Reviewer's report

Title: Pfizer's antifungal trials of voriconazole are misleading because of flaws in design, analysis and interpretation

Version: 1 Date: 21 November 2005

Reviewer: John Ioannidis

Reviewer's report:

I appreciate a lot your commentary and I have several suggestions that you may wish to consider. Nothing is a “compulsory” or “essential” revision, but you may wish to consider the following issues:

General comment:

The manuscript touches on an important general issue and is anchored around an influential specific example. I share your views, but I think that some of the language may need to be toned down. There is no need to overstate. This is a major problem and more people will be informed and convinced if more objective data are disseminated. There is less need to repeat terms such as “flawed”, “misleading”, etc. throughout the manuscript; just show the evidence, this speaks clearly.

Specific comments:

1. It would be good to know a bit more about what the authors and the company responded to your queries, when they responded and what they said (and how) when they refused to provide information.
2. I would be a little more tactful about who is to blame here. Is it the authors/investigators? Several of these people I happen to know professionally, I think they are very good scientists, and I cannot think that they are simply trying to cheat. Is it the company? Why make such blatant errors and mishandling of the data and their interpretation? I don’t think that the VIOXX scandal was eventually to the benefit of the company. Is it the journals? But why would they wish to have trials whose results and inferences may soon be rejected or attacked on so clear biases? I don’t have an answer here, and maybe I am just naïve and it is all the chasing of money and one-day glory, but maybe it is a multiplicative effect when all these forces/players interact. So, I would like to take a step back and instead of blaming only, try to think what is the cumulative motivation and thus how can it be corrected to the benefit of everybody. I am just afraid that if one ostracizes investigators, companies and journals, then who is left to correct things and create a better, healthy research environment?
3. Please give some more data, even if this is a commentary. For example, in page 4, I’d like to see the data for 1.5- and 2-fold creatinine.
4. “Without mention of pre-medication and substitution”: did you clarify this with the authors? Could you find out what really happened? Maybe these management items were considered so routine that not even a mention was made, but they were followed in most or all patients.
5. In page 5, refs. 12 and 13 – this is just two references. It would be useful to do a citation analysis and see how many of the citations are following this misleading interpretation.

Minor typo: p.6: alreday

What next?: Accept after discretionary revisions
Level of interest: An article of outstanding merit and interest in its field

Quality of written English: Acceptable

Declaration of competing interests:
I declare that I have no competing interests