

PHARMACEUTICAL INDUSTRY INVOLVEMENT IN NEUROLOGIC PUBLICATIONS

Robert C. Griggs, MD

University of Rochester School of Medicine
Rochester, NY

Conflict of interest: As a neuromuscular disease specialist who does not and has never been engaged in clinical neurophysiology, the speaker has taken what is tantamount to a vow of poverty. However, in academic pursuits, money is by no means the “currency of the realm.” In fact, I must note the pressures/conflicts inherent in each of three roles: As Editor (Table 1), as Department Chair (Table 2), and in research (Table 3).

Table 1: Disclosures as Editor-in-Chief, Neurology

The Editor is not responsible for ads, does not receive revenues from industry for journal activities. However... the Editor sits on the Board of Directors of the AAN and in this role has fiduciary responsibilities for the AAN.

- Ad revenues
- Supplement revenues
- International editions (5 languages) – industry-sponsored
- Overt pressure from Big Pharma to publish their papers
- Covert pressure from Big Pharma (via academic authors) to publish their papers

Astra-Zeneca Medical Advisory Board

Table 2: Disclosures as Department Chair – Industry Support

- Resident support
- Grand Rounds support
- \$10-15 million research support (most for studies that are investigator-initiated, investigators' own data, etc.)
- Technology-transfer agreements

Table 3: Disclosures as Chair of Muscle Study Group Executive Committee

- Joint industry/FDA sponsored clinical trials (3)
- Industry/NIH sponsored clinical trials (2)
- Many others pending

Pharmaceutical industry involvement in neurologic publications:

Advertisements:

Neurology is the leading clinical neuroscience journal in terms of industry-sponsored display advertisements. This position reflects the fact that Neurology has been repeatedly documented to have the largest number of readers --- “eyes on pages”. This position accounts for the large number of display advertisements in Neurology. The Editor has opportunity to review advertisements (with a 72 hour time window). The evolving policy of Neurology is shown in Table 4.

Table 4: Neurology: Display Advertisements

- Since 1998 – The publisher secures and manages all commercial advertising
- The Editor-in-Chief reviews ads (72 hr window)
 - until 2002 – for propriety
 - since 2002 Editorial Board discussion, for accuracy*
- 2002 strategic planning meeting (with Editors of the NEJM, BMJ) “The Editor is not responsible for ads”

* These reviews are obtained at the discretion of the editor. Approximately 20% of ads have been reviewed. About half of those reviewed have been delayed or modified.

Who takes responsibility for the review of advertisements?

The FDA, after a drug is approved, asks the company for INITIAL proofs of all advertising. If they change it after this stage to make claims that are inaccurate or misleading, the company is only turned in by the competition, watchful readers – as has been the case for Neurology – to the FDA. They then can be given severe penalties – including to cease and desist all advertising. The FDA has sent letters to Neurology thanking us for turning in inaccurate advertising. We do not have specific information on penalties. An NEJM staff person has indicated that pharmas don’t often break the rules re claims because the competition have dedicated people working to go through competitors’ ads to ensure that claims are true.

Table 5: The FDA as watchdog for truth in advertising?

- Must review and approve all initial advertisements for agent
- Do not review subsequent ads
- Monitoring of ads?
 - Competitors
 - Editors
 - Readers
 - Penalties?

Table 5A: The FDA as Watchdog? Neurology Experience

- Concerns about three ads reported to Editor-in-Chief
- FDA sanctions/fine for at least one of the three

- Rapid responses from FDA
- Penalties?

Table 5B: FDA Penalties

- The FDA sends a warning letter itemizing the problem(s) and ordering the company to cease and desist. Examples can be found at <http://www.fda.gov/cder/warn/index.htm>.
- The FDA may require the company to send a “Dear Doctor” letter to physicians to correct any misinformation.
The company may be required to publish the letter as paid advertising in leading journals in the field.
- The FDA may fine the company or require their product be taken off the market.

Why take advertisements at all?

There are two obvious answers to this frequently raised question:

- (1) Informing the practicing neurologist; (2) money. While one can object to a biased source providing CME to the practitioner, the “blame” must be shared by the readers of ads. Caveat emptor. (Table 6).

Table 6: Do display advertisements have benefits?

- Information for the practicing physician?
- Support for professional society.
- Support for peer-review process
- Support for editorial and production processes

On-line advertising:

There has not yet been any experience with banner ads. This fact reflects the reluctance of advertisers to move from the print to the electronic journal. Neurology has a policy on banner ads and has been proactive in seeking to secure ad revenues (Table 7).

Table 7: Neurology: On-line advertising?

- Editorial Board-approved – “Banner” ads – on generic pages (Table of Contents, etc), not on articles
- No takers
- Bundled with display ads at no cost to advertisers – starting soon

Table 7A: Risks of Editorial Review of Ads

- You second guess the FDA and circumvent their process for dealing with unsubstantiated advertising claims.
- You give up the protection of the disclaimer that says the AAN and Editors are not responsible for the content of ads
- If ads are, in effect, peer reviewed, an advertiser could legitimately claim that the journal has endorsed their advertising content.

- There is the risk of restraint-of-trade litigation if Neurology rejects ads that other journals accept.

Publication of industry-sponsored research:

Most large, definitive clinical trials have major industry support. Neurology has had an Author Disclosure policy for many years. This policy (Kieburtz, 1997) was updated in 1998. Following a further consideration of industry-sponsored research in major medical journals, Neurology joined other neurological journals in a recent joint policy statement (Rosenberg et al, 2002). Neurology's Information for Authors reflects these policies (www.neurology.org).

These policies have been implemented as noted in Table 8.

Table 8: Neurology: Publication of industry-sponsored research

- Disclosures required (Kieburtz, 1997, 1998)
- Careful review by:
 - peer-reviewers
 - statistician
 - editor
 - 3-4 revisions usual
- Policy editorial by editors of major neurology journals (Neurology 2002; 58:347)

Supplements:

Neurology supports peer-review of all materials in the editorial pages of the Journal (Table 9). The previous Editor-in-Chief initiated supplements (often industry-sponsored). Neurology has a Supplement Editor who reviews all supplements. They are not, however, peer-reviewed. The arguments for and against industry-sponsored supplements are presented in Tables 10 & 11; Neurology policy in Table 12.

Table 9: Neurology and Peer Review

- All articles now peer-reviewed (except Presidential Address)
- Editors discourage citing non peer-reviewed sources (texts, supplements, solicited review journals)
- Since 1998, all AAN position papers are peer- reviewed
- AAN position papers based on peer-reviewed papers

Table 10: The Case For Supplements

- Readers like them – generally excellent reviews
- Academic authors paid to write reviews
- Income generating for AAN

Table 11: The Case Against Supplements

- “It will tarnish the image of Neurology”
- The readers may be confused into thinking that a supplement is peer-reviewed
- The publication might be biased in favor of the sponsor
- The cost of supplements is ultimately passed on to our patients

Table 12: Neurology: Publication of Supplements

- Review of proposals by Supplement Editor for:
 - ◆ single product?
 - ◆ appropriate focus for neurologists?
 - ◆ appropriate authors?
- New standards (2004)
 - ◆ No “Guidelines”, etc.
 - ◆ Clear statements about being non-peer-reviewed, etc.
 - ◆ Conference reports

Table 13: The Case Against Supplements - Rebuttal

- Tarnishing Neurology? In whose eyes?
- Confusing the readers? Those who can't tell that a supplement is different are likely to be misled generally.
- Bias in favor of sponsor? Surely true of any non peer-reviewed work by an industry-supported person.
- Cost – agreed.

Support of AAN infrastructure:

Others at this colloquium will no doubt mention the other ways in which industry supports the AAN including: (1) Annual meeting monies from exhibits, course “sponsorships”, attendees expense payments, meeting sponsorships, meal sponsorships. (2) Foundation support by industry donations; (3) Academy Enterprises, Inc. (AEI) support for many projects, publications. The fact that many practicing and academic neurologists are recipients of industry research support doubtless contributes monies to dues and donations to the AAN and its Foundation.

Neurophilosophy and neurotheology:

When St. Paul wrote to the Thessalonians that we are “to abstain from all appearances of evil” (1 Thess. 5:22) he assuredly meant that we are not to think or do evil --- as opposed to just appearing not to misbehave. Regrettably, much current policy in grant, manuscript, other reviewing is designed to appear free of conflict, while not eliminating conflicts of interest in the least.

Journal reviewing as an example: Reviewers from the same institution are not considered appropriate. Those from an intensely competitive or rival institution are? If I have not been included as a center in your large, multi-institutional grant proposal --- and am furious or at a minimum, hurt, am I a reviewer without a conflict?

I am never quite certain if the potential reviewer who declines to do a review on a manuscript “because the author is a friend (collaborator, former collaborator, future collaborator, former fellow, former mentor, etc)” is honest, or simply indolent. Regardless, I generally respond to the handful that state the conflict as a question, “Should I review the paper?” --- “Yes. You’ve declared your conflict. The other reviewers probably haven’t. Moreover, if all the authors’ friends decline to review the thing, only their enemies are left.”

Policies concerning conflicts are unquestionably necessary to give an aura of probity. They no doubt prevent some abuses from occurring. But policies cannot prevent subtle biases any more than one can legislate morality. The pen is no easier to tame than the tongue.

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