



**Gene Transfer for X-SCID:  
Conclusions and Recommendations  
of the RAC**

**March 3, 2009**



# Previous RAC Gene Transfer Safety Symposia: Current Perspectives on Gene Transfer for X-SCID

**NIH RAC has reviewed the clinical and molecular data concerning the five previous serious adverse events that occurred in human gene transfer studies to correct X-linked SCID conducted in France and England.**

- December 5, 2002
- February 10, 2003
- March 15, 2005
- March 14, 2007
- March 11, 2008



# RAC Recommendations 2005-2008

- **Retroviral gene transfer studies for X-linked SCID should be reviewed, on a case-by-case basis, and limited, pending further data, to patients who have failed identical or haploidentical stem-cell transplantation or for whom no suitable stem cell donor can be identified. Case-by-case review would include appropriate risk:benefit analysis accompanied by implementation of appropriate informed consent and monitoring plans.**



# RAC Recommendations 2005-2008

- **There are not sufficient data or reports of adverse events directly attributable to the use of retroviral vectors at this time to warrant cessation of other retroviral human gene transfer studies, including studies for non-X-linked SCID. Such studies may be justified contingent upon appropriate risk:benefit analysis accompanied by implementation of appropriate informed consent and monitoring plans.**



# Proposed Revisions

- Gene transfer studies for X-linked SCID that propose to use **integrating vectors that have been shown in preclinical studies to reduce the risk of insertional mutagenesis compared to the retroviral vectors used in the original X-SCID trials that led to leukemias** should be reviewed, on a case-by-case basis, and should ordinarily exclude patients who:
  - Have an HLA identical **related** donor available for stem-cell transplantation, as this remains first line therapy, or
  - Patients who are younger than 3 ½ months who often have clinical improvement with haploidentical transplant.
- Case-by-case review of the other inclusion and exclusion criteria would include an appropriate risk:benefit analysis accompanied by implementation of appropriate informed consent and monitoring plans. Further revision of this recommendation will be developed once more data on the leukemogenic potential of these vectors is developed in clinical investigations.

