



National Poisons Information Service

Annual Report 2010/2011



National Poisons Information Service

Commissioned by the Health Protection Agency through its Centre for Radiation, Chemical and Environmental Hazards

The main role of the National Poisons Information Service is to advise NHS healthcare professionals on the diagnosis, treatment and care of cases of poisoning across the UK. Poisoning is an extremely common cause of hospital admissions in the NHS, being numerically similar to admissions for myocardial infarction. In addition, many cases of suspected poisoning are managed out of hospital following advice provided by the NPIS, thus reducing unnecessary use of NHS resources. The major workload falls on hospital emergency departments, but minor injuries units and primary care services also make major contributions – the latter to a large extent involving NHS telephone helplines (NHS Direct and NHS 24).

NPIS Units at 31 March 2011

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NPIS Cardiff Unit

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NPIS Edinburgh Unit

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Foreword

The National Poisons Information Service (NPIS) annual reports are published as statements of accountability and governance to its commissioners, the Health Protection Agency, as well as to the funding bodies for the service – the Department of Health in England, the Scottish Government, the Welsh Government, the Department of Health, Social Services and Public Safety for Northern Ireland and Beaumont Hospital, Dublin, on behalf of the Government of the Republic of Ireland.

The report for 2010/11 demonstrates the volume and quality of the work performed by the NPIS in providing essential support to front-line healthcare professionals in the management of the large numbers of people who present following suspected exposure to potential toxins. The complexity of this task is amplified by the large numbers and types of drugs and chemicals that are involved.

The report also demonstrates the value of NPIS activity data for public health surveillance purposes for following trends in enquiries related to poisons of interest, such as emerging recreational drugs or more established hazards such as carbon monoxide and pesticides. In addition, the report provides valuable information to support local commissioning of preventive programmes.

Following the establishment of Public Health England the commissioning arrangements for the NPIS may change. This report shows the NPIS to be an essential, high quality, cost-effective front-line service that is valued by the many NHS healthcare professionals who use it each year. We are confident of maintaining this position into the future.

Once again, the NPIS has had a very busy and productive year. The service has achieved a level of stability in its staffing and has, for the first time ever, written or revised around 4,000 entries on its online database, TOXBASE[®], during the course of the year, almost a third of the total.

Congratulations to all staff involved in such a challenging achievement.

Elaine Lynch-Farmery

Centre for Radiation, Chemical and Environmental Hazards, Health Protection Agency

Simon Thomas Chair, NPIS Clinical Standards Group

For	reword		1			
Exe	ecutive	Summary	3			
1	Introduction					
2	NPIS	Advice Service Structure	6			
3	NPIS	Activities in 2010/11	8			
	3.1	Overall Service Profile	8			
	3.2	Consultant Referrals	13			
	3.3	UKTIS	16			
	3.4	Product Data Centre	22			
	3.5	Current Awareness in Clinical Toxicology	22			
4	Clin	ical Governance	23			
	4.1	Analysis of Critical Events	23			
	4.2	Quality Assurance Exercises	24			
	4.3	Education and Training	26			
5	Area	as of Interest in 2010/11	29			
	5.1	Drugs of Misuse	29			
	5.2	Pesticide Poisonings	34			
	5.3	Carbon Monoxide	35			
	5.4	Antidote Availability	37			
	5.5	Toxic Alcohols and Glycols	38			
6	Reco	ommendations	40			
Ap	pendix	A NPIS Staff	41			
Ap	pendix	B Publications in 2010/11	45			



Background

The National Poisons Information Service provides information and advice to support the management of people admitted to hospitals with exposure to suspected poisons each year and the many seen and not admitted, or seeking advice in the community. This information is provided via the poisons information database TOXBASE[®] and, if needed, via the NPIS 24-hour telephone service. Support from a consultant clinical toxicologist is available at all times. The NPIS also provides the UK Teratology Information Service (UKTIS), which is the national source of information and advice about exposures to drugs and chemicals during pregnancy.

Activity

During 2010/11 there were 510,000 TOXBASE user sessions (1,420,000 separate product accesses), a 2.9% reduction on the previous year. NPIS telephone enquiries numbered almost 51,000, a fall of 4.9% compared with 2009/10, but over 1,500 of these enquiries were referred to a NPIS consultant, which is a 22.7% increase on the previous year. There were, in addition, 38,000 accesses to the information held on TOXBASE concerning exposure to drugs and chemicals in pregnancy (an increase of 4.5%) and 3,700 telephone enquiries to UKTIS.

Maintaining the 14,000 product entries in the TOXBASE database is the major workload for NPIS staff, but it is essential that this is done effectively to retain the confidence of healthcare professionals, allowing telephone call numbers to be maintained at manageable levels. During 2010/11 NPIS staff wrote or revised around 4,000 entries, almost a third of the total. These figures include 100 pregnancy exposure monographs, an increase of 85% on the number of pregnancy monographs written or revised in 2009/10.

Quality

There continues to be evidence of the high quality of services provided, with a low rate of critical incidents and excellent user approval ratings for TOXBASE (91%), NPIS telephone enquiries (96.5%) and UKTIS telephone enquiries (93%).

Surveillance

Data from the NPIS are useful for public health surveillance activities. Four issues of interest are highlighted in this report, as follows.

Drugs of misuse

NPIS data have demonstrated substantial reductions in enquiry numbers relating to mephedrone since this drug was controlled under misuse of drugs legislation in April 2010; enquiries relating to naphyrone and desoxypipradrol, which increased briefly after the legal control of mephedrone, have also become uncommon following further control measures. Enquiry numbers relating to other emerging agents remain low but continue to be monitored.

Pesticides

The NPIS has collected detailed information on exposure to pesticides since 2004, of which glyphosate, paraquat and organophosphorus insecticides have been most commonly encountered. Following accidental exposure, serious clinical features have been uncommon, with two deaths reported from almost 2,200 episodes. Higher rates of mortality occurred following deliberate self-harm using these agents, with organophosphorus insecticides (14%) and paraquat (13%) associated with a higher case fatality than glyphosate (7%).

Carbon monoxide

Poisoning with carbon monoxide continues to be an important preventable cause of morbidity and mortality. There were 286 telephone enquiries to the NPIS concerning this toxin during 2010/11, involving at least 385 individuals. Most exposures occurred in the home, with central heating boilers the most common source. While most episodes were associated with limited clinical effects, there were seven cases with severe poisoning, of which two are known to have died.

Toxic alcohols and glycols

Poisoning with these agents, including ethylene glycol and methanol, is not common, but when it does occur it can be severe and is one of the most common reasons for referral to an NPIS consultant. During the 2010 calendar year there were over 600 enquiries relating to these agents, of which 182 were systemic exposures; 99 of these required an antidote and 33 patients required haemodialysis and/or

 $[\]mathsf{TOXBASE}^{\odot}$ is a registered trademark of the UK National Poisons Information Service.

haemofiltration. Difficulties in obtaining the specialist assays and antidotes required for optimal management of this type of poisoning were often encountered.

Antidote availability

Antidotes are important for the management of some poisons, but there have been incidents when appropriate antidotes have not been available to treat patients who need them. The NPIS with the College of Emergency Medicine (CEM) issued guidance on stocking of antidotes by NHS trusts in 2008. During 2010/11 an audit of antidote holdings by hospitals was performed by the NPIS and CEM. While most commonly used antidotes were widely available, holdings of less commonly used antidotes were suboptimal. For example, the proportion of NHS trusts stocking pralidoxime (for organophosphorus insecticide poisoning) was 33% and viper venom antiserum was 50%. About 5% of hospitals stocked no antidotes for cyanide poisoning and 15% had no antidote available for treating poisoning with ethylene glycol or methanol.

Research

NPIS staff continue to be active in research, with over 90 contributions to the scientific literature, one-third of which were peer-reviewed papers, published during 2010/11.



Information on the work of the National Poisons Information Service (NPIS) in 2010/11 is given in this report. The report illustrates the increased activity in the UK Teratology Information Service (UKTIS) and highlights some areas of interest, including trends in enquiries on drugs of abuse, the UK exposures to toxic alcohols and glycols, and carbon monoxide exposures reported in 2010/11, together with work on symptoms from pesticide exposures and a survey of antidote holdings in UK hospitals.

The NPIS is a network of specialist units commissioned by the Health Protection Agency (HPA) on behalf of the UK health departments. All the units are linked to clinical treatment facilities within UK teaching hospitals.

The NPIS has provided information by telephone since 1963. The poisons information database, TOXBASE[®] (www.TOXBASE.org), introduced in 1982, was transferred to the internet and adopted as the first-line information source for healthcare professionals in the UK in 1999. While the structure of the NPIS has changed, the focus of the service has always been to assist colleagues in all parts of the NHS to manage cases of poisoning. The information and advice provided by the NPIS is updated regularly and is based on published literature, experience from NPIS telephone enquiries data and direct clinical experience of poisoning managed in NPIS-linked clinical departments.

Since 1995 UKTIS has been based in Newcastle as an integral component of NPIS activities. The activity of UKTIS is important both in supporting women of child-bearing age and their healthcare providers, and in collecting information on the potential effects of exposure to drugs and chemicals in pregnancy, including the therapeutic use of medicines.

Poisoning continues to be an important public health issue in the UK. It accounts for around 120,000 NHS hospital admissions in England each year (just under 1% of the total number), thus creating a significant workload for health service staff. Hospital emergency departments and minor injuries units are particularly involved. A major component in adults is related to self-harm, but accidental ingestion is common in children. Many thousands of different agents can be involved, and the appropriate management of poisoning is therefore a major, complex task for the NHS, especially when new or unfamiliar agents are involved. In addition, many adult ingestions also involve ethanol, making clinical assessment and management more difficult. A further concern is the holding as 'pets' of venomous exotic snakes and arthropods which require specific antidotes that are not held by NHS hospitals.

Over the past decade there has been a steady increase in patient admissions from poisoning to hospitals in England, from around 82,000 poisoning-related admissions in 2002/03 to just under 120,000 in 2009/10. Adding to the burden are new emerging trends; new drugs of abuse present a particular challenge. The patterns of prescription drugs taken has changed in line with new approaches to therapy. Newer antidepressants and antipsychotic drugs are increasingly involved, as older and often more toxic agents have been withdrawn. Furthermore, hospital admission data, illustrated by NHS finished consultant episodes, do not reflect the very many attendances to emergency departments of patients who do not require admission, nor the large numbers of enquiries through NHS public access helplines (NHS Direct in England and Wales and NHS 24 in Scotland), which are handled using information provided by the NPIS. The NPIS thus provides information to support and assist appropriate triage, referral, assessment and treatment of patients in all settings within the NHS.

The majority of people dying from poisoning do so before healthcare assistance is summoned. Nevertheless, there are still opportunities to improve care for those with more severe poisoning, thus reducing morbidity or mortality. At the same time NPIS advice reduces the need for unnecessary hospital attendance by those who have been exposed to substances of relatively low toxicity.

A key component of the work of the NPIS is obtaining information from treating clinicians on the effects and ultimate outcomes of cases of severe or unusual poisoning. This assists the service in providing current, accurate advice. A better interaction on this aspect is needed from NPIS users, and the NPIS seeks their future collaboration in improving feedback.

The NPIS is funded primarily through 'Government Grant in Aid' from the UK health departments, but receives some contract income and research income for specific projects, notably in 2009 the award of a three-year project from the Health and Safety Executive concentrating on monitoring health effects of exposures to pesticides and biocides.

 $[\]mathsf{TOXBASE}^{\circledast}$ is a registered trademark of the UK National Poisons Information Service.

The NPIS provides a 24-hour consultant-supported clinical toxicology advice service on the diagnosis and management of poisoning, including the clinical effects of exposures arising from chemical incidents and accidents.

The four NPIS units are currently based within NHS teaching hospital 'providers' (two in England and one each in Scotland and Wales):

- Cardiff and Vale University Health Board
- Newcastle upon Tyne Hospitals NHS Foundation Trust
- NHS Lothian University Hospitals Division
- Sandwell and West Birmingham Hospital NHS Trust.

The service has 24-hour consultant clinical toxicologist support provided by NHS consultant staff in all four NPIS units and colleagues in two other NHS hospitals (Guy's and St Thomas' NHS Foundation Trust and York Hospitals NHS Foundation Trust). NPIS consultant clinical staff also provide specialist clinical services to their local populations.

Over the past few years there has been an expansion in the number of consultant staff available to assist colleagues in the management of more seriously unwell cases. Some consultants working within the NPIS are now based in acute hospitals geographically separate from the four main NPIS units. This expansion in the availability of expertise is important for UK resilience. Since the NPIS also receives many enquiries about children, it has formalised existing support from expert paediatricians, particularly to assist in the review of standard advice for the management of poisoning in children.

The primary source of information provided by the NPIS is its online database, TOXBASE (www.TOXBASE.org), which is available free to all UK NHS healthcare professionals who register, including hospital staff, primary care and public health physicians, and NHS Direct and NHS 24 services. The NPIS also provides a 24-hour telephone information service for healthcare professionals using a single national telephone number (0844 892 0111) when further advice or information is needed. Enquiries are answered by specialists in poisons information (SPI); complex enquiries can be referred on to NPIS consultant staff as necessary on a 24-hours-a-day basis. All NPIS telephone enquiries are now recorded for governance purposes and data logged within a specially designed national database (UKPID). Data are uploaded on to a central server, allowing patient data to be accessed by other NPIS units that subsequently become involved in the management of that case and provision of easily accessible national data on the activity of the service and the patterns of enquiries received. The information available can then be used to inform clinical management of subsequent similar cases. Data from UKPID can also be used to support UK pharmaceutical licensing decisions by the Medicines and Healthcare products Regulatory Agency, and for studying the epidemiology of poisoning as reported to the NPIS.

In Northern Ireland, the Regional Medicines and Poison Information Service in Belfast provides a daytime poisons information service, with out-of-hours enquiries from healthcare professionals referred to the NPIS. The NPIS is also contracted to provide poisons information for users in the Republic of Ireland: TOXBASE is provided to major hospital emergency departments and to the National Poisons Information Centre in Dublin. Out-of-hours telephone support is provided by the NPIS.

Information on the potential toxicity of drugs and chemicals in pregnancy is provided by UKTIS. Information on aspects of the toxicity of drugs and chemicals in pregnancy is increasingly being made available on TOXBASE.

In order to maintain a consistent approach, irrespective of the NPIS provider unit answering an enquiry, it is essential to have national mechanisms for addressing issues that affect the service. A key development over recent years has been the formalisation of such arrangements within a UK strategic framework.

Commissioning issues are dealt with by the HPA NPIS Commissioning Group, which meets quarterly (or more often if required). Clinical issues, including clinical governance matters, are discussed at the NPIS Clinical Standards Group, which also meets quarterly, on the same day as the HPA NPIS commissioning meetings. These meetings are attended by a representative of the commissioner, a senior clinician from each provider unit, and a senior specialist in poisons information. Invitations are also sent to representatives of the National Poisons Information Centre in Dublin. Operating procedures are updated frequently and made available to NPIS staff via TOXBASE.

To ensure a common and evidence-based approach to the clinical management of poisoning, all NPIS clinical and information staff are invited to attend continuing professional development (CPD) meetings which deal with new data and important clinical issues. These occur three times a year and have now been taking place for five years. Each provider unit hosts the event in turn.

There are regular meetings and teleconferences of the TOXBASE Editing Group and the UKPID User Group. These also have representation from each provider unit and discuss issues relating to these IT platforms. The National Poisons Information Centre in Dublin and the Northern Ireland Regional Medicines and Poison Information Service also contribute to TOXBASE development.



How poisons enquiries are answered

3.1 Overall Service Profile

This report concentrates on NPIS activity in 2010/11, as reflected by TOXBASE user sessions, TOXBASE accesses, telephone enquiries and consultant referrals. The increasing use now being made of TOXBASE allows specialist staff to perform more strategic work for the service, ensuring that TOXBASE monographs are reviewed and updated in a timely, systematic manner.

The total number of TOXBASE user sessions (defined as one logon to the TOXBASE site during which the user may have accessed one or more products several times) was 509,503. This is a decrease of 2.9% on the number of sessions in 2009/10 (Figure 3.1), but remains above the levels in 2007/08. New software was implemented in 2008/09 accounting perhaps for the particular rise in that year, but overall the number of user sessions appear to be approaching a plateau.

The number of user sessions includes 4,513 educational sessions, an increase of 12.4% on the 2009/10 figure.

Sessions from all the NPIS units and from the Northern Ireland Regional Medicines and Poison Information Service have been excluded from further detailed analyses, as these units may access TOXBASE for training/educational purposes, for operating procedures or for monograph-writing purposes (NPIS units only), as well as for telephone answering. Therefore a total of 465,111 sessions originating in England, Northern Ireland, Scotland and Wales have been analysed further in this report. Sessions originating overseas are presented elsewhere (see Box 3.1, page 11).

There were 1,422,673 individual product accesses in 2010/11; applying the same criteria as for session data, 1,121,300 product accesses have been analysed further.

The total number of telephone enquiries received by the NPIS in 2010/11 was 54,538 (including 3,722 calls made to UKTIS; see page 16); this is a decrease of 5.2% from 2009/10 (Figure 3.1). The analyses presented in this report include only telephone enquiries to the NPIS which related to patients, of which there were 49,595. These data include the 1,528 referrals for specialist advice from NPIS consultants.

Table 3.1 shows the number of poisons enquiries from UK countries and relates these to population size. Table 3.2 shows the variation in TOXBASE use by strategic health authorities in England compared with use in Northern Ireland, Scotland and Wales. On the whole, telephone enquiries received and TOXBASE usage relative to population size have decreased apart from in North East England, where TOXBASE usage is up 8.9% on last year's figure.



FIGURE 3.1 Telephone enquiries and TOXBASE sessions from 2000 to 2010/11 (data for 2000–2003 by calendar year; subsequent years by financial year) (data from 2009/10 onwards include UKTIS telephone enquiries and pregnancy monograph accesses)

Figure 3.2 shows that hospital departments and NHS Direct/ NHS 24 users are responsible for the majority of TOXBASE

TABLE 3.1 Origin of poisons enquiries to the NPIS in 2010/11						
Telephone enquiries (about individual patients)		TOXBASE sessions Combined total			otal	
Country	Number	Rate per 100,000 population*	Number	Rate per 100,000 population*	Number	Rate per 100,000 population*
England	41,265	79.6	376,657	727.0	417,922	806.6
Northern Ireland	566	31.6	10,620	593.7	11,186	625.3
Scotland	2,063	39.7	49,807	958.9	51,870	998.6
Wales	3,442	114.8	28,027	934.4	31,469	1,049.2

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* Based on 2009 estimates from www.statistics.gov.uk/statbase/Product.asp?vlnk=15106, accessed June 2011 (and given in Table 3.2)

Strategic health authority	Number of TOXBASE sessions	TOXBASE sessions per 100,000 population	Population estimate (mid-2009)*
East Midlands	29,888	671.4	4,451,200
East of England	39,405	683.3	5,766,600
London	44,702	576.5	7,753,600
North East	25,122	972.1	2,584,300
North West	59,665	865.0	6,897,900
South Central	33,106	808.4	4,095,400
South East Coast	20,763	478.4	4,340,300
South West	39,183	749.0	5,231,200
West Midlands	39,687	730.7	5,431,100
Yorkshire and the Humber	45,136	858.4	5,258,100
-	10,620	593.7	1,788,900
-	49,807	958.9	5,194,000
-	28,027	934.4	2,999,300
	Strategic health authority East Midlands East of England London North East North West South Central South Central South East Coast South West West Midlands Yorkshire and the Humber - -	Number of TOXBASE sessionsStrategic health authorityTOXBASE sessionsEast Midlands29,888East of England39,405London44,702North East25,122North West59,665South Central33,106South East Coast20,763South West39,183West Midlands39,687Yorkshire and the Humber45,136-10,620-28,027	Number of TOXBASE sessionsTOXBASE sessions per 100,000 populationEast Midlands29,888671.4East of England39,405683.3London44,702576.5North East25,122972.1North West59,665865.0South Central33,106808.4South East Coast20,763478.4South West39,837749.0West Midlands39,68730.7Yorkshire and the Humber45,136593.7I10,620593.7I93,807958.9I28,027934.4

TARIF 3 2	Regional	distribution	of TOXBASE	sessions in	2010	/11
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* From www.statistics.gov.uk/statbase/Product.asp?vlnk=15106, accessed June 2011 (England total = 51,809,700)



FIGURE 3.2 Telephone enquiries and TOXBASE sessions by type of user in 2010/11

sessions; 288,062 (63.4%) and 126,620 (27.8%), respectively. In contrast, telephone enquiries received were distributed more evenly across hospital, primary care and NHS Direct/ NHS 24 users, 15,287 (30.8%), 14,617 (29.5%) and 10,817 (21.8%), respectively. This is because, as in previous years, GPs are more likely to call the NPIS than access TOXBASE.

The largest number (249,312 or 86.5%) of TOXBASE sessions were from emergency departments (Table 3.3). The second largest group of hospital users were medicines information departments and pharmacies (25,723 or 8.9%). Of the telephone enquiries, 44.3% (21,978) were made by doctors and 41.4% (20,559) by nurses; these proportions are almost identical to those in previous years.

TABLE 3.3 Hospital session data by department

Department	Number of sessions
Emergency	249,312
Medicines information and pharmacy	25,723
Admission/assessment	2,450
Poisons ward	1,825
Psychiatry	1,664
Paediatric	1,405
General medicine	674
Intensive care/treatment	787
Biochemistry and other laboratories	868
Other	2,897

The ages of patients who were the subject of telephone enquiries are shown in Figure 3.3; over a quarter (28.8%) involved children under the age of five years. Patients were female in 52% of telephone enquiries. These figures for age and sex distribution are similar to those in previous years.

Figure 3.4 shows the type of poisonings reported to the NPIS during telephone enquiries in 2010/11; the largest single category was accidental ingestions. Exposures in the home accounted for 86.7% of enquiries, while 2.7% were in the workplace and 2.1% in hospital or medical facilities. The majority (87.2%) of enquiries related to ingestion, while 3.7% related to inhalation, 1.4% to injection, 2.4% to eye contact and 2% to skin contact.



FIGURE 3.3 Age of poisoned patients reported in telephone enquiries to the NPIS in 2010/11



FIGURE 3.4 Types of poisonings reported in telephone enquiries to the NPIS in 2010/11

The types of agents that were the subject of TOXBASE sessions and telephone enquiries are shown in Figure 3.5. For both datasets pharmaceuticals are the most common source of enquiries (69.1% and 63.4%, respectively).

Table 3.4 shows the ten pharmaceutical agents that were the most frequent subject of telephone enquiries and TOXBASE accesses. It should be noted that the number of enquiries and accesses listed for paracetamol do not include those for compound analgesics (e.g. those containing both paracetamol and codeine), which are counted separately. The pattern of enquiries and accesses is similar to those in the previous



TOXBASE sessions

FIGURE 3.5 Types of agents involved in telephone enquiries and that users accessed during TOXBASE sessions in 2010/11

BOX 3.1 Non-UK and Subscription Users of the NPIS

The NPIS provides out-of-hours telephone support under contract to the Republic of Ireland. During 2010/11 there were 1,920 telephone enquiries routed to the NPIS national telephone service from this source. NPIS units also received 281 telephone enquiries from outside the British Isles.

As well as the out-of-hours contract, the NPIS provides TOXBASE specifically tailored to medical professionals in the Republic of Ireland; in 2010/11 there were 9,674 TOXBASE sessions made by 62 registered Irish users. There were 24,672 individual TOXBASE accesses and the majority of Irish accesses originated in hospital emergency departments.

TOXBASE is provided under special agreements to users in over 40 countries outside the British Isles; 12,705 TOXBASE sessions were made by these users, with those in Brazil (19%), Belgium (16%), Australia (13.5%) and Hong Kong (8.5%) the most frequent users, a pattern similar to that for last year. The majority of sessions were made by poison centres (42%) and hospital departments (12%).

	-3				
Telephone enquiries		TOXBASE accesses			
Agent	Number of enquiries	Agent	Number of accesses		
Paracetamol*	6,058	Paracetamol*	76,728		
Ibuprofen	2,447	Ibuprofen	40,028		
Co-codamol [†]	1,228	Salicylates [‡]	23,739		
Citalopram	1,054	Citalopram	22,832		
Diazepam	951	Diazepam	20,142		
Zopiclone	924	Zopiclone	17,226		
Salicylates [‡]	903	Compound analgesics [†]	15,795		
Codeine	693	Fluoxetine	14,230		
Fluoxetine	684	Tramadol	13,083		
Tramadol	656	Amitriptyline	12,307		
* Does not include compound analgesics					
† Containing paracetamol and codeine					

TABLE 3.4 Pharmaceutical agents: top telephone enquiries and TOXBASE accesses in 2010/11

TABLE 3.5 Pharmaceutical agents: to	o TOXBASE accesses by UK, Republic o	f Ireland and overseas users in 2010/11
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	UK		Republic of Ireland		Overseas	
Rank	Agent	Count (% of total)	Agent	Count (% of total)	Agent	Count (% of total)
1	Paracetamol*	76,728 (6.8%)	Paracetamol*	1,431 (5.8%)	Paracetamol*	596 (3.0%)
2	Ibuprofen	40,028 (3.6%)	Diazepam	679 (2.7%)	Ibuprofen	267 (1.3%)
3	Salicylates [‡]	23,739 (2.1%)	Zopiclone	592 (2.4%)	Amitriptyline	197 (1.0%)
4	Citalopram	22,832 (2.0%)	Ibuprofen	552 (2.2%)	Carbamazepine	186 (0.9%)
5	Diazepam	20,142 (1.8%)	Escitalopram (as oxalate)	436 (1.8%)	Piperonyl butoxide	185 (0.9%)
6	Zopiclone	17,226 (1.5%)	Compound analgesics [†]	393 (1.6%)	Clonazepam	184 (0.9%)
7	Compound analgesics [†]	15,795 (1.4%)	Salicylates [‡]	387 (1.6%)	Diazepam	168 (0.8%)
8	Fluoxetine	14,230 (1.3%)	Quetiapine	376 (1.5%)	Sertraline	159 (0.8%)
9	Tramadol	13,083 (1.2%)	Venlafaxine	369 (1.5%)	Salicylates [‡]	159 (0.8%)
10	Amitriptyline	12,307 (1.1%)	Alprazolam	359 (1.4%)	Fluoxetine	145 (0.7%)
* Does	* Does not include compound analgesics					
† Conta	aining paracetamol	and codeine				

‡ Includes aspirin

two years, with analgesics and antidepressants predominating. For comparison, the ten pharmaceutical agents that were the most frequently accessed on TOXBASE by users in the UK, Republic of Ireland and overseas are given in Table 3.5.

Table 3.6 shows the household agents most frequently accessed during TOXBASE sessions in 2010/11; as previously, by far the most commonly viewed were surfactants and bleaches.

TABLE 3.6 Household agents by ingredients: top TOXBASE accesses in 2010/11

Agent	Number of accesses
Surfactants plus detergents (e.g. washing powders, washing up liquids and 'liquitabs')	26,291
Bleaches	15,691
Ethylene glycol or methanol (e.g. antifreeze)	4,583
Isopropanol (e.g. hand gels and screen washes)	3,986
Batteries	1,996
Petroleum distillates	1,963
Silica gel	1,426
White spirit (e.g. paints and varnishes)	1,382
Cyanoacrylate (e.g. glues)	1,351
Descalers	1,311

BOX 3.2 TOXBASE Editing

With the increased use of TOXBASE by healthcare professionals as the first, and often only, source of advice, it is essential that the information it contains is kept as up to date as possible. Because of the numbers of monographs involved, this is a very substantial workload, which is shared by all the NPIS units. TOXBASE entries that are new to the database and major updates are circulated to all the NPIS units for review before going 'live'. The database is updated on a daily basis.

The HPA NPIS TOXBASE Editing Group includes representatives of clinical and information staff from all the NPIS units, together with representatives from related poisons centres, a public health physician and a scientist from the HPA Centre for Radiation, Chemical and Environmental Hazards. It meets around four times a year (two face-to-face meetings and two web/teleconferences) to agree policy for TOXBASE development, discuss the format of TOXBASE monographs, and agree and prioritise work programmes on the database content.

Areas of clinical controversy or uncertainty are discussed at regular meetings or teleconferences of the TOXBASE Editing Group or by the NPIS Unit Directors at the quarterly NPIS Clinical Standards Group meetings. Monthly literature reviews are circulated as *Current Awareness in Clinical Toxicology* (see Section 3.5), to assist in updating TOXBASE.

The NPIS aims to review each of the approximately 14,000 entries on TOXBASE at least every four years. During 2010/11, 3,947 entries were written or revised.

An important component in the review process is clinical data from users, especially on new products or unusual symptom patterns. We encourage all users to feed back information to NPIS by the forms on TOXBASE, via email, letter or telephone.

3.2 Consultant Referrals

Background

The NPIS has operated a national consultant clinical toxicology on-call rota since May 2005. Currently thirteen consultant clinical toxicologists from the four NPIS units (Birmingham, Cardiff, Edinburgh and Newcastle) participate, as well as three consultants from hospitals in York and London who also contribute to out-of-hours cover (18.00 to 09.00 hours Monday to Thursday, weekends and public holidays) for the UK and the Republic of Ireland. All staff on the rota are involved in the care of poisoned patients in their own local NHS poisons treatment facilities. A nationally agreed protocol is used to determine when specialists in poisons information should refer enquiries to a consultant. The national consultant rota is managed from NPIS Edinburgh; precise arrangements have been described in previous annual reports.

For telephone enquiries, details of the original call are available on the UKPID central server for audit and checking, and the call reference number is sent to the relevant consultant for audit purposes. In addition, consultants keep contemporaneous local records of advice given, which are passed to the NPIS unit that took the original call for addition to the call record. For the purposes of collating and auditing consultant referrals, NPIS Cardiff can export data from UKPID for analysis.

Referrals

There were 1,528 referrals made to NPIS consultants (daytime and out-of-hours) in 2010/11, an increase of 22.7% on 2009/10, but similar to referrals in 2008/09. Figure 3.6 shows the number of referrals by three-month period since April 2006.

The distribution by day of week is shown in Figure 3.7, with fewer referrals at the weekend. The average number of referrals per day was 4.2, with a range of 0–16 referrals. Consultant referrals by country are shown in Table 3.7.

The vast majority of consultant referrals came from hospitals (1,359 referrals or 88.9%), with GPs (105; 6.9%), NHS Direct/ NHS 24 (14; 0.9%) and others (40; 2.6%) making much smaller contributions. Hospital referrals by department are shown in Table 3.8. There was a slight decrease in the proportion of referrals from units other than emergency departments, compared with the previous year.



FIGURE 3.6 Quarterly NPIS consultant referrals (including out-of-hours and workday referrals) since April 2006

Country	Number of referrals	Poto por 100 000 population*	0/ 2010/11	
TABLE 3.7	NPIS consultant referrals by country in 2	010/11, with 2009/10 for comparis	on	

Country	Number of referrals	Rate per 100,000 population*	% 2010/11	% 2009/10
England	1,144	2.2	74.9	73.2
Northern Ireland	20	1.1	1.3	1.6
Scotland	245	4.7	16.1	15.8
Wales	77	2.6	5.1	6.9
Republic of Ireland	35	-	2.3	1.8
Other	7	-	1.5	0.7
Total	1,528			

* Based on 2008 estimates from www.statistics.gov.uk/cci/nugget.asp?id=1352, accessed June 2011

TABLE 3.8 NPIS consultant referrals from hospital by department in 2010/11				
Department	Number of referrals	% of total		
Emergency and minor injuries units	534	34.9		
High dependency and intensive care/treatment units	296	19.4		
Paediatric	112	7.3		
General medicine	105	6.9		
Admissions/short stay/assessment	93	6.1		
Medicines information and pharmacy	36	2.4		
Psychiatry	27	1.8		
Surgery	16	1.1		
Other	118	7.7		



FIGURE 3.7 Number of NPIS consultant referrals (including out-of-hours and workday referrals) in 2010/11 by day of the week

The enquiries

Table 3.9 shows the most common types of products involved in referrals to consultants. These were paracetamol-containing products, cardiac drugs, substances of abuse, benzodiazepines and toxic alcohols or glycols (e.g. ethylene glycol, methanol and antifreeze). In 97 referrals the product taken (if any) was unknown and help with diagnosis was required.

Feedback into NPIS services

Analysis of the consultant referrals is used to improve the services offered by the NPIS. This includes additions and changes to TOXBASE entries that reflect user needs. Issues highlighted by such calls, especially those that are difficult or complex, are discussed further amongst NPIS staff by email or telephone, and difficult enquiries may be examined in more detail at one of the NPIS CPD meetings. This year CPD topics have included poisoning with toxic alcohols and glycols, chemical exposures, snake bites, and antidote use in digoxin and cyanide poisoning. TABLE 3.9 Agents commonly involved in NPIS consultant referrals in 2010/11

Product	Number of referrals
Paracetamol*	302*
Substances of abuse	138
Antifreeze/ethylene glycol/methanol	87
Lithium	54
Citalopram	52
Digoxin	44
Diazepam	41
Iron	40
Ibuprofen	38
Lead	38
Amitriptyline	38
Amlodipine	34
Aspirin/salicylate	34
* Including 47 co-codamol	

Conclusions

The NPIS national out-of-hours on-call consultant rota is well established. Consistency of advice is assisted by audit, regular contact by email and telephone, and educational meetings. Information derived from analysis of the enquiries assists in identifying toxicological problems and new trends in severe poisonings, and improving the clarity of TOXBASE entries. It also informs the need for research in a number of areas.

3.3 UKTIS

The UK Teratology Information Service is a national service commissioned to provide information on all aspects of the toxicity of drugs and chemicals in pregnancy. Information is provided to healthcare professionals via a telephone information service and online through TOXBASE, which holds summaries on maternal exposures to various drugs and chemicals. UKTIS also plays a leading role in the collection of pregnancy outcome data in the UK.

UKTIS is a founder member of the European Network of Teratology Information Services (ENTIS) and senior UKTIS staff are members of the Organisation of Teratology Information Specialists (OTIS), which involves teratology services in the USA and Canada. Together with ENTIS and OTIS, UKTIS collaborates to improve data collection and surveillance methodology in the field of reproductive toxicology.

There is evidence to suggest that prescription rates increase during pregnancy, primarily for pregnancy-related symptoms. Exposure to prescribed medications or other substances may also occur in the peri-conception period before a woman is aware that she is pregnant, giving rise to maternal concern as to whether this exposure may cause adverse pregnancy outcomes such as miscarriage or birth defects. It is therefore essential that accurate information on the maternal and fetal effects of drug use in pregnancy is available. UKTIS plays an important role in this process by providing up-to-date, evidence-based written information and risk assessments via the telephone and internet to NHS healthcare professionals and their patients throughout the UK.

Telephone enquiries to UKTIS

During 2010/11 UKTIS answered 3,722 pregnancy-related telephone enquiries. The geographical distribution of these is shown in Table 3.10. UKTIS also took 64 calls from outside the UK, the majority from the Republic of Ireland. A regional breakdown of calls taken in England is shown in Table 3.11.

Data showing trends in enquiries answered by UKTIS over a five-year period indicate that antidepressant-related enquiries continue to be the most frequent, once calls relating to the influenza H1N1 pandemic in 2009/10 are excluded. In 2010/11, seven of the top ten most frequent enquiries to the service were regarding antidepressants, with the three most common being the serotonin selective reuptake inhibitors (SSRIs) – citalopram, sertraline and fluoxetine (Figure 3.8). The prevalence of antidepressant-related enquiries reflects both their high level of use and recent publications concerning their safety during pregnancy.

To optimise treatment during pregnancy and reduce fetal harm, enquirers are encouraged to contact the service before their patient conceives or before a drug is prescribed in pregnancy. In 2010/11 UKTIS saw similar rates as in previous years of these types of enquiries, with 11% of risk assessments being provided for women in the preconception period and 27% being for preprescription risk assessments. The opportunity to offer advice at this early stage, thereby reducing the potential for adverse maternal and fetal outcome, remains a challenge for healthcare professionals and UKTIS as around 50% of pregnancies are unplanned.

TABLE 5.10 Distribution of pregnancy-related enquines in 2010/11			
Country	Number of enquiries	% of enquiries	Enquiries per million population*
England	3,188	85.6	61.5
Scotland	254	6.8	48.9
Wales	167	4.5	55.7
Northern Ireland	49	1.4	27.4
Outside the UK (including the Republic of Ireland)	64	1.7	N/A
Total	3,722	100	

TABLE 3.10 Distribution of pregnancy-related enquiries in 2010/11

* Based on 2010 estimates from www.ons.gov.uk/ons/publications/re-reference-tables.html?edition=tcm%3A77-231847, accessed September 2011



FIGURE 3.8 Top agents involved in enquiries to UKTIS, from 2006/07 to 2010/11

TABLE 3.11	Regional distribution in England and the
Channel Isla	ands of pregnancy-related enquiries to UKTIS
in 2010/11	

England by region	Number of enquiries	% of enquiries
East Anglia	144	4.5
East Midlands	252	8.0
Greater London	587	18.4
Isle of Man	3	0.1
North East and Yorkshire	633	19.8
North West	424	13.3
South East	576	18.1
South West	253	8.0
West Midlands	312	9.7
Channel Islands	4	0.1
Total	3,188	100





The majority of calls (45%) were regarding pregnant women who had already been exposed to a drug or chemical. In these scenarios UKTIS is able to provide advice about risk to the fetus and, if required, recommendations for prenatal monitoring (Figure 3.9).

Therapeutic use of medicines during pregnancy remains the largest category about which enquiries are made (90%) (Table 3.12). Hospital pharmacists (35%) remain the most frequent type of caller, followed by GPs (28%), consultants (15%) and community pharmacists (10%) (Figure 3.10).

category in 2010/11		
Type of exposure	Number of enquiries	% of enquiries
Therapeutic	3,360	90.3
Drug overdose	95	2.6
Poisoning	117	3.2
Substance abuse	23	0.6
Complementary medicines	6	0.1
Occupational	35	1
Environmental	24	0.6
Other	62	1.6
Total	3,722	100

TABLE 3.12 Telephone enquiries to UKTIS by exposure



FIGURE 3.10 Telephone enquiries to UKTIS by type of user in 2010/11

Pregnancy monographs

UKTIS monographs provide a summary of all the available information relating to the teratogenicity or reproductive toxicology of a specific exposure in pregnancy. During the past year UKTIS has improved the accessibility of this information by reformatting the monograph content to include a detailed summary that can act as a concise stand-alone document (see Figure 3.11). The service plans to include these summary documents on the UKTIS website (www.uktis.org) in the near future, signposting registered users to TOXBASE for the full document. Where large volumes of published literature, e.g. multiple meta-analyses, cohort and case-control studies, and case reports are available for a specific exposure, this information is now summarised and presented in a tabulated format, thus facilitating rapid access to complex data, allowing more efficient dissemination of information by enquiry answerers and ultimately clearer discussions between the healthcare provider and the patient.

New operating procedures have been implemented to ensure that all relevant emerging data can be identified and incorporated into the monographs in 'real-time' such that documents remain as up-to-date as possible. An updated in-house review system is in place to ensure quality of content and maintenance of the standard of excellence that users demand.

UKTIS strives to ensure continued excellence of the service and regularly reviews comments made by users regarding suggestions for improvement of the service. These comments consistently request more monographs as a top priority. In light of these requests, UKTIS produced 100 new and updated pregnancy monographs during 2010/11, an increase of 85% on the previous year.

Monographs are updated as new data become available or on a rolling basis, with priority given to agents commonly involved in telephone enquiries. This year UKTIS produced a number of detailed monographs on the serotonin selective reuptake inhibitors (SSRIs) due to the controversy regarding their use in pregnancy. Other completed documents considered potential teratogens, including mycophenolate mofetil, leflunomide and misoprostol, providing practical advice when exposure has occurred.



USE OF CARBAMAZEPINE IN PREGNANCY

issue: June 20

SUMMARY: Carbamazepine is an iminostilbene used as an anticonvulsant, mood stabilizer and for the treatment of neuralgic pain.

Carbamazepine is teratogenic in humans with malformations reported following *in utero* exposure including neural tube defects, hypospadias, cardiac defects and microcephaly. Exposure to antiepilepitic polytherapy drug regimens which contain carbamazepine may further increase the risk of major congenital malformation. Due to inconsistencies in investigation methods, it is currently difficult to state an estimated percentage of the risk.

Carbamazepine may also have adverse effects on the neurodevelopment of infants following *in utero* exposure, although evidence is currently limited and subject to confounding. It is appropriate to warn pregnant patients taking carbamazepine as part of a polytherapy regimen of the potential risks.

In considering risk benefit balance during pregnancy, it is important to take into account the risks of maternal seizures, which can result in reduced placental perfusion, fetal anoxia and intrauterine death. Therefore, if a switch of therapy is being considered in epileptic patients, this should be attempted prior to pregnancy. Pregnant patients with bipolar affective disorder require good therapeutic control of the condition as a relapse in mental state could result in serious complications for both the patient and the pregnancy.

Carbamazepine has been shown to interfere with folate metabolism. In light of the risk of maternal folic acid deficiency and the detrimental effects this may have on a developing fetus, high dose folic acid supplementation (5 mg/day) is recommended preconceptionally and throughout pregnancy in all women taking carbamazepine.

The risks associated with carbamazepine therapy in pregnancy should be discussed when prescribing the drug to women of childbearing potential and highlighted when prenatal screening is discussed. In women exposed to carbamazepine during pregnancy, especially as part of polytherapy, detailed ultrasound scans should be considered to screen for major structural malformations such as oral clefts and neural tube defects. Exposure to carbamazepine at any stage in pregnancy would not usually be regarded as medical grounds for termination of pregnancy.

If you require assistance in making a patient-specific risk assessment, please telephone UKTIS on 0844 892 0909 to discuss the case with a teratology specialist. Please contact the service on 0844 892 0909 to inform us of any pregnancy where exposure to carbamazepine has occurred.

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FIGURE 3.11 Example of a UKTIS monograph summary document

UKTIS monographs on maternal and paternal exposures to drugs and chemicals are hosted on TOXBASE. The availability of these monographs allows immediate access at the time of prescribing or consultation for all registered UK-based NHS healthcare professionals. The pregnancy summaries (monographs) hosted by the TOXBASE website had approximately 37,600 accesses during 2010/11, an increase of 4.5% compared to 2009/10.

Since 1995, access to pregnancy-related information has increased year on year. Figure 3.12 shows the rise in access to information by healthcare professionals in the past five years and the change in the way that information is obtained. This long-term increase demonstrates the continuing demand for high quality information regarding exposure to drugs and chemicals in pregnancy, both in the online, immediately accessible monographs and also in the highly detailed patient-specific risk management advice provided via our telephone service.

Healthcare professionals most frequently accessed TOXBASE for documents relating to antidepressants, anti-infectives and antihistamines, as well as for general documents on nausea and vomiting, migraine, malaria prophylaxis and insect repellents. The top 20 most accessed TOXBASE pregnancy monographs for 2010/11 are listed in Table 3.13.

UKTIS summary sections of updated or new pregnancy monographs continue to be hosted by the National electronic Library for Medicines website (www.nelm.nhs.uk). These summaries are freely accessible on the internet with instructions to link to TOXBASE for access to the complete monographs. Alerts are sent to registered NHS users by email when any new or updated pregnancy summary is published.



FIGURE 3.12 Telephone enquiries and TOXBASE sessions on pregnancy-related information from 2006/07 to 2010/11

TABLE 3.13	Top 20 most accessed pregnancy summaries
on TOXBAS	E in 2010/11

Pregnancy monograph	Number of accesses
Nausea and vomiting	1,725
Antibiotics	1,227
Citalopram	933
Malaria prophylaxis	842
Codeine	821
SSRIs	742
Corticosteroids	685
Amitryptiline	673
Insect repellents	591
Metronidazole	566
Chlorphenamine	531
Loratadine	486
Fluoxetine	477
Trimethoprim	473
Cephalosporins	470
Migraine	464
Cetirizine	449
Antispasmodics	444
Quetiapine	435
Swine flu	428

Surveillance data

Limited data exist on the potential fetotoxicity of many drug and chemical exposures in pregnancy. Follow-up data providing information on pregnancy outcome when exposure has occurred are invaluable because these add to the, often inadequate, existing published literature and can often enable more accurate risk assessment This is particularly the case when few or no published data exist. Until recently, UKTIS has only followed up new (black triangle) drugs, known or potential teratogens, and exposures occurring either through poisoning, the environment or occupational exposure.

The return rate of pregnancy outcome questionnaires from enquiries the service has attempted to follow up has increased steadily in the past six years, rising from 23% to 34% in 2009/10. Owing to our increased activity in 2009/10, where the service attempted to obtain pregnancy outcome details for all enquiries where sufficient patient identification was provided, UKTIS saw an absolute increase in successful follow up of 44% compared to the average follow-up rate of the previous five years (26%).

Software development

In January 2011 a new UKTIS database went live. The software was designed to enable more rapid and accurate data entry by staff at the service and to allow more efficient checking and follow up of enquiries than could previously be achieved. The new system offers a more user friendly interface, greater automated functioning, drop down menus, improved searching facilities and batch processing. Improvements have been made to the way in which UKTIS stores and collects pregnancy outcome data. A function for generating automated reports now allows rapid analysis of the data and an improved ability for UKTIS to continue surveillance. The system also allows adverse pregnancy outcomes to be categorised using internationally recognised International Classification of Disease (ICD) codes, enabling surveillance of congenital malformations and ensuring that collection of UKTIS data is consistent with international surveillance methods.

UKTIS has developed new questionnaires to capture information concerning maternal health and exposures during pregnancy from healthcare professionals who telephone the service for advice for a particular patient. The data that have been returned using these forms, since their introduction in January 2011, are more detailed and comprehensive. We hope that these improved questionnaires will encourage our service users to report more detailed case histories of their patients and pregnancies to increase the quality of data collected by UKTIS.

Service profile

If UKTIS is to have an impact on maternal and fetal health in pregnancy, and to collect useful outcome data, it is important that healthcare professionals are aware of it and support it. UKTIS maintains its profile by performing outreach work and by presenting and publishing research and surveillance data, as well as by advertising new pregnancy monographs via NeLM. UKTIS has increased the amount of outreach work with user groups in the past year. Awareness of the service has been raised among clinicians by delivery of spoken presentations and at national training courses including the Drug and Safety Research Unit, the Education and Research Course and the Theoretical Course in Fetal Medicine organised by the Royal College of Obstetricians and Gynaecologists. UKTIS surveillance data have also been presented at national and international teratology and poisoning conferences, as well as at the annual British Isles Network of Congenital Anomaly Registers (BINOCAR) meeting.

Spoken and poster presentations on the H1N1 in Pregnancy Study have been delivered at regional days for GPs across the UK, as well as at international conferences. Interim results of this research have been published and the article circulated to all participating GP practices. A talk to the Regional Midwifery Neonatal Screening Committee has also been given. Attendance by the UKTIS staff at local fetal pathology meetings has increased the visibility of the service amongst local obstetricians, fetal pathologists and geneticists.

Material that provides contact details for the service has been distributed throughout the UK and to specifically targeted groups (see Figure 3.13). In November 2010 UKTIS provided information about the service at a stand at the Royal College of Midwives annual conference.

Research and development

During the H1N1 influenza ('swine flu') pandemic of 2009, UKTIS obtained research grants from the National Institute for Health Research (NIHR), and the H1N1 vaccine manufacturers GlaxoSmithKline and Baxter, to carry out a prospective observational study examining the effects of swine flu, antivirals and vaccination during pregnancy. Pregnancy outcome data have now been obtained from over 650 women and the study is soon coming to a conclusion, with data collection due to end in September 2011. A detailed statistical analysis of the data will be carried out at the end of the study, and it is expected that full analysis of the study findings will be available in advance of the 2011/12 influenza season.

In the past financial year UKTIS has continued to collaborate in a European multicentre research project with 31 public and private partners. The project, Pharmacoepidemiological



FIGURE 3.13 UKTIS flyer

Research on Outcomes of Therapeutics (PROTECT), has been funded by the Innovative Medicines Initiative to address limitations of current methods in the field of pharmacoepidemiology and pharmacovigilance. PROTECT will trial direct patient data collection using web-based and telephone systems. It will test the transferability of the data into a common language and explore linkages to data from electronic health records and registries.

During 2010/11 UKTIS initiated and led a collaborative project to improve understanding of the molecular mechanisms that orchestrate gene expression during fetal development. This work aims to identify epigenomic signatures during development and then to further interrogate these signatures in relation to exposures known to influence pregnancy outcomes (e.g. potential teratogens and maternal obesity). The ultimate goals are two-fold:

- a To define epigenetic signatures that may have clinical utility as early biomarkers of exposure and thus assist in more accurate and specific risk prediction and counselling
- b To increase our understanding of the molecular mechanisms occurring in fetal development and thus the pathogenesis of health problems later in the course of life that have antecedents *in utero*, therefore informing appropriate interventions.

An NIHR FSF grant and Newcastle Healthcare Charity award have been secured to fund the pilot work necessary to establish reference epigenetic signatures. It is hoped that this work will generate preliminary data that will underpin further funding applications and collaborations.

3.4 Product Data Centre

In order for the NPIS to provide accurate advice on the treatment and management of patients exposed to consumer products, reliable information on the composition of these products is necessary. Manufacturers' product safety datasheets (SDS) also provide information for updating TOXBASE, enabling users to obtain specific advice on many common products.

NPIS Birmingham has the responsibility of coordinating the NPIS Product Data Centre and liaising with manufacturers to ensure that the data held are comprehensive and up to date as far as is possible. In 2010/11, 9,069 datasheets were added to the NPIS Product Data Centre which now holds 63,256 current datasheets. The database is indexed by product name, manufacturer, date of datasheet, and the accession date for the datasheet to the database. Where these fields are insufficient, the database is also fully text searchable, which enables searches to be made on any other criteria, e.g. active ingredients or use.

NPIS Birmingham has also developed a database to support the NPIS Product Data Centre. This second database holds contact details for more than 2,300 companies and assists in the tracking of correspondence with companies; it includes data on the current marketing status of products.

3.5 Current Awareness in Clinical Toxicology

To ensure that NPIS staff are equipped to answer enquiries on all aspects of human toxicology and that TOXBASE is kept up to date, access to current scientific literature is essential. With the assistance of the other NPIS units, NPIS Birmingham produces *Current Awareness in Clinical Toxicology* each month. Citations are selected using searches specially developed for the purpose run against Medline, Embase and Science Direct. In addition, the tables of contents of key journals are scanned for suitable papers on publication. Each issue lists some 400 citations, with 15–20 key papers highlighted because of their importance to the clinical management of poisoning and the updating of TOXBASE.

In 2010/11, 6,240 references were added to the NPIS Literature Database, which currently contains 76,380 references. The database is fully searchable using keywords, authors, journals and text words and is available on a 24-hours-a day basis to all NPIS staff.

4 Clinical Governance

The NPIS needs to provide high quality evidence-based and consistent advice to its users. To ensure that this occurs, clinical governance arrangements have been developed – these are defined in operational procedures that are available to all staff via TOXBASE. Key components are

- a Appropriate induction, training and appraisal of staff
- b Availability of continuous professional development shared nationally where contentious issues can be discussed to ensure consistency of approach
- c Access to high quality information sources
- d Early peer review of enquiry answers
- e Continuous support from senior staff, including 24-hour availability of a consultant clinical toxicologist
- f Reporting and reviewing critical incidents, complaints and near misses so that lessons can be learned and shared throughout the service
- g Quality assurance exercises seeking the feedback of users in relation to use of TOXBASE, the telephone enquiry services for NPIS and UKTIS, and consultant advice.

UKTIS

This year UKTIS focused on reviewing its working practices and in doing so has produced new and updated existing operating procedures for the service. Operating procedures for staff working at the service have been updated to ensure that staff are logging, answering and peer-reviewing enquiries with consistency and accuracy, and in line with clinical governance standards. In light of the increasing involvement in research, there is scope for UKTIS staff to increase their publication portfolio; therefore, guidelines have also been developed to help with producing peer-reviewed journal articles.

In the past year all staff within UKTIS were required to undergo good clinical practice (GCP) and regulatory requirements training due to their involvement in clinical research. This training ensures that employees have a thorough understanding of European Union directives and UK legislation, their roles and responsibilities, data storage and protection, and ethical considerations to provide high quality research within the NHS.

4.1 Analysis of Critical Events

All NPIS staff are mandated to report critical events or near misses and any complaints or observations on the quality of the service are treated through the same system. Critical events are examined by the Director of the originating unit in the first instance and then reviewed at the Clinical Standards Group where recommendations on further actions are made. If urgent changes are required, there are mechanisms available for rapid discussion amongst the NPIS units and implementation of changes nationally.

During 2010/11 five critical incidents were reported and discussed at the Clinical Standards Group relating to clinical issues. Three involved a clinician or coroner raising issues relating to TOXBASE entries for specific products. The TOXBASE entries to which these cases related were all reviewed in detail by the Clinical Standards Group. In the event, none of the entries was considered inaccurate in content. However, aspects of style were changed in these entries to improve clarity.

One critical incident related to clinical advice provided by an NPIS consultant; following review of all pertinent information, the consultant's advice was endorsed by the Clinical Standards Group.

The final critical incident involved the lack of local availability of *vipera berus* antivenom to treat a patient with severe envenomation. Antidote stocking is not a responsibility for the NPIS but, following discussions by the Clinical Standards Group, it was agreed that advice be re-circulated jointly by the NPIS and the College of Emergency Medicine to the emergency departments of all acute NHS hospitals about appropriate stocking arrangements for this antivenom. A national audit of antidote stocking was also performed with the College of Emergency Medicine (see Section 5.4).

There were five further incidents involving misrouting of telephone enquiries to an NPIS unit that was not open on the 24-hour rota switching arrangements at that time. We continue to work with our telephone service provider to reduce the frequency of these episodes. There was also one brief episode of a lack of access to the TOXBASE main site, although the TOXBASE backup site remained operational.

4.2 Quality Assurance Exercises

TOXBASE

An online questionnaire is used to obtain formal quality assurance from TOXBASE users. An automated system asks a selection of users to complete and submit short quality assurance forms during their online session. Invitations can be set to be generated between every two and fifteen database logins and this number is varied throughout the year to achieve a reasonable return rate, whilst avoiding user fatigue.

A total of 1,018 returns were received between 1 April 2010 and 31 March 2011. The responders were nurses (278), junior hospital doctors (244), NHS Direct/NHS 24 staff (189), pharmacists (60), hospital consultants (64) and GPs (56). The remaining 127 indicated another designation – these included middle grade doctors, biomedical scientists and 52 ambulance staff/paramedics.

On type of enquiry, 557 users reported that they primarily used TOXBASE for 'routine enquiries', 312 for a 'triage decision' and 149 for 'complex enquiries'. On frequency of use, 430 reported using TOXBASE weekly, 347 daily and 241 accessed it only occasionally.

Users were asked to grade a series of statements on a scale of 1 to 6, where 1 = disagree completely and 6 = agree completely. Satisfaction scores were high (Table 4.1). When asked to indicate their overall satisfaction with TOXBASE on a scale of 1 to 6, where 1 = poor and 6 = excellent, 922 (91%) scored either 5 or 6.

Users commented on several issues, including IT problems and difficulties in searching the database. Where users provided

TABLE 4.1 Summary of user satisfaction scores

Rank	Question	Satisfaction score (%)*
1	I had confidence in the information for my query	92.9
2	The information was sufficient for managing this case	86.5
3	Logging on to the database was easy	85.1
* Satisfa	ction score is the proportion of responder	nts who agree

* Satisfaction score is the proportion of respondents who agree 'completely' or 'a lot' contact details responses were made to specific queries and comments; however, most users chose not to provide their contact details. Users were also directed to the help section on TOXBASE where a guide to searching is provided, and to the TOXBASE e-learning module available at www.TOXBASE.co.uk.

User suggestions are considered and discussed at the TOXBASE Editing Group and NPIS Clinical Standards Group meetings. Issues specific to entries are dealt with as they arise.

The questionnaire responses have improved feedback to the NPIS and the TOXBASE Editing Group and have enabled improvements to be made to the search facility. Further quality assurance returns on TOXBASE will be used to monitor progress and feedback to the service on these issues and aspects of data content and presentation.

In summary, the majority of respondents reported that use of TOXBASE was easy and that it provided the information they required.

Telephone information service

Since 2002 the NPIS units have collected information on user satisfaction with their telephone service to establish if it is meeting the needs of their users and to identify and address problems, both internal and external. During 2010/11 the eighth national telephone quality assurance exercise, conducted in accordance with national contractual arrangements with the HPA, was performed. Questionnaires were sent to a random sample of callers using a common methodology for random allocation of calls for stakeholder feedback.

During 2010/11 the four NPIS units sent out a total of 2,697 questionnaires (a 5.4% sample overall) and there were 1,171 responses (a response rate of 43%).

The proportion of callers who accessed TOXBASE before ringing the service increased to 42% from last year's figure of 37%. As in previous years, those accessing TOXBASE first made their telephone enquiry most often because they considered that there was too little information available on TOXBASE to answer their enquiry (60%) or that there were special circumstances (31%). During 2010/11 there was a reduction in the proportion of respondents who selected the option that the information on TOXBASE seemed to contradict other information they had. Of those who did not access TOXBASE first, the numbers who did not know about TOXBASE decreased to 32% from 36% last year. Most respondents in this group continue to be GPs. Access to TOXBASE continues to improve, with only 18% of respondents reporting that they do not have access, although some users still experience difficulty logging on (14%).

To assess the quality of the service as perceived by users, respondents were asked to what degree they agreed or disagreed with a series of statements relating to the particular enquiry they made to the NPIS. Although questions are framed differently, high scores always indicate a high overall satisfaction rating.

Respondents showed a high degree of satisfaction in the way they answered the various questions posed (Table 4.2). Especially good feedback was obtained for questions relating to the politeness of the staff, promptness of enquiry handling, confidence in the reply, and the speed of delivery of the information. Satisfaction scores were less favourable for the amount of information provided and time taken to answer the telephone, although satisfaction scores were still more than 90% for both these questions.

TABLE 4.2 Summary of satisfaction scores

Rank	Question	Satisfaction score (%)*
1	The person I spoke to was polite and pleasant	98.3
2	Once my call was answered by a specialist in poisons information the enquiry was dealt with promptly	97.4
3	I had confidence in the reply I was given	96.3
3	The information was given to me at an appropriate speed	96.3
5	The reply from NPIS was relevant and useful	95.4
6	I was given an appropriate amount of information for my needs	94.7
7	My telephone call was answered without delay by a specialist in poisons information	92.9
* Catiofa	ation accur is the preparties of responds	

* Satisfaction score is the proportion of respondents who agree 'completely' or 'a lot' There continues to be a very high rating of overall satisfaction with the service, defined as a score of 5 or 6 out of a total of 6, with an overall satisfaction score of 96.5% if non-responders are excluded from the denominator and 94.3% if they are included (Figure 4.1). Considering each NPIS unit separately, the proportions of respondents indicating high overall satisfaction scores were above 95% for all four units (Figure 4.2).



FIGURE 4.1 Overall quality scores (with 95% confidence intervals) for the NPIS units from 2004/05 to 2010/11, expressed as a percentage of respondents scoring 5 (\blacksquare) or 6 (\blacksquare) out of a possible 6. Non-respondents are excluded from the denominator



FIGURE 4.2 Overall quality scores (with 95% confidence intervals) for 2010/11 for the NPIS units, expressed as a percentage of respondents scoring 5 (\blacksquare) or 6 (\blacksquare) out of a possible 6. Non-respondents are excluded from the denominator

UKTIS telephone enquiries

As part of our interest in service user satisfaction UKTIS regularly asks for feedback from service users. During 2010/11 a random sample of 412 enquiries, 35 per month (11% of the total enquiries), made directly to UKTIS was selected for quality assurance monitoring. Questionnaires were sent out to enquirers between one and four weeks after the enquiry. As of May 2011, 187 (45%) of these forms had been returned.

The responders were hospital consultants (20), junior hospital doctors (12), pharmacists (49), GPs (78), nurses (18), pharmacy technicians (4), and health advisors (NHS Direct) (2). The occupation of four responders was not reported. Of the responders, 36% had used the service between one and five times previously, with a further 26% being firsttime enquirers. Satisfaction scores were high – in particular, 93% of responders agreed or strongly agreed that they were highly satisfied with the service they received, with 94% agreeing that they found it easy to contact UKTIS. The majority were happy with the amount of information they received from the service (84%). Of the enquirers, 93% reported that they spoke to someone who was polite and pleasant, and 91% had confidence in the reply that they were given (Table 4.3).

TABLE 4.3 Summary of UKTIS enquirer satisfaction scores

Rank	Question	Satisfaction score (%)*
1	The person I spoke to was polite and pleasant (agree)	93
2	I had confidence in the reply I was given (agree)	91
3	The reply from UKTIS was relevant and useful (agree)	86
4	The information was sufficient for my needs (agree)	84
5	Once I got through, the enquiry took a long time to be dealt with (disagree)	79
6	The information was given to me too quickly (disagree)	70
*		

* Satisfaction score is the proportion of respondents who scored 5 and 6 (in agreement) or 1 and 2 (in disagreement)

4.3 Education and Training

Training and continuing education of clinical and non-clinical staff are vital to ensure that the service is equipped at all times to provide pertinent, informed and evidence-based advice on all aspects of poisoning. Newly recruited scientific staff undergo in-house training for six to eight weeks before being allowed to answer telephone enquiries. Consistency and quality of training across the units is achieved by adherence to guidelines set out in the nationally agreed operating procedures on initial training and core competencies for NPIS specialists in poisons information. Figure 4.3 shows the

Competency Checklist for Specialists in Poisons Information

 (trainee's name)
Has been taught and assessed on each aspect of the NPIS core curriculum
Has a comprehensive understanding of TOXBASE and UKPID
Can use electronic and published reference sources competently
Has knowledge of the information sources available locally and nationally (see separate operational procedure)
Understands all the NPIS operational procedures available on the NPIS section of the specialist areas link on TOXBASE
Understands the procedures involved in reviewing and producing TOXBASE entries and the specific responsibilities of their Unit
Understands the structure and function of the NPIS and its role within the NHS and the Health Protection Agency (HPA) and specifically the Centre for Radiation, Chemical and Environmental Hazards, Chemical Hazards and Poisons Division
Understands the protocol to follow in the event of a chemical incident being reported to the NPIS, including the criteria determining what constitutes a chemical incident
Understands the NPIS clinical governance arrangements locally and nationally
Understands the importance and organisation of local and national audits of performance
Appreciates the importance of continuous professional development and involvement in the CPD programme locally and nationally
Has passed the final competency assessment conducted by the Unit's Director or their Deputy
Training Coordinator XXXX Unit Date

FIGURE 4.3 Competency checklist for NPIS specialists in poisons information

competency checklist used by supervisors to ensure staff have covered all aspects of training. At the end of the training period staff undergo a nationally agreed final competency assessment conducted by the Unit Director or their Deputy and are then presented with an NPIS certificate of competency as a specialist in poisons information.

One NPIS consultant, appointed by the Directors and the Commissioner, is responsible over a three-year term for the coordination of a rolling programme of continuing professional development (CPD) meetings for NPIS scientific and medical staff. These meetings serve not only to ensure that everyone involved in front-line delivery of advice is up to date with the latest developments within the specialty, but also that all staff are fully conversant with new or changing responsibilities and procedures within the NPIS. They provide an informal forum where colleagues can discuss difficult or controversial cases and where junior staff can present cases and voice concerns and questions in a supportive environment, and an opportunity for face-to-face contact between the scientific and consultant staff of different units who frequently discuss cases as part of the out-of-hours NPIS rota but may never otherwise meet. The venue rotates between the four UK NPIS units and sometimes to the NPIC in Dublin.

Topics covered in the last year include the pharmacology and toxicology of newer antiepileptic agents, emerging drugs of abuse, and adder bite management and foreign snake bites encountered in the UK. Other topics are shown in Figure 4.4, which is the programme from the meeting held in Newcastle in March 2011. In addition, in July 2010 NPIS Birmingham hosted the third annual Chemical Terrorism Symposium, jointly sponsored with the HPA and Dstl Porton Down. Topics included human decontamination, the national emergency response arrangements and an update on the management of poisoning with the nerve agents, ricin and botulinum.

All NPIS staff undergo regular appraisal and career development planning. Staff are encouraged to submit papers to national and international congresses and scientific meetings hosted by toxicological organisations such as the British Toxicology Society and the European Association of Poisons Centres and Clinical Toxicologists (EAPCCT). For example, NPIS and NPIC Ireland staff presented some 42 posters or oral presentations at the 30th International Congress of the EAPCCT held in Bordeaux, France, in May 2010.

NPIS CPD Meeting 15 MARCH 2011 **RESEARCH BEEHIVE, NEWCASTLE UNIVERSITY** 10.00 Coffee 10.30 Welcome and introduction Sally Bradberry Towards 2012 10.35 Dioxins Arvind Veiraiah Aluminium phosphide and phosphine 10.55 Allister Vale NPIS activities update 11.15 Antidote stocking audit Ruben Thanacoody 11.35 ACB/NPIS guidelines for availability of toxicological analyses John Thompson 11.55 'Toxic alcohols' audit Ruben Thanacoody From our Tox Correspondent 12.15 Society of Toxicology Meeting, Washington DC, 6-10 March 2011 Sally Bradberry 12.30 Lunch Hot topics for SPIs Expert panel: Nick Bateman, Paul Dargan, Michael Eddleston, Allister Vale 13.30 Sodium nitroprusside overdose in a neonate Sian Harbon, Cardiff Repeated reactions to acetylcysteine 13.45 Danielle Brackenridge, Birmingham 14.00 Treatment and complications of ethylene glycol poisoning David James, Newcastle 14.15 latrogenic morphine overdose in a neonate Pardeep Jagpal, Birmingham Rash complicating cocaine abuse 14.30 Gill Jackson, Edinburgh 14.45 Теа CSG Digest An update on recent decisions and deliberations of the 15.00 NPIS Clinical Standards Group Simon Thomas 15.15 Questions and discussion on the CSG Chair: Simon Thomas

- Closing comments/feedback forms 15.30 Sally Bradberry
- 15.45 Depart

FIGURE 4.4 CPD Programme of 15 March 2011

The need to develop clinical toxicology as a medical specialty is supported by government departments and agencies (particularly the Department of Health, the Health Protection Agency and the Ministry of Defence), by the Royal Colleges of Physicians and by the specialist societies (notably the British Toxicology Society and the British Pharmacological Society). NPIS Directors have led in the development of a special one-year training module in clinical toxicology which has been approved by the Specialist Advisory Committee for Clinical Pharmacology and Therapeutics. It is expected that this will be approved by the General Medical Council in autumn 2011 and will be available to provide accredited training soon after that.

e-learning



This clinical toxicology e-learning resource, developed by NPIS Edinburgh,

went live in September 2005 at www.toxbase.co.uk. Over 2,900 individuals have registered on the site between its launch and 31 March 2011. Registration and access are free to NHS users, who can work through the site at their own pace, save their work, obtain their scores and print a certificate of completion for their CPD file.

The resource was initially designed to be used for training new staff at NHS 24 centres on the use of TOXBASE; however, the content and scope of the resource have grown over the years to be of interest to a wide range of NHS users including doctors, nurses and paramedics. Three modules are currently available: on using TOXBASE, management of the poisoned patient and management of patients involved in chemical incidents.

Using TOXBASE

Two levels of the TOXBASE module are available, designed to support different users, Level 1 for NHS 24/NHS Direct users and Level 2 for emergency department nurses/junior doctors. As of 31 March 2011, a total of 2,763 users had completed the TOXBASE unit. Completion of the Level 2 unit represents 1.75 hours of study.

Management of the poisoned patient

Available since July 2008, this module is designed to help junior doctors and triage nurses improve their knowledge on the clinical management of the poisoned patient. Since its launch,

619 users have completed units. Completion of the whole module represents 3 hours of study. Units are available on:

- a General aspects
- b Common poisons
- c Problematic poisons
- d Drugs of misuse.

Management of patients involved in chemical incidents

Added to the site in September 2010, this module is designed to provide junior doctors and triage nurses with an introduction to the management of chemical incidents. Since its launch, 115 users have completed units. Completion of the whole module represents 3.5 hours of study. Units are available on:

- a Decontamination and incident management
- **b** Factory and motor vehicle accidents
- c Leaks and contamination
- d Riots and potential deliberate release.

The site also hosts, on behalf of the Scottish and Welsh governments, learning resources for pharmacy staff and healthcare professionals on medicines in a chemical, biological, radiological or nuclear incident.

The next module in production will be on natural toxins, including plants and venomous animals.

UKTIS

Staff in UKTIS maintain their CPD by attending national and international meetings, conferences and teratology-specific training courses. In addition to gaining knowledge of research and findings in the area of reproductive toxicology, and suspected new human teratogens, information obtained from these meetings has been incorporated into monographs and training materials and will continue to be disseminated through in-house CPD sessions, enabling telephone staff to remain up to date with current developments which underpin the quality of the service. Attendance at these meetings has also provided UKTIS staff with the opportunity to discuss the service delivery models of other teratology services across the world. This has proved beneficial not only in terms of developing UKTIS as a service, but also in facilitating future international collaborations. Much of the information given in this chapter would not have been available without the feedback provided by our users. We wish to thank all our users for their assistance in providing information that can be fed back into NPIS datasets and improve information provided to other clinicians or safety regulators.

There are several ways in which data can be fed back into the NPIS, these include follow-up questionnaires that are sent to every user who speaks with a NPIS consultant and online questionnaires that users can complete – these are accessed via alert boxes on TOXBASE entries (Figure 5.1).

NEW PRODUCTS

This is a new product. Knowledge of its toxicity is limited. To help other clinicians dealing with similar cases please click here to give us details of your case.

UNCOMMON PRODUCTS

This is a product about which little information is available. Knowledge of its toxicity is limited. To help other clinicians dealing with similar cases please click here to give us details of your case.

FIGURE 5.1 Example alert boxes added to TOXBASE entries to encourage user feedback

5.1 Drugs of Misuse

Enquiries about suspected toxicity following exposure to drugs of misuse are an important part of the NPIS workload. The recent, rapid emergence of newer recreational drugs, especially mephedrone, has been a particular challenge to the service, which needs to maintain awareness of new agents and be ready to collect and disseminate information on their likely toxic effects and the appropriate management of affected people.

This section provides an update on trends in NPIS activity relating to important drugs of misuse, including telephone enquiry and TOXBASE access statistics. As with all NPIS activity data, figures are not a direct measurement of the frequency of toxicity or of hospital admissions, but give an indirect indication of the substances being encountered by the NHS clinicians who use our services. It should be noted that analytical confirmation of exposure is rarely available and the statistics reflect what has been reported as being taken by the recreational drug users involved.

During the year the most common drugs of misuse involved in NPIS telephone enquiries or TOXBASE accesses were cocaine and mephedrone, with heroin, methadone, cannabis, MDMA ('ecstasy'), amphetamines and ketamine also frequently encountered (Figure 5.2). The NPIS continues to monitor enquiries relating to newer recreational drugs but, with the exception of mephedrone, naphyrone and 6-(2-aminopropyl) benzofuran (6-APB), enquiries relating to these compounds continue to be very uncommon (Figure 5.2).

Longer term trends are presented as proportions of the total numbers of calls received or TOXBASE accesses made each year. This adjustment is needed to take into account the increases in overall TOXBASE accesses and reductions in telephone enquiries that have occurred over the years. Over the last nine years there have been reductions in telephone enquiries and TOXBASE accesses relating to MDMA and heroin. Activity relating to cocaine had been increasing earlier in the decade but has not been as high in the last two years. The proportion of overall telephone and TOXBASE activity that relates to ketamine has been increasing in recent years (Figures 5.3 and 5.4).

Last year, the NPIS reported substantial increases in telephone and TOXBASE enquiries relating to synthetic cathinones, especially mephedrone. The clinical features reported in telephone enquiries to the NPIS have now been published * and preliminary data were provided as evidence to the Advisory Council on the Misuse of Drugs (ACMD) for its consideration of the cathinones [†]. Monthly activity data show telephone and TOXBASE enquiry numbers for mephedrone peaking in March 2010, with substantial subsequent reductions (Figure 5.5). These changes suggest that the legal control of mephedrone and other cathinones enacted in April 2010 had an impact on the frequency of associated toxicity. It is

^{*} James D, Adams R, Spears R, Cooper G, Lupton DJ, Thompson JP, Thomas SHL. Clinical characteristics of mephedrone toxicity reported to the UK National Poisons Information Service. Emerg Med J 2011; 28(8): 686–9 (Epub 2010 August 25).

[†] Advisory Council on the Misuse of Drugs. Consideration of the Cathinones, March 2010. Available at www.homeoffice.gov.uk.



FIGURE 5.2 Telephone enquiries and TOXBASE accesses relating to selected drugs of misuse, in 2010/11 *Abbreviations*

MDMA – methylene dioxymethamphetamine MDAI – 5,6-methylenedioxy-2-aminoindan PMA – paramethoxy-amphetamine 6-APB – 6-(2-aminopropyl)benzofuran LSD – lysergic acid diethylamide TFMPP – 1-(3-trifluoromethylphenyl) piperazine BZP – benzylpiperazine

acknowledged, however, that reductions in media reports and increasing familiarity of healthcare professionals with these substances may also have contributed to the observed pattern.

There were small increases in telephone and TOXBASE activity relating to naphyrone (naphthylpyrovalerone) after April 2010, until this was controlled in July 2010. It should be noted, however, that analysis has often found that products described as naphyrone instead contained mephedrone. In August and September 2010 a number of telephone enquiries were received relating to products termed 'Ivory Wave'. These exposures were often associated with severe clinical effects, including prolonged psychiatric features. Analysis of one batch of 'Ivory Wave' demonstrated desoxypipradrol as the constituent. After considering evidence about Ivory Wave and desoxypipradrol, including information provided from the NPIS, the ACMD advised an import ban, which was put into effect in November 2010. NPIS telephone enquiries relating to desoxypipradrol or 'Ivory Wave' have been very uncommon since September 2010 (Figure 5.5).







Other drugs

FIGURE 5.3 Proportion of TOXBASE accesses relating to selected drugs of misuse (data for 2002–2003 by calendar year; subsequent data by financial years)

(It should be noted that TOXBASE access data for MDMA for 2008/09 and 2009/10 were inaccurately recorded in last year's report due to a processing error; this has been corrected here)







Other drugs

FIGURE 5.4 Proportion of telephone enquiries relating to selected drugs of misuse (data for 2002–2003 by calendar year; subsequent data by financial years)



FIGURE 5.5 Monthly TOXBASE accesses and telephone enquiries relating to selected drugs of misuse, from March 2009 to March 2011

5.2 Pesticide Poisonings

Clinical features of common pesticide exposure in UK adults

Owing to recent work on the NPIS pesticide surveillance project we are able to examine symptoms reported from UK adult exposures (classified as those aged 13 years and over) involving common pesticides (glyphosate, paraquat and organophosphorus insecticides).

Between 1 April 2004 and 30 September 2010 data were collected on 5,210 UK exposures. In total, 2,690 adult patients were identified; 2,194 of these cases were due to accidental exposure. Of these, 283, 157 and 145 were reported in association with glyphosate, organophosphates and paraquat, respectively (paraquat was withdrawn from domestic use in 2005 and professional use in 2008). The majority reported minor symptoms. One death was reported for accidental poisoning with organophosphate and one with paraquat. No deaths were reported with accidental glyphosate poisoning.

Of the 496 deliberate self-harm (DSH) cases, paraquat (56 cases) was the pesticide most commonly involved. A higher mortality rate was seen with organophosphates (14%) and paraquat (13%) in comparison to glyphosate (7%). Death from paraquat ingestion was closely associated with multi-organ failure.

Glyphosate

Accidental exposure was the predominant method of poisoning. Of the 2,194 accidental adult exposures, 283 were exposed to glyphosate or glyphosate trimesium herbicides. In the 257 cases with a specific age recorded, the age group most frequently affected was of 40–49 year olds, with an overall male predominance. The majority of patients accidentally exposed to glyphosate were allocated severity grades of minor (58%) or asymptomatic (28%).

Among accidental exposures the most frequently reported symptoms were those affecting the gastrointestinal tract (87 cases, or 30.7%), eye (71) and skin (65). Common gastrointestinal features include nausea and vomiting (29 cases) followed by burning sensation or pain of mouth/ throat (17) and abdominal pain (13). Eye irritation/pain (52 cases) and skin irritation (47) were the most common features in their respective categories.

The majority of DSH exposures (42 cases) were graded asymptomatic (40%) or minor (32%), with moderate (14%), severe (7%) and fatal (7%) exposures less common. Gastrointestinal features were the most common in DSH cases, with 18 cases presenting with either nausea, vomiting, abdominal pain or diarrhoea. The next two most common organ categories involved were cardiovascular (11 cases) and respiratory (five).

Organophosphates

Of the insecticide exposures, 171 (16%) involved organophosphates. Regardless of exposure type, the age range most frequently involved was of 40–49 year olds. The male to female gender ratio in the UK was 3 : 1.

The majority (157 cases, or 92%) were accidental and most reported minor symptoms (79%). One fatal outcome occurred due to accidental exposure. Following accidental exposure, CNS features (72 cases) were the most common, with lethargy/ fatigue (14) and neurological symptoms (13; peripheral neuropathy/neuropathic pain in four cases). Other organ systems commonly affected were gastrointestinal (52 cases) and respiratory (36; including shortness of breath in 17 cases). Vomiting (18 cases) and diarrhoea (11) were common gastrointestinal symptoms. General malaise was reported in 13 cases.

For DSH exposures (eight cases) cardiovascular features were most frequent, with cardiac arrest (three cases, or 37.5%) being the most common symptom. Two patients died. There was a similar prevalence (seven cases) between gastrointestinal and CNS features. Vomiting (three cases) accounted for almost half of the gastrointestinal features. Coma/collapse/altered consciousness and uncontrolled movement/fasciculation (two cases for each) were reported in the CNS category.

Paraquat

Paraquat has been withdrawn from use in Europe, but occasional exposures occur from residual stored product in domestic use. Regardless of the method of paraquat poisoning, a male predominance was found. The age group in the accidental category most frequently affected was of 40–49 year olds, whereas in the DSH category it was of 50–59 year olds.

Accidental paraquat exposures in the UK (145 cases) resulted in eye (25 cases, or 17%) and skin (14) symptoms. Eye irritation/ pain (11 cases) and skin irritation (seven) were common. Shortness of breath accounted for 21 cases of respiratory symptoms reported. In the CNS category, headache (six cases) and dizziness (four) accounted for 40% and 27% of symptoms, respectively. Fatal outcome of accidental exposure in the UK was unusual (one case).

Of 56 patients with DSH exposures, seven died (13%). The majority of DSH exposures presented with gastrointestinal features (43 cases). Nausea and vomiting (19 cases) and mouth/throat symptoms (13) were among the common manifestations. Metabolic acidosis occurred in 11% of DSH exposures (six cases). Respiratory failure occurred in almost half of the patients who died. One case of liver failure was reported. Six patients presented with renal failure.

Discussion

The rate of fatal outcomes of reported accidental pesticide poisoning was low with organophosphates and paraquat having a mortality rate of 0.5% (one case) and 0.7% (one case), respectively. There were no fatal outcomes reported for accidental exposures with glyphosate. The majority of patients reported minor symptoms after accidental exposure with either glyphosate, organophosphate or paraquat. Regardless of the type of pesticide and method of poisoning, gastrointestinal features for the two herbicides were common. Skin and eye features also occurred frequently.

The mortality rates associated with deliberate ingestion of all three pesticides in the UK were higher compared to accidental exposures (glyphosate 7%, paraquat 13% and organophosphate 14%). Among deliberate self-harm exposures in the UK, organ failure was common with organophosphate (3 cases, or 21%) and paraquat (11 cases, or 20%) poisoning, but less common with glyphosate (4 cases, or 10%).

Conclusions

For the three pesticides most commonly reported to the NPIS, males aged 40–49 years are most commonly involved. Accidental exposures generally result in minor symptoms with

gastrointestinal features being common for herbicides. These findings suggest that improvements in the way these products are used could reduce accidental exposures.

5.3 Carbon Monoxide

Despite continuing public awareness campaigns, carbon monoxide poisoning remains an important preventable cause of morbidity and mortality in the UK. During 2010/11 there were 286 telephone enquiries to the NPIS (290 in 2009/10) regarding confirmed or suspected carbon monoxide exposures which involved one or more individuals. Thirty-eight enquiries involved multiple individuals so that the total number of patients involved was at least 385 (in some cases the number of individuals exposed was not known). The maximum number of individuals exposed in a single incident was 12 and involved the smoking of a 'water pipe' in a poorly ventilated bar.

In addition, there were 108 enquiries from the emergency services, health protection staff and the Environment Agency regarding potential carbon monoxide incidents and three enquiries were requests for general information.

The seasonal variation in the number of enquiries to the NPIS in 2009/10 and 2010/11 is shown in Figure 5.6. This demonstrates, as expected, that enquiries regarding carbon monoxide exposure were generally less frequent in the summer months (with the exception of May 2010).

Most enquiries (242 of 286; 85%) during 2010/11 involved carbon monoxide exposure at home, compared to just 16 (6%) occurring in the workplace and 12 (4%) reported in a public area. The suspected source of carbon monoxide in the domestic setting is known in 71% of cases; central heating boilers were implicated most often (Figure 5.7).

A majority of the enquiries (251 of 286) were reported to be accidental, 19 were deemed intentional and, in the remaining 16, the intention was uncertain but was probably accidental in ten. Of the 251 accidental exposures, 225 had a Poisons Severity Score (PSS) of 0 or 1 (minor toxicity) at the time of the enquiry, 12 (5%) had features of moderate toxicity (PSS 2) and seven (3%) were graded PSS 3, indicating features of



FIGURE 5.6 Number of enquiries regarding carbon monoxide received each month in 2009/10 and 2010/11



FIGURE 5.7 Suspected source of carbon monoxide exposure in a domestic environment

severe poisoning; a PSS was unavailable in the remaining seven enquiries. Six out of seven severe cases involved patients who had been exposed to carbon monoxide through smoke inhalation during a domestic fire, so factors such as thermal injury may also have contributed to their features. Carboxyhaemoglobin concentrations in these patients ranged from 11% to 48%. Follow up was attempted in all cases: one patient recovered completely and two died; in four cases either no or insufficient follow-up data were available.

Of the 19 intentional exposures, 13 involved vehicle exhaust fumes, three were attempted suicides which involved the lighting of a barbecue in a confined space, and two involved house fires. The carboxyhaemoglobin concentrations at presentation were known in 13 of 19 cases and ranged from 4.8% to 38.9%, with values of 30% or higher in four cases.

In two further cases involving victims of house fires, the circumstances of exposure were classified as 'unknown' but it was considered possible that the fires had been started deliberately. In both these cases, cyanide poisoning was also a factor and most probably contributed to the severity of the cases.

5.4 Antidote Availability

Guidelines for antidote stocking by acute hospital emergency departments in the UK were issued jointly by the NPIS and the College of Emergency Medicine in 2008. To assess compliance with this guidance, a national audit was undertaken by sending a short questionnaire regarding the availability of specific antidotes to the chief pharmacist in every acute hospital in the UK. This was sent by post or email from the NPIS units according to geographical area (Scotland – Edinburgh; Wales and South West England – Cardiff; Midlands – Birmingham; Northern England – Newcastle; London/South East – Birmingham and Newcastle). Questionnaires were sent to 224 acute hospitals in the UK and, of these, 196 were completed and returned (a response rate of 87.5%).

The results showed that most commonly used antidotes are available immediately or within one hour in acute hospitals in

the UK. There were, however, problems with the availability of less commonly used antidotes. For example, pralidoxime, used in the treatment of poisoning with organophosphorus compounds, was held in only 33% of hospitals. Similarly, stocking of other antidotes was patchy, with cyproheptadine and viper venom antiserum stocked by about 50% and calcium gluconate gel by 75% of acute hospitals. For the treatment of cyanide and toxic alcohol poisoning, more than one antidote is available. For cyanide poisoning, most hospitals held at least one antidote (usually dicobalt edetate), but nine (5%) held none of the four antidotes. For toxic alcohol and glycol poisoning, most hospitals held ethanol for intravenous use, with a minority stocking fomepizole. There were, however, 30 (15%) acute hospitals that had no antidote available locally for treatment of toxic alcohol and glycol poisoning.

There has been little change in antidote availability compared with a previous survey in 2007 (Figures 5.8 and 5.9).



FIGURE 5.8 Proportion of hospitals *not* holding stocks of antidotes that are recommended to be available immediately



FIGURE 5.9 Proportion of hospitals *not* holding stocks of antidotes recommended to be available within one hour

5.5 Toxic Alcohols and Glycols

Toxic alcohol and glycols, such as ethylene glycol and methanol, are present in a number of commercial products that are readily available to the public, including antifreeze, brake fluid, and wallpaper stripping, window-cleaning and windscreen-washing solutions. If ingested accidentally or deliberately, they can cause severe toxicity, including metabolic acidosis, coma, seizures, renal failure (especially for ethylene glycol) and blindness (methanol). Severe sequelae can be prevented by appropriate clinical management including administration of an antidote, either ethanol or fomepizole, together with appropriate use of haemodialysis. Episodes of severe poisoning are sometimes difficult to manage because of difficulties in obtaining the required laboratory analyses or in locating supplies of antidotes.

Little is known about the epidemiology of this relatively infrequent poisoning in the UK, although the complexity of patient management leads to this being one of the most common types of poisoning requiring referral to NPIS consultant clinical toxicologists for advice on management.

A prospective audit of toxic alcohol and glycol cases reported through telephone enquiries to the NPIS was therefore

conducted, during the 2010 calendar year, to provide information on the frequency, current management and outcomes of systemic toxic alcohol poisoning. The main aim was to provide information on which to base the planning of clinical services for this type of poisoning, including appropriate availability of assays and antidotes.

Over the year there was a total of 608 enquiries to the NPIS involving toxic alcohols and glycols, relating to 488 individual exposures. Of these, 250 originated from non-hospital sources. The vast majority of incidents (431) occurred in the home and most were acute ingestions. There were 89 cases involving children aged five years or less (Figure 5.10). Accidental exposures accounted for 328 cases, 119 were intentional exposures and four were described as recreational use. Of the people involved, 409 had no or minor symptoms only at the time of the call and 71 had moderate or severe symptoms. A Poisons Severity Score (PSS) was not available in eight enquiries. The products most commonly involved were antifreeze and screenwash, surgical spirit and methylated spirits (Figure 5.11); ethylene glycol was the most common ingredient.

Of the 238 calls originating from hospitals, 182 were potentially systemic exposures. Further follow up was attempted for these and complete information was obtained for 122 cases. Of these, 99 patients required treatment with an antidote and 33 patients underwent haemodialysis and/or haemofiltration. There were four fatalities.

Some of the difficulties encountered by clinicians in managing this relatively uncommon but potentially serious poisoning included a lack of availability of laboratory assays for toxic alcohols, inadequate stock of antidotes, and inadequate access to facilities for haemodialysis. Individual hospitals encounter clinically important systemic poisoning with toxic alcohols and glycols infrequently. As a result, they may not be well prepared to manage cases when they do occur, since stocking of appropriate antidotes and availability of specialist assays may not be considered a priority. NPIS data, however, indicate that there is an average of at least two severe cases each week nationally. To manage these more effectively, NHS hospitals need to consider how they can improve the local availability of assays and antidotes.



FIGURE 5.10 Enquiries to the NPIS involving toxic alcohols and glycols by age of patient, in 2010



FIGURE 5.11 Products involved in enquiries to the NPIS involving toxic alcohols and glycols, in 2010

6 Recommendations

Outcome of Recommendations for 2010/11

1 To work to ensure that future NPIS and UKTIS commissioning arrangements are appropriate and consistent with the evolving policy for public health

Outcome Being progressed, but delayed in line with national arrangements

2 To ensure arrangements are appropriate to enable the NPIS and UKTIS to provide optimal support to the London 2012 Olympic Games

Outcome The NPIS has prepared a capability summary for public health protection for the Olympic Games. It is preparing to provide high quality enhanced business as usual during the games by establishing the availability of laboratory assays and antidotes, improving protocols to support healthcare professionals in the management of radiation poisoning, updating information about chemical hazards held on TOXBASE and educating NHS staff about the management of people exposed to these agents

Recommendations for 2011/12

- 1 To complete preparations and provide health support for the London 2012 Olympic Games
- 2 To collaborate with the College of Emergency Medicine to produce and circulate updated guidelines for NHS trusts on recommended holdings of the antidotes required for the treatment of poisoning
- 3 To collaborate with the Association for Clinical Biochemistry to update recommendations on the use of specialist assays required for the management of poisoning and establish the availability of these assays nationally
- 4 To ensure TOXBASE remains a fit-for-purpose, front-line resource for UK healthcare professionals by maintaining the four-yearly review cycle for all entries on the database



NPIS Consultants

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Consultants providing on-call support for the NPIS

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Consultants providing specialist paediatric support for the NPIS

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Consultant Paediatrician, Newcastle upon Tyne Hospitals NHS Trust

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Consultant in Paediatric Emergency Medicine, Royal Hospital for Sick Children, Edinburgh

National and International Appointments of NPIS Consultants

NPIS staff have a role in supporting many important aspects of toxicology, both nationally and internationally. These include advisory roles to international and national bodies, including government, as well as academic activities. The range of their roles presented below provides a flavour of these activities and indicates the wider 'added value' of the NPIS.

NPIS Birmingham

Dr S M Bradberry

INTERNATIONAL ACTIVITIES

Board Member: European Association of Poison Centres and Clinical Toxicologists

Scientific Committee Member: European Association of Poison Centres and Clinical Toxicologists

INTERNATIONAL SOCIETIES

Fellow: American Academy of Clinical Toxicology

INTERNATIONAL JOURNALS

Senior Editorial Board Member: Clinical Toxicology

UK ADVISORY COMMITTEES

Member: Health and Safety Executive Pesticide Incident Appraisal Panel ACADEMIC ACTIVITIES

Honorary lecturer: School of Biosciences, University of Birmingham Joint Course Organiser: MSc (Toxicology), University of Birmingham Educational supervisor: Sandwell and West Birmingham Hospitals NHS Trust

Professor I A Vale

INTERNATIONAL ACTIVITIES

Member: Advisory Board Hong Kong Poisons Centre

INTERNATIONAL SOCIETIES

Fellow: American Academy of Clinical Toxicology

INTERNATIONAL JOURNALS

Reviews Editor: Clinical Toxicology Editorial Board Chairman: Medicine Editorial Board Member: Drugs

UK ADVISORY COMMITTEES

Chairman: Ministry of Defence Research Ethics Committee

Member: MHRA Clinical Trials Collaboration Group

Consultant: Dstl Porton Down

Member: Expert Advisory Group on Management of Casualties Caused by Chemical Terrorism (Blain II)

NHS NATIONAL AND REGIONAL COMMITTEES

Member: National Patient Safety Board: Medication Safety Board ACADEMIC ACTIVITIES

Joint Course Organiser: MSc (Toxicology), University of Birmingham Examiner: MRCP(UK) Part 2 Clinical Examination (PACES) External Examiner: Cardiff University Examiner: Faculty of Occupational Medicine Fellow: British Toxicology Society Fellow: Faculty of Occupational Medicine

NPIS Cardiff

Dr C V Krishna

NHS NATIONAL AND REGIONAL COMMITTEES

Chairman and Training Programme Director for Clinical Pharmacology Training in Wales

Member: New Medicines Group, All-Wales Medicines Strategy Committee Member: Joint Specialty Committee, Clinical Pharmacology and Therapeutics

Member: All-Wales Specialist Training Committee in Clinical Pharmacology ACADEMIC ACTIVITIES

Member: SAC, Clinical Pharmacology and Therapeutics, UK

Member: Prescribing Skills Assessment, Certificate/Diploma/MSc in Medical Toxicology, Cardiff University Deputy Course Coordinator: Certificate/Diploma/MSc in Medical Toxicology, Cardiff University Member: Steering Committee, Diploma in Therapeutics, Cardiff University PACES Examiner: Royal College of Physicians, UK

Professor P A Routledge

INTERNATIONAL ACTIVITIES

Associate Director: World Health Organization Clearing House for Chemical Incidents, Cardiff, Wales

INTERNATIONAL JOURNALS

Editorial Board Member: Adverse Reactions and Acute Poisoning Reviews Editorial Board Member: Adverse Drug Reactions Bulletin

ADVISORY COMMITTEES

Chairman: All-Wales Medicines Strategy Group Consultant Advisor in Toxicology to the Chief Medical Officer (Wales) NHS NATIONAL AND REGIONAL COMMITTEES

Chairman: UK Herbal Medicines Advisory Committee

ACADEMIC ACTIVITIES

President Elect: British Pharmacological Society External Advisory Board Member: Liverpool School of Biomedical Sciences Course Director: Postgraduate Diploma/MSc Programmes in Medical Toxicology, Therapeutics and Occupational Health, Cardiff University Faculty Lead: Medicines Management, 1000 Lives Plus Campaign, Wales Honorary Secretary: Clinical Pharmacology Colloquium

Dr A Thomas

ADVISORY COMMITTEES

Member: New Medicines Group, All-Wales Medicines Strategy Committee Member: All-Wales Specialist Training Committee in Clinical Pharmacology

NHS NATIONAL AND REGIONAL COMMITTEES

Deputy Director: Yellow Card Centre (Wales)

ACADEMIC ACTIVITIES

Member: Steering Committee, Diploma/MSc in Medical Toxicology, Cardiff University

Member: Steering Committee, Diploma in Therapeutics, Cardiff University

Dr J P Thompson

INTERNATIONAL ACTIVITIES

Member: Advisory Board Hong Kong Poisons Centre

INTERNATIONAL SOCIETIES

Chair: Human Toxicology Section British Toxicology Society Vice President (Clinical): British Pharmacological Society

ADVISORY COMMITTEES

Member: Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT)

Member: Appraisal Panel for Suspected Adverse Reactions to Veterinary Medicines

Member: Expert Advisory Group on Management of Casualties Caused by Chemical Terrorism (Blain II)

Senior Medical Officer: Yellow Card Centre (Wales)

NHS NATIONAL AND REGIONAL COMMITTEES

Member: New Medicines Group, All-Wales Medicines Strategy Committee Member: Joint Specialty Committee, Clinical Pharmacology and Therapeutics

Member: All-Wales Specialist Training Committee in Clinical Pharmacology

ACADEMIC ACTIVITIES

Member: Prescribing Skills Assessment and PRESCRIBE Task and Finish Group, British Pharmacological Society

Course Coordinator: Certificate/Diploma/MSc in Medical Toxicology, Cardiff University

Member: Steering Committee, Diploma in Therapeutics, Cardiff University Member: Steering Committee, MSc in Occupational Health, Policy and Practice, Cardiff University

NPIS Edinburgh

Professor D N Bateman

INTERNATIONAL ACTIVITIES

Advisor: World Health Organization/International Programme on Chemical Safety

INTERNATIONAL SOCIETIES

Scientific Committee Member: European Association of Poisons Centres and Clinical Toxicologists

Fellow: American Academy of Clinical Toxicology

INTERNATIONAL JOURNALS

Editor in Chief: Clinical Toxicology

UK ADVISORY COMMITTEES

Member: Pharmacovigilance Expert Advisory Group, Medicines and Healthcare products Regulatory Agency Member: Expert Advisory Group on Management of Casualties Caused by Chemical Terrorism (Blain II) Member: Pesticides Adverse Health Effects Surveillance Working Group of the Advisory Committee on Pesticides

NHS NATIONAL AND REGIONAL COMMITTEES

Board Member: Yellow Card Centre (Scotland) Expert Toxicology Advisor: Scottish Government

ACADEMIC ACTIVITIES

Training Programme Director: Scotland's Clinical Pharmacology and Therapeutics Programme *(from August 2009)* Member: Association of Physicians Fellow: British Toxicology Society Fellow: British Pharmacological Society

Dr J Dear

ACADEMIC ACTIVITIES

Tutor: MSc in Translational Medicine, Edinburgh University, PhD Student External Examiner: MRes in Translational Medicine, Newcastle University Member: British Pharmacological Society Member: Association of Physicians Member: Clinical Pharmacology Specialty Question Group, MRCP(UK)

NHS NATIONAL AND REGIONAL COMMITTEES

Member: Lothian Formulary Committee

Dr M Eddleston

INTERNATIONAL ACTIVITIES

Advisor: World Health Organization/Department of Mental Health and Evidence and Policy on Environmental Health

INTERNATIONAL SOCIETIES

Board Member: Asia Pacific Association of Medical Toxicology

INTERNATIONAL JOURNALS

Board Member: Clinical Toxicology

NPIS Newcastle (including UKTIS)

Dr S Stephens

INTERNATIONAL SOCIETIES

Member: The Teratology Society Member: Organisation of Teratology Information Specialists

Dr H K R Thanacoody

UK ADVISORY COMMITTEES

Member: Independent Scientific Advisory Committee, Medicines and Healthcare products Regulatory Agency Member: RCPath Toxicology Specialist Advisory Committee

ACADEMIC ACTIVITIES

Member: Question Writing Group: Joint Royal Colleges MRCP (Part 1) Examining Board

Module Leader: Certificate/Diploma in Therapeutics, University of Newcastle

Module Leader: Experimental Medicine and Therapeutics, MRes in Translational Medicine, University of Newcastle

External Examiner: Certificate/Diploma/MSc in Medical Toxicology, Cardiff University

Professor S H L Thomas

INTERNATIONAL SOCIETIES

President: European Association of Poisons Centres and Clinical Toxicologists

Expert Panel Member: European Medicines Agency

INTERNATIONAL JOURNALS

Senior Editorial Board Member: *Clinical Toxicology* International Editorial Board Member: *British Journal of Clinical Pharmacology*

UK ADVISORY COMMITTEES

Member: Commission for Human Medicines Member: MHRA Paracetamol Ad Hoc Group Co-opted Member: Technical Committee, Advisory Council on the Misuse of Drugs Member: Expert Advisory Group on Management of Casualties Caused by Chemical Terrorism (Blain II) Member: Ministry of Defence Advisory Committee on Military Medicine Member: Ministry of Defence Research Ethics Committee NHS NATIONAL AND REGIONAL COMMITTEES

Director: Yellow Card Centre (Northern and Yorkshire) Medical Director: Regional Drug and Therapeutics Centre, Newcastle Member: North East Treatment Advisory Group Member: North of Tyne Area Prescribing Committee Chair; North of Tyne Area Prescribing Committee, Formulary Subcommittee

ACADEMIC ACTIVITIES

Chair: Specialist Training Committee, Clinical Pharmacology and Therapeutics, Northern Deanery

Degree Programme Director: Certificate/Diploma in Therapeutics, Newcastle University

Strand leader: MRes in Translational Medicine and Therapeutics, Newcastle University

Dr L M Yates

INTERNATIONAL SOCIETIES

Member: The Teratology Society Member: Organisation of Teratology Information Specialists



Over 90 contributions to the scientific literature were published in 2010/11 by NPIS staff.

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Thomas SHL, James DA, Spears R, Cooper G, Wood K, Dyas J, Adams RD, Lupton DJ, Good AM. Effects of legal control on enquiries to the UK National Poisons Information Service relating to recreational cathinone use. Clin Toxicol 2011; 49: 214.

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Thanacoody HKR. Opiate overdose. Monograph for BMJ Best Evidence/Point of Care June 2010. Available at http://bestpractice.bmj.com/best-practice/monograph/339.html The following amendment has been made to this report since first publication on the website earlier this month

Page 38 – Figure 5.9 has been replaced since the previous version included some entries that appear (correctly) in Figure 5.8 (on page 37).

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