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- [Assessment of causality of individual adverse events following immunization \(AEFI\): a WHO tool for global use.](#)

Tozzi AE.Vaccine. 2013.

[Jacob Puliye2014 Feb 20 4:36 p.m.](#)

Tozzi and colleagues state that their article describes the new tool for causality assessment of AEFI as set out in the [User Manual for the Revised WHO Classification](#)

1) However this manual it seems has been developed without adequate care and without thinking through the consequences of the changes.

a) One pointer to this is how the manual cites an example of vaccines being wrongly blamed for events unrelated to its administration (Page 13). It says that vaccines were wrongly blamed for deaths resulting from consumption of the Cassia occidentalis beans causing a syndrome of acute hepato-myoenkephalopathy. However the article they quote describes Japanese B encephalitis being blamed for the deaths – not the vaccine [Panwar RS, 2008](#)

b) Dr Madhavi put the new classification to a simple test. She tested how the system would have responded if the revised AEFI classification been in place in 1999. She suggests that the intususceptions following use of RotaShield would have been classified as ‘inconsistent with causal association’ because:

i) other qualifying factors like previous similar reaction (re-challenge equivalent) were not available

ii) nor was biological plausibility demonstrated at that time

iii) and background rate, other exposures etc were not ruled out.

Under this category ‘inconsistent with causal association’ it would never activate the analysis reserved for ‘indeterminate’ reactions – “Information on AEFIs that are classified as indeterminate should be pooled and analyzed by time and place, in order to understand if the AEFI represents a new signal of an unrecognized event. Should this be the case, a more comprehensive epidemiological investigation should be performed.” [Tozzi AE, 2013](#)

These intususceptions would have continued for years before the vaccine was pulled off the shelves.

2) In my previous comment I had pointed out that the experts investigating the Sri Lanka deaths from Pentavalent vaccine deleted the categories ‘Probable’ and ‘Possible’ from the Brighton classification and reported that although they found no alternate explanation for the deaths, the deaths were unlikely to be related to the vaccine. An apologist for the distorted Brighton Classification told me at that time that it was ‘experts’ who developed the Brighton

Classification and it is alright for other experts to alter the classification. That was prescient. The new system makes a virtue of this ability to disregard the algorithm when it suits any expert. It says “Finally, instead of assigning a final category through an automatic classification process, the final outcome of the case investigation depends on the personal judgment of the assessor.” [Tozzi AE, 2013](#)

3) Post marketing surveillance is used to monitor the safety of a drug. Since drugs are approved on the basis of clinical trials which involve a relatively small numbers of people who have been selected for this purpose - meaning that they normally do not have other medical conditions which may exist in the general population - post marketing surveillance can further refine, or confirm or deny, the safety of a drug after it is used in the general population by large numbers of people who have a wide variety of medical conditions. (Abridged from Wikipedia)

The effort of the revised WHO [Causality assessment of an AEFI](#) is to deny adverse events noticed on post marketing surveillance, are caused by the vaccine (unless they had been observed in the original small clinical trials).

Events that occur 1 in 10,000, for example the intussusceptions with RotaShield will be noticed only in post marketing surveillance.

The AEFI in individuals was responsible for the ‘signal’. Evidence of causality in the individual provided evidence of causality in the population. The [new system](#) stands this logic on its head when it says on Page 5 that causality in the population must be known before causality in the individual can be ascribed.

“Causality assessment of AEFI should be performed at several different levels. The first is the population level, where it is necessary to test if there is a causal association between the use of a vaccine and a particular AEFI in the population. Secondly, at the level of the individual AEFI case report, one should review previous evidence and make a logical deduction to determine if an AEFI in a specific individual is causally related to the use of the vaccine. The third level of assessment is in the context of the investigation of signals.”

I am not stating that there is something sacrosanct about the [original Brighton Classification](#) but one has to evaluate the two schemes (Brighton vs CIOMS) from the point of view of patient safety to see which scheme would react to rare RotaShield-like-reactions first. The causality scheme that insists on calling all reactions as ‘indeterminate’ or ‘inconsistent/coincidental’ just because they were not noticed in the original small clinical trials, undermines the very raison d’être of post marketing surveillance. Patient safety (meaning protecting patients) rather than vaccine safety (protecting vaccines) is what is important.