Appendix I

Methods Used in OTA's Study of Success Rates for New Molecular Entities

As described in the text of chapter 6, OTA used data from the U.S. Food and Drug Administration (FDA) to compare development times for two cohorts of new molecular entities (NMEs) with their first commercial investigational new drug (IND) applications submitted during two 3-year intervals: 1976-78 and 1984-86. The FDA had already compiled IND, new drug application (NDA), and final approval data on the 1976-78 cohort for their own previous analysis (426), For this analysis, the FDA updated the 1976-78 database to record approvals through July 1991. At OTA's request, the FDA compiled similar data for the 1984-86 cohort. Because the FDA's computer data systems do not link IND and NDA records for the same N-ME, the agency manually integrated these records.

Both cohorts exclude insulins, insecticides, sunscreens, vaccines and antitoxins from a biological source, and veterinary products from the analysis (426) For the 1984-86 cohort, the FDA added therapeutic biological entities evaluated by it's Center for Biologics Evaluation and Research (CBER). This step was not necessary for the 1976-78 cohort because the FDA did not establish CBER until 1988; prior to this date, all therapeutic drugs, no matter what their source, were reviewed by the predecessor of the FDA's Center for Drug Evaluation and Research (CDER). A total of 7 percent of the later cohort are biologics.

The FDA purged the 1984-86 cohort of INDs that did not represent a first commercial filing for the NME. Using available reference materials such as *Pharmaprojects (328)* and the *Merck Index* (267), the FDA verified each IND sponsor was a commercial firm and then checked the *Ingredient Dictionary,* the Drug Product Reference File microfiche, and its own management information system to confirm that no commercial INDs had been filed for a related compound (salt or ester) prior to the 1984-86 interval.

During the 3-year period 1976-78, commercial sponsors filed 174 first NME INDs. Of these 40 resulted in an NDA, and the FDA had approved 27 for marketing as of July 1991. During the 1984-86 period, commercial sponsors filed 344 NME INDs. By July 1991,53 of these also resulted in an NDA, and 27 had received FDA marketing approval. All drugs in the 1984-86 cohort have at least 54 months experience following IND submission recorded in the database (the amount of time between December 1986 and July 1991).