In vitro Studies at Syngenta CTL

- *In vitro* studies conducted on rodent (rat & mouse) synaptosomes to investigate the potential for paraquat to interact with the dopamine transporter and dopamine receptors (radioligand binding studies).
- Dopamine re-uptake studies using [^{3}H]-dopamine:
  IC_{50} MPP^+ = 200 nM
  IC_{50} PQ = >1 mM
- Binding affinities for PQ >100 μM (K_i MPTP D_2 = 500 nM)
- Paraquat may display apparent structural similarities to MPTP however:
  paraquat is not a substrate for the dopamine transporter
  paraquat does not bind to post-synaptic dopamine receptors

Summary - Paraquat & Parkinson's disease literature findings

- Reports in the literature suggest that in a certain strain of pigmented mouse ($C_{57}Bl_6$), multiple i.p. injections of paraquat at relatively high doses can result in a 30% loss of dopaminergic neurones in the *substantia nigra*.
- These findings have been replicated in Syngenta studies.
- There are also claims that the effect can be observed in another rodent species (rat), however Syngenta studies have failed to repeat this finding.
- We should be aware that there may be NHP data with paraquat emerging in the near future that may replicate the findings already reported in rodent species - potential relevance to humans.