Medicines & Healthcare products Regulatory Agency

MHRA
Regulating Medicines and Medical Devices

James Kelly
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MHRA

151 Buckingham Palace Road
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www.gov.uk/mhra

06th July 2018

Dear Mr Kelly,

FOI 18/324

Thank you for your information request, dated 8th June 2018, where you have asked further questions based on the response previously provided. This FOI response addresses those additional questions which have been highlighted within the extracts from your email.

> *1) Copies of all the correspondence and dates of any telephone calls between ICO, PHSO, and MHRA between 3rd July and 11th December 2017 regarding my complaint?*
>
> *I find it difficult to believe that you failed to respond to my official complaint dated 03rd July 2017 by late November.*
>
> *Within weeks of my contact with PHSO a response from MHRA was received on 11th Dec 2017.*
> *(I don't think this was just a coincidence, and your response was totally irrelevant to the complaint)!*
>
> *Why was my complaint ignored for five Months?*

The MHRA would like to assure you that the agency does not ignore correspondence. We apologise for the delay that you experienced in response to your email dated 3 July 2017. Although you considered your correspondence to be an official complaint it was logged as a general query (GCEP-00122592) and allocated for a response. Unfortunately, the member of staff it was allocated to went on a prolonged period of sick leave and it was not picked up until they returned to work in November. MHRA has procedures in place that should ensure work is reallocated in order to meet deadlines but unfortunately the system failed on this occasion.

> *2) Copies of all the information MHRA and CSM sent out to GP's and other health professionals regarding any prescribing recommendations during 2005?*
>
> *The only document I could find on the internet was CSM Letter to GP's 31/01/2005. [Page 5 Four Steps]*
> *https://assets.publishing.service.gov.uk/media/547307ede5274a1303000023/con019461.pdf*
>
> *Was this the only Document?*

Details of additional communications issued by MHRA were provided in response to your original request for documentation. One of the links provided to you in the response (http://webarchive.nationalarchives.gov.uk/20141206152207/http://www.mhra.gov.uk/NewsCentre/CON2025739) contains a further link (http://webarchive.nationalarchives.gov.uk/20141205212718/http://www.mhra.gov.uk/Safetyinformation/Safetywarningsalertsandrecalls/Safetywarningsandmessagesformedicines/CON1004254) to all documents prepared by MHRA/CSM for healthcare professionals, i.e.:

- Letter to healthcare professionals dated 31 January 2005

- Questions and answers dated July 2005
- Outcome of the public request for information on the risks and benefits of co-proxamol dated January 2005
- Advice on analgesic options in treatment of mild to moderate pain in adults dated January 2005
- Advice from the CSM Expert Working Group on analgesic options in treatment of mild to moderate pain dated January 2005

The Agency can confirm that the 'Letter to healthcare professionals dated 31 January 2005' was sent to healthcare professionals, while the other documents were hosted on the Agency's website.

Press releases were also issued and the information was subsequently reported in publications for healthcare professionals.

http://webarchive.nationalarchives.gov.uk/20141206152209/http://www.mhra.gov.uk/NewsCentre/Pressreleases/CON002065

http://webarchive.nationalarchives.gov.uk/20141206152207/http://www.mhra.gov.uk/NewsCentre/CON2025739

An article was also published in the MHRA's bulletin Drug Safety Update in November 2007 reminding healthcare professionals that all licences were to be cancelled at the end of 2007.

https://www.gov.uk/drug-safety-update/co-proxamol-withdrawal-reminder-to-prescribers

> *This document MHRA and CSM recommended that patients should discuss their treatment with their healthcare professional as published at the website given above. All information that was sent to GPs and other health professionals is published on the internet.*
>
> *There were 1.75 million patients being forced to try the alternate analgesia during 2005 and 2006, they were forced to participate in the four recommendations set out in the 'CSM letter to Doctors: -*
>
> *Class I – Acute pain either as acute self-limiting episode or on a background of chronic pain: e.g. soft tissue injuries, post-operative pain, osteoarthritis, low back pain, dysmenorrhoea.*
>
> *Step 1: Paracetamol Step 2: Substitute ibuprofen Step 3: Add Paracetamol to Ibuprofen Step 4: Continue paracetamol and replace ibuprofen with an alternative NSAID*
>
> *This equated to a maximum of seven million additional GP appointments! This resulted in hundreds of thousands of patients being forced off Co-proxamol without the opportunity of a discussion with their GP! (I was informed by telephone by the surgery's Pharmacist).*
>
> *Did MHRA Honestly Believe That Seven Million Additional GP Appointments Would Be Available?*

The impact of regulatory action on health services is fully considered by the MHRA and ministers before action is taken.

GP's had the opportunity to raise any concerns regarding potential problems with resources or difficulties discussing the issue with patients within the public consultation.

> *3) Please can you explain why CSM felt it necessary to inform the FDA on their ill-informed findings six months before it was debated in parliament?*
>
> *The FDA dismissed this warning on two occasions prior to its final removal on Nov 19th 2010. FDA finally succumbed to the pressures from 'Public Citizen' by a very small majority of 14 to 12. This petition relied heavily on the lies and misinformation supplied by MHRA, and EMA.*

FDA stated the situation in the UK was completely different to the USA as DXP had always been a controlled drug and this wasn't' the case in the UK! (I have no doubt it should have been)

As the agency previously informed you; The MHRA has regular discussions with the FDA and other regulators concerning safety concerns that have been investigated or are under investigation. This action is taken to ensure that all available information can be considered to protect public health both in the UK and for patients travelling to other countries. Therefore, the FDA and other regulators were informed of the CSM recommendation in 2005.

Why did MHRA Not follow the advice from MP Howard Stoat during the Parliamentary debate (17th January 2007)? "A more sensible way forward, as my hon. Friend said, is to make co-proxamol a controlled drug under schedule 3 of the Misuse of Drugs Act 1971. The advantage of doing that is that the potential risks involved in prescribing would be flagged up, but GPs could still prescribe the drug when necessary, and it would be clearly acknowledged in doctors' minds that extra precautions and closer monitoring of patients would be advisable.

Schedule 3 status would also send a clear message that co-proxamol is not a first-line drug and that it should be used only after careful consideration of all the available alternatives it." would also give pharmacists the opportunity to reinforce guidance to patients who are on the drug and to ensure that they fully understand the risks and benefits of taking it.

Why has MHRA never explained why Schedule 3 status was not an option? Schedule 3 status was forced on Tramadol during June 2014 when the deaths from Tramadol poisoning (240) had reached the same level as Co-proxamol in 2005 (242).

As the agency previously informed you; Decisions to classify individual drugs as controlled drugs under the Misuse of Drugs Act 1971, is undertaken by the Home Office with advice from the Advisory Council on the Misuse of Drugs and is not confined to authorised medicines. Further information relating to the classification of dextropropoxyphene is available in the www.gov.uk webpages

It is not within the remit of the MHRA to change the schedule status of a medicine.

4) CSM had given five options for MHRA to consider, why did MHRA not disclose the other four options to Government during 2005?

[Hansard 17 Jan 2007: Column 341WH]

I have a copy of the paper considered by the Committee on Safety of Medicines in reaching its decision; an individual requested one under freedom of information legislation. That paper lists a complete ban as only one of five options. The Medicines and Healthcare products Regulatory Agency said that it decided in favour of a full ban because information and communication programmes had failed to alert prescribers and patients of the dangers of the drug. What the paper presented to the committee actually said was that the programmes had failed at national level as they had "been piecemeal activities rather than a concerted campaign using several vehicles simultaneously."

The paper goes further in its conclusions, saying that "It is possible on pharmacokinetic grounds that co-proxamol may only have a full therapeutic effect with chronic dosing. There may therefore be some justification for co-proxamol remaining a therapeutic option for the management of chronic pain." Another conclusion in the paper, on the clinical effectiveness of co-proxamol, was based on the contention that there were no robust data to prove that. Co-proxamol is an old drug that has been around since the 1950s. It has never been subject to testing to find out exactly how it works, as is done on modern drugs. Such testing has not been carried out even today. There are no robust data, because there are no data.

The conclusion drawn could quite easily have been the opposite—that there were no robust data, and that that proved that the drug was not effective. There are no robust data proving that full-strength paracetamol is as effective as co-proxamol either. From my experience, it most certainly is not. Despite my extensive searching on the internet I can't locate this CSM document which contains the other four options If this document is now archived I think you should have supplied the document or a link to it.

The MHRA have supplied all archived information available in our electronic records. Details of the 5 regulatory options considered by CSM were provided in the paper titled CSM 2004_18th.pdf

5) Did MHRA inform Ministers in 2005 that CSM's call for evidence had an extremely low response?

As The Government of the day appeared to have a poor understanding of the term 'Due Diligence' Does MHRA think a response of just 14.7% to CSM's 'call for evidence' was sufficient evidence to call for a complete ban on Co-proxamol?

In response to question 5 and 6c, the MHRA makes every effort to contact the most relevant stakeholders for any given consultation or 'call for evidence'. The call for evidence is also widely publicised and runs for at least a 12-week period. In our experience while not all stakeholders respond, those who do often represent a large number of people. In the case of the call for evidence on co-proxamol, representations were received from several Royal Colleges, Pharmacists and Pharmacy bodies, specialists in pain management, prescribers, patients and patient organisations, NHS Trusts and various other interested parties.

The Agency holds no correspondence with Ministers relating to the response rate for the public consultation on co-proxamol.

8b) Please could you inform me which Ministers responded, and supply all correspondence between Ministers and MHRA regarding a reconsideration of your decision to ban? We are unable to identify any correspondence between ministers and the MHRA on this subject from our electronic archives. The market authorisation Holders were able to appeal to the decision and CSM took on board their responses to CSM's concerns. Therefore, the decision was reconsidered, however the concerns of CSM were not addressed, and therefore the decision to withdraw Coproxamol licences was retained. The historical documentation concerning all decisions are attached.

In a previous response I received from MHRA the names of the 'Market Authorisation Holders' who appealed the decision had been redacted.

Why did MHRA feel that this was necessary?

The Marketing Authorisation Holders who supplied data or responses in relation to the appeal, supplied that information in confidence. Therefore their names were redacted on the FOI response.

In response to question 9, the letter by Hanks and Forbes (1998) was considered alongside all other data sources by CSM (see Annex 17, page 13 in document 'CSM 2004 8th, SCOP 2004 2nd pages 136-183.pdf', provided previously.)

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I hope the information provided is helpful; however, if you are dissatisfied with the handling of your request, you have the right to ask for an internal review. Internal review requests should be submitted within two months of the date of this response; and can be addressed to this email address.

Please remember to quote the reference number above in any future communications.

Yours sincerely,

FOI Team,
Vigilance and Risk Management of Medicines Division

If you have a query about this email, please contact us. If you are unhappy with our decision, you may ask for it to be reviewed. That review will be undertaken by a senior member of the Agency who has not previously been involved in your request. If you ish to pursue that option please write to the Communications Directorate, 4-T, Medicines and Healthcare products Regulatory Agency, (via this email address). After that, if you remain dissatisfied, you may ask the Information Commissioner at:

The Information Commissioner's Office
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