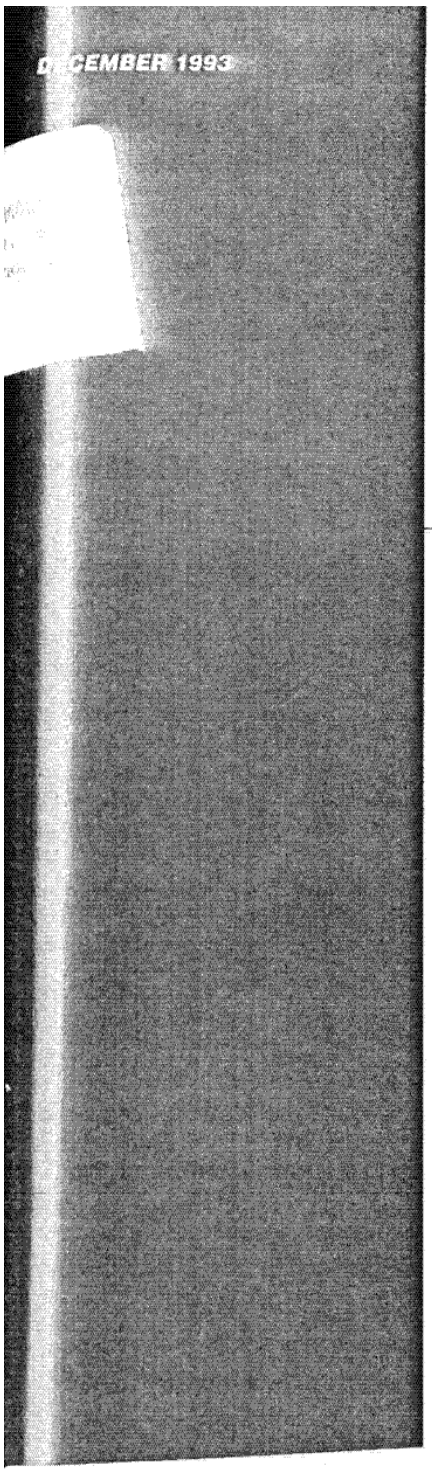

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LETTERS

Precipitation of paclitaxel during infusion by pump

Paclitaxel (Taxol, Bristol-Myers Squibb Oncology) is administered as a 24-hour continuous i.v. infusion. The use of an infusion-control device has been recommended. When diluted to a final concentration of 0.3 to 1.2 mg/mL, paclitaxel has been reported to be visually and chemically stable for up to 27 hours at room temperature and under ambient light.[1]

Investigational use of paclitaxel at our institution began in September 1991. Doses of paclitaxel were prepared in 1000 mL of 5% dextrose injection in glass bottles and infused through vented, polyethylene-lined solution administration sets (2C7552s, Baxter Healthcare Corporation) and 0.22-µm filters (Millex-GV, Millipore). Volumetric infusion pumps (Flo-Gard models 6200 [single chamber] and 6300 [dual chamber], Baxter) were used; these pumps infuse fluid by linear peristalsis—a series of rollers move against a small segment of polyvinyl chloride (PVC) tubing in a peristaltic motion that resembles pushing the fluid along the tubing path.

In August 1992, we received sporadic reports of fluffy, white precipitate in paclitaxel-exposed solution administration sets. The precipitate appeared throughout the section of tubing distal to the pump chamber but not in the glass bottle or the tubing leading to the chamber. The precipitation apparently began in the section of PVC tubing that came into direct contact with the peristaltic rollers of the pump. When precipitation was observed, the solution administration set and filter were changed and the balance of the infusion was administered. Partial doses were not remade, because precipitation was not found in the glass bottles. In most cases, precipitation was observed near the end of the 24-hour infusion period. The concentration of these solutions ranged from 0.2

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The Letters *column is a forum for rapid exchange of ideas among readers of* AJHP. *Liberal criteria are applied in the review of submissions to encourage contributions to this column.*

The Letters *column includes the following types of contributions: (1) comments, addenda, and minor updates on previously published work, (2) alerts on potential problems in practice, (3) observations or comments on trends in drug use, (4) opinions on public health issues of interest to pharmacists in institutional settings, (5) comments on ASHP activities, and (6) human interest items about life as a pharmacist.*

Short papers on practice innovations and other original work are included in the Notes *section rather than in* Letters.

Letters need not be submitted with AJHP*'s manuscript checklist. The following conditions, however, must be adhered to: (1) the body of the letter must be no longer than two typewritten pages, (2) the use of references and tables should be minimized, (3) the authors' names, affiliations, and mailing addresses must be typed at the end of the letter in the format used by* AJHP*, and (4) the entire letter (including references, tables, and authors' names) must be typed double-spaced on plain white paper (not letterhead). Following acceptance of a letter, the authors are required to sign an exclusive publication statement and a copyright transferal form. All letters are subject to revision by the editors. Authors do not receive proofs of edited letters.*

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to 0.3 mg/mL.

The use of paclitaxel vials and solution administration sets from other lots did not prevent precipitation. We notified the National Cancer Institute (NCI) and sent samples of tubing with precipitate for analysis. At that time, NCI had received no similar report of precipitation. In November 1992, following an amendment to NCI treatment referral center protocol 9103, we decreased the volume of a 24-hour dose of paclitaxel to 500 mL; we also began dividing the total daily dose into two 12-hour infusions (250 mL each) to decrease the length of time during which the drug could precipitate. Over the next six weeks, 18 incidents of precipitation (in approximately 150 doses) occurred in solution administration sets used to infuse paclitaxel 0.38–0.58 mg/mL.

Similar problems have been reported with teniposide (Vumon, Bristol-Myers Squibb Oncology),[2] which also contains polyoxyethylated castor oil and alcohol. According to the manufacturer, supersaturated solutions of teniposide rapidly precipitate after formation of seed crystals, a process that may be accelerated by agitation.[3] Agitation sufficient to induce precipitation could be produced by a mechanical pumping action. We suggest that a similar event occurs with our method of paclitaxel administration.

Further studies have been performed. Various types of agitation and manipulation appeared to induce precipitation earlier than was seen in the static samples. Also, higher paclitaxel concentrations began to precipitate sooner than lower concentrations. However, precipitation was not seen when another group repeated the procedure with the solutions and equipment that we routinely use to infuse paclitaxel (Trissel LA, personal communication, 1993 Feb 12).

We have not completely resolved our problem with precipitation, despite interventions to minimize agitation of paclitaxel solutions. Another, more costly option we are considering is to use cassette-type, positive-displacement, volumetric pump systems (e.g., Flo-Gard model 8000, Baxter) for administering paclitaxel. We would appreciate receiving suggestions or hearing about others' experiences with paclitaxel infusion solutions.

1. Bristol-Myers Squibb Company. Taxol package insert. Princeton, NJ: 1992 Dec.
2. Strong DK, Morris LA. Precipitation of teniposide during infusion. *Am J Hosp Pharm.* 1990; 47:512,518. Letter.
3. Bogardus JB, Kaplan MA, Carpenter JP. Precipitation of teniposide during infusion [response]. *Am J Hosp Pharm.* 1990; 47:518-9. Letter.

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Before we received a copy of the above letter, Bristol-Myers Squibb was not aware of clinical or laboratory conditions in which paclitaxel precipitated during infusion by peristaltic pump or with a specific type of infusion device.

The paclitaxel package insert cautions against the use of plasticized polyvinyl chloride (PVC) equipment or devices. The infusion set described by Mr. Pfeifer and Ms. Hale contains a small amount of PVC tubing in a segment where the PVC tubing comes in direct contact with the peristaltic rollers of the pump; however, a laboratory simulation at another institution did not produce paclitaxel precipitation.

Since paclitaxel became commercially available in December 1992, the company has received fewer than a dozen reports of precipitation. Information on the drug concentration, infusion set, and infusion pump used when the drug precipitated has not always been provided. In most cases when this information was provided, precipitation occurred in a PVC-containing segment of tubing.

For the mechanism of the reported precipitation to be identified, precipitation would have to be reproducible under controlled conditions. Perhaps the sample size used by Mr. Trissel during simulation was too small to represent the small number of occurrences in clinical practice.

Finally, we would like to emphasize the selection of infusion sets appropriate for the infusion pump chosen and the avoidance of PVC equipment, as directed in the paclitaxel package insert.

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Incompatibility of labetalol hydrochloride and furosemide

We report the apparent incompatibility of labetalol hydrochloride and furosemide injections.

A 60-year-old woman was receiving labetalol hydrochloride (Normodyne, Schering Laboratories, Kenilworth, NJ, lot 2 DDF 102) 1.6 mg/mL in 5% dextrose injection by continuous i.v. infusion at 30 mg/hr for treatment of systolic hypertension. Furosemide 40 mg (10 mg/mL, Elkins-Sinn, Cherry Hill, NJ, lot 033021) was to be given by i.v. push. Less than 0.5 mL of furosemide had been injected into the port of the labetalol i.v. line when white precipitation was noted. No further furosemide was injected, and the i.v. line was flushed with 0.9% sodium chloride injection.

The patient suffered no detectable adverse drug reaction from this event. The incompatibility was confirmed in the pharmacy department's laminar-airflow hood by using injectable solutions from the same lots and in the same concentrations as the patient received.

Schering Laboratories could provide no previous reports of this incompatibility (Newandee K, Drug Information Manager, personal communication, 1993 Jul 16). This incompatibility is not described in Trissel's *Handbook on Injectable Drugs*.[1] We suspect the incompatibility is due to the difference in solution pH between labetalol hydrochloride (pH 3–4) and furosemide (pH 8–9.3).[2]