To:
P. Nikiforos Diamanduris
The European Ombudsman
The European Union

Reply to the opinion provided by the European Medicines Agency (EMEA) to the European Ombudsman, regarding our appeal concerning denial of access to clinical study reports and corresponding trial protocols of the anti-obesity drugs, orlistat and rimonabant

Complaint 2560/2007/BEH

From:
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In their letter to the Ombudsman from 28 April 2008, EMEA gave its opinion on the issues that the Ombudsman raised.

EMEA stated that:

- clinical study reports contain considerable detail on the design and methodology of the trial, the data generated and on the analysis of the data, and represent the full detail of the clinical development programme for a medicinal product,

- the clinical development of a product represents the most substantial part of the applicant's investment up to the point of marketing approval,

- all requests for access to documents are handled in accordance with the rules for implementation of Regulation (EC) No 1049/2001.

EMEA concluded that:

- the clinical study reports and protocols contain commercially confidential information and substantial amounts of personal data,

- to give access to these documents requires time and resources that will divert attention from the core business of EMEA, which is to inform healthcare professionals and patients on data relating to medicinal products that are approved or rejected by EC, through science-based recommendations.

We have previously described that considerable details of the methodology of trials are needed to make reliable systematic reviews about benefit and harms of drugs. However, such information is rarely available, neither in medical journals, nor in EMEA's scientific assessment reports.

As an example of lack of details, EMEA's assessment report on Xenical (orlistat) does not mention anything about allocation concealment. The report on Acomplia (rimonabant) presents data from

49 trials, 8 of which are phase III trials that are relevant for us, but allocation concealment is only described for 4 of these. Details on concealment of allocation are very important. Inappropriate or unclear concealment of allocation introduces bias and overestimates the effect by 18% on average (2).

EMEA emphasises the degree of detail of the clinical study reports by referring to their guide on structure and content of clinical study reports. However, this describes general and well-known principles for drug trials. In contrast to EMEA's conclusion, this guide does not indicate that clinical study reports contain commercially confidential information.

We agree with EMEA that clinical trials require considerable resources, and that the clinical development may be a substantial part of the applicant's investment up to marketing approval. However, this only represents a minor part of the pharmaceutical industry's total expenses. In USA, the pharmaceutical industry spends about twice as much on drug promotion than on research and development (1). Furthermore, EMEA's deliberation is irrelevant for our request of access to data. In fact, we believe that if commercial success is dependent on withholding data that are important for rational decision-making for doctors and patients, then there is something fundamentally wrong with our priorities in health care.

We still find it highly unlikely that clinical study reports should contain commercially confidential information, as we did not find such information when we read the full contents of industry-sponsored trial protocols, as described previously in our letters to the Ombudsman.

Previously, we have been denied access to the requested documents because of the exceptions listed in article 3.2(a) of the Rules for the Implementation of Regulation (EC) No 1049/2001 on access to EMEA documents. It now seems EMEA also uses the exceptions in Art 3.1(b) to deny us access to clinical study reports, as these - according to EMEA's guide on structure and content of clinical study reports - contain tables with individual patient data. However, Art. 6 states that if only parts of the requested document are covered by any exceptions, the remaining parts of the documents shall be released.

According to EMEA, it is a long and complex work to provide the documents without the individual patient data. However, the structured nature of clinical study reports, as described by EMEA's guide on structure and content of clinical study reports, indicates that removing such information should be rather easy.

Finally, according to Regulation (EC) No 1901/2006 article 41.2, details of all paediatric trials submitted to EMEA shall be made public by the Agency. It would seem difficult, if not impossible, to defend a position that only details on trials in children and not those of trials in adults will be made publicly available.

To summarise our opinion:

- EMEA has again failed to specify why clinical study reports and protocols are to be considered as covered by commercial interests,

- Disclosure of the requested documents will benefit the members of the European Community and people in the rest of the world, as they would get a more reliable picture of the benefits and harms of drugs used against obesity. This is important for rational decision-making, and we therefore firmly believe that the interests of the patients should override the commercial interests of the companies marketing anti-obesity drugs.

We ask the Ombudsman also to consider our previous letters, where we documented that patients have been - and are likely to be in future - treated with inferior and sometimes harmful drugs, which have led to - and likely will lead to - the deaths of many patients, unless reliable information about the benefits and harms of drugs are made publicly available.

Yours sincerely,

Peter C Gøtzsche
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References

1. Gagnon MA, Lexchin J. The cost of pushing pills: a new estimate of pharmaceutical promotion expenditures in the United States. PLoS Med 2008;5:e1.

2. Pildal J, Hrobjartsson A, Jorgensen KJ, Hilden J, Altman DG, Gotzsche PC. Impact of allocation concealment on conclusions drawn from meta-analyses of randomized trials. Int J Epidemiol 2007; 36(4):847-57.