

FDA Fact Sheets: Premarket Approval

Premarket approval is the process of scientific and regulatory review of the safety and effectiveness of Class III medical devices; it is the most rigorous premarket device submission that FDA requires. Class III devices include those that support or sustain human life, are important to prevent impairment of human health, or present a potential, unreasonable risk of illness or injury.

To obtain approval to market a Class III device, the premarket approval application (PMA) must establish a “reasonable assurance of safety and effectiveness” as demonstrated by valid scientific evidence. Safety means that the device’s probable benefits outweigh its probable risks, and effectiveness is measured by looking at clinically significant results for the target population for the device. Valid scientific evidence includes clinical studies and trials, case histories, and reports of significant human experience.

Elements of a PMA application include:

- Reports of all known information about the device’s safety and effectiveness;
- Description of the device, including its components, ingredients, properties, and operating principles;
- Description of the device’s manufacturing and processing;
- Results of non-clinical trials (bench/animal testing);
- Results of any clinical studies;
- Proposed professional and patient labeling; and
- A summary of safety and effectiveness data.

PMA review is a multi-step process that typically includes an initial review to confirm that an application is complete; an in-depth scientific and regulatory review; a manufacturing quality and bioresearch audit (these may not be required depending on the company’s compliance history); review and recommendation by an advisory committee (these reviews are not conducted for all PMAs); and final deliberations and notification of FDA’s decision.

The applicant can make a complete application submission or use a modular format in which components are submitted and reviewed separately. FDA will notify the applicant of information required to complete the application through major/minor deficiency letters and, in some cases, through informal interaction. Required information typically will be submitted by the applicant as a PMA amendment.

The applicant has the right to request a meeting within 100 days of the filing of the PMA to discuss the review status of the application, and there are opportunities for other types of formal and informal interactions throughout the review process.

FDA may choose to refer the PMA to an outside panel of experts to advise FDA on the device's safety and effectiveness and risk versus benefit. The panel's recommendations to FDA are not binding but are frequently followed.

Under a current agreement with industry, FDA commits to issuing a decision on 90 percent of PMAs that do not require panel review within 180 FDA days.

A decision includes issuance of: an approval order, an approvable letter citing conditions for approval, a not approvable letter, or an order denying approval. Issuance of a "not approvable" letter means that FDA believes that the application may not be approved for statutory reasons that allow FDA to deny a PMA, or because FDA cannot reach an approvable decision because the PMA lacks significant information. The letter describes the PMA's deficiencies and may identify what is necessary to make the PMA approvable.

As a condition to PMA approval, an applicant may be required to conduct postmarket surveillance or a postapproval study. After PMA approval, all applicants must submit a postapproval "annual report" identifying changes to the device that are required to be reported to FDA. Additionally, the annual report must include an update of all available information and reporting on adverse reactions and device defects.

Before making a change to the device that affects its safety or effectiveness, FDA requires submission of a PMA supplement.