To assist Principal Investigators with their responsibilities for ensuring that recombinant or synthetic nucleic acid research utilizing new gene editing technologies is appropriately registered, reviewed and approved, the University of Utah Institutional Biosafety Committee (IBC) requires PIs to address risks associated with gene editing technology, such as CRISPR/Cas9, by requiring responses to the following questions:

1. Please specify which gene editing technology is being used (CRISPR/Cas9, Zinc Finger nucleases, TALENS, Meganucleases, other?).
2. How is the gene editing technology being delivered to cells (e.g., nanoparticles, plasmid, lentivirus, adeno-associated virus, etc.)?
3. What are the gene targets for these experiments?
4. Are any of the targets oncogenes, tumor suppressors, or genes involved in cell cycle regulation?
5. Are you targeting embryos or germ line cells?
6. Are you planning research using gene editing technologies in humans, human embryos, or human germ cells?

(No gene editing of the germ line, human embryos or germ cells for clinical application is allowed. Gene editing of human embryos and germ cells for scientific purpose may be allowed, but must be evaluated on a case-by-case basis by the appropriate federal and local scientific review committees.)

1. Please identify the cell types, tissues and/or organisms that are being targeted.

**Answer the following questions for studies involving CRISPR/Cas9:**

1. Are the guide RNA (gRNA) and nuclease encoded on the same plasmid, viral vector or other delivery vehicle? If yes, describe.
2. For gene editing research involving viral vectors, have potential off target effects by your gRNA been identified in the human genome? This is helpful in assessing the risk of potential exposure in the event of an incident. The IBC recommends GT Scan (<http://bioinformatics.csiro.au/gt-scan/>), but other utilities may be used. Please identify which utility you have used and provide a list of off target genes (with up to 3 mismatches).
3. Are you performing a “gene drive” experiment?

(A “gene drive” is established when Cas9 and gRNA are flanked by homology arms that match DNA sequences surrounding the genome of the gRNA target site. When such a system is introduced into the germ line of a sexually reproducing species, genomic alterations are continually transmitted to offspring. (**Reference:** Akbari, Omar S., et al. "Safeguarding Gene Drive Experiments in the Laboratory." *Science* 349.6251 (2015): 927-9)?

1. Does the construct encoding either Cas9 or gRNA also contain DNA with homology to genomic DNA that flanks the gRNA target site? If so, answer the questions below.
   1. Will the experiment introduce this construct into the germ line of an organism?
   2. Will the experiment result in a transgenic, sexually reproducing organisms?
   3. If the answer is yes to both 11 and 11a, provide a complete description of your experiment.

Please provide answers to these questions and attach the completed document to your registration in BioRAFT. The IBC will typically approve registrations at the containment required for the vector system. However, there are situations where higher containment will be required, including, but not limited to:

If the guide RNA and editing enzyme are encoded by the same vector and the vector/delivery vehicle can integrate into the genome, the University of Utah IBC requires BSL2+ containment,

If a search of off-target genes has not been performed and the vector/delivery vehicle can integrate into the genome, the University of Utah IBC requires BSL2+ containment, or

If a list of off-target sites with up to 3 mismatches identifies tumor suppressors or genes that regulate the cell cycle, and the vector/delivery vehicle can integrate into the genome, the University of Utah IBC requires BSL2+ containment.