

**Focus on procedures**

Project licence number	70/6524
Protocol number	2

What does this study involve doing to the animals?	What will the animals experience? How much suffering might it cause? What might make it worse?	How will suffering be reduced to a minimum?	
	Adverse effects and indicators of these	Methodology and interventions	Humane endpoints
Administration of rheumatoid arthritis inducer	<p><i>Capture and restraint – distress. Aggression, vocalisation, unwilling to be caught.</i></p> <p><i>Administration i.d. or s.c. – pain. Flinching, vocalisation, aggression.</i></p> <p><i>Pain or ulceration around injection site. Attention to site, reduction in</i></p>	<p><i>Competent, empathetic capture (e.g. not by tail) and handling, habituate to handling and restraint.</i></p> <p><i>Use gaseous anaesthesia for i.d.; inject into rump, not tail base (if tail base is painful, restraint by the tail will hurt). Minimise volumes and doses, use multiple sites if large volumes. Ensure injectate formulated to minimise adverse effects.</i></p> <p><i>Inject into rump (less risk of ulceration); never inject into the</i></p>	<p><i>Humane endpoints with respect to administration of inducer in general:</i></p> <ul style="list-style-type: none"> <li><i>- Ulceration that is painful, shows no signs of healing or becomes infected.</i></li> <li><i>- If an ulcer reaches &gt;5 mm, the vet or senior animal technologist should be informed and consulted about treatment. Animal should be humanely killed if no signs of healing within 3 days.</i></li> </ul>

	<p><i>nest quality, body weight/food intake reduction, reduced grooming, reduced social interaction, physical appearance of ulcers.</i></p> <p><i>Adverse effects due to adjuvant, e.g. granuloma, lesions. Indicators as for pain/ulceration above.</i></p>	<p><i>foot; if attention paid to site apply topical anaesthesia and review injection protocol; choose needle gauge with care.</i></p> <p><i>Ensure that least harmful adjuvant possible has been used; review literature and avoid FCA (e.g. trial incomplete Freund's).</i></p>	
<p><i>Allowing arthritis to develop</i></p>	<p><i>Painful joints, sore feet, lameness, disability – pain and distress. Altered gait, swollen paws, favouring paws, reduced grooming, discoloured skin. Acute pain. Flinching, vocalisation, attention to painful site.</i></p>	<p><i>Implement husbandry refinements e.g. long drinking nozzles; pick up and handle using washed Vetbed; give analgesia if possible, e.g. opioid during 'attack' phase, provide appropriate enrichment to 'shift' attention.</i></p>	<p><i>Prolonged failure to weight bear on a limb. Spontaneous vocalisation when picked up or handled. 20 % weight loss, or 15 % if this does not begin to reverse within 5 days. Severe paw swelling, using a numerical index or paw volume.</i></p>
<p><i>Other issues</i></p>	<p><i>Inherent severe arthritis in some models or strains.</i></p>	<p><i>Explore potential to answer the same question using a less severe model or less susceptible strain.</i></p>	

Note: This example is intended to give an indication of some of the points and factors that could be discussed when conducting this part of the review. It is for guidance only and is not intended to be exhaustive for this type of procedure. It is based on the RSPCA report on Applying refinement to the use of mice and rats in rheumatoid arthritis research, *Inflammopharmacol* DOI 10.1007/s10787-015-0241-4 which is open access here: <http://link.springer.com/article/10.1007/s10787-015-0241-4>