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Rodenticides (Anticoagulant)

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1. Introduction

Rodents occur worldwide and have adapted to most types of ecosystems. Rodents provide many important ecosystem functions and while most rodent species do not cause serious damage problems, a small number of species do. Rodent-caused damage includes crop and stored food consumption and contamination, forestry and nursery damage, rangeland damage, ornamental plant damage, property damage, cable and irrigation pipe damage, disease transmission, and, when introduced to islands, damage and even extinction of native flora and fauna. Many tools are used to reduce rodent populations and damage. Rodenticides are an especially important tool in rodent management. Many types of active ingredients and formulations are available for different species and situations. Rodenticides and their use are regulated by the United States Environmental Protection Agency (EPA) and authorized State agencies. Following regulatory review, the approved label dictates how the product must be used and who has authority to use the product. All labels contain mitigation measures to reduce the risk to workers, consumers, pets, livestock, non-target animals, and the environment. Recently, the EPA has been re-evaluating many of the major rodenticides as part of the periodic re-registration process. To reduce the number of accidental exposures by children and impacts to non-target wildlife, the EPA has proposed new mitigation measures to reduce the hazards of certain rodenticides that are used in and aroundhomes and other buildings. If implemented as proposed, these mitigation measures may affect the availability of some of the most common rodenticides (Witmer and Eiseman, 2007)

Rodenticides are defined as any substance that is used to control population of rats, mice, and other commensal rodents in and around the house or other facilities as one component of an integrated pest management program. Most commercial baits are registered for rats and mice, and they are usually based on new generation substances, such as Bromodiolone, Brodifacoum and Difenacoum. No rodent bait ingredient is universally highly acceptable, and regional differences are the rule rather than the exception. To achieve good control of commensal rodents using rodenticides, selection of the appropriate toxicant and formulation (i.e. grain, pelleted or wax block); as well as bait placement, are important considerations.

Contrary to popular belief, rats prefer fresh, high-quality foods and will reject spoiled or inferior food items when given a choice. Therefore, rodent baits should be made from high-quality food materials, and baits which have become rancid or insect-infested should be discarded. Usually wheat, barley, oats and corn are the grains most preferred by rodents. Preference varies between rodent population and among individuals. Baits similar to foods that rodents are accustomed to eating are often a good choice, particularly if their normal foods are limited or can be made less available to them.(EPA,2007)

2. RODENTICIDES CLASSIFICATION

Rodenticides are classified into two groups: anticoagulants and all other compounds (nonanticoagulants). Anticoagulant rodenticides were first discovered in the 1940's and have since become the most widely used ingredients for commensal rodent control. Rodents poisoned with anticoagulants die from internal bleeding, the results of loss of the blood's clotting and damage to the capillaries. Prior to death the animal exhibits increasing weakness due to blood loss, though appetite and body weight are not specifically affected. Because anticoagulant baits are slow in action (several days following the ingestion of a lethal dose), the target animal is unable to

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associate its illness with the bait eaten. Therefore, bait shyness does not occur. This delayed action also has a safety advantage because it provides time to administer the antidote (vitamin K1) to save pets, livestock, and people who may have accidentally ingested the bait. Anticoagulant rodenticides are also divided into two groups, commonly known as the first generation anticoagulants or multiple-feed rodenticides and the second-generation anticoagulants. Rodenticides from first generation are chronic in their action, requiring multiple feeding over several days to a week or more to produce death. Resistance to the lethal effects of the first-generation baits led to the development of the second-generation anticoagulants: Difenacoum, Bromadiolone, Brodifacoum and other active ingredients. These compounds are much more potent than the first-generations anticoagulants, making them effective for the control of rats and mice. As one feeding can produce death if a sufficient amount of bait is consumed, they are often referred to as single-feed anticoagulants. In commensal situations where rodents are often marginal or reluctant feeders, these compounds can be extremely effective. The effects of these compounds are also cumulative and will result in death after several feeding of even small amounts. As in the case of all anticoagulants, death is delayed for several days following the ingestion of a lethal dose.

Although all second-generation anticoagulants are very potent rodenticides currently available for commensal rodents, Difenacoum is less toxic to rodents as Brodifacoum or Bromadiolon but can results in the same level of control. Most important attribute of Difenacoum is small lethal dose for other warm-blooded animals. It has very targeted efficacy.

Difenacoum is the oldest second - generation anticoagulant, therefore acts by preventing the production of blood clotting factors and it is very effective against mice and rats, including warfarin resistant strains. After a couple of small feeds on any Difenacoum baits, clotting is slowed down, leaks in the vessels are not repaired and after 4-10 days the rodent dies due to low blood pressure. From professional point of view, Difenacoum is vitamin Kantagonist. The main site of its action is the liver, where several of the blood coagulation precursors under vitamin K dependent post translation processing take place before they are converted into the respective procoagulant zymogens. The point of action appears to be the inhibition of K1 epoxide reductase.

It does not enter the atmosphere, because of its low volatility and its stable under normal conditions. In addition, Difenacoum is slightly soluble in water and in bait formulation it is unlikely to be a source of water pollution. (Singleton *et al.*, 1999)

Mammalian	LD50 in mg/kg b.w.		
toxicology			
oral	Difenacoum	Bromadiolone	Brodifacoum
Rat	1.80	1.125	0.27
Mouse	0.80	1.75	0.40
Rabbit	2	1	0.30
Dog	>50	>10	0.25-1.00
Cat	100	>25	25
Guinea pigs	50	/	2.8
Dermal			
Rabbit	1000	2.1	/
Rat	27.4	/	0.25-0.63

 Table1. Difenacoum, Bromadiolone and Brodifacoum LD50 comparison

Table Comment: From LD50 in table is evident lesser toxicity of Difenacoum in comparison to Bromadiolone and Brodifacoum, but the effect on rodent control is similar. It provides the same level of protection against commensal rodents and it has targeted efficacy. That means it is less toxic to larger warm-blooded animals, such as domestic pets or even humans. Difenacoum is the oldest second – generation anticoagulant and for that reason furthest used in rodent control (Witmer et al., 1995).

3. RODENTICIDE PRODUCTS

Unichem rodenticides production is based on anticoagulant of the second generation in 0,005% concentration. This active substance is formulated in 4 different forms:

- Rodenticide pasta bait
- Rodenticide wax blocks

Rodenticides (Anticoagulant)

- Rodenticide pellets
- Rodenticide grain bait

3.1. Rodenticide Pasta Bait

Fresh bait rodenticide based on active Bromadiolene, Brodifacoum or Difenacoumfor house mice and black/grey rats control. It is becoming the most popular and used bait throughout the world. Both, composition of bait and added attractant increases bait attractiveness on such level that the rodents are more likely to consume pasta bait rather than their natural food.

Dosage:

house mice: 20 - 25 g

black/grey rats: 100 - 150 g

Advantages:

- 1. Especially suitable for rodents when there is enough of their natural food.
- 2. Contains added attractants.
- 3. Highly effective due to delayed action.
- 4. Moistureproof, thus suitable for indoor and outdoor use.
- 5. Added BHT compound that mummifies killed rodents, and Bitrex (detering agent).
- 6. Protection glove enclosed.
- 7. Test results show this is the most effective formulation.

Packaging:

125 g, 250 g, 500 g, 10 kg bulk

Transport Packaging:

125 g: 20/80 Ep; 250 g: 20/48 Ep; 500 g: 14/30 Ep, 10 kg bulk: 1/24 Ep

3.2. Rodenticide Wax Blocks

Description:

Wax blocks rodenticides based on active Bromadiolene, Brodifacoum or Difenacoum for house mice and black/grey rats control. Their waterproof quality and resistance to various environment conditions makes wax blocks suitable for outdoor use. Rodents like to nibble on hard objects, so this formulation is very suitable for all commensal rodents. Sharp edges are easy to check for rodent activity.

Dosage:

house mice: 20 - 25 g

black/grey rats: $100 - 150 \,\mathrm{g}$

Advantages:

- 1. Highly resistant to various environment specifics such as moisture. Especially suitable for moist places and outdoors.
- 2. Contains added attractants
- 3. Highly effective due to delayed action.
- 4. Added BHT (mummyfier) and Bitrex (detering agent).
- 5. Protection glove enclosed.

Packaging:

250 g, 10 kg bulk

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Transport Packaging:

250 g: 20/48 Ep

10 kg: 1/24 Ep

3.3. Rodenticide Pellets

Description:

Pelleted rodenticide based on active Bromadiolene, Brodifacoum or Difenacoum for house mice and black/grey rats control. Bait is made by grind wheat and pelleted to become more attractive to rodents. Substances to increase attractiveness are added. Recommended for indoor use.

Dosage:

house mice: 20 - 25 g

black/grey rats: 100 - 150 g

Advantages:

- 1. Due to large portion of wheat very tasteful to rodents.
- 2. Contain added attractants.
- 3. Highly effective due to delayed action.
- 4. Added BHT (mummyfier) and Bitrex (detering agent).

Packaging:

300 g, 25 kg bulk

Transport Packaging:

300 g: 20/54 Ep

25 kg bulk: 1/19 Ep

3.4. Rodenticide Grain Bait

Description:

Grain bait rodenticide based on active Bromadiolene, Brodifacoumor Difenacoumfor house mice and black/grey rats control (Desoky,2015).

Dosage:

house mice: 20 - 25 g

black/grey rats: 100 - 150 g

Advantages:

- 1. Contains the largest portion of grain which is favourite food of rodents.
- 2. Does not disperse due to bag packaging.
- 3. Contains added attractants.
- 4. Highly effective due to delayed action.
- 5. Added BHT (mummyfier) and Bitrex (detering agent).
- 6. Protection glove enclosed.

Packaging:

250 g, 500 g, 25 kg bulk

Transport Packaging:

250 g: 18/48 Ep 500 g: 14/30 Ep 25 g bulk: 1/19 Ep

4. MARKETING

4.1. An Overview of Unichem's Activities in Different Markets and Market Segments

Unichem d.o.o. has activities in 14 different countries across Europe. In 4 countries we have our own representative companies: Poland, Czech Republic, Hungary, Croatia (covering the whole area of ex-Yugoslavia). Other countries include both Eastern and Western European countries. We also have extensive knowledge of some other countries such as USA.

As Unichem is producing a wide product range for both plant protection and growth, as well as for biocides (insecticides and rodenticides) we are facing several different market segments. These product groups are not equally competitive so we are not present with the whole product range on all markets. The most attractive products are rodenticides (we are present in all 14 countries with this product group), followed by insecticides (present in 12 countries) and biological plant protection (Bio Plantella – present in 11 countries).

We are usually present in 5 major distribution channels with either all or at least some of our products:

• Market segment

Usually large retail stores with only small number of products from our product groups, however with large quantities sold. Competition are usually multinational companies such as Scotts, Bayer or similar. The shelf space needs to be bought and a lot of costs are present to enter this distribution channel, however with the right product and appropriate (intensive) marketing support the results can be very good. Their importance is increasing in all markets. Sometimes this segment is supplemented with a large number of small market retail shops, which have central purchase and the same rules apply.

DIY

(Do-it-yourself) centres – usually large retails stores with a large product range of all our product groups. Competitors are usually both multinational companies as well as local producers. A lot of products on the shelf and poor assistance of the selling staff result in the consumer confusion as the consumers are not able to differentiate between products. Special marketing tools are used to attract customer to your product although they usually need to be paid to the retailer: promotions, label designs, special 'action' sales, leaflets... Their importance is also increasing and the number of different centres is also increasing. It usually attracts people in bigger cities and as a consequence smaller shops are losing market share.

• Agricultural Shops (Small Specialized Stores)

Usually small to medium sized with a large product range. Seller is sometimes also an owner and has a lot of knowledge of the products. People come to buy not only a product but also an advice how to use it. These shops are usually in every village or town no mater how small – it makes them very attractive but also more difficult and expensive to cover. The most important is to get the seller to promote our products. They can also be motivated with special sales promotions and with wide product range – they prefer to buy different products from one supplier. This market segment is in certain countries not present however in most countries this is the most important segment, even though it is losing market share to DIY centres. Even if this segment is not present another very similar segment then evolves which is usually very similar (chemical stores instead of agricultural stores).

• Other Small Shops (Small General Shops)

Usually different retail formats such as flower shops, shops that sell live-plants, small hardware shops, veteranian shops, paint shops... Similar to Agricultural shops however the sellers usually do not have the knowledge of the products in our product groups. Sales are also usually lower. This segment is usually supplemental to other segments.

• Professional Buvers

Almost all our product is also sold to professionals – companies that perform services to the endbuyers and buy our materials as 'raw material'. Rodenticides and insecticides are sold to special companies that perform 'publichygiene' services either to private users, food industry (which needs these services if they have HACCP standard for public hygiene) and also to government agencies or ministers (or local municipalities) if they take care for public health (sewerage). These companies are usually connected into the Association which has the information about all such companies in the country. This association usually also has a monthly newspaper and a yearly trade fair where everybody in the industry meet – these two opportunities are the best for marketing. Large quantities (in large packaging – 5, 10, 25 kg) are usually both by these buyers at favourable prices although they sometimes prefer to prepare their own products instead of buying it from a supplier. Such products are always much less effective than professionally prepared products. Special offers are usually prepared for each buyer, both technical and price. Very similar is true for professional plant protection.

Unichem usually starts to cover professional buyers and continues with the Agricultural and DIY sectors. The remaining two sectors are covered only later.

5. REGISTRATION OF RODENTICIDES IN EC COUNTRIES

In the past for biocidal active substances and products different bregistration took place according each member state.

The European Parliament and the Council adopted the Directive 98/8 EC in 1998 concerning the placing of biocidal products on the EU market (Biocidal Products Directive, BPD). The background for this Directive is a need for harmonization of the legislation of the Member States regarding this type of substances. The Directive requires an authorization process for biocidal products containing active substances listed in "positive lists".

The notification procedure of existing active substances had started in 2000 and was finalized at the 31st January 2003 after the additional period for notification of certain active substances.

At the next step the full dossier including all test reports should be submitted to the Rapporteur Member State including the risk assessment of the active substance.

UNICHEM d.o.o. has contracts with companies which had prepared dossiers for active substances. In this moment UNICHEM d.o.o. has access to three rodenticide active substances for whole EC area: for bromadilone brodifacoum and difenacoum.

Preparing of dossiers and tests is connected with quite high costs, for example 3,2mio € for bromadiolone, 3,5mio € for brodifacoum and 3,8mio € for difenacoum.

In the next stage documentation for products have to be prepared. Unichem is also involved in this process. Preparing of dossiers and tests for products is also connected with quite high costs, from 80.000 to 120.000 \in .

When mentioned process will be finished all products will need new registrations in each member state. This process is connected with cost from 3.000 to some 10.000 € depends on product and Member state.

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