

Re: Comments on DRAFT GUIDANCE for Industry Good Pharmacovigilance Practices and Pharmacoepidemiologic Assessment

Introduction

The Brighton Collaboration, formed in 2000, is an international voluntary collaboration to facilitate the development, evaluation, and dissemination of high quality information about the safety of human vaccines by enabling comparability of data through the development of harmonized (or standardized) case definitions on adverse events following immunization. It is currently funded by the U.S. Centers for Disease Control and Prevention and the World Health Organization.

As of April 2004, the Collaboration included >500 scientists volunteering from industry, regulatory agencies, public health, clinical care and academic organizations coming from 57 countries. Six harmonized case definitions and guideline documents regarding “adverse events following immunization” (AEFI) have been published in January 2004¹⁻⁶ and 18 additional definitions and corresponding guidelines are at various stages of development. It plans to develop approximately harmonized case definitions of about 100 AEFI together with their respective guidelines.

The comments submitted in this document have been written by representatives of the Steering Committee (with the reclusion of Miles Braun from FDA from this submission) and the Secretariat of the Brighton Collaboration.

The Brighton Collaboration Steering Committee and Secretariat welcome the opportunity to comment on the draft guidance for Industry Good Pharmacovigilance Practices and Pharmacoepidemiologic Assessment, and support the guidance put forth in the document with the suggestion of referencing work that is already being done specifically in the area of case definitions and guidelines for adverse events following immunization.

Comments

In various locations throughout the proposed document is guidance given regarding information to be collected on an adverse event to “focus the line of questioning” for specific events, and the need for case definitions is highlighted. The Brighton Collaboration has created such targeted data collection tools in addition to recommendations for a standardized way to analyze collected data. The Brighton Collaboration also has created and continues to do so standardized case definitions of selective AEFI to standardize and improve our current understanding of these events.

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<http://brightoncollaboration.org>
secretariat@brightoncollaboration.org

PARTNERS

The European Research Program
for Improved Vaccine Safety Surveillance
EUSAFEVAC

Centers for Disease Control and Prevention
CDC

The World Health Organization
WHO

Few international and national surveillance groups have developed case definitions for use in immunization safety⁷⁻⁹. Those developed were neither widely implemented nor do they represent an exhaustive set of definitions, or provide guidelines for the standardized collection, analysis, and presentation of data which are needed to achieve comparability of data. The Brighton Collaboration is filling this need.

We stipulate that in surveillance systems and epidemiologic studies, the documents can be used to assist with follow up on reported cases to get complete information. The definitions or guidelines can also be used to classify coded events in a surveillance database, and to identify useful follow up information on reports of AEFIs. Another envisioned possibility for web-based reporting is to have a “pop-up window” based on certain key words (e.g., fever) provided by the reporter prompting that reporter for information specified in the respective definition and data collection guidelines. This would allow for more complete information at the reporting level. Standardized case definitions and guidelines are also valuable for case reports, and would help in the overall evaluation in the Periodic Safety Update Reports, if one and the same vocabulary and meaning of that vocabulary were used.

We believe that the Brighton Collaboration concept of global collaboration and a scientific approach towards best evidence-based standardization of public health tools such as case definitions and guidelines can serve as a model for other areas of medical interventions, especially other domains in patient safety.

On behalf of the Brighton Collaboration, I am pleased to submit these comments.

Katrin Kohl, MD, MPH, DTM
Coordinator, The Brighton Collaboration

Proposed additional wording:

We propose to include a reference to available case definitions and guidelines for data collection for adverse events following immunization developed by the Brighton Collaboration in either one or all of the following three sections:

Section IV. A. Good reporting practices

Line 149. Following the sentence: “FDA suggests that the queries be focused on clinically relevant information associated with the product and the adverse event.” we propose to add a footnote that could read: “For adverse events following immunization, the Brighton Collaboration -- an international voluntary Collaboration; see <http://brightoncollaboration.org> -- is developing standardized case definitions and guidelines for data collection, analysis, and presentation of adverse events following immunization for use in vaccine safety surveillance systems and clinical trials”.

Section IV. B. Characteristics of a Good Case Report

Line 163. Following the heading: “Good case reports include the following elements:” we propose to add a footnote that could read: “See <http://brightoncollaboration.org> for targeted standardized case definitions and guidelines for data collection, analysis, and presentation for specific adverse events following immunization”.

Section IV. C. Developing a Case Series and Assessing Causality of Individual Case Reports

Line 216. Following the sentence: “Where these are available, FDA recommends that case definitions (i.e., formal criteria for including or excluding a case) be used to assess cases.” we propose to add a footnote that could read: “See <http://brightoncollaboration.org> for targeted case definitions and guidelines for data collection, analysis, and presentation of specific adverse events following immunization.”

References

1. Bonhoeffer J, Vermeer P, Halperin S, Kempe A, Music S, Shindman J, Walop W, and The Brighton Collaboration Persistent Crying Working Group. Persistent crying in infants and children as an adverse event following immunization: case definition and guidelines for data collection, analysis, and presentation. *Vaccine* 2004; 22:587-592.
2. Marcy SM, Kohl KS, Ron Dagan R, et al., and The Brighton Collaboration Fever Working Group. Fever as an adverse event following immunization: case definition and guidelines of data collection, analysis, and presentation. *Vaccine* 2004;22:551-556.
3. Bonhoeffer J, Gold MS, Heijbel H, et al. and The Brighton Collaboration HHE Working Group. Hypotonic-Hypo-responsive Episode (HHE) as an adverse event following immunization: case definition and guidelines for data collection, analysis, and presentation. *Vaccine* 2004; 22:563-568.
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5. Rothstein E, Kohl KS, Ball L, et al., and The Brighton Collaboration Local Reaction Working Group. Nodule at injection site as an adverse event following immunization: case definition and guidelines for data collection, analysis, and presentation. *Vaccine* 2004;22:575-585.
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7. World Health Organization. Surveillance of adverse events following immunization. Field guide for managers of immunization programmes. Global Programme for Vaccines and Immunization. Expanded Programme on Immunization. World Health Organization, Geneva 1997. Report available on the world wide web at:
<http://www.who.int/vaccines-documents/DocsPDF/www9541.pdf>.
8. Ball R, Halsey N, Braun MM, et al. Development of case definitions for acute encephalopathy, encephalitis, and multiple sclerosis reports to the Vaccine Adverse Event Reporting System. *J Clin Epidemiol* 2002;55:819-24.
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