Chapter Forty-one

Packaging

Introduction

The packaging of cosmetics and toiletries is in principle no different from the packaging of any other product, but aspects of package design and development are of such prime importance in the successful marketing of cosmetic products that it has a more important role in this industry than in almost any other.

Packaging is very diverse, and utilizes a wide variety of materials such as plastics, glass, paper, board, metal and wood combined with a wide range of technologies including printing, machinery design and tool making. There is in fact no clearly defined packaging industry, since many companies in packaging also manufacture other products. The purpose of this chapter is to give a broad spread of information in this wide field; further details can be obtained from textbooks such as those of MacChesney,[1] Paine[2] and Park,[3] and from the *Modern Packaging Encyclopaedia*.[4]

Packaging has been defined as the means of ensuring the safe delivery of a product to the ultimate consumer, in sound condition at the minimum overall cost. Other definitions are:

> Packaging is the art or science of, and the operations involved in, the preparation of articles or commodities for carriage, storage and delivery to the customer (BSI *Glossary of Packaging Terms*[5]).

> Packaging sells what it protects and protects what it sells.

Principles of Packaging

Packaging must:

Contain the product
Restrain the product
Protect the product
Identify the product
Sell the product
Give information about the product

and do this within a cost related to the marketing, profit margin, selling price and image of the product.

Marketing and Packaging

The package projects the style and image, not only of the product, but often of the company which markets the brand. The pack must therefore project the

image that it has been designed for, not only to the customer through advertising and point of sale but also to the retailer and wholesaler chain.

Packaging is particularly important in the self-service retail trade. The package designer has a responsibility to ensure not only that the pack has the type of appeal that will make the customer pick it up and be encouraged to purchase on impulse, but also to ensure that the pack will stack on self-service shelves and give the retailer the maximum profit per linear unit of shelf space.

Advertising has ensured that the package is now more widely seen than ever before. With the predominance of colour in advertising—in television, cinema and press advertisements and on posters—the package must be made of materials that have good aesthetic appeal and which will take and hold colour.

TECHNOLOGY AND COMPONENTS

Plastics

The use of plastics for producing primary components and point-of-sale material now dominates packaging technology. Two main groups are used—thermoplastic resins and thermosetting resins. Thermoplastics can be extruded at their melt temperature and then blow moulded or injection moulded. After cooling, the resin can be remelted by heating to the limits of thermal fatigue and oxidation. Thermosetting resins, by contrast, are moulded using an irreversible chemical reaction and the resins tend to be rigid, hard, insoluble and unaffected by heat up to decomposition temperature.

Thermoplastic Resins

Polyvinyl chloride (PVC) is the most familiar of all plastics, certainly as far as the general public is concerned. The basic polymer varies from transparent to opaque. In its unplasticized state, known as UPVC, the product is rigid and is used chiefly for transparent bottles and blow mouldings of various kinds. Plasticized, or flexible, PVC is widely used in sheet form, either by itself or reinforced and supported by other materials, for flexible laminates.

Polyethylene is of the class known as polyolefins, which includes two types of polyethylene and an allied material, polypropylene. Low density polyethylene (LDPE) is the more flexible form. It has high cold flow characteristics with no indicated break point under flexing or impact; when formed into film, it can be stretched to cause an increase of up to 600 per cent in tensile strength, resulting from the realignment of molecules. It is chiefly used as film. About 70 per cent of output is in this form which can be used for packaging, and in building and horticulture. Its injection moulding characteristics are excellent and it is used for closures and fittings.

High density polyethylene (HDPE) is the stiffer, more rigid form of polyethylene with generally greater mechanical strength. Its chief use (about 40 per cent of output) is as a blow moulding material for bottles and small-to-medium size containers. HDPE does not mould as well as LDPE but finds outlets as polymer for injection moulded milk crates or general industrial pallets.

Polypropylene (PP) could be described as the best of LDPE and HDPE—at a competitive price. Its chief use is for blow and injection moulding in all kinds of

packaging. One particular quality is its high fatigue resistance which makes it popular for the manufacture of durable closures. To some extent PP is also used for making packaging film and extrusions.

Polystyrene (PS) is a rigid transparent material with excellent flow properties which allow it be formed into intricate shapes, so that it is principally processed by injection moulding. It is widely used for jars, bottles and mascara cases. It is somewhat brittle, but this can be remedied by mixing it with synthetic rubber to form toughened polystyrene (TPS) which is widely used for all types of packaging components where solvent attack is not a problem.

Expanded polystyrene (XPS) is used in sheet form for building and industrial insulation because of its low thermal conductivity. It is also moulded to provide close-fitting packs for fragile products and used as inert filler in secondary packaging.

Thermosetting Resins

The generic term 'aminoplastics' is used for plastics produced by reacting formaldehyde with amino compounds. These have the advantage of not being dependent on crude oil supplies for a feedstock and, because of this, in recent years have been in greater demand. Their applications range from electrical equipment such as switch plates, sockets or circuit breakers, to toilet seats, bathroom cabinets and work surface laminates. In packaging, caps and closures are the main uses. Generally aminoplastics are processed by compression moulding.

Phenolics (PF) are related to aminoplastics in that they are formed by a reaction between formaldehyde and phenol. Their general characteristics are similar but they are usually only available in black or brown, although they will accept paints without difficulty. Some grades can be injection moulded and compression moulded.

Plastics Technology

There are five main methods of converting plastic resin into packaging components:

(i) *Injection moulding* is used in thermoplastic conversion, where molten plastic is injected under pressure into a mould and allowed to cool. The mould is then split, the component is removed and the cycle repeated. This type of moulding is used mainly for caps, closures, fittings and small trays or boxes.

(ii) *Extrusion blow moulding*, again used in thermoplastic conversion, is a process in which a tube or 'parison' of molten plastic is extruded from a die. The tube is cut to length while still hot, and transferred to a blow mould where air pressure is applied through the tube, forcing it to expand into the shape of the mould. The mould is split, the component removed and the cycle repeated. Extrusion blow moulding is used mainly for bottles and jars.

(iii) *Compression moulding* is used in the conversion of thermosetting resins. The resin and catalyst are placed in a mould and held under pressure of up to 6000 psi (41 N mm^{-2}). The mould is then heated by steam, electricity or induction heaters until the reaction is complete (generally only a few

seconds). The mould is parted and the component is removed. The main uses in packaging are in high quality caps and closures.

(iv) In the process of *thermoforming*, a pre-extruded sheet of thermoplastic is placed over a table mould and the sheet is heated from above by infrared heaters. When the softening temperature of the sheet is reached, vacuum suction is applied from below the mould to pull the sheet tightly onto the mould table. The heat is switched off, the vacuum is released and the component is removed from the mould table. The process is used mainly for low quality trays and point-of-sale display items.

(v) *Injection blow moulding* is a combination of injection and extrusion blow moulding, and is used for bottles in which tight-tolerance neck and shoulder measurements are required. The parison, including the neck of the bottle, is first made in an injection mould and then transferred while still hot to another mould where the final bottle shape is blown.

It should be noted that all containers made from thermoplastics are permeable to air, perfume and water vapour to some degree, and furthermore the product may react chemically with the plastic. Full compatibility studies are essential, therefore, before packaging cosmetics in plastic.

Metals

The particular applications for which metals are most suited in cosmetics packaging are aerosol containers, powder dispensers, shallow tins and collapsible tubes. Tinplate is the most commonly used metal for the rigid packs, although aluminium also finds widespread use. As aerosols are by far the largest of these applications, the use of rigid tinplate and aluminium has already been discussed in the chapter on aerosol packaging (Chapter 40). The metal required for collapsible tubes has, on the other hand, to be readily deformable but must not fatigue or crack under stress. Suitable metals for this purpose are aluminium, tin and lead, when of the correct gauge and purity. The use of collapsible aluminium tubes in particular is extremely widespread, and almost all varieties of semi-solid, cosmetic and toiletry products, including emulsions, pastes and gels, can be purchased in collapsible tubes, but toothpaste remains the most popular application. The impervious nature of the metal gives the collapsible tube the great advantages of reduced risk of contamination of the product and reduced losses of volatile materials from the contents.

Lead. The use of lead for the manufacture of tubes varies to some extent with the availability and cost of the different metals in a particular area, but its use, particularly in Europe, is not widespread. Lead is more resistant to corrosion than aluminium, being much lower in the electrochemical series, and has been used for the packaging of products such as fluoride toothpaste that are acid and attack aluminium very rapidly. As lead can cause discoloration in some products, and as it might be a source of contamination, particularly undesirable in oral products such as toothpastes, the interior of lead tubes is usually lined with wax to reduce contact between the products and the metal. Apart from the high cost of lead tubes in many areas, their weight is an obvious disadvantage.

Tin. Tin (99·5% pure) has a great many properties which commend it for collapsible tubes and it held sway for many years in the first half of the century. However, by about 1950 the technology of aluminium had so improved that satisfactory tubes could be made from aluminium which was available in a purity of 99·7% at a considerably lower cost than tin.

In some places there has been an attempt to obtain some of the benefits of tin by using it in conjunction with lead, either as alloy or as an internal tin lining. Neither of these approaches has gained widespread acceptance, due largely to the large proportion of tin which has to be used to prevent contamination of the product by lead.

Aluminium. Structurally, high purity aluminium is a very suitable material for collapsible tubes as it is readily deformable, it is light, does not fracture under normal use conditions, and is totally impermeable to water, oils, solvents, and gases such as oxygen. Aluminium is, however, a reactive metal and one that is easily corroded. Compared with plastic tubes, aluminium tubes have the advantages of being impermeable and of being permanently deformable rather than flexible, so that there is no 'suck-back' on release of the tube, but they suffer from the disadvantages of having poor resistance to corrosion and of being rather unattractive in appearance when they have been squeezed or crumpled, particularly if there is a complex or colourful design on the pack.

When packing a product in an aluminium tube, careful attention must be paid to the problem of corrosion. Aluminium can be corroded by a galvanic action or a direct chemical reaction. Chemical attack is common at extremes of pH and corrosion is generally rapid and accompanied by hydrogen evolution. Very alkaline products such as depilatories and hair straighteners and acid products such as hydroquinone skin bleach creams cannot be packed in plain aluminium tubes. Internal coatings of lacquer, usually two, are required and in many cases, where the product is liable to strip the lacquer, a coat of wax over the lacquer is required. Galvanic corrosion of aluminium is very common and takes place under slightly acid or alkaline or, even neutral conditions if electrolytes are present. Migration of ionic dyestuffs is often a very good indication that galvanic action is taking place. It is accelerated by entrapped air, corrosion often taking place at the air–metal–product boundary, and also depends to a considerable extent on the purity of the aluminium. Sodium silicate is a very effective anodic corrosion inhibitor and can be used in mildly alkaline products such as chalk-based toothpastes and soap-based lather shaving creams. Corrosion in slightly acid conditions is rather more difficult to control chemically. Both types of corrosion can lead to hydrogen evolution and eventual blowing of tubes. The usual method of reducing or preventing galvanic corrosion is by internally lacquering the tubes so that the metal is insulated from the product. Vinyl, phenolic and epoxy resins are used as lacquers.

Laminates

The various requirements of packages for cosmetics and toiletries (such as attractive appearance; impermeability to water and volatile oils) are not always available from a single material. This problem can sometimes be solved by the

use of composite materials in laminar form. Laminates have found particular application in the production of sachets and of collapsible tubes as alternatives to pure metal tubes for toothpastes.

Laminates are used for *flat sachets* that are heat sealed around the periphery (as distinct from the fatter *pillow sachets* which are made from PVC tube and sealed ultrasonically). The laminate must be able to withstand the pressure of the contained product and provide leakproof seals. It must also prevent loss of water and other volatile substances such as perfume; these barrier properties can be provided by aluminium foil or by combinations of plastics with complementary properties, such as polyethylene and cellulose acetate films. Polyester films can be used to impart strength, and a paper layer will give both strength and stiffness. A typical three-ply laminate suitable for sachets is made up of cellulose acetate, aluminium foil and polyethylene, and a tougher four-ply laminate has a layer of paper between the aluminium and the polyethylene. Dweck[6] has described the manufacture of filled sachets from laminated materials.

Laminates for *collapsible tubes* aim to combine the appearance of plastics with the impermeability and collapsibility of aluminium. Tubes made from plastics material only—usually polyethylene, PVC or (to a lesser extent) polypropylene—do not collapse when squeezed: air is sucked back into the tube when the product has been dispensed. This is not acceptable for products such as toothpastes which are expected to be discharged as a continuous ribbon without air bubbles. A further disadvantage is that a plastics tube which retains its shape gives no indication of the amount of product remaining. The basic materials used for laminates to overcome these shortcomings are polyethylene film and aluminium foil, but complex combinations have been developed in order to achieve the desired properties. For example, a suitable laminate consists of polyethylene (or polypropylene) in contact with the product, then aluminium foil, polyethylene, paper and polyethylene.

A comparative review of the various metals, plastics and laminates available for the fabrication of tubes, together with a short description of tube filling and cartoning operations, has been given by Guise.[7]

Glass

Glass containers are still used widely in the toiletries industry by virtue of the basic packaging characteristics of glass. Glass is chemically very inert and generally will not react with or contaminate high quality cosmetic and perfume products; it has the approval of the US Food and Drug Administration (FDA) for a wide range of products. With a properly designed closure, glass is a 100 per cent barrier material and provides protection from oxidation, moisture loss or gain, perfume loss, etc. Glass is transparent, sparkles and provides an excellent point-of-sale display. Alternatively, for a product that is sensitive to light, amber glass or cartoning can be used. Finally, glass can be moulded into very attractive designs and provides an excellent brand or product image, especially at the high quality end of the market.

Glass is manufactured in many different formulations but the most common in packaging is soda lime glass composed as follows:

	per cent
Silica obtained from sand or quartz	72
Calcium carbonate (limestone)	11
Sodium carbonate (soda ash)	14
Aluminium oxide	2
Trace oxides	1

It is the trace oxides that provide colour to the glass, and green and amber containers are readily available. Trace selenium compounds are sometimes added as a decolorizer. An important 'raw material' in glass manufacture is the oil or gas required to melt the materials, which constitutes a very significant element in the cost of glass containers.

Glass Technology

The technology of glass making is thousands of years old but it is only in recent years that fully automatic methods have been developed for the manufacture of glass components. Molten glass is made in a furnace in a continuous flow, that is, the raw material input matches the rate at which the molten glass is drawn off. A furnace will run continuously for about eight years and during this time a temperature of around 1500°C must be maintained. The molten glass is fed to the conversion machines where the containers are made. Details of glass moulding processes have been described by Moody;[8] the basic techniques are the following.

The Suction Process. Molten glass is sucked into an initial or parison mould where the neck is formed. This parison shape is transferred to a blow mould where the final shape is made using air pressure.

Press and Blow Flow Process. A molten gob of glass of predetermined weight drops into the parison mould, a plunger presses the parison into shape. This is then transferred to a blow mould where the final shape is blown.

Blow and Blow Flow Process. The gob drops into the mould where the neck is formed, assisted by air pressure. A parison shape is then blown, which is then transferred to the final mould and the finished container is blown.

Glass, even with its inherent disadvantages of fragility and weight which generally cause transport and secondary packaging costs to be high, continues to provide the cosmetic industry with aesthetically pleasing, stable and high quality containers and bottles.

Paper and Board

Practically every cosmetic and toiletry product uses paper or paperboard in some form. Many grades of paper and board are available; the main types used in packaging are listed in Tables 41.1 and 41.2. Uses of paper and board in cosmetics packaging include labels, leaflets, corrugated cases, printed cartons and soap wraps.

Table 41.1 Main Types of Packaging Board

Type	Made from	Properties	Uses
Plain chipboard	100% low-grade waste, e.g. old newspapers	Cheap Prints poorly Light grey/tan colour Folds poorly	Rigid boxes Packing pieces
Cream-lined chipboard	Two layers: (a) cream liner from new pulp (b) as plain chipboard	Poor quality Folds satisfactorily	Low-quality cartons
Duplex board	Two layers, both from new pulp	Prints well Folds well Smooth surface	Quality cartons Point-of-sale displays
White-lined chipboard	Two layers: (a) white 100% chemical pulp (b) as plain chipboard	Prints well Folds well Smooth surface	Quality cartons Point-of-sale displays
Clay-coated boards	As duplex or white-lined + clay coat	Excellent print, fold and gloss	Top-quality cartons for high-price cosmetics
Solid bleached sulphate or sulphite boards	100% sulphate or sulphite pulps	Good strength Excellent print and whiteness Odourless for food contact	Frozen food, ice cream, etc.

Table 41.2 Main Types of Packaging Paper

Type	Made from	Weight ($g\ m^{-2}$)	Properties	Uses
Kraft	Sulphate pulp	65–300	Heavy duty paper	Corrugated case liners Multiwall sacks
Sulphite	Mixture of hardwood and softwood, i.e. mechanical and chemical pulp Usually bleached	34–300	Bright paper Prints well	Envelopes Foil lamination Labels Leaflets
Greaseproof	Heavily beaten pulp	65–150	Translucent Grease-resistant	Fatty products
Glassine	Greaseproof, calendered	39–150	Resistant to oil and grease Good odour barrier	Soap wraps
Vegetable parchment	Unsized paper treated with concentrated sulphuric acid	59–370	Non-toxic High wet strength Resistant to grease and oil	Mainly food products
Tissue	Any virgin pulp	20–50	Low strength Light weight	Wrapping of goods

Printing and Decoration

All packaging components can be printed to give a wide range of decorative effects. Different processes are used depending on the application. The five main processes used in the printing of packaging components are described briefly below.

Screen Printing
Method: porous stencil printing, in which a rubber blade forces ink through unblocked print areas of a screen. The screen is generally made from nylon sheet or, sometimes, silk.

Main packaging uses: printing of plastics and glass containers, point-of-sale display items.

Letterpress
Method: the face of the printed image is a raised surface above a metal blade—a relief print process. Ink is applied direct to the face and is transferred to paper or other printing surface directly.

Main packaging uses: all types of labels.

Flexography
Method: as in letterpress, but the raised image is made from a flexible rubber or composition plate. Similar in operation to a rubber stamp.

Main packaging uses: corrugated cartons and transit shippers, some films and labels.

Offset Lithography
Method: print and non-print areas are hydrophobic and hydrophilic areas in the same plane on the printing plate. The plate is wetted and the inked hydrophobic areas reject water and accept ink, whereas hydrophilic areas accept the water and thus reject ink. The image formed is transferred to a rubber-covered cylinder, which then transfers the ink to the printing substrate.

Main packaging uses: all types of cartons and high-quality metal containers.

Gravure Printing
Method: the reverse of letterpress. The image is made up from subsurface 'cells' etched into a metal cylinder. The depth of the cells varies according to the depth of ink to be transferred. The cylinder is inked, and excess ink is wiped from the surface by a wiper or 'doctor' blade. The ink in the subsurface cells is transferred to the printing surface.

Main packaging uses: long-run flexible package printing and label printing—a very high quality of work is achieved.

PACKAGE DEVELOPMENT AND DESIGN

Package development has the aim of increased sales and profit through the correct design of the package. Packaging must be considered as early as possible

in the development of a new product to allow time to ensure that pack and product are compatible. The development process begins with a detailed analysis of the product so that a pack can be designed to give protection. Marketing factors must also be considered—the pack must be suitable for the product and its market. Easy opening, convenience factors and ease of handling are of prime importance to the ultimate user. Graphics and aesthetic design should also be considered at this stage, any important related marketing criteria again being taken into account, and the interaction between the product and the primary container and other packaging should be investigated. Finally, in the development of the package the environmental aspects of the pack should be considered, not only in terms of disposability and litter, but also from the point of view of the re-use of scarce raw materials.

Technical Aspects of Design

The technical aspects of packaging design are rather diverse and too involved for any detailed discussion in this text, but, generally speaking, given a particular packaging material, the final pack must be sufficiently strong to survive any treatment that it is liable to receive from the time of first delivery at a factory, through to filling, distribution, sale and actual use. There is bound to be a certain failure of packs, largely due to accidents, but it is essential that this failure rate is very low if the product is to be a commercial success, and hence very strict testing and quality control of packs is essential in a factory producing toiletries or cosmetics. Typical problems that must be watched for in package design are thin areas in bottles, which are quite common in flat glass or plastic bottles, highly stressed areas, of particular importance when polyolefins are used, and very small radius convex areas on the outside of clear packs that can act as effective lenses for focusing ultraviolet radiation, and so concentrate its harmful effects on to small areas of a product. Bottles which are unstable on their bases can give rise to troubles on a mechanical filling line if they are unstable when empty, and to spillage and breakage in use if they are unstable when filled.

Not only must a pack be attractive to the consumer and contain the product in an efficient manner, but it must also render the product available as soon as the consumer desires to use it. There is nothing more infuriating to a consumer than a hand cream that will not come out of a bottle because the hole is too small, or a squeeze pack that squirts a direct jet of liquid rather than the expected fine spray. The simple example of a badly-judged orifice size is an extremely important one, as it is absolutely essential that the orifice size of a bottle or tube is correct so that the product is dispensed at the desired rate. Similarly, in the second example the orifice dimensions and design must be correct for the desired effect, that is a fine spray, but also the pack must be sufficiently flexible to allow the consumer to dispense easily the required volume of product. These points of orifice size and design, wall flexibility, and also general product accessibility in open containers such as jars, would seem to be somewhat obvious, but are factors that can be very easily overlooked and hence merit considerable emphasis.

Applicators are widely used for products such as antiperspirant–deodorants and the various forms of decorative make-up that require application to specific areas of the body. In the field of deodorants in particular, there has been

considerable activity in applicator design. Products in deodorant ranges can be obtained in the form of pressurized packs, finger-operated pumps, squeeze packs, roll-balls and sticks.

The roll-ball (or roll-on) type of pack is in widespread use and is particularly ingenious as it dispenses a convenient quantity of product only when the pack is actually applied to the skin. It usually consists of a glass or plastic bottle with a snap-on polyethylene housing containing a polystyrene or glass ball. On inversion of the pack the product flows through a hole in the centre of the housing on to the ball and can then be rolled on to the skin. The closure can be obtained in two ways, both of which are patented;[9,10] either a raised portion in the cap can be made to engage on the ball and push it on to a seating in the housing, so restricting flow, or the interior of the cap can be so shaped that, when it is replaced, the lip of the housing is compressed on to the ball, so giving the seal round the ball rather than below it. The development of the roll-ball applicator has been described by Hanlon.[11] Stick containers are generally polystyrene cylinders containing a polyethylene godet. The container containing the godet is used as a mould for the stick which can then be extended or retracted manually, or in more sophisticated packs by means of a screw device operated by revolving the base of the pack. It is of prime importance that the interior of the cylinder is true so that there is no possibility of evaporation of the water or alcohol in the stick past the godet. Lipstick containers can also be of the screw type and are generally made in metal. As evaporation is not a problem, lipsticks can be moulded separately.

Another interesting area, where there has been considerable activity, is in the design of collapsible tubes to contain two incompatible materials which are mixed on extrusion. A large number of patents have been filed for such a tube, which would have particularly wide application in the field of hair dyes and bleaches, but as yet no completely successful pack is available. A related design is that of the collapsible tube which dispenses product (usually a toothpaste) in a striped form. The separate parts of the extruded product may differ in colour but may also be different in other ways, for example clear gel and opaque toothpastes may be co-extruded. This is achieved by placing one product in a specially designed insert in the tube nozzle, so that, when the other product is extruded past the insert, the first product is drawn into the ribbon to form a stripe.[12]

Closures

No container, however perfect, is of any value unless it has an efficient closure. Ideally the closure should be easy to remove and replace, but should give a seal that prevents the diffusion of gases and vapours and the seepage of liquids. Many bottle and tube closures consist of a screw cap containing a compressible wad, but wadless closures—achieved by new designs of thermoplastic screw and snap-on caps—are now extensively used for liquid products such as shampoos and hair conditioners.

Caps containing wads are usually manufactured from a thermosetting plastics material such as urea- or phenol-formaldehyde, although metal caps are still sometimes used. Wads usually consist of a stiff base material such as wood pulp,

which can be treated in various ways. Wood pulp used alone gives only a poor seal but this can be very much improved by a coating of wax. This type of wad, however, has a rather poor resistance to moisture and oils and is inclined to become soggy on long-term storage. A more satisfactory wad for cosmetic packs is the vinyl-coated paper-faced wood pulp wad which is very resistant to moisture and oil, although the seal obtained on glass and metal rims is not particularly good. If products are to be packed that are sensitive to moisture loss, for example oil-in-water emulsions, the vinyl coating should be further coated with a layer of wax.

Where the neck of a container is small, as in a bottle, there is more choice of wadding material, as cork-backed wads can be used. Aluminium-foil-faced cork wads are quite common, but give a poor seal for oily materials. The vinyl-coated wads are rather superior in this respect, but are inclined to stick to the container and split when the cap is removed, if the product is resinous. Waxing should, however, overcome this problem. Solid, shaped flexible plugs or wads have also been used for bottles, particularly those with a sprinkler neck, where a central spike can be designed to engage in the sprinkler orifice to give a very effective seal.

The closures used for collapsible metal tubes are basically similar to those used for bottles. The caps are made of a thermosetting resin and the wads are usually of vinyl-coated paper-faced wood pulp. It is normally only necessary to use special wads where the product is air-sensitive or very sensitive to moisture loss, and in such cases solid polyethylene or polyethylene-coated paper-faced wood pulp wads are particularly suitable. An alternative is to use a solid moulded high-density polyethylene or polypropylene cap containing a flat area that seals on the neck of the tube. These caps give a good seal but are inclined to expand and loosen slightly at high temperatures. For extreme cases, to give a perfect seal, an aluminium tube with a pierceable membrane across the nozzle can be obtained. At the crimp end of an aluminium tube a latex end seal, an internal band of latex rubber about 6 mm in width, can be used to give a good seal, but care must be taken in filling to ensure that no product comes into contact with the latex. An end seal is not necessary, however, if the interior of the tube is waxed. In the case of plastic (polyethylene or PVC) tubes, a solid polypropylene cap is usual as the seal obtained between two fairly flexible plastics is usually quite adequate. Attractive designs for this type of package can be achieved by the use of caps of the same diameter as the body of the tube, so allowing stand-up storage on a shelf.

For some products with appropriate rheological characteristics, for example skin creams, the closure may incorporate a dispenser pump, so designed that a downward pressure causes the discharge of a fixed amount of product. Such dispensers are usually formed from a polyolefin material.

PACKAGE TESTING AND COMPATIBILITY

Testing

There are three main reasons for testing packaging materials and finished packs: to provide information vital to the designer to enable him to make effective

material selection; to assess the performance of a material in relation to the duty that it has to perform; and to provide an continuing check on quality.

Comparison of results is only valid if the same standard test method is used each time the test is performed, and the quotation of results without the relevant standard must be suspect. Therefore it is important to use an accepted standard method for testing whenever possible. Standard test methods are drawn up and published by national organizations such as the British Standards Institution (BSI), the American Society for Testing and Materials (ASTM), Deutsches Institut für Normung (DIN), etc., using panels of experts from industry and trade bodies, and are coordinated by the International Standards Organization (ISO). As with all testing procedures, a basic knowledge of statistical methods is essential, both in making sure that the sample selected for testing are representative, and in the interpretation of the results.

The main testing methods used in the packaging industry, both on materials and finished packs, investigate the following:

Mechanical properties, for example, compression, tensile, flexural and impact strengths.

Physical properties, for example, water absorption, moisture vapour transmission rates, accelerated aging, flammability and thermal conductivity.

Chemical properties, for example, resistance to the product or the chemical environment, and corrosion testing.

Compatibility

Compatibility testing is performed when the final product formulation and packaging system have been decided. Samples of the product should ideally be taken from trial batches, and the complete packaging system should be assembled using actual samples or pilot tooling samples representing the final component.

The general compatibility of the pack and product needs to be checked by storage testing which will enable an assessment to be made of the effect of the pack on the product as well as that of the product on the pack. It is important to remember that the effect of spillage on the outside of the pack is important, and should certainly be included in any testing schedule. For example, it is possible to formulate alcoholic products containing a small amount of non-volatile ester which have no effect on, say, polystyrene if the polystyrene is immersed in the product, but if the product is allowed to dry out on the surface of a polystyrene container, the evaporation of the alcohol allows a high concentration of ester to occur and this can dissolve in the polystyrene to make the pack sticky.

Shelf life testing is also necessary in order to determine the rate at which volatiles may be lost and this includes not only water or alcohol but the perfume. The assessment of loss of perfume can only sensibly be done by nose, although weighing will obviously allow determination to be made of the loss of solvents.

Finally, the convenience of any cosmetics pack must be tested by in-use tests as well as by laboratory tests and for this purpose it is necessary to take into account both the local customs and the climate of the country in which the product is to be marketed: for instance, bathrooms in the UK tend to be cold, and tests for pourability should reflect this; similarly, products for tropical countries should be tested in conditions of high temperature and humidity.

REFERENCES

1. MacChesney, J. C., *Packaging of Cosmetics and Toiletries*, London, Butterworth, 1974.
2. Paine, F. A., *Packaging Evaluation: The Testing of Filled Transport Packages*, London, Butterworth, 1974.
3. Park, W. R. R. (Ed.), *Plastics Film Technology*, New York, Van Nostrand Reinhold, 1970.
4. *Modern Packaging*, 1979, **52**(12).
5. BS 3130: 1973, *Glossary of Packaging Terms*.
6. Dweck, A. C., *Cosmet. Toiletries*, 1981, **96**(6), 17.
7. Guise, W., *Manuf. Chem.*, 1981, **52**(8), 24.
8. Moody, B. E., *Packaging in Glass*, London, Hutchinson Benham, 1977.
9. British Patent 740 220, Bristol-Myers Co., 17 March 1954.
10. British Patent 843 315, Owens Illinois Glass Co., 25 April 1958.
11. Hanlon, J. F., *Soap Cosm. Chem. Spec.*, 1981, **57**(6), 67.
12. British Patent 813 514, Marraffino, L. L., 11 June 1956.

Chapter Forty-two

The Use of Water in the Cosmetics Industry

Of all the raw materials used in the formulation and manufacture of cosmetics, water is almost certainly the most widely used. Without water, our range of cosmetic products would be drastically reduced, yet because it is relatively cheap and abundant, water is often taken for granted. We should not be so complacent: of all the fresh water on this planet (and there is not much of that) only 0·03 per cent is readily available to the world's population, which is growing at a staggering rate.

Properties and Cosmetic Uses of Water

Water is an extremely reactive substance, much more so than most of the raw materials of cosmetics. This is made manifest by its extreme corrosiveness—water rusts metals and rots animal and vegetable matter. It is surprising, therefore, that it should be physiologically innocuous—it rots dead, but not living, material.

Water takes part in four types of chemical reaction, namely oxidation, reduction, condensation and hydrolysis. All four are represented in the various biochemical processes in which water is involved. For this reason, water is an essential requisite of all living organisms—without water, life itself cannot exist. Once water is present, however, life of some kind will almost certainly be found. Moreover, water is distributed very heterogeneously among living organisms. For instance, the jellyfish is 97 per cent water, adult human beings 70 per cent and bacterial spores only 50 per cent, which seems to be about the lower limit at which life can continue.

In the manufacture of cosmetics, use is made of water as a solvent and a relatively innocuous raw material rather than as an essential biochemical ingredient. Among other applications, water forms a significant part of shampoos, bath products, spirituous preparations, soaps and emulsions. It is because of its easy availability and its cheapness that water plays an important part in these cosmetic products; it is, however, through neglect of the quality of the water used that many otherwise satisfactory cosmetic products can be made useless.

Composition of Mains Water

In many cosmetic-producing countries, water is available from the mains supply and may be obtained by the turn of a tap. Since pure water is an extremely

aggressive solvent, mains water will inevitably contain traces of contaminants and it is the presence of these that should be the concern of the cosmetic chemist. The identities of the contaminants that reach our manufacturing plants in mains water depend upon the original source of the water and upon the nature and the extent of any purification processes to which it may have been subjected by national or municipal water authorities. Generally, water from rural areas contains the following inorganic ions to varying extents: calcium, magnesium, sodium, potassium, bicarbonate, sulphate, chloride and silicate. In addition, the water may have a recognizable organic content, particularly humic and fulvic acids (polycarboxylic materials derived from the breakdown of natural vegetation), amino acids, carbohydrates and proteins (from decaying leaves), high molecular weight alkanes and alkenes (from algal growth) and possibly traces of organic sulphur compounds (from sewage effluent or contact with animal life).

From urban areas, more polluted water has a wider range of contaminants. Among inorganic traces to be found in polluted water are ammonia, phosphates, arsenates, borates, chromium, zinc, beryllium, cadmium, copper, cobalt, nickel, iron and manganese. Organic contaminants in polluted water include petrol, chlorinated solvents and traces of surface-active agents such as alkyl benzene sulphonic compounds (although the levels of these have been greatly reduced by the introduction of biodegradable surfactants). Whatever the origin of the water, it is almost certain to contain bacteria, viruses, pyrogens, moulds and yeasts.

Even relatively uncontaminated raw water from rural areas would no longer be deemed fit for municipal supply in most industrial countries today. Consequently, such water is purified before distribution. The object of such purification is not to produce completely pure water, but to produce potable water for general consumption that is pleasant to see, taste and drink and which contains nothing that is dangerous to human health. To reach this standard, the water is freed from most of the suspended solids, humic acids and living organisms but it still contains enough dissolved salts and gases to be pleasant to drink.

Water Purity Requirements for Cosmetics

Cosmetics were once made exclusively from mains water which had not been further purified. To meet today's high standards of product stability, however, two aspects of mains water contamination need to be investigated thoroughly.

The first of these is the inorganic ion concentration. Mains water, even after its initial purification, still contains the majority of its sodium, calcium, magnesium and potassium salts; it will also contain 50 per cent of its original concentration of heavy metals, particularly mercury, cadmium, zinc and chromium, as well as traces of iron and other materials that may be picked up from supply pipes.

In the manufacture of colognes and aftershaves (which usually contain between 15 and 40 per cent water), trace quantities of calcium, magnesium, iron and aluminium can give rise to the slow formation of unsightly insoluble residues—often made worse by the co-precipitation of the least soluble components of the perfume compound. In addition, the presence of phenolic organic

compounds such as antioxidants and UV-stabilizers can be the cause of discoloration in such cosmetics by reacting with trace metals to form coloured products.

In the field of emulsion technology, it is well known that the presence of large inorganic ions such as magnesium and zinc can, by interfering with the balance of static charges responsible for the proper functioning of certain surfactants, bring about the separation of otherwise stable emulsions. Even where complete separation is not caused, the presence of such ions in the water phase can give rise to extremely unpredictable viscosity characteristics in the cream or lotion, and similar viscosity effects can result in shampoos and other products containing surfactants.

The second aspect of unpurified mains water which should be of concern to cosmetic chemists is the presence in such water of micro-organisms. If micro-organisms are introduced into cosmetics and are allowed to thrive, the result will be spoilage of the product by the development of unpleasant odours, visible colonies of bacteria, moulds or fungi and eventually (in the case of emulsions) product separation—and all this in addition to potential harm to the consumer. Any cosmetic product containing even a surface coating of water is at microbiological risk and the most common source of such contamination is the water itself. Modern cosmetics manufacturing plants must therefore be supplied with water that is as free from microbiological contamination as is technically and economically feasible. (It is ironic, as will be seen, that a potential source of contamination with bacteria is the very apparatus that may be used to remove stray ion contamination from the water).

In general, the level of microbiological contamination of mains water from the tap is very variable; since microbes will multiply best in stagnant or quiescent water, the level of contamination by the time the water reaches the consumer depends not only on its purity on leaving the water authority's plant, but also upon the layout and frequency of use of the distributive system.

Further Purification of Mains Water

Deionization

The further deionization of mains water may be effected by means of ion-exchange systems, by reverse osmosis or by distillation. Of these, the most popular method is ion exchange.

In order to remove all ions from water completely, deionization systems comprise at least two types of resin—one to remove cations (and therefore called the cation resin) and a second, the anion resin, to remove anions. Figure 42.1 illustrates the principle diagrammatically. As the active sites on both types of resin become occupied with inorganic ions, the deionizer becomes increasingly ineffective until the feed water passes through the columns virtually unchanged. The resins must now be 'regenerated' in order to continue to function. During regeneration, the active sites are swamped with free hydrogen and hydroxyl ions by lengthy contact with strong mineral acid and base respectively, when the sorbed inorganic cations and anions are once more replaced by hydrogen and hydroxide. After thorough washing in deionized water, the resins are fit for use again.

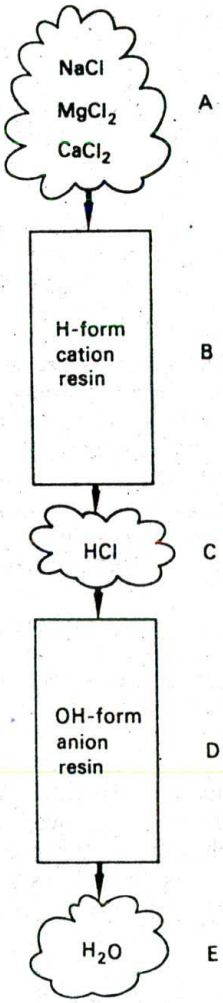

Figure 42.1 Principle of ion-exchange columns
The mains water (A) contains various inorganic ions to be removed by the process. The cation resin (B) through which this water passes is in the acid or hydrogen form. As water percolates through the resin beds, each cation becomes bound to an active site on the resin surface, replacing a hydrogen ion. Given a sufficient number of such sites and a long enough contact time between water and resin, quantitative replacement by hydrogen of all metal ions in the original solution is possible; the water then has the composition shown at C. This acidic water is now passed through the anion column (D) where a similar exchange of anions for hydroxyl ions takes place, so that the eluent at E contains a further concentration of hydrogen and hydroxyl ions equivalent to the quantities of ionizable inorganic impurities initially present.

Ion-exchange resins are used in three ways, each giving rise to a slightly different quality of water. In the first of these, the two resins are kept in separate columns (the 'twin bed' system). In this case, there is invariably a slight leakage of sodium salts from the cation column, to an extent depending on the ratio of sodium to total cation content in the feed water. Since these sodium salts leave the deionizer as sodium hydroxide, the purified water obtained from such a deionizer may have a pH as high as 10.

To overcome this problem, a second type of system exists in which both resins are mixed intimately together in one column (the 'mixed bed' system). This arrangement produces a higher quality water having a neutral reaction and an ionic concentration of less than 1 ppm. On exposure to the atmosphere, however, such water rapidly absorbs carbon dioxide to form carbonic acid and will therefore exhibit an acidic pH.

The third type of resin system combines a strong cationic with a weak anionic resin in either twin or mixed bed form. Naturally, such a system will not remove such weakly acidic materials as silica and carbon dioxide. The resulting purified water will therefore be undiminished in the concentration of these ionic species and frequently has a pH value of about 4. Such systems are used to purify water for the topping up of batteries or for glass-washing.

From a practical point of view, ion-exchange systems can be purchased or hired in three different forms: self-regeneratable, cartridge exchange or as throw-away resins.

As the name implies, self-regeneratable deionizers may be regenerated by the user either manually (by the manipulation of valves) or automatically at a pre-set time or when the effluent water reaches a predetermined quality. The convenience of the automatic type ensures that this is by far the most popular and such deionizers are available in twin or mixed bed form.

Cartridge deionizers, on the other hand, are usually of the mixed bed type, this being packed into a replaceable cartridge. When the mixed bed requires regeneration this cartridge is simply removed and replaced by a spare one containing fresh resin, the exhausted cartridge being returned to the manufacturer for regeneration. Depending on the uses to which they are put, cartridge deionizers have several advantages over the self-regeneratable variety. They produce purer water, shut-down time for regeneration is negligible (or nil if an automatic changeover device is installed), little skill is required, there are no chemicals to handle or effluent to dispose of and they are quick and easy to install. The main disadvantage is their comparatively high running cost, especially for larger throughputs of water. Throw-away cartridges are, as the name implies, designed to be discarded when they are exhausted. This is particularly useful in areas where regeneration facilities are not readily available.

Another type of ion-exchange technique in common use in the cosmetics industry is known as 'base-exchange' or 'water-softener'. In this case the feed water is passed over a cation resin in the sodium form. In this way, calcium and magnesium ions in the hard water are replaced by an equivalent number of sodium ions, so producing soft water. The equivalent ionic concentration of water treated this way therefore remains the same—only the nature of the cation changes.

Distillation

Ion-exchange resins do not provide the means for removing nonionic or weakly ionic contaminants from the water. In particular, deionized water may still contain pyrogens and, for this reason, distillation is sometimes used as an alternative or an adjunct to ion-exchange.[1] Although simple baffle stills are sometimes to be found in laboratories, the two most commonly used types of still for large volumes of water are the 'thermo-compression' and 'turn-back' types. The former, however, is difficult and complex to operate, while the latter utilizes comparatively large amounts of cooling water.

The latest development is to use multi-stage pressure column stills which require little or no cooling water. Generally, distillation is more commonly used in the pharmaceutical industry where the use of sterile water is a necessity. As a means of obtaining large quantities of pure water for cosmetic use, distillation is far too costly. The associated nature of the water molecule lends it a heat capacity and latent heat of evaporation which is disproportionately large for such a small molecule. If no heat is recovered from the distillation process, the minimum energy requirement for distillation is of the order of 0·8 kW of power for every kg of water distilled.

Ultrafiltration

Ultrafiltration is a simple and rapid method for separating dissolved molecules on the basis of size by pumping water through a filter of molecular size. Rates of throughput (up to 10 litres per hour) are far too low for this technique to be of much use for production purposes.

Reverse Osmosis

Reverse osmosis[2–5] is the most widely applicable of all the purification techniques involving membranes. The principle which gives rise to its name involves the forcing of water through a semi-permeable membrane from a concentrated solution to a weak one against osmotic pressure. Thus the concentrate becomes increasingly more concentrated in solutes. The value of this technique is that the dilute solution is exceedingly dilute: the membrane is able to prevent the passage of 95 per cent of inorganic ions, 100 per cent of bacteria and viruses and a very high percentage of other organic species, depending on their molecular weight.

As with the more familiar osmosis phenomenon, the membrane does not play a passive part, its nature and structure being of great importance to the efficiency of the process. Several types of membrane are available, but still the most widely used types are the anisotropic cellulose acetate and the hollow polyamide fibre. The latter suffers the disadvantage of being vulnerable to bacteriological attack, high temperatures and pH changes outside a narrow range, and this has led to the search for other anisotropic membranes, which are unfortunately more expensive.

Typical cellulose acetate membranes consist of a relatively dense non-porous layer (the 'active layer') with a thickness of 1500–2500 Å supported on a highly porous substructure which comprises the bulk of the membrane. This substructure contains about 55 per cent void space with pores of average diameter 20 Å.

Although the mechanism of rejection is not fully understood, it is apparently concerned with the formation of hydrogen bonds between the feed water and the membrane polymer, making the water less easily available to solvate the solutes.

The membranes are constructed in the form of cylinders capable of withstanding working pressures of 400–600 psi (2·7–4·1 N mm^{-2}), and the whole reverse osmosis device works on a continuous basis. Feed water passes across and through the membrane (through the 'active' layer first) and is collected as purified water on the other side of the membrane. Approximately 75 per cent of the feed water is collected as purified and 25 per cent continuously discarded as concentrate.

Reverse osmosis plants are available to suit almost any usage rate of water and, apart from the high initial capital cost, are an ideal way to provide pure water for cosmetics processing. The membranes need replacing typically at intervals of 5–10 years for continuous operation.

Microbiological Purification

In the UK, mains water from the tap is far from sterile. Plate counts of between 10^2 and 10^3 organisms per ml are often obtainable and if the supply is from storage tanks (commonly used in the cosmetics industry) these counts can easily reach 10^5 or 10^6 organisms per ml. The types of organisms that will actually thrive in tap water are limited to those of meagre nutritional requirements—largely Gram-negative types of which *Pseudomonas*, *Achromobacter* and *Alcaligenes* are representative. These, however, are precisely the organisms that will proliferate most readily in aqueous-based products such as emulsions.

Other types of organism may, once they have found their way into the water supply, survive the chlorination procedures and adapt to a non-proliferating form until suitable substrates become available—even spore-forming varieties can behave in this way. On leaving the treatment plant, however, the municipal water supply is likely to be free from pyrogens, algae and viruses and therefore the factory supply should also be free of these contaminants unless they are picked up in the supply pipework.

The raw material, before further purification, may therefore already be contaminated with micro-organisms to an unacceptable degree. Passage over ion-exchange resins can cause even higher contamination levels: these resins form an ideal breeding ground for microbes since they contain large areas of thin films of stagnant water. Even the manufacturing plant itself may not be free from contamination—every pump, metering device, joint, pipeline, gauge and valve can provide a stagnant pool of water in which microbial growth can take place.

There are five practical methods for the reduction or elimination of microbiological contamination of water in the cosmetics plant: chemical treatment, heat treatment, filtration, UV treatment and reverse osmosis. These may be used separately or in combination.

Chemical Treatment. Contaminated resin beds and distribution systems can be sterilized and cleaned by the use of dilute solutions of formaldehyde or of chlorine (usually in the form of hypochlorite solution). Before the resins are treated they must be completely exhausted by prolonged contact with brine; if this is not done, formaldehyde is likely to be converted into paraformaldehyde

(a polymer) and hypochlorite may give rise to free chlorine gas. The usual method of treatment is to leave the beds in contact with a 1 per cent aqueous solution of either chemical overnight.

Once water has passed through the deionizer, one method of ensuring that micro-organisms cannot thrive in the storage tank or supply system is to dose it with a very low concentration of either disinfectant. Cosmetics plants can be maintained at levels of contamination of less than 100 colony-forming units by dosing the post-deionized storage tank with between 1 and 4 ppm available chlorine (5 ppm is just detectable by smell without any apparent detrimental effect on the vast majority of cosmetic products). In order to achieve this, however, constant monitoring of the levels of chlorine must be carried out and re-dosing effected once the chlorine level falls below 1 ppm.

A less usual means of achieving sterile or near sterile water involves treatment with preservative and heat. For example, a 0·1–0·5 per cent solution of methyl parabens when heated to 70°C gives almost sterile water which can be used for cleaning out plant.

Heat Treatment. The decontamination of process water by heat treatment in the cosmetics industry is carried out most frequently in the process vessel itself. The vessel is charged with the appropriate quantity of water which may be heated to 85°–90°C and held at this temperature for at least 20 minutes. Such treatment is sufficient to eliminate all the common water-borne bacteria but will not destroy spore-formers—in the unlikely event of any being present. (In fact heat treatment such as this is likely to cause any spores to germinate. If spores are suspected to be present, the same heating procedure should be repeated a second time after the lapse of two hours and, for absolute safety, for a third time two hours later still.)

An alternative arrangement is available which heats the water to 120°C in a thin film and then instantaneously cools it again. This is an in-line device known as a UHST treatment unit ('ultra high short term'). It is claimed that such units are able to destroy all bacteria.

In some pharmaceutical manufacturing plants where sterilized water has to be stored, the storage tanks are maintained at a constant heat of 70°C to prevent the growth of any stray contaminants which may have escaped the sterilization procedures.

UV Radiation. Ultraviolet radiation of wavelengths below 300 nm has been shown to destroy most of the micro-organisms that commonly contaminate water—including viruses, bacteria and most moulds. The mechanism by which the organisms are killed appears to be the photochemical effect of such UV radiation on the DNA and RNA content of their thinly protected nuclei. Since light of this wavelength does not penetrate very far through water, however, the supply has to be brought into very close contact with the UV sources to prove effective; in effect, this means that the water has to be spread into a thin film, thus providing a restriction in the supply system and cutting down the flow rate.

Although UV sterilization is a useful means of microbiological control in some types of installation, care must be taken to ensure that the efficiency of the source does not become impaired either by the build-up of slime around the

source or the inevitable deterioration of the source itself. As with all cold methods of sterilization, UV radiation is never completely effective—a few organisms usually manage to escape even the most efficient systems and these will thrive and multiply if they are allowed to.

Filtration. In theory, all known bacteria can be removed from water by passing it through a filter having a pore size of 0·2 μm or less. Practically, such filters exist in cartridge form and are sometimes recommended as an in-line method of sterilizing water in cosmetics plants either alone or in conjunction with other means (although 0·45 μm filters are sometimes suggested as a more practical alternative).

While it can be shown that membrane filters can very effectively remove microbiological contamination from water, the method has a number of drawbacks. These filters create a very high resistance to flow and are extremely expensive to replace—running costs can be disproportionately large compared with other methods. A more fundamental objection, however, is that eventually the build-up of organisms caught in the filter matrix increases the resistance to flow of water until eventually the pressure reaches a point at which some organisms break through the membrane or the water ceases to flow at all. Moreover some organisms—particularly moulds—are able to multiply in the membrane matrix and literally grow through to the other side. The rate at which this happens depends upon the volume of water passing through and its level of contamination. Installations employing the constant recirculation principle are especially susceptible, since the constant passage of water through pumps and filters warms the circulating water and speeds up the rate of growth of organisms trapped in the membranes. For these reasons, many people believe that it is fundamentally wrong to use membrane filters to hold back living organisms in this way.

Finally, it should be noted that only distillation, ultra-filtration and reverse osmosis give water which is free from pyrogens.

Distribution Systems

The quality of the water obtainable from a practical piped distribution system depends substantially on the quality of water entering the system (if this is poor, there is no hope of obtaining good quality of water at the point of use), the nature of the materials which come into contact with the water; the design of the system and the maintenance of the system. Of these factors, the first has already been discussed in some detail while the second is usually assumed, for cosmetics purposes, to be relatively unimportant. This is far from true, however.[6–8]

There are two good reasons for concern about the nature of the materials from which the distribution system is constructed: the likelihood of contamination by substances leaching out into or reacting with the water, and the ease of cleaning the system. The ideal material from which to construct pipework for water distribution is probably stainless steel, but the prohibitively high cost normally precludes its use in most cosmetics plants. It is theoretically possible to manufacture pipework from other non-corroding metals, but such materials are

also relatively expensive and difficult to join together in such a way as to exclude bacteria and air. Many distribution systems employ plastic pipework, especially pipes fabricated from unplasticized polyvinyl chloride, polypropylene and acrylonitrile–butadiene–styrene (ABS). All three materials suffer the disadvantage of not being able to withstand sterilization by live steam and each contains a variety of additives that could leach out and contaminate the water. Such additives include catalysts, pigments, plasticizers, antioxidants, lubricants, stabilizers, antistatics, high impact modifiers, and monomers or low molecular weight polymers.

In practice, many cosmetics installations have been constructed of plastic with no obvious detriment to the products although it would be foolish to assume that interaction between product and contaminant could never occur.

Physical Layout of the Distribution System

The choice of material from which the pipework is to be made is only one design element of a distribution system which has to be decided upon. The choosing of the physical layout of the system is a very important part of the design process; even the best equipment will create serious problems in use if it is not correctly chosen for the purpose and connected together in a sensible and appropriate manner.

Probably the first step in this process is to decide which type of deionizer is to be used, bearing in mind the quality and quantity of water required, the level of expertise for use and maintenance that is available and the running and capital cost limitations that have to be met. This will to some extent help in the choice of equipment for controlling the microbiological quality of the water: filters, UV, chemical treatment or perhaps a combination. The distance over which the system is to stretch and the minimum number of outlets needed also has to be fixed before the first draft drawings can be made. The design engineer should then be in a position to decide on the fundamental features of the layout and, in particular, whether to choose a centralized or a peripheral purification system and whether to choose a 'ring main' or a 'dead leg' distributive system. These features are illustrated in Figures 42.2–4.

Figure 42.2 represents a conventional ring main, constant circulation system in which the water is continuously circulated through the pipework, the deionizer, the filters and/or UV sterilizer and back to its start point again. Thus circulation takes place 24 hours per day whether or not water is being drawn off, so that the system, if properly designed, has no dead spots where stagnant water can accumulate. By being continuously pumped through the purification system, the water improves in quality with every pass.

Provided that the pipework is properly laid out with no sagging or tight bends and that the take-off valves have a minimum of dead space within them, the constant circulation system has been shown to be very effective in supplying water of good quality. Its chief disadvantage is that the filters clog rapidly if the quality of the raw water coming from the mains is not good to start with. Once bacteriological growth begins in the filter system the increased pressure so generated and the constant passage of water through other restrictions in the layout can lead to a considerable rise in temperature, so encouraging further unwanted growth.

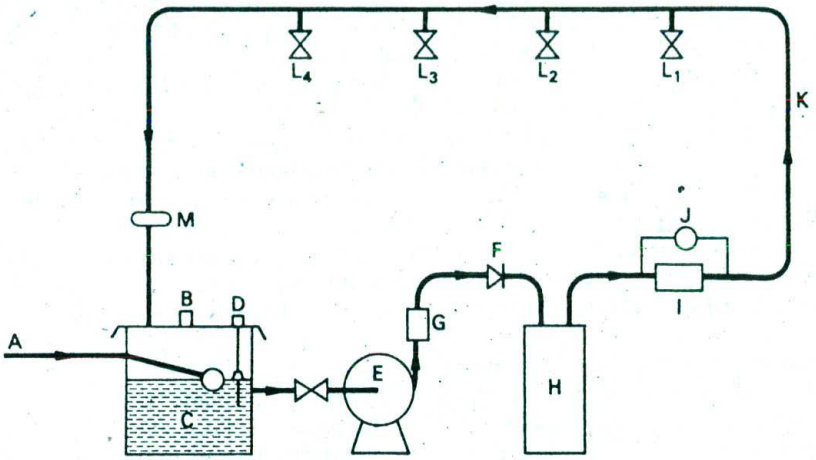

Figure 42.2 Ring main circulation system
The raw water supply (A) feeds directly into a break tank (C) fitted with a ball valve, a sealed top, a bacteriological air-filtered breather tube (B) and low-level float switch (D). The pump (E) pushes the water via a non-return valve (F) through a coarse pre-filter whose purpose is to protect the deionizer (H) from any suspended particulate matter. The deionized water emerges from H via microbiological control (I) (filter system or UV sterilizer) and on to take-off points L_1–L_4, finally returning via a constant-flow tank (M) to the break tank.

The popularity of the ring main system (especially with the suppliers of water purification equipment), has led to the underrating of the 'dead leg' system (Figure 42.3). The obvious disadvantage of such a system is that water lies stagnant in the pipes when it is not actually being drawn. Nevertheless, 'dead leg' layouts have proved their worth in certain circumstances, particularly in small plants where the distribution pipework can be kept short and all the take-off points are frequently used. Figure 42.3 shows two such deionizers installed in parallel. With the proper microbiological and chemical monitoring that is essential for any well-run purified water system, whatever its design, such a 'dead leg' layout can be effective, comparatively trouble-free and inexpensive to run.

For larger plants and where especially pure water is required, a decentralized system such as that shown in Figure 42.4 may be appropriate. In such a system, each take-off point is fitted individually with a deionizer and a microbiological control device. It will be obvious that high installation cost is a serious disadvantage of a layout of this kind; nevertheless in appropriate circumstances it represents the safest and most trouble-free system of all.

The range of possible designs is not limited to the three described here: combinations of all these illustrated layouts can be used as well as additional features such as cooling columns and UHST treatment units. Before installing any system it is wise to contact a reputable manufacturer of water-treatment equipment for advice on the most appropriate design.

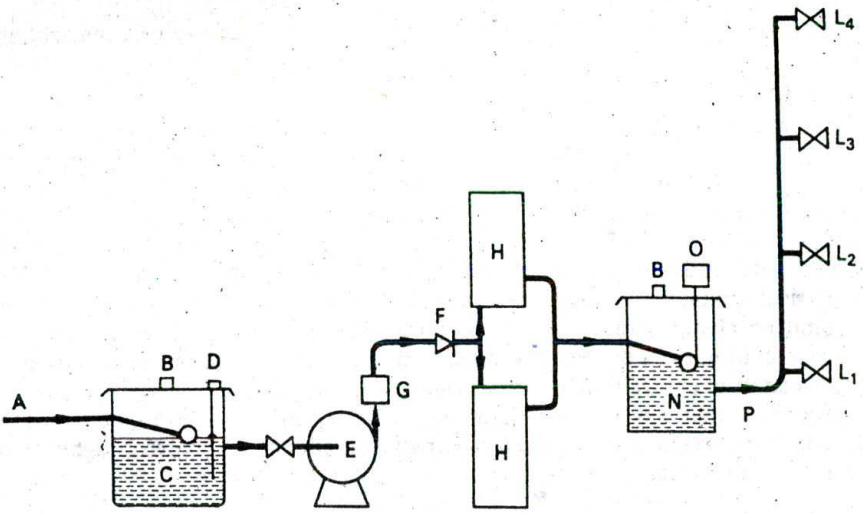

Figure 42.3 'Dead leg' distribution system
Water is pumped into a storage tank (N) fitted with a tight lid, a microbiologically filtered breather (B) and a chlorine dosing unit (O) which keeps the chlorine content of the water constant at 1 ppm. The distribution is gravity fed via a very short run of pipework (P). Before use, sufficient water is run to waste from each take-off point to empty P, thus ensuring that water that has remained stagnant in the part of the system after N is not used.

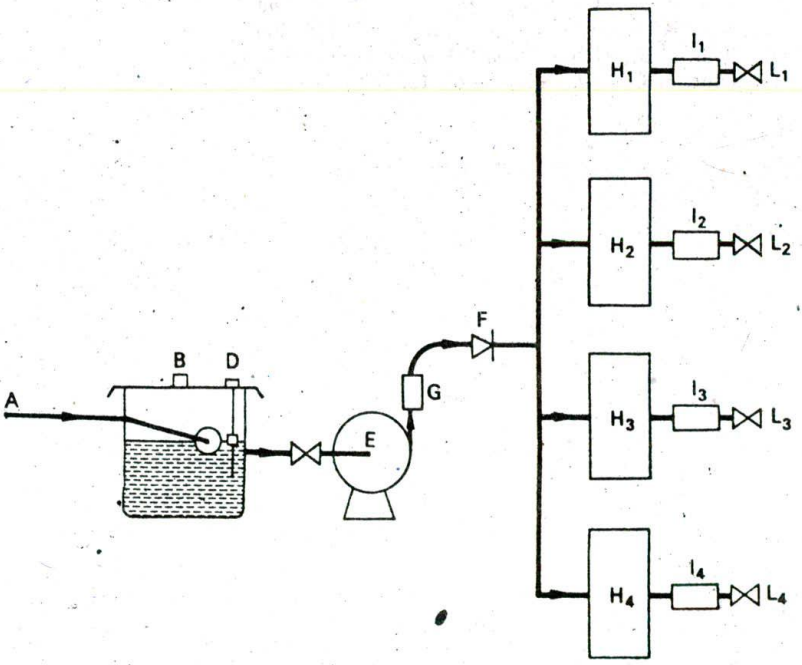

Figure 42.4 Decentralized distribution system (key as Figures 42.2 and 3)

Good Housekeeping

No matter how well it is designed and made, no purified water system is proof against neglect and bad management. Good housekeeping should begin at the time of installation by ensuring that all piping and fittings are stored carefully in clean conditions and that all end-caps and other dust-exclusion devices are properly fitted. After the system has been commissioned, it is essential to keep tanks clean and to change filters and UV lamps with sufficient frequency. The electrical conductance of the water should be monitored regularly and resins should be changed or recharged in good time. Similarly, the microbiological contamination must be checked at least once a week and the whole system must be cleaned chemically at the first sign of trouble.

Provided that it is properly designed, fitted and maintained, a modern water purification system can be relied on to give an adequate supply of highly pure water at all times.

REFERENCES

1. Shvedov, A., *Med. Tek.*, 1974, 36.
2. Reid, C. E. and Lonsdale, H. K., *Industrial Processing with Membranes*, ed. Lacy, R. E. and Loeb, S., London and New York, Wiley-Interscience, 1972.
3. Loeb, S. and Sourirajan, S., *Adv. Chem. Ser.*, 1963, **38**, 117.
4. Carter, J. W., Psaras, G. and Price, M. T., *Desalination*, 1973, **12**, 117.
5. Carter, J. W. and De, S. C., *Trans. Inst. Chem. Eng.*, 1975, **53**, 16.
6. Packham, R. F., *Water Treat. Exam.*, 1971, **20**, Parts 2 and 3.
7. Goodhall, J. B., *Manuf. Chem. Aerosol News*, 1973, **44**(9), 58.
8. Conacher, J. G., *Filtr. Sep.* 1976, **13**, 251.

Chapter Forty-three

Cleanliness, Hygiene and Microbiological Control in Manufacture

Introduction

The control of quality begins before any material is purchased, continues throughout manufacture, assembly and distribution and cannot be 'inspected into' a product at the end of the manufacturing process. Products of high microbiological quality do not just happen; they are so designed from the earliest stages of manufacture. Frequent occurrence of low-level microbial contamination of the finished product is a warning that the equipment on which it was made may not have been adequately sterilized. Finished product testing is a measure (and only a measure) of good manufacturing practice. Appropriate precautions should be taken against product contamination risks of all kinds. Insanitary processing and filling equipment can also be detrimental to the finished item. Dust, dirt or irregular air flow in the manufacturing area can easily compromise an otherwise acceptable product[1] and there should be a cleaning routine for all equipment and manufacturing areas. Toilet and washing facilities must be appropriately located, designed and equipped.

The following are some of the essential requirements for manufacturing a quality cosmetic:

The maintenance of clean premises
Attention to personal hygiene of operatives
Development of an effective cleaning and sterilization programme
Continuous monitoring of the water supply
Adherence to rigid microbiological criteria for raw materials
Incorporation of an adequate preservative system
Continuous microbiological monitoring of all stages of the cosmetic in production

The presence of micro-organisms in large numbers in cosmetic preparations is undesirable because spoilage of the product may result. The product can change in colour, odour or consistency, or manifest visible growth. Furthermore, the presence of microbial contaminants constitutes a potential hazard to public health, although reports of infections traced to contaminated cosmetics are rare. These problems were emphasized in the early 1970s by several surveys of cosmetic products on the US market; one showed a high proportion to be contaminated, some with bacteria counts as high as 12×10^6 per ml. A survey by the US Food and Drug Administration also showed a fairly high rate of heavy microbial contamination.[2]

SOURCES OF CONTAMINATION

Environment

Control of the manufacturing environment significantly reduces the risk of product contamination. Floors and wall surfaces should be impervious and resistant to antimicrobial agents. Walls should be washed periodically and floors should be washed each night. Puddles, dirt and debris should be removed as soon as practical. Drains on the floor should be kept covered and should receive particular attention as they can easily become sources of contamination. Air flow through production areas should be minimized. Air ducts, light fittings and other piping can create problems unless they are routinely cleaned. In general, an acceptable and effectively controlled production environment requires all exposed surfaces to be kept clean. Other potential hazards of contamination are cleaning utensils—buckets, mops, brushes, etc., should themselves be kept in a clinically clean condition. Sinks and areas where equipment is washed should be kept clean at all times. Traffic through production areas must be restricted to essential personnel and necessary equipment.

The factors mentioned above must be carefully considered as all can influence the microbial content of the environment. Although the product itself may be protected by the use of preservatives, the load of micro-organisms present in the environment of manufacture may affect the long-term activity of the preservative system. The presence of large numbers of micro-organisms in the manufacturing atmosphere will shorten the period of preservative efficacy. A product manufactured in a contaminated environment will have a reduced preservative activity and as a result, when some of the contents are withdrawn from the pack, further contamination may occur and present a hazard to the consumer.

Factory Buildings

Buildings should be constructed to protect as far as possible against the entrance and harbouring of vermin, birds and other pests. The buildings should be effectively lit and ventilated with air control facilities appropriate both to the operations undertaken within them and the external environment. Certain areas should not be used as a general right of way for materials or personnel passing through to other parts of the factory. Laboratories, processing areas, stores and the factory in general should be maintained in a clean, neat and tidy condition, and free from accumulated waste. Waste material should be collected into suitable receptacles for removal to collection points outside the buildings. It should be then disposed of at regular and frequent intervals. The operations carried out in any particular area of the premises should be such as to minimize the contamination of one product by another.

Floors and Walls

Floors should be made of impervious materials, laid to an even surface, and free from cracks and open joints. They should be maintained in a good state of repair. Dust, dirt and other contaminants that may be carried into manufacturing and filling areas on the soles of shoes and on trolley wheels can be collected on special plastic screens that pick up such material on their surface, have good non-slip properties and are easy to maintain.

Walls and ceilings should be finished with a smooth, impervious and washable surface and maintained in a good state of repair. Pipework should not contain uncleanable recesses and should be effectively sealed into walls and partitions through which it passes. Extraction fans should be sited to avoid cross-contamination hazards caused by intake or exhaust.

Equipment

Frequently, equipment is purchased with little regard for ease of clean-up or sanitization after breakdown. Before new equipment is bought, not only should rate of output be considered but also the susceptibility of the product to contamination. A piece of equipment may be installed in a manufacturing or filling area where there is no one who really knows how to dismantle, clean or sanitize it properly.

Hygienic considerations are often neglected in equipment design. Cooperation between production managers and microbiologists is essential and this applies even to minor modifications to existing equipment. Equipment should be made of materials capable of withstanding conventional cleaning methods, such as the use of steam, detergents and chemical antimicrobial agents; the most efficient and widely used material is stainless steel. Other essential components of production machinery such as gaskets, fittings, tubing and rails should also receive proper attention. Hoses that are old, cracked and decaying and equipment with crevices and corners are nearly impossible to clean and sanitize properly. Pumps that are old or frequently taken apart can be a major source of contamination. Such hazards can be avoided by establishing routine cleaning and maintenance procedures. Discretion and a general awareness of all aspects of sanitary hygiene on the part of the microbiologist and the engineering personnel enable appropriate equipment choices to be made and routine maintenance procedures to be established, so that unnecessary clean-up and prolonged stoppages in processing and filling are avoided.

The Manufacturing Process

Potential sources of microbial contamination during the manufacturing process can be summarized as follows:[3]

	Cause of contamination
Storage	Airborne micro-organisms
	Inadequate cleaning of vessel/tank
Filling	Airborne micro-organisms
	Transfer via filling machine
	Transfer via container
	Transfer via operator

Unsuspected Sources of Contamination

Where all reasonable precautions have been taken but sporadic and serious outbreaks of infection still occur, the source is likely to be an unsuspected reservoir of contamination. The underlying cause is probably among the

following:

Poor communication between management and staff
Poor supervision, especially early in the morning
Poor hygienic design of equipment or layout
Changes in cleaning/sterilizing procedure, introduced to reduce costs
Rapid staff turnover
Assumptions made without verification by laboratory test

CLEANING AND DISINFECTION

The utmost care taken in formulating a quality cosmetic, in purchasing raw materials to high specification and marketing elegant cosmetics can be defeated by failure to exercise the same strict control over the cleaning and sanitation of buildings, plant and equipment and over the conditions of bulk manufacture, filling and storage of products. Effective cleaning, when viewed as part of the normal production cycle, requires not only a detailed knowledge of the manufacturing operations and plant but also an appreciation of all aspects of cleaning. The decisions to be made relate to the labour requirement, the cleaning equipment, the detergents and the standard of cleanliness required. The following important considerations must be taken into account:

1. The quality and therefore the value of the end product depends essentially on the cleanliness of the production plant.
2. The sterilization capacity of the product is a function of the initial microbial count.
3. The shelf life of creams, lotions and powders that are made from sterilized ingredients is affected by reinfection during manufacture and filling.
4. Production of pathogenic micro-organisms such as staphylococci, *Pseudomonas*, coliforms, clostridia and *Candida* must be prevented.

Cleaning schedules can only be established by careful study of the problem, an appreciation of what is required, and a knowledge of how cleaning and sterilization are best carried out.

The Cleaning Logbook

Despite the exercise of every care in the cleaning and sterilization of equipment and plant, unexpected problems and unusual situations may occur. These can be detected easily by the senior staff of the production area if the senior cleaner or the operatives in manufacturing areas are responsible for keeping a logbook of daily occurrences reported. The supervisor or manager responsible can quickly make himself familiar with any variation from the expected pattern and take remedial action. When poor microbiological results are obtained from manufactured bulk or filled finished product, reference to the cleaning logbook can help to identify the cause if it lies in a variation in cleaning procedure.

Cleaning Staff

Because of the failure to appreciate that efficient cleaning can materially contribute to the total profitability of the business it has too often been a custom

in the past to employ for this purpose labour considered unsuitable for other activities. This is a grave error, for failure by these employees in the intelligent performance of their duties can do greater harm to a company's products and reputation than a mistake by the more highly regarded production line employees. Staff of suitable quality should be engaged, their role in the business should be explained to them and they should be instructed in the type of plant employed in the factory, and the cleaning equipment, procedures and materials to be used.

Cleaning staff should be supplied with overalls, rubber gloves, rubber boots and hats. Arrangements should be made to replace this equipment where necessary with adequately clean items in order to minimize the possibility of cross-infection from dirty clothing. The cleaner should be provided with a composite cleaning kit comprising brushes, abrasives, detergents and sterilants. Cleaning procedures will not be carried out correctly and within reasonable time if the cleaner has to interrupt his work to look for cleaning materials, and a trolley to carry this composite cleaning kit is strongly recommended. Also advantageous would be an equipment cupboard with glass sliding doors for stocking cleaned equipment; cleaning personnel should be given the responsibility for maintaining it in a scrupulously clean condition.

Many of the cleaning and disinfecting materials described later in this chapter are potentially hazardous, so it is essential to instruct and train cleaning personnel to handle them in a completely safe manner. Supervisors must know about the toxic properties and dangers of the chemicals used and be aware of suitable treatments for injuries arising from mishandling.

Equipment Cleaning

However well designed the equipment may be, unless the method of cleaning is effective all the design efforts will be nullified. Establishment of an effective cleaning method requires:

(a) An appreciation of the type of plant and equipment used, with special reference to the type of contamination likely to occur and the consequences of failure to remove it.
(b) Instruction in the need for a planned and rational approach to cleaning.
(c) The selection and use of appropriate cleaning equipment.
(d) The selection and use of correct detergent concentrations.
(e) The selection and use of correct sterilant and sterilant concentrations.

The method to be employed to clean a specific item of equipment will vary according to the nature of the product being processed and the quality of the surfaces, but certain general principles can be established (Figure 43.1). The equipment should first be dismantled and all product residues removed. Any part of the equipment that comes in contact with the product should be removed and cleaned: all processing vessels, pumps, hoses, valves, storage cans, various hand utensils, and the filling equipment should undergo this cleaning process. Inaccessible parts of this equipment should be given extra attention. This preparation may take a long time, but it is well worth the effort if a serious contamination problem is thereby avoided.

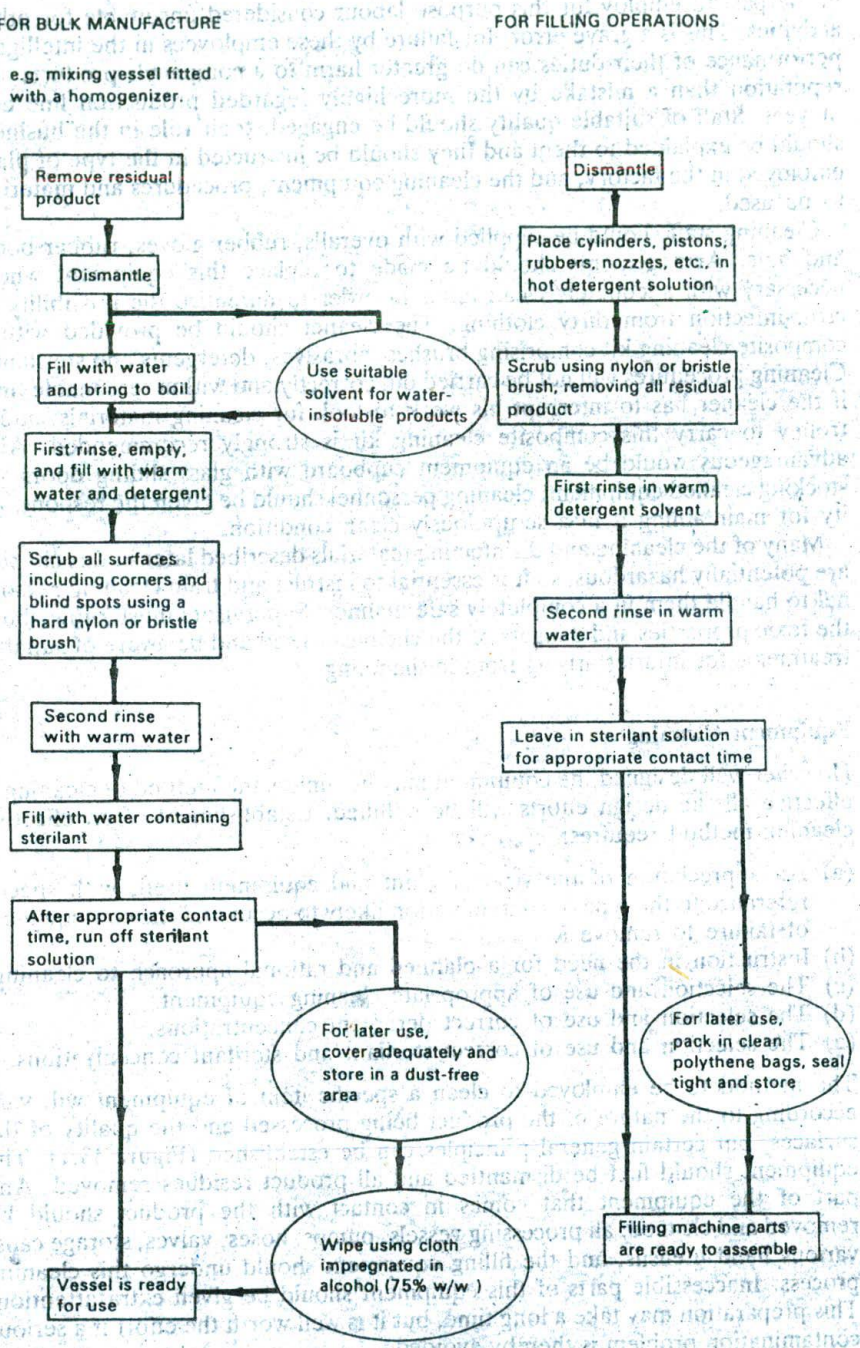

Figure 43.1 Sequence of equipment cleaning and sterilization operations

Detergents

Detergents employed in cleaning plant and equipment must be able:

(i) thoroughly to wet the surface to be cleaned;
(ii) to remove the residual product from the surface;
(iii) to hold the removed product in suspension;
(iv) to resist deposition of the residual product on dilution, that is, have good rinsability.

In addition, other factors need to be considered in choosing a suitable detergent, such as:

Prevention of corrosion
Dissolving and emulsifying action on cosmetic solids, that is, emulsification of dried cosmetic product.
Prevention of scale formation
Quick and complete solubility
Economy in use

No single detergent or class of detergents can meet all these requirements, and hence a vast range of detergents is offered for both domestic and industrial purposes. They fall into four main categories:

Soaps
Synthetic soapless detergents
Alkaline detergents
Specialized detergents

Soaps. Soaps are produced in flake, bar, tablet, liquid and powder form. Flake and powder soaps are used for laundry processes, tablet soap for personal hygiene, liquid soap for cleaning equipment, plant, etc. Soaps, however, lack the powerful wetting action of synthetic detergents and the powerful dissolving properties of alkalis.

Synthetic Soapless Detergents. Synthetic detergents are divided into four classes:

Cationic detergents
Anionic detergents
Nonionic detergents
Amphoteric surface-active agents

Cationic detergents are not normally used for detergent purposes but some are employed as sterilizers, since they possess bactericidal properties. The quaternary ammonium compounds belong to this group.

Anionic detergents, to which class belong the sulphated fatty alcohols and alkyl aryl sulphonates, are the most widely manufactured synthetic detergents.

Nonionic detergents have certain unique properties. In general they are unaffected by any ionic reactions, for example they do not react with the hardness of water. Foaming is generally less than with the anionics and their ability to remove oily product residues is excellent.

Amphoteric surface-active agents: amphoteric compounds exhibit the property of being able to function either as acids or as bases—the electrochemistry of the molecule depends on the pH of the medium in which it is present. They exhibit a very marked degree of detergent activity. In working solutions amphoteric compounds produce good wetting and penetrating effects and efficient grease-dissolving and cleaning action. Solutions at 0·5–1·0 per cent in water show adequate microbiocidal activity and therefore these are widely used as sterilant–disinfectants.

Synthetic detergents lack the powerful dissolving properties of alkalis.

Alkaline Detergents. Alkaline detergents (for example, solutions of sodium hydroxide or alkaline phosphates used with treatment times of at least 30 minutes) are very effective in removing hard product residues and therefore are invariably used in machine and plant cleaning where foam is a disadvantage. They do not, however, possess the same wetting properties as synthetic detergents or the same emulsifying properties as soap.

Although the first detergents ever to be used were alkaline, their continued use in the cleaning field is a clear indication of their adaptability and efficiency.

Specialized Detergents. These include the detergent sanitizers which are designed to incorporate bactericidal properties with the other desirable detergent features.

Bactericidal Action of Detergents. Many detergents have marked germicidal properties although they are used primarily as detergents. Hot water at 60°–80°C will kill most or all vegetative cells but few spores. A detergent will always enhance the killing effect of heat; probably the best example is sodium hydroxide: a treatment at 63°C for 30 minutes in water will kill all bacteria except thermoduric ones and spores, but a 1–3 per cent NaOH solution under these conditions will kill all thermoduric cells and a considerable proportion of spores. Detergents are nearly always used hot and so act by enhancing the bactericidal effects of heat. This effect is especially valuable against spores in those industrial applications, for example bottle-washing followed by cold filling, in which excessive temperatures have to be avoided. Detergent–sterilants are particularly useful when high temperatures cannot be used, as in manual dishwashing, or because of delicacy of materials. Even apparently innocuous detergents such as anionics, nonionics and trisodium phosphate exert a powerful killing effect against most pathogens but not against tubercle bacilli or spores.

Equipment Disinfection

Once equipment is thoroughly cleaned, the actual disinfection process can be initiated, using steam or chemical sterilants.

Disinfection by Steam

Steam is the most effective and reliable means of sterilizing equipment but the steam tolerance of equipment material should be checked before steam is used as a sterilizing agent. As with other sterilizing agents, contact time is important.

The minimum temperature at the exit end of the steam generating system should be in the range 72°–80°C. Contact times for open vessels are normally 30 minutes or more, since the steam is at zero pressure. For closed systems, contact times vary according to steam pressure; for example, at pressures of about 1–5 psi (5–100 kPa), a 20 minute contact time is necessary. At higher pressures the contact time may be as little as 5 minutes. In addition, the steam used must be free from particulate and other extraneous matter. This will eliminate the problem of residues remaining after the sterilization process.

Disinfection by Chemical Sterilants

At sufficiently high concentrations many chemicals, including nutrients such as oxygen and fatty acids, are bacteriostatic and even bactericidal. The term 'disinfectant' is restricted to substances that are rapidly bactericidal at low concentrations. Most sterilizing agents act either by dissolving lipids from the cell membrane (detergents, lipid solvents) or by damaging proteins (denaturants, oxidants, alkylating agents and sulphydryl reagents). The rate of killing by disinfectants increases with concentration and with temperature. Anionic compounds are more active at low pH and cationic compounds at high pH. This effect results from the greater penetration of the undissociated form of the inhibitor, and possibly also from the increase in opposite charges in cell constituents. Strongly acid and alkaline solutions are actively bactericidal. Weak acids exert a greater effect than can be accounted for by pH: the presence of highly permeable undissociated molecules promotes penetration of the acid into the cells, and increasing activity with chain-length suggests that direct action of the organic compound itself plays a part. Lactic acid is the natural preservative of many fermentation products, and salts of propionic acid are now frequently added to foodstuffs such as bread to retard mould growth. Halogens such as iodine and chlorine combine irreversibly with proteins and they are oxidizing agents. Chlorine was the antiseptic introduced as chlorinated lime by O. W. Holmes in Boston in 1835, and by Semmelweis in Vienna in 1847, to prevent transmission of puerperal sepsis by the physician's hands. Chlorine is a reliable, rapidly acting sterilant–disinfectant for 'cleaning' materials but it is less satisfactory for materials that are subject to attacked by chlorine.

Alkylating Agents. Suitable dilutions of formaldehyde and of ethylene oxide in carbon dioxide (in appropriate gastight enclosures) replace the labile H atoms on—NH_2 and—OH groups which abound in proteins and nucleic acids, and also on —COOH and—SH groups of proteins (Figure 43.2). The reactions of formaldehyde are in part reversible, but the high-energy epoxide bridge of ethylene oxide leads to irreversible reactions. These alkylating agents, in contrast to other disinfectants, are nearly as active against spores as against vegetative bacterial cells, presumably because they can penetrate easily (being small and uncharged) and do not require water for their action.

Phenols. Phenol itself is both an effective denaturant of proteins and a detergent. Its bactericidal action involves cell lysis. The antibacterial activity of phenol is increased by halogen or alkyl substitutes on the ring, which increase polarity of the phenolic OH group and also make the rest of the molecule more

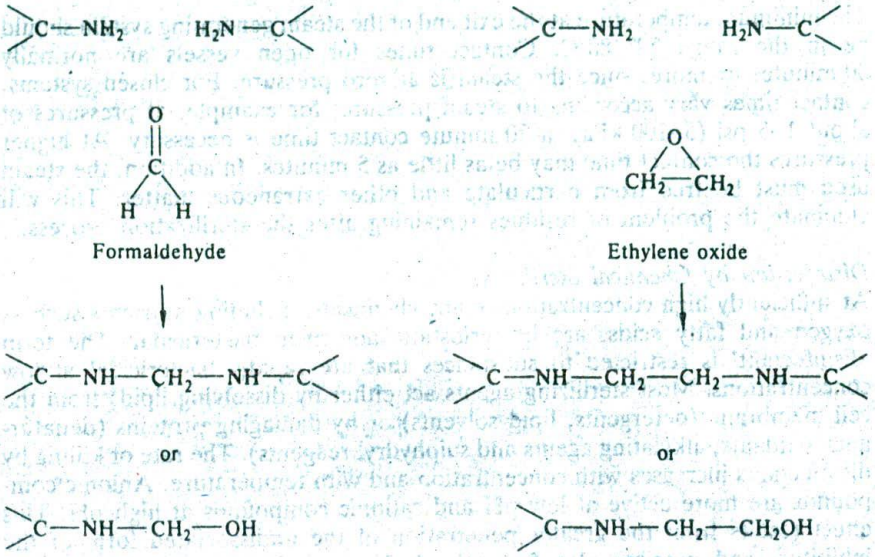

Figure 43.2 Reactions of formaldehyde and ethylene oxide with amino groups. Bridges may be formed between groups on the same molecule or on different molecules

hydrophobic; the molecule becomes more surface-active and its antibacterial potency may be increased a hundred-fold or more. Phenols are more active when mixed with soaps, which increase their solubility and promote penetration. However, too high a proportion of soap impairs activity, presumably by dissolving the disinfectant too completely in soap micelles. With increasing chain-length the potency of phenols first increases and then decreases, presumably because of low solubility; with Gram-negative organisms the maximum is reached at a relative short chain-length.

Alcohols. The sterilant–disinfectant action of the aliphatic alcohols increases with chain-length up to 8–10 carbon atoms, above which the water solubility becomes too low. Although ethyl alcohol has received the widest use, isopropyl alcohol has the advantages of being less volatile and slightly more potent. The sterilant–disinfectant action of alcohols, like the denaturing effect on proteins, involves the participation of water. Ethyl alcohol is most effective in 50–70 per cent aqueous solution; at 100 per cent it is a poor sterilant, in which anthrax spores have been reported to survive for as long as 50 days, and its bactericidal action is negligible at concentrations below 10–20 per cent. Some organic disinfectants such as formaldehyde and phenol are less effective in alcohol than in water because of the lower affinity of the disinfectant for the bacteria relative to the solvent. On the other hand, alcohol removes lipid layers that may protect skin organisms from some other disinfectants.

Other Chemical Sterilants. Organic solvents such as ether, benzene, acetone and chloroform also kill bacteria but are not reliable disinfectants. Glycerol is

bacteriostatic at concentrations exceeding 50 per cent and is used as a preservative for vaccines and other biologicals, since it is not irritating to tissues.

Propylene glycol and diethylene glycol reduce the bacterial count in air when dispersed in fine droplets at concentrations non-toxic to man, but their activity is unfortunately highly sensitive to humidity; at high humidities the glycol droplets take up water and become too dilute, while at low humidities the desiccated bacteria no longer attract glycols. Moreover, the glycols do not disinfect surfaces such as floors, walls or working surfaces, from which aerial contamination is renewed. The chemical sterilants mentioned above are widely used in the cosmetics industry. They are generally used on equipment that cannot tolerate steam or to which steam cannot be applied.

Chlorine is commonly used in the food and cosmetics industries, usually by employment of hypochlorites or chloramines, and has a relatively broad spectrum of activity. It is fairly inexpensive but it is corrosive and is not a cleaning agent. Equipment must be thoroughly cleaned or the chlorine will be inactivated.

Iodine-containing sterilants are useful and can be formulated with detergents in order both to clean and to sterilize. The disadvantages of materials containing iodine are their poor rinsability and their less than satisfactory effect against certain micro-organisms. Staining of equipment components may also be a problem.

Quaternary ammonium compounds are odourless and less corrosive than some of the other chemical agents. Their antimicrobial effectiveness is slightly less than that of alternative materials, but when used at appropriate concentrations and elevated temperatures they can be satisfactory. Quaternary ammonium compounds have the advantage of being non-toxic and are therefore more easily handled than other sterilizing agents.

Detergent sterilizers work more efficiently at higher temperatures, requiring a lower concentration of sterilant. At lower temperatures, on the other hand, not only may a higher concentration be needed but also increased contact time. Different types of surface may require different contact times with the sterilant; smooth, non-porous surfaces require less time than moving parts. Processing systems containing moving parts that are not always in contact with the sterilant will require frequent cycling of the parts during the exposure time to give adequate contact time.

Table 43.1 Properties of Some Major Classes of Antimicrobial Chemicals

Property	Inorganic hypochlorites	Detergent quaternaries	Detergent iodophors
Broad microbial spectrum	Yes	No	Yes
Activity against pseudomonads	Yes	No	Yes
Product stability	Limited	Yes	Yes
Interference by water hardness	No	Yes	Yes
Interference by alkalinity	Yes	No	Yes
Odour (use dilution)	Yes	No	Slight
Visual indicator of activity	No	No	Yes

Selection of the appropriate sterilant for sterilizing equipment is a difficult problem. The first step in the evaluation of a sterilant is to review the technical literature and set out its advantages and disadvantages. In the microbiological laboratory basic cleaning procedures, such as the determination of minimum inhibitory concentrations, should be conducted using a wide variety of possible contaminants and these should preferably be the types encountered in cosmetic products. The results will give information on both the spectrum of effectiveness and the potential range of concentration required for the sterilant. Once an effective concentration has been established, additional testing using equipment components can be conducted. From further investigations into temperatures and contact times, a degree of sterilant effectiveness may be established. Comparative testing of two or more sterilants or conditions of sterilization can also be conducted easily.

Once the new sterilant has demonstrated acceptable ability, it should be experimentally evaluated on full-scale equipment. Since all conditions of use have been previously established, this final evaluation should not create substantial difficulties.

Regular use of a single type of sterilant can result in the development of strains of organisms resistant to the antimicrobial agent in use. Over long periods of time organisms that were once eliminated are found to have adapted and to survive; this adaptation of equipment-borne micro-organisms can be prevented by the rotation of sterilants. Regular use of a different sterilant will eliminate the occurrence of resistant organisms. For instance, a quaternary sterilant may be used for a given period of time, followed by a chlorine-based sterilant for a further period of time. However, if steam is used as the sterilant, rotation is not normally necessary. In order to avoid serious equipment-borne contamination particular attention should be given to the phenomenon of microbial adaptation.

Parameters of Cleaning, Disinfection and Rinsing

Cleaning. In this procedure the dirt or the product residue is separated from the surfaces through the combined action of cleaning agent and mechanical energy. Investigations show that the removal of product residue or dirt proceeds formally as a chemical reaction of the first order. If m_A is the quantity of residue per unit surface area and t is the time taken to remove it, the relationship between them can be described as $dm_A/dt = -k_R m_A$, where k_R is a rate constant describing the velocity of cleaning. Thus a plot of t versus log m_A yields a straight line (Figure 43.3). This behaviour could be due to the removal of the residue in layers, there being only weak cohesive forces between the layers, but in the end the stronger adhesion force of the final residual layer to the walls of the vessel must be overcome.

The value of the constant k_R depends on several parameters:

1. Type and concentration of cleaning agent
2. Material and state of surface
3. Type and state of dirt or residue
4. Temperature of cleaning solution
5. Mechanical energy supplied.

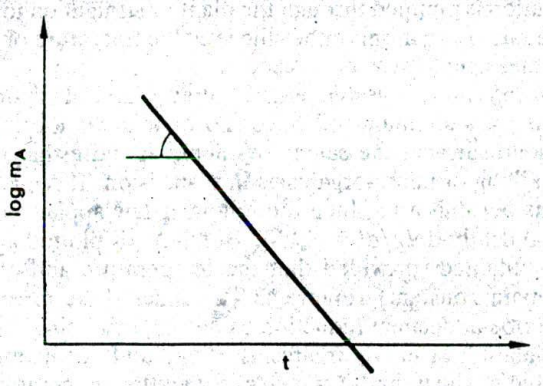

Figure 43.3 Kinetics of product residue removal: $dm_A/dt = -k_R m_A$

Schlussler[4] found that for many cleaning agents there is an optimum concentration at which the cleaning speed (defined as the amount of dirt or residual product removed in unit time) is maximal. This means that an overdose can hinder the cleaning action just as much as an underdose. It is well known that smooth surfaces can be cleaned more easily than rough surfaces. It is not only the depth of roughness, but also the structure of the roughness which influences the cleaning speed.

There are essentially two types of cleaning procedure: open cleaning and closed cleaning. In these two methods the same sequence of preparation is followed—firstly, removal of residual product and, secondly, disinfection followed by finally rinsing. When there is heavy residue to be removed there may be rinsing before disinfection; this sequence will avoid residues and detergents affecting the disinfectant. If the residue to be cleaned is light and the bacterial count is low, cleaning and disinfection can be carried out in one step.

(a) Open cleaning is used on open surfaces, such as working areas, open vessels and manufacturing equipment such as spatulas and stirrer blades. Strong foaming detergents can be used. This has the advantage that the cleaning foam can work longer on the surface than a quickly disappearing liquid film. The final outcome of cleaning operations in open cleaning, which forms the bulk of the cleaning in any industry, depends on the understanding of the procedure and the care taken by the cleaning personnel.

(b) Closed cleaning or CIP (cleaning in place) is used for plant and storage vessels that are connected together and consist of pipes and tanks. Here the cleaning or disinfectant solutions are held in storage tanks and supplied through the plant to be cleaned. Cleaning or disinfectant solutions are applied with a turbulence, often at high pressures in the form of a spray. CIP avoids operator errors but, because of the more complex cleaning machinery, there is an increased tendency for machine wear and, therefore, failure of some parts of the plant.

Disinfection. For disinfection of solid surfaces two processes are in general use: (i) the application of heat and (ii) the use of chemicals, when an aqueous

disinfecting solution is pumped through the plant or straight on to the surface. In order to kill the micro-organisms either the lethal temperature or the lethal dose of the disinfecting agent must be exceeded.

Kinetics of disinfection. Investigations by Prado[5] and Han[6] on the killing of micro-organisms on aluminium foil have shown that for the killing of micro-organisms on solid surfaces the same laws apply as those that have long been known for the killing of micro-organisms in suspension. If N_A is the number of micro-organisms per unit area, then the following law applies both for thermal and for chemical death: $dN_A/dt = -kN_A$. If $\log N_A$ is plotted against time, t, a straight line is obtained (provided that the temperature and concentration of disinfectant remain constant) (Figure 43.4). Under these circumstances, it is possible to describe a 'decimal reduction value', D, this being the time taken to reduce the population of micro-organisms to one-tenth of its initial concentration. It is possible to show that $D = 2{\cdot}3/k$. When the temperature is allowed to vary, D varies inversely with it. The temperature rise, Z, at which the value of D is reduced to one-tenth of the initial value, is also a useful practical parameter. For most micro-organisms Z is about 5°C, and for spores it is about 10°C.[7]

The effect of disinfecting agents can increase for a given surface through increasing concentration, but for disinfectants with active chlorine there is a corrosion-limited upper concentration. Increase in temperature enhances the action of the disinfectant. For a given temperature, a separation into thermal and chemical action is no longer possible. The effect of disinfectants also depends on the pH value. Active chlorine compounds develop their greatest effect when neutral, and iodophors are most effective at an acid pH.

The condition of the surface has a strong influence on disinfection. The rougher the surface, the greater is the danger of formation of nests of micro-organisms in the pores, and the more difficult is the disinfection. The presence of organic materials will greatly reduce the action of a disinfectant, and so pre-cleaning is necessary for efficient disinfection. Apart from removing undesirable organic material, pre-cleaning also reduces the bacterial population by washing out the micro-organisms.

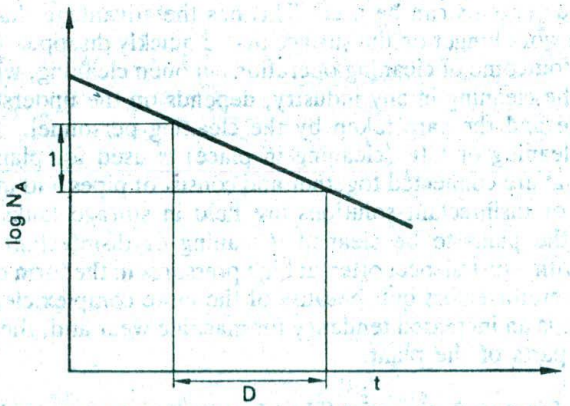

Figure 43.4 Kinetics of disinfection: $dN_A/dt = -kN_A$; $D = 2{\cdot}3/k$

CONTROL OF CONTAMINATION

Hazards from Personnel

Eating, drinking and smoking should be forbidden in all production areas, and high standards of personal hygiene should be observed by all persons concerned in production processes; direct contact between materials and operators' hands should be avoided by the use of correct and suitable equipment. All operatives should wear protective garments appropriate to the process being carried out. The garments should be regularly and frequently laundered. Persons not regularly employed in a production area, whether employees of the firm or not, should wear protective garments where appropriate and necessary. No person known to be suffering from a disease in communicable form, or to be the carrier of such disease, and no person with open lesions or skin infection on the exposed surface of the body, should be employed on production processes.

The bacteria that live on human skin are adapted to the skin habitat and use skin secretions such as sebum and sweat as food; furthermore, pores and cavities function as shelter. Skin bacteria such as *Staphylococcus epidermidis* and *Corynebacterium acnes* adhere to epithelial layers that form the cornified skin surface, and extend between the squames and down the mouths of the hair follicles and glands opening onto the skin surface. These bacteria can only be reduced in numbers, but never eliminated, by scrubbing and washing. They produce odoriferous substances by metabolizing secretions of the apocrine sweat glands, giving the body a smell that modern man, at least, finds offensive.

The ability of micro-organisms to spread from one host to another is of great importance for bacterial distribution and their eventual survival. Clearly if micro-organisms do not spread from individual to individual they will die with the host and will be unable to persist in nature. A classical example of this distribution is the spread of respiratory disease from one individual to a score of others in the course of an innocent hour in a crowded room. Thus, a successful parasitic micro-organism is one that lives on or in the individual host, multiplies, spreads to fresh individuals, leave descendants, and from an evolutionary point of view avoids its extinction and that of its host. On the other hand, if an infection is too lethal or crippling, there will obviously be a reduction in numbers of the host species and thus in the numbers of the micro-organisms. Although a few micro-organisms cause disease in the majority of those infected, it is to be expected that most are comparatively harmless, causing even no disease, or disease in only a small proportion of those infected. Successful parasites cannot afford to become too pathogenic; some degree of tissue damage may be necessary for the effective shedding of micro-organisms to the exterior, as for instance in the flow of infected fluids from the nose in the common cold or from the alimentary canal in infectious diarrhoea, but otherwise there is ideally very little tissue damage. A few microbial parasites achieve the supreme success of causing zero damage, thus failing to be recognized as parasites by the host. It is the virulence and pathogenicity of micro-organisms, their ability to kill and damage the host, that makes them important to the medical scientist and to the microbiologist.

Skin bacteria are mostly shed attached to desquamated skin scales, and an average of about 5×10^8 scales, 1×10^7 of them carrying bacteria, are shed per

person per day. The fine white dust that collects on surfaces in hospital wards and in bedrooms consists to a large extent of skin scales. Shedding also takes place from the nose and notably from the perineal area. Potentially pathogenic *Staphylococcus aureus* colonizes the nose, fingers and the perineum. The effect of shedding can be reduced by wearing suitable clothing. A good staphylococcal shedder can raise the staphylococcal count in the air from less than 36 per m^3 to 360 per m^3. It is not known why only some individuals are profuse shedders, but the phenomenon is significant in cross-infection in hospitals and other areas where cross-contamination is critical. Many micro-organisms are effectively transmitted from faeces to mouth after contamination of water used for drinking. In the bowel *E. coli*, *Cl. welchii*, and *Cl. tetani* are nearly always present. All these organisms are potentially pathogenic, and there can be little doubt that they can very easily be transferred and cause contamination and infection. Microbial transmission by the respiratory route depends on the production of aerosols containing micro-organisms. These are air-borne particles produced to some extent in the larynx, mouth, and throat during speech and normal breathing. Harmless commensal bacteria are shed and more pathogenic streptococci, meningococci and other micro-organisms are also spread in this way, especially when people are crowded in small rooms. Micro-organisms in the mouth, throat, larynx and lungs are expelled to the exterior with much great efficiency during coughing; a cough will project bacteria into the air.

In factory areas such as filling lines, where there is a high density of people, cough and sneeze spray is probably the most important vehicle or likely cause of contamination. In a sneeze up to 20 000 droplets carrying micro-organisms are produced and these droplets, depending on their size, may travel up to 5 metres. They evaporate and release micro-organisms into the environment.[8] A streptococcal sore throat can be acquired by subjects at a distance of 6 metres from a carrier. Dust, dandruff, hair, skin particles, dried sputum and droplets from coughing and sneezing have all been shown to harbour all types of bacteria associated with the human body, and these can obviously be transferred to products.

Washrooms and Toilets

Stringent procedures should be set up and adhered to for the cleaning and disinfection of sinks, toilets, showers, tools, lockers and floors. The use of tablet soap and roll towels for handwashing should be discouraged and discontinued. Instead, antiseptic liquid soap and disposable paper towel dispensers should be installed. Work clothing should be provided to employees and freshly laundered garments should be made available on a regular and frequent basis. Dirty clothing cannot be overlooked as a source of contamination and therefore every effort should be made to eliminate it.

Despite the fact that washrooms and toilets may be cleaned daily, bacteria originating from faeces are often found in large numbers on all surfaces. These areas readily come into contact with people. One third by weight of faeces is bacteria, many of which are alive.[9] The areas likely to cause cross-infection are the toilet seat, wash basin, overflow tap, handles, inside handle of the entrance door. Splashing of the water in the toilet pedestal during

defecation is another potential source of cross-infection; this varies with cistern height and bowl design. Contamination originating from these areas is unlikely, unless the handles or toilet seats are particularly soiled. This may happen in mental hospitals or children's wards, and outbreaks of bowel infections have occurred in such places, but it is unlikely elsewhere.[10] Salmonella are potentially dangerous organisms, because they resist drying and small-dose infection is thought to occur, but no evidence is available to incriminate the toilet in such infections. Water that 'looks clean' in pedestals is not necessarily bacteriologically clean. Bacterial populations of 1×10^6 organisms per ml have been found in fresh water in pedestals.[11] In the UK drought of 1976 when 'economy flush' systems were used, large numbers of bacteria remained unflushed, whereas with full flushing the bacteria were removed from the pedestals effectively. Thus simple cleaning and the maintenance of a good flushing cistern are the main principles of toilet care. Flush handles can be a source of transmission of contamination from one individual to another and foot-operated pedals for flushing are recommended.

Toilet care should be mainly mechanical: the ball valve should be set to the correct height and the flush mechanism made to work properly. The surfaces and handles must be kept clean. In the UK the best equipment is the British Standard wash-down bowl with a low cistern, but the latter must be capable of a good cleaning action. The care of the bowl should be restricted to cleaning. A standard scouring powder is adequate for this if used in conjunction with a brush and flushed away. It should not be just poured into the bowl and left, for it might choke up the toilet. The more conventional descaling agents may be required in hard-water areas. There is no reason to pour large quantities of disinfectant into the bowl; this is uneconomic and aimed at a non-existent danger. Finally, as always, the care of the hands is of paramount importance in preventing transmission of contamination; operatives can be encouraged to use paper tissues when handling flushing handles, water taps and door knobs in the toilet area. Also necessary is the provision of a wash-basin close to the toilet area.

Raw Materials

Ingredients used in cosmetic formulae should be quarantined until their quality is determined; those found to be acceptable should be protected from contamination during storage. Raw materials are likely sources of microbial contamination and should be examined microbiologically on a routine basis. A major raw material in cosmetic products is water. If contaminated, the entire water system should be shut down, emptied, thoroughly cleaned, and disinfected by disinfectant solution circulating throughout the entire system, including all feed lines, tanks, and resin beds. After disinfection the system should be drained and flushed with clean water until all traces of the disinfectant solution have been rinsed away. On the other hand if a reduced bacterial count is detected on routine testing, and found to be increasing, it may be sufficient to inject a small quantity of disinfectant solution (say, on Fridays) as a prophylactic measure in order to control the bacterial count. The water supply may be a major source of *Pseudomonas* contamination, and where ambient temperatures exceed 18°C few

bacterial cells should be allowed to reach over 10^6 bacteria per gramme. Raw materials of natural origin, such as the natural gums tragacanth and acacia, may be very heavily contaminated and so may kaolin, chalk and starch. Significant microbial contamination has been reported in bentonite, Quaternium-18, hectorite, sodium magnesium silicate and aluminium powder.

Among other raw materials, fats and waxes contain relatively few organisms but Hall (cited by Boehm and Maddox[2]) found counts of up to 16×10^6 bacteria per gramme in dried natural products such as gums and herbs. Also encountered were a variety of fungi and yeasts. Many synthetic materials may also be contaminated.

For microbiological examination of raw materials there is a number of methods for taking samples aseptically. The aim of aseptic sampling is to limit the possibility of adding contamination to the product, so that the test results indicate the microbial status of the material on its arrival at the plant. A sample is scooped or pipetted out from the raw material container, placed in a sterilized sample container and returned to the laboratory for immediate testing. The raw material container should immediately be sealed.

If, after completion of all microbiological tests, the material is accepted, it is then removed from the holding quarantine area and placed in stock. It should be borne in mind that excessive humidity and large fluctuations in temperature from ambient may effect the physical, chemical and microbial properties of raw materials. Raw materials that are retained for long periods of time should be retested at specific intervals (at least every six months). Raw materials that are purchased pre-sterilized to assure the microbiological quality should also be tested to verify (i) that the sterilization procedure was effective and (ii) that post-sterilization contamination has not occurred.

Storage Areas

All raw materials should be stored in such a way that the tested degree of microbial purity is maintained. Storage areas for raw materials should be maintained in as clean a condition as bulk product manufacturing and product filling areas.

When it is necessary to store raw materials, packing materials, intermediate products or finished products in a special environment, these goods should be stored off the floor where possible, to allow their maintenance in a clean dry and orderly condition. This does not, however, prevent outdoor storage of materials whose condition is not adversely affected thereby.

Product Packaging

The protection of the product, once it is filled into an adequate container, depends purely on the efficiency of the closure. The seal should be secured and tight, thus protecting the product from microbes for an indefinite period. This protection may be described as a criterion of the physical preservation of the product. Packaging components such as jars, bottles, tubes, container closures and closure liners should not be ignored as sources of contamination.[12] They should be stored in clean and dry areas and suitably packed or covered to

prevent dust-borne microbes from settling on them. Before use if possible they should be air-blown with dry, clean air to rid them of any extraneous particles. It is recommended strongly that air-blowing is carried out under an extraction hood with vacuum facilities so that the particles blown off are immediately extracted from the filling area. If possible, the supplier should be persuaded to supply the packaging components in sealed plastics bags which should be opened just prior to use. This will obviously avoid the complications of air rinsing.

Microbiological Standards

Microbiological standards serve several quite distinct purposes:

1. Control of the danger from pathogenic organisms
2. Assurance that the cosmetic product has never been grossly contaminated
3. Confirmation of a reasonable expected life in storage—that is, an estimate of perishability

Freedom from pathogens is the requirement that is usually paramount in microbiological standards. The usual guidance given to the industry is to exclude 'named pathogens' from cosmetics. With few exceptions, it is doubtful whether a single bacterial cell ever did anyone any harm. It appears to be necessary for growth that at least a few organisms should establish themselves and adapt to their environment. This is clearly illustrated by figures for the 'minimum effective dose' for well recognized diseases (Table 43.2).[13]

The need to ensure that the cosmetic product has never been seriously contaminated emphasizes the importance of quantitative tests in microbiological control. An attempt should always be made to assess the number of organisms present, even though the error may be large. The reason for this is that the onset of an infection, or the development of a microbiological defect in a product, is dependent on the number of organisms originally present.

The third consideration, that of shelf life or perishability, relates to the retail and consumer end of the cosmetics chain. In general, it is always better to prevent microbiological growth by formulation rather than to rely on preservatives. Preservatives, like antioxidants, are rarely completely satisfactory for a long period, especially where ambient temperatures are warm, whereas control by formulation lasts indefinitely.

Microbial specifications within the cosmetics industry are essential aids in maintaining the sanitary quality and stability of the end product, when used to control raw materials, processes and factory hygiene.

Table 43.2 Minimum Effective Doses (approx.) from Pathogens in Human Beings

Disease	Number of cells
Typhoid fever	3
Tuberculosis	100
Cutaneous moniliasis	100 000
Salmonelloses (other than typhoid fever)	100 000–1 000 000

If equipment has been properly cleaned and sterilized the number of bacteria left will not exceed one per cm^2 by a swab test or one per ml by a rinse test. These tests are therefore quite adequate to assess the efficiency of cleaning in a general sense. It can be assumed under ordinary working conditions that if the results are satisfactory (that is, less than 1 colony per cm^2 or ml) then all pathogens have been killed or removed. It is also unlikely that micro-organisms will have survived in sufficient numbers to cause trouble.

Conclusion

The cleanest factory conditions can easily be invalidated if unhygienic methods are practised; microbial contamination will only be avoided by careful attention to all aspects of production and control. Disregard for any of the following points results in weaknesses and, eventually, costly complications.

1. Check the quality of raw materials
2. Unpack raw materials in a separate building, especially if embedded in sawdust, cotton waste, straw, etc.
3. Apply a biocidal treatment where necessary if this is practicable
4. Control the quality of water used in the factory
5. Check the bacterial purity of the air near fillers, etc.
6. Check the hygienic condition of all containers
7. Remove all residue, broken or split containers, etc. as soon as possible
8. Do not use cloths for mopping up spillages, unless these are maintained in a clean condition; paper towels are much better
9. Thoroughly clean equipment immediately after use
10. Sterilize or cleanse all equipment, as may be necessary, immediately before use

Common Fallacies in Hygiene
It is not true that:

(a) splashing disinfectant over floors, etc., 'solves the hygiene problem';
(b) forcing steam round a circuit, with the production of great clouds of 'steam' and considerable noise, necessarily sterilizes the equipment;
(c) if equipment looks clean, then it must be clean—this is not true microbiologically.

'Window-dressing' devices, such as making people wear white coats and caps, provision of glaring UV lamps, use of disinfectant aerosols, may serve some useful purpose and undoubtedly exert a psychological influence, but in real terms their value is not great.

A cosmetic product contaminated by micro-organisms is generally held to be a potential danger to the user, especially if harmful pathogens are present. Paetzoid examined 129 products and found 17·1 per cent of them to be contaminated with bacteria that were 43·9 per cent pathogens and 56·1 per cent non-pathogens.[14] It has been pointed out by Knothe[15] that the skin possesses self-disinfection properties with a greater bactericidal effect on pathogens than on non-pathogens. The conclusion from his work is that cosmetic products need

not necessarily be sterile in order to protect the normal healthy user. So why does the cosmetics industry attempt to limit the micro-organism content of products? The answer is that if micro-organisms are introduced into a cosmetic product the general properties of the cosmetic can be altered (a) by the micro-organism, (b) by multiplication of the micro-organism and (c) by microbial metabolites.

The following phenomena are common in insufficiently preserved cosmetics: creams and lotions can exhibit visible mould colonies; products can separate with or without the production of a rancid or putrid odour; discoloration can occur; clear preparations can become turbid owing to precipitation; fermentation can produce gas, sometimes causing tubes to swell or glass bottles to burst. The result is that a product manufactured at high cost and believed to have received all possible care has become unsaleable.

The sanitary quality of a cosmetic product is normally the summation of the level of sanitation in the production of raw material ingredients, the sanitation quality of the finished raw materials, and level of sanitation in the cosmetic product manufacturing plant. The EEC definition of the term cosmetic is 'any substance or preparation intended to be placed in contact with various superficial parts of the human body (epidermis, hair system, nails, lips and external genital organs) or with the teeth and mucous membrane of the oral cavity with a view exclusively or principally to perfume them, clean them, protect them and keep them in good condition, to change their appearance or to correct body odours'. As such, cosmetics demonstrating poor microbiological quality have a potential for being 'injurious to health' with unpredictable frequencies and at unpredictable times.

REFERENCES

1. Yablonski, J. L., *Cosmet. Toiletries*, 1978, **93**(9), 37.
2. Boehm, E. E. and Maddox, D. N., *Manuf. Chem. Aerosol News*, 1971, **42**(4), 41.
3. Kano, C., Nakata, O., Kurosaki, S. and Yanagi, M., *J. Soc. cosmet. Chem.*, 1976, **27**, 73.
4. Schlüssler, H. J., *Milchwissenschaft*, 1970, **25**(3), 133.
5. Prado Fihlo, L. G., *Lebensm.-Wiss. Technol.*, 1975, **8**(1), 29.
6. Han, B-H., Dissertation, University of Karlsruhe, 1977.
7. Thor, W. and Loncin, M., *Chemie Ingenieur Technik*, 1978, **50**(3), 118.
8. Mims, C. A., *Pathogenesis of Infectious Disease*, London, Academic Press, 1977.
9. Mendes, M., *New Scientist*, 1977, **76**(1079), 507.
10. Newsom, S. W. B., *Lancet*, 1972, 30 September, 700.
11. *Guide to Good Pharmaceutical Manufacturing Practice*, London, HMSO, 1971.
12. Most, S. and Katz, A., *Am. Perfum. Cosmet.*, 1970, **85**(3), 67.
13. Davis, J. G., *Soap Perfum. Cosmet.*, 1973, **46**(1), 37.
14. Paetzoid, H., *Vortrag anl. der D. G. F.-Vortragstagung*, Mainz, 1967.
15. Knothe, H., *Referat anl. d. Vortrags- und Diskussionstagung der Gesellschaft deutscher Kosmetika-Chemiker e.V.*, Hamburg, 1967.