European Commission
Peer Review Programme

Paraquat

ADDENDUM

Further consideration following the publication of the Opinion of the Scientific Committee on Plants (Opinion adopted by the Scientific Committee on Plants on 20 December 2001) in the context of inclusion of the above mentioned active substance in Annex I of Council Directive 91/414/EEC

Pesticides Safety Directorate, UK.

Summary, Scientific Evaluation and Assessment

SEPTEMBER 2002

Contents

Introduction

This document provides the conclusions of the UK's Pesticides Safety Directorate (PSD) in response to the Opinion of the Scientific Committee on Plants (SCP) on specific questions from the Commission regarding the evaluation of paraquat in the context of Council Directive 91/414/EEC (Opinion adopted by the Scientific Committee on Plants on 20 December 2001).

The response of the notifier, Syngenta, is contained in their document dated 19 March 2002 (see Syngenta covering letter headed "Paraquat: EU Review under Council Regulation 3600/92; Comments on the SCP Opinion published in January 2002" and attached document, dated 19 March 2002). That document together with the supporting information has been considered and evaluated by PSD.

PSD's assessment in the context of the SCP Opinion is presented below.

Background

In 2001, the SCP were requested to respond to the following questions in the context of the review of paraquat as part of the Commission's work on the implementation of Council Directive 91/414/EEC concerning the placing of plant protection products on the market.

1. Can the Committee comment on the relevance for consumers and operators of the ocular and pulmonary changes, which were observed in the long-term rat study?

2. Can the Committee comment on the risk for operators, taking into particular account potential inhalatory and dermal exposure?

3. Can the Committee comment on potential long-term effects to soil dwelling organisms?

4. Can the Committee comment on the risks the intended uses might pose to reproducing birds and hares?

   Please note that question 4 consists of two questions, one relating to birds and one relating to hares, therefore for clarity the question has been considered separately in this paper.

The SCP addressed these questions and their full opinion, which was published on 16 January 2002, can be found at www.europa.eu.int/comm/food/fs/sc/scp/out122_en.pdf

Question 1:

Can the Committee comment on the relevance for consumers and operators of the ocular and pulmonary changes, which were observed in the long-term rat study?

Opinion of the Committee:

The toxic effects of paraquat are due to its ability to induce the production of reactive superoxide anions from molecular oxygen.

The pulmonary lesions observed in animals after paraquat oral treatment are the critical effect and are similar to those reported to occur in humans after deliberate or accidental oral ingestion of very high doses. Such effects, however, are not expected to occur under the exposure conditions that can take place in occupational settings or for consumers, when paraquat is used as a plant protection product as recommended.

The ocular lesions documented in the long-term rat study result from systemic action of paraquat after prolonged oral absorption and not as a result of direct local contact with the eye. This latter situation may cause irritative mucosal effects, different from the lenticular opacity observed in rats as a result of systemic toxicity. The systemic effects on the eye of paraquat, observed in rats and not in other species, are not relevant to the risk assessment for operators and consumers.

Further RMS consideration - question 1

The notifier has submitted no further information in response to the SCP Opinion on Question 1.

The opinion of the SCP is in agreement with the conclusions of the rapporteur as presented in the draft assessment report and the addendum and is also in agreement with the summary of the rapporteur Member State's (RMS) position given at 4.3 in the Evaluation Table.

The RMS also notes that in scientific background on which this opinion (and that for question 2) is based it is stated that the SCP is of the opinion that the NOAELs based on pulmonary effects observed in dogs should represent the basis to set short-term or medium-long-term AOELs and the ADI. This is also the conclusion reached by the RMS.

The rapporteur considers that these areas of concern have been satisfactorily resolved.

Question 2:

Can the Committee comment on the risk for operators, taking into particular account potential inhalatory and dermal exposure?

Opinion of the Committee:

While the use of predictive exposure models suggests that operator exposure to paraquat may exceed the proposed AOELs, the results of the field studies conducted in various countries indicate that the exposure models markedly overestimate the actual exposure to paraquat in real working situations. Thus modelled exposures cannot be used as the only basis for operator risk assessment. Based on the field exposure studies, corroborated by information on health surveys on operators, the SCP is of the opinion that when paraquat is used as a plant protection product as recommended under prescribed good working practices, its use does not pose any significant health risk for the operators.

The SCP is of the opinion that the NOAELs based on pulmonary effects observed in dogs should represent the basis to set short-term or medium-long-term AOELs.

Further RMS consideration - question 2

The notifier has submitted no further information in response to the SCP Opinion on Question 2.

The opinion of the SCP is in agreement with the conclusions of the rapporteur as presented in the draft assessment report and the addendum and is also in agreement with the summary of the RMS's position given at 4.2 (inhalation exposure) and 4.5 (operator exposure) in the Evaluation Table.

The rapporteur considers that these areas of concern have been satisfactorily resolved and shares the opinion of the SCP that when paraquat is used as a plant protection product as recommended under prescribed good working practices, its use does not pose any significant health risk for the operators.

Question 3

Can the Committee comment on potential long-term effects to soil dwelling organisms?

Opinion of the Committee:

Overall the SCP is satisfied with the data presented and concluded that if paraquat is used at recommended field rates then it is unlikely to pose a significant risk to soil-dwelling organisms. However, the Committee notes that the litter bag study was conducted at too high a dose rate to allow a reliable assessment of the likely effects of paraquat on the rate of organic matter decomposition under field conditions. Given this uncertainty and the persistence of paraquat in soil, the SCP feels that the Notifier should provide a more detailed appraisal of the likely effects of paraquat on the rate of degradation of organic material in soil.

Further RMS consideration - question 3

In their consideration of the potential long-term effects to soil dwelling organisms, the SCP state:

> Overall the SCP is satisfied with the data presented that if paraquat is used at recommended field rates then it is unlikely to pose a significant risk to soil-dwelling organisms. The high SAC-WB values compared to long-term PEC_S and general absence of significant effects at high field application rates, support the view that as a consequence of high adsorption, paraquat should not be bio-available in high concentrations to many soil organisms.
>
> The SCP notes that no laboratory sub-lethal test for earthworms was conducted despite the fact that paraquat may become available to these organisms through ingestion. However the Committee notes that the LC_{50s}[1] for earthworms were generally very high, and that field trials showed no significant differences in earthworm numbers 1 year following applications up to 90 kg a.s./ha.

Therefore, on the basis of the above, the SCP considered that paraquat is unlikely to pose a significant long-term risk to soil dwelling invertebrates.

However, the SCP do raise concern regarding the litter bag study and, in particular, the relevance of the high application rate and the method of application (i.e. the leaves were dipped into the paraquat).

Due to this concern the SCP requested that the Notifier should provide a more detailed appraisal of the likely effects of paraquat on the rate of degradation of organic material in soil. The Notifier's more detailed appraisal is presented in their response to the opinion of the SCP (see Syngenta covering letter headed "Paraquat: EU Review under Council Regulation 3600/92; Comments on the SCP Opinion published in January 2002" and attached document, dated 19 March 2002).
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[1] Lethal concentration, median

In this appraisal the Notifier cites the results from further litter bag studies (i.e. Cole J *et al* 'Paraquat: Long-term high rate trial, Frensham, UK. Crop and soil data for the period 8-12 years after treatment' ICI Report No RJ0355B, 30 April 1984; Gowman M A, Riley D, Newby S E (1980) 'Paraquat and diquat: Long-term high-rate trial, Frensham, UK. 2. Persistence and movement in soil and glasshouse bioassays' ICI Report No RJ0014B (submitted in EU dossier, 1995 and Dyson *et al* 'Paraquat: Long-term soil trial at Goldsboro, USA, 1979-1991. I. Trial description and crop measurements, Zeneca Report No TMJ3328B, 13 April 1995.) These reports were included in the original dossier in 1995. Summaries of these studies were included in the fate assessment in the monograph, rather than the ecotoxicology section. The Notifier has also submitted a further study on the microbial biodegradation of paraquat in soil. This study is summarised above.

These studies have been re-examined and presented below.

Data Evaluation

Field plots on a loamy sand with a paraquat 'Strong Adsorption Capacity (SAC) of 120 µg/g, were treated in November 1971 with 0, 90, 198 and 720 kg paraquat ion/ha incorporated to a depth of 15 cm. According to the study report this gave theoretical soil concentrations of 0, 50, 110 and 400% of the SAC value. In 1978 the site was sown with a ryegrass (*Lolium perenne*)/white clover (*Trifolium repens*) ley.

The effect of the above treatment regime was determined by measuring the vegetation cover and yield, soil pH and available nutrients (i.e. P, K and Mg) and uptake of nutrients by vegetation.

As regards the vegetation cover, there was no significant differences between the control and the 90 kg paraquat ion/ha paraquat ion/ha treatments at any of the assessment dates. At the 198 kg paraquat ion/ha there was one time point were there was a significantly lower *Trifolium repens* in the treatment compared to the control, however this did not appear to be treatment related as there was no significant difference for the preceding and following years. At the highest application rate of 720 kg paraquat ion/ha there was statistically less *Lolium perenne* at all three time points. In the highest treatment there was statistically more *Trifolium repens* than in the control. This effect was noted on the last two sampling dates. As regards yield there were no treatment related effects observed. The 90 and 198 kg paraquat ion/ha had no appreciable effect on soil pH. The top rate showed slightly reduced pH. The paraquat treatment generally had no significant effect on the available P, K and Mg levels in the soil. The nutrient contents of the vegetation on the paraquat treated plots were generally not significantly different from the control.

Cole *et al* (1984)

Field plots on a loamy sand with a low Strong Adsorption Capacity (SAC) of 120 µg paraquat ion/g soil were treated with paraquat and diquat at rates of 0, 90, 198 and 720 kg/ha incorporated to a depth of 15 cm. According to the study report this gave theoretical soil concentrations of 0, 50, 110 and 400% of the SAC value. During the 7 year period 14 normal applications of paraquat were made to all plots to control weeds (total 8.9 kg/ha).

The 90 and 198 kg/ha treatments had no appreciable effect on soil pH, at the highest application rate pH was reduced by between 0.3 and 0.5 pH units on two sampling dates. The treatments had no effect on available P, K and Mg levels.

It was noted that it took about two years for adsorption to reach equilibrium. It was also noted that the bipyridyl soil residues from the 90 and 198 kg/hg treatments had no effect on wheat growth once adsorption had reached equilibrium.

Information from this field study was used in the original assessment of paraquat (e.g. Edwards (1980), Drew and Davies (1980) and Cole and Wilkinson (1980).

Gowman *et al* (1980)

The long-term fate and effects of paraquat were studied on a sandy soil at Goldsboro, North Carolina, USA. As part of this study, the potential risk to plants from the repeated use of paraquat was assessed. Five paraquat treatments were replicated on 4 blocks – an annual treatment (1 kg/ha/yr), three single high rate treatments applied at the start of the trial, i.e. 50% 100% and 200% of the average SAC-WB value (28, 57 and 114 kg paraquat/ha incorporated to a depth of 15 cm) and an untreated control.

The potential effect on plant growth from residues of paraquat in the soil were measured from plant density, height of crops and crop yield. Paraquat residues did not affect stand counts. The plant heights of corn and wheat show in general, that they were very similar for all the paraquat treatments. (On one of the 200% SAC-WB treatments plant heights were reduced by 50%, however, all treatments including the control in this block also had reduced plant heights therefore it was concluded that other factors were affecting plant height.) The high-rate paraquat treatments only resulted in two statistically significant reductions in crop yield for wheat, but did not generally lead to statistically significant effects on stand counts, plant heights or grain weights.

Dyson *et al*(1995)

The microbial degradation of 14C paraquat using cultures from two agricultural soils was investigated. The experiment was carried out in the absence of light, under aerobic conditions. Degradation was rapid with 50% mineralisation to 14C carbon dioxide occurring within three weeks. HPLC, capillary electrophoresis and mass spectroscopy confirm that the majority (>85%) of the remaining radiochemical in solution was 14C oxalic acid and that no paraquat remained. This study, therefore demonstrated that bioavailable paraquat can be rapidly and completely degraded by micro-organisms.

Ricketts (1999)

Risk assessment

These above studies were designed to determine if very high applications of paraquat had an adverse effect on soil characteristics and yield. These data indicate that the functionality of the soil is not adversely affected and hence crop yields are comparable to the control. In one trial a difference in the ratio of ryegrass (*Lolium perenne*)/white clover (*Trifolium repens*) was noted at the maximum application rate, equivalent to 720 kg paraquat ion/ha, equivalent to approximately 700N. It was postulated, by the authors, that due to the presence of paraquat at the time of sowing *Lolium perenne* was suppressed. It should be noted that all three of these studies were carried out on a sandy soil with low organic matter and they were treated at rates in excess of their adsorption capacity. In light of the overall conclusion of the SCP and the studies summarised above, it is considered that the available data indicates that paraquat will not adversely affect soil function or fertility in the long-term, especially at the use rates supported.

In conclusion, it is proposed that the risk to soil dwelling organisms and the resulting soil function is acceptable.

<u>Question 4 (a)</u>

Can the Committee comment on the risks the intended uses might pose to reproducing birds ?

<u>Opinion of the Committee:</u>

As regards the risk to birds, the Committee concludes that the results of the egg dipping study demonstrate a hazard from paraquat to avian embryos, but the available information is not adequate for an assessment of risk (i.e. the likelihood that these effects will occur in practical use of the active substance). To provide a risk assessment would require tests with paraquat involving more realistic exposures.

<u>Further RMS consideration - question 4 (a)</u>

The Notifier has responded to the SCP Opinion (see Syngenta covering letter headed "Paraquat: EU Review under Council Regulation 3600/92; Comments on the SCP Opinion published in January 2002" and attached document, dated 19 March 2002).

Data on dipping eggs in paraquat presented in the original monograph indicated a potential hazard. When the SCP considered these data they concluded that in order to provide an appropriate risk assessment tests with paraquat involving more realistic exposures were required. The Notifier has submitted data on the risk to birds from overspraying of eggs. The studies submitted have been summarised and are presented below. The Notifier has also submitted a risk assessment and this is presented in their response to the opinion of the SCP (see Syngenta covering letter headed "Paraquat: EU Review under Council Regulation 3600/92; Comments on the SCP Opinion published in January 2002" and attached document, dated 19 March 2002).

Data evaluation

Paraquat was sprayed directly onto the eggs of Japanese quail, *Coturnix coturnix japonica*, prior to incubation, at rates equivalent to 0.20, 0.35, 0.78, 1.49 and 3.03 kg paraquat ion/ha, in a spray volume of 200 l/ha. The percentage of set eggs which hatched following these treatments was 58, 53, 47, 64 and 61% respectively, compared with 63 and 58% in the water and unsprayed control. There was no significant differences in the treatment levels. Paraquat residues in whole egg contents, 5 days after spraying at these rates were 0.02, 0.05, 0.05, 0.04 and 0.2 mg/kg respectively. The paraquat treatment had no effect on the length and width of the vestigial right Müllerian ducts attached to the caudal end of the cloaca in females. No Müllerian ducts in any form, were found in males. The treatments did not have any observable effects on the testes and ovaries.

Edwards *et al* (1979)

In a GLP study, mallard duck eggs were sprayed either with tap water (Control), or paraquat at rates of 0.56, 1.12 and 2.24 kg ion/ha using spray strength solutions containing 0, 2.8, 5.6 and 11.2 paraquat ion/l. Eggs were divided into 6 groups and each group was sprayed once either on day 0, 2, 4, 10, 14 or 20 of the incubation period. There were 4 replicates for each treatment regime. Eggs were candled at days

13 and 19 of the incubation period when infertiles, early embryonic deaths and late embryonic deaths were recorded and removed. Numbers of dead in shells, chicks hatched and 28-day survivors together with bodyweights at hatching and 28 days of age were recorded. In addition, any gross abnormalities in the embryos which died and the chicks which hatched were recorded together with any abnormalities in the chicks during the 28-day observation period.

The following significant treatment effect in comparison with the control are present in Table 1.

Table 1: Summary of the significant treatment effects on fertility of mallard eggs following spray treatment of paraquat

Parameter	Effect
Early embryonic deaths	There was a significantly greater proportion of early embryo deaths from eggs sprayed on day 0, 2 and 4 in the top dose compared to the control eggs.
Late embryonic deaths	There was a significantly greater proportion of late embryo deaths from eggs sprayed on days 10 and 14 in the top dose compared to the control eggs.
Dead in shell as a proportion of fertile eggs	There was a significantly greater proportion of dead in shell as a proportion of fertile eggs in eggs sprayed on day 0 and day 14 in the top dose compared to those in the control. When considered as a proportion of eggs viable at day 19, significantly more dead in shell occurred in the top dose than in the control group in eggs at all times of spraying except on day 20.
Eggs that hatch as a proportion of fertile eggs	There was a significantly lower proportion of chick hatch in the top dose compared to the control. This was observed in eggs that had been sprayed on days 0, 2, 4, 10 and 14.
Surviving chicks as a proportion of fertile eggs	There were a significantly lower number of survivors as a % of chicks hatched from eggs sprayed in the top dose compared to the control eggs.
Surviving chicks as a proportion of hatched chicks	There were a significantly lower number of survivors as a % of fertile eggs from eggs sprayed on day 20 in the top dose compared to the control eggs.
Chick bodyweight	Chick body weight in the top dose was significantly heavier than in the control group for eggs sprayed on day 2 and 10. At sacrifice, chicks from the top dose sprayed on day 14 weighed more than those in the control group.
Liver weights	There was an indication that, of the chicks surviving from eggs sprayed on day 14, the liver weights in the top dose were significantly higher than the control. After adjustment for final bodyweights, the liver weights for the top two doses were found to be significantly lower than the controls.

Significant adverse effects on early embryonic death, late embryonic death, dead in shell, hatchability and chick survivability occurred as a result of spraying fertile Mallard duck eggs with paraquat at an application rate of 11.2 g a.s./l, equivalent to 2.24 kg/ha. No adverse effects occurred in eggs sprayed at 2.8 g a.s./l or 5.6 g a.s./l, i.e. at rates equivalent to 0.56 and 1.12 kg/ha respectively.

Hakin and Chanter (1989)

In a GLP study, four replicates each comprising ten fertile Pheasant eggs were sprayed either with tap water (Control), or paraquat at rates of 0.56, 1.12 and 2.24 kg ion/ha. Spray solutions containing 0, 2.8, 5.6 and 11.2 paraquat ion/l were used. Eggs were divided into 6 groups and each group was sprayed once either on day 0, 2, 4, 10, 14 or 20 of the incubation period. There were 4 replicates for each treatment regime. Eggs were candled at days 13 and 19 of the incubation period when infertiles, early embryonic deaths and late embryonic deaths were recorded and removed. Numbers of dead in shells, chicks hatched and 28-day survivors together with bodyweights at hatching and 28 days of age were recorded. In addition, any gross abnormalities in the embryos which died and the chicks which hatched were recorded together with any abnormalities in the chicks during the 28-day observation period.

The following significant treatment effect in comparison with the control are presented in Table 2.

Table 2: Summary of the significant treatment effects on fertility of pheasant eggs following spray treatment of paraquat

Parameter	Effects
Early embryonic deaths	There was a significantly greater proportion of early embryo deaths from eggs sprayed on day 0, 2 and 10 in the top dose compared to the control eggs.
Late embryonic deaths	There were no statistical differences observed.
Dead in shell as a proportion of fertile eggs	There were no statistical differences observed.
Eggs that hatch as a proportion of fertile eggs	There was a significantly lower proportion of chick hatch in the top dose compared to the control. This was observed in eggs that had been sprayed on days 2 and 10. This difference was also evident in averages over spraying time.
Surviving chicks as a proportion of fertile eggs	Statistical analysis of the results showed that eggs sprayed on Day 2 showed significantly smaller proportions of fertile eggs surviving to 28 days in the top dose than in the control group. Eggs sprayed on day 4 showed a significantly smaller proportion of fertile eggs surviving to 28 days in the top two doses.
Surviving chicks as a proportion of hatched chicks	Eggs sprayed on Day 10 showed a significantly higher proportion of hatchlings surviving to day 28 in the top dose than in the control group.
Chick bodyweight	Initial chick bodyweights were higher in all the treated groups than in the control group for eggs sprayed on day 14. At sacrifice there were no significant differences between treatments in chick bodyweight.

Significant adverse effects on early embryonic death, hatchibility and chick survivability occurred as a result of spraying fertile pheasant eggs with paraquat at an application rate of 11.2 g a.s./l. The NOEL for the study was 5.6 g a.s./l, equivalent to 1.12 kg ion/ha.

Roberts *et al* (1989)

In a GLP study, one replicate, comprising 10 fertile Mallard duck eggs, was sprayed with either tap water or Gramoxone at concentrations of 2.8, 5.6 or 11. 2 g paraquat ion/l on day 0, 2, 4, 10, 14 or 20 of the incubation period. A second replicate also comprising ten fertile Mallard eggs was dipped for 30 seconds in tap water or Gramoxone at concentrations of 0.6, 1.2 or 2.4 g paraquat ion/l at the same time points.

All eggs were candled on day 13 and 19 of the incubation period when infertiles, early embryonic deaths and late embryonic deaths were recorded.

The following significant treatment effect in comparison with the control are presented in Table 3.

Table 3: Summary of the significant treatment effects on fertility of mallard eggs following spray and dip treatment of paraquat

Parameter	Effect from dipping	Effect from spraying
Infertile eggs	No significant difference from the control	No significant difference from the control
Early embryonic deaths	No significant difference from the control	Statistical analysis of the results showed that there was a significantly greater proportion of early embryonic deaths in the top dose of those eggs sprayed on day 4.
Late embryonic deaths	No significant difference from the control	Statistical analysis of the results showed that there was a significantly greater proportion of late embryonic deaths in the top dose of those eggs sprayed on day 10. This difference was detected for averages over times of spraying.
No of embryos alive on Day 19 as a proportion of the total fertile	There was a significantly smaller proportion of fertile eggs still viable at Day 19 in the top dose than in the eggs dipped on day 10.	There was a significantly smaller proportion of fertile eggs still viable at Day 19 in the top dose than in the eggs sprayed on day 4. The effect was detected for averages of sprayed eggs.
No of embryos alive on Day 19 as a proportion of the total set	No adverse effects were noted.	There was a significantly smaller proportion of alive embryos on day 19 as a proportion of those set in the top dose sprayed on day 4. The effect was detected for averages of sprayed eggs.

Hakin and Chanter (1988)

Paraquat was sprayed directly onto the eggs of pheasant, *Phasianus colchicus*, prior to incubation, at rates between 0.25 and 4.0 kg paraquat ion/ha in a spray volume of 200 l/ha. The study authors considered that late deaths were not attributable to paraquat and removed these from the analysis. Therefore, the assessment of effects was based on early embryo deaths. After the results had been corrected for control mortality, there was 24% and 100% mortality in the 2.0 kg/ha and 4.0 kg/ha application regimes respectively. The percentage of eggs which hatched indicated that the LD50 was between 2 and 4 kg/ha; 2 kg/ha had no effect on hatchibility. Chicks which hatched were dissected for examination of the reproductive organs. Right Mullerian ducts in all females were all vestigial, which is normal in birds, and no Mullerian ducts persisted in males. The left Mullerian duct in females was normal. No abnormalities in the gross structure of the gonads were noted in either sex.

Newman and Edwards (1980)

The Notifier submitted an extract from the above publication which summarised a trial where pheasant eggs were sprayed. The summary lacked detail, however the results are presented below in Table 4.

Table 4: Results of spraying pheasant eggs with Gramoxone without a wetting agent

Group no	No of eggs	Treatment	Infertile eggs	Early dead germ	Dead in shell	Hatched
1	100	Not sprayed	10	9	33	48
2	80	1.12 kg/ha	9	28	30	13
3	80	2.24 kg/ha	7	67	6	0

Eggs sprayed at 1.12 kg/ha had a concentration of 2.6 mg/kg in the shell, 0.33 mg/kg in the white and 0.10 mg/kg in the yolk. Eggs sprayed at 2.24 kg/ha had a concentration of 5.7 mg/kg in the shell, 1.3 mg/kg in the white and 0.10 mg/kg in the yolk. In a subsequent trial eggs were sprayed at the same rate, however a wetting agent was used. The results are presented in Table 5.

Table 5: Results of spraying pheasant eggs with Gramoxone with a wetting agent

Group no	No of eggs	Treatment	Infertile eggs	Early dead germ	Dead in shell	Hatched
1	100	Not sprayed	5	8	39	48
2	80	1.12 kg/ha	4	9	13	12
3	80	2.24 kg/ha	6	27	9	6

Analysis of the shell indicated that the residue was 17 mg/kg, whilst the ‘egg contents’ were 0.23 mg/kg.

Blank (1967/8)

Risk assessment

The studies indicate that at twice the application rate there was an overall reduction in the egg hatchability for the mallard duck and pheasant. The NOEC from these studies was equivalent to 1.12 kg/ha. The Japanese quail study indicated that there were no effects on egg hatchability at rates up to 3.0 kg a.s./ha. A study was submitted which compared the hazard of over spraying and dipping eggs (see Hankin and Chanter 1988). This study indicates that the hazard of dipping is greater compared to sprayed, (i.e. the NOEC from dipping was equivalent to 1.2 g a.s./l compared to a NOEC from spraying of 5.6 g a.s./l.).

Of the uses listed in the notifier's document "Summary of main use patterns for paraquat" (given as an Appendix to this document), the following uses are considered to pose a low risk due to the time of application – treatment of dormant lucerne, treatment of weeds in stubble prior to cultivation and land prior to cultivation. Furthermore the uses on lucerne following cutting and the use on land prior to cultivation are considered to pose a negligible risk to ground nesting birds due to disturbance by machinery. Likewise, the use of paraquat as a chemical pruner is unlikely to pose a risk due to the low probability of exposure. In addition, not all of the use situations outlined in the Appendix are considered suitable habitats for ground nesting birds. For example, it is highly unlikely for ground nesting birds to nest in orchards, olive groves or vineyards. Therefore, the RMS considers that the use of paraquat in these situations will pose a negligible risk to ground nesting birds.

Of the uses listed in the Appendix the following are considered possible suitable habitats for ground nesting birds:

?? treatment of early weed growth following cultivation and
?? treatment of inter-row in vegetable crops.

Whilst, the above habitats <u>may</u> be suitable, there is a lack of information available to the RMS to indicate whether they are in fact used by ground nesting birds and to what extent. This information will be MS specific and hence the risk should be determined at a MS level.

In conclusion, the NOEC from the studies submitted on the development of eggs is approximately equivalent to the maximum field rate, i.e. the NOEC from the studies is 1.12 kg paraquat/ha, whereas the application rate is 1.1 kg paraquat/ha. At an application twice the proposed maximum rate, adverse effects on hatchability have been observed.

It should be noted that this route of exposure is not normally considered in the risk assessment carried out under 91/414/EEC. Hence there is not a standard risk assessment model or appropriate Annex VI trigger value.

To conclude there are several situations where exposure to ground nesting birds will be negligible and hence the risk acceptable. However, there are certain uses where exposure may occur and it is proposed that the risk be assessed, and if necessary managed, at MS level.

Question 4 (b)

Can the Committee comment on the risks the intended uses might pose to hares?

Opinion of the Committee:

As regards the risk to hares, the SCP concluded that paraquat can be expected to cause lethal and sublethal effects for hares, and this is confirmed by field reports. However, the available data are inadequate to estimate the proportion of hares affected.

Further RMS consideration - question 4 (b)

The Notifier has responded to the SCP Opinion (see Syngenta covering letter headed "Paraquat: EU Review under Council Regulation 3600/92; Comments on the SCP Opinion published in January 2002" and attached document, dated 19 March 2002).

The RMS agrees with the SCP conclusion that paraquat can be expected to cause lethal and sublethal effects for hares. The SCP highlights the lack of data to estimate the proportion of hares affected. The Notifier has provided a further argument (see Syngenta covering letter headed "Paraquat: EU Review under Council Regulation 3600/92; Comments on the SCP Opinion published in January 2002" and attached document, dated 19 March 2002) which outlines why they consider that the incident data submitted provide a realistic indication of the number of incidents involving hares and paraquat. In addition to this the Notifier has submitted further studies on paraquat and these are summarised below.

These studies were cited in Edwards *et al* (2000). This paper was previously considered in detail by the RMS and an assessment included in their Addendum of 2001. The SCP also considered the paper by Edwards *et al*.

Data evaluation

NOTE – the following two studies were cited in Edwards et al (2000). This paper was previous considered in detail by the RMS in their Addendum of 2001.

Groups of two rabbits, given a single oral dose of 2, 4, 8 or 12 mg paraquat ion/kg showed no observable signs of toxicity over a 10 day period. Following a 16 mg/kg dose one rabbit showed some inappetence over the initial four days which then returned to normal. Inappetence was more marked following doses of 20 and 24 mg/kg paraquat with loss of body weight in one rabbit at 24 mg/kg, some haematuria was seen in this animal on day 8 after dosing. Increasing the dose to 30 mg/kg led to both animals not eating over the first two days. Four rabbits were dosed with 40 mg/kg paraquat, and these stopped eating over the first few days and then gradually consumed small quantities over the following days. One rabbit died on day 3. Body weight ranged from 11-13%. Following dosing at 50 mg/kg paraquat one rabbit died and another was terminated on day 3 while the remaining were terminated on day 8. The median lethal dose for paraquat to rabbits was determined to be between 40-50 mg paraquat ion/kg bw.

A single oral dose of 2 mg/kg paraquat ion resulted in no treatment related effects on organs. Details of tissue concentrations are presented in table 5 below. A single dose of 30 mg/kg paraquat resulted in multifocal regions of necrosis in the proximal tubule with the presence of tubular dilation and luminal casts. Details of tissue concentrations are presented in table 5.

Table 5: Tissue paraquat concentration (µg/g wet weight) and plasma paraquat (µg/ml) at various times following a single oral dose of 2 or 30 mg/kg paraquat ion.

Tissue	1 hour	4 hours	24 hours	48 hours	72 hours	168 hours
2 mg/kg						
Liver	n.d.	n.d.	n.d.	n.d.	n.d.	0.029
Lung	n.d.	n.d.	n.d.	n.d.	n.d.	0.076
Kidney	n.d.	n.d.	n.d.	n.d.	n.d.	0.023
Plasma	n.d.	n.d.	n.d.	n.d.	n.d.	<lod
30 mg/kg						
Liver	3.76	2.16	1.48	1.75	1.94	n.d.
Lung	1.85	1.48	1.23	1.12	1.00	n.d.
Kidney	14.71	3.03	1.23	2.48	2.67	n.d.
Plasma	5.39	2.01	0.35	0.11	0.48	n.d.

Farnworth *et al* (1993)

A rectangular plot 40 m by 80 m was fenced off in a wheat field by a wire netting fence 2 m high. It was protected on the outside by an electric fence. The enclosure was then divided in its length so as to provide on one side an acclimatization enclosure and on the other side 8 plots each measuring 20 m by 10 m. Four mobile shelters were set long the median fences. These, together with trough of pellets, were always available to the hares. The first trial was conducted with 4 'fairly old' hares, whilst the second trial involved six hares. One of the hares was incapable of running normally. A total of 4 treatments were used – (i) control water only, (ii) 'Gramoxone', (iii) sulphate of ammonia applied at 20 kg/ha and (iv) 'Gramoxone 2' at 2.5 l/ha together with 20 kg/ha sulphate of ammonia. All treatments were carried out as sprays and were applied on the basis of 200 l/ha. Animals were introduced once the spray deposits had dried. During each trial an assessment of feeding was made by counting the number and height of wheat tillers present in the plots.

Each trial involved an adaptation period of 10 days whilst the trial lasted 3 days. The first trial took place under very wet conditions, whereas the second trial was under 'good weather' conditions.

Of the four hares used in the first trial one died prior to being moved to the treated plot, whilst the remaining 3 died after returning to the post-treatment breeding cage. After post-mortem it was concluded that their death was due to infection (coccidiosos). As regards the second trial one of the six hares died as a result of shock, however of the five remaining no adverse effects were observed. Examination of the buccal mucous membranes of the 5 surviving hares noted no signs of ulceration. An assessment the foraging behaviour indicated that from both trials between 4.38-12.8% of tillers were grazed in the control treatment (i), compared to 0.08-3.43% in treatment (ii), 0-0.17% in treatment (iii) and 0-0.2 in treatment (iv). The 'Gramoxone 2' formulation reduced the number of shoots severed quite significantly from the first day even under rainy conditions. Higher consumption was observed in trial 1 from treatments (ii) and (iii) compared to trial 2. The study author considered that this was due to the wet weather adversely affecting the repellency of the compounds used.

The trial was poorly reported and lack detail regarding certain aspects, e.g. detailed weather records were not provided, no details of quantity of additional food provided and to what extent this was consumed etc.

Lagaude H. (1980)

The study demonstrates that ammonium sulphate can be used to avoid hare fatalities during applications of paraquat.

This report was presented in French, however the summary was in English.

Grolleau (1981)

Risk assessment

The study by Lagaude (1980) indicates that hares will avoid vegetation that has been treated with ammonium sulphate. The paper by Farnworth *et al* (1993) provides reassurance that the rabbit is of similar sensitivity to paraquat as the rat. The Notifier uses this paper to give reassurance that the incidents considered by both the UK Wildlife Incident Investigation Scheme (WIIS) and the French SAGIR scheme were assessed and categorised appropriately.

Regarding the risk to hares from the intended uses of paraquat, it is considered likely that a route of exposure will be via the consumption of treated foliage in an arable situation. This is due to the fact that hares will tend to inhabit arable environments in preference to orchards or vineyards etc.

Potential exposure via dermal penetration and/or grooming exists wherever paraquat is used and hares occur. The dermal LD50 for paraquat in rats is approximately 200 mg/kg bw (lowest value in original monograph). The oral LD50 for 'hares' is approximately 35 mg/kg (see Section 8.3.1 of the original monograph) Therefore, the oral route of exposure is probably a more sensitive route of exposure compared to the dermal route. If it is assumed that a hare has a surface area of approximately 3000 cm^2 and weighs 3 kg, then estimated exposure via grooming is approximately 10 mg/kg bw. This estimation assumes that the hare is totally covered by sprayed paraquat and then removes all applied paraquat during grooming. According to the original monograph a hare consuming treated vegetation would take in approximately 20.5 mg/kg bw. Therefore, based on this crude estimate described above, exposure via the consumption of treated food poses a higher risk than grooming.

Incidents have been reported following the use of paraquat on stubbles (UK), potatoes (UK) and lucerne (FR). Of these uses the use on lucerne and stubbles is highlighted as intended uses in the Appendix, whereas the use on potatoes is not an intended use. The analysis of the incident data would have covered all routes of exposure, dermal, consumption of treated vegetation and grooming.

When the SCP considered the risk to hares, they concluded that it was not possible to estimate the number of hares affected by the use of paraquat. In order to provide information to address this issue, the RMS proposes to concentrate on the use of paraquat on stubbles in the UK. This scenario has been selected as (i) this use was considered to have resulted in incidents in the 1960s, (ii) data on the usage of paraquat on stubbles in the UK are available and (iii) it is an intended use (see Appendix).

Data from the UK Pesticide Usage Survey Group (stratified survey conducted by interview) indicate that in the year 2000, paraquat was used between August and October on stubbles on 10834 ha. This compares to a total area of cereals grown in the UK of 2662013 ha (i.e. 0.4% of total cereal area). On individual farms sampled in 2000 that used paraquat on stubbles, the area treated ranged from 0.46-18.9% of the total arable area farmed. Therefore, it can be seen that the actual area of stubbles treated with paraquat is low and the percentage of a total farm treated is also relatively low. The usage of paraquat on stubbles is low due to reseeding immediately after harvest as well as the availability of alternative herbicides.

Data from Corbet and Harris (1991) indicate that the density of hares on farmland in England range from 1.5 to 147.0 hares per km squared, equivalent to 0.015 to 1.47 hares/ha. It is not known whether the fields treated in 2000 were representative of all fields, or were rich in hares or had low hare numbers. However, if as a worse case example, it is assumed that all the stubbles treated in 2000 contained hares at the highest density, then this would equate to approximately 1.3 to 1.9% of the UK population (see http://www.ukbap.org.uk for details of population levels). It should be noted that exposure in the field does not equate with death. No incidents have been reported to the UK WIIS from this use since 1974 (see Edwards *et al* 2000).

The SCP outlined that on the basis of the available data it was not possible to estimate the proportion of hares affected. Outlined above is a very crude estimate of the number of hares that may be exposed to paraquat used on stubbles in the UK. This is less than 2% of the total population. It is clear that potential exposure does not lead to death, as spray application may occur when hares are not present in the field (see below). It is assumed that if large numbers of hares were being killed by paraquat then some would be reported. This was the case in the 1960s, however no incidents have been reported following this use since the implementation of risk management measures.

When incidents first occurred in the UK, risk management measures were taken to reduce exposure and hence risk to hares (See RMS original monograph section 8.3.2 (a) (i)). These measures took the form of label instructions on when best to spray, for example the UK label carries the following phrase: ‘Paraquat may be harmful to hares. Where possible spray stubbles early in the day.’

The Notifier and the SCP have both outlined possible ways to manage the risk to hares. For example:

(a) no aerial spraying (to avoid over spraying);

(b) to spray in the early morning, to prevent hares from being exposed to paraquat before it has dried, as hares are active mainly at night;

(c) to add a repellent, if it is effective against hares e.g. ammonium sulphate;

(d) avoid spray patterns which would trap hares within the spray area e.g. spray from the centre of the field outwards;

(e) avoid spraying the whole field with paraquat on the same day if there is no alternative forage adjacent to the sprayed field.

It is proposed by the RMS that due to the specific nature of this risk, for example, hares that graze stubbles, that the risk to hares should be determined at Member State level and, if necessary, managed appropriately.

References – alphabetical by author

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SUMMARY OF MAIN USE PATTERNS FOR PARAQUAT

Paraquat is a non-selective herbicide and its uses are described most clearly by reference to agricultural activity rather than specific crops. Paraquat is used when a very broad spectrum of weeds needs to be treated rapidly to permit the farmer to progress to the next activity within a few days. Paraquat is a contact herbicide and therefore is most effective on small annual weeds.

Maximum single application rate	1.1 kg paraquat ion/ha (1 application per season)
Typical application rate	0.6 – 0.8 kg paraquat ion/ha

Use pattern	**Weeds status**	**Timing of application**
Land preparation prior to cultivation or direct drilling ('Spring cleaning')	No crop present, only volunteers/weeds germinating after autumn harvest	February – March
Treatment of early weed growth following cultivation and seed sowing, prior to crop emergence (arable and vegetable crops)	No crop present, only volunteers/weeds germinating after autumn harvest	February – April
Treatment of early weed growth following cultivation and seed sowing, prior to crop emergence (potatoes) (up to 10% emergence permitted, but use primarily pre-emergence)	No crop present, only volunteers and weeds germinating after harvest in the autumn	April – May
Treatment inter-row in vegetable crops (shielded spray to avoid crop)	Crop present (but not treated), only new spring weed growth	Exact timing is dependent on location
Treatment of weeds in orchards, vines and tree nurseries (around base of trees). Typically a strip beneath the trees are sprayed and inter-rows are left vegetated	Crop present but not treated	June – July
Treatment of weeds in olives (around base of trees), inter-row areas may be treated or untreated depending on farming practice	Crop present but majority not treated	Oct - Dec (Southern Member States)
Chemical pruning of suckers e.g. vines and strawberries	Crop present, only suckers are treated	May – June
Treatment of weeds in stubble prior to cultivation and sowing winter cereal	Stubble with cereal volunteers and weeds treated	September – October
Treatment of dormant Lucerne (alfalfa) prior growth for silage	Lucerne crop present and treated Note: Alfalfa canopy presents a low density at this stage. Most of the time alfalfa is grown in areas where cereals are a majority	January - February
Treatment of Lucerne immediately after cutting	Lucerne crop present and treated	April - May