"Add for the oral forms: Novobiocin may be useful in the few urinary tract infections caused by Proteus species sensitive to novobiocin but resistant to other therapy.

"CONTRAINDICATIONS

"This drug should not be administered to persons with known sensitivity to novobiocin.

"WARNING

"Because novobiocin has been shown to affect bilirubin metabolism adversely, its use should be avoided in newborn and premature infants.

"PRECAUTIONS

"Novobiocin possesses a high index of sensitization and appropriate precautions should be taken. If allergic reactions develop during treatment and are not readily controlled by the usual measures, the product should be discontinued.

"Hepatic and hematologic studies should be made routinely during treatment. In the case of development of liver dysfunction, the drug should be stopped. If hematologic studies show evidence of the development of leukopenia or other blood dyscrasias, the drug should be stopped.

"If new infections appear during therapy, appropriate measures should be taken and consideration given to discontinuance of novobiocin.

"ADVERSE REACTIONS

"A high incidence of adverse reactions has been reported with the use of this drug.

"Leukopenia and other blood dyscrasias, including anemia, pancytopenia, eosinopenia, agranulocytosis, and thrombocytopenia, have been reported.

"Reversible liver dysfunction has been reported.

"Skin eruption may take the form of urticarial, erythematous, maculopapular, or a erythema multiforme (Stevens-Johnson Syndrome).

"Pain at the site of injection as well as nausea and vomiting, loose stools, and diarrhea when the drug is taken orally may occur.

"Alopecia as well as intestinal hemorrhage have been reported.

"DOSAGE AND ADMINISTRATION

"1. *Parenteral.* This method of administration should be used only as a temporary measure in severe infections for those unable to take the preparation orally.

"Adults: 500 milligrams intramuscularly or intravenously every 12 hours.

"Children: Moderately acute infections—15 milligrams per kilogram per day in two divided doses at 12-hour intervals; severe infections—up to 30 milligrams per kilogram per day in two divided doses at 12-hour intervals.

"2. *Oral.* Adults: Usually 250 milligrams every 6 hours or 500 milligrams every 12 hours. In severe cases, 500 milligrams every 6 hours or 1.0 gram every 12 hours.

"Children: Moderately acute infections—15 milligrams per kilogram per day in divided doses: severe infections—30–45 milligrams per kilogram per day in divided doses."

The firms listed above have been mailed a copy of the NAS–NRC reports. Any manufacturer, packer, or distributor of a drug of composition and labeling similar to the subject drugs or any other interested person may also obtain a copy from the office named below.

Communications forwarded in response to this announcement should be directed to the attention of the appropriate office listed below and addressed to the Food and Drug Administration, 200 C Street SW., Washington, D.C. 20204.

Requests for NAS–NRC report: Press Relations Office (CE–300).

Supplements: Division of Anti-infective Drugs (MD–140), Office of New Drugs, Bureau of Medicine.

Comments on this announcement: Special Assistant for Drug Efficacy Study Implementation (MD–16), Bureau of Medicine.