Frequently Asked Questions About the Vaccine Exemption in the *NIH Guidelines for Research Involving Recombinant DNA Molecules*

Q. Are there any clinical trials involving the administration of recombinant DNA that are specifically exempted from the RAC review process?

A. Yes. Appendix M-VI-A of the *NIH Guidelines for Research Involving Recombinant DNA Molecules (NIH Guidelines)* exempts certain types of vaccine trials from the requirements for submission of the protocol to NIH OBA, RAC review, and subsequent reporting (Appendix M-I). Specifically, this exemption applies to clinical studies involving the administration of recombinant DNA in which "induction or enhancement of an immune response to a vector-encoded microbial immunogen is the major goal, such an immune response has been demonstrated in model systems, and the persistence of the vector-encoded immunogen is not expected." Trials fulfilling all three criteria do not have to be registered with NIH OBA, undergo RAC review, or adhere to clinical trial reporting requirements under Appendix M-I of the *NIH Guidelines*. These trials can be submitted on a voluntary basis, particularly if the investigator believes that a clinical trial involving the administration of recombinant DNA presents scientific, safety, or ethical issues that would benefit from RAC review and public discussion. Investigators who submit trials voluntarily will be expected to comply with all aspects of the protocol review and reporting requirements. OBA encourages investigators and institutional review bodies to contact us (oba@od.nih.gov) for assistance in determining whether this exemption applies to their specific trial.

Q. Do all clinical studies that involve the generation of an immune response to a microbial immunogen fall under the vaccine exemption?

A. No. This is just one of the three criteria that must be met for a trial to be exempted. The vaccine exemption was intended to streamline the development of new vaccines against infectious diseases. Some studies that involve generating an immune response to a microbial immunogen are targeting viruses that cause cancer. If the principal goal of the study is to treat a precancerous or cancerous lesion, the study does not fall under this section.

In addition, some human studies involve the administration of a microbial immunogen in combination with recombinant DNA that encodes for a cytokine or other immune stimulant, for example recombinant IL2, granulocyte macrophage-colony stimulating factor (GM-CSF), or IL12. Such trials

are also not exempt under Appendix M-VI-A since the recombinant DNA encoding the cytokine is not of microbial origin.

Q. Are clinical trials that fulfill all of the criteria as outlined in Appendix M-VI-A exempt from all other requirements specified in the *NIH Guidelines*?

A. No. Vaccine trials that meet the exemption criteria set forth in Appendix M-VI-A are exempt **only** from the requirements of Appendix M-I (*Requirements for Protocol Submission, Review and Reporting*) and are expected to follow all other requirements of the *NIH Guidelines.* This includes having the vaccine trial reviewed and approved by an Institutional Biosafety Committee (IBC) before research participants are enrolled. More information regarding the IBC's role in reviewing and overseeing trials involving the administration of recombinant DNA can be found on the IBC page of the OBA website.