EUROPEAN COMMISSION

ENTERPRISE DIRECTORATE-GENERAL
HEALTH AND CONSUMER PROTECTION DIRECTORATE-GENERAL

Reflection Paper on Residues in foodstuffs of animal origin

This discussion paper presents points that need to be considered and debated with a view to reconsider and modify Community legislation concerning residues of veterinary medicinal products. The goal is to determine new means to balance consumer protection, animal health, welfare and trade requirements concerning residues of pharmacologically active substance used in veterinary medicinal products in food producing animals.

Existing legislation on pharmacologically active substances used in veterinary medicinal products greatly increased consumer protection but also significantly contributed to the decreased availability of medicines for uses in food producing animals in the European Community. Moreover its construction has lead to various problems related to the implementation and enforcement of legislation related to the control of residues in foods of animal origin. These have also lead to difficulties in the functioning of the Single Market and in international trade.

This paper analyses the reasons for these difficulties and seeks to propose alternative ways to achieve a high level of consumer protection coupled with continued availability and development of veterinary medicinal products for the European market. It does, however, not intent to address every detail of the legislation in force.

The authors of this document are aware of the fact that there are certainly overlaps in respect to current legislation on residues of feed additives and of plant protection products (pesticides). As recent proposals to modify the legislation governing the authorisation and control of residues of these products have been made by the Commission, it is not feasible to cover these areas in this document. It should however be borne in mind that a number of pharmacologically active substances used in veterinary medicinal products are also used as pesticides or feed additives and a co-ordinated approach in supervision of residues in foodstuff should be one of the goals for future legislation.

On the basis of the comments received, the Commission will present a proposal for new legislation on the evaluation of residues of pharmacologically active substances and for their control. This exercise should also bring the relevant legislation in line with the principles of Regulation 178/2002 (‘Food Law’) and would include modification of the relevant legislative instruments, i.e. Regulation (EEC) No 2377/90, and Directive 96/23/EC. The ultimate goal is to have a more consistent approach for the risk analysis

and control of residues of pharmacologically active substances, which may appear in food produced in or imported into the European Union.

The main questions on which comments and proposals are solicited are the following:

1. Structures for the appropriate differentiation of risk assessment and risk management for the evaluation and control of residues in food of animal origin
2. Procedures for extrapolation of maximum residue limits
3. Procedures for provision of reference points for control purposes
4. Procedures for precautionary measures for substances in imported foodstuffs
5. Procedures for short-term risk assessments in crisis situations
6. Procedures for the evaluation of Third Countries residue control measures
7. Procedures for the nomination of Community reference laboratories
8. Procedures for the establishment of plans for monitoring and targeted controls
9. Financing of measures of interest to the Community related to food safety
10. Residue control specific enforcement measures

Please provide your comments no later than **20 March 2004** to the e-mailbox

comments-mrlpaper@cec.eu.int

or in writing to Mr. Philippe Brunet, Head of Unit DG Enterprise F2 and Mrs. Patricia Brunko, Head of Unit D3, DG Health and Consumer Protection, European Commission, Rue de la Loi 200, B-1049, Brussels, Belgium.

TABLE OF CONTENTS

INTRODUCTION

Residues of pharmacologically active substances in food of animal origin are essentially a side-effect of the use of medicines in food-producing animals. They are potentially toxic and consequently unwanted components of food.

Until the mid-1960s the general idea of food safety meant that food should not contain any potentially harmful residues of veterinary medicinal products. This was a realistic goal because at that time residues could only be determined in concentrations of around 1 mg/kg.

Since then the availability and sensitivity of methods of analysis has continuously improved and the detection of concentrations as low as 1 ng/kg are frequently state of the art today. These improvements mean that ever lower amounts of residues are detected, which would previously have gone undetected. Furthermore, the Member States developed threshold values or maximum residue limits on a national basis.

This development led to an increasing awareness of residues of potentially harmful substances in food in general and the demand for legislation that would take this into account. The adoption of the Single Act in 1986 and its call for the completion of the Single Market by 1992 made it necessary to address the issue at Community level. As a measure to harmonise the limits to be respected in residues testing, the Council adopted Community legislation that required withdrawal periods for veterinary medicinal products and/or residue limits for the pharmaceutical active substances.

The resulting legislation still forms the basis for the Community legislative framework on residues of pharmaceutically active substances or veterinary medicinal products in food.

This framework consists mainly of the following pieces of legislation:

Directive 2001/82/EC[1] provides that veterinary medicinal products can only be authorised or used in food producing animals if pharmacologically active substances contained therein have been assessed as safe according to Regulation (EEC) No 2377/90 (see below). Moreover it contains rules concerning on the documentation of use, re-designation ('off label use'), prescription and distribution of veterinary medicinal products intended for use in food producing animals.

Regulation (EEC) No 2377/90[2] ('MRL Regulation') introduced Community procedures to evaluate the safety of residues of pharmacologically active substances according to human food safety requirements. A pharmacologically active substance may be used in food producing animals only if evaluated favourably. If considered necessary for the protection of human health, maximum residue limits (MRLs) are established. They are the points of reference for the establishment of withdrawal periods in marketing authorisations as well as for the control of residues in the Member States and at Border Inspection Posts.

---

[1] Directive 2001/82/EC of the European Parliament and of the Council of 6 November 2001 on the Community Code relating to veterinary medicinal products, OJ L 311, 28.11.2001, p. 1

[2] Council Regulation (EEC) No 2377/90 of 26 June 1990 laying down a Community procedure for the establishment of maximum residue limits of veterinary medicinal products in foodstuffs of animal origin. OJ L 224, 18.8.1990, p. 1, as last amended by Commission Regulation (EC) No 1873/2003, OJ L 275 149, 25.10.2003, p. 9

Rules on food control in general can be found in a variety of Community legislative acts and is at this time under consideration[3]. Additionally **Directive 96/23/EC** ('Residue Control Directive')[4] contains specific requirements, in particular for the control of pharmacologically active substances that may be used as veterinary medicinal products in food producing animals. This includes primarily sampling and investigation procedures, requirements on the documentation of use, indication for sanctions in case of non-compliance, requirements for targeted investigations and for the establishment and reporting of monitoring programmes.

Moreover **Directive 96/22/EC**[5] prohibits the use of certain substances for specific purposes in food producing animals and **Decision 1999/879/EC** prohibits the use of bovine somatotropin for animal health reasons[6].

For completeness it has to be mentioned that none of the legislation mentioned above defines 'food producing animals'. However some indication on how this term is to be interpreted is provided in Directive 64/433/EEC ('Fresh Meat Directive')[7], Directive 96/22/EC and Directive 2001/82/EC.

The current legislative framework also contributed to the decreased availability of medicines for food producing animals in the European Community, a problem that has already been discussed in the *Communication from the Commission to the Council and the European Parliament on the availability of veterinary medicinal products*[8]. Moreover its implementation has lead to various problems related to the control and enforcement of legislation of residues in foods of animal origin including difficulties in intra-Community and international trade.

This framework has been designed in the late 1980s and early 1990s. Since then the Community and international legislation on food safety has developed further. The creation of the Word Trade Organization and the adoption of the SPS agreement[9] have had a significant impact on Community legislation related to international trade. For the

---

3 Proposal for a Regulation of the European Parliament and of the Council on official feed and food controls (COM/2003/0052 final - COD 2003/0030)

4 Directive 96/23/EC on measures to monitor certain substances and residues thereof in live animals and animal products. OJ L 125, 23.05.1996, p. 10

5 Directive 96/22/EC concerning the prohibition on the use in stockfarming of certain substances having a hormonal or thyrostatic action and of betaagonists, and repealing Directives 81/602/EEC, 88/146/EEC and 88/299/EEC. OJ No. L 125, 23.05.1996, p. 3, as amended by Directive 2003/74/EC OJ L 262, 14.10.2003, p. 17

6 Decision 1999/879/EC concerning the placing on the market and administration of bovine somatotrophin (BST) and repealing Decision 90/218/EEC OJ L 331, 23.12.1999, p. 71

7 Directive 64/433/EEC on health conditions for the production and marketing of fresh meat as incorporated by 94/103(51)/EEC,OJ L 1, 3.1.1994, p. 220, last amended by Council Directive 95/23/EEC, OJ L 243, 11.10.1995, p. 7

8 Communication from the Commission to the Council and the European Parliament - Availability of veterinary medicinal products COM (2000) 806 final

9 Uruguay Round of Multilateral Trade Negotiations (1986-1994) - Annex 1 - Annex 1A - Agreement on the Application of Sanitary and Phytosanitary Measures, *OJ L 336, 23.12.1994, p. 40*

Community the re-structuring of legislation initiated by the White Paper on Food Safety and the consequent adoption of Regulation (EC) N° 178/2002 ('Food Law')[10] represent a significant re-orientation of relevant Community legislation to consumer and international trade requirements. Moreover the European Court of Justice has released several rulings relevant in particular to the interpretation of Regulation 2377/90[11].

In consequence it seems appropriate to reconsider the adequacy of Community legislation on residues of veterinary medicinal products.

This paper analyses problems that have arisen in the implementation of the legislative framework in force and the impact of changes in general policies and modifications of basic Community food safety legislation.

1. PROBLEMS ARISING AS A CONSEQUENCE OF THE IMPLEMENTATION AND ENFORCEMENT OF THE LEGISLATIVE FRAMEWORK ON RESIDUES

In order to understand the problems that have arisen in the implementation and enforcement of the Community legislative framework on residues it is central to understand the impact that the introduction of Regulation 2377/90 had on the availability of veterinary medicinal products and the control of residues of pharmacologically active substances that may be contained in veterinary medicinal products used in food producing animals.

The Regulation's goal, as referred to in its recitals, is firstly to ensure food safety and secondly to allow the free movement of food of animal origin within the Single Market. Taking this as a starting point, Regulation 2377/90 has been quite successful as it let to the evaluation of over 700 substances in the last 8 years, more then any other legal constituency or international organisation was ever able to establish. However, it also had an impact on availability of veterinary medicinal products for food producing animals and the operation of food control that was not entirely foreseen at the time its was adopted.

1.1. Impact of the application of Regulation 2377/90 on the availability of veterinary medicinal products

Article 6 of Directive 2001/82/EC requires the inclusion of a pharmacologically active substance in annexes I, II or III of Regulation 2377/90 as a precondition for obtaining a marketing authorisation for veterinary medicinal products for food producing animals. The transitional period foreseen in Regulation 2377/90 came to an end on 1 January 2000. Since then, veterinary medicinal products containing pharmacologically active substances that are not listed in the above-mentioned annexes can neither be authorised nor used otherwise for food producing animals[12]. Existing authorisations containing such substances had to be withdrawn and off label use of medicines authorised for humans or companion animals prohibited.

---

[10] Regulation (EC) No 178/2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety OJ L 031, 1.02.2002 p.1

[11] C 32/00, C23/00, C-248/99, T-212/99, 125/96, T-152/96, C151/98, T-112/97, T-120/96, T-105/96

[12] Article 14 of Regulation 2377/90 and Article and 6 and 11 of Directive 2001/82/EC

As already discussed in the *Communication from the Commission to the Council and the European Parliament on the availability of veterinary medicinal products* this restrictions contributed significantly to the decreased availability of veterinary medicines for food producing species in the Community.

It is primarily up to the pharmaceutical companies to apply for the establishment of MRLs pharmacologically active substances to be included in the veterinary medicinal product under development and to provide all necessary information on potential residue in products obtained from animals that have been treated with these products. Results from pharmacological and toxicological studies and validation of methods of analysis are required. These data include a comprehensive dossier on the pharmacology, toxicology, pharmacokinetics and depletion of residues of the pharmacologically active substance(s) and possibly its (their) metabolites from target tissues to allow elaboration of a maximum safe limit for residues in for example meat, milk, eggs or honey. In addition, an analytical method to detect and quantify the residues at these limits has to be supplied. The high cost of the studies, not only on residues but also of those additionally necessary to obtain a marketing authorisation, has resulted in a certain reluctance of the industry to apply for the evaluation of substances not promising sufficient return on investment. Additionally once the substance has been included in annex I to III of the Regulation, any other pharmaceutical company can make reference to this. In consequence competitors of the companies that paid for the data may introduce a similar product without the need to recover the costs for the residue evaluation of the pharmacologically active substance contained therein.

It has to be mentioned that MRLs are only set for those species (cattle, horses, pigs, laying hens, fish, deer, etc.) and food commodities (muscle/meat, liver, kidney, skin and fat, eggs, milk and honey) for which data have been provided by the applicant. The requirement for species specific MRLs is not laid down in Regulation 2377/90, neither is a definition or subdivision of species or animal types foreseen. The practice gradually crept into the current evaluation process. It has been tacitly confirmed through the adopting of a fee regulation for the European Agency for the Evaluation of Veterinary Medicinal Products (EMEA)[13].

1.2. Impact of the legislative framework on the use of substances in food producing animals (authorisation and prohibition)

Veterinary medicinal products containing pharmacologically active substances intended for use in the European Community have to be authorised according to Directive 2001/82/EC ('decentralised procedure') or Regulation 2309/93[14] (centralised procedure). The requirements for both are laid down in Directive 2001/82/EC. As mentioned above, Directive 2001/82/EC requires the prior classification in annexes I, II or III of Regulation 2377/90 if a substance is to be authorised as veterinary medicinal product or to be used '*off label*' in food producing animals.

The use of substances not evaluated or listed in Annex IV of Regulation 2377/90 in food producing animals is prohibited. Moreover Directive 96/22/EC prohibits - with some

---

[13] Regulation 297/95 on fees payable to the European Agency for the Evaluation of Medicinal Products, OJ No L 35, 15.2.95, p. 1 as amended by Regulation 2743/98,OJ No. L 345, 19.12.1998, p. 3

[14] OJ L 214, 24.8.1993, p. 1, amended by Commission Regulation 649/98, OJ L 88, 24.3.1998, p. 7

exemptions - the use of certain substances for specific purposes in food producing animals and Decision 1999/879/EC prohibits the use of bovine somatotropin.

Therefore the explanation why it is illegal to use a certain pharmacologically active substance in a food-producing animal can de construed from different parts of Community legislation.

1.3. Impact of the application of Regulation 2377/90 on control of residues in food

The maximum residue limits established in Regulation 2377/90 are the point of reference for residue control of food of animal origin. Food that contains residues non-compliant with the limits established in Regulation 2337/90 is considered unfit for human consumption. As mentioned above, at the time of the adoption of this Regulation, MRLs were seen as the measure of choice to ensure food safety with respect to residues of veterinary medicinal products.

However, already at this time it was evident that it would not be appropriate to establish MRLs for every pharmacologically active substance authorised in the Community for use in veterinary medicinal products if the risk assessment procedure established by Regulation 2377/90 was to be based on a full-scale toxicological and residue evaluation.

This was because on one hand it was evident that there were substances used in veterinary medicine for which it would be impossible to establish toxicological end points (concentrations for which in studies no effect is observed) due to their well-known general or particular toxicity. On the other hand it was also evident that many substances were for different reasons (e.g. due to their chemical structure, metabolisation or specific use in the treatment of animals) unlikely to pose a health risk. It was considered exaggerated to require all the detailed studies needed to establish toxicological end points for these substances.

As a consequence, the evaluation procedure established in Regulation 2377/90 provides for three general legal tools to address the potential toxicity of residues of veterinary medicinal products:

1. establishment of MRLs (Annex I and III),
2. approval of the substance without the establishment of MRLs (Annex II) and
3. prohibition of the use of the substance (Annex IV).

A fourth tool was developed during the implementation of the Regulation for substances for which the information was considered insufficient to establish an MRL or tolerate the use without MRL, but the toxicological evidence was not strong enough to definitively prohibit their use. Here the applicant companies often decided to withdraw their applications. In these cases, of which the most famous one is phenylbutazone (a painkiller for horses and cattle) the evaluation could not be completed.

The decision which legal tool is to be used depends mainly on the outcome of the evaluation of the toxicity of potential residues of the pharmacologically active substance in question:

1. The complete prohibition of the substance by inclusion in Annex IV meaning that a maximum residue limit cannot be established because its residues in food constitute at whatever limit a hazard to the health of the consumer. This classification also results in the prohibition of the use of the substances in veterinary medicinal products;

2. The establishment of maximum residue limits by inclusion in Annex I (definitive MRLs) or III (provisional MRLs) of Regulation 2377/90;
3. The renunciation of the necessity to establishment of maximum residue limits by inclusion in Annex II of Regulation 2377/90 or
4. No proposal for inclusion in Annex I – IV of Regulation 2377/90 due to lack of data and unwillingness of the applicant to respond to the questions posed by the Committee for Veterinary Medicinal Products. Such withdrawn applications have produced a group of substances for which no MRLs have been established and use of which is indirectly prohibited since the full implementation of Regulation 2377/90 (from 1 January 2000).

The consequence is that, with respect to tool 1 (prohibition), tool 3 (no MRL necessary) and tool 4, the procedure does not provide a solid point of reference for the evaluation of compliance in the residue control system as no maximum limit is available. The same is of course true for substances for which an application for the establishment of MRLs was never presented.

Moreover MRLs are set for those species (cattle, horses, pigs, poultry, fish, deer, etc.) and food commodities (muscle/meat, liver, kidney, skin and fat, eggs, milk and honey) for which data have been provided by the applicant. As mentioned above, this is because the basis for the evaluation are studies provided by a sponsor or applicant, usually the pharmaceutical company that wants to market a veterinary medicinal product containing the substance. In consequence the evaluation according to Regulation 2377/90 only takes into account the risk that arises from the normal conditions of use of the veterinary medicinal product that contains the substance. It is also usually limited to the uses and routes of administration envisaged in the documentation provided by the sponsor.

The common practice, which has been followed up till now, is not to specify MRLs for those species or types of exploitation (e.g. dairy cows with respect to milk) for which the relevant substances have not been evaluated, i.e. not documented by the applicant.

As described above, the evaluation of pharmacologically active substances according to Regulation 2377/90 assumes that these substances are used legally in authorised veterinary medicinal products. This results in the situation that control authorities find themselves without a point of reference for the evaluation of compliance in the residue control in the following situations:

- A finding of residues of a substance listed in Annex II in food of animal origin: However, substances that do not present a hazard if used correctly can be used incorrectly and potentially lead to harmful residues. A particular group of substances within such potential hazards are some substances produced by the animals themselves (endogenous substances).
- A finding of residues a substance not listed in Regulation 2377/90 because an application for the evaluation of residues was never presented or it was not possible to conclude the evaluation procedure with a positive opinion. A particular case in this class are residues of substances not included in products having a marketing authorisation in the Community for food producing animals, which may be detected in food imported from Third Countries, where these products may be authorised.
- A finding of residues of a substance listed in Annex IV in food of animal origin. These substances were classified in Annex IV because their evaluation revealed that residues of these substances in food constitute at whatever limit a hazard to the health of the

consumer. In consequence, food containing the smallest amount of these residues is considered unfit for human consumption.

– A finding of residues of a substance in species or food commodities for which no MRL was established. However, such use may be in line with off-label use in accordance with Article 10 and 11 of Directive 2001/82/EC in exceptional circumstances.

In the above-mentioned cases, points of reference would, however, be necessary in order to judge whether a substance has been used illegally[15] unless any amount of the respective substance detected is considered non-compliant with Community legislation (*"zero-tolerance" approach)*. In some cases, such as for substances produced by the animals themselves or substances being used also in other fields such as feed additives or plant protection products, this concept to measure compliance is, however, not practicable.

1.4. Impact of Directive 96/23/EC and Regulation 2377/90 on the control of residues

Legislation on the control of food in general can be found in a variety of Community legislation on food. Additionally **Directive 96/23/EC** ('Residue Control Directive') contains specific requirements in particular for the control of pharmacologically active substances that may be used as veterinary medicinal products in food producing animals. The main purpose of Directive 96/23/EC is to provide an effective and uniform system for the monitoring and control of illegal substances or incorrect use of authorised substances in animal products intended for human consumption. In this respect it lays particular emphasis on those substances that have been prohibited due to the rules laid down in Directive 96/22/EC and Annex IV of Regulation 2377/90.

1.4.1. Reference points

According to of Directive 96/23/EC, the maximum residue limits established in Regulation 2377/90 are the tolerances to be applied in food control. As discussed above, the evaluation according to Regulation 2377/90 will in many cases not produce clear points of reference. Such points of reference may on the other hand be needed to decide whether a food containing residues is compliant with Community legislation. In cases where points of reference have not been established, the only safe ground for food inspectors is to apply a policy of "*zero tolerance*". In practice "*zero tolerance*" means not detectable with the method employed and is therefore determined under the competence of the laboratory in charge. Laboratory competence and therefore the actual amount of residues "*zero tolerance*" is associated with, has varied within and between Member States.

---

[15] Illegal treatment is defined Directive 96/23/EC as the "*use of unauthorised substances or products or the use of substances or products authorised under Community legislation for purposes or under conditions other than those laid down in Community legislation or, where appropriate, in the various national legislations*".

Commission Decision 2002/657/EC[16] introduced Minimum Required Performance limits (MRPLs) intended to promote harmonised implementation of Directive 96/23/EC for substances for which no permitted limited has been established. In contrast to MRLs, MRPLs are control tools based on expert advice on feasibility of controls, an 'other legitimate factor' in risk analysis (see Article 6 of Regulation 2002/178/EC 'Food Law'). This may be further developed into a more general framework for reference points for control purposes.

Moreover veterinary medicinal products not having a marketing authorisation in the European Community may be authorised in other countries. This may be because in other regions different diseases or target species prevail or that companies have chosen not to market a product in the Community. Non-authorisation in the Community does not necessarily indicate that the use of these substances is not safe. Nevertheless as there are no reference points established for these substances, any amount of residue found is considered non-compliant. Many Third Countries perceive this requirement as non-proportionate.

2. GENERAL CONTROL AND ENFORCEMENT ISSUES RELATED TO DIRECTIVE 96/23/EC

As mentioned earlier, Directive 96/23/EC includes provisions on:

1. Specific enforcement measures to be taken by Member States in the case of non-compliant results;
2. Planned sampling and analysis, usually addressed as residue monitoring according to national control plans;
3. Provisions related to the authorisation of imports of food of animal origin from Third Countries that may contain residues;
4. Provisions related to the establishment and maintenance of a network of Community and national (Member State) reference laboratories.

2.1. Specific enforcement measures

Directive 96/23/EC provides specific enforcement measures to be taken by Member States in the case of non-compliant results. These measures set out rules for e.g. investigations on farms, restrictions to the slaughter or movement of animals, evaluation and confiscation of products, search and inspection of suspect premises and imposition of penalties.

As mentioned above, the rules on feed and food control are at this time under consideration and will have been profoundly revised once the *"Proposal for a Regulation of the European Parliament and of the Council on official feed and food controls"* has been adopted. The adoption of this measure will call for reconsideration of enforcement measures. This document does for this reason not examine in detail which modifications

[16] Commission Decision 2002/657/EC: implementing Council Directive 96/23/EC concerning the performance of analytical methods and the interpretation of results, OJ L 221, 17.08.2002 p. 8

are needed to bring this part of Directive 96/23/EC in conformity with future requirements.

2.2. Residue monitoring and control plans

Council Directive 96/23/EC requires that Member States submit an annual national residue monitoring plan to the Commission. The national plan approach was already part of the precursor of Directive 96/23/EC[17]. Planned residues control was introduced to harmonise the control of residues in the Member States, thus ensuring a high level of health protection and avoiding disruption in intra Community trade. Directive 96/23/EC expanded the scope of commodities covered by the plans and introduced more detail on the sampling requirements, the residue plan design and the approval procedure. Decision 97/747/EC[18] again broadened the scope of the plans to cover residues most food commodities.

National residue monitoring plans according to Directive 96/23/EC are not designed to assess general consumer exposure to residues, but to reinforce supervision and monitoring with regard to illegal use of pharmacologically active substances[19]. To this end, every Member State proposes annually a residue monitoring plan that takes into account national specificities of animal production and evidence of illegal use of substances. The national plans target the combinations of product/residue to which non-compliance could be linked in the past ('targeted approach').

Incorporation of information and results generated during the year of application of the national residue monitoring plans is theoretically possible, but in practice hardly feasible. Moreover, the rigid timeframe of the adoption procedure and, occasionally delays in the presentation of results, only allow for the consideration of results in the plans 1 to 2 years after they have been established. This is in contradiction to the overall purpose of the targeted residues control. Therefore timeframe and procedure of the targeted residues control may need to be reconsidered.

Annex I of Directive 96/23/EC provides a list of substances that are to be investigated. It also provides a reference for the specific enforcement measures (non-compliance with requirement related to Group A substances is reckoned as more severe) and for the distribution of the tasks of the Community reference laboratories.

---

[17] Directive 86/469/EEC concerning the examination of animals and fresh meat for the presence of residues, OJ L 275, 26.09.1986, p. 36

[18] Commission Decision 97/747/EC fixing the levels and frequencies of sampling provided for by Council Directive 96/23/EC for the monitoring of certain substances and residues thereof in certain animal products, OJ L 303, 06.11.1997 p. 12

[19] including "*off-label use*" as defined in Article 1 (16) of Directive 2001/82/EC as: "*The use of a veterinary medicinal product that is not in accordance with the summary of the product characteristics, including the misuse and serious abuse of the product*" and "*illegal treatment*" defined in Article 2 (b) of Directive 96/23/EC as "*the use of unauthorised substances or products or the use of substances or products authorised under Community legislation for purposes or under conditions other than those laid down in Community legislation or, where appropriate, in the various national legislations*".

The Annex I list is divided in substances whose use is partly or entirely expressly prohibited in food producing animals (Group A), substances that may be authorised for use in veterinary medicinal products for food producing animals ('veterinary drugs' in Group B 1 and 2) and other substances and contaminants. Moreover, some pharmacologically active substances used in animals are also applied as plant protection products (pesticides). In contrast, substances addressed as '*environmental contaminants*' are not related to the general objective of the control plans to control illegal use, because the presence of these environmental pollutants in food is not due to intentional use. In short, the content of Annex I needs to be reconsidered taking primarily the purpose for residue control into account.

Annex IV of Directive 96/23/EC and Decision 97/747/EC determine minimum numbers of samples to be taken according to national residue monitoring plans per animal species. Moreover indications are made with respect to percentages of samples to be taken at different levels of the production chain (e.g. in slaughterhouses, farms). The number of samples is linked to the individual Member States' animal production in the preceding years. It does not consider the relatively small numbers certain animal species in some countries, which may render the current sampling requirements unrealistic (e.g. requiring 0.5 samples for Group A substances), while in countries with larger animal productions minimum requirements are in reality often exceeded.

Targeted sampling should be risk orientated. Risk may shift over time. It may therefore be argued that primary emphasis should be placed on a flexible framework to support the most effective method of detection and control of illegal use. This is because the determination of the most successful strategy will be dependant e.g. on the distribution chain of illegal substances and type of illegal use. Therefore the general sampling strategy may be reconsidered taking the aforementioned views and the overall goal of residue control (harmonised approach to residues control in the Community ensuring a high level of health protection while avoiding disruption in intra Community trade) into account.

It has also been argued that the targeted approach does not provide realistic information on the exposure of consumers to residues and therefore should not be called '*monitoring*' (sampling and testing on a regular or ongoing basis). In order to estimate consumer exposure, a new programme would be necessary. This programme would have to rely on consumption rather than on production figures. It would require that samples are taken randomly according to a consumption related plan and according to statistical considerations. A respective programme would result in additional costs for the Member States.

2.3. Residues in food of animal origin imported from Third Countries

Directive 96/23/EC constitutes the legal link between food imports of Third Countries and the residue legislation of the Community. It requires that Third Countries provide '*guarantees*' that have an '*equivalent*' effect as the measures that are to be implemented by Member States according to Directive 96/23/EC.

The Directive places particular emphasis on the presentation of the Third Country's residue monitoring plan; the requirements are essentially the same as for the Member States national residue monitoring plans. Directive 96/23/EC also requires that Third Countries provide details on their control system and guarantees that products of animal

origin obtained with the help of substances whose use is prohibited in stock-farming in the Community are not presented for import.

However, neither Directive 96/23/EC nor Decision 2000/159/EC[20], adopted to implement the approval of Third Country plans provide specific guidance (e.g. procedure/criteria for the evaluation) on how equivalence is to be determined.

Article 4 of the SPS Agreement defines '*equivalence*' as measures that achieve the importing Member's appropriate level of sanitary or phytosanitary protection. International guidance on the interpretation of equivalence in relation to residues of pharmacologically active substances contained in veterinary medicinal products is available in Codex alimentarius guidelines[21].

Time schedules and transparency of the current process have been criticised and may be reconsidered. However, a more systematic approach would also imply more standardized requirements for the input provided from Third Countries.

Article 13 of Regulation 2002/178/EC ('Food Law') requires that Member States and the Community "*give particular attention to the special development, financial and trade needs of developing countries, with a view to ensuring that international standards do not create unnecessary obstacles to exports from developing countries*" and to "*promote consistency between international technical standards and food law while ensuring that the high level of protection adopted in the Community is not reduced*".

Directive 96/23/EC and Decision 2000/159/EC may be modified in line with Codex alimentarius guidance. Whilst it is not possible to grant derogations to the health standards that are established under Community legislation[22], it should be possible to consider assistance to the least developed countries to provide the requisite guarantees, e.g. phased introduction of the requirements and assistance in the establishment of a control programme and analytical laboratories with adequate competence.

2.4. Laboratory network

Directive 96/23/EC established a Community network of laboratories for residue control involving Community reference laboratories (CRLs), national reference laboratories (NRLs) and routine laboratories designated by each Member State. According to Directive 96/23/EC are to fulfil the following requirements:

- designated as a NRL by a Member State;
- suitable qualified and adequately trained staff to perform the analysis of the substances for which the CRL has been designated;
- possess the facilities to perform the analysis of the substances for which the CRL has been designated;
- have an adequate administrative infrastructure;

---

[20] Decision 2000/159/EC on the provisional approval of residue plans of third countries according to Council Directive 96/23/EC, OJ L 051, 24.02.2000, p. 30

[21] *Codex Guidelines for the Establishment of a Regularly Control Programme for Control of Veterinary Drugs Residues in Foods (CAC/GL 16-1993)* at this time reviewed as draft *Codex Guidelines for the design and implementation of national and border chemical control and verification assurance programs for animal products* and *Guidelines for the design, operation, assessment and accreditation of food import and Export Inspection and certification Systems* (CAC/GL 26/-1997).

[22] Article 152 of the Treaty calls for a high level of consumer protection

- have sufficient data processing capacity to produce statistics and to enable rapid communication of those statistics and other information to NRL and the Commission;
- ensure that their staff respect the confidential nature of certain issues, results or communications;
- have sufficient knowledge of international standards and practices;
- have available an up to date list of reference materials and list of manufacturers and vendors of that material.

The Commission grants financial contributions to the CRLs on a yearly basis to perform the following functions as listed in Directive 96/23/EC:

- to promote and co-ordinate research into new analytical methods and to inform NRLs of advances in analytical methods and equipment;
- to help the NRLs for residues to implement quality assurance system;
- to provide the NRLs with the routine analytical methods accepted during the MRL procedure, with details of analytical methods and the comparative tests to be conducted and technical advice on the analysis of the substances for which they have been designated as CRL;
- to organise comparative tests for the benefit of NRLs;
- to identify residues and determine their concentrations in cases of disagreement between Member States;
- to conduct training courses for national laboratories;
- to provide the Commission services with technical and scientific assistance to compile a report on each year's work and transmit it to the Commission to liaise in the field of analytical methods and equipment with the NRL designated by Third Countries

Directive 96/23/EC does not provide a procedure nor specific performance criteria for the designation of CRLs. However, Article 32 (3) of the Commission's *"Proposal for a Regulation of the European Parliament and of the Council on official feed and food controls"* introduces general requirements that all CRLs will have to comply with. Moreover, with the enlargement of the Community the workload of the CRLs is bound to increase, in particular in relation to the support granted to the increased number of Member State laboratories. Therefore it may be opportune to reconsider the distribution of tasks attributed to CRLs and to verify if the general requirements proposed by the Commission are sufficient for the CRLs fulfilling the specific tasks under 96/23/EC.

3. NON-COMPATIBILITY OF TERMINOLOGY AND DEFINITIONS WITHIN THE LEGISLATIVE FRAMEWORK ON RESIDUES

Due to the fact that the legislation was developed in parallel over a long period of time, the terminology within the legislative framework is not entirely consistent. For example 96/23/EC has a different concept of non-authorised use as that of Directive 2001/82/EC and it is not entirely clear whether the '*farm animals*' in one Directive are the same as the '*food producing animals'* in the other Directive.

4. EVOLUTION OF COMMUNITY LEGISLATION AND POLICY APPROACHES AND RESPECTIVE CONSEQUENCES FOR COMMUNITY LEGISLATION ON RESIDUES

The legislative framework on residues of pharmacologically active substances has been designed in the late 1980s and early 1990s. In the meantime adoption of the SPS agreement of the Word Trade Organization in 1994 has triggered an evolution in the approach on decisions concerning measures to protect public and animal health. Article 2, paragraph 2 and Article 5, paragraph 7 of this agreement[23] require that sanitary measures are based on scientific principles and are not maintained without sufficient scientific evidence, unless, if this evidence is insufficient, provisional measures are adopted.

These provisions brought about more detailed discussions in Codex alimentarius (the reference international organisation according to SPS), which are summarised in the *Proposed Draft Working Principles for Risk Analysis*[24]. Moreover relevant WTO rulings[25] have further interpreted obligations of the SPS agreement.

Both have influenced the Community's approach on decision-making with respect to health protection and in particular the drafting of Regulation (EC) N° 178/2002 ('Food Law'). This recently adopted first overarching framework legislation for food and feed defines food law as *"the laws, regulations and administrative provisions governing food in general, and food safety in particular, whether at Community or national level; it covers any stage of production, processing and distribution of food, and also of feed produced for, or fed to, food-producing animals"*. In consequence the regulatory framework on residues of pharmacologically active substances falls also under the scope of Regulation 2002/178.

Article 6 of Regulation 2002/178 rules that food law shall be based on risk analysis. Article 3 of the same document provides the following definitions:

– *"risk analysis" means a process consisting of three interconnected components: risk assessment, risk management and risk communication;*

---

[23] 2.2: *"Members shall ensure that any sanitary or phytosanitary measure is applied only to the extent necessary to protect human, animal or plant life or health, is based on scientific principles and is not maintained without sufficient scientific evidence, except as provided for in paragraph 7 of Article 5"* and 5.7.:*"In cases where relevant scientific evidence is insufficient, a Member may provisionally adopt sanitary or phytosanitary measures on the basis of available pertinent information, including that from the relevant international organizations as well as from sanitary or phytosanitary measures applied by other Members. In such circumstances, Members shall seek to obtain the additional information necessary for a more objective assessment of risk and review the sanitary or phytosanitary measure accordingly within a reasonable period of time"*.

[24] available on ftp://ftp.fao.org/codex/alinorm03/Al03_33e.pdf

[25] The Decision of the Arbitrators on European Communities - Measures Concerning Meat and Meat Products (Hormones) - Recourse to arbitration by the European Communities under Article 22.6 of the DSU - is being circulated to all Members, pursuant to the DSU. The report is being circulated as an unrestricted document from 12 July 1999 pursuant to the Procedures for the Circulation and Derestriction of WTO Documents (WT/L/160/Rev.1) available on http://www.wto.int/

– *"risk assessment" means a scientifically based process consisting of four steps: hazard identification, hazard characterisation, exposure assessment and risk characterisation;*

– *"risk management" means the process, distinct from risk assessment, of weighing policy alternatives in consultation with interested parties, considering risk assessment and other legitimate factors, and, if need be, selecting appropriate prevention and control options.*

According to Article 4 of Regulation 2002/178 existing food law principles and procedures shall be adapted as soon as possible and by 1 January 2007 at the latest in order to comply with Articles 5 to 10.

The current implementation of Regulation 2377/90 has not always strictly followed this approach and the summary reports of the *scientific* evaluation do sometimes not clearly distinguish between what can be considered risk assessment and risk management, respectively. This is particularly obvious in reports on substances proposed for the inclusion in Annex II of the Regulation. In order to justify that maximum residue limits are not necessary, the evaluation committee follows criteria summarised in a guideline[26]. These criteria are mostly related to the authorised or intended use of the veterinary medicinal product in the framework of the marketing authorisation procedure in accordance with Directive 2001/82/EC, which is currently used as a reference in the risk assessment process. However, other criteria are also mentioned, for example that a substance is endogenous, a normal component of the human diet, generally recognised as safe for humans, used in a small number of animals, infrequent or non-regular treatments or the animal is unlikely to be sent to slaughter immediately after treatment. In this context it may be necessary from a public health point of view to address additional risk management considerations or 'other legitimate factors' in relation to food safety, i.e. in relation to control measures for certain substances currently included in Annex II of Regulation 2377/90.

Any future reorganisation and amendment of the Annexes to Regulation 2377/90, relating to substances with definite entries, should nevertheless not require new applications nor submission of new scientific data in order to meet with the legitimate expectations of marketing authorisation holders for products containing such substances.

Additionally, in the case of clenbuterol[27] it was disputed whether the strict limitation of the use of the substance established in Directive 96/22/EC could limit the validity of the human safety evaluation according to Regulation 2377/90. In its final ruling of 26 February 2002, the European Court of Justice (ECJ) confirmed that Community Institutions could limit or prohibit the authorisation of substances potentially harmful to human health in order to facilitate the control, despite of the fact that the correct use of

---

[26] Criteria for inclusion of substances into Annex II of Council Regulation 2377/90 and extension of Annex II classification to other species. in Appendix I to the Note for Guidance on the risk Analysis Approach for Residues of Veterinary Medicinal Products in Food of Animal Origin (EMEA/CVMP/187/00-FINAL available on www.emea.eudra.org)

[27] Clenbuterol is a substance effective against bronchial asthma, asthmatic bronchitis, chronic and acute spastic bronchitis, pulmonary emphysema and against premature contractions of the uterus in pregnancy that has also growth promoting properties

the substances was safe[28]. In this the ECJ confirmed that feasibility of control is an 'other legitimate factor'.

Article 6 of Regulation 2002/178/EC also establishes that risk management shall take the precautionary principle into account when establishing measures. With respect to the evaluation of residues according to Regulation 2377/90 the only option to appreciate this principle is the establishment of provisional maximum residues limits (classification in Annex III). At present, such provisional measures may only be instituted for a period of maximum seven years (Article 4 of Regulation 2377/90).

As mentioned before, legislation on official food and feed control is under revision, amongst other things to implement an overall 'stable to table approach'. In consequence many official control issues addressed with respect to residues in Directive 96/23/EC will be covered by general control requirements after the new legislation has been adopted. The chapter on control of illegal use of pharmacologically active substances in Directive 96/23/EC will have to be adjusted to these changes.

5. SUMMARY OF THE KEY PROBLEMS RELATED TO THE EXISTING LEGAL FRAMEWORK.

Community legislation on residues of pharmacologically active substances is insufficiently interconnected. In the present legislative framework relevant procedures and legislative tools are distributed over several pieces of legislation. This has lead to contradictions, inconsistencies and numerous difficulties in the implementation of the legislation and it has made unduly complex the weighing of risks and benefits and subsequent selection of appropriate measures to ensure consumer protection, animal health and animal welfare and facilitate trade.

Moreover the tools offered by the current legal framework are may be considered too inflexible. This is particular true for Regulation 2377/90, which requires the final classification of all substances into a specific annex. Furthermore, extrapolation of maximum residue limits from one species to another is not sufficiently considered in the legal framework. Additionally its evaluation procedures are not designed to always provide control authorities with references for enforcement in particular with respect to illegal use. Besides there is no procedure that would allow authorities to establish limits as a precautionary measure or for import purposes only. This contributes to the inflexibility of the Community's approach towards imports from Third Countries established in Directive 96/23/EC. Moreover, the system lacks procedures to deal with crisis situations, in particular with respect to the establishment of short-term risk assessment for certain substances detected in imported food.

The veterinary pharmaceutical companies operating in the Community are responsible for the use of the authorised products in accordance with the terms of the marketing authorisations. The pharmaceutical industry cannot be obliged carry the costs of ensuring the quality of food produced or imported in the European Union with respect to illegal use of substances included in authorised products or substances not authorised for use. Therefore, adequate alternative funding should be allocated for the establishment of reference points for enforcement and appropriate control instruments.

---

[28] Case C 23/2000- Council of the European Union v Boehringer Ingelheim Vetmedica GmbH and C. H. Boehringer Sohn - European Court reports 2002 Page I-01873

Specific enforcement measures for residue control will have to be reconsidered when the "*Proposal for a Regulation of the European Parliament and of the Council on official feed and food controls"* is adopted.

Independently from this exercise, the planned sampling and analysis (residue monitoring according to national plans), the provisions related to the authorisation of imports of food of animal origin from Third Countries and the provisions related to the establishment and maintenance of a network of Community and national (Member State) reference laboratories may be reconsidered.

The introduction of the national plan has improved the residue control in the Community and contributed significantly to the harmonisation of control. Nevertheless the system has also been criticised. This criticism of the system is primarily linked to:

1. the inflexibility of plans and the concurrent impossibility to react to recent residue findings and delay in obtaining and evaluating of results;
2. the list of substances in Annex I of Directive 96/23/EC;
3. the sampling requirements;
4. the inadequacy of the results to estimate Community consumer exposure to residues.

The system should therefore be reconsidered in order to identify an approach that further increases achievements of the overall goals of residue control: harmonised approach to residues control in the Community ensuring a high level of health protection while avoiding disruption in intra Community trade.

Directive 96/23/EC and Decision 2000/159/EC may have to be modified taking Codex alimentarius guidance into account. It should be possible to consider assistance to least developed countries to provide the requisite guarantees.

The laboratory network of the Community consists of four Community reference laboratories (CRLs) that work with national reference laboratories (NRLs) in 15 Member States. Following Enlargement the four CRLs would have to work with the increased number NRLs in 25 Member States. Because of this increase in workload, the distribution of tasks attributed to CRLs under Directive 96/23/EC may have to be reconsidered in the light of the requirements proposed in relation to general feed and food control and the increased workload due to enlargement.

Distribution of current legislative tools to prevent and control residues of pharmacologically active substances over Community Legislation	
authorisation of medicinal products according to specific requirements, including possible restrictions in the conditions of use	2001/82/EC (requirements, procedure) 2309/93 (centralised procedure only)
prohibition of use	2377/90 (Annex IV), 96/22/EC
off-label use	2001/82/EC
distribution of veterinary medicinal products (agriculture equipment shops, pharmacies, veterinarians; documentation and traceability)	2001/82/EC 96/23/EC (documentation) 96/22/EC (specific substances)
withdrawal time/periods	2001/82/EC marketing authorisation and default for off label use 96/22/EC (specific substances)
reference points: permitted limits, (import) tolerances, maximum residue limits, action limits	2377/90 2001/82/EC 96/23/EC and 2002/657/EC
slaughter, catch and harvest restrictions/ identification of animals	96/23/EC 64/433/EC (and other relevant vertical directives)
inspections (pharmaceutical industry, feed industry, pharmacies, veterinarians, sampling and analysis post and past slaughter, catch and harvest)	2001/82/EC 96/23/EC 2000/68/EC 97/747/EC
import restrictions	96/23/EC 72/462/EC 2000/159/EC
laboratory network	91/664/EEC 96/23/EC
measures with respect to non-compliance: investigations on farms, restrictions to the slaughter or movement of animals, evaluation and confiscation of products, search and inspection of suspect premises and imposition of penalties.	96/23/EC (and other relevant general or food product specific Directives)