GAO CITES SCIENCE, BUSINESS, REGULATORY, AND INTELLECTUAL PROPERTY ISSUES AS HAMPERING DRUG DEVELOPMENT EFFORTS

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On December 19, 2006, GAO released a new analysis of pharmaceutical drug development and the recent decline in the number of new drug applications submitted to FDA by major drug manufacturers.[1] The key findings of this analysis include:

- **Research breakthroughs have failed to keep up with R&D funding.** Between 1993 and 2004, pharmaceutical R&D expenses (adjusted for inflation) increased from $16 billion to $39 billion, a 147% increase. Over the same time period, the number of new drug applications (NDAs) has increased by only 38%, and the number of applications for potential breakthrough drugs (new molecular entities, or NMEs) has increased by only 7%. In both cases, the number of applications has declined since 1999. According to GAO, "the number of drugs developed has not been commensurate with research and development investments by the pharmaceutical industry."

- **FDA approval rates have remained the same.** In the period analyzed by GAO, FDA approved 76% of NDAs. Approval rates varied by only a small amount on a year-by-year basis.

- **The majority of drug applications are for non-breakthrough drugs.** Only 32% of drug applications are for NMEs; only 12% of drug applications are considered by FDA to be "priority" NMEs.

- **Drug approval times are declining.** Between 1993 and 2002, approval times for all NDAs declined from 669 days to 442 days — a 34% decline. Approval times for priority drugs were even faster, and declined by a similar amount — from approximately 375 days to approximately 200 days.

- **Reasons for the decline in the number of NDAs.** GAO convened a panel of experts to explore the reasons for the decline in the number of NDAs. This panel — which included representatives from industry, academia, FDA, consumer groups, and health care providers — identified four main reasons:

    1) **Difficulties in translating basic research discoveries into new medications.** These problems are driven by increasing complexity and lack of understanding of the diseases to be addressed, and the failure, to date, of new technologies (such as genomics) to be effectively translated into practical results. Panelists also identified a shortage of researchers who

[1] GAO, *New Drug Development: Science, Business, Regulatory, and Intellectual Property Issues Cited as Hampering Drug Development Efforts* (Nov. 2006) (GAO-07-49).

possess the expertise to take cutting-edge science from discovery to development.

2) **The business environment.** Recent trends in the pharmaceutical industry have been focused on developing two types of drugs: (1) blockbuster drugs, which are expensive to develop — expenses that result in the exclusion of research on highly innovative but lower-revenue drugs; and (2) "me-too" drugs, which are less risky to develop but offer little in the way of therapeutic breakthroughs. In addition, the large number of mergers and acquisitions in the drug industry has led to the discontinuation of many drug development efforts.

3) **Regulatory uncertainty.** The lack of precise FDA standards to outline what constitutes a safe and effective drug has adversely affected the drug development process. There is also a perception among some experts that FDA review requirements have become more stringent in the wake of drug safety problems identified in recent years.

4) **Patent law.** The ability of drug manufacturers to easily obtain patents for minor changes to products, or to receive patent exclusivity for new uses of existing products, have reduced incentives to develop new drugs.

Recommendations

The panel of experts convened by GAO made the following recommendations:

- Increase collaboration among government, industry, and academia to collect and analyze data on why drugs fail during clinical testing; develop validated biomarkers and end points to use when testing drug safety and efficacy; and develop a conditional, expedited review process for drugs to treat diseases in particular need of treatment.

- Academia, industry, and the government should make additional efforts to develop scientists who can translate scientific breakthroughs into practical results.

- The government could consider providing additional financial incentives — such as longer patent lives for innovative drugs and shorter patent terms for "me-too" drugs — to shape the drug development process.