July 25, 1967 J. G. VINCENT, JR., ET AL 3,333,031

SURFACE DYEING AND PIGMENT MARKING OF GELATIN CAPSULES

Filed June 14, 1963 5 Sheets-Sheet 1

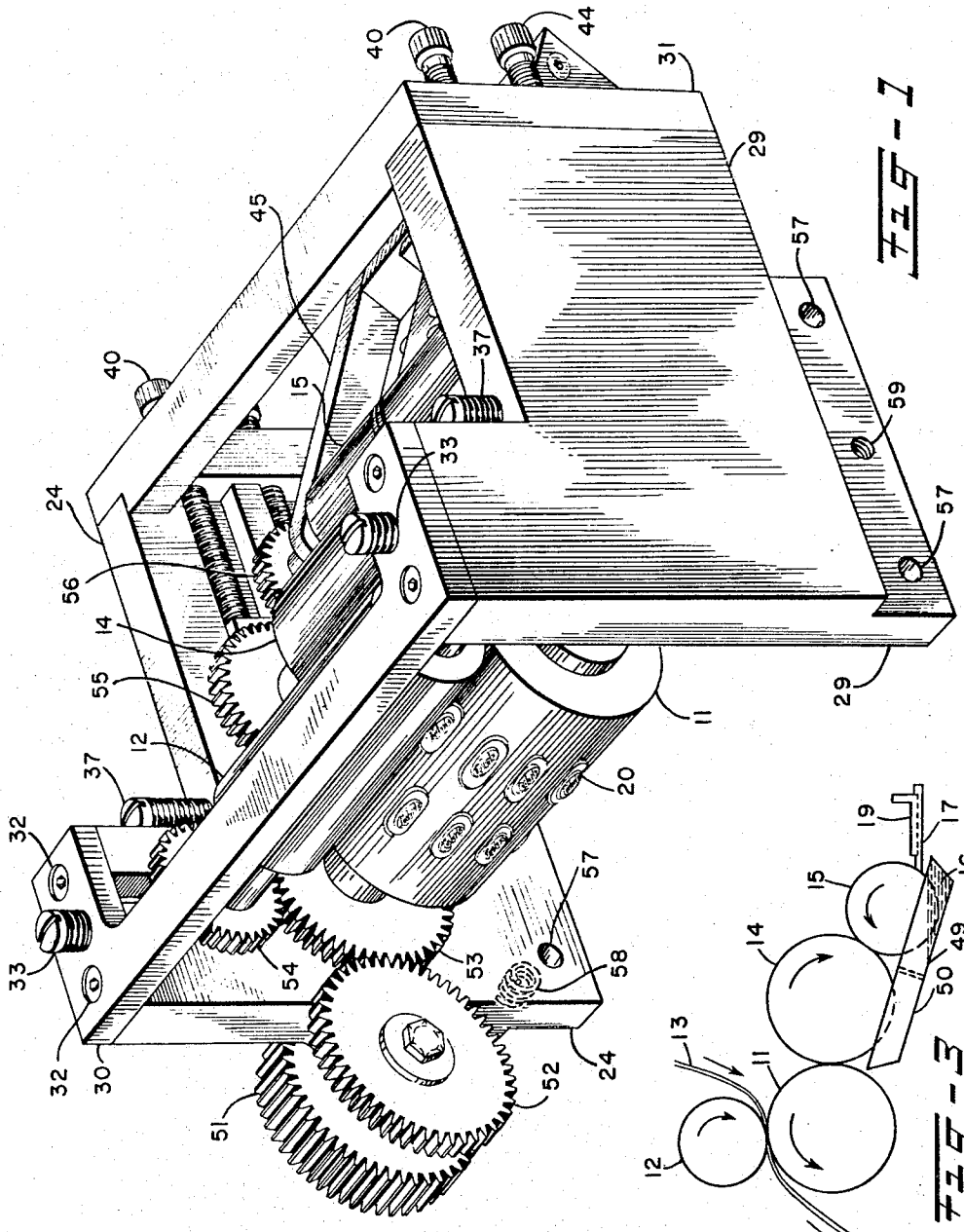


FIG - 1

FIG - 3

INVENTORS
JAMES G. VINCENT, JR.
LLOYD FRANK HANSEN
ERNEST CHU YEN
ARTHUR SINCLAIR TAYLOR
GEORGE SPENCER BOTT
MARTIN GREIF

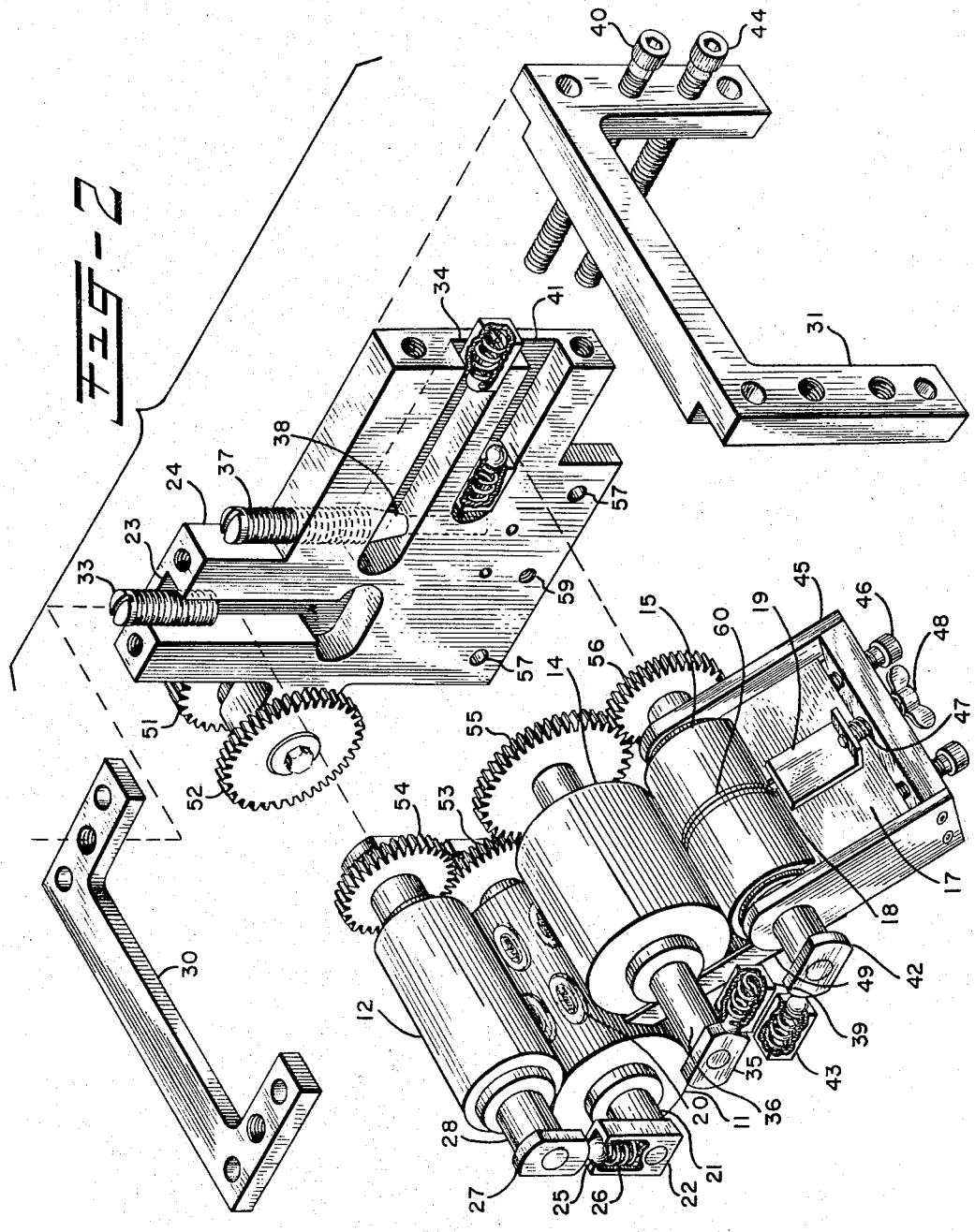
BY Samuel Frank Walker
ATTORNEY

July 25, 1967 J. G. VINCENT, JR., ET AL 3,333,031

SURFACE DYEING AND PIGMENT MARKING OF GELATIN CAPSULES

Filed June 14, 1963 5 Sheets-Sheet 2

FIG-2



INVENTORS
JAMES G. VINCENT, JR
LLOYD FRANK HANSEN
ERNEST CHU YEN
ARTHUR SINCLAIR TAYLOR
GEORGE SPENCER BOTT
MARTIN GREIF

BY Samuel Branch Walker
ATTORNEY

July 25, 1967 J. G. VINCENT, JR., ET AL 3,333,031

SURFACE DYEING AND PIGMENT MARKING OF GELATIN CAPSULES

Filed June 14, 1963 5 Sheets-Sheet 3

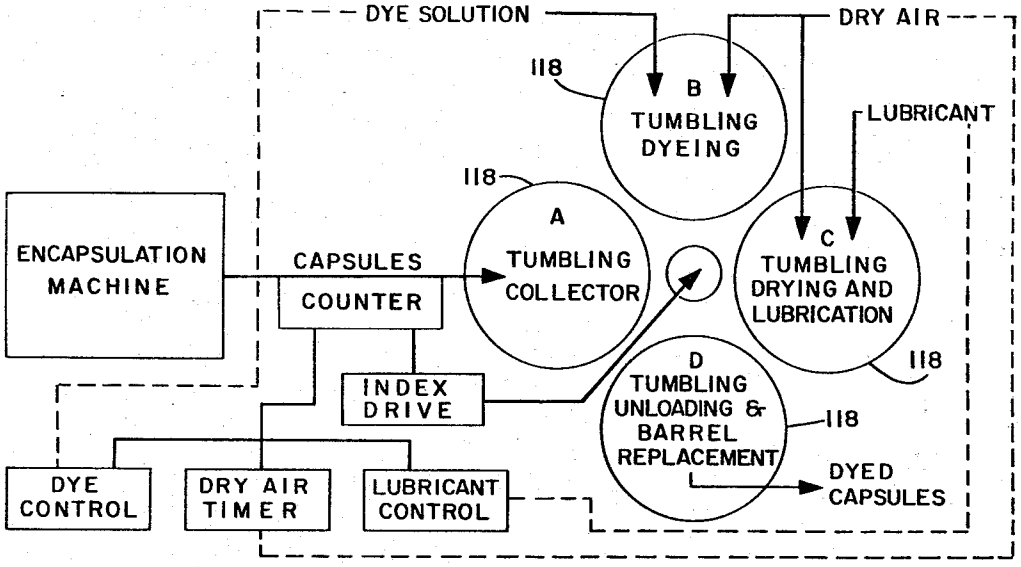


Fig-4

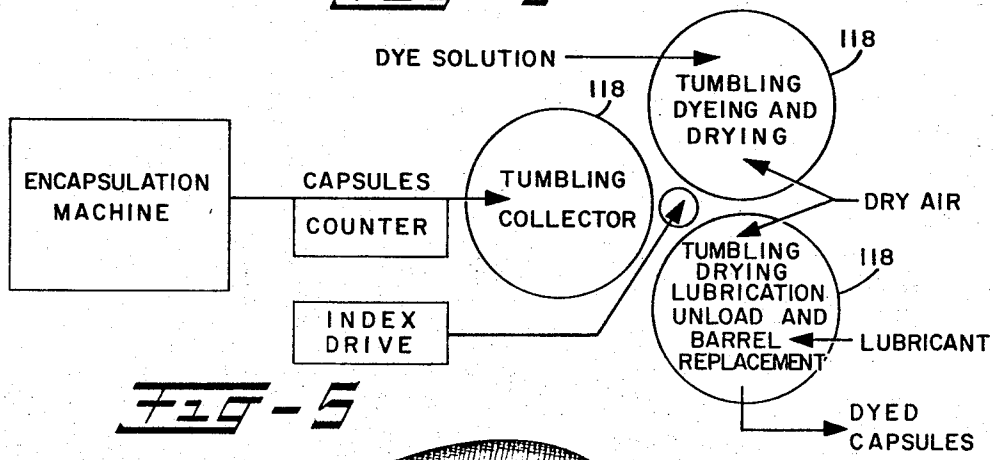


Fig-5

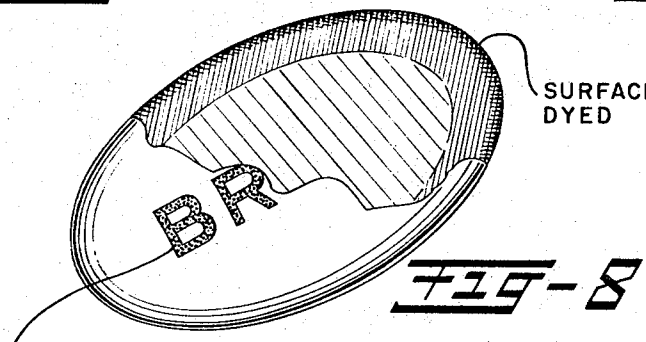


Fig-8

INVENTORS
JAMES G. VINCENT, JR.
LLOYD FRANK HANSEN
ERNEST CHU YEN
ARTHUR SINCLAIR TAYLOR
GEORGE SPENCER BOTT
MARTIN GREIF

BY Samuel Frank Walker
ATTORNEY

July 25, 1967 J. G. VINCENT, JR., ET AL 3,333,031

SURFACE DYEING AND PIGMENT MARKING OF GELATIN CAPSULES

Filed June 14, 1963 5 Sheets-Sheet 4

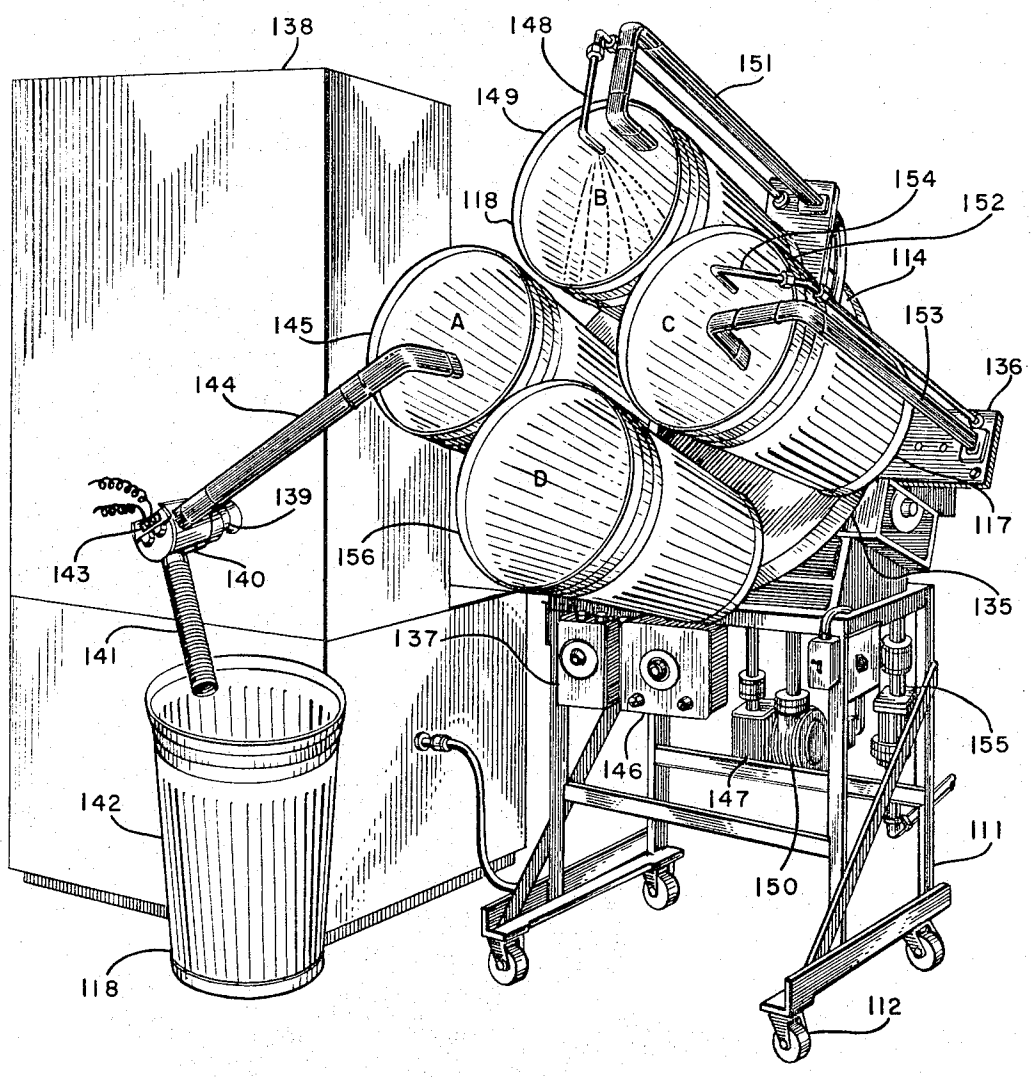


Fig-6

INVENTORS
JAMES G. VINCENT, JR.
LLOYD FRANK HANSEN
ERNEST CHU YEN
ARTHUR SINCLAIR TAYLOR
GEORGE SPENCER BOTT
MARTIN GREIF

BY Samuel Frank Walker
ATTORNEY

July 25, 1967 J. G. VINCENT, JR., ET AL 3,333,031

SURFACE DYEING AND PIGMENT MARKING OF GELATIN CAPSULES

Filed June 14, 1963 5 Sheets-Sheet 5

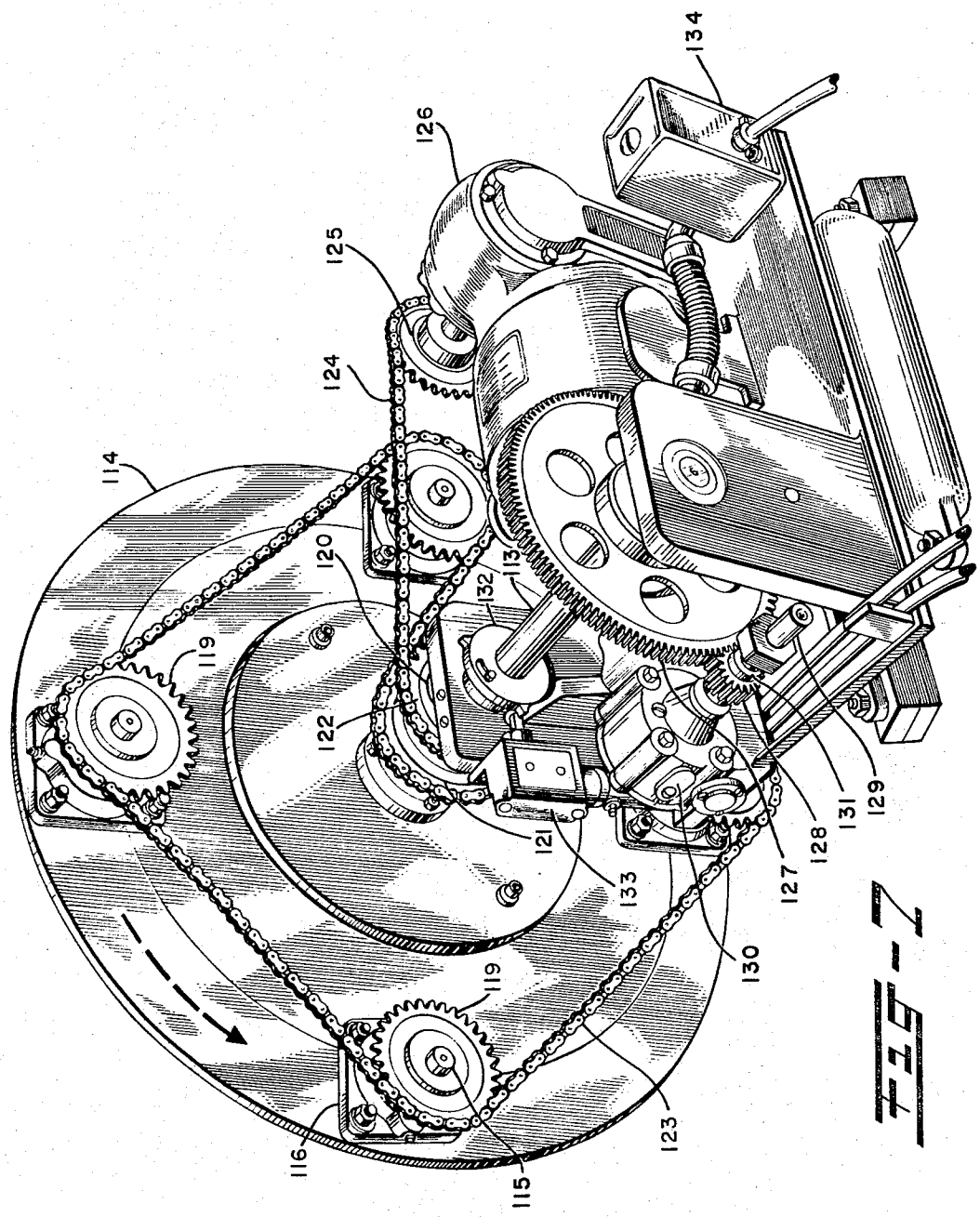


FIG. 7

INVENTORS
JAMES G. VINCENT, JR.
LLOYD FRANK HANSEN
ERNEST CHU YEN
ARTHUR SINCLAIR TAYLOR
GEORGE SPENCER BOTT
MARTIN GREIF

BY Samuel Frank Walker
ATTORNEY

United States Patent Office

3,333,031

Patented July 25, 1967

3,333,031

SURFACE DYEING AND PIGMENT MARKING OF GELATIN CAPSULES

James G. Vincent, Jr., West Nyack, Lloyd Frank Hansen, New City, Ernest Chu Yen, Orangeburg, and Arthur Sinclair Taylor, Spring Valley, N.Y., George Spencer Bott, Westwood, N.J., and Martin Greif, Bronx, N.Y., assignors to American Cyanamid Company, Stamford, Conn., a corporation of Maine

Filed June 14, 1963, Ser. No. 287,829

4 Claims. (Cl. 264—15)

This invention relates to a method for surface dyeing and surface marking capsules of plastic strip material, particularly soft gelatin capsules, in which the surfaces of the capsules are at one time colored by surface dyeing; and an identifying indicia is at another time marked on a portion of the capsule surface; as for example, by a printing step. Conveniently, but not necessarily, the indicia is marked on the surface of the strip before capsules are cut out from the strip. Apparatus for both the indicia marking and the surface dyeing are described, but not claimed in this application; and either indicia marking or surface dyeing may be used independently.

The printer herein shown in FIGURES 1, 2 and 3 is described and claimed in application Ser. No. 287,242, June 14, 1963, now Patent 3,203,347, Hansen and Bott, "Rotary Pigment Printer for Gelatin Strip for Capsules," Aug. 31, 1965.

Ingestible one-piece capsules, usually referred to as soft gelatin capsules, can be formed on machines such as disclosed in United States Patent 2,697,317, Stirn and Taylor, "Capsule Forming Die Roll," Dec. 21, 1954, from which the formed capsules are discharged in a current of air by an air conveyor. The gelatin strip for the capsules is conveniently formed from a mixture of primarily gelatin, glycerin and water, together with minor quantities of pigments, flavors and odors as desired, by methods such as disclosed in United States Patents 2,799,591, Michel and Knight, "Rapid Preparation of Encapsulation Formula," July 16, 1957; or 2,799,592, Hansen and Weidenheimer, "Rapid Preparation of Encapsulation Mixture," July 16, 1957; or 2,720,463, Stirn and Taylor, "Gelatin Capsule Casting Composition Preparation," Oct. 11, 1955. The gelatin composition may have other components, such as disclosed in United States Patent 2,770,553, Weidenheimer and Callahan, "Soft Gelatin Encapsulation," Nov. 13, 1956, showing certain amides, such as formamide or acetamide present, and United States Patent 2,776,220, Reed, Ritter, Valentine and Yen, "Gelatin Films and Capsules Made Therefrom," January 1, 1957.

Gelatin substituents may be used and hence the film in its broader sense is a pressure sealable plastic, referred to as plastic strip. Present commercial practice uses gelatin films exclusively—hence the invention is described with particular reference to gelatin films.

After manufacture, capsules have been dried in drum dryers, as disclosed in United States Patent 2,638,686, Stirn and Taylor, "Drying Gelatin Capsules," May 19, 1953.

Dyes are a foreign substance, not a natural food, so that the quantity to be ingested is preferably kept at a minimum.

The coloring of capsules is very useful for identification during manufacture, distribution and sale, and by the patient.

If the surface of the strip from which a capsule is formed is colored, during the cutting out procedures a narrow uncolored strip remains at the line of the seal.

We have now found that surface-dyed capsules can be formed from an undyed gelatin strip which may contain pigments such as titanium dioxide, calcium carbonate, barium sulfate or alumina, iron oxides or charcoal, to give either a white, gray or other color capsule and the outside surface only of the film forming the shell of the capsule is then colored by dyeing—giving capsules having a markedly lower quantity of dye than would be the case if the entire film were dyed. The appearance is elegant.

The capsules are marked by printing with identifying indicia either before or after dyeing by an edible pigment suspended in a water-polyhydric alcohol composition using methyl cellulose or sodum carboxymethyl cellulose as a binder. Printing of the strip before the formation of the capsules is preferred. An excellent composition consists of a suspension of a substantially water-insoluble non-toxic opaque material such as titanium dioxide, calcium carbonate or barium sulfate or iron oxide or charcoal suspended in an aqueous vehicle containing a polyhydric alcohol such as glycerin, propylene glycol, ethylene glycol, liquid polyethylene glycol or sorbitol with a small amount of a non-toxic surface active agent to maintain the pigment in suspension, aid penetration into the film, and aid in smooth spreading of the pigment composition on the marking type; and a water-soluble suspending and adhesive agent such as methyl cellulose or sodium carboxymethyl cellulose. Titanium dioxide is the strongest, and usually preferred pigment. Ethylene glycol is best used on capsules for other than ingestion, such as for dyes or bleaches.

The non-toxicity of propylene glycol renders propylene glycol the polyhydric alcohol of choice. Additionally, the volatility characteristics of propylene glycol are within a preferred range.

A particularly useful embodiment consists of titanium dioxide, propylene glycol, water, methyl cellulose and bis(2-ethylhexyl) sodium sulfosuccinate (Aerosol OT®).

Although the surface dyeing may be accomplished as a separate step, it is advantageous to accomplish the dyeing as part of a continuous operation. Labor and handling is minimized, the entire coloring is part of a single manufacturing operation under the control of a minimum crew, and the possibility of confusion of identity before dyeing is eliminated. The residual web is not colored, and may be conveniently used without color problems.

Any dye which is soluble in a solvent compatible with the film composition can be used. Water-soluble dyes can be added in water but usually dyes are preferred which are soluble in mixtures of lower alcohols and water as such dyes penetrate into the capsule surface more readily and the solvent system can be evaporated from the capsules.

Methanol is toxic, so usually its use is undesirable, for ingested capsules. Ethanol is technically very satisfactory, but in the United States at present taxation problems arise. Propanol or isopropanol are technically excellent, and available and economical. Tertiary-butanol is good, but slower in drying. Polyhydric alcohols, acetone, other ketones and other volatile water-miscible solvents may be used. From 25% to 75% alcohol in water is preferred (volume/volume basis).

For non-medicinal purposes any dyestuff may be used which has a satisfactory solubility and color. For most purposes non-toxic dyes are preferred. Among the dyes which are presently acceptable for food and drug use are those described in the article entitled "Colors for Food, Drugs and Cosmetics," published in the Encyclopedia of Technology, The Intersciene Encyclopedia, Inc. 1949, vol. 4, pages 287–313. This encyclopedia describes the production and use of various colors, giving the name and formula for the Food, Drug and Cosmetic dyes which are soluble colors. The FD&C alcohol-soluble dyes there listed are excellent for present purposes. Whereas dyes not presently known to be non-toxic can be used, and are

acceptable on proof of non-toxicity, the time and cost of proof of non-toxicity is such that for commercial purposes the dyes known to be acceptable are very much a matter of choice.

The capsules may be surface dyed after being dried, using the tumbling process; or may be dyed either wet or dry by immersion for controlled lengths of time in dye solutions of known strength. Tumble dyeing as part of a continuous process is preferred, and is accordingly described in detail.

The quantity of dye to be used can vary over very wide limits. The strength of the dye and the depth of color required, for a preferred value and chroma, are controlling factors. For any specific batch of capsules, a rather precise quantity of dye is required so that the finished capsules match arbitrary standards within acceptable limits.

The reduction in dye content of surface-dyed capsules over film-dyed capsules, in which the entire film is colored, is at least about 70% and usually more. Reproducibility of color is excellent.

A water-soluble flavor or perfume can be added to the dye solution to introduce a flavor or odor at this point. Flavors such as cherry, lemon, lime, orange, raspberry, vanilla, or Ethavan® synthetic vanilla are suitable.

In the drawings:

FIGURE 1 is a pictorial view of the assembled pigment printer.

FIGURE 2 is a pictorial exploded view of the pigment printer.

FIGURE 3 is a diagrammatic cross section of the roll system of the pigment printer.

FIG. 4 is a diagrammatic view showing the process steps of a four-barrel surface dyeing machine.

FIGURE 5 is a similar drawing of a three-barrel modification.

FIGURE 6 shows a pictorial view of the assembled dyeing machine.

FIGURE 7 is a partial view showing the drive mechanisms of the dyeing barrels with safety guards removed.

FIGURE 8 is a representation of the final surface-colored surface-marked capsule.

As shown in FIGURE 3, the essential elements of the pigment printer include a marking roll **11**, which corresponds to the printing roll of the more conventional printing couples; and adjacent thereto a pressure roll **12**. Between these two rolls passes the gelatin strip **13**. Adjacent to the marking roll **11**, and bearing against raised portions of the marking roll, is the pigment marking fluid transfer and spreading roll **14**, sometimes hereafter shortened to the transfer roll. In contact with the transfer roll is the pigment pick-up roll **15**. The pigment pick-up roll, which rotates in the pigment marking fluid **16**, bears against the transfer roll **14**, and a notched doctor blade **17** doctors or scrapes the pigment marking fluid from the pigment pick-up roll except at the notch **18**. The cross-section of the notch is varied by the notch adjusting doctor **19**.

Thus, a very narrow band of pigment marking fluid of adjustable cross section passes through the notch in the notched doctor blade and is spread over the surface of the transfer roll **14** as the pigment fluid passes between the bite of the transfer roll and the pigment pick-up roll, thus giving a uniform coating on the transfer roll which is transferred to the raised portions of the marking roll and thus to the gelatin strip being marked.

The marking roll **11** consists of a roll having integral or separate marking type **20** which are indicia or letters to be printed on a strip **13**. The marking roll **11** is mounted on the marking roll shaft **21** which is journaled at each end in a marking roll journal block **22**. The rear marking roll journal block **22** slides in the marking roll slot **23** in the rear side plate **24**. The marking roll journal block **22** has in its upper face a positioning ball **25** under which is a positioning ball spring **26**.

Also sliding in the marking roll slot **23** is the pressure roll journal block **27**. In the pressure roll journal block is journaled the pressure roll shaft **28** on which is mounted the pressure roll **12**.

A corresponding front side plate **29** is on the front side of the assembly and of the same general configuration, except for the driven gear support. Both side plates are shown in FIGURE 1. The front side plate is omitted in FIGURE 2 to show the details of roll construction. The front and rear side plates are held apart by a top side plate spacer **30** and an end side plate spacer **31**. The spacers are held to the side plates by spacer cap screws **32**. Through the top side plate spacer extends a pressure roll adjusting screw **33** which bears on the pressure roll journal block **27** pressing the pressure roll towards the marking roll. The positioning ball **25** loaded by the positioning ball spring **26** tends to press the pressure and marking rolls apart, thus taking up any lost motion and permitting a very fine adjustment of the spacing between the pressure roll **12** and the marking roll **11**. Thus the pressure on the gelatin strip **13** passing therebetween is readily and accurately controlled. It is necessary that only minimum pressure be used as the gelatin strip is tender and easily damaged by pressure.

At approximately right angles to the marking roll slot **23**, the side plates **24, 29** have therein the transfer roll slots **34**. The transfer roll journal blocks **35** slide in the transfer roll slots **34**. The transfer roll shaft **36** is journaled in the transfer roll journal blocks **35**. At the end of the transfer roll slots, closest to the pressure roll, are conical tapered positioning screws **37**. The transfer roll journal blocks **35** bear against the conical portions **38** of the positioning screws **37** and hence the entry depth of these blocks and the pressure between the transfer roll and the marking roll can be accurately controlled. Bearing against the transfer roll journal blocks are transfer roll balls and springs **39** which are compressed to increase pressure by transfer roll adjusting screws **40** threaded in the end side plate spacer **31**.

Partially under and adjacent to, and conveniently parallel to, the transfer roll slots **34** are pigment pick-up roll slots **41** in which slots slide the pigment pick-up journal blocks **42**, which in turn are urged backwards by the pick-up roll balls and springs **43** and which are pressed forward by the pick-up roll adjusting screws **44**. The shaft of the pick-up roll **15** is journaled in said blocks **42**. The spring loading of the blocks thus permits the use of the adjusting screws to give fine control over pressures and any lost motion is taken up by spring action. The action of the journal blocks and adjusting assemblies are the same for both side plates.

Also journaled on the shaft of the pigment pick-up roll **15** is a doctor blade frame **45**. In the doctor blade frame slides a notched doctor blade **17** which is held against the pigment pick-up roll **15** by the notched doctor adjusting screws **46**. A notch adjusting doctor **19** slides on the surface of the notched doctor blade **17** and is urged towards the pigment pick-up roll by a biasing spring **47** and is held open by a feed-adjusting screw **48**.

Under the pigment pick-up roll **15** is a pigment marking fluid trough **49** holding a pigment marking fluid **16**. Also in the trough is a spillage compartment **50** to pick up any marking fluid which is spilt during operation. A conventional fluid supply system is used to supply the pigment marking fluid to a constant level in the pigment marking fluid trough.

As shown in FIGURE 1, the shaft of each roll is gear driven. On the rear side plate only is mounted a wide driven gear **51** which is driven by an angularly adjustable gear on the encapsulation machine, the details of which are conventional. This is a spur gear which is wide enough so that the entire pigment marker assembly can be axially shifted for lateral register. An angularly adjustable drive gear on the encapsulating machine provides for linear register. The wide driven gear is fastened to a spur gear

52 which in turn drives the marking roll gear 53 which drives the pressure roll gear 54, and the transfer roll gear 55, which transfer roll gear drives the pigment pick-up roll gear 56.

In the lower part of the side plates are mounting holes 57 which permit the entire assembly to slide on mounting rods attached to the encapsulation machine so that the entire assembly may be axially adjusted for lateral register. Conveniently, the assembly is spring loaded in one direction by mounting springs 58 behind the assembly which is held against the spring action by an adjusting screw setting through an adjusting screw hole 59.

In operation the pigment printer assembly is mounted on the encapsulation machine so that the gelatin strip feeds between the marking roll 11 and the pressure roll 12 and the marking fluid composition is fed into the pigment fluid trough. The pigment fluid is picked up by the pigment pick-up roll. Most of the fluid is scraped off of the pigment pick-up roll by the notched doctor so that only a narrow ribbon of pigment marking fluid 60 is fed on the surface of the pigment pick-up roll and into the bite between the pigment pick-up roll and the transfer and spreading roll. Because this ribbon is comparatively narrow, about 2 mm., the volume may be more readily controlled than if a wider feed were used. Thus, the amount of pigment marking fluid fed can be exactly adjusted to a desired rate so that as the fluid is evenly spread over the surface of the transfer and spreading roll, just enough is fed to properly mark the gelatin strip.

Although the material of construction is not critical for effective results, the pigment printer has a longer effective life if the pick-up roll is of a hard material such as stainless steel, or chrome-plated steel, and the pressure roll and transfer and spreading roll are of a resilient material, such as rubber or a synthetic rubber, which is not swelled by the pigment marking fluid.

The carrier for the pigment is a mixture of water and a polyhydric alcohol. Propylene glycol is preferred because it has the characteristics of penetrating into the gelatin surface sufficiently rapidly that the marking composition hardens sufficiently to prevent offset during the formation of capsules from the strip and before their discharge from the encapsulation machine, which thus permits tumbling of the capsules immediately after formation. Such prompt tumbling aids in rounding powder-filled capsules and permits prompt coloration by a surface dye without storage problems, without inventory problems, with optimum ease of reusing web, and without the possibility of confusion between various batches of capsules. For best results, from about 30% to 60% of propylene glycol is preferred. The titanium dioxide gives excellent results in the range of from about 10 to 20% and the remainder is largely water.

About 0.5% to 3% of a suspending and binding agent is preferred. Methyl cellulose is the suspending and binding agent of choice as it forms a film binding the pigment to the surface of the capsule which is flexible and sufficiently hard without being brittle and is thus both rub resistant and chip resistant. Low viscosity methyl cellulose is preferred. A methoxyl content of from 20% to 32% gives good results. Sodium carboxymethyl cellulose and other water-soluble non-toxic adhesive suspending agents give good results.

A water-soluble, preferably non-toxic wetting agent increases the rate of penetration into the surface of the gelatin strip and improves the bond. Non-toxic wetting agents such as polyoxyethylene sorbitan monooleate, polyoxyethylene-polyoxypropylene condensation polymers (Pluronic F–68), sodium lauryl sulfate, and polyoxyethylene stearate give good results. Sodium bis(2-ethylhexyl) sulfosuccinate is preferred; it is well known to have extremely low toxicity. A concentration of about 0.05% of the wetting agent is preferred. A range of at least 0.005 to 2% is effective. The exact quantity varies in part with the state of subdivision of the pigment, and the degree of agitation and time of storage before use. Sufficient agent to maintain suspension and give a rapid penetration in the film and give smooth non-puddling spreading on the type is preferred.

A current list of wetting agents is given in an article by John W. McCutcheon, "Synthetic Detergents and Emulsifiers—Up-To-Date III," Soap and Chemical Specialties, July, August, September and October 1955. This list is expanded in "Detergents and Emulsifiers 1963 Annual," John W. McCutcheon, Inc., 236 Mt. Kemble Ave., Morristown, N.J., 1963. The surfactants there listed can be used for suspension of the pigments, but where toxicity is a problem, only those known to be non-toxic are acceptable. Rather than prove non-toxicity of some other surfactant, some form of bis(2-ethylhexyl) sulfosuccinic acid, such as its sodium salt, or polyoxyethylene sorbitan monooleate or polyoxyethylene stearate or other agent known to be non-toxic is usually used commercially.

Where desired, other non-toxic pigments, including iron oxides, charcoal, and the insoluble lakes of toxicologically approved dyes may be used independently or in combination with titanium dioxide. The lakes of the dyes acceptable for surface dyeing the capsules are acceptable pigments.

For convenience, the numbers assigned to the barrel dye apparatus start at 111 to differentiate from the pigment printer series.

The barrel dyeing apparatus is mounted on a support frame 111, mounted on casters 112. In the support frame is journaled a turntable shaft 113, which is at an angle, conveniently from 10 to 45° with the horizontal; 15° gives preferred results. On the turntable shaft is a turntable 114. Journaled in the turntable shaft are four barrel shafts 115. Conventional pillow block bearings 116 are used. On the upper end of the barrel shafts are located barrel supports 117. The barrel supports each hold a plastic barrel 118. Conveniently the plastic barrels are corrugated polyethylene or polypropylene barrels formed of one-piece. A twenty-gallon size is convenient. The barrel support 117 is of a size adapted to hold the particular plastic barrels being used at a given time. If the barrels are tapered so that they stack, the barrel support may be a barrel clamped to the upper end of the barrel shaft; or may be a stainless steel frame of rods. It should be of non-corrodible composition and readily cleaned. At the other end of the barrel shaft is a barrel shaft sprocket 119.

Mounted on the turntable shaft is a coaxial sprocket hub 120 having a shaft drive sprocket 121 and a drive sprocket 122. A barrel drive chain 123 is mounted around each of the barrel shaft sprockets 119, and extends around the shaft drive sprocket 121. A main drive chain 124 extends over the drive sprocket 122 and a motor sprocket 125 mounted on a reduction drive motor 126.

The reduction drive motor 126 drives its motor sprocket 125 and through the main drive chain 124 causes the coaxial sprocket hub with shaft drive sprocket 121 to rotate. The drive shaft sprocket 121 through the barrel drive chain 123 in turn causes each of the barrel shafts 115 and the associated barrels 118 to rotate. The barrels should rotate fast enough to give a tumbling action to the capsules contained therein, and well below the critical speed at which capsules would be held against the sides of the barrel by centrifugal force. A speed of 30 to 60 revolutions per minute gives good results. For the appended examples, a speed of 40 revolutions per minute was selected, where not otherwise set forth.

On the turntable shaft 113 is a turntable shaft gear 127 which in turn is driven by a turntable pinion gear 128. The turntable pinion gear is mounted on an indexing motor shaft 129. The indexing motor assembly 130 is an electric motor with an associated reduction drive to turn the indexing motor shaft. Between the indexing motor shaft and the turntable pinion gear is a slip clutch 131. This is a conventional slip clutch; conveniently a driven

member between spring loaded driving members; so that the starting and stopping of the rotation of the turntable is cushioned and if any of the equipment is jammed accidentally, slippage occurs without damage to the mechanism or operator.

An indexing cam **132** is adjustably mounted on the turntable shaft **113** and in turn has cam points operating the indexing switch **133**, the functioning of which is described later.

The reduction drive motor **126** is controlled by a tumbling switch **134**, which controls the barrel rotating action.

As shown in FIGURE 6, a drive safety shield **135** is placed over the barrel drive chain system to protect the operators from getting caught in the sprocket drive and to act as a grease catcher. Similarly, the turntable shaft and its associated mechanism is protected by a safety cover **136** which serves to enclose the drive system and also serves as a support for certain nozzles, as later described.

Also mounted on the support frame is a capsule counter **137**. The encapsulation machine **138** is shown diagrammatically. From the encapsulation machine the capsules are conveyed in an air stream by an air conveyor **139**. In the air conveyor is a conveyor valve **140** which in one position diverts capsules through a waste chute **141** to a waste container **142**. During start up and adjustment, capsules not known to be perfect are diverted through the waste chute to a waste container. On the conveyor valve **140** is a mercury switch **143** which closes only when the conveyor valve **140** is in position to feed capsules through the capsule transfer duct **144** which discharges capsules into the barrel at a first barrel position **145**, lettered as position A. The mercury switch **143** controls the capsule counter **137**. The capsule counter is synchronized with the speed of the encapsulation machine and counts capsules only while capsules are being fed through the capsule transfer duct **144**. The counter is preset to a capsule batch number, and when a desired number of capsules have been introduced into the barrel in position A, starts the rotation of the indexing motor assembly. From 1,000 to 16,000 capsules is a convenient batch size, depending in part on capsule size.

When the turntable shaft is rotated one-quarter turn the indexing cam **132** through the indexing switch **133** stops the rotation of the turntable. The counter also then actuates a sequence controller **146** which includes a dye control that actuates a dye solution pump **147** which injects a dye solution through a dye nozzle **148** into the rotating barrel containing capsules at the dyeing barrel position **149**, designated as position B. For best results, a multiple jet nozzle is preferred. A spray may produce a mist that causes loss of dye. Too coarse a nozzle, impinging at a single point, may cause uneven dyeing. A nozzle having fine streams that impinge diagonally across the face of the tumbling capsule mass gives excellent results over a wide range of coloring conditions. The sequence controller also includes a dry air timer that controls a dry air blower **150** which blows dry air through a dry air pipe **151** into the barrel in position B. The sequence controller operates the dry air control valves and regulates the interval between dye addition and air drying, and also turns off the air before the capsules are overdried if, for some reason the encapsulation machine does not keep up with the drying cycle.

In a drying and lubrication position **152**, designated as position C, a second dry air pipe **153** directs addtional dry air on the capsules. Also in this position a lubricant nozzle **154**, fed by a lubricant pump **155**, in turn operated by a lubricant control, which is part of the sequence controller **146**, directs a lubricant on to the capsules as they are tumbling, which gives a slightly soft sheen to the surface and prevents the capsules from sticking to each other. The fourth position is a loading and unloading position **156**, designated as position D. At this point the machine operator removes the barrel containing the dyed and lubricated capsules and replaces the barrel with an empty barrel ready for the next cycle. More than four operating positions can be used; four is preferred as these are enough stations for flexibility, and the machine is of convenient size. An alternative operating procedure uses station B to dry the marking on printed capsules using the air blower. Station C is fitted with a dye nozzle, and dyeing, drying and lubrication are performed sequentially at this station.

As shown in FIGURE 5, all operations can be conducted in three positions, although the nozzles may complicate barrel loading and unloading; and the timing of unloading may be less flexible.

The dye is conveniently added promptly if dried capsules are being colored. With wet capsules, that is freshly formed capsules, preferably the capsules are tumbled for a time to shape, and permit the capsules to partially dry, before dyeing. Hence it is advantageous to use the second barrel position to hold and tumble the capsules, the third to dye and dry and either the third or fourth position to add the lubricant. Drying air can be introduced in all positions, although such introduction is normally mandatory only after the addition of the dye solution. Where large barrels are used, at lower production rates, ambient air currents may be enough to dry, depending on fan locations, and air movement in the encapsulation room. Other variations within the scope of the appended claims are obvious to those skilled in the art.

As common in pharmaceutical practice, percentages are based on volume of liquids and weights of solids. Where not otherwise specified, the abbreviation w./v. for weight solids/volume of liquid, based on unit density for water, or v./v. is used in part for clarity.

EXAMPLE 1

A gelatin mix was prepared as described in Example 5 of United States Patent 2,799,591, supra, except that the red dye and red pigment were omitted. The gelatin was cast as a continuous strip and capsules were formed therefrom, as described in United States Patent 2,697,317, supra.

Forty-eight parts of titanium dioxide pigment were mixed with 72 parts of propylene glycol and passed through a three-roller paint mill until the pigment was smoothly dispersed. Separately 5 parts of low viscosity methyl cellulose were dispersed by stirring in 200 parts of hot water; 2 parts of a 10% aqueous solution of sodium bis(2-ethylhexyl) sulfosuccinate was added and the mixture cooled to room temperature, then mixed with the titanium dioxide dispersion in propylene glycol. Fifty-five additional parts of propylene glycol were added and the mixture stirred until a smooth uniform suspension was obtained. The suspension was used in the pigment printer above described. The marking composition was smoothly transferred onto the printing surface and transferred to the surface of a gelatin strip from which capsules were formed.

As the capsules were formed in the encapsulation machine and stripped from the residual web, the capsules were picked up by the air conveyor and transferred to tumbling drums. Capsules were manufactured in a flat oval size, the surface of which in finished form is approximately 493 square millimeters. (Capsules are about 21.8 mm. long and about 7.2 mm. in diameter.) Four thousand capsules were counted into a polyethylene tumbling barrel, the apparatus indexed and tumbled for 5 minutes to let the pigment set. Then 75 ml. of a dye solution containing 0.5% w./v. of FD&C Blue No. 1 in a 50% v./v. mixture of isopropanol and water was added automatically by the dye pump over a period of about 15 seconds in 5 jets across the face of the tumbling capsule mass. The capsules were tumbled for two minutes to smoothly and uniformly coat all of the capsules with the dye solution and then a current of room air was blown on the

capsules for two minutes, at the end of which time all of the dye solution was either absorbed in the capsules or evaporated. Five grams of powdered stearyl alcohol was dusted on the surface of the tumbling capsules by hand, and during an additional two-minute tumbling period spread over the capsule surfaces. The entire operation was carried out at normal operating room conditions of 68° F. and 35% relative humidity.

The barrel containing the capsules was then removed from the machine and the capsules were transferred to trays and spread out in a single layer. The capsules were then put in a dry room and allowed to remain until dry. The capsules were uniformly and evenly dyed. The pigment marking stood out clearly against the dyed background.

The capsules can be coated with an air drying resin such as disclosed in United States Patent 2,727,833, Yen and Stirn, "Capsule Finishing Process," if desired.

EXAMPLE 2

The dye in Example 1 is present to the extent of about 94 micrograms per capsule. The procedure of Example 1 is repeated using a concentration of 1.0% of FD&C Blue No. 1 in the dye solution. The capsules have about 188 micrograms per capsule and are a deeper blue than obtained in Example 1. The pigment marking stands out more clearly.

The run is repeated using 0.5% solution of FD&C Red No. 2, and containing 0.1% synthetic vanilla as a flavor. A red capsule is obtained. The pigment marking shows up clearly.

EXAMPLE 3

Using the gelatin formula and encapsulation machine referred to in Example 1, capsules are produced having a surface area of about 657 mm. with a length of about 25.4 mm. and a diameter of 8.25 mm. The printing is accomplished using the formula of Example 1, except that medium viscosity carboxymethyl cellulose is used as the binder.

Four thousand such capsules as they come from the encapsulation machine are collected in a rotating barrel, rotating at 30 r.p.m., the barrel is indexed to position B, and held there under a current of drying air until the machine is indexed to position C, then thereto is added 150 ml. of 50% isopropanol in water, v./v., containing 0.058%, w./v., of FD&C Violet No. 1, and 1.442%, w./v., of FD&C Red No. 4.

After tumbling for about 4 minutes air is turned into the tumbling drum and the capsules are dried by air for an additional 6 minutes, after which 10 ml. of 5% weight by volume of stearyl alcohol in isopropanol is added by the automatic sequence controlled pump, and the capsules are allowed to continue tumbling for another 4 minutes. After the barrel indexes to the loading and unloading position, D, the barrel containing the capsules is removed. The capsules are spread in a single layer in drying trays and dried.

The length of time capsules are tumbled after the addition of a lubricant before they are unloaded is not important and hence for production purposes the capsules are permitted to continue tumbling with or without air being blown upon them until subsequent batches of capsules are ready for dyeing. If, for example, the encapsulation rate is 400 per minute, and 4,000 capsules are used in a batch, the holding time is ten minutes per station for continuous production. If difficulties in encapsulation delay the production rate, a longer tumbling has no harmful effect on the final capsules. As the barrel is at the unloading and barrel replacing station for ten minutes, the operator may remove the barrel containing capsules and replace it with an empty barrel at his convenience at any time during this ten-minute period.

EXAMPLE 4

Using the encapsulation machine and the general formula of Example 1, two batches of capsules are produced in which for one strip the formula of Example 1 is used, and for the other strip a similar formula is used, except that the titanium dioxide is omitted.

Forty-eight parts of FD&C Blue No. 1 lake (a commercially-available triphenyl methane blue lake) are mixed with 72 parts of propylene glycol and passed through a three-roller paint mill until the lake is uniformly dispersed through the propylene glycol. Six parts of a low viscosity methyl cellulose are stirred into 100 parts of hot water to which are added 5 parts of a 10% aqueous solution of sodium bis(2-ethylhexyl) sulfosuccinate and the composition stirred while being cooled to room temperature. The two compositions are blended together and an additional 100 parts of propylene glycol are added and the composition stirred until uniform.

When placed in the printing machine, above described, a uniform blue pigment print is obtained on the surface of the capsules. The pigment shows a minimum of offset as the capsules are tumbled.

The depth of color of the printing may be reduced by using some titanium dioxide instead of all FD&C Blue No. 1.

A three-barrel machine, such as shown diagrammatically in FIGURE 5 is used. After 4,000 capsules are collected the machine indexes and tumbling is continued with drying air only for 8 minutes to permit the printing to dry. One hundred milliliters of a 50% v./v. isopropanol-water solution containing 0.05% w./v. FD&C Red No. 4 dye is then added. Tumbling is continued for three minutes, the machine is then indexed and 10 ml. of a 5% w./v. solution of stearyl alcohol in isopropanol is added. Tumbling is continued for a minimum of 30 seconds, after which the dyed capsules may be removed at the operator's convenience, at any time prior to the next indexing step.

The dye and lubricant are added by hand. Well formed, well dyed properly pigment marked capsules are obtained.

In one instance for spheroidal capsules having a surface area of 657 square millimeters, it was found that 50 micrograms of dye gave the same surface color as on capsules containing 750 micrograms of dye added to the gelatin formula. This is a ratio of 1/15 of dye usage.

As typical of the ranges to be expected, the following is given as a table of certain commercial products showing the micrograms of dye used for gelatin dyeing where the entire gelatin formula is used, as compared with the quantity of dye per capsule with surface-dyed capsules.

TABLE I

Capsule	Gelatin Dyed Standard, mcg.	Surface Dyed, mcg.
M	356	75
N	1,582	93.7
O	1,005	150
P	1,784	563
Q	880	250

EXAMPLE 5

Capsules are produced as in Example 1, except that the pigment printing and final stearyl alcohol are omitted. The capsules are placed in trays having oriented slots, to line up the capsules, and each capsule is hand stamped, using rubber type, and the same pigment formula as in Example 1. The capsules are permitted to dry for 30 minutes, and are then coated with stearyl alcohol. An excellent white pigment marking sharply contrasting against a blue capsule is obtained.

Where not otherwise specified in the claims, parts are by weight.

We claim:

1. The method of forming pigment marked colored soft gelatin capsules comprising: (a) casting a liquid gelatin composition, which seals on cutting out, to form a continuous soft gelatin strip, (b) forming a pigment marking fluid by suspending from 10 to 20 parts of a non-toxic water and alcohol insoluble pigment in 30 to 60 parts of a polyhydric alcohol and sufficient water to make a total of 100 parts with the aid of 0.005 to 2 parts of a non-toxic surface active suspending agent in the presence of from about 0.5 to 3 parts of a water-soluble non-toxic suspending agent, (c) printing the thus formed pigment marking fluid on parts only of the soft gelatin strip to form indicia, (d) forming, filling and cutting out soft gelatin capsules from parts of said soft gelatin strip having at least some printing thereon, (e) transferring the printed and filled capsules to a rotating barrel, (f) tumbling the capsules in the barrel to smooth the configuration of the capsules, (g) adding to the tumbling capsules a volatile liquid composition containing an alcohol-water soluble surface dye, (h) absorbing said dye evenly and uniformly on the surface of the capsules, and (i) evaporating the volatile components of the volatile liquid composition, thereby drying said capsules.

2. The method of claim 1 in which a solution of a lubricant in alcohol is added to the dyed and printed capsules.

3. The method of coloring and marking soft gelatin capsules comprising: (a) casting a liquid gelatin composition, which seals on cutting out, to form a continuous soft gelatin strip, (b) forming a pigment marking fluid by suspending from 10 to 20 parts of a nontoxic water and alcohol insoluble pigment selected from the group consisting of titanium dioxide, calcium carbonate, barium sulfate, charcoal, iron oxides and the lakes of dyes approved for drug and cosmetic use, in 30 to 60 parts of a polyhydric alcohol selected from the group consisting of propylene glycol, polyethylene glycol, sorbitol and glycerin and sufficient water to make a total of 100 parts with the aid of 0.005 to 2 parts of a non-toxic surface active suspending agent in the presence of from about 0.5 to 3 parts of a water-soluble non-toxic cellulose derivative selected from the group consisting of methyl cellulose and sodium carboxymethyl cellulose, (c) printing the thus formed pigment marking fluid on parts only of said gelatin strip to form indicia, (d) forming, filling and cutting out soft gelatin capsules from parts of said soft gelatin strip having at least some printing thereon, (e) transferring the printed and filled capsules to a rotating barrel, thereby tumbling the capsules, (f) after a predetermined number of capsules have been introduced into the barrel moving the barrel to a second position, (g) continuing the tumbling to smooth the configuration of the capsules and simultaneously drying the printed capsules by introducing an air current into the barrel, (h) adding to the tumbling capsules a predetermined quantity of a volatile liquid composition containing a surface dye, (i) absorbing the dye evenly and uniformly on the surface of the capsules, evaporating the volatile components of the volatile liquid composition, to dry the capsules, (j) moving the barrel to a third position, (k) introducing a predetermined quantity of a liquid lubricant, (l) introducing air into the barrel to continue the drying of the capsules, (m) moving the barrel to a fourth position and removing the treated capsules therefrom.

4. The method of coloring and marking soft gelatin capsules comprising: (a) casting a liquid gelatin composition, which seals on cutting out, to form a continuous gelatin strip, (b) forming a pigment marking fluid by suspending from 10 to 20 parts of titanium dioxide in 30 to 60 parts of propylene glycol and sufficient water to make a total of 100 parts with the aid of 0.005 to 1 part of sodium bis(2-ethylhexyl)sulfosuccinate in the presence of from about 0.5 to 3 parts of a water-soluble methyl cellulose, (c) printing the thus formed pigment marking fluid on parts only of said gelatin strip to form indicia, (d) forming, filling and cutting out soft gelatin capsules from parts of said soft gelatin strip having at least some printing thereon, (e) transferring the printed and filled capsules to a rotating barrel, thereby tumbling the capsules, (f) after a predetermined number of capsules have been introduced into the barrel moving the barrel to a second position, (g) continuing the tumbling to smooth the configuration of the capsules and simultaneously drying the printed capsules by introducing an air current into the barrel, (h) adding to the tumbling capsules a predetermined quantity of a volatile liquid composition containing an alcohol-water soluble surface dye, (i) absorbing the dye evenly and uniformly on the surface of the capsules, evaporating the volatile components of the volatile liquid composition to dry the capsules, introducing a predetermined quantity of a lubricant, introducing air into the barrel to continue the drying of the capsules, and (j) subsequently moving the barrel to another position and removing the treated capsules therefrom.

References Cited

UNITED STATES PATENTS

2,196,283	4/1940	Zick et al.	167—83
2,234,479	3/1941	Scherer	167—83
2,638,686	5/1953	Stirn et al.	264—15
3,070,927	1/1963	Lundahl	53—29
3,092,940	6/1963	David	53—29
3,149,039	9/1964	Jeffries	167—82

ROBERT F. WHITE, *Primary Examiner.*

JULIAN S. LEVITT, *Examiner.*

G. A. MENTIS, J. R. HALL, *Assistant Examiners.*