Accelerated Approval

When studying a new drug, it can sometimes take many years to learn whether a drug actually provides a real effect on how a patient survives, feels, or functions. A positive therapeutic effect that is clinically meaningful in the context of a given disease is known as “clinical benefit”. Mindful of the fact that it may take an extended period of time to measure a drug’s intended clinical benefit, in 1992 FDA instituted the *Accelerated Approval* regulations. These regulations allowed drugs for serious conditions that filled an unmet medical need to be approved based on a surrogate endpoint. Using a surrogate endpoint enabled the FDA to approve these drugs faster.

In 2012, Congress passed the Food and Drug Administration Safety Innovations Act (FDASIA). Section 901 of FDASIA amends the Federal Food, Drug, and Cosmetic Act (FD&C Act) to allow the FDA to base accelerated approval for drugs for serious conditions that fill an unmet medical need on whether the drug has an effect on a surrogate or an intermediate clinical endpoint.

A surrogate endpoint used for accelerated approval is a marker - a laboratory measurement, radiographic image, physical sign or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. Likewise, an intermediate clinical endpoint is a measure of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a drug, such as an effect on irreversible morbidity and mortality (IMM).

The FDA bases its decision on whether to accept the proposed surrogate or intermediate clinical endpoint on the scientific support for that endpoint. Studies that demonstrate a drug’s effect on a surrogate or intermediate clinical endpoint must be “adequate and well controlled” as required by the FD&C Act.

Using surrogate or intermediate clinical endpoints can save valuable time in the drug approval process. For example, instead of having to wait to learn if a drug actually extends survival for cancer patients, the FDA may approve a drug based on evidence that the drug shrinks tumors, because tumor shrinkage is considered *reasonably likely to predict* a real clinical benefit. In this example, an approval based upon tumor shrinkage can occur far sooner than waiting to learn whether patients actually lived longer. The drug company will still need to conduct studies to confirm that tumor shrinkage actually predicts that patients will live longer. These studies are known as phase 4 confirmatory trials.

Where confirmatory trials verify clinical benefit, FDA will generally terminate the requirement. Approval of a drug may be withdrawn or the labeled indication of the drug changedif trials fail to verify clinical benefit or do not demonstrate sufficient clinical benefit to justify the risks associated with the drug (e.g., show a significantly smaller magnitude or duration of benefit than was anticipated based on the observed effect on the surrogate).

More in Fast Track, Breakthrough Therapy, Accelerated Approval, and Priority Review (/ForPatients/Approvals/Fast/default.htm)

Fast Track (/ForPatients/Approvals/Fast/ucm405399.htm)

- **Breakthrough Therapy (/ForPatients/Approvals/Fast/ucm405397.htm)**
- **Accelerated Approval (/ForPatients/Approvals/Fast/ucm405447.htm)**
- **Priority Review (/ForPatients/Approvals/Fast/ucm405405.htm)**