European Medicines Agency 2560/2007/BEH

London, 26 February 2009
Doc. Ref.: EMEA/110754/2009

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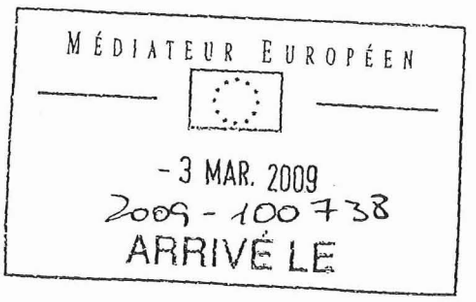

Re: Complaint 2560/2007/BEH

Dear Mr. Diamandouros,

Thank you for your letter dated 22.01.2009 concerning the proposal for a friendly solution in the case at object. After having taken in close consideration your arguments, I would like to submit the following observations and to provide further motivations in relation to our initial decision.

Summary of the facts

1) On 31 July 2007 the Danish Medicines Agency forwarded to the EMEA a letter from Mr Anders W. Jorgansen and Dr Peter C. Gotzsche, respectively PhD student and director of the Nordic Cochrane Centre in Copenhagen, sent on 29 June 2007 (to the National Competent Authority).

Their request was aimed at obtaining the clinical study reports and corresponding trial protocols for placebo-controlled trials concerning two anti-obesity medicinal products for which marketing authorisations had been granted, namely Rimonabant and Orlistat.

By letter of 20 August 2007, the EMEA informed the applicants that the requested documents fell under the exceptions set out in the implementing rules of Regulation (EC) No 1049/2001 on access to EMEA documents, and in particular Article 3.2 (a) of these rules, and therefore they could not be released.

2) The applicants lodged a confirmatory application on 24 August 2007 against EMEA's decision in accordance with Article 6.2 of Rules for the Implementation of Regulation (EC) 1049/2001. In its reply dated 17 September 2007, the EMEA confirmed its previous decision and denied access to the concerned documents for the abovementioned reasons.

3) On 8 October 2007, the applicants lodged a complaint to the Ombudsman concerning EMEA's denial of access to the requested documents.

On 30 January 2008 The EMEA sent accordingly an opinion to the European Ombudsman, with enclosed copy of EMEA rules for the implementation of Regulation (EC) No 1049/2001.

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4) By letter of 18 March 2008, the Ombudsman asked the EMEA for further information on the concerned issue. In its letter dated 28 April 2008, the EMEA submitted its observations in response to the Ombudsman's request.

Finally, on 22 January 2009, the Ombudsman sent the EMEA a letter with enclosed proposal for a friendly solution in the present case.

a)

Aspect of commercial confidentiality of the clinical study reports and corresponding trials protocols

The EMEA refused access to the documents the applicant requested on the basis of the exception foreseen by article 4.2.a of Regulation 1049/2001 (EC), in the view of the interest to protect commercially confidential information of a third party.

It's worth mentioning that although a sound and clear definition of commercially confidential information (CCI) cannot be found, neither in the legislation nor in the jurisprudence, generally CCI is defined as follows:

Information that could be of benefit for a competitor, the disclosure of which could cause a disproportionate prejudice to and seriously harm the commercial interest of the party. Under the definition of CCI fall the following categories:

a) Intellectual property: Concerns the development and research (very costly in the pharmaceutical sector) prior to the filing of a patent or a design. The disclosure of the information prior to obtaining a patent can prevent it from being registered. Therefore, high interest to put measure in place to keep it secret;

b) Trade secrets: Concern formulas, manufacturing and control processes which are or may be used in trade. They are generally not in the public domain and can draw a certain value from not being known. They are also subject to reasonable efforts of being kept secret;

c) Commercial confidences: Concern every piece of information which does not have a commercial value as such, but its disclosure might provoke damage to the party (e.g. structures and development plans of company, marketing strategies, etc.).

As already explained in our reply dated 28 April 2008, the data contained in those third parties documents have commercial value.

In particular, **clinical study reports** are integrated full reports of an individual study of any therapeutic, prophylactic, or diagnostic agent (referred to as drug or treatment) conducted in patients. The clinical and statistical description, presentations, and analyses are integrated into a single report, incorporating tables and figures into the main text of the report or at the end of the text, with appendices containing such information as the protocol, sample case report forms, investigator-related information, information related to the test drugs/investigational products including active control/comparators, technical statistical documentation, related publications, patient data listings, and technical statistical details such as derivations, computations, analyses, and computer output. I would also like to take the opportunity to note that a document concerning the structure and content of a clinical study report was already submitted in our reply to the Ombudsman dated 28 April 2008.

A **Clinical Trial Protocol** is instead a document that describes the objective(s), design, methodology, statistical considerations, and organization of a clinical trial. The protocol usually also gives the background and reason the trial is being conducted. The protocol contains a study plan on which the clinical trial is based. The plan is designed to safeguard the health of the participants (while limiting their financial liability) as well as answer specific research questions. The protocol describes, among other things, what types of people may participate in the trial; the schedule of tests, procedures, medications, and dosages; and the length of the study.

The format and content of clinical trial protocols sponsored by pharmaceutical, biotechnology or medical device companies in the United States, European Union, or Japan has been standardized: they are written to follow the Good Clinical Practice guidance issued by the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). Regulatory authorities in Canada and Australia also follow the ICH guidance.

The existence of a clinical trial protocol allows researchers at multiple locations (in a multicenter trial) to perform the study in exactly the same way, so that their data can be combined as though they were all working together. The protocol also gives the study administrators (often a contract research organization) as well as the local researchers a common reference document for the researchers' duties and responsibilities during the trial.

With reference to these two documents, I would like to draw the attention of the Ombudsman to the fact that it would be reasonably foreseeable that the disclosure of this information would specifically undermine the interest of the third party owner of the document. The data contained in the reports and protocols could in fact be used by competitors as a basis to start developing the same or a similar medicinal product on their own, using the information and data for their own economical advantage. And moreover from the data contained therewith, the competitors could gather valuable information on the long term clinical development strategy of the company.

b)
Evidence of an overriding public interest in disclosure

Article 4 2. a) of Regulation (EC) 1049/2001, foresees a, so called, relative exception to the general principle of transparency. In particular, whenever the institution denies access to certain documents on the basis of the exemptions foreseen by the article at stake, the applicant would still be in the position to prove the existence of a public interest which overrides the exception and therefore re-establish the general rule of transparency.

In relation to this aspect the EMEA attentively considered the motivations stated by the applicant - on whom the burden of proof lays - to demonstrate the existence of a public interest in disclosure. The Cochrane Centre arrived at the conclusion that as a consequence of the EMEA's refusal to give access to those documents, patients would die unnecessarily.

The Court of First Instance, in the Case T-36/04 has stated that:

"*It must be stated that Regulation No 1049/2001 does not define the concept of overriding public interest. It should also be pointed out that, in the case of interests protected by the exception in question (...) it is for the institution concerned to strike a balance between the public interest in disclosure and the interest which is served by a refusal to disclose, in the light, where appropriate, of the arguments put forward by the applicant in that connection.*"

The EMEA is of the opinion that the link between the sharing of the requested documents and the possibility of saving lives of patients was not satisfactorily proven by the applicant to justify the release of the clinical study reports and corresponding trials protocols. The EMEA believes that the underlying meaning of the principle of transparency is to enable citizens to scrutinize the activities of the Agency and strengthening, in this way, the democratic scrutiny and control over its functions.

To this purpose, the EMEA, according to article 80 of Regulation (EC) 726/2004, regularly publishes European public assessment reports and press releases through which the public is informed about EMEA's activities and can therefore gather information about the work of the Agency. On the other hand, it is important to underline that, the activity of evaluation on the safety and efficacy of a medicinal product during its whole lifecycle, is still expressively and specifically a task of the Agency, and not a shared responsibility of the general public. Therefore the EMEA considered that the motivations put forward by the applicant to try to prove the existence of an overriding public interest in the disclosure of the documents were not sufficient.

In addition to this, it worth noting that the EMEA has drafted an Access to Documents Policy - currently undergoing public consultation - which foresees the possibility for the public to have access to many documents related to the EMEA's activities, with particular reference to the CHMP Assessment Report and to the (Co)- Rapporteur Assessment Reports. In relation to these two categories of documents, the EMEA holds the view that the release of the assessment reports for the two medicinal products at stake, could satisfy the request of the complainants.

As also stated by the Ombudsman, regulatory agencies find themselves in a difficult position whenever they need to assess the balance between private and public interest. With reference to this, it is worth noting that the evaluation made by the EMEA in the case at stake involved not only the balance between the private interest of the marketing authorisation holder against the instances of pubic interest put forward by the applicant, but also considerations on the institutional tasks the Agency has been entrusted with by the legislator.

In this respect it is worth mentioning that, as stated by recital 13 of EMEA founding regulation (EC) 726/2004 "*in the interest of public health, authorisation decisions under the centralised procedure should be taken on the basis of the objective scientific criteria of quality, safety and efficacy of the medicinal product concerned, to the exclusion of economical consideration*" and amongst its tasks, the EMEA has indeed the responsibility to coordinate the scientific evaluation of the quality, safety and efficacy of medicinal products which are subject to community marketing authorisation. Moreover, the Agency provides the Member States and the institutions of the EU the best-possible scientific advice on any question relating to the evaluation of the quality, safety and efficacy of medicinal products for human or veterinary use referred to it in accordance with the provisions of EU legislation relating to medicinal products.

As known, in fact, the legislator, with the creation of the Agency, believed that the centralisation of the procedure of authorisation for marketing authorisation and of the evaluation of medicinal products - and not the opposite- would have been of benefit for the citizens. It is the EMEA, therefore, the reference point and the European Union body responsible for coordinating the existing scientific resources put at its disposal by Member States for the evaluation, supervision and pharmacovigilance of medicinal products.

The central position of responsibility of the Agency in the protection of public health is also supported and reinforced by the fact that, firstly with reference to the medicinal product Acomplia (Intellectual Non-proprietary Name "Rimonabat"), The European Medicines Agency recommended the suspension of the marketing authorisation. The EMEA's Committee for Medicinal Products for Human Use (CHMP) concluded in fact that, the benefits of Acomplia no longer outweigh its risks and the marketing authorisation should have been suspended across the European Union (EU). On 13 November 2008, the marketing of Acomplia was suspended in all the Member States in which the product was being marketed. After this decision, on 5 December 2008, the marketing authorisation holder (MAH) responsible for Acomplia, notified the European Commission of its decision to voluntarily withdraw its marketing authorisation. The MAH stated that no additional clinical data will be available to lift the suspension of the marketing authorisation for Acomplia following its decision to discontinue the ongoing rimonabant clinical development program in all indications.
Finally, on 16 January 2009, the European Commission issued a decision to withdraw the marketing authorisation for Acomplia. Pursuant to this decision the marketing authorisation is no longer valid.

Secondly, as far as the other medicinal product - Orlistat - is concerned, after evaluating safety and efficacy aspects, on 21 January 2009 the EMEA granted approval for the sale without prescription. EMEA recommended the switch as part of an extension of the marketing authorization in response to an application by the marketing-authorization holder for a lower-dose capsule (60 mg) with a new classification as a non-prescription medicine.

c)

Application of the principle of proportionality in the redaction of the documents

On the contrary, should the Ombudsman be of the opinion that the requested documents would need to be released, even in that case, only a partial disclosure could be granted. Due to the presence of a great amount of commercially confidential information and personal data, the documents would in fact need to be redacted and could only be partially released. It is also important to say that, as a result of the redaction exercise, the documents will be deprived of all the relevant information and the remaining parts of them will be worthless for the interest of the complainant.

As already mentioned the clinical study reports protocols are annexes of the dossier submitted by the pharmaceutical companies and in the present case comprise more than 500 volumes of documentation, each of which containing approximately 300-400 pages. Therefore, the redaction of these documents would nevertheless entail a disproportionate effort in term of time and human resources that would be distracted from their core activities. This would mean in practical terms the redaction of 300.000 - 400.000 pages for the two medicinal products at stake.

Considering this, access could be nevertheless refused in the light of the principles as stated by the judgment of the Court of First Instance quoted by the Ombudsman T-2/03, 102: "An institution must therefore retain the right, in particular cases where concrete, individual examination of the documents would entail an unreasonable amount of administrative work, to balance the interest in public access to the documents against the burden of work so caused, in order to safeguard, in those particular cases, the interests of good administration (see, by analogy, *Hautala* v *Council*, cited in paragraph 69 above, paragraph 86).

This principle is also supported and shared by some national legislation on access to information, amongst which the English Freedom of Information Act is an example. The English F.O.I. Act, Part 1, 12, foresees in fact the possibility for the institution to deny access whenever the cost of compliance exceeds appropriate limit:

Exemption where cost of compliance exceeds appropriate limit:

(1) Section 1(1) does not oblige a public authority to comply with a request for information if the authority estimates that the cost of complying with the request would exceed the appropriate limit.

(2) Subsection (1) does not exempt the public authority from its obligation to comply with paragraph (a) of section 1(1) unless the estimated cost of complying with that paragraph alone would exceed the appropriate limit.

(3) In subsections (1) and (2) "the appropriate limit" means such amount as may be prescribed, and different amounts may be prescribed in relation to different cases.

(4) The Secretary of State may by regulations provide that, in such circumstances as may be prescribed, where two or more requests for information are made to a public authority—

(a) by one person, or

(b) by different persons who appear to the public authority to be acting in concert or in pursuance of a campaign,

the estimated cost of complying with any of the requests is to be taken to be the estimated total cost of complying with all of them.

(5) The Secretary of State may by regulations make provision for the purposes of this section as to the costs to be estimated and as to the manner in which they are to be estimated.

In particular, in the explanatory note to the Statutory Instrument 2004 n. 3244, it is mentioned that in the case of public bodies (including governmental departments) an appropriate limit is to be considered an amount of £600 per request and an amount of £450 for other public authorities, the statutory instrument foresees also that the cost are to be estimated at a rate of £25 per person per hour.

For the above mentioned reasons the EMEA believes that also partial access to the documents should be denied since the completion of the request of the applicant would entail a disproportionate effort for

the Agency, which would need to distract human resources from their normal activities connected to the core business.

d)
Conclusions

In conclusion, the EMEA maintains that the information contained in the clinical study reports and in the corresponding trials protocols concerning the anti-obesity medicinal products Rimonabant and Orlistat, as requested by the applicant, cannot be disclosed due to the commercially confidential nature of the information contained and, moreover, that the applicant has not given evidence of the existence of an overriding public interest which could potentially justify the disclosure of the documents. In any case, should the Ombudsman still believe that the documents have to be released, the effort that the redaction of those documents would entail for the Agency in terms of time and human resources would be disproportionate and therefore access should be denied also in this case.

I trust the Ombudsman would consider the motivations and the arguments of the Agency as in compliance with the applicable rules on access to documents and information.

Yours sincerely,

Thomas Lönngren
Executive Director