

P/2/11/16

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LLS/JFM

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Dear Bob

Stuart Jagers has asked me to reply to your request for information that PP796 is absorbed from the stomach in sufficient amounts to cause emesis. There is no direct evidence that PP796 is absorbed from the stomach but because of the very rapid induction of emesis we believe this to be likely. However, even if PP796 were absorbed from the duodenum I think it unlikely that all the paraquat consumed with PP796 could pass from the stomach in the few minutes it takes to induce vomiting. Thus, I doubt if the value of PP796 in reducing the toxicity of paraquat would be seriously impaired if it were absorbed distal to the stomach.

Since the information you require has been requested by others I shall undertake to determine at least in rodents, the site of absorption of PP796. I have given consideration to these studies earlier this year, however I ran into serious problems with Home Office clearance. To do these studies it will almost certainly be necessary to keep the animals anaesthetised throughout since it will be necessary to ligate the intestine below the stomach. Nevertheless, I do not think the use of anaesthetic will invalidate the results. If I am to undertake these studies in a vomiting species i.e. dog, further discussion with the Home Office will be necessary.

In summary, therefore, I hope you will be able to reassure any interested parties that PP796 is likely to be absorbed from the stomach, is effective in causing vomiting rapidly enough to reduce the toxicity of paraquat and we are continuing to investigate some of the pharmacokinetic properties of the absorption of PP796.

I trust all is well with you and you enjoyed your trip to the UK.

Kind regards  
Yours sincerely

Lewis L Smith (Dr)