New Drug Application (NDA) Process

For decades, the regulation and control of new drugs in the United States has been based on the New Drug Application (NDA). Since 1938, every new drug or therapy has been the subject of an approved NDA before US commercialization. The NDA application is the vehicle through which drug sponsors, such as biotech and pharmaceutical companies, formally propose that the FDA approve a new pharmaceutical for sale and marketing in the US. The data gathered during the animal studies and human clinical trials of an Investigational New Drug (IND) become part of the NDA.

The goals of the NDA are to provide enough information to permit FDA reviewers to reach the following key decisions:

- Whether the drug is safe and effective in its propose use(s), and whether the benefits of the drug outweigh the risks.
- Whether the drug's proposed labeling (package insert) is appropriate, and what it should contain.
- Whether the methods used in manufacturing the drug and the controls used to maintain the drug's quality are adequate to preserve the drug's identity, strength, quality, and purity.

The documentation required in an NDA is supposed to tell the drug's whole story, including what happened during the clinical tests, what the ingredients of the drug are, the results of the animal studies, how the drug behaves in the body, and how it is manufactured, processed and packaged.

FDA Drug Review and Approval Time
FDA is often asked about the pace of drug approvals and how FDA review time for applications affects it. Since the Prescription Drug User Fee Act (PDUFA) was passed in 1992, FDA has met and often exceeded the vast majority of review-time goals established under the Act. New drug approval times also have been dramatically reduced (from a median of 22 months in 1992 to a median of less than 12 months in 1999), although a slight increase was seen for the year 2000.

Definitions
FDA Review Time: The time it takes FDA to review a new drug application. Review time goals are established under PDUFA.

Approval Time: Approval time is the time from first NDA submission to NDA approval. It includes the sum of: FDA review time for the first submission of an NDA to the Agency, plus any subsequent time during which a pharmaceutical sponsor addresses deficiencies in the NDA and resubmits the application, plus subsequent FDA review time.

New Molecular Entity (NME): A medication containing an active substance that has never before been approved for marketing in any form in the United States.

Priority New Drug Application (NDA): An application for a product determined to provide a

significant therapeutic or public health advance. Priority NDAs have a 6-month FDA review performance goal.

Standard New Drug Application (NDA): A NDA for a product that is not designated as a Priority NDA. The performance goal for FDA review for a standard NDA is 10-12 months.

FDA Approvable: The FDA has essentially approved the product but remaining questions will need to answered by the sponsor before an actual approval is received. Typically, the sponsor replies within three months with another three months for final review by the FDA. Therefore, the product would be approved for availability and marketing in the US six (6) months after receiving an FDA approvable.

FDA Approval: The sponsor has received final product approval by the FDA to sell and market a product in the US with no exceptions and/or questions.

The number of Priority NMEs, those with a 6-month review goal, reviewed in a given year impacts the median approval time for drugs. In 1999, 19 of 35 (54%) NMEs had priority designation. For 2000, only 9 of 27 (33%) of the NMEs had priority designation.

By definition, a drug's time to approval includes time that the NDA is under review by FDA, as well as any time it takes the pharmaceutical sponsor to address deficiencies identified by the FDA. Deficiencies can range from requiring new data analyses, to product labeling revisions, to the need for conducting additional clinical studies. Some applications go through more than one cycle of NDA submission followed by an FDA action other than approval. The percentage of NMEs that are approved within 12 months of submission has remained relatively constant in recent years at around 40%. However, products with longer regulatory NDA histories with multiple review cycles can significantly affect aggregate time to approval for drugs in a given year.

In summary, the applications approved in calendar year 2000 do, in aggregate, have a higher median time to approval compared to other recent years. However, the data show that factors underlying the change do not include any slowing by FDA in its review of NDAs. Instead, the smaller percentage of priority applications in 2000 and the high number of applications with prolonged regulatory histories are responsible for the increase.