspection program for incoming punches and dies was found to be necessary. Engineers and mechanics, utilizing appropriate instruments, developed standard techniques for checking all critical dimensions. Figure 4 presents a view of the inspection area showing the equipment used for checking all critical dimensions. Present are measuring tools, including indicating micrometers, gauge blocks, an indicating bore gauge, and a master form gauge. This precision equipment can measure to an accuracy range of ±0.0001 in. The inspector checks the dimensions against the drawings which were sent with the tool order to the manufacturer. Other inspection devices include a depth measuring stereomicroscope to measure punch face characteristics. A steel hardness tester is also available, so that punches and dies may be checked not only for conformance to specifications, but also for uniformity of steel temper throughout each tool. The steels currently used for tooling are based upon the suppliers' recommendations.

If the complete set of punches or dies meets all the standards, they are then accepted and etched



SIZE	"A"	"B"
20/32	.6235"	.6135"
19/32	.5935"	.5835"
18/32	.5635"	.5535"
17/32	.5335"	.5235"
16/32	.5035"	.4935"
15/32	.4735"	.4635"
14/32	.4432"	.4332"
13/32	.4052"	.3952"
12/32	.3740"	.3640"
11/32	.3425"	.3325"
10/32	.3115"	.3015"
9/32	.2802"	.2702"
8/32	.2490"	.2390"
7/32	.2177"	.2127"
6/32	.1865"	.1815"

Fig. 3.—Print showing punch body specifications.

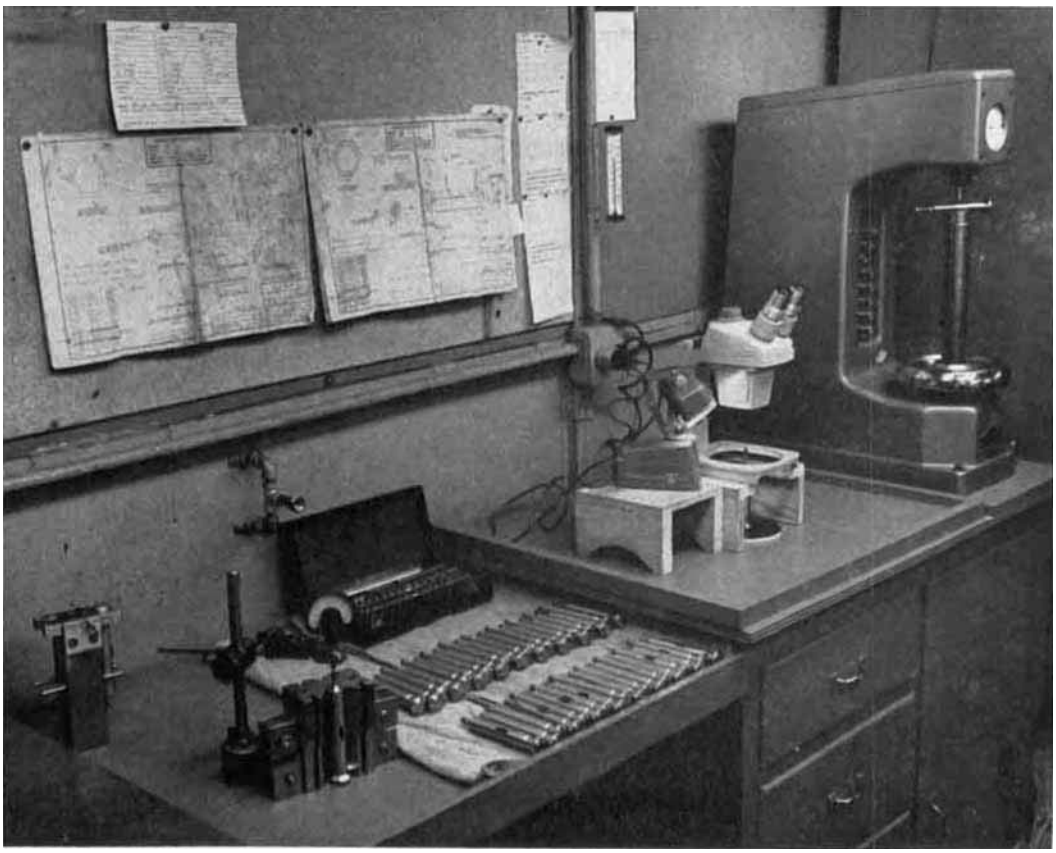


Fig. 4.—Tool inspection area with testing equipment.

with a control number for identification. Should the tools fail to meet specifications, they are rejected and returned to the manufacturer for reprocessing or replacement.

Considering aspects of the inspection procedure, all the dimensions defined are important and are checked. However, through our experience, several areas have been found to be of more critical concern and limits of ±0.0005 in. have been established for them. These regions include head thickness, overall punch length, and shank diameter. Justification for this may best be described by way of example. During compression, the influence of variation in overall length of the lower punches will affect weight variation between tablets, thus altering the dose finally administered to the patient. Hardness of the tablets will not be uniform and the mechanics of compression coating operations may be seriously affected. Tapered and oversized punch shanks can lead to seizing of the punch body in the head of the machine, with resultant severe turret damage. The concentricity of the die bore, in relation to the concentricity of the punch tip, if not within specified tolerances can seriously affect continuous machine operation.

After the first year of the program we were surprised to see that 33.8% of all incoming tooling was rejected as not conforming to specifications. This was particularly disturbing since these standards were set up in conjunction with our tooling suppliers, using their working tolerances. Since then, as can be noted in Fig. 5, we have experienced a steady reduction in the total number of tools returned to the fabricators. It is felt that a paramount factor in this reduction has been the establishment and maintenance of our vigorous inspection program. The continued progress achieved in this area is indicated by the further reduction of rejections to a level of 4.0% of all tooling received during 1961. While the decrease in the total number of rejections during the fourth year of the program is heartening and demonstrates positive action on the part of our suppliers, the continuing appreciable number of unsatisfactory punches and dies points to the need for maintenance of total inspection as it is presently being carried out.

Recording Tool Life History.—The establishment of specifications and subsequent quality control of the tools will insure a uniform high quality in the tools purchased. But, at our present level of knowledge in this area, we cannot be certain that the quality of tooling now used, however uniform, is the most satisfactory for uninterrupted production. So that we might obtain such information, a system for recording the life of the various tools has been developed which enables us to know the total number of tablets compressed with any given set of tools. In addition, information on the products prepared, machines the tools were used with, and the reason that the tools were eventually discarded is recorded. The careful evaluation of the facts obtained from these records will be useful in purchasing tooling with optimum wear characteristics and will result in a better finished product at reduced cost.

The tool life information is recorded on specially prepared cards. They may disclose the merits of refacing procedures, in those instances where refacing is feasible. The records will also show whether misuse by operators, excessive wear by the machine, or a particular granulation was the principal reason that the tools are no longer suitable for use. Since, for the purpose of accurate wear records it is necessary to employ tools only as complete sets, the record cards give the extra benefit of an auditing control of each set of punches for inventory purposes.

RESEARCH AND DEVELOPMENT ASPECTS

Over and above the advantages derived from a quality control viewpoint, the tableting tool control program as just outlined has been responsible for a number of benefits, of both a general and specific character, in tablet manufacturing at Ciba. The acquisition of tooling of desired specifications can now be assured regardless of the source of supply. From the point of view of research and development, the secondary benefits of the program allow the planning and execution of experiments leading to the evaluation of the effects of steels, tool shapes, tolerances, granulation, and tool maintenance on the effective life span of the tableting tools.

Although the program is of recent origin, a number of interesting projects are being pursued and will be discussed below.

Effect of Steel on Tool Life.—From intuitive and cursory evaluation of steels based on data gathered prior to the introduction of the punch and die program, it appeared evident that the type and hardness of steel used in the punches had a profound effect on the life of the tools being used. To accelerate the development of more basic scientific knowledge in this area, an experiment was devised in which a set of punches was prepared from four different types of steels, each being tempered to the same hardness. The test conditions were kept constant by the utilization of a 35-station tableting press and a single product, the only variable being the steel employed for the punches.

Although this study is still in progress, preliminary examination of punches by photomicrography indicates that there are definite differences in the wear qualities of each of the steels used, even though all have the same hardness. Upon completion of this study, or ones of similar design, one will be able to arrive at a scientific conclusion as to the relative merits of the various steels, based upon experimental data rather than speculation. It must be

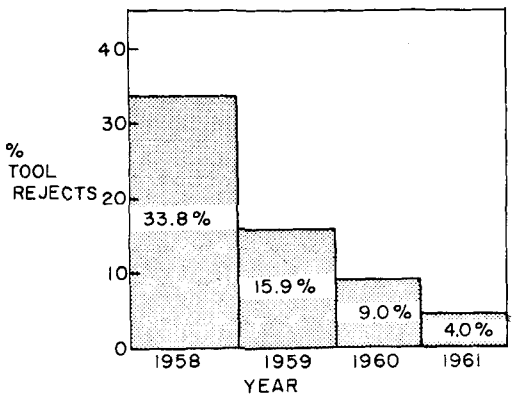


Fig. 5.—Rejection rate of tooling following the introduction of the control program.

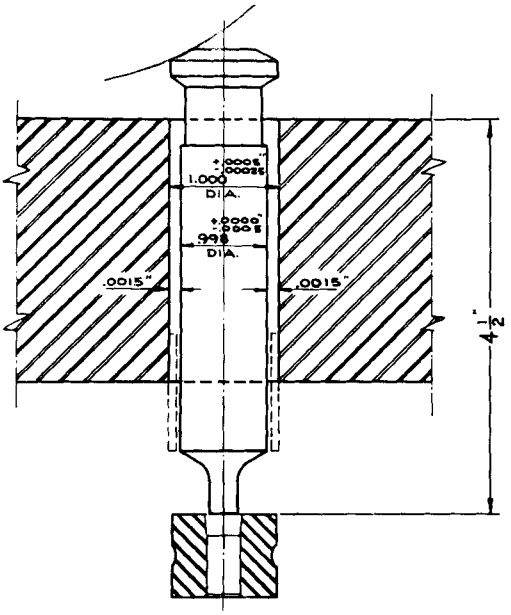


Fig. 6.—Cross-section of upper punch in guide bore with established specifications.

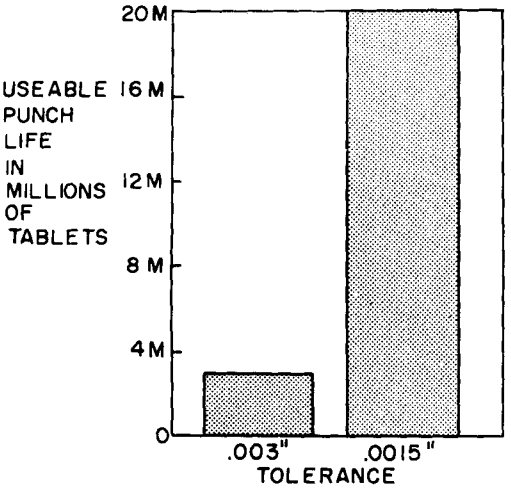


Fig. 7.—Added tool life attributed to closer tolerances.

emphasized that these results can only be accepted as valid in respect to the product tested as it has been shown that different formulations of the same product may possibly alter punch life characteristics.

Effect of Punch Shape.—As was noted earlier, evaluation of the records obtained to date indicated that the shape or geometry of punch tips had a marked influence on the life of punches. The following shapes commonly employed in the manufacture of pharmaceutical tablets are listed in an order of the most durable to the least durable shape: flat, shallow concave, standard concave, flat beveled, deep concave, modified ball punches.

The reason for the order, which has been established from examination of our records, can be explained on the basis of edge strength. It has been found, upon study of unsatisfactory punches, that a common reason for discarding them is the development of a rolled-in burr. It is readily apparent that a modified ball punch tip which, by design, has extremely sharp and narrow edges would be much more prone to this type of deformation than the flat punch, all other shapes fitting somewhere in between. It has been found that the shape of punch tips is also important with respect to misalignment or poor fit in the tableting press itself. This will be discussed in the next section.

Effects of Machine Tolerances.—During the evaluation of data it was noted that, in some cases, a marked decrease in the expected life of the tools resulted when tools were used on certain machines. It was found in all instances that the reduction of tool life was due to damage to the upper punches in the form of a rolled-in lip or burr. Stroboscopic examination of the machine in operation at production speeds indicated that enough clearance existed between the punch shank and machine bore to allow considerable "run out" of the tool at the die table during the compression cycle. This "run-out" results from the eccentric force exerted by the upper pressure roller which forced the tool out of line to as much as 0.010 inch off center at the point of entry into the die. This constant contact with the die edge very rapidly resulted in the lapped condition observed. The solution to this dilemma was a cooperative effort between ourselves and the manufacturer who prepared a new head for the machine in question utilizing tighter clearances for the upper punch, as noted in Fig. 6. Calculations indicated that reducing the clearances between the punch shank and the bore to 0.0015 in. from the 0.003 in. normally allowed on the machine would be the most suitable solution to the problem. Following the receipt of a head, machined to the dimensions specified, experiments were conducted to determine the influence of the turret with these closer tolerances on the actual wear characteristics of the punches in question. As evidenced in Fig. 7 there is no question about the added tool life which can be attributed to closer tolerances. The graph clearly illustrates that, to date, we have obtained at least six times greater usable life from the punches by the application of closer tolerances. It is readily apparent that although the original program was not intended to study the compression machines, *per se*, the availability of accurate, recorded data on punch life enabled us to become aware of a machine problem and to facilitate its solution readily. The economic advantages of a scientific approach to tableting are obvious in this instance.

Effect of Granulations.—Up to this point we have dwelled mainly upon the mechanical aspects of the program, but any tableting operation can be considered a three-component system consisting of the machine, the tools, and the granulation. All things being equal, the active agent and/or excipients of the granulations exert a profound effect on the life of the tools being used. Again, from experiences prior to the initiation of this program, it was our impression that the marked variations in the length of tool life were directly related to the products compressed. Examination of the records of discarded sets having been controlled and used under the conditions of the program indicated our conjec-

ture to be well founded. This can be most dramatically illustrated by the following: glutethimide (Doriden, Ciba) tablets are prepared utilizing $^{15}/_{32}$ in. flat beveled punches. Records indicate that, under the conditions of manufacture and using what will be called formula A, a yield of approximately 25,000,000 tablets per set of punches could be expected on a 35-station machine. For other technical reasons it became necessary to modify the formulation to formula B. Concurrently with this, a new set of punches meeting the same specifications as those previously used were ordered and used exclusively with formula B. The completed report on these tools indicates that 114,000,000 tablets have been compressed on the same machine under the same conditions. This 4.5-fold increase in the life of the tools is a significant change and can be wholly attributed to modification of the granulation components. Although a replacement set is still being used, a check at this date indicates that 80,000,000 tablets have been produced so far from this second set without deleterious effects on the tools. This would suggest that the initial results with the new formulation will be substantiated by the second set of punches now in use.

Relationship of Dies to the Life of Punches.—Our consideration thus far has been mainly devoted to the life of the punch due to the relative costs involved. Inasmuch as one would be prone to examine punches more thoroughly than dies, it should be pointed out that in the majority of our trials, carbide lined dies have been utilized. No data are available as yet on the length of service of controlled sets of these dies as the carbide lining appears impervious to normal wear, with the exception of damage brought about by sudden shocks. It has been noted that in the cases of modified ball, deep concave, and flat beveled punch tips, carbide dies, acting as honing surfaces, have a tendency to wear the edges of the punches rapidly.

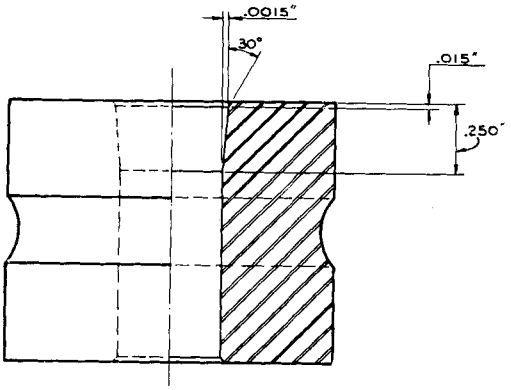


Fig. 8.—Die with tapered bore.

An interesting facet examined is the use of tapered dies. In these dies the bore is not a uniform cylinder but gradually tapers, as shown in Fig. 8, or is gradually tapered completely through the bore. It has been suggested that the tapering would reduce die wall friction during the ejection cycle by virtue of the increase in die diameter anywhere above the compression point. It was felt that if this were true it could be demonstrated by differences between edge

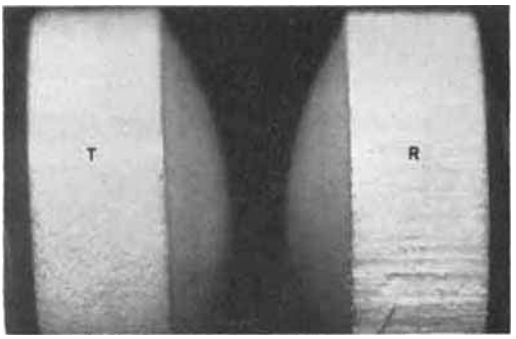


Fig. 9.—Tablets prepared using tapered (T) and regular (R) dies showing edge characteristics.

characteristics of tablets compressed in standard or tapered dies. Figure 9 shows the results of an experiment carried out at Ciba comparing tapered and standard dies. The test substance consisted of granulated magnesium oxide (granulated with sucrose solution) and stearic acid *q.s.* The amount of stearic acid was reduced successively until binding occurred in standard bore dies. At this point, tapered dies were substituted and the same granulation compressed. The different edge characteristics noted upon examination of Fig. 9 showing the regular signified by "R" and the "T" signifying tapering dies, clearly indicated that tapered dies prevented binding. It is fully recognized that this is a qualitative rather than a quantitative analysis, but it does indicate the possible value of the substitution of tapered dies in selected problem products. The reduction of binding by the tapered dies allows the use of lower concentrations of lubricants which, as shown by Strickland, *et al.* (3), generally results in lowering of disintegration time of tablets.

CONCLUSION

The comprehensive integration of pharmaceutical requirements and tool technology under the program has been found to be a valuable stimulus to investigation of tableting problems. It is impossible to contemplate research projects in tableting without a thorough understanding of the influence exerted by the tooling on the resultant data. It is obvious that marked variations of the tooling from established specifications could invalidate conclusions drawn from otherwise closely controlled experiments.

For years pharmaceutical manufacturers have accepted the expense of nonuniform punches and dies, fearing that a program to improve their caliber would be even more costly. It has been found that the ability to introduce new products on schedule, elimination of severe machine damage, and prolonging of tool life more than compensates for the costs involved. Aside from the technical and financial aspects, there is no question that well prepared tooling helps insure uniformity of finished tablets which is, after all, the paramount aim of our science.

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Acceptance Sampling of Finished Pharmaceutical Products

By H. LATHAM BREUNIG and E. P. KING

In this paper we describe some problems inherent in acceptance sampling of finished pharmaceuticals, and provide an expository account of the power and effectiveness of modern statistical methods in the solution of these problems.

STATISTICAL techniques form an integral part of every effective quality control program. Sound statistical procedures for accepting or rejecting batches of finished product based on evidence obtained from samples were given tremendous impetus during World War II through their recognition and application by military procurement agencies. Since that time, these methods have enjoyed a continually expanding circle of usage in the chemical and process industries.

On the other hand, criteria currently used for acceptance sampling of medicinal products, based upon chemical or biological assay, are susceptible to considerable improvement. It would further appear that as this need for improvement becomes recognized and as changes in the sampling procedures are proposed, even these revisions do not incorporate the efficient statistical methods now available.

The sampling procedures of today are probably the result of a natural process of evolution. For many years the majority of active drugs were dispensed in the form of fluid extracts and solutions. The first official sampling procedure to appear in the United States Pharmacopeia (1) pertained to the assay of crude drugs which were to be extracted. Because the liquid extract was recognized as homogeneous, it was natural that attention be shifted from the finished product and focused on accurately estimating the amount of active principle in a shipment of crude drug. It was logical to strive for a "representative sample" of the shipment, ignoring variation from portion to portion within a shipment, because the entire shipment would ultimately be extracted as one unit to form a homogeneous fluid. Hence the procedure called for taking core samples, compositing, quartering, and the like.

However, as time passed, new dosage forms came into prominence. Tablets and filled capsules replaced fluid extracts and solutions. Since this was a gradual process, the sampling procedures for crude drugs were carried over unchanged to the new forms. Unfortunately, however, the problem had changed. Unit-to-unit variation among finished tablets or capsules from the same batch is inherently greater than the variation from one portion of a fluid to another. A thoroughly mixed fluid is homogeneous throughout, but two tablets from the same batch can differ in potency because of composition variation in granulation and because of weight variation among the tablets after compression.

Both physician and patient are concerned with whether or not the amount of drug in a single dose conforms to label claim. Estimating the average amount of drug per unit weight in the parent batch is only a first step. The older sampling methods, aimed at assessing the amount of active ingredient in a crude drug shipment, simply cannot be depended upon to provide information about unit-to-unit differences in tablets and filled capsules. Hence the "representative sample" approach, although adequate for its original purpose, must now make room for techniques which concentrate on individual units of finished product; methods which are concerned not only with average drug content but also with variation in potency from unit to unit. Such a program is given further impetus by the development, in recent years, of analytical methods which permit

Received March 22, 1962, from Eli Lilly and Company, Indianapolis 6, Ind.
Accepted for publication May 10, 1962.
The authors wish to express their thanks to Dr. S. F. Kern and Mr. W. W. Hilty for helpful ideas and discussions during the development of this paper.