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9<sup>th</sup> June 2010

Dear Dr Raine

Thank you for your letter of 3<sup>rd</sup> June responding to my concerns regarding the safety of Ativan and Lorazepam. I would now like responses to the following questions:

1. You mention various updating and replacing of filing systems, a lack of available records, and that the original product licence application is unavailable as an explanation as to why you are unable to answer some of my questions.
  - a) Can you clarify what has happened to the original product licence and these other documents?
  - b) Were they destroyed or lost and when did this happen? Also, if they have been destroyed, then I request access to your document destruction log.
  - c) What other documents besides the original product licence application have been destroyed or lost?
  - d) What is the MHRA's legal duty with regard to retaining these documents and records?
2. The Ativan licence may have been cancelled in October 2008 but numerous Lorazepam licences have since been issued by the MHRA for its manufacture and distribution. Presumably, these Lorazepam licence holders did not have to provide clinical trial evidence on the safety of Lorazepam. This implies that the only evidence available to support these new licences has been lost or destroyed by the MHRA in the form of evidence supplied by Wyeth prior to 1981. As these records are unavailable how can the MHRA vouch for the safety of Lorazepam without them?
3. You state that in 2000 the MCA had not received formal notification of the De Buck study and had to ask Wyeth if they sent it. This is ridiculous because Wyeth would obviously confirm that they had sent this information because it was in their interest to do so. If, as you say '*...we no longer hold a copy of the original licence application the Agency cannot confirm exactly what details from the De Buck study were presented in the original dossier*' then how can you know that Wyeth sent them?
4. Lorazepam prescriptions are increasing and there were 852,000 in 2007 according to the Dept of Health statistics. It is one of the most problematic benzodiazepines and has caused hell for hundreds of thousands of patients and death for many others. In the benzodiazepine litigation 1986-96, the Department of Health and the CSM were originally joined with Wyeth as co-defendants accused of negligence. Legal aid certificates were issued by the Legal Aid Board to fund the litigation against them and they were represented by counsel at hearings in the High Court. The Ativan product licence application would have been one of the key documents and inevitably would

have been copied for the solicitors and barristers involved. In this light, how could the MHRA claim to have destroyed or lost such an important document?

5. When did anyone at the MHRA last see, use or refer to the Ativan product licence application and when did the MHRA realise it was destroyed or lost? How were the MHRA able to give assurances to Panorama, the Sunday Express, Phil Woolas MP and Barry Haslam that Ativan was safe without reference to these files and documents?
6. There has been endless controversy over Ativan and Lorazepam covered by countless television documentaries eg Panorama, Brass Tacks, the Cook Report, and newspaper articles and concerns raised by MPs, academics and the public. What justification did the MHRA have for ignoring widespread public concern?
7. Why did it take from 1972 until 1990 for convulsions to be listed as side effects? Do you consider this was a reasonable time span taking into account the hundreds of thousands of patients who were developing long-term addictions during this period of time?
8. It is irrelevant and misleading for you to say that 3000 people can be involved in clinical trials. This gives a false inference that large numbers of people were involved in the clinical trials of Ativan. There were not, and all the clinical trials of Ativan in my possession were short-term and of poor quality and concentrated on efficacy and not on safety. The obligation is on the pharmaceutical companies and the MHRA to produce evidence that the drug is safe – it is not the public's obligation to provide evidence that the drug is dangerous. What clinical trial evidence does the MHRA now rely upon to demonstrate that Lorazepam is safe and how many individuals were involved in those trials?
9. You state that '*Two cases from clinical trials, particularly if these included a confounded case, are unlikely to have roused suspicion*'. In fact, 2 cases of seizures out of 30 patients indicated that Ativan showed potentially highly addictive properties and should have prompted further trials. Also, the protocol violation within the trial should have raised additional suspicions with the MCA as to the integrity of Wyeth's clinical trials, not placated them. Why did this not happen?
10. If the UK dosage change was approved in 1988 then why did the MHRA make an announcement in the Drug Safety Update Vol.1 Issue 3 Page 8 in October 2007 that the UK maximum dosage would be reduced from 10mg to 4mg? Also, this is an error of 250% which is a catastrophic miscalculation in medical terms; How does the MHRA explain this and can the MHRA provide evidence of the variation approval in 1988 to which you refer regarding dosage? Also, why did it not go onto the datasheets?
11. You still have not answered why the product licence was not reviewed following Professor Tyrer's, Professor Einarson's and Professor Lader's investigations into convulsions and withdrawal symptoms in 1979/80. Who carried out the CRM review of 1980, what was its terms of reference and what records are available?
12. The answer to question 8 regarding the MHRA's objectives on patient safety is full of aspiration but far from reality. Just in this one case involving one drug, we have a catalogue of inaction, lost documents, unavailable files, information that you might or might not have, and in the meantime patients have become addicted by the thousands to a drug which is still prescribed

today, for which you now have no evidence to vouch for its safety. I would like to request that the Lorazepam licence be suspended immediately in the interests of public safety until credible scientific evidence is presented to demonstrate that the drug is safe.

13. The MHRA (MCA) has known that benzodiazepines have been used long-term since the 1960's and that they are highly addictive but has made no efforts to assess resulting long-term and permanent damage. Why not?
14. You say that you are sorry you have not been able to answer some of my questions but is the MHRA sorry that because of their lack of robust licensing and competent monitoring and a careless attitude to record keeping and a complacent regard to important information required from companies, I and many others have become unwittingly addicted to a drug and had to take it for decades unnecessarily and suffer the consequences of the side effects and horrific withdrawal symptoms?
15. To whom are the MHRA accountable for their mistakes and what is the procedure for complaints against the agency?

Yours sincerely

John Perrott