

Annex 2 - EU Poison Centre data – ECHA Analysis

1. Background

ECHA launched a consultation of EU Poison Centres using the EU Survey tool from February 2022 to April 2022 to collect information on anticoagulant rodenticides primary and secondary poisoning data and reports on accidental poisoning.

A total of 79 contact points were invited to contribute to the EU Survey and 19 contributions were received from the following 16 MSs: PT, IT, HR, FR, SE, IE, FI, NL, DE, NO, EE, ES, HU, BE, MT, LT.

The anticoagulant rodenticides in scope of the EU Survey are depicted in Table 1.

Table 1: Active substances in the scope of this request

Active substance	EC No.	CAS No.
Brodifacoum	259-980-5	56073-10-0
Bromadiolone	249-205-9	28772-56-7
Bromadiolone Difenacoum	-	-
Chlorophacinone	223-003-0	3691-35-8
Coumatetralyl	227-424-0	5836-29-3
Difenacoum	259-978-4	56073-07-5
Difethialone	600-594-7	104653-34-1
Flocoumafen	421-960-0	90035-08-8
Warfarin	201-377-6	81-81-2

2. Approach for the analysis

The input provided by the EU Poison Centres can be found in the following Annexes:

- The questions and answers received in Annex 1.
- An Excel overview of the input provided in Annex 2.
- The individual input and attachments provided by each Poison centre in Annex 3.

Several Member States answered that they are collecting primary and secondary poisoning data and/or preparing reports (e.g. annual reports) on accidental poisonings involving any of the anticoagulant rodenticides active substances in scope of the request.

The availability of data and reporting formats varied significantly between the EU Poison Centres. For example:

- Some Poison Centres provided data on anticoagulant rodenticides as a group, while others could also provide data on individual substances;
- Some data sets included substances not in scope of the request;
- Some Poison Centres differentiated intentional from unintentional/accidental poisonings, while this differentiation was not available for the data from other Poison Centres;
- Information on potential co-exposures was sometimes available, while this information was missing in other data sets;
- The case numbers (or calls) were sometimes provided per year, while other Poison Centres provided numbers on a period basis (covering multiple years);

- Some Poison Centres explained that they register calls, which are not per se linked to real poisoning cases;
- The Dutch poison centre clarified that in the Netherlands the Poisons Center is only available for medical professionals and not for the general public;
- The reporting format (e.g. intentional vs. unintentional; mono-intoxication vs. multi-intoxications) was not always detailed/specific enough;
- The reporting schemes and criteria applied to confirm a poisoning case, and/or to assess the severity of the symptoms observed or outcome, were not always provided or sufficiently detailed;
- Limited information was available regarding the dose intake for the reported poisoning cases;
- Most of the Poison Centres informed that the poisoning cases were not confirmed to be due to a specific anticoagulant rodenticide active substance since the substance was not analysed.

These limitations make the analysis and comparison of the poisoning cases between MSs challenging. Caution should therefore be applied when interpreting the data and drawing conclusions.

Whenever possible, ECHA has attempted to organize the data provided by the Poison Centres in a standardized way, in order to facilitate the comparison between MSs and to identify trends (e.g. by reporting the data in standardized tables). Human and animal poison cases were analysed separately.

In order to answer the question (f) from the mandate, ECHA focused its analysis on:

- data on the individual anticoagulant rodenticide substances in scope;
- unintentional/accidental cases;
- mono-intoxication cases with one anticoagulant rodenticide substance (by avoiding multiple-intoxications/co-exposures) when this information is available.

Information on the number of authorized biocidal products (BPs) containing a specific anticoagulant rodenticide substance in a specific Member State (MS) for the concerned period (for which the poisoning cases were reported) was extracted to put the number of poisoning cases in perspective, although acknowledging that this does not give information about sales volumes (or amounts of BPs used). This information was extracted from ECHA's dissemination website in June 2022 (See Annex 4).

3. Human poisoning cases

Number of cases

An overview of the number of human poisoning cases reported in the EU Survey is provided in the Table 15 to 16 below per MS.

Most of the human anticoagulant rodenticide poisonings occur without being able to identify the active substance. When the identity of the substance was known, most of the human poisoning cases reported related to SGAR substances. Poisoning cases were rarely reported with FGAR substances.

The anticoagulant rodenticide substances involved in most human poisoning cases per MS are highlighted in orange. Some variations were seen between MSs but **bromadiolone** and **difenacoum** were most often reported, followed by **brodifacoum** and **difethialone**.

The number of authorized BPs containing a specific active substance in a MS for the concerned period were included in the Tables (highest numbers are highlighted in green).

With some exceptions, the highest number of poisoning cases is usually correlated to anticoagulant rodenticide substances having the highest number of BPs authorized during the reporting period in that specific MS.

It therefore seems that the number of poisoning cases are linked to the availability of BPs containing a specific anticoagulant rodenticide substance on that market.

Table 2. France (intentional and unintentional cases; monoagent and “monoagent like”^{*} - polyagents cases excluded)

FRANCE Year	Total (2012 – 2021)	Number of authorized BPs (2012-2021)
Total	5622	
<i>First generation</i>		
Chlorophacinone	365	
Coumatetralyl	89	4
Warfarin	191	
<i>Second generation</i>		
Brodifacoum	789	55
Bromadiolone	1115	35
Bromadiolone Difenacoum	46	3
Difenacoum	2210	47
Difethialone	814	3
Flocoumafen	3	1

* FR: “monoagent like” exposure (=polyagent but with only one specific active substance).

Monoagent: intoxication cases with only one “agent” (i.e. one anticoagulant rodenticide substance);

Polyagent: intoxication case involving several agents (anticoagulant rodenticides or other types of product),

Table 3. Ireland (accidental, other and unknown cases – intentional cases excluded)

IRELAND Year	2017	2018	2019	2020	2021	Total (2017-2021)	Number of authorized BPs (2017-2021)
Total	48	34	54	27	34	197	
First generation							
Chlorophacinone							
Coumatetralyl	3	5	5	1	2	16	
Warfarin							1
Second generation							
Brodifacoum	1	3	2	6	8	20	47
Bromadiolone	11		14	3	1	29	27
Bromadiolone Difenacoum							1
Difenacoum	8	5	4	3	3	23	26
Difethialone							4
Flocoumafen	3	1	2		5	11	10
Unknown							
	22	20	27	14	15	98	
	46%	59%	50%	52%	44%	50%	

Numbers in table focus on AVK substances in scope and “unknowns” – “Anticoagulant Rodenticide Other” were excluded.

Table 4. The Netherlands (mono-intoxications with substances in scope; unintentional and not recorded cases – intentional case and multi-intoxications excluded)

THE NETHERLANDS Year	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	Total	Number of authorized BPs (2012- 2021)
Total (AVKs)	111	74	80	76	73	72	82	63	64	44	739	
First generation												
Chlorophacinone	2		1							1	4	1
Coumatetralyl							2				2	1
Warfarin												
Second generation												
Brodifacoum	3	4	1		1	2	9	12	14	12	58	23
Bromadiolone	11	9	13	12	13	3	3	2		2	68	12
Bromadiolone Difenacoum				1	1	3	12	8	11	5	41	
Difenacoum	39	26	27	26	23	30	32	19	11	8	241	29
Difethialone	56	35	37	37	34	34	23	21	27	16	320	4
Flocoumafen			1		1		1	1	1		5	6
Unknown												
	31	40	26	32	27	13	17	7	8	14	215	
	28%	54%	33%	42%	37%	18%	20%	11%	13%	32%	29%	

The NL Poison centre informed that “In the Dutch data ‘unknown’ is the category ‘other long-acting coumarine derivatives’.

Table 5. Estonia (accidental cases – intentional cases excluded)

ESTONIA Year	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	Total	Number of authorized BPs (2012- 2021)
Total	7	16	23	17	20	23	9	15	14	12	3	159	
First generation													
Chlorophacinone													
Coumatetralyl													
Warfarin													
Second generation													
Brodifacoum				2	1			3				6	15
Bromadiolone	3	5	2	6	3	8	1	5	2	1		36	18
Bromadiolone Difenacoum													1
Difenacoum				2								2	3
Difethialone													1
Flocoumafen													1
Unknown													
	4	11	21	7	16	15	8	7	12	11	3	115	
	57%	69%	91%	41%	80%	65%	89%	47%	86%	92%	100%	72%	

Table 6. Hungary (unintentional cases and others with rodenticides – suicidal and abusives cases excluded, co-exposures (e.g. with alcohol) excluded)

HUNGARY Year	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	Total	Number of authorized BPs (2012- 2021)
Total	64	50	66	39	47	50	46	40	25	23	450	
First generation												
Chlorophacinone			1								1	
Coumatetralyl												1
Warfarin		1	5	4		1	1				12	
Second generation												
Brodifacoum			1	1		1	1		4	1	9	56
Bromadiolone	15	8	10	13	9	10	11	8	1	6	91	49
Bromadiolone Difenacoum							1				1	2
Difenacoum					1						1	18
Difethialone												1
Flocoumafen	1										1	2
Unknown												
	48	41	49	21	37	38	32	32	20	16	334	
	75%	82%	74%	54%	79%	76%	70%	80%	80%	70%	74%	

Table 7. Belgium (anticoagulant rodenticides, mono-substance cases with the exception of “bromadiolone/difenacoum”)

BELGIUM Year	Total cases (2020)	Number of authorized BPs (2020)
Total	129	
First generation		
Chlorophacinone		
Coumatetralyl	2	3
Warfarin		
Second generation		
Brodifacoum	28	35
Bromadiolone	8	23
Bromadiolone Difenacoum	2	1
Difenacoum	54	34
Difethialone	19	13
Flocoumafen	3	2
Unknown		
	13	
	10%	

Note: From the BE reporting, it is understood that “rodenticides NOS” refers to rodenticide substances which were not identified; “Rodenticides – anticoagulant” to anticoagulant rodenticides which were not identified.

Table 8. Portugal (accidental AVK cases – Both human and animal cases)

PORTUGAL Year	2017	2018	2019	2020	2021	Total cases (2017-2021)	Number of authorized BPs (2017-2021)
Total cases	175	162	145	196	121	799	
Human cases	58	64	51	123	58	354	
Animal cases	115	98	91	73	63	440	
Unknown	2		3			5	
First generation							
Chlorophacinone							
Coumatetralyl	18	5	4		1	28	3
Warfarin							
Second generation							
Brodifacoum	22	13	11	8	3	57	65
Bromadiolone	64	76	63	85	52	340	54
Bromadiolone Difenacoum							
Difenacoum	11	5	1	9	13	39	35
Difethialone	2		2		5	9	9
Flocoumafen	3	4	2			9	1
Unknown							
	55	59	62	94	47	317	
	31%	36%	43%	48%	39%	40%	

Note: From the reporting from PT, no differentiation can be made between human vs. animal poisoning cases.

Table 9. Italy (all cases)

ITALY Year	Total cases (2000 – 2022)	Number of authorized BPs (2000-2022)
Total	220*	
First generation		
Chlorophacinone		4
Coumatetralyl	1	5
Warfarin		
Second generation		
Brodifacoum	27	131
Bromadiolone	31	126
Bromadiolone Difenacoum		6
Difenacoum	16	77
Difethialone	1	8
Flocoumafen		3
Unknown		
	144	
	65%	

*Number calculated based on AVKs in scope.

Table 10. Croatia (accidental cases and other reasons – attempted suicides excluded)

CROATIA Year	2017	2018	2019	2020	2021	Total cases (2017-2021)	Number of authorized BPs (2017-2021)
Total	25	15	16	12	16	84	
First generation							
Chlorophacinone		1				1	
Coumatetralyl							1
Warfarin							
Second generation							
Brodifacoum		1				1	36
Bromadiolone	2	1	3	2	2	10	46
Bromadiolone Difenacoum							2
Difenacoum							13
Difethialone							
Flocoumafen							2
Unknown							
	23	12	13	10	14	72	
	92%	80%	81%	83%	88%	86%	

Table 11. Finland

FINLAND Year	2016	2017	2018	2019	2020	Total (2016-2020)	Number of authorized BPs (2016-2020)
Total	66	66	52	55	37	276	
First generation							
Chlorophacinone							
Coumatetralyl	3	1	1			5	2
Warfarin							
Second generation							
Brodifacoum	1					1	2
Bromadiolone	11	7	8	3	2	31	1
Bromadiolone Difenacoum							
Difenacoum	17	19	12	9	9	66	3
Difethialone				1	2	3	4
Flocoumafen							1
Unknown							
	34	39	31	42	24	170	
	53%	59%	59%	76%	65%	62%	

Route of exposure

Based on the information received in the survey, the most common route of exposure is the oral/ingestion route (for both intentional and unintentional cases). Occasionally, the dermal and inhalation exposure routes were mentioned. Other routes (e.g. ocular, subcutaneous, intramuscular, nasal) were rarely reported.

For example, in France (years 2012-2021), 74% of the reported unintentional cases occurred by the oral route. In Finland (years 2016-2020), 63% of all the cases are linked to the oral route of exposure, followed by 10% via the dermal route.

Based on available data, there were no differences seen in the route of exposure between AVK substances, or between FGARs vs. SGARs.

Intentional vs. unintentional

Most of the human poisoning cases were reported as unintentional/accidents.

For example:

- In France (years 2012-2021), 79.2% of the poisoning cases with AVK substances were unintentional;
- In Croatia (years 2017-2021), 81% of the calls were linked to accidental ingestions;
- In Italy (years 2000-2022), 82.3% of the cases were unintentional;
- In Sweden (years 2012-2021), 92% of the calls relate to unintentional cases;
- In Finland (years 2016-2020), 90% of the calls relate to unintentional cases.

Based on the available data, no differences were seen between AVK substances, or between FGARs vs. SGARs.

Gender

For symptomatic unintentional cases, the gender distribution was rather equal. More variability was seen with the symptomatic intentional cases.

For example, in France (years 2012-2021), 50% of the unintentional cases occurred in males vs. 43% in females and 6% were unknown. When sufficient poisoning cases were available, the sex ratio was stable (around 1) for the symptomatic unintentional cases. No obvious differences in the sex ratio was seen between anticoagulant rodenticide substances.

Age groups

Most of the unintentional human poisoning cases occurred in a younger human population/children (age group <5 years).

Most of the intentional cases occurred in the adult population (e.g. age groups 40-60 years).

For example, in France (years 2012-2021), the majority of unintentional cases occurs in small children, age class [0-4.9 years], representing 57% of the unintentional cases. However, FR also informed that they are rarely symptomatic (6%) and that this is typical of poison control centres data, reflecting calls from worried parents after child exposure.

The majority (35%) of the unintentional symptomatic cases in the FR reporting is still in the [0-4.9 years] age group, followed by the [40-59.9 years] age group accounting for 24% of the cases. No clear differences in the impacted age groups between anticoagulant rodenticide substances could be seen.

Place of poisoning

The most common place of poisoning is at home (for both intentional and unintentional cases).

In France (years 2012-2022), 90% of the unintentional cases happened at home, followed by 3.5% at school.

No differentiation could be made between AVK substances, or between FGARs vs. SGARs, regarding the place of poisoning.

Symptomatic/asymptomatic

For most of the human poisonings, the cases were reported as asymptomatic.

It should however be noted that this may depend on the active substance but also on the dose taken, for which little information was available.

In France (years 2012-2021), 15.6% of all anticoagulant rodenticide poisoning cases were symptomatic. The proportion of symptomatic cases (36.2%) is higher in the intentional cases compared to the unintentional cases (11.9%). The oral route is the most frequent exposure route both for asymptomatic (77%) and symptomatic (50%) cases for unintentional cases.

In Italy (years 2000-2022), 95.4% of the victims remained asymptomatic.

In Croatia (years 2017-2021), 88% of the callers (accidental ingestions, attempted suicides and other reasons) and 81% of the callers (accidental ingestions only) were asymptomatic at the time of the call.

Severity and type of symptoms

An overview of the severity grades of the human poisoning cases reported per anticoagulant rodenticide substance is provided in the Table 12 to Table 17 below, per MS. The anticoagulant rodenticide substances and cases where the symptoms were categorized as most severe are highlighted in orange. The severity grades mostly reported are highlighted in green.

The symptoms for the symptomatic unintentional cases were mainly of minor severity. The symptoms for the symptomatic intentional cases, were also mainly of minor severity with some being moderate, severe and sometimes fatal. Whenever the information is available, the focus of the analysis was made on the severity/symptoms of the unintentional poisoning cases.

In France (years 2012-2021), the severity grade (based on the Poisoning Severity Score¹) was unknown for 27% of the unintentional symptomatic cases involving a monoagent. The majority (69%) of the cases were of "minor" (grade 1) severity, while 4% of the cases were of "moderate" severity (grade 2). One "severe" case (grade 3) was reported for **difethialone**.

Interestingly, the French input also referred to the fact that the anticoagulant rodenticides leading to the highest number of poisoning cases are not the anticoagulant rodenticide substances leading to the highest rate of symptomatic cases:

"Considering only monoagent and "monoagent like" cases, the top 3 active substances by number of cases in France are: difenacoum (n=2210), bromadiolone (n=1115) and difethialone (n=814).

Nevertheless, they are not the ones who have the highest rate of symptomatic cases. The active substances with the highest rate of symptomatic cases are warfarin (21.5%), chlorophacinone (16.4%) and coumatetralyl (13.5%) which are first generation anticoagulants."

This may indicate that the FGARs could give more symptoms than SGARs. A slightly higher proportion (see % in table) of "moderate" grade intoxications were reported with FGARs in comparison to SGARs. However, the only "severe" case was reported with a SGAR (i.e. **difethialone**).

¹ https://cdn.who.int/media/docs/default-source/chemical-safety/intox/pss95699a36-61ab-4be6-848f-c1d894d21fbd.pdf?sfvrsn=5750967e_10&download=true

Table 12. France (symptomatic, unintentional cases; monoagent and “monoagent like”^{*} - polyagents cases excluded)

FRANCE Severity	Severe (grade 3)	Moderate (grade 2)	Minor (grade 1)	Unknown	Total
	1	21	359	140	521
	0.2%	4%	69%	27%	
First generation					
Chlorophacinone		3 (8%)	26 (70%)	8 (22%)	37
Coumatetralyl		1 (9%)	8 (73%)	2 (18%)	11
Warfarin		2 (6%)	21 (68%)	8 (26%)	31
Second generation					
Brodifacoum		3 (4%)	45 (62%)	25 (34%)	73
Bromadiolone		1 (1%)	69 (66%)	34 (33%)	104
Bromadiolone Difenacoum			3 (75%)	1 (25%)	4
Difenacoum		7 (4%)	136 (74%)	42 (23%)	185
Difethialone	1 (1%)	4 (5%)	51 (67%)	20 (26%)	76
Flocoumafen					

^{*} FR: “monoagent like” exposure (=polyagent but with only one specific active substance).

From the FR reporting, most of the symptoms were of minor severity. Examples of impacted systems and frequent symptoms of “minor” severity observed included:

- the hepato-digestive system (e.g. vomiting, abdominal pain, oropharyngeal pain, nausea, diarrhoea, buccal irritation, epigastric pain);
- local and cutaneous effects (e.g. erythema, skin break, local cutaneous edema, rash, localized skin pain, eye pain);
- the nervous system (e.g. headache, paraesthesia, drowsiness, dysgeusia);
- general signs (e.g. asthenia, anorexia, vertigo, short term hyperthermia);
- the respiratory system (e.g. coughing, unspecified respiratory gene, upper airways irritation);
- coagulation disturbances & bleedings (e.g. epistaxis, hematuria, hematoma).

Table 13 provides an overview of the “moderate” and “severe” symptoms reported by the FR Poison Centre for the unintentional cases per anticoagulant rodenticide substance. Coagulation disturbances and bleedings were most often reported. **Chlorophacinone** and **difenacoum** poisoning were reported with “severe” symptoms.

Based on the available data, no clear differentiation in severity of poisoning cases can be made between anticoagulant rodenticides, or between FGARs and SGARs.

Table 13. Poisoning data provided by France for FGARs and SGARs from 2012 to 2021 – Moderate and Severe symptoms (symptomatic, unintentional cases; monoagent and “monoagent like”*)

Systems/ symptoms	General signs	Hepato-digestive system	Local and cutaneous effects	Nervous system	Musculoskeletal system	Cardiovascular system	Coagulation disturbances & bleedings	Psyche disorders
First generation								
Chlorophacinone				Motor deficit (1)			Hemoptysis (1)	Hallucinations (1)
						Pulmonary embolism (1)	Disseminated intravascular coagulation (1)	
Coumatetralyl							Hematemesis (1)	
Warfarin			Erythema multiforme (1)					
Second generation								
Brodifacoum			Skin burn (1)	Balance disorder (1)	Localized muscle hypertonia (1)	Unspecified sinus tachycardia (1)	Hemorrhage (3) hemoptysis (1)	
Bromadiolone							Lower gastrointestinal bleeding (2) Hematemesis (1)	
Bromadiolone Difenacoum			Skin burn (1)					
Difenacoum	Impaired general condition (2)		Skin burn (3) Giant hives (2)	Brief loss of consciousness (2) Mental confusion (1)			Hemorrhage (3) Lower gastrointestinal bleeding (2) Hematemesis (1) Gross hematuria (1)	
						Chest pain at rest (1)		
Difethialone	Impaired general condition (2)	Prolonged diarrhoea (1) Prolonged vomiting (1)					Hematemesis (2) Lower gastrointestinal bleeding (1) Metrorrhagia (1)	

* FR: “monoagent like” exposure (=polyagent but with only one specific active substance). Polyagents cases excluded. **Moderate symptoms. Severe symptoms.** Number of occurrences are reported in “()”.

In Ireland, most of the accidental cases were asymptomatic or with symptoms of “minor” severity. Two cases of “moderate” severity were reported with **difenacoum**.

Table 14. Ireland – poisoning severity scores (accidental, other and unknown cases – intentional cases excluded)

IRELAND Severity	Severe	Moderate	Minor	None/N.A.	Total (2017-2021)
Total	1	2	22	185	210
	0.5%	1%	11%	88%	
First generation					
Chlorophacinone					
Coumatetralyl				16 (100%)	16
Warfarin					
Second generation					
Brodifacoum			1 (5%)	19 (95%)	20
Bromadiolone			2 (7%)	27 (93%)	29
Bromadiolone Difenacoum					
Difenacoum		2 (9%)	3 (13%)	18 (78%)	23
Difethialone					
Flocoumafen			3 (27%)	8 (73%)	11
Other AVK					
			1 (9%)	10 (91%)	11
Unknown					
	1 (1%)		12 (12%)	87 (87%)	100

N.A: Not applicable

The data from Hungary informs that the AVK substance identity is unknown for the majority of the unintentional poisoning cases. For most of the cases, “no symptoms” or “no data” were reported. A case of “moderate” severity was reported for **bromadiolone**. Cases with “mild” or “moderate” symptoms were only reported with SGARs and none with FGARs.

The data from Hungary also informs of the consequences of the poisoning which can give an indication of the severity of the poisoning:

- In 18 cases (4%), 3 involving **bromadiolone** and 15 unknown AVK, further medical care was required. From these cases, severity was described as “no data”, “asymptomatic”, “mild symptoms”, “moderate symptoms” and “severe symptoms”;
- 421 cases (92%) were marked as “recovered in a few days”;
- 19 cases (4%) were “left at his own risk”.

Based on this information, further medical care was required only in a minority of the poisoning cases.

Table 15. Hungary - Symptoms (unintentional and other cases – suicidal and abusive cases excluded)

HUNGARY Years 2012-2021	Fatal	Severe	Moderate	Mild	No symptoms	No data	TOTAL (2020)
Total	0	2	25	63	151	217	458
	0%	0.5%	5.5%	14%	33%	47%	
First generation							
Chlorophacinone						1 (100%)	1
Coumatetralyl							
Warfarin					2 (17%)	10 (83%)	12
Second generation							
Brodifacoum				1 (11%)	6 (67%)	2 (22%)	9
Bromadiolone			2 (2%)	14 (15%)	30 (33%)	45 (50%)	91
Bromadiolone Difenacoum					1 (100%)		1
Difenacoum					1 (100%)		1
Difethialone							
Flocoumafen						1 (100%)	1
Unknown							
		2	23	48	111	158	342
		100%	92%	76%	74%	73%	75%

Information provided by The Netherlands also indicate that for the majority of the cases for which the management advice is known was: "observation at home". Only in about 3% of the cases, was the management advice: "observation in hospital", indicating a potential serious exposure.

No clear differentiation of the management advice could be seen for the different anticoagulant rodenticides, neither between SGARs in comparison to FGARs. The number of poisoning cases with FGARs is very low making the interpretation of the data challenging.

Table 16. The Netherlands – Management advice/Severity (mono-intoxications with AVKs in scope; unintentional and not recorded cases – intentional case and multi-intoxications excluded)

The Netherlands Years 2016-2021	Observation in hospital	Assessment by physician	Observation at home	Not recorded	TOTAL
Total	10	57	331		398
	3%	14%	83%		
First generation					
Chlorophacinone		1 (100%)			1
Coumatetralyl	1 (50%)	1 (50%)			2
Warfarin					
Second generation					
Brodifacoum	2 (4%)	7 (14%)	41 (82%)		50
Bromadiolone		3 (13%)	20 (87%)		23
Bromadiolone Difenacoum	1 (2%)	7 (18%)	32 (80%)		40
Difenacoum	2 (2%)	11 (9%)	110 (89%)		123
Difethialone	4 (2%)	24 (16%)	127 (82%)		155
Flocoumafen		3 (75%)	1 (25%)		4

NL: An indication can also be derived from the 'Management advice' provided, where 'observation in hospital' clearly indicates a potentially serious exposure. The NL Poison centre informed that "Management advice" is only recorded from 2016. So to get a realistic idea on severity based on this management advice information, the data from 2016-2021 was used.

In Belgium, most of the human poisoning cases were reported as having “no symptoms”, while a similar number of cases had symptoms categorized as “severe”, with **brodifacoum** and **difenacoum** being most involved. This contrasts with the information reported from other poison centres. It should however be noted that the higher proportion of “severe” cases could be linked to the fact that in this case, the unintentional cases were not differentiated from the intentional cases. More information would also be needed on the scheme/criteria applied to categorize the symptoms in the different severity grades to ensure a proper comparison between Poison Centres.

Table 17. Belgium (all reported cases of poisonings by rodenticides)

BELGIUM Year 2020	Fatal	Severe	Moderate	Mild	No symptoms	TOTAL (2020)
Total	0	39	15	13	42	214
First generation						
Chlorophacinone						
Coumatetralyl						2
Warfarin						
Second generation						
Brodifacoum		11 (39%)	7 (25%)	3 (11%)	7 (25%)	28
Bromadiolone		3 (38%)		2 (25%)	3 (34%)	8
Bromadiolone Difenacoum						2
Difenacoum		19 (35%)	7 (13%)	6 (11%)	22 (41%)	54
Difethialone		6 (32%)	1 (5%)	2 (11%)	10 (53%)	19
Flocoumafen						3
Unknown						
						98
						46%

Severity categories: No symptoms; Mild: mild symptoms; Moderate: no severe symptoms and conditional referral to a doctor; Severe: severe symptoms and referral to doctor; Fatal: deceased.

Italy reported that only 4.6% (11 cases) of the cases were symptomatic:

- 4 (36.4%) showed coagulation imbalance,
- 3 (27.2%) minor bleeding,
- 4 (36.4%) major bleeding with 2 fatalities.

The AVK substance identity was only identified in 4 cases as:

- brodifacoum (n 2),
- bromadiolone (n 1) and
- bromadiolone associated with denatomium (n 1).

One of the fatal cases (intracerebral hemorrhage) was associated with **bromadiolone** plus denatonium. It should also be noted that in this case, no differentiation between intentional vs. unintentional cases was made. No information on the dose intake was available either.

Overall, it should be highlighted that the symptoms may depend on the anticoagulant rodenticide active substance but also to the dose intake (which could be higher in intentional cases). Limited (or no) information on the dose intake was available in the data provided. In addition, different scoring systems of the severity of symptoms could also impact the reporting of the Poison Centres, thereby complicating the comparison and interpretation of the data.

Based on the available data on the human health poisonings collected in the EU survey, no clear trends could be identified on specific anticoagulant rodenticides being consistently linked to more (or less) severe poisoning cases in humans.

4. Animal poisoning cases

Number of cases

Based on the information provided in the EU Survey, an overview of the number of domestic animal poisoning cases (pets, livestock) is provided in the Tables below per Poison Centre.

Most of the animal poisonings occurred with the active substance being unknown/not identified. When information on the anticoagulant rodenticide substance is available, most of the animal poisoning cases reported related to SGARs. A similar trend was observed for human poisoning cases (section 2.3.3).

The anticoagulant rodenticide substances involved in most of the animal poisoning cases are highlighted in orange. Some variations were seen in the anticoagulant rodenticide active substances involved in most of the animal poisoning cases per Member State (MS). **Brodifacoum**, **bromadiolone**, **difenacoum** and **difethialone** were mostly reported as being involved in animal poisoning cases.

The highest numbers of authorized BPs containing a specific anticoagulant rodenticide active substance in the specific MS for the concerned period are highlighted in green in the Tables. In many cases, the highest number of poisoning cases relate to anticoagulant rodenticide substances having the highest number of BPs authorized during the reporting period in that MS.

Table 18. Ireland - Animal poisoning cases (accidental, other and unknown cases)

IRELAND Year	2017	2018	2019	2020	2021	Total (2017-2021)	Number of authorized BPs (2017-2021)
Total	10	6	12	21	16	65	
First generation							
Chlorophacinone							
Coumatetralyl		1	3	2		6	
Warfarin							1
Second generation							
Brodifacoum	1		2	5	5	13	47
Bromadiolone	3	1	3	3		10	27
Bromadiolone Difenacoum							1
Difenacoum	3	1		3	2	9	26
Difethialone							4
Flocoumafen			1			1	10
Other AVK							
	1	1		4	2	8	
Unknown							
	2	2	3	4	7	18	
	20%	33%	25%	19%	16%	28%	

Table 19. France – Total number of calls for animal poisoning cases.

FRANCE Year	2014	2015	2016	2017	2018	2019	Total (2014-2019)	Number of authorized BPs (2014-2019)
Total	488	523	481	445	519	535	2991	
First generation								
Chlorophacinone	17	21	18	12	12	6	86	
Coumatetralyl	11	10	11	4	9	11	56	4
Warfarin								
Second generation								
Brodifacoum	72	50	52	37	84	84	379	55
Bromadiolone	74	84	75	77	74	69	453	35
Bromadiolone Difenacoum								3
Difenacoum	142	165	174	152	146	196	975	47
Difethialone	93	107	75	84	122	85	566	3
Flocoumafen	0	0	0	0	0	0	0	1
Unknown								
	79	86	76	79	72	84	476	
	16%	16%	16%	18%	14%	16%	16%	

FR: The Center received 2,991 calls about anticoagulant rodenticides, which represents 6.4% of calls during this period. Calls to CAPAE-Ouest relating to anticoagulants follow the possible or certain ingestion of a rodenticide product whose composition is known. This is most often a question about risk assessment: "Is the ingested dose dangerous? ", and in a lesser number of cases of what to do "How to make the diagnosis? ", or when the diagnosis is made "What is the duration of treatment with vitamin K? ". Not all calls therefore correspond to poisonings, as many are received shortly after the animal is seen ingesting the product.

Table 20. The Netherlands (mono-intoxications with AVKs in scope; unintentional and not recorded cases – intentional case and multi-intoxications excluded)

The Netherlands Year	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	Total	Number of authorized BPs (2012- 2021)
Total (AVKs)	178	149	200	197	175	242	232	231	231	209	2044	
First generation												
Chlorophacinone	1	2	1				2	1			7	1
Coumatetralyl			2	1		1	1	1	1	2	9	1
Warfarin										1	1	
Second generation												
Brodifacoum	14	5	10	10	7	6	26	43	40	55	216	23
Bromadiolone	62	54	51	47	48	54	52	38	34	32	472	12
Bromadiolone Difenacoum				14	6	7	9	10	13	7	66	
Difenacoum	42	38	55	45	58	76	51	55	51	32	503	29
Difethialone	58	47	73	73	49	82	85	75	85	75	702	4
Flocoumafen	1	3	8	7	7	16	6	8	7	5	68	6
Unknown												
	64	67	66	54	75	45	36	48	30	60	545	
	36%	45%	33%	27%	43%	19%	16%	21%	13%	29%	27%	

The NL Poison centre informed that "In the Dutch data 'unknown' is the category 'other long-acting coumarine derivatives'.

Table 21. Estonia – Animal poisoning cases (accidental exposure)

ESTONIA Years	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	Total	Number of authorized BPs (2012- 2022)
Total	1			3	3	4	4	8	7	1	2	33	
First generation													
Chlorophacinone													
Coumatetralyl													
Warfarin													
Second generation													
Brodifacoum					1	1		1	1		1	5	15
Bromadiolone				2			3		1			6	18
Bromadiolone Difenacoum													1
Difenacoum													3
Difethialone													1
Flocoumafen													1
Unknown													
	1			1	2	3	1	7	5	1	1	22	
	100%			33%	66%	75%	25%	88%	71%	100%	50%	67%	

Table 22. Belgium – Animal poisoning cases (AVK rodenticides in scope)

BELGIUM Year	Total cases (2020)	Number of authorized BPs (2020)
Total	325	
First generation		
Chlorophacinone		
Coumatetralyl	6	3
Warfarin		
Second generation		
Brodifacoum	98	35
Bromadiolone	23	23
Bromadiolone Difenacoum	1	1
Difenacoum	113	34
Difethialone	54	13
Flocoumafen	10	2
Unknown		
	20	
	6%	

Note: From the BE reporting, it is understood that “rodenticides NOS” refers to rodenticides substances which were not identified (not considered in table above); “Rodenticides – anticoagulant” to AVK rodenticides which were not identified (identified as “Unknown” in table above).

Species

Data provided from the Poison Centres inform that several animal species may be affected by anticoagulant rodenticide poisonings. The animal species in which most of the poisoning cases were reported are highlighted in orange. Most of the animal poisoning cases occurred in dogs (usually more than 80% of the cases), followed by cats (about 5% of the cases). The same trend can be seen from the reporting from different poison centres. No clear differentiation between anticoagulant rodenticide substances could be seen in the animal species impacted.

Table 23. Estonia – Animal poisoning cases per species (accidental exposure)

ESTONIA Years 2012-2022	Cats	Dogs	TOTAL (2012-2022)
Total	3	29	32
	9%	91%	
First generation			
Chlorophacinone			
Coumatetralyl			
Warfarin			
Second generation			
Brodifacoum		5	5
Bromadiolone		6	6
Bromadiolone Difenacoum			
Difenacoum			
Difethialone			
Flocoumafen			
Unknown			
	3	18	21

Table 24. Ireland – Animal poisoning cases per species (accidental, other and unknown cases)

IRELAND Years 2017-2021	Cats	Cow	Dogs	Chicken	Ferret	Rabbit	Sheep	Horse	Pig	TOTAL (2017-2021)
Total	1	1	58	1		1		1	2	65
	2%		89%							
First generation										
Chlorophacinone										
Coumatetralyl			6							6
Warfarin										
Second generation										
Brodifacoum	1 (8%)		11 (85%)					1		13
Bromadiolone			10 (100%)							10
Bromadiolone Difenacoum										
Difenacoum			8 (89%)			1				9
Difethialone										
Flocoumafen			1 (100%)							1
Other AVK										
		1	4	1					2	8
Unknown										
			18							18

Table 25. France – Calls for animal poisonings per animal species (“certain ingestions” and “probable cases”)

FRANCE Years 2014- 2019	Cats	Cattle	Dogs	Donkey	Ferret	Hens	Rabbit	Sheep	Horse	Pig	Duck	Goat	Hamster	Pony	Tortoise	Guinea pig	Lizard	Parrot	Rat	Hedgehog	Pigeon	TOTAL (2014-2019)
Total	129	19	1719	13	1	30	19	11	26	10	5	28	1	11	2	1	1	1			2	2029
	6%	1%	85%	<1%	<1%	1.5%	1%	<1%	1.3%	<1%	<1%	1.4%	<1%	<1%	<1%	<1%	<1%	<1%			<1%	
First generation																						
Chlorophacinone	4 (7%)	2	46 (79%)	1	1	2	1	1														58
Coumatetralyl	2 (4%)		44 (85%)	1			2	1	1	1												52
Warfarin																						
Second generation																						
Brodifacoum	17 (5%)	3	278 (88%)	1		3	4	1	3	1		2		3								316
Bromadiolone	23 (7%)	7	282 (80%)	5		6	1	4	10	2	2	8	1	1	1							353
Bromadiolone Difenacoum																						
Difenacoum	50 (6%)	6	680 (87%)	2		13	6	2	6	3		7		2	1	1	1					780
Difethialone	33 (7%)	1	389 (83%)	3		6	5	2	6	3	3	11		5				1			2	470
Flocoumafen																						

FR: Calls classified as 'Probable' and 'Very probable' essentially correspond to the following 2 situations:

1°) ingestion is certain and the clinical picture is compatible with intoxication.

Ingestion is considered 'Certain' when the animal has been seen ingesting the rodenticide or when the toxicological analysis is positive (presence of the molecule in the blood or the liver)

2°) the clinical picture is compatible with anticoagulant poisoning, the rodenticide is present in the animal's environment, and there is no other explanation present to explain the symptoms.

It should be noted that when the case is considered probable and the animal has been exposed to two (or even more) anticoagulant molecules at the same time, it is not possible to attribute responsibility for the intoxication to one rather than to the other. The case will then be deemed 'Probable' for both molecules potentially involved.

Table 26. The Netherlands - Animal poisoning cases per species (mono-intoxications with anticoagulant rodenticides in scope; unintentional and not recorded cases – intentional case and multi-intoxications excluded)

The Netherlands Years 2012-2021	Cats	Cattle	Dogs	Rabbit	Horse/pony	Pig	Goat	Other	Rodent	Bird	TOTAL (2012-2021)
Total	138	5	1795	43	25	8	5	4	9	12	2044
	7%	0.2%	88%	2%	1%	0.4%	0.5%	0.4%	0.4%	0.6%	
First generation											
Chlorophacinone	4 (57%)		3 (43%)								7
Coumatetralyl			8 (89%)			1					9
Warfarin			1 (100%)								1
Second generation											
Brodifacoum	20 (9%)		186 (86%)	3	4	1	2				216
Bromadiolone	21 (4%)		432 (92%)	5	6	3	1		1	3	472
Bromadiolone Difenacoum	5 (8%)		56 (85%)	2	1				1	1	66
Difenacoum	38 (8%)	2	437 (87%)	12	3	1		2	5	3	503
Difethialone	48 (7%)	3	611 (87%)	21	7	2	1	2	2	5	702
Flocoumafen	2 (3%)		61 (90%)		4		1				68

Route of exposure

The main route of poisoning cases in animals was via the ingestion route.

Place of poisoning

The main place of poisoning is at home.

Symptoms and severity

The Table 27 to Table 29 report the severity grades of the animal poisoning cases. The mostly reported severity grades are highlighted in green – the anticoagulant rodenticide substance(s) involved in the most severe grade are highlighted in orange.

From the reporting from Ireland, most of the cases had no symptoms or symptoms of “minor” severity. One “severe” case was however reported for **Flocoumafen** which is a SGAR.

Table 27. Ireland – poisoning severity scores in dogs (unintentional and unknown cases)

IRELAND Years 2017-2021	Severe	Moderate	Minor	None/N.A.	Total (2017-2021)
Total	3		7	55	65
	4.5%		10.5%	85%	
First generation					
Chlorophacinone					
Coumatetralyl				6 (100%)	6
Warfarin					
Second generation					
Brodifacoum			2 (15%)	11 (85%)	13
Bromadiolone				10 (100%)	10
Bromadiolone Difenacoum					
Difenacoum			1 (11%)	8 (89%)	9
Difethialone					
Flocoumafen	1 (100%)				1
Other AVK					
				8 (100%)	8
Unknown					
	2		4	12	18

The management advice provided at the time of the poisonings in the data provided by the Netherlands can give an indication of the severity of the poisonings. For most of the cases, no information was recorded or the advice was “observation at home” (possibly indicating an intoxication of lower concern). Only poisoning cases involving SGARs resulted in “observations at hospital” (possibly indicating a more severe intoxication) – while none were reported for FGARs. No clear differentiation can however be done between AVK SGAR substances. The NL Poison Centre mentioned that one dog died – but no information was provided as to which substance may have been associated.

Table 28. The Netherlands – Animal poisoning cases - Management advice/Severity (mono-intoxications with AVKs in scope; unintentional and not recorded cases – intentional case and multi-intoxications excluded)

The Netherlands Years 2016-2021	Observation in hospital	Assessment by veterinarian	Observation at home	Not recorded	TOTAL
Total	50	462	808	1	1321
	4%	35%	61%	<1%	
First generation					
Chlorophacinone		1 (33%)	2 (67%)		3
Coumatetralyl		3 (50%)	3 (50%)		6
Warfarin		1 (100%)			1
Second generation					
Brodifacoum	12 (7%)	93 (53%)	72 (40%)		177
Bromadiolone	8 (3%)	97 (38%)	152 (59%)	1	258
Bromadiolone Difenacoum	3 (6%)	27 (52%)	22 (42%)		52
Difenacoum	14 (4%)	81 (25%)	228 (71%)		323
Difethialone	6 (1%)	134 (30%)	311 (69%)		451
Flocoumafen	7 (14%)	24 (49%)	18 (37%)		49
Third generation					
Alpha- bromadiolone					

NL: An indication can also be derived from the 'Management advice' provided, where 'observation in hospital' clearly indicates a potentially serious exposure.

The NL Poison centre informed that "Management advice" is only recorded from 2016. So to get a realistic idea on severity based on this management advice information, the data from 2016-2021 was used.

A higher proportion of "severe" cases were reported by Belgium. This could be partially due to differences in classification criteria between Poison Centres. It should also be noted that the severity of symptoms may depend on the active substance but also on the dose taken for which little (or no) data is available. Most of the animal poisoning cases reported by Belgium were from SGARs. All the "severe" cases were reported with SGARs but no clear differentiation could be made in the severity of the symptoms reported between SGAR substances.

Table 29. Belgium – Animal poisoning cases

BELGIUM Year 2020	Fatal	Severe	Moderate	Mild	No symptoms	Total cases (2020)
Total		177	40	3	68	288
		61.5%	14%	1%	23.5%	
First generation						
Chlorophacinone						
Coumatetralyl						6
Warfarin						
Second generation						
Brodifacoum		72 (73%)	11 (11%)	2 (2%)	13 (13%)	98
Bromadiolone		15 (65%)	1 (4%)	1 (4%)	6 (26%)	23
Bromadiolone Difenacoum						1
Difenacoum		59 (52%)	17 (15%)		37 (33%)	113
Difethialone		31 (57%)	11 (20%)		12 (22%)	54
Flocoumafen						10
Unknown						
						20

Severity categories: No symptoms ; Mild : mild symptoms ; Moderate : no severe symptoms and conditional referral to a doctor ; Severe : severe symptoms and referral to doctor ; Fatal : deceased.

Note: From the BE reporting, it is understood that “rodenticides NOS” refers to rodenticides substances which were not identified (not considered in table above); “Rodenticides – anticoagulant” to AVK rodenticides which were not identified (identified as “Unknown” in table above). Numbers in *italic* are number of animal cases reported but for which no severity scores were provided.

In France, the symptoms observed in animals poisoned were similar between species. 16.5% of probable cases were recorded as fatal (noting that the outcome was not always known). Using the antidote vitamin K1 for several weeks was considered a successful as treatment:

“The reported symptoms are similar in all species. we mainly note: lethargy, digestive and respiratory haemorrhages, cough, hematomas. Complementary examinations show an increase of coagulation times, and later anemia. Abdominal or thoracic effusion is not exceptional.

Of a total of 176 probable cases, we record 29 fatal outcome (but we do not know the outcome of all cases). The treatment of poisoning is implemented without difficulty by veterinarians, and consists of the administration of vitamin K1 for several weeks. It is generally followed by success if it is correctly implemented.”

Overall, most of the poisoning cases of domestic animals seem to be of minor severity. SGARs seem to be involved in the poisoning cases of highest severity – but these are also the anticoagulant rodenticide substances which are most involved in the highest number of poisoning cases. No clear differentiation can be made between the SGAR substances.

5. Conclusions

Human Poisonings

- Most of the human poisonings occurred with the active substance being unknown/not identified.
- When information on the substance was available, most of the human poisoning cases related to SGARs. Poisoning cases were rarely reported with FGAR substances.
- Some variations were seen in the anticoagulant rodenticide active substances involved in most of the human poisoning cases per Member State (MS). **Bromadiolone** and **difenacoum** were most often reported, followed by **brodifacoum** and **difethialone**.
- The highest number of poisoning cases is usually correlated to anticoagulant rodenticide substances having the highest number of BPs authorized during the reporting period in that specific MS. It therefore seems that the number of poisoning cases are linked to the availability of BPs containing a specific anticoagulant rodenticide substance on that market.
- The main route of poisoning was via the oral/ingestion route. Occasionally, the dermal and inhalation exposure routes were mentioned. Other routes (e.g. ocular, subcutaneous, intramuscular, nasal) were rarely reported. Based on available data, there were no differences seen in the route of exposure between anticoagulant rodenticide substances, or between FGARs vs. SGARs.
- Most of the human poisoning cases were reported as unintentional/accidents. Based on the available data, no differences were seen between AVK substances, or between FGARs vs. SGARs.
- Most of the unintentional human poisoning cases occurred in a younger human population/children (age group <5 years). Most of the intentional cases occurred in the adult population (e.g. age groups 40-60 years).
- The most common place of poisoning is at home (for both intentional and unintentional cases). No differentiation could be made between AVK substances, or between FGARs vs. SGARs, regarding the place of poisoning.
- Most of the reporting indicated that the poisoning cases had no symptoms or symptoms of minor severity.
- FR data indicated that FGARs may lead to more symptomatic cases than SGARs. Other Poison Centres reported an opposite trend where SGARs were associated more frequently with cases of "moderate" severity than FGARs. When looking in more details into the type and severity of the reported symptoms, it is difficult to make clear differentiations between anticoagulant rodenticide substances, or between FGARs and SGARs.
- The reported symptoms affected several functional systems, the most common being coagulation disturbances and bleeding. No clear differences were seen between anticoagulant rodenticide substances.
- It should be noted that the severity of the symptoms may depend on the anticoagulant rodenticide active substance but also to the dose for which only limited (or no) information on the dose was available. In addition, different scoring systems of the severity of symptoms could also impact the reporting of the Poison Centres, thereby complicating the comparison and interpretation of the data.

Based on the available data from the Poison Centres, no clear conclusions could be drawn regarding specific anticoagulant rodenticide substances being consistently linked to more (or less) severe poisoning cases in humans, and/or to conclude that some anticoagulant rodenticide substances would have a significantly better safety profile in humans than others.

Animal Poisonings

- Most of the animal poisonings occurred with the active substance being unknown/not identified.
- When information on the substance was available, most of the animal poisoning cases reported related to SGARs.
- Some variations were seen in the AVK active substances involved in most of the animal poisoning cases per MS. **Brodifacoum, bromadiolone, difenacoum and difethialone** were mostly reported as being involved in animal poisoning cases.
- In many cases, the highest number of poisoning cases relate to anticoagulant rodenticide substances having the highest number of BPs authorized during the reporting period in that specific MS.
- Several animal species may be affected by anticoagulant rodenticide poisonings, with most of the poisoning cases being reported in dog (more than 80% of cases) followed by cats (about 5% of cases). No clear differentiation between anticoagulant rodenticide substances could be seen in the animal species impacted.
- The main route of poisoning was via ingestion and most frequent location of poisoning is at home.
- With the exception of Belgium who reported a high proportion of severe cases, most of the reporting indicated that the poisoning cases had no symptoms or symptoms of minor severity.
- The more severe poisoning cases seem to occur with SGARs compared to FGARs – but SGARs are also the anticoagulant rodenticide substances involved in the highest number of poisoning cases overall (and with the highest number of authorized BPs).
- No clear differentiation can be done between SGARs when looking at the severity and/or management advice provided at the time of the poisonings.
- France reported that the symptoms observed in animals poisoned were similar between species, with 16.5% of cases being recorded as fatal.
- Using Vitamin K1 for several weeks was considered a successful treatment in animal poisoning cases.

In conclusion, based on the available data provided by the Poison Centres, it is not possible to identify an anticoagulant rodenticide substance that would have a significantly better safety profile than another for the safety of domestic animal species.

6. Annexes

Annex 1 - The questions in the EU Survey and answers received by EU Poison Centres - **CONF**

Annex 2 - Excel overview of the input received from the EU Poison Centres – **CONF**

Annex 3 - Individual inputs and attachments received by each Poison centre – **CONF**

Annex 4 - Information on the number of authorized biocidal products