

Commission proposal to include biocides used in animal husbandry in the legislation replacing Council Regulation 2377/90/EC establishing procedures for setting MRLs for veterinary medicinal products

This paper is to help discussion on this issue, and is not necessarily the UK's definitive view at this point.

The proposal

1. To include in the replacement of Council Regulation 2377/90 rules and procedures for establishing Maximum Residue Limits (MRLs) for residues of pharmacologically active substances in biocidal products used in animal husbandry. These may be present in food of animal origin.

Summary

2. It is recommended that biocides are removed from the proposal until the way forward is clearer. Substances which have a pharmacological/physiological action in the species in which they come into contact would be regarded as veterinary medicinal products (vmpps). Whilst it is logical that these substances should be evaluated by EMEA it must be recognised that there will be large areas of dossiers for biocidal products (eg environmental toxicity) which fall outside the remit of a vmp, and will therefore need new data.

3. Where data does exist, there are different concentrations in products at which the same substance can become pharmacologically active and therefore need MRLs. This will be the case between vmpps and biocidal products, and as there is no simple "read across" between products for a pharmacologically active substance the biocides products will potentially require a great deal of extra work.

4. In view of the funding and resourcing questions that have arisen it is recommended that the steps at the end of this paper are followed to clarify the position before committing MSs to obligations which we are unable to quantify at present. This will also make the position clearer on whether the EMEA's legal remit needs to be extended to include biocidal products in addition to evaluating medicinal products.

Background

5. Council Regulation 2377/90 lays down a Community procedure for the establishment of MRLs of vmpps in foodstuffs of animal origin. Annex V sets out the information to be included in an application for the establishment of a MRL for a pharmacologically active substance used in veterinary medicinal products. This includes a wide range of toxicological studies such as teratogenicity, mutagenicity and carcinogenicity. Other areas such as metabolic studies and residues studies are also included.

Regulatory Authority procedures for setting an MRL for a **veterinary medicinal product**, and funding

6. Pharmaceutical companies wishing to apply for an authorisation are legally required to provide fees to cover the cost of the work. If it is a centralised application, the payment will be made to the European Medicines Agency (EMA). The Committee for Veterinary Medicinal Products (CVMP), will then appoint a rapporteur Member State (RMS) and co-rapporteur from its members. The EMA pays the CVMP members for their work on an application. If it is a decentralised or mutual recognition application, the applicant nominates the Reference Member State (RMS) and will pay the relevant fees to the RMS and the Concerned Member States. In the case of national applications, the pharmaceutical company will pay the Regulatory Authority direct.

Evaluation work currently carried out on **biocide active substances** (including those with pharmacologically active substances), and funding

7. The Biocides Products Directive (98/8/EC) requires that all Member States recover the costs they incur in operating the regulatory process, with the cost of the work involved in evaluating an Active Substance dossier for a clearly identified customer being recovered by means of a fee. The evaluation work is carried out by the Member State Competent Authority (CA). In the UK this is the Health and Safety Executive (HSE). The fees for the evaluation of biocide active substances are not harmonised across the Community – some countries charge more than the UK; some charge less.

8. The evaluation work at this stage does not involve providing data specifically for setting an MRL. It follows that the fee charged does not therefore cover any further work that will be needed to set an MRL and withdrawal period.

The need to set MRLs for some active substances in biocides

9. Council Directive 98/8 sets out the legal framework for biocides and includes the need for a process in setting MRLs. Article 10.2(ii)(b) in particular allows the establishment “where relevant” of MRLs. There is no current legal framework to allow this to be taken forward in practice.

10. The Commission advises that it is very difficult to give an estimate of the number of substances under Council Directive 98/8 that will require MRLs. The Commission has suggested that around 60 substances may need to be evaluated. However, they believe that is a “worst-case” scenario, and it is more realistic that only 15-20 of those substances will actually need MRLs. Nevertheless, some work will have to be completed on all 60 substances to establish whether an MRL is needed or not.

11. Biocidal products are not intended to end up in the food chain after being used in connection with animal husbandry. They are not injected directly into food producing animals, and for those products such as teat dips

that may be applied directly to the skin of an animal it is anticipated that MRLs have already been set.

The Commission's preference for moving forward on setting MRLs for biocide active substances used in animal husbandry

12. The intention in Article 9(1)(c) of the proposal is that the Commission or Member States may forward to the EMEA requests for an opinion on MRLs for substances in biocidal products that are not intended for use in veterinary medicinal products. (This will presumably include data generated by companies and considered by MS Competent Authorities in producing evaluations/authorisations for biocides with pharmacologically active substances.)

13. The EMEA would then require Member States to volunteer to act as rapporteur or co-rapporteur in the same way as currently happens for veterinary medicinal products. It will be for the EMEA to recommend whether an MRL is needed for a biocide active substance.

14. The Commission is unclear on how the funding or resourcing of this will work. Clearly, the EMEA and MSs taking the lead in assessing dossiers for MRLs will face a resource issue, and very possibly conflicting priorities, in taking forward biocide active substances in addition to veterinary medicinal products. There is also no clear way forward on funding the EMEA and MSs if the biocides company is not required to submit data and pay a fee to the EMEA.

15. Factors in favour of EMEA taking this forward;

- no need to set up a new Agency/unit within the EU Chemicals Agency along the lines of the EMEA to consider biocides used in animal husbandry,
- it is unlikely that many new substances would emerge, which would make a new Unit almost redundant once it had considered the current substance list
- the EMEA is more likely to be clear about the quality and quantity of data that is needed to guarantee confidence in the MRL/withdrawal period,
- having the EMEA and MS vmp experts assess pharmacologically active substances in biocidal products ensures a consistent approach and avoids duplication
- the biocides sector working in isolation could result in different MRLs being set for the same pharmacologically active substance used in vmps and biocidal products.

16. Factors against the EMEA taking this forward

- the options for funding EMEA and MS involvement in setting MRLs have not been explored. The funding and resourcing positions are totally unclear, and need resolving first.
- the Commission believes that the workload for EMEA and MSs assessing substances for MRLs will be “very small” but there is no evidence to support this. Setting an MRL for biocides active substances needs to be a painstaking process, along the lines of setting those for vmps, if it is to be taken seriously by consumers and other stakeholders
- if there is a rush of biocide active substances needing assessment in the same timescale as veterinary medicinal products how do the EMEA and MSs cope in terms of prioritising in view of the funding and resourcing issue? Who decides the priorities? Presumably priority will be given to vmps, as these companies fund the EMEA and MS work. However, all applications will be subject to the same timescales if biocides are included in the legislation replacing Council Regulation 2377/90.

17. There are other factors which need to be considered in setting MRLs for biocide active substances

(i) Setting an MRL will also require a withdrawal period to be established to ensure safe usage of the product. This will be essential if a residues surveillance programme is introduced to monitor proper use of biocides with pharmacologically active substances.

Withdrawal periods will also be essential tools in deciding the level of action that is proportionate in the event of an accident leading to a food safety incident/emergency situation.

(ii) In the case of biocides the evaluation should be linked to a marketing authorisation, in the same manner as vmps. This would place a responsibility on the applicant company to provide the toxicological and other data for evaluation. Article 9(1)(c) of the proposal requires the Commission or Member States to do this, but unless the company provides the data to them it is difficult to see how they can do so, or, indeed, why they should.

18. Requiring the company to provide the data to acquire the Marketing Authorisation also means it takes full responsibility for the safety of the product, which puts them on the same footing as most other businesses engaged in producing and selling goods.

Discussion

19. There is logic in the EMEA taking on responsibility for evaluating biocides with pharmacologically active substances used in animal husbandry.

This avoids incurring expense in setting up a new Unit similar to the EMEA and the possibility of different standards being set for vmps and biocides containing the same active substance.

20. There are, however, very serious concerns about how the system would work. It seems illogical for the Commission/Member States to approach the EMEA with the request to determine whether an MRL is needed, and highly unlikely that the Commission/Member States could provide the comprehensive package of data likely to be required for an MRL (and withdrawal period) to be set with the necessary confidence required by consumers and stakeholders in general. Will an incentive be needed to encourage companies to provide the necessary comprehensive data?

21. There is also the issue of funding/resourcing the EMEA's workload (which is not yet quantified) and the work of the (probably few) Member States taking the lead in assisting the EMEA. The current funding arrangement covers only the evaluation work carried out by MS Competent Authorities in producing the Completeness Check for authorisation. This would not cover the EMEA and Member States carrying out the subsequent work checking safety and other data needed in setting an MRL and withdrawal period.

22. This could be a significant problem if, as the Commission indicates, about 60 substances require evaluation to decide if an MRL is needed. Whilst it is accepted that only 15-20 substances will probably need MRLs it will still be necessary to evaluate all 60 substances.

23. A logical approach is therefore needed to establish how much work is involved, including establishing how many of the pharmacologically active substances have already been evaluated in vmps. Indeed, should the biocides with pharmacologically active substances be classified as vmps anyway? Council Directive 2001/82 says a vmp is;

“any substance or combination of substances presented as having properties for treating or preventing disease in animals; or

any substance or combination of substances which may be used in, or administered to, animals with a view either to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis.”

Directive 2001/82 also says at Article 2.2 “In cases of doubt, where taking into account all its characteristics, a product may fall within the definition of a “veterinary medicinal product” and within the definition of a product covered by other Community legislation, the provisions of this Directive shall apply.” This would seem to present a strong case for any biocidal product with pharmacological activity to be regulated as a vmp.

Proposed way forward

24. It is suggested that the following steps are taken;

- (i) biocides are removed from the proposal for the moment,
- (ii) consideration should be given as to whether biocidal products with pharmacologically active substances should be classified as vmps,
- (iii) the biocides review starting in 2008 should formally consider whether it is appropriate to have a split in the legislative arrangements for biocides (ie, should those with pharmacologically active substances needing MRLs be covered by this legislation, and other biocides covered by Directive 98/8?),
- (iv) the list of active substances which may require MRLs is completed by the Commission. It would also be helpful if this list (i) estimated for each substance when it is likely to be ready for evaluation for an MRL and withdrawal period, and (ii) which Member State Competent Authority was responsible for studying the Active Substance dossier,
- (v) establish through EMEA/volunteer Member States which of the pharmacologically active substances already have a substantial body of data,
- (vi) on the basis that this will give a realistic estimate of the amount of money and resources needed to establish MRLs and withdrawal periods, produce a strategy for funding the work,

(this could be through the company with the Competent Authority authorisation applying to the EMEA for an MRL and EU Marketing Authorisation if there is not much further work required. Alternatively, if a great deal of further work is required the company can then choose between going to the EMEA, or making a national application (not necessarily choosing its own Competent Authority for this work). This could then go to Mutual Recognition.)
- (vii) prior to any applications going forward to EMEA, if the decision is to split the biocides between different legislation (see (ii)) then a separate section for biocides needing MRLs can be introduced into the replacement for Council Regulation 2377/90.
- (viii) the remit (and funding arrangements if necessary) of the EMEA should be amended in Council Regulation 726/2004, unless it is decided that biocidal products with pharmacologically active substances should be classified as vmps.
- (ix) it has been mentioned at Council Working Group that biocides with pharmacologically active substances should be part of a residues surveillance programme. There is merit in this idea, and this should be pursued as part of the revision of Council Directive 96/23 in due course.