Summary of positions of Stakeholders and Interested Parties in response to HPRA consultation on whether a change to the classification of the products concerned is needed to fulfil the requirements of the relevant EU legislation (Directive 2006/130/EC and Regulation 2019/6).

4 September 2019

The Task Force would like to thank all parties that engaged in the consultation that was conducted between 20 May and 21 June 2019. The survey was communicated to all marketing authorisation holders of veterinary medicinal products authorised by the HPRA, as well as stakeholders and interested parties, including farm, veterinary and pharmacy organisations, trade organisations, animal breeder organisations and other representative bodies. Responses were anonymous, although in a few cases the name of organisation making the response was self-declared within the response itself.

Overall there were 39 responses to the electronic survey, but not all respondents addressed every question. In addition, eight written submissions were separately received; many of these submissions were from the respondents who had also completed the on-line survey (in some cases this was self-declared). Furthermore, it is also clear from the wording of a number of the survey answers that there was a degree of coordination between a few of the individuals concerned. Most of the respondents focussed solely on resistance to anthelmintic drugs, rather than wider resistance in ectoparasites and coccidia.

The responses, including those made in written submissions, are summarised below. Wording in italics indicates direct quotations from individual responses. Note that the summary represents a general overview of the responses so that not every comment or reference cited is mentioned below.

Q.1 What would be the likely benefits, if any, associated with maintaining the current regulatory supply channels for antiparasitic veterinary medicines in food-producing animals? What evidence do you have to support the answer given?

There were 20 positive and 18 negative responses to this question.

Respondents who believed that the current regulations in place for antiparasitic medicine in food producing animals identified several benefits to support this viewpoint:

- Competitive pricing of products,
- Wide product choice from a variety of outlets, that are located throughout the country,
- Ease and timeliness of access to products by farmers,
- Traceability of products used,
- Low levels of residues in analysed food samples,
- Products are available in licensed merchants by a trained, 'Responsible Person'. These individuals have access to a wide range of resources provided by pharmaceutical companies and other bodies to maximise the quality of advice available to farmers,
- The potential for retailers and pharmaceutical companies to '*take ownership of knowledge transfer'* of best practice of antiparasitic medicines on farms [to educate end-users],
- Maintaining the current system would avoid the need to establish new systems and to [have to] educate users and prescribers accordingly.

Concerning those who have a contradictory opinion, most considered current regulatory supply channels for antiparasitic veterinary medicines allowed '*far too easy access without proper advice*'. The issue of resistance was raised by several respondents as a consequence of such use. Some considered that product price was the major driver amongst farmers for product choice and that the current system provided for greatest competition. However, it was stated that the result of such a system where product margins at retailers were lower than those available to vets was uninformed use, overuse and misuse,

One respondent considered the low price of antiparasitic veterinary medicines as one of the drivers of drug misuse '*the fact that a farmer can treat a 500 kg animal for 50 cents with an ivermectin results in widespread and indiscriminate use of these products'*.

It was stated that beekeepers could not afford to have a veterinary prescription, and might start accessing and using drugs illegally if that was to happen.

Limited scientific evidence in direct support of the positions cited was provided. One respondent quoted levels of compliance from the National Residue Control Plan reports from 2010 to 2017 as evidence for the high standard of traceability. The same respondent cited a reference by Charlier *et al.*[1] 2016 who advised that economic factors are not the sole driver of animal health decisions on farms. The authors of the paper advise that several diagnostic tools and methods are now available to assess the economic impact of helminth infections on dairy cattle farms, and they recommend that anthelmintics should be used on the basis of relevant diagnostic tests to prove the need and efficacy of treatment and to guide decision-making in the case of resistance.

Q. 2 What would be the expected risks, if any, associated with maintaining the current regulatory supply channels for antiparasitic veterinary medicines in food-producing animals? What evidence do you have to support the answer given?

Twenty-eight respondents cited the continuing development of anthelmintic resistance as an expected risk, as well as risk to consumers from residues due to misuse. One respondent opined that the products concerned were being supplied '*as commodities'* and that '*worming programmes [were] not planned in the majority of cases, but decided on price and non-scientific advice'*. Others considered that there are risks for not only resistance, but also regarding environmental risks, especially with long-acting anthelmintics. Others considered that an inadequate appreciation of how pour-on formulations should be properly administered could lead to under-dosing due to animal grooming. Other respondents opined that a significant proportion of farmers currently receive poor or no advice when purchasing antiparasitic products from licensed merchant outlets, and that there was poor understanding of rotation of anthelmintic drug classes or the epidemiology of the parasites involved. One opined that licensed merchants or other vendors might have limited knowledge of specific animal health issues on farms, or might not engage in discussion on parasite control at the point of sale, and this could possibly lead to misuse of antiparasitic drugs. Some felt that resistance would lead to reduced production efficiency on Irish farms as well as reduced welfare standards and a decline in farm profitability.

Nine respondents considered that there would be minimal risk with maintaining the current regulatory supply channels. For evidence, respondents gave the following reasons:

- General satisfaction amongst farmers for the products and services available to them currently,
- The existence of the current system for training and qualification of Responsible Persons,
- Growing awareness amongst farmers through media coverage and recent Teagasc publications on anthelmintic resistance,
- Research from the UK by Easton *et al.*[2] which showed equivalent knowledge of basic helminthology, best practice guides in anthelmintics intended for livestock and horses, and relevant dispensing legislation amongst veterinary practitioners and specially qualified persons.

[1] Charlier, J., De Waele, V., Ducheyne, E., Van Der Voort, M., Vande Velde, F. and Claerebout, E. 2016. Decision making on helminths in cattle: diagnostics, economics and human behaviour. Irish Veterinary Journal. 69; 14.

[2] Easton, S., Bartley, D.J., Hotchkiss, E., Hodgkinson, J.E., Pinchbeck, G.L., Matthews, J.B., 2016. Use of a multiple choice questionnaire to assess UK prescribing channels' knowledge of helminthology and best practice surrounding anthelmintic use in livestock and horses. Preventative Veterinary Medicine. 128; 70.

However, the authors of the reference point out that interpretation should be carried out with caution due to 'the poor response and completion rates [of the multiple choice online survey] and the unknown quality of knowledge in those who did not perform or complete the test'.

- *'Ultimately, it is the farmer that administers the product, so it was his/her responsibility to ensure correct use'*.

One respondent advised that neither the licensed merchant (LM) nor the prescription route of supply system could prevent improper anthelmintic use and considered that supply should be based on diagnostic tests with relevant advice. Other respondents felt that the basis of current system could be improved though education, diagnostic testing, and better communication / knowledge transfer. One respondent considered that '*the lack of a formal reaccreditation/continuous education system means that the knowledge level of responsible persons may vary, which could lead to inappropriate/outdated advice being given.*'

Q.3 What would be the likely risks, if any, associated with restricting antiparasitic veterinary medicines to prescription control? What evidence do you have to support the answer given?

Twenty-six respondents perceive possible risks with restricting antiparasitic veterinary medicine to prescription control. The main risks identified were:

- Reduction in competition, leading to increased prices in the cost of medicines. It was stated that currently only 26% of the products are supplied through vet practice channels and removing the products from LM outlets would lead to increased cost and inconvenience for farmers. It could also create a vested interest for the prescriber or anti-competition practices by vets who might promote the highest margin product rather than the most appropriate one,
- Less frequent worming of animals leading to animal welfare issues, as farmers would wait until a visit by a veterinary practitioner rather than paying separately for a veterinary prescription,
- Diseased animals or bees being left untreated,
- Sub-clinical infestations becoming established with consequential impact on animal productivity,
- Reduction in the number of products available, and possibly also in the number of retail outlets supplying the products,
- Development of a black market or on-line purchase, as farmer buyer groups or individual users would access medicines outside the State illegally,
- There might be a lack of sufficient numbers of veterinary practitioners in certain rural areas, thereby hampering access by farmers,
- Corporate veterinary practices or '*motorway vets'* supplying product without advice,
- Resistance to change by farmers, as such a decision is expected to be politically and commercially unpopular to vested interests,
- Reduction in employment opportunities for Responsible Persons, with a negative effect on the rural economy,
- Use of ineffective alternative feed supplements that carried claims for parasite control,
- Farmers might '*abdicate responsibility for mitigating the risk of anthelmintic resistance'* to the prescribing veterinarian.

Eight respondents foresaw no risks with implementing antiparasitic veterinary product restrictions. One respondent considered that '*veterinary practitioners … operate at much longer opening hours so access to medicine would not be compromised'*. Another pointed out that veterinary practices are present in every rural town in Ireland and antiparasitic products on sale there were as competitive as other retail outlets. Yet another pointed out that restrictions on the products concerned already operate in other EU countries and this was evidence of its feasibility. One respondent advised that restricting the supply of antiparasitic products to veterinary prescription-control would not change practices in parasitic

control that favour the development of resistance, such as dose-and-move and preventative blanket treatment.

Limited specific scientific evidence was submitted by respondents to this query e.g. Dillon *et al*,[3] 2018, Vande Velde *et al*.[4] 2018.

Q.4 What would be the likely benefits, if any, associated with restricting antiparasitic veterinary medicines to prescription control? What evidence do you have to support the answer given?

Twenty-seven respondents foresaw the potential benefits associated with restricting antiparasitic veterinary medicines to prescription control as:

- Reducing the risk of inappropriate or unnecessary use,
- Reducing antiparasitic resistance,
- Improving the quality of advice and implementation of best practices and health programmes on farm,
- Improving the standard of care of animals, where the correct dosage and drug substance is given,
- Reducing the risk of misuse due to a lack of knowledge about differential diagnoses amongst farmers regarding other possible causes of ill thrift and diarrhoea,
- Enabling better recording of product supply, thereby facilitating better monitoring and research,
- Compliance with the relevant EU legislation on the supply of veterinary medicinal products that are used for food-producing species.

Seven respondents did not see benefits. Another two felt that appropriate use of diagnostic tests was needed irrespective of where the products were obtained. One respondent drew attention to a UK paper (Easton *et al*, 2016, see footnote 2) which, under the conditions of the survey, showed a similar level of knowledge with regard to anthelmintic products and parasitology between those vets and specially qualified persons who had responded to the questionnaire.

Q.5 Without prejudice to the outcome of this review, should the weight of evidence lead to a conclusion that antiparasitic veterinary medicines no longer meet the criteria set out in Directive 2006/130/EC, how best should the change to prescription control be made (timeframe, logistics etc.)? What evidence do you have to support the answer given?

The respondents provided varied answers to this question, although nearly all respondents focussed on anthelmintic resistance rather than resistance to ectoparasiticides or coccidiostats. Sixteen respondents advised that a relative long transition period of perhaps 3 or 4 years would be appropriate for reasons such as to:

- Provide pharmaceutical companies with the time needed to make changes to their marketing authorisations, product labelling etc.,
- *'Take into consideration veterinary medicinal products that currently have expiry dates to 2023',*
- *'Allow for changes to supply chain',*

[3] Dillon, E. J., B. Moran, J. Lennon, and T. Donnellan. 2018. Teagasc National Farm Survey 2017 Results. Teagasc.

[4] Vande Velde, F., J. Charlier, L. Hudders, V. Cauberghe, and E. Claerebout. 2018. Beliefs, intentions, and beyond: A qualitative study on the adoption of sustainable gastrointestinal nematode control practices in Flanders' dairy industry. Prev Vet Med 153:15-23.

- Allow for sufficient time for an educational campaign and advice to be provided to all relevant parties,
- Allow for the development of national infrastructure on laboratory diagnostics,
- Allow for training of vets
- Allow for further consultation with interested parties/associated changes in legislation.

Ten respondents felt that any change should be carried out as quickly as possible or within two years given the increasing risk of anthelmintic resistance, risk of stockpiling by farmers and/or political backlash. Seven advised that a phased transition should be carried out over a few years. Three respondents opined that there was a need to maintain the broadest possible number of retail outlets, and in the event that a prescription would be required that licensed merchants should be allowed to dispense the products concerned. One respondent opined that the time needed to put in place the necessary infrastructure for diagnostic techniques should inform the timeline needed for any transition. One respondent advised that an all-industry approach to co-design a sustainable parasite control programme that mitigates the risk of the development of resistance was needed, and highlighted such an approach in relation to an udder health programme undertaken by dairy farmers (Devitt *et al.*[5] 2013) and its success in reducing somatic cell counts (Graham,[6]2016).

One respondent advised that their organisation had raised concerns in relation to the potential eventuality of anthelmintics requiring a prescription with the Department of Agriculture, Food and the Marine some years ago, and had been reassured on the point.

One respondent proposed that compliance with a veterinary prescription should be part of the Bord Bia quality compliance check. Another respondent advised that an exemption from any requirement for prescription would be needed for products for honey bees, due to the costs in obtaining a veterinary prescription.

Q.6 Are there any other relevant facts or scientific evidence that you wish to bring to the attention of the Task Force?

Eight respondents considered that there were no other relevant facts to be considered. Four respondents considered that evidence-based prescribing should be the goal, opining that prescribing behaviours of veterinary practitioners were not always based solely on clinical factors, but on non-clinical factors such as perceived client expectations to receive the product Gibbons *et al.*[7] (2013). There is '*no reason to assume that a similar pattern would not arise for the prescribing of antiparasitic medicines if this was their sole route of supply*'. These respondents also believe that some cooperatives are providing excellent service through routine bulk milk antibody testing, its faecal egg count testing services, promoting the responsible use of parasiticides, and raising awareness about antiparasitic resistance and medicines residues to farmers. One respondent opined that information from anthelmintic herd screening tests that are currently being undertaken by a service provider are not being widely used by veterinary practitioners to guide decision-making in the choice of an appropriate

[5] Devitt, C., K. McKenzie, S. J. More, K. Heanue, and F. McCoy. 2013. Opportunities and constraints to improving milk quality in Ireland: enabling change through collective action. J Dairy Sci 96(4); 2661

[6] Graham, D. 2016. National Cattle Health Programmes- an Irish Perspective. Proceedings of the 29th World Buiatrics Congress; 66.

[7] Gibbons, J.F., Boland, F., Buckley, J.F., Butler, F., Egan, J., Fanning, S., Markey, B.K. and Leonard, F.C., 2012, Influences on antimicrobial prescribing behaviour of veterinary practitioners in cattle practice in Ireland. Veterinary Record 172; 14.

anthelmintic for the farm. Another respondent opined that resistance is present or widespread both in countries with unrestricted access to anthelmintic as well as in countries with restricted access and that restricting supply would not change usage/behaviour *per se* (Becher *et al.*,[8] 2018, Mooney *et al.*,[9] 2009, O'Shaughnessy *et al.*[10], 2014, Geurden *et al.*,[11] 2015, Keegan *et al.*,[12] 2015, Martinez-Valladares *et al.*[13] 2015, Novobilsky *et al.*[14] 2016, Pena-Espinoza *et al.*[15] 2016).

Two respondents drew parallels with lessons regarding the control of antimicrobial resistance and advised that targeted, selective treatment should be the goal. Two respondents suggested that an interdepartmental / multi-stakeholder approach, such as that operated for animal disease control by Animal Health Ireland, offered a good model to ensure engagement and voluntary application of best practice. Another respondent advised that use of behavioural change science was key for success; legal instruments on their own would not achieve the desired outcome. Yet another respondent advised that in an ideal world the prescriber should not be the same person as the dispenser. Another respondent advised that the responsible persons dispensing the products should undergo independent accreditation in order to unsure objectivity and to avoid undue influence by pharmaceutical companies wishing to promote their own products.

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[8] Becher, A. M., D. C. van Doorn, K. Pfister, R. M. Kaplan, M. Reist, and M. K. Nielsen. 2018. Equine parasite control and the role of national legislation - A multinational questionnaire survey. Vet Parasitol 259; 6.

[9] Mooney, L., B. Good, J. P. Hanrahan, G. Mulcahy, and T. de Waal. 2009. The comparative efficacy of four anthelmintics against a natural acquired Fasciola hepatica infection in hill sheep flock in the west of Ireland. Vet Parasitol 164(2-4); 201.

[10] O'Shaughnessy, J., B. Earley, J. F. Mee, M. L. Doherty, P. Crosson, D. Barrett, R. Prendiville, M. Macrelli, and T. de Waal. 2014. Detection of anthelmintic resistance on two Irish beef research farms. Vet Rec 175(5); 120.

[11] Geurden, T., C. Chartier, J. Fanke, A. F. di Regalbono, D. Traversa, G. von Samson-Himmelstjerna, J. Demeler, H. B. Vanimisetti, D. J. Bartram, and M. J. Denwood. 2015. Anthelmintic resistance to ivermectin and moxidectin in gastrointestinal nematodes of cattle in Europe. Int J Parasitol Drugs Drug Resist 5(3); 163.

[12] Keegan, J. D., O. M. Keane, L. Farrell, W. Byrne, T. de Waal, and B. Good. 2015. Characterisation of ivermectin and multi-drug resistance in two field isolates of Teladorsagia circumcincta from Irish sheep flocks. Vet Parasitol: Regional Studies and Reports 1-2; 3.

[13] Martinez-Valladares, M., T. Geurden, D. J. Bartram, J. M. Martinez-Perez, D. Robles-Perez, A. Bohorquez, E. Florez, A. Meana, and F. A. Rojo-Vazquez. 2015. Resistance of gastrointestinal nematodes to the most commonly used anthelmintics in sheep, cattle and horses in Spain. Vet Parasitol 211(3-4); 228.

[14] Novobilsky, A., N. Amaya Solis, M. Skarin, and J. Hoglund. 2016. Assessment of flukicide efficacy against Fasciola hepatica in sheep in Sweden in the absence of a standardised test. Int J Parasitol Drugs Drug Resist 6(3); 141.

[15] Pena-Espinoza, M., S. M. Thamsborg, M. J. Denwood, M. Drag, T. V. Hansen, V. F. Jensen, and H. L. Enemark. 2016. Efficacy of ivermectin against gastrointestinal nematodes of cattle in Denmark evaluated by different methods for analysis of faecal egg count reduction. Int J Parasitol Drugs Drug Resist 6(3); 241.