PLANT REQUIREMENTS FOR MANUFACTURE OF PHARMACEUTICAL PRODUCTS

TECHNICAL AIDS BRANCH
INTERNATIONAL COOPERATION ADMINISTRATION
Washington, D. C.

FOREWORD

This brochure is one of a series of reports resulting from overseas technical inquiries on factory or commercial establishments, operation, management, and engineering. The report is designed to provide only a general picture of the factors that must be considered in establishing and operating a factory of this type. In most cases, plans for actual installations will require expert engineering and financial advice in order to meet specific local conditions.

Mention of the name of any firm, product, or process in this report is not to be considered a recommendation or an endorsement by the International Cooperation Administration, but merely a citation that is typical in its field.

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TABLE OF CONTENTS

	Page
Introduction	1
General Assumptions	1
Product Specifications	2
Production Capacity	3
Manufacturing Unit	3
Manufacturing Operations	3
Direct Materials	19
Supplies	19
Plant Layout	20
Plant Site	20
Building	20
Power	20
Water	21
Fuel	21
Production Tools and Equipment	22
Other Tools and Equipment	23
Furniture and Fixtures	23
Direct Labor	23
Indirect Labor	24
Depreciation	24
Manufacturing Overhead	25
Manufacturing Costs	25
Fixed Assets	26
Working Capital	26
Capital Requirements	26

	Page
Sales Revenue	27
Recapitulation of Costs, Sales and Profits	27
Budget Control	28
Budget Control Accounts	28
Purchase Requisition	29
Voucher Check	30
Engineers	31
Training	32
Safety	33
Other Considerations	34
Materials and Supplies	34
Market Factors	34
Export Markets	35
Marketing Problems	35
Economic Factors	36
Personnel	36
Laws and Regulations	36
Financial Factors	37
Financial Requirements of the Project	37
Short Term Bank Credits	37
Financial Plan	37
Suppliers of Equipment	38
Bibliography	38
Rotary Press	39
Automatic Tablet Machine	39
Mixer	40
Drying Oven	40

	Page
Punches and Dies	41
Flow Sheet for Tablet Manufacture	42
Flow Sheet for Pill Manufacture	43
Flow Sheet for Capsule Manufacture	44
Suggested Layout for Manufacture of Tablets, Pills and Capsules	45

PHARMACEUTICAL PRODUCTS

INTRODUCTION

The purpose of this report is to present basic information for establishing a plant in a foreign country to produce pharmaceutical products. The term pharmaceutical products includes tablets; pills, coated and uncoated; and capsules.

GENERAL ASSUMPTIONS

In order to make realistic estimates in this report, certain assumptions are made. These are:

1. The costs of the building and general facilities are based on United States prices.

2. Material costs are based on sizes and specifications of materials used in the United States.

3. Labor costs are based on the average for the industry as recently published by the United States Bureau of Labor Statistics.

4. Adequate power and water are available at the plant site.

5. Adequate transportation facilities are available at the plant site.

6. The plant operates eight hours a day, five days a week, fifty weeks a year.

7. No special provision is made for the training of new personnel. It is assumed that learner's rates are paid in such cases.

8. The following items cannot be estimated realistically:

   A. Land value.
   B. Distribution and selling costs.
   C. In-freight and out-freight.
   D. Administrative costs.
   E. Taxes.

   While general estimates will be made of each of these items, for the purpose of completing cost estimates, adjustment should be made in accordance with actual local costs.

   In fact, all cost estimates contained in this report should be adjusted to conform to local conditions.

9. Columns are provided in the tables included in this report to facilitate the conversion of cost figures to conform with local costs.

PRODUCT SPECIFICATIONS

A pharmaceutical plant usually produces a large variety of products in the form of tablets; pills, coated and uncoated; and capsules. These products are packaged in many different ways such as metal or cardboard boxes, glass or plastic bottles and packaged individually in polythylene strips before they are placed in boxes.

Obviously the cost figures on all of the various products and methods of packaging, including materials and labor for each product, cannot

be shown in this report.

For this reason, all cost figures contained in this report are based on the production of one product and one method of packaging in order to supply annual production cost figures. The product used for this purpose is five grain aspirin tablets in glass bottles.

PRODUCTION CAPACITY

The production capacity of this plant is based on a single product as stated above. The annual production of five grain aspirin tablets is 25,000,000.

MANUFACTURING UNIT

The manufacturing unit is one five grain aspirin tablet.

MANUFACTURING OPERATIONS

There are two methods used today for the manufacture of tablets: namely, the Wet Granulating Process and the Slugging Process.

The Wet Granulating Process

Choice of Binder or Granulating Solution

Choosing the proper binder or granulating solution is important in producing a good tablet. A liquid binder is more effective than the

same amount of material in powder form. The selection of a binder is determined by the ingredients which are to be made into tablets. Light ones require a heavy binder, while heavy ones require a lighter binder. Following are listed some binders in order of their ability to act as binders: glucose (corn syrup), gum acacia, gelatin, syrup (cane sugar), starch paste, water, alcohol.

Weighing and Mixing

All of the powdered drugs and chemicals to go into the tablet are weighed. The active ingredient is usually a very small portion of the finished tablet and in order to make a tablet of suitable size, diluents must be added.

After the proper weights of the various powdered chemicals and drugs are combined in a mixer, they are put through a #30 or #40 sieve to help mix thoroughly.

Potent drugs pose a problem all of their own. They must be thoroughly hand triturated with a small portion of diluent and then sifted and resifted to insure thorough mixing.

Granulating

(3)* This step is the basis of all good compressed tablets and therefore is most important.

* See Bibliography, page 38

This is the process whereby all of the ingredients of the tablet are converted into a granular form so that they will flow freely from the hopper into the tablet machine.

The granulation may be done by hand in a pan or in a granulating machine, the binder solution being added slowly, in small quantities, to allow thorough mixing. When finished, the mass should stick together when squeezed in the hand.

Screening Wet Mass

The wet granulation is forced through a #6 or #8 mesh screen either by hand or a power operated granulator, spread on drying pans and put into a circulating air drying cabinet with temperature control and heated to 130° Fahrenheit to 140° Fahrenheit. Larger lumps are broken up to insure quicker drying.

Screening Dry Granulation

This process is carried out as under screening wet mass except a finer screen is used.

Lubrication

Here a substance is added to facilitate the ejection of the finished tablet after compression.

The lubricant, such as a talc or sodium stearate, is screened through a #80 or #100 mesh sieve, sprinkled on small quantities of granulation

at a time, mixed by hand. A tumbling mixer with blades is used for larger quantities.

At this point a disintegrating agent, such as starch, is added solely for the purpose of speeding up the disintegration of the tablet in the stomach.

Compression

The choice of a punch and die with deep concave surfaces for round tablets to be coated is desirable, since a tablet with thin ends is produced and facilitates coating. For uncoated tablets, the regular punch and die for round tablets is desired.

Weigh out sufficient granulation for one tablet, fill die cavity of machine and make proper adjustments for weight.

It is advisable to check weight and thickness of tablets at frequent intervals to insure a uniform product.

Granulating by the Slugging Method (2)*

The cost figures shown in this report are based on this method. This method has many advantages over the Wet Method of Granulation, the most important of which are: (1) less machinery and floor space required; (2) eliminates wet mixing and simplifies combining of incompatible materials; (3) fewer number of steps prior to compression.

* See Bibliography, page 38

Weighing Ingredients

All ingredients should be weighed carefully and be in powder or fine granule form.

Sifting, Mixing and Lubricating

All ingredients, plus lubricant, are mixed and sifted thoroughly in a sifter and mixer, and then screened through a #30 or #40 mesh bolting cloth screen.

Slugging

The mixed powders are compressed into slugs. Their size is dependent on the size of the tablet machine.

Reducing Slugs to Granulation

The slugs are broken down by forcing through a hand screen or a granulator, depending on the size of the batch. The screen size for granulation depends on the size of tablet to be made from granulation.

Compressing into Tablets

Same as for wet granulation.

As experience increases and demand warrants, the more complicated tablets may be manufactured.

Tablet Coating Process (4)*

Tablet coating being a difficult job at best, several precautions should be observed in preparing tablets for coating. Many tablets, for example aspirin tablets, are not coated. The following information is for coated tablets only.

(1) Tablets should be made with deep concave punches, as large in diameter as the tablet will allow. The thinner the tablet edge, the less time is required for coating.

(2) A good firm tablet is necessary.

(3) Tablets should be clean and free from dust or broken tablets. Use a #2, #3, or #4 mesh sieve to accomplish this.

(4) Hygroscopic tablets should first be coated with several coats of certified confectioners shellac. It is advisable to dry these shellac coated tablets overnight in an atmospheric or vacuum dryer.

(5) Tablets must be at room temperature before subcoating, never below 70° Fahrenheit.

Sub-Coating

This process builds up the tablets with several layers of a thick

* See Bibliography, page 38

gelatin-syrup mixture aided by a dusting powder.

The tablets are placed in a rotating coating kettle, and the proper amount of warm (150° Fahrenheit) sub-coating is applied. Stir by hand, and add more sub-coating if necessary. The kettle is kept rotating until the tablets become tacky, and begin to roll free. The dusting powder is now sprinkled by hand over the turning tablets. Rotation is continued for five minutes, and then the warm air is turned on until the tablets are thoroughly dry.

When the tablets are dry, the process is repeated until the corners are well covered, and until the tablets are well rounded and in proper proportions.

In the process of making "chocolate coated tablets" or "chocolate colored tablets," the procedure is the same except that the "chocolate" or "chocolate coloring" is used in place of the white dusting powder. Coating and dusting powder formulas are on pages 17 and 18.

Syrup Coating (Smoothing)

The pan containing the tablets is set in motion and the proper amount of hot white under-coating is added. Stir by hand, rotating the tablets until they begin to dry. At this point only, may the warm air be turned on.

Test tablets for dryness. If dry, add subsequent coats of the white

syrup until tablets are smooth and without imperfection.

Where tablets are to be colored, a plain coating syrup is used instead of the white coating syrup. The coating process is the same except that less syrup is used. (See formulas, pages 17 and 18)

Coloring and Finishing

About six or seven coats of the plain coating syrup are necessary, drying each coat thoroughly. These coats should be dried without the aid of heat, especially the last two coats. The final or finishing coat is now given.

The syrup is applied as before and the tablets are allowed to rotate until they are evenly covered and just begin to dry. The pan is stopped, the pan opening covered with cheesecloth and the pan rotated 1/4 turn every five or ten minutes for the first hour, then every fifteen minutes for the next hour. The tablets are emptied onto trays with canvas bottoms, covered, and let dry at least two hours, but preferably overnight.

If the tablets are to be colored, the procedure is somewhat the same except that colored syrups of varying intensity would be employed, starting with light colored syrups and gradually increasing the intensity until the desired color is reached. A syrup consisting of one part colored syrup to three parts plain syrup may be used for the first six to eight coats. For the next six or seven coats, a mixture

of one part colored syrup to two parts plain syrup may be used.

When the color becomes fairly uniform, use a colored syrup in the ratio of one part colored syrup to one part plain syrup. For intense colors, use only colored syrup.

When the desired color is obtained, two coats of syrup (one part colored syrup to three parts plain syrup) should be given without the aid of heat. These last two coats should be applied as stated in "Coloring and Finishing" (page 10).

Polishing

The tablets are rotated in a canvas polishing kettle while the proper amount of hot polishing solution is added. (Formula on page 18) Rotation is continued until all the solvent is evaporated. One-half the original amount of polishing solution is then added, and rotation is resumed until the solvent has evaporated. Repeat this procedure, using one-quarter of the original amount of polishing solution. Do not rotate too long since chipping may result. Use no air during the polishing process.

Enteric Coating

There are a number of ways to enteric coat tablets. However, this report will deal with only one, the use of confectioners shellac. It has been proven over the years to be the most satisfactory.

It is recommended that two sub-coats, as previously described, be applied before the enteric coat is applied.

The method of enteric coating is comparatively simple. The shellac solution (formula on page 17) is added, spread by hand and the tablets rotated for several minutes. When they begin to stick to the back of the pan, a small amount of talc should be sprinkled on and mixed well. When rolling free, cool air may be turned on for a few minutes. Warm air may then be used to hasten drying, but should be followed by cool air since the next shellac coat should not be applied until the tablets are cool. It is recommended that seven or eight coats be applied in such manner.

The process for syrup coating, coloring and finishing, and polishing of enteric coated tablets is the same as for regularly coated tablets.

For Tropical Climates

A sugarless coating must be used since sugar is hygroscopic and would not stand up very long under conditions of excessive humidity. It is necessary to eliminate sugar as much as possible, especially from the outer coating. Where plain syrup and colored syrup were previously used, gelatin syrup is now used.

The sub-coating procedure is the same, but a heavy gelatin syrup is used instead of a sugar syrup.

A different dusting powder is used also, as follows:

Calcium carbonate, precipitated	77 pounds
Kaolin	12 pounds
Starch	16 pounds

Instead of smoothing with a plain syrup, as used for normal sugar coating, a gelatin syrup is used, as follows:

Granulated gelatin	8 ounces
Granulated acacia	4 ounces
Water	1 gallon

Pill Manufacture (5,6)*

Today the use and manufacture of pills has largely been replaced by compressed tablets and capsules. The preparation and coating of pills is very similar to that of tablet manufacture.

Preparation of Pill Mass

Among the most important factors influencing the pill mass, is the selection of a suitable excipient and the thorough mixing and kneading of the pill mass.

Mechanical mixers are needed to achieve the proper mixing and kneading of the pill mass. The active ingredients, diluents, and a small amount of excipient are thoroughly mixed. If the consistency is not correct, small amounts of excipient are added with thorough mixing until the

* See Bibliography, page 38

proper consistency is obtained. The mass is then placed in a kneading machine which consists of two steel rollers revolving in opposite directions, and at slightly different speeds. This machine is geared in such a manner that the direction of rotation can be reversed. The rollers may be hollow to admit steam for heating. The mass is passed repeatedly through this machine until thoroughly kneaded.

There are three essential requirements of a pill mass:

(a) Adhesiveness: The mass must be sufficiently adhesive to retain its shape, and yet soft enough to be worked into the desired form. This is accomplished by the use of the proper excipient.

(b) Firmness: This can be accomplished by the use of the right amount of the proper excipient. If too much is used, the pills will subsequently run together.

(c) Plasticity: This condition is dependent on the previous two requirements. Plasticity can usually be secured by properly working or kneading the mass.

Shaping and Cutting

The pill mass is now ready for the pill machines. There are two in number. The first is called the ball-making machine which takes the mass and delivers it, covered with dusting powder, in the shape of balls into the hopper of the second machine. In their course through

the second machine, the balls are elongated into rod-shaped pieces, which subsequently drop on revolving cutters where they are divided into pieces of uniform size and weight. These pieces drop into a chute, and are carried to the entrance of the pill-rounding belts where they are thoroughly rolled and shaped. From here, the pills go into a separator whereby the perfect pills are separated from the tailings.

If the pills are to be anything but round, they are fed into an attachment on the second machine which shapes them into the desired form.

Pill Coating (6)*

The process for coating pills is the same as for coating tablets with two exceptions.

(a) The sugar coating is made up of six parts milk sugar, one part starch and one part powdered acacia. It is applied in the dry state because the pills are somewhat damp, and also because the sugar mixture subsequently melts in the steam jacketed coating kettle. This precludes the need of a liquid sugar coating.

(b) In making chocolate coated pills, the use of a dry cocoa mixture does not produce a smooth pill. A strong syrup of the chocolate mixture is made and poured, while hot, over the pills in a coating pan. The warm air evaporates the water, and the constant rotation distributes the coating evenly. Several applications are necessary

* See Bibliography, page 38

to produce a sufficient thickness of coating. An under-coat containing iron oxide protects the pills from solvent action by the warm syrup.

Enteric coating of pills follows the same procedure as with compressed tablets.

Capsule Manufacture (5)*

Three forms of capsules are in use today. Two, the hard gelatin capsules and the soft gelatin capsules are the most common. The third, pearls, will not be dealt with in this report since they perform the same function as the soft gelatin capsules.

Hard Gelatin Capsules

The manufacture of empty hard gelatin capsules requires very complicated and expensive machinery. It is recommended that this type of capsule be purchased from present manufacturers.

Hand filling of capsules is a tedious and laborious job, and has been largely supplanted by semi-automatic and automatic machines. The semi-automatic machines only fill the bottom of the capsules. The caps must be removed and replaced manually. The completely automatic machines remove the caps, fill the base, replace the caps and clean the outside of the capsules.

* See Bibliography, page 38

The preparation of the mixture to be used for filling the hard gelatin capsules requires nothing more than thorough mixing of the ingredients, plus the possible addition of a diluent to make a suitable size capsule. Some incompatibilities may possibly be encountered, but these can usually be resolved with little or no trouble.

Soft Elastic Capsules

The smallest possible operation in the manufacture of soft elastic capsules is the plate process. This consists of two identical plates with matching depressions. A warm sheet of gelatin is placed on one plate and the liquid poured upon it. A second sheet of gelatin is carefully placed over this, and is then covered with the top plate of the mold. Pressure is applied to form the capsules which are then washed with a solvent to remove traces of oil.

For large production of soft elastic capsules, a rotary die machine is used. Such machines will produce upwards of 60,000 capsules per hour, but they are very complicated and require highly skilled operators. Some of these machines may be purchased outright, while others are only obtainable by leasing from the manufacturer.

Sub-Coating Formulas

Shellac Solution

Pharmaceutical glaze (arsenic-free shellac)	6 pounds
Denatured absolute alcohol (3A)	1 gallon

(Mix, and shake well before applying)

Sub-Coating Dusting Powder

Powdered precipitated calcium carbonate	48 pounds
Tapioca dextrin	25 pounds
Powdered talcum	2 pounds
Powdered sugar	25 pounds

Brown Sub-Coating Dusting Powder (Chocolate Color)

Powdered umber	8 ounces
Powdered iron oxide	4 ounces
Powdered precipitated calcium carbonate	24 pounds
Talc	2 pounds

Sub-Coating Syrup

Granular gelatin	3-3/4 pounds
Granular gum acacia	9-3/8 pounds
Granulated sugar	50 pounds
Water	6 gallons

Syrup Coating Formulas

White Under-Coating or Glossing Syrup (White Tablets Only)

Granulated sugar	8 pounds
Powdered corn starch	6 ounces
Powdered talc (white)	2 ounces
Water	4 pints

Dissolve sugar in three pints of water. Make a paste of the other ingredients, and add to the sugar solution. Bring to the boiling point, strain through cheesecloth, and add sufficient water to make one gallon paste. Keep at 140° Fahrenheit to 150° Fahrenheit while in use.

Plain Coating Syrup (For Smoothing Tablets to be Colored)

Coarse granulated sugar (brown)	15 pounds
Water	1 gallon

Mix sugar with previously heated water. Bring to a boil, and boil two minutes. Strain through muslin.

DIRECT MATERIALS

Item	Number Required	Unit Cost	Annual Cost Estimated	Annual Cost Actual
Acetylsalicylic acid	17,350 pounds	$ .561	$ 9,730	_____
Corn starch	1,735 pounds	.069	120	_____
Talc	1 ton	100	100	_____
Surgical cotton			50	_____
Labeled bottles	250,000	.03	7,500	_____
Cartons	2,500	.20	500	_____
Total			$ 18,000	_____

SUPPLIES

Item	Annual Cost Estimated	Annual Cost Actual
Lubricants and hand tools	$ 100	_____
Maintenance and spare parts	500	_____
Office supplies	200	_____
Total	$ 800	_____

PLANT LAYOUT

A suggested plant layout for the manufacture of tablets, pills, and capsules together with the work flow for each product is shown on the last four pages of this report.

PLANT SITE

In order to provide for future expansion a plant site of about 10,000 square feet will be required.

The estimated cost of this plant site is $1,000.

BUILDING

A one-story building 40 feet by 75 feet or 3,000 square feet is required for a pharmaceutical plant of this capacity. Any suitable local construction materials may be used.

The cost of the building is estimated at $12,000.

POWER

The connected load requirements amount to 18 horsepower. Based on an 80 percent load factor, the annual cost of power is estimated at $200.

WATER

The annual cost of water, including a small amount for production and the requirements for sanitary purposes, is estimated at $100.

FUEL

The annual cost of fuel for heating the building, sanitation purposes, and a small amount for production, is [illegible]mated at $300

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PRODUCTION TOOLS AND EQUIPMENT

The following items will be required for the processing of tablets, pills, and capsules.

Description	Number Required	Unit Cost	Cost Estimated	Cost Actual
Scales	1	$ 25	$ 25	_____
Scales	1	50	50	_____
Scales	1	225	225	_____
Mixer	1	3,600	3,600	_____
Tablet machine	1	750	750	_____
Tablet machine	1	2,300	2,300	_____
Tablet machine	1	4,100	4,100	_____
Drying oven	1	1,400	1,400	_____
Granulator	1	2,700	2,700	_____
Water still	1	350	350	_____
Coating and polishing machine	1	2,500	2,500	_____
Strip packaging machine	1	10,800	10,800	_____
Semi-automatic machine for hand capsules	1	4,000	4,000	_____
Press plates for soft capsules	2 sets	500	1,000	_____
Punches and dies	18 sets		2,000	_____
Tablet hardness testers	2	50	100	_____
Manual counters	20	5	100	_____
Total			$ 36,000	_____

OTHER TOOLS AND EQUIPMENT

Description	Cost Estimated	Cost Actual
Hand truck, tables, and bins	$ 475	_____
Air conditioner unit	500	_____
Gas burner	25	_____
Total	$ 1,000	_____

FURNITURE AND FIXTURES

Item	Number Required	Unit Cost	Cost Estimated	Cost Actual
Tables and chairs	3	$ 75	$ 225	_____
File cabinets	3	75	225	_____
Typewriter	1	150	150	_____
Adding machine	1	100	100	_____
Total			$ 700	_____

DIRECT LABOR

Occupation	Number Required	Hourly Rate	Annual Cost Estimated	Annual Cost Actual
Machine operator	2	$2.00	$ 8,000	_____
Helper	1	1.50	3,000	_____
Packaging	2	1.50	6,000	_____
Total	5		$ 17,000	_____

INDIRECT LABOR

Occupation	Number Required	Annual Cost Estimated	Annual Cost Actual
Manager (pharmacist)	1	$ 10,000	_____
Bookkeeper-clerk	1	5,000	_____
Maintenance	1	4,000	_____
Total	3	$ 19,000	_____

DEPRECIATION

Description	Estimated Cost	Years Life	Annual Cost Estimated	Annual Cost Actual
Building	$ 12,000	20	$ 600	_____
Production tools and equipment	36,000	10	3,600	_____
Other tools and equipment	1,000	10	100	_____
Furniture and fixtures	700	10	70	_____
Total			$ 4,370	_____

MANUFACTURING OVERHEAD

Item	Annual Cost Estimated	Annual Cost Actual
Depreciation	$ 4,370	_____
Indirect labor	19,000	_____
Power	200	_____
Water	100	_____
Fuel	300	_____
Supplies	800	_____
Total	$ 24,770	_____

MANUFACTURING COSTS

Item	Annual Cost Estimated	Annual Cost Actual
Direct materials	$ 18,000	_____
Direct labor	17,000	_____
Manufacturing overhead	24,770	_____
Total	$ 59,770	_____

FIXED ASSETS

Item	Cost Estimated	Cost Actual
Land	$ 1,000	_____
Building	12,000	_____
Production tools and equipment	36,000	_____
Other tools and equipment	1,000	_____
Furniture and fixtures	700	_____
Total	$ 50,700	_____

WORKING CAPITAL

Item		Cost Estimated	Cost Actual
Direct materials	30 days	$ 1,500	_____
Direct labor	30 days	1,400	_____
Manufacturing overhead	30 days	2,100	_____
Reserve for sales collections	30 days	7,500	_____
Total		$ 12,500	_____

CAPITAL REQUIREMENTS

Item	Cost Estimated	Cost Actual
Fixed assets	$ 50,700	_____
Working capital	12,500	_____
Total	$ 63,200	_____

SALES REVENUE

The annual production capacity of this plant is 25,000,000 five-grain aspirin tablets.

The current average sales price of these tablets is $3.60 per 1,000 tablets.

Based on these figures the annual sales revenue would amount to $90,000.

RECAPITULATION OF COSTS, SALES AND PROFITS

Item	Estimated Cost		Actual Cost
Direct materials	$ 18,000		_____
Direct labor	17,000		_____
Manufacturing overhead	24,770		_____
Total manufacturing cost		$ 59,770	_____
Interest on loans	$ 1,900		_____
Insurance	200		_____
Legal	600		_____
Auditing	1,200		_____
Unforeseen expense	2,230		_____
Total administrative costs		$ 6,130	_____
Sales commissions		5,000	_____
Travel, bad debts, discounts and allowances, freight-out		1,000	_____
Profit before taxes		18,100	_____
Total annual gross sales		$ 90,000	_____

BUDGET CONTROL:

A requisition form designed to provide accurate records of procurement and indicate the purpose of procurement with the least amount of time and effort is shown on the following page.

This form has an account number for each type of the various expenditures which the manager will review in detail, monthly or oftener, in order to control his expenses. Some items, such as power and water, are usually under contract and are easily checked by reference to monthly bills. For simplification, items (marked with an asterisk below) are omitted from the purchase requisition. Variations in the labor costs are easily reviewed by examination of the payroll vouchers. The simplified type of control thus provided makes certain that the manager can control expenditures promptly.

Following the requisition form, a sample voucher check is shown. Voucher checks should be used for the payment of all expenditures and the appropriate book account number placed on each voucher.

At the end of each month the manager will receive a statement of all expenditures broken down by budget accounts. If the expenditures exceed the budgeted monthly allowances of any of the accounts, the bookkeeper will furnish the manager with a break-down of all expenditures relative to the budgeted accounts exceeded. All these supporting data can be secured by reference to the purchase requisitions and the check vouchers. This reference will enable the manager to determine what caused the over-expenditure and take corrective action.

If at any time during each month it becomes apparent that expenditures will exceed any of the budget accounts, the bookkeeper will bring this to the attention of the manager for his information and action.

BUDGET CONTROL ACCOUNTS:

Account Number		Monthly Expense	Monthly Budget	Annual Budget	Actual
10	Administrative	$_____	$ 325	$ 3,900	$_____
20	Sales	_____	500	6,000	_____
30	Direct Materials	_____	1,500	18,000	_____
40	Supplies	_____	66	800	_____
51	Power*	_____	16	200	_____
52	Water*	_____	8	100	_____
53	Fuel	_____	25	300	_____
60	Unforeseen Expense (Reserve Account)	_____	185	2,230	_____
71	Direct Labor*	_____	1,416	17,000	_____
72	Indirect Labor*	_____	1,583	19,000	_____
80	Depreciation (Reserve Account)	_____	364	4,370	_____

PURCHASE REQUISITION	COMPANY NAME	DATE

- ☐ 10 ADMINISTRATION
- ☐ 20 SALES
- ☐ 30 MATERIALS
- ☐ 40 SUPPLIES
- ☐ 50 UTILITIES
- ☐ 60 UNFORESEEN EXPENSE

INDICATE BELOW THE USE OF MATERIALS

- ☐ DIRECT MATERIALS
- ☐ MAINTENANCE MATERIALS
- ☐ MAINTENANCE SERVICES
- ☐ OPERATING SUPPLIES

	PLEASE ORDER THESE MATERIALS OR SERVICES	DELIVERY WANTED	
QUANTITY	DESCRIPTION	UNIT	TOTAL

QUOTES FROM		REQUISITIONED BY	
QUOTES FROM		APPROVED BY	
QUOTES FROM		ORDER NO.	ORDER DATE

R. W. MITCHELL MANUFACTURING COMPANY

1422 BOSWORTH STREET, S. E.

65-22
514

ANYWHERE, U. S. A._____19____ No. 10000

PAY _____ DOLLARS $ _____

TO THE ORDER OF

R. W. MITCHELL MANUFACTURING COMPANY

TO FIRST NATIONAL BANK
ANYWHERE, U. S. A.

BY SAMPLE CHECK

VICE PRESIDENT

ACCOUNT NUMBER

Sample voucher check to be used for the payment of all expenditures in connection with Budget Control.

ENGINEERS:

The services of professional engineers are desirable in the design of this plant, even though the proposed plant is small.

A correct design is one which provides the greatest economy in the investment of funds and establishes the basis of operation that will be most profitable in the beginning and will also be capable of expansion without expensive alteration.

The addresses of professional engineers who specialize in industrial design, some of whom may be willing to undertake such work on low cost projects overseas, can be secured by reference to the published cards in various engineering magazines. They may also be reached through their national organizations, one of which is the

National Society of Professional Engineers
2029 K Street, Northwest,
Washington 6, D. C.

Manufacturers of industrial equipment employ engineers familiar with the design and installation of their specialized products. These manufacturers are usually willing to give prospective customers the benefit of technical advice by those engineers in determining the suitability of their equipment in any proposed project.

The equipment manufacturers also know, and can recommend, professional engineers in private practice, who are willing and able to provide appropriate consulting services.

TRAINING:

Manufacturing an inferior quality of product during the training period could create sales resistance that might be difficult to cope with later. To avoid such possibilities, the quality of the product should be maintained at all times, including the training period.

In some areas skilled operators may be available locally. In other areas all the operators may have to be trained.

If skilled operators are not available, adequate training would be assured by using one or more of the following methods:

A. If the plant is designed and installed by a competent engineering firm, the contract should be negotiated, if possible, on a turn-key basis. On this basis the contractor agrees to operate the plant and produce the quality and quantity of the product stated in the contract for an agreed period of time. Such a contract would assure adequate personnel training, since full quantity and quality could not be produced with an untrained organization.

B. The engineering firm that designs and installs the plant can usually make training arrangements to have key personnel placed, for training purposes, in a foreign industry that produces the same type of product. This would provide training for the key personnel while the plant is being installed.

C. If neither of the above methods is possible, then qualified and experienced individuals should be employed for the key positions, either permanently or temporarily, to perform the key operations and assist in training the organization, even if they must be secured outside the country.

D. The manager should have years of successful experience in this type of business and be fully qualified in all phases of management, including the training of employees.

SAFETY:

There is always danger of accident and injury in any industrial plant. Because of this, the manager should take specific action to bring to the attention of each employee the importance of safety precautions and intelligent first aid.

Practically all machines have safety appliances, and the manager should see that these are in good working condition and that the operators are making full use of them.

In addition to constant watchfulness to make sure that all practicable safety precautions are taken, first aid supplies should be readily available. One complete first aid kit should be maintained near the manager's office, and others at appropriate places throughout the plant. Some of the employees should be trained to provide first aid service.

The use of accident posters in the plant have proved to be of value in reducing accidents. It is recommended that such posters be used, and that some direct special action be taken by the manager, at least once each month, to bring to the attention of all personnel the importance of safety precautions.

A fire brigade should be established and each member trained as to his responsibility in case of fire. Fire drills should be conducted periodically.

It is recommended that the employees be encouraged to offer suggestions or recommendations relative to prevention of accidents, removal of fire hazards and maintaining general interest in all safety factors.

OTHER CONSIDERATIONS

There are other important subjects, shown below, that should be fully investigated and considered. Information on these subjects is usually available from such sources as banks, government agencies, exporters and importers, wholesalers, retailers, transportation companies and manufacturers.

MATERIALS AND SUPPLIES

1. Are all materials and supplies available locally?
2. Is the local material market competitive?
3. Is satisfactory delivery of local materials assured at reasonable prices?
4. What materials and supplies must be imported?
5. Are they available in world markets at competitive prices?
6. Would prompt delivery of imported materials and supplies be assured so that large inventories would not be required?

MARKET FACTORS

1. Is there already a demand for the product?
   - A. Who are the principal consumers?
   - B. Who are possible new consumers?

2. How is demand for the product now satisfied?
   - A. By local production? If so, what is the volume of annual production?
   - B. What percentage of consumption is filled by local production?
   - C. By imports? If so, what is the volume of annual imports?
   - D. What percentage of consumption is met by imports?
   - E. From what areas are imports derived?

3. What is the estimated annual increase in local consumption over the next five years?
   - A. How were such estimates made?
   - B. By reference to official figures on population growth, family budgets, imports, etc.?
   - C. By consultation with trade or industry, ministries, associations, bankers, commercial houses, wholesalers, retailers, industrial consumers, etc.?

4. If the product is already being manufactured, can the existing and estimated future local market absorb production of the new plant without price-cutting or other dislocations?

5. Would the estimated sales price and quality of the new product make it competitive with an imported equivalent?
   A. After adjusting cost to local conditions, is the estimated sales price of the product so high that tariff protection is necessary to protect it from imports?

EXPORT MARKETS:

1. Could the product compete in export markets on the basis of price, quality and dependability of supply?
2. Can export markets for the product be developed?
3. If so, in what areas and in what annual volume?
4. What procedures would be necessary to develop export markets?
5. What would it cost?

MARKETING PROBLEMS:

1. In calculating costs of the product, has adequate allowance been made for the expense of a sales department, advertising and promotion that might be required?

2. Do consumer prejudices against locally manufactured products exist?
   A. If so, why?
   B. Would they apply to the new product?
   C. If so, how could they be overcome and what would it cost to do so?

3. Do marketing and distribution facilities for the product exist?
   A. If not, can they be set up?
   B. What would it cost to do so?

4. Will the product be sold to:
   A. Wholesalers?
   B. Retailers?
   C. Direct to consumer?
   D. Other industries?
   E. Government?

ECONOMIC FACTORS:

1. How much foreign exchange (and in what currency) is required to import machinery, equipment and supplies:
   A. How much foreign exchange (and in what currency) is required for annual interest payments and amortization of any loans contracted to import machinery and equipment, or for payment of royalties and technical services?
   B. How much foreign exchange (and in what currency) is required for annual import of raw materials and supplies?
   C. What are estimated annual foreign exchange earnings and in what currencies?
   D. Has careful consideration been given to the possibility of depreciation in the foreign exchange value of the local currency?
   E. Has careful consideration been given to the possibility of import controls, or restrictions on availabilities of foreign exchange necessary to operate the business?
   F. What benefits would the new business bring to the economy in the use of local raw materials: in employment and in technology?
   G. Do dependable facilities exist for transportation, power, fuel, water and sewage?
      (1) If not, can existing deficiencies be eliminated satisfactorily?
      (2) What would be the cost to do so?

PERSONNEL:

1. Is there an adequate labor supply near the plant location?
   A. If not, how can the problem be solved?

2. Can the problem of training competent management and supervisory personnel be solved?
   A. Also, the training of skilled labor?
   B. Is technical advice available in the locality?
   C. If not, where can it be obtained and what will it cost?

LAWS AND REGULATIONS:

1. Do existing labor laws, government regulations, laws and taxes favor establishment of new business?
   A. If not, can existing obstacles be removed?
   B. If so, how and when?

FINANCIAL FACTORS:

1. Technical advice on selection of machinery and equipment.
   A. In selecting the machinery and equipment for the new plant, have reputable and competent engineers and technicians been consulted?
   B. Have they been asked for advice on the most suitable types of machinery and equipment for the process and locality?
   C. Have they carefully compared costs of various suppliers?
   D. Credit terms offered purchasers?

FINANCIAL REQUIREMENTS OF THE PROJECT:

1. In estimating the cost of the project, has careful consideration been given to:
   A. The effect on costs of delays in construction schedules?
   B. In delivery and installation of machinery and equipment?
   C. In import of essential raw materials and supplies?

2. In calculating cash flow and working capital requirements, has careful consideration been given to:
   A. Maintaining adequate inventories of raw materials?
   B. Supplies and spare parts?
   C. Seasonal fluctuations in the business?
   D. The time required to liquidate credit sales to customers and bad debts?
   E. The period necessary to get the plant into production?
   F. Cash required to amortize its principle loans?

3. If the economy is in a period of inflation, has full allowance been made for the influence of rising prices and wages on the cost of the project and on working capital requirements?

SHORT TERM BANK CREDITS:

1. Has it been possible to make arrangements with local banks to finance short-time working capital requirements of the business?

FINANCIAL PLAN:

1. Has a definite plan to finance the project been worked out?
   A. Is sufficient capital available locally?
   B. If not, what is the plan to obtain the required capital?

SUPPLIERS OF EQUIPMENT

The two major suppliers of manufacturing and accessory equipment are the F. J. Stokes Machine Company, Philadelphia, Pennsylvania; and the Arthur J. Colton Company, Detroit, Michigan.

Highly specialized equipment such as the rotary punch and die machine for filling elastic capsules, and the fully automatic machine for filling hard gelatin capsules may be obtained, usually on a rental basis, from the Norton Company (Capsule Division), Worcester, Massachusetts; Eli Lilly and Company, Indianapolis, Indiana; Parke, Davis and Company, Detroit, Michigan. Other manufacturers of specialized equipment include the Cowley Pharmaceutical Company, Auburn, Massachusetts; Scherer Corporation, Detroit, Michigan; and the Strong - Cobb Company, Columbus, Ohio.

Screens, balances, graduates, mortars and other laboratory style equipment may be obtained from laboratory supply houses such as: Fisher Scientific Company, Pittsburgh, Pennsylvania; Arthur H. Thomas Company, Philadelphia, Pennsylvania; Chicago Apparatus Company, Chicago, Illinois; Will Corporation, Baltimore, Maryland.

BIBLIOGRAPHY

1. Drug and Cosmetic Industry, Vol. 78 (No. 1), page 38 (1956). Drug Markets Inc., New York, New York.

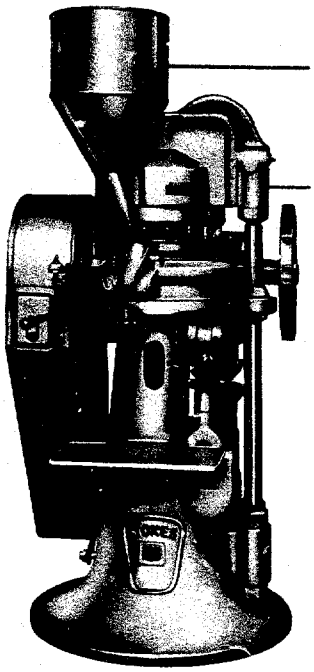
2. "Manufacture of Compressed Tablets" - J. A. Silver and R. Clarkson. F. J. Stokes Machine Company, Philadelphia, Pennsylvania.

3. Journal American Pharmaceutical Association, Scientific Edition: Vol. 44, page 291 (1955). American Pharmaceutical Association, Washington, D. C.

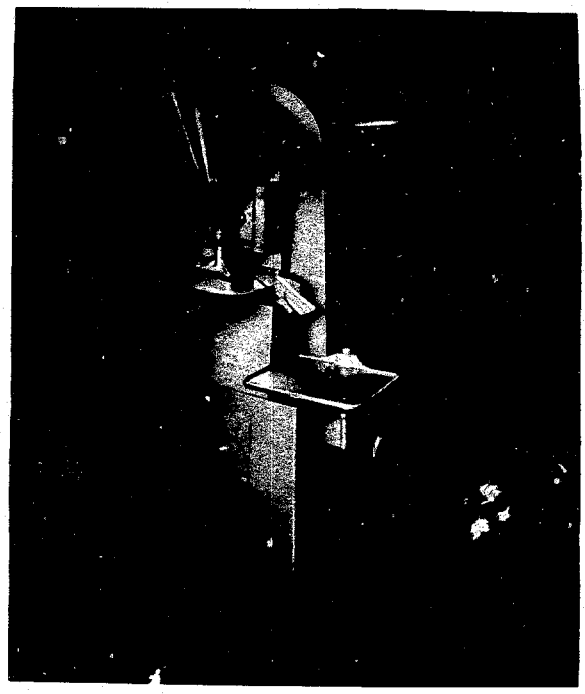
4. "The Art of Coating Tablets" - T. H. Rowell. Baudette, Minnesota (1949).

5. "Remington's Practice of Pharmacy" - E. W. Martin and E. F. Cook (Editors), 11th Edition (1956). Mack Publishing Company, Easton, Pennsylvania.

6. Scovill's "The Art of Compounding" - J. L. Powers and G. E. Grossen (Editors), 7th Edition. The Blakiston Company, Philadelphia, Pennsylvania.

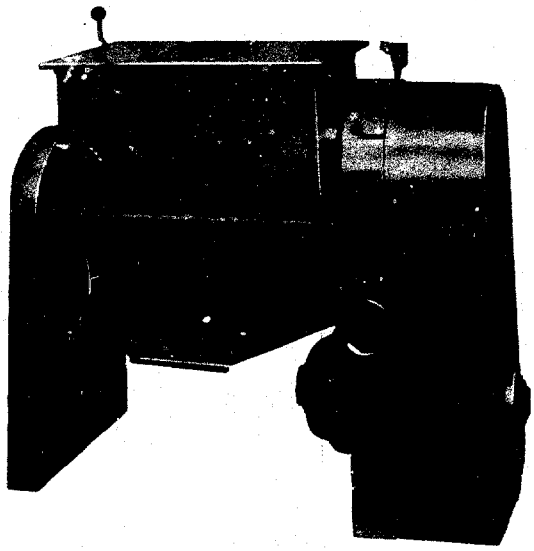


Sixteen-station automatic rotary press (tablet machine) for slugging or for final tabletting. Maximum tablet diameter 15/16 inch. 190 to 350 tablets per minute capacity.

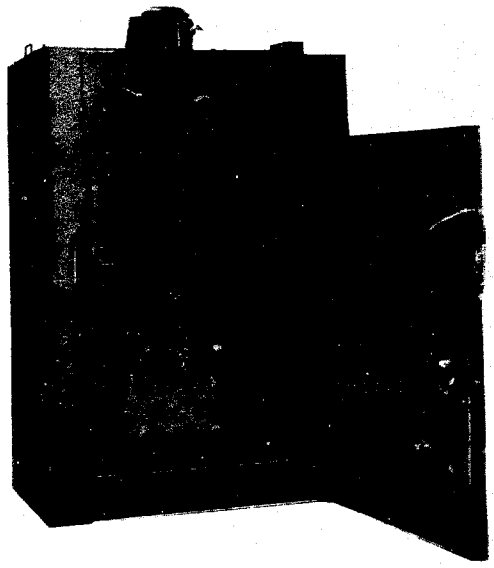


Automa ic tablet machine. Maximum table diameter 3/4 inch. 55 to 105 tablets per minute capacity.

Courtesy:
F. J. Stokes Corporation
Philadelphia, Pennsylvania

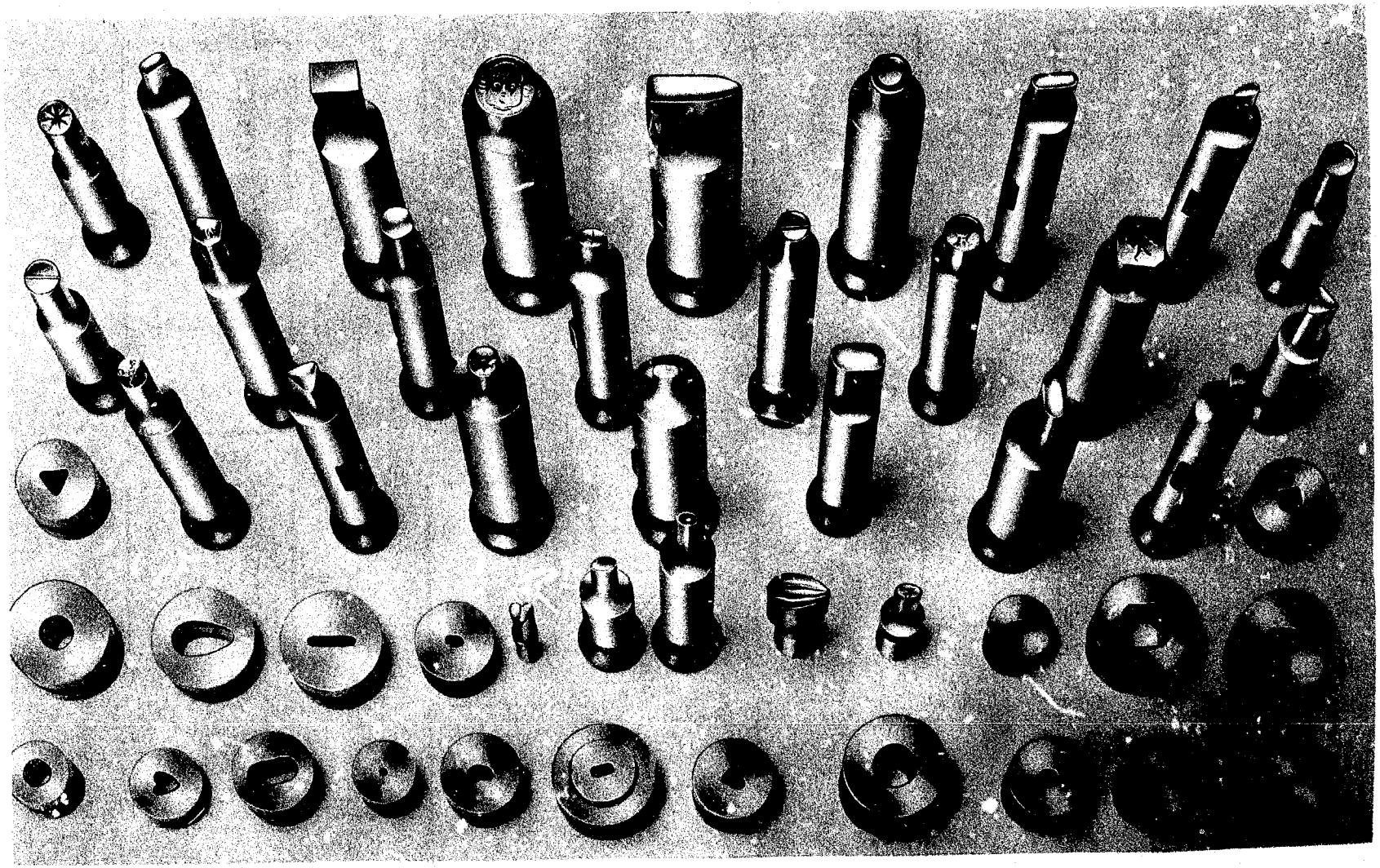


Mixer for wet mixing or blending of dry materials.



Drying oven for drying of all materials.

Courtesy:
F. J. Stokes Corporation
Philadelphia, Pennsylvania

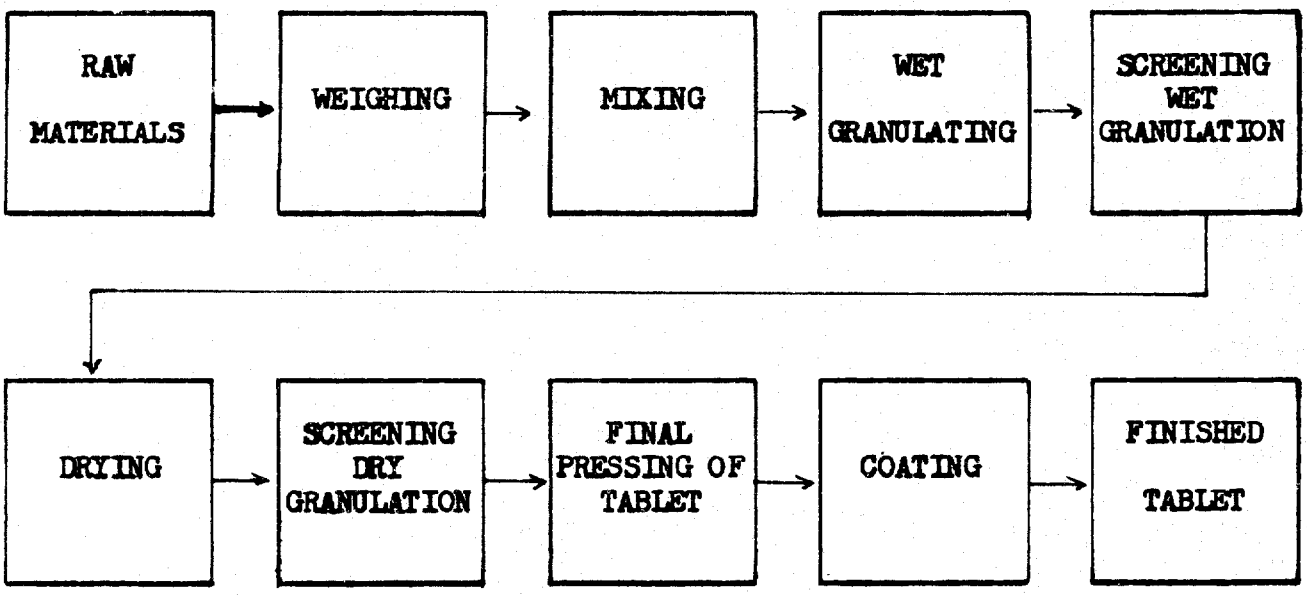


Punches and dies used in the production of tablets and pills.

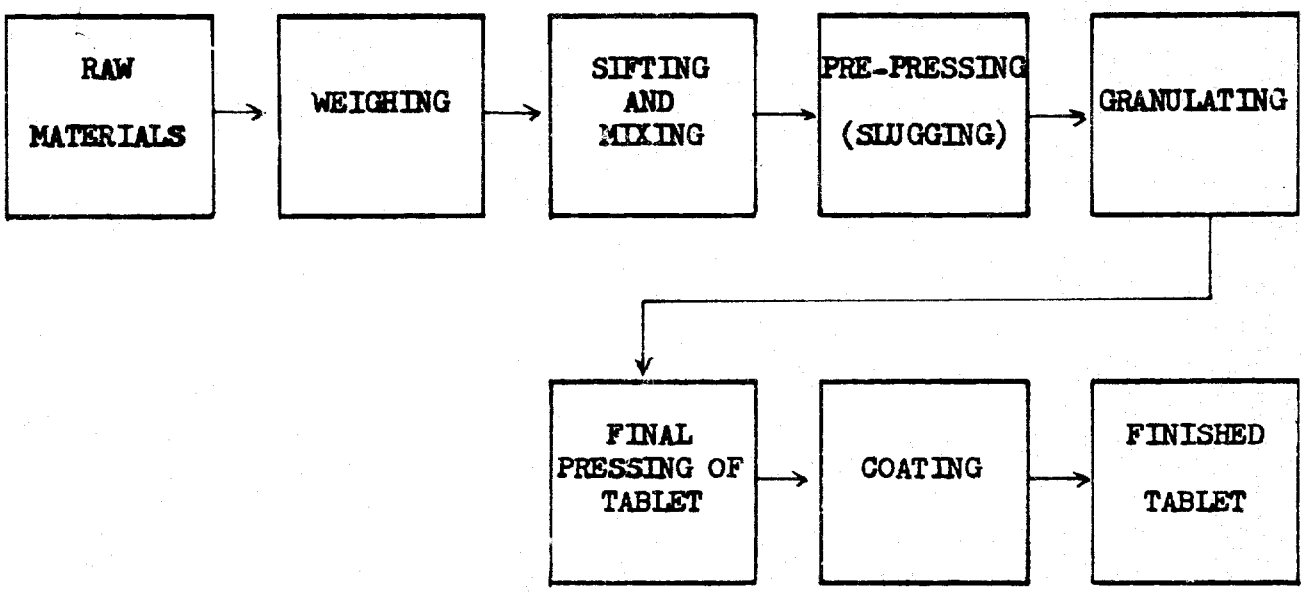
Courtesy:
F. J. Stokes Corporation
Philadelphia, Pennsylvania

FLOW SHEET FOR TABLET MANUFACTURE

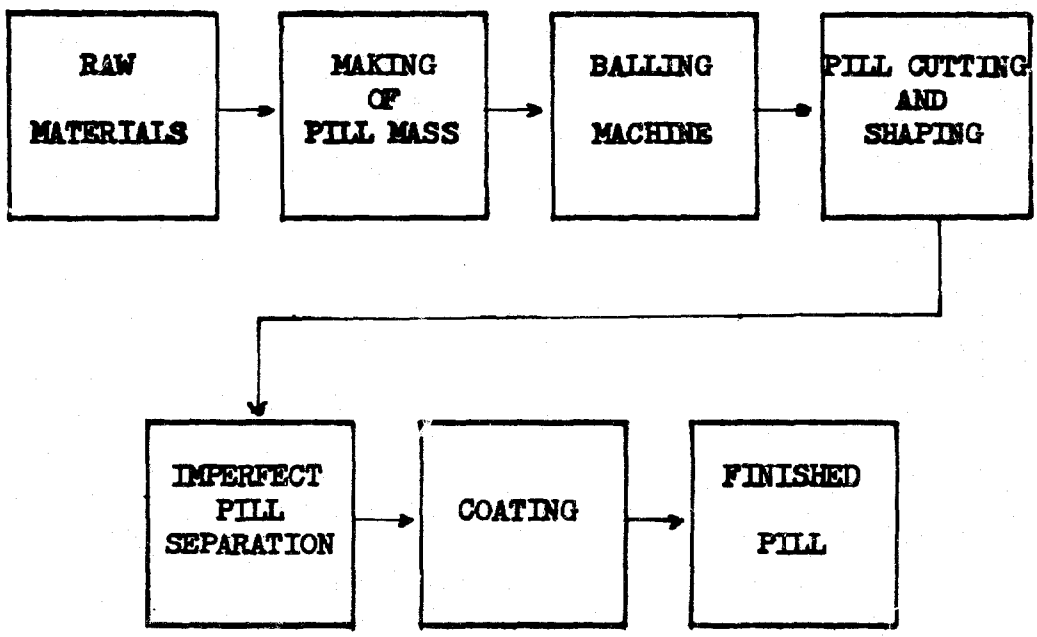
WET GRANULATION



SLUGGING METHOD

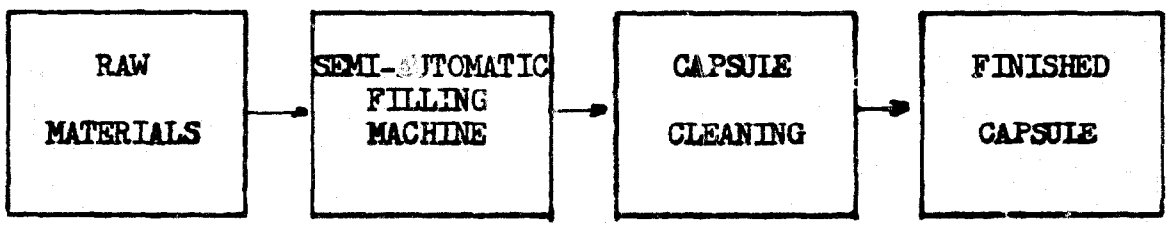


FLOW SHEET FOR PILL MANUFACTURE

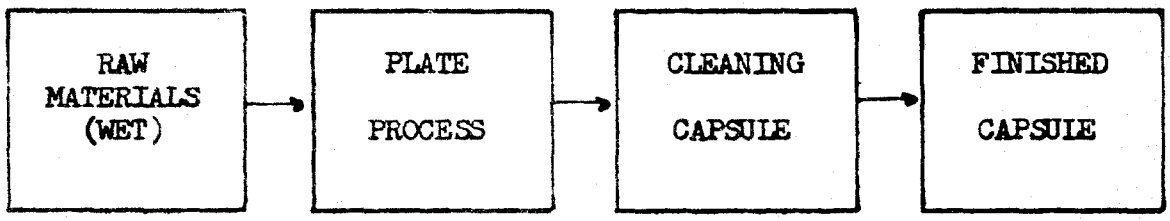
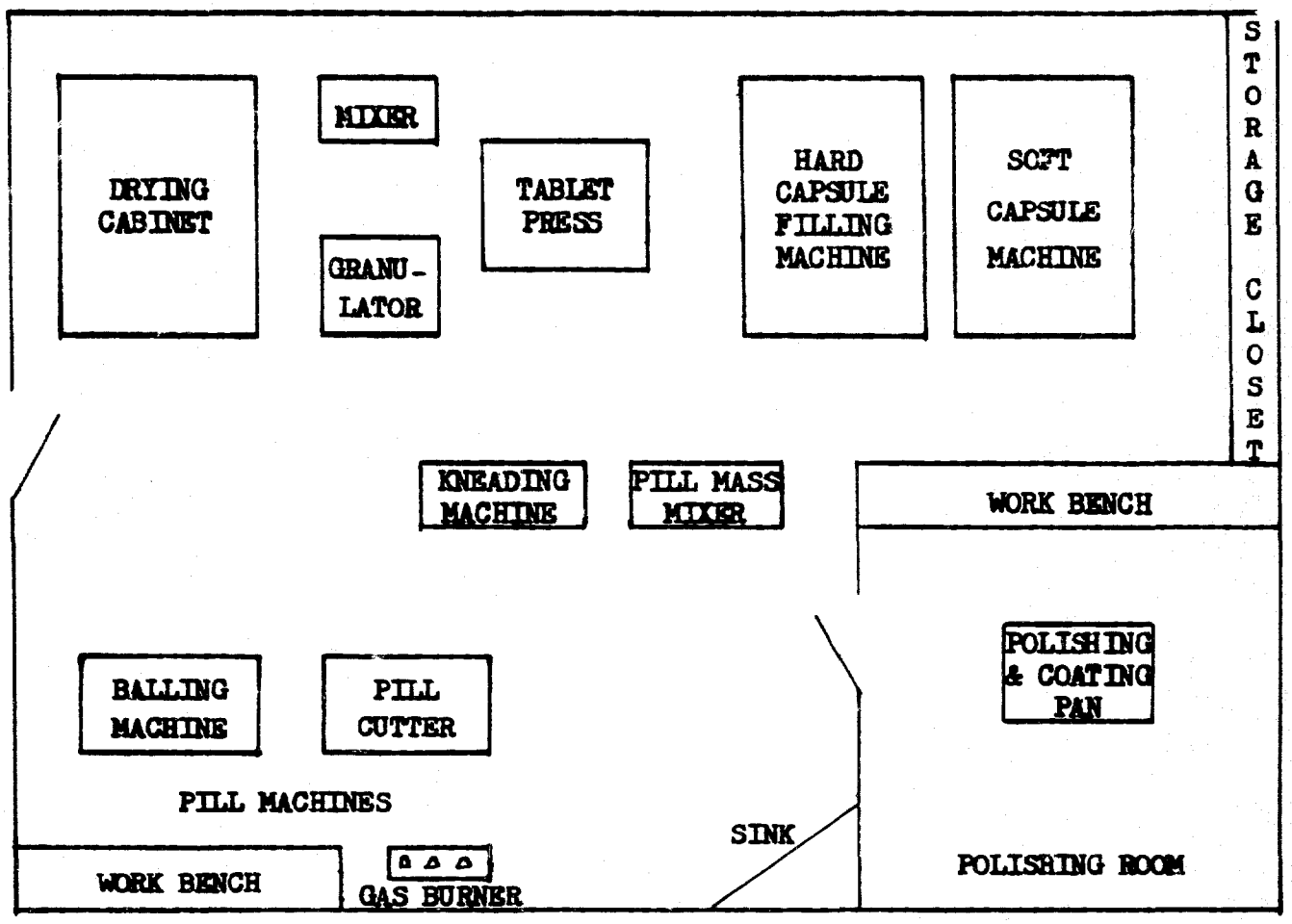


FLOW SHEET FOR CAPSULE MANUFACTURE

HARD GELATIN CAPSULES



SOFT GELATIN CAPSULES



SUGGESTED LAYOUT FOR MANUFACTURE OF TABLETS, PILLS AND CAPSULES