

Frequently Asked Questions about the Vaccine Exemption in the *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules*

(*NIH Guidelines*)

Are there any clinical trials involving the administration of recombinant or synthetic nucleic acid molecules to human research participants that are specifically exempted from the NIH human gene transfer protocol registration process and subsequent reporting requirements?

Yes. Appendix M-III-A of the *NIH Guidelines* exempts certain types of vaccine trials from the requirements for submission of the protocol to the NIH Office of Science Policy (OSP) and subsequent reporting (Appendix M-I of the *NIH Guidelines*). Specifically, this exemption applies to clinical studies involving the administration of recombinant or synthetic nucleic acid molecules 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 OSP or adhere to reporting requirements under Appendix M-I of the *NIH Guidelines*; they do, however, require Institutional Biosafety Committee (IBC) review and approval. These trials can be submitted to NIH OSP on a voluntary basis. Investigators who submit trials voluntarily will be expected to comply with all aspects of the protocol review and reporting requirements. Investigators and institutional oversight bodies are encouraged to contact NIH OSP by email at HGTprotocols@mail.nih.gov for assistance in determining whether this exemption applies to a specific trial.

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

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 exemption.

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 interleukin-2. Such trials are also not exempt under Appendix M-III-A since the recombinant DNA encoding the cytokine is not of microbial origin.

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

No. Vaccine trials that meet the exemption criteria set forth in Appendix M-III-A of the *NIH Guidelines* are exempt only from the requirements of Appendix M-I (Requirements for Protocol Submission, Review and Reporting – Human Gene Transfer Experiments) and are expected to follow all other requirements of the *NIH Guidelines*. This includes having the vaccine trial reviewed and approved by an IBC before research participants are enrolled.