tempt, we should use our full clinical acumen in assessing a patient with pharyngitis.

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Phase IV Drug Studies

To the Editor: I have serious concerns about the ethical appropriateness and scientific accuracy of a paper that recently appeared in *JABFP*, a report from the Clinical Experience Network exploring a variety of coronary heart disease risk factors in patients with high cholesterol levels. The study is billed as an epidemiologic study of the demography of a heterogeneous and representative group of dyslipidemic patients to be followed by a subsequent report of the efforts of diet, exercise, and gemfibrizol therapy. Parke-Davis paid for the study and also purchased a three-page advertisement for gemfibrizol in the same issue of *JABFP*, an advertisement that directly precedes the article in question. Even though this is probably a coincidence, the juxtaposition of the study and the advertisement exemplifies the dangers inherent in drug company funding of research evaluating drugs manufactured by the sponsoring company.

Let's discuss the science first. The major justification for publishing this manuscript is that the patient sample is representative of the general population and that the findings are generalizable. But what evidence do we have for this assertion? We know relatively little about the 327 family physicians who are part of the Clinical Experience Network, how they were selected, and whether they are, in fact, representative of the universe of American family physicians. We know nothing about the extent to which the patients studied are representative of other patients in their respective practices. What percentage of all patients with high cholesterol were enrolled, and how many refused to be studied? How many were excluded from the study based on the various exclusion criteria established by the authors? How many patients were enrolled from each practice, and does the sampling strategy actually yield a study population that represents the geographic and demographic distribution of hypercholesterolemic patients in the United States? The discussion of this critical element of the study is incomplete at best.

But the ethical considerations are even more troubling than the inadequate science. The involvement of the pharmaceutical company would appear to introduce a serious potential for conflict of interest in the sponsorship and administration of the study. It is impossible to know whether actual or potential conflict of interest exists because we are given no information about the relationships among the involved individuals and organizations. What are the commercial, contractual, and financial links between the Clinical Experience Network, Health Learning Systems, and Parke-Davis? Did any of the listed authors of the study receive financial compensation from any of the above organizations? Who owns the Clinical Experience Network and Health Learning Systems? Do any of the authors have investments in any of the involved organizational entities? How were the participating physicians recruited, and did they receive any inducements or compensation for participating?

In my opinion, this paper is of limited scientific value and raises serious ethical questions about the propriety of drug company sponsorship of research in primary care. Clinical networks have an important role to play in research, but it is critical that there be no possibility that the commercial interests of the sponsors influence the design of the studies, the analysis of the data, or the presentation of the results. Full disclosure of potential conflicts of interest should be part of the review of all manuscripts, and papers that may be tainted by such actual or potential conflicts should be rejected. Any lesser standard demeans our discipline and undermines the probity of

the journals upon which we depend for accurate and objective information.

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To the Editor: I read with some uneasiness the latest report from the Clinical Experience Network (CEN) on low HDL cholesterol and other risk factors.[1] The way I see it, this paper, like their two previous reports,[2,3] walks a thin line between advertising and science.

This network, a nationwide affiliation of family physicians, organized and led by five former presidents of the American Academy of Family Physicians or American Board of Family Practice, provides the opportunity for family physicians to engage in clinical investigation and learn from their experience in a systematic and scientific manner. Their stated goals include the enhancement of the practice of medicine and creation of educational opportunities. Based on their first three reports, I think we would have to add the promotion of marketing material for the pharmaceutical industry supporting the research as an additional goal.

Briefly, let me comment on the three reports and my experience with them:

The first report, "Managing Hypertension in Family Practice,"[2] was a prospective, nonexperimental study meant to examine the ways in which family physicians select from among four antihypertensive agents for their patients and provide an overall prospective on how these agents perform in the management of hypertension. We are told that patients were not preassigned to drugs randomly. Physicians could assign patients to receive any one of the four study drugs at their discretion. All drugs produced similar results in predetermined efficacy and toxicity rating systems. More than 3500 total patients were initially treated with atenolol (564 patients), enalapril (677 patients), hydrochlorothiazide-triamterene (506 patients), or verapamil, sustained release (1861 patients). Am I being too skeptical when I notice that twice as many patients were randomized to verapamil and then read the study was conducted under an educational grant from G.D. Searle and Company? My local Searle pharmaceutical sales representative (PSR) presented me with a reprint of the paper emphasizing that family physicians choose verapamil 2:1 over other first-step antihypertensive agents.

The second report, "A Large-Scale, Office-Based Study Evaluates the Use of a New Class of Nonsedating Antihistamines,"[3] meets the requirements of a postmarketing surveillance (phase IV) study. The two newest agents in the class of nonsedating antihistamines, terfenadine and astemizole, were studied in typical family practice patients. No clinically significant differences were seen between treatments. It was unfortunate that there were no comparisons versus the classical, much less expensive, H_1-antihistamine receptor antagonists. So 141 family physicians were taught to treat 1485 patients with expensive, nonsedating, second-line antihistamines. Again, I am not surprised to find that the study was conducted through an educational grant from Janssen Pharmaceutica, Inc. My local Janssen PSR tried to use the piece on me to sell the product.

Finally, the latest report, "Low High-Density Lipoprotein Cholesterol and Other Coronary Heart Disease Risk Factors,"[1] analyzes the demography of a large population of dyslipidemic patients. The report pushes HDL as an additional risk factor and alludes, unnecessarily, to a treatment arm of the study (presumably to be published later) utilizing gemfibrozil, a drug known to increase HDL cholesterol. The report was supported by an educational grant from Parke-Davis, makers of gemfibrozil.

The common denominator in all three of these reports is that the "research" appears to have been designed more as a way to promote certain medications rather than as a way to improve the care of patients. Drug advertising-promotion is big business. The industry spent $10 billion ($1 billion more than the amount spent on research) last year. Most physicians are appropriately skeptical of slick, "Madison Avenue," advertising pieces distributed by PSRs. The pharmaceutical industry is eager to camouflage its promotional material by disguising it as research. The problem is compounded when a reputable scientific journal publishes the material, without ensuring itself of the independence and objectivity of the authors and researchers.

I would suggest that all of us involved in the design, analysis, and publication of research maintain the highest possible vigilance to prevent commercial intrusion into the scientific enterprise. Those practitioners who participate in this type of study should ask themselves what are the motives of the sponsors of the study, what assurances are there that the study designs will answer key clinical questions, and who stands to benefit from publication of the results. Those who organize the studies and are involved in the writing should examine their own motives for participation. Referees, editors, and publishers should ensure that conflicts of interest do not distort the papers they select for publication.

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