In response to these reports, FDA conducted a nation-wide survey of case records in hospitals and clinics in an attempt to evaluate the magnitude of the problem and to determine whether a cause and effect relationship existed between the drug and the disease. This survey produced records of 410 cases of serious blood disorders, of which 177 were definitely known to have been associated with chloramphenicol. In 61 cases, chloramphenicol was the only drug administered. In half of these 177 cases, the blood disorders were fatal. They included aplastic anemia; hypoplastic anemia; thrombocytopenia; and granulocytopenia. In June 1952, the FDA discontinued certification of chloramphenicol, and in July 1952, the FDA referred the case histories obtained in the survey to the National Research Council (NRC). The NRC established a committee of outstanding hemotologists and internists, under the chairmanship of Dr. John Holmes Dingle, Professor of Preventive Medicine, Western Reserve University, to review and evaluate the chloramphenicol problem. On August 7, 1952, the Committee reported as follows:

"An *ad hoc* Conference was held on 6 August and reviewed all available data presented by the Food and Drug Administration and by Parke, Davis and Company.

"The consensus of the Conference was as follows:

"1. Certain cases of serious blood dyscrasias (aplastic anemia, thrombecytopenic purpura, granulocytopenia, and pancytopenia) have been associated with the administration of chloramphenicol.

"2. Although this complication has thus far been uncommon, it is sufficiently important to warrant a warning on the label of packages of the drug and in advertisements of the drug and the recommendation that chloramphenicol not be used indiscriminately or for minor infections.

"3. When prolonged or intermittent administration is required, adequate blood studies should be carried out.

"4. In view of the paucity of information at the present time the Conference hopes that further study of serious reactions to chloramphenicol and other drugs will be promoted. The records of the Veterans Administration and military forces could be of great value in providing some of the desired information."

The recommendations of the Committee were implemented and resumption of certification of the drug followed. All chloramphenicol was to be marketed with the following label warning: "Warning—Blood dyscrasias may be associated with intermittent or prolonged use. It is essential that adequate blood studies be made".

The following warning was to appear at the top of the package insert: "*Certain blood dyscrasias (aplastic anemia, thrombocytopenic purposa, granulocytopenia and pancytopenia) have been associated with the administration of Chloromycetin. It is essential that adequate blood studies be made when prolonged or intermittent administration of this drug is required. Chloromycetin should not be used indiscriminately or for minor infection*".

In announcing the reinstitution of certification for chloramphenicol, FDA said: "The administration has weighed the value of the drug against its capabilities for causing harm and has decided that it should continue to be available for careful use by the medical profession in those serious and sometimes fatal diseases in which its use is necessary".

FDA characterized its experience as "an impressive reminder that highly potent drugs must be treated with extreme care and should not be employed unless there is a clear-cut indication that they are needed".

The Kefauver Subcommittee on Anti-Trust and Monopoly subsequently reported that these warning measures were diluted by Parke-Davis instructions to its detail force, which the Subcommittee said presented the report of the National Research Council as a blanket clearance of the drug. Nonetheless, the use of the drug dropped off markedly after the new warning issued. This was a short-term reaction, however, and use of the antibiotic increased during the years that followed.

In 1955 Parke-Davis requested a deletion of part of the warning statement. The firm's letter pointed out that some patients with blood disorders attributable to Chloromycetin had received only a few capsules. The company regarded the warning, which referred to prolonged or intermittent therapy, as a legal liability in litigation.