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DRUGS PAST THEIR EXPIRATION DATE

Physicians and pharmacists are often asked if patients can use drugs after their expiration date. Pharmaceutical companies, because of legal restrictions and liability concerns, will not sanction such use and may not even comment on the safety or effectiveness of using their products beyond the date on the label.

THE EXPIRATION DATE — The expiration date on the manufacturer's package is based on the stability of the drug in its original closed container. The date does not necessarily mean that the drug was found to be unstable after a longer period; it means only that real-time data or extrapolations from accelerated degradation studies indicate that the drug will still be stable at that date. The expiration date for new drugs is usually 2-3 years from the date of manufacture. Once the original container is opened for use or dispensing, the expiration date on the container no longer applies. Retail pharmacists who repackage drugs, in accordance with the standards of the US Pharmacopoeia (USP), label them with a "beyond-use" date, generally one year from the date the prescription is filled.

SAFETY — The only report of human toxicity that may have been caused by chemical or physical degradation of a pharmaceutical product is renal tubular damage that was associated with use of degraded tetracycline (GW Frimpter et al, JAMA 1963; 184:111). Current tetracycline preparations have been reformulated with different fillers to minimize degradation and are unlikely to have this effect.

STABILITY — Shelf life is the time a product, stored under reasonable conditions, is expected to remain stable (generally retain >90% of potency) (B Kommanaboyina and CT Rhodes, Drug Dev Ind Pharm 1999; 25:857). Data from the Department of Defense/FDA Shelf Life Extension Program, which tests the stability of drug products past their expiration date, showed that 84% of 1122 lots of 96 different drug products stored in military facilities in their unopened original containers would be expected to remain stable for an average of 57 months after their original expiration date (JS Taylor et al, 2002 FDA Science Forum Poster Abstract, Board AC-08, www.fda.gov, search "2002 FDA science forum"). Storage in high humidity may interfere with the dissolution characteristics of some oral formulations. In one published study, however, captopril (*Capoten*) tablets, flucloxacillin sodium (*Flucloxin*) capsules (a penicillin not available in the US), cefoxitin sodium (*Mefoxin*) powder for injection and theophylline (*Theo-Dur*) tablets stored under both ambient and "stress" (40°C and 75% relative

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humidity) conditions remained chemically and physically stable for 1.5-9 years beyond their expiration dates (G Stark et al, Pharm J 1997; 258:637). Amantadine (*Symmetrel*) and rimantidine (*Flumadine*) remained stable after storage for 25 years under ambient conditions, and retained full antiviral activity after boiling and holding at 65-85°C for several days (C Scholtssek and RG Webster, Antiviral Res 1998; 38:213). In another report, theophylline retained 90% of potency for about 30 years (R Regenthal et al, Hum Exp Toxicol 2002; 21:343).

LIQUID DRUGS — Drugs in liquid form (solutions and suspensions) are not as stable as solid dosage forms. Suspensions are especially susceptible to freezing. Drugs in solution, particularly injectables, that have become cloudy or discolored or show signs of precipitation should not be used. When oral drugs are in solution with dyes, however, color changes may be due to degradation of the dye and not the drug. Epinephrine in *EpiPen* injections loses potency after its expiration date; in one study, 5 of 7 autoinjectors contained less than 90% of the labeled epinephrine content 10 months after the expiration date, without necessarily being discolored or showing signs of precipitation (FER Simons et al, J Allergy Clin Immunol 2000; 105:1025). Drugs prepared by addition of a solvent before dispensing or administration (such as suspensions of antibiotics for oral use or lyophilized drugs in vials for parenteral use) tend to be relatively unstable in the liquid state. With ophthalmic drugs, the limiting factor may not be the stability of the drug, but the continued ability of the preservative to inhibit microbial growth.

CONCLUSION — There are virtually no reports of toxicity from degradation products of outdated drugs. How much of their potency they retain varies with the drug and the storage conditions, especially humidity, but many drugs stored under reasonable conditions retain 90% of their potency for at least 5 years after the expiration date on the label, and sometimes much longer.

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