



# Position Paper—Recombinant DNA

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Office of Biotechnology Activities  
National Institutes of Health  
Building 1, Room 103  
Bethesda, MD 20892

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Dear Sirs,

The American Biological Safety Association (ABSA) is an organization of biological safety practitioners who work in a variety of academic, government, and private work environments. We have reviewed your Notice of Proposed Action under the National Institute of Health (NIH) Guidelines for Research Involving Recombinant DNA Molecules that was published in the December 12, 2000 issue of the *Federal Register*. Please consider the comments that follow.

We approve and support the general content and scope of the proposed changes to the guidelines. The refinement of the definition for sudden adverse events (SAEs) and the tightening of the timeframes for reporting them are positive steps for harmonization of NIH and Food and Drug Administration (FDA) SAE requirements that should be endorsed. These efforts will help to prevent SAEs from being considered trade secrets, but they also prevent the inclusion of patient identifiers and other confidential information in the report.

The Office of Biotechnology Activities' (OBA) changes in the review of SAEs are to be applauded. All Institutional Biosafety Committees (IBCs), even ones at large universities with major medical centers, do not always have the needed expertise for the SAE review. Some Institutional Review Boards (IRBs) are better equipped for these reviews, but they don't always have

expertise in gene therapy. The perspective of the OBA will also be of value, since it will have access to SAEs from other institutions. The OBA should warn all clinical sites of a potential problem with a gene therapy protocol before examination by the Gene Transfer Safety Assessment Board.

Local IRBs and IBCs should be party to communications between OBA and principal investigators on human gene therapy research projects. RAC decisions would also need to be communicated to IRBs and IBCs. The Gene Transfer Safety Assessment Board conclusions also would need to be disseminated to these parties in a timely manner.

Adverse event (AE) and SAE report forms should be identical to the FDA's. A subject identifier is a major benefit of these forms. This enables the Gene Transfer Safety Assessment Board and the public to determine if SAEs are in one or more subjects. NIH may want to consider reformatting its forms to more closely match FDA's. It is understood that the information collected in each form is destined for different uses.

The identification in applications of all IBCs, IRBs, and the proposed clinical sites that are required in Appendix M of the guidelines does not always occur. Some studies involve multiple clinical investigators at more than one hospital or university. It must be an absolute requirement to identify these investigators and locations in applications.

Despite the improved definitions, some Principal Investigators (PIs) may not recognize that an unexpected SAE is associated with a gene transfer project. The sponsor needs to train the PI, or provide PIs with information related to the gene therapy agent. Reporting as soon as possible or within 7 days of the PI's receipt of information of the event should be required.


The Gene Transfer Safety Assessment Board Working Group should include an epidemiologist and a pathologist. Inclusion of a molecular biologist/molecular virologist, preferably a basic scientist rather than a clinician, should also be considered. The basic science molecular biologists often bring to the discussion includes less well known aspects of molecular mechanisms associated with gene transfer. The perspective of a biological safety professional is not only beneficial, but ultimately necessary for this Working Group to address all aspects of health and safety. For this reason, an ABSA member who is also a certified biological safety professional (CBSP) should be appointed to this

group. ABSA reviews the areas of interest of CBSPs, and determines the willingness to serve of CBSPs with the pertinent expertise. The names of these individuals could be provided to the NIH Director, who would make the appointment.

We appreciate the opportunity to provide input to your proposals.

Sincerely,

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President, American Biological Safety Association



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