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Residue control in the European Union, the present and future challenges: Experiences from the Netherlands

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Abstract

Residue control in the European Union has the primary goal to protect consumers from intolerable health hazards which may be associated with residues of veterinary drugs or non-licensed or forbidden substances in animal products. The present situation regarding residue control in the EU is discussed. In the near future Directive 96/23 will be revised and residue monitoring will become more risk based, which will present challenges to laboratories. What are the new risks (compounds), and how can these be effectively identified and controlled? Techniques and matrices will change in the coming years to accommodate this new monitoring system.

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1. The European residue control system

According to Council Directive 96/23/EC[3], the European residue legislation provides for the establishment of a hierarchically structured system of European Union Reference Laboratories (EURLs), National Reference Laboratories (NRLs) and Official Laboratories (OLs)[1]. It also commits the Member States to establish a National Residue Control Plan. Official control in the EU is based also on Regulation EC No. 882/2004[2] on the official

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controls performed to ensure the verification of compliance with feed and food law, animal health and animal welfare rules.

For analysis, the samples should be in compliance with internationally approved procedures and supported by a network of laboratories. The cornerstones (Fig. 1) for residue control consist of a network of laboratories, analytical methods based on performance criteria and quality assurance systems and accreditation. The official laboratories can be either public laboratories, private laboratories or laboratories within Academia. However, they have to be designated by the competent authority in the Member State. They have the task of analysing samples and for this they have to be in accordance with EN/ISO/IEC/17025. They are assisted by NRLs. These NRLs have the task to develop routine methods for monitoring, perform the Quality Assurance for the OLs and coordinate the exchange of information between the OLs. For each task, one NRL is appointed. The NRLs are assisted by the EURLs. There is one EURL for each task. The tasks for the EURL are described in the EU legislation. EURLs act as an interface between the European Commission and the NRLs for technical issues, they develop confirmatory methods, support the Quality Assurance in the NRLs by, for example, organization of Proficiency Testing, they perform arbitration analysis and are a contact for Third Countries.

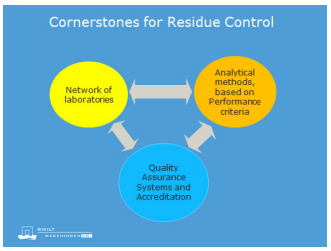

Fig. 1. Cornerstones of Residue control.

2. Results of residue control in the European Union

All Member States are required to report findings from National Residue Control Plans to Brussels before the 1st of April of the following year. The European Food Safety Authority (EFSA) compiles all these data in overall reports. However, the publication of these reports is not very timely; the 2012 report is the latest published[4]. The 2013 report will be shortly available[4a]. In 2012 and 2013, overall, 772540 and 1005835 samples, respectively, were analysed by 27 Member States, and 427193 and 419528, respectively, were collected under 96/23 Commission Decision for residue control. In total 1071 (2012) and 1443 (2013) non-compliant samples were reported. RIKILT, as a EURL, annually evaluates group A hormonal growth promoters. Table 1 shows an overview for the last 3 years.

Table 1. Non-compliant (NC) results in the EU for group A1-A4 compounds. Reproduced from EURL RIKILT data presented during annual workshop, June 2015.

Substance groups	NC 2012	Number of MS	NC 2013	Number of MS	NC 2014	Number of MS
A1 Stilbenes	0	0	3	2	1	1
A2 Antithyroid agents	36	8	68	9	54	7
A3 Steroids						
Androgens	40	3	49	4	50	7
Natural Hormones	0	0	0	0	0	0
Oestrogens	0	0	0	0	9	1
Gestagens	0	0	0	0	0	0

B2f Corticosteroids	68	6	33	7	47	8
Subtotal A3	108	7	82	8	106	12
A4 RALs	16	4	34	3	68	4
Total	160	13	187	13	229	15

An increase is seen in non-compliant results. Underlying this is the problem of (semi) naturally occurring compounds for which no effective control strategy is available at the moment.

3. Challenges in residue control for the future

With the upcoming revision of EU legislation, the National Residue Control Plan monitoring will probably change from the current fixed (production based) program to a more flexible risk-based monitoring. This allows the system more flexibility to focus on different substances and matrices and species depending on the actual risk in each Member State. In the laboratories, changes will also be needed to adapt to this challenge.

3.1. Growth promotors

With respect to the use of growth promotors, there seems to be a tendency to shift from the illegal use of synthetic steroids to the use of esters of natural steroids. For enforcement, it is difficult to determine whether concentrations of, for example, testosterone are physiological, with intra- or inter-individual fluctuations, or are due to illegal administration. New control strategies are put into place. In the recent Reflection paper of the EURL[5], different approaches are described. One is steroid profiling[6], used as a screening method where changes in the steroid profile of an animal, compared to reference profiles, are being picked up. The animals with deviations in their steroid profile will be selected for confirmatory analysis using Isotope Ratio Mass Spectrometry to determine if the testosterone is from a synthetic source[7,8]. These state of the art techniques are currently implemented in a number of NRLs.

On the other hand the detection of the synthetic esters of the steroid in hair[9,10] or serum[10] is direct proof of illegal administration. This, however, requires more effort in sample cleanup for hair or very sensitive methods for serum due to the low circulating concentrations of these steroid esters.

Risks can also come from new groups of growth promotors, eg. peptide or protein growth promotors[11] such as recombinant bovine growth hormone (rBST). Analysis of peptides and proteins in biological matrices is a great challenge compared to small molecule analysis[12]. Next to the targeted analyses for different substances, and untargeted screening and profiling, there is also a need for quick and sensitive on-site test devices. These can be used by enforcement bodies, the sector or industry, to determine to take (more) samples. A nice format is a cell phone-based[13], for biomarkers for rBST in milk. Although at the moment not yet applicable in routine control, in the future, such devices will certainly become available commercially for quick on-site testing.

3.2. Antibiotics

Due to antibiotic resistance issues, governments want to decrease the use of antibiotics in animal husbandry. Although antibiotic sales have decreased over the years, antibiotic residues still occur in biological matrices. For antibiotics there is also a need for quick tests to be used on-farm as control shifts from consumer products to on-farm testing. For analyses, the trend is for more focus on detecting lower concentrations, below the Maximum Residue Limit (MRL), in order to monitor the total use of antibiotics, including the illegal use of forbidden antibiotics. This includes, for example, testing for nitrofurans in bovine animals. For the laboratories this means that besides residue control at MRL levels, sub-MRL testing methods for on-site testing, and methods for new matrices need to be developed to monitor use on farms. For example, analysis of feathers[14] or manure[15] could be useful.

4. Conclusion

With the changes in legislation, substances used and concentrations found, the laboratories need to be better equipped for rapid analysis of a broad package of substances in different matrices. Combining state of the art equipment with clever screening strategies is necessary for effective monitoring in the future. The use of inexpensive on-the-spot-tests in combination with sophisticated techniques in the laboratories will enable successful monitoring and enforcement.

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