From

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To

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Dr A Calderbank, J. Hill
Dr M S Rose, CTL
Miss N T Frost, Fernhurst

Your ref	Our ref	Tel ext	Date
	LLS/JFM	Redacted - EU PII	28 Nov 78

Dear David

Re: Safer formulations of Gramoxone

I am writing to you to inform you of the views of Mike and myself on measures which might be taken to safen Gramoxone and related formulations. We feel that the experimental evidence in dogs and monkeys if applicable to man indicates that the addition of emetic to Gramoxone ought to reduce the hazard by a factor of at least three. This means that the likely lethal dose of Gramoxone plus emetic would then be 30-45 mls. We are confident that in accidental poisonings the addition of emetic together with prompt and effective treatment should markedly reduce the likelihood of mortality. Regrettably the vast majority of deaths following the ingestion of paraquat result from suicidal intent and this is especially so in Japan. Also, if the figures enclosed are to be believed the volume ingested by the 'typical Japanese suicide' tends to be large and about 50% of the deaths possibly result from the ingestion of more than 100 mls of Gramoxone. This has at least two consequences when discussing safer formulations.

1. The addition of an alerting agent by itself to Gramoxone will not prevent death since without emetic only 10-15 mls of Gramoxone can cause death and even with emetic 45 mls are probably lethal. A mouthful has a volume of 30-40 mls and it is unlikely that the alerting agent would prevent the consumption of two mouthfuls even if it were instantaneously irritant.

2. In order to maximise the benefit of adding emetic, dilution of Gramoxone is required (assuming that 45 mls of emeticised Gramoxone is lethal and that two mouthfuls is 60-80 mls). Even allowing for the vagueness of these figures the knowledge that the Japanese ingest large volumes argues that, at least in this market, dilution is required.

We of course recognise that the dilution of Gramoxone may pose serious commercial problems and it is difficult for us to be categoric as to the extent of dilution we should recommend. Obviously the greater this is the less toxic will be Gramoxone. We suggest that using the above figures a dilution of no less than three be your target. This should shift the lethal dose of emeticised Gramoxone from 30-45 mls to ∿ 100 mls. Provided the data we are using is correct and there is no alteration in the habits of those Japanese who use pesticides to commit suicide, this approach may significantly alter the number of deaths from Gramoxone in Japan. It follows that an alerting agent can only be of use in conjunction with the dual approach of emeticising and dilution.

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I hope my comments have clarified the current CTL view on this problem.

Best wishes
Yours sincerely

L L Smith

Lewis L Smith (Dr) pp LLS
(Dictated, signed in his absence)