Introduction

The UK welcomes this discussion paper from the European Commission, which we hope will stimulate discussion and find a harmonised way of moving forward. There have been many significant developments in Community legislation in recent years in all aspects of veterinary medicines, including setting MRLs, authorisations and surveillance. These developments have, as the Commission paper points out, led to a need to produce solutions to balance consumer protection, animal health, animal welfare and trade requirements in this important area. The UK is keen to take an active and constructive role in helping to determine new measures, where appropriate, to achieve a responsible balance in meeting these priorities and ensuring a level playing field for all stakeholders in these areas.

The UK stresses the need to ensure that consumer protection becomes a key consideration, in addition to the correct usage of veterinary medicines, when amending the regulatory framework for residues in foodstuffs.

In response to the ten main questions on which comments and proposals are sought, the UK interim comments are set out below. We may wish to refine these in the coming weeks;

- **Structures for the appropriate differentiation of risk assessment and risk management for the evaluation and control of residues in food of animal origin**

Section 4 of the Commission paper discusses the differentiation of “risk assessment” and “risk management” in the control of residues. It is clear from the discussion that the requirements of Commission Regulation 2002/178 as regards risk analysis will have a significant impact on this area. These requirements must be implemented by 1 January 2007 and will have an impact on the implementation of Commission Regulation 2377/90. Suggested changes to the Annexes of 2377/90 are set out in later paragraphs.

Whilst it can be argued that the process of setting an MRL is in its totality a risk assessment, the UK notes that the CVMP has set out in general terms which stages of the MRL setting procedure it considers to fall under the heading of "risk assessment" and which under the heading of "risk management" (EMEA/CVMP/187/00). To aid transparency, these general points could be incorporated into new MRL summary reports simply by modifying the CVMP guideline. Existing summary reports do not contain any reference to risk assessment, but there would be little to be gained from applying this process to existing summary reports, as the Commission’s paper indicates on page 17. The UK therefore supports this approach, except, of course, where a new and valid risk is identified which requires previous assessments to be re-visited.
It is clear from the reflections paper and the comments above that this is an area requiring further attention and that the EU appears to be moving closer towards the Codex approach to risk assessment. With the relatively recent accession of the EC as a member of Codex, the UK suggests that this is an ideal opportunity to adopt a more proactive role towards the CCRVDF to bring greater cohesion and synergy between the work being carried out on setting MRLs. It is to be hoped that the end benefit of this is more areas where the Codex and EU MRLs are the same, thereby improving international harmonisation of trade and consumer protection.

The parallel structures of the Commission and the EFSA, where risk assessment and risk management are separated are perhaps a model to be followed in differentiating between assessment and management. However, the UK acknowledges that in practice it is difficult to completely separate risk assessment from risk management, as seen for example with the problems with semicarbazide in baby food.

- Procedures for the extrapolation of maximum residue limits

The CVMP considered this issue in its guidance document EMEA/CVMP/187/00 and concluded that considerable extrapolation was acceptable. In principle the UK supports extrapolation, recognising that such an approach could benefit areas such as the honey industry. However, before taking such steps, there are several factors which need to be considered. Crucial among these is the need to critically examine the robustness of the data supporting the original MRL from which the extrapolation is to be made. There needs to be a very sound basis for determining the ratio of marker to total residues. Without this basis it is particularly difficult to provide a view on violative residues when asked to do so.

There are areas where the EU has not set MRLs. The UK therefore suggests that in cases where other regulatory authorities, countries or international organisations have set MRLs, a procedure could be adopted whereby the EU authorities responsible for veterinary medicines would have the opportunity to see if they could accept those MRLs. However, this must be on the basis that the scientific basis and risk assessment work in setting them are sufficiently robust to merit their adoption.

There has, over the years, been a move towards setting different MRLs for the same analyte/matrix combination in different animals. This has tended to lead to a rather confusing picture, and, whilst recognising the difficulties posed by the inter-species differences in metabolism, the UK suggests that these areas are reviewed to see if the position can be simplified.

- Procedures for the provision of reference points for control purposes

The procedures required in this area will vary according to the current classification of the residue, i.e. the Annex of Council Regulation 2377/90 into which the substance has been placed.
Annex I

This annex is straightforward and should be retained in its present format. If, as discussed above, a procedure is adopted for the EU accepting MRLs set by other regulatory authorities, then it is suggested that these form a new Annex to distinguish between those set by the EU and those set by others. Placing them in separate Annexes will show which have gone through the EU regulatory process, and in the case of “adopted” MRLs, where the data scrutinised has not been as extensive as under the EU process but is nevertheless sufficient for the EU to accept the MRL. It should, of course, be made clear that all of the MRLs are applicable across the EU and to third country trade entering the EU.

Annex II

It is for discussion whether reference points are necessary in this Annex, which covers substances for which it is considered no MRL needs to be set. Some substances (although not many) in Annex II have ADIs or other indications of acceptable levels, for example normal dietary intakes. It is suggested that it would make sense to re-organise the information in Annex II, as the categories currently used are not particularly helpful. One proposal for a different order might be to sub-divide the Annex into sections relating to the CVMP’s criteria for inclusion. This would help monitoring authorities to identify substances which need no MRL when used in the normal way but which might be harmful if used in other ways, and which might therefore need to be monitored.

The Commission paper highlights the implementation of Regulation 2377/90, particularly with regard to the summary reports of the scientific evaluation of substances allocated to Annex II. In the UK, the independent Veterinary Residues Committee (VRC) is strongly of the opinion that Annex II as a concept cannot be defended and that every product with an authorisation should have a MRL. The Committee recognises that dossiers may not always be complete, particularly for substances with limited use. However, the Committee advocates the use of the concept of “Threshold of Toxicological Concern”, which it suggests is finding application in other areas and might allow a default ADI to be set for any substance even with no experimental data. However, this should be based on sound scientific reasoning. At the other extreme if a product is demonstrated, in suitable studies, to have no adverse effects, even at high doses, an upper default value for an ADI may be applied. However, to make this approach workable, adequate consumption data on all products likely to contain the substance of interest must be available and should cover not only the UK but also across the EU.

Annex III

The UK suggests the future of Annex III should be discussed. This annex sets provisional MRLs whilst queries relating to the validity of analytical methods submitted with applications are resolved. We understand that Annex III is used infrequently now, and, as discussed later in this paper, it will be worthwhile exploring other options of ensuring analytical methods appropriate for large-scale surveillance programmes are available.
Annex IV

Substances placed in Annex IV should not be present in edible tissues produced in Member States, or contained in produce imported into the EU. These substances are in Annex IV because, as the Commission paper states, their evaluation revealed that residues of these substances in food at whatever limit constitute a hazard to the health of the consumer. In consequence, no safe limit can be set and food containing the smallest amount of these residues is considered unfit for human consumption. Equally clearly, it is impossible to measure "none" – it is only possible to measure "something" or "less than something". In view of the fact that the objective is effectively zero, it is vital that the "something" is as low as possible so that "less than something" is as close to zero as possible.

It is recognised that the analytical methods used to determine the presence in food of Annex IV substances such as chloramphenicol and nitrofurans have become increasingly sophisticated since 1990. This is to the extent that some Member States can confirm the presence of chloramphenicol in some foodstuffs at concentrations of less than one part per billion.

The UK supports the proposal that there should be an agreed European limit as to what value is acceptable for the lowest measurable concentration for substances contained in Annex IV. These limits should be reviewed at regular intervals (possibly every two years) to check whether, in the light of methodological developments, the limit should be amended. It is also suggested that there should be measures in place to ensure that surveillance results for these banned substances are clearly reported and explained; i.e. that there were residues present, but that residues were so low that there is no evidence of illegal use of a substance. (See also the comments on MRPLs later in this section.)

Substances not listed in Annexes I-IV

It is suggested that consideration is given to preparing a list of all substances which have been evaluated by the CVMP but for which no MRLs were set because of insufficient information. This list should include brief details of the data deficiencies. The information needed to do this should be readily available, as the CVMP has approved status reports for all substances which fall into this category. These status reports have never been made public but consideration could be given to whether this policy should change. It may be that a company might be prepared to provide the missing information if they knew what it was. Alternatively, if it was considered that there was a great need for a specific substance, consideration could be given to the possibility of providing EU funding to fill the data gaps, although the circumstances under which this might be done would have to be carefully defined. The list of substances in this category could be incorporated into a new Annex to the MRL regulation so that there is openness about the status of the substances.
It is also suggested that for substances which were placed in Annex I for only some of the species originally envisaged it might be more difficult to identify what data were missing for the species which were excluded. In the interests of extending MRLs to other species, it would be beneficial to identify the data gaps. Again these substances should be officially identified in an Annex to the MRL regulation.

In some cases the only missing data relate to validation of the monitoring method. It is open to discussion whether this should be a valid reason for not granting an MRL. Most methods are not suitable for large scale surveillance programmes, and their absence are therefore not significant. However, it is noted that the CCRVDF currently requires a validated analytical method which has been collaboratively trialled in a number of laboratories before granting an MRL.

The wider issue of the relevance of the analytical methods provided by companies in support of the MRL must also be considered, as the methods are designed to be both sensitive and highly specific. Such methods would find no application in a routine surveillance programme where the need is for high throughput, multi-residue methods. Perhaps a way forward in future would be to request “class specific” methods with proven sensitivity/selectivity for the range of substances to be considered? From a consumer safety point of view the UK suggests that it would be preferable to have more information on the ratio of marker: total residues, than on the monitoring method.

The outcome of Review 2001 opens up the possibility for standardising withdrawal periods where none are set for analyte/matrix combinations. The UK also notes that, in effect, Commission Decision 2000/68/EC permits the use in horses of substances not contained in Annexes I, II or III of Council Regulation 2377/90, provided a six month withdrawal period is observed. The UK suggests that this concept could be extended to other areas after a careful case by case analysis in order to increase the availability of medicines.

Substances having more than one authorised use

A further area not addressed in this reflection paper concerns the potential for active substances to have more than one authorised use. For example, some active ingredients of feed additives can also be used as veterinary medicines. In these cases, it will be difficult to be certain that the residue arose from veterinary medicinal usage if found in national surveillance programmes, particularly as MRLs are now being set for feed additives. The UK believes that the present position, whereby an MRL is set for a product rather than a substance, will prove very confusing, with a substance potentially having several different values. A similar issue where substances have more than one authorised use arises with some veterinary medicines which may also have pesticide use, such as thiabendazole.

Minimum Required Performance Limits (MRPLs)

The UK agrees with the concept of setting MRPLs for substances which do not have any other guideline (such as an MRL) in order to establish harmonised levels for
detection of the use of such substances. However, the UK is concerned that the purpose of the MRPL is misunderstood in many areas, and is keen to ensure that all Member States and third countries are in agreement on how products containing substances with MRPLs are dealt with after their presence is confirmed. This will ensure a level playing field which the UK recognises is one of the aims that the Reflections paper is seeking to achieve.

MRPLs have been set for substances which are not permitted for use in the EU in animals and animal products for human consumption. These substances are therefore not permitted in products exported to the EU. The UK is concerned that MRPLs are being seen as tolerance/action levels in some areas, and therefore the presence of a substance with an MRPL in produce is thought by some to be acceptable provided it is below the MRPL. There may be the unwanted effect that the MRPLs are actually encouraging the use of these substances in some cases. This is perhaps also partly because of the marked similarity between the acronyms MRL and MRPL.

The UK is also concerned that MRPLs are being set on the basis of advice from CRLs on the analytical limit of detection they feel all Member States should achieve for a particular substance, rather than any safety data. Whilst the UK recognises that these levels are necessary to harmonise analytical detection levels and trade it is a concern that these MRPLs are being set without any rigorous assessment of their safety, which is in marked contrast to the stringent requirements that have to be met before legitimate active ingredients are authorised. The position is then exacerbated by the increasing number of substances which are being given MRPLs, which increases the levels of banned substances appearing in the “food basket” on which Acceptable Daily Intakes (ADIs) are set for legitimate products.

The issue of how to deal with products in which the presence of non-permitted substances with MRPLs are found needs to be clarified. The UK independent Veterinary Residues Committee has recommended to the UK Government that all results where the presence of these substances are found should be reported, regardless of whether the confirmed presence is above or below the MRPL. The UK is of the opinion that retailers and their suppliers will wish to be aware of those cases where these substances have been found below the MRPL to enable those parts of the food chain to decide if they wish to continue obtaining their products from the same source. The Committee also feels that the consumer should be aware of these findings to help them make more informed decisions when purchasing. The VMD is continuing to notify the Chief Veterinary Officer in the country of origin of all confirmed findings of non-permitted substances, and it follows that the UK supports the issue of Rapid Alerts in all these cases. The position is more straightforward where non-permitted substances are confirmed above the MRPL.

Surveillance for Annex IV substances has identified unexpected analyte matrix combinations such as nitrofurans in honey which is not covered by current MRPL legislation. There is the potential for Member States to adopt different thresholds for enforcement action - some apply the MRPL set for other foodstuffs while others adopt the LOD. Further clarification/guidance might be included within the legislation to ensure a consistent approach to enforcement across the EU.
Procedures for precautionary measures for substances in imported foodstuffs

The UK feels that the Rapid Alert system that the Commission has in place to warn Member States of potential issues related to imports of animal derived foodstuffs functions well.

It is suggested that the intelligence obtained from Rapid Alerts and FVO Missions is used to enable countries to put in place contingency arrangements in the event of a crisis situation, or, preferably to prevent a crisis situation arising. The issue of several Commission Decisions over the past couple of years requiring immediate and large-scale testing of certain imports for chloramphenicol or nitrofurans has placed a strain on the analytical capacity in several Member States. If it is not being done already, it is suggested that the Rapid Alert information is collated by foodtype, substance and country of origin to enable Member States to assess the risk from imports into their countries, and ensure that their laboratories have the appropriate validated methods and capacity to deal with issues of concern.

There have been a number of occasions where the Commission has issued helpful advice to the UK on matters of interpretation of legislation, particularly regarding the restrictions on imports of products of animal origin from China. The UK appreciates the Commissions timely responses, and recommends that to promote consistent enforcement approaches across the EU such advice is published and disseminated to all Member States.

Unfavourable FVO report findings have the potential to raise concern among consumers and the media. To demonstrate that consumer health is being protected and ensure that consumer confidence is not undermined it would be helpful if DG SANCO were to make public, in a timely manner, its views about the implications for consumer health of adverse report findings, and its intentions as regards protective or other measures.

Procedures for short-term risk assessments in crisis situations

The crisis situation can be either a local food safety incident within a Member State, or a wider national crisis owing either to a problem with domestic production or imported produce. In each case it is important to have robust procedures for such assessments in order to safeguard consumers and animal welfare. MRLs are set on the basis of potential daily exposure, and the MRL summary report therefore rarely contains any useful information about effects following short-term exposure. However, in a crisis situation, it is information on effects resulting from a short-term exposure that is primarily required for a risk assessment. There is a common assumption that if a certain degree of exposure is acceptable on a daily basis, then a higher level of exposure is automatically acceptable on an occasional basis. This is not necessarily a safe assumption – for substances with allergic or pharmacological effects the single safe exposure dose would be as low as the safe repeated exposure dose.
In order to provide the information needed for such urgent risk assessments, the MRL assessment process would need to include more information on short-term exposure and this would have to be made available to monitoring authorities.

The value of the role of CRLs in crisis situations was demonstrated by the prompt response to the nitrofurans in poultry scenario in spring 2002, where NRLs were brought together at a workshop organised by the CRL to discuss methodology. Perhaps inevitably some Member States took longer than others to introduce and validate the methodology, and this is perhaps an area where, if they are not already doing so, the CRLs may be able to offer more assistance to an individual Member State to enable it to match the speed of others and ensure a more harmonised response across the EU in responding to an emergency.

- **Procedures for the evaluation of Third Country residue control measures**

The residue control measures in place in third countries are evaluated by FVO inspections. The UK would like to acknowledge the valuable work carried out by the FVO, both in Member States and third countries, which is not discussed in the Reflections paper. The UK has noted that many of the FVO reports focus on the areas that the countries under inspection do not do well, and suggests that the reports should, where appropriate, also pick out areas in which the FVO considers the countries are doing well to give a more encouraging overall picture. We can all learn from best practice in other Member States.

Member States are invited each year to agree the list of countries approved to export produce to the EU on the basis that the produce they export complies with the conditions set out in Council Directive 96/23/EC. However, it is clear from the list of Rapid Alerts that some of the produce imported into the EU from approved third countries does not comply with EU legislation. The UK suggests that if a country exceeds a pre-determined number of breaches of EU legislation in a 12 month rolling period then the country is formally warned that further breaches could result in a ban being placed on their products until the situation improves. This is an area where the production of a list of Rapid Alerts by categories such as country, as described in the previous section, will help in assessments of the residue status of all countries, including Member States.

The UK is aware that the Commission would appreciate help from Member States in assessing third country plans, but that many Member States do not have the resources to offer such assistance. It is an EU legislative requirement that Member States have a national imports surveillance plan, and the UK would like to see cooperation between Member States in pooling intelligence at regular intervals to ensure that testing is targeted in the right areas. It is to be hoped that the Commission could eventually be able to produce an annual report to the European Council and European Parliament on the testing of imports along the lines of the annual report on the surveillance that Member States have undertaken on national produce in accordance with Council Directive 96/23/EC.
The reflection paper notes that Directive 96/23/EC does not set out specific performance criteria for CRLs, nor does it provide a procedure for designating these laboratories. From the perspective of the Veterinary Medicines Directorate, as the Competent Authority for veterinary medicines in the UK, the work of the CRLs has not been transparent. However, the VMD welcomes the paper tabled by the Commission towards the end of last year, which set out the proposed work of the CRLs for 2004. The UK hopes that this will be a regular feature, and that the CRLs can produce a summary of their activity and achievements at the end of each year. If it is not already the case, performance criteria should be established for the CRLs and related to funding to ensure value for money.

The ten new Member States have drawn, and, we expect, will need to continue to draw on the expertise and resources of the CRLs. Some of the new Member States will require considerable assistance with their programmes of analyses, although others will be contracting this out to neighbouring countries where expertise is already established. In addition, there is the added pressure on all Member States to meet the requirements of Commission Decision 2002/657/EC for improved analytical methods. This is therefore an opportune time to consider the benefits obtained from the CRL network and whether or not the current structure is suited to the extra workload.

Feed additives are now subject to MRLs, and this new system will also require the establishment of a CRL to cover this area of work. The CRL to be appointed for this is the Joint Research Centre of the Commission. One of the responsibilities of this laboratory will be responsibility for the testing and evaluation or validation of the analytical method for detecting these feed additives. Firm links between these different areas should be established as part of this proposed overhaul of the veterinary medicines legislation. It would also be appropriate to consider the network of feed additive NRLs yet to be established and how they might interact with the existing residue NRLs – indeed, some NRLs may usefully serve both areas.

- **Procedures for the establishment of plans for monitoring and targeted controls**

Council Directive 96/23/EC currently requires annual residue testing plans to be submitted by 31 March. In practice, several Member States miss the deadline, and it is not unusual for some plans to be agreed in October or later. Indeed in 2003, several plans were sent to Member States for final approval in December. It is also of concern that some Member States are slow in producing their results. The addition of the ten new Member States will slow down the approval process further whilst they gain the necessary expertise. A complete review of this process is required to streamline it.

The UK proposes that the deadline for producing residue testing plans is brought forward to 31 January. This will allow more time for the Commission and Member States to examine plans in the calendar year, which will be essential with 25 Member States. Member States will have to closely monitor their results during the first three quarters of the previous year to enable them to base their plan for the following year on the latest intelligence.
The UK also suggests that the EU programme as a whole should be more targeted to make best use of limited resources. There is a case for dropping the requirements for testing in the analyte/matrix combinations where results have been negative for some time. It had been agreed that testing for thyrostats in poultry can stop but this should be extended to other areas such as growth promoting hormones in poultry and fish. These sample numbers can then either be focused in potential areas of more concern across the EU where it is felt that extra vigilance is needed (eg the use of non-permitted substances) or allowing Member States extra flexibility to test in areas where they feel they may have problems. Rationalising the matrix/analyte combinations will result in a more significant programme which reassures producers (who pay for the surveillance) and consumers that present day veterinary medicine usage is being effectively monitored. The collation of results for the past few years by the Commission is a useful source of information for spotting trends in medicine usage so that the programme can evolve using modern risk assessment techniques.

It is suggested that the Commission adopts an approach based more on risk analysis, which concentrates more on what Member States are doing to monitor the use of Group A and Annex IV substances. Whilst, in an ideal world, it would be helpful to have figures for commodities such as game presented to the Commission in the same format, this diverts time and effort away from the more important areas.

Under Council Directive 96/23/EC Member States are required to sample for substances which are not veterinary medicines. Substances within this group include dioxins, PCBs, lead, cadmium and mycotoxins. The UK suggests that it would be more appropriate to remove responsibility for these substances from a Directive specifically intended to deal with residues of veterinary medicines. The EFSA and related national agencies are developing control procedures in these areas and it would seem sensible to transfer the responsibility to these agencies so that they can control all aspects of dealing with potential sources and exposures to these substances.

The UK welcomes the Commission’s efforts in producing a proposal for harmonising the production of results, and hopes that the end result is simple to use but effective in providing a direct comparison between Member States. Whilst this in itself will be a major step forward, Member States also need to concentrate on harmonising areas such as the analytical methods and the matrices used in individual Member States to enable the most accurate comparisons to be made. The CRLs have an important role to play here in ensuring that best practice arising from the implementation of Commission Decision 2002/657 is disseminated to NRLs in Member States rather than all Member States duplicating time, effort and expense in producing their own versions of methods. This is particularly the case, for example, in determining the concepts of CCα and CCβ.

The UK agrees that targeted controls are essential to ensure that authorised veterinary medicines are used appropriately and the use of illegal substances detected. There appears to be some confusion within the EU over the definition of a targeted sample (as
opposed to a suspect sample), which needs to be clarified. The criteria for choosing a targeted sample also appears to cause confusion.

The current residue programme complying with the requirements of Directive 96/23/EC is, as the reflection paper states, targeted in structure. The suggestion in the paper that a “monitoring” programme may also be required is worthy of further consideration. By rationalising the targeted programme as suggested above, this could result in a smaller, more significant programme and release resources for a supplementary programme of true monitoring. The statutory powers should apply to both targeted surveillance and a monitoring programme.

The Commission’s paper also suggests that the new monitoring programme would need to be based on consumption rather than production figures to estimate consumer exposure to residues. A programme based on consumption figures, will, of course, need to include imported produce as well as national produce to give the most accurate picture. (For example, some Member States import a significant amount of poultry meat from third countries.) It can therefore be argued that the national programmes for testing of imports, which Member States are required to have, will cover part of the new monitoring programme envisaged.

- **Financing of measures of interest to the Community related to food safety**

The high cost of developing a veterinary medicine and the subsequent costs of preparing a dossier for an MRL application, in the knowledge that other pharmaceutical companies can benefit from the MRL when granted, may have reduced the number of new medicines coming forward. Companies developing veterinary medicines are required to provide residue depletion data and analytical methods, and it can be argued that this is their contribution to financing the food safety element of usage of veterinary medicines.

The cost of residue surveillance for veterinary medicines is currently recovered by way of a statutory levy from the relevant commodity sectors. This arrangement will be continued when the financial provisions of the Official Food and Feed Controls Regulations come into effect in January 2007. The UK agrees that this is an area where the food industry is required to meet the cost of surveillance, provided that the costs remain proportionate to the size of the problem. This is an area where it is essential that the Commission ensures that all Member States are implementing the legislation to ensure a level playing field.

- **Residue control specific enforcement measures**

Some of the measures discussed above will aid enforcement (eg where possible setting EU MRLs based on information from other sources).

An area where further discussion would be welcomed is on the analytical issue of “Measurement of Uncertainty” (MU). When deciding on an appropriate action for a positive result, we are advised that the MU must be taken into account. The concepts...
of CCα and CCβ have a good statistical basis but will be affected by the way in which the reproducibility study is conducted during the validation exercise. A harmonised approach on this would make it easier to compare what may appear to be different values when in fact they are effectively the same. However, they are only components of the overall MU surrounding a reported result. The major contributor to MU is sampling and the variability surrounding this. As a result of this, it is potentially possible to obtain a result which is in excess of the decision limit (CCα) but when MU is taken into account, as required by ISO17025, the result drops below the decision limit, with the effect that an action against the violative sample cannot proceed. The CRLs should be requested to take the lead in addressing this issue on behalf of the Commission and Member States.