CRACK IT

# Challenge 30: RaTS Surgery Q&As

**Q. How were the technical specifications for the Raman transmission spectroscopy defined?**

**A:** The technical specification values are the estimated improvements in Raman transmission spectroscopy that will be needed to solve the Challenge of early detection of bone and cartilage changes in the CIA rodent model. Alternative specifications that can potentially solve the Challenge are also welcome.

Presently, we are not aware of any data specifically published on *in vivo* Raman Transmission Spectroscopy for rats CIA models.

**Q: Are approaches other than Raman transmission spectroscopy within scope?**

**A:** Yes, the Sponsors welcome to any spectroscopic approach that can deliver the scientific and 3Rs requirements of the Challenge.

**Q: What molecular and chemical biomarkers do you expect to look for in assessing early joint damage?**

**A:** Molecular changes that we would be interested in detecting include the ratio of normal to denatured molecules of the extracellular matrix (e.g. proteoglycans) in the cartilage and the amount of key minerals in the bone (e.g. chondroitin sulfate, phosphated hydroxyapatite, and carbonated hydroxyapatite) and the bone density. Other inflammatory markers may include the amount of synovial swelling/oedema and vascular/blood flow changes in the paw.

**Q: Is it an absolute requirement for the device to be hand-held?**

**A:** The device must be small enough to use with conscious rodents in their home cage without excessive handling. A handheld or compact device that would permit this would be acceptable. It is OK to have a handheld probe with the laser emitter and detector that is connected via cable to a larger desktop device.

**Q: Are the bone changes you see in the disease model crystalline or amorphous?**

**A:** Bone is a complex structure that includes both crystalline and amorphous molecules. Potentially, all of them become degraded to some degree in the CIA model of RA.

**Q: Are you expecting the device to be used in other species, such as humans?**

**A:** The current Challenge is focused on non-clinical models, specifically the rat's CIA model. Future applicability to other species is encouraged but not a requirement of this Challenge.

**Q: Is there a preference for imaging or spectroscopy? Which is most important**?

**A:** There is no preference, as long as the proposed modality provides reliable quantified information with minimal manual analysis. The molecular information is most important for the evaluation of cartilage and bone degradation. This information can come from either imaging or spectroscopy.

NC 3Rs

**Q: What depth of penetration into the joint is required?**

**A:** Given the size of the rodent knee joint, we estimate that 5 mm depth of penetration is needed.

**Q: Is an approach that requires multiple injections acceptable?**

**A:** No, the technique should not increase the experimental burden on the animals used.

**Q: Is there a preference in the types of read outs you require? If you require both inflammation and bone changes, is there an order of priority?**

**A:** Measurement of the bone and cartilage damage has a higher priority, as there is a lack of objective measures for these pathological symptoms. Inflammation markers have a lower priority, as they can be objectively assessed using the systemic blood tests.