To:
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From:
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Regarding Dr Panos Tsintis' letter from 20 August, EMEA/372159/2007.

We hereby appeal against EMEA's decision to decline our initial application "Applying for access to the clinical study reports and protocols for placebo-controlled trials of anti-obesity drugs submitted for marketing approval" with reference to article 3.2(a) in the Rules for implementation of Regulation (EC) No 1049/2001.

Our application was forwarded to the European Medicines Agency (EMEA) by the Danish Medicines Agency on 31 July 2007. We applied for access to the clinical study reports of the placebo-controlled clinical trials and corresponding trial protocols of orlistat and rimonabant submitted to EMEA for marketing approval.

We offer additional arguments below on why it is highly important that researchers and others can get access to such documents, but ask EMEA also to consider the content of our initial letter.

According to Regulation (EC) No 1049/2001, "Openness enables citizens to participate more closely in the decision-making process and guarantees that the administration enjoys greater legitimacy and is more effective and more accountable to the citizen in a democratic system. Openness contributes to strengthening the principles of democracy and respect for fundamental rights as laid down in Article 6 of the EU Treaty and in the Charter of Fundamental Rights of the European Union".

In this case the citizens are primarily patients, doctors and taxpayers, and the decision maker is EMEA. We find it unacceptable and unethical that clinical study reports and protocols of drugs submitted to EMEA for marketing authorization are unavailable to the public, including independent researchers. It has been amply documented that the results of trials that are available to doctors and patients in medical journals are often seriously flawed, compared to the results that are known to the drug regulatory agencies.

We give three examples of this. First, the case of Vioxx has demonstrated that the withholding of unfavourable results from the public domain can have lethal consequences for the patients.

Second, Hans Melander et al. compared clinical study reports of placebo controlled trials of selective serotonin reuptake inhibitors submitted to the Medical Product Agency in Sweden as a basis for marketing approval for treating major depression with the published results. They found that studies showing significant effects of drugs were published as stand-alone publications more often than studies with non-significant results and that many publications ignored the results of intention to treat analyses and reported the more favourable per protocol analyses only (1).

Third, such selective reporting seems to be the rule, rather than the exception (2), and it has the consequence that doctors cannot select the best available treatments; they will therefore inevitably sometimes harm their patients unknowingly. We have compared 102 trial protocols with published reports of randomised controlled trials (2). The Scientific-Ethical Committees for Copenhagen and Frederiksberg in Denmark provided access to all the protocols. Half of the trials were funded by the drug industry. We believe that none of the protocols disclosed anything that could undermine the protection of commercial interests of a natural or legal person, including intellectual property. Apparently, the Scientific-Ethical Committees have come to the same conclusion or they at least concluded that there was an overriding public interest in our research.

It is particularly unlikely that clinical study reports should contain anything that could undermine the protection of commercial interests of a natural or legal person, including intellectual property, as one would not expect to find details of patented production processes, for example, in these reports.

We believe the current lack of openness and transparency in EMEA violates basic principles in the EU Treaty and must be changed, as it is also unethical. It is evident that this attitude leads to suboptimal treatment of the patients - and sometimes even to lethal harms - that could have been avoided.

We expect that your reply to our appeal will not merely refer to EU regulations, but will address, point by point, our documented concerns about secrecy in drug regulation and our arguments in favour of freedom of access. In case of continued denial of access to the requested documents, we also ask you to explain with what reasoning EMEA considers that the commercial interests of the drug industry should override the welfare of the patients, as this attitude will increase the risk that patients die because of the treatments their doctors prescribe to them out of ignorance about what the true ratio is between the benefits and harms. In particular, if EMEA not only denies us access to the protocols but also to the study reports, we expect to receive an explanation why.

Yours Sincerely,

Anders W. Jørgensen Peter C. Gøtzsche

References

1. Melander H, Ahlqvist-Rastad J, Meijer G, Beermann B. Evidence b(i)ased medicine - selective reporting from studies sponsored by pharmaceutical industry: review of studies in new drug applications. BMJ 2003;326:1171-3.

2. Chan A-W, Hróbjartsson A, Haahr MT, Gøtzsche PC, Altman DG. Empirical evidence for selective reporting of outcomes in randomized trials: comparison of protocols to published articles. JAMA 2004;291:2457-65.