RODENTICIDES – INDISPENSABLE FOR SAFE FOOD PRODUCTION

Stefan Endepols, Bayer CropScience–Environmental Science and Chairman of the Rodenticide Resistance Action Committee (RRAC), describes the work of the RRAC in establishing rodenticide resistance management strategies

Rodents are pests for crops and stored products; they also can constitute a high risk for the health and life of livestock and man. As an example, their faeces can shed pathogens such as *Salmonella* or the Foot-and-Mouth Disease virus. In contrast to most insect pests, which spend periods of their lives on crops or in stored products, synanthropic rodents usually visit plants, grain or food only to eat. The rest of their lives are spent somewhere else, often unnoticed. This frequently leads to an underestimation of infestations, resulting in insufficient control measures. In addition, the highly social organisation of rat populations and the various behaviours of individual rats make complete eradication very difficult. The incorrect use of rodenticides often causes inaccurate reports about the failure of the products.

Rodenticides are extremely valuable in the prevention of human and animal disease and the protection of property, agriculture and the environment. New molecules are difficult and expensive to bring to market. Through their activities, the overriding intention of the industry's working groups is to maintain the effectiveness of current rodenticides and to guide their sustainable use.

Various levels of reduced susceptibility to some anticoagulant rodenticides exist in certain localities, particularly in North America and northern Europe and in the species *Rattus norvegicus*, *Rattus rattus* and *Mus musculus*. Nevertheless, it remains possible to control rodents everywhere with currently available rodenticides and it is the opinion of Rodenticide Resistance Action Committee (RRAC) that this will remain the case for the foreseeable future.

The development of anticoagulant rodenticides

Early rodenticides were acute poisons. Today, slow-acting anticoagulants are used, especially to control Norway rats (*Rattus norvegicus*). The development of these compounds was a major step toward effective and safe rodent control during recent decades. Due to the slow action of these coumarins, rats do not develop conditioned aversion (bait shyness), and with vitamin K an antidote is available.

All anticoagulant rodenticides belong to the group of hydroxycoumarins or a related group of the indandiones. They act by interrupting the vitamin K cycle in liver microsomes (MacNicoll, 1986). As a result, the maintenance of a number of clotting factors is hampered, resulting in fatal haemorrhages after a few days. Based on their toxicity, these rodenticides can be separated into two main groups: the first generation comprising compounds such as warfarin with lower acute but high cumulative toxicity, and the second generation including compounds with higher acute toxicity. The latter consists of five commercialised compounds that were introduced in the 1970s and 1980s. Those anticoagulants currently in use are very close to having the optimal characteristics of a rodenticide, and attempts to develop better compounds have so far proven unsuccessful.

In 1958, for the first time, it was found that rats in one area of Scotland were impossible to control with warfarin (Boyle, 1960). As a consequence, the more complex hydroxycoumarin molecules of the second generation were developed. The first compound of this generation, difenacoum (Hadler and Shadbolt, 1975), was introduced to the market in 1976. But in 1978, rats were trapped on farms in Hampshire, UK, which survived treatments with common strength difenacoum (Greaves *et al.*, 1982). Subsequent investigations in the 1980s and 1990s revealed that some rat populations on farms in certain areas in Europe and in the U.S. contained individuals which were resistant to the second generation anticoagulant bromadiolone. House mice (*Mus musculus*) in Europe are predominantly resistant to first generation anticoagulants.

In response to concerns associated with the use of anticoagulant rodenticides, the industry established the Rodenticide Resistance Action Committee (RRAC) in 1990. The objective of the RRAC is to advise international agencies, governmental bodies, regulatory bodies and rodenticide users on technical matters related to the proper use of rodenticides. It carries out this objective by producing leaflets guiding the safe and effective use of rodenticide products, by developing and advocating the use of effective resistance management strategies, and by sponsoring research projects on rodenticide resistance. In addition, it organises seminars and conferences where industry members can meet and exchange ideas with experts from universities, governments and international organisations.

Current approaches to rodenticide stewardship

Research in the field of rodent control is complicated by various conditions, such as long rodent lifespans, their reproduction strategy, the wide range of social, learning and feeding behaviours, regulations with respect to animal welfare, and the considerable variations in rodent control techniques. These are some of the reasons why substantial data on resistance management strategies are rare. Before

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the RRAC could start to provide comprehensive advice on rodent control and resistance management strategies, intensive research was required to provide the basic tools for analysing the problems in rodent control.

Susceptibility to anticoagulant rodenticides varies, ranging from a factor of 1.1 up to 2000 between strains of Norway rats (Greaves and Cullen-Ayres, 1988). The practical significance of a proven decrease in susceptibility is therefore difficult to interpret. Not surprisingly, test protocols for susceptibility and resistance have been a major issue for the committee.

Anticoagulant susceptibility in rodents is usually studied by means of feeding tests to measure mortality, and by non-lethal blood-clotting response tests (BCR tests). Although feeding tests are the most conclusive method for determining whether rodents can be effectively controlled with the respective compound, more sensitive BCR tests have been preferred for determining sensitivity in recent decades. These tests can usually be performed easily, they do not rely on feeding behaviour, and can give results within 24 hours. Additionally, they are considered more humane than feeding tests, and animal subjects can be used for further breeding and study. A disadvantage is the significant number of variations in the test protocols for different compounds.

The first BCR tests were developed to distinguish homozygous resistant rat strains from a susceptible strain (Martin *et al.*, 1979, Gill *et al.,* 1993). Later tests were based on a discriminating dose that would make a high percentile of susceptible animals respond (Gill *et al.*, 1994, Prescott and Buckle, 2000). Differences between testing methods made it difficult to assess and compare results obtained from BCR tests for different compounds with wild rats, and to predict the result of control measures. The increasing sophistication of apparatus, statistics and procedures, has gradually made testing more difficult, less comprehensible, and remote from the realities of pest control. For future developments in methodology, standardisation is required. RRAC has, therefore, initiated a research program at the University of Reading that established BCR test protocols for commercial anticoagulants and base lines for the Norway rat and house mouse (Prescott, 2002). The development of these methodological standards is a major step toward the presentation of more sound advice in rodenticide use.

Future challenges

From farm to fork, the food production chain is a vulnerable network. Requirements for hygiene measures play an increasing role in the entire process of producing safe food. Vector control is an essential component of biosecurity and HACCP-based systems. Safe and effective pest control techniques are essential for governments and producers of livestock and food to fulfil consumers' requirements. Working groups like the RRAC acknowledge this political and economic challenge for sustainable pest management.

In the case of rodenticides, the situation is complicated. The vast majority of products currently in use share a common mode of action which is nearly perfect. A further increase in toxicity would not necessarily increase efficacy but may reduce safety. New compounds probably will not appear in the near future. The use of acute poisons as an alternative is limited by their disadvantages and by regulatory constraints, making the usual approach of general product group rotation as a tool in resistance prevention and management impossible. Future rodenticide resistance management strategies must reflect the full range of products and their benefits as well as reliable control practices. Sound recommendations must be given to prevent resistance in susceptible populations, and for the treatment of populations containing resistant individuals. It is the RRAC's objective to provide advice on the use of rodenticides so that their future effectiveness is guaranteed.

Compared with other pest control and crop protection products, the market for rodenticides is comparatively small. Therefore the responsibility to care for a few compounds with all the associated risks and opportunities lies in a few hands. Increasing regulatory and other stewardship costs may reduce the willingness of companies to invest in technological progress. There is opportunity for manufacturers, regulatory authorities, governmental bodies and others to acknowledge their responsibility and to pool their activities. RRAC will play a key role in providing information and in promoting active collaboration to maintain and develop effective rodent control techniques for the safe production of livestock and food, today and in the future.

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