COUMATETRALYL: PUBLIC CONSULTATION IN ACCORDANCE WITH ARTICLE 10(3) OF THE BIOCIDAL PRODUCTS REGULATION (528/2012)

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1. KEY MESSAGES

- Coumatetralyl is less acutely toxic to rodents and birds, it is less persistent in poisoned rodents and in the environment;
- Failure to control rodent populations adequately can result in serious consequences for human health and animal health - rats and mice are known to spread more than 35 diseases to humans and animals.
- The risk mitigation measures report concludes that 'It will be difficult to find a rodenticide that can meet more of the above features [of an ideal rodenticide] than the anticoagulant rodenticides' and also that 'alternatives to AVKs are limited today.'
- Although no single study has assessed all elements to determine the economic impacts that rodents have in one MS or within the EU overall it is clear that this is considerable.
- Coumatetralyl meets 2 of the 3 criteria specified in Article 5(2) of the BPR – it is essential for to prevent or control a serious danger to public health and its loss would have a disproportionate impact on society.

2. INTRODUCTION

An application for the active substance, Coumatetralyl (CAS N° 5836-29-3), was submitted to Denmark in accordance with the renewal procedure outlined in the Biocidal Products Regulation (BPR) (528/2012).

Currently there is no harmonised classification of Coumatetralyl in Annex VI of the Classification and labelling Regulation (1272/2008). However, following a decision of the ECHA's Risk Assessment Committee in March 2014[1], it is proposed that Coumatetralyl meets the criteria to be classified as toxic for reproduction category 1B. As Coumatetralyl meets the criteria listed in Article 5(1)(c), i.e. classified as toxic for reproduction category 1B. It is, therefore, considered as a potential candidate for substitution.

According to Article 10(3) of the BPR, the European Chemicals Agency (ECHA) shall make publicly available information on potential candidates for substitution during a period of no more than 60 days. During this time interested third parties are invited to submit relevant information, including information on available substitutes. At the end of the public consultation period, the Biocidal Product Committee will take due account of the information received before finalising its opinion.

The present position paper examines the derogation conditions outlined in Art 5(2) and shows that two out of the three derogations are met to justify that Coumatetralyl should be re-approved under the BPR.

3. COUMATETRALYL

Anticoagulant (anti-vitamin K) rodenticides (AVKs) are widely used in Europe for controlling the commensal rodents (*Mus musculus, Rattus rattus* and *Rattus norvegicus*). AVKs, which act by interfering with the normal synthesis of vitamin K-dependent clotting factors, fall into two classes,

[1] http://echa.europa.eu/documents/10162/13579/rac_meeting_28_minutes_final_en.pdf

namely the first generation anticoagulant rodenticide (FGAR) and the second generation anticoagulant rodenticide (SGAR).

Coumatetralyl is an FGAR. It acts, (like all AVK), by blocking the vitamin K cycle and resulting in the inability to produce blood clotting factors.

When compared to SGARs, Coumatetralyl is less acutely toxic to rodents and birds; it is less persistent in poisoned rodents and in the environment. In addition, it is not considered to be a persistent or bioaccumulative substance (when assessing environmental Persistent Bioaccumulative and Toxic criteria). As such, Coumatetralyl presents a better environmental profile and a lower primary (birds) and secondary poisoning toxicity when compared to the SGARs.

Coumatetralyl also presents a further advantage as it is formulated into different product types, which are complementary and ensure an efficient level of rodent control in various scenarios and situation. Coumatetralyl is widely used in Europe as a bait paste (Racumin paste) and as a contact product (Racumin foam). The contact product relies on the rodent self-grooming and therefore does not rely on palatability. It can be placed in, for example, cavity walls where normal baits could not be placed. It is uniquely different and a complementary weapon in the control of rodent populations in buildings.

4. CONSIDERATION OF THE DEROGATION PROVISIONS OUTLINED IN ARTICLE 5(2).

a. Are the AVKs, including Coumatetralyl, essential to prevent or control a serious danger to human health, animal health or the environment?

The main reasons for the need to control rodents are[2]:

i. Transmission of diseases to humans

Rodents, both rats and mice, carry a very wide range of disease organisms that are transmissible to humans.

Commensal rodents are reservoirs of a number of human diseases[3] e.g. plague, Hantavirus and leptospirosis[4] and Lassa fever. In fact, rats and mice are known to spread more than 35 diseases to humans and animals[13]. These diseases can be spread to humans directly, through handling of live or dead rodents, through contact with rodent feces, urine, or saliva, and through rodent bites. Diseases carried by rodents can also be spread to humans indirectly, through fleas, ticks, or mites that have fed on an infected rodent[5]. As rodents frequent sewers they can spread the disease over wide areas.

Failure to control rodent populations adequately can result in serious consequences for human health. For example, a selected number of leptospirosis strains are carried by rodents. The rodents do not become noticeably ill from the infection, and so leptospirosis is not a 'rat disease'. The reason it becomes important is that the strains rodents can carry are the same strains that cause

[2] The Sustainable use of rodenticides as biocides in the EU http://www.cefic.org/About-us/How-Cefic-is-organised/Fine-Speciality-and-Consumer-Chemicals/European-Biocidal-Products-Forum-EBPF/
[3] http://ecdc.europa.eu/en/healthtopics/climate_change/health_effects/Pages/rodent_borne_diseases.aspx
[4] https://www.gov.uk/government/publications/list-of-zoonotic-diseases/list-of-zoonotic-diseases
[5] http://www.pestworld.org/news-and-views/pest-health-hub/posts/health-hazards-posed-by-rodents/

severe illness in other animals, and in humans[6]. In the UK alone in 2014 there were 76 cases of leptospirosis, rising from 47 cases in 2013[7]. The disease is more common in Southern Europe e.g. in 2013 there were 385 cases in metropolitan France[8]. In the majority of cases (about 90%) the symptoms are only mild and include a high temperature, chills, conjunctivitis etc. In the remaining 10% of cases it leads to Weils disease and if left untreated can be life threatening and result in kidney failure[9]. In South Africa it was reported that a prisoner died due to leptospirosis as a result of a large rat infestation in the prison. In fact, more than 4000 prisoners had to be evacuated because of a failure to adequately control the rodent population[10].

A recent outbreak of Lassa fever in the North of Nigeria, has led to 82 causalities since August 2015. The fever is caused by rodent excreta and particularly to a West African commensal rodent from the genus *Mastomys*[11].

Coumatetralyl has been shown to be effective at controlling rats in urban and rural environments and therefore reducing the risk of disease transmission to humans and preventing a serious danger to human health.

ii. Transmission of diseases to animals

Modern humane systems of animal husbandry, which often rely on constant access of domestic stock to food, are highly prone to rodent infestation because it is impossible to prevent rodent access to them. Rodents carry a wide range of diseases that are transmitted to farm animals, some further transmissible to man; including cryptosporidiosis, campylobacter, salmonella, avian flu and Hanta viruses. It is a requirement of audit systems applied in animal husbandry across the EU that rodent infestations are absent from animal husbandry facilities.

Coumatetralyl has been shown to be effective at controlling rats on farms and therefore reducing the risk of disease transmission to animals. In a study by Endepols et al.,[12] rat-control strategies were examined on 25 farms (with 21 farms producing swine, 9 farms keeping dairy cattle (7 with bulls), and a few keeping chicken, horses or goats.) in Velen (Muensterland), Germany, where an average of 20% of trapped rats were resistant for bromadiolone according to a blood-clotting response (BCR) test. Baiting points were furnished with 200 g of rat bait, checked by the farmers after 3–4 days, and refilled. Baiting points that showed rat activity were tended once to twice weekly for up to 4 weeks. Baits used were Bayer's Racumin Paste (0.0375% coumatetralyl) and Rodilon Pellets (0.0025% difethialone). On 5 farms, the coumatetralyl based product was used alone and resulted in complete eradication of the population. Control success clearly depended on the distribution of baiting points according to the proposed scheme, independent of signs of rat activity.

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[6] http://www.leptospirosis.org/animals-species-at-risk
[7] https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/404107/hpr0515_zoos.pdf
[8] http://www.pasteur.fr/fr/institut-pasteur/presse/fiches-info/leptospirose
[9] http://www.nhs.uk/Conditions/Leptospirosis/Pages/Symptoms.aspx
[10] http://www.ghanaweb.com/GhanaHomePage/worldNews/Rats-chase-thousands-from-prison-in-South-Africa-383009

[11] http://www.who.int/csr/don/27-january-2016-lassa-fever-nigeria/en/
[12] Endepols, S., Klemann, H, Pelz, H-J., Ziebell, K-L. A scheme for the placement of rodenticide baits for rat eradication on confinement livestock farms. Preventive Veterinary Medicine 58, 115-123 (2003).

Controlling rodent populations adequately on farms prevents transmission of diseases to animals and prevents a serious danger to animal health.

iii. Consumption of foodstuffs intended for humans and animals

It was estimated in the UK that rats consume ~ 210 tonnes of food per day. This does not take into account food spoiled by rodents but not eaten, which normally occurs in far greater quantity.

iv. Soiling and spoilage of human and animal food and feedstuffs

In addition to losses caused by direct consumption, rodents' soil with urine, faeces and hair much more than they actually consume.

v. Damage to property, products and infrastructure

Rodents damage property and installations wherever their populations occur. Damage to electrical cables causes power outages and fires and damage to water pipes and sewage conduits causes flooding and the requirement for costly reconstruction. In domestic properties, rodents damage heat insulation, electrical wiring, wooden fittings and personal possessions.

It was estimated that in the United Kingdom, the costs to the economy of damage to infrastructure by rats could be between £61.9 million and £209.0 million. It was concluded that, based on the size of the rodent control industry, the higher figure was more likely[15]. Moreover, the damage caused by rats in Budapest, Hungary, was estimated at between US$ 6.4 million and US$ 8.5 million annually between the years 1978 and 1985[13].

vi. Public abhorrence and social implications

Because of the diseases they carry, and their association with filth, rodents are generally regarded with abhorrence by the public. Although mouse allergen is known to cause occupational asthma in laboratory workers, its potential significance in home environments has been underplayed. Through testing, 89 (18%) of 499 inner-city children were shown to be sensitised to mice[14].

Based on the information above it is considered that Coumatetralyl, and the AVKs, are essential for human and animal health and therefore meet the criteria specified in Article 5(2).

b. Would the loss of the AVKs, including Coumatetralyl, have a disproportionate negative impact on society when compared with the risk?

Battersby[15] noted that in order to properly assess the socio-economic effects of rodents the following aspects need to be considered:

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[13] Bonnerley, X., Kampen, H., Sweeney., K. Public health significance of urban pests. World Health Organisation (2008).

[14] Phipatanakul W, Eggleston PA, Wright EC, Wood RA; National Coooperative Inner-City Asthma Study. Mouse allergen. II. The relationship of mouse allergen exposure to mouse sensitization and asthma morbidity in inner-city children with asthma. J Allergy Clin Immunol 2000;106(6):1075-80

[15] Battersby, S., Public health policy – can there be an economic imperative? An examination of one such issue. Journal of Environmental Health Research, Volume 3, issue 1 (2004).

It is clear that no single study has assessed all of the above elements to determine the economic impacts that rodents have in one MS or within the EU overall. Work has been done on examining some of the effects and a summary of some of this work is outlined below.

Salmonella and *Campylobacter* are generally regarded as the most important food-borne pathogens in the world. Reduction or elimination of these pathogens in the first part of the food chain (on the farm) is important to prevent disease among consumers of animal products[16]. Within the summary by Meerburg and Kijlstra[16] further references are made on the links between rodents and these food-borne diseases:

In the EU and Norway in 2002 a total of 145,231 cases of human salmonellosis were reported (38 cases per 100 000 inhabitants). A total of 149,287 cases of human campylobacteriosis were reported in the EU and Norway in 20028 (39 cases per 100,000 inhabitants) [17].

Rodents can be long-term sources of *Salmonella* infection: it was found that 3-week-old chicks can acquire infection via mice artificially infected with *S. enteritidis* 2 and 5months previously[18]. The presence of rats on farms has been associated with an increased risk of *Campylobacter* introduction into broiler houses[19].

Besides health problems, economic losses due to human infection with *Salmonella* and *Campylobacter* are also considerable. In a study on the socio-economic impact of infectious intestinal disease in England, average costs per case were £606 for *Salmonella* and £315 for *Campylobacter*[20]. This would equate to a cost of £135 million in 2002 for the EU and Norway.

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[16] Meerburg, B.G. and Kijlstra, A., 'Review of rodents in transmission of salmonella and campylobacter'. Journal of the Science of food and agriculture, 87, 2274-2781 (2007).

[17] Trends and sources of zoonotic agents in animals, feedingstuffs, food and man in the European Union and Norway in 2002. *SANCO/29/2004*, European Commission, Health & Consumer Protection Directorate-General, Brussels (2004)

[18] Davies RH and Wray C,. Mice as carriers of *Salmonella enteritidis*on persistently infected poultry units. *Vet Rec* **137**:337–341(1995).

[19] Kapperud G, Skjerve E, Vik L, Hauge K, Lysaker A, Aalmen I, *et al*, Epidemiological investigation of risk factors for *Campylobacter* colonization in Norwegian flocks. *Epidemiol Infect* **111**:245–255 (1993).

[20] Roberts JA, Cumberland P, Sockett PN, Wheeler J, Rorigues LC, Sethi D, *et al*, The study of infectious intestinal disease in England: socio-economic impact. *Epidemiol Infect* **130**:1–11 (2003).

In a study assessing the effect of invasive species, Pimentel *et al.*,[21] explained that on farms, rats and mice are particularly abundant and destructive. They note that the US has an estimated 1.25 billion rats and that an individual adult rat causes US$ 15 of damage per year. This equates to causing equivalent to US$ 19 billion per year worth of damage. Pimentel *et a*l estimate a cost to the UK economy of damage from rats as 4.1 billion (estimation based on 4.6 rats per capita and US$ 15 damages/rat per year).

Battersby[15] stated that the total costs due to infrastructure damage by rodents were difficult to estimate. However, a model was constructed that estimated the cost to the economy of such rodent damage in the UK could be between £61.9m to £209m. The study indicated that the size of the rodent control industry in the UK indicates that the higher figure is more likely.

A summary of a report published in Pest magazine in December 2014[22] indicated that the cost of pest infestations to British businesses was £1.2 billion. It also found that more than 92% of British companies had suffered with pest problems over the past five years. Rats and mice were the most troublesome pest with 52% of companies having suffered a mouse problem in the past five years and 39% a rat problem. The impact of these infestations varied but a third (33%) of business owners said they had affected staff morale and 20% that the pests had damaged goods. 82% of the businesses taking part in the survey were aware that pest problems had increased their operating costs. But it wasn't just direct financial losses that were associated with pests. 55% of businesses said they had suffered a loss of at least one working day and just over a quarter (26%) had recorded the loss of at least five working days each year.

Although, no study has fully assessed the socio-economic effects of rodent damage it is clear that they have a significant impact on local businesses and the economy overall[23]. With risk mitigation measures (RMMs) appropriately applied, as detailed on current labels and in the risk mitigation measures report[25] the benefits of the coumatetralyl outweigh the risks.

5. ALTERNATIVES TO COUMATETRALYL

a. The Second Generation Anticoagulants (SGARs)[2]

This group include the active substances brodifacoum, bromadiolone, difenacoum, difethialone and flocoumafen, are capable of controlling rodents that are resistant to the first generation anticoagulants but are more acutely toxic and persistent in the environment.

b. Fumigants[2]

[21] Pimentel, D., McNair S., Janecka J., Wightman J., Simmonds C., O'Connell C., Wong E., Russel L., Zern J., Aquino T., Tsomondo., T. Economic and environmental threats of alien plant, animal, and microbe invasions. Agriculture, Ecosystems and Environment 84 (2001) 1–20

[22] Pest Magazine, issue number 42, December 2015 and January 2016. http://www.pestmagazine.co.uk/en/pest-magazine

[23] http://www.sudouest.fr/2015/06/15/bordeaux-les-souris-aiment-les-caneles-la-preuve-en-images-1952149-2780.php, http://www.evous.fr/Les-rats-de-Paris-et-d-Ile-de,1145320.html, http://www.sciencedirect.com/science/article/pii/S1201971211001305

Fumigants such as hydrogen cyanide and aluminium phosphide have to be used by specifically trained individuals.

Aluminium phosphide cannot be used in proximity to buildings because it works by the evolution of a toxic gas which cannot be fully controlled when it has been produced. Although valuable in some circumstances, this property makes aluminium phosphide inappropriate for most rodent control situations in the urban environment and in many rural environments.

Hydrogen cyanide can only be used in hermatically-closed structures.

c. Carbon dioxide[2]

This substance is currently restricted for use only against mice indoors. It is dispensed using a special automatic application device which is appropriate only in limited practical use situations.

d. Powdered corn cob

This substance is relatively new to the EU market and works by affecting the rodent's digestive system. Practical experience with its use is very low.

e. Alphachloralose

This substance is only approved for use against mice at temperatures below 15°C. The mice die as a result of hyperthermia . Its use is, therefore, only suitable in certain restricted circumstances.

f. Cholecalciferol[25]

Cholecalciferol has been recently submitted as a new active substance to the EU. It is not yet approved for use and recent experience with its use is low.

g. Alternatives to rodenticides

i. Rodent Traps

Rodent traps can be an effective way to control small rodent populations, particularly mice.

Break-back traps work by snapping onto the rodent and killing it instantly. In some case however, the rodent is not killed but severely injured and they can cause unnecessary suffering. In addition, they are known to cause shyness to rats in an established colony and therefore are not recommended for effective population management of rats.

Electronic traps work by luring the rodent into a box where it is electrocuted. They can be quite expensive if you have more than one or two rats or mice.

Live capture traps that if checked frequently that the captured rodent can be released unharmed. Any captured animals must be killed humanely in some countries it is illegal to translocate and release them[2].

In summary, controlling large rodent populations with traps is often seen as difficult and expensive.

ii. Glue boards

Glue boards are very simple forms of trap that contain an adhesive which the rodent sticks too and cannot escape. They do not kill the rodent automatically and if the rodent is left it can cause unnecessary suffering. This is because the rodent tries to escape and can bite itself in order to become free. They must be checked regularly (at least every 12 hours) and therefore can be an expensive option for rodent control. Due to their ability to cause unnecessary suffering they are often considered as a last resort in high risk environments[24]. They also create shyness among rat population and therefore it limits their use for practical population management of rats.

iii. Pest repellents

Repellents containing substances such as peppermint oil and garlic are available on the EU market. Currently these active substances have not been assessed to the requirements of the BPR for their effectiveness.

Ultrasonic rodent repellents are available on the market. These products emit a high frequency and high intensity sound which cannot be detected by the human ear. There is limited information available on their effectiveness as a rodent control technique.

iv. Rodent proofing

Proofing of building and structures is vital to prevent rodent ingress. It should form an important part of any integrated pest management approach (IPM). The use of biocides is minimised when effective rodent proofing has taken place[2].

Rodent proofing can be expensive for many low income families and can be difficult to do in many buildings on farms. In addition, some materials are easily gnawed by rodents e.g. plaster

v. Habitat modification

Rodents require food, harbourage and in the case of rats water to survive. Removal of all of these requirements will eliminate or reduce the rodent population[2].

6. CONCLUSIONS

In the RMM report, prepared by independent experts and published by the European Commission on anticoagulant rodenticides in October 2014[25], the Authors noted there is no evidence that effective chemical alternatives to anticoagulant rodenticides will be available in the next 5 years, (no results anticipated before 2020). The same report identifies the features of an ideal rodenticide and then concludes that 'It will be difficult to find a rodenticide that can meet more of the above features than the anticoagulant rodenticides' and also that 'alternatives to AVKs are limited today.'

For any IPM approach for rodents to be successful there must be complete removal of water, food and harbourage. In addition, buildings should be proofed to prevent rodent ingress. Small infestations of rodents may be adequately controlled using traps but require expertise in placing the traps in the correct locations. However, in order to ensure that these products do not cause rodents

[24] http://www.pestmagazine.co.uk/_attachments/resources/183_s4.pdf
[25] European Commission (2014) Risk Mitigation measures for anticoagulant rodenticides as biocidal products. https://circabc.europa.eu/sd/a/352bffd8-babc-4af8-9d0c-a1c87a3c3afc/Final%20Report%20RMM.pdf

unnecessary suffering they need to be checked regularly (twice a day), a resource intense investment.

Rodenticides are important tools of IPM and should be considered as part of any rodent control management plan.

The FGARs, particularly Coumatetralyl, offers an interesting and valuable solution for rodent control in light of their favourable environmental profile, in comparison the SGARs. In addition, Coumatetralyl offers products formulated as a foam and a bait, which offer complementary solutions for effective and rapid rodent control. Use of such products requires less resources than other solutions – increasing the speed of gaining control. In conclusion, based on the information provided above, Coumatetralyl, meets 2 of the 3 derogations given in Article 5(2) of BPR and therefore should be re-approved under the BPR.