

Regulatory Insights into Neurological Devices and Neurovascular Stent for Brain Aneurysm

P. Shailaja¹, K. SriDivya², D. Mounika Chowdary³, G. Snehalatha⁴

¹Associate Professor, Department of Pharmaceutical Regulatory Affairs, Andhra University College of Pharmaceutical Sciences, Visakhapatnam, India.

^{2,3}Students, Department of Pharmaceutical Regulatory Affairs, Andhra University College of Pharmaceutical Sciences, Visakhapatnam, India.

⁴Research Scholar, Department of Pharmaceutical Regulatory Affairs, Andhra University College of Pharmaceutical Sciences, Visakhapatnam, India.

Abstract

Neurology is concerned with diagnosing and treating neurological diseases and disorders affecting the brain and spinal cord. Numerous neurological disorders and conditions, such as Alzheimer's disease, Parkinson's disease, major depression, epilepsy, spinal cord injury, and brain damage, can now be diagnosed, prevented, and treated with the aid of neurological devices that can enhance function and restore hearing and vision. Neurovascular stents are an emerging treatment option for brain aneurysms that offer several advantages over traditional treatments. This article describes the most recent regulatory framework for neurological devices in the United States and the regulatory requirements for marketing clearance of neurological devices in the United States. The Centre for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) regulates neurological devices.

Keywords

Neurology, Neurological Device (ND), Neurovascular Stent, Aneurysm, Neurological Device Regulation, Neuro Stimulation, Neuro Intervention, Neuro Diagnostics, Centre for Device and Radiological Health (CDRH).

I. Introduction of Neurological Medical Device:

- Neurological devices have been shown to be more effective than pharmaceuticals in treating patients, so more patients are choosing to utilize them instead of taking drugs.
- The development of these gadgets has also been progressing quickly, with more routes to approval and favourable incentives.
- Because producers of neurological devices have been beating their pharmaceutical competitors, the way neurology is practised around the world is changing quickly.
- The multibillion-dollar market for neurological devices is anticipated to grow further result of population ageing, which has led to a sharp rise in the prevalence of neurological disorders.
- Neurological device regulations primarily aim to facilitate access to high-quality, safe, and effective medical equipment and prevent access to dangerous items.

- Many neurology-related items are advancing in clinical trials in the United States, where neurology research and development are accelerating.

II. History of Neurological Medical Devices

- Stephen Hales and Robert Whytt were the first to study animal neuron function scientifically in the eighteenth century. Traumatic brain damage produces aphasia, seizures, and movement problems. Jean-Martin Charcot and William Gowers classified nerve system disorders. Targeted electrical stimulation to map brain function began in the 19th century. In addition to these contributions, animal research and microscopic inspection of nerve cells underpin our brain and nervous system expertise.
- Hans Berger devised the electroencephalograph (EEG) in the 1920s to record brain activity. Neurologists can now make more accurate diagnoses and provide more specific treatments and rehabilitation thanks to the EEG, lumbar puncture, and cerebral angiography. In the early 1970s and 1980s, computerized axial tomography (CT) scanning and magnetic resonance imaging (MRI) provided detailed, noninvasive pictures of the brain's interior, making brain illnesses easier to diagnose and treat. Cerebral imaging. Many medications for neurological disorders like Parkinson's disease, multiple sclerosis, and epilepsy have been developed since the discovery of chemical agents in the central nervous system and their roles in transmitting and blocking nerve impulses. CT scanning and other more precise methods for identifying lesions and other neural tissue anomalies have also helped neurosurgery.

III. Classification of Neurological Medical Devices

A) Types of Neurological Devices, depending on the level of risk, medical devices are divided into one of three classifications:

CLASS	RISK LEVEL	EXAMPLES
I	Low	Ventricular needles and anvils
II	Moderate	Neurostimulators, aneurysm clips & blood clot retrievers
III	High	Deep brain stimulators

Class I neurological devices are not common. Class II or class III devices are the most common classifications for neurological devices.

B) Types of Neurological Devices Based on Usage

a) Neurodiagnostic Devices: These involve the investigation and recording of electrical activity in the brain, CNS and PNS. Observing the electrical signals of these nervous systems provides vital information that can assist in the diagnosis and treatment of a number of neurological conditions. Conditions include epilepsy, headaches, head and spinal traumas, seizures, sleep disturbances, strokes, and unexplained comas.

Examples of Neurodiagnostic Devices: Electroencephalography, long-term monitoring, intraoperative neuromonitoring, polysomnography, evoked potential studies and nerve conduction studies are the most common procedures performed by neurodiagnostic technicians.

b) Neurostimulation Devices: Neurostimulation technologies provide relief to an increasing number of individuals with chronic neurologic and mental disorders. Neurostimulation therapies employ both invasive and noninvasive electrical stimulation of brain circuits to control neural function. This article explores established invasive electrical stimulation techniques used clinically to induce neuromodulation

of damaged brain circuits. These implantable neurostimulation systems target specific deep subcortical, cortical, spinal, cranial, and peripheral nerve regions to modulate neuronal activity, thereby providing therapeutic benefits for a range of neuropsychiatric diseases.

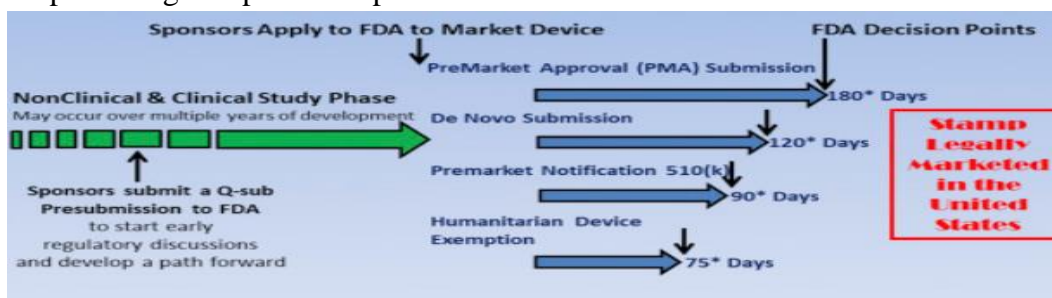
Example of Neurostimulation Device: Neuromodulation devices include pain pumps that deliver a preset dose of pain medication directly to the spinal cord for immediate pain relief.

c) Neurointerventional Device: It offers minimally invasive therapy for the vascular lesions of the CNS. These are used for persons who are suffering from serious neurological illnesses, such as stroke and aneurysms. It involves the delivery of drugs via a catheter or cannula implanted through microscopic incisions, which are invasive.

Examples of neuro-interventional Devices: Among the most significant varieties of neurointerventional devices are neurovascular stents, embolic coils, liquid embolic, embolic protection devices, flow diverters, balloons, neurovascular thrombectomy devices, stent retrievers, and intravascular devices.

IV. Regulatory Process

- Regulatory requirements for an experimental agent may be affected by considerations that are product-specific.
- During the pre-IND conference, where these subjects should be carefully discussed with the FDA, the IND sponsor should offer pertinent preclinical data, manufacturing information, and animal safety tests to support the intended clinical development route.
- The agency's engagement can help define the eventual growth strategy and recommend the kind of follow-up research that is pertinent to a particular agent.
- The development of a product will be aided by scheduling interactions with regulatory organizations at regular intervals.
- Regulatory agency standards tighten when a Neurological Medical device product moves through the trials and license processes from the first to the second the third phases.
- A sponsor should be able to evaluate the identification, purity, quality, dose, and safety of a Neurological Medical Device product for early-phase clinical research.
- A potency assay to evaluate the compatibility of the finished Neurological Medical Device, with applicable lot release parameters, should be established prior to starting the clinical investigations, which are intended to show compelling Safety and level of risk for a marketing application.
- To support the licensing of a neurological product, manufacturing procedures and all testing techniques for the product release (21 CFR 882) must be validated.
- Sponsors should speak with the FDA's CDRH early on in the development of the Device to address any issues pertaining to a particular product.



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Figure 1: Neurological Medical device regulatory pathway to Market

V. Regulatory Standards for Neurological Medical Devices

- In order to make the evaluation process rigorous and predictable, the FDA recognizes standards developed by organizations such as the International Organization for Standardization (ISO) and the American Society for Testing and Materials (ASTM) International (ISO).
- By selecting the "Neurology" category in the Specialty Task Group Section of the FDA Recognized Consensus Standards database, sponsors can access all of the national and international standards applicable to neurological devices that the FDA has recognized.
- Class II devices require additional controls besides traditional controls in order to provide a reasonable assurance of safety and efficacy.
- A producer must consistently comply with Section 513(a)(1)(A) of the Federal Food, Drug, and Cosmetic Act (the Act); address the specific health risks listed in Section 513(a)(1)(B) of the FD&C Act by adhering to the recommendations in the guidance or guidelines; or use another method that provides equivalent assurances of safety and efficacy.

VI. Considerations for Pre-Clinical Development of Neurological Medical Device

- In this step, in vitro or in vivo animal testing evaluates the device's toxicity, pharmacological effects, and safety.
- Preclinical requirements vary for lab animals. Pre-clinical research uses sheep, dogs, hounds, mice, pigs, and beagles.
- Studies use GLP and non-GLP. Discovery, foundational research, screening, and other non-GLP studies don't examine product safety.
- GLP studies examine non-clinical health and safety research execution, planning, monitoring, recording, archiving, and reporting.
- The preclinical team has veterinarians, technologists, project managers, and regulatory managers for this research.
- Animal models are chosen based on technology and human anatomy. If customers are unsure of the animal model needed for device testing, FDA consultants can help.
- The regulatory manager will monitor all industry GLP and non-GLP procedures.
- Animals undergo acute and chronic tests using the device. Acute investigations usually last one to two days. Chronic studies last three to 365 days.
- If the test fails and the animals die, a necropsy determines the device's failure. The animal tissue surrounding the device is removed and sent for pathological investigation.
- Failures must be reported to FDA. After the device fails, the client must figure out why and fix it. If the test works, the animal survives, and it's minimally invasive, they'll be used again.
- A client can request a necropsy after a successful test to see how the gadget impacts animal tissues.

VII. Considerations for Clinical Development of Neurological Medical Devices

Before evaluating new technologies, lab studies on animal and human cells take years. If early laboratory research is effective, the FDA approves additional laboratory and human trials. Human testing of an experimental technology is permitted. Medical device clinical trials use only patients with the product's intended disease. Drug clinical trials have several pathways. Medical device clinical trials depend on risk and class. Surgical gloves, bandages, and other low-risk devices don't need clinical trials.

Medication trials include a few healthy people. In medical device clinical trials, patients have the product's intended disease. Healthy people should not use it. Surgical implants such as cardiac pacemakers, coronary stents, prosthetic heart valves, etc. may not be tested in healthy people.

There are three different stages for medical device clinical studies. They are:

1) Pilot Study: To evaluate the viability, duration, cost, and adverse effects and to improve the study design, a small-scale preparatory investigation known as a "pilot study" is conducted. Another term for an important study is a feasibility study. Pilot studies are often single-centre studies with a small subject population that are intended to achieve any number of goals within a clinical development programme. The study, which aims to assess the preliminary performance and safety of the gadget, entails 10 to 30 participants with the disease or condition. It also provides guidelines for future study design and equipment adjustments.

2) Pivotal Study: Important research is also carried out to show that the gadget is safe and efficient for a particular purpose in a specified patient population. Typically, 150 to 300 people with the illness or condition take part in the trial to evaluate the device's preliminary performance and safety. A critical study's findings are utilized to get regulatory approval to market the gadget. All clinical trial results, additional data pertaining to the device's production, preclinical findings, and administrative data are being submitted to the FDA for review.

3) Post-Approval Study: This level is similar to Phase IV of clinical drug trials. The objective is to comprehend the device's long-term efficacy and any potential negative effects related to its use. The companies will now assess the device's cost-effectiveness in relation to current technology by comparing it to comparable goods. Even after the technology is made available to the general public, this research still goes on. By learning about medical device clinical and regulatory processes, products can be put on the market to benefit patients or society.

VIII. Considerations for Marketing And Post-Marketing Of Neurological Medical Devices

A. Marketing:

Submission Type	Description
Pre-submission	It enables applicants to obtain FDA feedback on future or approaching IDE applications or other premarket submissions, such as the review of automatic class III designations, PMA applications, premarket notice 510(k) and HDE applications.
IDE (Investigational Device Exemption)	It permits the use of an investigational device in a clinical trial to collect data on its safety and effectiveness. Unless an exemption applies, an Investigational Device Evaluation (IDE) must be approved prior to any clinical evaluation of an investigational device conducted in the United States.
HDE (Humanitarian Device Exemption)	An HDE is an application used for selling a HUD. An HDE is subject to numerous profits and uses constraints and is expected to prove safety and a likely benefit for the intended patient population.
De novo	Applicants may submit a de novo application to request a class II or class I classification for medical devices that are

	unique and lack a suitable predicate device. Class II de novo-classified devices can serve as predicates for future 510(k) submissions if they are commercially available.
510(k) Pre-market Notification	In terms of intended use, technological characteristics, and performance testing, a 510(k) indicates that the new device is almost identical to a predicate device.
PMA (Pre-Market Approval)	The PMA is the most stringent premarket filing type. The sponsor must provide sufficient assurance that the device is safe and effective for its intended use before the FDA will approve a PMA.

B. Post Marketing:

1) Reporting Adverse Events: MedWatch, the FDA's adverse event reporting program, functions as a repository for new safety information and a reporting portal for problems with medical products (drugs and devices). The option to sign up for frequent MedWatch safety alerts is provided.

The Medical Product Safety Network (MedSun), an adverse event reporting program, monitors the efficacy and safety of medical equipment. The FDA has enlisted 350 medical experts from across the nation to report any problems with medical devices that result in severe injuries or deaths. The FDA distributes a new issue of Med Sun every month. The newsletter provides consumers with essential information about the safety of medical equipment.

2) Active Surveillance: As part of the Sentinel Program, the FDA is constructing a new national system to identify potential safety concerns. The system will utilize extremely large electronic health databases, such as registries, administrative and insurance claims databases, and electronic health record systems, to continuously monitor the safety of licensed medicinal products. This technology will not replace the FDA's current methods for evaluating post-market safety but will supplement them.

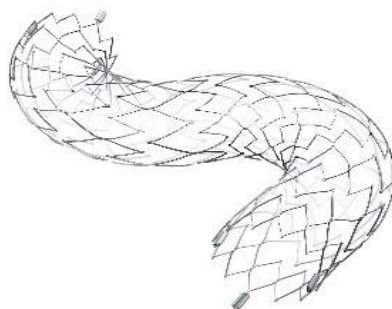
IX. Case Study of Neurological Medical Device

Neurointerventional device: A neurovascular stent

Example: DEVICE TRADE NAME: Neuro form Atlas Stent

DEVICE GENERIC NAME: Intracranial Coil-Assist System

COMPANY: Stryker



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A. Definition: The Neuroform Atlas Stent System is designed to keep coils used to close up aneurysms in the brain in place if they have a neck size of at least 4 mm or a dome-to-neck ratio of less than 2. (Wide-

necked brain aneurysms). A wire is used to insert the self-expanding metal (nitinol) tube-shaped device (stent) known as the Neuroform Atlas Stent System inside a brain artery.

B. Working:

A tiny catheter and delivery wire with the Neuroform Atlas stent is inserted by a doctor through an incision into the femoral artery. To maintain embolization coils put in the sac of the aneurysm in place, the Neuroform Atlas stent is precisely guided to the aneurysm and permanently implanted.

C. Contraindications:

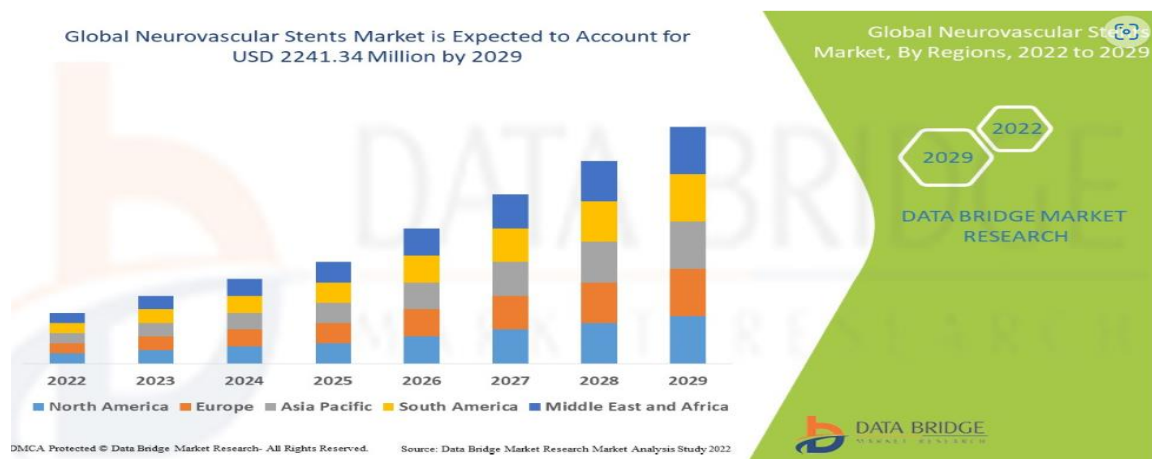
- Possess a parent vessel size outside the range mentioned
- Have not taken anti-platelet medications before having a stent implanted
- Possess an ongoing bacterial infection
- Are not suitable for use with anticoagulant and antiplatelet treatment
- Possess an already-existing stent in the parent artery at the intended intracranial aneurysm site.

D. Clinical study:

In the clinical study of 124 patients with posterior circulation wide-necked brain aneurysms treated with the Neuroform Atlas Stent System, 77% of the aneurysms were completely sealed off at one year without the need for re-treatment or significant constriction of the parent artery (stenosis). 18.1% of the patients in the research received treatment for significant adverse effects, such as mortality, stroke, or temporary blood supply obstruction (transient ischemic attack or TIA).

E. Regulatory aspects: As the device is high risk comes under class III. To market this device, it requires Premarket Approval To obtain PMA the manufacturer must provide the safety and efficacy data of the device through pre-clinical and clinical studies. The manufacturer must also comply with the quality and safety parameters as per US FDA Regulations. This stent recently got approval on 3rd June 2020, by FDA through a PMA application having safety and efficacy.

X.STATISTICS:



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Neurovascular stents are expected to grow 10% from 2022 to 2029. Neurovascular stents will be worth USD 2,241.34 million by 2029. BD, Cook, B. Braun Melsungen AG, Medtronic, Terumo Corporation, Lombard Medical, Johnson and Johnson Private Limited, Cardinal Health, Boston Scientific Corporation, MicroPort Scientific Corporation, and Merit Medical Systems are the major players in the Neurovascular Stents Market.

XI. Conclusion

- Neurological medical devices have evolved into indispensable instruments for treating a variety of neurological illnesses.
- Here is the neurovascular stent used to treat brain aneurysms, thereby decreasing the risk of stroke or possibly death.
- The importance of regulations in guaranteeing the safety and efficacy of these technologies cannot be overstated.
- Before authorizing a device for use, regulatory agencies such as the FDA conduct extensive testing and evaluation to see if it meets safety and efficacy standards.
- Hence, the FDA CDRH will establish techniques that customize a single scientific and regulatory examination to the unique characteristics of Neurological Medical Devices.
- Yet, these rules also add complexity and expense to the commercialization and development of these technologies.
- At Present the growth of the Neurovascular stents market has been the rising prevalence of cardiac illnesses, and has high demand due to less invasive procedures, more technical development, and quick uptake of less endovascular treatment, the market for neurovascular stents is now growing due to the increasing prevalence of cardiac ailments.
- Understanding the legislation governing Neurological Medical Devices is essential for successfully launching breakthrough technologies.
- To optimize market expansion, innovators must comply with restrictions imposed by regulatory bodies and collaborate with regulators to enhance public health by introducing safe and effective neurological medical devices.

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