Drug Safety 2008; 31 (3): 272-273
0114-5916/08/0003-0272/$48.00/0

© 2008 Adis Data Information BV. All rights reserved.

The Authors' Reply

We would like to thank Dr Karim and his colleagues for their valuable comments on our article.[1] In principle, we accept their assertion that the control of the sensitivity (Type II error) for the interested adverse event (AE)/drug combinations was more important than that of the specificity (Type I error).

In our article, we divided the AEs into two classes: regular events and rare events. Given an assumed spontaneous reporting model and the proposed criteria for the Bayesian Confidence Propagation Neural Network method, the sensitivity was 76% for regular events and 39% for rare events. In our study, regular events were almost equivalent to AEs in the context of the simple example demonstrated by Dr Karim and his colleagues. However, if we wish to rule out an expected proportional reporting ratio (PRR) >2 for rare events, the background reporting rate of which is 0.4 per 1000, with at least 80% certainty (power), then the signalling threshold would be 1 out of 2000. Irrespective of whether we accept Dr Karim's assertion, we could not propose to control the sensitivity as 80%, because this proposal generated too many false-positive signals for us to review.

We have examined the characteristic differences of several spontaneous reporting databases and found some differences among them.[2] The situations may differ depending on the size or component of the databases. To actualize the principle, we should prepare a better criterion adaptable to the specific characteristics of the database.

Regarding rare events, specific AEs such as the Stevens-Johnson syndrome, toxic epidermal necrolysis, agranulocytosis and rhabdomyolysis pointed out by Ståhl et al.,[3] may be marked targets for requesting high sensitivity. In fact, the ICH-E2E guideline describes that the important identified risks of a drug, important potential risks and important missing information should be summarized in the safety specification, and a pharmacovigilance plan should be based on this safety specification.[4] From this viewpoint, we consider a strategy to determine different signalling thresholds for different AE/drug combinations to improve our methodology. We hope our future efforts will actualize the assertion of Dr Karim and his colleagues.

Yasuyuki Matsushita,[1,2] *Yasufumi Kuroda*,[2] *Shinpei Niwa*,[2] *Satoshi Sonehara*,[2] *Chikuma Hamada*[1] and *Isao Yoshimura*[1]

1 Faculty of Engineering, Tokyo University of Science, Tokyo, Japan

2 Daiichi Sankyo Co. Ltd., Tokyo, Japan

Acknowledgements

Drs Chikuma Hamada and Isao Yoshimura have no conflicts of interest directly relevant to the content of this letter. Yasuyuki Matsushita, Yasufumi Kuroda, Shinpei Niwa and Satoshi Sonehara are all employees of Daiichi Sankyo Co. Ltd.

References

1. Matsushita Y, Kuroda Y, Niwa S, et al. Criteria revision and performance comparison of three methods of signal detection applied to the spontaneous reporting database of a pharmaceutical manufacturer. Drug Saf 2007; 30 (8): 715–26
2. Matsushita Y, Kuroda Y, Sonehara S, et al. Remarks on the characteristics of detected signals among spontaneous reporting databases (SRDs) from a US Regulatory Agency, a Japanese Regulatory Agency and a Japanese Company. Pharmacoepidemiol Drug Saf 2007; 16: S197
3. Ståhl M, Lindquist M, Edwards IR, et al. Introducing triage logic as a new strategy for the detection of signals in the WHO Drug Monitoring Database. Pharmacoipidemiol Drug Saf 2004; 13: 355–63
4. ICH-E2E-Expert Working Group. Pharmacovigilance planning [online]. Available from URL: http://www.ich.org/LOB/media/MEDIA1195.pdf [Accessed 2007 Nov 16]