

**Wellcome Trust, UK / National Health & Medical Research Council, Australia /
Health Research Council, New Zealand**

International Collaborative Research Grants

ANNUAL PROGRESS REPORT

Purpose

The annual report is intended as a mechanism to allow the funding partners, with the advice of their advisory committees, to monitor the scientific activities of major programmes on an annual basis. By this means, the Wellcome Trust, NHMRC and HRC can keep in touch with achievements, problems, changing circumstances, and opportunities in order to allow effective management and administrative support. While there is an element of performance review, the annual report is more for the purpose of informing the funders of ongoing progress and programme development.

Guidelines

1. The Annual Report is to be submitted by the Principal Investigators by **15th March each year**.
2. The report should be completed using the standard form (below) specifically provided for this purpose. Only brief descriptions are required to introduce the key elements of major studies or themes, bearing in mind that full details have previously been considered and approved.
3. The level of detail provided should allow the Trust, NHMRC and HRC and their advisory committees to assess the progress of the research programme over the previous 12 months.
4. The attached form provides guidance notes on the type of information required, but the precise format and subheadings may need to be tailored to the particular structure of each programme.
5. The report must be signed by the Principal Investigators on behalf of all the other investigators involved in the project and by the administering institution's Responsible Officer (Section F).

Please send the completed form by **15th March 2008** to:

Wellcome Trust

Ms Rebecca Erlich

Email: r.erlich@wellcome.ac.uk

Copies of the completed form should also be sent to NHMRC and/or HRC, as appropriate.

HRC, New Zealand contact:

Dr Vernon Choy

Group Manager, Investment Process

Email: vchoy@hrc.gov.nz

NHMRC, Australia contact:

Ms Sarojini (Ro) Martin

Email: ro.martin@nhmrc.gov.au

The NHMRC also requires a signed original to be submitted to the following address:

NHMRC Progress Reports
Research Funding Schemes
Centre for Research Management and Policy
National Health and Medical Research Council
MDP 33, GPO Box 9848
CANBERRA ACT 2601

SECTION A - Administration

Grant Type	International Collaborative Research Grant
Wellcome Trust Grant Number	GR071669MA
NHMRC Application ID	268053
HRC Contact Number	
Principal Investigator - Australia/New Zealand <i>Please provide title and full address</i>	A/Professor Nicholas Allan Buckley Clinical Pharmacology & Toxicology Australian National University Medical School PO Box 11 Woden ACT 2606 Australia
Principal Investigator - Developing country <i>Please provide title and full address</i>	Professor Nimal Senanayake Faculty of Medicine University of Peradeniya Peradeniya Sri Lanka
Project Title	Reducing deaths from pesticide poisoning - Establishing a regional toxicology research centre
Administering Institution - Australia/New Zealand	Australian National University
Date Funding Commenced	July 2004
Current Year for which progress report is presented (<i>e.g. Year 1 2004</i>)	Year 3/4 - 2007

SECTION B – General overview

*Please summarise the original objectives, timelines and milestones of the funded project **as specified in the original application.***
(Maximum of one side of A4 page)

Building on a collaboration previously funded by the Wellcome Trust, we proposed to establish an Australian/Sri Lankan based research collaboration to evaluate methods to reduce deaths from deliberate self-poisoning with pesticides. We have called this broader collaboration the South Asian Clinical Toxicology Research Collaboration (SACTRC). Specific questions we intended to address are as follows:

- Can the burden of disease in Sri Lanka attributable to pesticide poisoning be reduced through a coordinated clinical research programme?
- Is pesticide restriction an effective primary prevention strategy to reduce the severity or frequency of pesticide poisoning?
- Can detailed investigation of the clinical pathophysiology and epidemiology of the “intermediate syndrome” and organophosphorus induced delayed neuropathy (OPIDN) provide information that will enable a reduction in morbidity and mortality from these conditions?
- Can changes in serum creatinine predict outcome from paraquat poisoning?
- Can we provide evidence (Phase II studies) that the following antidotes are effective in humans sufficient to warrant definitive large (Phase III) trials?
 - Bicarbonate, clonidine and diazepam (organophosphorus pesticides (OP)
 - Bicarbonate (chlorophenoxy herbicides)
 - Antioxidant therapy (paraquat)
- What are the barriers to implementation of evidence based treatment of pesticide poisoning (including antidotes) and how can these be overcome?
- What is the marginal cost effectiveness of the common antidotes used as treatments for pesticide poisoning?

We also aimed to build the clinical and research capacity in Australia and the region to better deal with this and related problems

The main themes of our research program and the timelines we anticipated achieving by the 3 ½ year stage were as follows: (Y = achieved, N = not achieved)

- 1) Improving the delivery of care based on best evidence - we stated we would have collected baseline data on current treatment in Sri Lankan hospitals (Y), and be starting interventions to alter practices (Y) and have a new edition of the national guidelines and a PIC poisoning handbook which incorporates results from our current research (Y).
- 2) Increasing the knowledge of the clinical pathophysiology of pesticide poisoning – we stated we would have completed a study on the intermediate syndrome (Y) and on the prognosis of paraquat poisoning (Y) and be conducting a study of long-term neurotoxicity from OP (Y).
- 3) Increasing the evidence for antidote use – we stated we would have commenced phase II & III trials on antidotes (Y)
- 4) Pharmaco-economic assessment of antidote use – we stated we would be measuring resource use and cost-effectiveness in the phase II and III trials (Y).
- 5) Poisoning prevention – we demonstrated that targeted pesticide restrictions is effective in reducing mortality (Y) this has now been included into national policy.
- 6) Capacity building – we stated we would have enrolled 10 higher degree students (Y), have prepared new short course and distance education material (Y), and be running regular short courses and training programs (Y).

Has the direction of the research changed (from that specified in the original application)? If so how?

The broad research direction has remained unchanged. We have identified significant resources and knowledge gaps in primary care hospitals both. The identification of barriers to the implementation of evidence-based management has provided the impetus for studies to address these barriers which have commenced with the collaboration of the North Central & North Western Provincial Directors of Health. Specifically these studies examine implementing policy into practice within primary care hospitals using an academic detailing model. We are also evaluating a primary care mental health intervention. Poisoning & suicide has been identified as a health priority within North Central Province and have been included in the local policy planning.

As a consequence of our capacity development we have begun studies examining health effects of low dose exposure to agrochemicals. We completed a pilot study with local collaborators looking at DNA fragmentation in newborns associated with environmental use of pesticides. We also completed pilot studies of measuring cognitive function in occupationally exposed individuals. We believe that this may have important public health and socioeconomic implications.

We commenced an RCT of immunosuppression in paraquat poisoning. In addition we have received ethical approval for an additional phase II study examining salicylate in paraquat poisoning. This study is being done in collaboration with partners in Portugal. We have attracted additional funding for both of these studies.

Our original research and capacity building program was to be entirely based in Sri Lanka. However, the problem of pesticide poisoning is widespread in the region, particularly in India. We are supporting a number of complementary research activities in the SACTRC collaborating centre in CMC Vellore. One of our postgraduate Bangladesh students completed a phase II study of bolus doses of magnesium in OP poisoning this study was presented in the APAMT congress. These activities in South Asia will help us explore the generalisability of interventions .

Has the timeline changed (from that specified in the original application)? If so how?

The original timeline stated we would start in January 2004 – as contracts with the ANU were not signed off until January 2004, this proved impractical. Effectively we started work in July 2004 and by altering our start date with the Wellcome Trust and by suspending payments from the NHMRC for 6 months our funding is now in line with this revised start date.

SECTION C – Progress Report

Specify the milestones and timelines for the last 12 months and whether these have been achieved. Please describe scientific highlights and major achievements of this project during this period.

▪ *Significant research results*

The cohort study recruited a further **5601** patients during 2007, bringing the total number enrolled since 2002 to **18065**.

This data was used to complete a number of studies examining the relative toxicity of pesticides which in turn helped to inform regulatory authorities.

Notably our data demonstrating a reduction of deaths from regional restriction of dimethoate and fenthion and our data and publications related to paraquat toxicity has directly led to the withdrawal of all 3 products from Sri Lanka starting January 2008. In the interim paraquat concentration has been reduced from 20% to 6.5%.

We predict that these policy changes will lead to a 40-60% reduction in deaths i.e. approximately saving 1200 lives per year. This has also been driven by two studies published in the last year demonstrating a 40% reduction in suicides with pesticide restriction measures in the second half of the 90s without any adverse effect on agriculture.

We have also continued to demonstrate for the first time the safety in human overdose of a number of pesticides for which there were no human data (e.g. presentations 6, 14 & 36), as well as providing evidence on the relative toxicity of pesticides used for similar indications and we expect to submit papers on these subjects this year.

The identification by one of our postgraduate students of intermediate syndrome (IMS) as a spectrum disorder with objective changes occurring in approximately 40% of patients has enabled us to use this as an outcome in our Phase II/III clinical trials. We have also supported the development at CMC Vellore of a cheap bedside diagnostic instrument to detect IMS and facilitate clinical management and research

The development of an objective measure of cognitive deficit following acute organophosphate poisoning by another of our postgraduate students is being applied to the assessment of environmental exposure.

We demonstrated a paradoxical impact of providing locked boxes to improve safe storage of pesticides, with high rates of use of safe storage increasing the storage of pesticides within the home rather than within the field. This has led further development of storage devices designed to be used within the field or compound. We are currently designing a definitive larger trial to assess the efficacy of this widely promoted but unproven intervention. This development was aided by a workshop on safe storage organised by SACTRC that included other researchers in this field

▪ *Progress of ongoing clinical studies*

Paraquat Studies

A Phase III RCT of immunosuppression has recruited 72 of a target of 800 patients after commencing in March 2007 in Galle Hospital. It has recently expanded to 4 other clinical centers. We have also concluded studies looking at the role of paraquat concentrations in predicting outcome. Further small pilot studies are due to start shortly including a study of salicylate, vitamin C and acetylcysteine antioxidants and a more detailed study with markers of oxidative stress (collaborations with - Portugal and Vanderbilt Universities)

Can fructose-1,6-diphosphate reverse oleander-induced cardiac toxicity?

This Phase II RCT was completed in September. The results were encouraging and has led to ethical approval of a larger study which commenced in February 2008

RCT Magnesium in Organophosphate Poisoning

This study commenced in April 2007 and has recruited 35 patients (target 300). This trial is also including a sub-study of neurotoxicity.

Is clonidine an effective treatment for organophosphate poisoning?

This Phase II RCT has recruited 42 patients (target 64) and is expected to finish within the next few months.

A pilot study of the potential efficacy of FFP in acute OP poisoning

This open pilot study recruited 9 patients. We decided to expand the study to include an albumin arm and measure a number of biologically plausible intermediate markers. This larger study will be done by the SACTRC group in CMC Vellore.

Bedside testing of Methaemoglobin (MetHb)

We have previously identified the inability to monitor MetHb treatment responses as the major contributor to mortality. We have developed a novel and cheap method of quantifying MetHb at the bedside. This has been validated and is now being used in a clinical trial of the treatment of propanil poisoning. We are also validating the use of oximeters that can determine metHb.

Alcohol Community Studies

Alcohol use is highly associated with self-poisoning as well as many other public health and socioeconomic problems. We commenced a sociological based community study aimed at developing community based harm minimization strategies

Anti-venom for Snakebite

An RCT looking at the rate of infusion of anti-venom and its effect on adverse reactions has commenced and recruited 101 of the target of 494 patients. A separate study is examining the dose response of anti-venom in envenomated patients as this is a major cost to the Sri Lankan health system (Recruited 22 of 94).

Other Phase II/III RCTs

Trials of bicarbonate (MCPA & OP) and diazepam (OP poisoning) have all been approved by ethics committees and should start within the next few months now that the number of hospitals recruiting has expanded and as the clonidine OP trial concludes..

Oduvanthalai Poisoning

This plant poisoning is a significant problem in parts of Asia. We are supporting an integrated study of clinical and basic aspects to understand and refine the management of this poisoning

▪ *Other treatments tested*

We completed a study comparing two different treatment protocols for the use of atropine in organophosphate poisoning

▪ *Research results translated into policies and practice*

The new national guidelines incorporating our results have been published a trial of educational detailing to look at enhancing their uptake has commenced.

We have commenced production of an integrated uniform medical undergraduate curriculum for poisoning

Our research results have also been incorporated into two distance learning courses (Australia and Sri Lanka). In addition a new WHO guideline development for the treatment of pesticide poisoning started in December 2008 has incorporated SACTRC research.

Andrew Dawson attended as a WHO consultant for the WHO/IPCS meeting on the Development of a risk assessment toolkit for country use. This project seeks to provide tools to allow developing and emerging economy countries to inform local policy on chemical hazards.

▪ *Major recognition such as membership of committees*

Andrew Dawson remains President of the Asian Pacific Association of Medical Toxicology (APAMT), a board member of the European Association of Poison Centres and Clinical Toxicologists and member of the senior editorial board of Clinical Toxicology

Tharaka Dassanayake received a 4 year Australian Endeavour PhD scholarship (AusAid) to extend his cognitive impairment research that was described in his MPhil

Indika Gawarammana received a 4 year Australian Leader PhD Scholarship for clinical research into paraquat toxicity

Five postgraduate students received competitive travel scholarships from the APAMT to attend and present at the 6th scientific congress in Bangkok held in December 2007

If satisfactory progress towards achieving the milestones and timelines have not been achieved, please explain why this has occurred and how the issues are being addressed.

It is only practical to run one RCT on a particular poisoning in a hospital; this has delayed the commencement of the diazepam in organophosphate study. The RCT of Magnesium study started strongly in Anuradhapura but slowed when the postgraduate student became unwell and then eventually had to leave the program. We subsequently have identified another postgraduate student who has recommenced the study

List key problems encountered, if any.

The political situation and conflict in Sri Lanka still has some indirect repercussions on our program. It has proved difficult to recruit Australian higher degree students, and the very high-level travel advisory warnings from the Australian government are likely to be partly to blame as they now include areas where our clinical units function.

Following an attack in Anuradhapura the hospital was effectively closed by curfew for some days. Bomb attacks on public buses has made some staff reluctant to travel and alternate arrangements have had to be made.

The conflict and the escalating price of oil have led to a worsening economic situation in Sri Lanka causing levels of inflation in the order of 17-21%. This in turn has led to pressure on wages which has required careful and transparent discussion, it has also led to an increase of cost for most items and an increase in tariffs for imports of research related supplies. We have dealt with this by using direct imports of consumables where ever possible

How has the Collaborative Effort developed? List any new collaborations and links developed.
The original Sri Lankan-Australian-UK collaboration has continued to gain strength, with new associate investigators from all medical schools in Sri Lanka. There are a large number of Masters and PhD students. Most of these also have junior academic posts and at least one supervisor at these universities. We also have active collaborative partners in Denmark, USA, Germany and Portugal

The North Central Provincial Health Council

A MoU was signed between North Central Provincial Health Council and SACTRC to facilitate research in primary hospitals and the community. The major activities are "Policy into Practice" initiatives in treatment of poisoning, piloting and evaluating primary mental health intervention in primary hospitals. Continued refinement of the safe storage of pesticides program in the community and a community intervention of harm minimisation associated with alcohol misuse

The Sri Lankan Post Graduate Institute of Medicine (PGIM)

The PGIM is the Sri Lankan institution in charge of all specialist post-graduate medical education. A SACTRC initiated proposal for a distance learning Masters Program in clinical toxicology was agreed to in December 2007 and will start course delivery in June 2008. There are numerous international partners identified.

In addition the PGIM will provide certification of short courses in toxicology that are being delivered in provincial areas.

World Health Organisation

SACTRC has received funding from WHO to run a research program which investigates the determinants of pesticide selection in the southern province of Hambantota. The aim of this project is to understand what incentives may work in encouraging farmers to use less toxic pesticides. This has potential broad applicability in parts of the developing world with less developed or effective regulatory systems

Christian Medical College of Vellore (INDIA)

SACTRC helped develop and fund an integrated research project in Vellore related to various aspects of OP poisoning and plant poisoning

SACTRC - WHO IPCS Wiki project

This project continues under the name of www.wikitox.org. Components of Wikitox are supporting course development in Australia and Sri Lanka (see *The Sri Lankan Post Graduate Institute of Medicine, Masters of Toxicology*). This project continues to accrue new international partners.

University of Copenhagen

SACTRC has further developed its collaboration with the Public Health faculty of the University of Copenhagen. Public health students are sent to do field work with SACTRC for their graduate or master's thesis in areas related to poisoning. Currently SACTRC continues to support longer term follow-up studies of the previously implemented community-based interventions to promote pesticide safe

Asia-Pacific Association of Medical Toxicology

SACTRC co-organised the 6th International Congress of the APAMT in Bangkok. This provided an opportunity for our local and regional postgraduate students to present their work and to promote the development of networks within the region.

MANAS project Goa India

Following the Wellcome Networking meeting in Beijing (November 2006) and a subsequent visit to Goa SACTRC has entered into a collaborative project with Prof Vikram Patel's group to examine the generalisability of the MANAS primary psychiatric health care intervention in Sri Lanka

Dept of Pathology, University of Peradeniya 7

SACTRC has sourced a variety of laboratory equipment to enable the establishment of a multi-disciplinary toxicology research laboratory in Peradeniya University

Training summary

What training and career development has been achieved?

Please provide details of all staff, graduate and postgraduate students involved in this grant who have received training in the last 12 months, indicating the source of funding and any other relevant information.

Scientific training			
Name	Post	Degree or course	Source of funding
Pradeepa Jayawardena	Postgraduate Researcher	PhD (year 3) near completion	SACTRC & Sri Jayawardenapura University
Tharaka Dassanayake	Postgraduate Researcher	MPhil Completed	SACTRC & University of Peradeniya. AUSAID Endeavour Scholarship
Darren Roberts	Postgraduate Researcher	PhD Completed	SACTRC, NHMRC scholarship, Australian National University
Indika Gawarammana	Postgraduate Researcher	PhD Commenced	AUSAID Australian Leadership Scholarship. SACTRC, University of Peradeniya
Ganga Senarathna	Postgraduate Researcher	MPhil (year 3) near completion	SACTRC & Sri Jayawardenapura University
Bishan Rajapakse	Postgraduate Researcher	MPhil (year 2) converted to PhD	SACTRC, Australian National University
Fathima Shihan	Postgraduate Researcher	MPhil (year 2) in progress	SACTRC, University of Peradeniya
Mohammed Fahim Cader	Postgraduate Researcher	Masters of Applied Health Management Completes in 2008	SACTRC
Aroona Abdulla	Postgraduate Researcher	Diploma of Clinical Epidemiology: completed 2006 Masters of Clinical Epidemiology: in progress	SACTRC
Mark Perera	Postgraduate Researcher	Diploma of Clinical Epidemiology: completed MPhil enrolling	SACTRC
Ariful Bashar	Postgraduate Researcher	Diploma of Clinical Epidemiology: completed	SACTRC, Dhaka Medical College
Ayanthi Karunathne	Postgraduate Researcher	M Phil Enrolling	SACTRC, University of Peradeniya
Asfir Essa Lenne	Postgraduate Researcher	Research commenced PhD Enrolling	SACTRC University of Peradeniya
Sudheera Jayasinghe	Postgraduate Researcher	PhD commenced	SACTRC, University of Galle
Kavitha Valeriparambath	Postgraduate Researcher	Withdrew from Vellore	SACTRC, CMC Vellore, self funding
Mohamed (Shukry) Zawahir	Clinical Trial Coordinator	Diploma of Clinical Epidemiology: in progress MPhil enrolling	SACTRC
Mohamed Sharif	Postgraduate Researcher	Diploma of Clinical Epidemiology: in progress	SACTRC, Dhaka Medical College

Shanta De Silva	Sri Lankan Poisons Information Centre	Diploma of Clinical Epidemiology Completed M Phil Enrolling	SACTRC, Ministry of Health
Prabhash Siriwardhana	Postgraduate Researcher	Enrolling MPhil	SACTRC

Non-scientific training			
Name	Post	Type of training	Source of funding
Lumbini de Silva	Clinical Research Assistant	Graduate Certificate Toxicology Colombo: completed	SACTRC
Mark Perera	Clinical Research Manager	Graduate Certificate Toxicology Colombo: completed	SACTRC

How has the grant contributed to the professional development of the staff and PhD students?

The grant has provided an opportunity and infrastructure to undertake postgraduate training and conduct research. It also has allowed the creation of a “critical mass” of postgraduate activity with overlapping areas of interest and research.

Please list any other training provided through the project.

The Asia-Pacific Association of Medical Toxicology (APAMT) 6th International Congress
SACTRC was the major organiser of this 3-day conference which went from the 12th to 14th of December. The congress attracted over 200 delegates from 24 countries. The main themes of the meeting were acute human toxicity and pesticides. A pre-meeting workshop was conducted on Safe storage

Visiting American Fellows

The following emergency physicians visited and conducted a series of lectures and workshops in the clinical research centres

Dr. Mark Supino, Chicago Emergency Medicine

Dr Jennifer Schwieger, Chicago Emergency Medicine

SECTION D – Research outputs

Indicate any outputs to date directly associated with the ICRG award. Please indicate clearly publications and outcomes that have resulted directly from the ICRG award. (marked by *)

Research publications:

Please provide full citations. Include published and expected (in press and submitted) publications.

(* indicates publications including some original research, which was partly or wholly funded by the ICRG grant)

Published since January 2007 (see previous annual reports for earlier publications).

Systematic review texts

1. Roberts D, Buckley NA. Urinary alkalinisation for acute chlorophenoxy herbicide poisoning. In: **The Cochrane Library**, Issue 1 2007: CD005488. Oxford: Update Software.
2. Eddleston M, Singh S, Buckley NA. Acute organophosphorus poisoning. **Clinical Evidence**. 2007;16:1-13 (on-line only). Continually updated compendium of evidence published by the American Society of Internal Medicine and the BMJ Publishing Group, London

Original research articles (with 2006 ISI Impact factors (IF))

3. * Eddleston M, Juszczak E, Buckley NA, Senarathna L, Mohamed F, Allen S, Dissanayake W, Hittarage A, Azher S, Jeganathan K, Jayamanne S, Sheriff MHR, Warrell DA. Multiple-dose activated charcoal in acute self-poisoning: a randomised controlled trial. **Lancet** 2008;371:579-587 **IF:25.80**
4. Abeyasinghe R, Gunnell D. Psychological autopsy study of suicide in three rural and semi-rural districts of Sri Lanka. **Social Psychiatry and Psychiatric Epidemiology** 2008 February DOI 10.1007/s00127-008-0307-3 **IF: 1.58**
5. * Davies J, Buckley NA, Eddleston M. Poison Severity Scores for Organophosphate poisoning. **Quarterly Journal of Medicine** (accepted Jan 2008) **IF:2.77**
6. * Perera, PMS, Shahmy I, Gawarammana I, Dawson, AH. Comparison of two commonly practiced atropinisation regimens in acute organophosphorus and carbamate poisoning, doubling doses vs ‘*ad hoc*’ - a prospective observational study. **Human and Experimental Toxicology**. (accepted March 2008) **IF:1.12**
7. * Eddleston M, Eyer P, Worek F, Sheriff MHR, Buckley NA. Predicting Outcome using Butyrylcholinesterase Activity in Organophosphorus Pesticide Self-Poisoning. **Quarterly Journal of Medicine** 2008;(accepted Feb 2008) **IF:2.77**
8. * Manuweera G, Eddleston M, Egodage S, Buckley NA. Do Targeted Bans of Insecticides to Prevent Deaths from Self-Poisoning Result in Reduced Agricultural Output? **Environmental Health Perspectives** (accepted Jan 2008) **IF:5.86**
9. Li Y, Tse ML, Gawarammana I, Buckley NA, Eddleston M. Systematic review of controlled clinical trials of gastric lavage in acute organophosphorus pesticide poisoning. **Clinical Toxicology** (accepted Dec 2007) **IF:1.09**
10. * Wilks MF, Fernando R, Ariyananda PL, Eddleston M; Berry DJ, Tomenson JA, Buckley NA, Jayamanne S, Gunnell D, Dawson A. Improvement in survival after paraquat ingestion following introduction of a new formulation in Sri Lanka. **PloS Medicine** Vol. 5, No. 2, e49

11. * Samawickrema NA, Peiris-John R, Karunaratna M, Pathmeswaran A, Wickremasinghe AR, Buckley N, Dawson A, de Silva HJ. Environmental exposure of pregnant women and the foetus to organophosphate compounds in a rural farming community in Sri Lanka. **Clinical Toxicology** (accepted Nov 2007) **IF:1.09**
12. * Eddleston M, Haggalla S, Reginald K, Sudarshan K, Senthilkumaran M, Karalliedde L, Ariaratnam A, Sheriff MHR, Warrell DA, Buckley N. The hazards of gastric lavage for intentional self-poisoning in a resource poor location. **Clinical Toxicology** 2007;45(2):136-143. **IF:1.09**
13. * Davies J, Roberts D, Hittarage A, Buckley NA. Oral C-4 plastic explosive in humans – a prospective study. **Clinical Toxicology** 2007;45(5):454-457. **IF:1.09**
14. * Mohamed F, Senarathna L, Azher S, Sheriff MHR, Buckley NA, Eddleston M. Compliance for single and multiple dose regimens of superactivated charcoal: a prospective study of patients in a clinical trial, **Clinical Toxicology** 2007;45(2):132-135. **IF:1.09**
15. Eddleston M, Juszczak E, Buckley NA, Senarathna L, Mohamed F, Allen S, Dissanayake W, Hittarage A, Azher S, Jeganathan K, Jayamanne S, Sheriff MHR, Warrell DA. Study protocol: a randomised controlled trial of multiple and single dose activated charcoal for acute self-poisoning [ISRCTN02920054]. **BMC Emergency Medicine** 2007;7:2.
16. * Dassanayake T, Weerasinghe V, Dangahadeniya U, Kularatne K, Dawson A, Karalliedde L, Senanayake N. Cognitive processing of visual stimuli in patients with organophosphate insecticide poisoning. **Neurology** 2007;68:2027–2030 **IF:5.69**
17. Eddleston M, Haggalla S. Fatal injury in Eastern Sri Lanka, with special reference to cardenolide self-poisoning with *Cerbera manghas* fruits. **Clinical Toxicology** 2008 (in press)
18. * Dassanayake T, Weerasinghe V, Dangahadeniya U, Kularatne K, Dawson A, Karalliedde L, Senanayake N. Long-term event-related potential changes following organophosphorus insecticide poisoning. **Clinical Neurophysiology** Jan;119(1):144-50. Epub 2007 Nov 26 **IF:2.72**
19. * Manuel C, Gunnell DJ, van der Hoek W, Dawson A, Wijeratne IK, Konradsen F. Self-poisoning in Rural Sri Lanka: small-area variations in incidence. **BMC Public Health** 2008, 8:26doi:10.1186/1471-2458-8-26 **IF:1.60**
20. Eddleston M, Udayakumara N, Adhikari S, de Silva D, Sheriff MHR, Waidyaratne DL. The Importance of Poisoning vs. Road Traffic Injuries as a Cause of Death in Rural Sri Lanka **PLoS ONE** 2007;2(7): e599. doi:10.1371/journal.pone.0000599
21. * Gunnell D, Fernando R, Hewagama M, Priyangika WDD, Konradsen F, Eddleston M. The impact of pesticide regulations on suicide in Sri Lanka. **International Journal of Epidemiology** 2007; 36(6):1235-42. **IF:4.52**
22. * Konradsen F, Pieris R, Weerasinghe M, van der Hoek W, Eddleston M, Dawson AH. Community uptake of safe storage boxes to reduce self-poisoning from pesticides in rural Sri Lanka. **BMC Public Health** 2007, 7:134. **IF:1.60**

Review articles

23. Eddleston M, Buckley NA, Eyer P, Dawson AH. Medical Management of Organophosphorus Pesticide Poisoning (Invited review). **Lancet** 2008;371:597-607 **IF:25.8**
24. * Roberts D, Buckley NA. Pharmacokinetic Considerations in Clinical Toxicology: Clinical Applications (Invited Review). **Clinical Pharmacokinetics** 2007;46(11):897-939. **IF:4.12**

Invited commentary/editorials

25. * Dawson A, Buckley NA. Integrating approaches to paraquat poisoning (Invited Editorial). **Ceylon Medical Journal** 2007;52(2):45-47.

Research letters/case reports

26. Gunawardene G, Roberts D, Buckley NA. Randomised controlled trial of immunosuppression in paraquat poisoning. **Critical Care Medicine** 2007;35(1):330-331. **IF:6.60**
27. Roberts D, Ai P, Kaiyuan Z, Buckley NA. Extracorporeal blood purification for acute organophosphorus pesticide poisoning. **Journal of Intensive Care Medicine** 2007;22(2):124-126.
28. * Roberts DM, Dawson AH, Hittarage A, Jegenathen K, Sheriff, MHR, Buckley NA. Plasma alkalinisation for acute organophosphorus poisoning - is it a reality in the developing world? **Clinical Toxicology** 2007;45(1):90-91. **IF:1.09**
29. * Perera, PMS, Kularathne K, Gawarammana I. A case report of laryngeal oedema and metabolic acidosis after Omnicide® ingestion. **Clinical Toxicology** (accepted Dec 2007) **IF:1.09**

Submitted articles (not yet accepted)

30. * Moffatt A, Mohamed F, Azher S, Eddleston M, Buckley NA. The effects of organophosphate poisoning on thermoregulation in humans. **Critical Care** (submitted Feb 2008)
31. * Jayawardane P, Dawson AH, Weerasinghe V, Karalliedde L, Buckley NA, Senanayake N. Intermediate syndrome is a spectrum disorder: A prospective study of organophosphate poisoning. **PLoS Medicine** (submitted Nov 2007)
32. * Davies JO, Roberts DM, Eyer P, Buckley NA, Eddleston M. Hypotension in Severe Dimethoate Self-Poisoning. **Clinical Toxicology** (submitted Feb 2008)
33. * Weerasinghe M, Pieris R, Konradsen F, Dawson A Safe storage of pesticides in Sri Lanka - identifying important design features influencing community acceptance and use of safe storage devices **BMC Public Health** (submitted Dec 2007)
34. * Wickramasinghe K, Steele P, Dawson A, Dharmaratne D, Eddleston M, Gunawardane A, Senarathna L, de Silva D, Wijayaweera K, Konradsen F Financial costs to the government health care services for treating acute self-poisoning in a rural Asian district **Bulletin of the World Health Organization**. (submitted Feb 2008)

Other meetings (abstracts published in conference proceedings):

Oral Presentations

1. * Buckley NA. Controversies in paraquat poisoning (Invited Keynote presentation). **Asia Pacific Association of Medical Toxicology (APAMT) meeting**, Bangkok, December 2007
2. Eddleston M. Update on Insecticide poisoning (Invited Keynote presentation). **Asia Pacific Association of Medical Toxicology (APAMT) meeting**, Bangkok, December 2007
3. * Dawson A. Alternative Antidotes for Organophosphate Poisoning: Atropine, Pralidoxime and Beyond. (Invited Keynote presentation). **Asia Pacific Association of Medical Toxicology (APAMT) meeting**, Bangkok, December 2007
4. * Wilks MF, Tomenson JA, Buckley NA, Dawson A. Influence of gastric decontamination on patient outcome after paraquat ingestion. **Asia Pacific Association of Medical Toxicology (APAMT) meeting**, Bangkok, December 2007

5. * Perera P.M.S Shahmy S, Gawarammana I, Dawson AH. A prospective study on two atropine regimens in acute organophosphorus and carbamate poisoning. **Asia Pacific Association of Medical Toxicology (APAMT) meeting.** Bangkok, December 2007
6. * Mohamed FC, Roberts D, Palangasinghe C, Zawahir S, Jayamanne S , Jegenathen K , Eddleston M, Buckley N, Dawson A. Acute human self-poisoning with imidacloprid compound: A neonicotinoid insecticide **Asia Pacific Association of Medical Toxicology (APAMT) meeting.** Bangkok, December 2007
7. * Weerasinghe M, Pieris R, Konradsen F. Utilizing pesticide safe storage devices in village communities in Sri Lanka - a pilot study **Asia Pacific Association of Medical Toxicology (APAMT) meeting.** Bangkok, December 2007
8. * Manuel C, Gunnell DJ, van der Hoek W, Dawson A , Wijeratne IK , Konradsen F. Self-Poisoning in Rural Sri Lanka: Small-Area Variations in Incidence **Asia Pacific Association of Medical Toxicology (APAMT) meeting.** Bangkok, December 2007
9. * Shihana HSF , Dissanayake DM , Dawson A. Bedside screening test to determine methaemoglobin semi-quantitatively in patients with propanil self-poisoning **Asia Pacific Association of Medical Toxicology (APAMT) meeting.** Bangkok, December 2007
10. * Senarathna SMDKG, Sri Ranganathan S, Fernandopulle BMR. Cost-outcome description of management of patients with acute paracetamol poisoning **Asia Pacific Association of Medical Toxicology (APAMT) meeting.** Bangkok, December 2007
11. * Senarathna L, De Silva D, Buckley NA , Dawson AH. The pattern of initial treatments for poisoned patients in primary care hospital level in rural Sri Lankan districts: Are the standard protocols useful? **Asia Pacific Association of Medical Toxicology (APAMT) meeting.** Bangkok, December 2007
12. * Dassanayake T, Weerasinghe V, Dangahadeniya U, Kularatne K, Dawson A , Senanayake N. Long-lasting effects of acute organophosphorus insecticide poisoning on cognitive processing of visual information **Asia Pacific Association of Medical Toxicology (APAMT) meeting.** Bangkok, December 2007
13. * Jayawardane P, Dawson A, Senanayake N, Weerasinghe V, Buckley N, Eyer P. Biochemical Correlations of Acute Chlorpyrifos Poisoning **Asia Pacific Association of Medical Toxicology (APAMT) meeting.** Bangkok, December 2007
14. * Shukry M, Ashrafdeen M, Palagasinghe C, Dawson A, Gawarammana I, Buckley N, Mohamed F. Acute intentional self-poisoning with a selective herbicide Fenoxaprop-P-ethyl (FPPE). A prospective observational study. **Asia Pacific Association of Medical Toxicology (APAMT) meeting.** Bangkok, December 2007
15. * Dawson A, Mohamed F, Perera M, Gawarammana I, Jayamanne S, Karunathilake H, Abayasinghe C, Buckley N. A dose escalation study to determine the safety and efficacy of fructose 1, 6-diphosphate (FDP) in treating yellow oleander-induced cardiac toxicity. **Asia Pacific Association of Medical Toxicology (APAMT) meeting.** Bangkok, December 2007
16. * Dawson A, Fahim M, Gawarammana I, Buckley N, Eddleston M, Manuweera G. Relative toxicity of pesticides in the developing world. **Asia Pacific Association of Medical Toxicology (APAMT) meeting.** Bangkok, December 2007
17. * Dawson A, Eddleston M, Buckley N, Gawarammana I. Dying is too easy for death to be a “Hard Outcome” in the developing world. **Third International Clinical Trials Symposium.** Sydney, September 2007.

18. * Gawarammana I, Dawson A, Buckley N, Wilks M. Immunosuppression Treatment of Paraquat poisoning: Ethical dilemmas in the developing world. **Third International Clinical Trials Symposium**. Sydney, September 2007.
19. * Buckley NA. Acetylcysteine (Invited presentation). **Eleventh International Congress of Toxicology (ICTXI)**. Montreal July 2007.
20. * Eddleston M, Juszczak E, Buckley NA, Senarathna L, Mohamed F, Sheriff MHR, Warrell DA. Randomised controlled trial of routine single or multiple dose superactivated charcoal for self-poisoning in a region with high mortality. **Eleventh International Congress of Toxicology (ICTXI)**. Montreal July 2007.
21. * Dawson A. Sri Lankan Clinical Toxicology Research: Past, Present & Future. **Sri Lankan Medical Association Scientific Meeting** Colombo March 2007
22. * Dawson A. Inter-Regional Collaboration on Clinical Toxicology. **Hong Poison Centre Symposium**, Hong Kong April 21 2007
23. * Dawson A. (Invited Keynote Lecture) Multicentre International Research. **European Association of Poisons Centres & Clinical Toxicology Scientific Meeting**. Athens, May 2007
24. * Dawson A. Variability in Pesticide Toxicity: Integrating the clinical and research responses. **Iranian Toxicology Society Scientific Congress**. Shiraz, Iran May 2007
25. * Dawson A. Clinical Toxicology, Answering the Kandyan Challenge. **Kandy Society Medicine Foundation Sessions**. Kandy 3rd October 2007
26. * Senarathna SMDKG, Sri Ranganathan S, Dargan P, Fernandopulle BMR. Acute paracetamol poisoning: is the ingested dose a reliable indicator for N-acetylcysteine? **120th Scientific Congress Sri Lankan Medical Association** Colombo March 2007
27. * Jayawardane P. Effects of acute organophosphate poisoning on the neuromuscular junction. **120th Annual Scientific sessions Sri Lanka Medical Association**. Colombo 21st-24th March 2007
28. * Jayawardane P, Dawson A, Senanayake N, Weerasinghe V, Buckley N, Eyer P Time course of electrophysiological abnormalities in acute organophosphate poisoning and intermediate syndrome. **European Association of Poisons Centres & Clinical Toxicology Scientific Meeting**. Athens, May 2007
29. * Perera P.M.S Shahmy S, Gawarammana I, Dawson AH. A prospective study on two atropine regimens in acute organophosphorus and carbamate poisoning. **European Association of Poisons Centres & Clinical Toxicology Scientific Meeting**. Athens, May 2007
30. * Rajapakse B: The development of Emergency medicine in Sri Lanka **International Emergency Medicine Congress**, Cape Town, SA, Oct 4-6
31. * Rajapakse B. Emergency Medicine in Sri Lanka – Challenges to Training and Service. **Postgraduate Institute of Medicine 27th Annual Scientific Sessions** Colombo October 2007
32. * Fernando R. Study of suicides in the coroner's court, Colombo Sri Lanka **9th Indo-Pacific Congress on Legal Medicine & Forensic Sciences of the Indo-Pacific Association of Law, Medicine and Science**. Colombo, Sri Lanka, July 2007

Poster Presentations

33. * Rajapakse B, Jegenethan K, Buckley NA. The impact of the introduction of an Emergency Treatment Unit on the outcome of acutely poisoned patients presenting to a Sri Lankan General Hospital. **Asia Pacific Association of Medical Toxicology (APAMT) meeting**. Bangkok,

December 2007

34. * de Silva NGL , Gawarammana I , Ariyananda PL, Dawson AH. 'Prinso' poisoning in the southern province of Sri Lanka. **Asia Pacific Association of Medical Toxicology (APAMT) meeting.** Bangkok, December 2007
35. * Perera P.M.S, Kularathne K, Gawarammana I. A case report of laryngeal oedema and metabolic acidosis after Omnicide ingestion. **Asia Pacific Association of Medical Toxicology (APAMT) meeting.** Bangkok, December 2007
36. * Shahmy S, Suhitharan T, Sriskandarajah L, Dawson AH. Acute Human Self-Poisoning with the Substituted Aromatic (Organochlorine) Fungicide Chlorothalonil – Tetrachloroisophthalonitril **Asia Pacific Association of Medical Toxicology (APAMT) meeting.** Bangkok, December 2007
37. * Wickramasinghe K, Steele P, Dawson A, Dharmaratne D, Eddleston M, Gunawardane A , Senarathna L, de Silva D, Wijayaweera K, Konradsen F. Costs to Government Health Care Services of Pesticide Self-poisoning Treatments in Sri Lanka. **Asia Pacific Association of Medical Toxicology (APAMT) meeting.** Bangkok, December 2007
38. * Pieris R, Weerasinghe M, Konradsen F. Identifying key design issues for pesticides safe storage devices- a pilot study **Asia Pacific Association of Medical Toxicology (APAMT) meeting.** Bangkok, December 2007
39. * Fernando R. Acute paracetamol poisoning - a new epidemic in Sri Lanka. **Asia Pacific Association of Medical Toxicology (APAMT) meeting.** Bangkok, December 2007
40. * Dawson A. Propagation of evidence: WikiTox internet based open source curriculum in clinical toxicology. **Asia Pacific Association of Medical Toxicology (APAMT) meeting.** Bangkok, December 2007
41. * Manuel C, Gunnell DJ, van der Hoek W, Dawson A ,Wijeratne IK ,Konradsen F. Mapping intentional self-poisoning in Sri Lanka **Asia Pacific Association of Medical Toxicology (APAMT) meeting.** Bangkok, December 2007
42. * Manuweera G, Eddleston M, Egodage S, Gunnell D, Buckley NA. Do Targeted Bans of Insecticides to Prevent Deaths from Self-Poisoning Result in Reduced Agricultural Output? **Asia Pacific Association of Medical Toxicology (APAMT) meeting.** Bangkok, December 2007
43. * Moffatt A, Mohammed F, Eddleston M, Azher S, Buckley NA. The effects of organophosphorus poisoning on thermoregulation in humans. **Asia Pacific Association of Medical Toxicology (APAMT) meeting.** Bangkok, December 2007
44. * Shihana HSF, Dissanayake DM, Dawson A. A method of stabilizing blood for determination of methemoglobin. **Asia Pacific Association of Medical Toxicology (APAMT) meeting.** Bangkok, December 2007
45. * Roberts DM, Eddleston M , Eyer P, Senarathna L, Fahim M, Buckley NA. Toxicokinetic analyses in acute chlorpyrifos poisoning **Asia Pacific Association of Medical Toxicology (APAMT) meeting.** Bangkok, December 2007
46. * Senarathna SMDKG, Sri Ranganathan S, Soysa P, Fernandopulle BMR. Colorimetric Technique: a cheaper method to assess the risk of hepatotoxicity in patients with acute paracetamol poisoning. **Asia Pacific Association of Medical Toxicology (APAMT) meeting.** Bangkok, December 2007
47. * Senarathna L, De Silva D, Buckley NA , Eddleston M, Dawson AH. Effect of resource availability and medical staff workload on outcome for poisoning in rural Sri Lanka. **Asia Pacific Association of Medical Toxicology (APAMT) meeting.** Bangkok, December 2007

48. * Senarathna L, Adams J, De Silva D, Buckley NA, Dawson A. Personal and professional challenges in the management of deliberate self-poisoning in rural hospitals. Why some doctors feel “like frogs in a well”. **Asia Pacific Association of Medical Toxicology (APAMT) meeting**. Bangkok, December 2007
49. * Manuweera G, Eddleston M, Egodage S, Gunnell D, Buckley NA. Do Targeted Bans of Insecticides to Prevent Deaths from Self-Poisoning Result in Reduced Agricultural Output? **Eleventh International Congress of Toxicology (ICTXI)**. Montreal July 2007.
50. * Senarathna SMDKG, Sri Ranganathan S, Soysa P, Fernandopulle BMR. Costs of current management of acute paracetamol poisoning. **120th Annual Scientific sessions Sri Lanka Medical Association**. Colombo 21st-24th March 2007
51. * Senarathna SMDKG, Sri Ranganathan S, Fernandopulle R. Economic analysis of the current management of acute paracetamol poisoning in Sri Lanka **67th International Pharmaceutical Federation Annual sessions Beijing China** September 2007

Other meetings (abstracts not published in conference proceedings):

52. Dawson A, Suicide in Sri Lanka: Integrating capacity building research into clinical & societal responses. **Wellcome Networking Meeting, China** 28th October
53. Jensen NK, Kenborg L. Quality of Care for Deliberate Self-poisoning Patients - A qualitative study in Anuradhapura District, Sri Lanka. University of Copenhagen

List any other outputs:

(e.g. input into policy and practice; new links with National Health Department/Ministry; dissemination of results at national level, public engagement, etc.)

Policy changes

Import regulations on paraquat formulations have been amended to reduce all products concentration from 20% to 6.5%. In addition paraquat, dimethoate and fenthion are being withdrawn from the market over 3 years by effecting quotas on imports. We anticipate that these changes coupled with the documented effects of previous pesticide restrictions in the late 1990s (covered in Publications 7 and 20) will ultimately lead to the suicide rate in Sri Lanka being just 30-40% of its peak in 1995. We hope in the medium term this will have a flow on effect to other Asian states with high rates of fatal pesticide poisoning that do not have any public-health motivated pesticide restrictions.

Practice changes

The results of the current research have been incorporated into the national poison treatment guidelines which was published by the National Poisons Information Centre in 2007 and distributed to all public hospitals.

Theses

Darren Roberts PhD Australian National University
Tharaka Dassanayake MPhil University of Peradeniya

Poisoning texts

A new edition of the Sri Lankan Poisons Information Centre poisoning handbook was produced by Prof Ravindra Fernando. Many other members of SACTRC also commented or contributed to the revision process.

In addition, a number of monographs in on-line database have been written or updated by members of SACTRC (drawing on their research and clinical experience with SACTRC) within the last year these have been propagated to a number of information providers including Toxinz, Wikitox, HyperTox, WHO guidelines:

SECTION E - Networks

Indicate whether the project attracted funding additional to the ICRG grant. Tick Yes or No for each and specify name of the funder and scheme where applicable.

	YES	NO	Details of funding source and interaction with ICRG grant
Host institution (internal)			
Wellcome Trust		X	
NHMRC		X	
HRC		X	
Other Government competitive funds	X	X	PhD Scholarships from AusAid to Tharaka Dassanayake and Indika Gawarammana Total \$400,000
Government non-competitive funds	X		.
Funds from industry	X		Syngenta - \$250,000. Funding for the paraquat reformulation follow up study and the immunosuppression trial
Other competitive funds	X		University Copenhagen -\$128,000. Support of safe storage project and Danish Public Health student research into poisoning APAMT Travel Scholarships \$4,000
Other non-competitive funds		X	

SECTION F - Certification

I certify that:

1. All Principal Investigators agree that this report is an accurate representation of the progress to date of the funded project; and
2. Relevant Institutional Approvals have been maintained to date in accordance with Clause 2.2 of the Deed of Agreement (NHMRC).

<p>Name of Principal Investigator (Australia/New Zealand):</p> <p style="text-align: center;">Nick Buckley</p> <p>Signature of Principal Investigator</p> <p>.....</p>	<p>Date</p> <p style="text-align: center;">.15.../..3../..2008.</p>
<p>Name of Principal Investigator (Developing country):</p> <p style="text-align: center;">Nimal Senanayake</p> <p>Signature of Principal Investigator</p> <p>...../...../.....</p> <p>.....</p>	<p>Date</p> <p style="text-align: center;">...../...../.....</p>
<p>Name of Head of Department of institute administering the award (Australia/New Zealand):</p> <p>Signature of Head of Department</p> <p>.....</p>	<p>Date</p> <p style="text-align: center;">...../...../.....</p>
<p>Name of Responsible Officer or delegate (Australia/New Zealand institute):</p> <p>Signature of Responsible Officer or delegate</p> <p>.....</p>	<p>Date</p> <p style="text-align: center;">...../...../.....</p>
<p>Contact phone number of Responsible Officer or delegate (Australia/New Zealand institute):</p>	