



Public Health  
England



National Poisons  
Information Service

# National Poisons Information Service

Report 2012/13



The National Poisons Information Service is commissioned by  
Public Health England on behalf of the UK health departments

# National Poisons Information Service

*A service commissioned by Public Health England on behalf of the UK health departments*

The main role of the National Poisons Information Service is to advise NHS healthcare professionals on the diagnosis, treatment and care of poisoned patients across the UK. Poisoning is an extremely common cause of hospital admissions in the NHS, being similar in number to admissions for myocardial infarction. In addition, many cases of suspected poisoning are not treated in hospital following advice provided by the NPIS, thus reducing unnecessary use of NHS resources. The major workload of NPIS is advice to hospital emergency departments, but minor injuries units and primary care services are also significant users of the service – the latter to a large extent involving NHS telephone helplines (NHS Direct, NHS 111 and NHS 24).

## NPIS Units at 31 March 2013

### NPIS Birmingham Unit

City Hospital, Birmingham

hosted by Sandwell and West Birmingham Hospitals NHS Trust

Director: Professor J A Vale MD FRCP FRCPE FRCPG FFOM FAACT FBTS FBPharmacolS HonFRCPSG

### NPIS Cardiff Unit

Llandough Hospital, Cardiff

hosted by Cardiff and Vale University Health Board

Director: Dr J P Thomson BMedSci MBChB FRCP FBTS

### NPIS Edinburgh Unit

Royal Infirmary of Edinburgh

hosted by NHS Lothian – University Hospitals Division

Director: Dr M Eddleston MA PhD FRCPE

### NPIS Newcastle Unit

Regional Drug and Therapeutics Centre, Newcastle

hosted by Newcastle upon Tyne Hospitals NHS Foundation Trust

Director: Professor S H L Thomas BSc MD FRCP FRCPE

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*Front cover image*

*Antique poison bottle © Medical Photography Department, Royal Infirmary of Edinburgh*

# Foreword

The role of the National Poisons Information Service (NPIS) is to reduce the burden of healthcare associated with poisoning by the provision of rapidly available, consistent and evidence-based advice to front-line NHS healthcare professionals. The purpose of this advice is to facilitate optimal clinical management of patients with confirmed or suspected poisoning and those who are (or may be) exposed to medicines or other potential poisons during pregnancy. Key aims are better in-hospital care and the avoidance of unnecessary hospital attendances and admissions. In view of the numbers of patients presenting to health services with poisoning and the many thousands of different substances and products that may be involved, this is a challenging task.

Responsibility for commissioning the NPIS moved from the Health Protection Agency (HPA) to Public Health England (PHE) in April 2013, on the abolition of the HPA. This annual report is provided as a statement of activity, accountability and governance for PHE and for the main joint funders, who are the English Department of Health, the Scottish Government, the Welsh Government, the Northern Ireland Department of Health and Beaumont Hospital, Dublin, on behalf of the Government of the Republic of Ireland.

This report demonstrates the volume and quality of work provided by the NPIS during 2012/13, as evidenced by workload statistics, results of quality assurance exercises and surveillance activities. In addition to this routine work, the NPIS has faced some particular challenges during the year, and four of these are outlined below.

Our preparations for the London 2012 Olympic and Paralympic Games involved updating information relating to possible chemical threats, developing new operational systems for surveillance and new pathways of referral for clinical enquiries relating to radiation, and introducing mechanisms to allow up-scaling of staff numbers to handle a major event. These leave a lasting legacy so that the NPIS is now better prepared than ever to provide support during a major public health incident.

In September 2012, the UK Commission for Human Medicines recommended significant changes to

the management of paracetamol poisoning. This necessitated a major overhaul of NPIS advice for this, the most common poisoning presentation in the UK, and resulted in a substantial and sustained increase in enquiry numbers and consultant referrals concerning paracetamol poisoning.

Previous NPIS research has demonstrated that access to antidotes for less commonly encountered poisons has been suboptimal in UK hospitals, with the risk that treatment may be delayed. Work has been undertaken with the College of Emergency Medicine and the UK health departments to clarify antidote stocking requirements and develop mechanisms for supra-regional stocking of antidotes that are infrequently needed.

Until recently there has been no accredited training in clinical toxicology and this has inhibited training the next generation of NPIS consultant clinical toxicologists. This situation has been improved substantially by the contribution of NPIS staff to the development of an advanced speciality module in clinical toxicology, which is now approved by the General Medical Council, and by funding from our commissioners for clinical fellowships based on this module and located in the NPIS units.

This annual report once again demonstrates the NPIS to be a fully integrated, essential, national front-line service that is highly valued by its many NHS healthcare professional users. We can be justifiably proud of the achievements of the NPIS during the year and look forward to meeting the challenges of the forthcoming year with confidence.

**Elaine Lynch-Farmery**

Centre for Radiation, Chemical and Environmental Hazards  
Public Health England

**Simon Thomas**

Chair, NPIS Clinical Standards Group

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# Executive Summary

## Background

Suspected poisoning, which may include accidental exposures, deliberate self-poisoning, drug misuse and therapeutic errors, is a common reason for presentation to health services. About 140,000 people with suspected poisoning are admitted to hospitals across the UK each year. Many more are seen in emergency departments and discharged, or managed in primary care, frequently using NHS advice lines such as NHS Direct, NHS 24 and NHS 111.

The National Poisons Information Service (NPIS) is commissioned to provide information and advice to support the management of these patients. This is achieved by provision of the poisons information database TOXBASE<sup>®</sup>, which is available without cost to registered UK health professionals. If further advice is needed for more complex cases, the NPIS 24-hour telephone service is available at all times, together with support from a consultant clinical toxicologist as required. The UK Teratology Information Service (UKTIS), the national source of information and advice about exposures to drugs and chemicals during pregnancy, is also provided by the NPIS.

## Activity

During 2012/13 there were over 550,000 TOXBASE user sessions and around 1,650,000 separate product accesses, increases of 4.0% and 7.7%, respectively, on equivalent figures for the previous year. There were, in addition, over 57,000 hits to the information held on TOXBASE concerning exposure to drugs and chemicals in pregnancy, an increase of more than 20% on activity for 2011/12. There was also an increase of 4.7% in NPIS and UKTIS telephone enquiries, to around 54,000. The complexity of these telephone enquiries is illustrated by the number referred to an NPIS consultant, around 2,200 during 2012/13, an increase of 44% over the previous year.

It is essential to update the approximately 17,000 product entries in TOXBASE regularly, to maintain their quality

and the confidence of NHS staff, and to allow telephone call numbers to be maintained at manageable levels.

During 2012/13, NPIS staff wrote or revised around 3,300 entries – making a total of over 8,800 (or 50% of entries) during the last two years.

## Quality

As in previous years, quality assurance exercises were conducted by questionnaire to obtain evidence of user satisfaction with our services. Overall satisfaction scores continued to be very high for the three areas studied, which were the TOXBASE website (92%), the telephone poisons information service (96%) and the UKTIS telephone service (98%).

## Surveillance

NPIS data is valuable for public health surveillance activities. The NPIS has continued to develop an urgent alerting system to allow immediate follow-up of accesses to TOXBASE that involve specific agents of interest. During the year over 2,600 patient-specific alerts were received by this system. Of these, 273 were followed up, most commonly involving exposure to carbon monoxide, chlorine and hydrofluoric acid.

The NPIS has performed surveillance for pesticide exposures in the UK on behalf of the Department for Environment, Food & Rural Affairs since 2004 using healthcare worker accesses to TOXBASE and calls to the NPIS telephone service. Currently, over 1,900 TOXBASE entries for pesticide and biocide products are being tracked. During 2012/13, information has been gathered on nearly 1,200 potential exposures, with the agents most commonly implicated being permethrin and glyphosate. Only a minority of patients were classified as having moderate (3%) or severe (0.5%) poisoning; there were three fatalities during the year due to deliberate ingestion of paraquat (two cases) or aluminium phosphide.

Issues of interest highlighted in this year's report include the following.

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\* TOXBASE<sup>®</sup> is a registered trademark of the UK National Poisons Information Service



## Therapeutic errors with intravenous paracetamol

Following the introduction of intravenous paracetamol into clinical practice and subsequent reporting to the service of serious overdoses, the NPIS developed treatment guidelines for the management of intravenous paracetamol poisoning in 2010 and brought the potential risks to the attention of prescribers. We have continued to review these exposures.

In 2012/13, there were 30 reports of overdoses with intravenous paracetamol. Six occurred in children under one year old; another six occurred in children between one and nine years old. Although the numbers of enquiries concerning intravenous paracetamol exposure have remained similar for the last three years, there is the suggestion that paediatric enquiries are decreasing, while adult exposures may be increasing, possibly reflecting increased use of intravenous preparations in adults and/or awareness of safety issues in children.

## Therapeutic errors with ranitidine

NPIS staff are able to detect and investigate signals from telephone enquiries that involve medication errors. In 2012, paediatric patients were noted to be commonly receiving excessively large doses of ranitidine syrup. Ranitidine is formulated at a concentration that requires ten-fold smaller volumes of the syrup to be given, compared to the 5 mL teaspoon doses used for many paediatric medicines such as paracetamol. Patients were receiving, for example, 2.1 to 3.0 mL rather than 0.21 to 0.3 mL of the ranitidine syrup, suggesting that carers were confused about these small prescribed doses. As a result of this study, we recommend that a paediatric formulation of ranitidine syrup is produced to avoid such large overdoses and unnecessary presentations to healthcare practitioners.

This work illustrates the value of NPIS data for pharmacovigilance. Using this information to study overdoses spread across time and place allows data regarding relatively uncommon errors, possibly seen once by a primary care physician, to be noticed, analysed and acted upon.

## Drugs of misuse including newer stimulants

NPIS data is useful for tracking toxicity associated with drugs of misuse. During the year the most frequently implicated drugs were mephedrone, cocaine, MDMA ('ecstasy'), amphetamines, heroin and cannabis. Other than mephedrone, of the newer recreational drugs, those most frequently involved in telephone enquiries have been 'legal highs' (not otherwise specified), alpha-methyltryptamine (AMT), synthetic cannabinoids (eg 'spice'), 5 or 6-(2-aminopropyl)benzofuran (5/6-APB) and 25I-NBOMe. Compared with the previous year, substantial increases in the numbers of telephone enquiries (49%) and TOXBASE accesses (128%) relating to recreational substances not controlled under misuse of drugs legislation ('legal highs') occurred during 2012/13. Reductions in NPIS activity following legal control of methoxetamine were demonstrated.

The NPIS has continued to work closely with the UK Focal Point Early Warning System (Focal Point EWS) on new psychoactive substances. Eight reports were provided by the NPIS to the Focal Point EWS during the year; NPIS data was referenced in the recent ACMD recommendation to control 5/6-APB and related substances.

## Carbon monoxide

Despite public awareness campaigns, carbon monoxide poisoning continues to be an important preventable cause of morbidity and mortality. During 2012/13, there were 434 telephone calls to the NPIS concerning carbon monoxide, involving at least 630 individuals (increases of 52% and 100%, respectively, over 2011/12). As in previous years, most exposures occurred in the home, with faulty boilers or appliances being the most common source. While most episodes were associated with limited or no clinical effects, 24 people had moderate or severe poisoning, of whom three are known to have died.

## Liquid detergent capsules

The NPIS has just completed a large follow-up study of the toxicity of liquid detergent capsules involving almost 1,500 patients, of whom the great majority were children under five years old. Exposure was predominantly by the

oral route. Thirty-two patients presented with moderate toxicity (2.2%), while seven had severe toxicity (0.5%). The most common features were nausea and vomiting (49%); drowsiness occurred in 49 cases; features that developed in children with severe toxicity included pulmonary aspiration (three cases), stridor (four cases) and airway burn (one case). Four children were intubated and ventilated. Features that developed following ocular exposure included conjunctivitis (145 cases) and corneal conjunctivitis (six cases).

### Toxic alcohols and glycols

A prospective audit of toxic alcohol and glycol cases reported through telephone enquiries to the NPIS was conducted during 2010 and again during 2012. The study aimed to provide information on which to base planning of clinical services for this type of poisoning, including appropriate availability of assays and antidotes. Over the two one-year periods, there were 1,315 enquiries relating to 1,070 individual exposures, with hospitals being the source of enquiries in 548 cases. Of 329 systemic exposures, 216 patients received antidote treatment,

90 required extracorporeal treatment for toxic alcohol and glycol poisoning, 77 developed severe toxicity and eight patients died. In keeping with NPIS advice, use of fomepizole increased but antidote treatment was usually initiated based on surrogate markers of toxicity as laboratory assays of toxic alcohols and glycol were often unavailable. As a result, there was overuse of antidote with a consequent risk of adverse events and unnecessary expense.

NPIS data suggests that there is an average of at least three severe systemic exposures each week nationally. To manage these effectively, NHS hospitals need to consider how they can improve the local availability of assays and antidotes.

### Education and Research

NPIS staff continue to be active in education and research, with more than 70 contributions to the scientific literature published during 2012/13. A high proportion of these publications were peer-reviewed scientific papers.





# 1 Introduction

Information on National Poisons Information Service (NPIS) activity in 2012/13 is given in this report. It shows how different elements of the service work together and provides some examples of its activity – in particular relating to drugs of misuse, liquid detergents, paracetamol overdose and carbon monoxide poisoning.

The NPIS is a network of four dedicated units, all linked to clinical treatment facilities within UK teaching hospitals. Until 31 March 2013, the NPIS was commissioned by the Health Protection Agency (HPA). From 1 April the HPA was abolished and its functions transferred to Public Health England (PHE), including commissioning the NPIS on behalf of the UK health departments.

The NPIS has provided information to healthcare workers in the UK by telephone for 50 years, since 1963 (see the panel). The poisons information database, TOXBASE®\* ([www.TOXBASE.org](http://www.TOXBASE.org)), was developed in 1982 and transferred to the internet in 1999 where it was adopted as the first-line information source for healthcare professionals in the UK. While the structure of the NPIS has changed over the last 50 years, its focus has always been to assist colleagues in all parts of the NHS to manage poisoned patients. Information and advice provided by the NPIS are updated regularly and are based on the published literature, experience from NPIS telephone enquiries data and direct clinical experience of poisoning managed in NPIS-linked clinical departments.

In 1995 the UK Teratology Information Service (UKTIS) moved to Newcastle to become an integral component of NPIS activities. As shown in this report, the activity of UKTIS is important both in supporting women of child-bearing age and their healthcare providers, and also in collecting new 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 over 140,000 NHS hospital admissions in the UK 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 in particular are involved. The

majority of poisoning in adults is related to self-harm, while unintentional exposures are common in children. Many thousands of different agents can be involved, making it very difficult for NHS staff to keep up to date on diagnosis and management, especially when new or unfamiliar agents are involved. In addition, around 40% of adults who poison themselves take alcohol at the same time, making clinical assessment and management more difficult.

Over the past decade, there has been a small reduction in the number of patients admitted to hospitals throughout the UK for suspected poisoning. Part of this may be due to national strategies aimed at reducing rates of suicide and self-harm. Other reasons are unclear. At the same time, however, novel trends are emerging and new drugs of misuse present a particular challenge (see Section 6.2). The pattern of prescription drugs taken in poisoning has also changed in line with new approaches to therapy. For example, newer antidepressants and antipsychotic drugs are increasingly involved, as the older and often more toxic agents are withdrawn.

Hospital admission data, illustrated by NHS finished consultant episodes, does not reflect the very many poisoned patients who present to emergency departments across the UK but are discharged without being admitted. Nor does the data reflect the very large number of enquiries about poisoning received in primary care or by NHS public access helplines (NHS Direct or 111 in England and Wales and NHS 24 in Scotland). The NPIS provides advice to general practitioners, emergency departments and NHS public access helplines to help them decide which patients need hospital assessment or admission and which can be managed safely at home.

The NPIS thus provides information to support and assist appropriate triage, referral, assessment and treatment of patients at all levels of 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 patients with severe poisoning who do survive to hospital admission, reducing morbidity or mortality. At the same time, NPIS advice reduces the need for unnecessary hospital attendance from those who have been exposed to substances of relatively low toxicity.

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\* TOXBASE® is a registered trademark of the UK National Poisons Information Service

A key component of the service 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. 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.

## 50 Years of the NPIS

September 2013 marks the 50th anniversary of the NPIS. The service was originally established following the recommendations of a subcommittee of the Standing Medical Advisory Committee of the Central Health Services. This subcommittee had been set up in 1959 under the chairmanship of Professor Hedley Atkins of Guy's Hospital, London, to address the morbidity and mortality from acute poisoning. In 1959, for example, 20,100 patients had been admitted to hospitals in England and Wales as a result of acute poisoning and, in 1960, 5,016 individuals died from poisoning, usually outside hospital. One of the recommendations of the Atkins Committee was that an information service should be set up with central arrangements for coordination to support doctors wishing to identify the properties or ingredients of a substance known to have been ingested. Such poisons services were already available in the United States, where the first poisons information centre in the world had been established in Chicago, Illinois, in 1953. This recommendation led to the establishment of the National Poisons Information Service (NPIS).

The NPIS was established with two main purposes. First, it was to maintain an index of substances of common use, including medicinal, veterinary, industrial, agricultural, horticultural and household products, showing their composition and, wherever possible, their toxicity and corrective measures in cases of poisoning. Second, it was responsible for providing information for medical practitioners so as to facilitate treatment of cases of acute poisoning.

The first three national centres set up by the Ministry of Health were based in acute hospitals in Belfast, Edinburgh and London (Guy's). These began operating on 2 September 1963. A centre to provide poisons information had already been set up at the Leeds General Infirmary in August 1961 and also contributed to the new service. Other centres were subsequently

established in Cardiff (1964), Birmingham (1974) and Newcastle (1975). Today's NPIS units are located in Birmingham, Cardiff, Edinburgh and Newcastle.

Over the years the activity of the service has grown substantially. For example, there were 10,858 telephone enquiries to all the NPIS centres in 1968, while in 2012/13 there have been over 50,000 telephone enquiries and more than 1.6 million product accesses on TOXBASE, as detailed later in this report.

Some milestones in the evolution of the service are given below.

### NPIS Milestones

<b>1983</b>	Establishment of TOXBASE allowed doctors to access information by telephone and a television (later computer terminal) using the Viewdata system
<b>1995</b>	Establishment of the National Teratology Service (now the UK Teratology Information Service) as part of NPIS Newcastle
<b>1996</b>	Launch of the UK Poisons Information Database, allowing entry of enquiry details on to a computer database
<b>1998</b>	Establishment of the NPIS Product Data Centre, providing information on the composition of consumer products, including product safety datasheets (SDS)
<b>1999</b>	Migration of TOXBASE to the internet, allowing rapid access to poisons information by all UK health professionals who register for the service
<b>1999</b>	Establishment of the NPIS Literature Database to ensure that NPIS staff are equipped to answer enquiries on all aspects of human toxicology and that TOXBASE is kept up to date
<b>2000</b>	Launch of a single national telephone number for the NPIS
<b>2003</b>	Commissioning transferred to the Health Protection Agency with subsequent establishment of a fully integrated national service
<b>2011</b>	Establishment of the publicly available NPIS website
<b>2012</b>	Launch of the TOXBASE app for mobile devices
<b>2013</b>	Commissioning transferred to Public Health England

## 2 NPIS Advice Service Structure

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

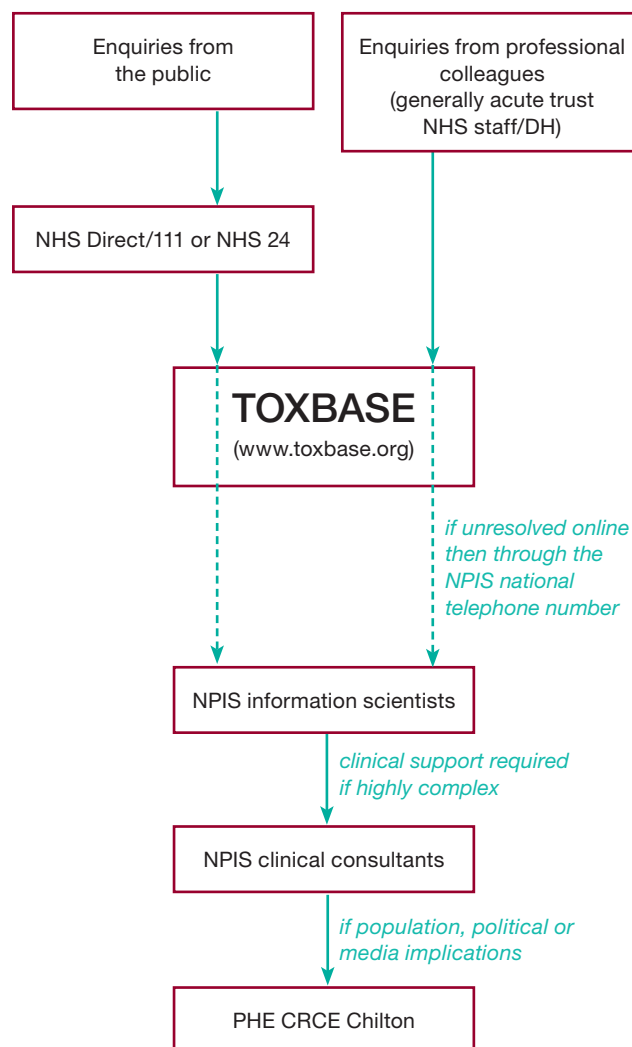
The four NPIS units are currently based within NHS teaching hospital 'providers' (two in England and one each in Scotland and Wales). The service has 24-hour consultant clinical toxicologist support provided by NHS consultant staff in all four NPIS units and colleagues in two other NHS hospitals (Guy's and St Thomas' NHS Foundation Trust and York Hospitals NHS Foundation Trust). These consultants are available to assist colleagues in the management of more seriously unwell patients. NPIS consultant clinical staff also provide specialist services in clinical toxicology to their local populations. Over recent years, there has been an expansion in the number of consultant staff available, increasing the resilience and sustainability of the service.

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](http://www.toxbase.org)), which is available free to all UK health professionals who register for it, including hospital staff, primary care physicians, and NHS Direct/111 and NHS 24 services staff. The NPIS also provides a 24-hour telephone information service for health professionals using a single national telephone number (0844 892 0111) when further advice or information is needed.

NPIS activity is reflected by the numbers of TOXBASE accesses or user sessions and telephone enquiries. The increasing use now being made of TOXBASE, encouraged by NPIS promotional exercises, releases NPIS staff-time for the performance of more strategic work for the service, including production of TOXBASE monographs.

When first received (Figure 2.1), telephone enquiries are managed by specialists in poisons information (SPI) who



**FIGURE 2.1** How poisons enquiries are answered

are graduates with a biomedical or nursing background. Complex enquiries are referred on to NPIS consultant staff as necessary on a 24-hours-a-day basis.

All NPIS telephone enquiries are recorded for governance purposes and the data is logged within a specially designed national database (UKPID). Data is 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 the provision of easily accessible national data on the activity of the service and the patterns of enquiries received. The information available can also be used to inform clinical management of subsequent similar cases. In addition, data from UKPID can 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. Out-of-hours enquiries from health professionals are referred to the NPIS. In addition, the NPIS is 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 to health professionals and members of the public in Ireland.

Information on the potential toxicity of drugs and chemicals in pregnancy is provided by the UK Teratology Information Service (UKTIS). This was established as part of NPIS Newcastle in 1995. 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 provider unit answering an enquiry, it is essential to have national mechanisms for addressing issues that affect the service. A key development has been the formalisation of such arrangements within a UK strategic framework.

Commissioning issues are dealt with by the PHE 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, usually on the same day as the PHE NPIS Commissioning Group 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 through TOXBASE.

To encourage 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 four times a year and have now been taking place for seven years. Each provider unit hosts the event in turn.

There are also regular meetings and teleconferences of the TOXBASE Editing Group and the UKPID User Group. These groups 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 and review.

## 3 NPIS Activities in 2012/13

### 3.1 Overall Service Profile

This report concentrates on NPIS activity in 2012/13, as reflected by TOXBASE user sessions, TOXBASE accesses, telephone enquiries and consultant referrals. Increased use of TOXBASE by healthcare professionals, encouraged by NPIS promotional exercises, allows NPIS staff to perform more strategic work for the service, including production and revision of TOXBASE monographs, research projects and follow-up of calls of interest.

The total number of TOXBASE user sessions (defined as one logon to the TOXBASE site during which the user may access one or more products several times) was 553,367. This is an increase of 4.0% on the number of sessions in 2011/12. In addition, 57,319 UKTIS monographs were accessed on TOXBASE during 2012/13, an increase of 20.2% compared to 2011/12.

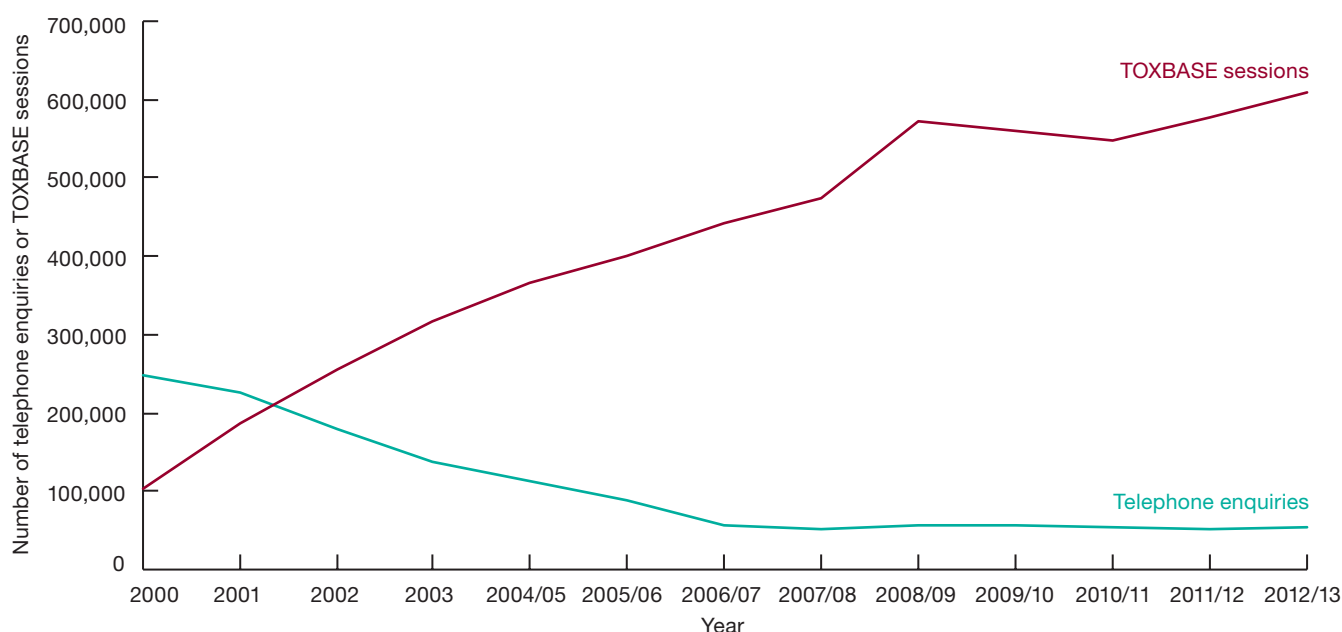
The number of user sessions includes 10,118 educational sessions, an increase of 45% on the 2011/12 figure. Sessions from all the NPIS units and from the Northern Ireland Regional Medicines and Poison Information Service have been excluded from further detailed analyses, as these units may access TOXBASE for training/ educational purposes, to access operating

procedures or for monograph-writing purposes (NPIS units only), as well as while answering telephone enquiries.

Therefore a total of 504,661 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).

There were 1,649,655 individual product accesses in 2012/13. Applying the same criteria as for session data gives a total of 1,380,258 product accesses from UK-based, non-poisons-centre users, which are analysed below. This number is an increase of 7.7% on the 2011/12 figure.

The total number of telephone enquiries received by the NPIS in 2012/13 was 53,796 (including 2,888 calls made to UKTIS), an increase of 4.7% on 2011/12 (Figure 3.1). The analyses presented in this report include only telephone enquiries to the NPIS that related to patients, of which there were 49,636 (an increase of 5.6% on 2012/13). The data includes the 2,219 referrals for specialist advice from NPIS consultants. The number of calls referred to consultants has increased by 44% from 2011/12; many of these calls were for advice on paracetamol following changes in national guidance in September 2012 (see Section 5.3).



**FIGURE 3.1** Annual number of telephone enquiries to the NPIS and TOXBASE sessions from 2000 to 2012/13 (data for 2000–2003 by calendar year; subsequent data by financial year)

Table 3.1 shows the number of poisons enquiries from countries in the UK and relates these to population size. Table 3.2 shows the variation in TOXBASE use by former strategic health authority areas in England, compared with use in Northern Ireland, Scotland and Wales. In 2012/13, the number of telephone enquiries received relative to population size increased in England and Scotland compared with last year's figure, but decreased in Northern Ireland and Wales. The number of TOXBASE sessions relative to population size increased in England, Northern Ireland and Scotland, but decreased in Wales.

Overall in 2012/13, the use of NPIS services, relative to population size, increased by 1.6% compared with the

2011/12 figure, demonstrating an increased demand for NPIS services within the UK. Within England, nine out of ten strategic health authorities showed an increased use of TOXBASE (as given in Table 3.2), with the West Midlands (11.6%) and East Midlands (10.6%) showing the largest increases in the numbers of TOXBASE sessions. The North East was the only former strategic health authority area to show a reduced usage of TOXBASE, a decrease of 5.1% compared to 2011/12, although this area still has the highest use of TOXBASE in England.

As in previous years, hospital departments and NHS Direct/111 and NHS 24 users were responsible for the majority of TOXBASE sessions: 339,772 (67.3%) and

**TABLE 3.1 Distribution of poisons enquiries to the NPIS in 2012/13**

Country	Telephone enquiries (involving patients)		TOXBASE sessions		Combined total	
	Number	Rate per 100,000 population (mid-2010)*	Number	Rate per 100,000 population (mid-2010)*	Number	Rate per 100,000 population (mid-2010)*
England	41,580	79.6	412,119	789.0	453,669	868.5
Northern Ireland	536	29.8	11,213	623.2	11,749	652.9
Scotland	2,190	41.9	53,227	1,019.3	55,417	1,061.2
Wales	3,149	104.7	28,102	934.7	31,251	1,039.5

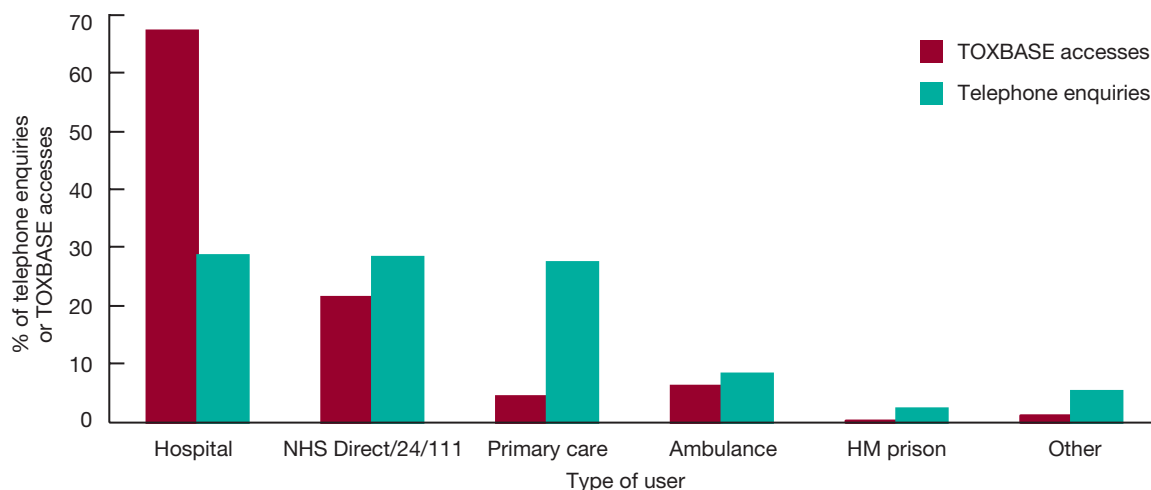
\* <http://www.ons.gov.uk/ons/rel/pop-estimate/population-estimates-for-uk--england-and-wales--scotland-and-northern-ireland/population-estimates-timeseries-1971-to-current-year/index.html> (accessed 06/2013), England total = 52,233,400

**TABLE 3.2 Regional distribution of TOXBASE sessions in 2012/13**

Country	Strategic health authority	Number of TOXBASE sessions	TOXBASE sessions per 100,000 population	Population estimate (mid-2010)*
England	East Midlands	32,858	733.2	4,481,400
	East of England	38,844	666.1	5,831,800
	London	47,850	611.5	7,825,200
	North East	25,782	989.1	2,606,600
	North West	65,590	945.7	6,935,700
	South Central	33,612	812.5	4,137,100
	South East Coast	25,181	574.2	4,385,400
	South West	43,639	827.5	5,273,700
	West Midlands	46,567	853.6	5,455,200
	Yorkshire and the Humber	52,196	984.6	5,301,300
Northern Ireland	–	11,213	623.2	1,799,400
Scotland	–	53,227	1,019.3	5,222,100
Wales	–	28,102	934.7	3,006,400

\* <http://www.ons.gov.uk/ons/rel/pop-estimate/population-estimates-for-uk--england-and-wales--scotland-and-northern-ireland/population-estimates-timeseries-1971-to-current-year/index.html> (accessed 06/2013), England total = 52,233,400





**FIGURE 3.2 TOXBASE accesses and telephone enquiries by type of user in 2012/13**

107,286 (21.3%), respectively (Figure 3.2). The number of sessions from NHS Direct/111 and NHS 24 users represents an 8.9% decrease in sessions compared to 2012/13, going against the overall increase in sessions of 3.6%. In contrast, telephone enquiries received were distributed more evenly across hospital, NHS Direct/111 and NHS 24, and primary care users: 14,187 (28.6%), 14,096 (28.4%) and 13,643 (27.5%). As has been found previously, GPs are more likely to call the NPIS than access TOXBASE.

The largest number of TOXBASE sessions from hospital users was from emergency departments (293,342 or

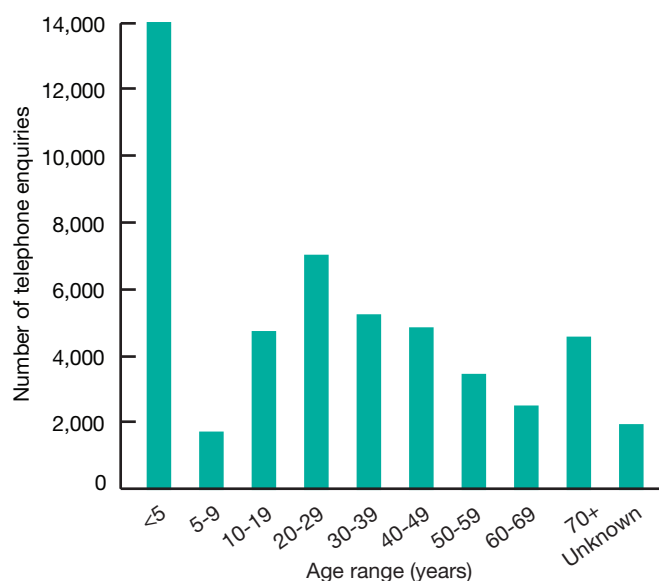
86.3%) (Table 3.3). Medicines information departments and pharmacies were the second largest group of hospital users (29,356 or 8.6%).

Of the telephone enquiries, 42.1% (20,900) were made by doctors and 46.7% (23,184) by nurses. This is the first year in which calls from nurses have exceeded the number of calls from doctors.

The age ranges of patients who were the subject of telephone enquiries are shown in Figure 3.3; over a

**TABLE 3.3 Hospital session data by department**

Department	Number of sessions
Emergency departments	293,342
Medicines information and pharmacies	29,356
Minor injuries unit	3,379
Admission/assessment	2,140
Paediatrics	2,026
Poisons wards	1,654
Intensive care/treatment	1,154
Urgent care	1,003
Psychiatry	912
General medicine	867
Biochemistry and other laboratories	685
Public health and Health Protection Agency	522
Other	2,732

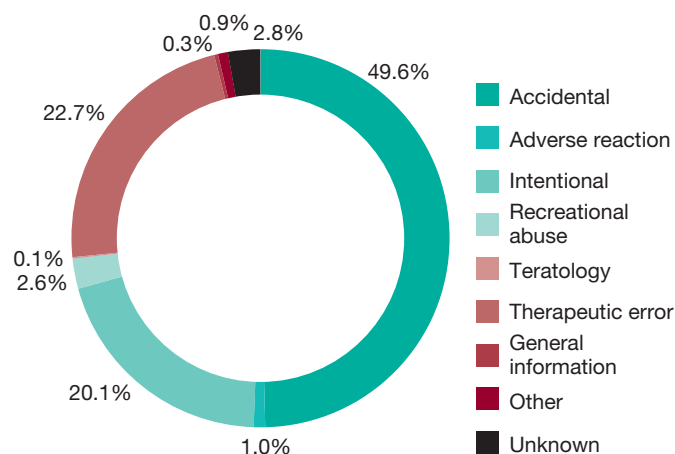


**FIGURE 3.3 Age range of poisoned patients reported in telephone enquiries to the NPIS in 2012/13**

quarter (28.2%) involved children under the age of five years and 52.0% of all telephone enquiries involved female patients. These figures for distribution by age and sex are similar to those in previous years.

The majority of exposures reported in telephone enquiries were accidental (49.6%), by ingestion (87.4%) and occurred at home (87.1%). Figure 3.4 shows the type of poisonings reported to the NPIS during telephone enquiries in 2012/13; as in previous years the largest single category was accidental ingestions.

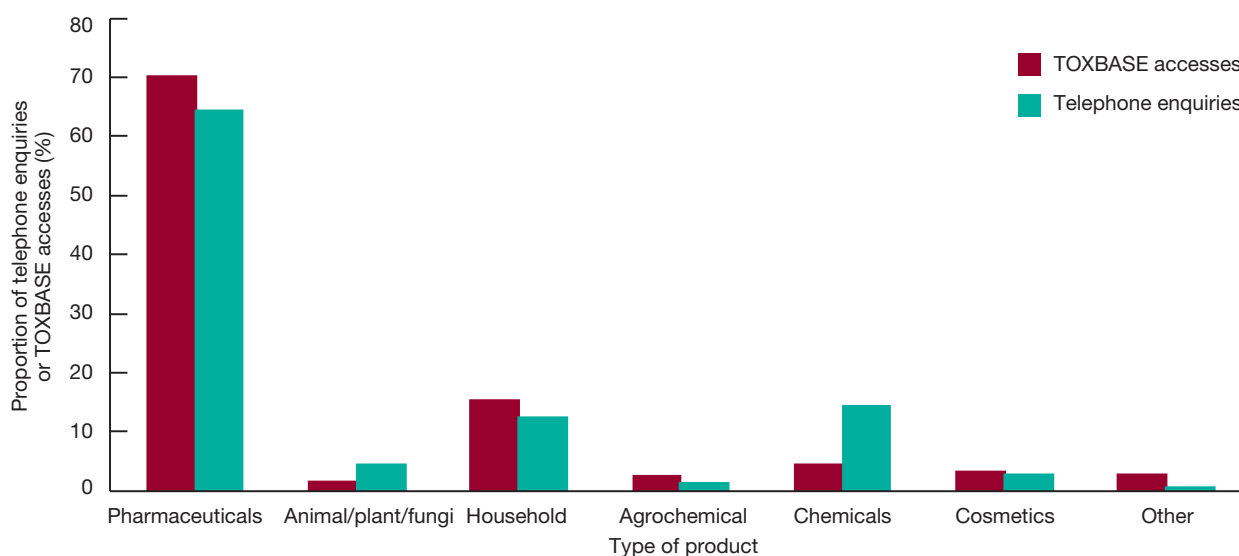
The types of agents that were the subject of TOXBASE accesses and telephone enquiries are shown in Figure 3.5. Pharmaceuticals were the most common source of enquiries (70.2% of accesses; 64.4% of telephone enquiries). As previously found, the percentages of accesses versus enquiries for each group of agents are similar except for the chemicals group (4.4% of accesses vs 14.2% of enquiries) and the animals/plants/fungi group (1.1% of accesses vs 3.9% of enquiries). There may be a number of reasons for the preference for telephoning the NPIS for these agents: users may wish to discuss such cases with the NPIS; users may be unsure regarding the management of poisoning with an unknown species of plant/fungus, or an unknown chemical; or a low toxicity species of plant, or rarely encountered chemical, may not be present



**FIGURE 3.4** Types of poisonings as reported in telephone enquiries to the NPIS in 2012/13

on TOXBASE, prompting the enquirer to contact the NPIS. A project is currently underway to add entries to TOXBASE where a telephone enquiry involves a product not found on the database.

Table 3.4 shows the ten pharmaceutical agents that were most frequently the subject of telephone enquiries and TOXBASE accesses. It should be noted that the numbers of enquiries and accesses listed for paracetamol exclude those for compound analgesics (eg those containing both paracetamol and codeine), which are counted separately. The numbers of enquiries and accesses for ethanol are also excluded. The pattern of enquiries and



**FIGURE 3.5** Types of agents involved in telephone enquiries and TOXBASE accesses in 2012/13

**TABLE 3.4 Pharmaceutical agents: top telephone enquiries and TOXBASE accesses in 2012/13**

Telephone enquiries		TOXBASE accesses	
Agent	Number of enquiries	Agent	Number of accesses
Paracetamol*	6,951	Paracetamol*	100,920
Ibuprofen	2,481	Ibuprofen	46,888
Co-codamol†	1,733	Diazepam	24,741
Diazepam	839	Citalopram	24,489
Citalopram	798	Zopiclone	19,731
Zopiclone	752	Tramadol	19,712
Tramadol	691	Fluoxetine	16,776
Aspirin	624	Mirtazapine	16,155
Mirtazapine	618	Amitriptyline	16,017
Quetiapine	580	Co-codamol†	15,894

\* Excludes compound analgesics

† Contains only paracetamol and codeine

### 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 2012/13 there were 1,865 telephone enquiries routed to the NPIS national telephone service from this source. The NPIS units also received 192 telephone enquiries from outside the British Isles.

As well as the out-of-hours contract, the NPIS provides TOXBASE to medical professionals in the Republic of Ireland; the majority of Irish users are hospital emergency departments. In 2012/13 there were 9,605 TOXBASE sessions made by 47 registered Irish users, accounting for 27,249 individual TOXBASE accesses.

TOXBASE is provided under special agreements to users in over 40 countries outside the British Isles; 14,740 TOXBASE sessions were made by these users in 2012/13, an increase of 0.6% on the 2011/12 figure. Users in Brazil access TOXBASE the most, accounting for 25.7% of all overseas sessions, followed by users in Australia (12.3%), Belgium (11.9%) and Austria (7.2%). A total of 43,653 product accesses were made during these sessions. A comparison of the top ten most frequently accessed pharmaceuticals by users in the UK, Republic of Ireland and overseas countries is shown in Table 3.5. While paracetamol is still the most accessed TOXBASE entry from overseas countries, as a proportion of total accesses, it is much lower than in the British Isles.

accesses is similar to those in the previous two years, with analgesics and antidepressants predominating.

Of particular note are the large increases in the numbers of telephone enquiries regarding paracetamol and co-codamol, amounting to 28.2% and 26.7%, respectively, compared with 2011/12. However, only paracetamol saw a substantial rise in the number of TOXBASE accesses (an increase of 13.6%); the number of accesses of co-codamol products increased by 2.8%, which is a 4.5% decrease relative to the total number of TOXBASE accesses for all products.

## 3.2 Consultant Referrals

The NPIS has operated a national consultant clinical toxicology on-call rota for the UK and the Republic of Ireland since May 2005. Thirteen consultant clinical toxicologists from the four NPIS units (Birmingham, Cardiff, Edinburgh and Newcastle), as well as three consultants from hospitals in York and London, contribute to out-of-hours cover (18:00 to 09:00 hours Monday–Thursday, weekends and public holidays). 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 (SPIs) should refer enquiries to a consultant. The national consultant rota is managed from NPIS Edinburgh.

**TABLE 3.5 Pharmaceutical agents: top TOXBASE accesses by users in the UK, Republic of Ireland and overseas in 2012/13**

UK		Republic of Ireland		Overseas	
Agent	Count (% of total)	Agent	Count (% of total)	Agent	Count (% of total)
Paracetamol*	100,920 (7.3%)	Paracetamol*	2,043 (7.5%)	Paracetamol*	852 (1.9%)
Ibuprofen	46,888 (3.4%)	Zopiclone	685 (2.5%)	Amitriptyline	698 (1.6%)
Diazepam	24,741 (1.8%)	Diazepam	655 (2.4%)	Clonazepam	623 (1.4%)
Citalopram	24,489 (1.8%)	Quetiapine	515 (1.9%)	Carbamazepine	571 (1.3%)
Zopiclone	19,731 (1.4%)	Escitalopram	482 (1.8%)	Quetiapine	539 (1.2%)
Tramadol	19,712 (1.4%)	Ibuprofen	461 (1.7%)	Sertraline	479 (1.1%)
Fluoxetine	16,776 (1.2%)	Venlafaxine	443 (1.6%)	Ibuprofen	476 (1.1%)
Mirtazapine	16,155 (1.2%)	Pregabalin	431 (1.6%)	Fluoxetine	453 (1.0%)
Amitriptyline	16,017 (1.2%)	Olanzapine	429 (1.6%)	Diazepam	382 (0.9%)
Co-codamol†	15,894 (1.2%)	Alprazolam	408 (1.5%)	Risperidone	354 (0.8%)

\* Excludes compound analgesics

† Contains only paracetamol and codeine

For daytime cover, units continue to make local arrangements and may be supported by consultants, academic clinical staff and specialist trainees (ST doctors) who are not on the UK NPIS consultant toxicologist rota, with all enquiries answered under the supervision of NPIS consultants. NPIS Edinburgh also provides consultant support for enquiries from Northern Ireland during the working week. The units provide cross-cover in emergencies and occasionally, in a planned manner, support colleagues in special circumstances during the working week.

For telephone enquiries, details of the original call are available on the UKPID central server for audit and checking purposes, and the call reference number is sent to the relevant consultant for audit purposes. The majority of consultant referrals now take place as a three-way call with the SPI listening into the conversation between the enquirer and consultant and recording the key information on to UKPID. Where three-way calls have not taken place, consultants keep contemporaneous local records of advice given and pass these on to the NPIS unit that took the original call for addition to the call record.

## Referrals

There were 2,219 referrals made to NPIS consultants (daytime and out-of-hours) in 2012/13, an increase of 44% on 2011/12). Figure 3.6 shows the number of referrals by month over the past three years. The

unprecedented increase in consultant referrals in September 2012 can largely be explained by the spike in enquiries received by the NPIS as a result of changes made to NPIS advice on paracetamol poisoning following recommendations issued by the Commission on Human Medicines.

Distribution by day of week is shown in Figure 3.7, with fewer referrals made at the weekend. The average daily number of referrals was 6.1 (with a range of 0–42 referrals). Over the first weekend following the change to NPIS advice on paracetamol poisoning (8 and 9 September) 81 referrals to consultants were made. This contrasts with a more typical weekend where 5–15 consultant referrals are made.

Table 3.6 shows the number of consultant referrals by country; although most referrals come from England, population-adjusted rates of referral are higher from Scotland and Wales.

The great majority of consultant referrals came from hospitals (1,857 or 83.7%), with GPs/primary care staff (160, 7.2%), NHS Direct/111 and NHS 24 staff (131, 5.9%) and others (71, 3.2%) making much smaller contributions. There was a 5% increase in the proportion of referrals from NHS Direct/111 and NHS 24 staff, compared to the previous year. Hospital referrals by department are shown in Table 3.7.

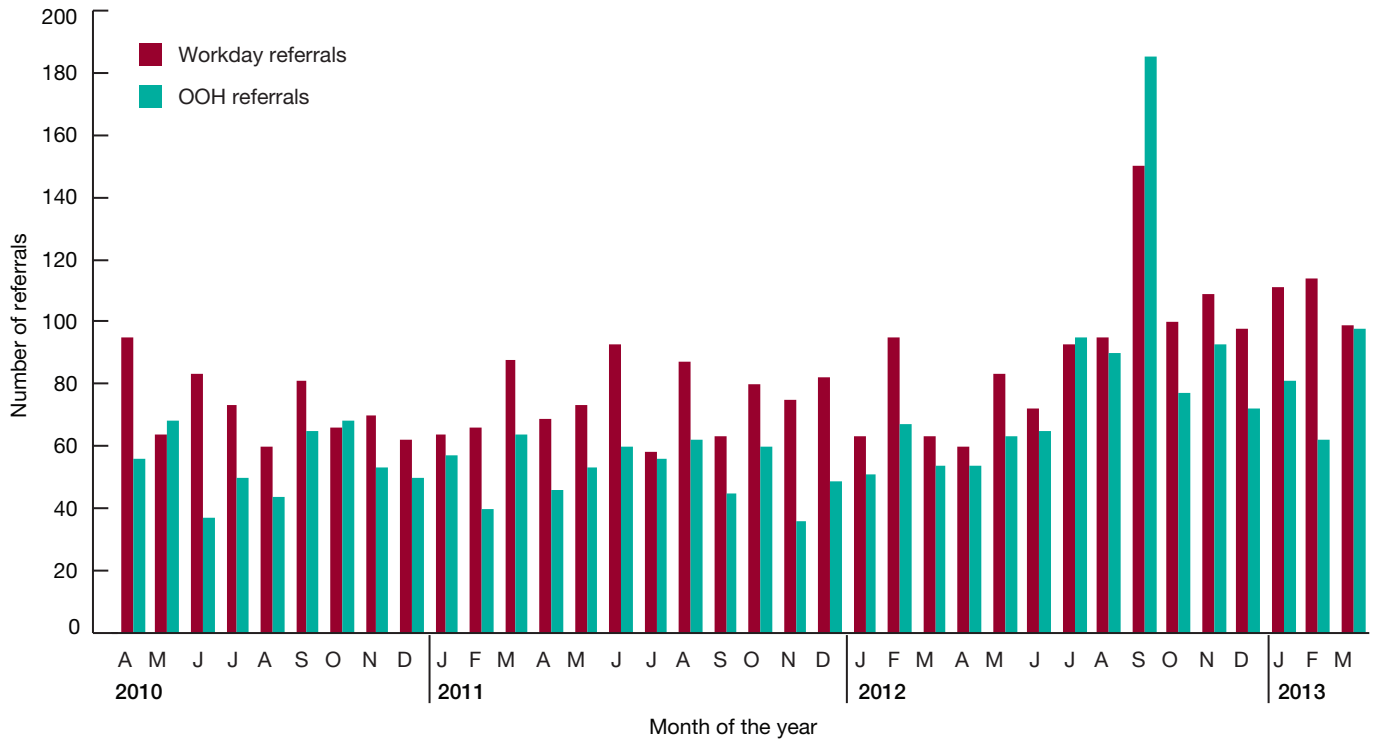


FIGURE 3.6 Monthly NPIS consultant referrals (showing out-of-hours and workday referrals) from 2010/11 to 2012/13

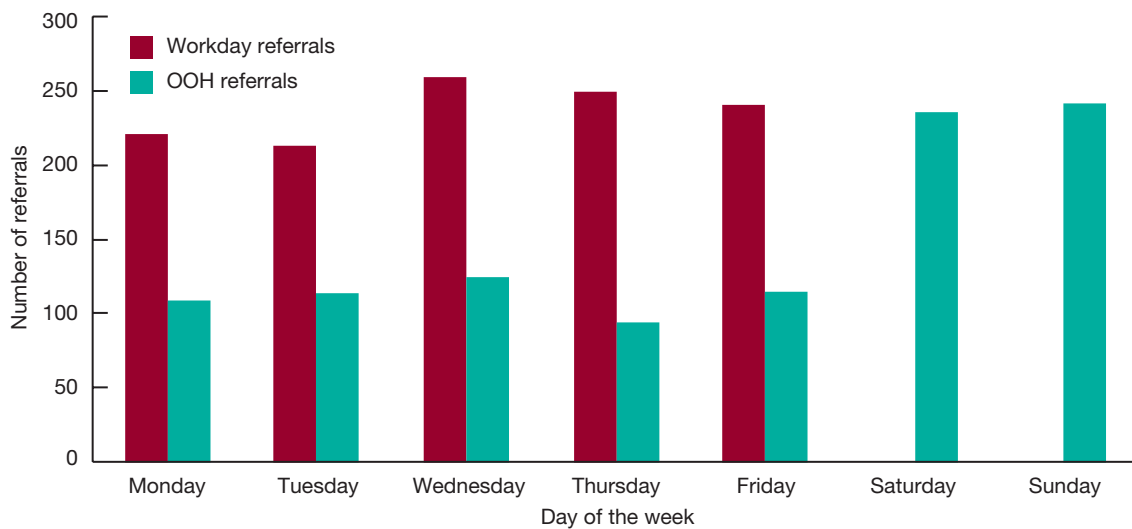


FIGURE 3.7 Number of NPIS consultant referrals by day of the week (showing out-of-hours and workday referrals) in 2012/13

**TABLE 3.6 NPIS consultant referrals by country in 2012/13, with corresponding 2011/12 proportions for comparison**

Country	Number of referrals	Rate per 100,000 population*	Proportion in 2012/13 (%)	Proportion in 2011/12 (%)
England	1,710	3.3	77.1	73.9
Northern Ireland	39	2.2	1.8	1.6
Scotland	285	5.5	12.8	18.0
Wales	133	4.2	6.0	4.4
Republic of Ireland	39	–	1.8	1.9
Other	13	–	0.6	1.2
<b>Total</b>	<b>2,219</b>			

\* Based on 2010 mid-year population estimates from <http://www.ons.gov.uk/ons/rel/pop-estimate/population-estimates-for-uk--england-and-wales--scotland-and-northern-ireland/mid-2010-population-estimates/index.html> (accessed 06/2013)

**TABLE 3.7 NPIS consultant referrals from hospitals by department in 2012/13 (83.7% of all referrals)**

Source	Number of referrals	Proportion of all referrals (%)
Emergency department and minor injuries unit	891	40.2
Intensive care/treatment	322	14.5
Paediatric	175	7.9
Admissions/short stay/assessment	119	5.4
General medicine	119	5.4
Medicines information and pharmacies	27	1.2
Surgery	24	1.1
Psychiatry	14	0.6
Other	122	5.5
Unknown	44	2.0

**TABLE 3.8 Agents commonly involved in NPIS consultant referrals in 2012/13**

Agent	Number of referrals
Paracetamol (including 95 co-codamol)	637
Drugs of misuse	178
Drug/substance (unknown)	177
Antifreeze/ethylene glycol/methanol	87
Digoxin	79
Ibuprofen	68
Aspirin/salicylate	63
Amitriptyline	58
Diazepam	57
Iron	52

## The enquiries

Table 3.8 shows the types of products most commonly involved in referrals to consultants. Topping the list are paracetamol-containing products, substances of misuse, and toxic alcohols or glycols (eg ethylene glycol, methanol and antifreeze). In 177 referrals the product taken (if any) was unknown and help with diagnosis was requested. Alcohol was involved in 143 consultant referrals.

## 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 at regular editing meetings. Difficult enquiries may be examined in more detail at one of the NPIS CPD meetings.

## Conclusions

The NPIS national out-of-hours on-call consultant rota continues to work well. Frequent contact by email and telephone, together with regular educational meetings, helps to ensure consistency of advice. Information gleaned from analysis of the enquiries has assisted in identifying toxicological and methodological problems, improving the clarity of TOXBASE entries, and informing the need for research in a number of areas.



### 3.3 UKTIS

#### Background

The UK Teratology Information Service (UKTIS), based within NPIS Newcastle, is commissioned to provide advice to health professionals across the UK on all aspects of the fetal effects of medicines, poisonings and hazardous chemical exposures in pregnancy. UKTIS also maintains detailed written reviews ('monographs') of animal and human pregnancy safety data for 345 drugs and chemicals; these monographs are currently available online to NHS and NHS-affiliated departments, units and

practices in the UK through TOXBASE. More recently, shorter abstracts of these monographs have been made openly accessible on the UKTIS website ([www.uktis.org](http://www.uktis.org)) (see Figure 3.8). UKTIS also provides information through a dedicated telephone enquiry line for health professionals, in concert with the NPIS.

UKTIS conducts surveillance of known and emerging teratogens by collecting pregnancy outcome data about women who have been exposed in pregnancy from health professionals who contact the service. Data obtained in this way is reported in UKTIS monographs, presented at scientific meetings internationally and/or published in peer-reviewed journals.

#### BOX 3.2 BT Cloud Telephone System

Since June 2012, enquiries to the NPIS have been delivered by the BT Cloud telephone system. This is a significant improvement over the Inbound Architect (IA) system that was used previously.

The IA system routed enquiries to specific units according to the national telephone rota, whereas the BT Cloud system can deliver enquiries to appropriately skilled NPIS staff who log into the system, irrespective of where they are located. IA used a complex call plan that was prone to human error, with a resulting negative impact on NPIS services.

The main advantages of the new system are improved functionality, increased resilience and more efficient co-operative working processes between the NPIS units. Enquiries may be transferred, conference calls may be established and real-time reporting facilities are available. NPIS staff can log in remotely if circumstances require, allowing rapid up-scaling of telephone staffing if this is needed.

BT Cloud has been designed to accommodate the various NPIS services (ie poisons, teratology and chemical) and the NPIS national rota.

The transition to BT Cloud from IA involved establishing NPIS needs, testing prior to implementation and training SPIs to use the system.

Our contract with BT allows us to report issues/faults and maintain a dialogue regarding current concerns and future developments. We are currently addressing NPIS reporting needs and further improving the disaster recovery system.

UKTIS also provides advice on drug and chemical exposures during pregnancy on request to official organisations such as the Medicines and Healthcare Products Regulatory Agency (MHRA), the Commission for Human Medicines (CHM), the European Medicines Agency (EMA), the British National Formulary (BNF) and the Neonatal Formulary.

UKTIS works closely with other international teratology services, including the European Network of Teratology Information Services (ENTIS), of which UKTIS is a founder member, and the Organisation of Teratology Information Specialists (OTIS) which encompasses teratology services in the USA and Canada.

#### UKTIS activity in 2012/13

##### Number and source of telephone enquiries to UKTIS

During 2012/13, UKTIS answered 2,888 pregnancy-related telephone enquiries, a reduction of 11.4% compared with 2011/12. These enquiries involved a total of 5,946 exposures. This decline in telephone call numbers is consistent with that observed over the past five years and corresponds with a managed increase in the availability of online information suitable for use in less complex enquiries. Analysis of telephone enquiries received by UKTIS suggests an increase in the complexity of telephone enquiries received in 2012/13, with 46% of calls relating to women taking more than one preparation, compared to 40% in 2008/09. This underscores the

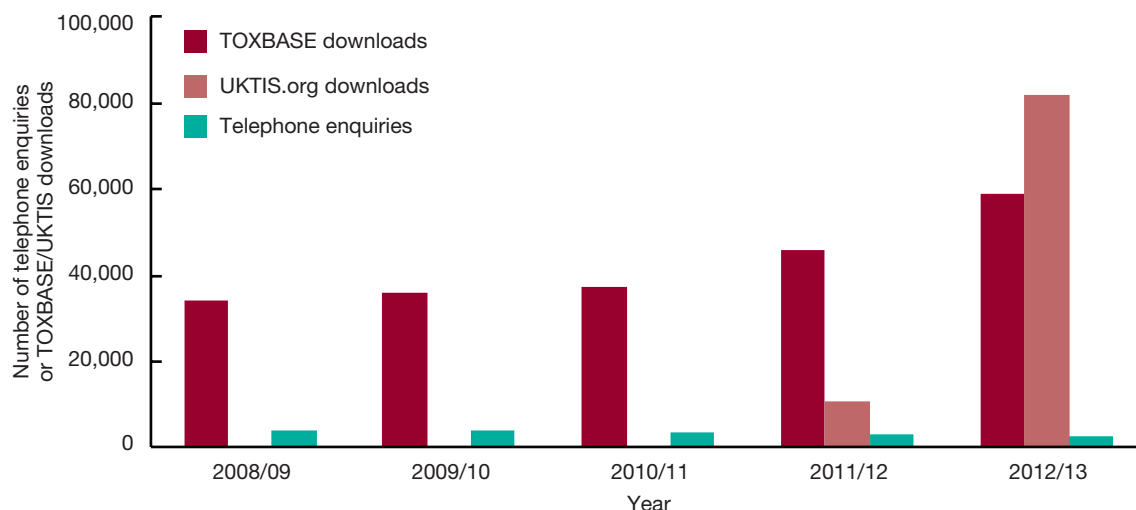


FIGURE 3.8 Telephone enquiries and monograph downloads from TOXBASE from 2008/09 to 2012/13 and UKTIS.org from November 2011 to March 2013

### BOX 3.3 UKTIS Key Achievements in 2012/13

In 2012/13 UKTIS provided information on pregnancy exposure in response to over 140,000 requests. These comprised:

- 58,000 TOXBASE pregnancy monograph downloads, an increase of 25% from 2011/12
- 82,000 monograph summaries downloaded by users worldwide from [www.uktis.org](http://www.uktis.org)
- 2,888 telephone enquiries

98.2% of users agreed or strongly agreed that they were highly satisfied with the service they received from UKTIS.

Awareness of the service has increased, with new users accounting for 45% of telephone enquiries in 2012/13, an increase of 15% from last year and 25% from three years previously.

continuing demand for specialist advice over and above the generic information provided in written monographs.

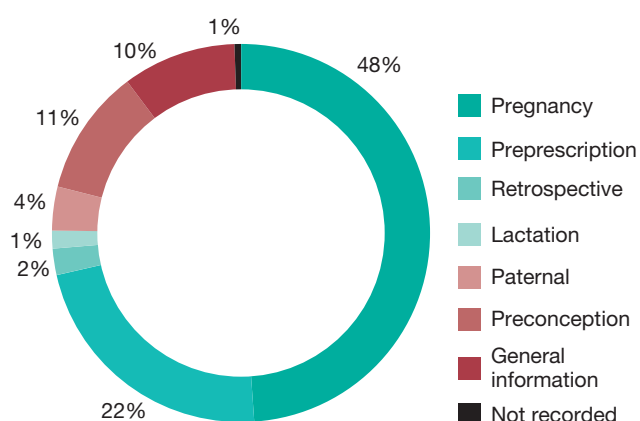
The geographical distribution of calls to UKTIS from the UK is shown in Table 3.9. UKTIS also took 47 calls from outside the UK, the majority from the Republic of Ireland.

A key role of teratology information services is to prevent birth defects and adverse neurodevelopmental effects due to known teratogens by providing information to healthcare professionals to support preconception prescribing of medicines. Of the enquiries to the service during 2012/13, 11% related to women on long-term therapy who were planning a pregnancy or to women of childbearing potential who were being considered for long-term treatment with a drug with known or suspected teratogenic effects. In such cases, the materno-fetal risks and benefits of both the proposed and potential alternative treatments need be considered. Where use of a drug associated with possible adverse fetal effects is deemed essential, advice regarding fetal monitoring and other methods of mitigating risk (eg use of high dose folic acid) is provided (Figure 3.9).

As in previous years, however, the majority of enquiries (48%) received by UKTIS related to women who have already been exposed to a drug or chemical in pregnancy (Figure 3.9). This is not unexpected as up to 50% of pregnancies are unplanned.

**TABLE 3.9 Distribution of teratology enquiries to UKTIS in 2012/13**

Country	Number of enquiries	Proportion of enquiries (%)
England	2,497	86.5
East Anglia	160	5.5
East Midlands	203	7.0
Greater London	471	16.3
North East and Yorkshire	476	16.5
North West	330	13.3
South East	392	11.4
South West	201	6.9
West Midlands	264	9.1
Northern Ireland	28	1.0
Scotland	187	6.5
Wales	126	4.4
Outside the UK	47	1.6
Republic of Ireland	36	1.2
Channel Islands	6	0.2
Isle of Man	2	0.1
Other	3	0.1
Location not provided	3	0.1
<b>Total</b>	<b>2,888</b>	<b>100</b>



**FIGURE 3.9 Telephone enquiries to UKTIS by stage of pregnancy, in 2012/13**

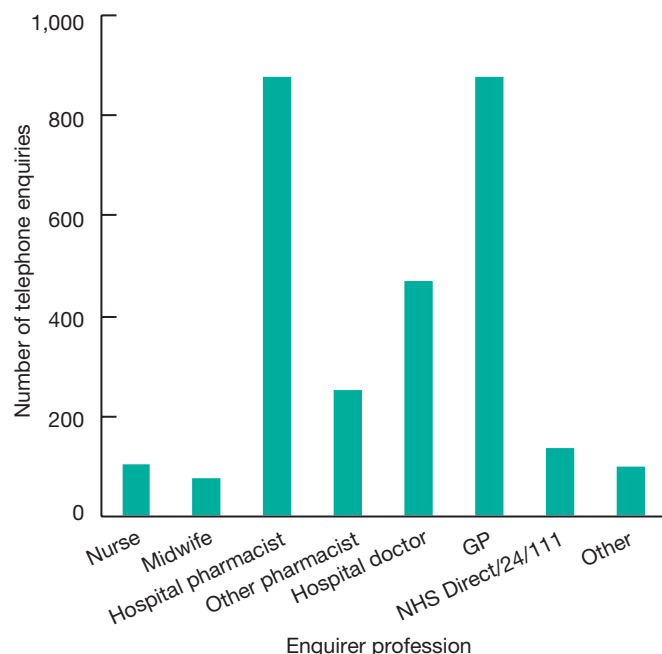
**TABLE 3.10 Telephone enquiries to UKTIS by exposure category, in 2012/13**

Type of exposure	Number of enquiries	Proportion of enquiries (%)
Therapeutic	2,558	88.6
Drug overdose	86	3.0
Poisoning	97	3.4
Substance abuse	21	0.7
Complementary medicines	7	0.2
Occupational	45	1.6
Environmental	38	1.3
Miscellaneous	36	1.2
<b>Total</b>	<b>2,888</b>	<b>100</b>

Therapeutic use of medicines during pregnancy comprises the largest enquiry category (88.6%) (Table 3.10). UKTIS staff are trained to assess the risk to the fetus as a result of the reported maternal exposure and, where appropriate, advise the enquirer about possible interventions and the need for enhanced fetal or maternal monitoring. In many instances, reassurance can be offered, thereby avoiding the unnecessary termination of an otherwise wanted pregnancy. The enquirer will also be provided with an assessment of the fetal risks should continued treatment of the maternal condition be deemed clinically appropriate. When this poses a teratogenic risk, consideration of other treatment options is encouraged and the risks associated with these options discussed in the context of the specific individual.

Hospital pharmacists (30.4%) remain the most frequent type of caller (these enquiries often originate from the prescriber), followed by GPs (30.3%), consultants (16.2%) and community pharmacists (8.7%) (Figure 3.10).

During 2012/13 UKTIS also advised on the management of 183 cases of poisoning (either deliberate or accidental) and 83 environmental or occupational exposures (Table 3.10) during pregnancy.



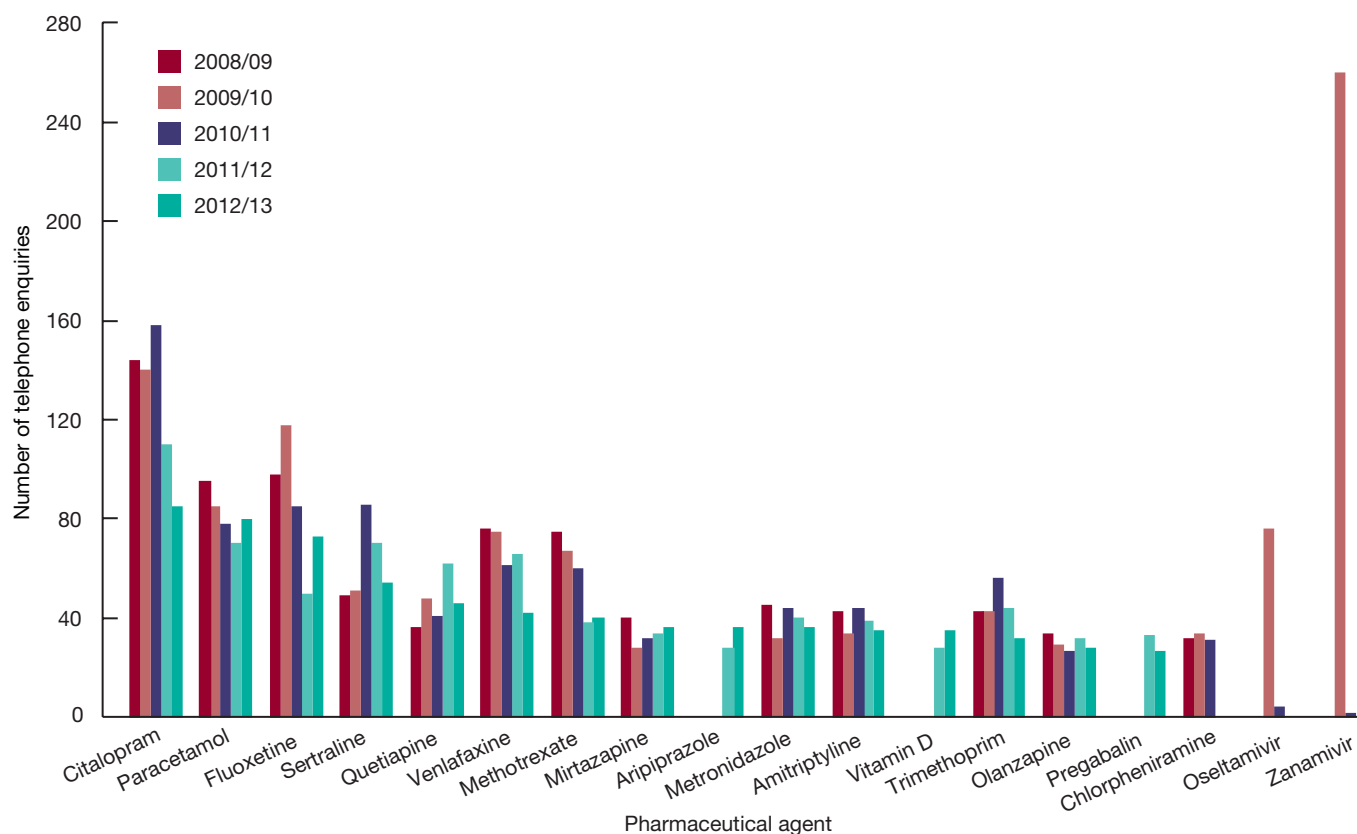
**FIGURE 3.10 Telephone enquiries to UKTIS by enquirer profession, in 2012/13**

### Substances involved in telephone enquiries

Enquiries relating to antidepressant and antipsychotic medication use in pregnancy continued to be the most common type, with these agents comprising seven of the ten enquiries most frequently made to the service. The selective serotonin reuptake inhibitor antidepressants (SSRIs) citalopram and fluoxetine were those most commonly involved (Figure 3.11).

### Pregnancy monographs

UKTIS monographs provide reviews of published, and in some instances unpublished, information relating to the teratogenicity or reproductive toxicology of specific exposures in pregnancy. Pregnancy surveillance data collected by UKTIS is also reported and, where no published information is available for a substance, the available unpublished data is reviewed. UKTIS recently adopted a new monograph format to facilitate interpretation of the data by service users, while providing sufficient detail of the available studies to permit critical



**FIGURE 3.11 Top telephone enquiries to UKTIS by type of pharmaceutical agent, for 2008/09 to 2012/13**

appraisal. All new and updated documents now include an abstract (summary) of the document, a brief overview of animal pregnancy data, with the available human data now considered by potential adverse pregnancy outcome including fetal loss, birth defects, neonatal complications and neurodevelopmental effects. Details of the human studies considered are appended as a table.

A significant portion of the 2012/13 workload involved the production of 63 monographs relating to exposures of special interest in support of planning and preparation for the London 2012 Olympics, along with monographs relating to anti-infectives and antidotes.

UKTIS has also remained responsive to current events and work completed during 2012/13 included monographs on metal-on-metal hip replacements, breast implants and the pertussis vaccine.

User feedback consistently requests UKTIS to make available more monographs as a priority; achieving this without compromising accuracy is a challenge, given the increasing complexity and volume of relevant published data. However, UKTIS was able to produce 119 new and updated pregnancy monographs during 2012/13, an increase of 10% on the previous year.

### Pregnancy information on TOXBASE and UKTIS.org

There were approximately 58,000 downloads of the 345 UKTIS monographs on TOXBASE during 2012/13, an increase of 25% compared to 2011/12, continuing the trend for increasing use of this online resource (see Figure 3.8). This was the first full 12-month period during which monograph abstracts were also freely available for download from the recently launched UKTIS.org website. Worldwide, 82,000 summary documents were downloaded in 2012/13.

The top 20 most frequently accessed full pregnancy monographs on TOXBASE and summary documents on UKTIS.org for 2012/13 are listed in Table 3.11. The documents most frequently accessed when hits for both websites during this period were combined, were on trimethoprim, codeine and amitriptyline.

**TABLE 3.11 Top 20 most frequently accessed pregnancy summaries on TOXBASE and UKTIS.org in 2012/13**

TOXBASE		UKTIS.org	
Pregnancy monograph	Number of hits	Pregnancy monograph abstracts	Number of hits
Insect repellents	2,785	Hyoscine	2,620
Nausea and vomiting	2,037	Mefenamic acid	1,870
SSRIs	1,150	Diclofenac	1,547
Paracetamol overdose	1,084	Trimethoprim	1,325
Codeine	968	Aspirin	1,667
Antibiotics	964	Propranolol	1,250
Constipation in pregnancy	954	Acetone	1,154
Malaria prophylaxis	942	Amitriptyline	1,074
Corticosteroids	888	Trazodone	938
Citalopram	834	Saunas and steam rooms	912
Amitriptyline	786	Zopiclone	929
Oseltamivir	770	Codeine	870
Sertraline	763	Metoprolol	884
Fluoxetine	757	Gentamicin	853
Anthelmintics	683	Quetiapine	823
Metronidazole	671	Diazepam	777
Paracetamol	652	Loperamide	791
Eye drops	650	Omeprazole	762
Chlorphenamine	638	Tramadol	780
Clarithromycin	637	Bisoprolol	700

### Teaching and training

During 2012/13 UKTIS staff have provided training on the principles of teratology and safe use of medications in pregnancy to a number of different audiences including geneticists, paediatricians, obstetricians, dentists, scientists and pharmacists. UKTIS staff also presented and discussed surveillance data at national and international teratology and poisoning conferences and this data has been included in a number of peer-reviewed journal papers.

### Service development

In the latter part of 2012, work began on a new public-facing website (Best Use of Medicines in Pregnancy – BUMPS) which will hold information leaflets regarding

medication and chemical exposures in pregnancy. The information in these leaflets will be consistent with that in UKTIS monographs, but will be written for the lay public. The website will also offer women the opportunity to provide information about themselves, their medication use, the outcome of their pregnancy and the health of their child, by means of an online pregnancy record. Users will be encouraged to update their information throughout their pregnancy, after the birth of the child and into late childhood. It is hoped that information collected in this way will provide a means of enhanced surveillance of drug use in pregnancy. The website is currently well under development and is expected to be completed by the end of 2013.

## Research and development

### Pharmacoepidemiological Research on Outcomes of Therapeutics (PROTECT)

UKTIS collaboration in a European multicentre research project with 31 public and private partners continues. The project has been funded by the EU Innovative Medicines Initiative (IMI) to address the limitations of current methods in the field of pharmacoepidemiology and pharmacovigilance. PROTECT will trial direct patient data collection using web-based and telephone systems, test the transferability of the data into a common language and explore linkages to data from electronic health records and registries. In the past year the project team from UKTIS has worked on finalising the promotional material and ethical requirements for the UK arm of the study. Data collection started in autumn 2012 and recruitment is approximately 30% complete.

### Schmallenberg virus (SBV)

In autumn 2011, maternal infection amongst cattle and sheep with the novel Schmallenberg virus (SBV) resulted in increased rates of stillbirth and congenital malformations including arthrogryposis in lambs and calves. Experience from similar viruses suggested that the risk of human disease was low, but it could not be excluded. UKTIS was tasked with coordinating surveillance for any early signals of a teratogenic effect from SBV infection in humans. A two-pronged approach was adopted, with 'astute clinicians' in the UK and worldwide being approached through links

with established paediatric pathology, neuromuscular paediatric and genetics networks to report unusual or unexplained cases or clusters of arthrogryposis to UKTIS. In addition, a collaboration with UK congenital malformation registries has been formalised to provide a review of arthrogryposis rates for previous years, with a view to registries analysing arthrogryposis and related malformation rates prospectively over five years on a quarterly basis.

As of April 2013, no cases of suspected SBV teratogenesis in humans had been reported to UKTIS. Baseline analysis of annual arthrogryposis and associated congenital anomaly rates before 2011 has been undertaken by congenital anomaly registries across the UK, and the rates for 2011 and 2012 are currently being analysed.

### Collaborative projects with other international teratology information services

Three collaborative peer-reviewed journal papers which included pregnancy exposure and outcome data collected for UKTIS surveillance have been published in 2012/13. UKTIS data and data from Europe and Canada were combined to report on the pregnancy outcomes of women exposed to statins, duloxetine and gabapentin in pregnancy.

## 3.4 NPIS 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 end-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 is comprehensive and up to date. In 2012/13, 9,665 SDS were added to the NPIS Product Data Centre, which now holds some 83,000 current SDS. The database is



indexed by product name, manufacturer, date of SDS and the accession date for the SDS 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, eg 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 2,400 companies and assists in the tracking of correspondence with companies and also includes data on the current marketing status of products.

### 3.5 NPIS Literature Database and *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. All NPIS staff have 24-hours-a-day access to the NPIS Literature Database, which is the responsibility of NPIS Birmingham. The database currently contains 91,846 citations on all aspects of clinical, occupational and environmental toxicology. In 2012/13, some 7,200 references were added to the database, which is fully searchable using keywords, authors, journals and text words. 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.

With the assistance of the other NPIS units, NPIS Birmingham also produces *Current Awareness in Clinical Toxicology* each month. Each issue lists some 400 citations, with some 15–20 key papers highlighted because of their importance to the clinical management of poisoning and the updating of TOXBASE. *Current Awareness* is distributed by the international clinical toxicological societies to all poisons units worldwide.

#### BOX 3.4 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 that 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 PHE 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 PHE Centre for Radiation, Chemical and Environmental Hazards. It meets approximately 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 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 17,200 entries on TOXBASE at least every four years. During 2012/13, 3,281 entries were added or edited; combined with the 5,600 entries reviewed in 2011/12, over 50% of the database content was reviewed between 2011 and 2013.

***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 the NPIS by the forms on TOXBASE, by email, letter or telephone.***

### 3.6 NPIS Website (www.npis.org)

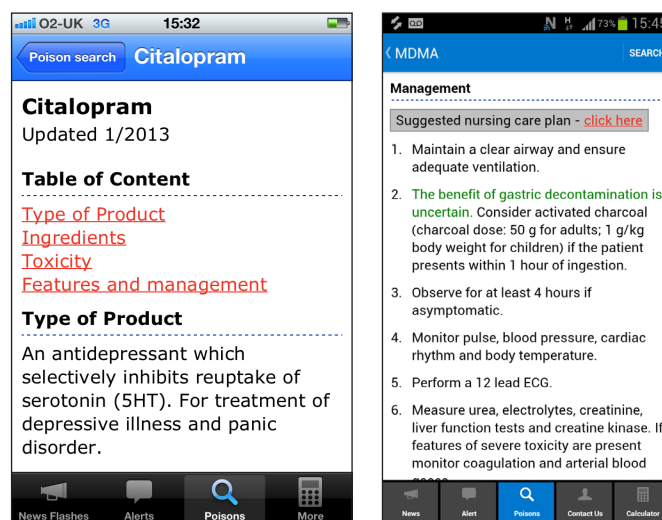
This website is focused primarily on providing information to members of the public. It contains information on the structure and function of the NPIS, details of the range of services provided to health professionals on all aspects of poisoning and links to affiliated organisations and relevant websites. Visitors to the website can also download NPIS publications including annual reports back to 2004.

The website has been created and is maintained by NPIS Birmingham with collaboration from the other units. The website is updated continuously, in particular with data from each annual report.

During 2012/13 the site had nearly 30,000 visitors and nearly 60,000 page views. The most popular documents downloaded were the low toxicity poster and the latest NPIS annual report.

### 3.7 TOXBASE App

Responding to advancing technology and user feedback, a TOXBASE app has been developed for use on iPhone and iPad (launch date 1 October 2012) and on Android phones and tablets (launch date 9 May 2013).



The app is available to individual healthcare professionals by paid annual subscription (through the Apple and Play app stores). Those who validate their registration with an NHS or PHE email address gain access to the 'full' version of the app, tailored for UK NHS users. Users from outside the NHS and PHE gain access to a 'global' version of the app, which contains more than 1,000 of the key TOXBASE entries considered by the NPIS to be most useful to those seeking poisons information from around the world.

The TOXBASE app offers greater user mobility and, for the first time, off-line availability of database content.

At 31 March 2013, 54% of all subscribers were doctors, while ambulance service personnel of all grades represented an additional 28% of users; 29% of users were based in hospital emergency departments. Around 20% of subscribers were located outside the UK.

In addition, all NPIS physicians and specialists in poisons information have been provided with access to the app to support their NPIS duties and increase service resilience.

## 4 Clinical Governance

The NPIS has developed robust and comprehensive clinical governance arrangements supported by detailed operational procedures to ensure that they are applied consistently in each contributing unit. These arrangements are important for ensuring patient safety and improving quality. A summary of the key features of the NPIS clinical governance arrangements is shown in Box 4.1.

### BOX 4.1 Key Features of NPIS Clinical Governance

Appropriate induction, training and appraisal of all staff

Nationally organised continuing professional development (CPD) with discussion of contentious issues, ensuring consistency of approach

Access to high quality information sources

Early peer review of enquiry answers and a programme of enquiry audit

Continuous support from senior staff including 24-hour availability of a consultant clinical toxicologist

Detailed and regularly updated national operational policies

Reporting and review of critical incidents, complaints and near misses so that lessons can be learned and shared throughout the service

Quality assurance exercises seeking the feedback of users in relation to use of TOXBASE, the telephone enquiry services for the NPIS and UKTIS and consultant advice

### 4.1 Analysis of Critical Events

NPIS staff are encouraged to report critical events or near misses. These are reviewed initially by the director of the originating unit. Complaints or observations on the quality of the service are treated in the same way. Those events that are confined to a single unit, where there is considered to be no relevance to the other units, are handled internally by the host NHS trust. Those with possible relevance to the service as a whole are shared between the units and reviewed at the NPIS Clinical

Standards Group meetings, where recommendations on further actions are made. If urgent changes are required, mechanisms are available for rapid discussion amongst the NPIS units and early national implementation of any required changes.

During 2012/13, a total of 16 events were reported and discussed nationally. Of these, two related to management guidance on TOXBASE: one concerned the system of dating entries; the second was to do with a possible risk of misinterpretation of an entry. Both of these were resolved by minor changes.

There were six episodes where TOXBASE functionality had been lost temporarily, with the result that enquirers could not access a full service, but on all occasions the service was restored promptly in collaboration with the website developers who maintain the site.

Five incidents involved a temporary loss of telephone services in one or more units. In one case this was due to a local power failure, in two cases because of a routing error by the telephone provider company and in the last two cases due to teething problems following installation of the new BT Cloud telephone system (see Box 3.2). It should be noted that the numbers of telephone routing problems have reduced since this new system was launched.

Two episodes related to information scientists not following operational procedures: in one case the scientist declined to provide advice as it was thought that the question being asked was outside the scope of the service; in the other case, advice on specific antidote use was provided without appropriate reference to the relevant clinician. Neither of these resulted in any risk to the patients involved. In both cases appropriate procedures were reiterated with the scientists involved and with the staff of the service as a whole.

The final case involved an enquiry from the coroner about advice provided by the service for a patient who had died from drug overdose. This advice was reviewed by the NPIS Clinical Standards Group, but no faults with it have been identified.

## 4.2 Quality Assurance Exercises

### TOXBASE

Formal quality assurance from TOXBASE users is obtained using an online questionnaire. A selection of users is automatically asked to complete and submit short quality assurance forms during their online session. To achieve a reasonable return rate invitations are set to be generated between every five and fifteen database logins; this number is varied throughout the year to avoid user fatigue.

A total of 924 returns were received between 1 April 2012 and 31 March 2013. The responders were nurses (214), junior hospital doctors (205), NHS Direct/111 and NHS 24 staff (133), pharmacists (71), hospital consultants (101) and GPs (78). The remaining 122 indicated another designation – these included middle grade doctors, biomedical scientists and 62 ambulance staff/paramedics.

On type of enquiry, 486 users reported that they primarily used TOXBASE for 'routine enquiries', 267 for a 'triage decision' and 171 for 'complex enquiries'. On frequency of use, 391 reported using TOXBASE weekly, 249 daily and 284 only occasionally.

Users were asked to grade a series of statements on a scale of one to six where one is disagree completely and six is agree completely. Satisfaction scores were high (Table 4.1).

When asked to indicate their overall satisfaction with TOXBASE on a scale of one to six where one is poor and six is excellent, 847 (91.7%) scored either five or six.

**TABLE 4.1 Summary of user satisfaction scores**

Rank	Statement	Satisfaction score* (%)
1	I had confidence in the information for my query	94.5
2	Logging on to the database was easy	88.7
3	The information was sufficient for managing this case	85.4

\* Satisfaction score is the proportion of respondents who agree 'a lot' (5) or 'completely' (6)

Users were invited to give comments and suggestions in a free text field. Any issues specific to entries were dealt with as they arose and the remainder were collated for discussion at the PHE NPIS TOXBASE Editing Group and NPIS Clinical Standards Group meetings.

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

### Telephones

Information on user satisfaction with the NPIS telephone service has been collected by the NPIS over the last decade to assess how the service meets customer expectations, to monitor user requirements and to identify external user problems such as inadequate access to TOXBASE.

During 2012/13, a random sample of 2,707 (5.4%) users was posted questionnaires and 1,012 completed questionnaires were returned, a response rate of 37.4% which is typical for surveys of this type.

Prior to telephoning the NPIS, 37.5% of respondents had looked on the TOXBASE website for guidance, a proportion that has changed little in recent years. Of those who had consulted TOXBASE prior to contacting the NPIS, the reason most often cited for the call was that they did not gain adequate information from TOXBASE to answer their enquiry (Table 4.2). The proportion making this response (51%) has fallen in recent years (from 59.2% in 2011/12, 60% in 2010/11 and 62% in 2009/10).

**TABLE 4.2 Reasons why the NPIS was contacted after TOXBASE was consulted**

Reason	Proportion (%)
We have a protocol telling us to ring NPIS for all cases of poisoning	3.8
I couldn't interpret the information on TOXBASE	51.0
The information on TOXBASE seemed to contradict other information I had	9.5
There was inadequate information on TOXBASE for the question I had	1.5
There were special circumstances or other reasons	32.2

**TABLE 4.3 Reasons why TOXBASE was not consulted first**

Reason	Proportion in 2012/13 (%)	Proportion in 2011/12 (%)
I don't know what TOXBASE is	26.3	27.9
We don't have it in our department	18.5	19.6
It was in part of the department that we didn't have access to	4.3	4.6
We couldn't get logged on/ connection wasn't working	12.5	14.3
We've not been trained to use it yet	12.3	8.7
Other	–	24.8

There has been a continued reduction in respondents reporting that local protocols required them to make telephone enquiries. A similar decline has been observed in respondents reporting that information on TOXBASE conflicted with other information sources.

Of the respondents who did not access TOXBASE first, the number giving their reason as not knowing what TOXBASE is has steadily decreased, to 26% this year (from 28% in 2011/12, 32% in 2010/11 and 36% in 2009/10). Amongst this group, GPs continue to be the most common designation (51.9%).

Respondents who reported that they were unable to access TOXBASE (38.5%) were asked to give a reason (Table 4.3). These figures have shown little change recently, but it is noteworthy that the number reporting that they have not been trained to use TOXBASE had been falling in recent years, although this year it increased to 12.3%.

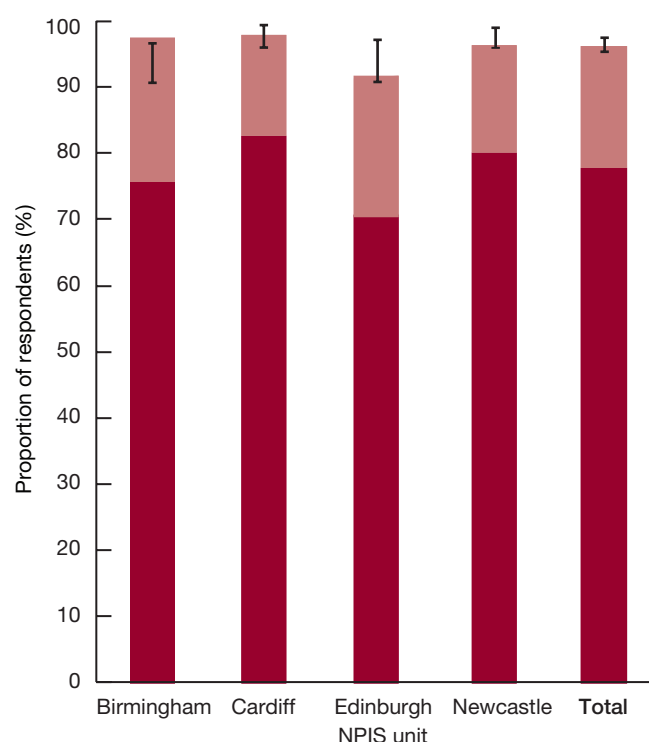
To assess the quality of the service as perceived by users, respondents agreed or disagreed with a series of statements relating to the particular enquiry they made to the NPIS. A high degree of satisfaction was demonstrated for each statement (Table 4.4), with the politeness of staff, promptness of enquiry handling and the speed of delivery of information all attaining particularly good feedback. In almost all categories satisfaction scores were slightly higher than those for last year.

The survey also asks about overall satisfaction with the service using a six-point scale (Figures 4.1 and 4.2). There continues to be a very high rating of overall satisfaction,

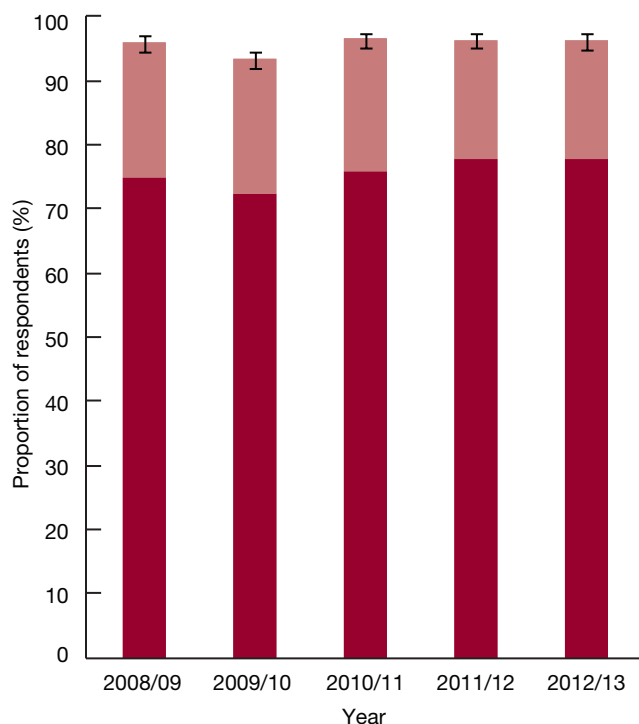
**TABLE 4.4 Summary of satisfaction scores**

Statement	Satisfaction score* in 2012/13 (%)	Satisfaction score* in 2011/12 (%)
The person I spoke to was polite and pleasant	98.9	97.8
Once my call was answered by a specialist in poisons information the enquiry was dealt with promptly	96.0	96.4
I had confidence in the reply I was given	96.7	96.3
The information was given to me at an appropriate speed	97.2	96.1
I was given an appropriate amount of information for my needs	96.2	96.1
The reply from the NPIS was relevant and useful	96.2	95.5
My telephone call was answered without delay by a specialist in poisons information	91.5	90.1

\* Satisfaction score is the proportion of respondents who agree 'a lot' (5) or 'completely' (6)



**FIGURE 4.1** Overall quality scores (with 95% confidence intervals) for 2012/13 for the NPIS units, expressed as a proportion of respondents scoring 5 (■) or 6 (■) out of a possible 6 (non-respondents are excluded from the denominator)



**FIGURE 4.2 Overall quality scores (with 95% confidence intervals) for the NPIS expressed as a proportion of respondents scoring 5 (■) or 6 (■) out of a possible 6 (non-respondents are excluded from the denominator)**

with 96.2% of respondents providing a score of five or six out of six if non-respondents are excluded from the denominator (93.3% if they are included).

The survey provides evidence of a very high degree of user satisfaction with the NPIS telephone service. No specific recommendations arise, other than the need to repeat the survey on an annual basis to ensure that this level of performance is being maintained.

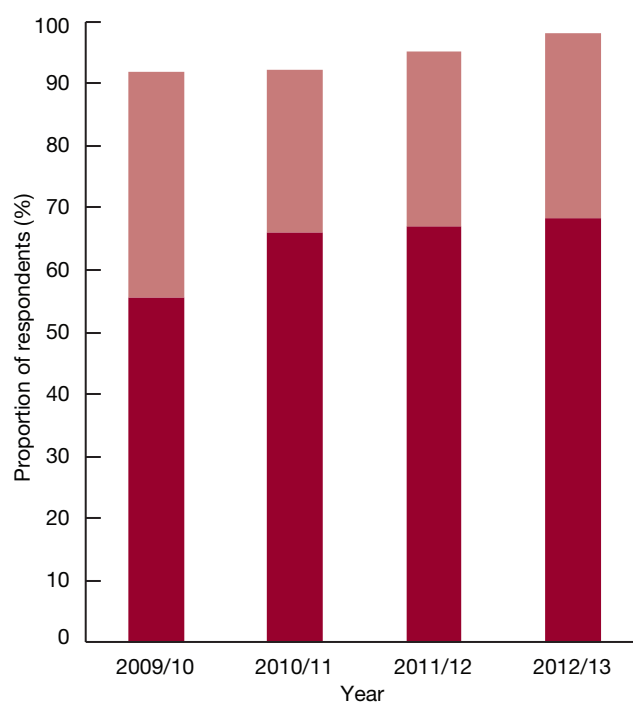
## UKTIS

During 2012/13, improvements to the service have been informed by both formal and informal feedback from service users. During the year a random sample of 350 enquiries (12% of the total number of enquiries) made directly to UKTIS were selected for quality assurance monitoring. Questionnaires were sent out to enquirers between one and four weeks after the enquiry. As of May 2013, 113 (32%) of these forms had been returned.

Over half the respondents were GPs (55%); the other responders included other health professionals (17%), hospital pharmacists (14%), hospital consultants (7%), nurses (4%) and junior hospital doctors (3%). Frequent users of the service (up to five times a year) made up 10% of the respondents and 45% were first-time users, an increase of 25% since 2009/10. Of the respondents, 36% reported that they had been informed about UKTIS by a colleague and 32% had found the details for UKTIS in the British National Formulary. Almost all (98%) said they would use the service again, with the remaining 2% not completing this question.

Satisfaction scores were increased compared to 2011/12 – in particular, 97% reported that the UKTIS staff member who dealt with their enquiry was polite and pleasant and 93% of respondents had confidence in the reply that they were given.

The survey also asked about overall satisfaction with the service using a six-point scale (see Figure 4.3). There was a very high rating of overall satisfaction, with 98.2%



**FIGURE 4.3 Overall quality scores for UKTIS from 2009/10 to 2012/13, expressed as a proportion of respondents scoring 5 (■) or 6 (■) out of a possible 6 (non-respondents are excluded from the denominator)**



of respondents providing a score of five or six out of six if non-respondents are excluded from the denominator (95.6% if they are included).

### 4.3 Service Improvements

#### TOXBASE user feedback

An important component in the review process of TOXBASE entries is feedback from users of the database. Feedback may be received from a variety of sources, eg the TOXBASE quality assurance forms (see Section 4.2), questionnaires on TOXBASE for new and unusual products, responses to follow up on cases of interest, or by email, letter or telephone. Users may also raise queries on existing entries or provide clinical data.

Any issues specific to entries are dealt with as they arise, and the remainder are collated for discussion at the PHE NPIS TOXBASE Editing Group and NPIS Clinical Standards Group meetings. Issues dealt with over the past year have included antidotes, iron poisoning and new psychoactive agents. A number of users provided feedback on the advice on paracetamol after the NPIS advice was revised following the Commission on Human Medicines changes to the licensed indication for acetylcysteine in September 2012.

*As randomised, controlled trial data is not easily obtained on the management of poisoned patients, a body of evidence on individual patients is a particularly valuable source of clinical evidence for the NPIS.*

*We encourage all users to feed back information to the NPIS by the forms on TOXBASE, or by email, letter or telephone.*

### 4.4 Training and Continuing Professional Development

Initial training and a national programme of continuing professional development (CPD) for all staff make an important contribution to the clinical governance structure of the NPIS, ensuring staff are equipped optimally to provide pertinent, informed and evidence-based advice on all aspects of poisoning.

#### Initial training

Newly recruited scientific staff undergo intensive in-house training and assessment in both theoretical clinical toxicology and communication skills before being allowed to answer telephone enquiries without direct supervision. Consistency and quality of training across the NPIS units are achieved by adherence to guidelines set out in the nationally agreed operating procedures, *Initial Training of Specialists in Poisons Information and Core Competencies for Specialists in Poisons Information*. At the end of the training period, staff undergo a final competency assessment conducted by the unit's director or their deputy and are then presented with an NPIS certificate of competency as a specialist in poisons information.

#### Continuing professional development

One NPIS consultant (currently Dr Sally Bradberry of NPIS Birmingham) is responsible for the coordination of a rolling programme of CPD meetings for NPIS scientific and medical staff.

These meetings serve to ensure not only 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 within the NPIS. They provide an informal forum where colleagues can discuss difficult or controversial clinical issues and where less experienced staff can present cases and voice concerns and questions in a non-threatening environment. These discussions also offer an opportunity for face-to-face contact between the scientific and medical staff of all the units who frequently discuss enquiries as part of the out-of-hours NPIS rota. Topics discussed at

CPD meetings are identified in part by internal review of audio recordings of challenging and complex inquiries, which occurs in all the units as part of the governance strategy.

CPD meetings this year have included the last in a series of five annual meetings in Birmingham hosted jointly between the NPIS and Dstl Porton Down on chemical terrorism as well as a meeting hosted in Newcastle, home of UKTIS, focusing on teratological aspects of poisoning and the management of poisoning in pregnancy. In September 2012 a special CPD meeting was held in honour of Professor Nick Bateman, retiring

Director of NPIS Edinburgh, focusing on important toxicological developments and achievements in Edinburgh, particularly with respect to the establishment of acetylcysteine as an antidote for paracetamol poisoning.

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 staff presented some 52 posters or oral presentations at the 32nd International Congress of the EAPCCT held in London in May 2012.

## 5 Surveillance and Research

### 5.1 Urgent Alerting System

Since March 2012, the NPIS has been able to rapidly detect users accessing TOXBASE entries that have been identified as being of special interest. Currently, the NPIS is monitoring 142 chemicals which have the potential to be involved in large deliberate exposures. As a healthcare professional accesses the TOXBASE entry of interest (eg chlorine, carbon monoxide, ammonia or hydrogen cyanide), they are asked whether they are managing a patient or not. If they are, they are then asked to enter their contact details to allow further assistance to be provided by the NPIS.

If an entry of interest is accessed, the NPIS receives an automatic email alert ('urgent alert') within five minutes, providing the time of access, the user's department and location, whether they are managing a patient and their contact details if entered. A specialist in poisons information (SPI) from NPIS Edinburgh, or the on-call centre at evenings and weekends, will contact the user as soon as possible to collect details on the case and to offer consultant advice if required. The SPI will then also contact PHE CRCE, other poisons centres and NPIS consultants as appropriate – for example, if there has been a large or serious exposure.

During 2012/13, the NPIS received 15,615 urgent alerts. Discounting access by the NPIS and educational users, 10,892 urgent alerts were received from 962 different users, regarding 127 entries. The most commonly accessed entry was carbon monoxide, at 2,837 times (26.0% of all urgent alert accesses) (see Table 5.1).

A total of 2,636 urgent alerts were marked as relating to a case where a patient was involved, and user contact details had been entered in 424 of these alerts. Cases where the user had inputted their details multiple times, the user was from an overseas poisons centre or where the user had already contacted the NPIS were discounted. As a result, 273 accesses were followed up by NPIS staff, regarding 48 different TOXBASE entries. The most commonly accessed entries, and the numbers of cases and follow-ups involving these chemicals, are given in Table 5.1.

As the NPIS is informed of all accesses within a five-minute period, multiple accesses from the same department or single accesses from geographically close departments can be noted. The NPIS can then follow up these accesses using contact details on record, in case there has been a chemical release in the area. During 2012/13 the NPIS followed up nine such cases, where no contact details were given but where there were multiple accesses to the same entry.

As an example, in December 2012, the aluminium phosphide entry was accessed four times by a single hospital and once by the local ambulance service within a 50-minute period. The NPIS contacted the hospital, where 19 patients were being treated following a potential exposure to aluminium phosphide/phosphine from a cargo ship. The NPIS was therefore able to inform PHE CRCE of the incident.

The NPIS can, in near real time, collect data on patients presenting with specific poisonings to hospitals across

**TABLE 5.1 Chemicals of interest: the ten most frequently accessed TOXBASE entries**

Agent	Number of alerts (% of 10,892)	Alerts relating to cases (% of 2,636)	Number of follow-ups (% of 273)
Carbon monoxide	2,837 (26.0%)	965 (36.6%)	80 (29.3%)
Chlorine	1,241 (11.4%)	322 (12.2%)	36 (13.2%)
Hydrogen cyanide	682 (6.3%)	61 (2.3%)	7 (2.6%)
Ammonia	446 (4.1%)	111 (4.2%)	13 (4.8%)
Hydrofluoric acid	332 (3.0%)	76 (2.9%)	16 (5.9%)
Paraquat	276 (2.5%)	36 (1.4%)	1 (0.4%)
CS gas	274 (2.5%)	101 (3.8%)	9 (3.3%)
Formaldehyde	219 (2.0%)	80 (3.0%)	10 (3.7%)
Pepper spray	201 (1.8%)	73 (2.8%)	9 (3.3%)
Digitalis purpurea	190 (1.7%)	35 (1.3%)	7 (2.6%)

different regions of the UK, while establishing a direct method of communication. The NPIS has several advantages for such a surveillance role: it offers a 24-hour service, it can act promptly on real-time alerts, disseminating the information appropriately and rapidly, and it is frequently used by and popular with hospital emergency departments across the country as the first port of call for advice on cases where poisoning might be suspected.

## 5.2 Pesticide Exposure Monitoring

Currently, 1,925 TOXBASE entries for pesticides and biocides are being tracked as part of an ongoing surveillance study funded by the Department for Environment, Food & Rural Affairs (Defra). Incident information is collected in two ways: TOXBASE enquiries by either online questionnaire or follow-up postal questionnaire and enquiries to the NPIS telephone enquiry service.

During the year, there were 4,108 enquiries to TOXBASE about pesticides of interest. From TOXBASE sessions, eight electronic and 410 follow-up post or email questionnaires were returned. Information on 743 potential incidents was available from the NPIS telephone enquiry service.

Cases involving animals or head lice treatment products, enquiry sessions from locations in the Republic of Ireland, identifiable duplicate sessions involving the same patient and sessions that were later reported not to have involved a pesticide were excluded from the analysis

As a result of the data collection methods outlined above, information was gathered on 1,161 potential exposures involving pesticides during 2012/13. This equates to an overall return rate of 23.9%. Multiple patients were involved in 15 exposures: this equates to 37 additional potential exposures.

Of the 1,198 potential exposures available for analysis, in 45 cases symptoms were thought on the balance of probabilities by the respondent or by NPIS Edinburgh not to be related to the pesticide exposure because of, for example, a pre-existing illness or reasonable grounds to link symptoms to a concomitant infection.

These cases have been excluded, leaving a total of 1,153 exposures involving patients for further analysis. The results displayed below include both accidental (91%) and deliberate self-harm exposures (9%).

### Agents of interest

The agents most commonly involved in exposures are shown in Table 5.2. In addition, there were 279 cases involving unknown agents: 155 cases involving unknown rodenticides, 36 ant killers, 30 herbicides, 27 insecticides, 26 pesticides and 5 wood preservatives.

In 2012/13, patients potentially exposed to pesticide products comprised 541 people aged over 12 years (46.9%) and 562 children aged 12 years or less (48.7%), with 50 cases of unknown age (4.3%). Among these patients, 54.7% were male and 41.8% were female (3.5% unknown).

The classes of product most commonly involved are shown in Figure 5.1. It is worth noting that more than one type of product was involved in some incidents.

**TABLE 5.2 Pesticides most frequently reported by respondents in suspected pesticide exposures in 2012/13 compared with 2011/12, ordered by rank in 2012/13**

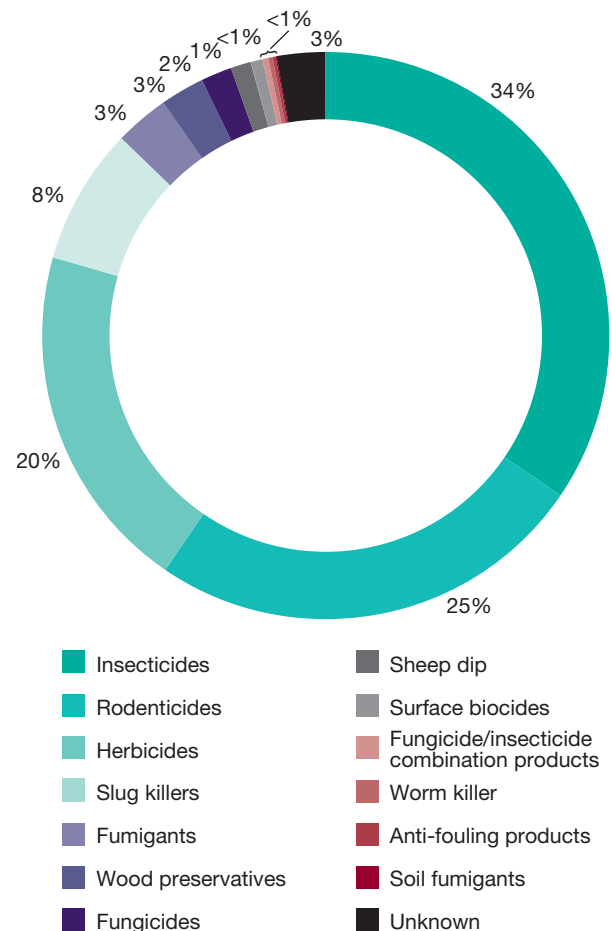
Ingredient	Number of reports by rank in 2012/13	
	2012/13	2011/12
Permethrin	121	95
Glyphosate	104	119
Metaldehyde	90	60
Bromadiolone	66	53
Difencoum	46	41
Diquat	39	31
Aluminium phosphide	33	20
Cypermethrin	32	17
Tetramethrin	27	41
Fipronil	22	20
Bendiocarb	22	32
2,4-D	21	26
Deltamethrin	21	20
Pyrethrins	19	12
Phenols	19	19
Imidacloprid	17	15
Mecoprop-P	15	19

## Severity

Most exposures were graded as poisoning severity score\* 0 (PSS 0, no features, 57.9%) or PSS 1 (mild, 35%) by the NPIS. Smaller proportions were graded as moderate (PSS 2, 3%), severe (PSS 3, 0.5%) or uncertain (3.2%). Three fatalities were reported during this period. These cases involved the deliberate ingestion of paraquat preparations (two cases) or an unknown quantity of aluminium phosphide pellets.

## Pregnancy

There were six enquiries about pesticides involving pregnant patients reported in 2012/13. Three of these were cases of deliberate self-harm involving ingestion of permethrin, in an ant powder or an unknown insecticide, and rat poison (active ingredient unknown). One involved an intentional daily inhalational exposure to fly spray (active ingredient unknown) over a two-week course and another dermal exposure to a small volume of 'Frontline Combo Spot On For Cats' (fipronil and (s)-methoprene). One enquiry regarding 'Ficam W' was precautionary in nature. Of these six exposures, three were graded PSS 0, two were graded PSS 1, and one was graded as uncertain.



**FIGURE 5.1 Pesticide exposures by class of product as reported by respondents, in 2012/13 (total = 1197)**

## 5.3 Changes in the Management of Paracetamol Poisoning

On 3 September 2012, the Commission for Human Medicines (CHM) recommended substantial changes to the use of the antidote acetylcysteine for the management of paracetamol poisoning. The licensed indication for acetylcysteine was changed to include all patients taking a staggered overdose of paracetamol and those for whom there was doubt about the timing of paracetamol ingestion. The blood paracetamol concentration at which acetylcysteine was indicated was lowered by 50% for most patients and risk factors (eg starvation and chronic excess alcohol use) were no longer to be considered. These recommendations impacted not only on the management of acute and

staggered paracetamol overdose, but also on the management of accidental therapeutic use of excessive doses of paracetamol, which is a common source of enquiries to the NPIS. Further CHM recommendations were to increase the duration of administration of the first dose of intravenous acetylcysteine from 15 minutes to one hour, to remove all contraindications to treatment with acetylcysteine and to introduce weight-based acetylcysteine dosing tables for adults and children.

These changes were intended to increase the numbers of patients with paracetamol poisoning receiving acetylcysteine to avoid the rare episodes of serious and sometimes fatal hepatotoxicity that have been reported in patients who had been not considered to require an antidote using previous guidance. The changes recommended by the CHM were endorsed by the

\* Persson H, Sjöberg G, Haines J, Pronczuk de Garbino J. Poisoning severity score: grading of acute poisoning. *J Toxicol Clin Toxicol* 1998; 36: 205–13

Chief Medical Officers and the NHS Clinical Director for Acute and Urgent Care.

The changes required extensive revision to TOXBASE advice and this was prepared by the NPIS in advance of the change, in discussion with the Medicines and Healthcare Products Regulatory Authority (MHRA). The new TOXBASE pages went live on the same day that the CHM issued its new guidance.

The change in management had a substantial impact on the NPIS workload (Figure 5.2). Comparing the month before and after the change, telephone enquiries relating to paracetamol increased by 117% from 524 to 1,139 and referrals to an NPIS consultant increased by 81% from 185 to 335. Similarly, accesses to the paracetamol pages on TOXBASE increased by 27% from 9,179 to 11,987. Although the rates of telephone enquiries have since fallen, these remain much above the baseline that existed before the change in management advice was announced. Over the seven months from September 2012 to March 2013 there was a 62% increase in telephone enquiries compared to the rate before the CHM advice was issued, equating to more than 2,300 additional enquiries. Similarly, there was

a 34% increase in enquiries that were referred to a consultant or 370 additional consultant referrals over the same period. The impact on consultant enquiries was especially marked immediately after the change, with 122 consultant enquiries about paracetamol handled during the first week. The higher rate of TOXBASE accesses, amounting to 25%, has continued since the change in guidance.

The impact of the changes has been limited by careful planning about the changes in TOXBASE guidance, in collaboration with the MHRA, to ensure that consistent advice was issued. However, there has been a substantial increase in the NPIS workload, which continues to this day. The persisting increases in TOXBASE accesses and enquiry numbers are likely to reflect an increase in hospital referrals and in the use of acetylcysteine involving patients with suspected paracetamol poisoning. These cannot be assessed directly using NPIS data; further research is underway to establish the impact of the new CHM guidance on rates of hospital admissions, use of acetylcysteine, adverse reactions, paracetamol-induced hepatotoxicity, paracetamol-related deaths and the cost-effectiveness of the change.

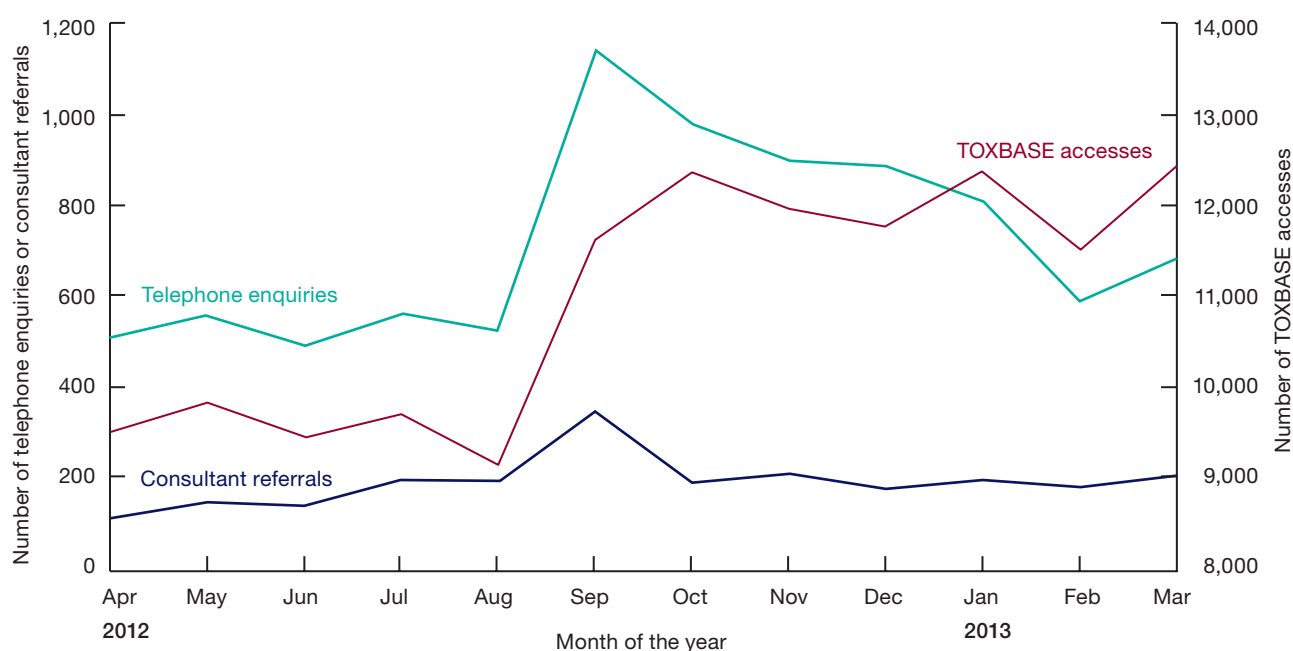


FIGURE 5.2 Impact on NPIS workload of changes to paracetamol management in 2012/13



## 6 Areas of Interest in 2012/13

### 6.1 Therapeutic Errors: Intravenous Paracetamol and Ranitidine

Although therapeutic errors are usually handled by medicines information departments, they are a common subject for telephone enquiries to the NPIS. During 2012/13, 11,247 telephone enquiries were made to the service concerning therapeutic errors, representing over 22% of all telephone enquiries. Here therapeutic errors with two particular medicines will be reviewed: intravenous paracetamol and ranitidine.

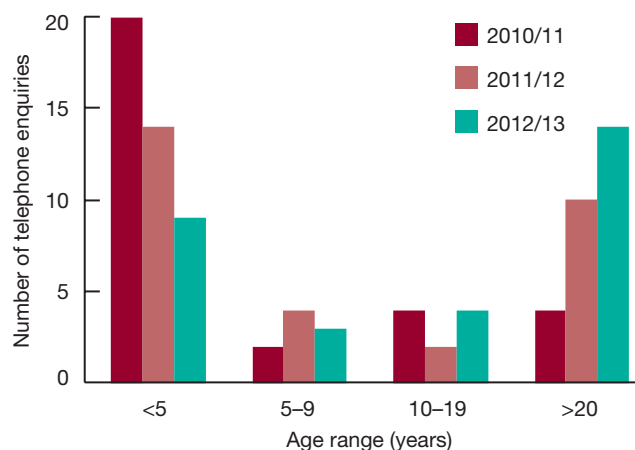
#### Intravenous paracetamol

Intravenous paracetamol preparations have now been available in the UK for several years. Following cases of intravenous overdoses reported to the service, the NPIS developed separate treatment guidelines for the management of intravenous paracetamol poisoning in 2010 and brought the potential risks to the attention of prescribers\*. Concerns over the risks of therapeutic dosing errors with intravenous paracetamol have been expressed by both patient safety groups and regulatory authorities.

There were 31 enquiries concerning intravenous paracetamol; of these, 30 were due to a therapeutic error and one involved an extravasation of the infusion. In 12 of these enquiries children less than ten years old were involved, three of whom were aged between one and five years, with six involving children under the age of one. In 11 cases there was acute administration of intravenous paracetamol, and a further 20 cases involved multiple doses of either IV paracetamol or combinations of both intravenous and oral paracetamol.

Medication errors with intravenous paracetamol arose for several reasons. In all cases where a ten-fold dosing error was made, these occurred in children less than one year old. Other cases involved the wrong dose being administered when the patient's weight was considered. In further cases, intravenous doses were administered in addition to previously administered oral paracetamol,

\* Beringer RM, Thompson JP, Parry S, Stoddart PA. Intravenous paracetamol overdose: two case reports and a change to national treatment guidelines. *Arch Dis Child – Fetal* 2011; 96: 307–8



**FIGURE 6.1** Number of enquiries concerning intravenous paracetamol exposure by age range of patients, from 2010/11 to 2012/13

resulting in an overdose. In one case paracetamol was injected inadvertently into the epidural space.

Although the number of enquiries concerning intravenous paracetamol exposure has remained similar for the last three years, there is the suggestion that paediatric enquiries are decreasing, while adult exposures may be increasing (Figure 6.1). This may reflect changes in the clinical use of intravenous paracetamol in the adult population or an increased awareness within the paediatric community of the potential for errors.

In using intravenous paracetamol it is recommended strongly that the patient's weight and drug history are checked carefully when prescribing is undertaken. It is also very important that the amount, volume and the timing of recently administered medicines are checked carefully before administration occurs, with particular attention paid to sections of medication charts relating to intravenous, oral, regular and 'as required' medicines.

#### Ranitidine

As well as employing automated surveillance techniques to analyse the use of TOXBASE (see Section 5.1), and protocols specifying manual follow-up on accesses to TOXBASE and telephone calls to the NPIS regarding specific products (see Section 5.2), NPIS staff are able to detect and investigate signals from telephone enquiries that involve similar features or medication errors. In 2012, NPIS staff noted that paediatric patients were commonly

being given excessively large doses of ranitidine syrup and investigated the nature of these therapeutic errors.

Patients are prescribed ranitidine for the treatment of gastro-oesophageal reflux disease and peptic ulceration. Neonatal and paediatric patients may be treated with ranitidine, at doses of 1–4 mg/kg; a 1 mg/kg dose equates to approximately 5 mg in an average two-month-old child. A syrup formulation allows the easy administration of appropriate doses to these patients; however, as the syrup is currently only available as a 75 mg/5 mL formulation, a 5 mg dose equates to 0.33 mL of syrup, which carers may not be used to administering.

Between 1 July 2007 and 31 March 2012 the NPIS took 374 calls relating to overdose of ranitidine; 315 of these (84.2%) involved children aged four years and under. Of these, 223 (70.8%) had ingested syrup and 218 (97.8%) of these syrup ingestions were therapeutic errors. The circumstances of the overdose were noted in 174 out of 218 calls, and the mean overdose taken by these patients was an 8x overdose. In 61 of the 174 documented cases (35.1%, or 16.3% of all cases involving ranitidine overdose in all patients) a child received a 10x overdose of ranitidine syrup.

The dose was recorded in 60 cases of 10x overdose, and most commonly involved 2.1–3 mL being given instead of 0.21–0.3 mL (16 patients, 26.7%) or 4.1–5 mL being given instead of 0.41–0.5 mL (20 patients, 33.3%). This suggests there may be confusion where patients are prescribed, for example, 0.5 mL doses of syrup and carers more used to giving ‘teaspoon’-sized doses give 5 mL instead.

The data was compared with that from telephone enquiries regarding another pharmaceutical which may be prescribed as a syrup formulation to children, chlorphenamine. A typical dose of ranitidine for a six-month-old child of 1 mg/kg, or 7.5 mg in total, is 0.5 mL of syrup (measured by syringe), whereas the dose of chlorphenamine for a child of the same age is 1 mg in total, equivalent to 2.5 mL, or half a teaspoon, of syrup.

Of the 629 enquiries taken about chlorphenamine, 316 (50%) involved children aged four years and under. Of these, 207 (66%) involved the administration of syrup and 137 of those (66%) were due to therapeutic error. In 68 of the 137 cases where the nature of the error was documented, 34 overdoses (50%) were due to a 2x dose, 10 calls (15%) involved a 4x overdose and one patient (1.5%) received a 10x overdose. The mean overdose in these patients was a 2.6x overdose.

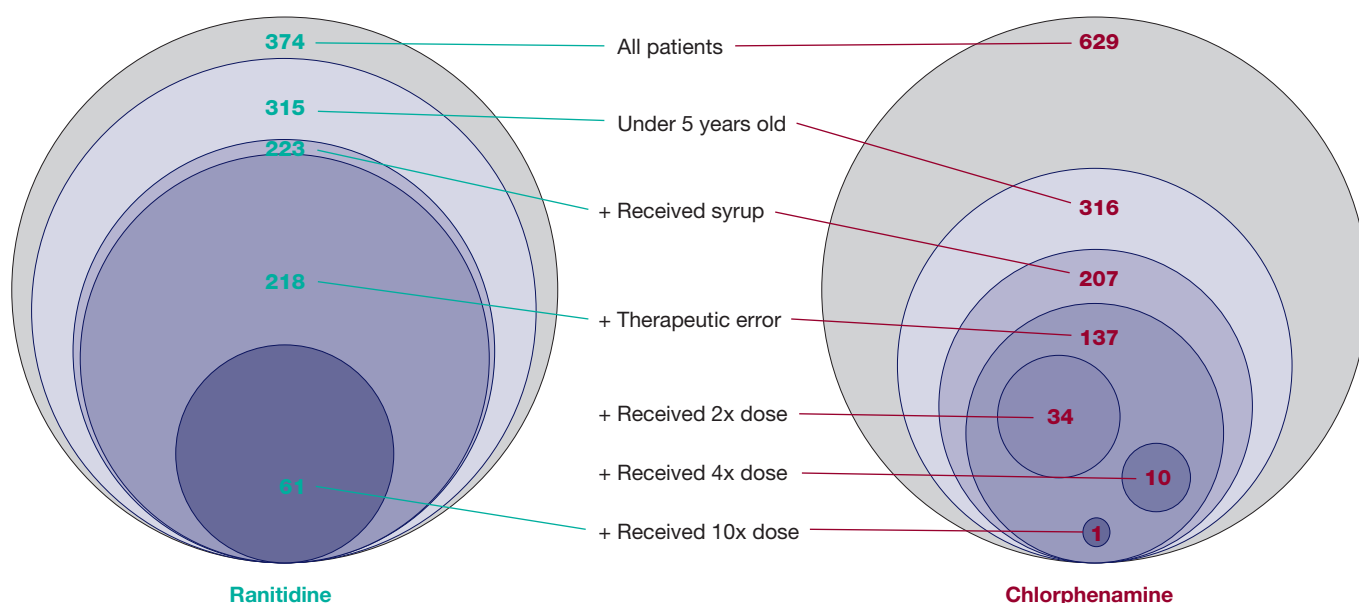


FIGURE 6.2 Nature of telephone enquiries made to the NPIS regarding overdose of ranitidine and chlorphenamine alone

A comparison of the natures of overdoses of ranitidine and chlorphenamine is shown in Figure 6.2.

The data suggests that carers are more likely to give larger overdoses with formulations that are not available in 'teaspoon'-sized doses, as they may not be used to measuring out such small volumes for administration. As this drug is so often prescribed to very young children, we would recommend that a paediatric formulation of ranitidine syrup is made available to avoid such large overdoses and unnecessary presentations to healthcare practitioners.

Call details collected by poisons centres can be a valuable resource for pharmacovigilance. Using this information to study overdoses spread across time and place allows data regarding relatively uncommon errors, possibly seen once by a primary care physician, to be noticed, analysed and acted upon.

## 6.2 Drugs of Misuse including Newer Stimulants

Provision of advice on the clinical features and management of toxicity associated with recreational drug use is an important component of NPIS work, but one which presents challenges. In recent years novel psychoactive substances, sometimes referred to as 'legal highs', have been encountered increasingly often. Provision of management advice for these new agents is particularly difficult because of a lack of information on the clinical effects of human exposure and the chemical content of proprietary brands, as well as a lack of analytical confirmation of exposure in cases referred to the service.

The NPIS is in a unique position to collect information directly from healthcare professionals throughout the UK who are managing toxicity associated with recreational drugs and who are a valuable source of information on features of toxicity with emerging novel psychoactive substances. As with all NPIS activity data, the numbers of telephone enquiries and TOXBASE accesses are not a direct measurement of the frequency of toxicity or hospital admission, but give an indirect indication

of the substances being encountered by the NHS clinicians using the NPIS services. It should be noted that analytical confirmation of exposure is rarely available and the statistics reported here reflect exposures reported by the enquirers involved.

### Enquiry numbers

During 2012/13 the NPIS has monitored telephone enquiry and TOXBASE access numbers relating to 56 different drugs of misuse. Over the year there were 1,201 telephone enquiries relating to these substances, a reduction of 1.3% compared with the figure for 2011/12. Enquiries relating to these drugs of misuse constituted 2.4% of all NPIS telephone enquiries. Over the same period there were 49,390 accesses to monographs on TOXBASE for these substances, a 10.3% increase on the previous year. This constitutes 4.0% of the overall TOXBASE activity.

TOXBASE and telephone activity for individual drugs during 2012/13 is summarised in Figure 6.3. Cocaine, MDMA, heroin, cannabis, 'legal highs' (not otherwise specified) and amphetamines were the six groups most commonly involved in telephone enquiries. Mephedrone remains the most commonly accessed drug of misuse on TOXBASE and is ranked seventh for telephone enquiries (Table 6.1).

Notable drugs outside the top ten for telephone enquiries in 2012/13 included alpha-methyltryptamine (AMT, ranked 13th), synthetic cannabinoids (eg 'spice', ranked 15th), 5 or 6-(2-aminopropyl)benzofuran (5/6-APB, ranked 16th) and 25I-NBOMe (ranked 22nd). Although ranked 17th, TOXBASE accesses relating to synthetic cannabinoids have increased seven-fold since 2011/12. There were substantial increases in the numbers of telephone enquiries (49%) and TOXBASE accesses (128%) relating to recreational substances that were not controlled under misuse of drugs legislation in either year, the so-called 'legal highs', comparing 2012/13 data with that of the previous year. These figures include the category 'legal highs' (not otherwise specified).

For longer term trends, the data is presented as a proportion of the total numbers of calls received or

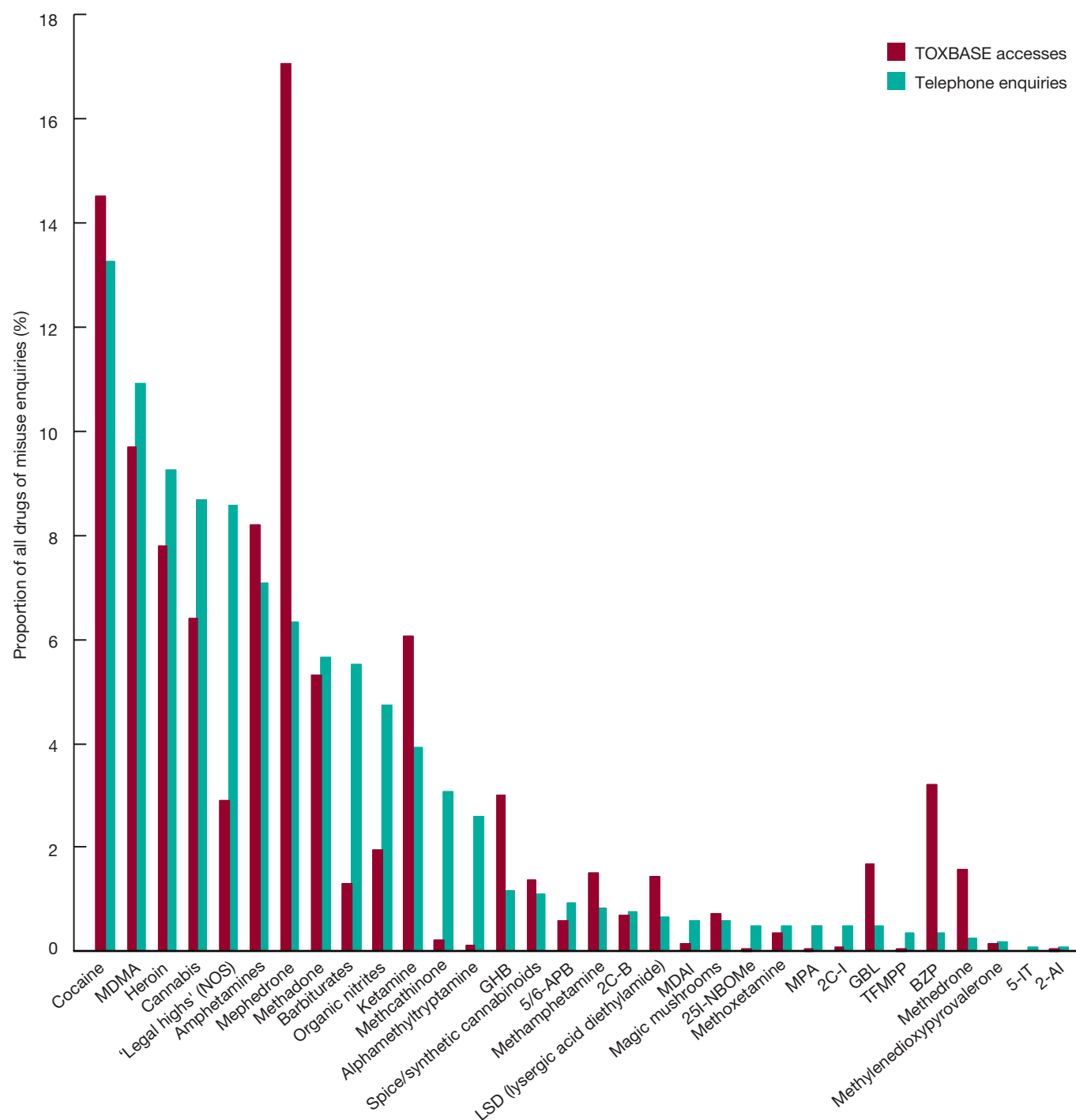


FIGURE 6.3 Drugs most commonly involved in telephone enquiries and TOXBASE accesses during 2012/13 (data presented as a proportion of the overall recreational drug telephone or TOXBASE activity)

Abbreviations	GHB	gamma hydroxybutyrate	2C-B	4-bromo-2,5-dimethoxyphenethylamine
	MDAI	5,6-methylenedioxy-2-aminoindane	MPA	Methiopropamine
	2C-I	2,5-dimethoxy-4-iodophenethylamine	GBL	gamma butyrolactone
	TFMPP	3-trifluoromethylphenylpiperazine	BZP	Benzylpiperazine
	5-IT	5-(2-aminopropyl)indole	2-AI	2-aminoindane

**TABLE 6.1 Top ten telephone enquiries and TOXBASE accesses for drugs of misuse**

Telephone enquiries			TOXBASE accesses		
Drug	Number in 2012/13	Percentage change from 2011/12 (%)	Drug	Number in 2012/13	Percentage change from 2011/12 (%)
Cocaine	159	-1.9	Mephedrone	8,432	36.1
MDMA	131	0.8	Cocaine	7,172	11.2
Heroin	111	-3.5	MDMA	4,778	12.8
Cannabis	104	-3.7	Amphetamines	4,055	-8.8
'Legal highs' (NOS)	103	33.8	Heroin	3,848	5.4
Amphetamines	85	-3.4	Cannabis	3,165	10.4
Mephedrone	76	-2.6	Ketamine	2,993	-14.2
Methadone	68	-32.7	Methadone	2,623	-14.4
Barbiturates	66	-8.3	BZP	1,574	-5.0
Organic nitrites	57	35.7	GHB	1,476	-13.7

TOXBASE accesses made each year. This is needed to adjust for the increases in overall TOXBASE accesses and reductions in telephone enquiries that have occurred over the last decade. During 2012/13 the downward trends in the proportion of telephone enquiries relating to traditional class A drugs of misuse, including MDMA, cocaine, heroin and methadone, have continued, without major changes to TOXBASE activity relating to these agents (Figure 6.4). For non-class-A drugs, downward trends in telephone enquiries and TOXBASE accesses relating to cannabis, amphetamines and ketamine were observed (Figure 6.5).

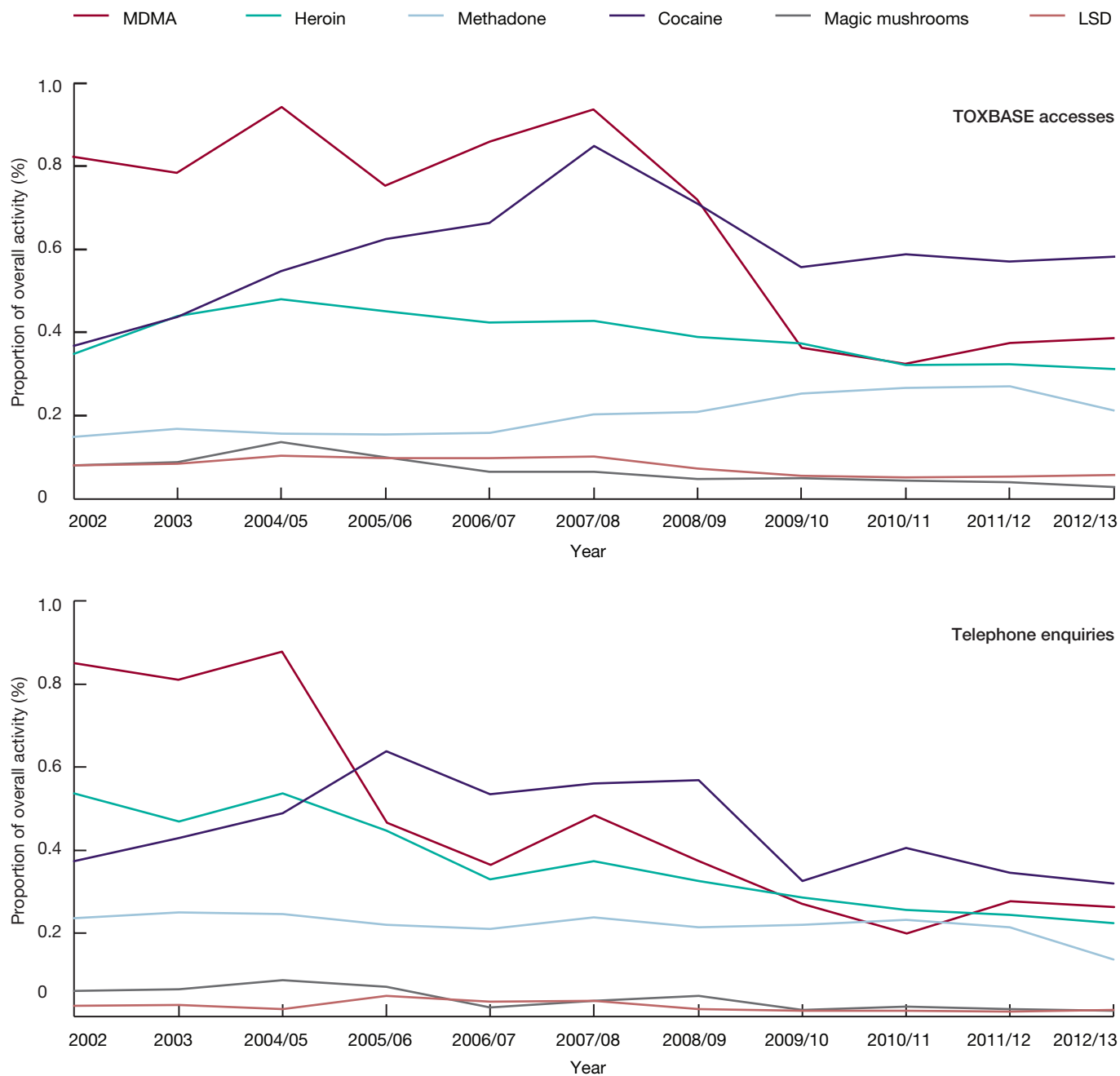
Monthly telephone enquiries and TOXBASE accesses for selected drugs of misuse are shown in Figure 6.6. Telephone enquiries relating to mephedrone have remained much less common than before classification as a class B drug of misuse in April 2010. TOXBASE activity, however, has increased this year, although the numbers of accesses have fallen since July 2012. Telephone enquiries and TOXBASE accesses relating to methoxetamine became infrequent immediately after this was subject to a temporary class drug order in April 2012. It should be noted, however, that NPIS activity relating to 6-(2-aminopropyl)benzofuran (6-APB, 'benzofury') has also been infrequent since 2010, although this drug remained uncontrolled throughout 2012/13.

## Data provision

Statistical data on enquiries relating to drugs of misuse, as well as being reported annually in this report, is provided periodically in response to requests from the UK Focal Point on Drugs Early Warning System (Focal Point EWS), the Advisory Council on Misuse of Drugs (ACMD) and the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA). Reports provided by the NPIS during 2012/13 are summarised in Table 6.2.

**TABLE 6.2 Reports on NPIS data on recreational agents submitted at the request of UK authorities, in 2012/13**

Date	Report title	UK authority
Jun 2012	Novel psychoactive substances – overview of NPIS data	Focal Point EWS
Sep 2012	NPIS telephone enquiries and TOXBASE accesses related to methoxetamine: updated information	ACMD
Sep 2012	NPIS information relating to 4-methylamphetamine (4-MA)	Focal Point EWS
Oct 2012	NPIS information relating to 5-(2-aminopropyl)indole (5-IT)	Focal Point EWS
Oct 2012	Novel psychoactive substances – overview of NPIS data	ACMD (NPS Working Group)
Nov 2012	NPIS information relating to synthetic cannabinoids	Focal Point EWS
Dec 2012	NPIS telephone enquiries and TOXBASE accesses related to nitrous oxide	ACMD
Feb 2013	5-(2-aminopropyl)indole (5-IT) – update	Focal Point EWS



**FIGURE 6.4** Proportion of TOXBASE accesses and telephone enquiries relating to selected class A drugs of misuse (data for 2002 and 2003 by calendar year; subsequent data by financial year)



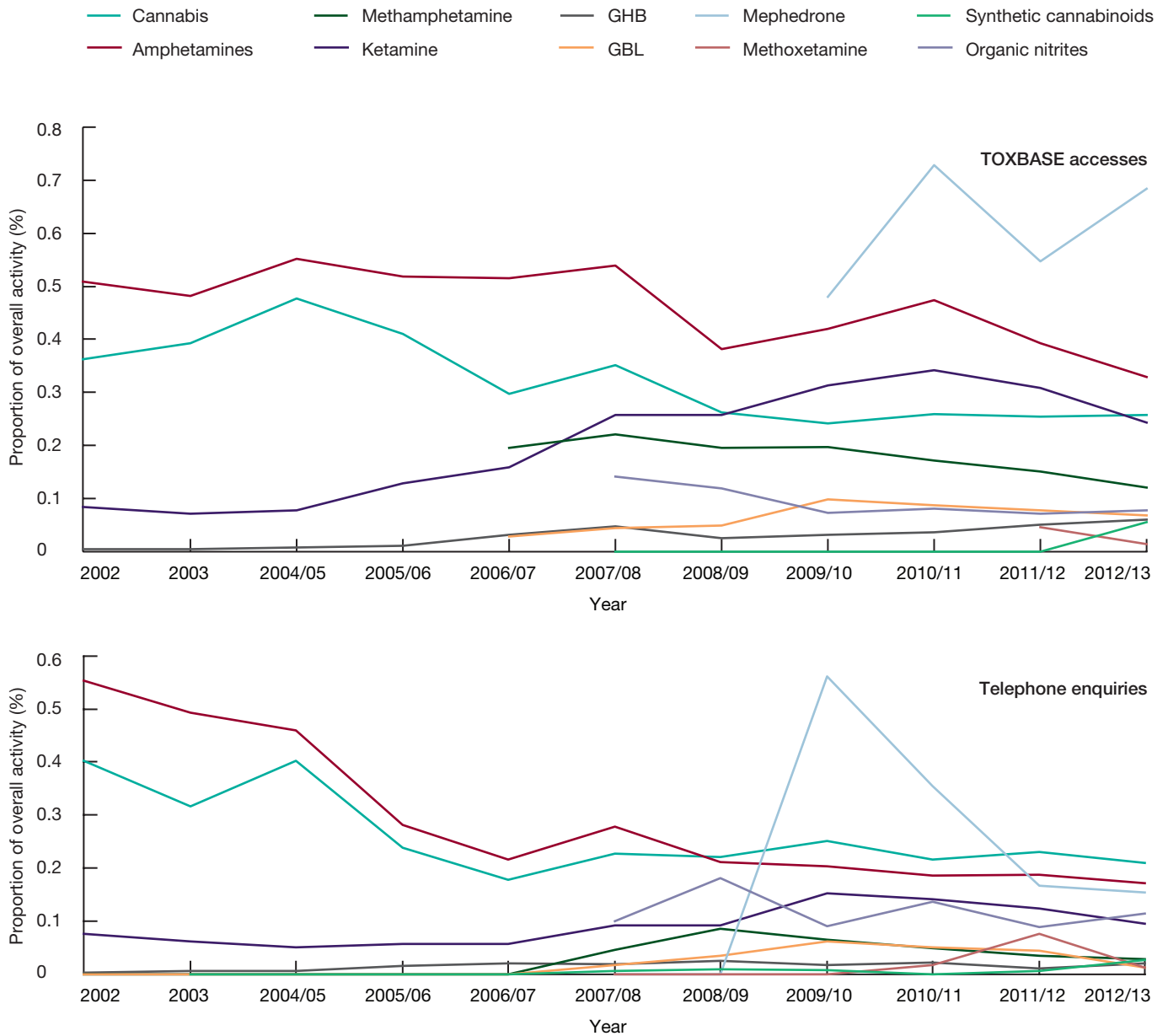
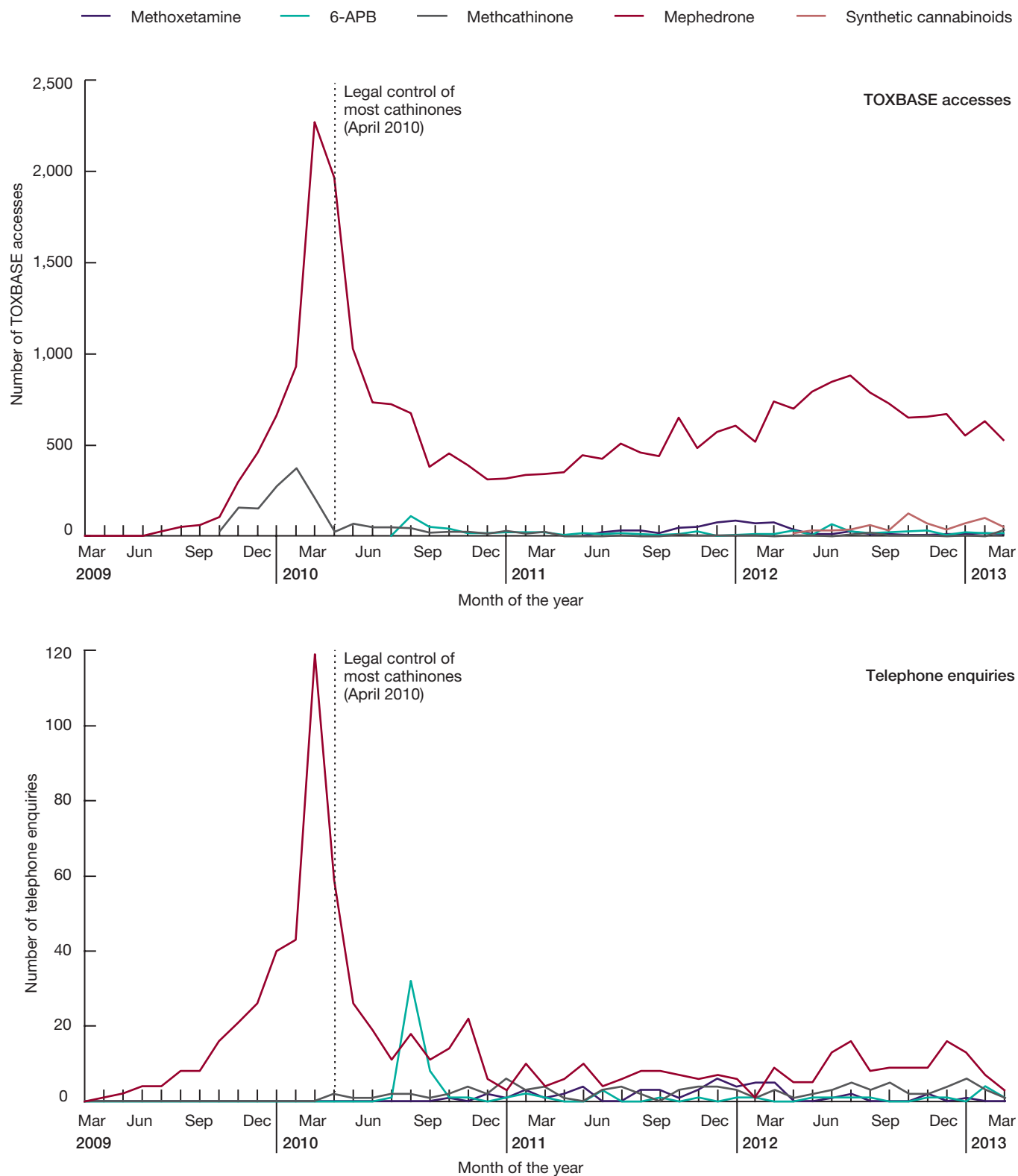


FIGURE 6.5 Proportion of TOXBASE accesses and telephone enquiries relating to drugs of misuse other than class A drugs (data for 2002 and 2003 by calendar year; subsequent data by financial year)



**FIGURE 6.6** Monthly TOXBASE accesses and telephone enquiries relating to selected drugs of misuse, from 2009/10 to 2012/13

This information is valuable when the need for legal control of new psychoactive substances is considered, as there must be evidence that the substance involved is associated with harmful effects. NPIS data can provide evidence of the extent and features of toxicity encountered in the UK and has previously formed part of the evidence base for the legal control of mephedrone, naphyrone and other cathinones (2010), desoxypipradrol (2010 and 2012) and methoxetamine (2012). Data collected during 2012/13 and provided to ACMD has demonstrated reduced enquiry numbers after legal control of mephedrone and methoxetamine. Data collected during 2012/13 has been referenced in the recent ACMD recommendation to control 5/6-APB and related substances.

During 2012/13, as recommended in last year's report, the NPIS explored arrangements for the exchange of data and information with the Focal Point EWS, including discussion of a good practice protocol. The Focal Point EWS has asked the NPIS to provide enquiry information on drugs notified to EMCDDA by member states. While the NPIS was keen to provide what it could within the available resources, it was agreed by both parties that the numbers of requests were such that data provision would need to be limited to priority issues.

### 6.3 Carbon Monoxide

During 2012/13 there were 434 telephone enquiries to the NPIS (248 in 2011/12 and 286 in 2010/11) regarding confirmed or suspected carbon monoxide exposures, involving one or more individuals. The apparent increase in the number of enquiries in 2012/13 was in part due to an actual increase in the number of enquiries and in part due to increased follow-up of the enquiries received following accesses to TOXBASE which prompted an urgent alert (see Section 5.1). Multiple individuals were involved in 67 enquiries. The total number of patients involved was at least 630, compared to at least 315 patients in 2011/12 and at least 385 in 2010/11. The maximum number of individuals exposed in a single incident in 2012/13 was 53. These exposures occurred at a car parts distribution plant.

In addition to the 434 patient-specific exposures in 2012/13, there were 136 general enquiries regarding potential carbon monoxide incidents, the majority of which were from the emergency services (85 enquiries), the Environment Agency (19) and the HPA (15).

The seasonal variation in the number of enquiries is shown in Figure 6.7, which also includes comparable

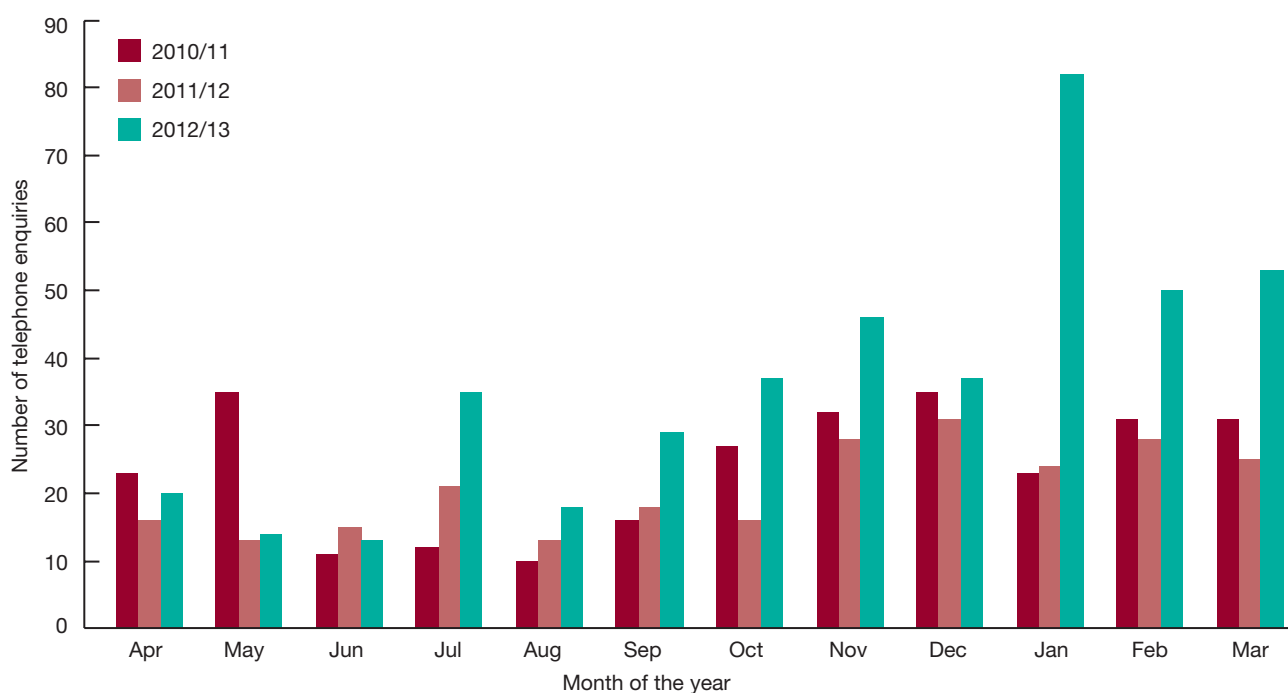


FIGURE 6.7 Number of enquiries regarding carbon monoxide exposures received each month from 2010/11 to 2012/13

data for 2010/11 and 2011/12. This demonstrates, as expected, that enquiries regarding carbon monoxide exposure were generally less frequent in the summer months.

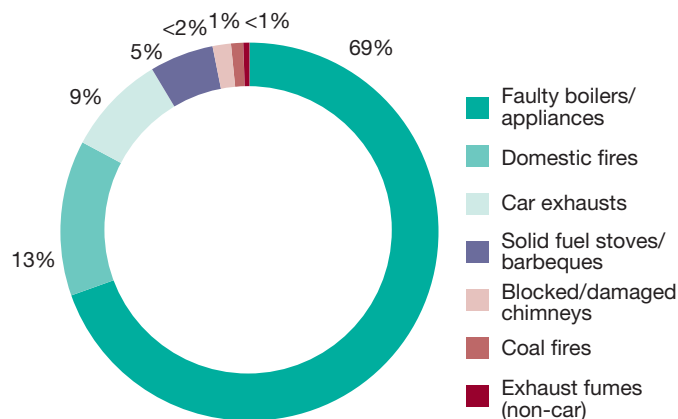
Most enquiries (384 out of 434, 88.5%) during 2012/13 involved carbon monoxide exposure at home, compared to just 29 (6.7%) occurring in the workplace, 16 (3.7%) in a public area and one (0.2%) in a nursing home; the location was unknown in four cases (0.9%). The suspected source of carbon monoxide in the domestic setting was known in all cases (see Figure 6.8); faulty boilers or appliances were implicated most often, accounting for 267 out of 384 enquiries (69%).

Exposure was accidental in 607 of 630 cases, 21 were deemed intentional and the intent was uncertain in two cases. Of the 21 intentional exposures, 13 involved vehicle exhaust fumes, seven involved the lighting of a barbecue in a confined space and one involved a house fire.

The poisoning severity score (PSS) was known in 612 of 630 patients: 588 patients had a PSS of 0 or 1 (minor toxicity), 18 had PSS 2 (moderate toxicity) and 6 were graded PSS 3 (severe toxicity). No PSS was available in the remaining 18 patients. There were multiple enquiries regarding two patients but only the most severe PSS was categorised. Three patients with a PSS 3 had been exposed to carbon monoxide during a domestic fire, so thermal injury may have also contributed to their features; three patients with PSS 3 died.

Carboxyhaemoglobin concentrations were known in 218 of 630 patients; the mean ( $\pm$ SD) carboxyhaemoglobin concentration in these 218 patients was 8.4 ( $\pm$ 9.5)%, in the six patients with PSS 3 was 38.6 ( $\pm$ 15.9)% and in 16 of 21 intentional exposures was 17.5 ( $\pm$  5.2)%.

Despite continuing public awareness campaigns, carbon monoxide poisoning remains an important preventable cause of morbidity and mortality in the UK. The NPIS is supporting these public awareness campaigns and, with public health authorities across the UK, is tracking the incidence of carbon monoxide exposures and helping to develop strategies for reducing these exposures.



**FIGURE 6.8** Source of carbon monoxide exposure in the domestic setting (total = 384)

## 6.4 Liquid Detergent Capsules

The NPIS first reported the toxicity of liquid detergent capsules in its 2009/10 annual report and this experience from 2008/09 was published subsequently\*. A larger study has now been completed covering the period from 1 May 2009 to 31 July 2012, with a particular focus on the ophthalmic damage and acute central nervous system (CNS) depression caused by these detergents. This more recent study involved 1,509 enquiries (there were 647 enquiries in 2008/09).

The 2009–2012 study involved 1,486 patients, the majority of whom (96%) were children less than five years of age. Exposure occurred mainly as a result of ingestion alone (82%), with eye contact alone (7%) and skin contact alone (1%) being less common. Multiple routes of exposure were involved in 9.5% of enquiries.

The poisoning severity score was known in 1,470 of 1,486 patients: no features were present in 478 cases; the features were minor (PSS 1) in 953, moderate (PSS 2) in 32 and severe (PSS 3) in seven cases (all children). Features that developed in those with PSS 3 included pulmonary aspiration (three cases), stridor (four cases) and airway burn (one case); four patients were intubated and ventilated.

\* Williams H, Bateman DN, Thomas SHL, Thompson JP, Scott RAH, Vale JA. Exposure to liquid detergent capsules: a study undertaken by the UK National Poisons Information Service. Clin Toxicol 2012; 50: 776–80

Only 14 adults ingested liquid detergent capsules; as stated above, the majority (96%) were children less than five years of age. The most common features reported following ingestion alone were nausea and vomiting (721 cases), followed by coughing (53), drowsiness (49, of whom 42 were children aged two years or less) and foaming (47). The mechanism by which the contents of these capsules cause drowsiness, particularly in very young children, is not fully understood. It is probable that the primary cause is the high concentration of non-ionic surfactants present in some capsules, together with anionic surfactants and ethanol; propylene glycol may also contribute.

Exposure for 20 patients was by the dermal route alone; they developed erythema (nine cases), rash (six cases) and burn (three cases). Following ingestion alone, 22 patients also apparently developed rashes; 21 of these were children aged three years or less. Rashes were reported to have developed 3–12 hours post-ingestion and were in many cases generalised, involving large areas of the body such as the trunk and arms. The mechanism by which rash appears to occur after ingestion (rather than following dermal exposure) is not known and requires further research.

The eye was involved in 212 cases; eye contact was the sole route of exposure in 110 of these patients and 195 (92%) were children aged less than five years of age. Features that developed following ocular exposure were conjunctivitis (145 cases out of 212, 68%) and corneal ulceration (six cases, 2.8%). In 41 cases no features were recorded. The ophthalmic damage is believed to be due primarily to the concentration of surfactants not the pH of the capsule ingredients, although in some formulations it may be as high as nine.

The NPIS is now working closely with the manufacturers of liquid detergent capsules to assess the impact of the new packaging that is currently being introduced.

## 6.5 Toxic Alcohols and Glycols

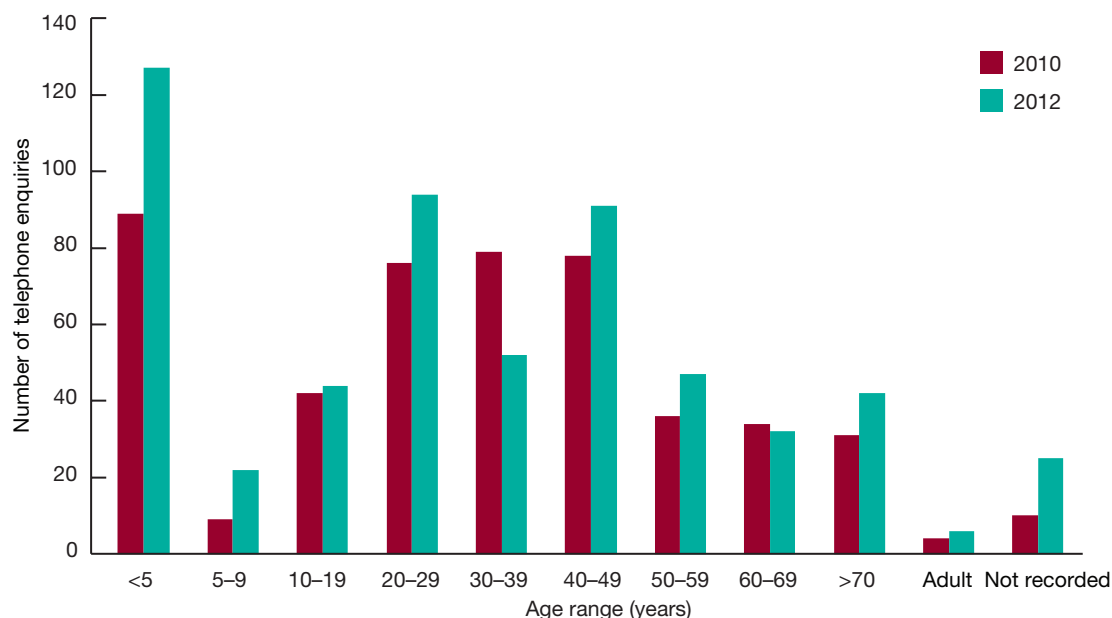
Toxic alcohols and glycols, such as ethylene glycol and methanol, are present in a number of commercial products that are readily available to the public, including antifreeze, brake fluid, and window-cleaning and windscreen-washing solutions. If ingested accidentally or deliberately, they can cause 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, in locating supplies of antidotes or in accessing facilities to perform haemodialysis.

Little is known about the epidemiology of this relatively infrequent poisoning in the UK, although the complexity of patient management leads to it being one of the most common types of poisoning referred 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 conducted during the 2010 calendar year and repeated during the 2012 calendar year, to provide information on the frequency, management and outcomes of systemic toxic alcohol poisoning. The 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.

During these two one-year periods, there was a total of 1,315 enquiries to the NPIS involving toxic alcohols and glycols, relating to 1,070 individual exposures. Of these, 522 originated from non-hospital sources. The vast majority of incidents (918, 86%) occurred in the home and were acute ingestions. Children aged five years or less were involved in 216 cases (Figure 6.9).

Accidental exposures accounted for 734 cases, 229 cases were intentional exposures and 13 described as recreational use. At the time of the enquiry, roughly



**FIGURE 6.9 Enquiries to the NPIS involving toxic alcohols and glycols by age range of patients, in 2010 and 2012**

half of the patients (544, 51%) were asymptomatic, 332 (31%) had minor features, 69 (6.4%) had moderate features and 77 (7.1%) had serious features. The products most commonly involved were antifreeze, screenwash, surgical spirit, window/glass cleaners and de-icers; ethylene glycol was the most common ingredient.

Of the 548 individual exposures originating from hospitals, there were 329 systemic exposures, for which 216 patients received antidote treatment and 90 required extracorporeal treatment (Figure 6.10). There were eight fatalities. In keeping with NPIS advice to use fomepizole as the antidote of choice for systemic toxic alcohol and glycol poisoning, there was an increase in the use of fomepizole in 2012 (75 out of 117, 64%) compared with 2010 (50 out of 99, 51%). However, antidote treatment was usually initiated based on surrogate markers of toxicity as laboratory assays of toxic alcohols and glycols were rarely available to guide management, leading to overuse of antidote and the risk of adverse events such as intoxication with ethanol and unnecessary expense with fomepizole. In 33 patients, antidote treatment was given until results of the assay showed undetectable concentrations of toxic alcohols and glycols.

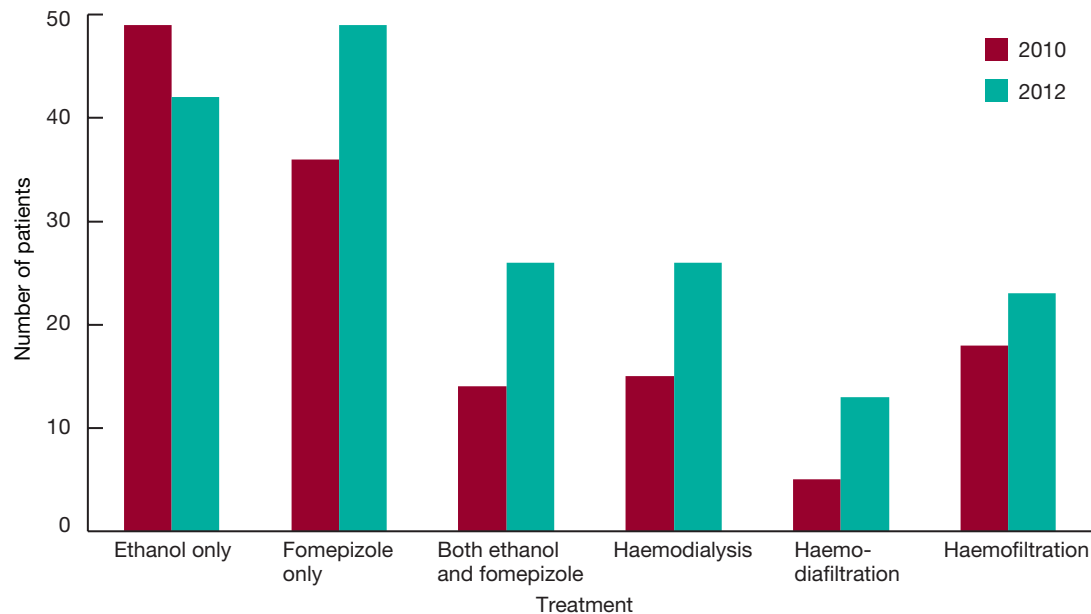
NPIS data suggests that there is an average of at least three severe systemic exposures each week nationally. To manage these effectively, NHS hospitals need to consider how they can improve the local availability of assays and antidotes. There are two or three reported accidental exposures to products containing toxic alcohols and glycols in children each week. Preventive measures such as improved labelling of products to warn parents of toxicity and the use of child-resistant containers would help reduce such exposures.

## 6.6 Antidote Holding

The NPIS and the College of Emergency Medicine (CEM) jointly issued guidelines for antidote stocking by acute hospital emergency departments in the UK in 2008. A national audit was undertaken in 2010 to assess compliance with this guidance. Questionnaires were sent by the NPIS units to the chief pharmacist in 224 acute hospitals in the UK and 196 were completed and returned (a response rate of 87.5%). The results, published in 2013\*, showed that commonly used

\* Thanacoody HKR, Aldridge G, Laing W, Nash S, Dargan PI, Vale JA, Bateman DN, Thompson JP, Thomas SHL. National audit of antidote stocking in acute hospitals in the United Kingdom. EMJ 2013; 30: 393–6.





**FIGURE 6.10** Patients requiring antidote treatment or extracorporeal treatment for toxic alcohol and glycol poisoning

antidotes were available immediately or within one hour in acute hospitals but highlighted problems with the availability of antidotes that are infrequently used, such as pralidoxime and viper venom antiserum, and antidotes for cyanide, toxic alcohol and heavy metal poisoning.

Following publication of this audit, the Department of Health set up a working group to look at ways of improving antidote stocking in acute hospitals in England. The NPIS and CEM have revised the joint guidelines and these will be published during 2013, accompanied by a letter of support from the Chief Pharmaceutical Officer of England. This will highlight the need to acute NHS trusts in England of ensuring adequate stocking of antidotes that are required either immediately or within one hour. This work is now being discussed with the Chief Pharmaceutical Officers of Wales and Scotland.

Further work is being undertaken to look at the feasibility and cost-effectiveness of having a small number of designated centres in the UK that would hold rarely used antidotes which are stocked supra-regionally.

# 7 Recommendations

## Outcome of Recommendations for 2012/13

- 1 To provide health support relating to chemical exposure and other forms of poisoning for the London 2012 Olympic and Paralympic Games

**Outcome** Completed.

- 2 To develop arrangements for the NPIS to act as the first point of contact for clinical enquiries relating to suspected radiation poisoning

**Outcome** Completed. Advice on management of radiation poisoning included in TOXBASE. Specific arrangements in place to access advice from specialists in radiation medicine for clinical cases of suspected radiation exposure

- 3 To explore arrangements for the exchange of data and information with the UK Focal Point on Drugs Early Warning System

**Outcome** Completed. Channels for two-way communication of information in place

- 4 To continue to ensure that TOXBASE remains a fit-for-purpose, front-line resource for UK healthcare professionals by maintaining a four-yearly review cycle for all database entries

**Outcome** Completed. More than 50% of all entries reviewed and revised as needed during the two years, 2011/12 and 2012/13

## Recommendations for 2013/14

- 1 To commission the UKTIS public facing website
- 2 To complete work with the UK health departments on antidote holding centres
- 3 To explore joint working with the Medicines and Healthcare Products Regulatory Agency to use data collected by the NPIS for monitoring drug safety
- 4 To encourage improved labelling of products containing toxic alcohols and glycols to warn parents of toxicity and the use of child-resistant containers
- 5 To encourage production of a low concentration paediatric formulation of ranitidine syrup to avoid large overdoses and unnecessary presentations to healthcare services

## APPENDIX A

# NPIS Staff

## NPIS Consultants

### NPIS Birmingham

**Dr S M Bradberry** BSc MD MRCP FAACT

Deputy Director, NPIS Birmingham and West Midlands Poisons Unit, City Hospital, Birmingham

**Professor J A Vale** MD FRCP FRCPE FRCPG FFOM FAACT FBTS FBPharmacolS HonFRCPSG

Director, NPIS Birmingham and West Midlands Poisons Unit, City Hospital, Birmingham; School of Biosciences and College of Medical and Dental Sciences, University of Birmingham

### NPIS Cardiff

**Dr C V Krishna** MD FRCP DipTox DipTher

Deputy Director, NPIS Cardiff, and Consultant Physician, Clinical Pharmacologist, Toxicologist and Honorary Clinical Senior Lecturer, Cardiff and Vale University Health Board and Department of Pharmacology, Therapeutics and Toxicology, Institute of Molecular and Experimental Medicine, School of Medicine, Cardiff University

**Professor P A Routledge** OBE MD FRCP FRCPE FBPharmacolS FBTS FRCGP FFPM

Professor of Clinical Pharmacology and Head of Department of Pharmacology, Therapeutics and Toxicology, Institute of Molecular and Experimental Medicine, School of Medicine, Cardiff University

**Dr A Thomas** MBChB MRCP

Senior Lecturer in Clinical Pharmacology and Honorary Consultant Physician, Department of Pharmacology, Therapeutics and Toxicology, Institute of Molecular and Experimental Medicine, School of Medicine, Cardiff University

**Dr J P Thompson** BMedSci MBChB FRCP FBTS

Director, NPIS Cardiff, and Senior Lecturer in Clinical Pharmacology, Department of Pharmacology, Therapeutics and Toxicology, Institute of Molecular and Experimental Medicine, School of Medicine, Cardiff University

### NPIS Edinburgh

**Professor D N Bateman** BSc MD FRCP FRCPE FBPharmacolS FBTS FAACT

Professor in Clinical Toxicology, University of Edinburgh, and former Consultant Physician, Royal Infirmary of Edinburgh

**Dr J W Dear** PhD FRCPE

NHS Research Scotland Career Research Fellow and Consultant in Acute Medicine and Clinical Toxicology, Royal Infirmary of Edinburgh

**Dr M Eddleston** MA PhD FRCPE

Director, NPIS Edinburgh, and Scottish Senior Clinical Research Fellow and Reader, University of Edinburgh, and Consultant Clinical Toxicologist, Royal Infirmary of Edinburgh

**Dr EA Sandilands** MBChB MRCP(UK)

Consultant in Acute Medicine and Toxicology, Royal Infirmary of Edinburgh

**Dr A Veiraiah** MB BS MRCP(UK)

Consultant in Acute Medicine and Toxicology, Royal Infirmary of Edinburgh

### NPIS Newcastle (including UKTIS)

**Dr S L Hill** BSc MB BS MRCP(UK)

Consultant Physician and Clinical Toxicologist, Newcastle upon Tyne Hospitals NHS Foundation Trust, and Honorary Senior Clinical Lecturer, Institute of Cellular Medicine, Newcastle University

**Dr H K R Thanacoody** MD FRCP FRCPE

Consultant Physician and Clinical Toxicologist, Newcastle upon Tyne Hospitals NHS Foundation Trust, and Honorary Senior Clinical Lecturer, Institute of Cellular Medicine, Newcastle University

**Professor S H L Thomas** BSc MD FRCP FRCPE

Director, NPIS Newcastle and UKTIS, Consultant Physician, Newcastle upon Tyne Hospitals NHS Foundation Trust, and Professor of Clinical Pharmacology and Therapeutics, Newcastle University

**Dr L Yates** MBChB PhD DRCOG MRCPCH

Head of Teratology, UKTIS, Consultant in Clinical Genetics, Institute of Genetic Medicine, Newcastle upon Tyne Hospitals NHS Foundation Trust, and Honorary Senior Clinical Lecturer, Institute of Genetic Medicine, Newcastle University

## Consultants providing on-call support for the NPIS

**Dr P I Dargan** FRCPE FACMT FRCP FAACT

Consultant Physician and Clinical Toxicologist, Clinical Director, Guy's and St Thomas' NHS Foundation Trust, and King's Health Partners, London, and Reader in Toxicology, King's College London, London

**Dr W S Waring** BMedSci MB PhD FRCPE FBPharmacolS

Consultant Physician in Acute Medicine and Clinical Toxicology, York Teaching Hospital Foundation Trust, and Honorary Senior Lecturer in Medicine, Hull York Medical School, York

**Dr D M Wood** MD FRCP FACMT FBPharmacolS

Consultant Physician and Clinical Toxicologist, Guy's and St Thomas' NHS Foundation Trust and King's Health Partners, London, and Honorary Senior Lecturer, King's College London, London

## Consultants providing specialist support for the NPIS

**Dr M Anderson** BSc BMedSci BM BS MRCPCH

Consultant Paediatrician, Great North Children's Hospital, Newcastle upon Tyne Hospitals NHS Foundation Trust

**Dr J M Wraight** MBChB MSc FACEM FCEM

Consultant Emergency Physician, St John's Hospital (NHS Lothian), Livingston

## Retirement of Professor D N Bateman

In March 2012 Professor Nick Bateman retired from Directorship of NPIS Edinburgh, a post he had held for 14 years. He continued to support the NPIS until March 2013, when he retired from clinical practice.

Professor Bateman qualified from Guy's Hospital, London, and trained at the Royal Postgraduate Medical School, London, and in Newcastle upon Tyne, UK. Between 1991 and 1998 he was Director of the Northern and Yorkshire Regional Drug and Therapeutics Centre, which included both the NPIS Newcastle Unit and the (then) National Teratology Information Service (now UKTIS), which he was instrumental in setting up. Soon after his move to Edinburgh in 1998, he took on the task of moving the NPIS poisons information database TOXBASE from the Viewdata platform to the internet, increasing its availability for healthcare workers around the country. This resulted in a large increase in accesses to the system, from around 100,000 in 2000 to 550,000 in 2012.



In addition to his post as consultant physician and clinical toxicologist in Edinburgh, Professor Bateman held many external positions, including Editor-in-Chief (2009–2011) of the journal *Clinical Toxicology*, the official journal of poison centres and clinical toxicologists in Europe and North America; President (2004–2006) of the European Association of Poisons Centres and Clinical Toxicologists; and Chair (2003–2008) of the Medical and Toxicology Sub-Committee of the Advisory Committee on Pesticides, Pesticides Safety Directorate. He is currently Chairman of the UK Poisons Board.

We thank Professor Bateman for his major contributions to the NPIS and to clinical toxicology both nationally and internationally, and for his mentoring of young researchers. We wish Nick, and his wife Judith, all the best for the future!

## 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

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

Member: Drugs and Therapeutics Committee, SWBH NHS Trust

#### Professor J A Vale

##### INTERNATIONAL ACTIVITIES

Member: Advisory Board Hong Kong Poisons Centre

##### INTERNATIONAL SOCIETIES

President: Clinical and Translational Specialty Section, Society of 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)

##### ACADEMIC ACTIVITIES

Joint Course Organiser: MSc (Toxicology), University of Birmingham

Examiner: MRCP(UK) Part 2 Clinical Examination (PACES)

Member: SAC in Toxicology, Royal College of Pathologists

Examiner: Faculty of Occupational Medicine

Fellow: American Academy of Clinical Toxicology

Fellow: British Pharmacological Society

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: 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

Course Organiser: 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

Member: Expert Panel of the Hong Kong Poison Control Network (HKPCN)

##### 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: British Pharmacological Society  
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

##### NHS NATIONAL AND REGIONAL COMMITTEES

Medical Director: Yellow Card Centre Wales  
Member: New Medicines Group, All-Wales Medicines Strategy Committee  
Member: All-Wales Specialist Training Committee in Clinical Pharmacology

##### ACADEMIC ACTIVITIES

Theme Lead: BDS Human Disease Course, Cardiff University  
Member: Steering Committee, Diploma/MSc in Medical Toxicology, Cardiff University  
Member: Steering Committee, Diploma in Therapeutics, Cardiff University  
Member: Final Year Exam Executive, Cardiff University

#### Dr J P Thompson

##### INTERNATIONAL ACTIVITIES

Member: Advisory Board Hong Kong Poisons Centre  
Consultant: WHO Collaborating Centre for Chemical Incidents

##### INTERNATIONAL SOCIETIES

Vice President (Clinical): British Pharmacological Society  
Chair: Human Toxicology Section British Toxicology Society  
Chair: EAPCCT Working Group on International Poisons Centre Activities and Regulatory Affairs

##### ADVISORY COMMITTEES

Member: Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT)  
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: Joint Specialty Committee, Clinical Pharmacology and Therapeutics  
Member: New Medicines Group, All-Wales Medicines Strategy Committee  
Member: Bro Taf Localities Drug and Therapeutics Committee  
Member: All-Wales Specialist Training Committee in Clinical Pharmacology

##### ACADEMIC ACTIVITIES

Member: Associate Course Director: Certificate/Diploma/MSc in Medical Toxicology; Therapeutics; and Occupational Health, Policy and Practice, Cardiff University  
Theme Lead: Prescribing and Therapeutics Education, School of Medicine, Cardiff University

## NPIS Edinburgh

#### Professor D N Bateman

##### INTERNATIONAL SOCIETIES

Scientific Committee Member: European Association of Poisons Centres and Clinical Toxicologists  
Fellow: American Academy of Clinical Toxicology

##### UK ADVISORY COMMITTEES

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

##### NHS NATIONAL AND REGIONAL COMMITTEES

Expert Toxicology Advisor: Scottish Government

##### ACADEMIC ACTIVITIES

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: Clinical Pharmacology Specialty Question Group, MRCP(UK)  
External Examiner: BSc Clinical Pharmacology, Kings College, London  
Member: British Pharmacological Society Clinical Section Committee

##### NHS NATIONAL AND REGIONAL COMMITTEES

Deputy Director: Yellow Card Centre, Scotland  
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 (until 31 Dec 2012)

##### INTERNATIONAL JOURNALS

Board Member: Clinical Toxicology

##### UK ADVISORY COMMITTEES

Member: MHRA Committee on Implementation of Changes to the Management of Paracetamol Overdose, Commission on Human Medicines, May–June 2012  
Member: UK Department of Health Committee on Antivenoms

##### ACADEMIC ACTIVITIES

Chairman of the Scientific Committee: Annual Congress of the Asia Pacific Association of Medical Toxicology



**Dr E A Sandilands****NHS NATIONAL AND REGIONAL COMMITTEES**

Member Lothian Drug and Therapeutics Committee

**ACADEMIC ACTIVITIES**

Lead: Undergraduate Educational Lead, Royal Infirmary of Edinburgh

**NPIS Newcastle (including UKTIS)****Dr S Hill****NHS NATIONAL AND REGIONAL COMMITTEES**

Member: UK Focal Point Early Warning System on Novel Psychoactive Substances

**ACADEMIC ACTIVITIES**

Module Lead: Drug Discovery and Development, MRes in Translational Medicine, Newcastle University

Member: Acute Medicine STC/DWDN Lead (Northern Deanery)

Member: Clinical Pharmacology and Therapeutics STC (Northern Deanery)

Educational Supervisor: PHE Funded Fellow in Clinical Toxicology

**Dr S Stephens****INTERNATIONAL SOCIETIES**

Member: European Network of Teratology Information Services

Member: The Teratology Society

Member: Organisation of Teratology Information Specialists

**ACADEMIC ACTIVITIES**

Honorary Associate Fellow: School of Cellular Medicine, Newcastle University

**Dr H K R Thanacoody****UK ADVISORY COMMITTEES**

Member: Independent Scientific Advisory Committee, MHRA

Member: Pharmacovigilance Expert Advisory Group, MHRA

**ACADEMIC ACTIVITIES**

Member: RCPATH Toxicology Specialist Advisory Committee

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**

Past 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

Co-opted Member: Technical Committee, Advisory Council on 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

**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

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

**Dr L Yates****INTERNATIONAL ACTIVITIES**

Member and Chair (from March 2013): European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP) Working Group 2: Independence and Transparency

**INTERNATIONAL SOCIETIES**

Member: European Network of Teratology Information Services

Member: Organisation of Teratology Information Specialists

Member: British Society of Human Genetics

Member: Clinical Genetics Society

Member: South African Society of Human Genetics

**NHS NATIONAL AND REGIONAL COMMITTEES**

Member: Northern Congenital Abnormality Survey (NorCAS) Steering Committee

**ACADEMIC ACTIVITIES**

Member of Organising Committee: British Association for Psychopharmacology (BAP) Guidelines on the Use of Psychotropic Medication Preconception, in Pregnancy and Postpartum

## APPENDIX B

# Publications in 2012/13

Seventy contributions to the scientific literature were published in 2012/13 by NPIS staff\*.

### Peer-reviewed papers

Antoine DJ, **Dear JW**, Starkey-Lewis P, Platt V, Coyle J, Masson M, **Thanacoody RH**, Gray AJ, Webb DJ, Moggs JG, **Bateman DN**, Goldring CE, Park BK. Mechanistic biomarkers provide early and sensitive detection of acetaminophen-induced acute liver injury at first presentation to hospital. *Hepatology* 2013; February [Epub ahead of print].

Antoine DJ, Jenkins RE, **Dear JW**, Williams DP, McGill MR, Sharpe MR, Simpson KJ, Craig DGN, Jaeschke H, Park K. Molecular forms of HMGB1 and Keratin-18 as mechanistic biomarkers for mode of cell death and prognosis during clinical acetaminophen hepatotoxicity. *J Hepatology* 2012; 56: 1070–79.

Benson BE, Hoppu K, Troutman WG, Bedry R, Erdman A, Höjer J, Mégarbane B, **Thanacoody R**, Caravati EM. Position paper update: gastric lavage for gastrointestinal decontamination. *Clin Toxicol* 2013; 51: 140–46.

Carroll R, Metcalfe C, Gunnell D, Mohamed F, **Eddleston M**. Diurnal variation in probability of death following self-poisoning in Sri Lanka – evidence for chronotoxicity in humans. *Int J Epidemiol* 2012; 41: 1821–8.

Chang SS, Lu TH, **Eddleston M**, Konradsen F, Sterne JAC, Lin JJ, Gunnell D. Factors associated with the decline in suicide by pesticide poisoning in Taiwan: a time trend analysis, 1987–2010. *Clin Toxicol* 2012; 50: 471–80.

Clutton RE, Dissanayake K, Lawson H, Simpson K, Thompson A, **Eddleston M**. The construction and evaluation of a device for mechanomyography in anaesthetized Göttingen minipigs. *Vet Anaesth Analg* 2013; 40: 134–41.

Conway BR, Manoharan D, Manoharan D, Jenks S, **Dear JW**, McLachlan S, Strachan MW, Price JF. Measuring urinary tubular biomarkers in type 2 diabetes does not add prognostic value beyond established risk factors. *Kidney Int* 2012; 82: 812–18.

**Coulson JM**, **Cooper G**, **Krishna C**, **Thompson JP**. Snakebite enquiries to the UK National Poisons Information Service: 2004–2010. *Emerg Med J* 2012; December [Epub ahead of print].

**Dear JW**, Street J, Bailey MA. Urinary exosomes: a reservoir for biomarker discovery and potential mediators of intra-renal signaling. *Proteomics* 2013; February [Epub ahead of print].

**Eddleston M**, Dawson AH. Triage and clinical management of patients with acute pesticide self-poisoning presenting to small rural hospitals. *Clin Toxicol* 2012; 50: 455–7.

Einarson A, Smart K, Vial T, Diav-Citrin O, **Yates L**, **Stephens S**, Pistelli A, Kennedy D, Taylor T, Panchaud A, Malm H, Koren G, Einarson TR. Rates of major malformations in infants following exposure to duloxetine during pregnancy: a preliminary report. *J Clin Psychiatry* 2012; 73: 1471.

Evan LC, Livingstone DE, Kenyon CJ, Jansen MA, **Dear JW**, Mullins JJ, Bailey MA. A urine-concentrating defect in 11 $\beta$ -hydroxysteroid dehydrogenase type 2 null mice. *Am J Physiol Renal Physiol* 2012; 303: F494–502.

**Hill SL**, **Harbon SCD**, **Coulson J**, **Cooper GA**, **Jackson G**, **Lupton DJ**, **Vale JA**, **Thomas SHL**. Methoxetamine toxicity reported to the National Poisons Information Service: clinical characteristics and patterns of enquiries (including the period of the introduction of the UK's first Temporary Class Drug Order). *Emerg Med J* 2013; January [Epub ahead of print].

Höjer J, Troutman WG, Hoppu K, Erdman A, Benson BE, Mégarbane B, **Thanacoody R**, Bedry R, Caravati EM. Position paper update: ipecac syrup for gastrointestinal decontamination. *Clin Toxicol* 2013; 51: 134–9.

Hughes D, **Routledge PA**. A prescribing partnership. *Public Service Review: Health Social Care* 2013; 35: 65–7.

**Murray DB**, **Eddleston M**, **Thomas S**, Jefferson R, **Thompson A**, Dunn M, Vidler D, Clutton REC, Blain PG. Rapid and complete bioavailability of antidotes for organophosphorus nerve agent poisoning and cyanide in minipigs after intraosseous administration. *Ann Emerg Med* 2012; 60: 424–30.

Nicholson Roberts T, **Thompson JP**. Illegal substances in anaesthetic and intensive care practices. *Cont Edu Anaesthes Crit Care Pain* 2012; August [Epub ahead of print].

**Pettie J**, **Dow M**, **Sandilands EA**, **Thanacoody HKR**, **Bateman DN**. An integrated care pathway improves the management of paracetamol poisoning. *Emerg Med J* 2012; 29: 482–6.

Povey AC, Rees HG, **Thompson JP**, Watkins G, Stocks SJ, Karalliedde L. Acute ill-health in sheep farmers following use of pesticides. *Occup Med (Lond)* 2012; 62: 541–8.

**Routledge PA**. A national inpatient prescription chart: the experience in Wales 2004–12. *Br J Clin Pharmacol* 2012; 74: 561–5.

**Routledge PA**. An agenda for UK clinical pharmacology; developing and delivering clinical pharmacology in the UK national health service. *Br J Clin Pharmacol* 2012; 73: 884–7.

**Routledge PA**. Safe prescribing: a titanic challenge. *Br J Clin Pharmacol* 2012; 74: 676–84. *Review*.

**Sandilands EA**, Crowe J, Cuthbert H, Jenkins PJ, Johnston N, **Eddleston M**, **Bateman DN**, Webb DJ. Histamine-induced vasodilatation in the human forearm vasculature. *Br J Clin Pharmacol* 2013; March [Epub ahead of print].

Schep L, Knudsen K, Slaughter RJ, **Vale JA**, Mégarbane B. The clinical toxicology of gamma-hydroxybutyrate, gamma-butyrolactone and 1,4-butanediol. *Clin Toxicol* 2012; 50: 458–70.

Starkey-Lewis P, Merz M, Couttet P, Grenet O, **Dear J**, Antoine D, Goldring C, Park BK, Moggs JG. Serum microRNA biomarkers for human drug-induced liver injury. *Clin Pharmacol Ther* 2012; 92: 291–3.

**Thanacoody HKR**. Serotonin syndrome. *Medicine* 2012; 40: 63–4.

\* NPIS staff are given in bold type

**Thanacoody HKR, Aldridge G, Laing W, Dargan PI, Nash S, Thompson JP, Vale A, Bateman N, Thomas S.** National audit of antidote stocking in acute hospitals in the UK. *Emerg Med J* 2012; 30: 393–6.

**Thanacoody HK, Gray A, Dear JW, Coyle J, Sandilands EA, Webb DJ, Lewis S, Eddleston M, Thomas SH, Bateman DN.** Scottish and Newcastle Antiemetic pre-treatment for paracetamol poisoning study (SNAP). *BMC Pharmacol Toxicol* 2013; 14: 20.

**Thomas SHL.** An agenda for UK clinical pharmacology: developing and delivering clinical toxicology in the UK National Health Service – clinical toxicology. *Br J Clin Pharmacol* 2012; 73: 878–83.

**Thomas SHL, Yates LM.** Prescribing without evidence – pregnancy. *Br J Clin Pharmacol* 2012; 74: 691–7.

**Thompson JP, Marrs TC.** Hydroxocobalamin in cyanide poisoning. *Clin Toxicol* 2012; 50: 875–85.

**Veiraiah A, Dyas J, Cooper G, Routledge PA, Thompson JP.** Flumazenil use in benzodiazepine overdose in the UK: a retrospective survey of NPIS data. *Emerg Med J* 2012; 29: 565–9.

**Williams H, Bateman DN, Thomas SHL, Thompson JP, Scott RAH, Vale JA.** Exposure to liquid detergent capsules: a study undertaken by the UK National Poisons Information Service. *Clin Toxicol* 2012; 50: 776–80.

**Williams H, Moyns E, Bateman DN, Thomas SHL, Thompson JP, Vale JA.** Hazard of household cleaning products: a study undertaken by the UK National Poisons Information Service. *Clin Toxicol* 2012; 50: 770–75.

Winterfeld U, Allignol A, Panchaud A, Rothuizen LE, Merlob P, Cuppers-Maarschalkerweerd B, Vial T, **Stephens S**, Clementi M, De Santis M, Pistelli A, Berlin M, Eleftheriou G, Manáková E, Buclin T. Pregnancy outcome following maternal exposure to statins: a multicentre prospective study. *BJOG* 2013; 120: 463–71.

**Yates LM, Thomas SHL.** Prescribing medicines in pregnancy. *Medicine* 2012; 40: 386–90.

## Book chapters

**Eddleston M.** Poisonous plants and fish: plant cardiac glycoside poisoning. In: *Hunter's Tropical Medicine and Emerging Infectious Diseases*, 9th edition (Magill A et al, eds). London: Saunders; 2013, 935–7.

**Eddleston M.** Poisons and contaminants in food. In: *Travellers' Health*, 5th edition (Dawood R, ed). Oxford: OUP; 2012, 44–7.

Rawlins M, **Vale JA.** Drug therapy and poisoning. In: *Kumar and Clark's Clinical Medicine*, 8th edition (Kumar P, Clark M, eds). Edinburgh: Elsevier Saunders; 2012; 899–927.

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## Published congress abstracts

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