To: Medicines and Healthcare products Regulatory Agency, FOIA-Department

January 10, 2009

FOIA-request about deaths from Strattera treatment

Background data about applicable rules

The MHRA is the Reference Member State (RMS) for the ADHD drug Strattera and as such assumes the responsibility of analysing and monitoring serious adverse reactions of the drug.

Per *Volume 9A of The Rules Governing Medicinal Products in the European Union (Guidelines on Pharmacovigilance for Medicinal Products for Human Use)* **[1]** "the Marketing Authorisation Holder should ensure that all serious adverse reactions occurring in the EU are reported in such a way as to be accessible to the RMS".

In the referenced Volume, Part I: *Guidelines for marketing authorisation holders,* Section 4 *The Requirements for Expedited Reporting of Individual Case Safety Reports,* the rules for Marketing Authorisation Holders (MAHs) in reporting serious adverse drug reactions are given.

For adverse drug reactions occurring within the EU it is stated (page 58): "For medicinal products authorised through the mutual recognition or decentralised procedures and for medicinal products which have been the subject of a referral procedure, *the Marketing Authorisation Holder is responsible for ensuring that all serious adverse reactions received from Healthcare Professionals or Competent Authorities within the EU are reported to the Reference Member State*." (Emphasis added.)

For *Individual Case Safety Reports on adverse reactions occurring outside the EU* it is stated (page 59): "For all medicinal products, independent of the authorisation procedure, *the Marketing Authorisation Holder should report on an expedited basis, all unexpected serious adverse reactions … occurring in the territory of a non-EU country, and initially reported (or confirmed) by a Healthcare Professional, to the Agency and to all Member States where the medicinal product is authorised."* (Emphasis added.)

As for the time frame of the reporting it is stated (page 57): "The Marketing Authorisation Holder should transmit all ICSRs requiring expedited reporting promptly and no later than 15 calendar days from receipt. This applies to initial and follow-up information."

In other parts of Section 4 the responsibility of the MAH for ensuring *the quality* of the Individual Case Safety Reports is stressed. It is stated (page 57): "The Marketing

Authorisation Holder is expected to validate all adverse reactions reported by Healthcare Professionals to ensure, prior to reporting to the Competent Authorities, that the minimum information required is included in the report". It is also stated: "Reports should be followed-up to obtain additional information relevant to the case as necessary, and relevant follow-up information should be reported to the Competent Authorities." It is further stated (page 62): It is essential for the Marketing Authorisation Holder to provide as many data elements as possible for cases of adverse reactions to facilitate assessment … *The Marketing Authorisation Holder is expected to follow-up all reports of serious adverse reactions to their medicinal product(s) to obtain comprehensive information where available. Additional information not available at the time of the initial report should be provided in the form of follow-up reports.*" (Emphasis added.)

It is understood that the RMS (in the case of Strattera, the MHRA) has the responsibility of ensuring that the MAH (in this case Eli Lilly) is following the rules listed above.

The medical agencies in Europe should cooperate with other regulatory authorities – for example the FDA – in the detection, assessment, understanding and prevention of adverse drug effects. It is stated (page 112): "Competent Authorities should also cooperate with regulatory authorities outside the EU on the basis of any formal arrangements in place for exchange of data and other information."

Background data about the investigation by the MHRA of Strattera death

In May 2008 I submitted detailed data about cases of Strattera death to the MHRA. 1st October I finally got an answer from the Scientific Assessor of the Vigilance and Risk Management of Medicines (VRMM). 7th October I got an answer from Professor Kent Woods, CEO of the MHRA, referring to the letter sent by the Scientific Assessor.

My data about Strattera deaths can be found in the letter *Strattera: Eli Lilly gave false information about deaths from Strattera treatment – a request for full investigation* from 15th May. **[2]**

The agency was in that letter provided with *specific data* (even ICSR numbers) about instances of death in connection with Strattera treatment.

In the letter 1st October the Scientific Assessor stated **[3]**:

"… in order to calculate the total number of reports with a fatal outcome ***it is not simply a case of adding up reports with a fatal outcome*** *mentioned in our assessment reports of the PSURs [Periodic Safety Update Reports] and those available on the FDA website as these different sources may contain duplicate information." [Emphasis added.]*

I would fully agree to this and it took only a casual reading of my letter from 15th May to find out that much care had been taken to *exclude* possible duplicates. It was quite easy to see that the data presented about fatal cases in my letter was NOT

"simply a case of adding up reports with a fatal outcome". (See also the EU Directive about the responsibility for the MAH and the Competent Authorities as regards duplicate information.)

However the MHRA ***did some form of investigation*** about the instances of death brought to the agency's attention by my letter. The MHRA assessor wrote:

"We have looked at the data you have sent us to see if they can add insight to the statutory sources of data we have received ***and do not think that they are of benefit as we cannot verify their source or accuracy.****"* (p. 3) [Emphasis added.]

My FOIA-request

In order to verify that the MHRA is adhering to the rules in the above described Directive from the EU Commission I request the following data:

I request to get the letter ***sent*** *by the MHRA* assessor to the MAH (Eli Lilly) to get data about all serious adverse events with outcome death, reported for Strattera. [With reference to the EU Directive the MAH is obliged to send all reported unexpected serious adverse drug reactions to the RMS, *also* those reported outside EU (I assume that serious adverse drug reactions with outcome *death* are considered *unexpected).* From my earlier communications with the MHRA it had become clear that the MAH had *not* sent these reports for Strattera to the agency. *So* I assume that the MHRA assessor as part of his investigation requested information from the MAH – I want to be sent a copy of this request.]

I request to get the documents ***submitted by the MAH*** (Eli Lilly) to the MHRA as a response to the above letter from the MHRA assessor about Strattera death.

I request to get the letter(s) demanding follow-up actions, ***sent*** by the MHRA assessor to the MAH *after* the above submission from the MAH. [With reference to the EU Directive the MAH is obliged to *"validate all adverse reactions reported"* and to "*obtain comprehensive information*" about the serious drug reactions reported. From the letter sent by the MHRA assessor to me it was clear that the MAH *at that time* had *not* done its required follow-up actions as regards cases with a fatal outcome, and I *assume* that the MHRA later demanded that these required follow-up actions were done - I want to be sent a copy of the letter from the MHRA requesting that these follow-up actions were done.]

I request to get the letter ***sent*** by the MHRA assessor to the FDA to get data about the serious drug reactions with outcome death (the data specified in my report from 15th May) and ***the answer sent by the FDA*** by reason of that data request. [With reference to the EU Directive the Competent Authorities should cooperate with regulatory authorities outside the EU for exchange of data and other information. This cooperation must be especially important when the the drug reaction had the outcome death.]

I request to get a compilation of all reported serious drug reactions in connection with Strattera treatment with the outcome death **now** available to the MHRA.

Yours sincerely,

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References:

[1] European Commission, *Volume 9A of The Rules Governing Medicinal Products in the European Union (Guidelines on Pharmacovigilance for Medicinal Products for Human Use)* September 2008, http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-9/pdf/vol9a_09-2008.pdf
[2] Larsson, *StratteraDeath*, May 15, 2008, http://jannel.se/StratteraDeath.pdf
[3] MHRA*, Re: letter of 9th September 2008 to "Assessor responsible for Strattera",* October 1, 2008, http://jannel.se/Reply.from%20MHRA.Assessor.October.pdf