MedicalXpress

Effects of Tamiflu still uncertain, warn experts, as Roche continues to withhold key trial data

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Two years after pharmaceutical giant Roche promised the *BMJ* it would release key Tamiflu trial data for independent scrutiny, the safety and effectiveness of this anti-influenza drug remains uncertain, warn experts today.

A new report by the Cochrane Collaboration says Roche's refusal to provide full access to all its data leaves critical questions about how well the drug works unresolved.

A *BMJ* investigation, published to coincide with today's report, also raises serious concerns about access to drug data, the use of ghost writers in drug trials, and the drug approval process.

Meanwhile, Tamiflu has become the mainstay of influenza treatment in the UK. It has also made it onto the World Health Organisation's list of Essential Medicines and Roche's claims continue to be supported by influential health agencies.

The Cochrane researchers set out to test Roche's claim that Tamiflu prevented complications and reduced the number of people needing hospital treatment. But their investigation was hampered by Roche's refusal to provide all of its trial data for analysis. The team obtained some clinical study reports from the European Medicines Agency (EMA), but found inconsistencies with published reports and possible

under-reporting of side effects.

When previously questioned by the *BMJ*, Roche also admitted that some of the published papers had been ghost written.

The *BMJ* investigation reveals how different regulators took different approaches to the data submitted to them, leading to conflicting messages about it effectiveness.

For example, the EMA released a proportion of the clinical study reports relating to the Tamiflu trials to Cochrane, but it admits that it did not ask for the remainder from the manufacturer, although it was legally entitled to do so. The EMA has since told the *BMJ* that it plans to start publishing reports for all drugs submitted for approval in the next few years.

Dr Fiona Godlee, *BMJ* Editor-in-Chief says: "We hope very much that the EMA will indeed take this important step in making the full study reports available. But we are still a long way away from having a full trial history for all drugs in clinical use. Public safety and the proper use of public money demands that we should stop at nothing less than this."

Meanwhile, the US Food and Drug Administration (FDA), which has reviewed the Tamiflu trial programme in perhaps more detail than anyone outside of Roche, chose not to review the largest ever trial of Tamiflu when considering the drug for approval. It states that "Tamiflu has not been shown to prevent such complications [serious bacterial infections]."

However, the US Centers for Disease Control and Prevention (CDC) continue to cite key published trials of Tamiflu, claiming a reduced risk of influenza complications, even after Roche admitted that some of these trials have been ghost written.

Dr Godlee says: "The discrepancies between the conclusions reached by different regulators around the world highlights the absurd situation we find ourselves in. In a globalised world, regulators should cooperate and pool their limited resources. Otherwise we will continue to waste money and risk people's health on drugs that don't work."

The investigation also raises questions about Tamiflu's clinical effects. After careful evaluation of trial data, the Cochrane group say that Tamiflu appears to affect antibody production – a claim that Roche refutes. This is important, say Cochrane, because influenza vaccination relies on an antibody response to be effective. But when asked by the *BMJ*, Roche refused to explain how the drug works.

As such, the Cochrane group say that "until more is known about the mode of action of neuraminidase inhibitors, health professionals, patients and other decision makers need to reflect on the findings of this review before making any decision about the use of the drug."

Cochrane also argue that Tamiflu's ability to prevent the spread of influenza has not been demonstrated in trials. Yet this is one of the main reasons governments around the world have spent billions of dollars stockpiling Tamiflu in case of a pandemic.

Roche maintain they provided the Cochrane team with enough information to conduct their evaluation, but the Cochrane team say this is not the case. Dr Peter Doshi from Johns Hopkins University School of Medicine says: "In the BMJ in December 2009, Roche promised full study reports to any legitimate investigators. They have not provided a single full study report to Cochrane, despite our repeated requests."

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