LINEAR QUADRUPOLE ION TRAP/FOURIER TRANSFORM ORBITRAP (LTQ-ORBITRAP) TO FIGHT AGAINST THE ILLEGAL USE OF GROWTH PROMOTERS IN CATTLE

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EU Council Directive 96/22/EC stated that "… substances having a hormonal action…" are prohibited for use in animals intended for meat production. Then, EU Council Directive 96/23/EC and Decision 2002/657/EC lay down requirements for residue testing, in order to ensure compliance with the prohibition. The continuous scientific and technological progresses in the field of analytical chemistry since the 70s' have permitted to improve significantly the detection limits over years. Nowadays, target concentrations are sometimes in the $ng.g^{-1}$ range (ppb), often in the $pg.g^{-1}$ (ppt) and progressively in the $fg.g^{-1}$ (ppq) range. In parallel, the specificity of the methods more often used for the control, especially based on mass spectrometry (MS), is also increasing continuously through the relative democratisation of multistage (MS^n) and high to ultra-high resolution (HRMS) mass spectrometry. High-resolution MS and accurate mass High-resolution MS (HRMS) is increasingly becoming more popular in laboratories, either in the form of TOF-MS, or magnetic sector, and more recently FT-ICR or Orbitrap mass spectrometer. If the target analyte contains chemical elements with an outstanding mass defect then HRMS becomes efficient in the suppression of matrix interference (mass clean-up). Hybrid mass spectrometers such as the linear quadrupole ion trap/Fourier transform ion cyclotron (LIT/FT-ICR) or linear quadrupole ion trap/Fourier transform orbitrap (LTQ-Orbitrap) combine large trapping capacity, MS^n capability with unsurpassed high mass accuracy, resolving power, sensitivity and dynamic range (better than the one observed on a TOFMS instrument). The high resolving power (>100,000) and excellent mass accuracy (specified as 2-5 ppm, but demonstrated to be as low as 0.2 ppm under favorable conditions) significantly reduce false positive identification. In the field of food safety (chemical hazard), this new perspective appears of valuable interest both for improving conventional targeted approaches and developing new global untargeted approaches (metabolomic). The advantage/disadvantage of Orbitrap technology will be illustrated through 3 different examples. The first will concern a targeted approach dedicated to growth hormone residues (somatotropin) in milk and blood. This application is still a real analytical challenge in the field; the benefits of high resolution MS will be discussed especially in a context where $pmol.L^{-1}$ of protein residues have to be identified and quantified. The second example will concern the direct measurement of hydrophilic phase II metabolites of boldenone, a well-known anabolic steroids which has been used in meat producing animals. The illustration will show how high resolution and mass accuracy permit the unambiguous identification of boldenone sulphate residues in urine at sub-$ng.mL^{-1}$ levels. The last example will focus on a novel untargeted approach for demonstrating the potential abuse of beta-agonists. The strategy is based on the fishing of indirect biomarkers by direct fingerprinting of the biological matrix (urine, blood). This application will show the promising features of this new approach which relies upon global biological effect modification induced by the administered of the drug. This new screening strategy constitutes a significant improvement in the fight against potential new frauds, e.g. unknowns compounds or cocktails of molecules at low dose.