AMMONIUM PERRHENATE: TOXICOLOGY STUDIES

Study	CRO	Contract signed	Protocol signed	Proposed start date	Proposed draft report date	Status	Comments
in vitro eye irritation (BCOP)	Harlan	29-Apr	29-Apr	3rd June (started)	August	on-going	**Statement from Harlan:** The BCOP study on Ammonium Perrhenate Pro No. 41100367 was terminated today due to solubility issues. We needed to prepare a 20% solution or suspension. However a suitable suspension was not even possible. There is the option to apply the neat solid Test Item. However applying neat Test Item has not been completely validated as respects to over or under prediction of ocular irritancy and is not the common application approach. The historical data is based on application of a 20% concentration. Another consideration taken into account to terminate the test is the increased amount of Test Item we'd used applying a sufficient amount to evenly cover each cornea for a 4 hour duration (see documentation regarding sample amounts required). Therefore the Study Director recommends another organotypic ex-vivo method. This would be the Isolated Rabbit Eye (IRE/REET) assay. Up to a maximum amount of 100mg of Test Item is applied to each eye (a much smaller volume than would be applied to the bovine cornea). The Test Item is commonly applied neat in this assay and therefore the common protocol would Following discussion with PMRC, it was agreed to cancel the BCOP assay and to
in vitro eye irritation (Isolated Chicken Eye)	LAB	awating contract					Request for protocol and contract sent 21 June 2011
in vivo eye irritation	Harlan	29-Apr	29-Apr	dependent on results from *in vitro* assay			this study depends on the results of the *in vitro* study
Local Lymph Node Assay	Harlan	29-Apr	29-Apr	7th June (preliminary work started)	August	on-going	The initial screening animal has been performed (25% in DMF) and no signs of toxicity or excessive irritation were noted at this concentration. The main test at dose levels of 25%, 10% & 5% will be started tomorrow (22 June 2011) with the result available next week.
in vitro mouse lymphoma assay	Covance	19-May	5 & 13 Apr	21 Apr (started)	end July	on-going	expt 1 showed no marked increase in mutant frequency. Expt 2 finished. No evidence of mutagenicity observed. Results discussed with Study Director, who confirmed that although there was some variability in expt 2, there was no linear trend dose-response seen, and no biologically significant mutant response. Therefore there is no requirement for colony sizing.
in vitro micronucleus assay	Covance	19-May	final protocol to be signed by 17 June	20-Jun	Nominally draft report issued 2.5 months from start	on-going	The study will start week commencing 20 June
28-day tox/reproscreen	Charles River	awaiting contract	protocol under review	to be agreed. Probably July	ca 7 months after start (Jan 12)	draft protocols in discussion	substance analysis in formulation to be conducted externally. Butterworth Laboratory chosen for analyses, and updated quotation available shortly. Note: Method validation will not be to GLP (only internal quality standard), but all formulation analyses will be to GLP. The CRL Study Director confirms that this is acceptable and is happy with this.