

REPORT TITLE

**A RANDOMISED DOUBLE BLIND ASCENDING SINGLE ORAL DOSE STUDY WITH
MALATHION TO DETERMINE THE NO EFFECT LEVEL ON PLASMA AND RBC
CHOLINESTERASE ACTIVITY**

DATA REQUIREMENTS

Not applicable

AUTHORS

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PERFORMING LABORATORY

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REPORT COMPLETION DATE

20 March 2000

SPONSOR

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SPONSOR'S REPRESENTATIVE/SUBMITTER

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1525 Wilson Boulevard
Suite 600
Arlington, VA 22209
USA**

LABORATORY PROJECT ID

ICR 013177

Volume 2 of 3

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APPENDIX B

Ethics Committee Constitution and Approvals Written Volunteer Information and Sample Consent Forms

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INDEPENDENT INVERESK RESEARCH ETHICS COMMITTEE - CONSTITUTION

The constitution of the Independent Inveresk Research Ethics Committee is as follows:

1. The Inveresk Research Ethics Committee is an *ad hoc* committee of independent advisors comprising a panel of consultant physicians and surgeons, general practitioners, lay persons (including ministers of religion) and nurses. Their function is to advise Inveresk Research on the ethical acceptability of clinical research.
2. A quorate Committee comprises a minimum of 5 members which must include medical practitioners and at least one lay member. Both sexes must be represented.
3. The normal composition of a Committee is 4 medical practitioners (to include 2 general practitioners and 2 consultants or equivalent), a lay member and a nurse.
4. A panel of nominated members who are willing to act as Chairmen is used. The Chairman is selected prior to each meeting and must be medically qualified.
5. The Committee meets at an appropriate venue to consider protocols. However, written comments from members can be used, exceptionally, for discussion purposes and for determining whether the meeting is quorate.
6. The Committee may invite specialist advisors to assist in determining the ethical suitability of a particular protocol, if required.
7. The Regulatory Affairs Department of Inveresk Research provides administrative assistance in the organisation of the Committee.

Date: 29 April 1997



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REGISTERED IN SCOTLAND NUMBER 91725



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INDEPENDENT INVERESK RESEARCH ETHICS COMMITTEE

The "Inveresk Research Ethics Committee" is completely independent of "Inveresk Research" and no member of the Committee is employed by the company. The Committee comprises of a panel of consultant physicians/surgeons, general practitioners, lay persons (including ministers of religion) and nurses. There are currently 36 members on the panel. There are 12 consultants (11 male, 1 female), 11 GPs (7 male, 4 female), 6 nurses (all female), 7 lay members (5 female, 2 male). The Committee adheres to the guidelines set down in the "Note for Guidance on Good Clinical Practice" (CPMP/ICH/135/95). Inveresk Research retains all relevant records (ie written procedures, memberships lists, lists of occupations/affiliations of members, submitted documents, minutes of meetings and correspondence), and would present them to the appropriate regulatory authorities on request.

SECRETARY: Sharon C Fisk DATE: 29-10-98



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ETHICS COMMITTEE MEETING

Tuesday 11 August 1998

"A randomised, double blind, ascending single oral dose study with malathion to determine the no effect level on plasma and RBC cholinesterase activity" (Draft 1 - 22 July 1998)

Jellinek, Schwartz & Connolly Inc (Cheminova), 1525 Wilson Boulevard, Suite 600,
Arlington, VA 22209, USA
Inveresk Project No: 961578
ICR Project No: 013177

Present:

Dr T M Chalmers MB ChB FRCP (Ed) (Consultant, Chair)
Dr G Smart FRCOG FRCSE (Consultant)
Dr L McSwan MB ChB D(Obst)RCOG (GP)
Dr J L Reeks MB ChB D(Obst)RCOG (GP)
Mrs A Campbell BSc (Hons) DIP (Nurse)
Mrs E Watson (Lay)

In attendance:

Ms S L Foster BSc (Hons) MSc (Secretary)



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REGISTERED IN SCOTLAND NUMBER 0176



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ETHICS COMMITTEE MEETING

11 August 1998

"A randomised, double blind, ascending single oral dose study with malathion to determine the no effect level on plasma and RBC cholinesterase activity" (Draft 1 - 22 July 1998)

Jellinek, Schwartz & Connoily Inc (Cheminova), 1525 Wilson Boulevard, Suite 600,
Arlington, VA 22209, USA
IRI Project No: 961578
ICR Project No: 013177

The Ethics Committee met on 11 August 1998 and approval has been granted provided that the points raised are addressed, or incorporated into a final protocol.

Secretary: Sharon L Foster Date: 29-9-98
Sharon L Foster

Chairman: Dr T M Chalmers Date: 30-9-98
Dr T M Chalmers



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REGISTERED IN SCOTLAND NUMBER 0175

ICR Study No: 013177 (Draft 1 - 22 July 1998)

GENERAL

The Chairman gave a brief review of the study.

Documents reviewed at the Ethics Committee Meeting were:

Volunteer Information/Informed Consent
Letter/Questionnaire to the Volunteer's GP
Clinical Protocol
Toxicology Review on Malathion

General Comments

- The Ethics Committee did not like the 'leading' design of this protocol. The study design is therefore being revised to incorporate a single cohort protocol style and *will be resubmitted in the near future.*
- The Committee were worried about the three fold jump in dose from 1.5 to 5.0 mg.kg⁻¹. An explanation of why these doses were chosen would be useful.

Questions asked by Clinical Investigator

- **Should the volunteers see the Toxicology Summary?**
The committee felt that the toxicology summary did not need to be shown to volunteers as long as the Ethics Committee are reviewing it.
- **Are there any objections to the toxicology summary being submitted as a separate document?**
There are no objections to the toxicology summary being submitted as a separate document.
- **Should the volunteers be given the results of long term, high exposure studies of compounds such as malathion in animals, even though they are not entirely relevant to a single dose study in humans?**
Yes.

VOLUNTEER INFORMATION

General

Smokers are excluded from this study (see Exclusion Criteria, page 17 of 67 in the protocol). Include a sentence which informs the volunteers that they must be non-smokers.

The medical risks of withdrawing from the study early should be given in the volunteer information (see page 18 of 67, para 2, line 1).

Specific

Page 45 of 67, para 5, line 1: Insert, "Your GP will be informed of your inclusion in this study".

Page 45 of 67, para 7, line 2: delete the word "a" and insert an "s" after "blood sample".

PROTOCOL

Page 14 of 67, para 5: the Committee felt that any significant changes in inhibition from baseline of red cell cholinesterase should not result in dose escalation. If a limit has to be set, please explain the rationale behind that level.

TOXICOLOGY REVIEW

Page 65 of 67, para 2, line 1: No details are given of how the malathion impurities Independent Inveresk Research Ethics Committee

ICR Study No: 013177 (Draft 1 - 22 July 1998)

were extracted from the early material. How is it known that these contaminants and break down products exaggerated malathion toxicity? More details are required. Page 66 of 67, para 7, line 2: the committee would like more details of the repeat oral dose study, including the number of volunteers that took part.

CONCLUSION

In conclusion, the protocol is being revised to incorporate a single cohort style of study. The points raised above should be addressed or incorporated into the revised protocol.

Secretary: Sharon L Foster Date: 11-8-98
Sharon L Foster

Chairman: J. M. Chalmers Date: 13.8.98
Dr T M Chalmers

Independent Inveresk Research Ethics Committee



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ETHICS COMMITTEE MEETING

11 August 1998

"A randomised, double blind, ascending single oral dose study with malathion to determine the no effect level on plasma and RBC cholinesterase activity" (Draft 2 - 21 August 1998)

Jellinek, Schwartz & Connolly Inc (Cheminova), 1525 Wilson Boulevard, Suite 600,
Arlington, VA 22209, USA
IRI Project No: 961578
ICR Project No: 013177

The Ethics Committee met on 11 August 1998 and approval has been granted provided that the points raised are addressed, or incorporated into a final protocol.

Secretary: Sharon L Foster Date: 12-10-98
Sharon L Foster

Chairman: Dr T M Chalmers Date: 13.10.98.
Dr T M Chalmers



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Addendum to Ethics Committee Minutes

Meeting of 11 August 1998

"A randomised double blind, ascending single oral dose study with malathion to determine the no effect level on plasma and RBC cholinesterase activity" (Final - 19 October 1998)"

Jellinek, Schwartz & Connolly Inc. (Cheminova), 1525 Wilson Boulevard, Suite 600,
Arlington, VA 22209, USA
Inveresk Project No: 961578
ICR Project No: 013177

The final protocol for the study detailed above has now been issued by ICR. This also addresses changes requested by the Ethics Committee.

The Chairman reviewed the attached documentation and gave it his approval.

Secretary: Sharon L Foster Date: 22-10-98
Sharon L Foster

Chairman: J. M. Chalmers Date: 29-10-98
Dr T M Chalmers



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Addendum to Ethics Committee Minutes

Meeting of 11 August 1998

"A randomised, double blind, ascending single oral dose study with malathion to determine the no effect level on plasma and RBC cholinesterase activity" (Amendment 1 - 3 November 1998)"

Jellinek, Schwartz & Connolly, Inc (Cheminova), 1525 Wilson Boulevard, Suite 600,
Arlington, VA 22209, USA
Inveresk Project No: 961578
ICR Project No: 013177

Amendment 1 for the study detailed above has now been issued by ICR.

The Chairman reviewed the attached documentation and gave it his approval.

Secretary: Sharon L Foster Date: 3/11/98
Sharon L Foster

Chairman: Dr T M Chalmers Date: 4. 11. 98
Dr T M Chalmers



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Addendum to Ethics Committee Minutes

Meeting of 11 August 1998

"A randomised, double blind, ascending single oral dose study with malathion to determine the no effect level on plasma and RBC cholinesterase activity" (Amendment 2 - 20 January 1999)"

Jellinek, Schwartz & Connolly (Cheminova), 1525 Wilson Boulevard, Suite 600,
Arlington, VA 22209, USA
Inveresk Project No: 961578
ICR Project No: 013177

Amendment 2 of the study detailed above has now been issued by ICR.

The Chairman reviewed the attached documentation and gave it his approval.

Secretary: Sharon L Foster Date: 28-1-99
Sharon L Foster

Chairman: J. M. Chalmers Date: 29.1.99.
Dr T M Chalmers



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MEMORANDUM

Date: 28 May 1999

To: Janet Dickson, Diane Gillies, AJR

c.c.: Central Files - Jellinek, Schwartz & Connolly (Cheminova), 1525
Wilson Boulevard, Suite 600, Arlington, VA 22209, USA
Inveresk Project No: 961578 - Ethics Committee File (original)
ICR Project No: 013177

From: Mary Pupkis

Subject: "A randomised, double blind, ascending single oral dose
study with malathion to determine the no effect level on
plasma and RBC cholinesterase activity" (Amendment 3 - 29
March 1999)

Amendment 3 for the study detailed above will not be sent to the Ethics Committee Chairman. This is because the changes do not affect the safety of the volunteers. Please accept my apologies for the administrative delay in responding to this Amendment.

Kind regards



Mary Pupkis

MEMORANDUM

Date: 20 September 1999

To: Diane Gillies, Steve Freestone

c.c.: Central Files: Jellinek, Schwartz 7 Connolly Incorporated, 1525
Wilson Boulevard, Suite 600, Arlington, VA 22209, USA
ICR Project No: 013177 - Ethics Committee Files (Original)

From: Susan Wilkie

Subject: "A Randomised Double-Blind Ascending Single Oral Dose
Study with malathion to Determine the No Effect Level on
Plasma and RBC Cholinesterase Activity" Amendment 4 - 06
September 1999

Amendment 4 of the study detailed above has no affect on the volunteers' as the clinical phase is complete. No review or approval is required from the Ethics Committee Chairman.

Kind regards



Susan Wilkie



Susan Wilkie

17/12/99 12:33

To: Diane Gillies/OA41/Riccarton/GB/Inveresk@Inveresk, Steve
Freestone/Executive/GB/Inveresk@Inveresk, Nichola
Erskine/OA14/Tranent/GB/Inveresk@Inveresk

cc:
Subject: Cheminova Study Number 013177 Amendment 5

Amendment 5 for the Cheminova Study 013177 has not been sent to the Ethics Committee Chairman for his approval as this amendment contains only administrative changes.

Kind regards

Susan Wilkie
Secretary to the Ethics Committee

Tel: +44 (0) 1875 618 196
e-mail: susan.wilkie@inveresk.com

ICR 013177 - FINAL - 19 OCTOBER 1998

APPENDIX A

Volunteer Consent Form

This agreement is between the volunteer _____ and Inveresk Clinical Research Limited (hereinafter referred to as ICR), and provides for the volunteer to take part in experiments, trial and/or tests of a chemical compound or compounds.

FOR ALL STUDIES

- 1) I, the undersigned voluntarily agree to take part in

Protocol No: 013177

Descriptive Study Title: A randomised double blind ascending single oral dose study with malathion to determine the no effect level on plasma and RBC cholinesterase activity.

I understand that the investigation will involve the administration of

Name(s) of compounds: Malathion

being the compound under test.

- 2) I have been given a full explanation by Dr _____ of the nature, purpose and likely duration of the study and what I will be expected to do and I have been advised about any discomfort and possible ill-effects on my health or well-being which he/she believes may result. The information document given to me is attached (Appendix A pages 49 of 69 to 52 of 69).
- 3) I have been given the opportunity to question Dr _____ on aspects of the study and have understood the advice and information given as a result.
- 4) I agree to Dr Freestone contacting my general practitioner (and teaching or university authority if appropriate) to make known my participation in the study and I authorise my general practitioner to report details of my relevant medical or drug history, in confidence.

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APPENDIX A (Continued)

- 5) I agree to comply with any instruction given during the study and to cooperate faithfully with Dr Freestone and to tell him immediately if I suffer from any deterioration of any kind in my health or well-being or any unexpected or unusual symptoms however they may have arisen.
- 6) I agree that I will not seek to restrict the use to which the results of the study may be put and, in particular, I accept that they may be disclosed to regulatory authorities for compounds in the UK and elsewhere.
- 7) I understand that I am free to withdraw from the study at any time without needing to justify my decision.
- 8) *The supervising doctor confirms that subject to overriding requirement of law necessitating the disclosure of documents relating to the study, the volunteer will not be referred to by name in any document concerning the study disclosed to any person not under the direct control of the supervising doctor;*
- 9) ICR confirms that:
 - (i) I shall receive in consideration for completing the study, the sum of £450 from the supervising doctor and that I shall receive the sum in full if it is necessary for me to withdraw from the study for medical reasons associated with participation in it. If I withdraw from the study for medical reasons not associated with the study a payment will be made to me proportional to the length of the period of participation, but if I withdraw for any other reason, the payment to be made, if any, shall be at the discretion of the supervising doctor;

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APPENDIX A (Continued)

- (ii) In the event of my suffering any bodily injury caused directly by my participation in the study, compensation will be paid to me by the company without having to prove that the injury arose through negligence or that the study compound was defective as set forth in the Association of the British Pharmaceutical Industry "Guidelines for medical experiments in non-patient human volunteers".
- (iii) The amount of such compensation shall be calculated by reference to the amount of damages commonly awarded for similar injuries by an English court if liability is admitted, providing that such compensation may be reduced to the extent that I, by reason of contributory fault through my actions or my failure to act, am partly responsible for the injury.
- (iv) Any dispute or agreement as to the application of clause 9 (ii) shall be referred to an arbitrator to be agreed between myself and the company, or in the absence of agreement, to be appointed by the President of the Royal College of Physicians of London with power in the arbitrator to consult a barrister of 10 years standing in respect of any issue of law including the amount of damages to be awarded as payment of compensation;
- (v) The agreement shall be construed in accordance with English law and subject to clause 9 (ii), (iii) and (iv) above the English courts shall have sole jurisdiction over any dispute which may arise out of it.

ICR 013177 - FINAL – 19 OCTOBER 1998

APPENDIX A (Continued)

Signed by the volunteer :

Dated :

Signed for on behalf
of the company by
its duly authorised
representative:

Dated :

I confirm that I
have explained the
nature, purpose and
possible hazards of
the above trial to :

Signed :

Dated :

I confirm that I have witnessed the above explanation :

Signed :
Witness Signature

Dated :

(NB-It may be appropriate for the supervising doctor to fulfil the obligations of the
duly authorised representative for the company.

Since signing the consent, the volunteer information sheet has been changed. I confirm
that I have read the revised information (dated / /) and still consent to participation in
the study.

Signed :

Dated :

ICR 013177 - FINAL - 19 OCTOBER 1998

APPENDIX A (Continued)Volunteer Information**A RANDOMISED DOUBLE BLIND ASCENDING SINGLE ORAL DOSE STUDY WITH MALATHION TO DETERMINE THE NO EFFECT LEVEL ON PLASMA AND RBC CHOLINESTERASE ACTIVITY.**Introduction

You are invited to take part in a study involving a pesticide called malathion proposed for use in controlling non-beneficial worms and insects which eat the plant leaves or fruit in a variety of fruit and vegetable crops, sugarbeets, cotton and ornamental plants.

Very small amounts of residue may exist at harvest on treated crops. To ensure the safety of these residues for human consumption, many studies have been performed in animals and one human study has already been conducted. These studies showed no side effects other than reducing the amount of an enzyme protein (cholinesterase) which breaks down a chemical substance (acetylcholine) in the body responsible for the transmission of nervous impulses. Large increases of acetylcholine in the nervous system can cause increased salivation, sweating, reduced blood pressure, nausea, vomiting and stomach cramps.

Although the mechanism of action of cholinesterase inhibitors is well understood, species differences do exist. This study is being conducted to reduce the uncertainties of species differences in determining a level of human exposure that causes minimal reduction of blood cholinesterase levels. A significant reduction of cholinesterase in the nervous system is required before any clinical effects are observed. The results of this study will further confirm that the use of malathion does not pose an unreasonable risk to either workers or consumers.

Aim

The aim of the study is to determine the highest dose at which no significant reduction of blood cholinesterase occurs.

Dose

The doses to be given are 0.5, 1.5, 5.0, 10.0 and 15.0 mg.kg⁻¹ body weight and placebo (inactive compound). A maximum of 48 of you will be tested in 7 groups. In the first group, one subject will receive placebo and three subjects the lowest dose of active compound (0.5 mg.kg⁻¹). In the second group, one subject will receive placebo and three subjects will receive 1.5 mg.kg⁻¹. In the third group three subjects will receive placebo and seven subjects will receive 5.0 mg.kg⁻¹. In the fourth group, one subject will receive placebo and three subjects will receive 10.0 mg.kg⁻¹. In the fifth group two subjects will receive placebo, four subjects will receive 10.0 mg.kg⁻¹ and three subjects will receive 15.0 mg.kg⁻¹. In the sixth group three subjects will receive placebo and four subjects will receive 15.0 mg.kg⁻¹. When the maximum dose that causes no significant inhibition of blood cholinesterase in men has been identified, this dose will be given to a group of 10 women (7 to receive active compound and 3 placebo).

Allocation to receive active compound or placebo (inactive compound) will be randomised. The compound or placebo will be administered as capsules by mouth.

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APPENDIX A (Continued)

Volunteer Information

Side Effects

While it is not anticipated that at the low doses to be used, any effects other than a reduced level of blood cholinesterase will occur, information from clinical effects caused by similar compounds at much higher dose levels suggests the following effects are possible:

Initial symptoms are headache and nausea, followed by a feeling of chest tightness and coughing. At dose levels much higher than those being used in this study other possible symptoms include vomiting, diarrhoea, abdominal pain, blurred vision, weakness, sweating, constricted pupils, excess saliva production, slow pulse, and involuntary muscle twitching. It is highly unlikely that any of these effects will occur.

In some animal studies (but not all) it has been shown that lifetime exposure to 1600 mg/kg daily of malathion (is more than 100 times the maximum dose in this study every day for a lifetime) in sensitive species caused an increased incidence of liver cancer. The dose level and duration of treatment bears no relationship to the single low doses to which volunteers will be exposed in this study.

Procedure

You will attend ICR for screening within 21 days of the start of the study. At screening, a complete medical history will be taken and you will have a complete physical examination, recordings of your pulse and blood pressure obtained, an ECG recorded (tracing of your heart's electrical activity) and blood samples taken for various safety tests. Samples of blood will also be taken to test for hepatitis B, hepatitis C and HIV, the virus that can cause AIDS. Urine will also be tested including a test for drugs of abuse.

Your GP will be informed of your participation and asked to confirm your medical history. If there are any objections expressed by your GP you will be excluded from the study.

Once you have successfully passed the screening examination, including acceptable blood and urine test results, your co-operation with the following will be required:

1. Up to a total of 48 of you will be studied.
2. If you smoke you must be able to abstain from smoking from 2h predose to 8h postdose.
3. You will require to attend the clinic for 4 outpatient visits on 9, 7, 5 and 2 days prior to dosing when a when a blood sample will be taken.
4. You will then be resident in the clinic on one occasion for 3 nights and will then return for 3 further outpatient visits 3, 6 and 13 days after dosing.
5. You will be admitted to the clinic between 10am and mid-day on the morning preceding the day of dosing. A brief examination including vital signs will be performed, and a blood sample taken for measurement of cholinesterase. A urine pregnancy test will be undertaken on female subjects. You will take no food or drink from 2300h.

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APPENDIX A (Continued)

Volunteer Information

6. On the day of dosing, you will be given breakfast and 5 min after completion you will receive either the active compound or placebo with 150 ml of water in the sitting position. You will then be required to remain seated or recumbent until 8h after dosing. You will be allowed water, fruit juice or decaffeinated drinks from approximately 3h after dosing. A light lunch will be provided approximately 4h after dosing. Normal activities excluding strenuous exercise will be allowed from approximately 4h after dosing.
7. Before dosing, a cannula (plastic tube inserted by a needle into a vein) will be inserted into your arm in order to allow samples of your blood to be obtained at regular intervals throughout the day of dosing. A needle and syringe can be used repeatedly to obtain blood samples if preferred. Repeated blood tests and cannulae can cause soreness and bruising of the arms or even, rarely, blockage of a vein, but those problems usually clear up within a few days to a few weeks.
8. Blood pressure, heart rate and a tracing of your heart's electrical activity will be recorded at intervals before and after dosing.
9. You will also be monitored for the presence or absence of the clinical signs listed in the introduction. A continuous recording of your heart's electrical activity will be displayed on a bedside monitor from 30mins before dosing to 4h after dosing.
10. You will be discharged 48h after dosing. Before discharge, a physical examination will be performed and blood samples will be taken for safety assessments.
11. You will return to the clinic in the morning 3, 6 and 13 days after dosing when a blood sample will be taken and to ensure continued well-being and for completion of any outstanding enquiry/adverse events.
12. Approximately 235 ml of blood will be taken during the study (compared with 480ml which is a standard blood donation).
13. You should avoid medication (including over-the-counter products) for 5 days before the start of the study.
14. You will not be allowed to take alcohol or other drugs on each resident study day or until after the last blood sample has been taken. It is recommended that you should refrain from alcohol as far as possible until the follow-up visit on Day 14.

If anything abnormal occurs, judged by the supervising clinician, or if laboratory investigations change, you may be withdrawn from the study. In addition, you may withdraw at any time without needing to justify your decision. (You are strongly advised not to leave the clinical unit within 24h after dosing as this may involve risk to your health). If you decide to withdraw before completion of the study a medical examination including blood pressure and heart rate, blood sampling, urine sampling and an ECG will be performed.

You should inform the supervising physician of any symptoms. After the study is over, you will be given a telephone number to call if you have any questions or worries.

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APPENDIX A (Continued)

Volunteer information

It is essential that you should adhere to all of these requirements. The supervising physician will be pleased to supply any further information at any time.

All information will be treated in a confidential manner but anonymised data will be seen by authorised persons involved in the study and possibly by compound regulating authorities.

Supervising Physicians

Dr J Dickson and Dr S Freestone
Inveresk Clinical Research
Riccarton
Edinburgh
EH14 4AP Tel: (0131) 451 5080

ICR 013177 – AMENDMENT 1 – 3 NOVEMBER 1998

APPENDIX A

Volunteer Consent Form

This agreement is between the volunteer _____ and Inveresk Clinical Research Limited (hereinafter referred to as ICR), and provides for the volunteer to take part in experiments, trial and/or tests of a chemical compound or compounds.

FOR ALL STUDIES

- 1) I, the undersigned voluntarily agree to take part in

Protocol No: 013177

Descriptive Study Title: A randomised double blind ascending single oral dose study with malathion to determine the no effect level on plasma and RBC cholinesterase activity

I understand that the investigation will involve the administration of

Name(s) of compounds: Malathion .
being the compound under test.

- 2) I have been given a full explanation by Dr _____ of the nature, purpose and likely duration of the study and what I will be expected to do and I have been advised about any discomfort and possible ill-effects on my health or well-being which he/she believes may result. The information document given to me is attached (Appendix A pages 50 of 70 to 53 of 70).
- 3) I have been given the opportunity to question Dr _____ on aspects of the study and have understood the advice and information given as a result.
- 4) I agree to Dr Freestone contacting my general practitioner (and teaching or university authority if appropriate) to make known my participation in the study and I authorise my general practitioner to report details of my relevant medical or drug history, in confidence.

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ICR 013177 – AMENDMENT 1 – 3 NOVEMBER 1998

APPENDIX A (Continued)

- 5) I agree to comply with any instruction given during the study and to cooperate faithfully with Dr Freestone and to tell him immediately if I suffer from any deterioration of any kind in my health or well-being or any unexpected or unusual symptoms however they may have arisen.
- 6) I agree that I will not seek to restrict the use to which the results of the study may be put and, in particular, I accept that they may be disclosed to regulatory authorities for compounds in the UK and elsewhere.
- 7) I understand that I am free to withdraw from the study at any time without needing to justify my decision.
- 8) The supervising doctor confirms that subject to overriding requirement of law necessitating the disclosure of documents relating to the study, the volunteer will not be referred to by name in any document concerning the study disclosed to any person not under the direct control of the supervising doctor.
- 9) ICR confirms that:
 - (i) I shall receive in consideration for completing the study, the sum of £450 from the supervising doctor and that I shall receive the sum in full if it is necessary for me to withdraw from the study for medical reasons associated with participation in it. If I withdraw from the study for medical reasons not associated with the study a payment will be made to me proportional to the length of the period of participation, but if I withdraw for any other reason, the payment to be made, if any, shall be at the discretion of the supervising doctor.

ICR 013177 – AMENDMENT 1 – 3 NOVEMBER 1998

APPENDIX A (Continued)

- (ii) *In the event of my suffering any bodily injury caused directly by my participation in the study, I may elect to proceed in accordance with the following optional procedure.*
- (a) *Compensation will be paid to me by ICR without my having to prove that the injury arose through negligence or that the study compound was defective as set forth in the Association of the British Pharmaceutical Industry "Guidelines for medical experiments in non-patient human volunteers".*
- (b) *The amount of such compensation shall be calculated by reference to the amount of damages commonly awarded for similar injuries by an English court if liability is admitted, providing that such compensation may be reduced to the extent that I, by reason of contributory fault through my actions or my failure to act, am partly responsible for the injury.*
- (c) *Any dispute or agreement as to the application of clause 9(ii) (a) and (b) may at my option be referred to an arbitrator to be agreed between myself and ICR, or in the absence of agreement, to be appointed by the President of the Royal College of Physicians of London with power in the arbitrator to consult a barrister of 10 years standing in respect of any issue of law including the amount of damages to be awarded as payment of compensation;*
- (d) *The agreement shall be construed in accordance with English law and subject to clause 9(ii) (a), (b) and (c) above the English courts shall have sole jurisdiction over any dispute which may arise out of it.*

ICR 013177 – AMENDMENT 1 – 3 NOVEMBER 1998

APPENDIX A (Continued)

Signed by the volunteer :

Dated :

Signed for on behalf
of ICR by its duly
authorised
representative :

Dated :

I confirm that I
have explained the
nature, purpose and
possible hazards of
the above trial to :

Signed :

Dated :

I confirm that I have witnessed the above explanation :

Signed :
Witness Signature

Dated :

**(NB-It may be appropriate for the supervising doctor to fulfil the obligations of the
duly authorised representative for ICR.**

Since signing the consent, the volunteer information sheet has been changed. I confirm
that I have read the revised information (dated / /) and still consent to participation in
the study.

Signed :

Dated :

ICR 013177 – AMENDMENT 1 – 3 NOVEMBER 1998

APPENDIX A (Continued)Volunteer information**A RANDOMISED DOUBLE BLIND ASCENDING SINGLE ORAL DOSE STUDY WITH MALATHION TO DETERMINE THE NO EFFECT LEVEL ON PLASMA AND RBC CHOLINESTERASE ACTIVITY.**Introduction

Malathion is an organophosphorus (OP) insecticide, one of a family of cholinesterase inhibitor compounds that includes many widely used insecticides. These pesticides have essentially no effects on mammals at sufficiently low levels. At higher levels they reduce the amount of an enzyme (cholinesterase) that breaks down a chemical substance (acetylcholine) in the body that is responsible for the transmission of nerve impulses, with the effect increasing as the dose increases. At yet higher levels, sufficient to reduce considerably the levels of acetylcholine in the nervous system, mild to serious physical effects can result (see the paragraph entitled Side Effects, below). Of all the OP insecticides, malathion has been shown to be among the lowest in acute toxicity (toxicity from a single dose) in animals and humans.

Very small amounts of residues of malathion may exist at harvest on treated crops. To determine whether these residues pose any risk to food consumers, many toxicity studies in animals, and one human study, have already been conducted. The animal studies showed that single doses at levels well above those that will be involved in this study produced no reduction in cholinesterase levels and no toxic effects.

Although the mechanism by which OPs act to inhibit cholinesterase is well understood, differences in behaviour of compounds from species to species do exist. This study is being conducted to reduce the uncertainties of species differences in determining a level of human exposure that causes measured reduction of blood cholinesterase levels. Prior testing has shown that a relatively large reduction of blood cholinesterase is required before any resulting clinical effects are observed. The results of this study are expected to be useful in showing that the use of malathion on crops does not pose health risks to food consumers, and also may be useful in evaluating whether workers who use malathion are thereby at risk.

Aim

The aim of the study is to determine the highest dose at which no significant reduction of blood cholinesterase occurs.

Dose

The doses to be given are 0.5, 1.5, 5.0, 10.0 and 15.0 mg.kg⁻¹ body weight and placebo (inactive compound). A maximum of 48 of you will be tested in 7 groups. In the first group, one subject will receive placebo and three subjects the lowest dose of active compound (0.5 mg.kg⁻¹). In the second group, one subject will receive placebo and three subjects will receive 1.5 mg.kg⁻¹. In the third group three subjects will receive placebo and seven subjects will receive 5.0 mg.kg⁻¹. In the fourth group, one subject will receive placebo and three subjects will receive 10.0 mg.kg⁻¹. In the fifth group two subjects will receive placebo, four subjects will receive 10.0 mg.kg⁻¹ and three subjects will receive 15.0 mg.kg⁻¹. In the sixth group three subjects will receive

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APPENDIX A (Continued)

Volunteer information

placebo and four subjects will receive 15.0 mg.kg⁻¹. When the maximum dose that causes no significant inhibition of blood cholinesterase in men has been identified, this dose will be given to a group of 10 women (7 to receive active compound and 3 placebo).

Allocation to receive active compound or placebo (inactive compound) will be randomised. The compound or placebo will be administered as capsules by mouth.

Side Effects

In view of the low doses of malathion to be used in this study and the results of earlier studies, it is not anticipated that any of the subjects of the study will experience any adverse effects other than a reduced level of blood cholinesterase. However, human studies with other more potent organophosphorus compounds suggest that the following effects can result from sufficiently high doses. Initial symptoms typically are headache and nausea, followed by a feeling of chest tightness and coughing. At dose levels much higher than those being used in this study other possible symptoms include vomiting, diarrhoea, abdominal pain, blurred vision, weakness, sweating, constricted pupils, excessive saliva preparation, slow pulse, and involuntary muscle twitching or spasm. A few reported cases of coma or death from ingestion of large quantities of malathion have been reported. However, the doses that cause these effects are very much higher than the ones to be used in this study. In some animal studies (but not all) it has been shown that lifetime exposure to 1600 mg/kg daily of malathion (ie more than 100 times the maximum dose in this study every day for a lifetime) in sensitive species caused an increased incidence of liver cancer. The dose level and duration of treatment bears no relationship to the single low doses to which volunteers will be exposed in this study.

Procedure

You will attend ICR for screening within 21 days of the start of the study. At screening, a complete medical history will be taken and you will have a complete physical examination, recordings of your pulse and blood pressure obtained, an ECG recorded (tracing of your heart's electrical activity) and blood samples taken for various safety tests. Samples of blood will also be taken to test for hepatitis B, hepatitis C and HIV, the virus that can cause AIDS. Urine will also be tested including a test for drugs of abuse.

Your GP will be informed of your participation and asked to confirm your medical history. If there are any objections expressed by your GP you will be excluded from the study.

Once you have successfully passed the screening examination, including acceptable blood and urine test results, your co-operation with the following will be required:

1. Up to a total of 48 of you will be studied.
2. If you smoke you must be able to abstain from smoking from 2h pre-dose to 8h post-dose.

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APPENDIX A (Continued)

Volunteer information

3. You will require to attend the clinic for 4 outpatient visits on 9, 7, 5 and 2 days prior to dosing when a blood sample will be taken.
4. You will then be resident in the clinic on one occasion for 3 nights and will then return for 3 further outpatient visits 3, 6 and 13 days after dosing.
5. You will be admitted to the clinic between 10am and mid-day on the morning preceding the day of dosing. A brief examination including vital signs will be performed, and a blood sample taken for measurement of cholinesterase. A urine pregnancy test will be undertaken on female subjects. You will take no food or drink from 2300h.
6. On the day of dosing, you will be given breakfast and 5 min after completion you will receive either the active compound or placebo with 150 ml of water in the sitting position. You will then be required to remain seated or recumbent until 8h after dosing. You will be allowed water, fruit juice or decaffeinated drinks from approximately 3h after dosing. A light lunch will be provided approximately 4h after dosing. Normal activities excluding strenuous exercise will be allowed from approximately 4h after dosing.
7. Before dosing, a cannula (plastic tube inserted by a needle into a vein) will be inserted into your arm in order to allow samples of your blood to be obtained at regular intervals throughout the day of dosing. A needle and syringe can be used repeatedly to obtain blood samples if preferred. Repeated blood tests and cannulae can cause soreness and bruising of the arms or even, rarely, blockage of a vein, but those problems usually clear up within a few days to a few weeks.
8. Blood pressure, heart rate and a tracing of your heart's electrical activity will be recorded at intervals before and after dosing.
9. You will also be monitored for the presence or absence of the clinical signs listed in the introduction. A continuous recording of your heart's electrical activity will be displayed on a bedside monitor from 30mins before dosing to 4h after dosing.
10. You will be discharged 48h after dosing. Before discharge, a physical examination will be performed and blood samples will be taken for safety assessments.
11. You will return to the clinic in the morning 3, 6 and 13 days after dosing when a blood sample will be taken and to ensure continued well-being and for completion of any outstanding enquiry/adverse events.
12. Approximately 235 ml of blood will be taken during the study (compared with 480ml which is a standard blood donation).
13. You should avoid medication (including over-the-counter products) for 5 days before the start of the study.
14. You will not be allowed to take alcohol or other drugs on each resident study day or until after the last blood sample has been taken. It is recommended that you should refrain from alcohol as far as possible until the follow-up visit on Day 14.

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APPENDIX A (Continued)

Volunteer information

If anything abnormal occurs, judged by the supervising clinician, or if laboratory investigations change, you may be withdrawn from the study. In addition, you may withdraw at any time without needing to justify your decision. (You are strongly advised not to leave the clinical unit within 24h after dosing as this may involve risk to your health). If you decide to withdraw before completion of the study a medical examination including blood pressure and heart rate, blood sampling, urine sampling and an ECG will be performed.

You should inform the supervising physician of any symptoms. After the study is over, you will be given a telephone number to call if you have any questions or worries.

It is essential that you should adhere to all of these requirements. The supervising physician will be pleased to supply any further information at any time.

All information will be treated in a confidential manner but anonymised data will be seen by authorised persons involved in the study and possibly by compound regulating authorities.

Supervising Physicians

Dr J Dickson and Dr S Freestone
Inveresk Clinical Research
Riccarton
Edinburgh
EH14 4AP Tel: (0131) 451 5080

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APPENDIX A

Volunteer Consent Form

This agreement is between the volunteer _____ and Inveresk Clinical Research Limited (hereinafter referred to as ICR), and provides for the volunteer to take part in experiments, trial and/or tests of a chemical compound or compounds.

FOR ALL STUDIES

- 1) I, the undersigned voluntarily agree to take part in

Protocol No: 013177

Descriptive Study Title: A randomised double blind ascending single oral dose study with malathion to determine the no effect level on plasma and RBC cholinesterase activity.

I understand that the investigation will involve the administration of

Name(s) of compounds: Malathion

being the compound under test.

- 2) I have been given a full explanation by Dr _____ of the nature, purpose and likely duration of the study and what I will be expected to do and I have been advised about any discomfort and possible ill-effects on my health or well-being which he/she believes may result. The information document given to me is attached (Appendix A pages 50 of 70 to 53 of 70).
- 3) I have been given the opportunity to question Dr _____ on aspects of the study and have understood the advice and information given as a result.
- 4) I agree to Dr Freestone contacting my general practitioner [and teaching or university authority if appropriate] to make known my participation in the study and I authorise my general practitioner to report details of my relevant medical or drug history, in confidence.

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APPENDIX A (Continued)

- 5) I agree to comply with any instruction given during the study and to cooperate faithfully with Dr Freestone and to tell him immediately if I suffer from any deterioration of any kind in my health or well-being or any unexpected or unusual symptoms however they may have arisen.
- 6) I agree that I will not seek to restrict the use to which the results of the study may be put and, in particular, I accept that they may be disclosed to regulatory authorities for compounds in the UK and elsewhere.
- 7) I understand that I am free to withdraw from the study at any time without needing to justify my decision.
- 8) The supervising doctor confirms that subject to overriding requirement of law necessitating the disclosure of documents relating to the study, the volunteer will not be referred to by name in any document concerning the study disclosed to any person not under the direct control of the supervising doctor.
- 9) ICR confirms that:
 - (i) I shall receive in consideration for completing the study, the sum of £450 from the supervising doctor and that I shall receive the sum in full if it is necessary for me to withdraw from the study for medical reasons associated with participation in it. If I withdraw from the study for medical reasons not associated with the study a payment will be made to me proportional to the length of the period of participation, but if I withdraw for any other reason, the payment to be made, if any, shall be at the discretion of the supervising doctor.

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APPENDIX A (Continued)

- (ii) In the event of my suffering any bodily injury caused directly by my participation in the study, I may elect to proceed in accordance with the following optional procedure.
- (a) Compensation will be paid to me by ICR without my having to prove that the injury arose through negligence or that the study compound was defective as set forth in the Association of the British Pharmaceutical Industry "Guidelines for medical experiments in non-patient human volunteers".
- (b) The amount of such compensation shall be calculated by reference to the amount of damages commonly awarded for similar injuries by an English court if liability is admitted, providing that such compensation may be reduced to the extent that I, by reason of contributory fault through my actions or my failure to act, am partly responsible for the injury.
- (c) Any dispute or agreement as to the application of clause 9(ii) (a) and (b) may at my option be referred to an arbitrator to be agreed between myself and ICR, or in the absence of agreement, to be appointed by the President of the Royal College of Physicians of London with power in the arbitrator to consult a barrister of 10 years standing in respect of any issue of law including the amount of damages to be awarded as payment of compensation;
- (d) The agreement shall be construed in accordance with English law and subject to clause 9(ii) (a), (b) and (c) above the English courts shall have sole jurisdiction over any dispute which may arise out of it.

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APPENDIX A (Continued)

Signed by the volunteer :

Dated :

Signed for on behalf
of ICR by its duly
authorised
representative :

Dated :

I confirm that I
have explained the
nature, purpose and
possible hazards of
the above trial to :

Signed :

Dated :

I confirm that I have witnessed the above explanation :

Signed :
Witness Signature

Dated :

(NB-It may be appropriate for the supervising doctor to fulfil the obligations of the
duly authorised representative for the company.

Since signing the consent, the volunteer information sheet has been changed. I confirm
that I have read the revised information (dated / /) and still consent to participation in the
study.

Signed :

Dated :

ICR 013177 – AMENDMENT 2 – 20 JANUARY 1999

APPENDIX A (Continued)Volunteer information**A RANDOMISED DOUBLE BLIND ASCENDING SINGLE ORAL DOSE STUDY WITH MALATHION TO DETERMINE THE NO EFFECT LEVEL ON PLASMA AND RBC CHOLINESTERASE ACTIVITY.**Introduction

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Aim

The aim of the study is to determine the highest dose at which no significant reduction of blood cholinesterase occurs.

Dose

The doses that have been given are 0.5, 1.5, 5.0, 10.0 and 15.0 mg.kg⁻¹ body weight and placebo (inactive compound). There has been no significant inhibition of blood cholinesterase in men. A group of women will receive the same dose as the last group of men (15.0mg.kg⁻¹). This will be given to 10 women (7 to receive active compound and 3 placebo).

Allocation to receive active compound or placebo (inactive compound) will be randomised. The compound or placebo will be administered as capsules by mouth.

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APPENDIX A (Continued)Volunteer informationSide Effects

In view of the low doses of malathion to be used in this study and the results of earlier studies, it is not anticipated that any of the subjects of the study will experience any adverse effects other than a reduced level of blood cholinesterase. However, human studies with other more potent organophosphorus compounds suggest that the following effects can result from sufficiently high doses. Initial symptoms typically are headache and nausea, followed by a feeling of chest tightness and coughing. At dose levels much higher than those being used in this study other possible symptoms include vomiting, diarrhoea, abdominal pain, blurred vision, weakness, sweating, constricted pupils, excessive saliva production, slow pulse, and involuntary muscle twitching or spasm. A few reported cases of coma or death from ingestion of large quantities of malathion have been reported. However, the doses that cause these effects are very much higher than the ones to be used in this study. In some animal studies (but not all) it has been shown that lifetime exposure to 1600 mg/kg daily of malathion (ie more than 100 times the maximum dose in this study every day for a lifetime) in sensitive species caused an increased incidence of liver cancer. The dose level and duration of treatment bears no relationship to the single low doses to which volunteers will be exposed in this study.

Procedure

You will attend ICR for screening within 21 days of the start of the study. At screening, a complete medical history will be taken and you will have a complete physical examination, recordings of your pulse and blood pressure obtained, an ECG recorded (tracing of your heart's electrical activity) and blood samples taken for various safety tests. Samples of blood will also be taken to test for hepatitis B, hepatitis C and HIV, the virus that can cause AIDS. Urine will also be tested including a test for drugs of abuse.

Your GP will be informed of your participation and asked to confirm your medical history. If there are any objections expressed by your GP you will be excluded from the study.

Once you have successfully passed the screening examination, including acceptable blood and urine test results, your co-operation with the following will be required:

1. Up to a total of 48 of you will be studied.
2. If you smoke you must be able to abstain from smoking from 2h predose to 8h postdose.
3. You will require to attend the clinic for 4 outpatient visits on 9, 7, 5 and 2 days prior to dosing when a blood sample will be taken.
4. You will then be resident in the clinic on one occasion for 3 nights and will then return for 3 further outpatient visits 3, 6 and 13 days after dosing.

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APPENDIX A (Continued)

Volunteer information

5. You will be admitted to the clinic between 10am and mid-day on the morning preceding the day of dosing. A brief examination including vital signs will be performed, and a blood sample taken for measurement of cholinesterase. A urine pregnancy test will be undertaken on female subjects. You will take no food or drink from 2300h.
6. On the day of dosing, you will be given breakfast and 5 min after completion you will receive either the active compound or placebo with 150 ml of water in the sitting position. You will then be required to remain seated or recumbent until 8h after dosing. You will be allowed water, fruit juice or decaffeinated drinks from approximately 3h after dosing. A light lunch will be provided approximately 4h after dosing. Normal activities excluding strenuous exercise will be allowed from approximately 4h after dosing.
7. Before dosing, a cannula (plastic tube inserted by a needle into a vein) will be inserted into your arm in order to allow samples of your blood to be obtained at regular intervals throughout the day of dosing. A needle and syringe can be used repeatedly to obtain blood samples if preferred. Repeated blood tests and cannulae can cause soreness and bruising of the arms or even, rarely, blockage of a vein, but those problems usually clear up within a few days to a few weeks.
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12. Approximately 235 ml of blood will be taken during the study (compared with 480ml which is a standard blood donation).
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14. You will not be allowed to take alcohol or other drugs on each resident study day or until after the last blood sample has been taken. It is recommended that you should refrain from alcohol as far as possible until the follow-up visit on Day 14.

If anything abnormal occurs, judged by the supervising clinician, or if laboratory investigations change, you may be withdrawn from the study. In addition, you may withdraw at any time without needing to justify your decision. (You are strongly advised not to leave the clinical unit within 24h after dosing as this may involve risk to your

ICR 013177 – AMENDMENT 2 – 20 JANUARY 1999

APPENDIX A (Continued)

Volunteer information

health). If you decide to withdraw before completion of the study a medical examination including blood pressure and heart rate, blood sampling, urine sampling and an ECG will be performed.

You should inform the supervising physician of any symptoms. After the study is over, you will be given a telephone number to call if you have any questions or worries.

It is essential that you should adhere to all of these requirements. The supervising physician will be pleased to supply any further information at any time.

All information will be treated in a confidential manner but anonymised data will be seen by authorised persons involved in the study and possibly by compound regulating authorities.

Supervising Physicians

Dr J Dickson and Dr S Freestone
Inveresk Clinical Research
Riccarton
Edinburgh
EH14 4AP Tel: (0131) 451 5080

APPENDIX C

**List of investigators and other significant
personnel involved in study (CVs included)**

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Personnel involved in study	329
Curriculum vitae	330-345
Final page	345

PERSONNEL INVOLVED IN PROJECT 013177

<u>Study Director</u>	Dr S Freestone MD FRCPEdin
<u>Clinical Investigators</u>	Dr W S Nimmo BSc MD FRCP FRCA FANZCA FFPM Dr S Freestone MD FRCPEdin Dr N Watson BSc MBChB MRCGP MFPM Dr S Mair MBChB DCCPSA Dr J Dickson MBChB Dr G Dennis MB BCh BAO MRCGP MICGP
<u>Project Physician</u>	Dr J Dickson MBChB
<u>Project CRA</u>	K Whalley RSCN D Gillies RGN RM
<u>Pharmacist</u>	D Lyall BSc MSc MRPharmS
<u>Clinical Pathology</u>	P Hudson FIBMS MBA
<u>Statistics and Data Management</u>	D Chalmers MSc CStat
<u>Principal Investigator (Bioanalytical)</u>	D L Scott HND GRSC
<u>Quality Assurance</u>	E J Elliott BSc SRN



STEPHEN FREESTONE

MEDICAL DIRECTOR

EDUCATION

Graduated MB ChB (with Honours) from Sheffield University (1975).
Awarded MRCP (UK) (1978).
Awarded MD (1991).
Awarded FRCPEdin (1998).

POST GRADUATE/INDUSTRIAL APPOINTMENTS

1976-79: General Medical Training Rotation – Royal Hospital, Royal Infirmary and Royal Hallamshire Hospitals, Sheffield.
1979-82: Research Fellow, Department of Therapeutics, Sheffield.
1983-95: Lecturer in Clinical Pharmacology and Medicine, University of Edinburgh.
1995-96: Co-director of Clinical Research Centre and Honorary Consultant Physician, Western General Hospital, Edinburgh.
1996-present: Inveresk Research (see below).

SOCIETIES/COMMITTEES/AWARDS

Member of British Pharmacological Society.
Member of the British Hypertension Society.
Member of the Medical Research Society.
Member of the Executive Committee of the Association of Independent Clinical Research Contractors.

EXPERTISE/RESEARCH INTERESTS

Dr Freestone has more than 20 years experience in Clinical Pharmacology and General (Internal) Medicine. As a hospital physician he was responsible for treating patients with a wide range of medical conditions. He has been involved with well over 150 research projects and has been Study Director/Principal Investigator on more than 75 studies. These have included patients with hypertension, diabetes, renal impairment and epilepsy in addition to healthy volunteers. Dr Freestone joined Inveresk Research in 1996 as Medical Director.

His research interests include the clinical pharmacology of cardiovascular drugs, the treatment of hypertension, the effect of drugs on the kidney and adverse drug reactions.

PUBLICATIONS

See attached list.

(CVs_OA41/1098)



STEPHEN FREESTONE – SELECTED PUBLICATIONS

Dr Freestone has written or been a co-author of more than 50 papers and 70 presentations to Learned Societies. The following are selected papers:

1. Ramsay, L E, Silas, J H, and Freestone, S, 1980. Diuretic treatment of resistant hypertension. *British Medical Journal*, 281, pp. 1101-1103.
2. Silas, J H, Phillips, F C, Freestone, S, Tucker, G T, and Ramsay, L E, 1981. A clinical and pharmacokinetic evaluation of tolmesoxide in hypertensive patients. *European Journal of Clinical Pharmacology*, 19, pp. 113-118.
3. Freestone, S, Jackson, P R, and Ramsay, L E, 1981. Life-threatening ventricular arrhythmia. *Practitioner*, 225, pp. 541-542.
4. Ramsay, L E, Freestone, S, and Silas, J H, 1982. Drug-related acute medical admissions. *Human Toxicology*, 1, pp. 379-386.
5. Freestone, S, Silas, J H, and Ramsay, L E, 1982. Sample size for short-term trials of antihypertensive drugs. *British Journal of Clinical Pharmacology*, 14, pp. 265-268.
6. Freestone, S, and Ramsay, L E, 1982. Effect of coffee and cigarette smoking on the blood pressure of untreated and diuretic-treated hypertensive patients. *American Journal of Medicine*, 73, pp 348-353
7. Silas, J H, Ramsay, L E, and Freestone, S, 1982. Hydralazine once daily in hypertension. *British Medical Journal*, 284, pp. 1602-1604.
8. Lennard, M S, Silas, J H, Freestone, S, and Trevethick, J, 1982. Defective metabolism of metoprolol in poor hydroxylators of debrisoquine. *British Journal of Clinical Pharmacology*, 14, pp. 301-303.
9. Lennard, M S, Silas, J H, Freestone, S, Ramsay, L E, Tucker, G T, and Woods, H F, 1982. Oxidation phenotype - a major determinant of metoprolol metabolism and response. *New England Journal of Medicine*, 307, pp 1558-1560.
10. Ramsay, L E, and Freestone, S, 1983. The management of resistant hypertension: a systematic approach. *Practical Cardiology*, 9, pp 70-83.
11. Lennard, M S, Jackson, P R, Freestone, S, Tucker, G T, Ramsay, L E, and Woods, H F, 1984. The relationship between debrisoquine oxidation phenotype and pharmacokinetics and pharmacodynamics of propranolol. *British Journal of Clinical Pharmacology*, 17, pp 679-685.
12. Silas, J H, Freestone, S, Lennard, M S, and Ramsay, L E, 1985. Comparison of two slow-release formulations of metoprolol with conventional metoprolol and atenolol in hypertensive patients. *British Journal of Clinical Pharmacology*, 20, pp 387-391.

(CVs_OA41/1098)



STEPHEN FREESTONE – SELECTED PUBLICATIONS

13. Freestone, S, Thomas, H M, Bhamra, R K, and Dyson, E H, 1986. Severe atenolol poisoning: treatment with prenalterol. *Human Toxicology*, 5, pp 343-345.
14. Freestone, S, 1987. Drug interactions with warfarin. *Edinburgh Medicine*, 43, pp. 16-17.
15. Jeffrey, R F, MacDonald, T M, Rutter, M K, Freestone, S, Brown, J, Samson, R R, and Lee, M R, 1987. The effect of intravenous frusemide on urine dopamine in normal volunteers: studies with indomethacin and carbidopa. *Clinical Science*, 73, pp. 151-157.
16. Capewell, S, Freestone, S, Critchley, J A J H, Pottage, A, and Prescott, L F, 1988. Reduced felodipine bioavailability in patients taking anticonvulsants. *Lancet*, 2, pp 480-482.
17. Freestone, S, MacDonald, T M, Jefferey, R F, Brown, J, and Lee, M R, 1989. The renal effects of atrial natriuretic peptide in man are not attenuated by (+)-sulpiride. *British Journal of Clinical Pharmacology*, 27, pp 13-18.
18. Freestone, S, Jeffrey, R F, Bonner, C V, and Lee, M R, 1990. The effect of lithium on the renal actions of atrial natriuretic peptide in normal man. *Clinical Science*, 78, pp 371-375.
19. Prescott, L F, Freestone, S, and McAuslane, J A N, 1991. Reassessment of the single intravenous injection method with inulin for measurement of the glomerular filtration rate in man. *Clinical Science*, 80, pp 167-176.
20. Freestone, S, McAuslane, J A N, and Prescott, L F, 1991. Effect of tenoxicam on renal function and the disposition of inulin and p-aminohippurate in healthy volunteers and patients with chronic renal failure. *British Journal of Clinical Pharmacology*, 32, pp 495-500.
21. MacDonald, T M, Sharp, K, Fowler, G, Lyons, D, Freestone, S, Lovell, H G, Webster, J, and Petrie, J C, 1991. Caffeine restriction: effect on mild hypertension. *British Medical Journal*, 303, pp 1235-1238.
22. Eadington, D W, Freestone, S, Waugh C J, Swainson, C P, and Lee, M R, 1992. Lithium pretreatment affects renal and systemic responses to angiotensin II infusion in normal man. *Clinical Science*, 82, pp. 543-549.
23. Prescott, L F, Freestone, S, and McAuslane, J A N, 1993. The concentration-dependent disposition of intravenous p-aminohippurate in subjects with normal and impaired renal function. *British Journal of Clinical Pharmacology*, 35, pp 20-29.
24. Freestone, S, Li Kam Wa, T C, and Lee, M R, 1993. Further studies on gludopa in man: the effect of the monoamine oxidase inhibitor selegiline. In: Soares-da-Silva P, ed *Advances in the Biosciences*, Vol. 88, Cardiovascular and Renal Actions of Dopamine. Oxford: Pergamon Press, pp. 195-201.

(CVs_QA41/1098)



STEPHEN FREESTONE – SELECTED PUBLICATIONS

25. Li Kam Wa, T C, Freestone, S, Samson, R R, Johnston, N R, and Lee, M R, 1993. A comparison of the renal and neuroendocrine effects of two 5 -hydroxytryptamine renal prodrugs in normal man. *Clinical Science*, 85, pp. 607-614.
26. Li Kam Wa, T C, Freestone, S, Samson, R R, Johnston, N R and Lee, M R, 1994. The antinatriuretic action of γ -L-glutamyl-5-hydroxy-L-tryptophan is dependent on its decarboxylation to 5-hydroxytryptamine in normal man. *British Journal of Clinical Pharmacology*, 38, pp 265-269.
27. Freestone, S, Yeo, W W, and Ramsay, L E, 1995. Effect of coffee and cigarette smoking on the blood pressure of patients with accelerated (malignant) hypertension. *Journal of Human Hypertension*, 9, pp 89-91.
28. Li Kam Wa, T C, Freestone, S, Samson R R, Johnston, N R, and Lee, M R, 1996. Renal metabolism and effects of the glutamyl derivatives of L-dopa and 5-hydroxytryptophan in man. *Clinical Science*, 91, pp. 177-185.

(CVs_OA41/1098)



WALTER S NIMMO
CHIEF EXECUTIVE OFFICER

EDUCATION

Graduated from Edinburgh University, Faculty of Medicine and several Royal Colleges in the UK and abroad. BSc (Med.Sci) Edinburgh 1968, MBChB Edinburgh 1971, MRCP UK 1975, FFARCS (now FRCA) England 1977, MD Edinburgh 1982, FRCP Edinburgh 1984, FRCP Glasgow 1984, FFARCS (now FANZCA) Australia 1989, FFPM 1993.

POST-GRADUATE/INDUSTRIAL APPOINTMENTS

1971-73: Various posts in Medicine, Surgery and Anaesthesia in the Royal Infirmary, Edinburgh.
1973-76: Research Fellow/Lecturer in Clinical Pharmacology, University of Edinburgh.
1976-79: Lecturer in Anaesthesia, University of Edinburgh
1979-84: Senior Lecturer in Anaesthesia, University of Glasgow.
1984-88: Professor of Anaesthesia, University of Sheffield.
1988-96: Medical Director/CEO, Inveresk Clinical Research Limited.
1996-present: CEO, Inveresk Research

SOCIETIES/COMMITTEES/AWARDS/EXAMINERSHIPS

Member of British Pharmacological Society, Anaesthetic Research Society, International Anaesthesia Research Society.
Past Chairman of Education and Research Committee, Association of Anaesthetists of Great Britain and Ireland.
Past Member of the Safety, Efficacy and Adverse Reactions Committee (SEAR) and the Adverse Reactions Group of SEAR (sub-committees of the CSM).
Examiner in Physiology and Pharmacology for several Royal Colleges in the UK.
Member of Editorial Board Br. J. Clin Pharmacol.
Member of PMIB of Medical Research Council.
Member of Council, Royal College of Physicians of Edinburgh

EXPERTISE/RESEARCH INTERESTS

Gastric emptying and drug absorption
Pharmacokinetics
Analgesia
CNS drugs
Rate Controlled Drug Therapy

Editor of 11 textbooks and more than 100 papers.

(CVs__Exec.0299)



NORMA WATSON

MEDICAL ADVISER

EDUCATION

Awarded BSc (MedSci) from Edinburgh University (1976).
Graduated with MBChB from Edinburgh University (1979).
Awarded MRCP from London College of General Practitioners (1983).
Awarded MFPM from Joint Colleges of Physicians, (Edinburgh, Glasgow, London) (1995).

POST-GRADUATE/INDUSTRIAL APPOINTMENTS

1979-80: Medical and surgical house jobs at Eastern General Hospital, Edinburgh.
1980-82: Senior House Officer Posts:
Surgical Paediatrics - Royal Hospital for Sick Children, Edinburgh.
Obstetrics and Gynaecology - Royal Infirmary, Edinburgh.
Neonatal Paediatrics - Simpson Memorial Maternity Pavilion, Edinburgh.
Medical Paediatrics - Royal Hospital for Sick Children, Edinburgh
1982-85: General Practitioner, Newport-on-Tay.
1987-90: Part-time General Practitioner, Crewe Medical Group, Edinburgh.
1989-present: Inveresk Research (see below).

EXPERTISE/RESEARCH INTERESTS

Dr Watson has been Study Director on over 150 Phase I, II and III studies. She has considerable experience of new chemical entities and various routes of drug delivery including transdermal and electrotransport.

Her particular interests include abnormalities in volunteers presenting for screening - in particular liver function tests and the importance of information obtained from General Practitioners in the screening of potential volunteers.

(CV₆_OA41/0887)



STUART J MAIR

CLINICAL RESEARCH PHYSICIAN

EDUCATION

Graduated with MBChB from University of Aberdeen (1990).
Awarded DRCOG from The Royal College of Obstetricians and Gynaecologists (1994).
(Diploma in clinical pharmacology awarded by The Society of Apothecaries of London)
1999 DCPSA

POST-GRADUATE/INDUSTRIAL APPOINTMENTS

1990-91: JHO General Surgery/Urology, Aberdeen Royal Infirmary.
1991-91: JHO General Medicine, Woodend Hospital, Aberdeen.
1991-92: SHO General Medicine, Aberdeen Royal Infirmary.
1992-92: SHO A & E, Dr Grays Hospital, Elgin, Moray.
1992-93: **FIFE GPVTS**
1992-93: SHO A & E, Victoria Hospital, Kirkcaldy.
1993-93: SHO OBS and Gynae, Forth Park Hospital, Kirkcaldy.
1993-94: SHO Psychiatry, Stratheden Hospital, Cupar, Fife.
1994-94: SHO Ophthalmology, Queen Margaret Hospital, Dunfermline.
1994-94: SHO ENT, Victoria Hospital, Kirkcaldy.
1994-95: General Practice Trainee with Dr R Robertson and Partners, The Health Centre, Kirkcaldy.
1995-96: SHO 2nd On Call/Infectious Diseases/Respiratory Medicine, Victoria Hospital, Kirkcaldy.
1996-present: Inveresk Research (see below).

EXPERTISE/RESEARCH INTERESTS

Dr Mair's responsibilities include supervising all aspects of Phase I clinical trials (safety, tolerability and pharmacokinetics in healthy volunteers) involving both licensed and unlicensed products delivered by oral, intravenous, inhalation and transdermal routes. Specific roles in individual studies include protocol design, supervising the clinical phase and writing reports.

(CVs_OA41/0489)



JANET E A DICKSON
CLINICAL RESEARCH PHYSICIAN

EDUCATION

Graduated with MBChB from University of Aberdeen (1977).

POST GRADUATE/INDUSTRIAL APPOINTMENTS

1977-78: Pre-registration - Medicine, Middlesborough General Hospital
1978: Pre-registration - Surgery, Woodend Hospital, Aberdeen
1978-79: SHO - Psychiatry and Mental Handicap, Royal Edinburgh and Gogarburn Hospitals
1979: SHO - Geriatrics, Royal Victoria Hospital, Edinburgh
1979-80: SHO - ENT, City Hospital, Edinburgh
1980: SHO - Obstetrics and Gynaecology, Eastern General Hospital, Edinburgh
1980-81: GP trainee, Sighthill Health Centre, Edinburgh
1981: General Practice and Hospital Locums
1981-82: SHO - Accident and Emergency, Western General Hospital, Edinburgh
1982: SHO - Paediatrics, Stirling Royal Infirmary and Falkirk Infirmary
1982-83: General Practice and Hospital Locums
1983-84: SHO - Anaesthetics, Western General Hospital, Edinburgh
1984-85: SHO - Anaesthetics, Royal Infirmary, Edinburgh
1985-86: Locum Registrar - Anaesthetics, Royal Infirmary, Edinburgh
1987-96: Sessional Medical Officer, Scottish National Blood Transfusion Service, Edinburgh
1994-95: GP Trainee (part-time), Craiglockhart Surgery and Bruntsfield Health Centre
1996-present: Inveresk Research (see below).

EXPERTISE/RESEARCH INTERESTS

Dr Dickson joined Inveresk Research in 1996 and since then has worked on all aspects of Phase I clinical trials.

(CVs_OA41/1097)



Inveresk Research

GERALDINE DENNIS

CLINICAL RESEARCH PHYSICIAN

EDUCATION

Graduated with MB B Ch BAO (Hons) from University College, Dublin, Ireland (1988).
Awarded Diploma in Obstetrics and Gynaecology (D.Obs) from Royal College of Physicians in Ireland (1991).
Completed vocational training with the Dublin Regional Training Scheme for General Practitioners (1992).
Awarded Membership of the Irish College and Royal Colleges of General Practitioners -MICGP and MRCGP (1992).
Awarded the Certificate of Family Planning from the Irish Family Planning Association (1993).

POST-GRADUATE/INDUSTRIAL APPOINTMENTS

1988-89: Pre-registration House Officer in St Vincent's Hospital, Dublin (General Medicine and General Surgery).
1989-90: House Officer in Mater Misericordial Hospital, Dublin (accident and emergency medicine and general medicine).
1990-91: House Officer in Temple Street and Coombe Hospitals, Dublin (Paediatrics and Obstetrics/Gynaecology).
1991-92: Trainee General Practitioner in Clane, Co Kildare, Ireland.
1992-93: Assistant General Practitioner in Clane, Co Kildare, Ireland.
1993-present: Inveresk Research (see below).

SOCIETIES/COMMITTEES

Member of the Irish College of General Practitioners.
Member of the Royal College of General Practitioners.

EXPERTISE/RESEARCH INTERESTS

Dr Dennis joined Inveresk Research in 1993 and since then has worked on Phase I and II clinical trials involving a wide range of compounds. She has been project manager on many studies and since 1996 has been study director on several studies.

(CVr_0A11/0997)



KAY WHALLEY

CLINICAL RESEARCH ASSOCIATE

EDUCATION

Registered General Nurse, South Lothian College of Nursing & Midwifery, Edinburgh, (1984-1987),
ENB, Care of the critically ill patient, St Thomas Hospital, London, (1989-1990).
Registered Sick Childrens Nurse, Guys Hospital, London, (1991-1992).

POST-GRADUATE/INDUSTRIAL APPOINTMENTS

1987-88: Staff Nurse, Surgical Ward, Edinburgh Royal Infirmary.
1988-89: Staff Nurse, Coronary Care Unit, Edinburgh Royal Infirmary.
1989: Staff Nurse, Acute Admissions Ward, St Thomas Hospital, London.
1990-91: Staff Nurse, Intensive Care, St Thomas Hospital, London.
1991: Staff Nurse, Intensive Care, Kings College Hospital, London.
1993-94: Staff Nurse, Intensive Care, Western General Hospital, Edinburgh.
1994-present: Inveresk Research (see below).

EXPERTISE/RESEARCH INTERESTS

Ms Whalley joined Inveresk as a clinical research nurse in 1994. In January 1998 she was appointed Clinical Research Associate Phase I.

Her duties include client liaison to ensure an accurate reflection of the sponsor's needs and requirements when writing protocols.

She has a very active role to play in ensuring efficient and effective communication between the Clients and Study Team.

Her duties as project manager and study co-ordinator include management of Phase I studies from initial sponsor contact through data monitoring quality assurance case report form writing to report writing.

She has become increasingly involved in professional development of colleagues in the areas of ECG, medilog holter monitors, Hewlett Packard bedside monitors and other equipment, by giving presentations and providing written information; also co-ordinating other personnel to give presentations in their areas of expertise.

Ms Whalley has skills for venepuncture, basic laboratory techniques and currently acquiring skills in venous cannulation.

(CT 0441/0198)



DIANE GILLIES

CLINICAL RESEARCH ASSOCIATE

EDUCATION

Registered General Nurse, North Lothian College of Nursing and Midwifery (1987-90).
Registered Midwife, North Lothian College of Nursing and Midwifery (1992-93).
Ongoing – BSc Combined Health Studies

POST-GRADUATE/INDUSTRIAL APPOINTMENTS

1991-92: Staff Nurse, Surgical High Dependency, Western General Hospital, Edinburgh.
1993-95: Midwife – rotational post, Riyadh Armed Forces Hospital, Saudi Arabia.
1996: Nurse, Midwife for BNA, Edinburgh.
1996-1998: Clinical Research Nurse, Inveresk Research
1999-present: Clinical Research Associate, Inveresk Research

SOCIETIES/COMMITTEES/AWARDS

Member of the Royal College of Midwives.

EXPERTISE/RESEARCH INTERESTS

Ms Gillies joined Inveresk as a Clinical Research Nurse in 1996. In January 1999 she was appointed Clinical Research Associate Phase I.

Her duties include client liaison to ensure an accurate reflection of the sponsor's needs and requirements when writing protocols.

She has a very active role to play in ensuring efficient and effective communication between the clients and study team.

Her duties as project manager and study coordinator include management of Phase I studies from initial sponsor contact through data monitoring, quality assurance, case report form writing to report writing.

(CVs_QA41/0198)



DAVID LYALL

PHARMACIST

EDUCATION

Graduated with BSc (Hons) in Pharmacy from Robert Gordon's Institute of Technology, Aberdeen (1979).

Awarded MSc in Pharmaceutical Analysis by Strathclyde University (1982).

POST-GRADUATE/INDUSTRIAL APPOINTMENTS

1979-80: Pre-registration Pharmacist, Grampian Health Board, Aberdeen.
1980-83: Pharmacist, Lothian Health Board, Edinburgh.
1983-85: Radiopharmacist, Grampian Health Board, Aberdeen.
1985-88: Quality Assurance Pharmacist, Royal Infirmary of Edinburgh.
1988-90: Laboratory Manager/Quality Assurance, Bioseparation Associates Limited, Livingston.
1990-93: Pharmacist Manager in Community Pharmacy for The Red Band Chemical Company Limited and McWhinnie (Scotland) Ltd.
1993-present: Inveresk Research (see below).

SOCIETIES/COMMITTEES

Member of the Royal Pharmaceutical Society of Great Britain.

EXPERTISE/RESEARCH INTERESTS

Mr Lyall duties include the application of the quality system of Good Manufacturing Practice, Good Laboratory Practice and Good Clinical Practice to the clinical and preclinical dispensary operations, particularly in the areas of radiopharmaceutical dose preparation, aseptic assembly of parenterals and their sterilisation, formulation development, process validation and control documentation.

(CVs_QA41/0599)



PAUL HUDSON

HEAD, DEPARTMENT OF BIOCHEMICAL PHARMACOLOGY

EDUCATION

Fellow of the Institute of Biomedical Sciences, Caledonian University, Glasgow
Master of Business Administration, Edinburgh University

INDUSTRIAL APPOINTMENTS

- 1971-77: Department of Laboratory Medicine, Ruchill Hospital, Glasgow: experience in haematology, clinical chemistry, bacteriology and histopathology.
- 1977-80: Syntex Research Centre, Edinburgh: Responsible for haematology and clinical chemistry in laboratory species. Promoted to the position of regulatory affairs/quality assurance officer. Worked on the UK submission for Nicardipine and regulatory clearance for European clinical trials.
- 1980-81: Haematology Department, Falkirk Royal Infirmary: Senior Scientific Officer in large haematology and serology laboratory. Responsible for staff supervision and a range of routine and investigative techniques.
- 1981-present: Inveresk Research (see below).

SOCIETIES

Member of the International Society for Thrombosis and Haemostasis
Member of the Animal Clinical Chemistry Association
Member of the Animal Haematology Association

EXPERTISE/RESEARCH INTERESTS

Since joining Inveresk in 1981 Paul Hudson has had responsibility for Clinical Pathology which provides a service for preclinical and clinical research. Following integration of Clinical Pathology with the Biochemical Pharmacology Group he has acted as Functional Manager and latterly Operational Area Manager. He has been Study Director on a number of investigative studies mainly in the field of thrombosis and atherosclerosis. He has prepared several publications.

Mr Hudson has a senior supervisory role in assuring that high standards are maintained in his Area, particularly in terms of QC and GLP. He has obtained extensive experience over a number of years in the broad field of biomedical science. He is also responsible for business development in his Department.

(CVs_QA04/05598)

**DAVID CHALMERS****HEAD OF STATISTICS AND DATA MANAGEMENT****EDUCATION**

Graduated with a BSc in Mathematics specialising in Statistics, from Strathclyde University (1981).

Graduated with MSc in Medical Statistics from London School of Hygiene and Tropical Medicine (1982).

POST GRADUATE/INDUSTRIAL APPOINTMENTS

- 1982-87: Hoechst UK Limited as Medical Statistician involved in the design and analysis of Phase II-III clinical trials. In 1985 promoted to Senior Statistician.
- 1987-89: Glaxo Pharmaceuticals Limited as Senior Statistician involved in the design and analysis of Phase III-IV clinical trials. In 1988 promoted to Principal Statistician, responsible for the quality of all statistical analyses performed within the Statistics and Data Management Department. Also responsible for providing specialist computer support within the department.
- 1989-present: Inveresk Research (see below)

SOCIETIES

Member of Royal Statistical Society (Chartered Statistician)
Associate member of PSI (Statisticians in Pharmaceutical Industry)
Member of Drug Information Association

EXPERTISE/RESEARCH INTERESTS

Mr Chalmers joined Inveresk as Company Statistician and in 1996 was promoted to Head of Statistics and Data Management (Operational Area Manager). The department is now responsible for the management, pharmacokinetics, statistical analysis and reporting of data from both clinical and non-clinical studies.

Mr Chalmers now has a mainly managerial role and is responsible for assuring that all procedures and output from the department satisfy the relevant regulatory guidelines including both GLP and GCP. He is also responsible for assuring effective communication between the various disciplines within the department (eg data management and clinical statistics). He has obtained extensive experience over a number of years in many aspects of drug development including design and analysis of Phase I-III studies, clinical data management, medical writing and regulatory issues. On a number of occasions he has represented Sponsors at regulatory meetings in both Europe and the US. He is also responsible for business development within his department.

(CVs_OA12/1298)



DAVID LAW SCOTT
STUDY DIRECTOR
DEPARTMENT OF BIOANALYTICAL CHEMISTRY

EDUCATION

HND, Chemistry, Napier Polytechnic, Edinburgh (1989).
GRSC Part I, Napier Polytechnic, Edinburgh (1990).
Individual Open University courses: Biology (2nd Level), Animal Physiology,
Biochemistry and Cell Biology (3rd Level).

POST GRADUATE/INDUSTRIAL APPOINTMENTS

1988: Chemist, Navigation Systems Department, Ferranti Defence Systems Limited, Edinburgh.
1989-90: Research Assistant, Blending and Bottling Section, Pentlands Scotch Whisky Research Limited, Edinburgh.
1990-present: Inveresk Research (see below).

EXPERTISE/RESEARCH INTERESTS

Mr Scott has considerable expertise in Modern Instrumental Analytical Techniques, particularly HPLC, GC, CE and UV/VIS Spectroscopy; and in Immunoassays, particularly RIA and ELISA.

Mr Scott was initially an Analyst, then Project Leader in the Department of Product Chemistry.

In 1994 he joined the Department of Bioanalytical Chemistry as a Project Leader. In his current position, Mr Scott is involved in the development, validation and routine use of Analytical Methodology; particularly HPLC, ELISA and RIA; associated with pharmaceuticals and their metabolites, in body fluids and tissue samples. Mr Scott is involved in the area of toxicology and clinical support as a Study Director.

(CVs_OA07/0598)



ELIZABETH J ELLIOTT

**FUNCTIONAL MANAGER (CLINICAL)
QUALITY ASSURANCE UNIT**

EDUCATION

Graduated with BSc (Hons) in Classical and Religious Studies from University College of Wales, Aberystwyth (1977).
State Registered Nurse (1981).
Gained Orthopaedic Nursing Certificate (1984).
Gained Diploma in Clinical Science from the Welsh School of Pharmacy (1995).

POST GRADUATE/INDUSTRIAL APPOINTMENTS

1978-81:	Student/Staff Nurse, Royal Masonic Hospital, London.
1981-83:	Staff Nurse, Hôpital de District, Moutier, Switzerland.
1983-84:	Staff Nurse, Princess Margaret Rose Orthopaedic Hospital, Edinburgh.
1984-85:	Staff Nurse, Addenbrooke's Hospital, Cambridge
1985-87:	Staff Nurse, Princess Margaret Rose Orthopaedic Hospital, Edinburgh
1987-88:	Senior Staff Nurse, Aberdeen Royal Infirmary.
1988-92:	CRA/Senior CRA/Regulatory Compliance Auditor, ClinTrials Research (formerly Clinical Research International).
1995-96:	Senior CRA, Inveresk Clinical Research.
1996-present:	Inveresk Research (see below).

SOCIETIES/COMMITTEES

Member of ACRPI.
Member of BARQA and MENSA.

EXPERTISE/RESEARCH INTERESTS

Miss Elliott has considerable nursing experience, with special expertise in orthopaedics. She has extensive experience in clinical research, including monitoring, project management and auditing, mainly in Phase II-IV research to GCP standards in the UK, Europe and the USA.

Miss Elliott is currently employed as Functional Manager, Quality Assurance (Clinical) assisting the QA Manager to lead a team of Quality Assurance specialists responsible for providing a GCP inspection and audit service for clinical studies conducted by Inveresk Research and Inveresk Clinical Research. She is responsible for the conduct of study and procedure inspections and the audit of draft and final reports; as well as having managerial responsibilities within the team.

(CVs_OA14/0398)

APPENDIX D

Quality Assurance Audits and QA Statement

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QUALITY ASSURANCE STATEMENT

The conduct of this study has been subjected to periodic inspections by the Inveresk Research Quality Assurance Unit. The dates of inspection are given below.

<u>Date of QA Inspection</u>	<u>Phase</u>	<u>Date of Report to Management/SD</u>
5 November 1998	Dosing and Protocol Compliance	5 November 1998
13 November 1998	CRF Data Review	13 November 1998
2 June 1999	Plasma Analysis	4 June 1999

This report has been audited by Inveresk Research Quality Assurance Personnel according to the appropriate Standard Operating Procedure and is considered to describe the methods and procedures used in the study. The reported results accurately reflect the original data of the study.

Signed:  Date: 24 Mar 00
(Quality Assurance)

APPENDIX E

Randomisation schemes and codes

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Randomisation Code Prepared by IRI Statistics Department

Project No. : 013177

Sponsor : Cheminova

Session 1

Date Prepared: 15-10-1998

Centre: ICR

Patient	Treatment
1	0.5 mg/kg Malathion
2	0.5 mg/kg Malathion
3	Placebo
4	0.5 mg/kg Malathion

*Randomisation by
D. Cathiona Murray
- 15 Oct '98*

*checked by
Mason Thom
15 Oct 98*

Randomisation Code Prepared by IRI Statistics Department

Project No. : 013177

Sponsor : Cheminova

Session 2

Date Prepared: 15-10-1998

Centre: ICR

Patient	Treatment
5	1.5 mg/kg Malathion
6	1.5 mg/kg Malathion
7	Placebo
8	1.5 mg/kg Malathion

*Randomisation by
J. Catherine Murray
15 Oct '98*

*Checked by
Marian Thom
15 Oct 98*

Randomisation Code Prepared by IRI Statistics Department

Project No. : 013177

Sponsor : Cheminova

Session 3

Date Prepared: 15-10-1998

Centre: ICR

Patient	Treatment
9	5.0 mg/kg Malathion
10	5.0 mg/kg Malathion
11	5.0 mg/kg Malathion
12	5.0 mg/kg Malathion
13	Placebo
14	5.0 mg/kg Malathion
15	Placebo
16	Placebo
17	5.0 mg/kg Malathion
18	5.0 mg/kg Malathion

*Randomization by
T. Cathiona Murray
15 Oct '98*

*Checked by
Maia Thom
15 Oct 98*

Randomisation Code Prepared by IRI Statistics Department

Project No. : 013177

Sponsor : Cheminova

Session 4

Date Prepared: 15-10-1998

Centre: ICR

Patient	Treatment
19	10.0 mg/kg Malathion
20	10.0 mg/kg Malathion
21	Placebo
22	10.0 mg/kg Malathion

*Randomisation by
O. Catherine Murray
15 Oct '98*

*checked by
Marian Thom
15 Oct 98*

Randomisation Code Prepared by IRI Statistics Department

Project No. : 013177

Sponsor : Cheminova

Session 5

Date Prepared: 15-10-1998

Centre: ICR

Patient	Treatment
23	10.0 mg/kg Malathion
24	Placebo
25	Placebo
26	15.0 mg/kg Malathion
27	10.0 mg/kg Malathion
28	10.0 mg/kg Malathion
29	15.0 mg/kg Malathion
30	10.0 mg/kg Malathion
31	15.0 mg/kg Malathion

*Randomisation by
G. Gibson Murray
15 Oct '98*

*Checked by
Nelson Thom
15 Oct 98*

Randomisation Code Prepared by IRI Statistics Department

Project No. : 013177

Sponsor : Cheminova

Session 6

Date Prepared: 15-10-1998

Centre: ICR

Patient	Treatment
32	Placebo
33	15.0 mg/kg Malathion
34	15.0 mg/kg Malathion
35	Placebo
36	Placebo
37	15.0 mg/kg Malathion
38	15.0 mg/kg Malathion

*Randomisation by
G. Gibson Murray
15 Oct '98.*

*checked by
Marian Thom
15 Oct 98*

Randomisation Code Prepared by IRI Statistics Department

Project No. : 013177

Sponsor : Cheminova

Session 7

Date Prepared: 15-10-1998

Centre: ICR

Patient	Treatment
39	NOEL Malathion
40	NOEL Malathion
41	Placebo
42	NOEL Malathion
43	NOEL Malathion
44	NOEL Malathion
45	Placebo
46	NOEL Malathion
47	Placebo
48	NOEL Malathion

*Randomisation by
J. Catherine Murray
15 Oct '98*

checked by

*Monica Thom
15 Oct 98*

APPENDIX F

Batch numbers of material used and their certificates of analysis

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Cheminova Agro A/S
P.O. Box 8
DK-7820 Lemvig
Denmark

Phone (+45) 97834100
Fax (+45) 97834633
Telex 86614 CHEMIV DK
A/S reg.no. 177122

Date:

BATCH ANALYTICAL CERTIFICATE

ARTICLE IDENTIFICATION				
Article Name: Fyfanon Technical		Reg. Dept. Code :		
Manufacturer: Cheminova Agro A/S		Batch No. : 50913-01		
Origin of Production: Commercial <input checked="" type="checkbox"/> ; Pilot plant <input type="checkbox"/> ;		Laboratory <input type="checkbox"/> ;		
PHYSICAL PROPERTIES				
Technical <input checked="" type="checkbox"/> ; Preparation of technical Product <input type="checkbox"/> ; Analytical <input type="checkbox"/> ; Liquid <input checked="" type="checkbox"/> ; Solid <input type="checkbox"/> ; Colour: Amber				
Recommended storage conditions				
Ambient temperature in the dark _____		Expiry Date: _____		
In refrigerator <input checked="" type="checkbox"/> _____		The article is stable at least <u>4</u> year from date		
In deep freezer _____		of analysis/last date of reanalysis when stored at recommended conditions.		
Additional Comments:				
ACTIVE INGREDIENT IDENTIFICATION				
Common Name/ISO-Name : Malathion		CAS-Name: Butanedioic acid, ((dimethoxyphosphorothioyl) thio)-, diethyl ester		
CAS No : 121-75-3		Structural Formula:		
Empirical Formula : C ₁₀ H ₁₉ O ₆ PS ₂				
Molecular Weight : 330.4				
Identified by means of:				
NMR <input checked="" type="checkbox"/> ; IR <input checked="" type="checkbox"/> ; UV <input checked="" type="checkbox"/> ; MS <input checked="" type="checkbox"/> ; Other Methods:				
ANALYTICAL DATA				
Certified Purity/Content of a.i.: 95.64 w/w				
Analytical Method: VAM 301-01.				
Analytical Report (incl. amendments): IZN 010-01				
Date of analysis/ reanalysis (yy/mm/dd)	95/004	960916	970911	980908
-For article stored at -	Cheminova Agro. Regist. storage, DK	Cheminova Agro. Regist. storage, DK	Cheminova Agro. Regist. storage, DK	Cheminova Agro. Regist. storage, DK
GLP-COMPLIANCE				
The identification and determination of purity/content of active ingredient were performed at Cheminova Agro A/S and conducted in accordance with FIFRA Good Laboratory Practice Standards, 40 CFR Part 160 and the OECD Principles of Good Laboratory Practices. All raw data, documentation, records, protocols, test articles, reference samples, and report are retained in the GLP archives of Cheminova Agro A/S, Denmark.				
Date: <u>September 10</u> 1998		Signature: <u>Elsa V. Sørensen</u> Elsa V. Sørensen		



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BATCH ANALYTICAL CERTIFICATE

ARTICLE IDENTIFICATION					
Article Name:		Fyfanon Technical		Reg. Dept. Code:	
Manufacturer:		Cheminova Agro A/S		Batch No.: 50913-01	
Origin of Production:		Commercial <input checked="" type="checkbox"/>	Pilot plant <input type="checkbox"/>	Laboratory <input type="checkbox"/>	
PHYSICAL PROPERTIES					
Technical <input checked="" type="checkbox"/>		Preparation of <input type="checkbox"/>	Analytical <input type="checkbox"/>	Liquid <input checked="" type="checkbox"/>	Solid <input type="checkbox"/>
Product		technical Product	Standard		Colour: Amber
Recommended Storage Conditions					
Ambient temperature in the dark		Expiry Date:			
In refrigerator		The article is stable at least 4 year from date			
In deep freezer		of analysis/last date of reanalysis when stored at recommended conditions.			
Additional Comments:					
ACTIVE INGREDIENT IDENTIFICATION					
Common Name/ISO-Name:		Malathion		CAS-Name: Butanedioic acid, ((dimethoxyphosphinothioyl)thio)-, diethyl ester	
CAS No.:		121-75-5		Structural Formula:	
Empirical Formula:		C ₁₀ H ₁₉ O ₆ PS ₂			
Molecular Weight:		330.4			
Identified by means of:					
		NMR <input checked="" type="checkbox"/>	IR <input checked="" type="checkbox"/>	UV <input checked="" type="checkbox"/>	MS <input checked="" type="checkbox"/>
Other Methods:					
ANALYTICAL DATA					
Certified Purity/Content of a.i.: 95.4% w/w					
Analytical Method: VAM 001-01.					
Analytical Report (incl. amendments): TEM 010-01					
Date of analysis/ reanalysis (yyymmdd)	951004	980908	990628		
-for article stored at -	Cheminova Agro. Reg. storage, DK	Cheminova Agro. Reg. storage, DK	Inveresk, Scotland		
GLP-COMPLIANCE					
The identification and determination of purity/content of active ingredient were performed at Cheminova Agro A/S and conducted in accordance with FITRA Good Laboratory Practice Standards, 40 CFR Part 160 and the OECD Principles of Good Laboratory Practices. All raw data, documentation, records, protocols, test articles, reference samples, and report are retained in the GLP archives of Cheminova Agro A/S, Denmark.					
Date: November 1, 1999		Signature: <u>Elsa V. Sørensen</u> Elsa V. Sørensen			



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BATCH ANALYTICAL CERTIFICATE
TEST/REFERENCE ARTICLE

Addendum				
Article Name: Fyfanon Technical				
Batch No.: 50913-01				
ANALYTICAL DATA				
Impurities:		Reference, Analytical Report: TEM 010-01		
CAS No.	CAS name/other name: (Cheminova name)	% by weight	Analytical method	Date of analysis (yy/mm/dd)
152-18-1	Phosphorothioic acid, O,O,O- trimethyl ester; (MeOOPS-triester)	0.19	VAM 006-01	980909
2953-29-9	Phosphorodithioic acid, O,O,S- trimethyl ester; (MeOOSPS-triester)	0.91	VAM 006-01	980909
623-91-6	2-Butanedioic acid (E)-, diethyl ester; (FE)	0.59	VAM 006-01	951005
17596-10-0	Succinic acid, ethoxy-, diethyl ester; (NE+EtOH)	0.14	VAM 006-01	951005
97998-25-9	Butanedioic acid mercaptomethyl, diethyl ester; (NE+CH ₃ SH)	0.32	VAM 006-01	951005
5930-73-4	Thiodiphosphoric acid, tetramethyl ester; (MP 11/2)	0.12	VAM 006-01	951005
71133-15-8	Butanedioic acid, ((ethoxymethoxyphosphino- thioyl)thio)-, diethyl ester; (EM-Fyfanon)	0.14	VAM 006-01	951005
21761-80-8	Succinic acid, 2,2'-thiodi- , tetraethyl ester; (Monosulfid)	0.082	VAM 006-01	951005
3344-12-5	Succinic acid, mercaptodi- ethyl ester, S-ester with O,S-dimethyl phosphoro- dithioate; (Isomalathion)	0.24	VAM 005-02	990630
1634-78-2	Butanedioic acid, [(dimethoxyphosphinyl) thio]-, diethyl ester; (Malaaxon)	< 0.02	VAM 008-01	990629
33779-98-5	Butanedioic acid, ((dimethoxyphosphinothioyl) thio)-, 4-ethyl 1-methyl ester and Butanedioic acid, ((dimethoxyphosphinothioyl) thio)-, 1-ethyl 4-methyl ester; (Mixed ester)	0.15	VAM 008-01	950927
7732-18-5	Water	0.037	VAM 022-01	950922
GLP-COMPLIANCE				
The identification and determination of the impurities were performed at Cheminova Agro and conducted in accordance with FIFRA Good Laboratory Practice Standards, 40 CFR Part 160 and the OECD Principles of Good Laboratory Practices. All raw data, documentation, records, protocols, test articles, reference samples, and report are retained in the GLP archives of Cheminova Agro, Denmark.				
Date: November 1, 1999		Signature: <i>Elsa V. Sørensen</i> Elsa V. Sørensen		

APPENDIX G

Dosing details – Individual values

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TABLE G1
Dosing Details
Individual Values: All Subjects

Subject	Dose of Malathion	Date of Dosing	Fasted From 23:00h	Time of Breakfast Completion (h:min)	Formulation Administered Whilst Sitting	150 mls Water Given With Formulation	Time of Administration (h:min)	Seated/ Recumbent For 8h Postdose
001	0.5 MG/KG	05NOV1998	YES	8:25	YES	YES	8:30	YES
002	0.5 MG/KG	05NOV1998	YES	8:26	YES	YES	8:36	YES
003	PLACEBO	05NOV1998	YES	8:35	YES	YES	8:40	YES
004	0.5 MG/KG	05NOV1998	YES	8:40	YES	YES	8:45	YES
005	1.5 MG/KG	11NOV1998	YES	8:55	YES	YES	9:05	YES
006	1.5 MG/KG	11NOV1998	YES	9:05	YES	YES	9:10	YES
007	PLACEBO	11NOV1998	YES	9:10	YES	YES	9:15	YES
008	1.5 MG/KG	11NOV1998	YES	9:15	YES	YES	9:20	YES
009	5.0 MG/KG	25NOV1998	YES	8:55	YES	YES	9:05	YES
010	5.0 MG/KG	25NOV1998	YES	9:05	YES	YES	9:10	YES
011	5.0 MG/KG	25NOV1998	YES	9:10	YES	YES	9:15	YES
012	5.0 MG/KG	25NOV1998	YES	9:15	YES	YES	9:20	YES
013	PLACEBO	25NOV1998	YES	9:20	YES	YES	9:26	YES
014	5.0 MG/KG	25NOV1998	YES	9:25	YES	YES	9:30	YES

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TABLE G1
Dosing Details
Individual Values: All Subjects

Subject	Dose of Malathion	Date of Dosing	Fasted From 23:00h	Time of Breakfast Completion (h:min)	Formulation Administered Whilst Sitting	150 mls Water Given With Formulation	Time of Administration (h:min)	Seated/ Recumbent For 8h Postdose
015	PLACEBO	25NOV1998	YES	9:30	YES	YES	9:35	YES
016	PLACEBO	25NOV1998	YES	9:35	YES	YES	9:40	YES
017	5.0 MG/KG	25NOV1998	YES	9:40	NO	YES	.	.
917	5.0 MG/KG	25NOV1998	YES	9:55	YES	YES	10:45	YES
018	5.0 MG/KG	25NOV1998	YES	9:45	YES	YES	9:50	YES
019	10.0 MG/KG	09DEC1998	YES	8:55	YES	YES	9:00	YES
020	10.0 MG/KG	09DEC1998	YES	9:00	YES	YES	9:05	YES
021	PLACEBO	09DEC1998	YES	9:05	YES	YES	9:10	YES
022	10.0 MG/KG	09DEC1998	YES	9:09	YES	YES	9:15	YES
023	10.0 MG/KG	16DEC1998	YES	9:00	YES	YES	9:05	YES
024	PLACEBO	16DEC1998	YES	9:05	YES	YES	9:10	YES
025	PLACEBO	16DEC1998	YES	9:10	YES	YES	9:15	YES
026	15.0 MG/KG	16DEC1998	YES	9:15	YES	YES	9:20	YES
027	10.0 MG/KG	16DEC1998	YES	9:20	NO	YES	.	.

Note: Subject 917 replaces subject 017 who was unable to swallow capsule and withdrew from study
Subject 927 replaces subject 027 who was unable to swallow capsule and withdrew from study

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TABLE G1
Dosing Details
Individual Values: All Subjects

Subject	Dose of Malathion	Date of Dosing	Fasted From 23:00h	Time of Breakfast Completion (h:min)	Formulation Administered Whilst Sitting	150 mls Water Given With Formulation	Time of Administration (h:min)	Seated/ Recumbent For 8h Postdose
927	10.0 MG/KG	16DEC1998	YES	9:50	YES	YES	9:55	YES
028	10.0 MG/KG	16DEC1998	YES	9:30	YES	YES	9:35	YES
029	15.0 MG/KG	16DEC1998	YES	9:35	YES	YES	9:40	YES
030	10.0 MG/KG	16DEC1998	YES	9:40	YES	YES	9:45	YES
031	15.0 MG/KG	16DEC1998	YES	9:45	YES	YES	9:50	YES
032	PLACEBO	20JAN1999	YES	9:25	YES	YES	9:30	YES
033	15.0 MG/KG	20JAN1999	YES	9:30	YES	YES	9:35	YES
034	15.0 MG/KG	20JAN1999	YES	9:35	YES	YES	9:40	YES
035	PLACEBO	20JAN1999	YES	9:40	YES	YES	9:45	YES
036	PLACEBO	20JAN1999	YES	9:45	YES	YES	9:50	YES
037	15.0 MG/KG	20JAN1999	YES	9:50	YES	YES	9:55	YES
038	15.0 MG/KG	20JAN1999	YES	9:58	YES	YES	10:04	YES
039	15.0 MG/KG	03FEB1999	YES	9:10	YES	YES	9:15	YES
040	15.0 MG/KG	03FEB1999	YES	9:15	YES	YES	9:24	YES

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TABLE G1
Dosing Details
Individual Values: All Subjects

Subject	Dose of Malathion	Date of Dosing	Fasted From 23:00h	Time of Breakfast Completion (h:min)	Formulation Administered Whilst Sitting	150 mls Water Given With Formulation	Time of Administration (h:min)	Seated/ Recumbent For 8h Postdose
041	PLACEBO	03FEB1999	YES	9:20	YES	YES	9:30	YES
042	15.0 MG/KG	03FEB1999	YES	9:30	YES	YES	9:35	YES
043	15.0 MG/KG	03FEB1999	YES	9:35	YES	YES	9:40	YES
044	15.0 MG/KG	19FEB1999	YES	9:08	YES	YES	9:15	YES
045	PLACEBO	19FEB1999	YES	9:15	YES	YES	9:22	YES
046	15.0 MG/KG	19FEB1999	YES	9:19	YES	YES	9:30	YES
047	PLACEBO	02MAR1999	YES	8:55	YES	YES	9:05	YES
948	15.0 MG/KG	09MAR1999	YES	9:25	YES	YES	9:30	YES

Note: Subject 948 replaces subject 048 who withdrew from study before dosing

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Table G2

Dosing details: Actual dose received (mg)/bodyweight

Individual values: All subjects

Subject No.	Dose Group	Actual Dose Received (mg)	Bodyweight
1	0.5	37.59	78.4
2	0.5	26.51	54.0
3	Placebo	37.96	75.2
4	0.5	35.89	74.0
5	1.5	126.23	80.5
6	1.5	131.69	85.2
7	Placebo	120.79	79.1
8	1.5	112.07	77.6
9	5.0	329.08	69.0
10	5.0	447.85	93.2
11	5.0	339.92	70.6
12	5.0	358.60	72.9
13	Placebo	416.58	84.4
14	5.0	321.05	67.2
15	Placebo	325.37	67.3
16	Placebo	408.86	84.3
917	5.0	365.77	70.3
18	5.0	368.78	75.7
19	10.0	733.05	73.4
20	10.0	726.72	72.0
21	Placebo	574.63	58.0
22	10.0	654.04	64.7
23	10.0	821.20	80.6
24	Placebo	1026.96	69.4
25	Placebo	1064.35	70.3
26	15.0	1060.85	72.9
927	10.0	927.01	92.9
28	10.0	731.74	74.0
29	15.0	914.47	60.8
30	10.0	541.09	53.9
31	15.0	948.51	61.6
32	Placebo	886.76	58.6
33	15.0	925.48	61.6
34	15.0	1095.82	73.0
35	Placebo	962.34	65.0
36	Placebo	1114.89	74.4
37	15.0	1084.62	71.1
38	15.0	926.67	62.1
39	15.0	1148.93	77.3
40	15.0	829.76	54.8
41	Placebo	1169.96	80.1
42	15.0	1040.43	70.1
43	15.0	1082.56	71.4
44	15.0	953.29	61.7
45	Placebo	954.08	63.5
46	15.0	1024.61	66.9
47	Placebo	884.20	60.7
948	15.0	1064.30	71.6

APPENDIX H

Demographic data: Summary tables and individual data listings

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TABLE H1
Demographic Details
Summary Statistics: All Dosed Subjects

MALE

Dose of Malathion		PLACEBO	0.5 MG/KG	1.5 MG/KG	5.0 MG/KG	10.0 MG/KG	15.0 MG/KG	ALL
Age (yrs)	Mean	35.4	31.7	31.0	35.5	32.8	30.1	33.4
	SD	7.8	13.5	8.2	9.2	8.4	5.6	8.1
	Min	21	18	22	22	22	22	18
	Max	47	45	38	48	47	39	48
	N	11	3	3	8	8	7	40
Height (cm)	Mean	170.4	171.7	175.7	176.0	175.8	173.9	173.7
	SD	5.0	2.5	0.6	6.0	7.7	4.9	5.8
	Min	164	169	175	169	165	168	164
	Max	180	174	176	188	188	182	188
	N	11	3	3	8	8	7	40
Weight (kg)	Mean	71.45	68.80	81.10	74.04	74.71	66.16	72.22
	SD	9.08	13.00	3.84	8.19	12.19	5.82	9.50
	Min	58.0	54.0	77.6	67.2	53.9	60.8	53.9
	Max	84.4	78.4	85.2	93.2	92.9	73.0	93.2
	N	11	3	3	8	8	7	40

(CONTINUED)

Note: Data summarised in the above table are listed in table H2.1.1

Subjects 017, 027 and 048 withdrew from study before dosing and are replaced by subjects 917, 927 and 948 respectively
All withdrawn subjects and their replacements are included in the demographic summary statistics

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TABLE H1
Demographic Details
Summary Statistics: All Dosed Subjects

MALE

Dose of Malathion		PLACEBO	0.5 MG/KG	1.5 MG/KG	5.0 MG/KG	10.0 MG/KG	15.0 MG/KG	ALL
Caliper Size (cm)	Mean	7.21	7.17	7.43	7.39	7.20	7.37	7.29
	SD	0.25	0.31	0.12	0.32	0.35	0.24	0.28
	Min	6.9	6.9	7.3	7.0	6.6	7.1	6.6
	Max	7.7	7.5	7.5	7.9	7.7	7.8	7.9
	N	11	3	3	8	8	7	40
Race								
WHITE								
	N	11	3	3	8	8	7	40

Note: Data summarised in the above table are listed in table H2.1.1
Subjects 017, 027 and 048 withdrew from study before dosing and are replaced by subjects 917, 927 and 948 respectively
All withdrawn subjects and their replacements are included in the demographic summary statistics

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TABLE H1
Demographic Details
Summary Statistics: All Dosed Subjects

FEMALE

Dose of Malathion		PLACEBO	15.0 MG/KG	ALL
Age (yrs)	Mean	25.7	28.0	27.4
	SD	3.2	7.2	6.3
	Min	22	18	18
	Max	28	41	41
	N	3	8	11
Height (cm)	Mean	168.0	167.1	167.4
	SD	0.0	4.4	3.7
	Min	168	162	162
	Max	168	174	174
	N	3	8	11
Weight (kg)	Mean	68.10	65.76	66.40
	SD	10.49	8.76	8.77
	Min	60.7	52.3	52.3
	Max	80.1	77.3	80.1
	N	3	8	11

(CONTINUED)

Note: Data summarised in the above table are listed in table H2.1.1
Subjects 017, 027 and 048 withdrew from study before dosing and are replaced by subjects 917, 927 and 948 respectively
All withdrawn subjects and their replacements are included in the demographic summary statistics

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TABLE H1
Demographic Details
Summary Statistics: All Dosed Subjects

FEMALE					
Dose of Malathion			PLACEBO	15.0 MG/KG	ALL
Caliper Size (cm)	Mean		6.60	6.69	6.66
	SD		0.36	0.30	0.30
	Min		6.3	6.3	6.3
	Max		7.0	7.1	7.1
	N		3	8	11
Race					
WHITE		N	3	8	11

Note: Data summarised in the above table are listed in table H2.1.1
Subjects 017, 027 and 048 withdrew from study before dosing and are replaced by subjects 917, 927 and 948 respectively
All withdrawn subjects and their replacements are included in the demographic summary statistics

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TABLE H2.1.1
Demographic Details
Individual Values: All Subjects

Subject	Dose of Malathion	Initials	Date of Birth	Age (yrs)	Sex	Race	Height (cm)	Weight (kg)	Caliper Size (cm)	Frame Size
001	0.5 MG/KG	SRC	08APR1966	32	MALE	WHITE	174	78.4	7.5	MEDIUM
002	0.5 MG/KG	APS	25FEB1980	18	MALE	WHITE	169	54.0	6.9	MEDIUM
003	PLACEBO	MWM	30MAR1968	30	MALE	WHITE	175	75.2	7.3	MEDIUM
004	0.5 MG/KG	RM	15MAR1953	45	MALE	WHITE	172	74.0	7.1	MEDIUM
005	1.5 MG/KG	G DY	26NOV1964	33	MALE	WHITE	176	80.5	7.5	MEDIUM
006	1.5 MG/KG	RWC	17MAR1960	38	MALE	WHITE	176	85.2	7.5	MEDIUM
007	PLACEBO	KFB	02NOV1966	32	MALE	WHITE	164	79.1	7.0	MEDIUM
008	1.5 MG/KG	SM	10FEB1976	22	MALE	WHITE	175	77.6	7.3	MEDIUM
009	5.0 MG/KG	SNC	16OCT1976	22	MALE	WHITE	174	69.0	7.4	MEDIUM
010	5.0 MG/KG	BDB	21JUN1954	44	MALE	WHITE	188	93.2	7.7	MEDIUM
011	5.0 MG/KG	RC	15NOV1959	38	MALE	WHITE	175	70.6	7.2	MEDIUM
012	5.0 MG/KG	PD	08JUN1950	48	MALE	WHITE	169	72.9	7.9	LARGE
013	PLACEBO	MIF	03MAR1951	47	MALE	WHITE	175	84.4	7.3	MEDIUM
014	5.0 MG/KG	WRS	26MAY1955	43	MALE	WHITE	172	67.2	7.5	MEDIUM
015	PLACEBO	KMT	11JUL1958	40	MALE	WHITE	180	67.3	6.9	SMALL

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TABLE H2.1.1
Demographic Details
Individual Values: All Subjects

Subject	Dose of Malathion	Initials	Date of Birth	Age (yrs)	Sex	Race	Height (cm)	Weight (kg)	Caliper Size (cm)	Frame Size
016	PLACEBO	GHK	04OCT1970	28	MALE	WHITE	169	84.3	7.7	LARGE
017	5.0 MG/KG	WDF	06MAY1970	28	MALE	WHITE	173	73.4	7.0	MEDIUM
917	5.0 MG/KG	LAH	16JUL1965	33	MALE	WHITE	181	70.3	7.4	MEDIUM
018	5.0 MG/KG	AJL	03AUG1970	28	MALE	WHITE	176	75.7	7.0	MEDIUM
019	10.0 MG/KG	MTP	05JAN1960	38	MALE	WHITE	176	73.4	7.3	MEDIUM
020	10.0 MG/KG	AM	30JAN1951	47	MALE	WHITE	170	72.0	7.3	MEDIUM
021	PLACEBO	AMC	12JUN1955	43	MALE	WHITE	166	58.0	7.2	MEDIUM
022	10.0 MG/KG	SJF	31MAR1976	22	MALE	WHITE	165	64.7	7.1	MEDIUM
023	10.0 MG/KG	JBK	18MAR1962	36	MALE	WHITE	182	80.6	7.4	MEDIUM
024	PLACEBO	TAH	23JUN1956	42	MALE	WHITE	171	69.4	7.4	MEDIUM
025	PLACEBO	JD	29JUN1977	21	MALE	WHITE	167	70.3	7.4	MEDIUM
026	15.0 MG/KG	PJH	03SEP1970	28	MALE	WHITE	182	72.9	7.8	MEDIUM
027	10.0 MG/KG	GG	11NOV1964	34	MALE	WHITE	180	86.2	7.4	MEDIUM
927	10.0 MG/KG	RGB	22OCT1971	27	MALE	WHITE	188	92.9	7.7	MEDIUM
028	10.0 MG/KG	KMM	10DEC1962	35	MALE	WHITE	177	74.0	6.8	SMALL

Note: Subject 917 replaces subject 017 who withdrew from study before dosing
Subject 927 replaces subject 027 who withdrew from study before dosing

TABLE H2.1.1
Demographic Details
Individual Values: All Subjects

Subject	Dose of Malathion	Initials	Date of Birth	Age (yrs)	Sex	Race	Height (cm)	Weight (kg)	Caliper Size (cm)	Frame Size
029	15.0 MG/KG	KD	18DEC1968	29	MALE	WHITE	178	60.8	7.3	MEDIUM
030	10.0 MG/KG	IRD	30OCT1975	23	MALE	WHITE	168	53.9	6.6	SMALL
031	15.0 MG/KG	AMC	11JAN1959	39	MALE	WHITE	174	61.6	7.2	MEDIUM
032	PLACEBO	JSB	03JUN1960	38	MALE	WHITE	172	58.6	6.9	MEDIUM
033	15.0 MG/KG	LIW	29APR1962	36	MALE	WHITE	173	61.6	7.1	MEDIUM
034	15.0 MG/KG	RRK	02JUL1970	28	MALE	WHITE	173	73.0	7.6	MEDIUM
035	PLACEBO	IB	20JAN1960	38	MALE	WHITE	164	65.0	7.0	MEDIUM
036	PLACEBO	TM	21FEB1968	30	MALE	WHITE	171	74.4	7.2	MEDIUM
037	15.0 MG/KG	MF	08DEC1969	29	MALE	WHITE	168	71.1	7.3	MEDIUM
038	15.0 MG/KG	KSA	23JUN1976	22	MALE	WHITE	169	62.1	7.3	MEDIUM
039	15.0 MG/KG	CES	30NOV1972	26	FEMALE	WHITE	168	77.3	6.8	LARGE
040	15.0 MG/KG	LCC	16MAY1969	29	FEMALE	WHITE	163	54.8	6.4	MEDIUM
041	PLACEBO	LMC	05SEP1970	28	FEMALE	WHITE	168	80.1	7.0	LARGE
042	15.0 MG/KG	DLA	13NOV1977	21	FEMALE	WHITE	169	70.1	6.6	MEDIUM
043	15.0 MG/KG	ALB	26NOV1980	18	FEMALE	WHITE	174	71.4	7.1	LARGE

TABLE H2.1.1
Demographic Details
Individual Values: All Subjects

Subject	Dose of Malathion	Initials	Date of Birth	Age (yrs)	Sex	Race	Height (cm)	Weight (kg)	Caliper Size (cm)	Frame Size
044	15.0 MG/KG	MM	22NOV1964	34	FEMALE	WHITE	172	61.7	6.9	LARGE
045	PLACEBO	EH	26MAY1971	27	FEMALE	WHITE	168	63.5	6.5	MEDIUM
046	15.0 MG/KG	PJ	15JUL1957	41	FEMALE	WHITE	164	66.9	6.4	MEDIUM
047	PLACEBO	JCM	30JUL1976	22	FEMALE	WHITE	168	60.7	6.3	MEDIUM
048	15.0 MG/KG	CAC	12OCT1971	27	FEMALE	WHITE	165	52.3	6.3	MEDIUM
948	15.0 MG/KG	KJO	13OCT1970	28	FEMALE	WHITE	162	71.6	7.0	LARGE

Note: subject 948 replaces subject 048 who withdrew from study before dosing

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TABLE H2.1.2

Demographic Details
Smoking And Alcohol Consumption
Individual Values: All Subjects

Subject	Dose of Malathion	Smoker	Date Stopped Smoking	Amount Smoked	Drinks Alcohol	Alcohol Intake
001	0.5 MG/KG	NON-SMOKER			YES	12 UNITS PER WEEK
002	0.5 MG/KG	NON-SMOKER			YES	10 UNITS PER WEEK
003	PLACEBO	SMOKER		20 CIGARETTES PER DAY	YES	02 UNITS PER WEEK
004	0.5 MG/KG	SMOKER		01 CIGARS PER DAY	YES	21 UNITS PER WEEK
005	1.5 MG/KG	NON-SMOKER			YES	06 UNITS PER WEEK
006	1.5 MG/KG	NON-SMOKER			YES	10 UNITS PER WEEK
007	PLACEBO	SMOKER		08 CIGARETTES PER DAY	YES	06 UNITS PER WEEK
008	1.5 MG/KG	SMOKER		15 CIGARETTES PER DAY	YES	20 UNITS PER WEEK
009	5.0 MG/KG	SMOKER		15 CIGARETTES PER DAY	YES	12 UNITS PER WEEK
010	5.0 MG/KG	SMOKER		10 CIGARETTES PER DAY	NO	
011	5.0 MG/KG	SMOKER		15 CIGARETTES PER DAY	NO	
012	5.0 MG/KG	SMOKER		10 CIGARETTES PER DAY	YES	12 UNITS PER WEEK
013	PLACEBO	SMOKER		10 CIGARETTES PER DAY	NO	
014	5.0 MG/KG	SMOKER		18 CIGARETTES PER DAY	YES	02 UNITS PER WEEK

Note: One unit of alcohol is defined as one glass of wine, half a pint of lager/beer or one measure of spirits

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TABLE H2.1.2

**Demographic Details
Smoking And Alcohol Consumption
Individual Values: All Subjects**

Subject	Dose of Maltathion	Smoker	Date Stopped Smoking	Amount Smoked	Drinks Alcohol	Alcohol Intake
015	PLACEBO	SMOKER		15 CIGARETTES PER DAY	YES	08 UNITS PER WEEK
016	PLACEBO	SMOKER		03 CIGARETTES PER DAY	YES	14 UNITS PER WEEK
017	5.0 MG/KG	SMOKER		05 CIGARETTES PER DAY	YES	10 UNITS PER WEEK
917	5.0 MG/KG	SMOKER		10 CIGARETTES PER DAY	YES	14 UNITS PER WEEK
018	5.0 MG/KG	SMOKER		10 CIGARETTES PER DAY	NO	
019	10.0 MG/KG	SMOKER		10 CIGARETTES PER DAY	YES	04 UNITS PER WEEK
020	10.0 MG/KG	SMOKER		05 CIGARETTES PER DAY	YES	02 UNITS PER WEEK
021	PLACEBO	SMOKER		03 CIGARETTES PER DAY	YES	02 UNITS PER WEEK
022	10.0 MG/KG	SMOKER		10 CIGARETTES PER DAY	YES	04 UNITS PER WEEK
023	10.0 MG/KG	SMOKER		15 CIGARETTES PER DAY	YES	02 UNITS PER WEEK
024	PLACEBO	SMOKER		05 CIGARETTES PER DAY	YES	06 UNITS PER WEEK
025	PLACEBO	SMOKER		20 CIGARETTES PER DAY	NO	
026	15.0 MG/KG	SMOKER		06 CIGARETTES PER DAY	NO	
027	10.0 MG/KG	SMOKER		15 CIGARETTES PER DAY	NO	

Note: One unit of alcohol is defined as one glass of wine, half a pint of lager/beer or one measure of spirits
 Subject 917 replaces subject 017 who withdrew from study before dosing
 Subject 927 replaces subject 027 who withdrew from study before dosing

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TABLE H2.1.2

Demographic Details
Smoking And Alcohol Consumption
Individual Values: All Subjects

Subject	Dose of Malathion	Smoker	Date Stopped Smoking	Amount Smoked	Drinks Alcohol	Alcohol Intake
927	10.0 MG/KG	SMOKER		10 CIGARETTES PER DAY	YES	08 UNITS PER WEEK
028	10.0 MG/KG	SMOKER		05 CIGARETTES PER DAY	YES	10 UNITS PER WEEK
029	15.0 MG/KG	SMOKER		10 CIGARETTES PER DAY	YES	14 UNITS PER WEEK
030	10.0 MG/KG	SMOKER		07 CIGARETTES PER DAY	YES	04 UNITS PER WEEK
031	15.0 MG/KG	SMOKER		07 CIGARETTES PER DAY	YES	20 UNITS PER WEEK
032	PLACEBO	SMOKER		10 CIGARETTES PER DAY	YES	20 UNITS PER WEEK
033	15.0 MG/KG	SMOKER		10 CIGARETTES PER DAY	YES	10 UNITS PER WEEK
034	15.0 MG/KG	SMOKER		02 CIGARETTES PER DAY	YES	02 UNITS PER WEEK
035	PLACEBO	SMOKER		06 CIGARETTES PER DAY	YES	20 UNITS PER WEEK
036	PLACEBO	SMOKER		08 CIGARETTES PER DAY	YES	10 UNITS PER WEEK
037	15.0 MG/KG	SMOKER		15 CIGARETTES PER DAY	YES	02 UNITS PER WEEK
038	15.0 MG/KG	NON-SMOKER			YES	14 UNITS PER WEEK
039	15.0 MG/KG	SMOKER		05 CIGARETTES PER DAY	YES	14 UNITS PER WEEK
040	15.0 MG/KG	PREVIOUS	JAN1999		YES	06 UNITS PER WEEK

Note: One unit of alcohol is defined as one glass of wine, half a pint of lager/beer or one measure of spirits

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TABLE H2.1.2

Demographic Details
Smoking And Alcohol Consumption
Individual Values: All Subjects

Subject	Dose of Malathion	Smoker	Date Stopped Smoking	Amount Smoked	Drinks Alcohol	Alcohol Intake
041	PLACEBO	SMOKER		10 CIGARETTES PER DAY	YES	01 UNITS PER WEEK
042	15.0 MG/KG	PREVIOUS	10/JAN1999		YES	02 UNITS PER WEEK
043	15.0 MG/KG	SMOKER		10 CIGARETTES PER DAY	YES	10 UNITS PER WEEK
044	15.0 MG/KG	SMOKER		10 CIGARETTES PER DAY	YES	04 UNITS PER WEEK
045	PLACEBO	SMOKER		10 CIGARETTES PER DAY	YES	01 UNITS PER WEEK
046	15.0 MG/KG	NON-SMOKER			NO	
047	PLACEBO	SMOKER		05 CIGARETTES PER DAY	YES	04 UNITS PER WEEK
048	15.0 MG/KG	SMOKER		15 CIGARETTES PER DAY	YES	01 UNITS PER WEEK
948	15.0 MG/KG	PREVIOUS	JAN1999		YES	12 UNITS PER WEEK

Note: One unit of alcohol is defined as one glass of wine, half a pint of lager/beer or one measure of spirits
Subject 948 replaces subject 048 who withdrew from study before dosing

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TABLE H2.2.1

Medications Taken One Month Prior To Screening
Individual Values: All Subjects Who Received Medications

Subject	Dose of Malathion	Drug Number	D:Drug I:Indication	S:Start E:End	D:Dosage F:Frequency R:Route	Side Effects
004	0.5 MG/KG	1	D:CO-PROXAMOL I:HEADACHE	S:14OCT1998 E:14OCT1998	D:2 TABLET F:ONE DOSE ONLY R:ORAL	NO
005	1.5 MG/KG	1	D:PARACETAMOL I:HEADACHE	S:01OCT1998 E:01OCT1998	D:1 G F:ONE DOSE ONLY R:ORAL	NO
008	1.5 MG/KG	1	D:ANADIN EXTRA I:HEADACHE	S:22OCT1998 E:22OCT1998	D:2 TABLET F:ONE DOSE ONLY R:ORAL	NO
008	1.5 MG/KG	2	D:BOOTS COUGH MIXTURE I:COUGH	S:05OCT1998 E:19OCT1998	D:5 CC OR ML F:FOUR TIMES A DAY (QID) R:ORAL	NO
008	1.5 MG/KG	3	D:MULTIVITAMINS + IRON I:COLD SYMPTOMS.	S:05OCT1998 E:22OCT1998	D:1 TABLET F:ONCE DAILY R:ORAL	NO
009	5.0 MG/KG	1	D:LEMSIP I:COLD SYMPTOMS.	S:02OCT1998 E:04OCT1998	D:1 SACHET/POWDER/PACKET F:EVERY 4-6 HOURS R:ORAL	NO
013	PLACEBO	1	D:ASPIRIN I:HEADACHE	S:19OCT1998 E:19OCT1998	D:300 MG F:ONE DOSE ONLY R:ORAL	NO

TABLE H2.2.1

Medications Taken One Month Prior To Screening
Individual Values: All Subjects Who Received Medications

Subject	Dose of Malathion	Drug Number	D:Drug I:Indication	S:Start E:End	D:Dosage F:Frequency R:Route	Side Effects
023	10.0 MG/KG	1	D:DIHYDROCODEINE I:POST ACCIDENT ANALGESIA.	S:23OCT1998 E:10NOV1998	D:60 MG F:FOUR TIMES A DAY (QID) R:ORAL	NO
023	10.0 MG/KG	2	D:IBUPROFEN I:POST ACCIDENT INFLAMMATION.	S:23OCT1998 E:10NOV1998	D:400 MG F:THREE TIMES A DAY (TID) R:ORAL	NO
927	10.0 MG/KG	1	D:PARACETAMOL I:HEADACHE	S:18NOV1998 E:18NOV1998	D:1 G F:ONE DOSE ONLY R:ORAL	NO
034	15.0 MG/KG	1	D:PARACETAMOL I:HEADACHE	S:01JAN1999 E:01JAN1999	D:1 G F:ONE DOSE ONLY R:ORAL	NO
039	15.0 MG/KG	1	D:MICROGYNON I:CONTRACEPTION	S:1991 E:CONTINUED	D:1 TABLET F:ONCE DAILY R:ORAL	NO
040	15.0 MG/KG	1	D:DAKTACORT CREAM I:DRY PATCH UNDER RIGHT EYE.	S:15DEC1998 E:15JAN1999	D:CREAM APPLICATION F:TWICE DAILY (BID) R:TOPICAL	NO
040	15.0 MG/KG	2	D:CILEST I:CONTRACEPTION	S:1992 E:CONTINUED	D:1 TABLET F:ONCE DAILY R:ORAL	NO

TABLE H2.2.1

Medications Taken One Month Prior To Screening
Individual Values: All Subjects Who Received Medications

Subject	Dose of Medication	Drug Number	D:Drug I:Indication	S:Start E:End	D:Dosage F:Frequency R:Route	Side Effects
041	PLACEBO	1	D:IBUPROFEN I:BACK PAIN.	S:12JAN1999 E:19JAN1999	D:400 MG F:THREE TIMES A DAY (TID) R:ORAL	NO
044	15.0 MG/KG	1	D:OVRANETTE I:CONTRACEPTION	S:1993 E:CONTINUED	D:1 TABLET F:ONCE DAILY R:ORAL	NO
046	15.0 MG/KG	1	D:ASPIRIN I:DYSMENORRHOEA	S:18JAN1999 E:18JAN1999	D:600 MG F:ONE DOSE ONLY R:ORAL	NO
047	PLACEBO	1	D:LIGNOCAINE HYDROCHLORIDE I:TOOTH EXTRACTION.	S:25JAN1999 E:25JAN1999	D:VARIABLE DOSE F:ONE DOSE ONLY R:GINGIVAL	NO
047	PLACEBO	2	D:PANADOL I:DENTAL PAIN.	S:25JAN1999 E:26JAN1999	D:2 TABLET F:AS REQUIRED (PRN) R:ORAL	NO
047	PLACEBO	3	D:CILEST I:CONTRACEPTION	S:JUN1998 E:CONTINUED	D:1 TABLET F:ONCE DAILY R:ORAL	NO
948	15.0 MG/KG	1	D:MICROGYNON I:ORAL CONTRACEPTIVE PILL.	S:DEC1996 E:CONTINUED	D:1 TABLET F:ONCE DAILY R:ORAL	NO

Note: Subject 948 replaces subject 048 who withdrew from study before dosing

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TABLE H2.2.2
Medication Changes Since Screening
Individual Values: All Subjects With Medication Changes

Patient	TREAT	DGNUM	D:Drug I:Indication	S:Start E:End	D:Dosage F:Frequency R:Route	Side Effects
6	1.5	1	D:PARACETAMOL I:HEAD COLD/NASAL CONGESTION.	S:17OCT1998 E:19OCT1998	D:2 TABLET F:EVERY 6 HOURS R:ORAL	NO
8	1.5	1	D:BENYLIN I:SORE THROAT.	S:15NOV1998 E:CONTINUED	D:2 TEASPOON F:EVERY 6 HOURS R:ORAL	NO
10	5.0	1	D:PARACETAMOL I:HEADACHE	S:25NOV1998 E:25NOV1998	D:1 G F:EVERY 6 HOURS R:ORAL	NO
14	5.0	1	D:PARACETAMOL I:PAIN IN PERINEUM.	S:26NOV1998 E:27NOV1998	D:1 G F:EVERY 4-6 HOURS R:ORAL	NO
14	5.0	2	D:DIAMORPHINE I:POST OPERATIVE PAIN FOLLOWING SURGERY : EXCISION AND DRAINAGE OF PERIANAL ABSCESS.	S:28NOV1998 E:28NOV1998	D:20 MG F:ONE DOSE ONLY R:INTRAMUSCULAR	NO
14	5.0	3	D:IBUPROFEN I:PAIN RELIEF FOLLOWING SURGERY.	S:30NOV1998 E:30NOV1998	D:400 MG F:THREE TIMES A DAY (TID) R:ORAL	NO
19	10.0	1	D:PARACETAMOL I:HEADACHE	S:09DEC1998 E:15DEC1998	D:1 G F:EVERY 4-6 HOURS R:ORAL	NO

TABLE H2.2.2
Medication Changes Since Screening
Individual Values: All Subjects With Medication Changes

Patient	TREAT	DGNUM	D:Drug I:Indication	S:Start E:End	D:Dosage F:Frequency R:Route	Side Effects
21	0	1	D:PARACETAMOL I:HEADACHE	S:09DEC1998 E:09DEC1998	D:1 G F:EVERY 4-6 HOURS R:ORAL	NO
22	10	1	D:PARACETAMOL I:HEADACHE	S:09DEC1998 E:09DEC1998	D:1 G F:EVERY 4-6 HOURS R:ORAL	NO
40	15	1	D:DAKTACORT I:DRY PATCH UNDER RIGHT EYE.	S:15FEB1999 E:16FEB1999	D:CREAM APPLICATION F:TWICE DAILY (BID) R:TOPICAL	NO
42	15	1	D:PENICILLIN V I:PAINFUL WISDOM TOOTH.	S:13FEB1999 E:19FEB1999	D:250 MG F:FOUR TIMES A DAY (QID) R:ORAL	NO
45	0	1	D:PARACETAMOL I:HEADACHE OR STOMACH CRAMP.	S:20FEB1999 E:20FEB1999	D:1 G F:EVERY 4-6 HOURS R:ORAL	NO
45	0	2	D:PARACETAMOL I:TOOTHACHE	S:24FEB1999 E:24FEB1999	D:1 G F:ONE DOSE ONLY R:ORAL	NO
46	15	1	D:PARACETAMOL I:HEADACHE	S:20FEB1999 E:20FEB1999	D:1 G F:EVERY 4-6 HOURS R:ORAL	NO

TABLE H2.3.1

Medical History At Screening
Individual Values: All Subjects

Subject	Dose of Malathion	E,E,N,T	Respiratory	Cardiovascular	Gastrointestinal	Genitourinary	Musculoskeletal	Neurological
001	0.5 MG/KG	NO	NO	NO	NO	YES	NO	NO
002	0.5 MG/KG	NO	NO	NO	NO	NO	NO	NO
003	PLACEBO	NO	NO	NO	NO	NO	NO	NO
004	0.5 MG/KG	NO	NO	NO	NO	YES	YES	YES
005	1.5 MG/KG	YES	NO	NO	YES	YES	NO	YES
006	1.5 MG/KG	NO	NO	NO	NO	YES	NO	NO
007	PLACEBO	NO	NO	YES	YES	YES	YES	NO
008	1.5 MG/KG	YES	NO	NO	YES	NO	NO	YES
009	5.0 MG/KG	NO	YES	NO	NO	NO	YES	NO
010	5.0 MG/KG	YES	NO	NO	NO	YES	YES	YES
011	5.0 MG/KG	YES	YES	NO	YES	NO	NO	NO
012	5.0 MG/KG	NO	NO	NO	NO	NO	NO	NO
013	PLACEBO	YES	NO	YES	NO	NO	NO	NO
014	5.0 MG/KG	YES	NO	NO	NO	NO	NO	YES
015	PLACEBO	YES	NO	NO	YES	YES	YES	NO

TABLE H2.3.1

Medical History At Screening
Individual Values: All Subjects

Subject	Dose of Malathion	E,E,N,T	Respiratory	Cardiovascular	Gastrointestinal	Genitourinary	Musculoskeletal	Neurological
016	PLACEBO	NO	NO	NO	NO	NO	NO	NO
017	5.0 MG/KG	NO	NO	NO	NO	NO	YES	NO
917	5.0 MG/KG	NO	NO	NO	NO	NO	NO	NO
018	5.0 MG/KG	NO	NO	NO	NO	NO	YES	NO
019	10.0 MG/KG	YES	NO	NO	YES	NO	NO	NO
020	10.0 MG/KG	YES	NO	NO	NO	NO	YES	NO
021	PLACEBO	YES	YES	NO	NO	NO	YES	NO
022	10.0 MG/KG	YES	NO	NO	NO	NO	NO	NO
023	10.0 MG/KG	NO	NO	NO	NO	NO	YES	NO
024	PLACEBO	YES	NO	NO	YES	NO	NO	NO
025	PLACEBO	YES	NO	NO	YES	NO	YES	NO
026	15.0 MG/KG	YES	NO	NO	NO	NO	NO	NO
027	10.0 MG/KG	NO	NO	NO	NO	NO	NO	YES
927	10.0 MG/KG	NO	NO	NO	YES	NO	YES	YES
028	10.0 MG/KG	YES	NO	NO	NO	NO	YES	NO

Note: Subject 917 replaces subject 017 who withdrew from study before dosing
Subject 927 replaces subject 027 who withdrew from study before dosing

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TABLE H2.3.1

Medical History At Screening
Individual Values: All Subjects

Subject	Dose of Malathion	E,E,N,T	Respiratory	Cardiovascular	Gastrointestinal	Genitourinary	Musculoskeletal	Neurological
029	15.0 MG/KG	NO	NO	YES	NO	NO	YES	NO
030	10.0 MG/KG	YES	NO	NO	NO	NO	NO	NO
031	15.0 MG/KG	YES	NO	NO	NO	NO	NO	NO
032	PLACEBO	NO	NO	NO	NO	NO	YES	YES
033	15.0 MG/KG	NO	NO	NO	NO	NO	YES	NO
034	15.0 MG/KG	NO	NO	NO	YES	NO	YES	NO
035	PLACEBO	NO	NO	NO	NO	NO	YES	NO
036	PLACEBO	YES	NO	NO	NO	NO	NO	NO
037	15.0 MG/KG	NO	NO	NO	NO	NO	NO	NO
038	15.0 MG/KG	NO	NO	NO	NO	NO	YES	YES
039	15.0 MG/KG	YES	NO	NO	NO	NO	NO	NO
040	15.0 MG/KG	YES	NO	NO	NO	NO	NO	NO
041	PLACEBO	NO	NO	NO	NO	YES	YES	NO
042	15.0 MG/KG	NO	NO	NO	NO	NO	NO	NO
043	15.0 MG/KG	NO	NO	NO	NO	NO	NO	NO

TABLE H2.3.1

Medical History At Screening
Individual Values: All Subjects

Subject	Dose of Malathion	E,E,N,T	Respiratory	Cardiovascular	Gastrointestinal	Genitourinary	Musculoskeletal	Neurological
044	15.0 MG/KG	NO	NO	NO	NO	NO	NO	NO
045	PLACEBO	NO	NO	NO	NO	NO	NO	NO
046	15.0 MG/KG	NO	NO	NO	NO	NO	NO	NO
047	PLACEBO	YES	NO	NO	NO	NO	YES	NO
048	15.0 MG/KG	NO	NO	NO	NO	NO	NO	NO
948	15.0 MG/KG	YES	NO	NO	NO	NO	NO	NO

Note: Subject 948 replaces subject 048 who withdrew from study before dosing

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TABLE H2.3.1
Medical History At Screening
Individual Values: All Subjects

Subject	Dose of Malathion	Endocrine/ Metabolic	Haemopoietic/ Lymphatic	Dermatological	Psychological	Other Chronic System Disease	Surgical History	Allergies
001	0.5 MG/KG	NO	NO	NO	NO	NO	YES	NO
002	0.5 MG/KG	NO	NO	YES	NO	NO	NO	NO
003	PLACEBO	NO	NO	NO	NO	NO	YES	NO
004	0.5 MG/KG	NO	NO	YES	NO	NO	NO	NO
005	1.5 MG/KG	NO	NO	NO	NO	NO	YES	NO
006	1.5 MG/KG	NO	NO	YES	NO	NO	NO	YES
007	PLACEBO	NO	NO	NO	NO	NO	YES	NO
008	1.5 MG/KG	NO	NO	YES	NO	NO	NO	YES
009	5.0 MG/KG	NO	NO	NO	NO	NO	YES	NO
010	5.0 MG/KG	NO	NO	NO	YES	NO	NO	NO
011	5.0 MG/KG	NO	NO	NO	NO	NO	YES	NO
012	5.0 MG/KG	NO	NO	NO	NO	NO	NO	NO
013	PLACEBO	NO	YES	NO	YES	NO	YES	YES
014	5.0 MG/KG	NO	NO	NO	NO	NO	YES	NO
015	PLACEBO	NO	NO	NO	YES	NO	YES	YES

TABLE H2.3.1

Medical History At Screening
Individual Values: All Subjects

Subject	Dose of Malathion	Endocrine/ Metabolic	Haemopoietic/ Lymphatic	Dermatological	Psychological	Other Chronic System Disease	Surgical History	Allergies
016	PLACEBO	NO	NO	NO	YES	NO	NO	NO
017	5.0 MG/KG	NO	NO	NO	NO	NO	YES	NO
917	5.0 MG/KG	NO	NO	NO	NO	NO	NO	NO
018	5.0 MG/KG	NO	NO	NO	NO	NO	NO	NO
019	10.0 MG/KG	NO	NO	NO	NO	NO	YES	YES
020	10.0 MG/KG	NO	NO	NO	YES	NO	NO	NO
021	PLACEBO	NO	NO	NO	NO	NO	NO	NO
022	10.0 MG/KG	NO	NO	NO	NO	NO	YES	YES
023	10.0 MG/KG	NO	NO	NO	YES	NO	YES	NO
024	PLACEBO	NO	NO	NO	NO	NO	YES	NO
025	PLACEBO	NO	NO	YES	NO	NO	YES	NO
026	15.0 MG/KG	NO	NO	NO	NO	NO	YES	YES
027	10.0 MG/KG	NO	NO	NO	NO	NO	NO	NO
927	10.0 MG/KG	NO	NO	NO	NO	NO	YES	NO
028	10.0 MG/KG	NO	NO	NO	YES	NO	YES	NO

Note: Subject 917 replaces subject 017 who withdrew from study before dosing
Subject 927 replaces subject 027 who withdrew from study before dosing

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TABLE H2.3.1

Medical History At Screening
Individual Values: All Subjects

Subject	Dose of Malathion	Endocrine/ Metabolic	Haemopoietic/ Lymphatic	Dermatological	Psychological	Other Chronic System Disease	Surgical History	Allergies
029	15.0 MG/KG	NO	NO	YES	YES	NO	NO	NO
030	10.0 MG/KG	NO	NO	NO	NO	NO	YES	NO
031	15.0 MG/KG	NO	NO	NO	NO	NO	YES	NO
032	PLACEBO	NO	NO	NO	NO	NO	NO	NO
033	15.0 MG/KG	NO	NO	NO	NO	NO	YES	NO
034	15.0 MG/KG	NO	NO	NO	NO	NO	NO	NO
035	PLACEBO	NO	NO	YES	NO	NO	NO	NO
036	PLACEBO	NO	NO	NO	NO	NO	NO	YES
037	15.0 MG/KG	NO	NO	NO	YES	NO	NO	NO
038	15.0 MG/KG	NO	NO	NO	NO	NO	NO	NO
039	15.0 MG/KG	NO	NO	NO	NO	NO	NO	NO
040	15.0 MG/KG	NO	NO	YES	NO	NO	NO	NO
041	PLACEBO	NO	NO	NO	NO	NO	YES	NO
042	15.0 MG/KG	NO	NO	NO	NO	NO	YES	NO
043	15.0 MG/KG	NO	NO	NO	NO	NO	NO	NO

TABLE H2.3.1

Medical History At Screening
Individual Values: All Subjects

Subject	Dose of Malathion	Endocrine/ Metabolic	Haemopoietic/ Lymphatic	Dermatological	Psychological	Other Chronic System Disease	Surgical History	Allergies
044	15.0 MG/KG	NO	NO	NO	NO	NO	NO	NO
045	PLACEBO	NO	NO	NO	YES	NO	YES	NO
046	15.0 MG/KG	NO	NO	NO	NO	NO	YES	YES
047	PLACEBO	NO	NO	NO	NO	NO	YES	NO
048	15.0 MG/KG	NO	NO	YES	NO	NO	YES	NO
948	15.0 MG/KG	NO	NO	YES	NO	NO	NO	NO

Note: Subject 948 replaces subject 048 who withdrew from study before dosing

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TABLE H2.3.2
Medical History At Screening
Details of Abnormalities: All Subjects with Abnormalities

Subject	Dose of Malathion	Body System	Result	Details
001	0.5 MG/KG	GENITOURINARY SURGICAL HISTORY	YES YES	UNDESCENDED TESTES, AGED 5 YRS CORRECTIVE SURGERY. SURGERY FOR UNDESCENDED TESTES AGED 5 YRS.
002	0.5 MG/KG	DERMATOLOGICAL	YES	DRY SKIN PATCHES ON BOTH ARMS - NO TREATMENT.
003	PLACEBO	SURGICAL HISTORY	YES	REPAIR OF SQUINT IN LEFT EYE AGED 5 YRS.
004	0.5 MG/KG	GENITOURINARY MUSCULOSKELETAL NEUROLOGICAL DERMATOLOGICAL	YES YES YES YES	INFECTION OF TESTES 1996 - 1997 - RESOLVED. FRACTURED NOSE 1997. BUMP ON HEAD - KNOCKED OUT FOR 2 MINUTES 1992. NO PROBLEMS. SCARS ON BACK FROM BURNS AGED 5. COLD SORE ON LEFT LOWER LIP PRESENT AT SCREENING.
005	1.5 MG/KG	E.E.N.T. GASTROINTESTINAL GENITOURINARY NEUROLOGICAL SURGICAL HISTORY	YES YES YES YES YES	ADENOIDECTOMY - AGE 5. WEARS GLASSES. BLEEDING DUODENAL ULCER 1980. SELECTIVE VAGOTOMY 1981. RENAL CALCULI - ULTRASOUND TREATMENT 1995. LOSS OF CONSCIOUSNESS - KNOCK TO HEAD AS CHILD. SELECTIVE VAGOTOMY 1981. ADENOIDECTOMY - AGE 5.
006	1.5 MG/KG	GENITOURINARY DERMATOLOGICAL ALLERGIES	YES YES YES	INVESTIGATIONS FOR RENAL COLIC 1995 NIL FOUND. DERMATITIS ON HANDS 1994 NIL SINCE ? STRESS RELATED. HYPERSENSITIVITY TO TETANUS INJECTION AND ALGIPAN - BOTH LOCALISED. NO TREATMENT.

TABLE H2.3.2

Medical History At Screening
Details of Abnormalities: All Subjects with Abnormalities

Subject	Dose of Methathion	Body System	Result	Details
007	PLACEBO	CARDIOVASCULAR	YES	CARDIAC INVESTIGATIONS ECHO DONE 1995 - NO ABNORMALITIES FOUND.
		GASTROINTESTINAL	YES	NON-SPECIFIC ABDOMINAL PAIN: CO-PROXAMOL PRESCRIBED BY GP 31/08/98.
		GENITOURINARY	YES	TORSION RIGHT TESTICLE 1996.
		MUSCULOSKELETAL	YES	FRACTURED WRIST - RIGHT 1979. BACKACHE - NO SYMPTOMS FOR 2 MONTHS.
		SURGICAL HISTORY	YES	SUTURING TO RIGHT MIDDLE FINGER AS A CHILD - GENERAL ANAESTHETIC. ORCHIDOPEXY 1996.
008	1.5 MG/KG	E.E.N.T	YES	WEARS GLASSES. SINUSITIS 1997.
		GASTROINTESTINAL	YES	ENDOSCOPY 4/12 AGO - INVESTIGATION NORMAL.
		NEUROLOGICAL	YES	MIGRAINE: EEG 1994 - NO SYMPTOMS FOR 3 YEARS. EEG NORMAL.
		DERMATOLOGICAL	YES	ACNE - MILD NO TREATMENT.
		ALLERGIES	YES	NICKLE & BEE STINGS.
009	5.0 MG/KG	RESPIRATORY	YES	CHEST ABSCESS RIGHT UPPER LOBE AS A BABY 1977.
		MUSCULOSKELETAL	YES	FRACTURED RIGHT HAND 1992.
		SURGICAL HISTORY	YES	THORACOTOMY 1977.
010	5.0 MG/KG	E.E.N.T	YES	BROKEN NOSE 1993.
		GENITOURINARY	YES	RENAL CALCULI 1994.
		MUSCULOSKELETAL	YES	FRACTURED RIBS AGE 8 - ROAD TRAFFIC ACCIDENT.
		NEUROLOGICAL	YES	ROAD ACCIDENT AGE 8 KNOCKED OUT FOR 2 HOURS.
		PSYCHOLOGICAL	YES	STRESS AT WORK FEB 1998. ATTENDED GP NO MEDICATION.

TABLE H2.3.2

Medical History At Screening
Details of Abnormalities: All Subjects with Abnormalities

Subject	Dose of Malathion	Body System	Result	Details
011	5.0 MG/KG	E.E.N.T	YES	TONSILLECTOMY AS A CHILD. SHORTSIGHTED
		RESPIRATORY	YES	OCCASIONAL BRONCHIAL INFECTIONS.
		GASTROINTESTINAL	YES	APPENDICECTOMY 1994. GASTRIC ULCER 1970 - HEALED.
		SURGICAL HISTORY	YES	HAEMORRHOIDS 1988. TONSILLECTOMY AS A CHILD. APPENDICECTOMY 1994. HAEMORRHOIDECTOMY 1988.
013	PLACEBO	E.E.N.T	YES	LAZY LEFT EYE.
		CARDIOVASCULAR	YES	RIGHT BUNDLE BRANCH BLOCK ON ECG 1960. INVESTIGATIONS 1994. NO ABNORMALITY.
		HAEMOPOIETIC/LYMPHATIC	YES	ANAEMIA OCT 1997 NOW RESOLVED.
		PSYCHOLOGICAL	YES	PANIC ATTACKS 1979 - NIL RECENTLY.
014	5.0 MG/KG	SURGICAL HISTORY	YES	ABSCESS DRAINED LEFT BUTTOCK 1996.
		ALLERGIES	YES	LOCALISED RASH FROM SHAMPOO.
		E.E.N.T	YES	TONSILLECTOMY AGED 11. SHORTSIGHTED
		NEUROLOGICAL	YES	LOSS OF CONSCIOUSNESS AGED 13 PLAYING FOOTBALL.
015	PLACEBO	SURGICAL HISTORY	YES	TONSILLECTOMY AGED 11 YRS.
		E.E.N.T	YES	WEARS CONTACT LENSES - SHORTSIGHTED. RHINOPLASTY 1988.
		GASTROINTESTINAL	YES	APPENDICECTOMY 1980.
		GENITOURINARY	YES	TESTICULAR TORSION 1984.
016	PLACEBO	MUSCULOSKELETAL	YES	KNEE OPERATIONS FOR OVERGROWTH OF BONE: 1973 AND 1990.
		PSYCHOLOGICAL	YES	1993 - REACTIVE DEPRESSION AFTER MARRIAGE BREAKDOWN.
		SURGICAL HISTORY	YES	RHINOPLASTY 1988. APPENDICECTOMY 1980. SURGERY FOR TESTICULAR TORSION. KNEE OPERATIONS 1973 AND 1990.
		ALLERGIES	YES	HAYFEVER AS A CHILD.
016	PLACEBO	PSYCHOLOGICAL	YES	WILD DEPRESSION JAN 1998 DUE TO UNEMPLOYMENT - TOOK PROZAC FOR 4 WEEKS UNTIL MAR 1998. NO PROBLEMS SINCE MAR 1998.

TABLE H2.3.2

Medical History At Screening
Details of Abnormalities: All Subjects with Abnormalities

Subject	Dose of Malathion	Body System	Result	Details
017	5.0 MG/KG	MUSCULOSKELETAL SURGICAL HISTORY	YES YES	FRACTURED RIGHT MIDDLE FINGER 1994. PIN INSERTED RIGHT MIDDLE FINGER 1995. LENGTHENING ACHILLES TENDON (RIGHT) 1978.
018	5.0 MG/KG	MUSCULOSKELETAL	YES	SECONDARY OSTEOARTHRITIS LEFT HIP. NO MEDICATION TAKEN IN PAST 3 MONTHS.
019	10.0 MG/KG	E.E.N.T GASTROINTESTINAL SURGICAL HISTORY ALLERGIES	YES YES YES YES	OCCASIONAL ITCHY EYE. TONSILLECTOMY AGE 9. APPENDICECTOMY AGE 13. TONSILLECTOMY AGE 9. APPENDICECTOMY AGE 13. HAD A RASH AFTER MEDICATION AGE 15 - NO FURTHER SYMPTOMS. HAS OCCASIONAL HAYFEVER - NO SYMPTOMS SINCE JUN 1998.
020	10.0 MG/KG	E.E.N.T MUSCULOSKELETAL PSYCHOLOGICAL	YES YES YES	SHORT-SIGHTED - GLASSES FOR READING. FRACTURED LEFT WRIST 1963. 1986 DEPRESSION - NIL SINCE.
021	PLACEBO	E.E.N.T RESPIRATORY MUSCULOSKELETAL	YES YES YES	SHORT-SIGHTED CHESTY COUGH VENTOLIN PRESCRIBED NOT ASTHMA - 1996. FRACTURED RIGHT COLLAR BONE AS CHILD.
022	10.0 MG/KG	E.E.N.T SURGICAL HISTORY ALLERGIES	YES YES YES	SHORTSIGHTED - WEARS GLASSES. REMOVAL OF IMPACTED WISDOM TEETH UNDER GENERAL ANAESTHETIC. 1996 ORANGES CAUSE RASH.

Note: Subject 917 replaces subject 017 who withdrew from study before dosing

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TABLE H2.3.2
Medical History At Screening
Details of Abnormalities: All Subjects with Abnormalities

Subject	Dose of Malathion	Body System	Result	Details
023	10.0 MG/KG	MUSCULOSKELETAL PSYCHOLOGICAL SURGICAL HISTORY	YES YES YES	FRACTURED RING FINGER LEFT HAND AS A CHILD. BRUISED STERNUM FOLLOWING ROAD ACCIDENT OCT 1998. DEPRESSION 1997 FOLLOWING MARITAL PROBLEMS. LIP SUTURED UNDER LOCAL ANAESTHETIC OCT 1998 FOLLOWING ROAD TRAFFIC ACCIDENT.
024	PLACEBO	E.E.N.T GASTROINTESTINAL SURGICAL HISTORY	YES YES YES	TONSILS & ADENOIDS REMOVED AS A CHILD. APPENDIX REMOVED AGE 18. HAEMORRHOIDS 1995. TONSILLECTOMY & ADENOIDECTOMY AS A CHILD. APPENDICECTOMY - AGE 18. HAEMORRHOIDECTOMY 1995.
025	PLACEBO	E.E.N.T GASTROINTESTINAL MUSCULOSKELETAL DERMATOLOGICAL SURGICAL HISTORY	YES YES YES YES YES	SHORT-SIGHTED. TONSILLECTOMY AS A CHILD. APPENDICECTOMY 1994. 26 OPERATIONS TO CORRECT CONGENITAL BILATERAL CLUBBED FEET. AGED 2 - 20. MILD ACNE. AGE 2 - 20 26 OPERATIONS FOR BILATERAL CLUBBED FEET. APPENDICECTOMY 1994.
026	15.0 MG/KG	E.E.N.T SURGICAL HISTORY ALLERGIES	YES YES YES	TONSILLECTOMY 1980. TONSILLECTOMY 1980. PENICILLIN AS A CHILD.
027	10.0 MG/KG	NEUROLOGICAL	YES	KNOCKED OUT BRIEFLY 1982. NOT HOSPITALISED.
927	10.0 MG/KG	GASTROINTESTINAL MUSCULOSKELETAL NEUROLOGICAL SURGICAL HISTORY	YES YES YES YES	APPENDICECTOMY 1988. FRACTURED RIGHT WRIST 1990. UNCONSCIOUS FOR 30 SECONDS WHILE IN BOXING MATCH 1987. APPENDICECTOMY

Note: Subject 927 replaces subject 027 who withdrew from study before dosing

TABLE H2.3.2

Medical History At Screening
Details of Abnormalities: All Subjects with Abnormalities

Subject	Dose of Malathion	Body System	Result	Details
028	10.0 MG/KG	E.E.N.T	YES	IMPAIRED VISION IN LEFT EYE SINCE CHILDHOOD. TONSILLECTOMY 1968.
		MUSCULOSKELETAL	YES	FRACTURED LEFT ARM 1976.
		PSYCHOLOGICAL	YES	REACTIVE DEPRESSION 1994. MEDICATION FOR 2 MONTHS.
		SURGICAL HISTORY	YES	TONSILLECTOMY 1968. ROAD ACCIDENT 1965 - OPERATION TO ? BLADDER.
029	15.0 MG/KG	CARDIOVASCULAR	YES	VARICOSE VEINS LEFT LEG.
		MUSCULOSKELETAL	YES	FRACTURED COLLAR BONE 1992 LEFT.
		DERMATOLOGICAL	YES	HISTORY OF ACNE, NOT ACTIVE.
		PSYCHOLOGICAL	YES	DEPRESSION & ALCOHOL PROBLEM MAY 1997.
030	10.0 MG/KG	E.E.N.T	YES	LEFT EYE SQUINT REPAIR AGE 9.
		SURGICAL HISTORY	YES	LEFT EYE SQUINT REPAIR AGE 9.
031	15.0 MG/KG	E.E.N.T	YES	TONSILLECTOMY AGE 5.
		SURGICAL HISTORY	YES	TONSILLECTOMY AGE 5.
032	PLACEBO	MUSCULOSKELETAL	YES	FRACTURED RIGHT THUMB 1974. FRACTURED LEFT PATELLA 1996.
		NEUROLOGICAL	YES	CONCUSSED 1983 - OVERNIGHT IN HOSPITAL FOLLOWING ROAD ACCIDENT.
033	15.0 MG/KG	MUSCULOSKELETAL	YES	FRACTURED NOSE 1985.
		SURGICAL HISTORY	YES	RHINOPLASTY 1985.
034	15.0 MG/KG	GASTROINTESTINAL	YES	PARASITICAL INFECTION 1995 RESOLVED WITH TREATMENT. ANAL FISSURE 1982.
		MUSCULOSKELETAL	YES	FRACTURED RIGHT WRIST 1981.

TABLE H2.3.2

Medical History At Screening
Details of Abnormalities: All Subjects with Abnormalities

Subject	Dose of Malathion	Body System	Result	Details
035	PLACEBO	MUSCULOSKELETAL DERMATOLOGICAL	YES YES	FRACTURED LEFT ANKLE 1979. SCAR ON CHEST WALL FROM A BURN.
036	PLACEBO	E.E.N.T ALLERGIES	YES YES	RECURRENT TONSILLITIS, LAST HAD 10 WEEKS AGO - ANTIBIOTICS TAKEN. LONG-HAIRED CATS CAUSE SNEEZING - NEVER REQUIRED MEDICATION.
037	15.0 MG/KG	PSYCHOLOGICAL	YES	1994 REACTIVE DEPRESSION AMYTRIPLINE PRESCRIBED FOR 1 YEAR BY GP.
038	15.0 MG/KG	MUSCULOSKELETAL NEUROLOGICAL	YES YES	FRACTURED NOSE JULY 1995. FEBRILE CONVULSION AS INFANT.
039	15.0 MG/KG	E.E.N.T	YES	SHORT-SIGHTED
040	15.0 MG/KG	E.E.N.T DERMATOLOGICAL	YES YES	SHORTSIGHTED ECZEMA AS A CHILD. NO PROBLEMS AT PRESENT.
041	PLACEBO	GENITOURINARY MUSCULOSKELETAL SURGICAL HISTORY	YES YES YES	OVARIAN CYST. BACK PAIN 'PULLED A MUSCLE' MID JAN 1999. OVARIAN CYST EXCISED JUL 1998.
042	15.0 MG/KG	SURGICAL HISTORY	YES	BREAST REDUCTION AUG 1998.
045	PLACEBO	PSYCHOLOGICAL SURGICAL HISTORY	YES YES	1995 IMPULSIVE OVERDOSE NO DIAGNOSIS OR FOLLOW-UP BY GP. STERILIZATION TWICE IN 1997 AND 1998.
046	15.0 MG/KG	SURGICAL HISTORY ALLERGIES	YES YES	ADENOIDS REMOVED AT AGE 12 YRS. HAY FEVER.

TABLE H2.3.2

Medical History At Screening
Details of Abnormalities: All Subjects with Abnormalities

Subject	Dose of Malathion	Body System	Result	Details
047	PLACEBO	E.E.N.T	YES	TONSILLECTOMY AS A CHILD.
		MUSCULOSKELETAL	YES	FRACTURED COLLAR BONE AS A CHILD.
		SURGICAL HISTORY	YES	TONSILLECTOMY AS A CHILD.
048	15.0 MG/KG	DERMATOLOGICAL	YES	PSORIASIS - FOR A FEW YEARS NO TREATMENT FOR THE PAST 2 MTHS
		SURGICAL HISTORY	YES	MAINLY ON KNEES. DILLATION AND CURTERLIGE APR 1994. STERILIZATION SEP 1994.
948	15.0 MG/KG	E.E.N.T	YES	SHORT-SIGHTED
		DERMATOLOGICAL	YES	CONTACT DERMATITIS 1991. NO PROBLEMS SINCE.

Note: Subject 948 replaces subject 048 who withdrew from study before dosing

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TABLE H2.4.1

Physical Examination
General Appearance and Respiratory System
Individual Values: All Subjects

Subject	Dose of Maltathion	Study Day	Skin	Hands	Lymph Nodes	Chest Movement	Trachea	Percussion	Breath Sounds
001	0.5 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
002	0.5 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
003	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
004	0.5 MG/KG	SCREENING COMPLETION	ABNORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
005	1.5 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
006	1.5 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
007	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
008	1.5 MG/KG	SCREENING COMPLETION	ABNORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
009	5.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
010	5.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE

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TABLE H2.4.1
Physical Examination
General Appearance and Respiratory System
Individual Values: All Subjects

Subject	Dose of Methathion	Study Day	Skin	Hands	Lymph Nodes	Chest Movement	Trachea	Percussion	Breath Sounds
011	5.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
012	5.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
013	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
014	5.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
015	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
016	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
017	5.0 MG/KG	SCREENING	NORMAL	ABNORMAL	NORMAL	NORMAL	NORMAL	NORMAL	NORMAL
917	5.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
018	5.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
019	10.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE

Note: Subject 917 replaces subject 017 who withdrew from study before dosing

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TABLE H2.4.1
Physical Examination
General Appearance and Respiratory System
Individual Values: All Subjects

Subject	Dose of Methathion	Study Day	Skin	Hands	Lymph Nodes	Chest Movement	Trachea	Percussion	Breath Sounds
020	10.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
021	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
022	10.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
023	10.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
024	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
025	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
026	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
027	10.0 MG/KG	SCREENING	NORMAL	NORMAL	NORMAL	NORMAL	NORMAL	NORMAL	NORMAL
927	10.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
028	10.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE

Note: Subject 927 replaces subject 027 who withdrew from study before dosing

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TABLE H2.4.1

Physical Examination
General Appearance and Respiratory System
Individual Values: All Subjects

Subject	Dose of Malathion	Study Day	Skin	Hands	Lymph Nodes	Chest Movement	Trachea	Percussion	Breath Sounds
029	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
030	10.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
031	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
032	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
033	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
034	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
035	PLACEBO	SCREENING COMPLETION	ABNORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
036	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
037	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
038	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE

TABLE H2.4.1

Physical Examination
General Appearance and Respiratory System
Individual Values: All Subjects

Subject	Dose of Malthion	Study Day	Skin	Hands	Lymph Nodes	Chest Movement	Trachea	Percussion	Breath Sounds
039	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
040	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
041	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
042	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
043	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
044	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
045	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
046	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
047	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
048	15.0 MG/KG	SCREENING	NORMAL	NORMAL	NORMAL	NORMAL	NORMAL	NORMAL	NORMAL

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TABLE H2.4.1

Physical Examination
General Appearance and Respiratory System
Individual Values: All Subjects

Subject	Dose of Malathion	Study Day	Skin	Hands	Lymph Nodes	Chest Movement	Trachea	Percussion	Breath Sounds
948	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE

Note: Subject 948 replaces subject 048 who withdrew from study before dosing

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TABLE H2.4.2
Physical Examination
Cardiovascular System
Individual Values: All Subjects

Subject	Dose of Methathion	Study Day	Peripheral Pulses	JVP	Heart Sounds	Murmurs
001	0.5 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
002	0.5 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
003	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
004	0.5 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
005	1.5 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
006	1.5 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
007	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
008	1.5 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
009	5.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
010	5.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE

TABLE H2.4.2

Physical Examination
Cardiovascular System
Individual Values: All Subjects

Subject	Dose of Methathion	Study Day	Peripheral Pulses	JVP	Heart Sounds	Murmurs
011	5.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
012	5.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
013	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
014	5.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
015	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
016	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
017	5.0 MG/KG	SCREENING	NORMAL	NORMAL	NORMAL	NORMAL
917	5.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
018	5.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
019	10.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE

Note: Subject 917 replaces subject 017 who withdrew from study before dosing

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TABLE H2.4.2
Physical Examination
Cardiovascular System
Individual Values: All Subjects

Subject	Dose of Mafathion	Study Day	Peripheral Pulses	JVP	Heart Sounds	Murmurs
020	10.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
021	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
022	10.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
023	10.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
024	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
025	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
026	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
027	10.0 MG/KG	SCREENING	NORMAL	NORMAL	NORMAL	NORMAL
927	10.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
028	10.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE

Note: Subject 927 replaces subject 027 who withdrew from study before dosing

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TABLE H2.4.2
Physical Examination
Cardiovascular System
Individual Values: All Subjects

Subject	Dose of Methathion	Study Day	Peripheral Pulses	JVP	Heart Sounds	Murmurs
029	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
030	10.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
031	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
032	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
033	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
034	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
035	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
036	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
037	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
038	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE

TABLE H2.4.4.2
Physical Examination
Cardiovascular System
Individual Values: All Subjects

Subject	Dose of Mafathion	Study Day	Peripheral Pulses	JVP	Heart Sounds	Murmurs
039	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
040	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
041	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
042	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
043	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
044	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
045	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
046	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
047	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
048	15.0 MG/KG	SCREENING	NORMAL	NORMAL	NORMAL	NORMAL

TABLE H2.4.2						
Physical Examination						
Cardiovascular System						
Individual Values: All Subjects						
Subject	Dose of Malathion	Study Day	Peripheral Pulses	JVP	Heart Sounds	Murmurs
948	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE

Note: Subject 948 replaces subject 048 who withdrew from study before dosing

TABLE H2.4.3
Physical Examination
Gastrointestinal System
Individual Values: All Subjects

Subject	Dose of Methathion	Study Day	Mouth and Lips	Abdomen: Scars	Abdomen: Tenderness	Spleen	Liver	Kidneys
001	0.5 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	ABSENT NO CHANGE	ABSENT NO CHANGE	NOT PALPABLE NO CHANGE	NOT PALPABLE NO CHANGE	NORMAL NO CHANGE
002	0.5 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	ABSENT NO CHANGE	ABSENT NO CHANGE	NOT PALPABLE NO CHANGE	NOT PALPABLE NO CHANGE	NORMAL NO CHANGE
003	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	ABSENT NO CHANGE	ABSENT NO CHANGE	NOT PALPABLE NO CHANGE	NOT PALPABLE NO CHANGE	NORMAL NO CHANGE
004	0.5 MG/KG	SCREENING COMPLETION	ABNORMAL NO CHANGE	ABSENT NO CHANGE	ABSENT NO CHANGE	NOT PALPABLE NO CHANGE	NOT PALPABLE NO CHANGE	NORMAL NO CHANGE
005	1.5 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	PRESENT NO CHANGE	ABSENT NO CHANGE	NOT PALPABLE NO CHANGE	NOT PALPABLE NO CHANGE	NORMAL NO CHANGE
006	1.5 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	ABSENT NO CHANGE	ABSENT NO CHANGE	NOT PALPABLE NO CHANGE	NOT PALPABLE NO CHANGE	NORMAL NO CHANGE
007	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	ABSENT NO CHANGE	ABSENT NO CHANGE	NOT PALPABLE NO CHANGE	NOT PALPABLE NO CHANGE	NORMAL NO CHANGE
008	1.5 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	ABSENT NO CHANGE	ABSENT NO CHANGE	NOT PALPABLE NO CHANGE	NOT PALPABLE NO CHANGE	NORMAL NO CHANGE
009	5.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	ABSENT NO CHANGE	ABSENT NO CHANGE	NOT PALPABLE NO CHANGE	NOT PALPABLE NO CHANGE	NORMAL NO CHANGE
010	5.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	ABSENT NO CHANGE	ABSENT NO CHANGE	NOT PALPABLE NO CHANGE	NOT PALPABLE NO CHANGE	NORMAL NO CHANGE

TABLE H2.4.3
Physical Examination
Gastrointestinal System
Individual Values: All Subjects

Subject	Dose of Methathion	Study Day	Mouth and Lips	Abdomen: Scars	Abdomen: Tenderness	Spleen	Liver	Kidneys
011	5.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	PRESENT NO CHANGE	ABSENT NO CHANGE	NOT PALPABLE NO CHANGE	NOT PALPABLE NO CHANGE	NORMAL NO CHANGE
012	5.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	ABSENT NO CHANGE	ABSENT NO CHANGE	NOT PALPABLE NO CHANGE	NOT PALPABLE NO CHANGE	NORMAL NO CHANGE
013	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	ABSENT NO CHANGE	ABSENT NO CHANGE	NOT PALPABLE NO CHANGE	NOT PALPABLE NO CHANGE	NORMAL NO CHANGE
014	5.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	ABSENT NO CHANGE	ABSENT NO CHANGE	NOT PALPABLE NO CHANGE	NOT PALPABLE NO CHANGE	NORMAL NO CHANGE
015	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	PRESENT NO CHANGE	ABSENT NO CHANGE	NOT PALPABLE NO CHANGE	NOT PALPABLE NO CHANGE	NORMAL NO CHANGE
016	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	PRESENT NO CHANGE	ABSENT NO CHANGE	NOT PALPABLE NO CHANGE	NOT PALPABLE NO CHANGE	NORMAL NO CHANGE
017	5.0 MG/KG	SCREENING	NORMAL	ABSENT	ABSENT	NOT PALPABLE	NOT PALPABLE	NORMAL
917	5.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	ABSENT NO CHANGE	ABSENT NO CHANGE	NOT PALPABLE NO CHANGE	NOT PALPABLE NO CHANGE	NORMAL NO CHANGE
018	5.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	ABSENT NO CHANGE	ABSENT NO CHANGE	NOT PALPABLE NO CHANGE	NOT PALPABLE NO CHANGE	NORMAL NO CHANGE
019	10.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	PRESENT NO CHANGE	ABSENT NO CHANGE	NOT PALPABLE NO CHANGE	NOT PALPABLE NO CHANGE	NORMAL NO CHANGE

Note: Subject 917 replaces subject 017 who withdrew from study before dosing

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TABLE H2.4.3
Physical Examination
Gastrointestinal System
Individual Values: All Subjects

Subject	Dose of Methathion	Study Day	Mouth and Lips	Abdomen: Scars	Abdomen: Tenderness	Spleen	Liver	Kidneys
020	10.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	ABSENT NO CHANGE	ABSENT NO CHANGE	NOT PALPABLE NO CHANGE	NOT PALPABLE NO CHANGE	NORMAL NO CHANGE
021	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	ABSENT NO CHANGE	ABSENT NO CHANGE	NOT PALPABLE NO CHANGE	NOT PALPABLE NO CHANGE	NORMAL NO CHANGE
022	10.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	ABSENT NO CHANGE	ABSENT NO CHANGE	NOT PALPABLE NO CHANGE	NOT PALPABLE NO CHANGE	NORMAL NO CHANGE
023	10.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	ABSENT NO CHANGE	ABSENT NO CHANGE	NOT PALPABLE NO CHANGE	NOT PALPABLE NO CHANGE	NORMAL NO CHANGE
024	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	PRESENT NO CHANGE	ABSENT NO CHANGE	NOT PALPABLE NO CHANGE	NOT PALPABLE NO CHANGE	NORMAL NO CHANGE
025	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	PRESENT NO CHANGE	ABSENT NO CHANGE	NOT PALPABLE NO CHANGE	NOT PALPABLE NO CHANGE	NORMAL NO CHANGE
026	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	ABSENT NO CHANGE	ABSENT NO CHANGE	NOT PALPABLE NO CHANGE	NOT PALPABLE NO CHANGE	NORMAL NO CHANGE
027	10.0 MG/KG	SCREENING	NORMAL	ABSENT	ABSENT	NOT PALPABLE	NOT PALPABLE	NORMAL
927	10.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	PRESENT NO CHANGE	ABSENT NO CHANGE	NOT PALPABLE NO CHANGE	NOT PALPABLE NO CHANGE	NORMAL NO CHANGE
028	10.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	ABSENT NO CHANGE	ABSENT NO CHANGE	NOT PALPABLE NO CHANGE	NOT PALPABLE NO CHANGE	NORMAL NO CHANGE

Note: Subject 927 replaces subject 027 who withdrew from study before dosing

TABLE H2.4.3
Physical Examination
Gastrointestinal System
Individual Values: All Subjects

Subject	Dose of Methathion	Study Day	Mouth and Lips	Abdomen: Scars	Abdomen: Tenderness	Spleen	Liver	Kidneys
029	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	ABSENT NO CHANGE	ABSENT NO CHANGE	NOT PALPABLE NO CHANGE	NOT PALPABLE NO CHANGE	NORMAL NO CHANGE
030	10.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	ABSENT NO CHANGE	ABSENT NO CHANGE	NOT PALPABLE NO CHANGE	NOT PALPABLE NO CHANGE	NORMAL NO CHANGE
031	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	ABSENT NO CHANGE	ABSENT NO CHANGE	NOT PALPABLE NO CHANGE	NOT PALPABLE NO CHANGE	NORMAL NO CHANGE
032	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	ABSENT NO CHANGE	ABSENT NO CHANGE	NOT PALPABLE NO CHANGE	NOT PALPABLE NO CHANGE	NORMAL NO CHANGE
033	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	ABSENT NO CHANGE	ABSENT NO CHANGE	NOT PALPABLE NO CHANGE	NOT PALPABLE NO CHANGE	NORMAL NO CHANGE
034	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	ABSENT NO CHANGE	ABSENT NO CHANGE	NOT PALPABLE NO CHANGE	NOT PALPABLE NO CHANGE	NORMAL NO CHANGE
035	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	ABSENT NO CHANGE	ABSENT NO CHANGE	NOT PALPABLE NO CHANGE	NOT PALPABLE NO CHANGE	NORMAL NO CHANGE
036	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	ABSENT NO CHANGE	ABSENT NO CHANGE	NOT PALPABLE NO CHANGE	NOT PALPABLE NO CHANGE	NORMAL NO CHANGE
037	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	ABSENT NO CHANGE	ABSENT NO CHANGE	NOT PALPABLE NO CHANGE	NOT PALPABLE NO CHANGE	NORMAL NO CHANGE
038	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	ABSENT NO CHANGE	ABSENT NO CHANGE	NOT PALPABLE NO CHANGE	NOT PALPABLE NO CHANGE	NORMAL NO CHANGE

TABLE H2.4.3
Physical Examination
Gastrointestinal System
Individual Values: All Subjects

Subject	Dose of Malathion	Study Day	Mouth and Lips	Abdomen: Scars	Abdomen: Tenderness	Spleen	Liver	Kidneys
039	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	ABSENT NO CHANGE	ABSENT NO CHANGE	NOT PALPABLE NO CHANGE	NOT PALPABLE NO CHANGE	NORMAL NO CHANGE
040	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	ABSENT NO CHANGE	ABSENT NO CHANGE	NOT PALPABLE NO CHANGE	NOT PALPABLE NO CHANGE	NORMAL NO CHANGE
041	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	PRESENT NO CHANGE	ABSENT NO CHANGE	NOT PALPABLE NO CHANGE	NOT PALPABLE NO CHANGE	NORMAL NO CHANGE
042	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	ABSENT NO CHANGE	ABSENT NO CHANGE	NOT PALPABLE NO CHANGE	NOT PALPABLE NO CHANGE	NORMAL NO CHANGE
043	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	ABSENT NO CHANGE	ABSENT NO CHANGE	NOT PALPABLE NO CHANGE	NOT PALPABLE NO CHANGE	NORMAL NO CHANGE
044	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	ABSENT NO CHANGE	ABSENT NO CHANGE	NOT PALPABLE NO CHANGE	NOT PALPABLE NO CHANGE	NORMAL NO CHANGE
045	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	ABSENT NO CHANGE	ABSENT NO CHANGE	NOT PALPABLE NO CHANGE	NOT PALPABLE NO CHANGE	NORMAL NO CHANGE
046	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	ABSENT NO CHANGE	ABSENT NO CHANGE	NOT PALPABLE NO CHANGE	NOT PALPABLE NO CHANGE	NORMAL NO CHANGE
047	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	ABSENT NO CHANGE	ABSENT NO CHANGE	NOT PALPABLE NO CHANGE	NOT PALPABLE NO CHANGE	NORMAL NO CHANGE
048	15.0 MG/KG	SCREENING	NORMAL	ABSENT	ABSENT	NOT PALPABLE	NOT PALPABLE	NORMAL

TABLE H2.4.3
Physical Examination
Gastrointestinal System
Individual Values: All Subjects

Subject	Dose of Malathion	Study Day	Mouth and Lips	Abdomen: Scars	Abdomen: Tenderness	Spleen	Liver	Kidneys
948	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	ABSENT NO CHANGE	ABSENT NO CHANGE	NOT PALPABLE NO CHANGE	NOT PALPABLE NO CHANGE	NORMAL NO CHANGE

Note: Subject 948 replaces subject 048 who withdrew from study before dosing

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TABLE H2.4.4
Physical Examination
Central Nervous System
Individual Values: All Subjects

Subject	Dose of Malthion	Study Day	Pupils	Ophthalmoscopy	Cranial Nerves	Power	Sensation	Reflexes	Cerebellar Function
001	0.5 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
002	0.5 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
003	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
004	0.5 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	ABNORMAL NO CHANGE
005	1.5 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
006	1.5 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
007	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
008	1.5 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
009	5.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
010	5.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE

TABLE H2.4.4
Physical Examination
Central Nervous System
Individual Values: All Subjects

Subject	Dose of Methathion	Study Day	Pupils	Ophthalmoscopy	Cranial Nerves	Power	Sensation	Reflexes	Cerebellar Function
011	5.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
012	5.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
013	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
014	5.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
015	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
016	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
017	5.0 MG/KG	SCREENING	NORMAL	NORMAL	NORMAL	NORMAL	NORMAL	ABNORMAL	NORMAL
917	5.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
018	5.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
019	10.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE

Note: Subject 917 replaces subject 017 who withdrew from study before dosing

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TABLE H2.4.4
Physical Examination
Central Nervous System
Individual Values: All Subjects

Subject	Dose of Maltathion	Study Day	Pupils	Ophthalmoscopy	Cranial Nerves	Power	Sensation	Reflexes	Cerebellar Function
020	10.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
021	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
022	10.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
023	10.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
024	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
025	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
026	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
027	10.0 MG/KG	SCREENING	NORMAL	NORMAL	NORMAL	NORMAL	NORMAL	NORMAL	NORMAL
927	10.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
028	10.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE

Note: Subject 927 replaces subject 027 who withdrew from study before dosing

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TABLE H2.4.4
Physical Examination
Central Nervous System
Individual Values: All Subjects

Subject	Dose of Maltathion	Study Day	Pupils	Ophthalmoscopy	Cranial Nerves	Power	Sensation	Reflexes	Cerebellar Function
029	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
030	10.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
031	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
032	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
033	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
034	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
035	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
036	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
037	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
038	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE

TABLE H2.4.4
Physical Examination
Central Nervous System
Individual Values: All Subjects

Subject	Dose of Malthion	Study Day	Pupils	Ophthalmoscopy	Cranial Nerves	Power	Sensation	Reflexes	Cerebellar Function
039	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
040	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
041	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
042	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
043	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
044	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
045	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
046	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
047	PLACEBO	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE
048	15.0 MG/KG	SCREENING	NORMAL	NORMAL	NORMAL	NORMAL	NORMAL	NORMAL	NORMAL

TABLE H2.4.4
Physical Examination
Central Nervous System
Individual Values: All Subjects

Subject	Dose of Malthion	Study Day	Pupils	Ophthalmoscopy	Cranial Nerves	Power	Sensation	Reflexes	Cerebellar Function
948	15.0 MG/KG	SCREENING COMPLETION	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE	NORMAL NO CHANGE

Note: Subject 948 replaces subject 048 who withdrew from study before dosing

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TABLE H2.4.5

Physical Examination
Details of Abnormalities: All Subjects with Abnormalities

Subject	Dose of Malathion	Study Day	Body System	Normal/Abnormal	Description
004	0.5 MG/KG	SCREENING SCREENING SCREENING	SKIN MOUTH & LIPS CEREBELLAR FUNCTION	ABNORMAL ABNORMAL ABNORMAL	MILD GENERALISED ERYTHEMA UPPER BACK AS RESULT OF OLD BURNS. COLD SORE LEFT LOWER LIP. LATERAL NYSTAGMUS AT EXTREMES OF EYEMOVEMENT - NOT PATHOLOGICAL.
005	1.5 MG/KG	SCREENING	ABDOMEN: SCARS	PRESENT	SELECTIVE VAGOTOMY SCAR.
008	1.5 MG/KG	SCREENING	SKIN	ABNORMAL	MILD FACIAL ACNE.
011	5.0 MG/KG	SCREENING	ABDOMEN: SCARS	PRESENT	APPENDICECTOMY SCAR IN RIGHT ILIAC FOSSA.
015	PLACEBO	SCREENING	ABDOMEN: SCARS	PRESENT	APPENDICECTOMY SCAR.
016	PLACEBO	SCREENING	ABDOMEN: SCARS	PRESENT	SMALL SCAR OPERATIVE AREA FROM LACERATION.
017	5.0 MG/KG	SCREENING SCREENING	HANDS REFLEXES	ABNORMAL ABNORMAL	FIXED FLEXION DEFORMITY RIGHT DISTAL PHALANX MIDDLE FINGER. RIGHT ANKLE JERK ABSENT - OPERATION TO LENGTHEN TENDON.
019	10.0 MG/KG	SCREENING	ABDOMEN: SCARS	PRESENT	APPENDICECTOMY SCAR RIGHT ILIAC FOSSA.
024	PLACEBO	SCREENING	ABDOMEN: SCARS	PRESENT	APPENDIX
025	PLACEBO	SCREENING	ABDOMEN: SCARS	PRESENT	APPENDICECTOMY SCAR.
927	10.0 MG/KG	SCREENING	ABDOMEN: SCARS	PRESENT	APPENDICECTOMY SCAR.
035	PLACEBO	SCREENING	SKIN	ABNORMAL	SCAR ON LEFT CHEST WALL FROM BURN - NCS.
041	PLACEBO	SCREENING	ABDOMEN: SCARS	PRESENT	(1) UPPER ABDOMEN - TRAUMA. (2) OVARIAN SURGERY.

Note: Subject 917 replaces subject 017 who withdrew from study before dosing

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TABLE H2.5
Inclusion/Exclusion Details
Individual Values: All Subjects Who Violate Criteria

Subject	
002	Failed Inclusion Criterion (f)
007	Failed Inclusion Criterion (f)
047	Failed Exclusion Criterion (b)
048	Failed Inclusion Criterion (c)

Note: Subjects 002, 007 weight outwith allowance, approved by study director
Subject 047 had taken medication (contraceptive pill) during the period 0 to 5 days before entry onto study, approved by study director
Subject 048 predose cholinesterase samples low, subject withdrawn from study and replaced by subject 948

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TABLE H2.6
Laboratory Sample Collection
Individual Values: All Subjects

Subject	Dose of Malathion	Study Day	Sample	Sample Collected
001	0.5 MG/KG	SCREENING	CLINICAL CHEMISTRY	YES
			HAEMATOLOGY	YES
			CHOLINESTERASE (4.5ml EDTA)	YES
			URINE TOXILAB	YES
002	0.5 MG/KG	SCREENING	CLINICAL CHEMISTRY	YES
			HAEMATOLOGY	YES
			CHOLINESTERASE (4.5ml EDTA)	YES
			URINE TOXILAB	YES
003	PLACEBO	SCREENING	CLINICAL CHEMISTRY	YES
			HAEMATOLOGY	YES
			CHOLINESTERASE (4.5ml EDTA)	YES
			URINE TOXILAB	YES
004	0.5 MG/KG	SCREENING	CLINICAL CHEMISTRY	YES
			HAEMATOLOGY	YES
			CHOLINESTERASE (4.5ml EDTA)	YES
			URINE TOXILAB	YES
005	1.5 MG/KG	SCREENING	CLINICAL CHEMISTRY	YES
			HAEMATOLOGY	YES
			CHOLINESTERASE (4.5ml EDTA)	YES
			URINE TOXILAB	YES

TABLE H2.6
Laboratory Sample Collection
Individual Values: All Subjects

Subject	Dose of Malathion	Study Day	Sample	Sample Collected
006	1.5 MG/KG	SCREENING	CLINICAL CHEMISTRY	YES
			HAEMATOLOGY	YES
			VIROLOGY	YES
			CHOLINESTERASE (4.5ml EDTA)	YES
007	PLACEBO	SCREENING	URINE TOXILAB	YES
			CLINICAL CHEMISTRY	YES
			HAEMATOLOGY	YES
			VIROLOGY	YES
008	1.5 MG/KG	SCREENING	CHOLINESTERASE (4.5ml EDTA)	YES
			URINE TOXILAB	YES
			CLINICAL CHEMISTRY	YES
			HAEMATOLOGY	YES
009	5.0 MG/KG	SCREENING	VIROLOGY	YES
			CHOLINESTERASE (4.5ml EDTA)	YES
			URINE TOXILAB	YES
			CLINICAL CHEMISTRY	YES
010	5.0 MG/KG	SCREENING	HAEMATOLOGY	YES
			VIROLOGY	YES
			CHOLINESTERASE (4.5ml EDTA)	YES
			URINE TOXILAB	YES

TABLE H2.6
Laboratory Sample Collection
Individual Values: All Subjects

Subject	Dose of Malathion	Study Day	Sample	Sample Collected
011	5.0 MG/KG	SCREENING	CLINICAL CHEMISTRY	YES
			HAEMATOTOLOGY	YES
			VIROLOGY	YES
			CHOLINESTERASE (4.5ml EDTA) URINE TOXILAB	YES
012	5.0 MG/KG	SCREENING	CLINICAL CHEMISTRY	YES
			HAEMATOTOLOGY	YES
			VIROLOGY	YES
			CHOLINESTERASE (4.5ml EDTA) URINE TOXILAB	YES
013	PLACEBO	SCREENING	CLINICAL CHEMISTRY	YES
			HAEMATOTOLOGY	YES
			VIROLOGY	YES
			CHOLINESTERASE (4.5ml EDTA) URINE TOXILAB	YES
014	5.0 MG/KG	SCREENING	CLINICAL CHEMISTRY	YES
			HAEMATOTOLOGY	YES
			VIROLOGY	YES
			CHOLINESTERASE (4.5ml EDTA) URINE TOXILAB	YES
015	PLACEBO	SCREENING	CLINICAL CHEMISTRY	YES
			HAEMATOTOLOGY	YES
			VIROLOGY	YES
			CHOLINESTERASE (4.5ml EDTA) URINE TOXILAB	YES

TABLE H2.6

Laboratory Sample Collection
Individual Values: All Subjects

Subject	Dose of Malathion	Study Day	Sample	Sample Collected
016	PLACEBO	SCREENING	CLINICAL CHEMISTRY	YES
			HAEMATOLOGY	YES
			VIROLOGY	YES
			CHOLINESTERASE (4.5ml EDTA)	YES
017	5.0 MG/KG	SCREENING	URINE TOXILAB	YES
			CLINICAL CHEMISTRY	YES
			HAEMATOLOGY	YES
			VIROLOGY	YES
917	5.0 MG/KG	SCREENING	CHOLINESTERASE (4.5ml EDTA)	YES
			URINE TOXILAB	YES
			CLINICAL CHEMISTRY	YES
			HAEMATOLOGY	YES
018	5.0 MG/KG	SCREENING	VIROLOGY	YES
			CHOLINESTERASE (4.5ml EDTA)	YES
			URINE TOXILAB	YES
			CLINICAL CHEMISTRY	YES
019	10.0 MG/KG	SCREENING	HAEMATOLOGY	YES
			VIROLOGY	YES
			CHOLINESTERASE (4.5ml EDTA)	YES
			URINE TOXILAB	YES

Note: Subject 917 replaces subject 017 who withdrew from study before dosing

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TABLE H2.6
Laboratory Sample Collection
Individual Values: All Subjects

Subject	Dose of Malathion	Study Day	Sample	Sample Collected
020	10.0 MG/KG	SCREENING	CLINICAL CHEMISTRY	YES
			HAEMATOLOGY	YES
			VIROLOGY	YES
			CHOLINESTERASE (4.5ml EDTA) URINE TOXILAB	YES
021	PLACEBO	SCREENING	CLINICAL CHEMISTRY	YES
			HAEMATOLOGY	YES
			VIROLOGY	YES
			CHOLINESTERASE (4.5ml EDTA) URINE TOXILAB	YES
022	10.0 MG/KG	SCREENING	CLINICAL CHEMISTRY	YES
			HAEMATOLOGY	YES
			VIROLOGY	YES
			CHOLINESTERASE (4.5ml EDTA) URINE TOXILAB	YES
023	10.0 MG/KG	SCREENING	CLINICAL CHEMISTRY	YES
			HAEMATOLOGY	YES
			VIROLOGY	YES
			CHOLINESTERASE (4.5ml EDTA) URINE TOXILAB	YES
024	PLACEBO	SCREENING	CLINICAL CHEMISTRY	YES
			HAEMATOLOGY	YES
			VIROLOGY	YES
			CHOLINESTERASE (4.5ml EDTA) URINE TOXILAB	YES

TABLE H2.6
Laboratory Sample Collection
Individual Values: All Subjects

Subject	Dose of Malathion	Study Day	Sample	Sample Collected
025	PLACEBO	SCREENING	CLINICAL CHEMISTRY	YES
			HAEMATOTOLOGY	YES
			VIROLOGY	YES
			CHOLINESTERASE (4.5ml EDTA) URINE TOXILAB	YES
026	15.0 MG/KG	SCREENING	CLINICAL CHEMISTRY	YES
			HAEMATOTOLOGY	YES
			VIROLOGY	YES
			CHOLINESTERASE (4.5ml EDTA) URINE TOXILAB	YES
027	10.0 MG/KG	SCREENING	CLINICAL CHEMISTRY	YES
			HAEMATOTOLOGY	YES
			VIROLOGY	YES
			CHOLINESTERASE (4.5ml EDTA) URINE TOXILAB	YES
927	10.0 MG/KG	SCREENING	CLINICAL CHEMISTRY	YES
			HAEMATOTOLOGY	YES
			VIROLOGY	YES
			CHOLINESTERASE (4.5ml EDTA) URINE TOXILAB	YES
028	10.0 MG/KG	SCREENING	CLINICAL CHEMISTRY	YES
			HAEMATOTOLOGY	YES
			VIROLOGY	YES
			CHOLINESTERASE (4.5ml EDTA) URINE TOXILAB	YES

Note: Subject 927 replaces subject 027 who withdrew from study before dosing

TABLE H2.6
Laboratory Sample Collection
Individual Values: All Subjects

Subject	Dose of Malathion	Study Day	Sample	Sample Collected
029	15.0 MG/KG	SCREENING	CLINICAL CHEMISTRY	YES
			HAEMATOLOGY	YES
			VIROLOGY	YES
			CHOLINESTERASE (4.5ml EDTA) URINE TOXILAB	YES
030	10.0 MG/KG	SCREENING	CLINICAL CHEMISTRY	YES
			HAEMATOLOGY	YES
			VIROLOGY	YES
			CHOLINESTERASE (4.5ml EDTA) URINE TOXILAB	YES
031	15.0 MG/KG	SCREENING	CLINICAL CHEMISTRY	YES
			HAEMATOLOGY	YES
			VIROLOGY	YES
			CHOLINESTERASE (4.5ml EDTA) URINE TOXILAB	YES
032	PLACEBO	SCREENING	CLINICAL CHEMISTRY	YES
			HAEMATOLOGY	YES
			VIROLOGY	YES
			CHOLINESTERASE (4.5ml EDTA) URINE TOXILAB	YES
033	15.0 MG/KG	SCREENING	CLINICAL CHEMISTRY	YES
			HAEMATOLOGY	YES
			VIROLOGY	YES
			CHOLINESTERASE (4.5ml EDTA) URINE TOXILAB	YES

TABLE H2.6
Laboratory Sample Collection
Individual Values: All Subjects

Subject	Dose of Malathion	Study Day	Sample	Sample Collected
034	15.0 MG/KG	SCREENING	CLINICAL CHEMISTRY	YES
			HAEMATOLOGY	YES
			VIROLOGY	YES
			CHOLINESTERASE (4.5ml EDTA) URINE TOXILAB	YES
035	PLACEBO	SCREENING	CLINICAL CHEMISTRY	YES
			HAEMATOLOGY	YES
			VIROLOGY	YES
			CHOLINESTERASE (4.5ml EDTA) URINE TOXILAB	YES
036	PLACEBO	SCREENING	CLINICAL CHEMISTRY	YES
			HAEMATOLOGY	YES
			VIROLOGY	YES
			CHOLINESTERASE (4.5ml EDTA) URINE TOXILAB	YES
037	15.0 MG/KG	SCREENING	CLINICAL CHEMISTRY	YES
			HAEMATOLOGY	YES
			VIROLOGY	YES
			CHOLINESTERASE (4.5ml EDTA) URINE TOXILAB	YES
038	15.0 MG/KG	SCREENING	CLINICAL CHEMISTRY	YES
			HAEMATOLOGY	YES
			VIROLOGY	YES
			CHOLINESTERASE (4.5ml EDTA) URINE TOXILAB	YES

TABLE H2.6
Laboratory Sample Collection
Individual Values: All Subjects

Subject	Dose of Malathion	Study Day	Sample	Sample Collected
039	15.0 MG/KG	SCREENING	CLINICAL CHEMISTRY	YES
			HAEMATOLOGY	YES
			VIROLOGY	YES
			CHOLINESTERASE (4.5ml EDTA)	YES
040	15.0 MG/KG	SCREENING	URINE TOXILAB	YES
			CLINICAL CHEMISTRY	YES
			HAEMATOLOGY	YES
			VIROLOGY	YES
041	PLACEBO	SCREENING	CHOLINESTERASE (4.5ml EDTA)	YES
			URINE TOXILAB	YES
			CLINICAL CHEMISTRY	YES
			HAEMATOLOGY	YES
042	15.0 MG/KG	SCREENING	VIROLOGY	YES
			CHOLINESTERASE (4.5ml EDTA)	YES
			URINE TOXILAB	YES
			CLINICAL CHEMISTRY	YES
043	15.0 MG/KG	SCREENING	HAEMATOLOGY	YES
			VIROLOGY	YES
			CHOLINESTERASE (4.5ml EDTA)	YES
			URINE TOXILAB	YES
043	15.0 MG/KG	SCREENING	CLINICAL CHEMISTRY	YES
			HAEMATOLOGY	YES
			VIROLOGY	YES
			CHOLINESTERASE (4.5ml EDTA)	YES
043	15.0 MG/KG	SCREENING	URINE TOXILAB	YES
			CLINICAL CHEMISTRY	YES
			HAEMATOLOGY	YES
			VIROLOGY	YES

TABLE H2.6
Laboratory Sample Collection
Individual Values: All Subjects

Subject	Dose of Malathion	Study Day	Sample	Sample Collected
044	15.0 MG/KG	SCREENING	CLINICAL CHEMISTRY	YES
			HAEMATOLOGY	YES
			VIROLOGY	YES
			CHOLINESTERASE (4.5ml EDTA)	YES
045	PLACEBO	SCREENING	URINE TOXILAB	YES
			CLINICAL CHEMISTRY	YES
			HAEMATOLOGY	YES
			VIROLOGY	YES
046	15.0 MG/KG	SCREENING	CHOLINESTERASE (4.5ml EDTA)	YES
			URINE TOXILAB	YES
			CLINICAL CHEMISTRY	YES
			HAEMATOLOGY	YES
047	PLACEBO	SCREENING	VIROLOGY	YES
			CHOLINESTERASE (4.5ml EDTA)	YES
			URINE TOXILAB	YES
			CLINICAL CHEMISTRY	YES
048	15.0 MG/KG	SCREENING	HAEMATOLOGY	YES
			VIROLOGY	YES
			CHOLINESTERASE (4.5ml EDTA)	YES
			URINE TOXILAB	YES

TABLE H2.6
Laboratory Sample Collection
Individual Values: All Subjects

Subject	Dose of Malathion	Study Day	Sample	Sample Collected
948	15.0 MG/KG	SCREENING	CLINICAL CHEMISTRY HAEMATOLOGY VIROLOGY CHOLINESTERASE (4.5ml EDTA) URINE TOXILAB	YES YES YES YES YES

Note: Subject 948 replaces subject 048 who withdrew from study before dosing

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TABLE H2.7

Admission Assessment
Individual Values: All Subjects

Subject	Dose of Methathion	Admission Date	Admission Time (h:min)	Alcohol Taken in Last 48 Hours	Alcohol Intake	Unwell Since Last Visit	Subject Taken Medications in Last 5 Days
001	0.5 MG/KG	04NOV1998	12:08	NO		NO	NO
002	0.5 MG/KG	04NOV1998	11:45	YES	3 PINTS BEER LAST EVENING.	NO	NO
003	PLACEBO	04NOV1998	12:02	NO		NO	NO
004	0.5 MG/KG	04NOV1998	12:43	NO		NO	NO
005	1.5 MG/KG	10NOV1998	11:30	NO		NO	NO
006	1.5 MG/KG	10NOV1998	11:45	NO		NO	NO
007	PLACEBO	10NOV1998	11:58	NO		NO	NO
008	1.5 MG/KG	10NOV1998	12:05	NO		NO	NO
009	5.0 MG/KG	24NOV1998	11:32	NO		NO	NO
010	5.0 MG/KG	24NOV1998	12:08	YES	1 PT BEER 23:00 23/11/98.	NO	NO
011	5.0 MG/KG	24NOV1998	11:37	NO		NO	NO
012	5.0 MG/KG	24NOV1998	11:58	NO		NO	NO
013	PLACEBO	24NOV1998	12:21	NO		NO	NO
014	5.0 MG/KG	24NOV1998	11:41	NO		NO	NO
015	PLACEBO	24NOV1998	11:45	NO		NO	NO

TABLE H2.7
Admission Assessment
Individual Values: All Subjects

Subject	Dose of Malathion	Admission Date	Admission Time (h:min)	Alcohol Taken in Last 48 Hours	Alcohol Intake	Unwell Since Last Visit	Subject Taken Medications in Last 5 Days
016	PLACEBO	24NOV1998	11:49	NO		NO	NO
017	5.0 MG/KG	24NOV1998	11:52	NO		NO	NO
917	5.0 MG/KG	24NOV1998	12:33	NO		NO	NO
018	5.0 MG/KG	24NOV1998	11:55	NO		NO	NO
019	10.0 MG/KG	08DEC1998	12:10	NO		NO	NO
020	10.0 MG/KG	08DEC1998	13:10	NO		NO	NO
021	PLACEBO	08DEC1998	12:12	NO		NO	NO
022	10.0 MG/KG	08DEC1998	13:10	NO		NO	NO
023	10.0 MG/KG	15DEC1998	10:50	NO		NO	NO
024	PLACEBO	15DEC1998	11:02	NO		NO	NO
025	PLACEBO	15DEC1998	11:06	NO		NO	NO
026	15.0 MG/KG	15DEC1998	11:30	NO		NO	NO
027	10.0 MG/KG	15DEC1998	11:23	NO		NO	NO
927	10.0 MG/KG	15DEC1998	11:25	NO		NO	NO
028	10.0 MG/KG	15DEC1998	12:24	NO		NO	NO

Note: Subject 917 replaces subject 017 who withdrew from study before dosing
Subject 927 replaces subject 027 who withdrew from study before dosing

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TABLE H2.7
Admission Assessment
Individual Values: All Subjects

Subject	Dose of Malathion	Admission Date	Admission Time (h:min)	Alcohol Taken in Last 48 Hours	Alcohol Intake	Unwell Since Last Visit	Subject Taken Medications in Last 5 Days
029	15.0 MG/KG	15DEC1998	11:30	YES	14 DEC 1998 PM 4 PINTS - LAGER WITH LEMONADE.	NO	NO
030	10.0 MG/KG	15DEC1998	11:35	NO		NO	NO
031	15.0 MG/KG	15DEC1998	13:34	YES	LUNCHTIME 14/12/98 X 1 BOTTLE BUDWEISER.	NO	NO
032	PLACEBO	19JAN1999	10:40	NO		NO	NO
033	15.0 MG/KG	19JAN1999	11:34	NO		NO	NO
034	15.0 MG/KG	19JAN1999	11:34	NO		NO	NO
035	PLACEBO	19JAN1999	11:50	NO		NO	NO
036	PLACEBO	19JAN1999	11:30	NO		NO	NO
037	15.0 MG/KG	19JAN1999	11:34	NO		NO	NO
038	15.0 MG/KG	19JAN1999	12:00	NO		NO	NO
039	15.0 MG/KG	02FEB1999	14:00	NO		NO	NO
040	15.0 MG/KG	02FEB1999	11:50	NO		NO	YES
041	PLACEBO	02FEB1999	11:30	NO		NO	NO
042	15.0 MG/KG	02FEB1999	11:24	NO		NO	NO
043	15.0 MG/KG	02FEB1999	11:35	NO		NO	NO

TABLE H2.7
Admission Assessment
Individual Values: All Subjects

Subject	Dose of Malahion	Admission Date	Admission Time (h:min)	Alcohol Taken in Last 48 Hours	Alcohol Intake	Unwell Since Last Visit	Subject Taken Medications in Last 5 Days
044	15.0 MG/KG	18FEB1999	11:15	YES	2 UNITS EVENING PRIOR TO ADMISSION.	NO	YES
045	PLACEBO	18FEB1999	11:00	NO		NO	NO
046	15.0 MG/KG	18FEB1999	11:15	NO		NO	NO
047	PLACEBO	01MAR1999	11:45	NO		NO	YES
048	15.0 MG/KG	01MAR1999	13:10	NO		NO	NO
948	15.0 MG/KG	08MAR1999	12:00	NO		NO	YES

Note: Subject 948 replaces subject 048 who withdrew from study before dosing

TABLE H2.8
Pregnancy Test
Individual Values: All Female Subjects

Subject	Dose of Malathion	Study Day	Result
039	15.0 MG/KG	SCREENING ADMISSION	NEGATIVE NEGATIVE
040	15.0 MG/KG	SCREENING ADMISSION	NEGATIVE NEGATIVE
041	PLACEBO	SCREENING ADMISSION	NEGATIVE NEGATIVE
042	15.0 MG/KG	SCREENING ADMISSION	NEGATIVE NEGATIVE
043	15.0 MG/KG	SCREENING ADMISSION	NEGATIVE NEGATIVE
044	15.0 MG/KG	SCREENING ADMISSION	NEGATIVE NEGATIVE
045	PLACEBO	SCREENING ADMISSION	NEGATIVE NEGATIVE
046	15.0 MG/KG	SCREENING ADMISSION	NEGATIVE NEGATIVE
047	PLACEBO	SCREENING ADMISSION	NEGATIVE NEGATIVE
048	15.0 MG/KG	SCREENING ADMISSION	NEGATIVE NEGATIVE

TABLE H2.8
Pregnancy Test
Individual Values: All Female Subjects

Subject	Dose of Malathion	Study Day	Result
948	15.0 MG/KG	SCREENING ADMISSION	NEGATIVE NEGATIVE

Note: Subject 948 replaces subject 048 who withdrew from study before dosing

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TABLE H3

Individual Values: All Subjects							
Subject	Dose of Malathion	Meal	Breakfast Start Time (h:min)	Breakfast Finish Time (h:min)	Target Time (h:min)	Actual Time (h:min)	Comments
001	0.5 MG/KG	BREAKFAST LUNCH	8:16	8:25	12:30	12:35	LATE DUE TO SLOW BLOOD SAMPLE.
002	0.5 MG/KG	BREAKFAST LUNCH	8:18	8:26	12:36	12:37	
003	PLACEBO	BREAKFAST LUNCH	8:20	8:35	12:40	12:47	
004	0.5 MG/KG	BREAKFAST LUNCH	8:35	8:40	12:45	12:56	
005	1.5 MG/KG	BREAKFAST LUNCH	8:40	8:55	13:05	13:10	
006	1.5 MG/KG	BREAKFAST LUNCH	8:45	9:05	13:10	13:10	
007	PLACEBO	BREAKFAST LUNCH	8:55	9:10	13:15	13:20	
008	1.5 MG/KG	BREAKFAST LUNCH	9:00	9:15	13:20	13:22	
009	5.0 MG/KG	BREAKFAST LUNCH	8:40	8:55	13:05	13:07	
010	5.0 MG/KG	BREAKFAST LUNCH	8:42	9:05	13:10	13:12	

TABLE H3
Meals
Individual Values: All Subjects

Subject	Dose of Malathion	Meal	Breakfast Start Time (h:min)	Breakfast Finish Time (h:min)	Target Time (h:min)	Actual Time (h:min)	Comments
011	5.0 MG/KG	BREAKFAST LUNCH	8:47	9:10	13:15	13:17	
012	5.0 MG/KG	BREAKFAST LUNCH	8:52	9:15	13:20	13:23	
013	PLACEBO	BREAKFAST LUNCH	8:59	9:20	13:26	13:28	
014	5.0 MG/KG	BREAKFAST LUNCH	9:05	9:25	13:30	13:33	
015	PLACEBO	BREAKFAST LUNCH	9:07	9:30	13:35	13:37	
016	PLACEBO	BREAKFAST LUNCH	9:12	9:35	13:40	13:43	
017	5.0 MG/KG	BREAKFAST LUNCH	9:17	9:40	.	.	
917	5.0 MG/KG	BREAKFAST LUNCH	9:35	9:55	14:45	14:53	
018	5.0 MG/KG	BREAKFAST LUNCH	9:24	9:45	13:50	13:55	
019	10.0 MG/KG	BREAKFAST LUNCH	8:43	8:55	13:00	13:00	

Note: Subject 917 replaces subject 017 who withdrew from study before dosing

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TABLE H3
Meals
Individual Values: All Subjects

Subject	Dose of Malathion	Meal	Breakfast Start Time (h:min)	Breakfast Finish Time (h:min)	Target Time (h:min)	Actual Time (h:min)	Comments
020	10.0 MG/KG	BREAKFAST LUNCH	8:44	9:00	13:05	13:06	
021	PLACEBO	BREAKFAST LUNCH	8:51	9:05	13:10	13:13	
022	10.0 MG/KG	BREAKFAST LUNCH	8:50	9:09	13:15	13:18	
023	10.0 MG/KG	BREAKFAST LUNCH	8:37	9:00	13:05	13:10	
024	PLACEBO	BREAKFAST LUNCH	8:45	9:05	13:10	13:13	
025	PLACEBO	BREAKFAST LUNCH	8:51	9:10	13:15	13:18	
026	15.0 MG/KG	BREAKFAST LUNCH	8:56	9:15	13:20	13:22	
027	10.0 MG/KG	BREAKFAST LUNCH	9:01	.	.	.	
927	10.0 MG/KG	BREAKFAST LUNCH	8:41	9:50	13:55	13:58	
028	10.0 MG/KG	BREAKFAST LUNCH	9:08	9:30	13:35	13:39	

Note: Subject 927 replaces subject 027 who withdrew from study before dosing

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TABLE H3
Meals
Individual Values: All Subjects

Subject	Dose of Malathion	Meal	Breakfast Start Time (h:min)	Breakfast Finish Time (h:min)	Target Time (h:min)	Actual Time (h:min)	Comments
029	15.0 MG/KG	BREAKFAST LUNCH	9:17	9:35	13:40	13:44	
030	10.0 MG/KG	BREAKFAST LUNCH	9:25	9:40	13:45	13:48	
031	15.0 MG/KG	BREAKFAST LUNCH	9:30	9:45	13:50	13:56	
032	PLACEBO	BREAKFAST LUNCH	9:10	9:25	13:30	13:30	
033	15.0 MG/KG	BREAKFAST LUNCH	9:15	9:30	13:35	13:37	
034	15.0 MG/KG	BREAKFAST LUNCH	9:20	9:35	13:40	13:43	
035	PLACEBO	BREAKFAST LUNCH	9:25	9:40	13:45	13:48	
036	PLACEBO	BREAKFAST LUNCH	9:30	9:45	13:50	13:54	
037	15.0 MG/KG	BREAKFAST LUNCH	9:35	9:50	13:55	13:57	
038	15.0 MG/KG	BREAKFAST LUNCH	9:40	9:58	14:04	14:06	

TABLE H3

Meals						
Individual Values: All Subjects						
Subject	Dose of Malathion	Meal	Breakfast Start Time (h:min)	Breakfast Finish Time (h:min)	Target Time (h:min)	Actual Time (h:min)
039	15.0 MG/KG	BREAKFAST LUNCH	8:50	9:10	13:15	13:20
040	15.0 MG/KG	BREAKFAST LUNCH	8:55	9:15	13:24	13:24
041	PLACEBO	BREAKFAST LUNCH	9:00	9:20	13:30	13:35
042	15.0 MG/KG	BREAKFAST LUNCH	9:06	9:30	13:35	13:43
043	15.0 MG/KG	BREAKFAST LUNCH	9:12	9:35	13:40	13:47
044	15.0 MG/KG	BREAKFAST LUNCH	8:50	9:08	13:15	13:15
045	PLACEBO	BREAKFAST LUNCH	8:55	9:15	13:22	13:25
046	15.0 MG/KG	BREAKFAST LUNCH	9:00	9:19	13:30	13:30
047	PLACEBO	BREAKFAST LUNCH	.	8:55	13:05	13:10
948	15.0 MG/KG	BREAKFAST LUNCH	9:10	9:25	13:30	13:30

START TIME UNKNOWN.

Note: Subject 948 replaces subject 048 who withdrew from study before dosing

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APPENDIX I

Vital Signs: Summary tables and individual data listings

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TABLE I1.1
Vital Signs
Supine Systolic Blood Pressure (mmHg)
Summary Statistics, Change from Baseline and Shift Values: All Dosed Subjects

MALE

Dose of Malathion		Result				Change From Baseline				Abnormal Decrease	No Change	Abnormal Increase
		Mean	SD	Min	Max	N	Mean	SD	Min	Max		
PLACEBO	PREDOSE	116.4	13.2	100	140	11						
	+2 H	111.5	13.6	88	135	11	-4.9	6.9	-18	5		11
	+4 H	115.1	12.4	96	135	11	-1.3	10.1	-20	15		11
	+8 H	114.5	6.1	108	128	11	-1.9	11.4	-22	20	1	10
	+24 H	113.2	7.9	100	125	11	-3.2	11.4	-24	14	2	9
0.5 MG/KG	PREDOSE	130.0	17.3	110	140	3						
	+2 H	126.3	10.0	115	134	3	-3.7	7.8	-10	5		3
	+4 H	110.7	5.1	105	115	3	-19.3	12.5	-28	-5	2	1
	+8 H	115.3	6.4	108	120	3	-14.7	11.0	-22	-2	1	2
	+24 H	115.0	10.0	105	125	3	-15.0	10.0	-25	-5	1	2

(CONTINUED)

Note: Data summarised in this table is listed in table I2

Baseline is defined as predose

Key for shift values: abnormal decrease from baseline <-20 mmHg abnormal increase from baseline >20 mmHg
Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics

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TABLE I1.1
Vital Signs
Supine Systolic Blood Pressure (mmHg)
Summary Statistics, Change from Baseline and Shift Values: All Dosed Subjects

MALE

Dose of Malathion		Result				Change From Baseline				Abnormal Decrease	No Change	Abnormal Increase
		Mean	SD	Min	Max	N	Mean	SD	Min	Max		
1.5 MG/KG	PREDOSE	114.0	9.2	104	122	3						
	+2 H	118.0	6.0	112	124	3	4.0	9.2	-4	14		3
	+4 H	111.3	8.1	104	120	3	-2.7	9.0	-12	6		3
	+8 H	117.3	8.3	108	124	3	3.3	12.1	-8	16		3
	+24 H	118.0	9.2	110	128	3	4.0	9.2	-6	12		3
5.0 MG/KG	PREDOSE	132.1	9.5	120	145	7						
	+2 H	127.6	10.6	115	140	7	-4.6	16.9	-27	15	2	5
	+4 H	120.7	7.3	110	130	7	-11.4	16.0	-30	10	2	5
	+8 H	121.4	8.8	106	130	7	-10.7	15.2	-34	8	2	5
	+24 H	121.9	7.7	110	135	7	-10.3	14.3	-30	10	1	6

(CONTINUED)

Note: Data summarised in this table is listed in table I2
Baseline is defined as predose
Key for shift values: abnormal decrease from baseline <-20 mmHg abnormal increase from baseline >20 mmHg
Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics

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TABLE I1.1
Vital Signs
Supine Systolic Blood Pressure (mmHg)
Summary Statistics, Change from Baseline and Shift Values: All Dosed Subjects

MALE

Dose of Malathion		Result						Change From Baseline				Abnormal Decrease	No Change	Abnormal Increase
		Mean	SD	Min	Max	N		Mean	SD	Min	Max			
10.0 MG/KG	PREDOSE	121.4	12.3	112	140	7								
	+2 H	121.1	10.5	102	138	7		-0.3	9.0	-14	10		7	
	+4 H	117.4	9.1	108	132	7		-4.0	5.7	-12	6		7	
	+8 H	120.9	8.8	110	130	7		-0.6	16.7	-30	18	1	6	
	+24 H	115.9	11.4	106	136	7		-5.6	14.5	-31	12	1	6	
15.0 MG/KG	PREDOSE	106.3	6.3	98	114	7								
	+2 H	108.0	7.4	98	118	7		1.7	5.5	-4	12		7	
	+4 H	107.4	9.3	100	124	7		1.1	7.8	-12	12		7	
	+8 H	112.6	7.8	100	122	7		6.3	6.5	-2	14		7	
	+24 H	112.4	12.5	100	134	7		6.1	8.4	-2	20		7	

Note: Data summarised in this table is listed in table I2

Baseline is defined as predose

Key for shift values: abnormal decrease from baseline <-20 mmHg abnormal increase from baseline >20 mmHg
Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics

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TABLE I1.1
Vital Signs
Supine Systolic Blood Pressure (mmHg)
Summary Statistics, Change from Baseline and Shift Values: All Dosed Subjects

FEMALE

Dose of Malathion		Result					Change From Baseline				Abnormal Decrease	No Change	Abnormal Increase
		Mean	SD	Min	Max	N	Mean	SD	Min	Max			
PLACEBO	PREDOSE	116.0	5.3	110	120	3							
	+2 H	110.0	10.0	100	120	3	-6.0	12.2	-20	2		3	
	+4 H	112.3	7.5	105	120	3	-3.7	12.1	-13	10		3	
	+8 H	104.0	5.3	100	110	3	-12.0	10.4	-18	0		3	
	+24 H	108.7	4.2	104	112	3	-7.3	7.0	-14	0		3	
15.0 MG/KG	PREDOSE	113.6	8.6	100	124	7							
	+2 H	111.7	13.5	96	130	7	-1.9	8.5	-12	12		7	
	+4 H	109.7	10.8	100	130	7	-3.9	6.8	-16	6		7	
	+8 H	112.0	9.7	102	130	7	-1.6	8.9	-16	10		7	
	+24 H	111.1	11.8	102	134	7	-2.4	9.4	-16	14		7	

Note: Data summarised in this table is listed in table I2

Baseline is defined as predose

Key for shift values: abnormal decrease from baseline <-20 mmHg abnormal increase from baseline >20 mmHg
Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics

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TABLE I1.2
Vital Signs
Supine Diastolic Blood Pressure (mmHg)
Summary Statistics, Change from Baseline and Shift Values: All Dosed Subjects

MALE

Dose of Malathion		Result						Change From Baseline				Abnormal Decrease	No Change	Abnormal Increase
		Mean	SD	Min	Max	N		Mean	SD	Min	Max			
PLACEBO	PREDOSE	75.5	11.9	60	92	11								
	+2 H	70.4	10.1	60	90	11		-5.2	7.6	-22	5	1	10	
	+4 H	70.2	8.8	58	82	11		-5.4	12.5	-27	18	1	10	
	+8 H	66.5	5.9	58	76	11		-9.0	11.2	-22	12	2	9	
	+24 H	70.1	8.9	56	85	11		-5.5	6.5	-15	5		11	
0.5 MG/KG	PREDOSE	75.0	15.0	60	90	3								
	+2 H	78.7	2.3	76	80	3		3.7	15.2	-10	20		3	
	+4 H	74.0	4.0	70	78	3		-1.0	19.0	-20	18		3	
	+8 H	71.3	3.1	68	74	3		-3.7	17.2	-22	12	1	2	
	+24 H	70.0	0.0	70	70	3		-5.0	15.0	-20	10		3	

(CONTINUED)

Note: Data summarised in this table is listed in table I2
Baseline is defined as predose
Key for shift values: abnormal decrease from baseline <-20 mmHg abnormal increase from baseline >20 mmHg
Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics

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TABLE I1.2
Vital Signs
Supine Diastolic Blood Pressure (mmHg)
Summary Statistics, Change from Baseline and Shift Values: All Dosed Subjects

MALE

Dose of Malathion		Result			Change From Baseline				Abnormal Decrease	No Change	Abnormal Increase
		Mean	SD	Min	Max	N	Mean	SD	Min	Max	
1.5 MG/KG	PREDOSE	63.3	6.1	58	70	3					
	+2 H	67.3	9.2	62	78	3	4.0	12.0	-8	16	3
	+4 H	64.7	11.7	56	78	3	1.3	15.0	-14	16	3
	+8 H	66.7	4.2	62	70	3	3.3	10.3	-8	12	3
	+24 H	74.0	8.7	68	84	3	10.7	11.0	0	22	1
5.0 MG/KG	PREDOSE	83.6	7.5	70	90	7					
	+2 H	77.4	10.1	65	90	7	-6.1	7.8	-20	2	7
	+4 H	73.6	10.3	60	90	7	-10.0	11.9	-30	10	6
	+8 H	79.9	6.6	70	90	7	-3.7	6.4	-11	5	7
	+24 H	76.6	6.5	68	86	7	-7.0	7.9	-17	6	7

(CONTINUED)

Note: Data summarised in this table is listed in table I2
Baseline is defined as predose

Key for shift values: abnormal decrease from baseline <-20 mmHg abnormal increase from baseline >20 mmHg
Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics

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TABLE I1.2
Vital Signs
Supine Diastolic Blood Pressure (mmHg)
Summary Statistics, Change from Baseline and Shift Values: All Dosed Subjects

MALE

Dose of Malathion		Result					Change From Baseline				Abnormal Decrease	No Change	Abnormal Increase
		Mean	SD	Min	Max	N	Mean	SD	Min	Max			
10.0 MG/KG	PREDOSE	79.7	5.8	70	90	7							
	+2 H	77.0	4.2	70	82	7	-2.7	9.6	-20	12		7	
	+4 H	77.0	7.9	70	90	7	-2.7	8.3	-10	10		7	
	+8 H	77.1	11.1	60	90	7	-2.6	7.3	-10	10		7	
	+24 H	73.3	11.3	52	82	7	-6.4	12.0	-26	11	1	6	
15.0 MG/KG	PREDOSE	63.0	8.3	52	78	7							
	+2 H	66.3	4.8	60	72	7	3.3	6.4	-8	10		7	
	+4 H	66.3	7.3	58	80	7	3.3	6.9	-8	15		7	
	+8 H	69.4	7.6	58	80	7	6.4	6.2	-2	13		7	
	+24 H	71.4	11.7	60	88	7	8.4	7.8	-3	23		6	1

Note: Data summarised in this table is listed in table I2
Baseline is defined as predose
Key for shift values: abnormal decrease from baseline <-20 mmHg abnormal increase from baseline >20 mmHg
Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics

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TABLE I1.2
Vital Signs
Supine Diastolic Blood Pressure (mmHg)
Summary Statistics, Change from Baseline and Shift Values: All Dosed Subjects

FEMALE

Dose of Malathion		Result						Change From Baseline					Abnormal Decrease	No Change	Abnormal Increase
		Mean	SD	Min	Max	N	Mean	SD	Min	Max					
PLACEBO	PREDOSE	71.0	9.6	60	78	3									
	+2 H	69.3	10.1	60	80	3	-1.7	18.9	-15	20			3		
	+4 H	65.7	8.0	58	74	3	-5.3	11.1	-17	5			3		
	+8 H	63.3	15.3	50	80	3	-7.7	8.7	-15	2			3		
	+24 H	66.7	10.1	56	76	3	-4.3	2.5	-7	-2			3		
15.0 MG/KG	PREDOSE	66.3	5.0	56	70	7									
	+2 H	65.4	6.2	54	70	7	-0.9	4.3	-8	6			7		
	+4 H	72.0	14.3	54	100	7	5.7	11.5	-4	30			6		1
	+8 H	68.0	6.1	60	78	7	1.7	7.5	-8	14			7		
	+24 H	66.9	9.2	52	80	7	0.6	5.9	-6	10			7		

Note: Data summarised in this table is listed in table I2

Baseline is defined as predose

Key for shift values: abnormal decrease from baseline <-20 mmHg abnormal increase from baseline >20 mmHg
Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics

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TABLE I1.3
Vital Signs
Supine Pulse (b.p.m.)
Summary Statistics, Change from Baseline and Shift Values: All Dosed Subjects

MALE

Dose of Malathion		Result					Change From Baseline				Abnormal Decrease	No Change	Abnormal Increase
		Mean	SD	Min	Max	N	Mean	SD	Min	Max			
PLACEBO	PREDOSE	66.5	12.5	46	84	11							
	+2 H	69.1	10.1	56	88	11	2.6	8.9	-14	18		10	1
	+4 H	63.6	9.4	50	79	11	-2.8	10.7	-24	12	1	10	
	+8 H	63.6	10.4	50	80	11	-2.8	11.3	-26	16	1	9	1
	+24 H	63.9	7.2	50	73	11	-2.5	11.2	-24	17	1	9	1
0.5 MG/KG	PREDOSE	68.0	6.9	60	72	3							
	+2 H	62.0	3.5	60	66	3	-6.0	6.0	-12	0		3	
	+4 H	59.7	4.5	55	64	3	-8.3	8.5	-17	0	1	2	
	+8 H	61.7	5.5	58	68	3	-6.3	6.8	-14	-1		3	
	+24 H	60.7	5.0	56	66	3	-7.3	4.2	-12	-4		3	

(CONTINUED)

Note: Data summarised in this table is listed in table I2

Baseline is defined as predose

Key for shift values: abnormal decrease from baseline <-15 b.p.m., abnormal increase from baseline >15 b.p.m.
Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics

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TABLE I1.3
Vital Signs
Supine Pulse (b.p.m.)
Summary Statistics, Change from Baseline and Shift Values: All Dosed Subjects

MALE

Dose of Malathion		Result				Change From Baseline				Abnormal Decrease	No Change	Abnormal Increase
		Mean	SD	Min	Max	N	Mean	SD	Min	Max		
1.5 MG/KG	PREDOSE	64.7	11.5	58	78	3						
	+2 H	74.7	2.3	72	76	3	10.0	13.9	-6	18	1	2
	+4 H	64.7	5.0	60	70	3	0.0	7.2	-8	6	3	
	+8 H	63.0	5.3	57	67	3	-1.7	11.0	-13	9	3	
	+24 H	73.3	4.2	70	78	3	8.7	14.7	-8	20	2	1
5.0 MG/KG	PREDOSE	66.9	11.7	52	80	7						
	+2 H	69.1	7.4	62	80	7	2.3	8.0	-8	10	7	
	+4 H	65.4	15.1	42	88	7	-1.4	9.1	-12	16	6	1
	+8 H	61.3	7.5	52	70	7	-5.6	5.5	-14	1	7	
	+24 H	63.1	9.4	44	72	7	-3.7	6.3	-12	6	7	

(CONTINUED)

Note: Data summarised in this table is listed in table I2

Baseline is defined as predose

Key for shift values: abnormal decrease from baseline <-15 b.p.m. abnormal increase from baseline >15 b.p.m. Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics

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TABLE I1.3
Vital Signs
Supine Pulse (b.p.m.)
Summary Statistics, Change from Baseline and Shift Values: All Dosed Subjects

MALE

Dose of Malathion		Result					Change From Baseline				Abnormal Decrease	No Change	Abnormal Increase
		Mean	SD	Min	Max	N	Mean	SD	Min	Max			
10.0 MG/KG	PREDOSE	64.7	4.2	59	70	7							
	+2 H	69.4	6.5	62	80	7	4.7	4.3	-2	10		7	
	+4 H	66.7	5.2	61	76	7	2.0	5.5	-6	12		7	
	+8 H	64.6	8.7	56	80	7	-0.1	8.2	-8	15		7	
	+24 H	69.6	7.3	56	81	7	4.9	4.9	-3	11		7	
15.0 MG/KG	PREDOSE	61.0	6.2	54	72	7							
	+2 H	61.4	5.9	52	71	7	0.4	8.8	-12	11		7	
	+4 H	58.3	5.3	50	64	7	-2.7	10.5	-22	10	1	6	
	+8 H	60.3	4.2	54	68	7	-0.7	5.4	-10	6		7	
	+24 H	62.9	8.3	54	80	7	1.9	8.4	-12	16		6	1

Note: Data summarised in this table is listed in table I2

Baseline is defined as predose

Key for shift values: abnormal decrease from baseline <-15 b.p.m. abnormal increase from baseline >15 b.p.m. Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics

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TABLE I1.3
Vital Signs
Supine Pulse (b.p.m.)
Summary Statistics, Change from Baseline and Shift Values: All Dosed Subjects

FEMALE

Dose of Malathion		Result						Change From Baseline				Abnormal Decrease	No Change	Abnormal Increase
		Mean	SD	Min	Max	N	Mean	SD	Min	Max				
PLACEBO	PREDOSE	70.7	11.5	64	84	3								
	+2 H	67.3	8.1	60	76	3	-3.3	5.0	-8	2			3	
	+4 H	70.7	8.3	64	80	3	0.0	4.0	-4	4			3	
	+8 H	70.0	10.0	60	80	3	-0.7	15.3	-14	16			2	1
	+24 H	68.0	8.7	62	78	3	-2.7	17.0	-20	14	1		2	
15.0 MG/KG	PREDOSE	67.7	7.8	54	76	7								
	+2 H	68.6	9.1	58	80	7	0.9	5.8	-8	6			7	
	+4 H	64.1	8.0	50	76	7	-3.6	4.5	-11	2			7	
	+8 H	67.9	5.4	64	78	7	0.1	7.6	-12	10			7	
	+24 H	64.7	7.4	58	79	7	-3.0	10.7	-18	10	1		6	

Note: Data summarised in this table is listed in table I2

Baseline is defined as predose

Key for shift values: abnormal decrease from baseline <-15 b.p.m. abnormal increase from baseline >15 b.p.m.
Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics

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TABLE I1.4
Vital Signs
Erect Heart Rate (b.p.m.)
Summary Statistics, Change from Baseline and Shift Values: All Dosed Subjects

MALE

Dose of Malathion		Result						Change From Baseline				Abnormal Decrease	No Change	Abnormal Increase
		Mean	SD	Min	Max	N	Mean	SD	Min	Max				
PLACEBO	PREDOSE	82.8	9.6	68	96	11								
	+2 H	87.7	12.0	74	118	11	4.9	15.5	-13	46			10	1
	+4 H	81.7	8.9	67	96	11	-1.1	13.9	-29	18	1		8	2
	+8 H	80.7	8.0	68	96	11	-2.1	11.0	-24	16	1		9	1
	+24 H	80.3	11.8	56	96	11	-2.5	14.0	-24	24	2		8	1
0.5 MG/KG	PREDOSE	74.7	4.6	72	80	3								
	+2 H	73.0	13.5	60	87	3	-1.7	9.6	-12	7			3	
	+4 H	68.0	0.0	68	68	2	-8.0	5.7	-12	-4			2	
	+8 H	68.0	2.6	65	70	3	-6.7	3.5	-10	-3			3	
	+24 H	64.7	5.0	60	70	3	-10.0	2.0	-12	-8			3	

(CONTINUED)

Note: Data summarised in this table is listed in table I2

Baseline is defined as predose

Key for shift values: abnormal decrease from baseline <-15 b.p.m. abnormal increase from baseline >15 b.p.m.
Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics

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TABLE I1.4
Vital Signs
Erect Heart Rate (b.p.m.)
Summary Statistics, Change from Baseline and Shift Values: All Dosed Subjects

MALE

Dose of Malathion		Result					Change From Baseline					Abnormal Decrease	No Change	Abnormal Increase
		Mean	SD	Min	Max	N	Mean	SD	Min	Max				
1.5 MG/KG	PREDOSE	81.3	8.3	72	88	3								
	+2 H	80.0	15.9	68	98	3	-1.3	17.2	-20	14	1	2		
	+4 H	78.7	7.6	70	84	3	-2.7	13.3	-14	12		3		
	+8 H	70.0	7.2	64	78	3	-11.3	15.0	-20	6	2	1		
	+24 H	82.7	3.1	80	86	3	1.3	5.8	-2	8		3		
5.0 MG/KG	PREDOSE	83.1	6.9	72	92	7								
	+2 H	86.9	5.8	78	94	7	3.7	5.4	-1	14		7		
	+4 H	82.3	13.0	60	96	7	-0.9	11.9	-24	16	1	5	1	
	+8 H	85.4	6.9	76	96	7	2.3	7.2	-12	8		7		
	+24 H	78.3	13.1	51	90	7	-4.9	8.5	-21	4	1	6		

(CONTINUED)

Note: Data summarised in this table is listed in table I2

Baseline is defined as predose

Key for shift values: abnormal decrease from baseline <-15 b.p.m. abnormal increase from baseline >15 b.p.m. Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics

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TABLE I1.4
 Vital Signs
 Erect Heart Rate (b.p.m.)
 Summary Statistics, Change from Baseline and Shift Values: All Dosed Subjects

MALE

Dose of Malathion		Result						Change From Baseline				Abnormal Decrease	No Change	Abnormal Increase
		Mean	SD	Min	Max	N		Mean	SD	Min	Max			
10.0 MG/KG	PREDOSE	77.7	7.4	65	86	7								
	+2 H	84.4	7.2	74	98	7		6.7	6.2	-2	15		7	
	+4 H	79.3	9.9	68	96	7		1.6	7.7	-4	18		6	1
	+8 H	81.7	10.9	64	96	7		4.0	12.1	-12	22		6	1
	+24 H	79.7	8.1	68	92	7		2.0	11.2	-12	15		7	
15.0 MG/KG	PREDOSE	69.6	10.3	58	88	7								
	+2 H	77.6	9.9	66	96	7		8.0	2.6	4	12		7	
	+4 H	72.9	10.5	62	94	7		3.3	2.9	-2	6		7	
	+8 H	78.3	11.6	64	96	7		8.7	16.5	-24	24	1	3	3
	+24 H	80.6	7.4	68	88	7		11.0	6.4	0	18		5	2

Note: Data summarised in this table is listed in table I2

Baseline is defined as predose

Key for shift values: abnormal decrease from baseline <-15 b.p.m., abnormal increase from baseline >15 b.p.m., Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics

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TABLE I1.4
 Vital Signs
 Erect Heart Rate (b.p.m.)
 Summary Statistics, Change from Baseline and Shift Values: All Dosed Subjects

FEMALE

Dose of Malathion		Result				Change From Baseline				Abnormal Decrease	No Change	Abnormal Increase
		Mean	SD	Min	Max	N	Mean	SD	Min	Max		
PLACEBO	PREDOSE	85.3	11.0	78	98	3						
	+2 H	87.7	6.0	82	94	3	2.3	5.7	-4	7		3
	+4 H	87.3	9.5	80	98	3	2.0	3.5	0	6		3
	+8 H	93.3	5.8	90	100	3	8.0	14.4	-8	20		2
	+24 H	89.0	7.0	82	96	3	3.7	17.2	-16	16	1	1
15.0 MG/KG	PREDOSE	80.1	9.0	63	88	7						
	+2 H	82.3	10.6	68	94	7	2.1	7.1	-7	13		7
	+4 H	81.4	9.4	67	92	7	1.3	7.2	-12	12		7
	+8 H	83.4	8.2	76	98	7	3.3	7.6	-8	13		7
	+24 H	85.3	10.2	67	98	7	5.1	12.0	-8	29		6
												1

Note: Data summarised in this table is listed in table I2

Baseline is defined as predose

Key for shift values: abnormal decrease from baseline <-15 b.p.m., abnormal increase from baseline >15 b.p.m.
 Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics

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TABLE I1.5
Vital Signs
Temperature (°C)
Summary Statistics and Change from Baseline: All Dosed Subjects

MALE

Dose of Malathion		Result						Change From Baseline			
		Mean	SD	Min	Max	N	Mean	SD	Min	Max	
PLACEBO	PREDOSE	36.39	0.21	36.0	36.6	11					
	+2 H	36.62	0.32	36.0	37.0	11	0.23	0.34	-0.4	0.8	
	+4 H	36.49	0.22	36.2	37.0	11	0.10	0.34	-0.4	0.8	
	+8 H	36.65	0.43	36.0	37.8	11	0.26	0.50	-0.4	1.6	
	+24 H	36.49	0.27	36.0	36.8	11	0.10	0.26	-0.2	0.6	
0.5 MG/KG	PREDOSE	36.73	0.12	36.6	36.8	3					
	+2 H	36.60	0.35	36.2	36.8	3	-0.13	0.42	-0.6	0.2	
	+4 H	36.47	0.42	36.0	36.8	3	-0.27	0.50	-0.8	0.2	
	+8 H	36.27	0.47	35.9	36.8	3	-0.47	0.59	-0.9	0.2	
	+24 H	36.43	0.12	36.3	36.5	3	-0.30	0.20	-0.5	-0.1	
1.5 MG/KG	PREDOSE	36.47	0.25	36.2	36.7	3					
	+2 H	36.37	0.23	36.1	36.5	3	-0.10	0.36	-0.4	0.3	
	+4 H	36.53	0.25	36.3	36.8	3	0.07	0.25	-0.2	0.3	
	+8 H	36.53	0.32	36.3	36.9	3	0.07	0.35	-0.3	0.4	
	+24 H	36.70	0.17	36.5	36.8	3	0.23	0.12	0.1	0.3	

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Note: Baseline is defined as predose
Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics
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TABLE I1.5
Vital Signs
Temperature (°C)
Summary Statistics and Change from Baseline: All Dosed Subjects

MALE

Dose of Malathion		Result					Change From Baseline				
		Mean	SD	Min	Max	N	Mean	SD	Min	Max	
5.0 MG/KG	PREDOSE	36.40	0.33	36.0	36.8	7					
	+2 H	36.66	0.23	36.4	37.0	7	0.26	0.30	-0.3	0.6	
	+4 H	36.59	0.27	36.2	37.0	7	0.19	0.23	-0.1	0.5	
	+8 H	36.49	0.48	36.0	37.3	7	0.09	0.32	-0.4	0.5	
	+24 H	36.74	0.10	36.6	36.8	7	0.34	0.33	0.0	0.8	
10.0 MG/KG	PREDOSE	36.51	0.33	36.2	37.1	7					
	+2 H	36.50	0.28	36.2	36.9	7	-0.01	0.32	-0.5	0.4	
	+4 H	36.34	0.28	36.0	36.9	7	-0.17	0.24	-0.6	0.2	
	+8 H	37.01	0.81	36.4	38.8	7	0.50	0.57	0.0	1.7	
	+24 H	36.60	0.22	36.4	37.0	7	0.09	0.30	-0.3	0.6	
15.0 MG/KG	PREDOSE	36.33	0.30	35.8	36.7	7					
	+2 H	36.37	0.34	35.8	36.8	7	0.04	0.43	-0.8	0.4	
	+4 H	36.44	0.46	36.0	37.4	7	0.11	0.35	-0.4	0.7	
	+8 H	36.63	0.51	36.0	37.4	7	0.30	0.46	-0.2	1.2	
	+24 H	36.09	0.22	35.8	36.4	7	-0.24	0.26	-0.7	0.1	

Note: Baseline is defined as predose
Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics
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TABLE I1.5
Vital Signs
Temperature (°C)
Summary Statistics and Change from Baseline: All Dosed Subjects

FEMALE

Dose of Malathion		Result					Change From Baseline				
		Mean	SD	Min	Max	N	Mean	SD	Min	Max	
PLACEBO	PREDOSE	36.73	0.21	36.5	36.9	3					
	+2 H	36.77	0.40	36.4	37.2	3	0.03	0.23	-0.1	0.3	
	+4 H	37.37	0.91	36.7	38.4	3	0.63	0.75	0.2	1.5	
	+8 H	37.37	0.98	36.8	38.5	3	0.63	0.85	0.0	1.6	
	+24 H	37.03	0.93	36.4	38.1	3	0.30	0.78	-0.2	1.2	
15.0 MG/KG	PREDOSE	36.64	0.25	36.2	36.9	7					
	+2 H	36.61	0.30	36.2	37.0	7	-0.03	0.39	-0.5	0.6	
	+4 H	36.71	0.38	36.2	37.2	7	0.07	0.39	-0.2	0.8	
	+8 H	36.81	0.30	36.4	37.1	7	0.17	0.35	-0.4	0.7	
	+24 H	36.54	0.27	36.2	36.8	7	-0.10	0.29	-0.4	0.4	

Note: Baseline is defined as predose
Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics
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TABLE I1.6
 Vital Signs
 Respiratory Rate (breaths per minute)
 Summary Statistics and Change from Baseline: All Subjects

MALE

Dose of Malathion		Result					Change From Baseline			
		Mean	SD	Min	Max	N	Mean	SD	Min	Max
PLACEBO	PREDOSE	17.6	2.2	14	22	11				
	+2 H	16.6	0.9	15	18	11	-1.0	1.9	-5	3
	+4 H	16.5	1.2	14	18	11	-1.1	2.3	-5	2
	+8 H	16.7	1.7	15	21	11	-0.9	2.3	-4	3
	+24 H	17.1	0.9	16	18	11	-0.5	2.6	-4	4
0.5 MG/KG	PREDOSE	17.3	1.2	16	18	3				
	+2 H	16.0	3.5	12	18	3	-1.3	4.2	-6	2
	+4 H	14.7	3.1	12	18	3	-2.7	3.1	-6	0
	+8 H	14.7	1.2	14	16	3	-2.7	1.2	-4	-2
	+24 H	14.7	1.2	14	16	3	-2.7	1.2	-4	-2
1.5 MG/KG	PREDOSE	17.7	2.9	16	21	3				
	+2 H	16.0	1.0	15	17	3	-1.7	2.1	-4	0
	+4 H	16.0	0.0	16	16	3	-1.7	2.9	-5	0
	+8 H	17.7	2.1	16	20	3	0.0	1.0	-1	1
	+24 H	16.7	1.2	16	18	3	-1.0	1.7	-3	0

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Note: Baseline is defined as predose
 Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics
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TABLE I1.6
 Vital Signs
 Respiratory Rate (breaths per minute)
 Summary Statistics and Change from Baseline: All Subjects

MALE

Dose of Malathion		Result						Change From Baseline			
		Mean	SD	Min	Max	N	Mean	SD	Min	Max	
5.0 MG/KG	PREDOSE	19.9	2.6	15	24	7					
	+2 H	18.0	1.2	16	20	7	-1.9	1.5	-4	1	
	+4 H	18.4	2.5	17	24	7	-1.4	3.4	-6	4	
	+8 H	18.4	3.3	16	24	7	-1.4	3.5	-4	4	
	+24 H	16.0	0.8	15	17	7	-3.9	2.5	-7	1	
10.0 MG/KG	PREDOSE	16.0	1.3	14	18	7					
	+2 H	16.0	1.2	14	18	7	0.0	1.7	-2	2	
	+4 H	16.6	1.5	14	18	7	0.6	2.4	-4	3	
	+8 H	15.9	0.4	15	16	7	-0.1	1.6	-3	2	
	+24 H	16.0	2.0	14	20	7	0.0	2.4	-2	4	
15.0 MG/KG	PREDOSE	14.6	1.5	12	16	7					
	+2 H	16.3	1.0	15	18	7	1.7	1.9	-1	4	
	+4 H	15.0	1.3	13	16	7	0.4	1.1	-1	2	
	+8 H	15.1	1.1	14	16	7	0.6	1.0	0	2	
	+24 H	16.1	1.9	14	20	7	1.6	2.0	-1	4	

Note: Baseline is defined as predose
 Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics
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TABLE I1.6
 Vital Signs
 Respiratory Rate (breaths per minute)
 Summary Statistics and Change from Baseline: All Subjects

FEMALE

Dose of Malathion		Result					Change From Baseline				
		Mean	SD	Min	Max	N	Mean	SD	Min	Max	
PLACEBO	PREDOSE	16.3	0.6	16	17	3					
	+2 H	18.0	2.0	16	20	3	1.7	1.5	0	3	
	+4 H	17.0	1.7	15	18	3	0.7	1.5	-1	2	
	+8 H	17.7	0.6	17	18	3	1.3	0.6	1	2	
	+24 H	17.0	1.0	16	18	3	0.7	1.2	0	2	
15.0 MG/KG	PREDOSE	17.6	1.6	16	20	7					
	+2 H	17.3	0.8	16	18	7	-0.3	1.4	-2	2	
	+4 H	18.3	1.9	16	22	7	0.7	1.5	-2	2	
	+8 H	16.6	1.5	14	18	7	-1.0	1.9	-4	2	
	+24 H	17.4	1.1	16	19	7	-0.1	1.6	-3	2	

Note: Baseline is defined as predose
 Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics
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TABLE 12
Vital Signs
Individual Values: All Subjects

Subject	Dose of Malathion	Sex	Study Day	Time Point	Supine Systolic BP (mmHg)	Supine Diastolic BP (mmHg)	Supine Pulse (b.p.m.)	Temperature (°C)	Respiration Rate (breaths per min)	Erect Heart Rate (b.p.m.)
001	0.5 MG/KG	MALE	SCREENING ADMISSION ON-STUDY	PREDOSE	120	70	56	36.6	16	56
				+2 H	120	75	64	37.0	16	73
				+4 H	140	90	72	36.8	16	72
				+8 H	130	80	60	36.2	18	60
				+24 H	115 D	70	55 D	36.0	14	.
002	0.5 MG/KG	MALE	SCREENING ADMISSION ON-STUDY	PREDOSE	118 D	68 D	58	36.1	14	65
				+8 H	125	70	60	36.3	14	64
				+24 H	104	78	58	36.6	18	74
				+2 H	110	60	62	36.9	18	72
				+4 H	140	75	60	36.6	18	72
003	PLACEBO	MALE	SCREENING ADMISSION ON-STUDY	PREDOSE	134	76	60	36.8	18	72
				+2 H	112 D	74	60	36.8	12	68
				+4 H	120	74	59	36.8	14	69
				+8 H	115 D	70	56	36.5	14	60
				+24 H	118	68	56	36.3	16	72
				PREDOSE	120	70	62	36.8	16	80
				+2 H	120	90	78	36.6	18	96
				+4 H	112	68 D	64	36.8	18	83
				+8 H	124	80	54 D	36.5	14	67 D
				+24 H	112	68 D	52 D	36.6	15	72 D
					125	80	54 D	36.5	16	72 D

Note: Values marked # indicate a repeat value not included in the summary statistics
 Values marked ## indicate a repeat value replacing the original value at that time point in the summary statistics
 Values marked I or D indicate increase or decrease from baseline of greater than +20 mmHg for blood pressure and greater than ±15 bpm for pulse and heart rate
 Baseline is defined as predose

TABLE I2
Vital Signs
Individual Values: All Subjects

Subject	Dose of Maltathion	Sex	Study Day	Time Point	Supine Systolic BP (mmHg)	Supine Diastolic BP (mmHg)	Supine Pulse (b.p.m.)	Temperature (°C)	Respiration Rate (breaths per min)	Erect Heart Rate (b.p.m.)
004	0.5 MG/KG	MALE	SCREENING ADMISSION ON-STUDY		118	84	74	36.4	18	82
					110	68	68	36.0	12	76
				PREDOSE	110	60	72	36.8	18	80
				+2 H	115	80	66	36.8	12	87
				+4 H	105	78	64	36.6	18	68
005	1.5 MG/KG	MALE	SCREENING ADMISSION ON-STUDY	+8 H	108	72	68	35.9	16	70
				+24 H	105	70	66	36.5	16	70
					126	78	74	36.8	16	78
					122	62	64	36.6	16	74
				PREDOSE	116	70	78	36.7	16	88
006	1.5 MG/KG	MALE	SCREENING ADMISSION ON-STUDY	+2 H	112	62	72	36.5	15	68 D
				+4 H	104	56	70	36.8	16	82
				+8 H	108	62	65	36.4	16	68 D
				+24 H	110	70	70	36.8	16	86
					122	76	80	36.1	15	82
	1.5 MG/KG	MALE	SCREENING ADMISSION ON-STUDY		120	60	62	36.8	15	66
					122	62	58	36.2	16	72
				PREDOSE	124	78	76 I	36.5	16	74
				+2 H	120	78	64	36.5	16	84
				+4 H	124	68	67	36.3	17	78
	1.5 MG/KG	MALE	SCREENING ADMISSION ON-STUDY	+8 H	124	68	78 I	36.5	16	80
				+24 H	128	84 I	78 I	36.5	16	

Note: Values marked # indicate a repeat value not included in the summary statistics
 Values marked ## indicate a repeat value replacing the original value at that time point in the summary statistics
 Values marked I or D indicate increase or decrease from baseline of greater than ±20 mmHg for blood pressure and greater than ±15 bpm for pulse and heart rate
 Baseline is defined as predose

TABLE 12

Vital Signs
Individual Values: All Subjects

Subject	Dose of Malathion	Sex	Study Day	Time Point	Supine Systolic BP (mmHg)	Supine Diastolic BP (mmHg)	Supine Pulse (b.p.m.)	Temperature (°C)	Respiration Rate (breaths per min)	Erect Heart Rate (b.p.m.)
007	PLACEBO	MALE	SCREENING ADMISSION ON-STUDY		144	78	62	36.0	16	93
				PREDOSE	130	75	76	36.8	15	80
				+2 H	130	64	71	36.0	18	90
				+4 H	112	66	70	36.3	17	84
				+8 H	124	82	64	36.6	18	78
008	1.5 MG/KG	MALE	SCREENING ADMISSION ON-STUDY	+24 H	128	76	62	36.5	18	80
					108 D	64	64	36.4	16	86
					122	58	78	36.6	16	96
				PREDOSE	125	72	79	36.7	15	89
				+2 H	104	58	58	36.5	21	84
009	5.0 MG/KG	MALE	SCREENING ADMISSION ON-STUDY	+4 H	118	62	76 I	36.1	17	98
				+8 H	110	60	60	36.3	16	70
				+24 H	120	70	57	36.9	20	64 D
					116	68	72	36.8	18	82
					140	80	76	36.6	14	84
			SCREENING ADMISSION ON-STUDY		105	80	72	36.4	16	88
				PREDOSE	125	80	52	36.5	20	84
				+2 H	120	70	62	36.6	18	84
				+4 H	130	90	52	36.4	17	60 D
				+8 H	130	85	52	36.4	16	86
				+24 H	135	86	58	36.8	15	78

Note: Values marked # indicate a repeat value not included in the summary statistics
 Values marked ## indicate a repeat value replacing the original value at that time point in the summary statistics
 Values marked I or D indicate increase or decrease from baseline of greater than ± 20 mmHg for blood pressure and greater than ± 15 bpm for pulse and heart rate
 Baseline is defined as predose

TABLE I2
Vital Signs
Individual Values: All Subjects

Subject	Dose of Malathion	Sex	Study Day	Time Point	Supine Systolic BP (mmHg)	Supine Diastolic BP (mmHg)	Supine Pulse (b.p.m.)	Temperature (°C)	Respiration Rate (breaths per min)	Erect Heart Rate (b.p.m.)
010	5.0 MG/KG	MALE	SCREENING ADMISSION ON-STUDY		124	88	54	36.6	15	68
				PREDOSE	125	80	68	36.0	18	76
				+2 H	140	90	64	36.0	20	88
				+4 H	120	80	70	36.6	18	87
				+8 H	130	80	64	36.4	17	88
011	5.0 MG/KG	MALE	SCREENING ADMISSION ON-STUDY	+24 H	120	78	58	36.0	16	76
							66	36.8	15	78
					118	62	74	36.8	16	80
				PREDOSE	104	74	68	36.4	18	72
				+2 H	145	90	68	36.6	24	80
012	5.0 MG/KG	MALE	SCREENING ADMISSION ON-STUDY	+4 H	118 D	70	62	36.9	20	82
				+8 H	115 D	60 D	68	36.8	18	78
				+24 H	120 D	80	60	36.2	22	82
					125	78	66	36.6	17	79
					112	67	61	36.4	14	87
			SCREENING ADMISSION ON-STUDY		115	72	76	36.2	18	96
				PREDOSE	125	90	80	36.2	20	88
				+2 H	140	90	72	36.7	18	94
				+4 H	120	80	76	36.7	18	88
				+8 H	120	90	66	36.7	16	96
				+24 H	118	80	68	36.8	17	90

Note: Values marked # indicate a repeat value not included in the summary statistics
 Values marked ## indicate a repeat value replacing the original value at that time point in the summary statistics
 Values marked I or D indicate increase or decrease from baseline of greater than ±20 mmHg for blood pressure and greater than ±15 bpm for pulse and heart rate
 Baseline is defined as predose

TABLE I2
Vital Signs
Individual Values: All Subjects

Subject	Dose of Malathion	Sex	Study Day	Time Point	Supine Systolic BP (mmHg)	Supine Diastolic BP (mmHg)	Supine Pulse (b.p.m.)	Temperature (°C)	Respiration Rate (breaths per min)	Erect Heart Rate (b.p.m.)
013	PLACEBO	MALE	SCREENING ADMISSION ON-STUDY		108	70	78	36.5	16	.
				PREDOSE	118	85	88	36.4	18	100
				+2 H	125	92	68	36.4	20	90
				+4 H	130	90	64	36.8	18	94
				+8 H	115	65 D	57	36.4	17	94
014	5.0 MG/KG	MALE	SCREENING ADMISSION ON-STUDY	+24 H	115	70 D	60	36.0	16	96
					120	85	66	36.6	17	91
					105	60	80	36.4	18	80
				PREDOSE	130	90	76	36.4	15	92
				+2 H	120	80	80	36.8	20	92
015	PLACEBO	MALE	SCREENING ADMISSION ON-STUDY	+4 H	135	82	76	37.0	18	91
				+8 H	130	70	68	37.0	18	96
				+24 H	128	80	70	37.3	24	92
					125	78	72	36.8	16	90
					144	88	76	36.8	18	84
					145	85	88	36.8	17	100
				PREDOSE	120	80	52	36.6	18	80
				+2 H	120	75	60	36.8	17	79
				+4 H	135	78	64	36.5	16	80
				+8 H	110	60	68 I	36.7	21	74
				+24 H	115	66	69 I	36.8	17	79

Note: Values marked # indicate a repeat value not included in the summary statistics
 Values marked ## indicate a repeat value replacing the original value at that time point in the summary statistics
 Values marked I or D indicate increase or decrease from baseline of greater than ±20 mmHg for blood pressure and greater than ±15 bpm for pulse and heart rate
 Baseline is defined as predose

TABLE 12
Vital Signs
Individual Values: All Subjects

Subject	Dose of Methathion	Sex	Study Day	Time Point	Supine Systolic BP (mmHg)	Supine Diastolic BP (mmHg)	Supine Pulse (b.p.m.)	Temperature (°C)	Respiration Rate (breaths per min)	Erect Heart Rate (b.p.m.)
016	PLACEBO	MALE	SCREENING ADMISSION ON-STUDY		122	78	60	36.8	16	72
				PREDOSE	115	82	76	36.5	18	80
				+2 H	140	90	80	36.6	22	88
				+4 H	135	85	78	36.8	17	79
				+8 H	120	70	66	36.6	17	76
017	5.0 MG/KG	MALE	SCREENING ADMISSION ON-STUDY	+8 H	118 D	70	68	36.6	18	84
				+24 H	116 D	75	69	36.5	18	79
					115	70	62	36.2	14	68
				PREDOSE	125	82	76	36.4	16	88
					140	90	72	36.5	20	100
917	5.0 MG/KG	MALE	SCREENING ADMISSION ON-STUDY		110	65	60	36.5	15	66
				PREDOSE	120	75	80	36.2	16	96
				+2 H	140	70	72	36.7	15	78
				+4 H	115 D	65	80	36.4	16	92
				+8 H	110 D	65	88 I	36.6	17	94 I
				+24 H	106 D	70	70	36.6	18	86
					110 D	68	68	36.8	16	82

Note: Values marked # indicate a repeat value not included in the summary statistics
 Values marked ## indicate a repeat value replacing the original value at that time point in the summary statistics
 Values marked I or D indicate increase or decrease from baseline of greater than ± 20 mmHg for blood pressure and greater than ± 15 bpm for pulse and heart rate
 Baseline is defined as predose
 Subject 917 replaces subject 017 who withdrew from study and is not included in the summary statistics

TABLE I2
Vital Signs
Individual Values: All Subjects

Subject	Dose of Malathion	Sex	Study Day	Time Point	Supine Systolic BP (mmHg)	Supine Diastolic BP (mmHg)	Supine Pulse (b.p.m.)	Temperature (°C)	Respiration Rate (breaths per min)	Erect Heart Rate (b.p.m.)	#
018	5.0 MG/KG	MALE	SCREENING ADMISSION ON-STUDY		110	70	52	36.0	14	60	
					115	75	52	36.0	16	64	
				PREDOSE	130	85	52	36.0	20	72	
				+2 H	125	75	62	36.4	18	78	
				+4 H	120	70	42	36.2	24	72	
							45				#
019	10.0 MG/KG	MALE	SCREENING ADMISSION ON-STUDY		116	74	53	36.0	17	80	
					120	68	44	36.6	16	51 D	
							45				#
					112	72	60	36.7	16	72	
					104	70	55	36.4	15	64	
				PREDOSE	118	78	59	36.4	16	65	
				+2 H	122	78	65	36.8	14	74	
				+4 H	112	84	61	36.2	18	68	
				+8 H	110	70	56	37.0	16	64	
				+24 H	106	52 D	56	36.5	14	80	

Note: Values marked # indicate a repeat value not included in the summary statistics
 Values marked ## indicate a repeat value replacing the original value at that time point in the summary statistics
 Values marked I or D indicate increase or decrease from baseline of greater than ±20 mmHg for blood pressure and greater than ±15 bpm for pulse and heart rate
 Baseline is defined as predose

TABLE I2
Vital Signs
Individual Values: All Subjects

Subject	Dose of Malathion	Sex	Study Day	Time Point	Supine Systolic BP (mmHg)	Supine Diastolic BP (mmHg)	Supine Pulse (b.p.m)	Temperature (°C)	Respiration Rate (breaths per min)	Erect Heart Rate (b.p.m.)	#
020	10.0 MG/KG	MALE	SCREENING		140	90	104	36.8	16	101	#
							84			100	##
			ADMISSION		130	84	82	36.7	18	96	
			ON-STUDY	PREDOSE	140	80	70	36.8	17	74	
				+2 H	138	74	80	36.9	16	86	
				+4 H	128	90	64	36.2	16	72	
				+8 H	110 D	80	66	36.8	16	86	
				+24 H	136	82	81	36.5	16	86	
021	PLACEBO	MALE	SCREENING		120	80	80	36.2	18	98	
			ADMISSION		100	66	82	36.2	18	106	
										102	#
			ON-STUDY	PREDOSE	112	70	84	36.3	18	90	
				+2 H	108	75	80	36.9	16	94	
				+4 H	126	80	79	36.2	18	84	
				+8 H	110	70	80	36.4	16	84	
				+24 H	107	72	73	36.2	16	80	

Note: Values marked # indicate a repeat value not included in the summary statistics
 Values marked ## indicate a repeat value replacing the original value at that time point in the summary statistics
 Values marked I or D indicate increase or decrease from baseline of greater than ± 20 mmHg for blood pressure and greater than ± 15 bpm for pulse and heart rate
 Baseline is defined as predose

TABLE I2
Vital Signs
Individual Values: All Subjects

Subject	Dose of Malathion	Sex	Study Day	Time Point	Supine Systolic BP (mmHg)	Supine Diastolic BP (mmHg)	Supine Pulse (b.p.m.)	Temperature (°C)	Respiration Rate (breaths per min)	Erect Heart Rate (b.p.m.)
022	10.0 MG/KG	MALE	SCREENING ADMISSION ON-STUDY		126	78	52	36.3	15	62
					110	60	58	37.0	16	78
				PREDOSE	138	70	65	37.1	15	74
				+2 H	124	82	68	36.6	16	82
				+4 H	132	70	69	36.9	18	70
023	10.0 MG/KG	MALE	SCREENING ADMISSION ON-STUDY	+8 H	130	60	80	38.8	16	96 I
				+24 H	107 D	81	72	37.0	16	68
					110	68	64	36.4	18	76
					110	78	67	36.4	16	79
				PREDOSE	118	80	64	36.5	18	84
024	PLACEBO	MALE	SCREENING ADMISSION ON-STUDY	+2 H	120	80	62	36.2	16	82
				+4 H	112	70	56	36.3	14	82
				+8 H	118	70	56	36.7	15	80
				+24 H	106	68	68	36.4	16	72
					150	84	80	36.4	16	94
					124	80	73	36.2	17	88
				PREDOSE	124	80	70	36.5	18	85
				+2 H	115	70	74	36.7	16	92
				+4 H	118	72	72	36.6	16	96
				+8 H	118	70	68	36.6	16	86
				+24 H	122	78	70	36.8	16	94

Note: Values marked # indicate a repeat value not included in the summary statistics
 Values marked ## indicate a repeat value replacing the original value at that time point in the summary statistics
 Values marked I or D indicate increase or decrease from baseline of greater than ± 20 mmHg for blood pressure and greater than ± 15 bpm for pulse and heart rate
 Baseline is defined as predose

TABLE I2

Vital Signs
Individual Values: All Subjects

Subject	Dose of Malathion	Sex	Study Day	Time Point	Supine Systolic BP (mmHg)	Supine Diastolic BP (mmHg)	Supine Pulse (b.p.m.)	Temperature (°C)	Respiration Rate (breaths per min)	Erect Heart Rate (b.p.m.)	#
025	PLACEBO	MALE	SCREENING ADMISSION ON-STUDY		102	68	66	37.0	16	74	
				PREDOSE	108	70	64	36.2	18	74	
				+2 H	105	75	46	36.2	16	68	
				+4 H	98	65	58	36.5	16	74	
				+8 H	102	65	54	36.4	16	86 I	
					110	70	50	37.8	16	68	
				+24 H	110	70	58	36.0	18	82	
026	15.0 MG/KG	MALE	SCREENING ADMISSION ON-STUDY		128	65	85	36.7	14	91	
				PREDOSE	112	72	77	36.1	18	88	
				+2 H	112	65	72	36.6	14	76	
				+4 H	110	72	62	35.8	18	84	
				+8 H	124	80	50 D	36.2	14	78	
					110	78	62	36.4	14	82	
				+24 H	125	88 I	60	35.9	16	88	
027	10.0 MG/KG	MALE	SCREENING ADMISSION ON-STUDY		120	88	76	36.4	18	80	
				PREDOSE	120	76	64	36.6	15	73	
					118	85	72	36.9	16	90	

Note: Values marked # indicate a repeat value not included in the summary statistics
 Values marked ## indicate a repeat value replacing the original value at that time point in the summary statistics
 Values marked I or D indicate increase or decrease from baseline of greater than ± 20 mmHg for blood pressure and greater than ± 15 bpm for pulse and heart rate
 Baseline is defined as predose
 Subject 927 replaces subject 027 who withdrew from study and is not included in the summary statistics

TABLE I2
Vital Signs
Individual Values: All Subjects

Subject	Dose of Maltathion	Sex	Study Day	Time Point	Supine Systolic BP (mmHg)	Supine Diastolic BP (mmHg)	Supine Pulse (b.p.m.)	Temperature (°C)	Respiration Rate (breaths per min)	Erect Heart Rate (b.p.m.)
927	10.0 MG/KG	MALE	SCREENING ADMISSION ON-STUDY		135	86	80	36.7	15	82
				PREDOSE	108	78	64	36.5	14	70
				+2 H	112	80	61	36.2	14	78
				+4 H	122	80	70	36.4	16	83
				+8 H	108	70	64	36.4	16	96 I
028	10.0 MG/KG	MALE	SCREENING ADMISSION ON-STUDY	+24 H	130	90	68	36.4	16	92
					120	80	70	36.5	16	92
					135	90	78	35.8	20	84
				PREDOSE	124	82	77	35.9	18	88
				+2 H	112	90	64	36.4	16	86
029	15.0 MG/KG	MALE	SCREENING ADMISSION ON-STUDY	+4 H	102	70	65	36.2	16	86
				+8 H	112	80	76	36.4	18	82
				+24 H	128	90	58	36.6	16	74
					124	82	70	36.5	20	82
					118	72	60	36.2	14	76
					112	80	73	36.5	14	83
				PREDOSE	114	78	54	36.2	14	65
				+2 H	118	70	59	36.4	16	75
				+4 H	102	70	64	36.3	13	70
				+8 H	118	80	54	37.4	14	70
				+24 H	134	88	60	36.3	16	78

Note: Values marked # indicate a repeat value not included in the summary statistics
 Values marked ## indicate a repeat value replacing the original value at that time point in the summary statistics
 Values marked I or D indicate increase or decrease from baseline of greater than ± 20 mmHg for blood pressure and greater than ± 15 bpm for pulse and heart rate
 Baseline is defined as predose

TABLE 12
Vital Signs
Individual Values: All Subjects

Subject	Dose of Malathion	Sex	Study Day	Time Point	Supine Systolic BP (mmHg)	Supine Diastolic BP (mmHg)	Supine Pulse (b.p.m.)	Temperature (°C)	Respiration Rate (breaths per min)	Erect Heart Rate (b.p.m.)
030	10.0 MG/KG	MALE	SCREENING ADMISSION ON-STUDY		137	74	77	36.8	16	88
				PREDOSE	112	80	66	36.0	15	69
				+2 H	112	80	70	36.2	16	83
				+4 H	120	75	76	36.4	18	98
				+8 H	118	75	70	36.0	16	85
				+24 H	120	80	68	36.8	16	80
031	15.0 MG/KG	MALE	SCREENING ADMISSION ON-STUDY		112	68	70	36.8	14	78
					120	80	89	36.5	16	98
				PREDOSE	118	68	89	35.7	18	99
				+2 H	98	60	60	35.8	12	88
				+4 H	110	70	71	36.2	16	96
				+8 H	102	64	58	36.0	14	94
032	PLACEBO	MALE	SCREENING ADMISSION ON-STUDY		110	70	58	36.0	14	64 D
				+24 H	108	70	60	35.8	16	88
					110	70	56	36.0	14	68
				PREDOSE	120	80	66	36.8	16	84
				+2 H	104	70	60	36.6	16	84
				+4 H	104	60	68	36.2	16	88
				+8 H	104	62	64	36.2	18	78
				+24 H	108	60	60	36.8	16	76
					118	60	62	36.6	18	68 D

Note: Values marked # indicate a repeat value not included in the summary statistics
 Values marked ## indicate a repeat value replacing the original value at that time point in the summary statistics
 Values marked I or D indicate increase or decrease from baseline of greater than ±20 mmHg for blood pressure and greater than ±15 bpm for pulse and heart rate
 Baseline is defined as predose

TABLE 12
Vital Signs
Individual Values: All Subjects

Subject	Dose of Malathion	Sex	Study Day	Time Point	Supine Systolic BP (mmHg)	Supine Diastolic BP (mmHg)	Supine Pulse (b.p.m.)	Temperature (°C)	Respiration Rate (breaths per min)	Erect Heart Rate (b.p.m.)	#
033	15.0 MG/KG	MALE	SCREENING ADMISSION ON-STUDY	PREDOSE +2 H	105	60	66	36.5	15	70	
					104	60	60	36.6	14	64	
					102	52	54	36.4	16	60	
					98	60	60	36.2	15	72	
					94	62	62				
					100	58	56	36.2	16	66	
034	15.0 MG/KG	MALE	SCREENING ADMISSION ON-STUDY	PREDOSE +2 H	100	64	60	36.3	16	68	
					100	60	54	36.0	16	68	
					110	60	84	36.2	16	90	
					120	76	78	37.0	16	88	
					108	68	63	36.4	16	72	
					112	66	60	36.8	16	78	
				+4 H	116	68	62	36.6	16	70	
					122	68	68	36.7	16	96 I	
					110	65	66	36.2	20	80	

Note: Values marked # indicate a repeat value not included in the summary statistics
 Values marked ## indicate a repeat value replacing the original value at that time point in the summary statistics
 Values marked I or D indicate increase or decrease from baseline of greater than ± 20 mmHg for blood pressure and greater than ± 15 bpm for pulse and heart rate
 Baseline is defined as predose

TABLE I2
Vital Signs
Individual Values: All Subjects

Subject	Dose of Malathion	Sex	Study Day	Time Point	Supine Systolic BP (mmHg)	Supine Diastolic BP (mmHg)	Supine Pulse (b.p.m.)	Temperature (°C)	Respiration Rate (breaths per min)	Erect Heart Rate (b.p.m.)
035	PLACEBO	MALE	SCREENING ADMISSION ON-STUDY		130	70	68	36.4	16	88
					110	78	62	36.7	18	84
				PREDOSE	100	60	52	36.3	16	68
				+2 H	88	60	56	36.0	15	80
					92	60				#
				+4 H	98	60	50	36.4	16	72
					96	62				#
				+8 H	120	60	52	36.6	16	80
				+24 H	100	65	50	36.2	18	56
036	PLACEBO	MALE	SCREENING ADMISSION ON-STUDY		102	72	64	36.8	20	76
					118	78	86	36.8	18	96
				PREDOSE	100	60	70	36.2	14	72
				+2 H	104	60	88 I	37.0	17	118 I
										#
				+4 H	102	58	76	37.0	16	112 I
				+8 H	110	58	80	36.6	16	88 I
				+24 H	104	56	68	36.0	18	96 I

Note: Values marked # indicate a repeat value not included in the summary statistics
 Values marked ## indicate a repeat value replacing the original value at that time point in the summary statistics
 Values marked I or D indicate increase or decrease from baseline of greater than ±20 mmHg for blood pressure and greater than ±15 bpm for pulse and heart rate
 Baseline is defined as predose

TABLE 12
Vital Signs
Individual Values: All Subjects

Subject	Dose of Methathion	Sex	Study Day	Time Point	Supine Systolic BP (mmHg)	Supine Diastolic BP (mmHg)	Supine Pulse (b.p.m.)	Temperature (°C)	Respiration Rate (breaths per min)	Erect Heart Rate (b.p.m.)
037	15.0 MG/KG	MALE	SCREENING ADMISSION ON-STUDY		130	70	60	36.5	16	70
					120	80	60	36.8	18	62
				PREDOSE	110	58	64	36.7	16	58
				+2 H	110	60	52	36.7	17	66
				+4 H	108	60	54	37.4	16	62
038	15.0 MG/KG	MALE	SCREENING ADMISSION ON-STUDY	+8 H	120	68	60	37.2	16	80 I
				+24 H	108	64	80 I	36.4	15	76 I
					110	64	70	36.3	16	86
					104	60	64	36.0	16	76
				PREDOSE	100	60	60	36.2	14	68
039	15.0 MG/KG	FEMALE	SCREENING ADMISSION ON-STUDY	+2 H	98	66	66	36.5	16	72
					104	64	64			
				+4 H	100	64	64	36.4	16	70
				+8 H	108	58	60	36.4	16	88 I
				+24 H	102	65	60	36.0	14	86 I
					110	78	82	36.2	18	92
					130	80	76	36.8	18	76
				PREDOSE	100	68	76	36.2	16	88
				+2 H	96	60	80	36.5	17	88
039	15.0 MG/KG	FEMALE	SCREENING ADMISSION ON-STUDY		98	58	58			
				+4 H	100	70	76	36.2	18	76
				+8 H	106	72	64	36.5	18	80
				+24 H	104	62	58 D	36.2	16	88

Note: Values marked # indicate a repeat value not included in the summary statistics
 Values marked ## indicate a repeat value replacing the original value at that time point in the summary statistics
 Values marked I or D indicate increase or decrease from baseline of greater than ± 20 mmHg for blood pressure and greater than ± 15 bpm for pulse and heart rate
 Baseline is defined as predose

TABLE I2
Vital Signs
Individual Values: All Subjects

Subject	Dose of Malathion	Sex	Study Day	Time Point	Supine Systolic BP (mmHg)	Supine Diastolic BP (mmHg)	Supine Pulse (b.p.m.)	Temperature (°C)	Respiration Rate (breaths per min)	Erect Heart Rate (b.p.m.)
040	15.0 MG/KG	FEMALE	SCREENING ADMISSION ON-STUDY		102	80	70	36.0	18	82
				PREDOSE	105	65	76	37.0	12	88
				+2 H	108	68	70	36.8	16	88
				+4 H	108	70	64	36.8	18	94
				+8 H	104	68	68	37.2	18	89
041	PLACEBO	FEMALE	SCREENING ADMISSION ON-STUDY	+8 H	102	68	68	37.0	16	88
				+24 H	104	64	70	36.8	18	90
					110	80	68	37.0	16	76
				PREDOSE	105	70	80	36.8	12	86
				+2 H	110	78	64	36.5	17	80
042	15.0 MG/KG	FEMALE	SCREENING ADMISSION ON-STUDY	+4 H	110	68	60	36.4	20	87
				+8 H	120	74	68	36.7	18	80
				+24 H	110	80	60	36.8	18	100 I
					110	76	62	36.4	17	96 I
					100	58	64	36.0	16	50
				PREDOSE	105	60	76	36.2	18	82
				+2 H	107	56	54	36.7	18	63
				+4 H	100	54	58	36.2	17	71
				+8 H	104	54	50	36.5	18	67
				+24 H	108	70	64	37.0	16	76
					104	52	64	36.3	18	92 I

Note: Values marked # indicate a repeat value not included in the summary statistics
 Values marked ## indicate a repeat value replacing the original value at that time point in the summary statistics
 Values marked I or O indicate increase or decrease from baseline of greater than ± 20 mmHg for blood pressure and greater than ± 15 bpm for pulse and heart rate
 Baseline is defined as predose

TABLE I2
Vital Signs
Individual Values: All Subjects

Subject	Dose of Maltathion	Sex	Study Day	Time Point	Supine Systolic BP (mmHg)	Supine Diastolic BP (mmHg)	Supine Pulse (b.p.m.)	Temperature (°C)	Respiration Rate (breaths per min)	Erect Heart Rate (b.p.m.)
043	15.0 MG/KG	FEMALE	SCREENING ADMISSION ON-STUDY		122	67	83	36.5	18	82
					110	70	68	36.2	12	84
				PREDOSE	118	68	72	36.7	19	87
				+2 H	106	66	64	36.3	18	86
				+4 H	102	64	61	36.5	17	90
044	15.0 MG/KG	FEMALE	SCREENING ADMISSION ON-STUDY	+8 H	120	66	72	36.6	18	98
				+24 H	102	68	62	36.3	18	98
					110	60	65	36.2	16	74
					130	70	68	36.0	16	90
				PREDOSE	118	64	60	36.4	20	75
				+2 H	130	70	60	37.0	18	68
				+4 H	110	70	62	37.2	22	74
				+8 H	110	60	65	37.1	16	76
				+24 H	110	66	60	36.8	17	67

Note: Values marked # indicate a repeat value not included in the summary statistics
 Values marked ## indicate a repeat value replacing the original value at that time point in the summary statistics
 Values marked I or D indicate increase or decrease from baseline of greater than ±20 mmHg for blood pressure and greater than ±15 bpm for pulse and heart rate
 Baseline is defined as predose

TABLE I2
Vital Signs
Individual Values: All Subjects

Subject	Dose of Methathion	Sex	Study Day	Time Point	Supine Systolic BP (mmHg)	Supine Diastolic BP (mmHg)	Supine Pulse (b.p.m.)	Temperature (°C)	Respiration Rate (breaths per min)	Erect Heart Rate (b.p.m.)	
045	PLACEBO	FEMALE	SCREENING ADMISSION ON-STUDY		130	75	76	36.8	18	76	
					100	70	62	36.9	16	66	
				PREDOSE	118	60	64	36.9	16	78	
				+2 H	120	80	66	37.2	18	82	
				+4 H	105	65	64	38.4	18	84	#
046	15.0 MG/KG	FEMALE	SCREENING ADMISSION ON-STUDY		100	50	80 I	37.6	17	90	#
					104	56	78	38.1	18	89	#
				+24 H				38.1			#
					120	82	72	36.2	18	80	
					130	90	84	37.0	16	96	
				PREDOSE	124	70	70	36.9	18	80	
				+2 H	130	68	76	36.9	17	76	
				+4 H	130	100 I	68	36.8	19	92	
					128	90					#
				+8 H	108	62	64	37.1	18	78	
				+24 H	120	80	79	36.6	19	84	

Note: Values marked # indicate a repeat value not included in the summary statistics
 Values marked ## indicate a repeat value replacing the original value at that time point in the summary statistics
 Values marked I or D indicate increase or decrease from baseline of greater than ± 20 mmHg for blood pressure and greater than ± 15 bpm for pulse and heart rate
 Baseline is defined as predose

TABLE I2
Vital Signs
Individual Values: All Subjects

Subject	Dose of Mefenamic Acid	Sex	Study Day	Time Point	Supine Systolic BP (mmHg)	Supine Diastolic BP (mmHg)	Supine Pulse (b.p.m.)	Temperature (°C)	Respiration Rate (breaths per min)	Erect Heart Rate (b.p.m.)	#
047	PLACEBO	FEMALE	SCREENING ADMISSION		110	54	60	36.6	18	80	
					132	74	100	36.6	16	100	
				PREDOSE	120	75	84	36.8	16	98	
				+2 H	100	60	76	36.7	16	94	
				+4 H	112	58	80	37.0	15	98	
048	15.0 MG/KG	FEMALE	SCREENING ADMISSION	+8 H	102	60	70	36.8	18	90	
				+24 H	112	68	64 D	36.6	16	82 D	
					122	78	72	36.4	18	88	
					100	60	62	36.0	16	68	
					110	72	68	36.6	15	74	
948	15.0 MG/KG	FEMALE	SCREENING ADMISSION		110	70	60	36.7	16	72	
				PREDOSE	120	70	72	36.8	16	80	
				+2 H	112	70	78	36.6	16	93	
				+4 H	118	78	64	36.6	16	82	
				+8 H	130	78	78	36.4	14	88	
948	15.0 MG/KG	FEMALE	ON-STUDY	+24 H	134	76	60	36.8	16	78	

Note: Values marked # indicate a repeat value not included in the summary statistics
 Values marked ## indicate a repeat value replacing the original value at that time point in the summary statistics
 Values marked I or D indicate increase or decrease from baseline of greater than ±20 mmHg for blood pressure and greater than ±15 bpm for pulse and heart rate
 Baseline is defined as predose
 Subject 948 replaces subject 048 who withdrew from study and is not included in the summary statistics

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APPENDIX J

Electrocardiographs: Summary tables and individual data listings

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TABLE J1.1
ECG
Ventricular Rate (b.p.m.)
Summary Statistics and Change from Baseline: All Dosed Subjects

MALE

Dose of Malathion		Ventricular Rate (b.p.m)					Change From Baseline				
		Mean	SD	Min	Max	N	Mean	SD	Min	Max	
PLACEBO	PREDOSE	65.5	10.3	46	80	11					
	+2 H	64.9	7.8	51	78	11	-0.5	5.9	-13	10	
	+4 H	57.4	7.4	48	73	11	-8.1	7.6	-21	2	
	+8 H	57.4	6.1	47	64	11	-8.1	6.3	-17	3	
	+24 H	62.0	5.7	52	71	11	-3.5	9.0	-21	9	
0.5 MG/KG	PREDOSE	61.0	1.0	60	62	3					
	+2 H	57.3	4.0	53	61	3	-3.7	3.5	-7	0	
	+4 H	52.3	3.8	48	55	3	-8.7	3.1	-12	-6	
	+8 H	56.7	1.5	55	58	3	-4.3	2.3	-7	-3	
	+24 H	56.3	7.5	52	65	3	-4.7	7.6	-10	4	

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Note: Data summarised in this table are listed in table J2.1

Baseline is defined as predose

Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics

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TABLE J1.1
ECG
Ventricular Rate (b.p.m.)
Summary Statistics and Change from Baseline: All Dosed Subjects

MALE

Dose of Malathion		Ventricular Rate (b.p.m)						Change From Baseline			
		Mean	SD	Min	Max	N	Mean	SD	Min	Max	
1.5 MG/KG	PREDOSE	59.3	1.2	58	60	3					
	+2 H	65.0	3.0	62	68	3	5.7	4.0	2	10	
	+4 H	62.3	2.1	60	64	3	3.0	1.0	2	4	
	+8 H	59.3	3.5	56	63	3	0.0	2.6	-2	3	
	+24 H	64.0	3.6	60	67	3	4.7	2.5	2	7	
5.0 MG/KG	PREDOSE	61.4	11.5	43	78	7					
	+2 H	65.4	10.1	51	80	7	4.0	5.5	-3	10	
	+4 H	62.6	12.9	39	78	7	1.1	6.9	-5	12	
	+8 H	58.0	12.3	40	80	7	-3.4	4.2	-10	2	
	+24 H	62.0	13.2	41	84	7	0.6	4.7	-4	8	

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Note: Data summarised in this table are listed in table J2.1

Baseline is defined as predose

Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics

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TABLE J1.1
ECG
Ventricular Rate (b.p.m.)
Summary Statistics and Change from Baseline: All Dosed Subjects

MALE

Dose of Malathion		Ventricular Rate (b.p.m)						Change From Baseline			
		Mean	SD	Min	Max	N	Mean	SD	Min	Max	
10.0 MG/KG	PREDOSE	62.7	6.4	55	75	7					
	+2 H	66.1	7.1	56	76	7	3.4	7.4	-4	13	
	+4 H	61.9	7.9	48	71	7	-0.9	6.2	-7	11	
	+8 H	58.9	11.9	45	83	7	-3.9	12.4	-14	23	
	+24 H	62.6	7.6	51	76	7	-0.1	6.7	-9	12	
15.0 MG/KG	PREDOSE	60.6	6.2	50	69	7					
	+2 H	60.9	9.3	51	77	7	0.3	9.2	-12	14	
	+4 H	54.0	4.6	49	61	7	-6.6	5.0	-13	0	
	+8 H	58.3	3.5	54	63	7	-2.3	4.3	-7	5	
	+24 H	58.6	3.7	54	63	7	-2.0	5.3	-8	4	

Note: Data summarised in this table are listed in table J2.1

Baseline is defined as predose
Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics

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TABLE J1.1
ECG
Ventricular Rate (b.p.m.)
Summary Statistics and Change from Baseline: All Dosed Subjects

Dose of Malathion		Ventricular Rate (b.p.m)					Change From Baseline				
		Mean	SD	Min	Max	N	Mean	SD	Min	Max	
PLACEBO	PREDOSE	64.7	7.4	59	73	3					
	+2 H	69.3	6.1	64	76	3	4.7	3.8	2	9	
	+4 H	64.0	4.6	59	68	3	-0.7	8.7	-8	9	
	+8 H	74.3	11.6	61	82	3	9.7	12.2	-1	23	
	+24 H	72.7	6.7	65	77	3	8.0	7.8	3	17	
15.0 MG/KG	PREDOSE	64.1	9.6	51	77	7					
	+2 H	66.0	6.1	56	75	7	1.9	5.9	-8	11	
	+4 H	62.9	7.1	52	72	7	-1.3	5.6	-12	6	
	+8 H	68.0	7.3	57	77	7	3.9	4.1	-2	10	
	+24 H	65.9	7.4	56	76	7	1.7	4.4	-5	9	

Note: Data summarised in this table are listed in table J2.1

Baseline is defined as predose
Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics

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TABLE J1.2

ECG
PR Interval (s)
Summary Statistics and Change from Baseline: All Dosed Subjects

MALE

Dose of Malathion		PR Interval (s)						Change From Baseline			
		Mean	SD	Min	Max	N	Mean	SD	Min	Max	
PLACEBO	PREDOSE	0.1478	0.0173	0.125	0.172	11					
	+2 H	0.1465	0.0152	0.126	0.174	11	-0.0013	0.0075	-0.013	0.008	
	+4 H	0.1502	0.0165	0.124	0.175	11	0.0024	0.0101	-0.013	0.021	
	+8 H	0.1446	0.0159	0.122	0.170	11	-0.0032	0.0091	-0.019	0.015	
	+24 H	0.1502	0.0162	0.124	0.174	11	0.0024	0.0125	-0.015	0.033	
0.5 MG/KG	PREDOSE	0.1453	0.0225	0.120	0.163	3					
	+2 H	0.1487	0.0165	0.132	0.165	3	0.0033	0.0081	-0.004	0.012	
	+4 H	0.1473	0.0147	0.136	0.164	3	0.0020	0.0135	-0.011	0.016	
	+8 H	0.1443	0.0172	0.132	0.164	3	-0.0010	0.0141	-0.016	0.012	
	+24 H	0.1497	0.0083	0.143	0.159	3	0.0043	0.0162	-0.006	0.023	

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Note: Data summarised in this table are listed in table J2.1

Baseline is defined as predose

Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics

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TABLE J1.2
ECG
PR Interval (s)
Summary Statistics and Change from Baseline: All Dosed Subjects

MALE

Dose of Malathion		PR Interval (s)					Change From Baseline				
		Mean	SD	Min	Max	N	Mean	SD	Min	Max	
1.5 MG/KG	PREDOSE	0.1583	0.0081	0.149	0.163	3					
	+2 H	0.1483	0.0142	0.132	0.157	3	-0.0100	0.0197	-0.031	0.008	
	+4 H	0.1470	0.0123	0.133	0.156	3	-0.0113	0.0185	-0.030	0.007	
	+8 H	0.1457	0.0145	0.129	0.155	3	-0.0127	0.0194	-0.034	0.004	
	+24 H	0.1460	0.0164	0.128	0.160	3	-0.0123	0.0230	-0.035	0.011	
5.0 MG/KG	PREDOSE	0.1683	0.0154	0.147	0.189	7					
	+2 H	0.1626	0.0139	0.143	0.175	7	-0.0057	0.0084	-0.017	0.008	
	+4 H	0.1664	0.0133	0.146	0.181	7	-0.0019	0.0071	-0.011	0.010	
	+8 H	0.1623	0.0161	0.141	0.183	7	-0.0060	0.0084	-0.023	0.005	
	+24 H	0.1593	0.0152	0.129	0.172	7	-0.0090	0.0079	-0.018	0.001	

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Note: Data summarised in this table are listed in table J2.1

Baseline is defined as predose

Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics

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TABLE J1.2
ECG
PR Interval (s)
Summary Statistics and Change from Baseline: All Dosed Subjects

MALE

Dose of Malathion		PR Interval (s)					Change From Baseline				
		Mean	SD	Min	Max	N	Mean	SD	Min	Max	
10.0 MG/KG	PREDOSE	0.1687	0.0166	0.142	0.185	7					
	+2 H	0.1597	0.0235	0.118	0.187	7	-0.0090	0.0252	-0.066	0.002	
	+4 H	0.1637	0.0219	0.130	0.191	7	-0.0050	0.0240	-0.054	0.019	
	+8 H	0.1620	0.0168	0.135	0.186	7	-0.0067	0.0207	-0.049	0.011	
	+24 H	0.1623	0.0214	0.124	0.193	7	-0.0064	0.0265	-0.060	0.018	
15.0 MG/KG	PREDOSE	0.1634	0.0250	0.142	0.202	7					
	+2 H	0.1574	0.0159	0.138	0.178	7	-0.0060	0.0115	-0.025	0.003	
	+4 H	0.1620	0.0279	0.139	0.204	7	-0.0014	0.0055	-0.009	0.009	
	+8 H	0.1594	0.0280	0.137	0.207	7	-0.0040	0.0111	-0.019	0.015	
	+24 H	0.1590	0.0312	0.133	0.207	7	-0.0044	0.0076	-0.014	0.006	

Note: Data summarised in this table are listed in table J2.1

Baseline is defined as predose
Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics

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TABLE J1.2
ECG
PR Interval (s)
Summary Statistics and Change from Baseline: All Dosed Subjects

FEMALE

Dose of Malathion		PR Interval (s)					Change From Baseline			
		Mean	SD	Min	Max	N	Mean	SD	Min	Max
PLACEBO	PREDOSE	0.1463	0.0187	0.125	0.160	3				
	+2 H	0.1433	0.0158	0.126	0.157	3	-0.0030	0.0087	-0.013	0.003
	+4 H	0.1403	0.0130	0.127	0.153	3	-0.0060	0.0075	-0.013	0.002
	+8 H	0.1380	0.0161	0.121	0.153	3	-0.0083	0.0102	-0.020	-0.001
	+24 H	0.1377	0.0127	0.124	0.149	3	-0.0087	0.0100	-0.020	-0.001
15.0 MG/KG	PREDOSE	0.1661	0.0124	0.154	0.186	7				
	+2 H	0.1664	0.0155	0.146	0.192	7	0.0003	0.0070	-0.011	0.007
	+4 H	0.1593	0.0265	0.107	0.187	7	-0.0069	0.0187	-0.047	0.012
	+8 H	0.1594	0.0202	0.125	0.180	7	-0.0067	0.0131	-0.029	0.012
	+24 H	0.1634	0.0225	0.119	0.188	7	-0.0027	0.0147	-0.035	0.008

Note: Data summarised in this table are listed in table J2.1

Baseline is defined as predose

Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics

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TABLE J1.3
ECG
QRS Interval (s)
Summary Statistics and Change from Baseline: All Dosed Subjects

MALE

Dose of Malathion		QRS Interval (s)					Change From Baseline			
		Mean	SD	Min	Max	N	Mean	SD	Min	Max
PLACEBO	PREDOSE	0.0856	0.0119	0.069	0.105	11				
	+2 H	0.0853	0.0097	0.073	0.100	11	-0.0004	0.0050	-0.011	0.007
	+4 H	0.0854	0.0121	0.067	0.101	11	-0.0003	0.0073	-0.020	0.008
	+8 H	0.0849	0.0089	0.068	0.098	11	-0.0007	0.0072	-0.014	0.008
	+24 H	0.0865	0.0103	0.070	0.099	11	0.0008	0.0074	-0.010	0.015
0.5 MG/KG	PREDOSE	0.0887	0.0070	0.082	0.096	3				
	+2 H	0.0883	0.0095	0.079	0.098	3	-0.0003	0.0025	-0.003	0.002
	+4 H	0.0900	0.0105	0.079	0.100	3	0.0013	0.0038	-0.003	0.004
	+8 H	0.0897	0.0090	0.081	0.099	3	0.0010	0.0020	-0.001	0.003
	+24 H	0.0850	0.0096	0.078	0.096	3	-0.0037	0.0035	-0.007	0.000

(CONTINUED)

Note: Data summarised in this table are listed in table J2.1

Baseline is defined as predose

Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics

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TABLE J1.3
ECG
QRS Interval (s)
Summary Statistics and Change From Baseline: All Dosed Subjects

MALE

Dose of Malathion		QRS Interval (s)					Change From Baseline				
		Mean	SD	Min	Max	N	Mean	SD	Min	Max	
1.5 MG/KG	PREDOSE	0.0940	0.0066	0.088	0.101	3					
	+2 H	0.0967	0.0042	0.092	0.100	3	0.0027	0.0032	-0.001	0.005	
	+4 H	0.0923	0.0085	0.084	0.101	3	-0.0017	0.0021	-0.004	0.000	
	+8 H	0.0937	0.0071	0.086	0.100	3	-0.0003	0.0021	-0.002	0.002	
	+24 H	0.0913	0.0087	0.084	0.101	3	-0.0027	0.0023	-0.004	0.000	
5.0 MG/KG	PREDOSE	0.0883	0.0064	0.083	0.102	7					
	+2 H	0.0881	0.0060	0.082	0.099	7	-0.0001	0.0045	-0.005	0.008	
	+4 H	0.0867	0.0066	0.082	0.101	7	-0.0016	0.0032	-0.005	0.003	
	+8 H	0.0864	0.0062	0.078	0.098	7	-0.0019	0.0034	-0.007	0.004	
	+24 H	0.0894	0.0035	0.083	0.093	7	0.0011	0.0054	-0.010	0.007	

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Note: Data summarised in this table are listed in table J2.1
Baseline is defined as predose
Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics

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TABLE J1.3

ECG
QRS Interval (s)
Summary Statistics and Change from Baseline: All Dosed Subjects

MALE

Dose of Malathion		QRS Interval (s)					Change From Baseline			
		Mean	SD	Min	Max	N	Mean	SD	Min	Max
10.0 MG/KG	PREDOSE	0.0911	0.0125	0.075	0.107	7				
	+2 H	0.0881	0.0099	0.074	0.100	7	-0.0030	0.0028	-0.007	0.0000
	+4 H	0.0889	0.0095	0.077	0.099	7	-0.0023	0.0039	-0.009	0.0023
	+8 H	0.0906	0.0113	0.078	0.104	7	-0.0006	0.0029	-0.003	0.0040
	+24 H	0.0923	0.0124	0.077	0.114	7	0.0011	0.0040	-0.003	0.0077
15.0 MG/KG	PREDOSE	0.0923	0.0056	0.083	0.100	7				
	+2 H	0.0883	0.0037	0.083	0.092	7	-0.0040	0.0028	-0.008	0.0010
	+4 H	0.0893	0.0027	0.086	0.093	7	-0.0030	0.0038	-0.009	0.0040
	+8 H	0.0893	0.0049	0.081	0.095	7	-0.0030	0.0024	-0.007	0.0000
	+24 H	0.0889	0.0038	0.086	0.097	7	-0.0034	0.0034	-0.008	0.0030

Note: Data summarised in this table are listed in table J2.1

Baseline is defined as predose

Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics

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TABLE J1.3

ECG
QRS Interval (s)
Summary Statistics and Change from Baseline: All Dosed Subjects

FEMALE

Dose of Malathion		QRS Interval (s)					Change From Baseline			
		Mean	SD	Min	Max	N	Mean	SD	Min	Max
PLACEBO	PREDOSE	0.0830	0.0072	0.077	0.091	3				
	+2 H	0.0827	0.0057	0.078	0.089	3	-0.0003	0.0015	-0.002	0.001
	+4 H	0.0840	0.0056	0.079	0.090	3	0.0010	0.0017	-0.001	0.002
	+8 H	0.0877	0.0050	0.083	0.093	3	0.0047	0.0023	0.002	0.006
	+24 H	0.0870	0.0036	0.084	0.091	3	0.0040	0.0036	0.000	0.007
15.0 MG/KG	PREDOSE	0.0813	0.0058	0.074	0.090	7				
	+2 H	0.0833	0.0079	0.074	0.098	7	0.0020	0.0033	-0.001	0.008
	+4 H	0.0817	0.0073	0.077	0.096	7	0.0004	0.0044	-0.006	0.006
	+8 H	0.0869	0.0089	0.079	0.105	7	0.0056	0.0099	-0.001	0.027
	+24 H	0.0820	0.0057	0.077	0.093	7	0.0007	0.0036	-0.005	0.006

Note: Data summarised in this table are listed in table J2.1

Baseline is defined as predose
Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics

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TABLE J1.4

ECG
QT Interval (s)
Summary Statistics and Change from Baseline: All Dosed Subjects

MALE

Dose of Malathion		QT Interval (s)						Change From Baseline			
		Mean	SD	Min	Max	N	Mean	SD	Min	Max	
PLACEBO	PREDOSE	0.3700	0.0305	0.329	0.428	11					
	+2 H	0.3638	0.0261	0.322	0.397	11	-0.0062	0.0118	-0.034	0.006	
	+4 H	0.3713	0.0238	0.336	0.408	11	0.0013	0.0164	-0.020	0.025	
	+8 H	0.3763	0.0227	0.346	0.413	11	0.0063	0.0153	-0.015	0.033	
	+24 H	0.3685	0.0223	0.338	0.406	11	-0.0015	0.0188	-0.037	0.024	
0.5 MG/KG	PREDOSE	0.3810	0.0148	0.364	0.391	3					
	+2 H	0.3777	0.0187	0.364	0.399	3	-0.0033	0.0206	-0.027	0.011	
	+4 H	0.3890	0.0241	0.366	0.414	3	0.0080	0.0286	-0.025	0.026	
	+8 H	0.3883	0.0189	0.372	0.409	3	0.0073	0.0228	-0.019	0.021	
	+24 H	0.3793	0.0151	0.362	0.390	3	-0.0017	0.0257	-0.029	0.022	

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Note: Data summarised in this table are listed in table J2.1

Baseline is defined as predose

Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics

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TABLE J1.4
ECG
QT Interval (s)
Summary Statistics and Change from Baseline: All Dosed Subjects

MALE

Dose of Malathion		QT Interval (s)					Change From Baseline				
		Mean	SD	Min	Max	N	Mean	SD	Min	Max	
1.5 MG/KG	PREDOSE	0.3783	0.0169	0.359	0.390	3					
	+2 H	0.3580	0.0171	0.340	0.374	3	-0.0203	0.0265	-0.050	0.001	
	+4 H	0.3563	0.0061	0.351	0.363	3	-0.0220	0.0175	-0.039	-0.004	
	+8 H	0.3743	0.0159	0.356	0.384	3	-0.0040	0.0017	-0.006	-0.003	
	+24 H	0.3597	0.0140	0.346	0.374	3	-0.0187	0.0107	-0.031	-0.012	
5.0 MG/KG	PREDOSE	0.3660	0.0301	0.325	0.419	7					
	+2 H	0.3553	0.0283	0.326	0.415	7	-0.0107	0.0148	-0.030	0.011	
	+4 H	0.3664	0.0333	0.322	0.421	7	0.0004	0.0174	-0.024	0.024	
	+8 H	0.3730	0.0360	0.313	0.434	7	0.0070	0.0173	-0.012	0.041	
	+24 H	0.3701	0.0273	0.323	0.415	7	0.0041	0.0124	-0.011	0.026	

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Note: Data summarised in this table are listed in table J2.1
Baseline is defined as predose
Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics

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TABLE J1.4
ECG
QT Interval (s)
Summary Statistics and Change from Baseline: All Dosed Subjects

MALE

Dose of Malathion		QT Interval (s)					Change From Baseline				
		Mean	SD	Min	Max	N	Mean	SD	Min	Max	
10.0 MG/KG	PREDOSE	0.3659	0.0200	0.341	0.388	7					
	+2 H	0.3650	0.0239	0.337	0.408	7	-0.0009	0.0322	-0.029	0.067	
	+4 H	0.3623	0.0225	0.330	0.388	7	-0.0036	0.0079	-0.014	0.009	
	+8 H	0.3623	0.0404	0.286	0.410	7	-0.0036	0.0254	-0.055	0.024	
	+24 H	0.3670	0.0144	0.339	0.381	7	0.0011	0.0230	-0.026	0.040	
15.0 MG/KG	PREDOSE	0.3856	0.0259	0.360	0.433	7					
	+2 H	0.3620	0.0131	0.344	0.380	7	-0.0236	0.0217	-0.053	0.004	
	+4 H	0.3899	0.0293	0.357	0.428	7	0.0043	0.0183	-0.031	0.023	
	+8 H	0.3906	0.0455	0.359	0.490	7	0.0050	0.0466	-0.047	0.102	
	+24 H	0.3750	0.0071	0.364	0.383	7	-0.0106	0.0231	-0.051	0.019	

Note: Data summarised in this table are listed in table J2.1

Baseline is defined as predose

Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics

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TABLE J1.4
ECG
QT Interval (s)
Summary Statistics and Change From Baseline: All Dosed Subjects

FEMALE

Dose of Malathion		QT Interval (s)					Change From Baseline				
		Mean	SD	Min	Max	N	Mean	SD	Min	Max	
PLACEBO	PREDOSE	0.3780	0.0122	0.364	0.386	3					
	+2 H	0.3597	0.0102	0.348	0.367	3	-0.0183	0.0032	-0.022	-0.016	
	+4 H	0.3717	0.0214	0.356	0.396	3	-0.0063	0.0215	-0.030	0.012	
	+8 H	0.3577	0.0238	0.342	0.385	3	-0.0203	0.0226	-0.044	0.001	
	+24 H	0.3623	0.0134	0.347	0.372	3	-0.0157	0.0217	-0.039	0.004	
15.0 MG/KG	PREDOSE	0.3707	0.0208	0.341	0.396	7					
	+2 H	0.3651	0.0161	0.345	0.389	7	-0.0056	0.0135	-0.035	0.004	
	+4 H	0.3740	0.0131	0.356	0.392	7	0.0033	0.0126	-0.021	0.021	
	+8 H	0.3767	0.0274	0.344	0.421	7	0.0060	0.0228	-0.027	0.047	
	+24 H	0.3747	0.0127	0.351	0.388	7	0.0040	0.0112	-0.011	0.019	

Note: Data summarised in this table are listed in table J2.1

Baseline is defined as predose

Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics

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TABLE J1.5
ECG
QTc Interval (s)
Summary Statistics and Change from Baseline: All Dosed Subjects

MALE

Dose of Malathion		QTc Interval (s)					Change From Baseline			
		Mean	SD	Min	Max	N	Mean	SD	Min	Max
PLACEBO	PREDOSE	0.3828	0.0228	0.361	0.429	11				
	+2 H	0.3763	0.0154	0.357	0.405	11	-0.0065	0.0115	-0.032	0.006
	+4 H	0.3607	0.0156	0.338	0.385	11	-0.0221	0.0114	-0.044	-0.008
	+8 H	0.3662	0.0155	0.350	0.395	11	-0.0166	0.0115	-0.034	-0.001
	+24 H	0.3730	0.0167	0.351	0.398	11	-0.0098	0.0117	-0.037	0.004
0.5 MG/KG	PREDOSE	0.3840	0.0125	0.370	0.394	3				
	+2 H	0.3683	0.0061	0.363	0.375	3	-0.0157	0.0103	-0.027	-0.007
	+4 H	0.3623	0.0108	0.350	0.370	3	-0.0217	0.0207	-0.044	-0.003
	+8 H	0.3767	0.0185	0.365	0.398	3	-0.0073	0.0199	-0.029	0.010
	+24 H	0.3660	0.0089	0.359	0.376	3	-0.0180	0.0070	-0.025	-0.011

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Note: Data summarised in this table are listed in table J2.1

Baseline is defined as predose

Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics

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TABLE J1.5
ECG
QTc Interval (s)
Summary Statistics and Change from Baseline: All Dosed Subjects

Dose of Malathion		QTc Interval (s)					Change From Baseline			
		Mean	SD	Min	Max	N	Mean	SD	Min	Max
1.5 MG/KG	PREDOSE	0.3760	0.0148	0.359	0.386	3				
	+2 H	0.3717	0.0097	0.361	0.380	3	-0.0043	0.0186	-0.022	0.015
	+4 H	0.3627	0.0104	0.351	0.371	3	-0.0133	0.0196	-0.032	0.007
	+8 H	0.3710	0.0075	0.364	0.379	3	-0.0050	0.0092	-0.013	0.005
	+24 H	0.3710	0.0159	0.359	0.389	3	-0.0050	0.0165	-0.024	0.006
5.0 MG/KG	PREDOSE	0.3661	0.0169	0.343	0.391	7				
	+2 H	0.3680	0.0159	0.346	0.393	7	0.0019	0.0190	-0.034	0.028
	+4 H	0.3690	0.0198	0.339	0.400	7	0.0029	0.0254	-0.015	0.057
	+8 H	0.3616	0.0156	0.343	0.393	7	-0.0046	0.0234	-0.035	0.040
	+24 H	0.3716	0.0168	0.343	0.386	7	0.0054	0.0143	-0.013	0.027

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Note: Data summarised in this table are listed in table J2.1

Baseline is defined as predose

Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics

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TABLE J1.5
ECG
QTc Interval (s)
Summary Statistics and Change from Baseline: All Dosed Subjects

MALE

Dose of Malathion		QTc Interval (s)					Change From Baseline				
		Mean	SD	Min	Max	N	Mean	SD	Min	Max	
10.0 MG/KG	PREDOSE	0.3734	0.0303	0.341	0.431	7					
	+2 H	0.3817	0.0275	0.356	0.437	7	0.0083	0.0437	-0.038	0.0966	
	+4 H	0.3661	0.0249	0.338	0.416	7	-0.0073	0.0151	-0.029	0.017	
	+8 H	0.3546	0.0288	0.328	0.413	7	-0.0189	0.0115	-0.039	-0.005	
	+24 H	0.3737	0.0245	0.344	0.420	7	0.0003	0.0162	-0.015	0.028	
15.0 MG/KG	PREDOSE	0.3854	0.0148	0.371	0.413	7					
	+2 H	0.3626	0.0202	0.344	0.403	7	-0.0229	0.0119	-0.035	-0.006	
	+4 H	0.3690	0.0293	0.340	0.423	7	-0.0164	0.0151	-0.033	0.010	
	+8 H	0.3841	0.0429	0.344	0.477	7	-0.0013	0.0484	-0.033	0.103	
	+24 H	0.3700	0.0147	0.348	0.389	7	-0.0154	0.0142	-0.033	0.004	

Note: Data summarised in this table are listed in table J2.1

Baseline is defined as predose
Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics

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TABLE J1.5

ECG
QTc Interval (s)
Summary Statistics and Change from Baseline: All Dosed Subjects

FEMALE

Dose of Malathion		QTc Interval (s)						Change From Baseline			
		Mean	SD	Min	Max	N	Mean	SD	Min	Max	
PLACEBO	PREDOSE	0.3910	0.0095	0.382	0.401	3					
	+2 H	0.3857	0.0061	0.379	0.391	3	-0.0053	0.0090	-0.011	0.005	
	+4 H	0.3823	0.0084	0.377	0.392	3	-0.0087	0.0136	-0.024	0.002	
	+8 H	0.3953	0.0064	0.388	0.399	3	0.0043	0.0110	-0.002	0.017	
	+24 H	0.3977	0.0159	0.387	0.416	3	0.0067	0.0091	-0.003	0.015	
15.0 MG/KG	PREDOSE	0.3807	0.0164	0.355	0.400	7					
	+2 H	0.3816	0.0140	0.361	0.401	7	0.0009	0.0108	-0.017	0.014	
	+4 H	0.3813	0.0192	0.351	0.404	7	0.0006	0.0068	-0.010	0.012	
	+8 H	0.3990	0.0222	0.376	0.434	7	0.0183	0.0156	0.003	0.042	
	+24 H	0.3914	0.0192	0.372	0.422	7	0.0107	0.0152	-0.013	0.027	

Note: Data summarised in this table are listed in table J2.1

Baseline is defined as predose

Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics

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TABLE J2.1

ECG Individual Values: All Subjects												
Subject	Dose of Malathion	Sex	Study Day	Time Point	Ventricular Rate (b.p.m)	Rhythm	PR Interval (s)	QRS Interval (s)	QT Interval (s)	QTc Interval (s)	QRS Axis (°)	ECG Normal/ Abnormal
001	0.5 MG/KG	MALE	SCREENING ON-STUDY	PREDOSE	52	SR	0.168	0.101	0.409	0.380	27	NORMAL
				+2 H	60	SR	0.163	0.096	0.388	0.388	39	NORMAL
				+4 H	53	SR	0.165	0.098	0.399	0.375	36	NORMAL
				+8 H	48	SB	0.164	0.100	0.414	0.370	35	NORMAL
				+24 H	57	SR	0.164	0.099	0.409	0.398	29	NORMAL
002	0.5 MG/KG	MALE	SCREENING ON-STUDY	PREDOSE	52	SR	0.159	0.096	0.390	0.363	32	NORMAL
				+2 H	53	SR	0.143	0.089	0.374	0.351	90	NORMAL
				+4 H	62	SR	0.120	0.088	0.364	0.370	92	NORMAL
				+8 H	58	SR	0.132	0.088	0.370	0.363	90	NORMAL
				+24 H	54	SR	0.136	0.091	0.387	0.367	94	NORMAL
003	PLACEBO	MALE	SCREENING ON-STUDY	PREDOSE	55	SR	0.132	0.089	0.384	0.367	92	NORMAL
				+2 H	52	SR	0.143	0.081	0.386	0.359	96	NORMAL
				+4 H	54	SR	0.146	0.104	0.396	0.375	74	NORMAL
				+8 H	68	SR	0.148	0.092	0.350	0.372	78	NORMAL
				+24 H	67	SR	0.151	0.091	0.356	0.376	78	NORMAL
004	0.5 MG/KG	MALE	SCREENING ON-STUDY	PREDOSE	49	SB	0.156	0.091	0.375	0.338	72	NORMAL
				+2 H	54	SR	0.142	0.093	0.383	0.363	81	NORMAL
				+4 H	54	SR	0.155	0.099	0.372	0.352	74	NORMAL
				+8 H	70	SR	0.142	0.080	0.361	0.389	1	NORMAL
				+24 H	61	SR	0.153	0.082	0.391	0.394	2	NORMAL
Key for rhythm: SR=sinus rhythm SA=sinus arrhythmia SB=sinus bradycardia ST=sinus tachycardia												
Note: # indicates a repeat value not included in the summary statistics												

Key for rhythm: SR=sinus rhythm SA=sinus arrhythmia SB=sinus bradycardia ST=sinus tachycardia
Note: # indicates a repeat value not included in the summary statistics

TABLE J2.1

ECG Individual Values: All Subjects												
Subject	Dose of Malathion	Sex	Study Day	Time Point	Ventricular Rate (b.p.m)	Rhythm	PR Interval (s)	QRS Interval (s)	QT Interval (s)	QTc Interval (s)	QRS Axis (°)	ECG Normal/ Abnormal
005	1.5 MG/KG	MALE	SCREENING ON-STUDY	PREDOSE	70	SR	0.146	0.090	0.360	0.388	51	NORMAL
				+2 H	60	SR	0.163	0.088	0.386	0.386	50	NORMAL
				+4 H	62	SR	0.156	0.092	0.374	0.380	56	NORMAL
				+8 H	63	SR	0.152	0.084	0.363	0.371	42	NORMAL
				+24 H	59	SR	0.155	0.086	0.383	0.379	52	NORMAL
006	1.5 MG/KG	MALE	SCREENING ON-STUDY	PREDOSE	61	SR	0.159	0.094	0.369	0.372	15	NORMAL
				+2 H	60	SR	0.149	0.093	0.359	0.359	17	NORMAL
				+4 H	65	SR	0.157	0.098	0.360	0.374	16	NORMAL
				+8 H	64	SR	0.156	0.092	0.355	0.366	6	NORMAL
				+24 H	63	SR	0.153	0.095	0.356	0.364	14	NORMAL
007	PLACEBO	MALE	SCREENING ON-STUDY	PREDOSE	70	SR	0.143	0.089	0.343	0.370	43	NORMAL
				+2 H	59	SA	0.125	0.081	0.367	0.363	51	NORMAL
				+4 H	61	SA	0.131	0.088	0.362	0.365	48	NORMAL
				+8 H	58	SR	0.146	0.089	0.355	0.349	51	NORMAL
				+24 H	58	SR	0.122	0.089	0.357	0.350	61	NORMAL
008	1.5 MG/KG	MALE	SCREENING ON-STUDY	PREDOSE	80	SR	0.126	0.100	0.316	0.364	75	NORMAL
				+2 H	58	SR	0.163	0.101	0.390	0.383	72	NORMAL
				+4 H	68	SA	0.132	0.100	0.340	0.361	77	NORMAL
				+8 H	60	SR	0.133	0.101	0.351	0.351	74	NORMAL
				+24 H	56	SR	0.129	0.100	0.384	0.370	68	NORMAL
				PREDOSE	60	SR	0.128	0.101	0.359	0.359	69	NORMAL
				+2 H	60	SR	0.128	0.101	0.359	0.359	69	NORMAL
				+4 H	60	SR	0.128	0.101	0.359	0.359	69	NORMAL
				+8 H	60	SR	0.128	0.101	0.359	0.359	69	NORMAL
				+24 H	60	SR	0.128	0.101	0.359	0.359	69	NORMAL

Key for rhythm: SR=sinus rhythm SA=sinus arrhythmia SR=sinus bradycardia ST=sinus tachycardia
 Note: # indicates a repeat value not included in the summary statistics

TABLE J2.1

ECG
Individual Values: All Subjects

Subject	Dose of Malathion	Sex	Study Day	Time Point	Ventricular Rate (b.p.m)	Rhythm	PR Interval (s)	QRS Interval (s)	QT Interval (s)	QTc Interval (s)	QRS Axis (°)	ECG Normal/ Abnormal
009	5.0 MG/KG	MALE	SCREENING ON-STUDY	PREDOSE	71	SR	0.166	0.093	0.334	0.363	68	NORMAL
				+2 H	53	SR	0.179	0.086	0.366	0.343	73	NORMAL
				+4 H	59	SR	0.172	0.084	0.358	0.355	46	NORMAL
				+8 H	65	SR	0.181	0.088	0.385	0.400	70	NORMAL
				+24 H	51	SR	0.156	0.086	0.373	0.343	66	NORMAL
010	5.0 MG/KG	MALE	SCREENING ON-STUDY	PREDOSE	50	SR	0.174	0.089	0.381	0.347	35	NORMAL
				+2 H	57	SR	0.189	0.088	0.382	0.372	28	NORMAL
				+4 H	66	SR	0.175	0.089	0.352	0.369	15	NORMAL
				+8 H	55	SR	0.178	0.083	0.384	0.367	26	NORMAL
				+24 H	55	SR	0.183	0.086	0.383	0.366	33	NORMAL
011	5.0 MG/KG	MALE	SCREENING ON-STUDY	PREDOSE	67	SR	0.161	0.098	0.365	0.385	86	NORMAL
				+2 H	64	SR	0.164	0.102	0.368	0.380	86	NORMAL
				+4 H	61	SR	0.147	0.099	0.344	0.346	86	NORMAL
				+8 H	68	SR	0.156	0.101	0.351	0.373	87	NORMAL
				+24 H	56	SR	0.161	0.098	0.371	0.358	84	NORMAL
012	5.0 MG/KG	MALE	SCREENING ON-STUDY	PREDOSE	60	SR	0.161	0.092	0.380	0.380	84	NORMAL
				+2 H	65	SR	0.179	0.080	0.361	0.375	58	NORMAL
				+4 H	65	SR	0.176	0.085	0.340	0.353	55	NORMAL
				+8 H	64	SR	0.175	0.082	0.351	0.362	61	NORMAL
				+24 H	60	SR	0.172	0.083	0.364	0.364	52	NORMAL
				+8 H	64	SR	0.172	0.082	0.381	0.393	47	NORMAL
				+24 H	65	SR	0.163	0.087	0.366	0.380	49	NORMAL

Key for rhythm: SR=sinus rhythm SA=sinus arrhythmia SB=sinus bradycardia ST=sinus tachycardia
Note: # indicates a repeat value not included in the summary statistics

TABLE J2.1

ECG
Individual Values: All Subjects

Subject	Dose of Mefenamic Acid	Sex	Study Day	Time Point	Ventricular Rate (b.p.m.)	Rhythm	PR Interval (s)	QRS Interval (s)	QT Interval (s)	QTc Interval (s)	QRS Axis (°)	ECG Normal/ Abnormal
013	PLACEBO	MALE	SCREENING ON-STUDY	PREDOSE	76	SR	0.150	0.086	0.384	0.432	21	NORMAL
				+2 H	63	SR	0.145	0.103	0.394	0.403	24	NORMAL
				+4 H	58	SR	0.148	0.098	0.397	0.390	21	NORMAL
				+8 H	53	SR	0.150	0.101	0.397	0.373	22	NORMAL
				+24 H	51	SR	0.149	0.098	0.404	0.372	25	NORMAL
014	5.0 MG/KG	MALE	SCREENING ON-STUDY	PREDOSE	72	SR	0.147	0.086	0.347	0.380	89	NORMAL
				+2 H	78	SR	0.150	0.085	0.325	0.370	88	NORMAL
				+4 H	77	SR	0.143	0.093	0.326	0.369	88	NORMAL
				+8 H	73	SR	0.146	0.082	0.322	0.355	84	NORMAL
				+24 H	80	SR	0.145	0.078	0.313	0.361	85	NORMAL
015	PLACEBO	MALE	SCREENING ON-STUDY	PREDOSE	84	SR	0.151	0.092	0.323	0.382	88	NORMAL
				+2 H	67	SR	0.162	0.082	0.372	0.393	63	NORMAL
				+4 H	80	SR	0.172	0.078	0.372	0.429	67	NORMAL
				+8 H	67	SR	0.161	0.080	0.376	0.397	72	NORMAL
				+24 H	59	SR	0.171	0.082	0.389	0.385	74	NORMAL
016	PLACEBO	MALE	SCREENING ON-STUDY	PREDOSE	63	SR	0.166	0.083	0.366	0.385	76	NORMAL
				+2 H	59	SR	0.171	0.083	0.396	0.392	76	NORMAL
				+4 H	68	SR	0.154	0.076	0.352	0.374	6	NORMAL
				+8 H	72	SR	0.163	0.071	0.332	0.363	7	NORMAL
				+24 H	71	SR	0.157	0.073	0.334	0.363	9	NORMAL
				+4 H	61	SR	0.150	0.072	0.353	0.355	7	NORMAL
				+8 H	62	SR	0.144	0.077	0.346	0.351	11	NORMAL
				+24 H	71	SR	0.156	0.075	0.338	0.367	4	NORMAL

Key for rhythm: SR=sinus rhythm SA=sinus arrhythmia SB=sinus bradycardia ST=sinus tachycardia
Note: # indicates a repeat value not included in the summary statistics

TABLE J2.1

ECG Individual Values: All Subjects													
Subject	Dose of Malathion	Sex	Study Day	Time Point	Ventricular Rate (b.p.m)	Rhythm	PR Interval (s)	QRS Interval (s)	QT Interval (s)	QTc Interval (s)	QRS Axis (°)	ECG Normal/Abnormal	
017	5.0 MG/KG	MALE	SCREENING ON-STUDY	PREDOSE	61	SR	0.137	0.115	0.387	0.390	6	NORMAL	
					71	SR	0.143	0.111	0.358	0.389	-1	NORMAL	
917	5.0 MG/KG	MALE	SCREENING ON-STUDY	PREDOSE	57	SR	0.131	0.091	0.406	0.395	78	NORMAL	
					70	SR	0.147	0.089	0.362	0.391	81	NORMAL	
					80	SR	0.155	0.084	0.341	0.393	79	NORMAL	
					+4 H	78	SA	0.157	0.084	0.338	0.385	86	NORMAL
					+8 H	60	SR	0.141	0.088	0.356	0.356	75	NORMAL
018	5.0 MG/KG	MALE	SCREENING ON-STUDY	PREDOSE	66	SR	0.129	0.093	0.361	0.378	83	NORMAL	
					40	SB	0.174	0.089	0.411	0.335	7	NORMAL	
					43	SB	0.173	0.083	0.419	0.354	2	NORMAL	
					51	SR	0.171	0.086	0.415	0.382	18	NORMAL	
					+4 H	39	SB	0.175	0.086	0.421	0.339	16	NORMAL
019	10.0 MG/KG	MALE	SCREENING ON-STUDY	PREDOSE	40	SB	0.178	0.087	0.434	0.354	4	NORMAL	
					41	SB	0.172	0.083	0.415	0.343	6	NORMAL	
					52	SR	0.158	0.091	0.388	0.361	31	NORMAL	
					55	SA	0.169	0.091	0.384	0.367	24	NORMAL	
					+2 H	66	SR	0.168	0.088	0.377	0.377	23	NORMAL
					48	SB	0.166	0.090	0.378	0.338	21	NORMAL	
					+4 H	45	SB	0.164	0.088	0.379	0.328	31	NORMAL
					+8 H	67	SR	0.163	0.090	0.358	0.378	24	NORMAL

Key for rhythm: SR=sinus rhythm SA=sinus arrhythmia SB=sinus bradycardia ST=sinus tachycardia
 Note: # indicates a repeat value not included in the summary statistics
 Subject 917 replaces subject 017 who withdrew from study and is not included in the summary statistics

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TABLE J2.1

ECG
Individual Values: All Subjects

Subject	Dose of Methathion	Sex	Study Day	Time Point	Ventricular Rate (b.p.m)	Rhythm	PR Interval (s)	QRS Interval (s)	QT Interval (s)	QTc Interval (s)	QRS Axis (°)	ECG Normal/ Abnormal
020	10.0 MG/KG	MALE	SCREENING ON-STUDY	PREDOSE	83	SR	0.150	0.097	0.347	0.408	76	NORMAL
				+2 H	75	SR	0.142	0.101	0.386	0.431	80	NORMAL
				+4 H	73	SR	0.144	0.096	0.357	0.393	83	NORMAL
				+8 H	69	SR	0.142	0.099	0.388	0.416	70	NORMAL
				+24 H	61	SR	0.149	0.103	0.410	0.413	85	NORMAL
021	PLACEBO	MALE	SCREENING ON-STUDY	PREDOSE	72	SR	0.137	0.092	0.342	0.374	77	NORMAL
				+2 H	73	SR	0.125	0.078	0.355	0.391	71	NORMAL
				+4 H	71	SR	0.126	0.079	0.345	0.375	76	NORMAL
				+8 H	73	SR	0.125	0.080	0.336	0.370	78	NORMAL
				+24 H	60	SR	0.140	0.083	0.365	0.365	77	NORMAL
022	10.0 MG/KG	MALE	SCREENING ON-STUDY	PREDOSE	45	SB	0.190	0.084	0.368	0.318	66	NORMAL
				+2 H	60	SR	0.185	0.077	0.341	0.341	68	NORMAL
				+4 H	69	SR	0.187	0.077	0.408	0.437	58	NORMAL
				+8 H	71	SR	0.191	0.079	0.330	0.358	59	NORMAL
				+24 H	83	SR	0.176	0.078	0.286	0.336	69	NORMAL
023	10.0 MG/KG	MALE	SCREENING ON-STUDY	PREDOSE	51	SR	0.169	0.083	0.381	0.351	39	NORMAL
				+2 H	64	SR	0.195	0.081	0.362	0.373	1	NORMAL
				+4 H	60	SR	0.175	0.086	0.388	0.388	-12	NORMAL
				+8 H	56	SR	0.177	0.086	0.386	0.372	1	NORMAL
				+24 H	57	SR	0.186	0.082	0.383	0.373	2	NORMAL
				+8 H	52	SR	0.186	0.083	0.389	0.362	-2	NORMAL
				+24 H	60	SR	0.193	0.085	0.378	0.378	-22	NORMAL

Key for rhythm: SR=sinus rhythm SA=sinus arrhythmia SB=sinus bradycardia ST=sinus tachycardia
Note: # indicates a repeat value not included in the summary statistics

TABLE J2.1

ECG

Individual Values: All Subjects

Subject	Dose of Malathion	Sex	Study Day	Time Point	Ventricular Rate (b.p.m)	Rhythm	PR Interval (s)	QRS Interval (s)	QT Interval (s)	QTc Interval (s)	QRS Axis (°)	ECG Normal/ Abnormal
024	PLACEBO	MALE	SCREENING ON-STUDY	PREDOSE	74	SR	0.162	0.066	0.364	0.404	55	NORMAL
				+2 H	72	SR	0.166	0.069	0.376	0.411	65	NORMAL
				+4 H	69	SR	0.155	0.073	0.378	0.405	81	NORMAL
				+8 H	62	SR	0.158	0.070	0.378	0.384	56	NORMAL
				+24 H	64	SR	0.163	0.068	0.379	0.391	53	NORMAL
025	PLACEBO	MALE	SCREENING ON-STUDY	PREDOSE	54	SR	0.140	0.096	0.394	0.364	12	NORMAL
				+2 H	52	SR	0.144	0.094	0.408	0.379	14	NORMAL
				+4 H	51	SR	0.131	0.093	0.395	0.364	12	NORMAL
				+8 H	49	SB	0.138	0.097	0.391	0.353	23	NORMAL
				+24 H	47	SB	0.132	0.092	0.398	0.352	11	NORMAL
026	15.0 MG/KG	MALE	SCREENING ON-STUDY	PREDOSE	61	SR	0.145	0.095	0.371	0.374	8	NORMAL
				+2 H	76	SR	0.135	0.092	0.347	0.390	-60	NORMAL
				+4 H	59	SR	0.148	0.096	0.381	0.377	-48	NORMAL
				+8 H	52	SR	0.138	0.091	0.371	0.345	-78	NORMAL
				+24 H	49	SB	0.139	0.093	0.402	0.363	-56	NORMAL
027	10.0 MG/KG	MALE	SCREENING	+4 H	54	SR	0.137	0.089	0.363	0.344	-58	NORMAL
				+8 H	62	SR	0.140	0.088	0.375	0.381	-66	NORMAL
				+24 H	62	SR	0.153	0.078	0.340	0.345	55	NORMAL

Key for rhythm: SR=sinus rhythm SA=sinus arrhythmia SB=sinus bradycardia ST=sinus tachycardia
 Note: # indicates a repeat value not included in the summary statistics
 Subject 927 replaces subject 027 who withdrew from study and is not included in the summary statistics

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TABLE J2.1

ECG
Individual Values: All Subjects

Subject	Dose of Malathion	Sex	Study Day	Time Point	Ventricular Rate (b.p.m.)	Rhythm	PR Interval (s)	QRS Interval (s)	QT Interval (s)	QTc Interval (s)	QRS Axis (°)	ECG Normal/ Abnormal
927	10.0 MG/KG	MALE	SCREENING ON-STUDY	PREDOSE	69	SR	0.155	0.100	0.374	0.401	81	NORMAL
				+2 H	66	SR	0.150	0.101	0.363	0.380	86	NORMAL
				+4 H	62	SR	0.152	0.096	0.353	0.358	79	NORMAL
				+8 H	63	SR	0.169	0.097	0.363	0.371	83	NORMAL
				+24 H	56	SR	0.159	0.099	0.375	0.362	84	NORMAL
028	10.0 MG/KG	MALE	SCREENING ON-STUDY	PREDOSE	60	SR	0.120	0.104	0.349	0.349	17	NORMAL
				+2 H	60	SR	0.184	0.107	0.348	0.348	37	NORMAL
				+4 H	61	SR	0.118	0.100	0.354	0.356	31	NORMAL
				+8 H	59	SR	0.130	0.098	0.357	0.354	11	NORMAL
				+24 H	55	SR	0.135	0.104	0.357	0.341	30	NORMAL
029	15.0 MG/KG	MALE	SCREENING ON-STUDY	PREDOSE	61	SR	0.138	0.096	0.365	0.368	66	NORMAL
				+2 H	50	SR	0.145	0.100	0.433	0.395	56	NORMAL
				+4 H	54	SR	0.148	0.092	0.380	0.360	60	NORMAL
				+8 H	50	SR	0.143	0.091	0.428	0.390	61	NORMAL
				+24 H	55	SR	0.137	0.095	0.386	0.369	68	NORMAL
030	10.0 MG/KG	MALE	SCREENING ON-STUDY	PREDOSE	54	SR	0.143	0.097	0.382	0.362	59	NORMAL
				+2 H	69	SR	0.162	0.084	0.346	0.371	97	NORMAL
				+4 H	63	SR	0.176	0.075	0.351	0.359	98	NORMAL
				+8 H	76	SR	0.172	0.074	0.337	0.379	97	NORMAL
				+24 H	66	SR	0.162	0.077	0.337	0.363	100	NORMAL
				+8 H	60	SR	0.165	0.079	0.340	0.340	97	NORMAL
				+24 H	62	SR	0.173	0.077	0.339	0.344	101	NORMAL

Key for rhythm: SR=sinus rhythm SA=sinus arrhythmia SB=sinus bradycardia ST=sinus tachycardia
Note: # indicates a repeat value not included in the summary statistics

TABLE J2.1

ECG
Individual Values: All Subjects

Subject	Dose of Malathion	Sex	Study Day	Time Point	Ventricular Rate (b.p.m)	Rhythm	PR Interval (s)	QRS Interval (s)	QT Interval (s)	QTc Interval (s)	QRS Axis (°)	ECG Normal/ Abnormal
031	15.0 MG/KG	MALE	SCREENING ON-STUDY	PREDOSE	93	ST	0.172	0.079	0.328	0.408	94	NORMAL
				+2 H	63	SR	0.202	0.088	0.404	0.413	91	NORMAL
				+4 H	77	SR	0.177	0.083	0.356	0.403	90	NORMAL
				+8 H	59	SR	0.199	0.086	0.427	0.423	96	NORMAL
				+24 H	57	SR	0.207	0.087	0.393	0.383	88	NORMAL
032	PLACEBO	MALE	SCREENING ON-STUDY	PREDOSE	62	SR	0.207	0.086	0.383	0.389	88	NORMAL
				+2 H	57	SR	0.172	0.074	0.372	0.362	70	NORMAL
				+4 H	61	SR	0.166	0.067	0.359	0.361	78	NORMAL
				+8 H	65	SR	0.174	0.076	0.343	0.357	78	NORMAL
				+24 H	57	SR	0.175	0.067	0.362	0.352	77	NORMAL
033	15.0 MG/KG	MALE	SCREENING ON-STUDY	PREDOSE	60	SR	0.170	0.075	0.354	0.354	80	NORMAL
				+2 H	63	SR	0.174	0.077	0.348	0.356	76	NORMAL
				+4 H	52	SR	0.187	0.092	0.374	0.348	75	NORMAL
				+8 H	56	SR	0.195	0.095	0.388	0.374	75	NORMAL
				+24 H	65	SR	0.178	0.092	0.354	0.368	76	NORMAL
034	15.0 MG/KG	MALE	SCREENING ON-STUDY	PREDOSE	55	SR	0.204	0.092	0.357	0.341	76	NORMAL
				+2 H	57	SR	0.190	0.095	0.490	0.477	84	NORMAL
				+4 H	58	SR	0.201	0.090	0.368	0.361	74	NORMAL
				+8 H	84	SR	0.156	0.082	0.328	0.388	47	NORMAL
				+24 H	69	SR	0.164	0.083	0.363	0.389	61	NORMAL
				PREDOSE	64	SR	0.165	0.084	0.355	0.366	52	NORMAL
				+2 H	61	SR	0.160	0.087	0.386	0.389	56	NORMAL
				+4 H	62	SR	0.145	0.081	0.359	0.364	59	NORMAL
				+8 H	63	SR	0.150	0.086	0.374	0.383	54	NORMAL
				+24 H								

Key for rhythm: SR=sinus rhythm SA=sinus arrhythmia SB=sinus bradycardia ST=sinus tachycardia
Note: # indicates a repeat value not included in the summary statistics

TABLE J2.1

ECG
Individual Values: All Subjects

Subject	Dose of Mefenamic Acid	Sex	Study Day	Time Point	Ventricular Rate (b.p.m.)	Rhythm	PR Interval (s)	QRS Interval (s)	QT Interval (s)	QTc Interval (s)	QRS Axis (°)	ECG Normal/ Abnormal
035	PLACEBO	MALE	SCREENING ON-STUDY	PREDOSE	67	SR	0.147	0.083	0.376	0.397	63	NORMAL
				+2 H	46	SB	0.145	0.105	0.428	0.374	56	NORMAL
				+4 H	56	SA	0.147	0.100	0.394	0.380	55	NORMAL
				+8 H	48	SB	0.159	0.101	0.408	0.364	62	NORMAL
				+24 H	49	SB	0.136	0.091	0.413	0.373	49	NORMAL
036	PLACEBO	MALE	SCREENING ON-STUDY	PREDOSE	73	SR	0.128	0.082	0.328	0.361	6	NORMAL
				+2 H	74	SR	0.127	0.084	0.329	0.365	4	NORMAL
				+4 H	78	SR	0.131	0.087	0.322	0.367	7	NORMAL
				+8 H	62	SR	0.124	0.089	0.340	0.345	4	NORMAL
				+24 H	63	SR	0.127	0.085	0.354	0.362	2	NORMAL
037	15.0 MG/KG	MALE	SCREENING ON-STUDY	PREDOSE	64	SR	0.124	0.080	0.340	0.351	5	NORMAL
				+2 H	58	SR	0.144	0.088	0.379	0.372	91	NORMAL
				+4 H	63	SR	0.142	0.092	0.370	0.379	90	NORMAL
				+8 H	51	SA	0.145	0.087	0.374	0.344	89	NORMAL
				+24 H	53	SR	0.140	0.088	0.380	0.357	95	NORMAL
038	15.0 MG/KG	MALE	SCREENING ON-STUDY	PREDOSE	60	SR	0.157	0.088	0.371	0.371	95	NORMAL
				+2 H	55	SR	0.133	0.087	0.364	0.348	96	NORMAL
				+4 H	73	SR	0.145	0.089	0.325	0.358	84	NORMAL
				+8 H	64	SR	0.148	0.092	0.360	0.371	85	NORMAL
				+24 H	63	SR	0.151	0.089	0.344	0.352	89	NORMAL
				PREDOSE	51	SR	0.149	0.088	0.369	0.340	83	NORMAL
				+2 H	51	SR	0.143	0.090	0.372	0.381	87	NORMAL
				+4 H	63	SR	0.139	0.088	0.379	0.366	87	NORMAL
				+8 H	56	SR						
				+24 H								

Key for rhythm: SR=sinus rhythm SA=sinus arrhythmia SB=sinus bradycardia ST=sinus tachycardia
Note: # indicates a repeat value not included in the summary statistics

TABLE J2.1
ECG
Individual Values: All Subjects

Subject	Dose of Malathion	Sex	Study Day	Time Point	Ventricular Rate (b.p.m)	Rhythm	PR Interval (s)	QRS Interval (s)	QT Interval (s)	QTc Interval (s)	QRS Axis (°)	ECG Normal/ Abnormal
039	15.0 MG/KG	FEMALE	SCREENING ON-STUDY	PREDOSE	70	SR	0.161	0.088	0.348	0.375	36	NORMAL
				+2 H	57	SA	0.159	0.084	0.396	0.385	53	NORMAL
				+4 H	68	SR	0.163	0.084	0.361	0.384	60	NORMAL
				+8 H	63	SR	0.156	0.087	0.375	0.384	53	NORMAL
				+24 H	67	SR	0.156	0.083	0.369	0.389	59	NORMAL
040	15.0 MG/KG	FEMALE	SCREENING ON-STUDY	PREDOSE	66	SR	0.102	0.082	0.399	0.418	74	NORMAL
				+2 H	67	SR	0.154	0.078	0.379	0.400	71	NORMAL
				+4 H	65	SR	0.146	0.083	0.376	0.391	72	NORMAL
				+8 H	70	SR	0.107	0.078	0.386	0.401	72	NORMAL
				+24 H	71	SR	0.125	0.105	0.396	0.427	78	NORMAL
041	PLACEBO	FEMALE	SCREENING ON-STUDY	PREDOSE	67	SR	0.119	0.077	0.388	0.422	75	NORMAL
				+2 H	62	SR	0.146	0.085	0.357	0.377	25	NORMAL
				+4 H	64	SR	0.160	0.077	0.384	0.390	19	NORMAL
				+8 H	59	SR	0.147	0.078	0.367	0.379	34	NORMAL
				+24 H	61	SR	0.153	0.079	0.396	0.392	23	NORMAL
042	15.0 MG/KG	FEMALE	SCREENING ON-STUDY	PREDOSE	65	SR	0.140	0.083	0.385	0.388	33	NORMAL
				+2 H	48	SB	0.140	0.084	0.372	0.387	19	NORMAL
				+4 H	51	SR	0.173	0.090	0.392	0.350	62	NORMAL
				+8 H	56	SR	0.175	0.090	0.392	0.361	54	NORMAL
				+24 H	52	SR	0.164	0.098	0.389	0.375	57	NORMAL
				+4 H	57	SR	0.171	0.096	0.392	0.364	60	NORMAL
				+8 H	57	SR	0.166	0.091	0.386	0.376	55	NORMAL
				+24 H	60	SR	0.173	0.093	0.381	0.381	59	NORMAL

Key for rhythm: SR=sinus rhythm SA=sinus arrhythmia SB=sinus bradycardia ST=sinus tachycardia
Note: # indicates a repeat value not included in the summary statistics

TABLE J2.1

ECG Individual Values: All Subjects												
Subject	Dose of Malathion	Sex	Study Day	Time Point	Ventricular Rate (b.p.m)	Rhythm	PR Interval (s)	QRS Interval (s)	QT Interval (s)	QTc Interval (s)	QRS Axis (°)	ECG Normal/ Abnormal
043	15.0 MG/KG	FEMALE	SCREENING ON-STUDY	PREDOSE	82	SR	0.174	0.076	0.333	0.389	86	NORMAL
				+2 H	77	SR	0.186	0.074	0.341	0.386	80	NORMAL
				+4 H	69	SR	0.192	0.075	0.345	0.369	76	NORMAL
				+8 H	65	SR	0.182	0.077	0.362	0.376	82	NORMAL
				+24 H	77	SR	0.180	0.079	0.344	0.389	82	NORMAL
044	15.0 MG/KG	FEMALE	SCREENING ON-STUDY	PREDOSE	72	SR	0.188	0.080	0.351	0.384	74	NORMAL
				+2 H	63	SR	0.167	0.096	0.403	0.412	87	NORMAL
				+4 H	66	SR	0.175	0.085	0.374	0.392	73	NORMAL
				+8 H	68	SR	0.182	0.085	0.377	0.401	71	NORMAL
				+24 H	64	SR	0.187	0.080	0.380	0.404	75	NORMAL
045	PLACEBO	FEMALE	SCREENING ON-STUDY	PREDOSE	66	SR	0.178	0.086	0.421	0.434	81	NORMAL
				+2 H	66	SR	0.180	0.080	0.375	0.393	73	NORMAL
				+4 H	49	SB	0.128	0.090	0.413	0.373	70	NORMAL
				+8 H	59	SR	0.125	0.091	0.386	0.382	69	NORMAL
				+24 H	68	SR	0.126	0.089	0.364	0.387	71	NORMAL
046	15.0 MG/KG	FEMALE	SCREENING ON-STUDY	PREDOSE	68	SR	0.127	0.090	0.356	0.378	71	NORMAL
				+2 H	82	SR	0.121	0.093	0.342	0.399	56	NORMAL
				+4 H	76	SR	0.124	0.091	0.347	0.390	64	NORMAL
				+8 H	71	SR	0.152	0.081	0.356	0.387	48	NORMAL
				+24 H	74	SR	0.158	0.083	0.348	0.386	36	NORMAL
				PREDOSE	75	SR	0.159	0.084	0.349	0.390	41	NORMAL
				+2 H	72	SR	0.153	0.077	0.356	0.389	40	NORMAL
				+4 H	77	SR	0.170	0.082	0.346	0.391	30	NORMAL
				+8 H	77	SR	0.163	0.081	0.367	0.413	36	NORMAL
				+24 H	76	SR	0.163	0.081	0.367	0.413	36	NORMAL

Key for rhythm: SR=sinus rhythm SA=sinus arrhythmia SB=sinus bradycardia ST=sinus tachycardia
 Note: # indicates a repeat value not included in the summary statistics

TABLE J2.1

ECG
Individual Values: All Subjects

Subject	Dose of Malathion	Sex	Study Day	Time Point	Ventricular Rate (b.p.m)	Rhythm	PR Interval (s)	QRS Interval (s)	QT Interval (s)	QTc Interval (s)	QRS Axis (°)	ECG Normal/ Abnormal
047	PLACEBO	FEMALE	SCREENING ON-STUDY	PREDOSE	71	SR	0.150	0.089	0.359	0.390	79	NORMAL
				+2 H	73	SR	0.154	0.081	0.364	0.401	87	NORMAL
				+4 H	76	SA	0.157	0.081	0.348	0.391	81	NORMAL
				+8 H	65	SA	0.141	0.063	0.363	0.377	83	NORMAL
048	15.0 MG/KG	FEMALE	SCREENING	+24 H	80	SR	0.153	0.087	0.346	0.399	79	NORMAL
					77	SA	0.149	0.086	0.368	0.416	83	NORMAL
					65	SR	0.148	0.084	0.372	0.387	80	NORMAL
948	15.0 MG/KG	FEMALE	SCREENING ON-STUDY	PREDOSE	63	SR	0.149	0.082	0.365	0.374	36	NORMAL
				+2 H	57	SR	0.156	0.075	0.365	0.355	32	NORMAL
				+4 H	61	SR	0.159	0.074	0.359	0.361	35	NORMAL
				+8 H	55	SR	0.159	0.077	0.367	0.351	35	NORMAL
				+24 H	64	SA	0.141	0.082	0.375	0.387	38	NORMAL
					60	SR	0.154	0.077	0.375	0.375	35	NORMAL

Key for rhythm: SR=sinus rhythm SA=sinus arrhythmia SB=sinus bradycardia ST=sinus tachycardia
 Note: # indicates a repeat value not included in the summary statistics
 Subject 948 replaces subject 048 who withdrew from study and is not included in the summary statistics

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TABLE J2.2

ECG Comments
Individual Values: All Subjects with Comments

Subject	Dose of Malathion	Study Day	Time Point	Comments
009	5.0 MG/KG	ON-STUDY	+4 H	ISOLATED SVES NORMAL.
013	PLACEBO	SCREENING		T WAVE INVERSION NOTED - ANTERIOR CHEST LEADS. PREVIOUSLY INVESTIGATED AND NO ABNORMALITY.
026	15.0 MG/KG	SCREENING		LEFT AXIS DEVIATION - NOT CLINICALLY SIGNIFICANT.
		ON-STUDY	PREDOSE	LEFT AXIS DEVIATION - NOT CLINICALLY SIGNIFICANT.
		ON-STUDY	+2 H	LEFT AXIS DEVIATION - NOT CLINICALLY SIGNIFICANT.
		ON-STUDY	+4 H	LEFT AXIS DEVIATION - NOT CLINICALLY SIGNIFICANT.
		ON-STUDY	+8 H	LEFT AXIS DEVIATION - NOT CLINICALLY SIGNIFICANT.
		ON-STUDY	+24 H	LEFT AXIS DEVIATION - NOT CLINICALLY SIGNIFICANT.
047	PLACEBO	ON-STUDY	PREDOSE	SINOATRIAL PAUSES - NOT CLINICALLY SIGNIFICANT.

Note: # indicates a comment for a repeat reading

TABLE J3
Continuous ECG Monitoring
Individual Values: All Subjects

Subject	Dose of Malathion	Study Day	ECG Monitoring Started	Monitoring Time	Target Time (h:min)	Actual Time (h:min)
001	0.5 MG/KG	ON-STUDY	YES	MONITORING START TIME MONITORING FINISH TIME	12:30	7:55 12:30
002	0.5 MG/KG	ON-STUDY	YES	MONITORING START TIME MONITORING FINISH TIME	12:36	8:06 12:36
003	PLACEBO	ON-STUDY	YES	MONITORING START TIME MONITORING FINISH TIME	12:40	8:10 12:40
004	0.5 MG/KG	ON-STUDY	YES	MONITORING START TIME MONITORING FINISH TIME	12:45	8:15 12:45
005	1.5 MG/KG	ON-STUDY	YES	MONITORING START TIME MONITORING FINISH TIME	13:05	8:35 13:06
006	1.5 MG/KG	ON-STUDY	YES	MONITORING START TIME MONITORING FINISH TIME	13:10	8:44 13:11
007	PLACEBO	ON-STUDY	YES	MONITORING START TIME MONITORING FINISH TIME	13:15	8:48 13:16
008	1.5 MG/KG	ON-STUDY	YES	MONITORING START TIME MONITORING FINISH TIME	13:20	8:50 13:24
009	5.0 MG/KG	ON-STUDY	YES	MONITORING START TIME MONITORING FINISH TIME	13:05	8:30 13:05

TABLE J3
Continuous ECG Monitoring
Individual Values: All Subjects

Subject	Dose of Mafathion	Study Day	ECG Monitoring Started	Monitoring Time	Target Time (h:min)	Actual Time (h:min)
010	5.0 MG/KG	ON-STUDY	YES	MONITORING START TIME MONITORING FINISH TIME	13:10	8:35 13:10
011	5.0 MG/KG	ON-STUDY	YES	MONITORING START TIME MONITORING FINISH TIME	13:15	8:40 13:17
012	5.0 MG/KG	ON-STUDY	YES	MONITORING START TIME MONITORING FINISH TIME	13:20	8:45 13:22
013	PLACEBO	ON-STUDY	YES	MONITORING START TIME MONITORING FINISH TIME	13:26	8:50 13:26
014	5.0 MG/KG	ON-STUDY	YES	MONITORING START TIME MONITORING FINISH TIME	13:30	8:55 13:31
015	PLACEBO	ON-STUDY	YES	MONITORING START TIME MONITORING FINISH TIME	13:35	8:50 13:36
016	PLACEBO	ON-STUDY	YES	MONITORING START TIME MONITORING FINISH TIME	13:40	9:00 13:40
017	5.0 MG/KG	ON-STUDY	YES	MONITORING START TIME MONITORING FINISH TIME		9:00
917	5.0 MG/KG	ON-STUDY	YES	MONITORING START TIME MONITORING FINISH TIME	14:45	10:15 14:45

Note: Subject 917 replaces subject 017 who withdrew from study before dosing

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TABLE J3
Continuous ECG Monitoring
Individual Values: All Subjects

Subject	Dose of Malathion	Study Day	ECG Monitoring Started	Monitoring Time	Target Time (h:min)	Actual Time (h:min)
018	5.0 MG/KG	ON-STUDY	YES	MONITORING START TIME MONITORING FINISH TIME	13:45	9:05 13:47
019	10.0 MG/KG	ON-STUDY	YES	MONITORING START TIME MONITORING FINISH TIME	13:00	8:28 13:00
020	10.0 MG/KG	ON-STUDY	YES	MONITORING START TIME MONITORING FINISH TIME	13:05	8:35 13:05
021	PLACEBO	ON-STUDY	YES	MONITORING START TIME MONITORING FINISH TIME	13:10	8:40 13:11
022	10.0 MG/KG	ON-STUDY	YES	MONITORING START TIME MONITORING FINISH TIME	13:15	8:43 13:15
023	10.0 MG/KG	ON-STUDY	YES	MONITORING START TIME MONITORING FINISH TIME	13:05	8:35 13:05
024	PLACEBO	ON-STUDY	YES	MONITORING START TIME MONITORING FINISH TIME	13:10	8:43 13:10
025	PLACEBO	ON-STUDY	YES	MONITORING START TIME MONITORING FINISH TIME	13:15	8:47 13:15
026	15.0 MG/KG	ON-STUDY	YES	MONITORING START TIME MONITORING FINISH TIME	13:20	8:49 13:20

TABLE J3

Continuous ECG Monitoring
Individual Values: All Subjects

Subject	Dose of Mafathion	Study Day	ECG Monitoring Started	Monitoring Time	Target Time (h:min)	Actual Time (h:min)
927	10.0 MG/KG	ON-STUDY	YES	MONITORING START TIME MONITORING FINISH TIME	13:55	9:53 13:55
028	10.0 MG/KG	ON-STUDY	YES	MONITORING START TIME MONITORING FINISH TIME	13:35	8:57 13:35
029	15.0 MG/KG	ON-STUDY	YES	MONITORING START TIME MONITORING FINISH TIME	13:40	9:05 13:40
030	10.0 MG/KG	ON-STUDY	YES	MONITORING START TIME MONITORING FINISH TIME	13:45	9:24 13:45
031	15.0 MG/KG	ON-STUDY	YES	MONITORING START TIME MONITORING FINISH TIME	13:50	9:29 13:50
032	PLACEBO	ON-STUDY	YES	MONITORING START TIME MONITORING FINISH TIME	13:30	8:55 13:30
033	15.0 MG/KG	ON-STUDY	YES	MONITORING START TIME MONITORING FINISH TIME	13:35	8:58 13:35
034	15.0 MG/KG	ON-STUDY	YES	MONITORING START TIME MONITORING FINISH TIME	13:40	9:03 13:40
035	PLACEBO	ON-STUDY	YES	MONITORING START TIME MONITORING FINISH TIME	13:45	9:04 13:45

TABLE J3
Continuous ECG Monitoring
Individual Values: All Subjects

Subject	Dose of Malathion	Study Day	ECG Monitoring Started	Monitoring Time	Target Time (h:min)	Actual Time (h:min)
036	PLACEBO	ON-STUDY	YES	MONITORING START TIME MONITORING FINISH TIME	13:50	9:06 13:50
037	15.0 MG/KG	ON-STUDY	YES	MONITORING START TIME MONITORING FINISH TIME	13:55	9:09 13:55
038	15.0 MG/KG	ON-STUDY	YES	MONITORING START TIME MONITORING FINISH TIME	14:04	9:12 14:04
039	15.0 MG/KG	ON-STUDY	YES	MONITORING START TIME MONITORING FINISH TIME	13:15	8:50 13:15
040	15.0 MG/KG	ON-STUDY	YES	MONITORING START TIME MONITORING FINISH TIME	13:24	8:55 13:24
041	PLACEBO	ON-STUDY	YES	MONITORING START TIME MONITORING FINISH TIME	13:30	9:00 13:35
042	15.0 MG/KG	ON-STUDY	YES	MONITORING START TIME MONITORING FINISH TIME	13:35	9:00 13:40
043	15.0 MG/KG	ON-STUDY	YES	MONITORING START TIME MONITORING FINISH TIME	13:40	9:10 13:44
044	15.0 MG/KG	ON-STUDY	YES	MONITORING START TIME MONITORING FINISH TIME	13:15	8:43 13:30

TABLE J3
Continuous ECG Monitoring
Individual Values: All Subjects

Subject	Dose of Malathion	Study Day	ECG Monitoring Started	Monitoring Time	Target Time (h:min)	Actual Time (h:min)
045	PLACEBO	ON-STUDY	YES	MONITORING START TIME MONITORING FINISH TIME	13:22	8:55 13:40
046	15.0 MG/KG	ON-STUDY	YES	MONITORING START TIME MONITORING FINISH TIME	13:30	9:00 13:45
047	PLACEBO	ON-STUDY	YES	MONITORING START TIME MONITORING FINISH TIME	13:05	8:30 13:08
948	15.0 MG/KG	ON-STUDY	YES	MONITORING START TIME MONITORING FINISH TIME	13:30	9:00 13:30

Note: Subject 948 replaces subject 048 who withdrew from study before dosing

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APPENDIX K

**Haematology (including normal ranges):
Summary tables and individual data listings**

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APPENDIX K (continued)**Methods, Abbreviations and Units Used in Laboratory Investigations**Haematology

<u>Parameter</u>	<u>Method</u>	<u>Normal Range</u>	<u>Units</u>
Haemoglobin: (Hb)	Technicon H1 Analyser, Bayer UK Limited	12.8-16.3♂ 10.8-15.3♀	g.dl ⁻¹
Total Red Blood Cell Count: (RBC)	Technicon H1 Analyser, Bayer UK Limited	4.17-5.55♂ 3.60-5.06♀	x 10 ¹² .l ⁻¹
Haematocrit: (Hct)	Technicon H1 Analyser, Bayer UK Limited	0.382-0.478♂ 0.321-0.457♀	l.l ⁻¹
White Blood Cell Count: (WBC)	Technicon H1 Analyser, Bayer UK Limited	3.62-10.49♂ 3.84-10.82♀	x 10 ⁹ .l ⁻¹
Absolute Values			
Mean Cell Haemoglobin: (MCH)	Technicon H1 Analyser, Bayer UK Limited	27.4-32.3♂ 27.5-32.2♀	pg
Mean Cell Volume: (MCV)	Technicon H1 Analyser, Bayer UK Limited	81.4-96.3♂ 82.0-97.8♀	fl
Mean Cell Haemoglobin Concentration: (MCHC)	Technicon H1 Analyser, Bayer UK Limited	31.9-35.6♂ 31.6-34.9♀	g.dl ⁻¹

APPENDIX K (continued)Haematology (continued)

<u>Parameter Method</u>	<u>Normal Range</u>	<u>Units</u>
Differential White Cell Count		
Neutrophils: (Neut)	Technicon H1 Analyser Bayer UK Limited	1.58-7.47♂ 1.86-7.43♀ $\times 10^9.l^{-1}$
Lymphocytes: (Lymp)	Technicon H1 Analyser Bayer UK Limited	1.01-3.03♂ 1.09-3.16♀ $\times 10^9.l^{-1}$
Monocytes: (Mono)	Technicon H1 Analyser Bayer UK Limited	0.18-0.75♂ 0.16-0.67♀ $\times 10^9.l^{-1}$
Eosinophils: (Eos)	Technicon H1 Analyser Bayer UK Limited	0.04-0.47♂ 0.03-0.48♀ $\times 10^9.l^{-1}$
Basophils: (Baso)	Technicon H1 Analyser Bayer UK Limited	0.02-0.09♂ 0.02-0.11♀ $\times 10^9.l^{-1}$
Large Unclassified Cells: (LUC)	Technicon H1 Analyser Bayer UK Limited	0.07-0.32♂ 0.09-0.36♀ $\times 10^9.l^{-1}$
Platelets: (Plat)	Technicon H1 Analyser Bayer UK Limited	128-331♂ 108-362♀ $\times 10^9.l^{-1}$

TABLE K1.1
Haematology
Hb (g/dl)
Summary Statistics: All Dosed Subjects

MALE

Dose of Malathion		Result				Change From Baseline				LOW	NORMAL	HIGH
		Mean	SD	Min	Max	N	Mean	SD	Min	Max		
PLACEBO	PREDOSE	14.69	1.19	12.4	16.0	11					1	10
	+24 H	14.53	0.87	12.9	16.1	11	-0.16	0.63	-1.5	0.7		11
0.5 MG/KG	PREDOSE	15.33	0.45	14.9	15.8	3						3
	+24 H	14.93	0.64	14.2	15.4	3	-0.40	0.82	-1.1	0.5		3
1.5 MG/KG	PREDOSE	15.27	0.45	14.8	15.7	3						3
	+24 H	14.97	0.86	14.2	15.9	3	-0.30	0.44	-0.6	0.2		3
5.0 MG/KG	PREDOSE	15.26	0.48	14.4	15.9	7						7
	+24 H	15.70	0.72	14.7	16.8	7	0.44	0.63	-0.1	1.4		5
10.0 MG/KG	PREDOSE	14.89	1.10	13.6	17.0	7						6
	+24 H	14.76	1.25	13.2	16.9	7	-0.13	0.35	-0.7	0.4		6
15.0 MG/KG	PREDOSE	14.43	0.84	13.2	15.4	7						7
	+24 H	14.36	0.71	13.1	15.2	7	-0.07	0.70	-0.8	1.2		7

Note: Data summarised in the above table are listed in table K2.1
 LOW/NORMAL/HIGH indicate values below/within/above normal range
 Baseline is defined as predose
 Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics
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TABLE K1.1
Haematology
Hb (g/dl)
Summary Statistics: All Dosed Subjects

FEMALE

Dose of Malathion		Result				Change From Baseline				NORMAL
		Mean	SD	Min	Max	N	Mean	SD	Min	Max
PLACEBO	PREDOSE	12.80	0.90	11.9	13.7	3				
	+24 H	13.07	0.68	12.3	13.6	3	0.27	0.61	-0.4	0.8
15.0 MG/KG	PREDOSE	12.77	0.74	11.5	13.7	7				
	+24 H	12.97	1.06	11.8	14.9	7	0.20	0.82	-0.6	1.2

Note: Data summarised in the above table are listed in table K2.1
 LOW/NORMAL/HIGH indicate values below/within/above normal range
 Baseline is defined as predose
 Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics
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TABLE K1.2
Haematology
RBC ($\times 10^{12}/l$)
Summary Statistics: All Dosed Subjects

MALE

Dose of Malathion		Result				Change From Baseline					LOW	NORMAL	HIGH
		Mean	SD	Min	Max	N	Mean	SD	Min	Max			
PLACEBO	PREDOSE	5.072	0.316	4.71	5.66	11						10	1
	+24 H	5.015	0.242	4.79	5.59	11	-0.057	0.209	-0.51	0.24		10	1
0.5 MG/KG	PREDOSE	4.993	0.040	4.97	5.04	3						3	
	+24 H	4.853	0.287	4.59	5.16	3	-0.140	0.251	-0.38	0.12		3	
1.5 MG/KG	PREDOSE	5.113	0.142	4.95	5.20	3						3	
	+24 H	5.113	0.046	5.06	5.14	3	0.000	0.168	-0.13	0.19		3	
5.0 MG/KG	PREDOSE	5.069	0.418	4.34	5.53	7						7	
	+24 H	5.173	0.392	4.39	5.57	7	0.104	0.241	-0.12	0.49		6	1
10.0 MG/KG	PREDOSE	4.956	0.433	4.25	5.46	7						7	
	+24 H	4.849	0.465	4.21	5.41	7	-0.107	0.140	-0.26	0.13		7	
15.0 MG/KG	PREDOSE	4.866	0.365	4.38	5.35	7						7	
	+24 H	4.783	0.407	4.12	5.28	7	-0.083	0.265	-0.31	0.45	1	6	

Note: Data summarised in the above table are listed in table K2.1

LOW/NORMAL/HIGH indicate values below/within/above normal range

Baseline is defined as predose

Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics
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TABLE K1.2
Haematology
RBC (x10¹²/l)
Summary Statistics: All Dosed Subjects

FEMALE

Dose of Malathion		Result					Change From Baseline					LOW	NORMAL	HIGH
		Mean	SD	Min	Max	N	Mean	SD	Min	Max				
PLACEBO	PREDOSE	4.363	0.161	4.18	4.48	3						3		
	+24 H	4.397	0.161	4.28	4.58	3	0.033	0.161	-0.15	0.15		3		
15.0 MG/KG	PREDOSE	4.217	0.400	3.67	4.66	7						7		
	+24 H	4.291	0.504	3.52	5.11	7	0.074	0.253	-0.15	0.45	1	5	1	

Note: Data summarised in the above table are listed in table K2.1
 LOW/NORMAL/HIGH indicate values below/within/above normal range
 Baseline is defined as predose
 Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics
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TABLE K1.3
Haematology
Hct (L/L)
Summary Statistics: All Dosed Subjects

MALE

Dose of Malathion		Result					Change From Baseline					NORMAL	HIGH
		Mean	SD	Min	Max	N	Mean	SD	Min	Max			
PLACEBO	PREDOSE	0.4409	0.0305	0.386	0.491	11					10	1	
	+24 H	0.4367	0.0218	0.410	0.482	11	-0.0042	0.0201	-0.047	0.024	11		
0.5 MG/KG	PREDOSE	0.4497	0.0060	0.444	0.456	3					3		
	+24 H	0.4347	0.0281	0.405	0.461	3	-0.0150	0.0256	-0.039	0.012	3		
1.5 MG/KG	PREDOSE	0.4443	0.0084	0.439	0.454	3					3		
	+24 H	0.4440	0.0242	0.430	0.472	3	-0.0003	0.0159	-0.010	0.018	3		
5.0 MG/KG	PREDOSE	0.4537	0.0166	0.430	0.476	7					7		
	+24 H	0.4651	0.0217	0.432	0.503	7	0.0114	0.0253	-0.009	0.057	6	1	
10.0 MG/KG	PREDOSE	0.4469	0.0345	0.406	0.509	7					6	1	
	+24 H	0.4366	0.0346	0.393	0.490	7	-0.0103	0.0156	-0.027	0.012	6	1	
15.0 MG/KG	PREDOSE	0.4331	0.0239	0.400	0.465	7					7		
	+24 H	0.4261	0.0262	0.390	0.470	7	-0.0070	0.0292	-0.035	0.052	7		

Note: Data summarised in the above table are listed in table K2.1
LOW/NORMAL/HIGH indicate values below/within/above normal range
Baseline is defined as predose
Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics

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TABLE K1.3
Haematology
Hct (L/L)
Summary Statistics: All Dosed Subjects

FEMALE

Dose of Malathion	Result				Change From Baseline				NORMAL
	Mean	SD	Min	Max	N	Mean	SD	Min	Max
PLACEBO	0.3820	0.0269	0.353	0.406	3				
	0.3860	0.0243	0.358	0.402	3	0.0040	0.0115	-0.008	0.015
15.0 MG/KG	0.3766	0.0185	0.347	0.401	7				
	0.3843	0.0296	0.356	0.445	7	0.0077	0.0252	-0.021	0.044

Note: Data summarised in the above table are listed in table K2.1
 LOW/NORMAL/HIGH indicate values below/within/above normal range
 Baseline is defined as predose
 Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics
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TABLE K1.4
Haematology
MCH (pg)
Summary Statistics: All Dosed Subjects

MALE

Dose of Malathion		Result			Change From Baseline			LOW	NORMAL	HIGH
		Mean	SD	Min	Max	N	Mean	SD	Min	Max
PLACEBO	PREDOSE	28.95	1.43	26.3	30.8	11				
	+24 H	29.01	1.41	26.0	30.7	11	0.06	0.30	-0.4	0.5
0.5 MG/KG	PREDOSE	30.77	1.05	29.7	31.8	3				
	+24 H	30.83	0.96	29.8	31.7	3	0.07	0.15	-0.1	0.2
1.5 MG/KG	PREDOSE	29.90	1.54	28.6	31.6	3				
	+24 H	29.27	1.48	28.0	30.9	3	-0.63	0.06	-0.7	-0.6
5.0 MG/KG	PREDOSE	30.26	1.65	28.1	33.1	7				
	+24 H	30.41	1.63	28.4	33.4	7	0.16	0.37	-0.4	0.6
10.0 MG/KG	PREDOSE	30.10	1.31	27.9	31.9	7				
	+24 H	30.51	1.33	28.5	32.3	7	0.41	0.33	0.0	1.0
15.0 MG/KG	PREDOSE	29.71	1.21	28.1	32.0	7				
	+24 H	30.13	1.54	28.3	33.1	7	0.41	0.47	-0.2	1.1

Note: Data summarised in the above table are listed in table K2.1
 LOW/NORMAL/HIGH indicate values below/within/above normal range
 Baseline is defined as predose
 Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics
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TABLE K1.4
Haematology
MCH (pg)
Summary Statistics: All Dosed Subjects

FEMALE

Dose of Malathion		Result				Change From Baseline				LOW	NORMAL	HIGH
		Mean	SD	Min	Max	N	Mean	SD	Min	Max		
PLACEBO	PREDOSE	29.33	1.10	28.6	30.6	3					3	
	+24 H	29.63	0.95	28.7	30.6	3	0.30	0.44	0.0	0.8	3	
15.0 MG/KG	PREDOSE	30.47	2.88	26.2	34.5	7					1	4
	+24 H	30.46	2.82	26.1	34.3	7	-0.01	0.27	-0.3	0.3	1	4

Note: Data summarised in the above table are listed in table K2.1
 LOW/NORMAL/HIGH indicate values below/within/above normal range
 Baseline is defined as predose
 Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics
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TABLE K1.5
Haematology
MCV (fl)
Summary Statistics: All Dosed Subjects

MALE

Dose of Malathion		Result					Change From Baseline					NORMAL	HIGH
		Mean	SD	Min	Max	N	Mean	SD	Min	Max			
PLACEBO	PREDOSE	86.96	3.25	82.0	91.4	11						11	
	+24 H	87.10	3.00	82.7	92.2	11	0.14	0.84	-0.8	1.4		11	
0.5 MG/KG	PREDOSE	90.07	1.42	89.1	91.7	3						3	
	+24 H	89.53	1.53	88.2	91.2	3	-0.53	0.65	-1.2	0.1		3	
1.5 MG/KG	PREDOSE	87.00	3.99	84.5	91.6	3						3	
	+24 H	86.80	4.39	83.6	91.8	3	-0.20	0.61	-0.9	0.2		3	
5.0 MG/KG	PREDOSE	89.86	4.70	85.0	99.1	7						6	1
	+24 H	90.14	4.41	84.6	98.4	7	0.29	1.06	-0.7	2.5		6	1
10.0 MG/KG	PREDOSE	90.29	3.27	86.0	95.6	7						7	
	+24 H	90.21	3.84	84.9	97.2	7	-0.07	1.14	-1.6	1.6		6	1
15.0 MG/KG	PREDOSE	89.19	3.53	84.6	95.5	7						7	
	+24 H	89.31	3.03	85.2	94.7	7	0.13	1.44	-1.3	2.7		7	

Note: Data summarised in the above table are listed in table K2.1
LOW/NORMAL/HIGH indicate values below/within/above normal range
Baseline is defined as predose
Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics

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TABLE K1.5
Haematology
MCV (fl)
Summary Statistics: All Dosed Subjects

FEMALE

Dose of Malathion		Result				Change From Baseline				LOW	NORMAL	HIGH
		Mean	SD	Min	Max	N	Mean	SD	Min	Max		
PLACEBO	PREDOSE	87.50	3.00	84.6	90.6	3					3	
	+24 H	87.77	4.15	83.6	91.9	3	0.27	1.17	-1.0	1.3	3	
15.0 MG/KG	PREDOSE	89.86	8.28	78.7	104.0	7					5	1
	+24 H	90.21	8.18	78.5	102.7	7	0.36	1.01	-1.3	1.8	4	2

Note: Data summarised in the above table are listed in table K2.1
 LOW/NORMAL/HIGH indicate values below/within/above normal range
 Baseline is defined as predose
 Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics
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TABLE K1.6
Haematology
MCHC (g/dl)
Summary Statistics: All Dosed Subjects

MALE

Dose of Malathion		Result					Change From Baseline					LOW	NORMAL
		Mean	SD	Min	Max	N	Mean	SD	Min	Max			
PLACEBO	PREDOSE	33.28	0.91	32.1	35.1	11							11
	+24 H	33.32	1.08	31.4	35.3	11	0.04	0.51	-0.7	0.7	1		10
0.5 MG/KG	PREDOSE	34.17	0.76	33.3	34.7	3							3
	+24 H	34.43	0.83	33.5	35.1	3	0.27	0.31	0.0	0.6			3
1.5 MG/KG	PREDOSE	34.33	0.67	33.6	34.9	3							3
	+24 H	33.70	0.75	33.0	34.5	3	-0.63	0.25	-0.9	-0.4			3
5.0 MG/KG	PREDOSE	33.66	0.53	33.0	34.6	7							7
	+24 H	33.73	0.50	33.0	34.4	7	0.07	0.71	-1.3	0.6			7
10.0 MG/KG	PREDOSE	33.31	0.46	32.4	33.8	7							7
	+24 H	33.84	0.61	33.2	34.8	7	0.53	0.70	-0.2	1.4			7
15.0 MG/KG	PREDOSE	33.33	0.36	32.8	33.9	7							7
	+24 H	33.73	0.96	32.4	35.0	7	0.40	0.95	-1.1	1.5			7

Note: Data summarised in the above table are listed in table K2.1
 LOW/NORMAL/HIGH indicate values below/within/above normal range
 Baseline is defined as predose
 Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics
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TABLE K1.6
Haematology
MCHC (g/dl)
Summary Statistics: All Dosed Subjects

FEMALE

Dose of Malathion		Result						Change From Baseline				NORMAL	HIGH
		Mean	SD	Min	Max	N	Mean	SD	Min	Max			
PLACEBO	PREDOSE	33.50	0.52	32.9	33.8	3						3	
	+24 H	33.80	0.50	33.3	34.3	3	0.30	0.72	-0.5	0.9		3	
15.0 MG/KG	PREDOSE	33.91	0.80	33.1	35.2	7						6	1
	+24 H	33.76	0.68	33.2	35.2	7	-0.16	0.53	-1.0	0.3		6	1

Note: Data summarised in the above table are listed in table K2.1
 LOW/NORMAL/HIGH indicate values below/within/above normal range
 Baseline is defined as predose
 Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics
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TABLE K1.7
Haematology
WBC (x10⁹/l)
Summary Statistics: All Dosed Subjects

MALE

Dose of Malathion		Result					Change From Baseline					LOW	NORMAL	HIGH
		Mean	SD	Min	Max	N	Mean	SD	Min	Max				
PLACEBO	PREDOSE	7.578	1.590	4.84	10.02	11							11	
	+24 H	7.143	1.283	4.89	8.90	11	-0.435	0.982	-2.66	0.85			11	
0.5 MG/KG	PREDOSE	5.867	0.728	5.25	6.67	3							3	
	+24 H	6.150	0.386	5.71	6.43	3	0.283	0.461	-0.24	0.63			3	
1.5 MG/KG	PREDOSE	6.390	0.447	5.92	6.81	3							3	
	+24 H	7.037	0.361	6.72	7.43	3	0.647	0.807	-0.09	1.51			3	
5.0 MG/KG	PREDOSE	7.701	3.196	4.89	13.57	7							5	2
	+24 H	7.987	3.032	4.47	13.73	7	0.286	0.998	-1.28	1.92			6	1
10.0 MG/KG	PREDOSE	8.717	2.415	5.10	12.64	7							6	1
	+24 H	7.399	1.733	5.03	9.64	7	-1.319	2.520	-4.81	1.69			7	
15.0 MG/KG	PREDOSE	6.640	1.644	4.40	8.89	7							7	
	+24 H	6.759	2.853	3.41	10.29	7	0.119	1.341	-1.89	2.10	1		6	

Note: Data summarised in the above table are listed in table K2.1
LOW/NORMAL/HIGH indicate values below/within/above normal range
Baseline is defined as predose
Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics

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TABLE K1.7
Haematology
WBC ($\times 10^9/l$)
Summary Statistics: All Dosed Subjects

FEMALE

Dose of Malathion		Result				Change From Baseline				NORMAL
		Mean	SD	Min	Max	N	Mean	SD	Min	Max
PLACEBO	PREDOSE	6.917	0.319	6.68	7.28	3				
	+24 H	6.690	1.163	5.58	7.90	3	-0.227	0.923	-1.21	0.62
15.0 MG/KG	PREDOSE	6.657	0.828	5.15	7.61	7				
	+24 H	7.214	1.011	5.41	8.64	7	0.557	0.603	-0.57	1.25

Note: Data summarised in the above table are listed in table K2.1
 LOW/NORMAL/HIGH indicate values below/within/above normal range
 Baseline is defined as predose
 Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics
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TABLE K1.8
Haematology
Neut (x10⁹/l)
Summary Statistics: All Dosed Subjects

MALE

Dose of Malathion		Result				Change From Baseline				N	Mean	SD	Min	Max	NORMAL	HIGH
		Mean	SD	Min	Max											
PLACEBO	PREDOSE	4.600	1.382	2.53	6.70	11									11	
	+24 H	4.078	1.125	2.30	6.34	11	-0.522	0.998	-3.09	0.40					11	
0.5 MG/KG	PREDOSE	3.270	1.090	2.32	4.46	3									3	
	+24 H	3.447	1.056	2.37	4.48	3	0.177	0.246	0.02	0.46					3	
1.5 MG/KG	PREDOSE	3.937	0.197	3.79	4.16	3									3	
	+24 H	4.543	0.696	4.05	5.34	3	0.607	0.853	-0.11	1.55					3	
5.0 MG/KG	PREDOSE	4.811	2.658	2.31	9.64	7									6	1
	+24 H	5.014	2.645	2.15	10.15	7	0.203	0.791	-1.21	1.30					6	1
10.0 MG/KG	PREDOSE	5.911	2.388	2.71	9.57	7									5	2
	+24 H	4.479	1.072	3.17	6.12	7	-1.433	2.645	-5.30	1.39					7	
15.0 MG/KG	PREDOSE	4.141	1.166	2.41	5.66	7									7	
	+24 H	4.014	1.979	1.65	6.89	7	-0.127	1.017	-1.79	1.23					7	

Note: Data summarised in the above table are listed in table K2.1
LOW/NORMAL/HIGH indicate values below/within/above normal range
Baseline is defined as predose
Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics

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TABLE K1.8
Haematology
Neut (x10⁹/l)
Summary Statistics: All Dosed Subjects

FEMALE

Dose of Malathion		Result					Change From Baseline				
		Mean	SD	Min	Max	N	Mean	SD	Min	Max	NORMAL
PLACEBO	PREDOSE	4.567	1.219	3.53	5.91	3					3
	+24 H	4.310	2.057	2.36	6.46	3	-0.257	0.865	-1.17	0.55	3
15.0 MG/KG	PREDOSE	3.763	0.813	2.36	5.00	7					7
	+24 H	3.904	0.684	2.63	4.78	7	0.141	0.621	-1.22	0.69	7

Note: Data summarised in the above table are listed in table K2.1
LOW/NORMAL/HIGH indicate values below/within/above normal range
Baseline is defined as predose
Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics

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TABLE K1.9
Haematology
Lymph (x10⁹/l)
Summary Statistics: All Dosed Subjects

MALE

Dose of Malathion		Result					Change From Baseline					LOW	NORMAL
		Mean	SD	Min	Max	N	Mean	SD	Min	Max			
PLACEBO	PREDOSE	1.921	0.390	1.59	2.76	11							11
	+24 H	1.995	0.405	1.50	2.93	11	0.075	0.302	-0.54	0.47			11
0.5 MG/KG	PREDOSE	1.743	0.355	1.34	2.01	3							3
	+24 H	1.823	0.509	1.26	2.25	3	0.080	0.160	-0.08	0.24			3
1.5 MG/KG	PREDOSE	1.640	0.440	1.15	2.00	3							3
	+24 H	1.607	0.448	1.10	1.95	3	-0.033	0.029	-0.05	0.00			3
5.0 MG/KG	PREDOSE	1.963	0.227	1.74	2.37	7							7
	+24 H	1.983	0.153	1.72	2.16	7	0.020	0.206	-0.27	0.24			7
10.0 MG/KG	PREDOSE	1.831	0.745	0.66	2.76	7					1		6
	+24 H	1.956	0.647	1.09	2.62	7	0.124	0.209	-0.14	0.43			7
15.0 MG/KG	PREDOSE	1.614	0.444	0.97	2.24	7					1		6
	+24 H	1.831	0.840	1.05	3.02	7	0.217	0.544	-0.27	1.11			7

Note: Data summarised in the above table are listed in table K2.1
LOW/NORMAL/HIGH indicate values below/within/above normal range
Baseline is defined as predose
Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics

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TABLE K1.9
Haematology
Lyp (x10⁹/l)
Summary Statistics: All Dosed Subjects

FEMALE

Dose of Malathion		Result					Change From Baseline					LOW	NORMAL	HIGH
		Mean	SD	Min	Max	N	Mean	SD	Min	Max				
PLACEBO	PREDOSE	1.590	0.676	0.87	2.21	3						1	2	
	+24 H	1.643	0.756	0.84	2.34	3	0.053	0.080	-0.03	0.13		1	2	
15.0 MG/KG	PREDOSE	2.214	0.480	1.68	2.94	7							7	
	+24 H	2.536	0.467	1.94	3.21	7	0.321	0.306	-0.07	0.76			6	1

Note: Data summarised in the above table are listed in table K2.1
 LOW/NORMAL/HIGH indicate values below/within/above normal range
 Baseline is defined as predose
 Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics
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TABLE K1.10
Haematology
Mono (x10⁹/l)
Summary Statistics: All Dosed Subjects

MALE

Dose of Malathion		Result					Change From Baseline					NORMAL	HIGH
		Mean	SD	Min	Max	N	Mean	SD	Min	Max			
PLACEBO	PREDOSE	0.583	0.154	0.35	0.89	11					9	2	
	+24 H	0.575	0.179	0.30	0.81	11	-0.007	0.200	-0.36	0.27	9	2	
0.5 MG/KG	PREDOSE	0.457	0.040	0.42	0.50	3					3		
	+24 H	0.443	0.140	0.30	0.58	3	-0.013	0.101	-0.12	0.08	3		
1.5 MG/KG	PREDOSE	0.367	0.021	0.35	0.39	3					3		
	+24 H	0.463	0.059	0.42	0.53	3	0.097	0.072	0.05	0.18	3		
5.0 MG/KG	PREDOSE	0.470	0.306	0.19	1.11	7					6	1	
	+24 H	0.536	0.257	0.32	1.06	7	0.066	0.102	-0.05	0.21	6	1	
10.0 MG/KG	PREDOSE	0.576	0.277	0.35	1.17	7					6	1	
	+24 H	0.523	0.167	0.31	0.81	7	-0.053	0.184	-0.36	0.21	6	1	
15.0 MG/KG	PREDOSE	0.499	0.142	0.33	0.76	7					6	1	
	+24 H	0.450	0.137	0.30	0.63	7	-0.049	0.131	-0.25	0.15	7		

Note: Data summarised in the above table are listed in table K2.1
 LOW/NORMAL/HIGH indicate values below/within/above normal range
 Baseline is defined as predose
 Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics
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TABLE K1.10
Haematology
Mono (X10⁹/l)
Summary Statistics: All Dosed Subjects

FEMALE

Dose of Malathion		Result					Change From Baseline					NORMAL	HIGH
		Mean	SD	Min	Max	N	Mean	SD	Min	Max			
PLACEBO	PREDOSE	0.337	0.091	0.24	0.42	3						3	
	+24 H	0.387	0.045	0.34	0.43	3	0.050	0.070	-0.03	0.10		3	
15.0 MG/KG	PREDOSE	0.350	0.111	0.22	0.49	7						7	
	+24 H	0.410	0.145	0.25	0.69	7	0.060	0.121	-0.09	0.25		6	1

Note: Data summarised in the above table are listed in table K2.1
LOW/NORMAL/HIGH indicate values below/within/above normal range
Baseline is defined as predose
Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics
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TABLE K1.11

Haematology
Eos (x10⁹/l)
Summary Statistics: All Dosed Subjects

MALE

Dose of Malathion		Result				Change From Baseline					LOW	NORMAL
		Mean	SD	Min	Max	N	Mean	SD	Min	Max		
PLACEBO	PREDOSE	0.258	0.100	0.14	0.44	11						11
	+24 H	0.242	0.098	0.12	0.40	11	-0.016	0.058	-0.12	0.09		11
0.5 MG/KG	PREDOSE	0.150	0.089	0.05	0.22	3						3
	+24 H	0.140	0.085	0.05	0.22	3	-0.010	0.056	-0.07	0.04		3
1.5 MG/KG	PREDOSE	0.237	0.152	0.10	0.40	3						3
	+24 H	0.217	0.126	0.10	0.35	3	-0.020	0.026	-0.05	0.00		3
5.0 MG/KG	PREDOSE	0.233	0.115	0.12	0.42	7						7
	+24 H	0.219	0.092	0.10	0.34	7	-0.014	0.070	-0.09	0.12		7
10.0 MG/KG	PREDOSE	0.177	0.124	0.07	0.36	7						7
	+24 H	0.220	0.136	0.02	0.38	7	0.043	0.119	-0.07	0.28	1	6
15.0 MG/KG	PREDOSE	0.219	0.127	0.10	0.42	7						7
	+24 H	0.217	0.100	0.12	0.42	7	-0.001	0.054	-0.09	0.06		7

Note: Data summarised in the above table are listed in table K2.1
LOW/NORMAL/HIGH indicate values below/within/above normal range
Baseline is defined as predose
Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics

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TABLE K1.11
Haematology
Eos (x10⁹/l)
Summary Statistics: All Dosed Subjects

FEMALE

Dose of Malathion		Result				Change From Baseline					LOW	NORMAL
		Mean	SD	Min	Max	N	Mean	SD	Min	Max		
PLACEBO	PREDOSE	0.283	0.186	0.07	0.41	3						3
	+24 H	0.190	0.159	0.01	0.31	3	-0.093	0.031	-0.12	-0.06	1	2
15.0 MG/KG	PREDOSE	0.156	0.039	0.10	0.20	7						7
	+24 H	0.163	0.050	0.10	0.24	7	0.007	0.023	-0.03	0.04		7

Note: Data summarised in the above table are listed in table K2.1
LOW/NORMAL/HIGH indicate values below/within/above normal range
Baseline is defined as predose
Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics
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TABLE K1.12
Haematology
Baso (x10⁹/l)
Summary Statistics: All Dosed Subjects

MALE

Dose of Malathion		Result						Change From Baseline					LOW	NORMAL	HIGH
		Mean	SD	Min	Max	N	Mean	SD	Min	Max					
PLACEBO	PREDOSE	0.068	0.027	0.03	0.10	11							8	3	
	+24 H	0.073	0.026	0.03	0.11	11	0.005	0.016	-0.02	0.04			8	3	
0.5 MG/KG	PREDOSE	0.043	0.015	0.03	0.06	3							3		
	+24 H	0.037	0.015	0.02	0.05	3	-0.007	0.015	-0.02	0.01			3		
1.5 MG/KG	PREDOSE	0.073	0.012	0.06	0.08	3							3		
	+24 H	0.053	0.006	0.05	0.06	3	-0.020	0.010	-0.03	-0.01			3		
5.0 MG/KG	PREDOSE	0.069	0.029	0.03	0.12	7							6	1	
	+24 H	0.059	0.034	0.03	0.12	7	-0.010	0.013	-0.03	0.00			6	1	
10.0 MG/KG	PREDOSE	0.053	0.023	0.02	0.08	7							7		
	+24 H	0.054	0.033	0.01	0.11	7	0.001	0.017	-0.02	0.03	1		5	1	
15.0 MG/KG	PREDOSE	0.043	0.018	0.02	0.06	7							7		
	+24 H	0.050	0.025	0.02	0.08	7	0.007	0.010	0.00	0.02			7		

Note: Data summarised in the above table are listed in table K2.1
 LOW/NORMAL/HIGH indicate values below/within/above normal range
 Baseline is defined as predose
 Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics
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TABLE K1.12
Haematology
Baso (x10⁹/l)
Summary Statistics: All Dosed Subjects

FEMALE

Dose of Malathion		Result						Change From Baseline				
		Mean	SD	Min	Max	N	Mean	SD	Min	Max	NORMAL	
PLACEBO	PREDOSE	0.040	0.010	0.03	0.05	3					3	
	+24 H	0.040	0.000	0.04	0.04	3	0.000	0.010	-0.01	0.01	3	
15.0 MG/KG	PREDOSE	0.041	0.011	0.03	0.05	7					7	
	+24 H	0.047	0.018	0.03	0.08	7	0.006	0.013	-0.01	0.03	7	

Note: Data summarised in the above table are listed in table K2.1
LOW/NORMAL/HIGH indicate values below/within/above normal range
Baseline is defined as predose
Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics
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TABLE K1.13
Haematology
LUC (x10⁹/l)
Summary Statistics: All Dosed Subjects

MALE

Dose of Malathion		Result				Change From Baseline						NORMAL	HIGH
		Mean	SD	Min	Max	N	Mean	SD	Min	Max			
PLACEBO	PREDOSE	0.150	0.037	0.10	0.22	11						11	
	+24 H	0.179	0.080	0.09	0.39	11	0.029	0.079	-0.06	0.24		10	1
0.5 MG/KG	PREDOSE	0.203	0.032	0.18	0.24	3						3	
	+24 H	0.250	0.053	0.21	0.31	3	0.047	0.025	0.02	0.07		3	
1.5 MG/KG	PREDOSE	0.133	0.032	0.11	0.17	3						3	
	+24 H	0.153	0.015	0.14	0.17	3	0.020	0.020	0.00	0.04		3	
5.0 MG/KG	PREDOSE	0.157	0.062	0.09	0.25	7						7	
	+24 H	0.179	0.051	0.10	0.26	7	0.021	0.048	-0.04	0.11		7	
10.0 MG/KG	PREDOSE	0.166	0.073	0.07	0.30	7						7	
	+24 H	0.167	0.054	0.09	0.24	7	0.001	0.029	-0.06	0.02		7	
15.0 MG/KG	PREDOSE	0.124	0.021	0.09	0.15	7						7	
	+24 H	0.196	0.092	0.07	0.35	7	0.071	0.094	-0.02	0.24		6	1

Note: Data summarised in the above table are listed in table K2.1
 LOW/NORMAL/HIGH indicate values below/within/above normal range
 Baseline is defined as predose
 Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics
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TABLE K1.13
Haematology
LUC (x10⁹/l)
Summary Statistics: All Dosed Subjects

FEMALE

Dose of Malathion		Result				Change From Baseline					LOW	NORMAL
		Mean	SD	Min	Max	N	Mean	SD	Min	Max		
PLACEBO	PREDOSE	0.097	0.060	0.04	0.16	3					1	2
	+24 H	0.120	0.026	0.10	0.15	3	0.023	0.042	-0.01	0.07		3
15.0 MG/KG	PREDOSE	0.136	0.046	0.09	0.22	7						7
	+24 H	0.154	0.050	0.08	0.24	7	0.019	0.053	-0.07	0.08	1	6

Note: Data summarised in the above table are listed in table K2.1
LOW/NORMAL/HIGH indicate values below/within/above normal range
Baseline is defined as predose
Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics
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TABLE K1.14
Haematology
Plat (X10⁹/l)
Summary Statistics: All Dosed Subjects

MALE

Dose of Malathion		Result					Change From Baseline					NORMAL	HIGH
		Mean	SD	Min	Max	N	Mean	SD	Min	Max			
PLACEBO	PREDOSE	250.9	65.4	179	377	11						10	1
	+24 H	247.8	67.6	172	377	11	-3.1	6.5	-14	5		9	2
0.5 MG/KG	PREDOSE	236.0	9.2	226	244	3						3	
	+24 H	236.0	31.3	215	272	3	0.0	25.9	-23	28		3	
1.5 MG/KG	PREDOSE	228.3	61.1	180	297	3						3	
	+24 H	224.3	46.5	197	278	3	-4.0	19.5	-19	18		3	
5.0 MG/KG	PREDOSE	243.1	54.3	146	299	7						7	
	+24 H	239.7	59.1	130	297	7	-3.4	13.6	-24	16		7	
10.0 MG/KG	PREDOSE	222.1	40.4	155	267	7						7	
	+24 H	214.3	31.8	174	262	7	-7.9	14.4	-26	19		7	
15.0 MG/KG	PREDOSE	233.3	30.1	193	268	7						7	
	+24 H	233.1	37.8	186	291	7	-0.1	12.3	-10	26		7	

Note: Data summarised in the above table are listed in table K2.1
LOW/NORMAL/HIGH indicate values below/within/above normal range
Baseline is defined as predose
Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics

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TABLE K1.14
Haematology
Plat (x10⁹/l)
Summary Statistics: All Dosed Subjects

FEMALE

Dose of Malathion		Result				Change From Baseline					NORMAL
		Mean	SD	Min	Max	N	Mean	SD	Min	Max	
PLACEBO	PREDOSE	213.0	65.6	145	276	3					3
	+24 H	227.0	67.2	155	288	3	14.0	5.3	10	20	3
15.0 MG/KG	PREDOSE	232.1	43.8	182	301	7					7
	+24 H	230.3	29.0	199	263	7	-1.9	21.3	-45	17	7

Note: Data summarised in the above table are listed in table K2.1
 LOW/NORMAL/HIGH indicate values below/within/above normal range
 Baseline is defined as predose
 Subjects 017, 027 and 048 withdrew from study before dosing and are not included in the summary statistics
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TABLE K2.1
Haematology
Individual Values: All Subjects

Subject	Dose of Malathion	Sex	Time Point	Hb (g/dl)	RBC (x10 ¹² /l)	Hct (l/l)	MCH (pg)	MCV (fl)	MCHC (g/dl)	WBC (x10 ⁹ /l)
001	0.5 MG/KG	MALE	SCREENING	15.0	5.06	0.441	29.7	87.1	34.1	5.33
			PREDOSE +24 H	14.9 15.4	5.04 5.16	0.449 0.461	29.7 29.8	89.1 89.2	33.3 33.5	5.25 5.71
002	0.5 MG/KG	MALE	SCREENING	15.4	5.07	0.439	30.5	86.6	35.2	5.68
			PREDOSE +24 H	15.3 14.2	4.97 4.59	0.444 0.405	30.8 31.0	89.4 88.2	34.5 35.1	5.68 6.31
003	PLACEBO	MALE	SCREENING	14.4	4.86	0.433	29.7	89.1	33.3	6.85
			PREDOSE +24 H	14.4 14.5	4.83 4.79	0.433 0.432	29.9 30.3	89.6 90.1	33.3 33.7	6.75 7.44
004	0.5 MG/KG	MALE	SCREENING	15.3	4.87	0.447	31.4	91.9	34.1	5.16
			PREDOSE +24 H	15.8 15.2	4.97 4.81	0.456 0.438	31.8 31.7	91.7 91.2	34.7 34.7	6.67 6.43
005	1.5 MG/KG	MALE	SCREENING	14.6	5.11	0.428	28.6	83.8	34.1	5.32
			PREDOSE +24 H	14.8 14.2	5.19 5.06	0.440 0.430	28.6 28.0	84.9 85.0	33.6 33.0	5.92 7.43
006	1.5 MG/KG	MALE	SCREENING	15.3	5.19	0.436	29.5	84.0	35.1	6.71
			PREDOSE +24 H	15.3 14.8	5.20 5.14	0.439 0.430	29.5 28.9	84.5 83.6	34.9 34.5	6.81 6.72
007	PLACEBO	MALE	SCREENING	15.2	5.09	0.447	29.8	87.8	33.9	9.12
			PREDOSE +24 H	15.4 15.5	5.16 5.22	0.467 0.470	29.9 29.8	90.6 90.0	33.0 33.1	7.88 8.73

Note: Values marked H/L indicate values above/below the normal range
indicates a repeat or unscheduled value not included in the summary statistics

TABLE K2.1
Haematology
Individual Values: All Subjects

Subject	Dose of Malathion	Sex	Time Point	Hb (g/dl)	RBC (x10 ¹² /l)	Hct (l/l)	MCH (pg)	MCV (fl)	MCHC (g/dl)	WBC (x10 ⁹ /l)
008	1.5 MG/KG	MALE	SCREENING	16.1	5.17	0.475	31.1	91.8	33.9	7.89
			PEDOSE	15.7	4.95	0.454	31.6	91.6	34.5	6.44
			+24 H	15.9	5.14	0.472	30.9	91.8	33.6	6.96
009	5.0 MG/KG	MALE	SCREENING	15.6	5.11	0.448	30.4	87.7	34.7	7.09
			PEDOSE +24 H	15.4 16.8 H	5.08 5.57 H	0.446 0.503 H	30.4 30.1	87.8 90.3	34.6 33.3	5.75 6.26
010	5.0 MG/KG	MALE	SCREENING	16.2	5.14	0.473	31.6	92.1	34.3	6.92
			PEDOSE +24 H	15.1 16.4 H	4.82 5.21	0.442 0.477	31.3 31.5	91.8 91.6	34.1 34.4	6.75 7.57
011	5.0 MG/KG	MALE	SCREENING	14.6	4.79	0.426	30.5	88.8	34.4	8.37
			PEDOSE +24 H	15.5 15.6	5.23 5.16	0.462 0.456	29.7 30.3	88.4 88.4	33.6 34.2	6.66 8.58
012	5.0 MG/KG	MALE	SCREENING	16.3	5.49	0.478	29.7	87.1	34.1	10.61 H
			PEDOSE +24 H	15.9 15.8	5.52 5.40	0.476 0.468	28.8 29.2	86.3 86.7	33.4 33.7	10.67 H 9.39
013	PLACEBO	MALE	SCREENING	12.4 L	4.85	0.402	25.7 L	82.9 L	30.9 L	8.51
			PEDOSE +24 H	12.4 L 12.9	4.71 4.95	0.386 0.410	26.3 L 26.0 L	82.0 L 82.7 L	32.1 L 31.4 L	8.01 7.83
014	5.0 MG/KG	MALE	SCREENING	15.5	4.81	0.439	32.2	91.4	35.2	8.17
			PEDOSE +24 H	15.0 15.1	4.96 5.03	0.449 0.458	30.4 30.0	90.6 91.0	33.5 33.0	13.57 H 13.73 H

Note: Values marked H/L indicate values above/below the normal range
indicates a repeat or unscheduled value not included in the summary statistics

TABLE K2.1

Haematology
Individual Values: All Subjects

Subject	Dose of Methathion	Sex	Time Point	Hb (g/dl)	RBC (x10 ¹² /l)	Hct (l/l)	MCH (pg)	MCV (fl)	MCHC (g/dl)	WBC (x10 ⁹ /l)
015	PLACEBO	MALE	SCREENING	15.5	5.30	0.464	29.3	87.6	33.4	6.04
			PREDOSE +24 H	14.0	4.83	0.429	29.0	88.8	32.7	7.02
016	PLACEBO	MALE	SCREENING	15.5	5.09	0.443	30.4	87.0	35.0	5.21
			PREDOSE +24 H	15.2	4.93	0.432	30.8	87.7	35.1	4.84
017	5.0 MG/KG	MALE	SCREENING	15.1	4.93	0.429	30.7	87.0	35.3	4.89
			SCREENING	14.9	5.17	0.450	28.9	86.9	33.2	5.23
917	5.0 MG/KG	MALE	SCREENING	14.5	4.16	0.409	35.0	98.5	35.5	4.43
			PREDOSE +24 H	14.4	4.34	0.430	33.1	99.1	33.4	4.89
018	5.0 MG/KG	MALE	SCREENING	14.7	4.39	0.432	33.4	98.4	34.0	4.47
			SCREENING	15.0	5.24	0.448	28.6	85.6	33.4	5.42
019	10.0 MG/KG	MALE	PREDOSE +24 H	15.5	5.53	0.471	28.1	85.0	33.0	5.62
			SCREENING	15.7	5.45	0.462	28.4	84.6	33.5	5.91
020	10.0 MG/KG	MALE	SCREENING	15.9	5.18	0.464	30.3	89.6	33.8	7.84
			PREDOSE +24 H	14.6	4.97	0.447	30.0	89.9	33.4	9.31
020	10.0 MG/KG	MALE	SCREENING	13.7	4.71	0.420	31.0	89.1	34.8	8.04
			PREDOSE +24 H	13.6	4.24	0.417	32.4	98.5	32.9	8.31
020	10.0 MG/KG	MALE	SCREENING	13.6	4.25	0.406	31.9	95.6	33.4	12.64
			PREDOSE +24 H	13.6	4.21	0.409	32.3	97.2	33.2	7.83

Note: Values marked H/L indicate values above/below the normal range
 # indicates a repeat or unscheduled value not included in the summary statistics
 Subject 917 replaces subject 017 who withdrew from study and is not included in the summary statistics

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TABLE K2.1
Haematology
Individual Values: All Subjects

Subject	Dose of Methionine	Sex	Time Point	Hb (g/dl)	RBC ($\times 10^{12}/L$)	Hct (L/L)	MCH (pg)	MCV (fL)	MCHC (g/dL)	WBC ($\times 10^9/L$)
021	PLACEBO	MALE	SCREENING	16.0	5.37	0.449	29.8	83.6	35.6	8.33
			PREDOSE	15.1	5.37	0.444	28.1	82.7	33.9	9.46
			+24 H	14.6	5.24	0.441	27.9	84.1	33.2	8.27
022	10.0 MG/KG	MALE	SCREENING	13.6	4.47	0.400	30.3	89.4	33.9	7.42
			PREDOSE +24 H	13.9	4.57	0.411	30.4	90.0	33.7	9.75
023	10.0 MG/KG	MALE	SCREENING	15.1	5.24	0.453	28.7	86.4	33.3	8.93
			PREDOSE	15.3	5.28	0.461	29.0	87.2	33.2	7.95
			+24 H	15.7	5.41	0.473	29.1	87.4	33.2	9.64
024	PLACEBO	MALE	SCREENING	15.8	5.46	0.471	28.9	86.2	33.5	10.51 H
			PREDOSE	16.0	5.66 H	0.491	28.3	86.8	32.6	9.36
			+24 H	16.1	5.59 H	0.482	28.7	86.3	33.3	8.90
025	PLACEBO	MALE	SCREENING	15.3	5.21	0.441	29.4	84.6	34.8	5.85
			PREDOSE	16.0	5.47	0.465	29.2	85.0	34.4	5.97
			+24 H	14.5	4.96	0.418	29.3	84.3	34.8	6.15
026	15.0 MG/KG	MALE	SCREENING	13.8	4.60	0.408	30.1	88.9	33.9	5.91
			PREDOSE	14.0	4.76	0.425	29.3	89.2	32.8	7.59
			+24 H	14.5	4.80	0.424	30.3	88.3	34.3	7.98
027	10.0 MG/KG	MALE	SCREENING	14.3	4.70	0.427	30.4	90.9	33.4	4.79

Note: Values marked H/L indicate values above/below the normal range
indicates a repeat or unscheduled value not included in the summary statistics

TABLE K2.1
Haematology
Individual Values: All Subjects

Subject	Dose of Maltathion	Sex	Time Point	Hb (g/dl)	RBC (x10 ¹² /l)	Hct (l/l)	MCH (pg)	MCV (fl)	MCHC (g/dl)	WBC (x10 ⁹ /l)
927	10.0 MG/KG	MALE	SCREENING	14.1	4.64	0.433	30.4	93.4	32.6	8.63
			PEDOSE +24 H	14.8	4.87	0.439	30.5	90.2	33.8	6.75
028	10.0 MG/KG	MALE	SCREENING	14.9	4.84	0.441	30.8	91.0	33.9	6.80
			PEDOSE +24 H	17.1 H	5.52	0.518 H	30.9	93.9	32.9	6.76
029	15.0 MG/KG	MALE	SCREENING	17.0 H	5.46	0.509 H	31.0	93.1	33.3	5.10
			PEDOSE +24 H	16.9 H	5.36	0.490 H	31.5	91.5	34.5	5.44
030	10.0 MG/KG	MALE	SCREENING	15.4	5.03	0.452	30.6	89.8	34.1	10.28
			PEDOSE +24 H	15.4	5.10	0.465	30.2	91.1	33.2	8.19
031	15.0 MG/KG	MALE	SCREENING	14.6	4.79	0.430	30.6	89.8	34.0	10.29
			PEDOSE +24 H	14.0	4.96	0.411	28.2	82.9	34.1	6.81
032	PLACEBO	MALE	SCREENING	14.7	5.29	0.455	27.9	86.0	32.4	9.52
			PEDOSE +24 H	14.4	5.06	0.430	28.5	84.9	33.6	9.01
033	15.0 MG/KG	MALE	SCREENING	14.8	4.54	0.428	32.6 H	94.3	34.5	4.78
			PEDOSE +24 H	14.0	4.38	0.418	32.0	95.5	33.6	5.30
032	PLACEBO	MALE	SCREENING	13.7	4.12 L	0.390	33.1 H	94.7	35.0	3.41 L
			PEDOSE +24 H	12.7 L	4.54	0.382	28.0	84.1	33.3	6.14
033	15.0 MG/KG	MALE	SCREENING	12.8	4.76	0.397	26.9 L	83.4	32.3	6.46
			PEDOSE +24 H	13.5	4.95	0.419	27.4	84.7	32.3	5.54
033	15.0 MG/KG	MALE	SCREENING	15.9	5.65 H	0.498 H	28.1	88.1	31.9	6.10
			PEDOSE +24 H	14.0	4.83	0.418	29.0	86.4	33.5	6.47
033	15.0 MG/KG	MALE	SCREENING	15.2	5.28	0.470	28.8	89.1	32.4	6.56
			PEDOSE +24 H	15.2	5.28	0.470	28.8	89.1	32.4	6.56

Note: Values marked H/L indicate values above/below the normal range
indicates a repeat or unscheduled value not included in the summary statistics
Subject 927 replaces subject 027 who withdrew from study and is not included in the summary statistics

TABLE K2.1
Haematology
Individual Values: All Subjects

Subject	Dose of Mafathion	Sex	Time Point	Hb (g/dl)	RBC (x10 ¹² /l)	Hct (l/l)	MCH (pg)	MCV (fl)	MCHC (g/dl)	WBC (x10 ⁹ /l)
034	15.0 MG/KG	MALE	SCREENING	15.5	5.08	0.442	30.5	87.0	35.1	5.65
			PREDOSE	15.4	5.18	0.454	29.7	87.7	33.9	5.64
			+24 H	14.8	4.94	0.430	30.0	87.1	34.4	4.78
035	PLACEBO	MALE	SCREENING	16.2	5.43	0.471	29.8	86.8	34.3	8.46
			PREDOSE	15.2	5.15	0.456	29.4	88.6	33.2	7.59
			+24 H	14.4	4.87	0.428	29.6	87.8	33.7	6.66
036	PLACEBO	MALE	SCREENING	15.3	4.82	0.446	31.9	92.5	34.4	5.88
			PREDOSE	15.1	4.92	0.450	30.6	91.4	33.5	10.02
			+24 H	14.5	4.80	0.443	30.2	92.2	32.8	7.36
037	15.0 MG/KG	MALE	SCREENING	15.5	5.44	0.463	28.5	85.1	33.5	8.88
			PREDOSE	15.0	5.35	0.452	28.1	84.6	33.2	8.89
			+24 H	14.6	5.15	0.439	28.3	85.2	33.3	10.26
038	15.0 MG/KG	MALE	SCREENING	13.7	4.61	0.403	29.7	87.6	33.9	5.15
			PREDOSE	13.2	4.46	0.400	29.7	89.8	33.1	4.40
			+24 H	13.1	4.40	0.400	29.8	91.0	32.7	4.03
039	15.0 MG/KG	FEMALE	SCREENING	11.7	3.54	0.363	33.1	102.5	32.3	9.43
			PREDOSE	12.7	3.67	0.382	34.5	104.0	33.1	7.61
			+24 H	12.1	3.52	0.361	34.3	102.7	33.4	8.64
040	15.0 MG/KG	FEMALE	SCREENING	12.6	4.45	0.372	28.2	83.7	33.7	7.34
			PREDOSE	13.2	4.57	0.391	28.8	85.4	33.7	6.93
			+24 H	12.8	4.42	0.377	29.0	85.3	34.0	7.66

Note: Values marked H/L indicate values above/below the normal range
indicates a repeat or unscheduled value not included in the summary statistics

TABLE K2.1
Haematology
Individual Values: All Subjects

Subject	Dose of Methathion	Sex	Time Point	Hb (g/dl)	RBC (x10 ¹² /l)	Hct (l/l)	MCH (pg)	MCV (fl)	MCHC (g/dl)	WBC (x10 ⁹ /l)
041	PLACEBO	FEMALE	SCREENING	13.8	4.83	0.404	28.5	83.6	34.1	6.50
			PREDOSE +24 H	12.8 13.6	4.43 4.58	0.387 0.402	28.8 29.6	87.3 87.8	32.9 33.8	6.68 6.59
042	15.0 MG/KG	FEMALE	SCREENING	11.5	3.96	0.342	29.0	86.3	33.6	4.76
			PREDOSE +24 H	11.5 12.5	3.93 4.22	0.347 0.375	29.4 29.7	88.5 88.9	33.2 33.4	6.57 7.82
043	15.0 MG/KG	FEMALE	SCREENING	13.4	4.82	0.419	27.9	87.1	32.0	7.53
			PREDOSE +24 H	13.7 14.9	4.66 5.11	0.401 0.445	29.4 29.1	85.9 87.0	34.3 33.5	7.51 6.94
044	15.0 MG/KG	FEMALE	SCREENING	13.4	4.38	0.401	30.5	91.4	33.4	6.18
			PREDOSE +24 H	12.8 13.8	4.08 4.35	0.365 0.393	31.5 31.8	89.6 90.4	35.2 35.2	6.45 7.26
045	PLACEBO	FEMALE	SCREENING	11.9	4.36	0.374	27.2	85.8	31.7	5.57
			PREDOSE +24 H	11.9 12.3	4.18 4.28	0.353 0.358	28.6 28.7	84.6 83.6	33.8 34.3	7.28 7.90
046	15.0 MG/KG	FEMALE	SCREENING	11.4	4.51	0.356	25.3	78.9	32.1	6.32
			PREDOSE +24 H	12.2 11.8	4.64 4.54	0.365 0.356	26.2 26.1	78.7 78.5	33.3 33.2	6.38 6.77
047	PLACEBO	FEMALE	SCREENING	13.5	4.33	0.400	31.2	92.5	33.7	4.42
			PREDOSE +24 H	13.7 13.3	4.48 4.33	0.406 0.398	30.6 30.6	90.6 91.9	33.8 33.3	6.79 5.58

Note: Values marked H/L indicate values above/below the normal range
indicates a repeat or unscheduled value not included in the summary statistics

TABLE K2.1
Haematology
Individual Values: All Subjects

Subject	Dose of Malathion	Sex	Time Point	Hb (g/dl)	RBC ($\times 10^{12}/L$)	Hct (L/L)	MCH (pg)	MCV (fL)	MCHC (g/dL)	WBC ($\times 10^9/L$)
048	15.0 MG/KG	FEMALE	SCREENING	13.9	4.52	0.404	30.8	89.4	34.4	6.78
948	15.0 MG/KG	FEMALE	SCREENING	13.0	4.02	0.401	32.2	99.7 H	32.3	6.96
			PREDOSE	13.3	3.97	0.385	33.5 H	96.9	34.6	5.15
			+24 H	12.9	3.88	0.383	33.2 H	98.7 H	33.6	5.41

Note: Values marked H/L indicate values above/below the normal range
 # indicates a repeat or unscheduled value not included in the summary statistics
 Subject 948 replaces subject 048 who withdrew from study and is not included in the summary statistics

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TABLE K2.1
Haematology
Individual Values: All Subjects

Subject	Dose of Malathion	Sex	Time Point	Neut. (x10 ⁹ /l)	Lymp (x10 ⁹ /l)	Mono (x10 ⁹ /l)	Eos (x10 ⁹ /l)	Baso (x10 ⁹ /l)	LUC (x10 ⁹ /l)	Plat (x10 ⁹ /l)
001	0.5 MG/KG	MALE	SCREENING	2.37	1.92	0.53	0.27	0.05	0.20	288
			PREDOSE	2.32	2.01	0.50	0.18	0.06	0.18	244
			+24 H	2.37	2.25	0.58	0.22	0.05	0.23	272
002	0.5 MG/KG	MALE	SCREENING	3.62	1.33	0.45	0.02 L	0.04	0.21	248
			PREDOSE +24 H	3.03 3.49	1.88 1.96	0.45 0.45	0.05 0.05	0.03 0.04	0.24 0.31	238 215
003	PLACEBO	MALE	SCREENING	4.01	1.70	0.68	0.23	0.06	0.17	191
			PREDOSE	4.00	1.70	0.53	0.25	0.10 H	0.17	194
			+24 H	4.27	1.99	0.72	0.21	0.08	0.17	189
004	0.5 MG/KG	MALE	SCREENING	3.80	0.70 L	0.40	0.08	0.09	0.08	240
			PREDOSE	4.46	1.34	0.42	0.22	0.04	0.19	226
			+24 H	4.48	1.26	0.30	0.15	0.02	0.21	221
005	1.5 MG/KG	MALE	SCREENING	3.23	1.24	0.45	0.28	0.13 H	0.11	191
			PREDOSE	3.79	1.15	0.39	0.40	0.08	0.12	208
			+24 H	5.34	1.10	0.44	0.35	0.06	0.14	197
006	1.5 MG/KG	MALE	SCREENING	3.57	2.32	0.45	0.11	0.06	0.20	324
			PREDOSE	4.16	2.00	0.36	0.10	0.08	0.11	297
			+24 H	4.05	1.95	0.42	0.10	0.05	0.15	278
007	PLACEBO	MALE	SCREENING	5.92	2.08	0.51	0.17	0.08	0.37 H	286
			PREDOSE	4.48	2.18	0.68	0.31	0.09	0.15	279
			+24 H	4.88	2.28	0.77 H	0.34	0.08	0.39 H	265

Note: Values marked H/L indicate values above/below the normal range
indicates a repeat or unscheduled value not included in the summary statistics

TABLE K2.1
Haematology
Individual Values: All Subjects

Subject	Dose of Malathion	Sex	Time Point	Neut (x10 ⁹ /l)	Lymp (x10 ⁹ /l)	Mono (x10 ⁹ /l)	Eos (x10 ⁹ /l)	Baso (x10 ⁹ /l)	LUC (x10 ⁹ /l)	Plat (x10 ⁹ /l)
008	1.5 MG/KG	MALE	SCREENING PREDOSE +24 H	5.92 3.86 4.24	1.38 1.77 1.77	0.35 0.35 0.53	0.10 0.21 0.20	0.07 0.06 0.05	0.07 0.17 0.17	202 180 198
009	5.0 MG/KG	MALE	SCREENING PREDOSE +24 H	4.02 2.79 3.27	2.07 1.99 2.09	0.44 0.35 0.32	0.18 0.32 0.28	0.13 H 0.09 0.09	0.25 0.20 0.21	301 263 266
010	5.0 MG/KG	MALE	SCREENING PREDOSE +24 H	3.96 4.11 4.71	1.65 1.79 1.87	0.62 0.41 0.55	0.37 0.30 0.21	0.13 H 0.06 0.03	0.19 0.09 0.20	267 247 263
011	5.0 MG/KG	MALE	SCREENING PREDOSE +24 H	5.25 4.22 5.52	2.08 1.76 2.00	0.56 0.33 0.54	0.27 0.18 0.30	0.06 0.06 0.04	0.15 0.12 0.17	269 269 275
012	5.0 MG/KG	MALE	SCREENING PREDOSE +24 H	6.79 7.23 6.02	2.34 2.11 2.16	0.61 0.58 0.59	0.45 0.42 0.34	0.16 H 0.12 H 0.12 H	0.27 0.21 0.17	263 284 260
013	PLACEBO	MALE	SCREENING PREDOSE +24 H	5.55 5.22 4.45	1.87 1.70 2.17	0.63 0.54 0.70	0.19 0.33 0.21	0.09 0.07 0.11 H	0.18 0.16 0.18	335 H 330 335 H
014	5.0 MG/KG	MALE	SCREENING PREDOSE +24 H	4.93 9.64 H 10.15 H	2.35 2.37 2.10	0.66 1.11 H 1.06 H	0.16 0.12 0.10	0.07 0.07 0.05	0.25 0.26	292 299 297

Note: Values marked H/L indicate values above/below the normal range
indicates a repeat or unscheduled value not included in the summary statistics

TABLE K2.1
Haematology
Individual Values: All Subjects

Subject	Dose of Methionine	Sex	Time Point	Neut (x10 ⁹ /l)	Lymph (x10 ⁹ /l)	Mono (x10 ⁹ /l)	Eos (x10 ⁹ /l)	Baso (x10 ⁹ /l)	LUC (x10 ⁹ /l)	Plat (x10 ⁹ /l)
015	PLACEBO	MALE	SCREENING	3.76	1.32	0.66	0.11	0.07	0.11	251
			PEDOSE +24 H	4.05 3.81	1.68 1.62	0.62 0.68	0.38 0.38	0.07 0.07	0.22 0.23	237 232
016	PLACEBO	MALE	SCREENING	2.84	1.47	0.39	0.34	0.06	0.12	243
			PEDOSE +24 H	2.53 2.30	1.59 1.84	0.35 0.43	0.20 0.12	0.04 0.05	0.12 0.15	241 228
017	5.0 MG/KG	MALE	SCREENING	2.95	1.53	0.52	0.05	0.05	0.13	273
917	5.0 MG/KG	MALE	SCREENING	2.44	1.45	0.40	0.07	0.06	0.11	132
			PEDOSE +24 H	2.31 2.15	1.98 1.72	0.32 0.34	0.12 0.12	0.05 0.05	0.10	146 130
018	5.0 MG/KG	MALE	SCREENING	3.02	1.67	0.39	0.16	0.03	0.15	177
			PEDOSE +24 H	3.38 3.28	1.74 1.94	0.19 0.35	0.17 0.18	0.03 0.03	0.12 0.14	194 187
019	10.0 MG/KG	MALE	SCREENING	4.92	1.75	0.65	0.24	0.07	0.22	269
			PEDOSE +24 H	5.44 4.40	2.76 2.62	0.51 0.46	0.36 0.34	0.06 0.05	0.17 0.17	266 248
020	10.0 MG/KG	MALE	SCREENING	4.93	1.86	0.89	0.09	0.17	0.37	301
			PEDOSE +24 H	9.57 4.62	1.54 1.87	1.17 0.81	0.07 0.19	0.08 0.11	0.21 0.23	214 212

Note: Values marked H/L indicate values above/below the normal range
indicates a repeat or unscheduled value not included in the summary statistics
Subject 917 replaces subject 017 who withdrew from study and is not included in the summary statistics

TABLE K2.1
Haematology
Individual Values: All Subjects

Subject	Dose of Malathion	Sex	Time Point	Neut ($\times 10^9/L$)	Lymp ($\times 10^9/L$)	Mono ($\times 10^9/L$)	Eos ($\times 10^9/L$)	Baso ($\times 10^9/L$)	LUC ($\times 10^9/L$)	Plat ($\times 10^9/L$)
021	PLACEBO	MALE	SCREENING	5.24	1.97	0.33	0.49	0.13	0.17	291
			PREDOSE	6.70	1.60	0.51	0.44	0.10	0.12	309
			+24 H	5.20	1.97	0.50	0.40	0.10	0.09	312
022	10.0 MG/KG	MALE	SCREENING	4.77	1.65	0.70	0.09	0.02	0.18	202
			PREDOSE +24 H	8.47 3.17	0.66 1.09	0.44 0.65	0.09 0.02	0.03 0.01	0.07 0.09	208 193
023	10.0 MG/KG	MALE	SCREENING	5.96	2.13	0.52	0.08	0.09	0.16	233
			PREDOSE	4.73	2.39	0.50	0.12	0.05	0.15	246
			+24 H	6.12	2.61	0.57	0.11	0.06	0.17	220
024	PLACEBO	MALE	SCREENING	7.79	1.50	0.79	0.14	0.13	0.15	229
			PREDOSE	6.45	1.66	0.89	0.14	0.10	0.11	188
			+24 H	6.34	1.53	0.64	0.14	0.10	0.16	190
025	PLACEBO	MALE	SCREENING	3.47	1.52	0.48	0.19	0.05	0.15	202
			PREDOSE	3.41	1.77	0.52	0.14	0.03	0.10	179
			+24 H	3.46	1.96	0.30	0.23	0.03	0.17	172
026	15.0 MG/KG	MALE	SCREENING	3.29	2.02	0.22	0.10	0.04	0.23	230
			PREDOSE	4.92	1.98	0.43	0.10	0.04	0.12	245
			+24 H	4.30	2.84	0.36	0.16	0.05	0.27	242
027	10.0 MG/KG	MALE	SCREENING	2.83	1.32	0.27	0.14	0.10	0.13	195

Note: Values marked H/L indicate values above/below the normal range
indicates a repeat or unscheduled value not included in the summary statistics

TABLE K2.1
Haematology
Individual Values: All Subjects

Subject	Dose of Malathion	Sex	Time Point	Neut (x10 ⁹ /l)	Lymp (x10 ⁹ /l)	Mono (x10 ⁹ /l)	Eos (x10 ⁹ /l)	Baso (x10 ⁹ /l)	LUC (x10 ⁹ /l)	Plat (x10 ⁹ /l)
927	10.0 MG/KG	MALE	SCREENING	5.82	1.72	0.72	0.17	0.03	0.17	169
			PREDOSE	4.37	1.65	0.42	0.15	0.02	0.13	155
			+24 H	4.43	1.63	0.42	0.16	0.03	0.13	174
028	10.0 MG/KG	MALE	SCREENING	4.33	1.28	0.34	0.42	0.07	0.33 H	275
			PREDOSE	2.71	1.34	0.35	0.35	0.05	0.30	267
			+24 H	3.21	1.31	0.31	0.34	0.04	0.24	262
029	15.0 MG/KG	MALE	SCREENING	7.97 H	1.42	0.56	0.07	0.09	0.17	337 H
			PREDOSE	5.20	1.91	0.76 H	0.15	0.06	0.11	239
			+24 H	6.02	3.02	0.63	0.19	0.08	0.35 H	242
030	10.0 MG/KG	MALE	SCREENING	4.01	1.99	0.30	0.26	0.08	0.18	193
			PREDOSE	6.09	2.48	0.64	0.10	0.08	0.13	199
			+24 H	5.40	2.56	0.44	0.38	0.08	0.14	191
031	15.0 MG/KG	MALE	SCREENING	3.27	0.87 L	0.31	0.10	0.10 H	0.13	204
			PREDOSE	3.44	0.97 L	0.58	0.14	0.02	0.15	196
			+24 H	1.65	1.10	0.33	0.16	0.02	0.15	186
032	PLACEBO	MALE	SCREENING	3.14	1.98	0.39	0.32	0.12 H	0.19	363 H
			PREDOSE	3.21	2.04	0.79 H	0.22	0.06	0.14	377 H
			+24 H	3.15	1.50	0.43	0.26	0.06	0.14	377 H
033	15.0 MG/KG	MALE	SCREENING	3.82	0.76 L	0.81 H	0.50 H	0.07	0.15	297
			PREDOSE	4.00	1.32	0.53	0.42	0.06	0.14	265
			+24 H	4.37	1.05	0.51	0.42	0.06	0.15	291

Note: Values marked H/L indicate values above/below the normal range

indicates a repeat or unscheduled value not included in the summary statistics
Subject 927 replaces subject 027 who withdrew from study and is not included in the summary statistics

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TABLE K2.1
Haematology
Individual Values: All Subjects

Subject	Dose of Malathion	Sex	Time Point	Neut (x10 ⁹ /l)	Lymp (x10 ⁹ /l)	Mono (x10 ⁹ /l)	Eos (x10 ⁹ /l)	Baso (x10 ⁹ /l)	LUC (x10 ⁹ /l)	Plat (x10 ⁹ /l)
034	15.0 MG/KG	MALE	SCREENING PREDOSE +24 H	3.49 3.36 2.89	1.51 1.49 1.29	0.33 0.39 0.30	0.19 0.30 0.21	0.03 0.02 0.02	0.10 0.09 0.07	199 193 191
035	PLACEBO	MALE	SCREENING PREDOSE +24 H	5.19 4.36 3.90	2.24 2.45 2.16	0.70 0.44 0.35	0.09 0.15 0.12	0.06 0.03 0.04	0.18 0.16 0.10	255 235 239
036	PLACEBO	MALE	SCREENING PREDOSE +24 H	2.69 6.19 3.10	2.31 2.76 2.93	0.45 0.54 0.81	0.20 0.28 0.25	0.21 H 0.06 0.08	0.22 0.20 0.19	202 191 187
037	15.0 MG/KG	MALE	SCREENING PREDOSE +24 H	6.14 5.66 6.89	1.60 2.24 2.18	0.54 0.47 0.62	0.33 0.32 0.26	0.13 H 0.06 0.08	0.14 0.14 0.22	256 268 262
038	15.0 MG/KG	MALE	SCREENING PREDOSE +24 H	3.23 2.41 1.98	1.23 1.39 1.34	0.42 0.33 0.40	0.08 0.10 0.12	0.05 0.04 0.04	0.14 0.12 0.16	227 227 218
039	15.0 MG/KG	FEMALE	SCREENING PREDOSE +24 H	5.89 3.77 4.46	2.41 2.94 3.04	0.77 H 0.49 0.69 H	0.17 0.20 0.24	0.06 0.05 0.08	0.12 0.16 0.13	281 301 256
040	15.0 MG/KG	FEMALE	SCREENING PREDOSE +24 H	4.70 3.46 3.69	1.90 2.74 3.21	0.42 0.34 0.35	0.08 0.14 0.13	0.06 0.03 0.04	0.16 0.22 0.24	247 205 202

Note: Values marked H/L indicate values above/below the normal range
indicates a repeat or unscheduled value not included in the summary statistics

TABLE K2.1
Haematology
Individual Values: All Subjects

Subject	Dose of Malathion	Sex	Time Point	Neut (x10 ⁹ /l)	Lymp (x10 ⁹ /l)	Mono (x10 ⁹ /l)	Eos (x10 ⁹ /l)	Raso (x10 ⁹ /l)	LUC (x10 ⁹ /l)	Plat (x10 ⁹ /l)
041	PLACEBO	FEMALE	SCREENING	4.07	1.49	0.39	0.34	0.06	0.14	316
			PREDOSE +24 H	4.26 4.11	1.69 1.75	0.24 0.34	0.37 0.25	0.03 0.04	0.09 0.10	218 238
042	15.0 MG/KG	FEMALE	SCREENING	2.68	1.53	0.43	0.04	0.03	0.07 L	188
			PREDOSE +24 H	4.36 4.78	1.76 2.28	0.23 0.48	0.10 0.10	0.03 0.03	0.09 0.15	201 207
043	15.0 MG/KG	FEMALE	SCREENING	5.28	1.42	0.56	0.06	0.07	0.14	235
			PREDOSE +24 H	5.00 3.78	1.68 2.44	0.45 0.44	0.18 0.15	0.05 0.05	0.15 0.08 L	210 224
044	15.0 MG/KG	FEMALE	SCREENING	3.06	2.58	0.24	0.08	0.04	0.19	178
			PREDOSE +24 H	3.64 3.88	2.24 2.69	0.28 0.31	0.12 0.14	0.05 0.06	0.13 0.18	182 199
045	PLACEBO	FEMALE	SCREENING	3.78	1.31	0.19	0.11	0.04	0.14	155
			PREDOSE +24 H	5.91 6.46	0.87 L 0.84 L	0.35 0.43	0.07 0.01 L	0.04 0.04	0.04 L 0.11	145 155
046	15.0 MG/KG	FEMALE	SCREENING	3.67	2.00	0.30	0.14	0.03	0.18	307
			PREDOSE +24 H	3.75 4.11	1.92 1.94	0.44 0.35	0.15 0.16	0.05 0.04	0.09 0.17	254 263
047	PLACEBO	FEMALE	SCREENING	2.17	1.57	0.30	0.22	0.05	0.11	295
			PREDOSE +24 H	3.53 2.36	2.21 2.34	0.42 0.39	0.41 0.31	0.05 0.04	0.16 0.15	276 288

Note: Values marked H/L indicate values above/below the normal range
indicates a repeat or unscheduled value not included in the summary statistics

TABLE K2.1
Haematology
Individual Values: All Subjects

subject	Dose of Malathion	Sex	Time Point	Neut (x10 ⁹ /l)	Lymp (x10 ⁹ /l)	Mono (x10 ⁹ /l)	Eos (x10 ⁹ /l)	Baso (x10 ⁹ /l)	LUC (x10 ⁹ /l)	Plat (x10 ⁹ /l)
048	15.0 MG/KG	FEMALE	SCREENING	3.90	2.06	0.37	0.26	0.09	0.10	311
948	15.0 MG/KG	FEMALE	SCREENING	4.00	2.34	0.26	0.19	0.03	0.13	314
			PREDOSE +24 H	2.36	2.22	0.22	0.20	0.03	0.11	272
				2.63	2.15	0.25	0.22	0.03	0.13	261

Note: Values marked H/L indicate values above/below the normal range
 # indicates a repeat or unscheduled value not included in the summary statistics
 Subject 948 replaces subject 048 who withdrew from study and is not included in the summary statistics

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