Systematic account of animal poisonings in Germany, 2012–2015


A systematic retrospective study on animal poisonings in Germany (wildlife excluded) between January 2012 and December 2015 was conducted. Data were collected on animal exposure calls to German poison centres, poisoning cases presenting to the University of Veterinary Medicine, Hannover Small Animal and Equine Clinics, cases involving off-label use of veterinary medicinal products reported to the Federal Office of Consumer Protection and Food Safety and toxicological submissions to the Institute of Pharmacology, Toxicology, and Pharmacy, Faculty of Veterinary Medicine, Ludwig-Maximilians-University, Munich.

Descriptive statistics were used to characterise animal type, exposure reason, type and substance, year/month of exposure, case severity and outcome. An evaluation of the data and data sources was also carried out. Variation in poisoning patterns was seen. However, dogs and cats were the most frequently reported species and medicinal products, pesticides and plants were consistently implicated as top causes of poisoning. Advantages and disadvantages were associated with each data source; bias was found to be an important consideration when evaluating poisoning data. This study provided useful information on animal poisonings in Germany and highlights the need for standardised approaches for the collection, evaluation and integration of poisoning data from multiple sources.

Animal poisonings within Germany and the EU are not required to be reported; both Germany and the EU lack a centralised veterinary poisoned database as well as centralised process for toxicology laboratories that analyse veterinary samples to reports case findings. There are also no veterinary-specific poison centres (PCs) within Germany. As a result, the eight human PCs within Germany advise and record data on animal poisoning inquiries, in addition to their main role of providing medical advice 24 hours a day, seven days a week for toxic exposures in human beings (BfR 2016). This situation mirrors many other European countries as currently only two countries, France and the UK, have veterinary-specific PCs that deal exclusively with animal poisonings (Caloni and others 2012a).

Several recent publications have provided a review on animal poisonings in Europe (Berny and others 2010, Guitart and others 2010, Caloni and others 2012b, Schediwy and others 2015). This contrasts with Germany, where there is a lack of publicly available data regarding animal poisonings apart from case reports, information included in yearly reports of the eight German PCs and a recently published survey of samples from suspected animal poisoning cases sent to a toxicology laboratory between 1998 and 2006 for analysis (Ailkämper and others 2015). Additionally, as available information is fragmented and non-standardised, it is a challenge for the veterinary profession within Germany to obtain a comprehensive overview of animal poisonings as well as up-to-date information that can be used for case management and poisoning risk assessment.

The main objective of this study was to systematically collect, assess and analyse information on poisonings in companion animals and livestock in Germany. Data were gathered from multiple sources and included animal exposure calls to five German PCs, poisoning cases presenting to the University of Veterinary Medicine, Hannover (TiHo) Small Animal and Equine Clinics, cases involving off-label use of veterinary medicinal products (VMPs) reported to the Federal Office of Consumer Protection and
Food Safety (BVL) and submissions for toxicological analysis to the Institute of Pharmacology, Toxicology, and Pharmacy, Faculty of Veterinary Medicine, Ludwig-Maximilians-University, Munich (IFTP, LMU). A secondary objective was to evaluate and compare the data in order to determine where efforts could be focused to optimise approaches for collection and use of information on animal poisonings.

**Materials and methods**

**Poison centres**

Data on animal 9168 exposure calls to five German PCs were collected retrospectively for the time period January 1, 2012, to December 31, 2014. The date of inquiry, type of caller, animal details (species, age, sex), exposure reason (eg, accidental), type (eg, acute) and route (eg, oral) and main exposure agent were collected retrospectively for the time period January 1, 2012, to December 31, 2014. Analysis of samples was carried out using the keywords “poisoning” and “intoxication” with the categories “diagnosis”, “finding” and “text”. For horses, cases were collected based on clinician recall. Case records were screened and selected for inclusion if the likelihood of exposure was probable or definite and/or causality was possible or probable. Animal details, location of exposure, reason for exposure, type and route of exposure and causative agent were extracted from the case notes. Case severity was assessed and outcome was evaluated at the time of discharge from the clinic.

**University of Veterinary Medicine, Hannover (TiHo)**

Poisoning cases (n=215) in cats, dogs and horses presenting to the TiHo were retrospectively collected for the time period January 1, 2013, to December 31, 2015. Other species were excluded (eg, cattle, exotics) due to the lack of poisoning cases treated at these clinics. For cat and dog cases, a search was carried out in the medical record software program (easyVet) using the keywords “poisoning” and “intoxication” with the categories “diagnosis”, “finding” and “text”. For horses, cases were collected based on clinician recall. Case records were screened and selected for inclusion if the likelihood of exposure was probable or definite and/or causality was possible or probable. Animal details, location of exposure, reason for exposure, type and route of exposure and causative agent were extracted from the case notes. Case severity was assessed and outcome was evaluated at the time of discharge from the clinic.

**Federal Office of Consumer Protection and Safety (BVL)**

Reports (n=150) to the BVL involving off-label use of VMPS in cats, dogs, rabbits, horses and livestock (including poultry) in Germany were collected retrospectively for the time period January 1, 2012, to December 31, 2015. Only cat and dog cases were assessed due to the small number of reports for the other species that met the inclusion criteria. Cases were screened and selected for inclusion if the likelihood of exposure was probable or definite and/or causality was possible or probable. Cases were excluded that resulted from veterinary instruction and/or error (eg, inaccurate dosing or use of a contraindicated medicine by a veterinarian). Animal details, route of exposure, reason for the reported adverse event and veterinary medicine/product were extracted from case records. Case severity and outcome were also evaluated.

**Institute of Pharmacology, Toxicology, and Pharmacy, Ludwig-Maximilians-University**

Data recorded on 393 samples from cats, dogs, horses and farm animal species (including poultry) sent for toxicological analysis to the IFTP, LMU were collected for the time period January 1, 2012, to December 31, 2014. Analysis of samples was carried out using gas chromatography mass spectrometry (GC-MS), GC-MS combined with thin-layer chromatography (TLC), high-performance liquid chromatography (HPLC) and/or photometry for 119 (30.3 per cent) submissions, and TLC, HPLC and/or photometry alone or in combination for 75 (19.1 per cent) submissions. Information on the date of submission, postcode of submission, species, test methods and substances detected was assessed. Submissions from outside Germany were excluded; submissions that tested positive but only included substances most likely involved in veterinary treatment/intervention (eg, metamizole, phenobarbital, pentobarbital) were categorised as negative.

**Results**

**Poison centres**

From January 1, 2012, to December 31, 2014, there were 9168 animal exposure calls to the five German PCs, representing 68 per cent of all animal exposure calls to German PCs (eight total). Animal calls comprised 1.4–3.7 per cent (average 2.1 per cent) of all exposure calls (human and animal) and numbered 3085 (35.6 per cent), 2868 (31.3 per cent) and 3215 (35.1 per cent) in 2012, 2013 and 2014, respectively.

Seasonal peaks were seen with calls regarding chocolate (February, April, December), cyanobacteria (August, September), mushrooms (September to November) and fertilisers and pesticides (Fig 1). The majority of calls were from laypersons (52.6 per cent) and veterinary personnel (46.5 per cent). Dogs were the species most frequently inquired about (75.8 per cent of all calls), followed by cats (18.2 per cent) and horses (2.2 per cent). Age and sex information is included in Table 1.

The majority of exposures were acute (n=8845, 96.4 per cent), 2.7 per cent (n=243) were chronic and 0.9 per cent (n=80) other/unknown. Oral exposure was the most common route (n=8514, 92.9 per cent), followed by dermal (n=294, 3.2 per cent), inhalation (n=97, 1.1 per cent), bite/sting (n=66, 0.7 per cent) and other/unknown (n=197, 2.1 per cent).

Reasons for exposure included accidental (n=8719, 95.1 per cent), criminal/malice (n=115, 1.2 per cent), unwanted effect (n=38, 1.0 per cent), misuse of medicinal products (n=44, 0.5 per cent) and other/unknown (n=202, 2.2 per cent).

The top three causative agent categories were medicinal products (n=2001, 21.8 per cent), plants and mushrooms (n=1703, 18.6 per cent) and pesticides (including plant protection agents) (n=1583, 17.3 per cent). Variation was seen for different species; Table 2 shows the distribution of exposures by species and poison category. NSAIDs (n=236, 16.3 per cent) and hormonal contraceptives for systemic use (n=115, 8.2 per cent) were the top causes of

**Documentation and analysis**

Definitions for exposure reason and type, likelihood of exposure, causality and case outcome were based on those established by the Society of Clinical Toxicology for German speaking PCs (Kliniktox 2016a); the poisoning severity score (PSS) was used for case severity assessment (Persson and others 2009). Toxic agents were classified according to Version 2.0 of the toxicological Category System (TDI-CSA, TKS) for poisonous agents (Kliniktox 2016b). Human medicinal products (HMPs) and veterinary medicinal products (VMPs) were classified according to the Anatomical Therapeutic Chemical (ATC) classification system and Anatomical Therapeutic Chemical Classification System for veterinary medicinal products (ATCvet), respectively (WHO 2016a, 2016b). A descriptive analysis of the data was carried out using Microsoft Excel (2010) and R (Version 3.2.3.).

FIG 1: Monthly distribution of animal exposure calls involving pesticides (n=1489) and fertilisers (n=444) to five German poison centres, 2012–2014
One poison centre. The top three exposure categories for this centre were pesticides plus plant protection agents (n=370, 20.2 per cent), medicines (n=550, 19.1 per cent) and plants and mushrooms (315, 17.2 per cent). For calls involving a known substance (n=1752), plant and mushroom exposures were responsible for the greatest number of fatal cases (n=9, 25.7 per cent), followed by pesticides (n=6, 17.1 per cent) and bites/envenomations (n=4, 11.4 per cent). The greatest number of severe cases involved pesticides (n=18, 24.7 per cent), medicines (n=15, 17.8 per cent) and plants and mushrooms (n=9, 12.3 per cent) (Table 3 and Fig 5).

University of Veterinary Medicine, Hannover (TiHo)

A total of 213 cases (n=198 incidents) in cats (n=29, 13.6 per cent), dogs (n=172, 80.8 per cent) and horses (n=12, 5.6 per cent) presented to the TiHo between 2013 and 2015. For cats and dogs, 98 per cent of cases were seen during emergency hours. Seasonal patterns were seen in cases involving chocolate, with peaks in April, May and December; all suspected exposure to yew (Acer species) in horses occurred in October to December. The majority of dogs were purebred (n=130, 75.6 per cent) and cats were feral (n=29, 13.6 per cent). The majority of horses were purebred (n=12, 5.6 per cent) and the majority of cases were seen during emergency hours (n=172, 80.8 per cent). The greatest number of severe cases involved pesticides (n=18, 24.7 per cent), medicines (n=15, 17.8 per cent) and plants and mushrooms (n=9, 12.3 per cent) (Table 3 and Fig 5).

### Table 1: Animal type, age and sex for all animal exposure calls with species information to five German poison centres (PCs), 2012–2014

Table 1 presents a summary of animal type, age, and sex for all animal exposure calls with species information to five German poison centres (PCs). The total number of cases (n=9168) includes all animal exposures presented to the five poison centres between 2012 and 2015. The majority of dogs were purebred (n=130, 75.6 per cent) and cats were feral (n=29, 13.6 per cent). The majority of horses were purebred (n=12, 5.6 per cent) and the majority of cases were seen during emergency hours (n=172, 80.8 per cent). The greatest number of severe cases involved pesticides (n=18, 24.7 per cent), medicines (n=15, 17.8 per cent) and plants and mushrooms (315, 17.2 per cent). For calls involving a known substance (n=1752), plant and mushroom exposures were responsible for the greatest number of fatal cases (n=9, 25.7 per cent), followed by pesticides (n=6, 17.1 per cent) and bites/envenomations (n=4, 11.4 per cent). The greatest number of severe cases involved pesticides (n=18, 24.7 per cent), medicines (n=15, 17.8 per cent) and plants and mushrooms (n=9, 12.3 per cent) (Table 3 and Fig 5).

### Table 2: Agents by category and species (N, %) for all animal exposure calls to five German poison centres, 2012

Table 2 presents a summary of agents by category and species for all animal exposure calls to five German poison centres (PCs) between 2012 and 2015. The table includes a breakdown of agents by category and species for all animal exposure calls to the five poison centres (PCs). The total number of cases (n=9168) includes all animal exposures presented to the five poison centres between 2012 and 2015. The majority of cases were seen during emergency hours (n=172, 80.8 per cent). The greatest number of severe cases involved pesticides (n=18, 24.7 per cent), medicines (n=15, 17.8 per cent) and plants and mushrooms (315, 17.2 per cent). For calls involving a known substance (n=1752), plant and mushroom exposures were responsible for the greatest number of fatal cases (n=9, 25.7 per cent), followed by pesticides (n=6, 17.1 per cent) and bites/envenomations (n=4, 11.4 per cent). The greatest number of severe cases involved pesticides (n=18, 24.7 per cent), medicines (n=15, 17.8 per cent) and plants and mushrooms (n=9, 12.3 per cent) (Table 3 and Fig 5).
cent) and the majority of cats were non-purebred (n=21, 72.4 per cent). Age and sex details are reported in Table 1.

Acute exposures were the most common (n=175, 82.2 per cent), two cases (0.9 per cent) involved subacute exposures, and 36 (16.9 per cent) were unknown. The reason for exposure was accidental for the majority of cases (n=183, 85.9 per cent), 73 (36.0 per cent) were unknown. The reason for exposure was accidental for the majority of cases (n=183, 85.9 per cent), 73 (36.0 per cent) were unknown. The reason for exposure was accidental for the majority of cases (n=183, 85.9 per cent), 73 (36.0 per cent) were unknown.

Oral exposure was the primary route (n=199, 93.4 per cent), 8 (4.1 per cent) were unknown. The reason for exposure was accidental for the majority of cases (n=183, 85.9 per cent), 73 (36.0 per cent) were unknown. The reason for exposure was accidental for the majority of cases (n=183, 85.9 per cent), 73 (36.0 per cent) were unknown. The reason for exposure was accidental for the majority of cases (n=183, 85.9 per cent), 73 (36.0 per cent) were unknown.

Inhalation. Information on location of exposure was not available for 66.7 per cent (n=134) of cat and dog cases. For cases with location information (n=67), the majority (53.1 per cent) occurred in or around the home.

VMPs (n=8, 27.6 per cent) followed by HMPS (n=6, 20.7 per cent) were the top two causes of poisoning in cats; chocolate (n=52, 50.2 per cent) followed by rodenticides (n=45, 26.2 per cent) the top two causes in dogs; suspected exposure to sycamore (Acer species) (n=7, 58.3 per cent) followed by herbicides (n=5, 25 per cent) the top two causes in horses (Table 4). The majority of cat cases were of minor severity (n=15, 44.9 per cent), the majority of dog cases involved no symptoms (n=94, 54.7 per cent) and 50 per cent of equine cases were of minor severity and 50 per cent fatal (Fig 4). Four of the six severe cases in cats involved application of canine ectoparasiticide spot-on preparations containing permethrin and the other two, anticoagulant rodenticides. Two of the four fatal cases in dogs involved anticoagulant rodenticides, one cyanobacteria exposure and one molluscicide exposure. Of the severe cases (n=27) in dogs, 21 (77.8 per cent) involved anticoagulant rodenticides, 3 molluscicides (11.1 per cent), 1 cannabis, 1 the plant Leonotis leonurus and 1 suspected accidental consumption of a horse parasiticide. All fatal equine cases (n=6) involved suspected exposure to sycamore (Acer species).

FIG 2: Anticoagulant exposures by type of anticoagulant for animal exposure calls to five German poison centres, 2012–2014 (inquiries, n=367; no. of substances, n=370). *Second-generation anticoagulant

<p>| TABLE 3: Poisoning severity score by agent (N, %) for all animal exposure calls with species information to one German poison centre, 2012 to 2014 |
|---|---|---|---|---|---|---|</p>
<table>
<thead>
<tr>
<th>None</th>
<th>Minor</th>
<th>Moderate</th>
<th>Severe</th>
<th>Fatal</th>
<th>NAD/NR</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biocides</td>
<td>13 (1.4)</td>
<td>13 (3.0)</td>
<td>3 (1.4)</td>
<td>3 (1.4)</td>
<td>5 (3.6)</td>
<td>37 (2.0)</td>
</tr>
<tr>
<td>Bites/envenomations</td>
<td>6 (0.6)</td>
<td>20 (4.6)</td>
<td>13 (6.0)</td>
<td>2 (2.7)</td>
<td>4 (11.4)</td>
<td>73 (4.0)</td>
</tr>
<tr>
<td>Chemical agents for technical equipment, products, processes</td>
<td>28 (3.0)</td>
<td>11 (3.0)</td>
<td>3 (1.4)</td>
<td>2 (2.7)</td>
<td>1 (2.9)</td>
<td>52 (2.8)</td>
</tr>
<tr>
<td>Cleaning and maintenance products</td>
<td>42 (4.5)</td>
<td>22 (5.1)</td>
<td>6 (2.8)</td>
<td>7 (5.0)</td>
<td>77 (4.2)</td>
<td>183 (9.9)</td>
</tr>
<tr>
<td>Construction materials and agents</td>
<td>22 (2.4)</td>
<td>8 (1.9)</td>
<td>1 (0.5)</td>
<td>1 (0.5)</td>
<td>1 (0.7)</td>
<td>32 (1.8)</td>
</tr>
<tr>
<td>Consumer items/products</td>
<td>43 (4.6)</td>
<td>14 (3.2)</td>
<td>3 (1.4)</td>
<td>1 (2.9)</td>
<td>1 (3.2)</td>
<td>63 (3.3)</td>
</tr>
<tr>
<td>Cosmetics/PERSONAL care products</td>
<td>12 (1.3)</td>
<td>5 (1.2)</td>
<td>1 (0.5)</td>
<td>1 (0.5)</td>
<td>2 (1.4)</td>
<td>19 (1.0)</td>
</tr>
<tr>
<td>Dyes, paints, lacquers, varnishes</td>
<td>20 (2.1)</td>
<td>7 (1.6)</td>
<td>1 (0.5)</td>
<td>1 (0.5)</td>
<td>1 (0.7)</td>
<td>28 (1.5)</td>
</tr>
<tr>
<td>Food</td>
<td>62 (6.6)</td>
<td>27 (6.2)</td>
<td>12 (5.6)</td>
<td>5 (6.9)</td>
<td>3 (8.6)</td>
<td>119 (6.5)</td>
</tr>
<tr>
<td>Fuels, inflammable agents, scents</td>
<td>21 (2.2)</td>
<td>5 (1.2)</td>
<td>1 (0.5)</td>
<td>1 (0.5)</td>
<td>1 (0.7)</td>
<td>29 (1.6)</td>
</tr>
<tr>
<td>Medicines/medicinal products</td>
<td>216 (23.0)</td>
<td>68 (15.7)</td>
<td>29 (13.5)</td>
<td>17 (12.8)</td>
<td>23 (16.4)</td>
<td>350 (19.1)</td>
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<tr>
<td>Human medicinal products</td>
<td>181 (19.3)</td>
<td>45 (10.4)</td>
<td>18 (8.4)</td>
<td>10 (13.7)</td>
<td>17 (12.1)</td>
<td>271 (14.8)</td>
</tr>
<tr>
<td>Veterinary medicinal products</td>
<td>15 (1.6)</td>
<td>18 (4.2)</td>
<td>6 (2.8)</td>
<td>3 (4.1)</td>
<td>3 (2.1)</td>
<td>46 (2.5)</td>
</tr>
<tr>
<td>Unclassified medicinal products</td>
<td>20 (2.1)</td>
<td>5 (1.2)</td>
<td>1 (0.5)</td>
<td>1 (0.5)</td>
<td>1 (0.7)</td>
<td>32 (1.8)</td>
</tr>
<tr>
<td>Pesticides plus plant protection agents</td>
<td>195 (20.8)</td>
<td>70 (16.2)</td>
<td>45 (20.9)</td>
<td>18 (24.7)</td>
<td>6 (17.1)</td>
<td>361 (19.9)</td>
</tr>
<tr>
<td>Plants and mushrooms</td>
<td>134 (14.3)</td>
<td>97 (22.4)</td>
<td>46 (21.4)</td>
<td>9 (12.3)</td>
<td>9 (13.7)</td>
<td>317 (17.1)</td>
</tr>
<tr>
<td>Products for plants and animals</td>
<td>53 (5.4)</td>
<td>23 (5.3)</td>
<td>13 (6.1)</td>
<td>4 (5.3)</td>
<td>2 (2.7)</td>
<td>80 (4.4)</td>
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<tr>
<td>Tobacco/nicotine/illegal drugs</td>
<td>10 (1.1)</td>
<td>1 (0.2)</td>
<td>1 (0.5)</td>
<td>1 (0.5)</td>
<td>1 (0.7)</td>
<td>12 (0.7)</td>
</tr>
<tr>
<td>Agents, unknown application/category</td>
<td>23 (2.5)</td>
<td>15 (3.5)</td>
<td>9 (4.2)</td>
<td>1 (1.4)</td>
<td>2 (2.7)</td>
<td>27 (1.5)</td>
</tr>
<tr>
<td>Other§</td>
<td>23 (2.5)</td>
<td>10 (2.3)</td>
<td>11 (5.1)</td>
<td>2 (2.7)</td>
<td>1 (2.9)</td>
<td>49 (2.7)</td>
</tr>
<tr>
<td>Unknown</td>
<td>17 (1.8)</td>
<td>15 (3.5)</td>
<td>20 (9.3)</td>
<td>13 (17.8)</td>
<td>5 (6.8)</td>
<td>82 (4.5)</td>
</tr>
<tr>
<td>Total</td>
<td>938 (51.2)</td>
<td>433 (23.6)</td>
<td>215 (11.7)</td>
<td>73 (4.0)</td>
<td>35 (1.9)</td>
<td>1834 (100)</td>
</tr>
</tbody>
</table>

Percentages under the column and row labelled ‘Total’ are based on the total number of cases (n=9168). Percentages under the columns labelled ‘Bird’ through ‘Unknown’ are based on the total number of cases in the row labelled ‘Total’

†Includes disinfectants, hygiene and protection agents
‡Includes adhesives, bonding agents, sealants
§Includes desiccants/oxygen absorbers, foreign objects, hot/cold packs, packaging material, toys
$Includes waste and other residues, weapons and pyrotechnical agents
NAD/NR, not able to be determined/not recorded
Contact with a PC was indicated in the case notes for 12 incidents; six of these were identical to exposures reported by the PCs. Outcome at the time of discharge for non-fatal cat and dog cases with symptoms (n=95) was recovered for 69 cases (72.6 per cent), still open for 15 cases (15.8 per cent) and unknown/not able to be determined for 11 cases (11.6 per cent). All non-fatal horse cases were recovered at the time of discharge.

Federal Office of Consumer Protection and Safety (BVL)
From 2012 to 2015 there were 150 incidents involving off-label use of VMPs in 191 cats and dogs reported to the BVL. Cats comprised 69.6 per cent (n=133) and dogs 30.4 per cent (n=58) of cases. The majority of dogs were purebred (n=46, 79.3 per cent); the majority of cats were non-purebred (n=65, 48.9). Age and sex information is reported in Table 1.

Acute exposures were the most common (n=188, 98.4 per cent); the main routes of exposure were dermal (n=100, 52.4 per cent), followed by oral (n=82, 42.9 per cent). The majority of cat (n=132, 99.2 per cent) and dog cases (n=42, 72.4 per cent) involved antiparasitics and the majority of cases were severe/fatal (n=100, 52.4 per cent) (Fig 5). Administration of canine spot-on ectoparasiticide products containing permethrin (n=92, 69.7 per cent) and overdosing of oral antiparasitics (n=18, 13.6 per cent) were the top two reasons for all reported cat cases. They were also the top two reasons for severe/fatal cases in cats, involving 77.6 per cent (n=59) and 7.9 per cent (n=6, all kittens) of severe/fatal cases, respectively. Accidental consumption of VMPs (n=25, 43.1 per cent) and use of oral antiparasitics contraindicated in breeds at risk for a mutation in the multidrug resistance gene (MDR1) (n=14, 24.1 per cent) were the top two reasons for reported dog cases; exposure to antiparasitics was the top cause of severe/fatal cases in dogs (n=18, 75 per cent). Seven (38.9 per cent) of these cases involved application of spot-on preparations orally, five (22.2 per cent) accidental consumption of various preparations (n=2, collars; n=2, pour-on for ruminants; n=1, injectable) and two (8.3 per cent) overdose of oral antiparasitics.

Contact with a PC was indicated in the case notes for five incidents; three of these were identical to reported exposures by the PCs. Outcome was recovered for 157 (71.7 per cent) cases, still open for 3 (1.6 per cent) cases and unknown for 51 (26.7 per cent) cases.

Institute of Pharmacology, Toxicology, and Pharmacy, Ludwig-Maximilians-University
From 2012 to 2014, there were 393 samples from cats, dogs and farm animals in Germany submitted to the IFTP, LMU. The greatest number of submissions occurred in May (n=45); most submissions were from Bavaria (n=234, 50.5 per cent), where the laboratory is located, 42 (10.7 per cent) were from Lower Saxony, 33 (8.4 per cent) Rhineland Palatinate and 84 (21.4 per cent) from other German federal states. Of the species considered in the analysis, the majority of samples were from dogs (n=237, 60.3 per cent), followed by horses (n=57, 14.5 per cent), cats (n=48, 12.2 per cent) and ruminants (n=43, 10.9 per cent).

A total of 150 (38.2 per cent) submissions involving 166 substances tested positive; of these, 33.7 per cent were anticoagulants, 20.5 per cent organophosphates, 18.1 per cent metaldehyde, 11.4 per cent carbamates, 4.8 per cent alkaloids and 11.4 per cent other substances (Table 5). For all species, anticoagulants were the most frequently detected substance class; of these first-generation anticoagulants coumatetralyl and warfarin were the most common (n=38, 67.9 per cent) (Fig 6).

Organophosphates included parathion (n=15), paraoxon (n=14), diazinon (n=2), sulfotep (n=2) and triphenylphosphate (n=1, possible contaminant/secondary finding); carbamates included carbofuran (n=15), promecarb (n=5) and methiocarb (n=1); alkaloids included colchicine (n=5, all involving horses),
strychnine (n=2) and brucine (n=1). Other substances included the pyrethroids bifenthrin, cypermethrin (both n=1), cyanide (n=2), 4-hydroxybenzonitrile, paracetamol, azobenzene, benzenesulfonamide, benzofuran, bromethaline, caffeine, crimidine, lindane, phenanthrene, pyrogallol, tetrahydrocannabinol and xylitol (all n=1).

**Discussion**

Based on the collected data, dogs and cats were the most common species involved in poisoning incidents; poisonings involving food-producing animals, small mammals (eg, rabbits, rodents) and exotics (eg, birds, reptiles) were not frequently reported. Variation in the top common exposures was seen among the different species and data sources. However, medicinal products (both HMPs and VMPs), pesticides and plants were consistently implicated as top causes of poisoning (Table 6). These findings are similar to reports from other European countries as well as the USA (Berny and others 2010, Buttke and others 2012, Guitart and others 2010, Vandenburgroucke and others 2010, Gwaltney-Brant 2012, Caloni and others 2012a).

For the PCs and clinics, the majority of exposures were acute, accidental and involved the oral route (Table 6). This also fits with data reported from other countries (Berny and others 2010, Gwaltney-Brant 2012). For reported incidents to the BVL involving off-label use of VMPs, the majority of exposures were acute, involved incorrect use of VMPs and were dermal (Table 6). Although there was a wide range of ages of animals involved in poisonings, the median age ranged from 1.5 to 3 years for all
species and from 1.5 to 2.8 years for cats and dogs, indicating, as other studies have, that there may be an increased risk of toxic exposures in younger animals, in particular, in cats and dogs (Berny and others 2010, Buttke and others 2012, Gwaltney-Brant 2012).

HMPs and VMPs were frequently implicated in poisoning cases in cats and dogs and have also been cited as a main cause of poisonings in small animals (Caloni and others 2014, Cortinovis and others 2015, Schediwy and others 2015). NSAIDs and hormonal contraceptives for systemic use drugs the most common HMPs involved in the small animal clinic cases. For VMPs, antiparasitics were responsible for the vast majority of exposures. These findings fit with reports in the literature (Caloni and others 2014, Cortinovis and others 2015, Schediwy and others 2015), with the exception that hormonal contraceptives have not been widely reported as a top cause of exposures involving HMPs. Additionally, care should be taken when comparing results as the categorisation and classification of medicinal products may differ across studies.

Rodenticides, in particular, anticoagulant rodenticides, were responsible for the majority of pest exposures; anticoagulants were the most commonly detected substance class by the laboratory. Although anticoagulant rodenticides have been widely reported as a frequent cause of poisoning in animals (Caloni and others 2012a, Allkämper and others 2015, Caloni and others 2016), this finding contrasts with recent studies that reported insecticides as the most common pesticide involved in animal poisonings (Wang and others 2007, Vandenbroucke and others 2010, Allkämper and others 2015, Caloni and others 2016). Additionally, the finding that first-generation anticoagulants were most commonly detected by the laboratory differs with results from the PCs as well as recent reports in the literature, which implicate second-generation anticoagulant rodenticides as being responsible for the majority of cases involving anticoagulants (Wang and others 2007, Vandenbroucke and others 2010, Caloni and others 2016).

After rodenticides, insecticides and molluscicides were the next most common class of pesticides. Pyrethroids/pyrethrins were the most frequent insecticide subcategory involved in PC inquiries but were detected in only 2 out of the 150 laboratory submissions. Metaldehyde was the most common molluscicide reported to the PCs and detected by the laboratory. Organophosphates were the second most common subcategory of insecticide involved in PC inquiries and were, followed by carbamates, the most common insecticide detected by the laboratory (Table 5). Although it has been banned in the EU, the carbamate carbofuran was detected in 15 laboratory samples. Other studies on animal poisonings have also reported detection of banned pesticides (Caloni and others 2016).

Plants were responsible for the majority of reported exposures in equines, ruminants and rabbits/rodents. They were also the top cause of PC exposure inquiries involving cats and the third cause of inquiries involving dogs. Apart from Hedera species, the top five plant exposure inquiries to the PCs (Prunus species, T. baccata, Euphorbia species, Rhododendron species) have also been described in recent publications detailing plant poisonings in domestic animals in Europe and Italy (Caloni and others 2013, Cortinovis and Caloni 2013). Atypical myopathy due to suspected exposure to Acer species was an important finding regarding plant poisonings in horses. Also, 7 out of 12 cases presenting to the equine clinics involved suspected atypical myopathy; six out of the seven cases were fatal. Over the past decade, occurrence of atypical myopathy in Europe has been gaining attention due to repeated occurrences of equine cases, the majority of which are fatal (Norton 2016).

Although it was not among the top three causative agent categories for the PCs, food, in particular chocolate, was a

<p>| TABLE 5: Substances (N, %) detected in submissions involving cats, dogs, equines and farm animals to the Institute of Pharmacology and Toxicology, Faculty of Veterinary Medicine, Munich, Germany, 2012–2014 |
|-----------------------------------------------|--------|--------|--------|--------|--------|</p>
<table>
<thead>
<tr>
<th>Substance</th>
<th>Cat</th>
<th>Dog</th>
<th>Equine</th>
<th>Poultry</th>
<th>Ruminant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alkaloids</td>
<td>1 (7.1)</td>
<td>2 (1.7)</td>
<td>5 (20.0)</td>
<td>1 (50.0)</td>
<td>1 (28.6)</td>
</tr>
<tr>
<td>Anticoagulants</td>
<td>4 (28.6)</td>
<td>37 (31.4)</td>
<td>12 (48.0)</td>
<td>2 (8.0)</td>
<td>1 (50.0)</td>
</tr>
<tr>
<td>Carbamates</td>
<td>4 (28.6)</td>
<td>12 (10.2)</td>
<td>2 (8.0)</td>
<td>1 (50.0)</td>
<td>19 (11.5)</td>
</tr>
<tr>
<td>Metaldehyde</td>
<td>2 (14.3)</td>
<td>27 (22.9)</td>
<td>4 (16.0)</td>
<td>1 (4.8)</td>
<td>30 (18.1)</td>
</tr>
<tr>
<td>Organophosphates</td>
<td>2 (14.3)</td>
<td>26 (22.0)</td>
<td>11 (44.0)</td>
<td>2 (8.0)</td>
<td>2 (28.6)</td>
</tr>
<tr>
<td>Other</td>
<td>1 (7.1)</td>
<td>14 (11.9)</td>
<td>2 (8.0)</td>
<td>2 (28.6)</td>
<td>19 (11.4)</td>
</tr>
<tr>
<td>Total</td>
<td>14 (8.4)</td>
<td>118 (71.1)</td>
<td>25 (15.1)</td>
<td>2 (12)</td>
<td>7 (4.2)</td>
</tr>
</tbody>
</table>

Submissions, n=150; substances, n=166
frequent cause of exposure inquiries to the PCs involving dogs and the top cause of dog cases presenting to the small animal clinic. The second most common food inquiry at the PCs and small animal clinic involved grape/raisin exposure in dogs. Both chocolate and grapes/raisins are well-known causes of poisonings involving food in dogs; chocolate has consistently been reported as a top cause of poisoning in dogs in both Europe and the USA (Caloni and others 2012a, Gwaltney-Brant 2012, Schedewy and others 2015, Votion 2015).

Agents consistently implicated in severe exposures included canine spot-on preparations containing permethrin in cats, anticoagulant rodenticides in dogs and sycamore (Acer species) in horses. These have also been extensively reported in the literature (Berny and others 2010, Caloni and others 2012a, Allkämper and others 2015, Schedewy and others 2015, Votion 2016). Seasonal peaks were seen with certain exposures such as chocolate around Valentine’s Day and the Easter and winter holidays, insecticides and herbicides in the spring months, rodenticides in the fall months, and cyanobacteria and mushrooms in the late summer and fall months. This has also been reported in other studies (Gwaltney-Brant 2012).

From this study, variation was seen with regard to the most commonly affected species, the most common causative agents for each species, as well as patterns of case severity. Therefore, when evaluating animal poisoning data, it is essential to consider the strengths, weaknesses and biases associated with available information.

Poison centres

The majority of exposure data from this study came from German PCs. PCs are also a primary source of data for published information on animal poisoning in other countries, which illustrates their importance in providing information on poisoning as well as potential for identifying poisoning trends and risks. However, as studies on the incidence of human poisonings have indicated that PC data underestimates the possible true incidence of poisoning by at least one-half (Wolkin and others 2012), it should be kept in mind that PC data also likely underestimate the true incidence of animal poisonings. Certain poisonings as well as species (companion animals vs food-producing animals) may be over or under-represented, reported cases may be more likely to involve acute than chronic exposures, and fatal cases are typically under-reported (Blanc and others 1995, Wolkin and others 2012). It is also possible that cases advised by PCs are more likely to involve exposures which are unfamiliar than those that are well-known, especially with regard to veterinary personnel calling for case management advice.

The primary focus of the PCs in Germany is to provide advice for medical treatment of human toxic exposures. Inquiries are handled by trained physicians, nurses, toxicologists and pharmacists; none of the staff has veterinary-specific training. No financial support is provided for the documentation and advising of animal poisoning cases; as a result, the German PCs have limited time and resources to invest in the recording, assessment, and quality control of animal exposure inquiries.

Although several German PCs use the same documentation system and method for recording information on animal exposures, there is currently no standard method or computer system used by all PCs. This also applies to some PCs in other countries and presents a challenge when evaluating as well as comparing poisoning data from different centres. Further to this, a substantial percentage of cases handled by PCs have no follow-up, which precludes complete assessment of cases and outcomes (Buttke and others 2012, Caloni and others 2012a, Caloni and others 2012b, Wolkin and others 2012). For the PCs participating in this study, there was variation in the percentage of cases (from 0.8 per cent to 50 per cent) with follow-up information.

Veterinary clinics

Veterinary centres have the potential to provide important information on animal poisonings. A major advantage is that detailed case information (including outcome) is likely to be available, allowing for a more thorough assessment of cases. However, as data typically exist as separate records, it can be difficult and time-consuming to collate. In addition, differences in documentation practices, investigative and treatment protocols, as well as coding of cases among centres can limit comparison of cases (Bartlett and others 2010).

For this study, data on poisonings were collected from clinics at a veterinary teaching hospital. The majority of cat and dog cases presented during emergency hours and over half (56 per cent) of the equine cases involved atypical myopathy, a
debilitating and often fatal condition associated with exposure to sycamore (Acer species). As veterinary teaching and specialist hospitals tend to treat more complicated cases and provide emergency services, cases may not be representative, causing referral bias. Other possible limitations of data from clinics include the geographical proximity of owners to clinics and cost of treatment, both of which may influence presentation of animals for veterinary attention (Thrusfield 2007).

Reporting of adverse events to veterinary medicines

As veterinary medicines have been cited as an important cause of poisonings in animals, reports of incidents due to off-label use of veterinary medicines in cats and dogs were collected for this study. The finding that antiparasitics were responsible for a large percentage of adverse events fits with reports in the literature as well as from the PCs and clinics participating in the study (Caloni and others 2012a, b, 2014, Curti and others 2009). However, caution should be used when interpreting the results as there is significant under-reporting of adverse events to veterinary medicines. For example, a recent study in the UK estimated that per year only one adverse event is reported by one in every ten veterinarians. Studies on adverse events in human beings have estimated that over 90 per cent of all adverse events involving medicines are not reported (Hazell and Shakir 2006, O’Neill and others 2014). Further to this, the 2015 veterinary pharmacovigilance report by the European Medicines Agency states that under-reporting in food-producing animals is a major concern and that 90 per cent of adverse events reported are for companion animals (EMA 2016). In addition, data can be misleading, particularly with regard to severe cases, which are more likely to be reported than mild cases (Hazell and Shakir 2006, Thrusfield 2007). This could explain the study finding that the majority (52.4 per cent) of reported adverse events were severe/fatal.

Laboratories

Information from laboratories is useful as it allows for evaluation of cases with confirmed exposures. However, samples from suspected poisonings cases are not commonly submitted to laboratories for toxicological testing; therefore, reported cases are likely to grossly underestimate the true incidence of poisoning. Laboratories also have different protocols, equipment, as well as diagnostic capabilities, which can limit the number of agents able to be tested for as well as comparison of results between laboratories.

Samples submitted to laboratories are also more likely to involve severe cases (Allkämper and others 2015); as a result, certain poisonings are likely to be under-represented or over-represented. In this study, agents used in pesticides were responsible for the majority of positive submissions; this has also been reported in other studies (Berny and others 2010, Guitart and others 2010, Vandenbroucke and others 2010).

This study involved certain limitations. For the PC data, exposures may not be representative of all animal exposures within Germany as many owners may not be aware that the German PCs take animal calls. Additionally, caller location, the number of animals involved per inquiry, as well as whether separate inquiries involved the same animal/incident could not be assessed. As a result, it is possible that some calls were from outside of Germany, involved multiple animals and/or that inquiries counted as separate involved the same incident. This is however likely to involve only a small percentage of the cases. Care should also be taken when interpreting case severity as likeliness of exposure and causality were not taken into account and the PC staff that assessed case severity have no veterinary-specific training. Additionally, the PC case severity data reported was based on what was recorded at the time of inquiry and no further probing of severity scores was carried out.

Results from the clinics and laboratory participating in this study should not be assumed to represent the situation for all clinics and laboratories throughout different regions of Germany. Due to the fact that cases were retrospectively collected from participating clinics, all poisoning cases may not have been captured. There was also overlap for a small number of cases, with six from the clinics and three involving reported adverse events being matched with cases handled by the PCs. Lastly, for all data sources, case severity assessment results should be interpreted with caution as the scale used (PSS) is not veterinary specific.

Conclusion

Data from this first systematic account of animal poisonings in Germany from multiple data sources indicate that dogs and cats, followed by horses, are the species most frequently involved in reported toxic exposures. Poisonings in food-producing animals and exotics were rarely reported. The main causative agents varied by species as well as data source; however, medicinal products, pesticides and plants were top causes of poisoning. For severe cases, canine spot-on preparations containing permethrin in cats, anticoagulant rodenticides in dogs and sycamore (Acer species) in horses played an important role. These findings largely reflect reports from other European countries (Berny and others 2010, Guitart and others 2010, Caloni and others 2012a). However, due to a lack of standardised protocols and definitions for the documentation and assessment of poisoning cases, care should be taken when comparing results to other countries.

Of the data sources in this study, PCs provided the most information in terms of numbers of exposures. They also were a major source of information on animal poisonings from other countries (Berny and others 2010, Vandenbrouck and others 2010, Caloni and others 2012a, b, Schiedwy and others 2015). Cases from the veterinary centres and reports of adverse events involving veterinary medicines, although less in number, provided valuable clinical information and allowed for thorough assessment of symptoms, case severity, as well as outcomes. Laboratory results allowed for insight into confirmed poisoning cases and were particularly useful with regard to pesticide exposures. As each data source provides biased information, collation and assessment of poisoning data from multiple sources has the potential to provide a more comprehensive overview of animal poisonings. Approaches within Germany as well as other countries to systematically collect and integrate poisoning data in a standardised format from multiple sources, for example, by the establishment of sentinel laboratories, clinics and PCs, could greatly facilitate the identification of poisonings trends and risks as well as the evaluation, management and treatment of poisonings.

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