Reply to 'Truth in Numbers'

To the editor:

Merck is committed to the highest standards of scientific integrity and patient safety. Your editorial "Truth in Numbers" (January 2006) incorrectly characterizes how we disclosed information regarding the VIGOR study. I am writing to set the record straight.

As we have previously stated, Merck submitted cardiovascular data from the VIGOR study to the *New England Journal of Medicine (NEJM)* that were reported to Merck as of a prespecified cutoff date. One of the reasons for specifying a cutoff date in advance is precisely to avoid any later allegation that the data were manipulated.

Any suggestion that Merck improperly hid data from *NEJM* is simply false. The editorial states that "three additional heart attacks had been omitted from the published data" and that "relevant data were removed from the manuscript before its submission to the journal." These statements are incorrect. As we have stated previously, these data were never included in the draft manuscript. During revision, the authors did change the format of presentation—from table to text—for the cardiovascular data. But, at all times, the data were those obtained as of the prespecified cutoff date.

The final data were provided to the US Food and Drug Administration (FDA) a month before publication of the article and were discussed at the public February 2001 meeting of the FDA Advisory Committee. In addition, the final data were widely disseminated and discussed in the scientific community at large and in the public media. Moreover, the small difference between the earlier and final data did not change the article's conclusion that there was a statistically significant difference in the rate of heart attacks between individuals taking Vioxx and individuals taking naproxen in the VIGOR study.

Merck has a long-standing tradition of providing innovative, safe drugs and vaccines that address unmet medical needs. We remain committed to this mission and to upholding the highest standards of scientific integrity.

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Reply to 'Encephalitis outbreak finds Indian officials unprepared'

To the editor:

We have found that the Japanese encephalitis outbreak in India, described in a recent news article[1] by T.V. Padma, is overblown, leading to erroneous diagnosis of many encephalitis cases.

Media reports have attributed the outbreak primarily to Japanese encephalitis, but that is misleading. According to the World Health Organization, only 37% of the reported 1,116 cases tested positive for the virus that causes Japanese encephalitis[2]. We also found a similar trend (S.K.S. *et al.*, unpublished data). Most of those cases therefore remain undiagnosed.

In 2005, encephalitis struck 6,097 individuals, mostly children, and claimed 1,398 lives, making it one of the deadliest outbreaks of the disease in India. The true incidence is likely to be much higher because a large proportion of sick individuals did not receive medical attention and even for those who did, diagnosis was difficult. Because the virus that causes Japanese encephalitis is widely recognized, experts have a tendency to attribute all outbreaks of brain disease in children to it. It is easy to recognize the clinical and laboratory information fitting with the diagnosis of Japanese encephalitis, but fine points of differentiation between other entities should also be considered carefully. A few individuals may have aseptic meningitis, or encephalopathy. The clinical features of the encephalopathy syndrome also clearly suggest an acute brain disease of children in outbreaks, for which reason the illness is often mistakenly diagnosed as encephalitis[3]. Expert teams calling it an outbreak of Japanese encephalitis, collecting samples of serum and cerebrospinal fluid for identifying the hypothetical virus causing the disease, reinforce the misdiagnosis of encephalitis. In addition, there were a few individuals who had a low platelet count with fever. This clinical picture, although described as another form in which the outbreak disease presented itself, was clearly different from encephalopathy or encephalitis, and was most probably due to dengue fever. In summary, different children's diseases affecting the brain and causing death should not be categorized together simply because they occurred in the same time period, assuming that all of them represented one epidemic. But it appears this was done to fulfill the saying that "one outbreak is due to one disease, caused by one agent."

The quality of management and care may also alter some of the features. Exposure to salicylate (aspirin) may be a cofactor for pathogenesis. Precisely for this reason, aspirin should not be used in children below 12 years of age. Early diagnosis and appropriate steps taken to reduce brain edema are lifesaving. Otherwise mortality may be very high.

The epidemiology of this outbreak presented a complex interplay of climatic, entomologic, human behavioral, viral and host factors, which are not completely understood. Considering the seriousness of inconclusive diagnoses, it is imperative to proceed with a sense of urgency and not merely to reclassify all cases with the best-fit diagnosis but to turn our attention to culprits like other flaviviruses