

## Review Article

# Medical device: a complete overview

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### ABSTRACT

Medical device means any instrument, apparatus, machine, appliance, implant, reagent for in vitro use, software, material or other similar or related article, intended by the manufacturer to be used, alone or in combination, for human beings, for one or more of the specific medical purpose. Medical devices are generally classified based on risks; the actual risk-based classification of the medical device depends upon its intended use and purpose. Development of an entirely new device typically begins with a concept by a physician or bioengineer for a solution to a medical problem. If the idea is determined to be workable and practical (proof of concept) an early design of the device, known as a prototype, will be built. A prototype device will undergo a cycle of preclinical testing, redesigning, preclinical testing of the redesign and so forth, until the design has been refined and tested to a point that it is ready for production and testing in humans. Preclinical animal tastings are conducted to provide reasonable evidence that novel technologies and therapies are safe and effective. When studying medical devices, clinical trials are not always required, and whether or not one will be conducted depends on a risk assessment. Post marketing surveillance is the practice of monitoring the safety of a medical device after it has been released on the market.

**Keywords:** Medical Device, Idea, Discovery, Prototype, Preclinical research, Clinical trials, Regulatory review and Decision, Product launch, Post marketing surveillance

### INTRODUCTION

WHO defines 'medical device' as any instrument, apparatus, machine, appliance, implant, reagent for in vitro use, software, material or other similar or related article, intended by the manufacturer to be used, alone or in combination, for human beings, for one or more of the specific medical purpose(s) of; diagnosis, prevention, monitoring, treatment or alleviation of disease; diagnosis, monitoring, treatment, alleviation of or compensation for an injury; investigation, replacement, modification, or support of the anatomy or of a physiological process; supporting or sustaining life; control of conception; disinfection of medical devices and providing information by means of *in vitro* examination of specimens derived from the human body; and does not achieve its primary

intended action by pharmacological, immunological or metabolic means, in or on the human body, but which may be assisted in its intended function by such means.<sup>1</sup>

In the past, medical devices were regulated as drugs in India under the drugs and cosmetics rules, 1945. The medical devices rules, 2017 of the Drugs and Cosmetics Act, 1940 came into force with effect from January 1, 2018.

In pursuance of sub-clause (iv) of clause (b) of section 3 of the Drugs and Cosmetics Act, 1940 (23 of 1940), the Central Government, after consultation with the drugs technical advisory board, specified the following devices intended for use in human beings or animals as drugs with effect from the 1st of April, 2020, namely; all

devices including an instrument, apparatus, appliance, implant, material or other article, whether used alone or in combination, including a software or an accessory, intended by its manufacturer to be used specially for human beings or animals which does not achieve the primary intended action in or on human body or animals by any pharmacological or immunological or metabolic means, but which may assist in its intended function by such means for one or more of the specific purposes of; diagnosis, prevention, monitoring, treatment or alleviation of any disease or disorder; diagnosis, monitoring, treatment, alleviation or assistance for, any injury or disability; investigation, replacement or modification or support of the anatomy or of a physiological process; supporting or sustaining life; disinfection of medical devices and control of conception

Medical devices are generally classified based on risks; the actual risk-based classification of the medical device depends upon its intended use and purpose. Following are the CDSCO classification for medical devices: low risk, class A (absorbent cotton wools, surgical dressing, alcohol swab, etc); low moderate risk, class B (thermometer, BP monitoring device, disinfectants, etc); moderate high risk, class C (defibrillator, dialysis machine, etc); high risk, class D (cardiac stent, heart valve, etc).<sup>2</sup>

## **IDEA AND DISCOVERY**

Development of an entirely new device typically begins with a concept by a physician or bioengineer for a solution to a medical problem, as opposed to a new drug, which usually comes from basic laboratory research.

Defining new invention is the first step and this can be accomplished by answering 3 questions;

### ***Market assessment***

What problem in the medical industry is your device addressing? How is it different than other devices trying to address this problem?

### ***Business model***

How much will production cost? How will you sell it and who are your investors?

### ***Engineering***

Is existing technology used to develop the product? Are the components available for use or new components are needed to be manufactured to help create the invention?<sup>3</sup>

## **PROTOTYPE**

If the idea is determined to be workable and practical (proof of concept) an early design of the device, known as a prototype, will be built.

### ***Appearance prototype***

This medical device prototype lets you see and “feel” how the device will look and function once it’s completed. In some cases, the appearance model may be a series of drawings that explore a number of configurations for the product. This prototype facilitates feedback from all stakeholders regarding the shape, size, color, location, other visual features and gross function of the final product, before you invest in detailed design, implementation, and testing.

### ***Proof of concept prototype***

The first physical model created along the product roadmap is the proof of concept prototype. This medical device prototype is used to analyze the business risks of the envisioned solution, performance of a subsystem or technical component for feasibility. Designed to answer the question "will it work?", “they’re usually functional, not really aesthetic. These evaluations and feasibility reports assist with component selection and specification development, and are part of the device’s design.

### ***Alpha prototype***

The Alpha prototype is the initial attempt at designing and fabricating the product to meet the Product Requirements Specification. It also is the first attempt to make a prototype that both looks like and works like the final product.

The Alpha may be constructed with 3D-printed enclosures and components for physical fit and performance evaluation. It will have initial printed circuit board and enclosure designs for internal testing and evaluation of performance, safety, Electromagnetic compatibility (EMC), usability, and appearance. Alpha development is expensive compared to previous stages, and requires months to iterate and refine the design.

The Alpha design and testing are essential in understanding the product’s limitations and in refining the design. The Alpha prototype development phase will involve development of design specifications for hardware and software that define performance specifications and incorporate safety mitigation for hazards identified.

### ***Beta prototype***

The Beta prototype development incorporates the design refinements found in Alpha development and implements them into production tooling, molds, printed circuit Board, subassemblies, enclosures, good User Interface designs, etc. Test plans and verification protocols are prepared. Software is refined and prepared for the first release. Documentation is updated and prepared for releasing the device master record (DMR). Production testing and assembly protocols are drafted.

Beta prototypes are assembled and tested per the production procedures, and hazard mitigations are documented in the risk management report. The Beta prototypes are ready for verification and preliminary validation testing, safety and EMC testing, and performance testing to verify compliance with the Product Requirements Specification.

Refinements will be required after assembly of the Beta prototypes, and these refinements should be under configuration control to reflect the reasons for the changes and how they make the Beta prototype overcome any deficiencies in meeting specifications and standards. Beta prototype development will involve the development of verification specifications for hardware and software to ensure that the product meets design requirements. These are used in clinical trials.

### ***Pilot production***

The pilot production phase is where the refinements from the Beta prototype verification and validation testing are incorporated into the design and into the production process. The documentation for the device master record and risk management report are updated. The design transfer to manufacturing and the implementation of the quality management system is done for pilot production.

These units may be used as a final prototype for sales and marketing purposes, allowing stakeholders to test the user experience and evaluate its performance before production tooling is created. The design and the production process are relatively stable.<sup>4</sup>

## **PRECLINICAL RESEARCH**

A prototype device will undergo a cycle of preclinical testing, redesigning, preclinical testing of the redesign, and so forth, until the design has been refined and tested to a point that it is ready for production and testing in humans. Preclinical testing may involve the following:

### ***Bench testing***

A crucial step in the early device design process. Bench testing is used as a low cost method to validate the engineering functions, features and to tease out mechanical and design flaws in your device before committing to costlier animal and highly expensive human studies. Early bench testing for small products is often done on a larger size version to emphasize the desired interaction. When developing a test plan for the bench tests, the designer must determine the key objectives of the study that anticipate the desired results and plan the protocols accordingly. In addition, the data needed to be collected defines the methods and materials required for the testing and can help guide how realistic the test needs to be. Low resolution, low cost models used to screen early prototype ideas, such as chicken

breast or beef liver obtained from the supermarket, or delivery system testing in vascular models crafted from silicone tubing from a hardware store.

Once a given design has completed the initial screening process, it will undergo a series of optimization steps, more realistic models used to further optimize product designs or to simulate various use states. Some medical devices are tested in anatomical models that match the targeted patient disease state, through advanced imaging of patient anatomy followed by accurate 3D printing of the model. Realistic anatomical models to support the design freeze decision. These models can also be used to educate and train physicians prior to the initiation of training in a preclinical model. Negative bench testing results are informative in the sense that if you find something not working during bench testing, you can be well assured that it is certainly not going to work inside the body. In contrast, if it works well during bench testing, obviously that is reassuring, but it is still no guaranteeing that it will work inside the body.<sup>5</sup>

### ***Technical testing***

Engineering and quality testing of the materials and the electronic/mechanical elements of the device for accuracy and reliability are done. The prototype will usually be rebuilt using different materials. Medical devices are critical since they have a direct impact on human lives. Medical devices are highly regulated by multiple regulatory bodies and compliances. On the other hand, end users expect exceptional performance, effectiveness, and safety from the device they are using. This compels medical device manufacturers to define and implement medical device testing strategy that turns to be effective throughout the development cycle, starting from the concept and design phase to production stage. A medical device testing strategy must incorporate compliance processes and technical testing strategies for better performance and effectiveness of medical devices. If they test manufactured devices for the functionalities and find issues with the device, it will be very costly and time consuming to go back to the design phase and find appropriate solutions for the issues.

### ***Devising an effective medical device testing strategy***

Testing team should utilize design team as a source of knowledge. Design input can help to derive the test structure that matches with the hardware, software or other technical requirements. The design class modes, effects, and criticality analysis can be used to derive test requirements of the device for risk mitigation. An effective medical device testing strategy needs several sets of test requirements. These sets of requirements are required to ease the test implementation as tests are carried out continuously at different stages of the complete manufacturing process, from component selection to a final assembly of a medical device, and

each stage has different requirements and different parameters to be satisfied.

### **Validation process**

Once everything is in place, the medical device test system must be validated, including software and hardware. The process of software and hardware validation for medical devices must be detail specific. The purpose of validation is to test if the device meets specific user needs or not. Hence, the structure and approach are very crucial to apply validation methodology. The testing team should work with the manufacturing team to validate those specifications and then testing and verification of the performance of individual block should be done to document the result, which should be then reviewed. The functional block test comes handy for validation of custom developed hardware or software for medical devices.

### **Verification testing**

Verification is a process to confirm whether the examination and provision of objective evidence that specified requirements of the device have been fulfilled. Verification process starts with clear and well-defined product requirements. These product requirements must be measurable in order to verify. We must know what the answer should be as verification is not an experiment. A strongly defined and implemented medical device testing strategy can save dollars for manufacturers and ensure that devices meet the end user expectations. It also decreases the risk of devices recall.<sup>6</sup>

### **Computer modelling and simulation**

The medical device industry has traditionally developed a process flow to test the innovation on the bench, do animal trials and human trials, and then apply for regulatory approval once confident in the performance and safety of the device. While computer modelling and simulation (CM&S) is typically used in the early design and development of devices, it has been less common in downstream activities, especially in the rigorous testing required to meeting regulatory requirements.

Traditional method can also be slow, costly, and limited. Testing on humans, for example, runs into practical constraints, such as the difficulty of measuring the performance of a device when it is in a person, the inability to quickly test variations of a device, and ethical considerations or because of the difficulties presented in testing sophisticated equipment. CM&S provides another avenue for looking at devices. Companies can build models of devices and the body's systems, and run simulations of how the device will perform when it is deployed. They can quickly adjust variables to try out different scenarios, making it possible to run through a large number of possibilities in a relatively short time to find the optimal result. One of the key advantages

simulation offers is the ability to reduce physical prototyping. Challenging designs and new ideas can be built and tested without having to be physically constructed. In an industry where safety is of paramount importance, the ability to investigate different scenarios by specifying boundary conditions, material properties, and physiological mechanisms allows for early and harmless correction of design mistakes. But that does not mean that these tests are expected to totally replace the traditional in vivo and in vitro tests. Rather, they can complement them, allowing researchers to shift more of the overall testing workload to CM&S and hopefully reduce reliance on bench, animal, and human testing. CM&S has the potential to be applied at points throughout the product lifecycle, from discovery and ideation to regulatory decision making, product launch, and post-market monitoring.

CM&S can also be used to assess certain qualities of devices that are already on the market. Clinical simulation helps doctors by performing virtual surgeries, such as stent deployment in the heart or the brain. These include models of anatomy, such as musculoskeletal structures; people can perform statistical shape modelling to understand population distributions of different anatomical characteristics, which can be important for understanding its impact on the design and sizing for devices. Physiology of various organ systems; modelling the electrophysiology of the heart for simulating arrhythmias is a growing area of research. It is needed to be able to simulate those arrhythmias in order to simulate the therapies that can treat those arrhythmias. The device can then be "virtually placed" in simulated/anatomy models for testing. Similarly, device parts can be modelled and tailored to individual patients and drive the 3-D printing of custom parts. With patient-specific implants, you can bring together a simulation of the anatomy and the device, so you can design the device to fit that anatomy before it's printed.

Researchers have plans to build on increasingly sophisticated CM&S capabilities, and bring together various models to create a "virtual patient" to test devices and treatments in order to augment clinical trials with human beings. Where a clinical trial might look at 500 or 1,000 patients with an actual implanted device, the virtual patient could potentially simulate thousands of patients and identify problems early on, before the devices are tested with humans. These simulations could be used in the design of clinical trials. Eventually, this approach could lead to researchers using a combination of real patients and "virtual patients" in clinical trials, which could reduce the number of humans, required and help speed up the process significantly.

While CM&S is finding a range of applications in the medical device field, it is still not used as widely as it could be, and there are still scientific and technical challenges that need to be overcome before that happens. A key one is lack of readily available information about

the human body that can be put into models. For example, the properties of materials used in medical devices are typically well understood, but not so the tissues in the human body. If we want to know the electrical conductivity of copper, that's easy to look up or measure, what about the electrical conductivity of muscle or fat at 400 kilohertz, roughly the frequency that is applied in tissue ablation? That's hard to find, and it varies with temperature. At the same time, materials in the body can differ from person to person, and they can change as people age or as tissue is affected by disease. There are efforts underway to gather more of this type of data, but doing so will take time. Another key hurdle is regulatory uncertainty, that is, the question of whether evidence from computer models will be accepted by regulators in the rigorous device-approval process.<sup>7</sup>

### ***Animal testing***

The purpose of preclinical animal testing is to provide reasonable evidence prior to early feasible testing in humans and human clinical trials to demonstrate that novel technologies and therapies are safe and effective, these data are an integral part of medical device development and necessary to make these decisions.

Testing of a novel device material involves *in vitro* assays in cell cultures and *in vivo* tests using animal models. The purpose of *in vitro* tests is usually to assess cell toxicity and DNA damage in animal and human cell lines and in primary human cells. Animal studies must be undertaken when cell studies are inapplicable, for example to study the systemic toxicological response, elimination pathway of a material, local and systemic immunological responses, or carcinogenicity of a material. Animal models can also be used to study *in vivo* chemical interactions or degradation of a material. The device materials may be injected or implanted in laboratory animals to study animal behaviour and physiology over short or long time frames. Extensive biochemical analysis can be carried out by harvesting various organs and tissues from the experimental animals.

### ***Elements to be considered for the animal study***

In the process of designing preclinical animal research, rationale animal models that are best representative of the human clinical trials must be chosen this will improve the success rate of clinical trials. The elements of risk analysis and limitations are addressed by describing the similarities and differences between the selected animal model and humans for utilizing device implantation; the surgical technique and location of device insertion and size and anatomy.

In addition, medical devices can cause mechanical or biological stresses when placed *in vivo*. Therefore, it is important to identify physiological response variables on the body, to improve the chances of success for human trials.

In preclinical animal research, it is recommended that the methods and materials utilized for the assessment of medical devices be similar to those utilized in humans. It is important to include adequate controls to minimize experimental variables and errors. In disease models, background levels of disease and psychological stress should be controlled as much as possible to generate data that can support the safety and performance of a medical device and obtain predictive outcomes. In addition, when considering the number of animals needed, it is important to decide which disease model to use (naturally occurring disease model vs. induced or experimental disease model).

### ***ISO standards for animal testing of medical devices***

The main ISO standards which covers quality management of animal testing, in addition to the quality management of all stages of medical device development, is ISO13485; 5. Both animal testing and *in vitro* testing are covered by the ISO10993 series<sup>6</sup> that is comprised of 18 parts including general evaluation, animal welfare requirements, tests for DNA damage, interactions with blood components, etc based on characterization of the device by type of tissue and contact duration. Advantages of standardization are; the ISO standards facilitate the use of replacement, reduction, and refinement in animal research, for example, by defining the minimum sample size for studies, and indicating where *in vitro* assays can be used instead. The documentation of device testing required by ISO standards ensures accurate records of any testing procedures carried out.

Individual tests for consideration systemic toxicity; acute, sub chronic, chronic, and pyrogenicity (ISO 10993-11A). Device and its constituent materials can potentially impact the macro and microstructure and function of organs as well as generalized physiologic homeostasis beyond the site of device-body contact. Toxic effects can be seen at any point along a continuum from acute (anaphylaxis) to chronic (renal insufficiency secondary to particulate accumulation). Methods of testing (ISO 10993-11) summarize the various routes of administration for toxicity testing, including implantation, intramuscular, subcutaneous, intravenous, and intraperitoneal. The standard states that the most relevant route of administration shall be used (International Standards Organization 2017). It follows, logically, that toxicity testing for a particular device should be performed using device components and exposure routes that reflect the intended clinical use of the device and that failure to do so can lead to findings that are inconclusive or confounding

Evaluation of testing evidence of systemic toxicity is obtained through three major routes in any animal model; clinical evaluation, clinical pathology, and anatomic pathology. Clinical evaluation ideally yields *in-life* information regarding an animal's overall clinical status including behaviour, appetite and water intake, presence

of overt signs of pain or distress, and signs of systemic compromise (dyspnea, seizure activity, haemorrhage, and profound lameness). Clinical pathology provides time point and trend data for hematologic and biochemical parameters that can be compared to individual baseline as well as accepted species and breed-specific standards. Anatomic pathology permits the gross and histological assessment of major and minor organs, including those with direct device contact as well as downstream and end-organ targets. Taken together, these data sets create an overall clinical picture of animal health and systemic stability following treatment with a device and can reveal evidence of toxicity throughout the observation period.

Chronic implant testing, (ISO 10993-6: 2016), the local tissue response to a chronically implanted device is also of interest. In general, chronic tissue responses are evaluated in tests longer than 3 months as in muscle and connective tissue a steady state tends to be seen in the cell population between 9 and 12 weeks (International Standards Organization 2016). The standard describes implantation in subcutaneous, muscle, bone, and brain tissue but states that the test sample shall be implanted into the tissues most relevant to the intended clinical use of the material (International Standards Organization 2016). Semi-quantitative and quantitative scoring systems have been described for evaluation of local biological effects, including capsule formation, inflammation, presence of different types of leukocytes, and degradation of the test material (International Standards Organization 2016).

*In Vivo* thrombogenicity testing, (ISO 10993-4: 2017), thrombogenicity testing is generally required as part of overall hemocompatibility testing when devices are in contact with the blood. There are many factors that can influence the thrombogenicity of a device tested *in vivo*, including species, subject positioning, anticoagulation regimen, implantation technique, device design and coating characteristics, and implantation location (International Standards Organization 2017a). Depending on the nature of the device and its intended clinical use, thrombus formation can occur on an acute (procedural or periprocedural) and/or chronic timescale. It is critically important that, as much as possible, the thrombogenicity testing be performed in a model that closely approximates its clinical use and that if multiple componentry such as delivery systems for short-term intravascular use and chronic intravascular implants receives adequate evaluation.<sup>8</sup>

## CLINICAL TRIALS

Before a clinical trial involving a new device may begin, the proposed study and device must undergo a regulatory review and notification process for the purpose of ensuring the safety of study participants. Data needed for regulatory review and approval includes; design analysis data, biocompatibility and animal performance study data, investigator's brochure, clinical

investigational plan, case report form, serious adverse event report form, informed consent form, investigator's undertaking, ethics committee approval and regulatory status in other countries proposed instruction for use or directions for use and labels.

In case of medical device of which drugs are also a part the submission of requirements relating to animal toxicology, reproduction studies, teratogenic studies, perinatal studies, mutagenicity and carcinogenicity may be relaxed in case of drugs already approved and marketed in India and supported by adequate published evidence regarding safety of the drug.

In India permission to conduct clinical investigation for an investigational medical device will be granted in form MD-23 by CDSCO, if not satisfied with the requirements as referred, CDSCO may reject the application for reasons to be recorded in writing, within a period of ninety days, from the date of application. Clinical investigation shall be initiated after approval of clinical investigation plan by the registered ethics committee.

Clinical investigation shall be conducted in accordance with the approved clinical investigation plan, good clinical practices guidelines issued by the central drugs standard control organization. Clinical investigation shall be registered with the clinical trial registry of India (CTRI) before enrolling the first participant for such clinical investigation. Annual status report of each clinical investigation, as to whether it is ongoing, completed or terminated, shall be submitted to the central licensing authority by the sponsor, and, in case of termination of any clinical investigation, the detailed reasons for the same shall be communicated to the central licensing authority within thirty days of such termination. Information about any report of suspected unexpected serious adverse event occurring during clinical investigation on the subject shall, after due analysis, be submitted by the sponsor to the central licensing authority within fourteen days of the knowledge of its occurrence. In case of an injury or death during clinical investigation of a subject, attributable to the use of investigational medical device the applicant/sponsor shall provide complete medical management or compensation.

The clinical investigation shall be initiated by enrolling first participant within a period of one year from the date of grant of permission, failing which prior permission from the central licensing authority shall be required to initiate clinical investigation. The sponsor holding permission shall maintain data, record, registers and other documents for a period of seven years after completion of such investigation.<sup>9</sup>

### *Clinical investigation of medical devices for human subjects*

ISO 14155:2011 addresses good clinical practice for the design, conduct, recording and reporting of clinical

investigations carried out in human subjects to assess the safety or performance of medical devices for regulatory purposes.

ISO 14155:2011 specifies general requirements intended to protect the rights, safety and well-being of human subjects, ensure the scientific conduct of the clinical investigation and the credibility of the results, define the responsibilities of the sponsor and principal investigator, and assist sponsors, investigators, ethics committees, regulatory authorities and other bodies involved in the conformity assessment of medical devices.<sup>10</sup>

### ***Clinical trial classifications***

Clinical trials for medical devices have many similarities to those for pharmaceuticals, but there are some necessary differences in the way the trials are designed and carried out. And in some cases, for medical devices, clinical trials may not even be required.

#### ***Feasibility (pilot) study***

Feasibility studies are intended to acquire specific essential information about a device, before going to pivotal study, conducted in small number of patients/sites 10-30 patients at 3-4 sites. It is exploratory in nature, gain initial safety data, answer study design and technique related issues.

The objectives of a pilot clinical investigation include assessing feasibility (preliminary device performance), exploring eligibility criteria and their practical application for pivotal controlled investigation, ascertaining potential harm (preliminary safety evaluations), studying device mechanism, validating a method for determining an outcome measure, provide guidance for pivotal study

#### ***Pivotal clinical investigation***

Pivotal clinical investigation shall be carried out on the basis of data emerging from pilot clinical investigation. The pivotal clinical investigation is a definitive study in which evidence is gathered to support the safety and effectiveness evaluation of the medical device for its intended use. The study is confirmatory that may be conducted in large number of patients (150-300 subjects) with disease or condition being studied and scope to provide the effectiveness and adverse effects. For investigational medical device which does not have a predicate device but has been approved for sale or distribution in any country other than India pivotal studies need to be carried out primarily to generate evidence of safety and effectiveness the medical device in Indian patients. Prior to conduct of pivotal clinical investigation in Indian subjects, the Central Licensing Authority may require the pilot study data to assess whether the pilot data is in conformity to the data already generated outside the country. The data is used for supporting marketing authorization application.

### ***Clinical trial design***

Clinical trial design may include randomization to ensure there is no bias for treatment outcomes. Randomization, which places subjects randomly into either the treatment or control, ensures that investigators could not choose subjects who would likely have better outcomes to be in the study group, while those who would likely have worse outcomes go into the control group. Many times, the controls used are previously approved devices, in order to show how the new product compares to current therapies. In medical device studies, it is often unethical to use a placebo, and for many devices it would be impossible for example, if a subject enrolled in a study of an artificial hip, the subject could not be given a placebo, or "sham" operation and be withheld treatment for the diseased joint. Another common way to design a trial is to use "blind" or "double blind" controls. A blind study means the subject is unaware of which treatment group they are assigned to, and double blind means both the subject and the physician are not aware of the treatment being provided. With new drug trials, double blind trials are commonly used. However, as one can imagine, it is nearly impossible to blind subjects or investigators with a device trial, there are exceptions, but they are rare.

Clinical trials need a way to measure the success of a new product. For drug trials, standard follow-up might collect blood pressures, heart rates, ECGs, etc. to determine the effect the drug has on the body. But in device trials, there is a way to actually visualize the performance of the device through imaging. There will likely be at least one imaging modality used to enable the sponsor to see the device and ensure it is still functioning appropriately.

### ***Clinical trial requirements***

When studying new drugs, a clinical trial is required in every case. Minute changes to the composition of a drug may result in unexpected effects. However, when studying medical devices, clinical trials are not always required, and whether or not one will be conducted depends on a risk assessment. For example, a tongue depressor and an adhesive bandage are considered medical devices. They pose little risk to human subjects, and therefore do not require a clinical trial. On the other hand, a drug-eluting stent, or a new material for a hip replacement, introduce higher levels of risk and may require a clinical trial. Medical devices can be broken out into classes, with class A being low risk, class B being low to moderate risk, class C being moderate to high risk, and class D being high risk. Mostly class A medical devices does not require clinical trial, class B and C may require and class D definitely requires clinical trials.

The central licensing authority may, in public interest, abbreviate, defer, or waive the requirement of animal data or clinical data for conducting clinical investigation. If the device is indicated in life threatening, serious diseases or disease of special relevance to the Indian health

scenario, national emergencies, extreme urgency, epidemic and medical devices indicated for conditions, disease or which there is no therapy.

The results of clinical investigation may not be required to be submitted where the investigational medical device is approved by the regulatory authorities of either UK or USA or Australia or Canada or Japan and the said device has been marketed for at least two years in that country and the central licensing authority is satisfied with the data of safety, performance and pharmacovigilance of the device, and there is no evidence or theoretical possibility, on the basis of existing knowledge, of any difference in the behaviour and performance in Indian population. The applicant needs to give an undertaking in writing to conduct post marketing clinical investigation with the objective of safety and performance of such investigational medical device as per protocol approved by the central licensing authority.<sup>11</sup>

## **REGULATORY REVIEW AND DECISION**

Medical devices approval is the process of scientific and regulatory review to evaluate the safety and effectiveness of medical devices. Medical devices are those that support or sustain human life, are of substantial importance in preventing impairment of human health, or which present a potential, unreasonable risk of illness or injury. Due to the level of risk associated with Medical devices, CDSCO has determined that general and special controls alone are insufficient to assure the safety and effectiveness of Medical devices. Therefore, these devices require a premarket approval.

The applicant must receive CDSCO approval prior to marketing the device. Medical Devices approval is based on a determination by CDSCO that there is sufficient valid scientific evidence to assure that the device is safe and effective for its intended use(s).

### ***Data requirements non-clinical laboratory studies section***

Non-clinical laboratory studies section includes information on microbiology, toxicology, immunology, biocompatibility, stress, wear, shelf life, and other laboratory or animal tests, the rationale for the model selection, the similarity of the selected model compared to humans, and the general animal study methodology used. In addition, it is important to include the rationale for the transition from the pilot, validation, or proof-of-concept studies to pivotal animal studies, as this information provides an understanding of how device safety was assessed. If any design changes have been made to the device, they should also be described in the regulatory submission, and there should be a performance report of the device across multiple studies.

Non-clinical studies for safety evaluation must be conducted in compliance good laboratory practice for nonclinical laboratory studies. For relatively simple devices, conclusions of substantial equivalence may be drawn from preclinical testing alone. When complex devices are considered, preclinical testing serves as the foundation for more extensive clinical testing.

### ***Data requirements clinical investigations section***

Clinical investigations section includes study protocols, safety and effectiveness data, adverse reactions and complications, device failures and replacements, patient information, patient complaints, tabulations of data from all individual subjects, results of statistical analyses, and any other information from the clinical investigations.

If the reports are vague or lack sufficient detail, the regulatory body reviewer may struggle. It is important to remember that anything the sponsor can do to make the reviewer's job easier will ultimately be an advantage. Failure to present data appropriately can result in regulatory body responding with deficiencies. Such deficiencies require a resubmission.

Include raw data. Another common error is to omit raw data. Sponsors often provide only the summary reports written by themselves or the contract laboratory. Providing only summary data almost always results in a significant deficiency. As noted earlier, reviewers want as much information as possible so that they can come to the independent conclusion that the data are valid and acceptable for supporting the application.

Submission that appears of poor quality can leave the impression that the science and entire operation is not of sufficient quality, even if all the actual science provided in the submission is good. Grammatical and typographical errors can be easily avoided by implementing several proofreading steps. Refine intended use and indications for use. It is common for submissions to have either no statement of intended use, or a statement of intended use that is too vague.

Provide description of the device, theory of operation, indication for use and method of manufacture. In addition, the sponsor should provide corresponding description of how each risk is mitigated or minimized via the device design, instructions for use, selection of patient population, and justification for the sample size.<sup>12</sup>

## **PRODUCT LAUNCH**

So much work goes into designing a product and submitting a regulatory submission that many people assume the work stops there. However, there is still much work that lies ahead to make sure there is adequate supply of your product and that it is actually used in the field. In order to execute a successful product launch, it is again wise to adhere to a plan.



### Design transfer

The design transfer process is all about handing over the necessary information to your manufacturing team so they can make your product. It is vital that the products made during the manufacturing stage match the products made during the verification and validation phase.

### Setup distribution network

The phrase “your product won’t sell itself” is one you’ve probably heard before. You are going to need a solid network of sales and marketing professionals. With the ever changing global economy, there are many companies throughout the world who have a proven infrastructure in place to focus on selling product and growing revenue.

### Develop marketing materials

The buyers of your device may be hospital systems, physicians, patients, distributors, and maybe even the government in some countries. Because of this, you need to have a marketing plan that considers all of these stakeholders. You will need everything from social media posts to catch the attention of patients to technical documentation so a physician can better understand the capabilities of your product. Remember that marketing materials may also be reviewed by regulatory bodies.<sup>13</sup>

## POST MARKETING SURVEILLANCE

Post marketing surveillance (PMS) is the practice of monitoring the safety of a medical device after it has been released on the market. Post marketing surveillance guidelines are a collection of processes and activities used to monitor the safety and effectiveness of medical devices. These activities are designed to generate information to quickly identify poorly performing devices and other safety problems and accurately characterize real-world device performance and clinical outcomes. The post-marketing surveillance includes the handling of the customer complaints, handling of the corrective and preventive action (CAPA) arising from the Customer complaints.<sup>14</sup>

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