TOXIC RESIDUES IN MEAT

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Introduction:

In January 2000, the European Commission issued the White Paper on Food Safety setting out the objectives to achieve the highest possible level of health protection for consumers in Europe. A central project in this program is the establishment of a Community Agency, the European Food Safety Authority (EFSA). Although the EFSA might not be operational before the end of 2002, the efforts to renew European legislation towards a transparent and consistent frame of legislative measures is progressing rapidly. Among others, milestones of recent activities are the two legislative proposals defining the regulatory framework on the used of genetically modified organisms (GMOs) in Europe, and the structured program towards Community activities in the field of public health. The latter comprise eight sectorial action programs, including health monitoring and injury prevention, devoted to the harmonization of safety rules for food supplements (vitamins, minerals a.o.), critical contaminants (for example dioxins) and communicable diseases (with particular reference to TSE/BSE, but also relating to food-borne microbiological risks such as *Salmonella, Campylobacter,* verocytotoxinogenic *E.coli* (VTEC) *Trichinella spp*, food-borne viruses and other zoonoses).

Harmonization of Risk Assessment

The effort to harmonize risk assessment procedures was intensified in the recent couple of years. A task force group was established given the mandate to (1) harmonize the risk assessment procedures within the scientific committees, and (2) to work towards a harmonization at the international level. The mandate given to the task force group was: to provide a standard format (and terminology) which should improve transparency and risk communication, thus enabling the Commission to demonstrate externally a consistent high quality scientific approach for all risk assessments conducted on its behalf pertaining to the protection of human health and the environment. The Scientific Steering Committee covering both, proposals for toxicological risks and microbiological risks published the first extensive document in December 2000 (http://europa.eu.int/comm./food/fs/sc/ssc/out82_en.html). This document is undergoing a continuos scrutinizing process, particularly in the areas of quantitative (probabilistic) risk assessment, and the introduction of stepwise approaches towards a consistent exposure assessment including common exposure model scenarios, which can be validated. Finally, the scientific validity of 'thresholds of concern' is evaluated for each category of sources.
A standardized risk assessment falls into a cascade of events, initiated by a scientific assessment addressing the following items:

Hazard identification: the identification of a risk source(s), capable of causing adverse effect(s)/event(s) to humans or the environment, together with a qualitative description of the nature of these effect(s)/event(s).

Hazard characterisation: the quantitative of semi-quantitative evaluation of the nature of the adverse health effects to humans and/or the environment following exposure to the risk source(s). This must, where possible, include a dose-response assessment.

Dose-response-assessment: the determination of the relationship between the magnitude of exposure to risks source(s) <dose> and the magnitude or frequency and/or severity of associated adverse effects <response>.

Exposure assessment: the quantitative or semi-quantitative evaluation of the likely exposure of man and/or the environment to risk sources from one or more media.

Risk characterisation: the quantitative or semi-quantitative estimate, including attendant uncertainties, of the probability of occurrence and severity of adverse effect(s)/event(s) in a given population under defined exposure conditions based on hazards identification, hazard characterisation and exposure assessment.

This scientific approach should – if necessary - be followed by legislative measure in the frame of:
Risk Management: the process of weighing the result of risk assessment and other relevant factors and, if required, selecting and implementing appropriate control measures (including where appropriate, monitoring and surveillance programs).

Risk Communication: the interactive exchange of information and science based opinions concerning the risk among risk assessors, risk managers, actual and potential stakeholders, and the public (consumers).

Risk benefit analysis and quality of life

Despite this efforts to base any legal decision on a sound scientific risk assessment, the European Commission has clearly committed herself to the 'Precautionary Principle' which implies that legal decisions will take into account emerging risks, even if uncertainties remain concerning the nature and of potential harmful effects of the substances or infectious organisms under investigation, on human health or the environment.
Handling the precautionary principle also implies an enlargement of the scope of scientific risk assessment towards an assessment of the quality of life and thus an evaluation of the perception of a certain risk level by consumers. This perception has a direct impact on the well-being by its psychological component, but it can also have a psychosomatically induced physical health effect due to undefined anxiety. In many cases, threats to health will be suspected in cases were transparency of food production methods are lacking. Subsequently, the impression of the public that it losses any independent control of life conditions, results in an undefined anxiety towards new technical developments. This mechanism is exemplified by the negative perception of genetically modified food commodities *versus* the positive acceptance of genetically modified organisms (or therapeutic methods) in curative medicine. Thus, in addition to a scientific risk assessment with the classical endpoints (mentioned above) a risk perception analysis should acknowledge the impact of a certain measure (food safety measures, environmental risks and protection) on people's life as experienced by the people, taking into account social and ethical

perceptions. The final goal is to communicate risk and benefits of any technological process to the public in an effective way and to create a culture of fairness and mutual understanding between stakeholders, risk managers and the public at large.

The farm-to table approach

The White Paper of Food Safety defines also new elements of food safety objectives in the 'from farm to table' concept. The basic principle remains the consistent monitoring of the entire production chain, accompanied by a prospective and structured assessment of all critical steps during production, followed by pre-set control measures. Thus, this objective exhibits obvious similarities with the well-established HACCP concept as applied in food processing. A rigorous HACCP analysis of the pre-slaughter phase of farm animals (pigs, veal calves, poultry and other food producing animals such as dairy cows and laying hens) would allow moving the present end-product control towards integrated quality guarantees at different stages of the production chain. A prerequisite for this approach is the identification of the critical control points, which in turn will increase not only the transparency of production methods – a demand of consumers – but will also increase the responsibility of all stakeholders.

Definition of critical control points

Past experience has indicated that the quality of animal derived foods is strongly influenced by the following factors:

Animal genetics: Breeding programs, particularly for pigs, focussed in the past on expected consumer demands towards low fat/low calorie products, whilst at the same time trying to meat the economic objectives of farmers. It seems unnecessary to recall the pitfalls and drawbacks of these breeding programs on meat quality as such. Advanced breeding programs, however, should include selection for stress resistance and resistance to infectious diseases with the aim to avoid the need for intensive vaccination and treatment protocols to maintain animal health. The objective has not only been debated under the aspects of animal welfare, but also in relation to consumer's concerns on possible residues of veterinary drugs and the risk for selection of antibiotic resistant bacteria, which might be transmissible to consumers thus comprising a public health threat.

Animal husbandry: Optimal conditions should be created for animals at all stages of life, again, not only with the aim to guarantee animal welfare and integrity, but also with the ultimate goal to avoid intensive intervention via vaccination and treatment programs.

Animal Feeds: Setting quality parameters for all components in animals feed and water supplies, is one of the most critical points in the production chain. The recent incidents with dioxins, steroid hormones, antibiotic residues and finally TSE/BSE point towards the pivotal role of feed quality monitoring. At present, Council directive 1999/29/EC and its recent amendments provide a list of undesirable substances in animal feeds. This list has been subjected to several changes in the past and needs to be updated for new emerging contaminants. However, considering the increasing global trade in feed commodities, it becomes obvious that any given list will remain incomplete. Thus, the same guideline states in Article 3 that 'materials intended for animal nutrition may be put into circulation and used in the Community only if they are sound, genuine and of merchantable quality'. This demand transfers a high degree of responsibility to feed industry, a questionable approach considering the numerous incidents related to feed contaminants in the last decade. Assuming that the definition of an undesirable contaminant refers to the ability of a compound (or living organism) to induce adverse effects in the animal and/or being disposed in edible tissues of the animal, a sound risk assessment would be necessary for all major feed ingredients. However, whilst the database for industrially produced feed additives and production aids is very comprehensive (meeting the requirements as defined in 70/524/EEC and corresponding guidelines), comparable sound data are lacking for natural toxicants with respect to their toxicological profile, kinetic behavior and residue disposition (carry-over). Thus, the priorities in risk assessment exercises need to be re-considered, and the efforts to avoid the use of bye-products (see dioxins in oils, mineral clays and mineral premixes) and to avoid contamination by natural toxins (such as microbial toxins, mycotoxins and phycotoxins) need to be strengthened. This approach would meet the intentions towards the establishment of a Rapid Alert System for Food and Feed (RASFF) as indicated in Regulation 178/2002/EC.

Animal health products: In the past two decades regulatory attempts and quality control measures focussed on the potential public health risk arising from residues of veterinary medicinal products in edible tissues or produces of animal origin (see for example 2377/90/EC providing the procedure to set maximum residue limits (MRL's) for veterinary medicinal products). For all substances used intentionally in animals health care, such as vaccines, therapeutic agents such as antibiotics, antiparasitic drugs and other medicinal products, a pre-marketing approval is mandatory. The assessment of the potential toxic hazards to public health from residual amounts of these products in edible tissues, milk and eggs, which is part of the licensing procedure, has been conducted under very stringent rules. The latter has created the favorable situation that all those compounds having the potential to cause harmful effects (even with delay) have been excluded from veterinary therapy (see Annex IV of 2377/90/EC). However, the stringent application of the 'Precautionary principle' has resulted in the non-availability of licensed drugs for the treatment of certain minor diseases and in a shortage of an appropriate spectrum of licensed drug for the so-called minor species (including horses, goats, sheep, geese, rabbits and others). This implies that the individual veterinarian has the responsibility to select an appropriate drug for these species in case of disease, which will be used off-label and thus without any detailed knowledge on target animal safety and residue disposition. Attractive incentives for pharmaceutical industries providing the essential information related to the use of medicinal products in minor species and for minor indications need to be discussed. This discussion should also consider an approach towards risk quantification, as current practice in the regulation of veterinary medicinal products neglects the issue of exposure assessment (see above).

Whilst the toxicological risk assessment following a standardized decision tree system, is well established for all medicinal products, the assessment of microbiological risks, originating from the use of antibiotics in farm animals has been a subject of recent debate (92/18/EC; as well as: Opinion of the Scientific Steering Committee on Antimicrobial Resistance; http://europa.eu.int/comm/food/fs/sc/ssc/out_50en.html; EMEA/CVMP/818/99). Antibiotics are able to induce various forms of antimicrobial resistance towards individual, groups and classes of antibiotics. Transfer of resistant bacterial strains from farm animals to humans comprises the risk that individual human patients needing antibiotic medication are found to be therapy-resistant. As bacterial resistance is predominantly induced following along-term use at low doses of antibiotics, the first precautionary measure was the ban of certain antimicrobials (97/6/EC; 98/19/EC; 2821/98/EC; 2788/98 and others), which had been licensed in the past as feed additives to improve animal health and productivity. Whilst the outcome of this recent ban of antibiotic growth promoters on the prevalence of resistant bacteria in farm animals is still under investigation, critical comments arise

stating that bacterial resistance in humans is related to an unrestricted used of antibiotics in human medicine rather than the use in farm animals. The latter would certainly apply in a world were veterinarians use antibiotics only under the rules set by Good Veterinary Practice. As these rules have not been formalized as yet (the first amendments of national legislation with respect to veterinary practice have been issued by individual member states), GVP compliance cannot be guaranteed as yet. Subsequently, an epidemiological surveillance network on antimicrobial resistance has been initiated in several member states (in accordance with Commission Decision 2000/96/EC).
Reliable GVP protocols allow residue avoidance in the majority of necessary treatments and should embrace the demand for transparency in production methods by documenting all necessary therapeutic interventions at the farm level. A prerequisite of this concept is the enforcement that antibacterial agents are available by prescription only (POM-status) and by enhancing the knowledge on the prudent use of antibiotics by specialized education programs for veterinarians. In parallel, the medical profession and the public at large should be informed about the risks linked to an uncontrolled use of antibiotics and the principles of prudent use of these compounds.
Finally, developing the rules of GVP further towards a complete documentation of all treatments, offers the possibility to wave end-product controls in all uncomplicated cases (guarantee of the absence of drug residues and resistant bacteria), which would reduce the costs of quality control programs devoted to the final product. At the same time this approach allows an intensification of residue analysis in those cases where incidental disease outbreaks result in emergency treatments (and early slaughter) and thus a higher risk of exposure to residues and resistant bacteria.

Transport and culling: Animal transport towards abattoirs deserves attention to avoid undesirable stress situations affecting meat quality and – even more important – to avoid impairment of animal welfare and integrity. Recently, in ruminants potentially exposed to TSE/BSE culling procedures have been re-evaluated with the aim to guarantee the proper dissection of specified risk material (SRM) and to avoid the dissemination of potentially infected organs (brain, spinal cord a.o.) into the carcass (MRM-ban). Conservative measures in the past demanded the discharge of certain organs at risk for high contamination with environmental pollutants (for example heavy metals) such as kidneys from horses and dairy cows. A major pre-requisite for all control measures is a consistent individual identification of the animal's carcass.

Meat inspection procedures: In the past, meat inspection procedures were designed to ensure consumer's safety by identifying any transmissible diseases. Conservative meat inspection in based on clinical examination prior to slaughter, and post-mortem gross examination for pathological alterations, indicative for infectious diseases. The examination of the carcass and organs was complete by bacteriological investigations were appropriate. Awareness of the possibility of contamination with residues from environmental pollutants and animal health products as well as from the illegal use of growth promoting agents resulted in numerous regulations directed towards analytical (residue) control measures, which need not to be explained in detail. The conservative meat inspection procedures, however, have recently been subjected to a critical review. Professional animal husbandry has irradiated most of the previously important infectious diseases. Industrialized slaughter procedures require a high throughput of animals per slaughter unit. Meat inspection 'with knives' bares a risk of cross contamination of carcasses, but fails to detect emerging risks like TSE/BSE, sub-clinical bacterial or parasitic infections (carriers of zoonotic pathogens) and sub-clinical intoxications (accumulation of contaminants). Thus, there is a strong need for a re-evaluation of current meat inspection protocols towards more risk targeted controls measures. Pre-set control measures, demonstrating that a flock of slaughter animals is free of typical zoonoses (for example trichinellosis in pigs when the animals have in raised under strict health control systems: indoor with carefully monitored feed supplies) would allow to replace routine individual carcass control by global sanitary measures (control of control-systems).

In conclusion, recent concept towards an improvement of food safety focus on shared responsibility of all stakeholders. In turn, stakeholders need to acknowledge that the society demands a high degree of transparency with respect to the production methods applied. **Quality of life** issues directed to both, animal health an welfare as well as consumer's perception of technical processes, need to be included not only in risk communication related to toxic or infectious agents, but also in the risk-benefit and cost-risk analysis of any (food) production process.

References:
Available upon request; the reader is particularly referred to the Internet Service of the European Commission http://europa.eu.int/comm/food/fs/sc_en.html.