5. Zanders' comparison of new Monograph with U.S. label.

* Comparison of the Parke-Davis Newly-Revised Chloromycetin Monograph Sent to All International Locations and the Parke-Davis U.S. Chloromycetin Label (and Physicians' Comments).

A great improvement warning of fatal aplastic anemia and against trivial use. However. The United States label begins with a very strong, boxed, and at times underlined WARNING that serious and fatal blood dyscrasias, including aplastic anemia are known to occur after administration of chloramphenicol, that it must not be used in trivial illnesses or when not indicated or as a prophylactic to prevent bacterial infection, and that blood studies during treatment are essential. In contrast, the Parke-Davis Monograph begins with a very positive descriptive statement on the drug: "Clinical use has established chloramphenicol (Chloromycetin, Parke-Davis) as an effective antibiotic in a wide variety of bacterial and rickettsial infections." The U.S. descriptive statement which follows the WARNING box, on the contrary, is in essentially restrictive terms, stating that it is an antibiotic that " should be reserved for serious infections caused by organisms susceptible to its antimicrobial effects when less potentially hazardous therapeutic agents are ineffective or contraindicated. Sensitivity testing is essential to determine its indicated use, but may be performed concurrently with therapy initiated on clinical impression that one of the indicated conditions exists (see "Indication" section)."

Parke-Davis does discuss adverse hematological reactions from use of Chloromycetin including aplastic anemia but in general the Monograph downplays both the incidence and mortality rate of irreversible aplastic anemia and gives less detailed information than the U.S. label so that the importance of this adverse reaction is diminished. The one good important principle of use that Parke-Davis states clearly, but without the U.S. examples and emphasis, is that Chloromycetin should not be used for trivial illnesses. However, this is not enough.

As we understand it, the basic concept of the U.S. label is that because of the possible adverse reactions, especially the serious and fatal hematological reactions, use of Chloromycetin should be restricted even in treatment of serious diseases to those which cannot be treated by any less potentially hazardous drug and that this need for Chloromycetin must be determined by prior sensitivity testing of the microorganism involved (except for a few very serious conditions where initial treatment with Chloromycetin may be instituted concurrently with sensitivity testing in order to change to another less hazardous therapeutic agent as soon as possible) and its use must be accompanied by blood studies, preferably while the patient is in a hospital. In contrast, the Parke-Davis Monograph, instead of severely restricting use (except for trivial illnesses) in the manner in which it is now restricted in the U.S., still seems to us to encourage unnecessary use. The major point of the U.S. label is to restrict unnecessary use as much as possible in order to limit the number of unnecessary aplastic anemia deaths. The Parke-Davis Monograph pays lip-service to the U.S. basic principle by listing the adverse reactions (without the extremely

* We have a very detailed comparative analysis to back up this summary statement.