# Challenge 21: InMutaGene Surgery Q and As.

**Q. Are the Sponsors interested in *in silico* approaches?**

A. Yes, the Sponsors would be interested in novel understanding that an *in silico* approach might offer.

**Q. The immune system is often key in the oncogenic events that might develop from insertional mutagenesis. What are your thoughts on this in the context of this Challenge?**

A. Yes, we recognise the importance of the immune system. In relation to this Challenge it should be remembered that the immune systems of current nonclinical models are very different to the human population which might impact on their ability to predict human risk.

**Q. Lentiviral vectors are now performing well in the clinical arena- is there a need to consider these vectors?**

A. The area is broader than lentiviral vectors- novel information on these as well as other available and perhaps novel vectors would be beneficial.

**Q. What kind of 'product' are the Sponsors expecting? Different gene therapies carry different risks- can a single assay assess all these risks?**

A. Sponsors would be happy with a suite of technologies and a decision tree to enable them to make internal company decisions in the first instance. Ideally, Sponsors would like useable and reproducible assays that integrate data on all relevant risk factors including vector design, disease-specific factors, tumour surveillance, etc. Sponsors also require information on the sensitivity and reproducibility of the assays.

**Q. What would a Phase 1 proof-of-concept look like?**

A. Sponsors are looking for proposals with evidence that applicants can achieve all the deliverables (ideally), or enough deliverables to provide confidence that the applicants can meet the Challenge. Applicants are encouraged to discuss their proposals with Sponsors to better understand if their approach would be considered appropriate.

**Q. Could an *in vitro* model fully replace *in vivo* models at this stage?**

A. There is no gold standard *in vivo* model, but developing an *in vitro* approach (or a suite of them) through this Challenge could be used as an early screen and refine and reduce future *in vivo* models. Sponsors emphasised that the expectation is not that this Challenge will prevent all further animal use, but to develop more predictive models that will impact on the 3Rs.

**Q. Should applicants focus efforts on understanding the commonalities between different diseases and create an assay to explore these?**

A. Sponsors agreed that this approach was of interest but that the key outcome would be to

identify what factors lead to an elevated risk of an oncogenic event.

**Q. The Challenge scope is broad - is it possible to solve all the issues?**

A. Sponsors agree that the Challenge is broad in scope and that it might not be possible to solve every aspect. It is the responsibility of the applicant to discuss their ideas with the Sponsors to ascertain if the proposed work would help address the Challenge.

**Q. Who should we email with questions?**

A. General questions can be sent to the NC3Rs. Questions regarding a specific Challenge can be sent to the Sponsors, but enquiries should be sent to ALL Sponsor parties for a particular Challenge. If preferred, please email the NC3Rs to introduce you to the Sponsors at CRACKITenquiries@nc3rs.org.uk.