

## **Author's response to reviews**

**Title:** Differential correlation of medical/laboratory examinations with blood levels of polychlorinated biphenyls, polychlorinated quarterphenyls and 2,3,4,7,8-pentachlorodibenzofuran in Yusho patients from 2001 to 2004

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**Version:** 2 **Date:** 29 May 2008

**Author's response to reviews:** see over

### Comments of referee and Correspondence of the author

**Version: 1 Date:** 17 March 2008

**Reviewer:** Paolo Mocarelli

Reviewer's report	Correspondence of the author
<p>The authors have done a huge work (maybe too much) to try to correlate many variables and the blood level of PCBs and PCDFs. It is difficult to follow the paper.</p>	<p>Thank you for pointing out these matters.</p>
<p>The results and discussion sections should be heavily reviewed to implement the understanding: for example Table 4 comes in the discussion. Why? The first page of discussion should be in the introduction etc.</p>	<p>Thank you for pointing out these matters. We have reexamined the Results and Discussion. Specifically, we have corrected the overlapping parts of the Results and Discussion to simplify the Discussion. In addition, the diagnostic criteria of Yusho, described in the first half of the Discussion, have been deleted and described in the Introduction as an explanation of Yusho. Furthermore, Table 4 containing the Yusho criteria has been changed to Table 1. Therefore, the other table numbers have been altered appropriately.</p>
<p>Without a very strong reviewing I do not suggest the publication, but I encourage the Authors to simplify the paper.</p>	<p>Thank you for pointing out these matters. We have shortened the parts related to the explanation about Yusho, which were described in the Discussion, and described them to the Introduction. In addition, we have deleted the overlapping parts of the Results regarding the logistic regression analysis, which were described in both the Results and Discussion, and simplified these parts wherever possible. Furthermore, we have clarified the definitions and variables of the analytical method as pointed out by the other reviewers. According to these indications, we have corrected the entire manuscript and revised almost half of the original manuscript.</p>

## Comments of referee and Correspondence of the author

**Version: 1 Date:** 22 March 2008

**Reviewer:** Leon Guo

Reviewer's report	Correspondence of the author
<p><b>Major Compulsory Revisions</b></p> <p>This investigation examined potential health effects and the serum levels of PCBs, PeCDF, and PCQ ~35 years after the 1968 Yusho episode of intoxication. The findings are based on health examinations 2001-2004. Thus, them looks like analysis of aggregation of data, rather than the results of carefully designed study. Specific concerns included</p>	<p>Thank you for pointing out these matters. As you pointed out, this research is based on the results from medical checkups of Yusho patients between 2001 and 2004.</p> <p>However, this study is considered to be significant, since no previous studies have analyzed the relationships among the clinical symptoms in patients who took dioxins more than 30 years ago and the dioxin levels.</p>
<p>1. Using serum levels as “objective” variable sounds strange to me, since from an environmental health point of view, serum level is the “exposure variable” which predicts the occurrence of outcomes</p>	<p>Thank you for pointing out these matters. It seems that the present blood concentration is correlated with the amount of exposure at the time of generating. Because, the serum half-life of PeCDF is long.</p>
<p>2. The variables are not clearly defined. For example, what do the authors mean by “Sputum” in tables 1, 2, and 3-2?</p>	<p>Thank you for pointing out these matters. We have clarified the definitions of the variables. The 49 factors extracted by the principal component analysis were classified into normal and abnormal categories in consideration of the characteristics of the data for each item. We have described a concrete normal/abnormal classification method in the text.</p>
<p>3. For some clinical findings, principal component analysis might not be adequate statistical method for analysis. However, it is not easy to judge because most of the variables are not clearly defined.</p>	<p>Thank you for your indication. To extract variables that represent each component in conducting the logistic analysis, we conducted a principal component analysis. However, we only conducted the principal component analysis as an aid for conducting the main analysis, i.e., the logistic regression analysis. Furthermore, we have made drastic revisions by deleting and shortening the overlapping parts of the Introduction, Results and Discussion as pointed out by the other reviewers.</p>
<p><b>• Minor Essential Revisions</b></p>	
<p>1. P5, line 10: “With recent advances in techniques for measuring dioxins such as PeCDF...”, PeCDF is not dioxin, better to change to “dioxin-like chemicals”</p>	<p>Thank you for pointing out this matter. We have corrected the phrase to "dioxin-like chemicals".</p>
<p>2. The author used “0.05% level of significance”, which should be “0.05” or “5%”.</p>	<p>Thank you for pointing out this matter. We have corrected the text to "0.05".</p>

## Comments of referee and Correspondence of the author

**Version: 1 Date:** 19 March 2008

**Reviewer:** Yoshito Masuda

Reviewer's report	
The manuscript is worth publishing to Environmental health as the study explained the relationship between the levels of 2,3,4,7,8-PeCDF, PCBs and PCQs in Yusho patients and the affected symptoms for 38 years by logistic regression analysis. The results are valuable for understanding the effects of the chemicals to human.	
This paper is acceptable after minor essential revisions	
Chemical names have to be correctly indicated including abbreviation and singular or plural. Slash combined chemicals, such as PeCDF/PCB/PCQ, are not clear whether individual or total chemicals.	Thank you for pointing out these matters. We have corrected the names of the chemicals as indicated.
Tow abbreviations, 2,3,4,7,8-PeCDF and PeCDF, for 2,3,4,7,8-pentachlorodibenzofuran --> It is better to use one abbreviation after clear indication of the abbreviation, 2,3,4,7,8-PeCDF or PeCDF	Thank you for pointing out this matter. For 2,3,4,7,8-pentachlorodibenzofuran, we have used the same abbreviation, namely 2,3,4,7,8-PeCDF.
Page 3, line 5 and Page 5, line 6 2,3,4,7,8-pentachlorodibenzofuran (PeCDF) --> polychlorinated dibenzofurans (PCDFs)	Thank you for pointing out these matters. We have corrected these phrases to "polychlorinated dibenzofurans (PCDFs)".
Page 3, line 7 PeCDF --> individual PCDF congeners	Thank you for pointing out this matter. We have corrected this phrase to "individual PCDF congeners".
Page 3, line 8 and 10 PeCDF/PCB/PCQ --> 2,3,4,7,8-pentachlorodibenzofuran (2,3,4,7,8-PeCDF), PCBs and PCQs	Thank you for pointing out. these matters. We have corrected these phrases to "2,3,4,7,8-pentachlorodibenzofuran (2,3,4,7,8-PeCDF), PCBs and PCQs" in line 8 and "2,3,4,7,8-PeCDF, PCBs and PCQs" on line 10.
Page 3, line 14 PeCDF/PCB/PCQ --> 2,3,4,7,8-PeCDF, PCB and PCQ	Thank you for pointing out this matter. We have corrected the phrase to "2,3,4,7,8-PeCDF, PCB and PCQ".
Page 3, line 18 PCB and PCQ --> PCBs and PCQs	Thank you for pointing out this matter. We have corrected the phrase to "PCBs and PCQs".
Page 4, line 2 A/G ratio; the level of PCB --> albumin/globulin (A/G) ratio; the level of PCBs	Thank you for pointing out this matter. We have corrected the phrase to "albumin/globulin (A/G) ratio; the level of PCBs".
Page 5, line 10 Dioxins such as PeCDF --> individual PCDF congeners	Thank you for pointing out this matter. We have corrected the phrase to "individual PCDF congeners".
Page 5, line 11 PeCDF --> 2,3,4,7,8-pentachlorodibenzofuran (2,3,4,7,8-PeCDF)	Thank you for pointing out this matter. We have corrected the phrase to "2,3,4,7,8-pentachlorodibenzofuran (2,3,4,7,8-PeCDF)".
Page 5, line 23 (81 individuals in 2001, 371 in 2002, 343 in 2003, and 292 in 2004) --> (81 individuals in 2001, 371 in 2002, 343 in 2003, and 292 in 2004, including multiple health checks)	Thank you for pointing out this matter. We have corrected the sentence to "81 individuals in 2001, 371 in 2002, 343 in 2003, and 292 in 2004, including multiple health checks".
Page 6, line 11 and 12 Missing under half --> Coefficient and Objective	Thank you for pointing out this matter. We have corrected this to "Coefficient and Objective".
Page 7, line 24 and Page 11, line 13 PCQ/PCB --> PCB and PCQ	Thank you for pointing out these matters. We have corrected the phrase to "PCB and PCQ".

Table 3 Explanations for * and **	Thank you for pointing out these matters. We corrected it to * and ** in Table 3.
Table 4 2,3,4,7,8-penta-chlorodibenzofurans (PeCDF) --> 2,3,4,7,8-PeCDF	Thank you for pointing out this matter. We have corrected this phrase to 2,3,4,7,8-PeCDF.