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Review on Bioburden Studies on Medical Devices

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ABSTRACT

Producing safe products is a core goal of all medical device manufacturers and sterility assurance is a key component in achieving that goal. Many single use medical devices are terminally sterilized by ethylene oxide or radiation methods such as gamma or e-beam. The FDA and other regulatory bodies requiring that the sterilization process be validated and these validations typically require a bioburden and sterility testing. Sterility testing and bioburden testing are also performed on devices as part of routine quality control. By conducting this test on medical device we can assure the in-house sterility; during production, packaging (primary and secondary) and dispatch. To avoid the any error or contamination attacks on the product.

Keywords: Bioburden, Medical Device, IUD, Sterility

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1. Introduction

Medical Devices types

a. Intra uterine devices[1]

b. Female sterilization devices[1]

1.1 Intrauterine devices[2]

Intrauterine device is a small contraceptive device, often 'T'-shaped, often containing either copper or levonorgestrel, which is inserted into the uterus. They are one form of long-acting reversible contraception which is the most effective types of reversible birth control. Failure rates with the copper IUD is about 0.8% while the levonorgestrel IUD has a failure rate of 0.2% in the first year of use. Among types of birth control they, along with birth control implants, result in the greatest satisfaction among users. [2] As of 2007, IUDs are the most widely used form of reversible contraception, with more than 180 million users worldwide. Intrauterine device definition lies in its main principle of work that IUD simply does not allow the egg to grow, i.e. to attach to the uterus, and thus the pregnancy does not occur. In addition, these products are made of copper that contributes to the production of liquid which has a spermicidal effect. Copper intrauterine devices can serve up to 10 years. [3]Copper IUDs primarily work by disrupting sperm mobility and damaging sperm so that they are prevented from joining with an egg. Copper acts as a spermicidal within the uterus, increasing levels of copper ions, prostaglandins, and white blood cells within the uterine and tubal fluids. The increased copper ions in the cervical mucus inhibit the sperm's motility and viability, preventing sperm from travelling through the cervical mucus, or destroying it as it passes through. Copper can also alter the endometrial lining, but studies show that this alteration can prevent implantation, but not disrupt implantation. Copper IUDs have a first year failure rate ranging from 0.1 to 2.2%. Most copper IUDs have a plastic T-shaped frame that is wound around with pure electrolytic copper wire and/or has copper collars (sleeves). The arms of the frame hold the IUD in place near the top of the uterus. The Paragard TCu 380A measures 32 mm (1.26") horizontally (top of the T), and 36 mm (1.42") vertically (leg of the T). Copper IUDs are becoming increasingly popular because they are more resistant to corrosion. [4] In the "Eurogine Gold T IUD, which is made in Spain, there is a gold core, which further prevents the copper from fragmenting or corroding. Goldring Medusa is a differently-shaped German version of the Gold T. Another form of AuCu IUD is called Goldlily which is made by the Hungarian company, Radelkis. Goldlily consists of a layer of copper wires wrapped around an original layer of gold wires, and it provides electrochemical protection in addition to ionic protection. Silver IUDs alsoexist. Radelkis also makes Silverlily, which is similar to Goldlily, and Goldring Medusa is available in an AgCu version as well. Nova-T 380 contains a strengthening silver core, but does not incorporate silver ions themselves

to provide electrochemical protection. Other shapes of IUD include the so-called U-shaped IUDs, such as the Load and Multi load, and the frameless IUD that holds several hollow cylindrical minuscule copper beads. It is held in place by a suture (knot) to the fundus of the uterus. It is mainly available in China, Europe, and Germany, although some clinics in Canada can provide it. A framed copper IUD called the IUB SCu300A coils during deployment to form a three dimensional spherical shape and is based on a shape memory alloy core. Advantages of the copper IUD include its ability to provide emergency contraception up to five days after unprotected sex. It is the most effective form of emergency contraception available. It works by preventing fertilization or implantation; however does not affect already implanted embryos. It contains no hormones, so it can be used while breast feeding, and fertility returns quickly after removal. Copper IUDs are also available in a wider range of sizes and shapes than hormonal IUDs. [5] Disadvantages include the possibility of heavier menstrual periods and more painful cramps. In addition to copper, noble metal and progestrogen IUDs, patients in China can get copper IUDs with indomethacin. This non-hormonal compound reduces the severity of menstrual bleeding, and these coils are popular. For women who have such a shape of the uterus that it's inconvenient to use the classical IUD like "the letter "T", there were created birth control intrauterine device with the semi-oval shape with some projections. [6] It is difficult to say what kind of intrauterine device is the best one, because it is always selected together with a doctor and only a health professional can define intrauterine device that will be the most suitable for a woman. For some women there are quite suitable IUDs with silver in a small amount, it has anti- inflammatory effects, and someone even chooses IUDs with some gold. [3, 6, 9]

Types of Intra uterine devices:

A. Copper T 380A

It consists of T- shaped body, made from polyethylene compounded with barium sulphate, which bears a coil of copper wire (99.99 % pure) on its arm, 2 copper sleeves (99.99 %) one on each of the horizontal arm and 2 monofilament threads tied with the bottom of the vertical arm. This whole assembly is called Cu T 380 A and remains in the body. Other components like Insertion tube, Solid Rod, Flange and Arm folder are assist devices used for insertion purpose. All the components are packaged in an individual pouch. The pouch is then sterilized can be stored for a long term. [7, 8, 10]

B. Copper T 380

A was invented by the population council, USA. The population council developed its manufactured specification and submitted New Drugs Application NDA 18-650 to US FDA and got permission for marketing in the year 1984. The manufacturing specification provided by The Population Council became guideline for manufacturer world over. [9, 11, 13]

Mechanism of Action Copper bearing IUDs works primarily by causing chemical changes that prevent fertilization. Studies show that the copper IUD effectively interrupts the reproductive process before implantation and pregnancy. It does not act by initiating an abortion. In addition to the contraceptive effect of a foreign body in the uterus, the Copper T380A functions by way of continuous release of copper ions into the uterine fluids. This interferes with some enzymatic functions, immobilizes sperm cells and inhibits fertilization. In addition, growth and development of the ovum, tubal function and implantation are inhibited and the biochemical environment of the uterus is ahead. [9, 12, 14]

C. Cu 375

Cu 375 consists of a U-shaped body, made from polyethylene compounded with barium sulphate which bears a coil of copper wire (99.99 % pure) on its vertical arm and two monofilament nylon threads tied to the bottom of the vertical arm. The vertical arm length is 29 mm only instead of 35 mm in Cu 375. The width is same i.e. 18mm. Copper wire of 0.4 mm diameter is wound 41 turns on the vertical arm to achieve a surface area of Copper 375 sq mm. These components U-frame, copper wire nylon threads remain inside the body. Shelf life- 4 years effective use life- 5 years, from insertion. [14, 15, 16]

D. Effects of Copper

Cu375 has copper as an integral part. Copper is released in the uterine cavity, on a continuous basis, during the lifetime of the device. Studies suggest that the copper acts as a medicinal substance and has a role in improving the contraceptive efficacy of the device. Additional amounts of copper available to the body from the Cu375 may precipitate symptoms in women with Wilson's disease. [9, 11, 18]

Figure 1: Copper T (IUD)

Table 1: Efficacy of the IUD's

S.N.	Product	Life span	Shelf life
1	Copper T 380A	10 years	7 years
2	Cu 375	5 years	4 years

E. IUDs' not an Abortifacient

It is important to understand that the IUD is not an abortifacient but, rather prevents conception. This position is supported by studies that have sought the presence of human chorionic gonadotropin in the presence of human chorionic gonadotropin in IUD users and compared tubal flushing of IUD users with those of non contraceptive control subjects. The copper IUD is effective as an EC when inserted up to 5 days following intercourse. Copper ions released from IUD create an environment that is toxic to sperm, preventing fertilization and implantation but not disrupt implantation. Because copper IUDs prevent Copper can also alter the endometrial lining, but studies show this alteration can rather than disrupt pregnancy, they too are properly classified as contraceptives, not abortifacient. To intended therapeutic and/or diagnostic indication. Copper is the only component on the device that gets released slowly and therefore the effectiveness of the device, if

calculated on the basis of the amount of copper released from the device, will be several years. [19, 20, 21]

F. Female Sterilization Device

Surgical sterilization is a safe, highly effective, permanent, and convenient form of contraception. The most common surgical sterilization procedure for women is called a tubal ligation or having the "tubes tied." The fallopian tubes are the passageway for the egg to travel from the ovary to the uterus. This is where the egg becomes fertilized by the male's sperm prior to traveling to the uterus. In tubal sterilization, the fallopian tubes are both cut and separated or they are sealed shut. This prevents the egg and sperm from meeting and thus prevents pregnancy. Tubal ligation (incorrectly referred to as tubectomy) is considered major surgery requiring the patient to undergo spinal anesthesia. It is advised that women should not undergo this surgery if they currently have or had a history of bladder cancer. After the anesthesia takes effect, a surgeon will make a small incision at each side of, but just below the navel in order to gain access to each of the two fallopian tubes. With traditional tubal ligation, the surgeon severs the tubes, and then ties (ligates) them off thereby preventing the travel of eggs to theuterus. Other methods include using clips or rings to clamp them shut, or severing and cauterizing them. Tubal ligation is usually done in a hospital operating-room setting. This is a permanent sterilization procedure. The mechanical properties of tubal ring are such that the ring compresses the fallopian tube fully, blocking the passage from the ovary to the uterus within minutes. In about ten days necrosis is complete and the loop of the tube withers away into the abdominal. [19, 22, 23]

2. Tubal Lignation Methods

2.1 Bipolar coagulation

The most popular method of laparoscopic female sterilization, this method uses electric current to cauterize sections of the fallopian tube.

2.2 Monopolar coagulation

Less common than bipolar coagulation, mono polar coagulation uses electric current to cauterize the tube together, but also allows radiating current to further damage the tubes as it spreads from the coagulation site. Many cases involve a cutting of the tubes after the procedure. [19, 20, 21]

2.3 Fimbriectomy

By removing a portion of the fallopian tube closest to the ovary, fimbriectomy eliminates the fallopian tubes ability to capture eggs and transfer them to the uterus. [24, 25]

2.4 Irving Procedure

This procedure calls for placing two ligatures (sutures) around the fallopian tube and removing the segment of tubing between the ligatures. Then to complete the procedure, the ends of the fallopian tubes are connected to the back of the uterus and the connective tissue respectively.

2.5 Tubal clip

The tubal clip (Filshie clip or Hulka clip) technique involves the application of a permanent clip onto the fallopian tube. Once applied and fastened, the clip disallows movement of eggs from the ovary to the uterus.

2.6 Tubal ring

The silastic band or tubal ring method involves a doubling over of the fallopian tubes and application of a silastic band to the tube.

2.7 Pomeroy tubal ligation

In this method of tubal ligation, a loop of tube is “strangled” with a suture. Usually, the loop is cut and the ends cauterized or “burned“. This type of tubal ligation is often referred to as cut, tied, and burned.

2.8 Essure tubal ligation

In this method of tubal ligation, two small metal and fiber coils are placed in the fallopian tubes. After insertion, scar tissue forms around the coils, blocking off the fallopian tubes and preventing sperm from reaching the egg. [26]

2.9 Adiana tubal ligation

In this method of tubal ligation, two small silicone pieces were placed in the fallopian tubes. During the procedure, the health care provider heated a small portion of each fallopian tube and then inserted a tiny piece of silicone into each tube. After the procedure, scar tissue formed around the silicone inserts, blocking off the fallopian tubes and preventing sperm from reaching the egg. The procedure can no longer be performed due to a lawsuit and judgment brought by the company responsible forEssure.

3. Devices

3.1 Tubal Rings [27, 28, 29]

The tubal ring (also called the Falope ring, Yoon ring, or Lay loop) is a small silastic band placed around a loop of the fallopian tube. With this method of tubal ligation, a 2-3 cm segment of fallopian tube is drawn inside a narrow cone-shaped applicator. The silastic ring (that previously has been stretched over the outside of the applicator) is then released onto the tubal loop. As the ring contracts due to its elasticity, it constricts the base of the loop and blocks the fallopian tube. Deprived of its blood supply, the constricted loop is replaced with scar tissue, and the remaining healthy tubal segments separate, similar to the Pomeroy tuballigation method. The pregnancy rate is 65% at one year following reversal of tubal ring procedures and continues to rise with the passage of time.

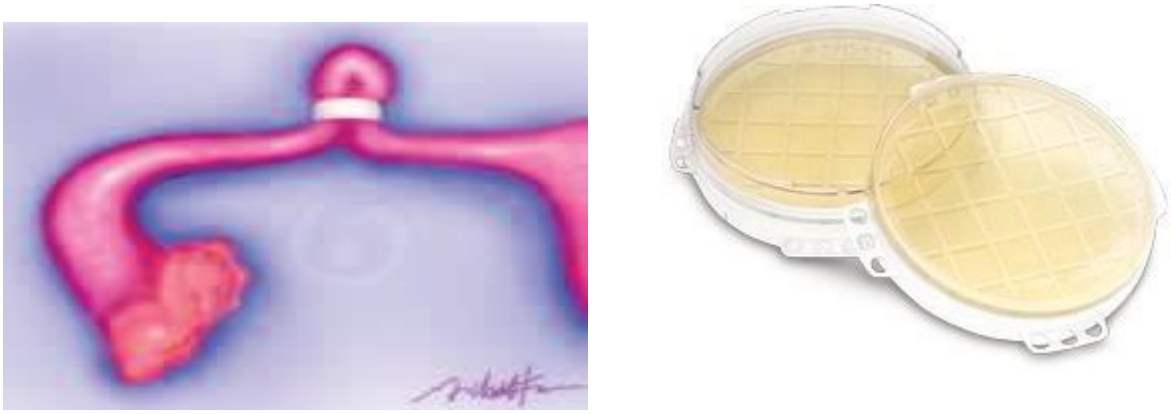

Figure 2: Tubal ring and Plates for Bioburden testing

4. Bioburden [27, 28]

The Bioburden test determines the total number of viable microorganisms in or on a medical device, container or component. It is performed on any product that requires control and/or monitoring of bioburden counts, usually as part of a sterilization program. This test acts as an early warning system for possible production problems that could lead to inadequate sterilization. It is also to calculate the necessary dose for effective radiation sterilization and to monitor product routinely as a part of quarterly dose audits. Bioburden is not a test your product passes or fails- It is information. Bioburden is normally defined as the number of bacteria living on a surface that has not been sterilized. The term is most often used in the context of bioburden testing, also known as microbial limit testing, which is performed on pharmaceutical products and medical products for quality control purposes. Products or components used in the pharmaceutical or medical field require control of microbial levels during processing and handling. Bioburden or microbial limit testing on these products proves that these requirements have been met. Bioburden testing for medical devices made or used in the USA is governed by Title 21of the Code of Federal Regulations and worldwide by ISO 11737. The aim of bioburden testing is to measure the total number of viable micro-organisms (total microbial count) on a medical device prior to its final sterilization before implantation or use. Bioburden in-process testing must be conducted pursuant to written procedures during the manufacturing process of drug products. The United States Pharmacopeia (USP) outlines several tests that can be done to quantitatively determine the bioburden of non- sterile drug products. It is important when conducting these tests to ensure that the testing method does not either introduce bacteria into the test sample or kill bacteria in the test sample. To prepare drug products for testing, they must be dissolved in certain substances based on their "physical characteristics. For example, a water-soluble drug product should be dissolved in "Buffered Sodium Chloride-Peptone Solution pH 7.0, Phosphate Buffer Solution pH 7.2, or Soybean-Casein Digest Broth. The Membrane-Filtration Method and Plate Count Method can be used to measure the number of microbes in a sample. In the Membrane-Filtration Method, the sample is passed through a membrane filter with a pore size of 0.45 micrometers or less. The membrane filter is then placed onto Soybean-Casein Digest Agar and incubated in order to be able to determine the total aerobic microbial count (TAMC).In the Plate Count Method, the sample of drug product to be tested and Soybean-Casein Digest Broth is poured into a Petri dish. The Petri dish is then incubated. The most probable number method (MPN) can also be performed for products considered to have a low bioburden[clarification needed]. The MPN is considered to be one of the least accurate tests. The bioburden quantification is expressed in colony forming unit (CFU). There are generally established guidelines for the maximum CFU that a drug product can contain. Contact plates or sterile swabs can also be used to test for microbes on a surface when compounding sterile products to ensure compliance with USP 797. Bioburden is also associated with biofouling, where microbes collect on the surface of a device or inside of fan cooled equipment. In healthcare settings, this increases the risk of Healthcare-associated infections (HAIs) or Hospital-acquired infections as pathogens can be spread through contact or through the air to new patients and hospital staff. Fan cooled system are generally avoided in critical care and operating rooms, thus relying on natural convection or liquid cooling to cool devices and equipment. These rooms are also required to maintain negative air pressure so that air may enter the room, but the air cannot exit into other rooms. HEPA filters are also used to collect airborne pathogens larger than 0.3 microns.[3, 28, 29]

Figure 3: Soybean Caesin Digest Media

5. Sources

A. Air/Particulate matter
B. Human handling
C. Contact with surfaces
D. Contact with liquids(endotoxins)
E. Can also come from previous use of a device on humans (reusable devices)

6. Determining Bioburden

A. First: Recovery is the best method to extract bioburden Factors affecting

B. Antimicrobials

C. Device Geometry

7. Bioburden result reported in CFUs

Collecting samples for Bioburden

A. Large and frequent production: 3 lots of 10 for initial bioburden

B. Smaller or infrequent production: 10products

8. Bioburden Enumeration Testing

The microbial enumeration test, also called the bioburden test or the microbial load test, is performed to monitor the microbial content in raw materials, in-process samples, and finished product in the pharmaceutical, biological, cosmetics, nutritional products, and medical device industry. The FDA expects companies to monitor the bioburden load in products used for humans and animals.

The bioburden test can be performed by several methods based on the nature of the material tested. The following is a list of the extraction methods offered. The extraction method is the procedure for removing the microorganisms from the product being tested.

A. Immersion

B. Flush /Rinse

C. Surface Sampling

D. Dilution

The following is a list of the enumeration methods offered. The enumeration method is the procedure used to determine the number of viable microorganisms that are extracted from the product being tested.

A. Membrane Filtration

B. Direct Plating

C. Most Probable Number(MPN)

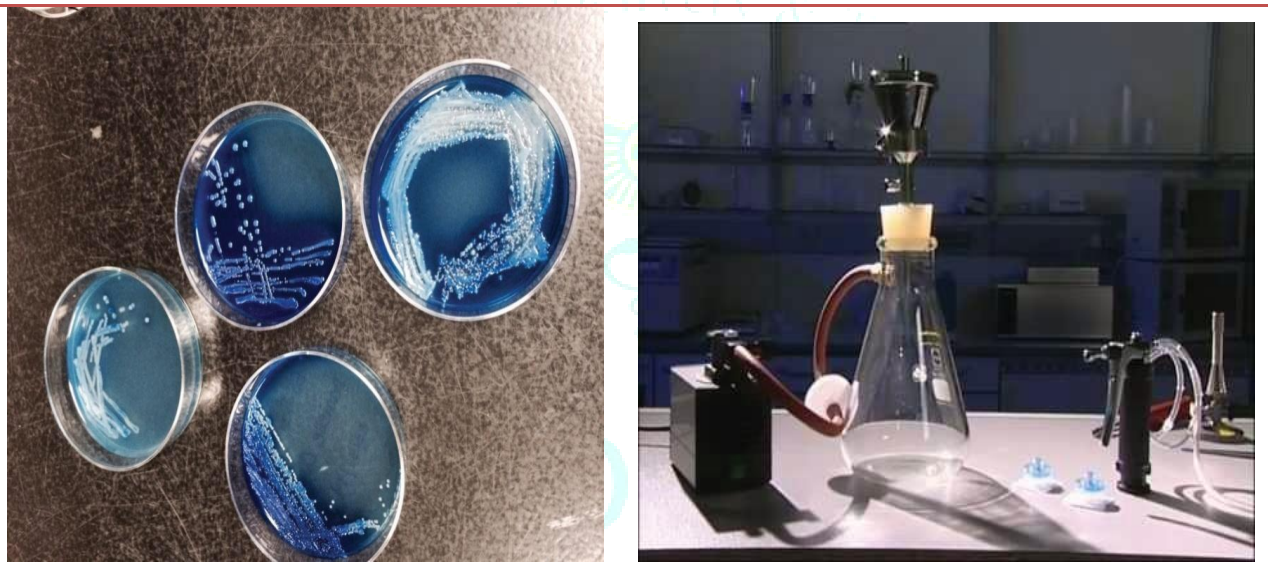

Figure 4: Direct Plate Method and Assembly of Membrane Filtration

The microbial load test should be validated to ensure that the method is effective, accurate, and reproducible in determining the material's microbial load in a test article. The most suitable methodology should be determined as part of method development. Validation will be performed with the method that shows the best recovery of organisms with no inhibition. Validation is performed per USP/EP for Pharmaceutical or Biotechnology products, and AAMI for medical devices. Cosmetics are tested per FDA BAM manual. MQA can also develop custom bioburden procedures for samples that are difficult to test.

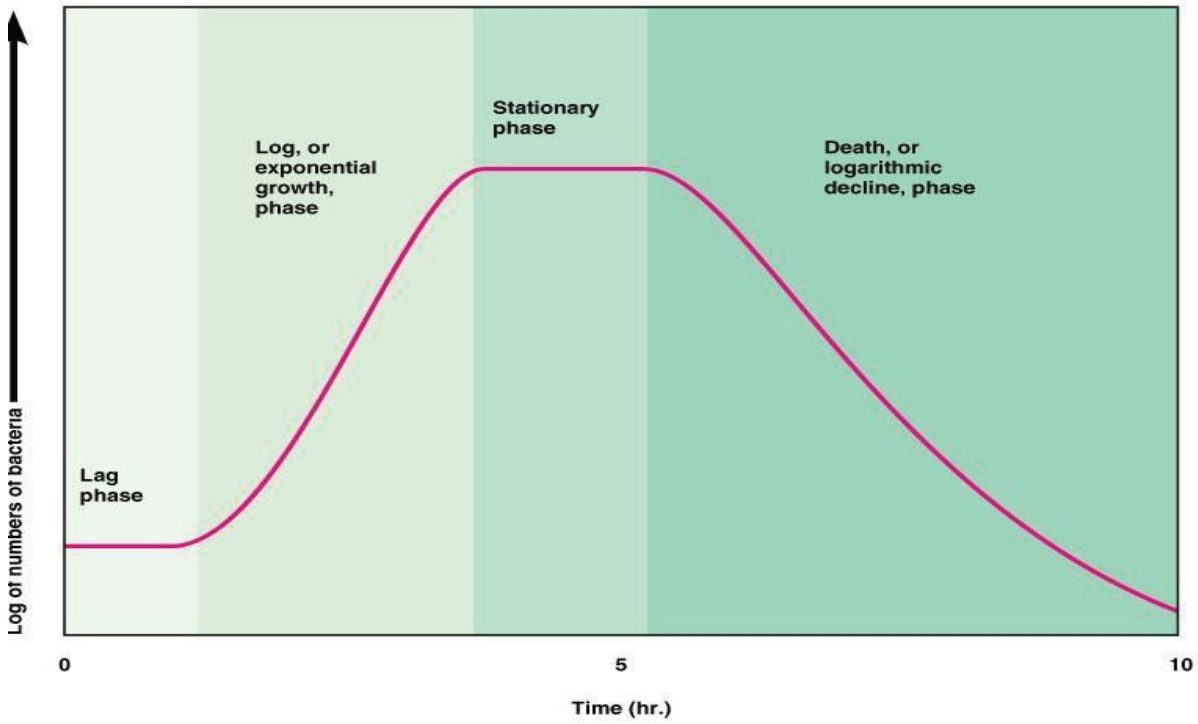

Figure 5: Microbiological Growth Curve

Table 2: Overview of Contamination Control [27, 28, 29, 30]

Content	Validation	Control	Monitoring
Facility	Qualification the clean Room area and HVAC	Maintenance of facilities in sanitization revision of barriers, traffic patterns or air balance	Environmental monitoring
HVAC	Qualification of the clean room area and HVAC system	Certification and prevention, maintenance of system repair of HEPA filter	Environmental monitoring
Water	Qualification of water system	Certification and personnel monitoring regular sanitization of system	Environment monitoring of water system
Equipment	Qualification of the equipment as suitable for its intended use	Certification and preventative monitoring regular sanitization	Environmental monitoring finished product release testing
Sanitization	Validation of cleaning , sanitization sporicidal treatments	Regular cleaning and sanitization of facilities and equipment	Environmental monitoring
Personnel	Proficiency criteria participation in media fills trending data by operator	Training discipline	Personnel monitoring trending data by operator
Process	**Process validation**	Acceptance testing of raw material and containers	In-process bioburden monitoring finished product release testing

9. Routine Monitoring

Routine monitoring procedures for the manufacturing environment and equipment may involve the following methods.

9.1 Surface testing

Testing of surfaces may be carried out using swabs, contact plates, contact slides or the rapid bioluminescence test. Contact plates and slides are designed so that the surface of the solid media may be directly applied to the test surface and then incubated. Such tests are quick and easy to use, and results are directly related to the contact area. The disadvantage is that possibly not all organisms will adhere to the media, and the plates or slides can be used only on flat surfaces. Determining bioburden by use of swabs is particularly useful for monitoring irregularly shaped equipment and difficult-to-access surfaces. Swabs are normally moistened in a liquid medium and then rubbed across a predetermined area. The swab may be directly applied to agar medium, or the swab may be immersed in liquid media, agitated to remove organisms and the TVC completed as for liquid testing. Direct application of the swab to the agar may not remove all organisms from the swab, whereas using an intermediate liquid stage will improve recovery of the organisms. Bioluminescence testing is especially helpful for examining surface bioburden because results are rapidly obtained and will confirm

whether cleaning procedures have been carried out correctly. This will enable a quick response to any problem areas identified, thereby preventing product contamination.

The test method utilizes the reaction that occurs between bacterial adenosine triphosphate (ATP) and firefly luciferin/luciferase, resulting in emission of light.

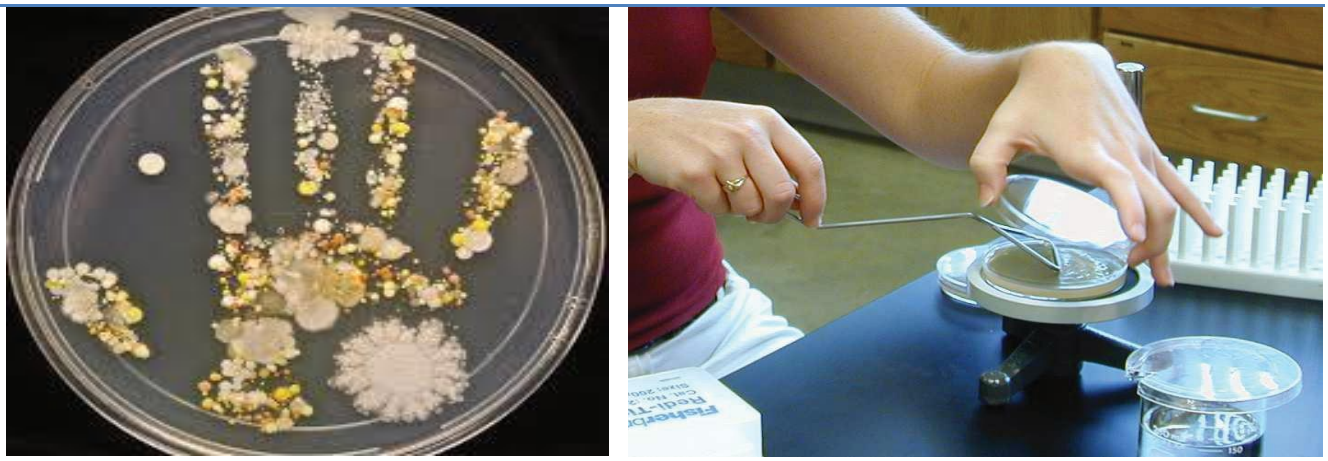

Figure 6: Contact Plate Method and Slide Method

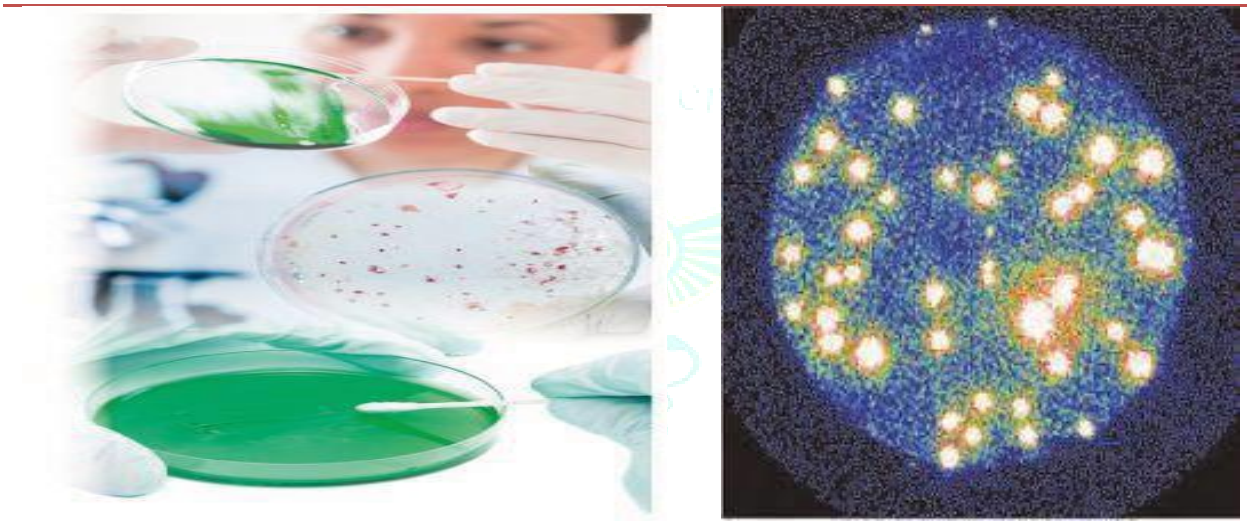

Figure 7: Swab Method and ATP Bioluminescence

9.2 Powders and liquids

Microbiological testing of powders and liquids can be achieved utilizing pour plates, spiral plating/spread plates, membrane filtration or the dilution droplet technique of Miles and Misra. In the case of water testing, the Most Probable Number (MPN) method can also be considered A measured amount of powder can be dissolved in either a suitable solvent or in liquid culture media. Testing then proceeds as for liquid samples. Solvents and powder samples may have an inhibitory effect, however. Therefore, suitable dilutions or neutralizing agents should be used. For the pour plate method, samples of liquid are added to cooled molten agar and mixed, and plates are poured. When set, plates are incubated at appropriate temperatures and times, and colonies are counted. Alternatively, a liquid sample may be directly applied to the agar surface, spread and then incubated. A smaller sample may be required in order to ensure that discrete colonies are cultured and so enable accurate counting. Samples may be delivered and spread using spiral plating equipment. The number of colonies can be related to the volume of suspension delivered and the total count calculated. For the Miles and Misra method, a series of dilutions are made from the samples. Then measured drops are placed on the agar surface. A minimum of five separated drops from each dilution is required. Plates are allowed to dry and are incubated, and counts are made. When large sample volumes are available, particularly as in the case of water testing, the MPN method may be used. A range of dilutions is made in liquid growth medium. The range must be selected so that the lowest dilutions do not show microbial growth. Tables have been produced, such as those by DeMan, using statistical assessments to determine the MPNs of organisms present in the initial sample. In tests of chlorinated water, any residual antimicrobial effect of the chlorine may be neutralized with sodium thiosulphate. The membrane filtration technique utilizes a membrane with a sub-micron pore size, large enough to enable large volumes to pass under pressure, but small enough to retain bacteria. The membrane is then placed onto an agar plate and incubated, and colonies are counted. This technique is particularly useful when there are low numbers of microbes or when there may be interfering substances in the liquid sample beingtested.[3, 5, 12, 29, 31]

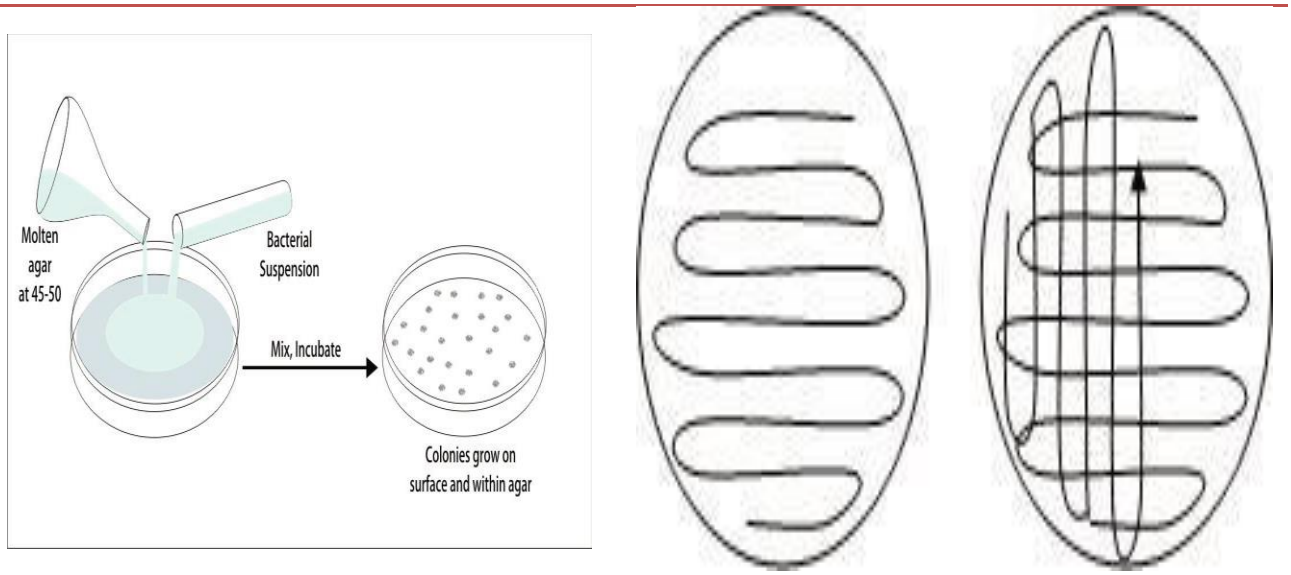

Figure 8: Pour Plate Method and Spiral Method

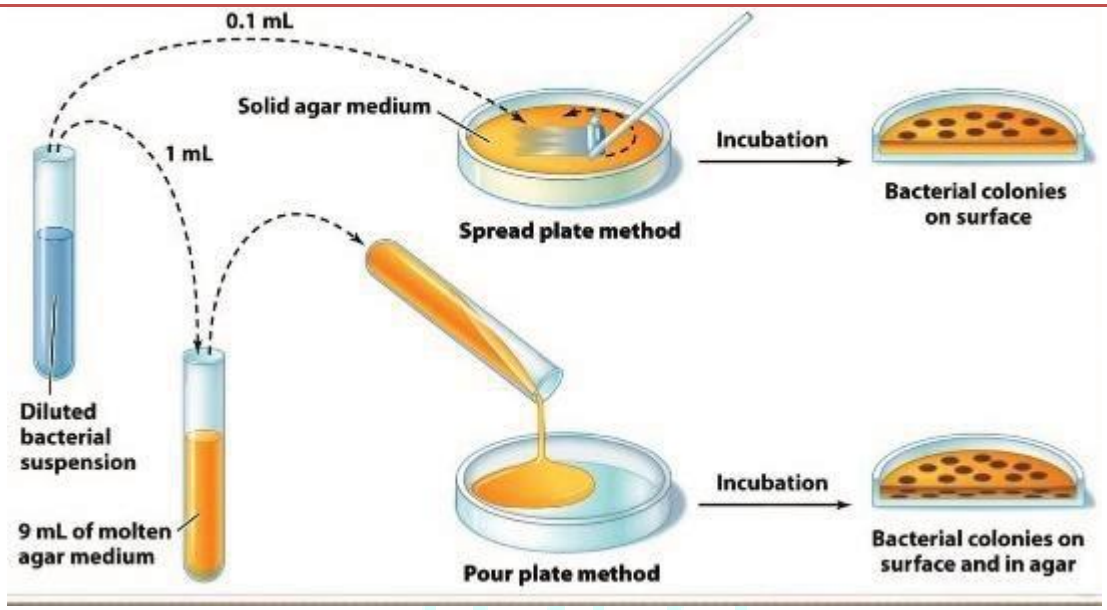

Figure 9: Spread Plate Method

9.3 Air Sampling

Microbiological testing of air samples may be achieved by using settle plates or by active air sampling. Agar plates are left exposed for a defined period of time in the area under test. They are then incubated and colonies are counted. Whyte has established that, for a bioburden of 100 cfu per m^3, a 90 mm diameter plate exposed for an hour will show 10 or 11 cfu. Active sampling systems are also available. Air is drawn into a device for a measured period of time. The micro-organisms are deposited onto agar, which is then incubated. Types of active air samplers available are slit samplers, centrifugal samplers and impaction samplers. The cost of equipment and consumables may be high. Membrane filtration may also be used. Air samples are passed through a sub-micron membrane filter pad for a designated time. The membrane is subsequently placed on an agar surface and then cultured to determine bacterial numbers present in the air sample. In the case of all air sampling techniques, loss of viability may occur due to desiccation of the organisms. Hence, prolonged sampling times should be avoided.[31, 32]

9.4 Identification of micro-organism

On completion of the primary testing, additional tests may be required to identify any organisms isolated, in order to confirm that none of the prohibited organisms are present. A gram stain, coagulase test and oxidase test will indicate whether species identification is required. Biochemical profiles may be used to identify organisms to species level.

9.5 Rapid test method

There are rapid test methods available that may be considered for testing materials and product and for environmental testing. Rapid test technology obtains bioburden measurement by utilizing turbidity, bioluminescence, conductance or impedance of preliminary testing will determine baseline counts to enable routine test limits to be established. When defined, the recommended limits must be at a level that will ensure product safety. After bioburden limits have been established, routine testing programmes can be installed for all stages of the manufacturing process.

10. Equipments

All manufacturing equipment, including tote bins, should be cleaned and sanitized at regular intervals to a written schedule. Cleaning should be microbiologically validate dusting surface test methods to ensure the efficacy of the cleaning procedures and to ensure that there is no cross-contamination onto product. [27, 28]

11. Environment

The manufacturing environment should be controlled to minimize microbial contamination and to ensure that pests such as rodents, birds and insects do not gain access to any manufacturing areas. This is especially important in the manufacturing stages after final drying. It is recommended that air sampling be regularly conducted, particularly in areas where the condoms are most vulnerable to microbial contamination, until product has been foiled.

12. Personnel

Microbial contamination may also arise from personnel. When standing still, a person will normally shed 1,00,000 particles per minute. Moving may increase this to more than one million particles per minute. These particles will contain microbes normally present on skin. Coughing, sneezing and touching product or equipment will also greatly add to the bioburden. Suitable protective clothing and gloved hands will give a measure of protection against this contamination. GMP training will help to enforce correct handling procedures to ensure that contact and cross-contamination between personnel and product are minimized. [27, 28]

13. Raw materials

All raw materials, including water and packaging materials, should be tested at regular intervals. Some materials may have an inherent antimicrobial effect. If this has been confirmed, then monitoring may continue at a much reduced rate on these particular materials.

14. Water

Water is a major material used during manufacturing, and so it must be controlled microbiologically and chemically. Some incoming water supplies may contain extremely high bioburden levels, particularly in adverse local weather conditions such as very heavy rainfall or drought, and must be treated before storage. Treatment methods may include filtration, reverse osmosis (RO) ultraviolet irradiation (UV) or chemical treatment. It should be noted that chemical treatment may interfere with production processes and, depending on the chemicals used, may also cause adverse reactions in personnel. After initial treatment the stored water should be kept under controlled conditions to minimize any further contamination or growth of micro-organisms. Additional treatment of water may be necessary to produce deionised (DI) or softened water. Many microorganisms find favour able conditions for growth on the DI resin beds and on RO membranes. It is essential, therefore, that the servicing protocols be followed rigorously to prevent colonization of the equipment with microbes. If UV irradiation is used, monitoring of the system to confirm correct UV emission is essential in order to ensure that the UV lamps have not become partially obscured and therefore ineffective.[5, 27, 28]

15. Dipping, stripping and drying

Dipping lines utilize large volumes of process water, which is sometimes re-circulated at certain points of the process. It is recommended that there is no recirculation, but, if recirculation is necessary, it should be kept to a minimum and only re-circulated for short periods of time or for a single re-use. [5, 27, 28]

16. Conclusion

Microbiological testing will confirm whether bioburden is being properly controlled under these circumstances. All equipment should be regularly monitored, using surface testing methods that will confirm the efficacy of cleaning.

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