support the position that HDL is a significant cardiovascular risk factor. With regard to Dr. Ellsworth's suggestion that a less expensive H_1 antihistamine should have been studied in CEN's antihistamine report, the Board respects this opinion and would encourage him or any other clinician-researcher to conduct such a trial in an equally large and geographically diverse population. We believe, however, that our model of a Phase IV project comparing head to head the two new drugs in a new class of antihistamines is in and of itself a meaningful contribution. Nowhere did we encourage or "teach" practitioners to use the nonsedating antihistamines rather than other antihistamines.[1]

Dr. Ellsworth's comment that his "local Searle pharmaceutical sales representative" inaccurately emphasized certain sections of the hypertension study is unfortunate. It is unrealistic to think that CEN can control the use of data that this *Journal* or any other journal puts into the public domain.

Dr. Ellsworth has stated in his letter that "all of us involved in the design, analysis, and publication of research should maintain the highest possible vigilance to prevent commercial intrusion into the scientific enterprise." It should, therefore, be most surprising to the readers of *JABFP* to learn that Dr. Ellsworth is the lead author of at least two publications funded by industry. Furthermore, two of these publications were funded by companies he is now calling into question: Searle Pharmaceuticals, Inc., and Parke-Davis, Division of Warner-Lambert Company. The complete references for these studies are included at the end of this letter.[4,5] The Advisory Board of CEN is not calling into question Dr. Ellsworth's science or ethics. We are interested to know, however, just how he distinguishes between conflicts of interest in manufacturer-funded studies in which he participates and studies funded by the same manufacturers in which he does not. Has he considered the possibility that a sales representative somewhere may be using his paper[5] to defend disopyramide?

Drs. Rosenblatt and Ellsworth have raised many questions about CEN. Some of the information provided here to answer them has not been published specifically before, but much of it is self-evident from the published papers. Indeed, many of the questions raised by Drs. Rosenblatt and Ellsworth are not questions at all but accusations against the integrity of the advisors and investigators of CEN and the editors of this *Journal*. This type of attack is not consistent with the legitimate, scientific critique by which investigators and readers can build on each others' learnings. We know of no other accusations from any other physicians at any other universities directed at CEN during the 5 years it has been conducting studies. The few unsolicited comments that have been received were positive and encouraged the continued involvement of family physicians in conducting clinical studies on drugs in actual conditions of clinical use. The professionals involved with the Clinical Experience Network reaffirm their support for the peer review process of *JABFP* and the CEN investigative process.

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References

1. A large-scale, office-based study evaluates the use of a new class of nonsedating antihistamines. A report from CEN. J Am Board Fam Pract 1990; 3:241-52.
2. Managing hypertension in family practice: a nationwide collaborative study of the use of four antihypertensives in the treatment of mild-to-moderate hypertension. A report from CEN. J Am Board Fam Pract 1989; 2:172-90.
3. Low high-density lipoprotein cholesterol and other coronary heart disease risk factors in patients with total cholesterol levels greater than 5.17 mmol/L (200 mg/dL) in family practice. A report from CEN. J Am Board Fam Pract 1991; 4:285-97.
4. Ellsworth AJ, Christensen DB, Volpone-McMahon MT. Prospective comparison of patient tolerance to enteric-coated vs. nonenteric-coated erythromycin. J Fam Pract 1990; 31:265-70.
5. Ellsworth AJ, Horn JR, Raisys VA, Miyagawa LA, Bell JL. Disopyramide and N-monodesalkyl disopyramide in serum and breast milk. DICP 1989; 23:56-7.

Editor's Comment

The above Letters to the Editor raise concerns about the process of Phase IV drug studies as represented by recent articles in *JABFP*. The preceding letters and response illustrate a myriad of procedural and process points at which either perceived or actual conflicts of interest could occur during Phase IV drug monitoring studies. The foregoing letters also indicate the need to communicate openly the process of Phase IV drug studies in order to allow readers of published reports to assess and interpret their findings. In view of the importance and complexity of the many issues involved, our usual space limitations for editorial correspondence have been relaxed in this instance in order to facilitate a full response by the Advisory Board of the Clinical Experience Network, the organization involved in all three studies called into question.

There is an important place for collaborative research in primary care and family practice settings. The Clinical Experience Network has been organized to facilitate involvement of practicing family physicians in collaborative research and so

far has reported on three postmarketing surveillance (Phase IV) drug studies. As noted and discussed by Dr. Young in an earlier editorial comment, the FDA has encouraged the conduct of Phase IV studies of approved drugs in order to provide monitoring of drug safety and efficacy in actual practice settings and expects pharmaceutical companies to pay for such studies.[1] In an effort to guard against potential bias from the pharmaceutical industry sponsoring a wide range of educational and scientific activities, the FDA has recently developed some proposed guidelines for investigators, participants, and their sponsors for the conduct of these activities. These guidelines have been made available to the pharmaceutical industry for comment and are expected to become law later this year. Although the final regulations are not yet available, it can be anticipated that Phase IV drug studies will be expected to meet FDA-designed standards assuring independence, objectivity, balance, and scientific rigor.

As a peer-reviewed journal, *JABFP* maintains total independence of the editorial process. It is the job of the editorial staff to assure objective and unbiased review of submitted manuscripts and to select papers for publication that best meet the editorial goals of the *Journal* and needs of the readership. Authors are expected to divulge any potential financial relations with sponsors of their studies or potential conflicts of interest in their submission letter. With regard to advertising, the editorial office is not involved with this part of the *Journal's* operations. It is involved exclusively with editorial matters, including the sequencing of articles in any given issue. The proximity of the gemfibrizol advertisement to the recently published article on low high-density lipoprotein cholesterol and other coronary heart disease risk factors[2] is entirely coincidental. The production staff of *JABFP*, located in the offices of the *New England Journal of Medicine*, is solely responsible for the acquisition and placement of journal advertising under a contractual agreement with the American Board of Family Practice.

The letters by Drs. Rosenblatt and Ellsworth are appreciated as is the response and further clarification by the Advisory Board of the Clinical Experience Network. It is hoped that this dialogue will result in wider understanding of the role, value, and limitations of Phase IV drug studies and at the same time assist editors, peer reviewers, and readers in their assessment of reports of these studies.

John P. Geyman, M.D.
Editor

References

1. Young PR. Editorial comment. J Am Board Fam Pract 1990; 3:252.
2. Low high-density lipoprotein cholesterol and other coronary heart disease risk factors in patients with total cholesterol levels greater than 5.17 mmol/L (200 mg/dL) in family practice. A report from CEN. J Am Board Fam Pract 1991;4:285-97.