OBSERVATIONS

BMJ OPEN DATA CAMPAIGN

Open letter to Roche about oseltamivir trial data

Roche promised in 2009 to release full reports from clinical trials of oseltamivir in response to an investigation by the *BMJ* and the Cochrane Collaboration. In this open letter to John Bell, regius professor of medicine at Oxford University and a Roche board member, the *BMJ*'s editor in chief further urges the company to disclose the full data

Fiona Godlee *editor in chief*

Dear John

I am writing to you in your capacity as a member of the board of Roche. As you may be aware, the *BMJ* has been working with the Cochrane Collaboration in its efforts to get Roche to release the raw data on the effects of oseltamivir (Tamiflu) so that Cochrane can properly fulfil the UK government's commission for a systematic review of neuraminidase inhibitors based on clinical study reports.

To remind you of the background to this, in 2009 the *BMJ* published the updated Cochrane review of neuraminidase inhibitors in healthy adults.¹ This took the view that, since eight of the 10 randomised controlled trials on which effectiveness claims were based were never published and because the only two that had been published were funded by Roche and authored by Roche employees and external experts paid by Roche, the evidence could not be relied on. The *BMJ* also published an article summarising the Cochrane team's efforts to obtain the data from these randomised controlled trials and a feature investigation exploring the underlying issues.^{2 3}

After these articles were published, we and the Cochrane Collaboration received public assurances from Roche that the data from these 10 trials would be made available to physicians and scientists.⁴ Although some further data have been released to the Cochrane reviewers, the data that were promised ("full study reports") have not been made available.

Below is a table showing which "modules" (sections) of the 10 trials Roche has so far refused to make available.↓ Also attached is a graphic, taken from a single study report, which explains the kind of content contained in each module of a full study report. This gives an indication of what can be expected in the modules that Roche has as yet not provided.

Tamiflu® (oseltamivir phosphate) 75mg Capsules, Hard 12 mg/mL Oral Suspension			5.3.5.4.6 CSR WV15799 (W-144170)	16
CLINICAL STUDY REPORT MODULES				
This report consists of 5 modules.				
Those not supplied in this submission are obtainable from the sponsor on request.				
MODULE I:	CORE REPORT			
	Background and Rationale Objectives Materials and Methods Efficacy Results Safety Results Discussion Conclusion Appendices			
MODULE II:	STUDY DOCUMENTS			
	Protocol and Amendment History Blank Case Report Form (CRF) Subject Information Sheet and Consent Form Glossaries of Original and Preferred Terms Randomization List Reporting Analysis Plan (RAP) Certificates of Analysis List of Investigators List of Ethics Committee			
MODULE III:	LISTINGS OF DEMOGRAPHIC AND EFFICACY DATA			
MODULE IV:	LISTINGS OF SAFETY DATA			
MODULE V:	STATISTICAL REPORT AND APPENDICES			
	Statistical Analysis Efficacy Results			

Example of content of each of the five modules of a full study report

The Cochrane reviewers now know that there are at least 123 trials of oseltamivir and that most (60%) of the patient data from Roche's phase III completed treatment trials remain unpublished. We have concerns on a number of fronts: the likely overstating of effectiveness and the apparent under-reporting of potentially serious adverse effects. Meanwhile, oseltamivir has just been

added to the World Health Organization's List of Essential Medicines, alongside aspirin and β blockers.

On behalf of the Cochrane collaborators and public health decision makers around the world, I ask Roche to honour its publicly stated promise to make available the full clinical study reports. In order for the Cochrane collaborators to properly analyse these data they will need individual patient data in electronic format.

Oseltamivir has been a great commercial success for Roche. Billions of pounds of public money have been spent on it, and yet the evidence on its effectiveness and safety remains hidden from appropriate and necessary independent scrutiny. I am appealing to you, as an internationally respected scientist and clinician and a leader of clinical research in the United Kingdom, to bring your influence to bear on your colleagues on Roche's board. As company directors, responsibility for Roche's behaviour rests with you, as individuals and collectively. In refusing to release these data of enormous public interest, you put Roche outside the circle of responsible pharmaceutical companies. Releasing the data would do a great deal to restore confidence in the company and its board of directors.

We plan to publish this letter in the *BMJ*, and we would welcome a reply from you to publish alongside it. We would need to receive your reply by Thursday 18 October or Friday 19 at the latest. I look forward to hearing from you.

With best wishes

Yours sincerely

Fiona Godlee

Competing interests: None declared.

This is an edited version of the letter sent to Roche on 11 October 2012; the original is at bmj.com/tamiflu. John Bell has responded saying that he has referred the letter to Roche.

bmj.com Editorial: Clinical trial data for all drugs in current use (2012;345:e7304, doi:10.1136/bmj.e7304); Feature: Tamiflu: the battle for secret drug data (2012;345:e7303, doi:10.1136/bmj.e7303)

- 1 Jefferson T, Jones M, Doshi P, Del Mar C. Neuraminidase inhibitors for preventing and treating influenza in healthy adults: systematic review and meta-analysis. *BMJ* 2009;339:b5106.
- 2 Doshi P. Neuraminidase inhibitors—the story behind the Cochrane review. *BMJ* 2009;339:b5164.
- 3 Cohen D. Complications: tracking down the data on oseltamivir. *BMJ* 2009;339:b5387.
- 4 Smith J, on behalf of Roche. Point-by-point response from Roche to BMJ questions. *BMJ* 2009;339:b5374.
- 5 Kaiser L, Wat C, Mills T, Mahoney P, Ward P, Hayden F. Impact of oseltamivir treatment on influenza-related lower respiratory tract complications and hospitalizations. *Arch Intern Med* 2003;163:1667-72.
- 6 Treanor JJ, Hayden FG, Vrooman PS, Barbarash R, Bettis R, Riff D, et al. Efficacy and safety of the oral neuraminidase inhibitor oseltamivir in treating acute influenza: a randomized controlled trial. US Oral Neuraminidase Study Group. *JAMA* 2000;283:1016-24.
- 7 Nicholson KG, Aoki FY, Osterhaus AD, Trottier S, Carewicz O, Mercier CH, et al. Efficacy and safety of oseltamivir in treatment of acute influenza: a randomised controlled trial. Neuraminidase Inhibitor Flu Treatment Investigator Group. *Lancet* 2000;355:1845-50.

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Table

Table 1 | The 10 trials included in the Kaiser et al 2003 review,⁵ showing number of modules in the full study report, which modules have been provided to the Cochrane reviewers by Roche to date, and which are being requested

Trial ID	No of patients	Primary publication of trial	Secondary publication of trial	No of modules in full study report	Modules provided by Roche	We are therefore requesting modules
WV15671	629	Treanor et al 2000 ⁶	Kaiser et al 2003	5	1	2-5
WV15670	726	Nicholson et al 2000 ⁷	Kaiser et al 2003	5	1	2-5
M76001	1459	Unpublished	Kaiser et al 2003	5	1	2-5
WV15707	27	Unpublished	Kaiser et al 2003	4	1	2-4
WV15730	60	Unpublished	Kaiser et al 2003	4	1	2-4
WV15812, WV15872	404	Unpublished	Kaiser et al 2003	5	1	2-5
WV15876, WV15819, WV15978	741	Unpublished	Kaiser et al 2003	5	1	2-5