Appendix H

Methods of OTA's Survey of Clinical Trial Size

The Office of Technology Assessment (OTA) conducted a survey of sponsors of new molecular entities (NMEs) that received U.S. Food and Drug Administration (FDA) marketing approval during certain years to estimate systematic changes over time in the number of participants in clinical trials conducted before new drug applications (NDA) approval.

To construct its sample, OTA began with 57 NMEs that had a first NDA approved between 1978-83 or 1986-90. OTA chose drugs approved during these periods to ensure the sample represented enough years to detect any trend in trial size while also ensuring all NMEs examined faced essentially the same regulatory guidelines. Because OTA hypothesized that there would be systematic variation in clinical trial size across product classes, OTA chose to focus on three very different therapeutic classes of drugs: antimicrobial, antihypertensives, and nonsteriodial anti-inflammatories (NSAIDs) in order to provide diversity in the analysis. (OTA analyzed data from each class separately), Before arriving at its final sample, OTA eliminated two NMEs from its sample because they were qualitatively different from other drugs in the class: one drug labeled by the FDA as an antihypertensive is not actually an antihypertensive, and another antihypertensive is actually a diagnostic agent rather than a therapeutic drug. This left a final sample consisting of 18 antihypertensives (9 for 1978-83 and 9 for 1986-90),27 antimicrobials (15 for 1978-83 and 12 for 1986-90), and 8 NSAIDs (4 for 1978-83 and 4 for 1986-90).

OTA staff developed the survey instrument with the assistance of OTA project advisory panel members and Pharmaceutical Manufacturers Association (PMA) senior management. It contained seven questions pertaining to total clinical trial enrollment, total number of therapeutic indications for which the company sought FDA approval, the total number of clinical studies completed (both pre-and post-NDA), and the total number of trial sites. OTA asked companies to provide these numbers broken down by foreign and domestic research and by whether or not the clinical studies were completed before or after first FDA (NDA) marketing approval.

To ensure a timely response, OTA mailed identical survey packages to two contacts at the company manufacturing each drug, Each package contained a cover letter, a description of OTA's project and its advisory panel membership, a project fact sheet, a return envelope, and survey forms for each drug in the sample developed by that company. OTA made two followup calls to contacts that did not return their surveys. OTA received usable responses for all but two drugs-one antihypertensive and one NSAID (both from the 1978-83 period) for an overall response rate of 96 percent.