The University of Sheffield

Bone metabolism Group

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24 June 2005

Ms R Valerio

Head, Department of Human Resources

The University of Sheffield

Western Bank, Sheffield, S10 2TN

Dear Ms Valerio

Re: Request to meet Professor Boucher

Thank you for your letter of 17/6/2005. I am disappointed that the Vice Chancellor has chosen not to meet with me given the seriousness of this matter and given that it is already at a late stage. I do however thank you for your response.

The actions recommended in your letter are based on a misunderstanding of the normal process of scientific scholarly inquiry, the obligations of clinical academics and of the recent international problems and resulting precedents in clinical pharmaceutical research. All academics seek to publish information that is truthful. They seek advice about methodology, statistics, procedure or other matters and make academic public comment through a variety of mechanisms. This is entirely normal. I do not believe that University "authorisation", warnings of "public dissociation" or "public interest disclosure legislation" have any relevance to this.

A University has an obligation to protect and support their academics where this usual process is not allowed to operate. Integrity of the process has particular relevance in clinical medicine where there is a serious risk of harm, and clinical academics have overriding statutory and ethical responsibilities.

I would stress that I wish this problem to remain separate from the other problems that were allowed to progress to such a serious extent within Professor Eastell's unit while he was Research Dean. That he acquiesced with an inappropriate scientific process involving a sponsor, and that he allowed colleagues to be implicated in this process can be dealt with at some other point, if at all. Initiation of a further protracted University "investigation" of Professor Eastell would be implausible and is not required. I simply require the support of the University to raise a critical and urgent procedural problem involving a pharmaceutical sponsor and with bearing on public safety.

I am, as you can imagine very fearful of the consequences for me. The immediate problem is simple and can be summarised in a single paragraph:

I performed a large-scale research project involving samples collected as part of FDA trials used to register the drug Risedronate (RJ102356). Measurements were performed in my laboratory, and Professor Eastell was coinvestigator. The aim of the study was to address an important and controversial question relating to this class of drugs. The company failed to allow investigators access to randomisation and event codes from the study. They continued to refuse access to this information to authors even after ghost-authoring work in the names of myself and Professor Eastell, and after substantial and increasing information emerged to suggest that the company data analysis could not be trusted. This breached their contract with the university, although restrictive contracts are widely held to be unenforceable in any event. The procedure was in conflict with all of the norms of usual legitimate scientific conduct. It is not necessary for me to demonstrate exactly how data analysis was perverted. Nor is it necessary to elaborate the effect that this may have on patient care. The principle at stake is clear, and such a process involving a sponsor is not ever appropriate in clinical medicine, or in any other branch of science.

I believe it is vital that the University get proper advice. I am fully aware that there are no appropriate clinical academics within Sheffield who would wish to be associated directly. Professor Peter Jackson (Clinical Pharmacology) would probably provide useful impartial advice to the University. I have already discussed this matter with him, but have not discussed what advice he would give. I know that he will not thank me for involving him, but he could advise the University in private. He will also be aware of the current context, the outcome of recent related scandals, legislative guidelines and recent discussion (such as the recent House of Commons Report) and the way in which this is likely to be viewed by the profession. I enclose some recent correspondence which will provide further details of fact.

I simply wish to know whether the University will support me in upholding such an important principle. I fear that the University will look foolish if it fails to uphold the principles inherent in this matter. I will however have to proceed to raise the matter regardless of such support. I believe it will be in the interests of the University to work with me. Given that we wrote to the Vice Chancellor some time ago and that the matter was raised with the previous Research Dean, I would appreciate a reply within the next week.

Yours Sincerely

Dr Aubrey Blumsohn
Senior Lecturer in Metabolic Bone Disease
Honorary Clinical Consultant in Metabolic Bone Disease

The University of Sheffield

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26th May 2004

Professor Richard Eastell
Research Dean
University of Sheffield
Clinical Sciences Centre
Herries Road
Sheffield S5 7AU

Dear Richard

I have had several E-mails relating to a planned meeting about the HIP/vert data at the ECTS meeting. My previous and often-stated concerns relating to the probity of this data analysis have been largely ignored. Another meeting to pressurise me to acquiesce with this process would not be feasible.

To summarise our previous and extensive conversations:

1) No self-respecting scientist could ever be expected to publish findings based on data to which they do not have free and full access.

2) This is particularly so when
a) there is a preconceived desirable result which is dictating statistical analysis, b) the results are likely to benefit a pharmaceutical company patron,
c) results are likely to have a direct impact on patient care,
d) results are likely to influence our scientific understanding of drug action, and
e) where the experiment is unlikely to be repeated or refuted by subsequent work.

2) It is inappropriate for a head of a University Department to pressurise a colleage (let alone a senior one) to get involved in such activities based on data generated by that colleague, to accept blindly the findings of company statisticians or the use of particular statistical techniques, or to accept other misleading aspects of the treatment of data.

3) Based on my limited view of this data I have every reason to believe that the proposed and previous presentation of the data is misleading in several respects. I have already discussed these concerns with you on several occasions over many months and do not plan to reiterate them.

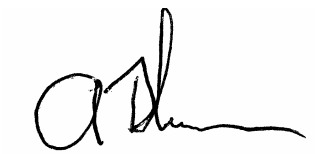
4) I also have reason to believe that several aspects of the existing three abstract presentations relating to this data and published in my name are incorrect and misleading. This contamination of the scientific record has to be corrected as soon as possible.

5) I do not believe that attempts to alter the unit of analysis (t-score approach), to ignore analyses already done, to repeat/add assays (to allow different statistical analysis) or to add authors will solve the fundamental problem we have.

6) I have severe ethical concerns about the way in which this process has worked, irrespective of the way in which this might have altered the perception of the data. I cannot reconcile this with my personal values or statutory responsibilities as a clinician, pathologist or responsible scientist.

This obfuscating process has been going on for a year now, and the misleading analyses have been in the public domain for 7 months. Given the persistent attempts to a) prevent full and proper examination and presentation of these data, and b) to prevent correction of the scientific record, I can only assume that you have not conveyed my views to the company. If you feel that you have not properly represented my concerns in your private meetings with the company about a) the data generated by me in my laboratory or b) the data analysis, please do let me know.

Yours Sincerely



Dr Aubrey Blumsohn MBBCh, BSc(hons), MSc, PhD, MRCPath
Senior Lecturer in Metabolic Bone Disease
Honorary Consultant in Metabolic Bone Disease
University of Sheffield and Sheffield Teaching Hospitals

Info: As also emailed

Dr Larry Games
Vice President Research and Development
The Procter & Gamble Company (P&G)
Miami Valley Laboratories
P.O. Box 538707
Cincinnati, OH 45253-8707

Our ref: SM/DO
Your ref:
Date: 25th May 2005

Dear Dr Games,

We are instructed by Dr Aubrey Blumsohn.

We are writing in relation to matters of serious concern which have been raised about proper procedure and data analysis in trials involving Risedronate carried out in Sheffield (United Kingdom). Our client has serious questions about studies involving himself as academic investigator, and we are advising him in this matter.

The studies in question were carried out as part of an agreement with the University of Sheffield dated July 2002 and signed by yourself on behalf of Procter & Gamble Pharmaceuticals.

Our client has raised matters of procedure and scientific honesty which he understands were conveyed to Procter & Gamble Pharmaceuticals by Professor Richard Eastell of Sheffield University. Our client has also discussed the most important aspect of the problem mentioned below with Dr David Cahall, but resolution was refused.

Information has been published in our client's name while denying him access to the raw data upon which such publication was based. Our client will allege that this flouts fundamental principles of science, and of clinical pharmaceutical collaboration in particular. Further our client believes that several aspects of data analysis and or presentation were false.

We write to ask that all of the raw data pertaining to this study is disclosed to our client immediately.

Yours sincerely,

McKAY LAW

The University of Sheffield

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19th May 2005

Professor John A Eisman
Editor-in-Chief
Journal of Bone and Mineral Research
c/o Managing Editor: Amber Williams
3209 Guess Road, Suite 201
Durham
NC 27705, USA

Dear Professor Eisman

I am writing about a rather troubling matter. I understand that you have already received some information about this from a colleague without specific detail.

I have substantial reason to doubt the integrity of clinical trial data and the analysis of that data relating to two recent ASBMR abstracts submitted by a pharmaceutical company in my name

1. ASBMR 2003: Relative Contributions Of The Early Changes In Bone Resorption And Later Changes In Hip Bone Mineral Density To The Reduction In Vertebral Fracture Risk With Risedronate. A. Blumsohn, IP Barton, A Chines, R Eastell.

2. ASBMR 2003: Relationship Of Early Changes In Bone Turnover To The Reduction In Vertebral Fracture Risk With Risedronate - The HIP Study. A. Blumsohn, IP Barton, A Chines, R Eastell.

Since I am first author on these abstracts it might be assumed that I vouch for this work and was able to verify the findings. Sadly this is not the case. A third abstract with similar text (almost verbatim) was also submitted to another international meeting by the company involved (Am College of Rheumatology: 2003). The underlying data has not been revealed to the academics involved, although considerable evidence has emerged to cause concern that the results are not correct.

I would wish to dissociate myself formally from these ASBMR abstracts, although clearly not from the underlying work. Might there be some mechanism to enable me to do this within the JBMR? This information placed in the public domain is currently not amenable to formal correction or dissemination via proper publication in the absence of data.

I also have concerns about the probity of a related paper in the Journal of Bone and Mineral Research (Eastell R, Barton I, Hannon RA, Chines A, Garnero P, Delmas PD. Relationship of early changes in bone resorption to the reduction in fracture risk with risedronate. J Bone Miner Res. 2003;18(6):1051-1056) which did not involve my co-authorship. The supposed data on which this paper was based is a subset of the data which formed part of the more recent meeting abstracts to which I refer. Partial data available to me has raised significant concerns.

A number of academics in the UK and the US have been helping me to frame concerns about the procedure that has led to the current situation. You will be aware of significant current concerns relating to the influence of pharmaceutical companies on research. The detailed scenario raises severe and illustrative concerns, and the feeling was that the "process" issues as well as selected data should be submitted to the Lancet, perhaps following further discussion with the company and collaborators. There may however be other alternatives, and I would appreciate it if we could discuss this matter.

Yours Sincerely

Dr Aubrey Blumsohn MBBCh, BSc(hons), MSc, PhD, MRCPath
Senior Lecturer in Metabolic Bone Disease
Honorary Consultant in Metabolic Bone Disease
University of Sheffield and Sheffield Teaching Hospitals

Professor Richard Eastell
Clinical Sciences Centre (North)
Northern General Hospital
Herries Road,
SHEFFIELD
S5 7AU

Our ref: SM/DO
Your ref:
Date: 25th May 2005

Dear Professor Eastell,

We are instructed by Dr Aubrey Blumsohn.

You will be aware that our client has serious concerns and questions relating to studies carried out in Sheffield regarding pharmaceutical clinical trials involving the drug Risedronate. He has instructed us to request that you to send all raw data relating to three scientific abstracts published in his name relating to this drug. Two of these abstracts are:

1. Relative Contributions Of The Early Changes In Bone Resorption And Later Changes In Hip Bone Mineral Density To The Reduction In Vertebral Fracture Risk With Risedronate. A. Blumsohn, IP Barton, A Chines, R Eastell. American Society for Bone and Mineral Research, 2003

2. Relationship Of Early Changes In Bone Turnover To The Reduction In Vertebral Fracture Risk With Risedronate - The HIP Study. A. Blumsohn, IP Barton, A Chines, R Eastell. American Society for Bone and Mineral Research, 2003

The third abstract contains identical information. Further my client requests that you make available to him all raw data relating to the following published scientific paper relating to the drug Risedronate:

> Eastell R, Barton I, Hannon RA, Chines A, Garnero P, Delmas PD. Relationship of early changes in bone resorption to the reduction in fracture risk with risedronate. J Bone Miner Res. 2003;18(6):1051-1056

You will be aware that the data underlying the information presented in this paper forms a subset of the data underlying the two abstract presentations published in our client's name. Our client wishes to compare data obtained with other information and data in his possession. He believes that the scientific process leading to these publications was improper. Further, he believes that the presentation of information in all these publications was false.

Our client has requested this data previously. We would appreciate it if you would send the raw and full data in electronic form to the writer's email address, simon.mckay@mckaylaw.co.uk within the next seven days. Data should include all variables required to reconstruct the analyses referred to in these publications, as well as the information pertaining to therapeutic adherence within the studies as requested by our client previously.

Data should be sent on a read-only CD-Rom, properly labelled and signed. If you wish, data may be sent in a password encoded file, and you may transfer the password to our client separately.

Yours sincerely

McKAY LAW